

EVALUATION OF A PERSONAL MOBILE TRAINER SYSTEM  
DESIGNED FOR FACILITATING EXERCISE THERAPY FOR  
TRAUMATIC BRAIN INJURY PATIENTS

by

AHMAD FAWZI G TURKI

DISSERTATION

Submitted in partial fulfillment of the requirements  
for the degree of Doctor of Philosophy at  
The University of Texas at Arlington  
August, 2021

Arlington, Texas

Supervising Committee:

Dr. George Alexandrakis

Dr. Khosrow Behbehani, Supervising

Dr. Kan Ding

Dr. Rong Zhang

## ABSTRACT

Evaluation of a Personal Mobile Trainer System  
Designed for Facilitating Exercise Therapy for  
Traumatic Brain Injury Patients

Ahmad Fawzi G Turki, Ph.D.

The University of Texas at Arlington, 2021

Supervising Professor: Khosrow Behbehani

There are no effective pharmacological agents that can prevent or treat post-TBI cognitive deterioration. Previous research has shown that exercise can be an effective means of enhancing the patients condition with mild traumatic brain injury (TBI). However, compliance with the prescribed exercise regimen has been low, as TBI patients often suffer from poor executive function and need assistance with complying with their prescribed exercise program. This study aims to design, build, and test a system based on a wearable exercise tracker to assist and encourage patients by facilitating doing the prescribed exercises at a place and time that is convenient to the patient. It is hypothesized that such a personal mobile trainer (PMT) system increases the compliance level of TBI patients with their prescribed exercise.

A PMT system using a commercially available wrist-worn fitness tracking (WFT) device was designed and built. To choose a suitable WFT for the project, four most popular WFT's were evaluated for their accuracy of measuring heart rate: 1) Apple Watch (AW); 2) Polar Watch (PW); 3) Fitbit (FB); and 4) Samsung Watch (SW). Recording heart rate from 5 volunteer healthy subjects (2F & 3M; age  $26.4 \pm 3.20$  years; BMI  $24.7 \pm 1.92$  kg/m<sup>2</sup>) while doing a 5-min of fast walk, as perceived by a volunteer, on a treadmill while using the WFT's and concurrently recording the heart rate by an electrocardiogram (ECG) showed that AW had the lowest least mean squared error (AW= $3.98 \pm 1.74$ ; PW= $20.9 \pm 14.6$ , FB= $27.74 \pm 14.0$ , SW= $62.6 \pm 73.6$ ). Hence, AW together with Apple iPhone was chosen to design the PMT for monitoring TBI patients exercise activity and to provide encouragements and reminders to assist patients to stay with their prescribed exercise program. Custom built software for AW and iPhone was developed to provide a patient interface both on AW and iPhone. Further, communication software was developed to transmit the collected data to a cloud-based server to make the status of the patient compliance instantly available to the attending clinicians.

To test the said hypothesis using the proposed PMT system, we tested the system on 9 participants (7 males, 2 females, aged  $55.2 \pm 7.5$  years, BMI  $28.4 \pm 5.0$  lb./in<sup>2</sup>) with TBI (3 with mild physical disability and six without physical disability) for 3 months. Two measure of compliance was devised that measure the percentage of the duration that the subjects performed the prescribed exercise (Duration Compliance,  $80.64\% \pm 17.23\%$ ) and the percentage of achieving the prescribed heart rate (Hear Rate Compliance,  $55.68\% \pm 33.80\%$ ). These results showed that the PMT system could increase TBI patient's adherence to prescribed physical exercises.

Investigators have shown that improvement in cognitive function may be associated with improved heart rate variability (HRV) [1]. Hence, time and frequency domain HRV metrics for the patient

sample population was measured using a 5-min ECG recording while TBI patient rested in supine position both at prior to patients start the 3-month exercise program and at the conclusion of the exercise program. No change in either time or frequency domain HRV metrics was detected. As the p-values for comparison in time domain was 0.94 and for comparison in frequency domain was 0.60.

Additionally, we studied the active energy value in kilocalories that was measured by AW and recorded in the PMT cloud-based system for each patient. A strong positive correlation was obtained between the exercise duration and active energy measurements ( $R\text{-value}=0.94\pm 0.7$ ) and between the Duration Compliance and the active energy measurements ( $R\text{-value}=0.85\pm 0.12$ ).

Finally, the patient's subjective ratings of the designed PMT system were studied using the System Usability Scale (SUS). The patients filled out the SUS surveys at the conclusion of their 3-month exercise program. The SUS average score for the PMT was ( $71.67\pm 21.40$ ), which indicated that the patients believe that the applications are acceptable, but it needs some improvements.

Copyright © by Ahmad Fawzi G Turki  
2021  
All Rights Reserved



## ACKNOWLEDGEMENTS

First and foremost, I would like to praise Allah the Almighty, the Most Gracious, and the Most Merciful for His blessing given to me during my study and in completing this dissertation. Then I would like to express my sincere gratitude to my advisor Professor Khosrow Behbehani for the continuous support of my Ph.D study and research. It has been an honor to be his Ph.D. student. I appreciate all his contributions of time, ideas, and funding to make my Ph.D. experience productive and stimulating. The joy and enthusiasm he has for his research was contagious and motivational for me, even during tough times in the Ph.D. pursuit. I am also thankful for the excellent example he has provided by his respectful character and personality. Besides my advisor, I would like to thank the rest of my dissertation committee members (Dr. Rong Zhang, Dr. Kan Ding and Dr. George Alexandrakis) for their insightful comments and invaluable advice. I am also thankful to Dr. Ming Li, from the UTA Department of Computer Science and Engineering, for her assistance and advise in building the PMT system. Also, I am thankful to Dr. Kathleen Bell and Stephanie Neaves for their help and support with the patient recruitment, I am also thankful to the rest of all the medical team members form UTSW that we collaborated with in this study. I am also grateful to my fellow colleagues at Bio-signal processing lab, Mahrshi B. Jani, Pegah Askari and Chuang, Yao Shun for extending their help and support in all possible ways.

I also, thank the King Abdulaziz University for providing me the sponsorship to continue my graduate studies abroad. My gratitude goes to the faculty and staff of Bioengineering department for their support throughout my PhD study. Special thanks to Ms. Julia Rockow for all her help and encouragement from the day I arrived at UTA to the last day.

## DEDICATION

*I dedicate this thesis to my family and friends for their unwavering support. A special feeling of gratitude to my loving parents, Fawzi and Raja, whose words of encouragement and push for tenacity ring in my ears. All my childhood memories are full of sweet things you did for me. I appreciate how you raised me and all the extra love that you gave me.*

*I also dedicate this work to my lovely wife, Dr. Enas, who has always accepted me for me and supported my hustle, drive and ambition. You have been my inspiration and my soul mate. I also dedicate this work to my lovely children, Turki and Reema, who they have been the power that always motivate me to work harder.*

*At the end, I would like to thank my sisters, and my Friend Dr. Alaa Bashake and all my friends whose encouragement made me able to achieve such success and honor.*

*Ahmad Fawzi G Turki*

*July 19, 2021*

# TABLE OF CONTENTS

<b>CHAPTER 1</b>	<b>1</b>
<b>Introduction</b>	<b>1</b>
<b>1.1 Traumatic Brain Injury: Definition and Prevalence</b>	<b>1</b>
1.1.1 Categories of TBI	3
<b>1.2 Physiological Impacts of TBI</b>	<b>4</b>
1.2.1 Pathophysiology of TBI	4
1.2.2 Secondary Brain Injuries:	4
<b>1.3 Current Treatment of TBI</b>	<b>7</b>
1.3.1 Non-technology Based Physiotherapy for TBI patient	8
1.3.2 Physical Exercise Effect on Brain Health	8
<b>1.4 Current Limitation of Exercise as Method of Therapy</b>	<b>10</b>
<b>1.5 Study Motivations and Objectives</b>	<b>10</b>
1.5.1 Significance of the Study	10
1.5.2 Use of Technology to Support Physical Therapy with other Medical Conditions	11
1.5.3 Novelty of the Study	11
1.5.4 Hypotheses and Specific Aims	13
<b>1.4 Current Limitation of Exercise as Method of Therapy</b>	<b>16</b>
<b>1.5 Study Motivations and Objectives</b>	<b>16</b>
1.5.1 Significance of the Study	16
1.5.2 Use of Technology to Support Physical Therapy with other Medical Conditions	17
1.5.3 Novelty of the Study	18
1.5.4 Hypotheses and Specific Aims	20



<b>CHAPTER 2</b>	<b>22</b>
<b><i>Accuracy Of Heart Rate Sensing of Wrist-Worn Fitness Tracking Devices</i></b>	<b>22</b>
<b>2.1 Method</b>	<b>22</b>
WFT accuracy Evaluation Protocol	22
Data Analysis	24
Statistical Analysis	25
<b>2.2 Results</b>	<b>27</b>
<b>2.4 Discussion</b>	<b>38</b>
<b>2.5 Conclusion</b>	<b>41</b>
<b>CHAPTER 3</b>	<b>42</b>
<b><i>The Designed Wearable Fitness Tracking Ecosystem for Exercise Therapy for Traumatic Brain Injury Patients</i></b>	<b>42</b>
<b>3.1 System Design Overview</b>	<b>43</b>
<b>3.2 PMT System Function Design</b>	<b>46</b>
<b>3.3 iPhone Application and Apple Watch Application Performance</b>	<b>52</b>
<b>CHAPTER 4</b>	<b>61</b>
<b><i>Methods Used to Measure the Effect of Exercise</i></b>	<b>61</b>
<b>4.1 Physiological Effects of Exercise</b>	<b>61</b>
<b>4.2 Measurement of energy expenditure</b>	<b>62</b>
Calculate Energy Expenditure Based on MET and Physical Activity	63
<b>4.3 Activity Level</b>	<b>65</b>

<b>4.4 Maximum Heart rate Equation</b>	<b>65</b>
<b>4.5 Exertion Level</b>	<b>66</b>
<b>4.6 Measurement of Heart rate</b>	<b>67</b>
VLF Band	70
Low-Frequency Band	71
HF Band	72
LF/HF Ratio	72
<b>4.7 Study Population</b>	<b>73</b>
4.7.1 Inclusion Criteria	73
4.7.2 Exclusion Criteria	73
<b>CHAPTER 5</b>	<b>74</b>
<b><i>TBI PATIENT COMPLIANCE WITH THE PRESCRIBED PHYSICAL EXERCISES USING THE PMT</i></b>	
<b>SYSTEM</b>	<b>74</b>
<b>5.1 Introduction</b>	<b>74</b>
<b>5.2 Exercise Compliance Definition</b>	<b>76</b>
<b>5.3 Means and Method</b>	<b>77</b>
5.3.1 Heart Rate Compliance	78
5.3.4 Compliance as Adherence to Perform the Required Exercise Duration	85
5.3.5 Exercise Frequency Compliance	92
5.3.2 Compliance of Achieving the Heart Rate Momentarily	98
5.3.3 Proposed Compliance Metrics by the PMT vs. Medical Team Pilot Study Home Exercise Compliance Metric Without the PMT	104
<b>5.7 Discussion</b>	<b>106</b>

5.8 Conclusion	108
<b>CHAPTER 6</b>	<b>109</b>
<b><i>PMT Effects on Heart Rate Variability Measurements</i></b>	<b>109</b>
6.1 Introduction	109
6.2 Evaluation of Apple Watch in Estimating Heart Rate Variability Measures in Traumatic Brain Injury Patients	110
Method	110
Comparison of HRV Metrics Derived From AW and ECG	116
Discussion of the Results of Comparing HRV Metrics Obtained from AW with those Obtained from ECG	119
Conclusion	128
6.3 Measuring the Changes in HRV, Post Physical Exercise Interventions Using the PMT System, Compared to Baseline	129
Results of Measuring the Changes in HRV, Post Physical Exercise Interventions Using the PMT System, Compared to Baseline	130
Discussion of Measuring the Changes in HRV, Post Physical Exercise Interventions Using the PMT System, Compared to Baseline	141
6.4 Conclusion	142
<b>CHAPTER 7</b>	<b>143</b>
<b><i>Estimation of Energy Expenditure</i></b>	<b>143</b>
7.1 Introduction	143
7.2 Method	144
7.3 Results	146

7.4 Discussion:	163
7.5 Conclusion	165
<b>CHAPTER 8</b>	<b>167</b>
<b><i>PMT User Rating</i></b>	<b>167</b>
8.1 Introduction	167
8.2 Method	168
8.3 Results	170
8.4 Discussion	171
8.5 Conclusion	172
<b>CHAPTER 9</b>	<b>173</b>
<b>CONCLUSIONS AND FUTURE WORK</b>	<b>173</b>
9.1 Conclusions	173
9.2 Future Work	176
<b>Appendices</b>	<b>177</b>
<b>A.2 CHAPTER 2 APPENDIX:</b>	<b>177</b>
<b>A.2.1: ECG and WFT Heart Rate Measurements Comparison</b>	<b>177</b>
Slow Walk Mode	177
Fast Walk Mode	188
Sitting Mode	198
Slow Bike Mode	208
Fast Bike Mode	218

<b>A.2.2: WFTs Bland and Altman Plots</b>	<b>228</b>
APPLE WFT Bland and Altman Plots	228
Polar WFT Bland and Altman Plots	241
Fitbit WFT Bland and Altman Plots	254
Samsung WFT Bland and Altman Plots	266
<b>A.2.3: WFTs Error Plots</b>	<b>277</b>
<b>A.2.4: Statistical Tests Results Tables</b>	<b>288</b>
<b>A5 CHAPTER 5 APPENDIX</b>	<b>292</b>
<b>Patient 1 Attempts</b>	<b>292</b>
<b>Patient 2 Attempts</b>	<b>313</b>
<b>Patient 3 Attempts</b>	<b>335</b>
<b>Patient 4 Attempts</b>	<b>353</b>
<b>Patient 5 Attempts</b>	<b>363</b>
<b>Patient 6 Attempts</b>	<b>377</b>
<b>Patient 7 Attempts</b>	<b>400</b>
<b>Patient 8 Attempts</b>	<b>422</b>
<b>Patient 9 Attempts</b>	<b>444</b>
<b>Patients Heart Rate Compliance Figures</b>	<b>464</b>
<b>Patients Duration Compliance Figures</b>	<b>469</b>
<b>Patients Frequency Compliance Figures</b>	<b>474</b>
<b>Patients Momentarily Heart Rate Compliance Figures</b>	<b>479</b>

<b>A.6 Chapter 6 Appendix</b>	<b>484</b>
<b>Patients Initial and Exit Visits Readings</b>	<b>484</b>
<b>Patient 1 Initial Visit Readings</b>	<b>484</b>
<b>Patient 1 Exit Visit Readings</b>	<b>488</b>
<b>Patient 2 Initial Visit Readings</b>	<b>492</b>
<b>Patient 2 Exit Visit Readings</b>	<b>496</b>
<b>Patient 3 Initial Visit Readings</b>	<b>500</b>
<b>Patient 3 Exit Visit Readings</b>	<b>504</b>
<b>Patient 4 Initial Visit Readings</b>	<b>508</b>
<b>Patient 5 Exit Visit Readings</b>	<b>512</b>
<b>Patient 5 Initial Visit Readings</b>	<b>516</b>
<b>Patient 5 Exit Visit Readings</b>	<b>519</b>
<b>Patient 6 Initial Visit Readings</b>	<b>524</b>
<b>Patient 6 Exit Visit Readings</b>	<b>528</b>
<b>Patient 7 Initial Visit Readings</b>	<b>532</b>
<b>Patient 7 Exit Visit Readings</b>	<b>536</b>
<b>Patient 8 Initial Visit Readings</b>	<b>540</b>
<b>Patient 8 Exit Visit Readings</b>	<b>544</b>
<b>Patient 9 Initial Visit Readings</b>	<b>548</b>
<b>Patient 9 Exit Visit Readings</b>	<b>552</b>

<b>A.7 Chapter 7 Appendix</b>	<b>556</b>
<b>Patient 1 Active Energy</b>	<b>556</b>
<b>Patient 2 Active Energy</b>	<b>559</b>
<b>Patient 3 Active Energy</b>	<b>562</b>
<b>Patient 3 Active Energy</b>	<b>563</b>
<b>Patient 4 Active Energy</b>	<b>565</b>
<b>Patient 5 Active Energy</b>	<b>569</b>
<b>Patient 6 Active Energy</b>	<b>572</b>
<b>Patient 7 Active Energy</b>	<b>575</b>
<b>Patient 9 Active Energy</b>	<b>581</b>
<b>References</b>	<b>584</b>

## List of Tables

TABLE 2.1: T-TEST RESULTS FOR COMPARING THE HEART RATE OF EACH WFT <sub>HR</sub> WITH ECG <sub>HR</sub> DURING FAST WALK MODE .....	37
TABLE 2.2: T-TEST RESULTS FOR COMPARING THE HEART RATE OF EACH WFT <sub>HR</sub> WITH ECG <sub>HR</sub> DURING SITTING MODE .....	37
TABLE 2.3: TESTING OF POSSIBLE DIFFERENCE BETWEEN WFT'S RMSE VALUES RESULTING FROM COMPARING THEIR MEASUREMENTS OF HEART RATE WITH ECG HEART RATE MEASUREMENT DURING FAST WALK USING KRUSKAL WALLIS TEST.....	37
TABLE 2.4: FAST WALK APPLE WFT <sub>HR</sub> RMSE WITH OTHER WFT'S USING WILCOXON RANK SUM TEST .....	38
TABLE 2.5: TESTING OF POSSIBLE DIFFERENCE BETWEEN WFT'S RMSE VALUES RESULTING FROM COMPARING THEIR MEASUREMENTS OF HEART RATE WITH ECG HEART RATE MEASUREMENT DURING SITTING USING KRUSKAL WALLIS TEST .....	38
TABLE 3.6: PMT SYSTEM'S MODELS AND THEIR RESPECTIVE INTERCONNECTIONS .....	51
TABLE 4.7: MET VALUES FOR DIFFERENT TYPES OF ACTIVITIES [83].....	63
TABLE 5.8: HEART RATE COMPLIANCE BOX PLOT VALUES .....	84
TABLE 5.9: DURATION COMPLIANCE BOX PLOT VALUES .....	90
TABLE 5.10: FREQUENCY COMPLIANCE BOX PLOT VALUES.....	96
TABLE 5.11: MOMENTARILY COMPLIANCE BOX PLOT VALUES .....	103
TABLE 5.12: DURATION AND FREQUENCY COMPLIANCES AND THEIR AVERAGES .....	106
TABLE 5.13: COMPLIANCE CLASSIFICATIONS FOR THE PROPOSED COMPLIANCE METRICS .....	107
TABLE 6.14: 2-TAIL WILCOXON RANK-SUM TEST RESULTS FOR HRV METRIC DERIVED FROM ECG AND AW. ....	117
TABLE 6.15: 2-TAIL WILCOXON RANK-SUM TEST RESULTS FOR HRV METRIC DERIVED FROM ECG PRE- VS. POST-INTERVENTION AND AW PRE VS. POST-INTERVENTION. ....	130
TABLE 7.16: PATIENTS WEEKLY TOTAL EXERCISE DURATION VS. WEEKLY TOTAL ACTIVE ENERGY.....	147
TABLE 7.17: PATIENTS ALL DURATION SESSIONS VS. ALL ACTIVE ENERGY SESSIONS.....	149
TABLE 7.18: PATIENT'S WEEKLY DURATION COMPLIANCE VS. WEEKLY TOTAL ACTIVE ENERGY .....	152
TABLE 7.19: PATIENTS WEEKLY MEAN OF AVERAGE HEART RATE VS. WEEKLY TOTAL ACTIVE ENERGY .....	155
TABLE 7.20: PATIENT'S WEEKLY HEART RATE COMPLIANCE VS. WEEKLY TOTAL ACTIVE ENERGY .....	158
TABLE 7.21: PATIENTS AVERAGE HEART RATE SESSIONS VS. ACTIVE ENERGY SESSIONS .....	161



TABLE 8.22: AVERAGE OF WEEKLY HEART RATE COMPLIANCE, DURATION COMPLIANCE, FREQUENCY COMPLIANCE, AND MOMENTARILY HEART RATE COMPLIANCE METRICS AND SUS SCORES FOR EACH PATIENT. ....	170
TABLE 8.23: SUS SCORES AND EACH COMPLIANCE METRIC PEARSON LINEAR CORRELATION DETERMINATION COEFFICIENTS .....	171
TABLE A2. 24: SLOW WALK T-TEST RESULTS FOR ECG VS WFT HRS .....	288
TABLE A2. 25: FAST WALK T-TEST RESULTS.....	288
TABLE A2. 26: SITTING T-TEST RESULTS.....	289
TABLE A2. 27:SLOW BIKE T-TEST RESULTS .....	290
TABLE A2. 28: FAST BIKE T-TEST RESULTS.....	290
TABLE A2. 29: SLOW WALK KRUSKALWALLIS TEST.....	291
TABLE A2. 30: SLOW BIKE KRUSKALWALLIS TEST.....	291
TABLE A2. 31:FAST BIKE KRUSKALWALLIS TEST.....	291

# CHAPTER 1

## Introduction

### 1.1 Traumatic Brain Injury: Definition and Prevalence

Traumatic brain injury (TBI) is a nondegenerative, noncongenital insult to the brain from an exterior mechanical force, perhaps leading to lasting or temporary impairment of cognitive, physical, and psychosocial functions, accompanied by a diminished or altered state of consciousness [2]. Worldwide, over 54 to 60 million people annually suffer from a traumatic brain injury, leading to either hospitalization or mortality [3] with incidence rates of 369 per 100,000 population per year [4]. The primary causes of traumatic brain injury differ by age, socioeconomic factors, and geographical area, so any planned interventions must consider this variability [4]. As World Health Organization (WHO) claims 98% occurrence in low medium-income countries and five times greater frequency than in industrialized nations, childhood injuries are most likely within the poorest countries.

In recent years a decrease in mortality post-traumatic brain injury has been observed [5]. Known fatality ranges in the U.S. are from 0.9 to 7.6 per 100 traumatic brain injury patients [5]. The fatality of severe traumatic brain injury ranges from 29 to 55 per 100 TBI patients [5]. Mean mortality is 10.53 per 100,000 per year, with 68% of the individuals dying before hospital arrival [5]. About 80% of individuals suffering from traumatic brain injury-related impairment live in low-middle-income countries [6]. Only 2% of these patients have access to rehabilitation services to brace their quality of life [6]. In the United States, annually, almost two million patients are cured and released from hospital emergency departments due to traumatic brain injury [7]. Approximately 56,000 individuals lose their life as a result of a traumatic brain injury [7]. At

the same time, 80,000 individuals are estimated to be discharged from the hospital with some impairment and require assistance with daily living activities [7]. Today, approximately 5.3 million patients in the U.S. live with impairment due to traumatic brain injury [7]. That costs the country more than \$56 billion per year because of care costs and earnings loss [7]. A tremendously growing population of traumatic brain injury survivors in the United States are veterans, with 350,000 troops diagnosed with traumatic brain injury by the Department of Defense between 2000 and 2017 due to the worldwide war on terror [6]. The type of present battle has been a reason for increasing blast related TBI. Indeed, enhanced armor technologies and emergency medicine protocols have increased veterans' survival rates with TBI [6].

Nowadays, mild traumatic brain injury mainly occurs from concussions [9]. However, not all blows or shocks to the head cause traumatic brain injury; others can just cause light damage to the skull without consequent injury to the brain [5]. In addition, some motor impairment from traumatic brain injury does not always be evident [8]. Hidden symptoms can arise with traumatic brain injuries such as the one related to cognition and behavior [9]. The traumatic brain injury can be named the "silent epidemic" because its population lives largely invisible and does not declare their needs, plus the widespread misunderstanding of the impact of related conditions [9]. Mild TBI can easily be unrecognized until their patients experience difficulty doing their daily activities [10].

TBI is a chronic health condition that can cause a lifelong effect on brain structure and function [2]. As TBI patients grow older, the high risk of neurodegenerative syndromes, like dementia and Parkinsonism, is a growing concern among patients, caregivers, and clinicians [11]. Research on individuals with TBI has shown accelerated brain aging compared to healthy controls

[12]. TBI patients with moderate to severe TBI over the age of 55 or with mild TBI over 65 can have premature brain aging and an increased risk of developing dementia [3].

### ***1.1.1 Categories of TBI***

There are several categories which are utilized to classify TBI [13]. One category based on the severity of a TBI is mild, moderate, or severe, relying on the Glasgow Coma Scale (GCS) that depends on the extent of the damage to the brain [8]. Glasgow Coma Scale is a point scale used to evaluate a patient's level of consciousness and neurological execution post brain injury [8]. The scoring is constructed on the best eye-opening response (1-4 points), best motor response (1-6 points), and best verbal response (1-5 points), with the cutoff point for coma at 8 points [8]. Another classification of TBI is based on the physical mechanisms of insult, (i) closed head; (ii) penetrating; (iii) explosive blast TBI. The degree of TBI can be classified based on several factors [8].

Mild TBI patients have a GCS score of more than 12, no abnormalities on CT scan, no operative lesions, length of hospital stay less than 48 hours, and brief loss of consciousness (LOC) [8]. For moderate TBI patients will have a GCS score of 9-12, length of hospital stay of at least 48 hours, and usual LOC lasting from 30 minutes to 6 hours [8]. In addition, severe TBI patients will have a GCS of less than 9 and a period of unconsciousness of more than 6 hours [8]. Approximately 80% of TBIs are mild [14]. A patient with a mild TBI or concussion may stay conscious but appear confused [7].

In some cases, there is a brief loss of consciousness for a few seconds or minutes. MRI or CT brain scans may appear nonspecific [15]. It is estimated that approximately 7-33% of patients continue to experience significant symptoms that persist and significantly disrupt daily functioning [10]. Furthermore, for mild TBI patients, post-TBI concussion symptoms may include headache,

confusion, light headedness, dizziness, ringing within the ears, blurred vision or tired eyes, fatigue or lethargy, awful taste within the mouth, a change in sleep patterns, behavioral or mood changes, difficulty with concentration, as well as trouble with memory, attention, and thinking [16].

An individual who suffers from a moderate or severe TBI may show the same symptoms as in the case of a patient with mild TBI and have a severe headache that doesn't disappear, repeated vomiting or nausea, seizures, and dilation of one or both pupils of the eyes [7]. Furthermore, patients with moderate TBI may experience an inability to wake up from sleep, weakness or numbness within the extremities, loss of coordination, slurred speech, increased confusion, restlessness, and agitation [7].

## **1.2 Physiological Impacts of TBI**

### ***1.2.1 Pathophysiology of TBI***

Injuries due to trauma to the brain can also be categorized as Primary injury and secondary injury [17]. A primary injury is an injury that is caused by the mechanical force to the head during the initial trauma. Secondary injury is the damage that occurs to the brain cellular tissues post the primary injury [17]. Focal and diffuse brain injuries are primary injuries that occur instantaneously from different mechanical traumas [17]. Moderate to severe TBI patients most likely would suffer from both types. However, secondary injuries are often more extensive.

### ***1.2.2 Secondary Brain Injuries:***

Secondary damages can last from hours to years, resulting from the biochemical, cellular, and physiological incidents that follow a primary injury [17]. Various elements can create secondary injuries such as follows:

*Excitotoxicity-* During a TBI, excessive release of excitatory amino acids as glutamate and aspartate from presynaptic nerve terminals will flow, owing to the

breakdown of BBB and primary cell death [18]. Excitotoxicity is the fast excess and inflow of calcium into the cell cytoplasm, stimulating a series of toxic signaling cascades, causing the cell to undergo apoptosis [18].

*Mitochondrial Dysfunction* - it involves metabolic and physiological deregulations that cause cell death [17]. Intracellular  $\text{Ca}^{2+}$  confiscation and excessive ions influx in mitochondria will lead to depolarization of the mitochondrial membrane, the production of reactive oxygen species, and ATP synthesis inhibition [17].

*Release of Reactive Oxygen Species (ROS) and Lipid Peroxidation* - Oxidative stress effect TBI pathogenesis to a significant degree [17]. Following a TBI, endogenic ROS and free radicals are continuously produced from numerous sources, such as enzymatic processes, activated neutrophils, excitotoxic pathways, and dysfunctional mitochondria [17]. After TBI, the insistent discharge of highly reactive oxygen free radicals and the allied rise in the level of ROS-mediated lipid peroxidation can enforce adversative effects in brain plasticity, cerebral blood flow and promote immunosuppression [17].

*Neuroinflammation* - It is an inflammatory response within the brain or spinal cord. Production of cytokines, chemokines, ROS, and secondary messengers will mediate the inflammation. Resident CNS glia (microglia and astrocytes), endothelial cells, and peripherally derived immune cells are the producers of these mediators [17]. For sure, there are immune, physiological, biochemical, and psychological consequences of these neuroinflammatory responses [19].

*Axonal Degeneration* - Axonal degeneration will arise as minutes after diffuse axonal injury (DAI), Wallerian degeneration will be observed [20]. Axonal degeneration remains years after injury and plays a role in developing Alzheimer's disease [20].

*Glial Scar and Myelin-Associated Axonal Growth Inhibitors* - Multiple barriers arise to axonal growth that causes mature axons to regenerate after injury [11]. Myelin-associated inhibitors signify one group of barriers extrinsic to the injured neurons. Nogo, MAG, and OMgp are three prototypical myelin inhibitors that signal through multiple neuronal receptors to exert growth inhibition [11].

*Apoptotic Cell Death* - Apoptosis is a hallmark of secondary brain injury [17]. Also, neuronal cell death is evident in the human hippocampus for up to 1-year post a TBI [17]. Following a brain injury, apoptotic cells have been observed alongside degenerating cells exhibiting classic necrotic morphology [17].

*Impairment of Autophagy and Lysosomal Pathways* - Autophagy is an adaptive homeostatic process that plays an essential role in eliminating abnormal intracellular proteins or organelles to sustain cell stability through the lysosome-dependent degradation pathway [21]. Also, it plays a critical role in cryoprotection and cell survival by eliminating abnormal intracellular proteins or organelles when cells are severed or under stress [21].

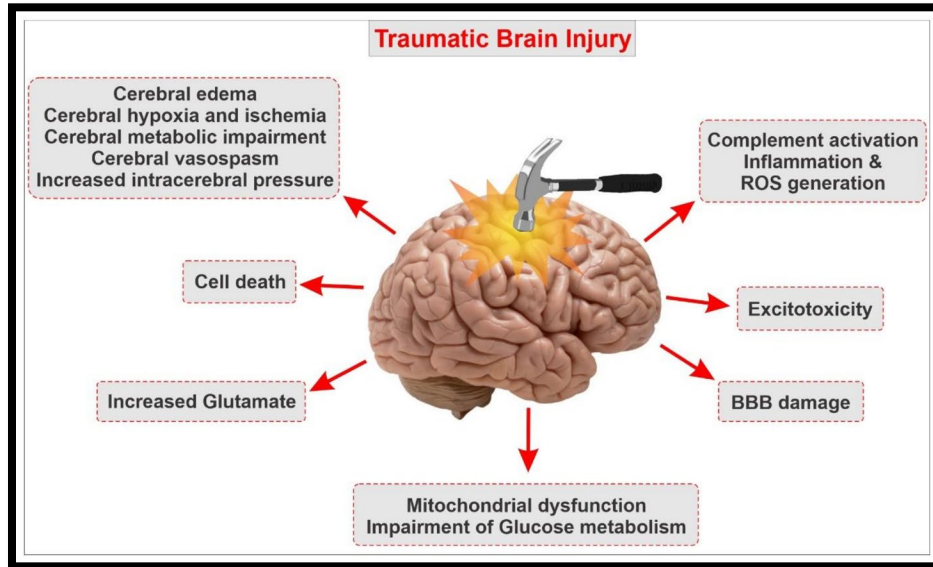


Figure 1.1 pathophysiological responses following TBI and the complex outbreak of secondary impairments. Adopted from [22].

### 1.3 Current Treatment of TBI

Treatment of TBI patients will depend on the severity of the injury [7]. Various types of treatment can aid a TBI patient to recover from TBI and decrease or remove specific physical, psychological, and cognitive deficits related to TBI [7].

*Medication Treatment for TBI* -Different medications can help treat physiological and psychological TBI symptoms and decrease the risk of some conditions related to it [23]. For instance, TBI patients can be administered to long-term management medications such as antidepressants, muscle relaxers, pain relievers, and stimulants to treat deficits in cognitive functions such as attention, memory, learning, and language [23]. However, no medication aids recovery from TBI, yet researchers are working to find cures to help patients recover from TBI [7].

*Rehabilitation Therapies* - Rehabilitation therapies can aid TBI patients to regain functions, relearn skills and uncover new methods to perform things that take their unique health status into account [24]. Different types of rehabilitation therapies may apply to TBI patients, Such as



physical therapy, occupational therapy, speech therapy, psychological counseling, vocational counseling, and cognitive therapy [24].

*Emergency Treatment for TBI* - Usually, emergency care concentrates on stabilizing a patient's conditions, such as ensuring enough oxygen reaching the brain, stabilizing brain and blood pressure, and avoiding additional injury to the head or neck [2]. In particular, in some cases, surgical treatment would be required as part of emergent treatment to decrease the damage that occurred to the brain. Once the medical care team stabilizes the patient's condition, they move forward with TBI medication treatment and rehabilitation therapies.

### ***1.3.1 Non-technology Based Physiotherapy for TBI patient***

Over the last decade, animal studies and clinical trials in healthy mid-aged and older adults have demonstrated that aerobic exercise attenuates age-related cognitive decline linked to preserving brain tissue volume and white structural integrity and cerebral perfusion [25]. A recent feasibility study [26] by our team demonstrated the feasibility of aerobic exercise training on persons with TBI as the study conducted by the research team found that 85% of the participants were able to complete a prescribed, individualized physical fitness level-based aerobic exercise training, with an average of 70% compliance. Compared to stretching, three months of aerobic exercise significantly improved cardiorespiratory fitness level. This trend was more significant in executive and memory performance and cerebral perfusion in parahippocampal regions.

### ***1.3.2 Physical Exercise Effect on Brain Health***

Several studies have shown that brain health can improve by regular aerobic exercise [27]. Physiological indicators such as brain perfusion and brain structure and function can enhance exercise-induced cardiovascular adaptation [27] [28]. Exercise can increase elasticity in cerebral

arteries and positively affect cerebral blood flow regulations [27] by improving vascular endothelial function via upregulation of nitric oxide bioavailability [28]. Consistent with this finding, exercise-related enhancements in endothelial can function as a risk reducer of atherosclerosis and may facilitate cerebral perfusion [29]. Alternatively, exercise can also affect attenuation in the transmission of excessive blood pressure pulsatility, reduce cerebrovascular resistance, stabilize blood pressure control, and increase cerebral blood flow [30].

Performing aerobic exercises regularly can attenuate age-related cognitive decline, which often can affect episodic memory and attention-executive function [31]. These positive outcomes from aerobic exercises link exercise in preserving brain tissue volume and white structural integrity and cerebral perfusion [32]. The level of cognitive improvements is strongly related to the gains in cardiorespiratory fitness [33]. Cognitive enhancements are observed in the domains of processing speed, aspects of executive function, and overall cognitive function. Of particular interest for the present study is the finding that vigorous aerobic exercise training may improve certain aspects of cognitive function in individuals with Traumatic Brain Injury [34]. Long-term treatment outcomes in TBI are difficult to predict and can be associated with either measurable improvement or deterioration for many years after an injury.

Adhering to a regimen of exercise, patients with head injuries respond well to physical conditioning with increases in the effectiveness of the cardiovascular system, improvements in muscular strength, and increases in the number of synapses per Purkinje cell [35]. The advances in muscular strength may be due to cerebral blood flow linking to neuronal firing rates and shifts in regional flow varying with the metabolic demands of different brain regions. Enlarged perfusion levels in the prefrontal, somatosensory, and primary motor areas have been discovered following

exercise performance in animals. Perfusion increase could enhance the process of recovery in these areas in the injured brain [36].

#### **1.4 Current Limitation of Exercise as Method of Therapy**

The exercise activity that a clinician could prescribe might depend on the nature and extent of the patient's physical and brain injuries. The need to get to health care facilities to perform the prescribed exercise regimen impedes TBI patients [37]. It is reasonable to suspect that such an impediment may contribute to low compliance with the prescribed exercise regimen, along with other factors affecting compliance such as personal habits and physical disabilities [37].

There are several barriers to conduct a clinical trial exercise in persons with TBI, including lack of transportation, poor organization and initiation, and challenges in fully implementing the prescribed exercise program for all participants [38] [39]. Investigators have reported that a personal mobile device that provides instruction and motivates the patients to perform the prescribed exercise may influence them to exercise efficiently and consistently, therefore improving their recovery process [40] [41].

#### **1.5 Study Motivations and Objectives**

##### ***1.5.1 Significance of the Study***

Aerobic exercise is a promising strategy to improve neurocognitive decline in TBI patients [42]. Employing a personal mobile trainer (PMT) system, as will be described in detail later in this document, for treatment of TBI patients will allow studying the efficacy of physical exercises in treating TBI patients. Our proposed PMT system consists of a smartphone and a watch with a customized app that presents daily prescribed exercises to the user, improves two-way communication with a healthcare provider, and is simple and accessible. Further, it will have

cognitive strategies such as reminders, notifications, calendars, care partner support. It will be customizable and adaptable as well as informative and educational.

Furthermore, it may be possible to increase patient compliance with the prescribed exercise program by removing barriers preventing patients from exercising. The proposed (PMT) system for traumatic brain injury patients will reduce visit burden, improve adherence to the exercise and increase recovery progress. In addition, the PMT ecosystem that contains of Apple Watch application, iPhone application, and clinician portal system will give the possibility to tailor and adapt the exercise protocols for each patient on a more frequent basis and improve the likelihood of finding suitable exercise protocols for each patient based on the patient's condition and observed adherence to the prescribed program.

### ***1.5.2 Use of Technology to Support Physical Therapy with other Medical Conditions***

Several studies have demonstrated the potential benefits of using mobile phone applications in home health therapy and recovery. For instance, the Corrie Health app [43] by John Hopkins Hospital helps with cardiac patient recovery. Also, the Start app [44] by Iodine Inc. (Iodine, San Diego, CA USA) for depression utilized this type of technology to support home therapy with other medical conditions. All these studies support: (1) the potential of this technology intervention to improve patient experience and outcomes, (2) ease of improvement in end-user experience, and (3) the ability of the technology to reach and empower underserved patients. Therefore, building an app that can serve with TBI patient recovery could significantly add value to the remote health care systems.

### ***1.5.3 Novelty of the Study***

This project is innovative because it focuses on increasing the compliance of TBI patients with their prescribed exercise. All the studies that recommend physical exercise as medicine for

TBI patients emphasize the chief challenge with the success of such therapy is the adherence of TBI patients to exercise regimens. Therefore, we will use state-of-the-art cloud-based mobile technology designed to meet the needs of persons with TBI. Precisely, the proposed system delivers personalized “exercise dose” (intensity, duration, and frequency) recommendations to each participant, monitors compliance and adherence in real-time, and provides timely feedback to facilitate exercise training and participant retention. The literature survey suggests that the PMT system will be the first individualized exercise training app used in a clinical trial for persons with TBI.

There are several innovations this study brings about:

1) *Develop an individualized exercise training multiple featured PMT system to be used in a clinical trial for persons with TBI.* The PMT system can monitor exercise by TBI patients, improve two-way communication with a health care provider, and be simple and easy to use. In addition, it will provide cognitive assistance such as reminders, notifications, calendars, care provider support. It will be customizable and adaptable as well as informative and educational.

2) *“Real World” evaluation of the PMT usability in person with TBI with varied literacy and disability.* Testing the PMT system usability for TBI patients that have moderate to severe TBI injury levels. Furthermore, investigating how the adherence to the treatment plan can be affected by the injury level can help determine how to adjust the treatment based on the patient's different levels of physical disability and cognitive impairment.

3) *Quantitative assessment of the efficacy of the built-in patient encouragement strategies.* We will apply different encouragement methods to study its effectiveness in enhancing compliance. This capability will be a built-in feature of the system and provide reminders, progress badges, progress points for the users, etc.

4) *Minimization of exercise barriers for TBI patients.*

The PMT system will remove many obstacles preventing a TBI patient from following and adhering to the rehabilitation treatment plan. The PMT system will eliminate environmental barriers such as transportation and geography, lack of motivation, lack of access to physical therapy clinics or gyms, and limited time to exercise at rehabilitation centers.

5) *Capability of customizing (tailoring) exercise training for each patient.* As brain injuries are entirely different, tailoring the physical exercises for TBI patients to meet each patient's needs may provide a better healing outcome. Change of exercise protocols for each subject is not readily possible without the PMT. However, PMT makes it possible to make such changes frequently, rapidly, and reliably.

6) *Providing the capability of monitoring and adjusting exercise levels for the TBI patients at any time during treatment without delay.* Continual tracking of patient performance on the prescribed exercise protocol will delineate the efficacy of the prescribed exercises. It will allow frequent adjustment to the treatment to optimize patient compliance; and

7) *Efficacy of patient compliance on HRV.* Studying the HRV will indicate the brain's health status. As compliance with the PMT system increases, heart rate variability will give evidence of improvement in the patient's brain health.

#### ***1.5.4 Hypotheses and Specific Aims***

We propose developing a personalized mobile trainer (PMT) phone application for traumatic brain injury patients to reduce the burden of clinical visits for performing the prescribed exercise, improving exercise compliance, studying the efficacy of tailored physical exercises on TBI patients, and enhancing patient recovery progress. The proposed method can provide means to study the effect of the PMT system by measuring compliance, heart rate variability, energy

expenditure, and ease of use rating evaluation. This continuous monitoring is superior to periodic clinical monitoring of the progress of traumatic brain injury patients [45].

In this regard, we have formulated three hypotheses to be investigated, and some specific aims for each hypothesis are described as follows:

**Hypothesis 1:** The proposed personal mobile trainer (PMT) system increases the compliance level of traumatic brain injury patients to their prescribed exercise.

**Aim 1.1:** Using Apple Watch and iPhone, design and deploy a PMT system for use by TBI patients, which provides them with their prescribed exercise protocol, tracks the patients' exercise activities, and issues reminders and encouragements to the patients to enhance the exercise compliance.

**Aim 1.2:** Using Apple Watch and iPhone, design and deploy a two-way communication system for the proposed PMT system that transmits the patients' exercise data to a server for clinician review and receives and displays clinician's instructions.

**Aim 1.3:** Quantify patient compliance based on the duration to maintain prescribed heart rate, frequency of performing the prescribed exercises over the prescribed treatment period, and duration of performed exercise.

**Aim 1.4:** Using the proposed PMT system and its two-way communication system, quantify and assess the level of TBI patient's compliance with their prescribed exercise protocol and compare that with the compliance levels previously observed for in-clinic exercise treatment of the TBI patient.

**Aim 1.5:** Using the proposed PMT system, measure changes in energy expenditure of TBI patients after normalization with the relation of compliance with their prescribed exercise protocol.

**Hypothesis 2:** Compliance with the prescribed exercise protocol improves the TBI patient's heart rate variability compared to their heart rate variability baseline (i.e., their heart rate variability before the exercise program).

**Aim 2.1:** Using the proposed PMT system, measure the changes in heart rate variability (HRV) and determine the association of improvements in the patient HRV compared to baseline HRV with the proposed compliance measures (obtained under Aim 1.3).

**Hypothesis 3:** Personal trainer applications for iPhone and Apple watch as health and well-being application will have acceptable rating scale using a well-established mobile health rating scale.

**Aim 3.1:** Use System Usability Scale to assess iPhone and Apple watch applications usability from the patient perspective

ate age-related cognitive decline, which often can affect episodic memory and attention-executive function [31]. These positive outcomes from aerobic exercises link exercise in preserving brain tissue volume and white structural integrity and cerebral perfusion [32]. The level of cognitive improvements is strongly related to the gains in cardiorespiratory fitness [33]. Cognitive enhancements are witnessed in the areas of processing speed, aspects of executive function, and overall cognitive function. Of particular interest for the present study is the finding that vigorous aerobic exercise training may improve certain aspects of cognitive function in individuals with Traumatic Brain Injury [34]. Long-term treatment outcomes in TBI are difficult to predict and can be associated with either measurable improvement or deterioration for many years after an injury.

Adhering to a regimen of exercise, patients with head injuries respond well to physical conditioning with increases in the effectiveness of the cardiovascular system, improvements in muscular strength, and increases in the number of synapses per Purkinje cell [35]. The



improvements in muscular strength may be due to cerebral blood flow linking to neuronal firing rates and shifts in regional flow varying with the metabolic demands of different regions of the brain. Enlarged perfusion levels in the prefrontal, somatosensory, and primary motor areas have been discovered following exercise performance in animals. Perfusion increase could enhance the process of recovery in these areas in the injured brain [36].

#### **1.4 Current Limitation of Exercise as Method of Therapy**

The exercise activity that a clinician could prescribe might depend on the nature and extent of the patient's physical and brain injuries. The need to get to health care facilities to perform the prescribed exercise regimen impedes TBI patients [37]. It is reasonable to suspect that such an impediment may contribute to low compliance with the prescribed exercise regimen, along with other factors affecting compliance such as personal habits and physical disabilities [37].

There are several barriers to conduct a clinical trial exercise in persons with TBI, including lack of transportation, poor organization and initiation, and challenges in fully implementing the prescribed exercise program for all participants [38] [39]. Investigators have reported that a personal mobile device that provides instruction and motivates the patients to perform the prescribed exercise may influence them to exercise efficiently and consistently, therefore improving their recovery process [40] [41].

#### **1.5 Study Motivations and Objectives**

##### ***1.5.1 Significance of the Study***

Aerobic exercise is a promising strategy to improve neurocognitive decline in TBI patients [42]. Employing a personal mobile trainer (PMT) system, as will be described in detail later in this document, for treatment of TBI patients will allow studying the efficacy of physical exercises in treating TBI patients. Our proposed PMT system consist of a smart phone and a watch with

customized app that present daily prescribed exercises to the user, improve two-way communication with a health care provider, and be simple and accessible. Further, it will have cognitive strategies such as reminders, notification, calendars, care partner support. It will be customizable and adaptable as well as informative and educational.

Furthermore, it may be possible to increase patient compliance with the prescribed exercise program by removing barriers preventing patients from exercising. The proposed (PMT) system for traumatic brain injury patients will reduce visit burden, improve adherence to the exercise and increase recovery progress. In addition, the PMT ecosystem that contain of Apple Watch application, iPhone application and clinician portal system, will give the possibility to tailor and adapt the exercise protocols for each patient on a more frequent basis and improve the likelihood of finding suitable exercise protocols for each patient based on the patient's condition and observed adherence to the prescribed program.

### ***1.5.2 Use of Technology to Support Physical Therapy with other Medical Conditions***

Several studies have demonstrated the potential benefits of using mobile phone applications in-home health therapy and recovery. For instance, the Corrie Health app [43] by Johns Hopkins Hospital helps with cardiac patient recovery. Also, the Start app [44] by Iodine Inc. (Iodine, San Diego, CA USA) for depression utilized this type of technology to support home therapy with other medical conditions. All these studies support: (1) the potential of this technology intervention to improve patient experience and outcomes, (2) ease of improvement in end-user experience, and (3) the ability of the technology to reach and empower underserved patients. Therefore, building an app that can serve with TBI patient recovery could significantly add value to the remote health care systems.

### ***1.5.3 Novelty of the Study***

This project is innovative because it focuses on increasing the compliance of the TBI patients with their prescribed exercise. All the studies that recommend physical exercise as medicine for TBI patients emphasize the chief challenge with the success of such therapy is the adherence of TBI patients with exercise regimens. Therefore, we will use state-of-the-art cloud-based mobile technology, designed to meet the needs of persons with TBI. Specifically, the proposed system delivers personalized “exercise dose” (intensity, duration, and frequency) recommendations to each participant, monitors compliance and adherence in real-time, and provides timely feedback to facilitate exercise training and participant retention. The literature survey suggests that the PMT system will be the first individualized exercise training app used in a clinical trial for persons with TBI.

There are several innovations this study brings about:

- 1) *Development of an individualized exercise training multiple featured PMT system to be used in a clinical trial for persons with TBI.* The PMT system has the capability of monitoring exercise by TBI patients, improve two-way communication with a health care provider, and be simple and easy to use. In addition, it will provide cognitive assistance such as reminders, notifications, calendars, care provider support. It will be customizable and adaptable as well as informative and educational.
- 2) *“Real World” evaluation of the PMT usability in person with TBI with varied literacy and disability.* Testing the PMT system usability for TBI patients that have moderate to severe TBI injury levels. Furthermore, investigating how the adherence to the treatment plan can be affected by the injury level can help determine how to adjust the treatment based on the patient's different levels of physical disability and cognitive impairment.

3) *Quantitative assessment of the efficacy of the built-in patient encouragement strategies.* We will apply different encouragement methods to study its efficacy in enhancing compliance. This capability will be a built-in feature of the system and will provide reminders, progress badges, progress points for the users, etc.

4) *Minimization of exercise barriers for TBI patients.*

The PMT system will remove many obstacles preventing a TBI patient from following and adhering to the rehabilitation treatment plan. Environmental barriers such as transportation and geography, lack of motivation, lack of access to physical therapy clinics or gyms, and limited time to exercise at rehabilitation centers will all be eliminated by the PMT system.

5) *Capability of customizing (tailoring) exercise training for each patient.* As brain injuries are entirely different, tailoring the physical exercises for TBI patients to meet each patient's needs may provide a better healing outcome. Change of exercise protocols for each subject is not readily possible without the PMT. However, PMT makes it possible to make such changes frequently, rapidly, and reliably;

6) *Providing the capability of monitoring and adjusting exercise level for the TBI patients at any time during treatment without delay.* Continual tracking of patient performance on the prescribed exercise protocol will delineate the efficacy of the prescribed exercises. It will allow frequent adjustment to the treatment to optimize patient compliance; and

7) *Efficacy of patient compliance on HRV. Studying the HRV will indicate the brain's health status.* As compliance will increase by the PMT system, heart rate variability will give evidence of improvement in the patient's brain health.

#### ***1.5.4 Hypotheses and Specific Aims***

We propose developing a personalized mobile trainer (PMT) phone application for traumatic brain injury patients to reduce burden of clinical visits for performing the prescribed exercise, improving exercise compliance, studying the efficacy of tailored physical exercises on TBI patients, and enhancing the patient recovery progress. The proposed method can provide means to study the effect of the PMT system by measuring compliance, heart rate variability, energy expenditure, and ease of use rating evaluation. This continuous monitoring is superior to periodic clinical monitoring of the progress of the traumatic brain injury patients [45].

In this regard, we have formulated three hypotheses to be investigated and some specific aims for each hypothesis described as follows:

**Hypothesis 1:** The proposed personal mobile trainer (PMT) system increases the compliance level of traumatic brain injury patients to their prescribed exercise.

**Aim 1.1:** Using Apple Watch and iPhone, design and deploy a PMT system for use by TBI patients, which provides them with their prescribed exercise protocol, tracks the patients' exercise activities, and issues reminders and encouragements to the patients to enhance the exercise compliance.

**Aim 1.2:** Using Apple Watch and iPhone, design and deploy a two-way communication system for the proposed PMT system that transmits the patients' exercise data to a server for clinician review and receives and displays clinician's instructions.

**Aim 1.3:** Quantify patient compliance based on the duration to maintain prescribed heart rate, frequency of performing the prescribed exercises over prescribed treatment period, and duration of performed exercise.

**Aim 1.4:** Using the proposed PMT system and its two-way communication system, quantify and assess the level of TBI patient's compliance with their prescribed exercise protocol and compare

that with the compliance levels previously observed for in-clinic exercise treatment of the TBI patient.

*Aim 1.5:* Using the proposed PMT system, measure changes in energy expenditure of TBI patient after normalization with the relation of compliance with their prescribed exercise protocol.

***Hypothesis 2:*** Compliance with the prescribed exercise protocol improves the TBI patient's heart rate variability compared to their heart rate variability baseline (i.e., their heart rate variability before the exercise program).

*Aim 2.1:* Using the proposed PMT system, measure the changes in heart rate variability (HRV) and determine the association of improvements in the patient HRV compared to baseline HRV with the proposed compliance measures (obtained under Aim 1.3).

***Hypothesis 3:*** Personal trainer applications for iPhone and Apple watch as health and well-being application will have acceptable rating scale using a well-established mobile health rating scale.

*Aim 3.1:* Use System Usability Scale to assess iPhone and Apple watch applications usability from the patient perspective

## CHAPTER 2

### Accuracy Of Heart Rate Sensing of Wrist-Worn Fitness Tracking Devices

#### 2.1 Method

In our preliminary study, we tested four popular wrist-worn fitness trackers (WFT). Then, we applied the assessment by measuring the heart rate accuracy of the selected smartwatches during treadmill walking and stationary biking. We choose Apple Watch Series 3 (Apple, Cupertino, CA USA), Samsung Gear S3 (Samsung, Seoul, South Korea), Polar M600 (Polar, Kempele, Finland), and Fitbit Charge 2 (Fitbit, San Francisco, CA USA), for this study due to their wide availability in the U.S. market.

Exercising on an exercise machine such as a treadmill or a stationary bike is commonly used to do at-home exercises. Hence, for this study, we choose walking and stationary biking to measure heart rate to test the accuracy of the fitness trackers in measuring heart rate. In addition, testing the WFT's during different exercises can elucidate how the WFT's perform when used in various exercise modes.

***WFT accuracy Evaluation Protocol-*** The heart rate recordings were compared with concurrently recorded electrocardiography (ECG) using a 5-electrode configuration and the Biopac MP 150 ECG system (BIOPAC Systems, Goleta, CA USA). The ECG data were sampled at 256 samples/s and stored using a Dell Latitude E640 laptop computer (Dell, Round Rock, TX USA) and National Instrument NI-USB-6128 analog-to-digital converter (National Instruments, Austin, TX USA). The data acquisition software was N.I. LabVIEW 2017 (National Instruments, Austin, TX USA). The data analysis is done offline. The subjects used Xterra Fitness TR150 Treadmill (XTERRA FITNESS, Jonesboro, AK USA) for walking exercise with an average speed of 3 MPH for a slow

walk and 6 MPH for a Fast Walk. IMPEX Marcy (IMPEX FITNESS, Pomona, CA USA) Magnetic-Resistance Upright Bike ME-708 for biking exercise. The Bike tension control is set to level 1 with an average speed of 18 MPH slow bike and level 3 with an average speed of 25 MPH for a fast bike.

We acquired the exercise data from 5 healthy (i.e., no known disease), non-smoker, adult volunteer subjects (2F & 3M; age  $26.4 \pm 3.20$  years; BMI  $24.7 \pm 1.92$  kg/m<sup>2</sup>). Our institutional review board (IRB) approved the protocol for the study, and the subjects signed an informed consent form that our IRB also approved.

The total duration of the experiment was approximately 60 minutes per subject for testing all WFT's for both rounds. Each measurement started with 5 minutes of low-speed walking with a pace that the subject found comfortable on the treadmill, followed by 5 minutes of walking faster. After finishing both walking exercises, the subject rested for 5 minutes in a Sitting position on a comfortable chair. Next, each subject started pedaling on the stationary bike at a rate that the subject found comfortable for 5 minutes. This was followed by an additional 5 minutes at a faster speed and increased resistance. However, in this preliminary study, slow walk, Fast Walk, Sitting, slow biking, and fast biking are reported. Since we evaluated 4 WFT's and could place only one on each wrist, the subjects performed the exercise protocol twice in the same way. Each mode was for about five minutes, and subjects performed the slow and fast modes continuously. Also, the subjects had Sitting mode between the walking and biking modes. They placed the Apple Watch on the right wrist and Samsung Gear G3 on the left wrist during the first round. They wore Polar M600 on the right wrist and Fitbit Charge 2 on the left wrist for the second round. Apple and Polar watches were tested together, and Fitbit and Samsung were tested together. The order by which the pair of watches were tested was random.



The data collected by Apple WFT's were collected using the Fitiv Pulse application on an iPhone (MOTIFIT, Moncton, Canada). For Polar WFT data retrieval, we used Polar Flow (Polar, Kempele, Finland). For Fitbit WFT, we applied the Fitbit application software (Fitbit, San Francisco, CA USA) for use on an iPhone. Finally, for the Samsung Gear S3 WFT, we used the Samsung S Health app on Samsung Galaxy J3 mobile phone. These apps allowed us to download the recorded heart rates from the WFT devices into a computer for further analysis.

**Data Analysis-** Stored ECG's QRS complex waveform data uploaded and plotted using MATLAB R2018 software (MathWorks, Natick, MA USA) and finding R wave peaks by applying peak detection *findpeak* algorithm; we computed beat-to-beat heart rate (H.R.). The interpolation of heart rates from the four WFT's and ECG was achieved using a cubic spline interpolation method. The interpolated H.R.'s were then uniformly sampled at 256 samples/s, using *interp1* MATLAB functions.

We used the temporal location of the peak of the R wave of the concurrently recorded ECG QRS complex to mark the time instance of each heartbeat. To calculate heart rate obtained from ECG recording,  $ECG_{HR}$ , the interval between consecutive detected R peaks were interpolated and uniformly resampled at 256 samples/s, using the *findpeak* and *interp1* function provided by the MATLAB. Likewise, WFT's heart rate readings ( $WFT_{HR}$ ) were transmitted from the WFT to the corresponding WFT phone's application. Following this, the values were first saved into a Microsoft Excel (Excel) file and then uploaded into the MATLAB software to be interpolated and uniformly resampled at 256 samples/s.

We computed the moving average on the interpolated  $WFT_{HR}$  and  $ECG_{HR}$  samples for every 100 points as we have 78600 interpolated points. The averaging smoothed the data by

reducing the momentarily jumps in the recorded heart rates due to movement of the sensing device or environmental noise.

**Statistical Analysis-** Following this, we used Bland-Altman (B&A) plot to assess the agreement between  $WFT_{HR}$  and  $ECG_{HR}$  [47]. Averaged interpolated measurements represented on the B&A plot by assigning the mean difference (Bias) of the two measurements (i.e.,  $ECG_{HR}$  and each of the  $WFT_{HR}$ ) on the x-axis and the difference between the two measurements on the y-axis, then Bias and limits of agreement (*LOA*) were calculated as follows:

$$Bias = \frac{1}{n} \sum_{i=1}^n (y_i - x_i) \quad (1)$$

$$LOA = Bias \pm 1.96SD \quad (2)$$

where *Bias* is an average shift in the values  $x_i$  ( $WFT_{HR}$ ) relating to the reference data  $y_i$  ( $ECG_{HR}$ ),  $n$  is the number of samples compared with each other, and *S.D.* denotes the standard deviation of the difference.

We assessed the accuracy of measured heart rate by WFT's by computing the mean and standard deviation of the sample-by-sample error between the interpolated  $WFT_{HR}$  measurements and interpolated  $ECG_{HR}$ -derived values. Therefore, we calculated sample error to study discrepancy between the WFT's detected heart rate and the  $ECG_{HR}$  for each interpolated sample ( $E_i$ ) as follows:

$$E_i = (ECG_{HR})_i - (WFT_{HR})_i \quad (3)$$

where  $E_i$  is the  $i^{th}$  sample error (WFT error),  $(ECG_{HR})_i$  is an  $i^{th}$  sample of the heart rate value calculated from ECG, and  $(WTF_{HR})_i$  is the  $i^{th}$  sample heart rate value that is calculated from one of the four WFT's.

Furthermore, we calculated the mean error between the interpolated  $WFT_{HR}$  measurements and interpolated  $ECG_{HR}$ -derived values as the following:

$$\text{Mean Error} = \frac{1}{N} \times \sum_{i=1}^N E_i \quad (4)$$

where  $E_i$  is the  $i^{\text{th}}$  WFT<sub>HR</sub> error as shown in Eq. (3), and  $N$  is the number of WFT<sub>HR</sub> sample points used for computing the error.

Further, the root means square error (RMSE) for the difference between each WFT<sub>HR</sub> and ECG<sub>HR</sub> was calculated as:

$$\text{RMSE} = \sqrt{\frac{\sum_{i=1}^n E_i^2}{n}} \quad (5)$$

where  $E_i$  is the  $i^{\text{th}}$  WFT<sub>HR</sub> error as shown in Eq. (3), RMSE is the root mean square error, and  $n$  is the number of WFT<sub>HR</sub> sample points used for computing the error.

Moreover, a *t-test* ( $\alpha = 0.05$ ) was applied to study the mean difference between WFT<sub>HR</sub> and ECG<sub>HR</sub> samples to examine the statistical significance. The *t-test* was calculated as follows:

$$t = \frac{\overline{ECG}_{HR} - \overline{WFT}_{HR}}{\sqrt{\frac{S_{ECG}^2}{n} + \frac{S_{WFT}^2}{m}}}$$

where,  $\overline{ECG}_{HR}$  is ECG<sub>HR</sub> readings mean and,  $\overline{WFT}_{HR}$  is WFT<sub>HR</sub> readings mean,  $S_{ECG}$  is ECG<sub>HR</sub> readings standard deviation and,  $S_{WFT}$  is WFT<sub>HR</sub> readings standard deviation and  $n$  is the ECG<sub>HR</sub> sample size and,  $m$  is the WFT<sub>HR</sub> sample size and in our study  $n$  and  $m$  are equal.

In addition, the *Kruskal Wallis test* ( $\alpha = 0.05$ ) was applied to the RMSE of WFT<sub>HR</sub> values to examine if the means of the WFT<sub>HR</sub> RMSE values are statistically different from each other. The *Kruskal Wallis test* is a non-parametric equivalent of the *one-way ANOVA* [48]. It is different from the *ANOVA* in the assumption of normally distributed responses is not necessary [48]. The test was calculated as follows:

$$H = (N - 1) \frac{\sum_{i=1}^g n_i (\bar{r}_i - \bar{r})^2}{\sum_{i=1}^g \sum_{j=1}^{n_i} (r_{ij} - \bar{r})^2} \quad (6)$$

$N$  is the total number of observations across all WFT's, (i.e., in our study  $N=20$ ),  $g$  is the number of the WFT's groups, (i.e., in our study  $g= 4$ ),  $n_i$  is the number of observations in WFT group  $i$  (i.e. in our study is 5 for each WFT),  $r_{ij}$  is the rank (among all observations) of observation from WFT group  $i$ ,  $\bar{r}_i = \frac{\sum_{j=1}^{n_i} r_{ij}}{n_i}$  is the average rank of all observations. For Fast Walk the rank were 4 (Apple) , 11.2 (Fitbit), 12 (Polar), and 14.8 (Samsung),  $\bar{r} = \frac{1}{2} (N + 1)$  is the average of all the  $r_{ij}$  ( $\bar{r} = 11.5$ )

If the results showed a significantly different P-value, a follow-up test, the *Wilcoxon Rank Sum test* ( $\alpha = 0.05$ ), was applied to identify the unequal pairs. The *Wilcoxon rank-sum test* is equal to the *one-sample t-test* [48]. The *signed-rank test* can be used to make implications about a population mean or median without necessitating the assumption of normally distributed data [48]. As its name denotes, the *Wilcoxon signed-rank test* is based on the ranks of the data [48]. The approximation test can be calculated using *Mann-Whitney U-test* as follows

$$U = W - \frac{n_x(n_x+1)}{2} \quad (7)$$

where  $U$  is the test result,  $W$  is the rank sum (i.e. for WFT<sub>Apple</sub>vs WFT<sub>Samsung</sub> Fast Walk was 17) and  $n_x$  is sample size of WFT<sub>x</sub> (i.e. WFT<sub>Apple</sub> for Fast Walk is 5).

## 2.2 Results

The collected results for all five modes and 4 WFT's (i.e., 20 combinations) were analyzed for all the participants. However, due to the large volume of the results, only Sitting and Fast Walk modes are reported in the chapter, and the rest are displayed in the appendix. We selected to report Fast Walk in the chapter because walk is the most common exercise users, in general, would perform. In addition, the Fast Walk will show the WFT stability and agreement performance with

fast movements and high artifacts. Also, we reported Sitting mode in the chapter as we will use Sitting mode readings to test the heart rate variability measurement in resting mode throughout the study. For the remaining 12 combinations, the results are reported in appendix A2.

Figure 2.1 shows plots of ECG for subject No.1 during Fast Walk recording and peak detection for the first 5 seconds at Apple and Samsung fitness trackers testing.

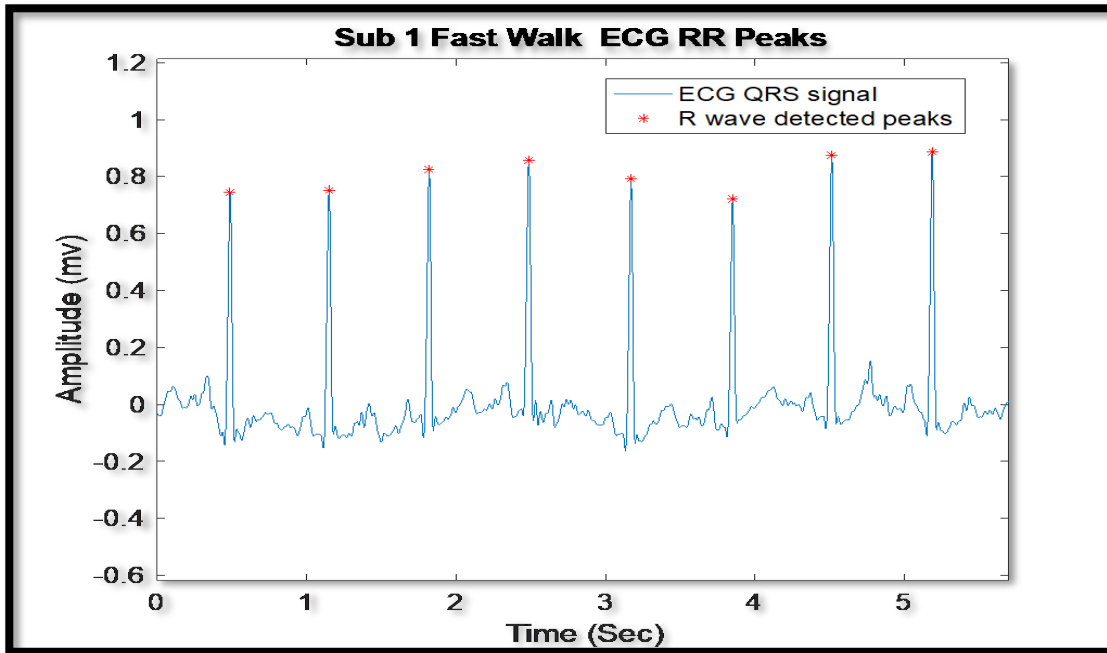


Figure 2.1: Subject No. 1 Fast Walk ECG RR Peaks detection

After that, ECG heart rate values interpolated over-exercise duration. Figure 2.2 shows ECG heart rate values and interpolation values for the Fast Walk from subject No. 1. Next, WFT's heart rate values for a pair of the WFT's were interpolated and plotted with the corresponding ECG's interpolated waveform. Figure 2.3 shows Apple and Samsung compared to the ECG. Polar and Fitbit WFT's were compared at different Fast Walk stages, as two WFT's were tested at a time. Figure 2.4 shows the results of comparing Polar and Fitbit heart rates with the ECG

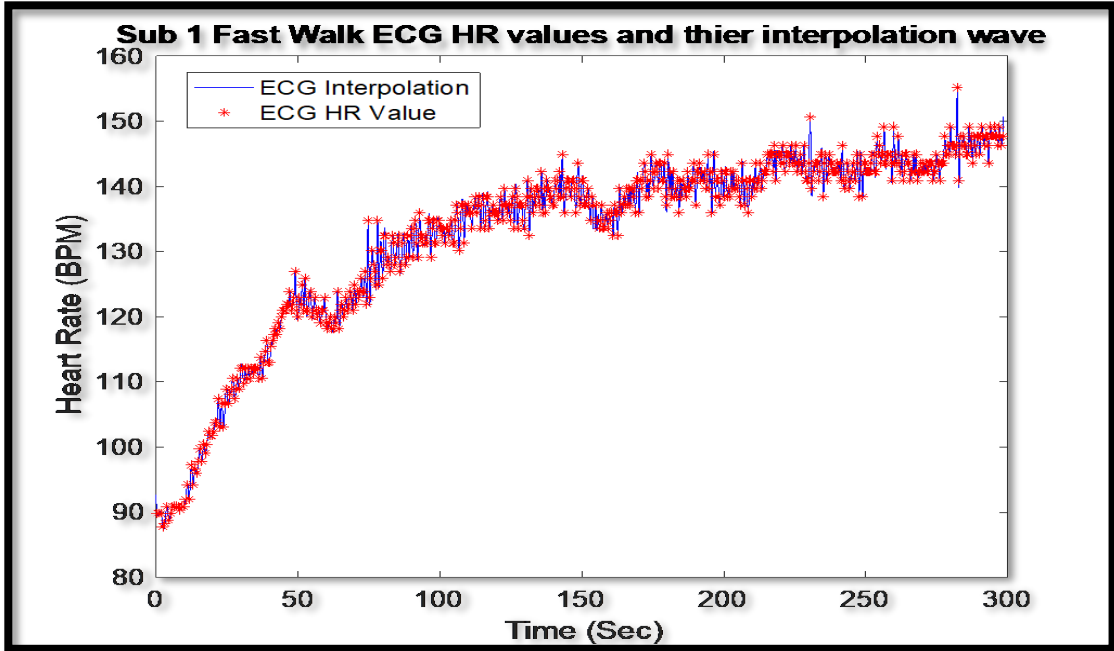


Figure 2.2: Subject No.1 Slow Walk exercise ECG interpolation

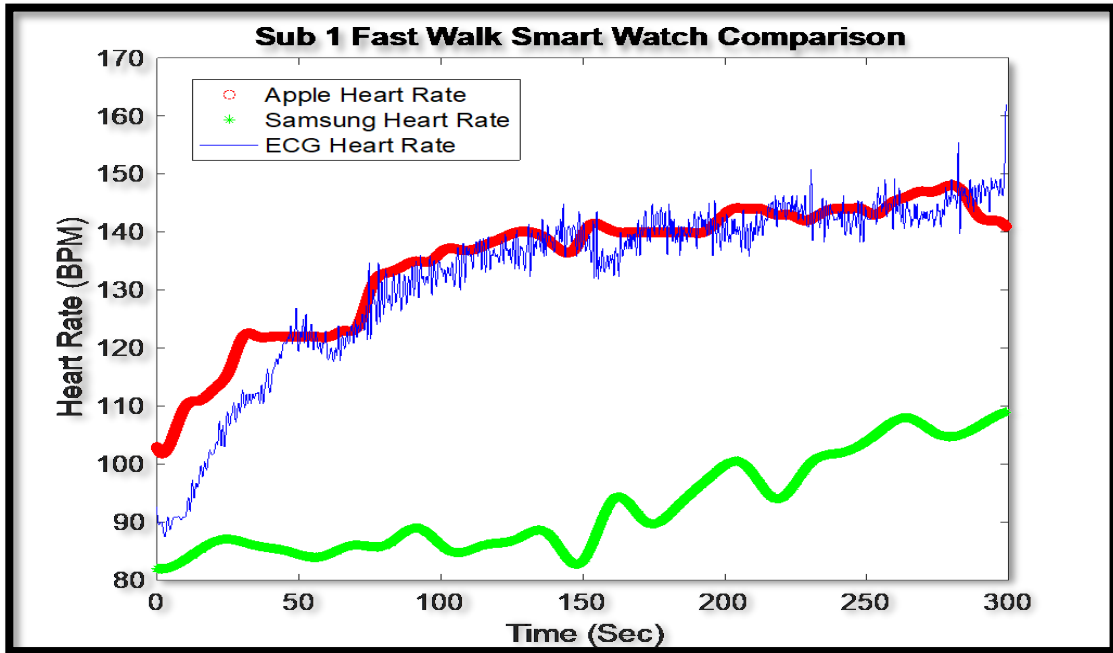


Figure 2.3: Subject No.1 Fast Walk Apple and Samsung WFT compared to ECG

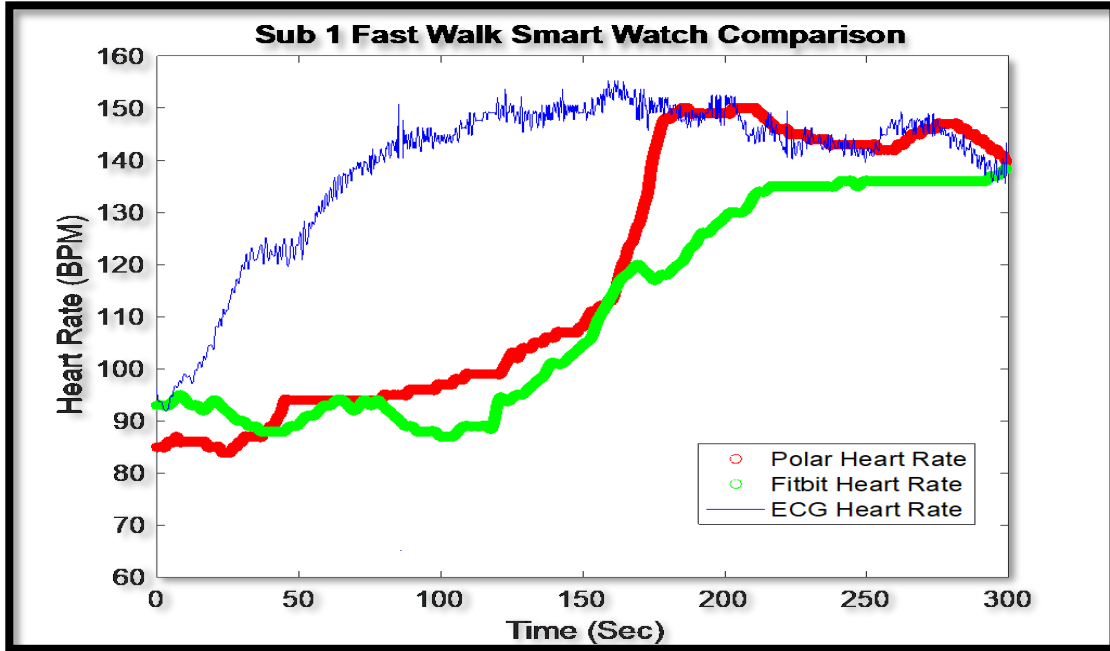


Figure 2.4: Subject No.1 Slow Walk Polar and Fitbit WFT's compared to ECG

To quantify WFT's accuracy and agreement, we studied B&A plots and calculated statistical measures. Figure 2.5 and 2.6 shows Apple WFT for Fast Walk and Sitting stages. Also, Samsung B&A plots are presented in figure 2.7 and figure 2.8 for Fast Walk and Sitting modes. The error means for both exercise modes were calculated and compared between the WFT's. Figures 2.9 and 2.10 show the WFT's error mean comparison. Moreover, RMSE comparison for both phases was calculated and compared between the WFT's; figures 2.11 and 2.12 display the comparisons for both modes.

Table 2.1 and Table 2.2 are showing the *t-test* results for the Fast Walk and Sitting modes, respectively. The *t-test* was conducted between the heart rate readings of the  $ECG_{HR}$  and each  $WFT_{HR}$ . The tables are showing the P-value of each *t-test* result for alpha value  $\alpha = 0.05$ .

Table 2.3 and Table 2.5 show the *Kruskal Wallis test* results for the Fast Walk and Sitting modes. The test was conducted between the RMSE values of WFT's with each other to examine the statistical significance. In addition, as *Kruskal Wallis test* results for the Fast Walk mode

showed a statistical difference between the WFT RMSEs, Table 2.4 shows the Wilcoxon rank-sum test results between Apple and each other WFT's.

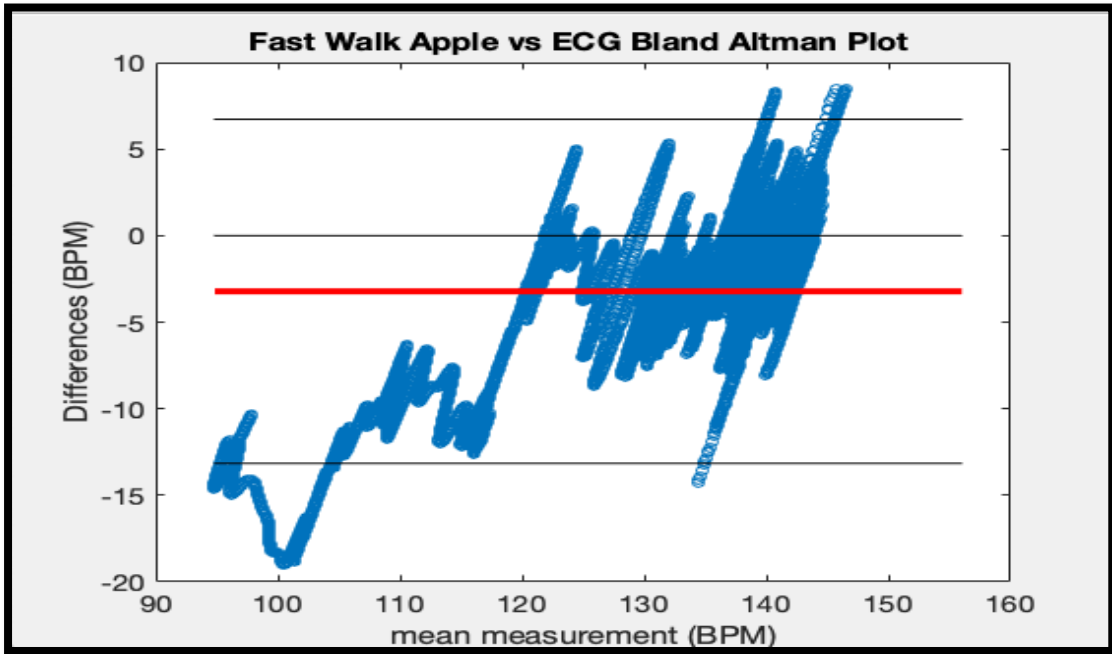


Figure 2.5: Fast Walk Apple B&A Plot (for 409k points), the upper solid black line is the upper value of the level of agreement (LOA), the lower black line represents the lower value of LOA, and the mean difference is shown in bold red line

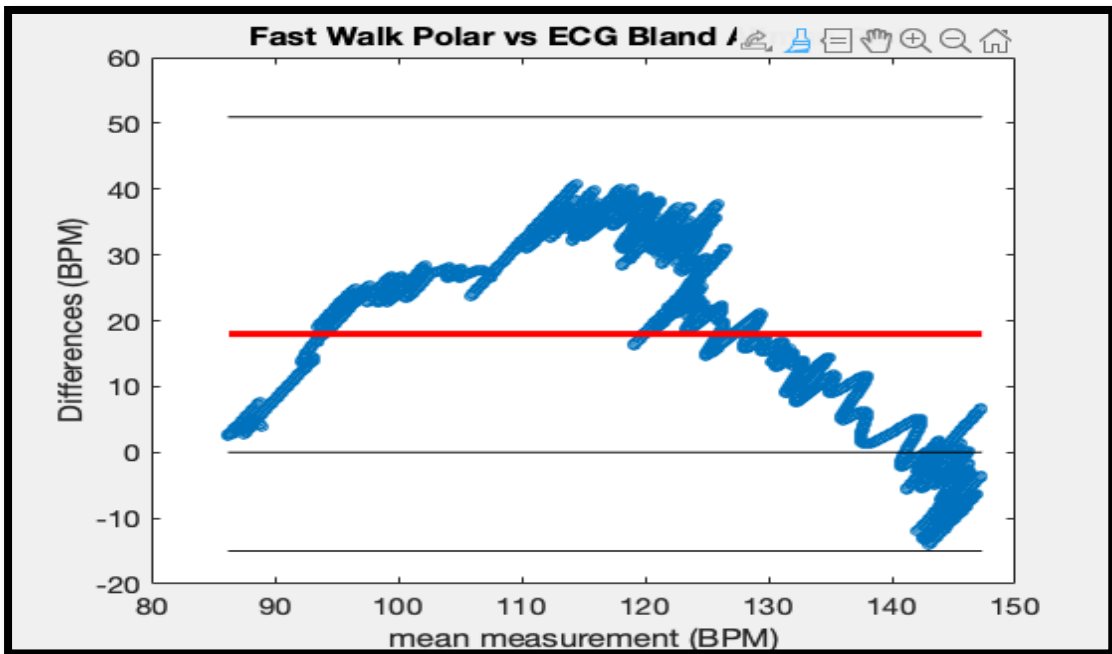


Figure 2.6: Fast Walk Polar B&A Plot (for 409k points), the upper solid black line is the upper value of the level of agreement (LOA), the lower black line represents the lower value of LOA, and the mean difference is shown in bold red line



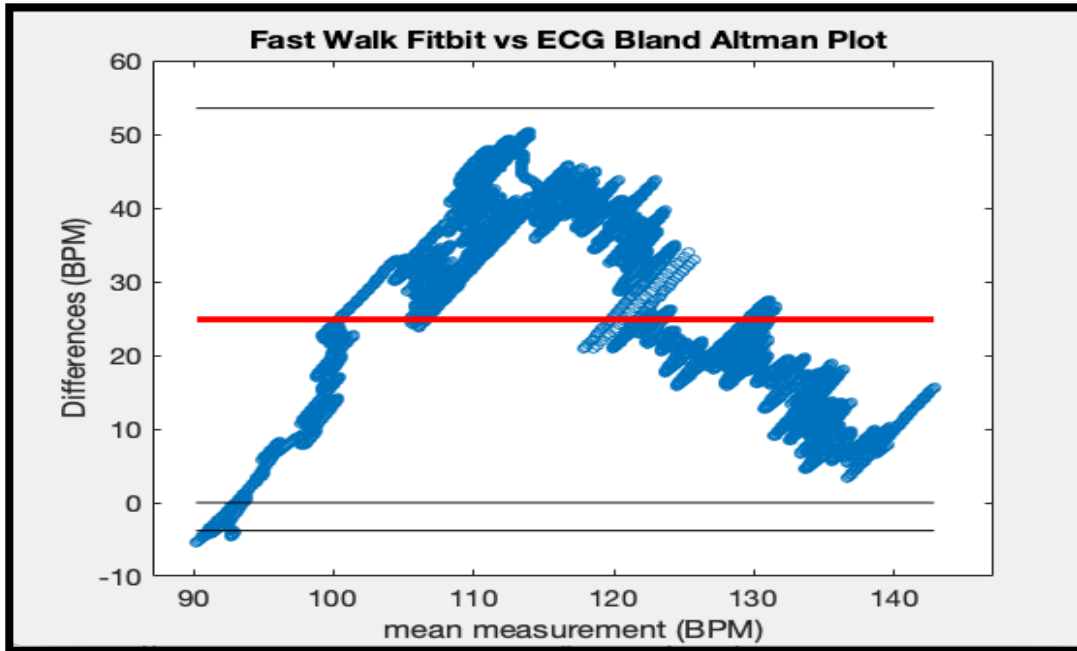


Figure 2.7: Fast Walk Fitbit B&A Plot (for 409k points), the upper solid black line is the upper value of the level of agreement (LOA), the lower black line represents the lower value of LOA, and the mean difference is shown in bold red line

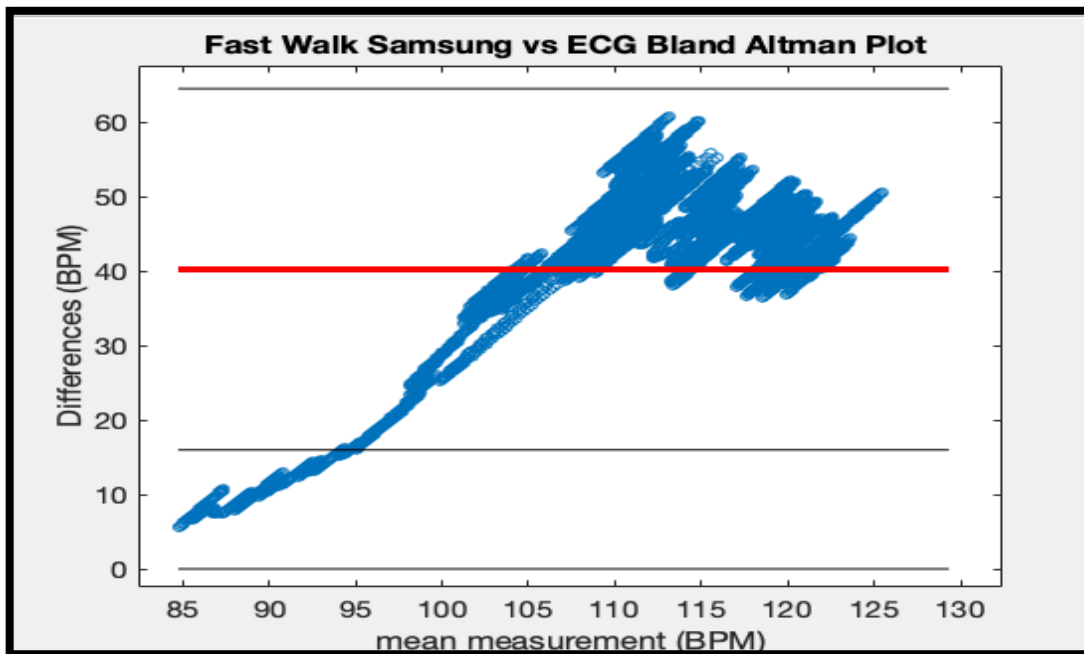


Figure 2.8: Fast Walk Samsung B&A Plot (for 409k points), the upper solid black line is the upper value of the level of agreement (LOA), the lower black line represents the lower value of LOA, and the mean difference is shown in bold red line

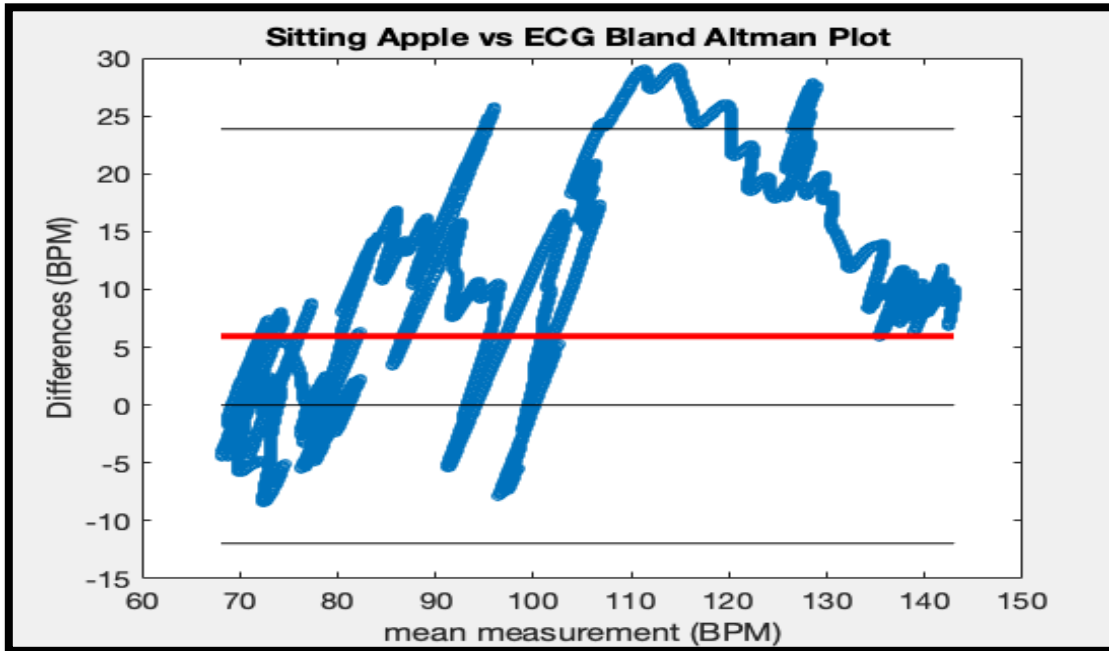


Figure 2.9: *Sitting Apple B&A Plot (for 409k points), the upper solid black line is the upper value of the level of agreement (LOA), the lower black line represents the lower value of LOA, and the mean difference is shown in bold red line*

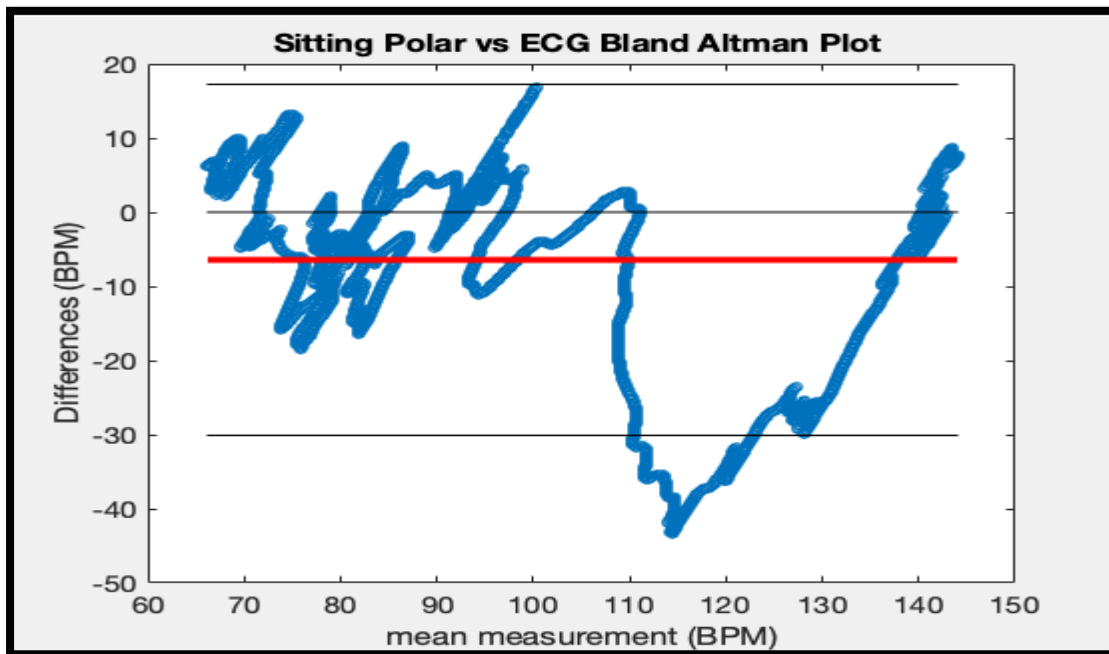


Figure 2.10: *Sitting Polar B&A Plot (for 409k points), the upper solid black line is the upper value of the level of agreement (LOA), the lower black line represents the lower value of LOA, and the mean difference is shown in bold red line*

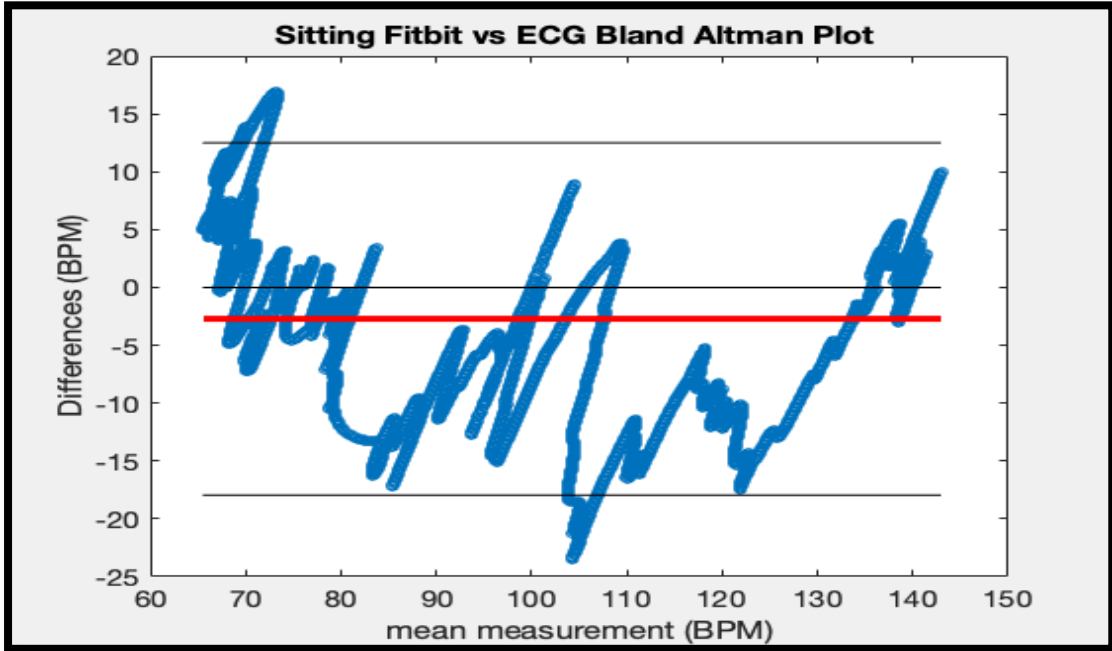


Figure 2.11: Sitting Fitbit B&A Plot (for 409k points), the upper solid black line is the upper value of the level of agreement (LOA), the lower black line represents the lower value of LOA, and the mean difference is shown in bold red line

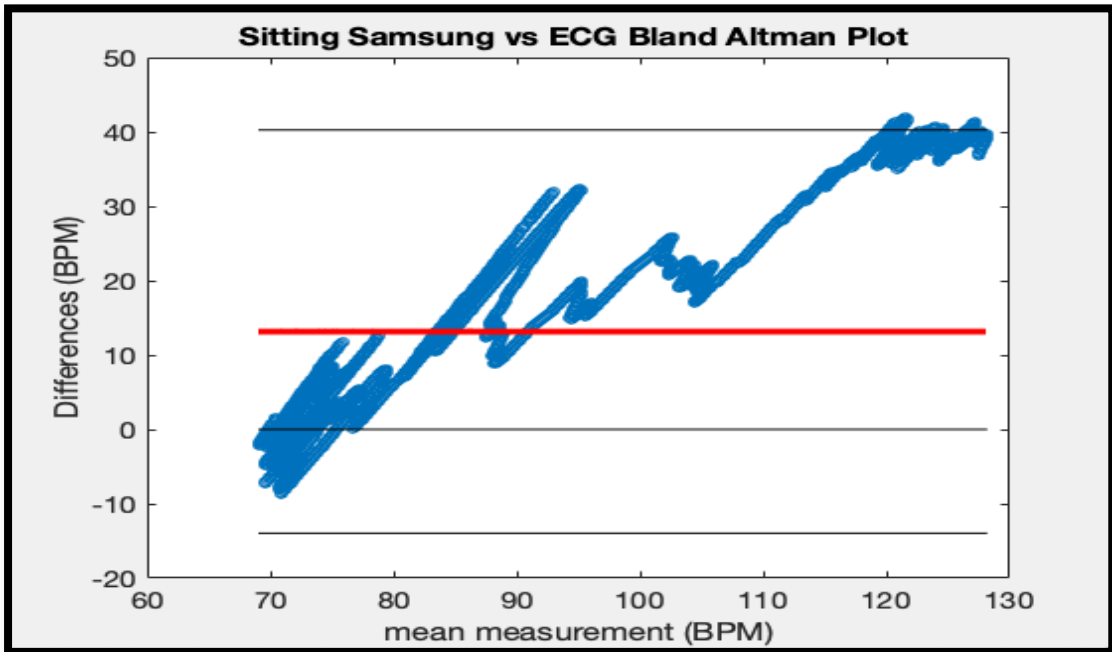


Figure 2.12: Sitting Samsung B&A Plot (for 409k points), the upper solid black line is the upper value of the level of agreement (LOA), the lower black line represents the lower value of LOA, and the mean difference is shown in bold red line

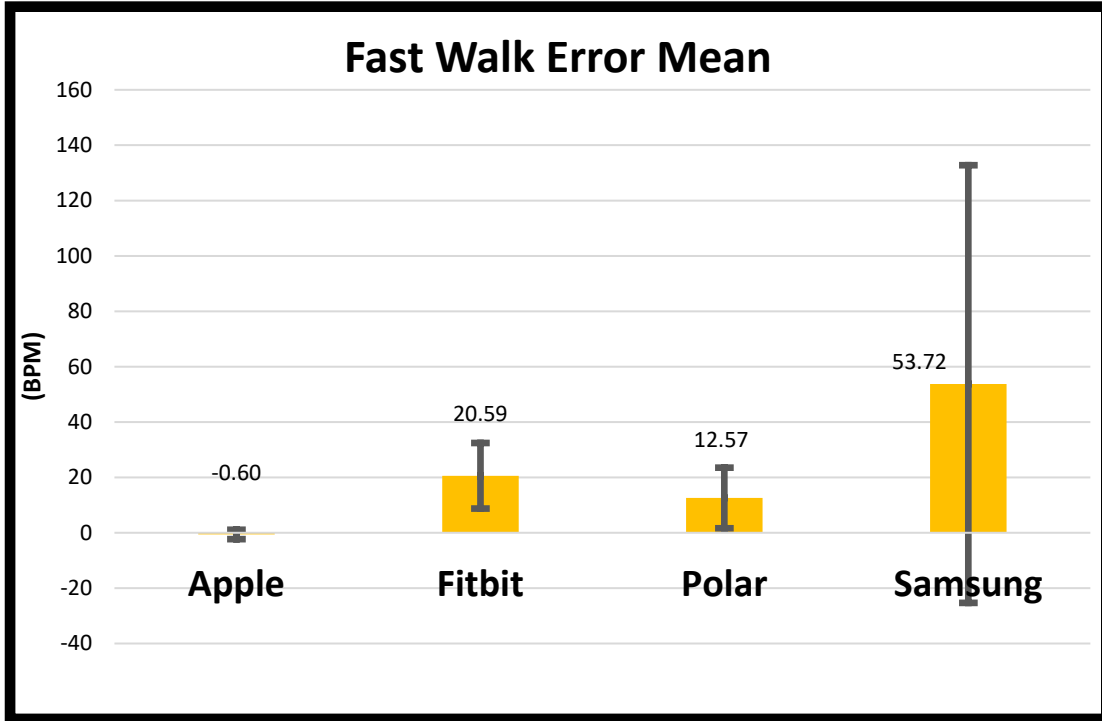


Figure 2.13: Fast Walk error mean (yellow bars),  $\pm$  one standard deviation of the error mean (vertical black lines)

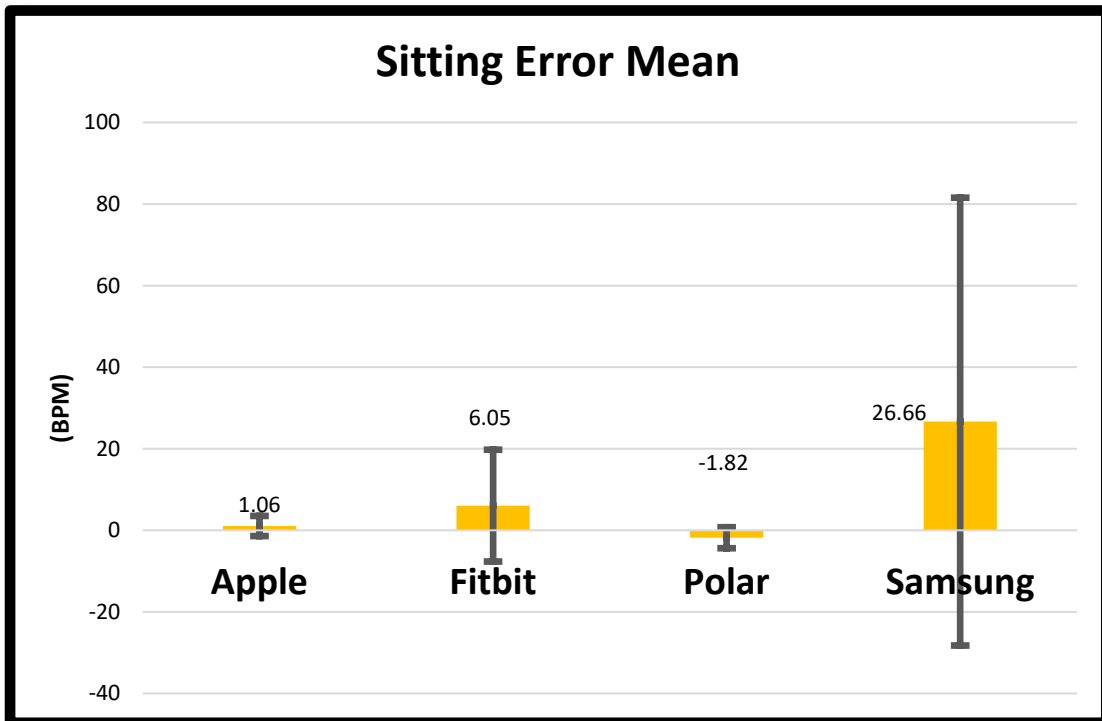


Figure 2.14: Fast Walk error mean (yellow bars),  $\pm$  one standard deviation of the error mean (vertical black lines)

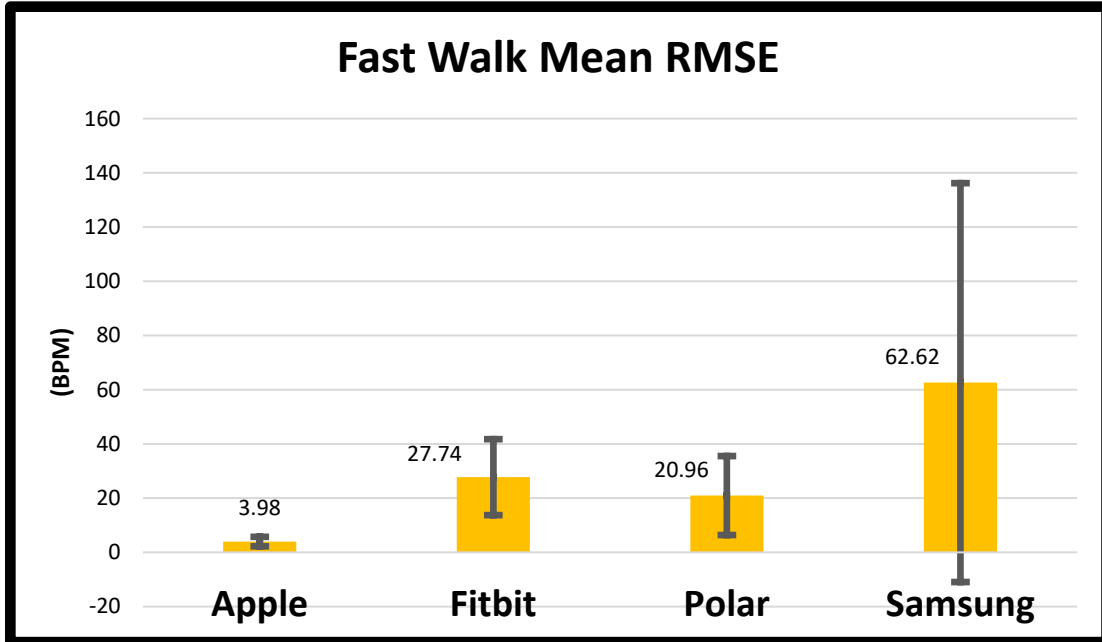


Figure 2.15: Fast Walk exercise WFT's mean RMSE (yellow bars),  $\pm$  one standard deviation of the RMSE (vertical black lines)

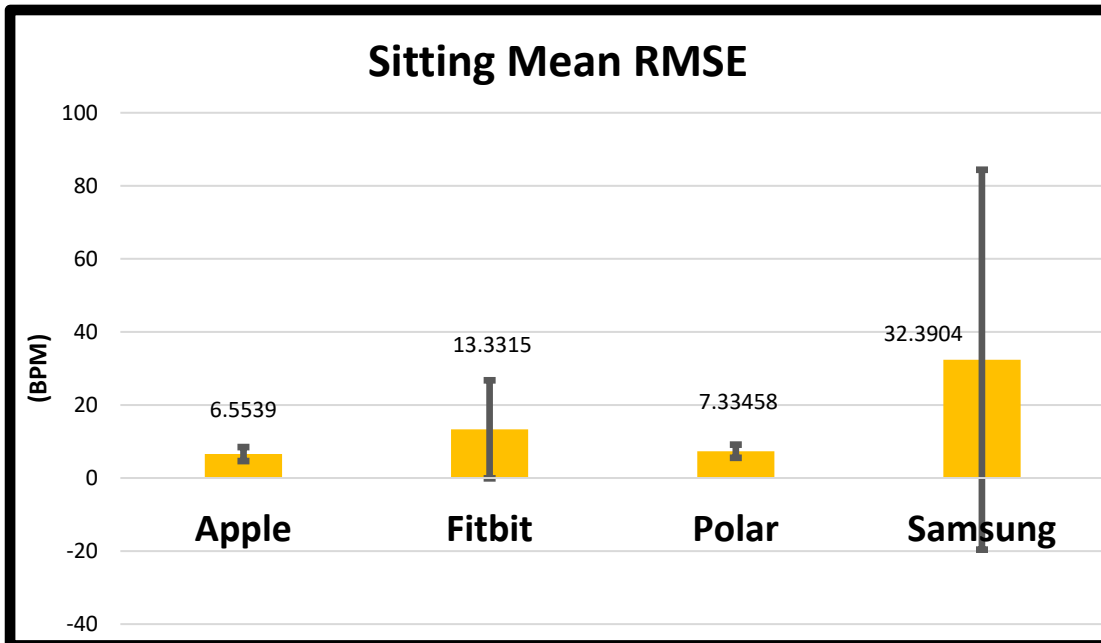


Figure 2.13: Sitting WFT's mean RMSE (yellow bars),  $\pm$  one standard deviation of the RMSE (vertical black lines)

Table 2.1: t-test Results for comparing the heart rate of each WFT<sub>HR</sub> with ECG<sub>HR</sub> during Fast Walk mode

T-test	P-Value
Apple	>0.05
Fitbit	<0.05
Polar	<0.05
Samsung	<0.05



Denotes no significant difference ( $\alpha = 0.05$ )

Table 2.2: t-test Results for comparing the heart rate of each WFT<sub>HR</sub> with ECG<sub>HR</sub> during Sitting mode

T-test	P-Value
Apple	>0.05
Fitbit	<0.05
Polar	<0.05
Samsung	<0.05



Denotes no significant difference ( $\alpha = 0.05$ )

Table 2.3: Testing of possible difference between WFT's RMSE values resulting from comparing their measurements of heart rate with ECG heart rate measurement during Fast Walk using Kruskal Wallis Test

Source	Sum of Squares	Degree of Freedom	Mean Squared Error	Chi-sq	Prob.>Chi-sq
Columns (between-groups variation)	317.4	3	105.8	9.07	0.03
Error (within-groups variation)	347.6	16	21.73		
Total	665	19			



Denotes significant difference ( $\alpha = 0.05$ )

Table 2.4: Fast Walk Apple WFT<sub>HR</sub> RMSE with other WFT's using Wilcoxon Rank Sum Test

Wilcoxon Rank Sum Test	P-Value
Apple vs. Fitbit	0.032
Apple vs. Polar	0.016
Apple vs. Samsung	0.032
Fitbit vs. Polar	0.690
Fitbit vs. Samsung	0.309
Polar vs. Samsung	0.309



Denotes significant difference ( $\alpha = 0.05$ )

Table 2.5: Testing of possible difference between WFT's RMSE values resulting from comparing their measurements of heart rate with ECG heart rate measurement during Sitting using Kruskal Wallis Test

Source	Sum of Squares	Degree of Freedom	Mean Squared Error	Chi-sq	Prob>Chi-sq
Columns (between-groups variation)	73.8	3	24.6	2.11	0.55
Error (within-groups variation)	591.2	16	36.95		
Total	665	19			

## 2.4 Discussion

The preliminary results show that the level of accuracy for WFT's is varied. In Fast Walk, between all the WFT's, Apple WFT had the least error with respect to ECG. For the *t-test* results for comparing the Apple WFT<sub>HR</sub> and the ECG<sub>HR</sub> in the Fast Walk mode, Apple showed no significant difference among all 5 subjects (Table 2.1). Apple's Fast Walk had an error mean of around -0.6 BPM, different than the ECG (Figure 2.13). Also, for this mode, Apple WFT had the least mean root mean square error with respect to ECG among all other WFT as it was around +3.98 BPM (Figure 2.15). This means that the Apple WFT had the highest agreement to the ECG among all other WFT's. Conversely, Samsung had the highest mean RMSE with respect to ECG

in Fast Walk compared to the other WFT's, as it reached +62 BPM, different from ECG (Figure 2.15), which means Samsung readings had the least agreement to the ECG readings.

B&A plot for the agreement between Apple and ECG Fast Walk showed LOA between -13 to +7 BPM, mean difference at -3.21 BPM, and 1.14% of the points were outside the LOA (Figure 2.5). On the other hand, Samsung B&A plot LOA for the Fast Walk was between 15.96 to 64.46 BPM, with a mean difference at 40.21 BPM and, despite the wide LOA, still 1.7 % of the difference points were outside the LOA (Figure 2.8).

Due to the small sample size (5 subjects), the RMSE data was not normally distributed. Therefore, we applied the non-parametric *Kruskal Wallis test* on the RMSE values to examine the WFT's with each other. Fast Walk *Kruskal Wallis test* results showed that the WFT RMSE's are significantly different from each other (Table 2.3). In addition, the paired Wilcoxon Rank Sum tests for the Fast Walk mode showed that the Apple WFT RMSE is different than Polar, Fitbit, and Samsung WFT. (Table 2.4).

In the Sitting mode, Apple had the least mean RMSE between all the watches as the error reached +6.55 BPM (Figure 2.16) and no significant differences in *t-test* results among all subjects (Table 2.2). On the other hand, Samsung had a high mean RMSE in the Sitting modes as the error reached +32.39 BPM, different from the ECG, which means less agreement to the ECG.

Also, in the Sitting mode, Apple's B&A plot showed LOA between -12 to +24 BPM, mean differences were 5.96 BPM, and 1.3% of the points were outside the LOA (Figure 2.9). Samsung's B&A plot showed LOA between -14 to 40 BPM, mean differences at 13.15 BPM, and 0.5% of the points are outside the LOA (Figure 2.12).

Furthermore, studying the RMSE for different exercise modes revealed that the least error with respect to ECG occurred in the slow biking mode. We observed that since the subjects were



in a sitting position while performing the exercise with their arms still on the bike's handlebars that led to fewer body movements compared to the walking modes. However, due to hand bending when subjects hold the bike's handlebars, the bottom surface of the WFTs had less contact to the skin under the wrist area and this introduced error in the measured heart rates by WFTs. The average of the RMSEs between measured heart rates by WFTs and ECG was 8.3 BPM. Moreover, all the WFT's performed the worst in the fast-walk exercise where the mean of the WFT's RMSE with respect to ECG reached 28.8 BPM, this may be due to the body movements being the highest when compared to the other modes.

Tallying the *t-test* results, Apple's *t-test* results showed the best result compared to the other three WFT's. Based on the *t-test* comparison results of each WFT to ECG, the Apple watch showed no significant differences between the watch and ECG in the majority of the exercise modes. For example, by observing all the *t-test* results between WFT'SHR and ECGHR readings, Apple WFT showed no significant difference 18 times, Samsung 10 times, Fitbit 3 times, and Polar 2 times out of 25 times that the *t-test* has been conducted (Appendix A2 Tables 1-5).

Body movements during exercise make heart rate measurement with both ECG and WFT's challenging, as movements can cause motion artifacts on ECG electrodes or WFT's photoplethysmography (PPG) sensor. WFT's accuracy varies with exercise mode and level. WFT's must be fitted well on the wrist to increase readings accuracy. Loose-fitted WFT's could not show accurate reading. WFT's shape design also affects how well the WFT fits different wrists, which will affect heart rate readings accuracy. The Apple watch's bottom design is wider, increasing the contact surface area to the skin surface. However, the Fitbit watch has a limited PPG light sensor area, and a relatively small body, causing the watch to be vulnerable to arm movements, leading to less accuracy.

## **2.5 Conclusion**

The results of assessing the accuracy of heart rate measurements by four wrist-worn fitness tracking devices during slow walking, fast walking, Sitting, slow biking, and fast biking in five healthy subjects were reported in this chapter. The results reveal that the accuracy varies depending on the WFT exercise mode. The Apple watch showed the highest agreement, followed by the Polar watch compared to ECG.

## CHAPTER 3

### **The Designed Wearable Fitness Tracking Ecosystem for Exercise Therapy for Traumatic Brain Injury Patients**

As we presented in Ch.1, physical exercise is a promising method of improving traumatic brain injury (TBI) patient's condition. However, this patient group can have some barriers to perform the prescribed physical exercises. TBI patients can suffer from poor executive function after the injury [33]. Further, TBI patients may need more assistance to manage their schedules and stay in an exercise program [49]. To enable and encourage TBI patients to follow an exercise prescription, one needs to study TBI patients' personal preferences, interests, and concerns. In particular, if one is to deploy mobile communication devices, such as smartphones, one needs to assess the patient's ability to use smartphone applications to manage various aspects of personal health after acquired brain injury (ABI). Our medical team conducted a feasibility study, 85% (17 out of 20 participants) were able to complete the study. However, the compliance to the exercise program was 70% on average, which was lower than aimed 80% as a threshold for achieving maximal exercise benefit. Given the poor executive function after TBI, these participants may require more assistance to manage their schedule and stay in the exercise program. The medical team found that seven broad themes that an ecosystem's phone application should have emerged as:

- (1) We Need to create one app that includes all the needed features for the patient to avoid using multiple apps that could cause user confusion.
- (2) It is essential to have easy-to-use two-way communication with the healthcare team.

- (3) Need to create a simple and easily accessible app; this involved having multiple modalities for the user interface and being easy to navigate.
- (4) Phone and watch applications need to include cognitive tactics, such as cognitive strategies like reminders, notifications, and calendars, to be integrated. Involve the potential for notifications to enhance emotional regulation through biofeedback.
- (5) Application must include care associate assistance. Importance of care partner encouragement as participants discussed methods to incorporate care associate support into mobile health systems.
- (6) Application must be customizable and adaptable for each user. Therefore, the app's content and interface should be customizable for each individual and can modify needs over time.
- (7) Application should provide educational/ provide instructional information. Integrating a resource library or direct link to resources (e.g., websites) was viewed as helpful.

### **3.1 System Design Overview**

As indicated in Ch. 2, our investigations have shown that the Apple watch has higher accuracy of measuring heart rate during exercise than other WFT's that we tested [50]. Hence, our proposed personal mobile trainer (PMT) system design is based on utilizing Apple Watch as our WFT device in conjunction with the Apple iPhone. Many available health monitoring apps for Apple Watch use tools offered by Apple (Apple Inc., Cupertino, CA USA) as an integral part of their design. Apple provides an open-source software development kit (SDK) called CareKit. CareKit allows developers to build apps that leverage a variety of customizable modules rapidly. In addition, since CareKit is open-source software, developers can build upon existing modules and contribute new code [51]. For example, many health care monitoring apps have been developed using CareKit,

which includes cardiac applications [52] and depression treatment [53]. Such apps can incorporate the capabilities of regularly tracking care plans, monitoring patients' progress, and sharing patients' insights and feedback with care teams. Therefore, building an app that can help with TBI patient recovery using CareKit was selected for the design of the PMT system.

An overview block diagram of the designed PMT system structure is presented in Figure 3.10. As shown in Figure 3.10, the PMT system has four major components: 1) the Apple watch; 2) Apple iPhone; 3) a cloud-based server; and 4) the care team portal. A brief description of the function of each of the four major components is as follows.

Apple Watch: The critical component of the system is the Apple Watch. It performs several essential functions of the system: 1) measurement of the heart rate; 2) measurement of exercise duration; 3) measurement of exercise intensity; 4) displaying reminders or encouragement messages to the patient, and 5) transmitting information collected during exercise to a Bluetooth paired Apple iPhone.

In collecting the exercise data, the Apple Watch utilizes many internal sensors such as a photoplethysmography sensor to determine heart rate [54]; an accelerometer to measure the number of steps whenever the subject exercise involves spatial movements [55]; a gyroscope to establish the direction of actions [45], and a barometric altimeter to measure the elevation when patient's exercise involves climbing such climbing stairs [56].

iPhone: The iPhone is a central component of the designed PMT system. It hosts and executes the application software to communicate with the Apple Watch. Further, it provides an additional interface for communication with the patient. The iPhone also communicates with the cloud-based server of the PMT system, transmitting patient's exercise information and receiving updates to the prescribed exercise regimen.

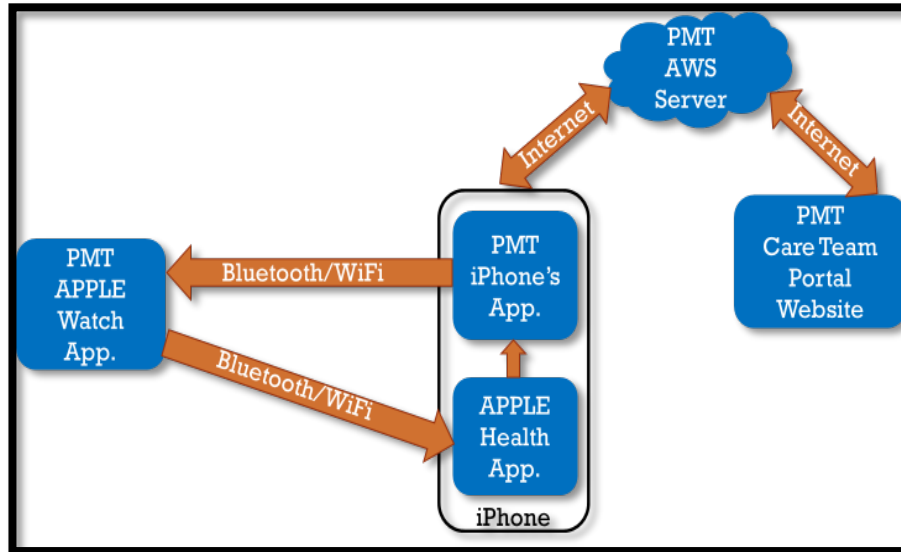


Figure 3.14: PMT system block diagram overview

Cloud-based Server: Incorporating a cloud-based server in the PMT hardware design structure allows a convenient and highly flexible means of accessing patient's exercise activities at any place and point in time that Internet access is available. The ubiquitous availability of the Internet and mobile devices makes this quite feasible [57]. In addition, the server chosen for this purpose is capable of enforcing the Health Insurance Portability and Accountability Act (HIPAA) to receive, store, and transmit data between the patient's application on the Apple Watch, Apple iPhone, and the care team portal (Figure 3.10) [57].

For this purpose, we used Amazon Web Services (AWS) (Amazon Inc., Seattle, Washington) to host The PMT server. AWS is an on-demand cloud computing platform and APIs to individuals, companies, and governments on a metered pay-as-you-go basis [58].

Care Team Portal Website: This portal is for clinicians prescribing and administering the exercise regimen to TBI patients. It enables them to monitor the effects of the prescribed exercise, adjust the prescribed regimen as needed, and communicate with the patients by pop-up messages.

### 3.2 PMT System Function Design

We designed the ensemble of the PMT application programs operating by the system components shown in Figure 3.10 to provide the following functions:

- 1) Aid the patient in remembering to perform the prescribed exercises at the specified times daily
- 2) Offer encouragement and feedback to the patient on the level of exercise achievements
- 3) Obtain quantitative data (e.g., time and date of doing the exercises, heart rate, count of steps taken, and exercise duration) from the Apple Watch
- 4) Record patient's subjective assessment of their condition (e.g., exercise rate of excretion)
- 5) Transmit and make available subjective and objective measures of patient performance (i.e., items 3 and 4 above) to the care team professionals at all times

iPhone Apps: Apple CareKit framework in iPhone is organized based on the user interface modules and data types in the Care Plan Store and Contacts. The Care Plan Store is a persistent database that holds the data that describes the care plan and the user interface (UI) modules. It displays or modifies the data as depicted in Figure 3.11. [55].

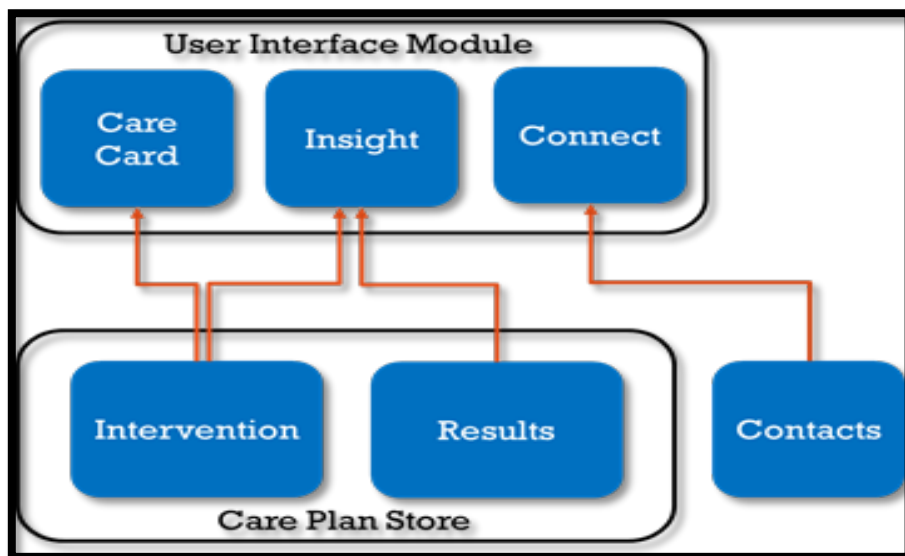


Figure 3.15: Structure of the iPhone app [55]

Specifically, we only utilized the Care Card, Insights, and Connect modules available from the user interface modules from the CareKit framework (Figure 3.11). The Care Card module presents and manages the tasks that the user is expected to perform as part of their treatment. Such as exercise types, frequency, and description. To store the information related to the Care Card function, the Apple Care Plan Store is used to store the data displayed by the Care Card locally. CareKit automatically loads the store's data as soon as the store is created and automatically saves changes. In addition, this part of the framework handles the data transmission and receiving to/from the PMT system server.

The Insights module displays charts and widgets that show the relationship between a user's treatment and their progress [55]. The Insights module can also include tips, alerts, notifications and reminders, and thresholds that help patients stay on track with their treatment plan goals. For example, it will issue reminders for performing the prescribed daily exercise training program simultaneously on both the Apple Watch and iPhone to increase the patient's likelihood of receiving such reminders on time.

The Connect module helps the user communicate with care team members [55]. This part of the app will be utilized to store care team contact information and integrate communication features to interact with the software residing on the Care Team Portal (Figure 3.10).

The iPhone application programmed to send and receive the following data structure and modules to and from the server (Table 3.1):

Patient Model: Has patient information such as name, detailed information, image

Contact Model: It has contact type as (care team, personal), name, relation (physician roll, etc.), contact items (phone number, SMS, email for the point of contact on the care team) and allows for photos to be included.



Activity Model: Includes multiple fields, some of which are:

- 1) ID number that is unique for every activity
- 2) Activity Type reflects whether this an intervention or assessment, and almost all the activities are of intervention type; that is, they require the patient to do an activity
- 3) Location Type can be either indoor, outdoor, or unknown
- 4) Activity instructions: They describe what type of intervention is needed and are read-only
- 5) Target heart rate: Receives the target heart rate value set by the clinician and transmitted from the Care Team Portal

Schedule Model: Controls the temporal aspect of the system functions. It includes several fields such as

- 1) Start date: Activity start date as prescribed by the clinician
- 2) End date: Activity end date as prescribed by the clinician
- 3) Type (i.e., periodicity): It holds whether the exercise is to be performed on a weekly or daily basis
- 4) Activity frequency: Specifies the number of times that the exercise is performed during each period. For instance, for a week that starts on Sunday, a value array of the form [0,3,0,3,0,0,0] means three repetitions on Monday and Wednesday and no activity on other days of the week. In the daily schedule type, the array contains one number only representing frequency per day.

Event Model: Contains the following fields.

- 1) Number of Days: It counts the number of days since the start of an event (i.e., exercise activity)

2) Occurrence Index of Day: The index of an event on a particular date. For example, if an activity has three occurrences in a day, then it would be represented by three Care Plan Event objects with index 0, 1, 2, respectively

3) State: The state of this event (0 Initial / 1 Not Completed / 2 Completed).

Attempt Model: (i.e., exercise outcome model): This structure contains the relevant fields that hold the outcomes of the exercise attempts. Some of the areas are:

1) Heart Rates: The heart rates recorded during an exercise session stored in an array with variable length, depending on the duration of the exercise and the intensity of the activity. Apple Watch sets the governing rules for the number of entries to the array, and they are not under the control of the developer or the user.

2) Number of Steps: This field holds the number of steps taken during the session

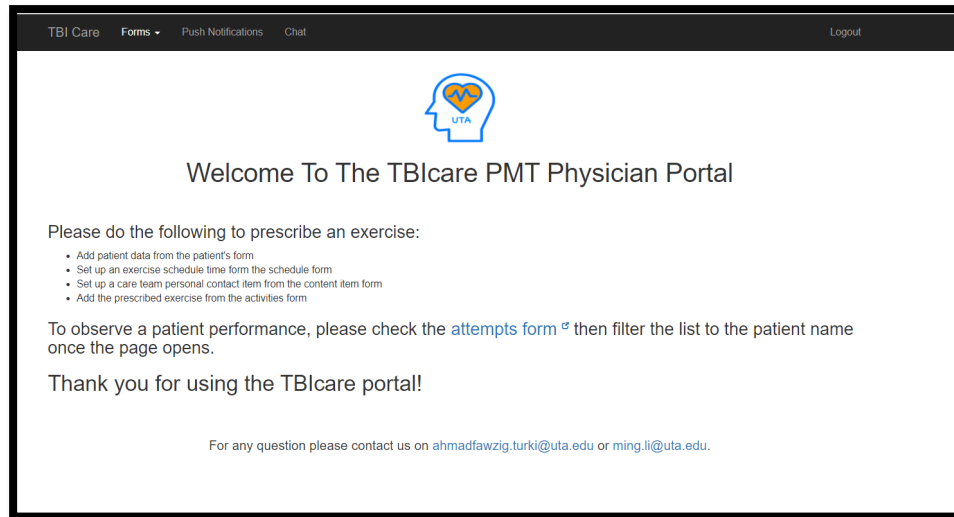
3) Distance value: This field holds the distance value with the units set for feet

4) Energy Expenditure: This field holds the energy expenditure value computed by Apple's proprietary algorithm.

Apple Watch Apps: We developed the application residing on the Apple Watch to collect all the health data of interest that the Apple Watch sensors can capture. The apps synchronize and fetch all the measured health data to the Apple Health module, which resides on the Apple Watch. Apple does not provide for third-party iPhone applications to receive the Apple Watch health data independently. The PMT system iPhone apps, in turn, fetch all the measured data by the Apple Watch from its Apple Health app.

Care Team Portal: We deployed a collection of functions on the Care Team Portal. The portal organizes the received information in a user-friendly format for presentation to the clinicians. Second, it allows the clinicians to customize messages of encouragement and feedback for each

patient based on their adherence to the prescribed exercise regimen. Finally, the portal provides the clinicians the freedom to modify the parameters of the prescribed exercise regimen. Such parameters of the prescribed exercise are the exercise's type, frequency, duration, and intensity.



*Figure 3.16: Clinician Portal main page*

PMT Server: As we mentioned before, we utilized Amazon Web Services to host the PMT. We built the server using the relational database MYSQL. Structured Query Language (SQL) is used by MySQL that is an easily accessible open-source Relational Database Management System (RDBMS) [57].

Table 3.6: PMT system's models and their respective interconnections

Patient Model	Contact Model	Activity Model	Schedule Model	Event Model	Attempt Model
Name	Type (care team, personal)	ID (to identify one activity from another)	Start date	Number of days since the start	Heart rates
Detailed info	Name	Group ID (to group similar activity in the app)	End date	Occurrence index of the day	Number of Steps
Color for Title's Circle	Relation	Type (intervention, assessment, random)	Type (weekly, daily)	State	Distance value
Image URL	Contact item type (phone, SMS, email)	Location type (unknown, indoor, outdoor)	Frequency	Link to activity model <->*	Energy Expenditure
Care Team Contacts	Contact item value	Title	Skips		Rate of excretion
Link to Activity Model <->*	Contact Color	Instruction			Link to event model <->*
Link to Contact Model <->*	Contact image URL	Image URL			
		Font Color			
		Result resettable			
		Schedule (follow schedule model)			
		Optional (give the option if it is an optional exercise)			
		Target heart rate			
		Target Steps			
		Target distance			
		Target Energy			
		Link to Schedule Model <->			

<->\*: Linkage to another model

### 3.3 iPhone Application and Apple Watch Application Performance

iPhone app login page: Each user is provided with a login page. We designed the page to safeguard patient privacy and the integrity of collected data. A view of the login page is shown in (Figure 3.13).

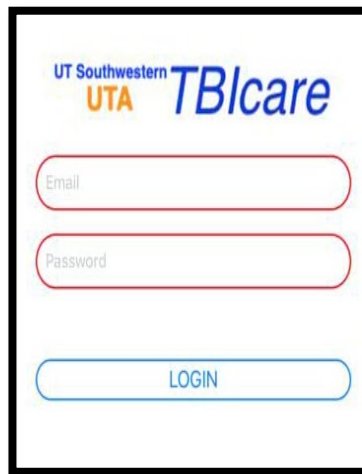


Figure 3.17: iPhone app. login page

Care Contents: This page shows the type of prescribed exercises for a specific day with the associated instruction, explaining some of the activity and frequency of prescribed exercise by displaying the corresponding number of circles as shown in the sample output in (Figure 3.14)

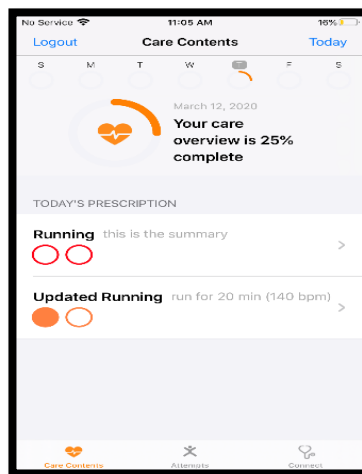


Figure 3.18: iPhone app. Care Contents page sample

Gamification Part and Attempt History Page: The phone application's second page contains the gamification part that shows the exercise percentage completion and collected badges throughout

the treatment. The percentage completion depends on the total time spent exercising out of the total required workouts target time. The patient will gain a bronze badge if they reach 1-49%, a silver badge if they earn more than 50%, and a gold badge if they achieve 100% before the end of the week. (Figure 3.15)

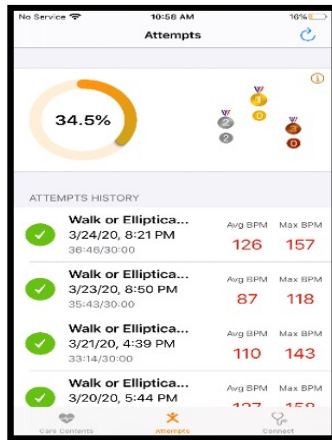


Figure 3.19: iPhone App Gamification Part and Attempt History Page

iPhone app connect page: The connects page shows care team contact information (Figure 3.16).

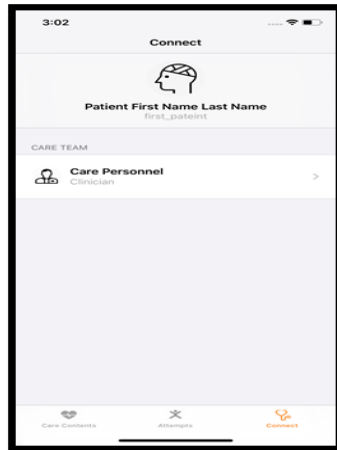


Figure 3.20: iPhone Connect page

iPhone app Care Personnel page: Displays the information about the care person assigned to the patient (Figure 3.17).

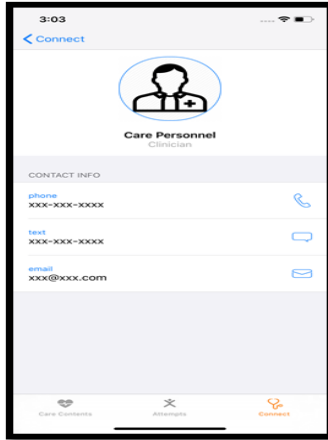


Figure 3.21: iPhone Care Personnel page

Samples of the screens of the Apple Watch app are presented below.

Apple Watch applications list page: TBIcare app icon will be displayed on the Apple watch applications list page, as shown in (Figure 3.18).

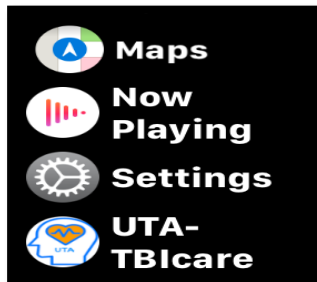


Figure 3.22: Apple Watch app icon (UTA TBIcare)

Apple Watch prescription page: Once the user opens the PMT's watch app, the prescribed exercises list for the specific day will appear (Figure 3.19).

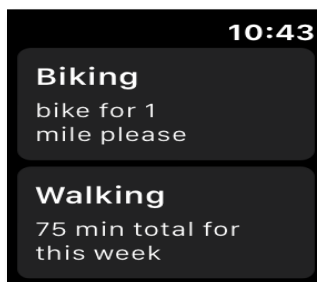
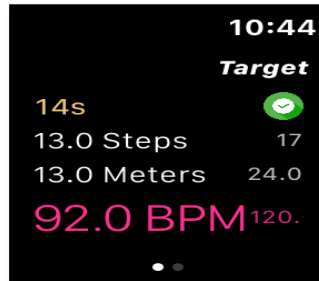


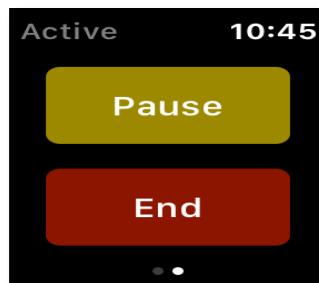
Figure 3.23: Apple Watch app prescription page

Apple Watch measurement page: Once the user chooses a prescribed exercise from the list, the measurement page will appear and show time elapsed since activity started, number of steps, distance, and current heart rate value. Each measurement will have a target value that the care team assigns, which will appear next to it, and a green mark would arise if the target value were achieved (Figure 3.20).



*Figure 3.24: Apple Watch app measurement page, displaying user's progress with the prescribed exercise.*

Apple Watch app measurement ending page: If the user wants to pause or end an exercise session, they will need to scroll on the watch's screen to the right and choose to pause/complete the exercise (Figure 3.21).



*Figure 3.25: Apple Watch app measurement ending page*

The Apple Watch reminder page: Shown in Figure 3.22, reminds the patient to fill out the iPhone app survey form pages shown in Figures 3.23 and 3.24.



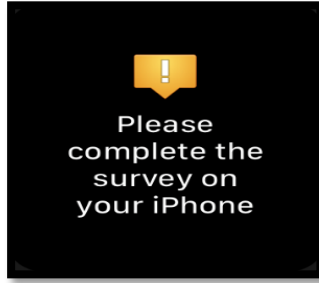


Figure 3.26: Apple Watch app showing a reminder to the user to complete the surveys on iPhone after ending an exercise

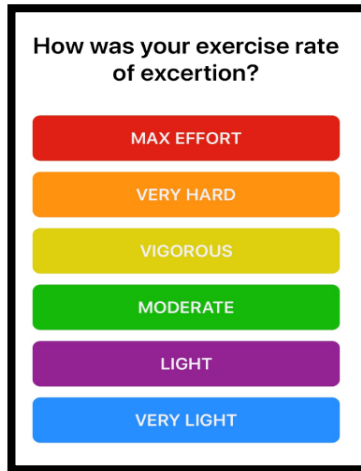


Figure 3.27: iPhone app showing the Rate of Perceived Exertion (RPE) survey regarding the completed exercise session

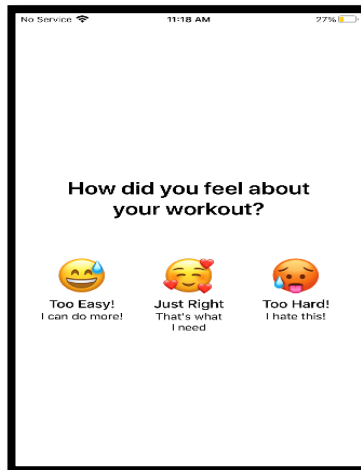


Figure 3.28: iPhone app exercise displaying the perceived level of exercise challenge of the completed prescribe exercise.

Completed Exercise page: If a user has performed all the required frequency of a prescribed exercise, the exercise icon on the watch app list would be shaded and blocked (Figure 3.25).

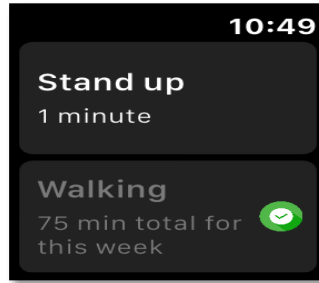


Figure 3.29: Completed exercise marked by green mark on the TBicare Apple watch app

Apple Watch ending exercise reminder: If the user forgot to turn off the exercise after reaching the target time, a notification would appear on the watch app to remind the user to turn off the activity (Figure 3.26).

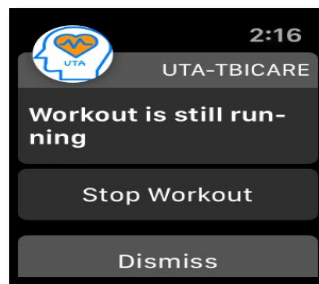


Figure 3.30: Apple Watch showing a reminder about not to user forgot to stop the workout in the app

iPhone survey questions pages: Once a user finishes a prescribed exercise on the PMT watch application, a survey of the Rate of Perceived Exertion level questionnaire will appear on the iPhone application (Figure 3.23). The system will transmit the user's response to the cloud along with the performed exercise data. Further, the user will be asked to answer the perceived level of workout difficulty question on the following page of the app, as shown in Figure 3.24.

Encouragement messages: The app will send automatic encouragement messages from the care team personnel to patients. (Figure 3.27 and Figure 3.28).

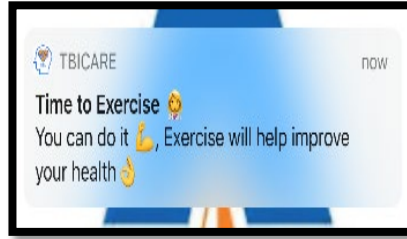


Figure 3.31: Partial view of the encouragement message that appears on iPhone screen

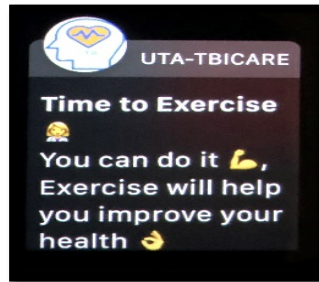


Figure 3.32: Encouragement message appear on Apple Watch screen

Several advantages are associated with the proposed design, such as the simplicity of the designed system on the Apple iPhone and Apple Watch for the user interface. In addition, to the simplicity is the accuracy of the Apple Watch in measuring heart rate, as our previous study showed the accuracy of the Apple devices compared to an accurate ECG [50]. Also, the availability of both the iPhone and Apple Watch in the U.S. market provides an advantage to the PMT system. The design aims to provide ease of use by people of various backgrounds, including those with some cognitive challenges, accommodated by having simple controls and displays. Other advantages of the PMT include providing encouragement and reminders to the participants and the ability for the care team to review the exercise data in real-time and adjust the exercise prescription in a timely fashion.

The use of the Apple Carekit framework gives an advantage of utilizing a tested, maintained, and easy to upgrade application programmed interface. In addition, the framework provides the possibility of a dynamic care plan, tracking user's performance, and connect users to the care team. The framework also offers appealing design elements that facilitate user engagement. The framework is written entirely in the Swift programming language [59]. The Swift programming

language is a general-purpose, multi-paradigm, compiled programming language developed by Apple Inc. and the open-source community.

That allows integrating the Swift programming powerful language features into the PMT design. Also, the integration of Apple Healthkit as the central repository for health and fitness data in IOS and watchOS ensures health data privacy in the system. Furthermore, having the PMT server hosted by the Amazon Rational Database Service (RDS) enhances data security as it meets HIPPA compliance requirements. Also, the RDS allows for straightforward setup, operation, and scaling. It delivers cost-efficient and resizable capacity while automating time-consuming administration tasks such as hardware provisioning, database setup, patching, and backups. Also, using the SQL used by MySQL enhances the usability of the accessible open-source Relational Database Management System (RDBMS). Furthermore, the designed PMT platform may apply to other chronic disorders such as diabetes, asthma, chronic obstructive pulmonary sleep disease, dementia, respiratory disease, and cardiovascular disease. The feedback features of the system, such as the Borg Scale rating, can be used to improve the design and therapy for a variety of patient groups.

There are some limitations to the proposed design, such as the requirement of specific hardware (i.e., Apple iPhone and Apple Watch); as well as the need for the patient to have hands-on interaction with the phone and watch, which may prove to be a barrier for some physically or cognitively impaired individuals. Also, the necessity of having internet connectivity for data transfers to the cloud can limit the system's usability. Nonetheless, the designed PMT system demonstrated how wrist-worn fitness tracking devices might play an influential role in engaging the person with TBI in successful exercise participation through remotely prescribed physical exercise with bidirectional communication between the study participant and the study clinician.

This system will allow the collection of physiological data and patient self-report of perceived exertion and challenge. Additionally, the system provides communication channels to deliver encouragement, reminders, or exercise prescription updates. Furthermore, the designed PMT system provides an alternate delivery model that can be utilized to monitor and encourage persons with TBI who cannot attend TBI rehabilitation centers or exercise programs conducted at facilities other than the patient's residence. Finally, the real-time visual response of the software to the patient software provides rapid real-time information to the patient and clinician.

## CHAPTER 4

### Methods Used to Measure the Effect of Exercise

#### 4.1 Physiological Effects of Exercise

Multiple retrospective studies have stated that regular physical activity (PA) is correlated with a lower probability of cardiovascular (CV) mortality and morbidity [59] [60]. Furthermore, prospective studies have shown that implementing a physically active lifestyle may postpone all-cause mortality and prolong longevity [61]. Furthermore, exercise-based rehabilitation is related to a decrease in CV mortality and fewer hospital admissions [62]. In particular, it decreases the risk for CV mortality by 42–44%, compared with persistently unfit men [63] [64]. However, the relationship between PA and CV risk shows a curvilinear dose-response outline [65] with growing but lessening returns at higher activity levels [66]. Until recently, the basis for the promotion of exercise and methods of prescribing it were founded on the belief that exercise produced its advantages by "secondary" effects. Exercise effectiveness was considered to be actualized by its capacity to adjust CV risk factors such as blood pressure (BP), lipids, insulin resistance, smoking, and obesity [67]. Indeed, studies connecting exercise to alterations in CV risk factors report significant enhancement in individual CV risk factors [68] [69].

At a minimum, there are two ways that blood pressure can affect vascular cells. First, cell culture experiments have demonstrated that the exposure of endothelial cells to acute elevated pressure affects their growth rate, where pressures of 20–100 mmHg increase growth compared with no pressure [70]. Second, the pressure can expand arteries, thus stretching vascular cells in the wall [71]. Since arteries are compliant, changes in pressure accordingly produce

circumferential stress (i.e., strain) [71]. Since the nature of arterial blood pressure is pulsatile, this circumferential strain leads to in cyclic circumferential strain [71]. Increase expression of some beneficial endothelial cells genes can be produced by circumferential wall stress [68]. That is, there is a crucial role that interactions of arterial pressure and fluid shear stress play in arterial vascular health by producing a healthy arterial endothelial phenotype [68].

Physiologically, there is a direct relationship between regular aerobic exercise and higher oxygen and glucose consumption, leading to increased energy expenditure. Higher glucose consumption is associated with energy expenditure related to increased energy metabolism and insulin sensitivity and decreasing resistance to leptin and insulin [72]. In insulin resistance, the ability of cells to respond to the action of insulin in transporting glucose into tissues is diminished; consequently, the resistant individual begins secreting above-normal amounts of insulin to obtain a quantitatively normal response [73]. Thus, if a person has insulin resistance, the person will have low insulin sensitivity. Conversely, if a person is sensitive to insulin, the person will have low insulin resistance. Therefore, while insulin resistance damages a person's health, insulin sensitivity is beneficial [73].

#### **4.2 Measurement of energy expenditure**

An essential element of the inefficacy of an exercise regime is the level of body energy expenditure. To define energy expenditure (EE), metabolic equivalent (MET) exercise intensity needs to be determined [75]. Haskell et al. provide a table using the MET level to categorize everyday physical activities as light, moderate or vigorous in intensity [76]. MET is an objective quantity of the ratio of the rate at which an individual expends energy relative to that person's body mass while performing some specific physical activity compared to a reference (Table 4.1). One MET is described as the quantity of oxygen consumed per kilogram of a person's body weight

per min while sitting at rest. Thus, one MET is the energy a person spends sitting at rest. It equals 3.5 ml of oxygen consumed per kilogram of body weight per minute [76]. The cells in the body muscles utilize oxygen to help create the energy needed to move the muscles. For example, at rest, the body will use about 254 milliliters of oxygen per minute if the body weighs 160 pounds (72.5 kg) ( $72.5 \text{ kg} \times 3.5 \text{ mL} = 253.75 \text{ mL of O}_2$ ) [77].

Table 4.7: MET values for different types of activities [83]

Physical activity	MET
<b>Light intensity activities</b>	
	<b>&lt; 3</b>
sleeping	0.9
watching television	1.0
writing, desk work, typing	1.8
walking, 1.7 mph (2.7 km/h), level ground, strolling, very slow	2.3
walking, 2.5 mph (4 km/h)	2.9
<b>Moderate intensity activities</b>	
	<b>3 to 6</b>
bicycling, stationary, 50 watts, very light effort	3.0
walking 3.0 mph (4.8 km/h)	3.3
calisthenics, home exercise, light or moderate effort, general	3.5
walking 3.4 mph (5.5 km/h)	3.6
bicycling, <10 mph (16 km/h), leisure, to work or for pleasure	4.0
bicycling, stationary, 100 watts, light effort	5.5
<b>Vigorous intensity activities</b>	
	<b>&gt; 6</b>
jogging, general	7.0
calisthenics (e.g. pushups, situps, pullups, jumping jacks), heavy, vigorous effort	8.0
running jogging, in place	8.0
rope jumping	10.0

### Calculate Energy Expenditure Based on MET and Physical Activity

Calculating metabolic equivalents is known as MET that is used to estimate the body's energy expenditure. MET can be utilized to describe the intensity of an exercise or activity. The metabolic equivalent task represents a straightforward, practical, and quickly understood technique for expressing the energy cost of physical activities as a multiple of the resting metabolic rate [77]. Applying the MET concept can offer an appropriate method to describe an individual's functional capacity or exercise tolerance [77]. For instance, one MET is the energy expended by sitting at



rest (resting or basal metabolic rate) [77]. In an activity with a 4 MET value, the body will exert four times more energy than sitting still [77].

Energy expenditure values units are expressed in kcal/kg, kcal/min, kcal/h, or kcalx24/h. Defining the kcal expended during resting, i.e., resting metabolic rate (RMR), and multiplying that value by MET values found to be the most accurate method of determining energy expenditure RMR, and it is close to 1 kcal/(kg.hr). It is feasible to approximate a kcal energy expended by a person during an activity by multiplying the body weight in kg by the MET value and duration of the activity. For instance, bicycling at a 4 MET value expends 4 kcal/(kg.h). Bicycling for 40 min by a 60-kg individual expands the following:  $(4 \text{ METs} \times 60 \text{ kg}) \times (40 \text{ min}/60 \text{ min}) = 160 \text{ kcal}$  [78]. It is noteworthy that *calorie* (gram calorie) is a unit of energy in a metric system needed to heat one gram of water by one Celsius degree [79]. *Kilocalorie* (food calorie) (Cal, Calorie, or kcal) is known as the energy needed to heat one kilogram of water by one Celsius degree [79]. If the word calorie is capitalized as *Calorie* is generally means Kilocalorie and also it means that it refers to the food calorie [79]. In several countries, labels of industrialized food products are obligated to indicate the nutritional energy value (kilo or capital C) calories per serving or weight [79]. For instance in the United States the labels of industrialized food have the calories unit with capitalized C which mean kilocalorie.

However, energy expenditure may vary from person to person based on several factors, including body mass, body consumption, body fat percentage, gender, age, fitness and activity level, hormonal status, ethnicity and genetics, and environmental influences. For example, a young athlete who exercises daily won't need to expend the same amount of energy during a brisk walk as an older and sedentary person [77].

### 4.3 Activity Level

An exercise prescription program needs to include frequency, intensity, duration, and specific exercise mode. To explore definitions of adherence to exercise classes, Vissek et al. [80] discussed four measures for adherence to structured exercise in trials: (1) completion, (2) attendance (the number of sessions attended over the follow-up period), (3) duration adherence (how long they exercised during each session) and (4) intensity adherence (the physical exertion level).

Indeed, these measures are distinct. For example, one could attend every exercise session for the entire length of the study but not achieve either the intensity or the duration prescription on any or every occasion. Because adherence to the exercise prescription is such an essential factor in the integrity of any intervention study, the knowledge of its determinants will maximize the validity of the scientific findings.

### 4.4 Maximum Heart rate Equation

An adult maximum heart rate can be estimated by Fox and Haskell maximum heart rate equation [81]:

$$\text{Maximum Heart Rate} = 220 - \text{subject age}$$

the formula and associated concepts are contained in most certification exams within sports medicine, exercise physiology, and fitness. A study established by Sporis et al. [82] examined the validity and reliability of different equations for predicting maximal heart rate value on 509 members of military personal, all males (age  $29.1 \pm 5.5$  years, height  $180.1 \pm 6.6$  cm). The graded exercise test (GTX) was used to test the maximum heart rate. The authors found that the Fox and Haskell equation is one of the recommended formulas to predicts maximum heart rate. The

examination revealed a correlation between the  $HR_{max}$  values determined during (GTX) and  $(HR_{max}=220 - \text{age})$  to be around  $(r = 0.41)$ .

#### 4.5 Exertion Level

The BORG Rate of Perceived Exertion Scale (RPE) (Figure 4.1) utilizes a subjective numeric rating (range 1-10) of exercise intensity according to how a subject feels or perceives the level of difficulty in the exercise [83].

RPE SCALE	RATE OF PERCEIVED EXERTION
<b>10</b> /	<b>MAX EFFORT ACTIVITY</b> Feels almost impossible to keep going. Completely out of breath, unable to talk. Cannot maintain for more than a very short time
<b>9</b> /	<b>VERY HARD ACTIVITY</b> Very difficult to maintain exercise intensity. Can barely breathe and speak only a few words
<b>7-8</b> /	<b>VIGOROUS ACTIVITY</b> Borderline uncomfortable. Short of breath, can speak a sentence
<b>4-6</b> /	<b>MODERATE ACTIVITY</b> Breathing heavily, can hold a short conversation. Still somewhat comfortable, but becoming noticeably more challenging
<b>2-3</b> /	<b>LIGHT ACTIVITY</b> Feels like you can maintain for hours. Easy to breathe and carry a conversation
<b>1</b> /	<b>VERY LIGHT ACTIVITY</b> Hardly any exertion, but more than sleeping, watching TV, etc

Figure 4.33:Rate of Perceived Exertion Scale Table [84]

For example, RPE of 7-8 (exercise that feels “somewhat hard”) coincides with an exercise heart rate of about 70% of the maximum heart rate for a subject [85].

In 1962 Borg presented the novel development of quantifying RPE. He established perceived exertion’s 21-point categorical rating scale, with verbal expressions to match with different levels along the scale. The scale was founded upon a correlation between heart rate and perceived exertion. By 1970 a modified 15-point scale was established to raise the linearity between the ratings and workloads [85]. The 1970’s scale has a lowered mid-point and marginally changed verbal expressions. In 1982 Borg established the last version of his scale with a 10-point category scale with ratio properties to include decimals in RPE determination. The 10 points scale has been

proven to be beneficial in anaerobic activity due to the verbal expressions fixed so that the semantic intensity raises according to a power function.

By the 1970s, perceived exertion became very widespread in research. Borg created high correlations between heart rate and RPE that were around (0.77-0.90). Nevertheless, there was some suspicion that this relationship might be owing to the experimental protocol or technique artifact [86]. That inspired Stamford to conduct an experiment using the 15-point RPE scale to test the reliability and validity of the perceptual responses of 14 sedentary females. Each subject participated in five tests at the same time each day. Two tests were executed on a bicycle ergometer, two tests on a treadmill, and one stepping test. Heart rate and perceived exertion were recorded at random times during each test. Subjects were unaware of the details of the trial in respect to length and intensity. 10 Results indicated that perceptual ratings of exertion were “Highly reproducible under various experimental circumstances” [86].

Reliability of effort related to fluctuations in workloads was demonstrated in this study. A significant finding in this study was the high reliability of terminal ratings of perceived exertion of 0.90. This finding suggests that the RPE was just as reliable as heart rate in the final minute of exercise. According to Stamford, the RPE scale is supported “As a valid and reliable instrument for the assessment of the degree of encountered stress during work effort” [86].

#### **4.6 Measurement of Heart rate**

Heart rate is universally defined as the number of times a person's heartbeats per minute [87]. The average heart rate range for adults has often specified as 60 to 100 beats per minute. However, resting heart rate varies significantly from person to person. TBI patient's resting heart rate range is reported to be between 60-80 beats per minute [88]. Heart rate indicates the amount of effort and the body's physiological adaptation [89]. Therefore, heart rate monitoring is an

effective means for cardiovascular fitness assessment in training programs [90]. A sedentary person's heart rate can increase up to 150 beats per minute (BPM) during moderate physical activity as jogging for less than 10 minutes, while a fit person typically might reach only 100 for the period of moderate exercise [91]. Hence, using heart rate as a measure of the efficacy of exercise therapy for enhancing cardiovascular fitness is used for the present study, as it is corroborated [32] by previous investigations [92] [93] [94].

In addition to heart rate measurement, we can utilize heart rate variability to study exercise efficacy. Heart rate variability (HRV) is the oscillation in the elapsed time interval between adjacent heartbeats [95]. HRV indexes neurocardiac function and is produced by heart-brain interaction in conjunction with the dynamic nonlinear autonomic nervous system (ANS) processes [95]. HRV reflects the regulation of autonomic balance, blood pressure (BP), gas exchange, gut, heart, and vascular tone is an effective noninvasive means of identifying ANS imbalances [95]. Qualitatively, when the variation in the elapsed time interval between successive heartbeats is low (the intervals between heartbeats are restively constant), a person's body system tends to be in a fight-or-flight mode. Conversely, when the variation of the temporal distance between consecutive beats is high, a person's body tends to be in a relaxed state [96]. In other words, the healthier the ANS, the higher variability in the duration of the inter-beat intervals is associated with more rapid alteration of the heart rate to cope with the emotional or psychological stimulation and showing more resilience and flexibility [97]. Over the past few decades, researchers have also demonstrated a relationship between low HRV and worsening depression or anxiety [98] [99] [100] [101]. The high-frequency band (0.15–0.40 Hz) within the HRV frequency spectrum relates to parasympathetic cardiac action [95]. The successful adaptation of the person's heart rate to changing environmental demands is influenced by the parasympathetic nervous system [102] [103]

[99] [104]. A reduction in vagal control could indicate a difficulty in responding flexibly to varying demands (i.e., decreased high-frequency power of HRV). It reflects decreasing the range of possible cognitive and emotional options and thus limiting the individuals' ability to generate appropriate responses and inhibit inappropriate ones [105].

Three time-domain measures of HRV were assessed by quantifying the variations in inter-beat intervals (IBI). IBI is defined as the elapsed time between consecutive heartbeats [95]. Specifically, the mean and standard deviations (Eqs. 1 & 2) of the IBI were computed over a specified time epoch. In our study, we used a 5-min interval.

$$\overline{IBI} = \frac{\sum_{i=1}^N IBI_i}{N} \quad (1)$$

where  $IBI_i$  is the  $i^{\text{th}}$ , inter-beat interval  $\overline{IBI}$  is the mean of recorded IBI's,  $\sum_{i=1}^N IBI_i$  is the sum of the IBI's, and  $N$  is the number of IBI values.

$$\sigma_{IBI} = \sqrt{\frac{\sum_{i=1}^N |IBI_i - \overline{IBI}|^2}{N-1}} \quad (2)$$

where  $\sigma_{IBI}$  is the standard deviation of IBI's over the recording interval. In addition to the mean and standard deviations of IBI, the coefficient of variation of IBI was also computed as:

$$CV_{IBI} = \frac{\sigma_{IBI}}{\overline{IBI}} \quad (3)$$

There are several frequency-domain measures of HRV that have been proposed in the literature [95]. HRV frequency-domain estimates can be calculated by obtaining a power spectral density (PSD) of the IBI measurements. The PSD can be obtained by applying the Fast Fourier Transform on the IBI measurements. Once the PSD is obtained, the HRV frequency measures can be calculated by investigating several frequency ranges in the PSD. Such frequency bands are:

- Ultra-Low Frequency (ULF) that has a frequency range of  $\leq 0.003$  Hz

- Very-Low-Frequency (**VLF**) that in the field of 0.0033–0.04 Hz
- Low Frequency (**LF**) band that is in the range of 0.04–0.15 Hz
- High Frequency (**HF**) is in the range of 0.15-0.4 Hz.

Another HRV frequency metric that can be considered is the ratio of LF to HF power (**LF/HF** ratio). This ratio could estimate the activity between the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) within regulated conditions [106]

The HRV measurements in the frequency domain can be expressed in absolute or relative power [106]. Absolute power is computed as  $\text{ms}^2/\text{Hz}$  [105]. Relative power is approximated as the percentage of total HRV power or in normal units (nu), which is obtained by dividing the absolute power for a specific frequency band by summing LF and HF band's absolute powers [101]. This computation method allows to evaluate and compares the frequency-domain HRV metrics for patients despite possible differences in specific band powers and total power within [106].

As ULF requires HRV recording for at least 24 hours, in this study, we focused on four frequency-domain measures of HRV that can be calculated from five-minute heart rate recording (VLF, LF, HF, and LF/HF).

### ***VLF Band***

The very-low-frequency (**VLF**) reflects the oscillations in IBI, with periods between 25 and 300 s [95]. The heart's intrinsic nervous system affects the VLF rhythm, and the SNS affects the amplitude and frequency of its oscillations [95]. Very low-frequency power might also be produced by physical activity [107], thermoregulatory, renin-angiotensin, and endothelial effects on the heart [108] [109]. In addition, VLF power might be affected by PNS activity; for instance, blocking parasympathetic activity could eliminate the VLF power [110]. Conversely, sympathetic

obstruction does not influence VLF power, and VLF action is observed in people with tetraplegia, whose SNS innervation of the heart and lungs is interrupted [111] [112].

Armour [113] and Kember et al. mentioned [114] [115] that the VLF rhythm appears to be produced by stimulating afferent sensory neurons in the heart. That will trigger numerous levels of feedback and feed-forward loops in the heart's intrinsic cardiac nervous system and between the heart, the extrinsic cardiac ganglia, and the spinal column [116]. Therefore, this suggestion recommends that the heart intrinsically produces the VLF rhythm and efferent SNS activity as the band amplitude and frequency control stress reactions and physical activity [116].

### ***Low-Frequency Band***

The low frequency (LF) band is in the range of 0.04–0.15 Hz; this range contains patterns with periods between 7 and 25 s [95]. Also, this frequency band used to be called the baroreceptor range since it mostly echoes baroreceptor activity throughout resting conditions [117]. Different physiological activities might generate LF power. PNS and SNS activities together could generate the LF power [118]. Moreover, Blood pressure regulation *through* baroreceptors could also cause an increase in LF power band [118] [119] [120] [121]. However, PNS activities have a higher effect on the LF band [122], and the baroreflex activity alone could generate the LF band [123]. The SNS does not generate rhythms with more than 0.1 Hz frequency, although the parasympathetic system found to affect heart rhythms down to 0.05 Hz (20 s beat) [95]. In resting conditions, the LF band echoes baroreflex activity and not cardiac sympathetic innervation [124].

Throughout epochs of slow respiration rates, vagal activity can rapidly produce low-frequency oscillations in the heart rhythms that cross into the LF band [125] [126]. Hence, respiratory-related efferent vagally-mediated effects primarily exist in the LF band when



respiration rates are lower 8.5 bpm or 7 s periods [126] [127] or when one sighs or takes a deep breath.

### ***HF Band***

High frequency (**HF**) or respiratory band (0.15–0.40 Hz) is conventionally recorded over a minimum of 1 min interval [95]. The HF frequency can be affected by breathing rate from 9 to 24 bpm [95].

The HF band echoes parasympathetic activity and is named the respiratory band because it matches the HR variations associated with the respiratory cycle [128]. These phasic HR changes are recognized as respiratory sinus arrhythmia (RSA) and may not be a clean index of cardiac vagal control [128]. Heart rate accelerates throughout inspiration and slows during expiration [124]. During inhalation, the cardiovascular center prevents vagal outflow resulting in increasing the HR [124]. Conversely, through exhalation, it reinstates vagal flow, causing the HR's deceleration through the discharge of acetylcholine [129]. Total vagal obstruction nearly eliminates HF oscillations and decreases power in the LF range [124]. HF band power may rise at night and decline throughout the day [117]. Lower HF power is correlated with stress, panic, anxiety, or worry [116]. The modulation of vagal tone aids preserves the dynamic autonomic regulation, which is essential for cardiovascular health [130]. Lacking vagal inhibition is involved in increased morbidity [130].

### ***LF/HF Ratio***

The LF/HF ratio assumes that the SNS may produce LF power while the PNS has HF power [95]. In this model, a low LF/HF ratio echoes parasympathetic dominance [124]. This is observed when we preserve energy and involve in tend-and-befriend behaviors [95]. Conversely,

a high LF/HF ratio reveals sympathetic power that appears when we apply in fight-or-flight actions or parasympathetic withdrawal [95].

#### **4.7 Study Population**

We tested the PMT system on 9 participants (7 males, 2 females, aged  $55.2 \pm 7.5$  years, BMI  $28.4 \pm 5.0$  lb./in<sup>2</sup>) with TBI (3 with mild physical disability and six without physical disability). The mild physical disability participants do not have any gait and balance difficulty that prevent them from performing any aerobic exercise activities. The participants were selected based on the defined inclusion and exclusion criteria described below and determined by the medical team.

##### ***4.7.1 Inclusion Criteria***

The Participants 1) were between 45-75 years old; 2) had moderate to severe TBI, based on posttraumatic amnesia (PTA) > 24 hours or loss of consciousness (LOC) >30 minutes, or Glasgow Coma Scale (GCS) <13 or intracranial neuroimaging abnormalities within 72 hours before emergency department admission; 3) at least one year had passed since the initial injury, but no more than five years; 4) walking was their primary mean of locomotion (FIM locomotion score >5); 5) they had not participated in any structured exercise or physical activity program (e.g., >3 times/week, 30-40 minutes per session) for the past six months or more; and 6) they could communicate in English.

##### ***4.7.2 Exclusion Criteria***

The exclusion criteria were defined by the medical team as the follows:

1) Contraindication to magnetic resonance imaging (MRI) and 2) had any major pre-existing medical, neurological, and psychiatric conditions other than TBI.

## CHAPTER 5

### TBI PATIENT COMPLIANCE WITH THE PRESCRIBED PHYSICAL EXERCISES USING THE PMT SYSTEM

#### 5.1 Introduction

Many remarkable pieces of evidence showed that intensive strength and endurance training could improve the physical condition of brain-injured patients and decreases the risk of further stroke incidents [131]. Also, some evidence revealed that physical exercise could positively affect emotions and cognitive functions [131]. There is also proof that brain-injured patients feel/perceive the positive outcome of cognitive and physical training themselves [132]. Individuals with (traumatic brain injury) TBI who reported no interest in being active or interested but not currently being active also perceived more barriers to exercising than those who were already regularly active [133]. In addition, poor self-management skills and lack of motivation can be a barrier for persons with TBI-related neurocognitive impairment [134].

Training program beneficial effects vary between patients, as a successful treatment with one patient would not be necessarily successful with another patient. That is partly due to how each patient adheres to and performs the training. Indeed, there is strong attention to analyzing the therapeutic process and the influence of elements of patient training compliance on outcome in psychotherapy research. The effect of patient compliance and the cost of non-compliance is well-documented in prior studies [135] [136] [137].

Treatment can be efficient only if the patient complies with the treatment program. However, Petermann and Mühlhling (1998) [138] reveal that compliance is more than just the patient's eagerness to do the exercise they are asked to do. A complex therapeutic intervention can

efficient only if the patient keeps on the therapeutic advice and contributes and gets involved aggressively and independently [138]. Compliance is a complex, dynamic, and situation-specific phenomenon that can be influenced and altered during therapy [135] [138]. TBI patients have impaired self-awareness and lack of motivation for participation in treatment; therefore, for a successful therapeutic work compliance is a requirement [139].

A positive relation between compliance with memory rehabilitation and the advancement of neuropsychological functions in a single-case study was demonstrated by Kime et al. [140]. Also, a therapist-rated measure of patients' acceptance of and coping with the program routines and patients' active engagement in a program has been reported to be the essential predictors of employment outcome after program completion [141]. This relation was replicated by Schönberger, Humle, Zeeman, & Teasdale (2006) [142] as compliance with holistic outpatient rehabilitation and follow-up outcome. The conclusions by Schönberger et al. also supported the efficacy of patient compliance and showed that the relationship between adherence and development based on what patients complied with [143]. All these studies demonstrated the relationship between compliance and outcome. In conclusion, brain injury rehabilitation compliance is not just defined by performing the exercises, rather how intense and properly the performed exercise was has a significant role in the rehabilitation and healing process [144].

To design an ideal exercise prescription, a balance between the frequency, intensity, duration, and exercise mode must be attained. To explore definitions of adherence to exercise classes, Visek et al. [80] discussed four measures used for adherence to structured exercise in trials: (1) completion, (2) attendance (the number of sessions attended over the follow-up period), (3) duration adherence (how long they exercised during each session) and (4) intensity adherence (the physical exertion).

In this chapter, four compliance measures will be presented, and the results of applying these measures to the performance of the patients will be offered.

## **5.2 Exercise Compliance Definition**

The World Health Organization (WHO) has defined compliance or adherence as "*the extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider*" [145]

As WHO defines a unit of measurement for compliance, the ratio of the duration of performed exercise sessions over the duration of the prescribed exercise sessions duration. For example, a subject who performs exercise sessions that constitutes 60% of the prescribed exercise duration is 60% compliant as measured with this compliance unit. Another measure of compliance proposed by the WHO is frequency compliance. It is the ratio of the number of performed exercise sessions over the total number of the prescribed exercise sessions. For example, a subject who performs exercise sessions that constitutes 70% of the prescribed exercise frequency is 70% compliant, as measured with this compliance method. Exercise determination is the accumulation of time from beginning to the cessation of therapy, measured by time metric (e.g., number of weeks to discontinuation) [145]. Furthermore, patient compliance can be calculated for different intervals; for example, we will calculate the compliances for each week in three months periods in this study.

Patients can be allocated into three classifications based on their compliance to prescribed exercise. The first category is complying patients, i.e., patients who comply both to the number of training sessions prescribed and the duration of the prescribed cycle (e.g., the duration of a structured program) by at least 80%. The second category consists of non-comply

patients, who comply <20% to the prescribed number of training sessions and their durations [145]. The third category corresponds to the partially compliant patients who perform the prescribed exercises but tend to neglect some of them or do not perform them for the prescribed duration [145].

### 5.3 Means and Method

In the following, we will discuss several methods of quantifying the level of compliance for 9 TBI patients (7 males, 2 females, aged  $55.2 \pm 7.5$  years, BMI  $28.4 \pm 5.0$  lb./in<sup>2</sup>) with TBI (3 with mild physical disability and six without physical disability) who participated in our study and were assigned to the aerobic exercises (presented in Ch4 section 4.7). The compliance calculations were based on 3-months (13 weeks) of automatic data collection by the patients by the PMT system based on the prescriptions that the care team prescribed for the patients. For these computations, only exercise sessions that were 10 minutes or longer were considered. The three main metrics we calculated were the following:

- The time interval during which the patient maintained the prescribed heart rate
- Total time that patient exercised for each prescribed instance of exercise
- The number of times or the frequency that each patient exercised in comparison to the prescribed exercise frequency.

Since the prescribed levels of exercise were reviewed and potentially adjusted every week, the number of exercise sessions per week was used to quantify the exercise frequency.

The compliance percentages are calculated for each week as follows:

$$\text{Heart Rate Compliance \%} = \frac{\text{duration of performed Exercise while maintaining or exceeding the prescribed HR}}{\text{prescribed duration of maintaing the prescribed HR}} \times 100 \quad (1)$$

$$\text{Duration Compliance \%} = \frac{\text{TotalDuration of Perofrmed Exercise}}{\text{Prescribed Exercise Duration}} \times 100 \quad (2)$$

$$\text{Freaquancy Compliance \%} = \frac{\text{Total Number of Peromed Exercise}}{\text{Prescribed Number of Exercise}} \times 100 \quad (3)$$

We also analyzed the *Momentarily Heart Rate Compliance* to investigate if the patients achieved the prescribed heart rate at least once in their exercises attempts. We calculated if the patients attain a heart rate equal to or above the prescribed heart rate at least once in an exercise session that lasted 10 minutes or longer.

$$\text{Momentarily HR Compliance \%} = \frac{\# \text{ of Peromed Exercise}(\text{HR} \geq \text{Target}) \text{ at least once}}{\text{Prescribed Number of Exercise}} \times 100 \quad (4)$$

### 5.3.1 Heart Rate Compliance

Heart Rate is known as the number of times a person's heartbeats per minute [87]. A typical range for adults is 60 to 100 beats per minute; however, heart rate varies from person to person. TBI patients are reported to have a range between 60-80 beats per minute [88]. The amount of effort and the body's physiological adaptation can be indicated by heart rate [89].

Heart rate monitoring is an essential element specifically in cardiovascular fitness assessment and training programs [90]. A sedentary person's heart rate can increase up to 150 (BPM), while a fit person might reach only 100 (BPM) for the period of moderate exercise [146]. Hence, using heart rate as a measure of compliance proposed for the present research is corroborated by previous investigations. Based on this compliance measure, the average patient adherence to the prescribed Heart Rate Compliance was 51.63%, where the highest adherence was 94.32%, and the lowest was 13.87%.

**Method:** We analyzed the patients' adherence to the prescribed heart rate throughout the exercise duration for this compliance metric. We calculated each exercise compliance based on the prescribed heart rate value for each week of the study. Then, we figured the average weekly

compliances for each patient as the prescription is updated every week. For example, suppose a patient prescribed 3 exercises per week. In that case, each for 30 minutes with a prescribed heart rate of 100 (BPM), then the patient has to archive 90 minutes of exercise while maintaining or exceeding 100 BPM to achieve 100% of compliance.

Therefore, we looked into each week's prescribed heart rate then analyzed the duration the patient maintained or exceeded the prescribed heart rate for each exercise. Then, we divided the calculated duration value over the prescribed exercise duration value.

**Results:** (Figure 5.34) Represent the patient's overall weekly Heart Rate Compliance. Then Figure 5.35 Shows the average Heart Rate Compliance overall view for the 3-months period.

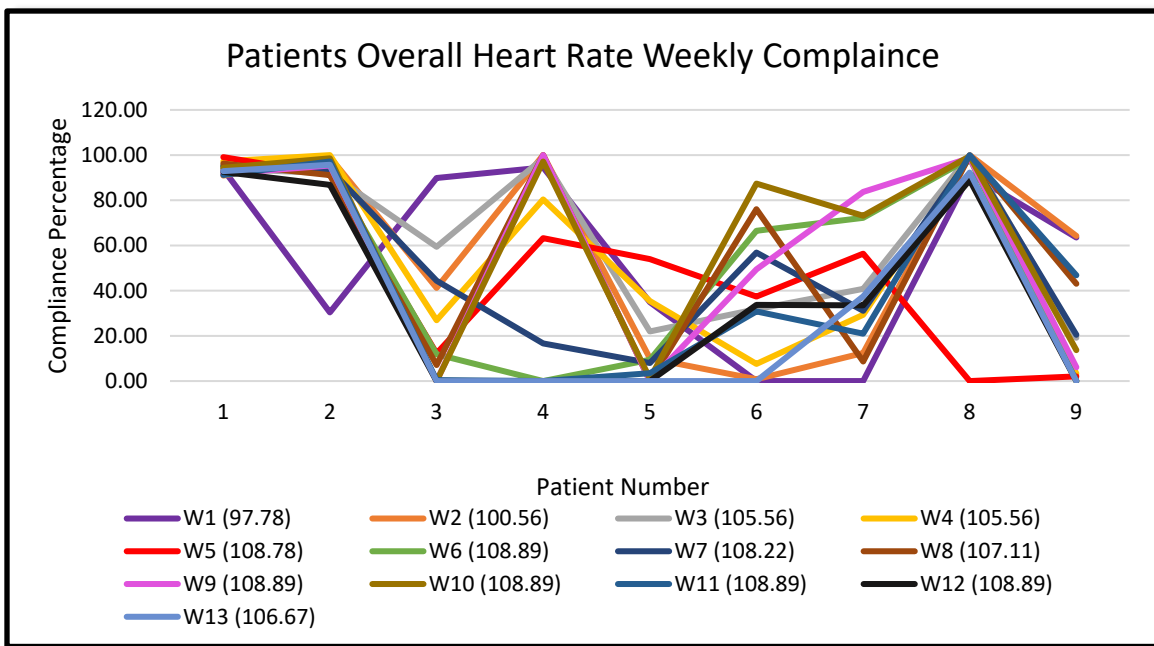


Figure 5.34: Patients Overall Weekly Heart Rate Compliance, the week numbers are shown as W1, W2, etc., and the numbers in the parentheses after that are the patients average prescribed heart rate for that week



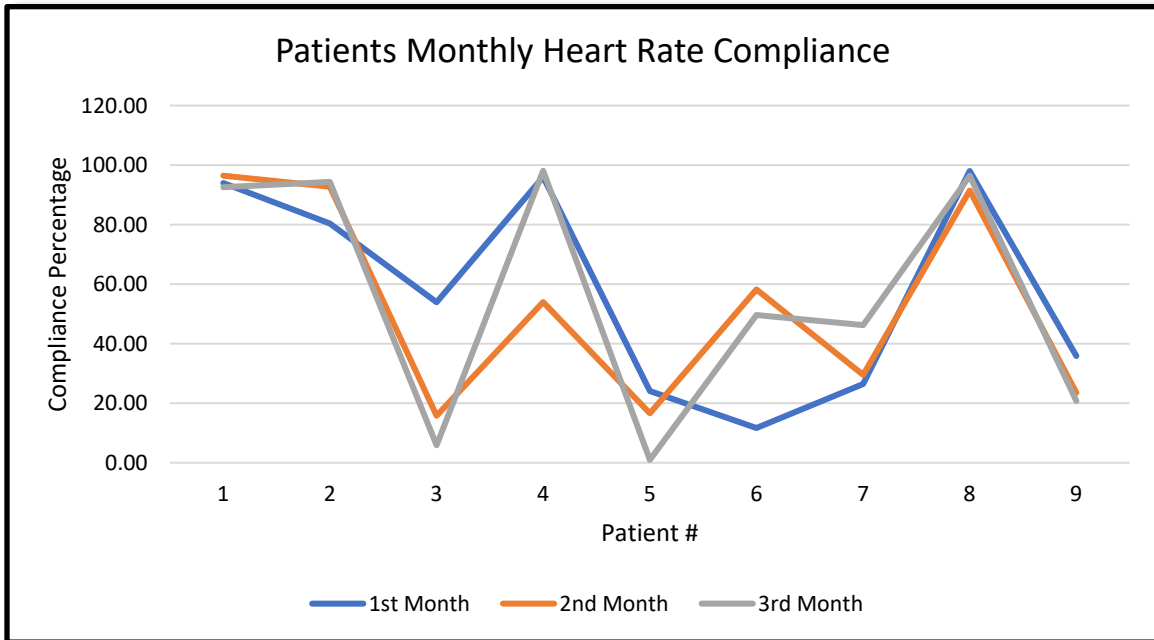


Figure 5.35: Patients Monthly Heart Rate Compliance

Patient number 1 achieved the highest Heart Rate Compliance among patients in all the compliance metrics. Patient number 1 achieved Heart Rate Compliance with an average of 94.32% within 3 months of the program (Figure 5.36).

The average patient compliance among the 3-months program was 51.63%. Patient number 3 had decreasing Heart Rate Compliance over the 13 weeks of the 3 months program (Figure 5.37). Figure 5.38 shows Patient number 4 high Heart Rate Compliance for the first month; then the compliance decreases at the second month; the patient tried to increase the compliance in weeks 8,9, and 10 then lost the compliance again. The patient weekly compliance percentage is demonstrated in (Figure 5.39). Patient number 5 had the lowest Heart Rate Compliance among the subjects. However, Patient number 7 maintained high Heart Rate compliance even though the patient was on Beta Blocker medication while the patient was in the program (Figure 5.40). For more details, the other patient's plots are demonstrated in Appendix A.2.

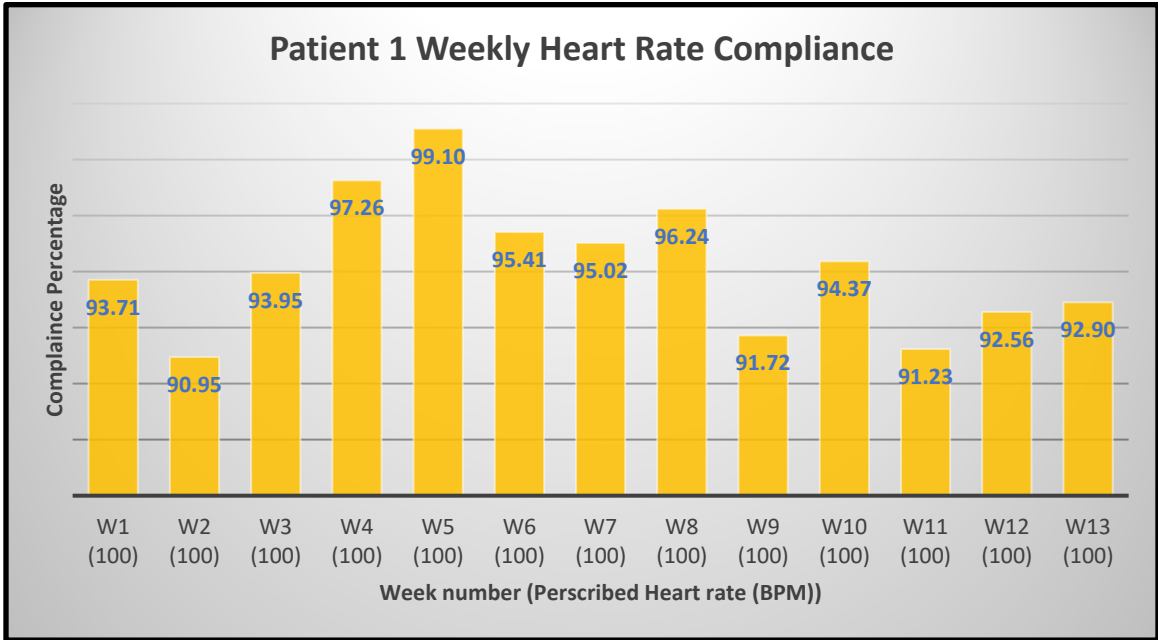


Figure 5.36: Patient#1 Heart Rate Weekly Compliance (Highest Compliance among patients), the week numbers are shown as W1, W2, etc., and the numbers in the parentheses below that are the prescribed heart rate for that week.

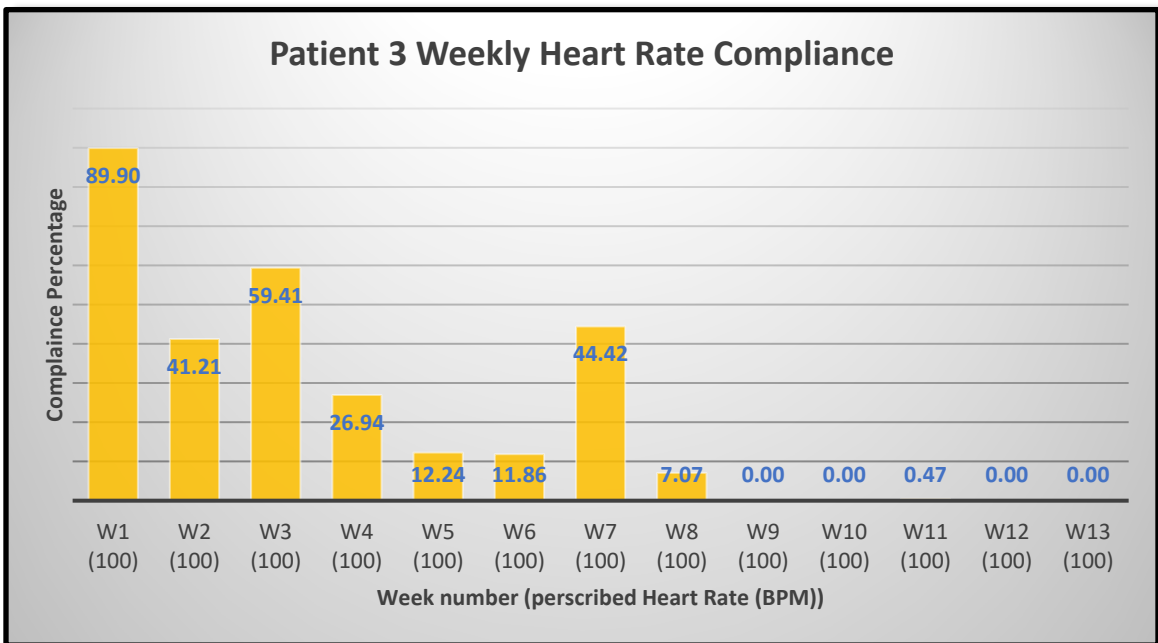


Figure 5.37: Patient#3 Heart Rate Weekly Compliance, the week numbers are shown as W1, W2, etc., and the numbers in the parentheses below that are the prescribed heart rate for that week.

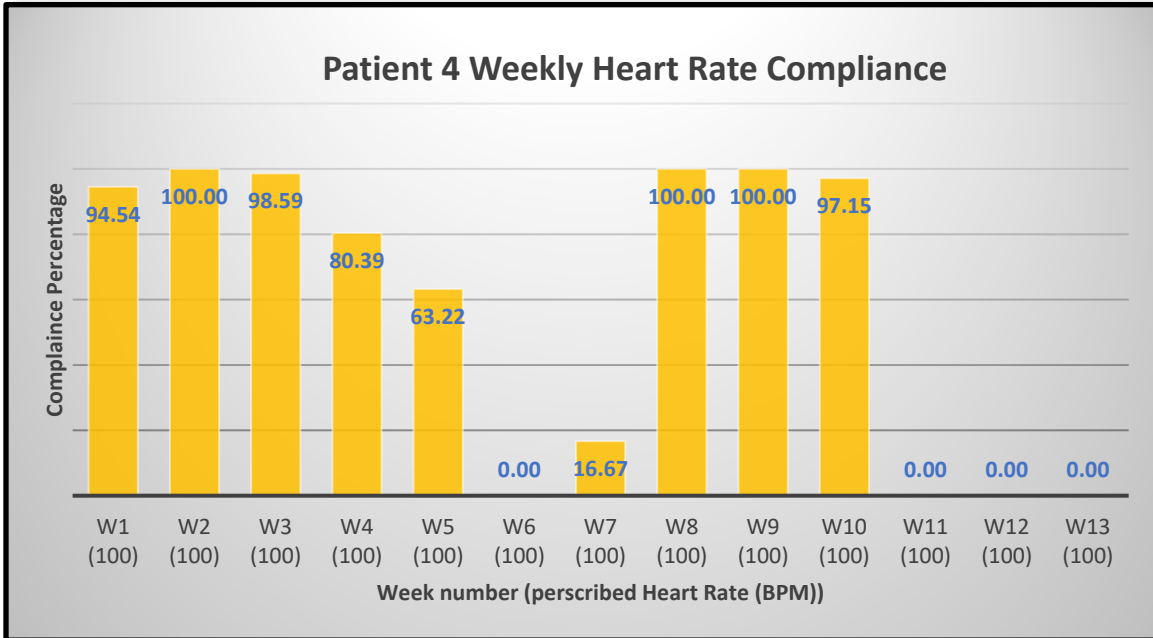


Figure 5.38: Patient#4 Heart Rate Weekly Compliance, the week numbers are shown as W1, W2, etc., and the numbers in the parentheses below are the prescribed heart rate for that week.

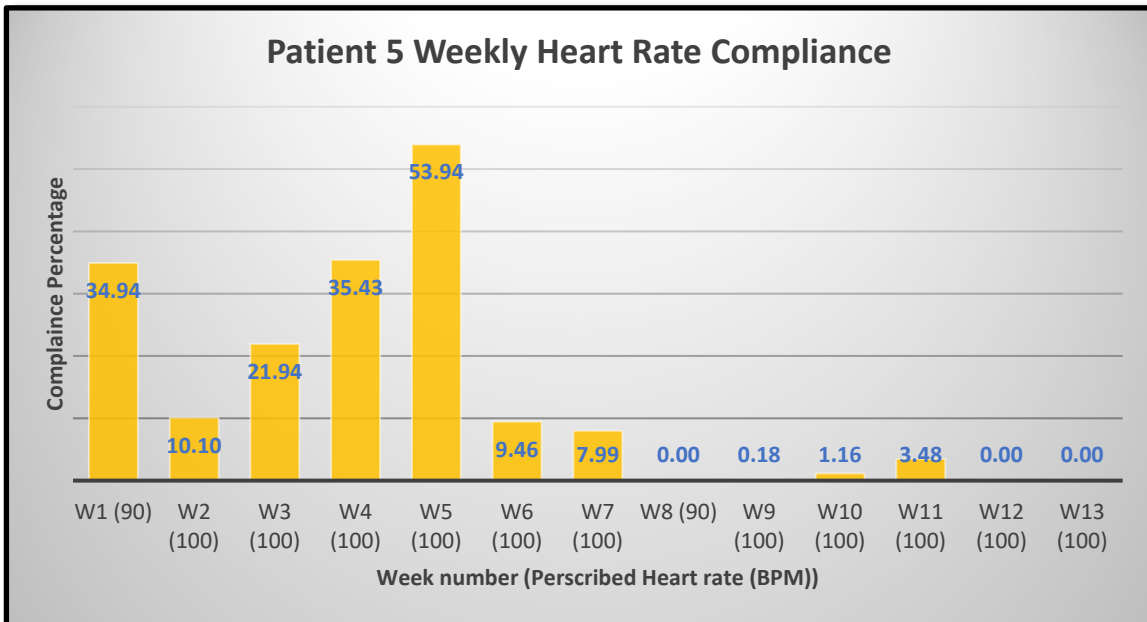


Figure 5.39: Patient#5 Heart Rate Weekly Compliance (lowest among patients), the week numbers are shown as W1, W2, etc., and the numbers in the parentheses below that are the prescribed heart rate for that week

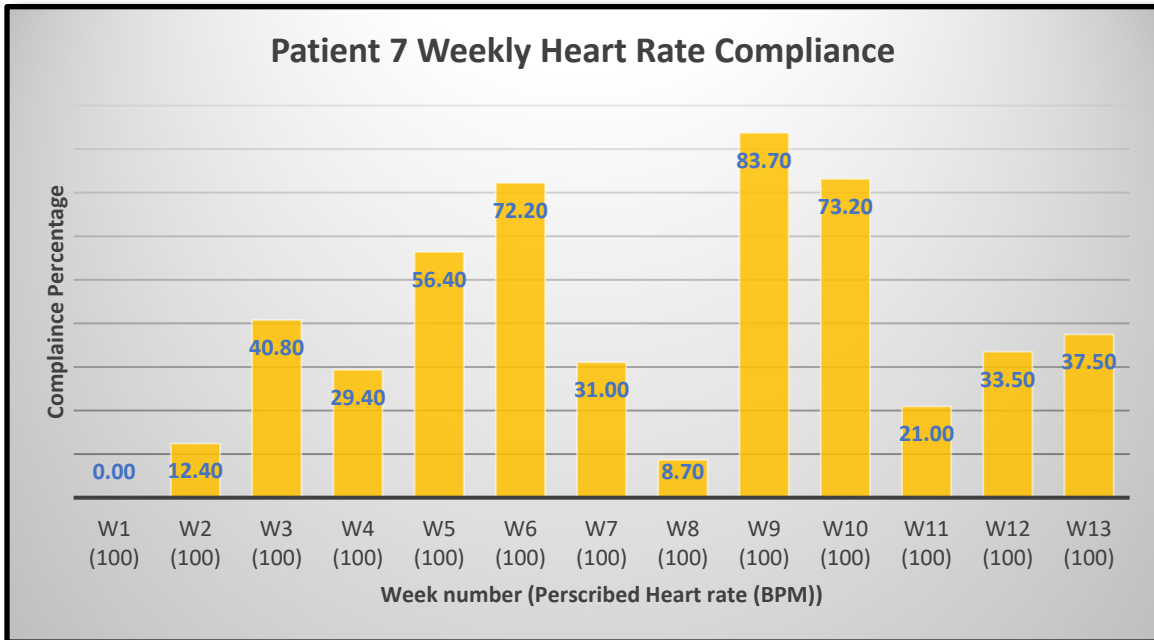


Figure 5.40: Patient#7 Heart Rate Weekly Compliance (lowest among patients), the week numbers are shown as W1, W2, etc., and the numbers in the parentheses below that are the prescribed heart rate for that week

One-way ANOVA ( $\alpha = 0.05$ ) test was applied to the monthly Heart Rate Compliance metric to study the mean differences of average compliance for each month. No statistically significant difference was found for the heart rate compliance over the three months, as the p-value was 0.96, which indicates no significant differences. Heart Rate Compliance Box Plot for each month was plotted as it is presented below.

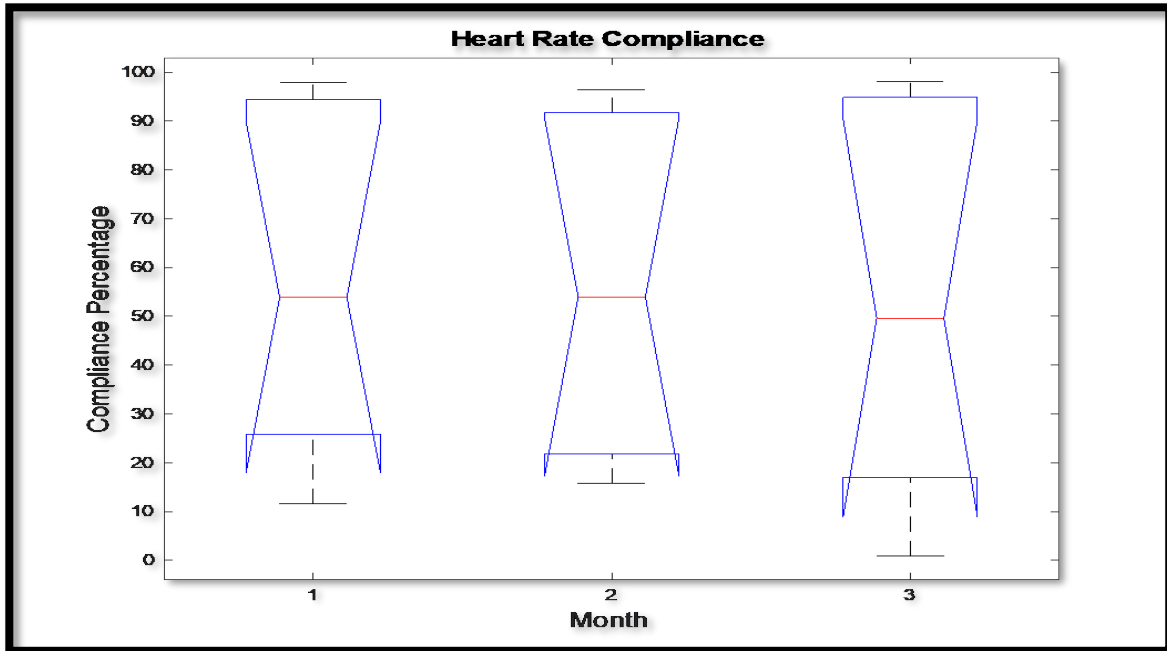


Figure 5.41: The Total Patient Average of Heart Rate Compliance Box Plot for each month, the lowest black bar (lower whisker) represents the lowest compliance among all patients. The top black bar (higher whisker) represents the highest compliance value among all patients. The low blue bar represents the 25<sup>th</sup> percentile, and the top blue bar represents the 75<sup>th</sup> percentile, and the medium red bar represents the median compliance value.

Table 5.8: Heart Rate Compliance Box Plot Values

Heart Rate Compliance Box Plot			
Box Plot Values	1st Month	2nd Month	3rd month
Lowest Compliance (bottom whisker)	11.66	15.79	0.96
Highest Compliance (top whisker)	98.02	96.44	98.01
25th Percentile (lower blue line)	25.86	21.78	17.03
75th Percentile (upper blue line)	94.48	91.77	94.86
Median (Red line)	53.92	53.97	49.64

**Discussion:** The patient Heart Rate Compliance average over 3 months was 51.63%. Overall, 4 patients out of the 9 patients maintain high Heart rate Compliance in most of the program weeks; they were patients 1,2,4 and 8 (Figure 5.34). Furthermore, some of the patients' Heart Rate Compliance did not vary significantly over the three months of study, such as patients 1,8, and 9

(Figure 5.35). For patients' numbers, 2 and 6, the second and third-month compliance increased comparing to the first month (Figure 5.35). Patient number 7 third month compliance was higher than first and second months even though the patient was on Beta-blockers where such medication can cause the heart rate to decrease. For Patients number 3 and 5, the compliance fell over the three-month program (Figure 5.35). Patient number 4 had higher compliance for the first and third months comparing to the second month (Figure 5.35 and Figure 5.38).

Moreover, no statistically significant difference was found for the Heart Rate Compliance over the three-months. The p-value was 0.98, which indicated no significant differences in Heart Rate Compliance among the three months. The Box plot showed no variations in the first and second months as the lowest compliance was 11.66% and 15.79%. The highest is 98.02% and 96.44% for the first and the second month, respectively. The median was 75.76% and 78.56% for the first and the second month, respectively. The third month's lowest was 35.15% percent, and the highest was 111.08% and the median 94.44% Figure 5.46.

Also, some patients' compliances did not change even when the prescribed heart rate decreased, such as patient number 5 (Figure 5.39). Some patients also did not achieve the prescribed heart rate regardless that they reached the initial clinic visit walking test more than the prescribed heart they missed, as was the case with patient number 4 (Figure 5.38.)

**Conclusion:** This section represented the Heart Rate Compliance metric that calculated patient compliance with prescribed heart rates. The average Heart Rate Compliance for all the patients was 51.63%

#### ***5.3.4 Compliance as Adherence to Perform the Required Exercise Duration***

Adherence to the exercise duration prescription is an essential factor in the integrity of any intervention study. The knowledge of its determinants will maximize the validity of the scientific

findings in any physical exercise therapy. Therefore, we propose to define adherence or compliance to the prescribed exercise based on the duration of keeping the prescribed exercise duration at the specified level. Indeed, another compliance metric we analyzed based on the exercises prescriptions is the duration of the exercises. Each patient may be prescribed duration of exercise session at the beginning of every week of the study. Therefore, the compliance for each week is based on the prescribed value for that week. The average patient adherence to the prescribed duration was 80.37%. The highest patient adherence to the prescribed exercise duration was 97.84%. The lowest adherence was 44.14%.

**Method:** The duration compliances metric was calculated by summing the duration of the performed exercises for sessions that were performed 10 minutes or longer and dividing that by the prescribed duration for each week for every patient. For example, if a patient did 80 min of exercise in a week for which the prescribed duration was 100 min, then the weekly compliance for that patient during that week would be 80%. We calculated each exercise compliance based on the prescribed total duration value for each week of the study. Then, we figured the average weekly compliances for each week as the prescription is updated every week. For example, if a patient is prescribed 3 exercises per week, each for 30 minutes, the patient has to archive 90 minutes of exercise to archive 100% of compliance.

Therefore, we examined each week's prescribed duration. Then, we analyzed the duration the patient maintained for each exercise; then, we divided the calculated duration value over the prescribed exercise duration value.

Based on this compliance measure, the average patient adherence to the prescribed duration was 80.37%. The highest patient adhered to the prescribed exercise duration was 97.84%. The lowest adherence was 44.14%.

**Results:** We represented in Figure 5.34-

Figure 5.43 patient's overall weekly Duration Compliance. Then (Figure 5.44) shows the average Duration Compliance overall view for the 3 months period.

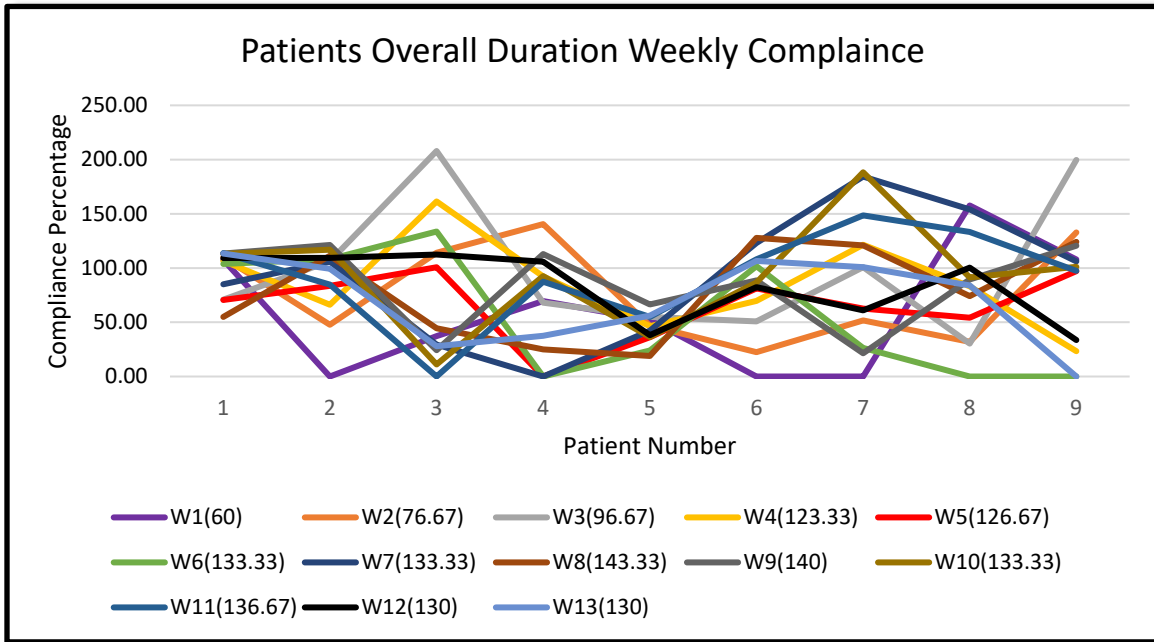


Figure 5.42: Patients overall weekly Duration Compliance, the week numbers are shown as W1, W2, etc., and the numbers in the parentheses below that are the average prescribed duration for that week

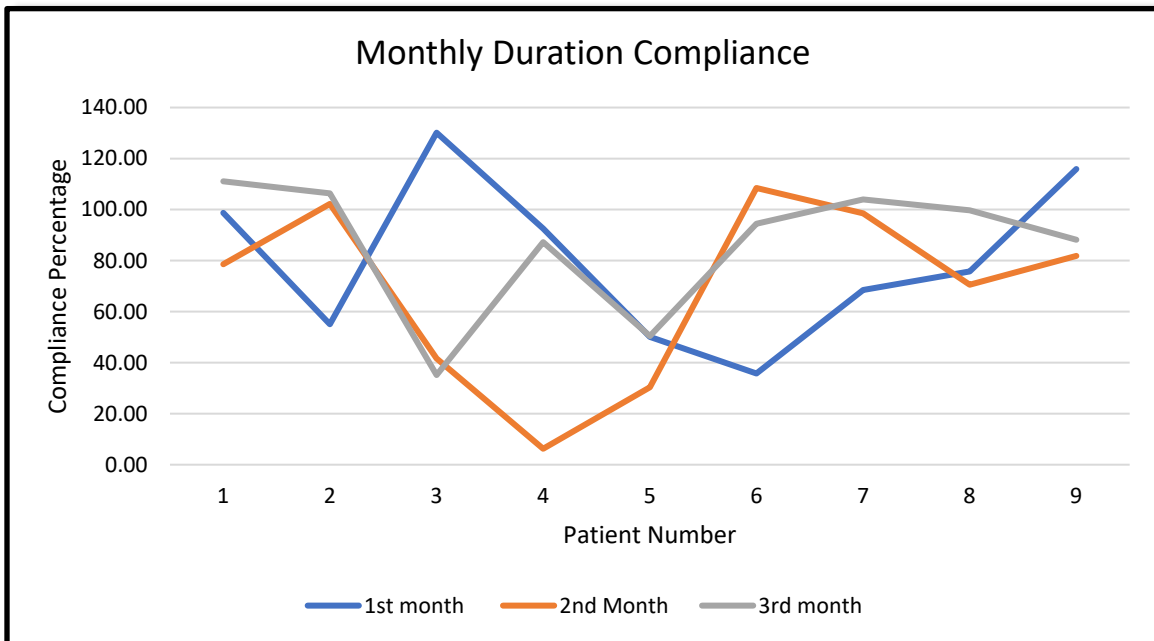


Figure 5.43: Patients Monthly Duration Compliance



Patient number 1 reached the highest Duration Compliance with an average of 97% within 3 months of the program (Figure 5.45).

Patient number 5 had the lowest Duration Compliance among the subjects. The average patient compliance for all patients over the 3 months program was 44.14%. The patient weekly compliance percentage is demonstrated in (Figure 5.46). For the detail, the other patient's plots are shown in Appendix A.2.

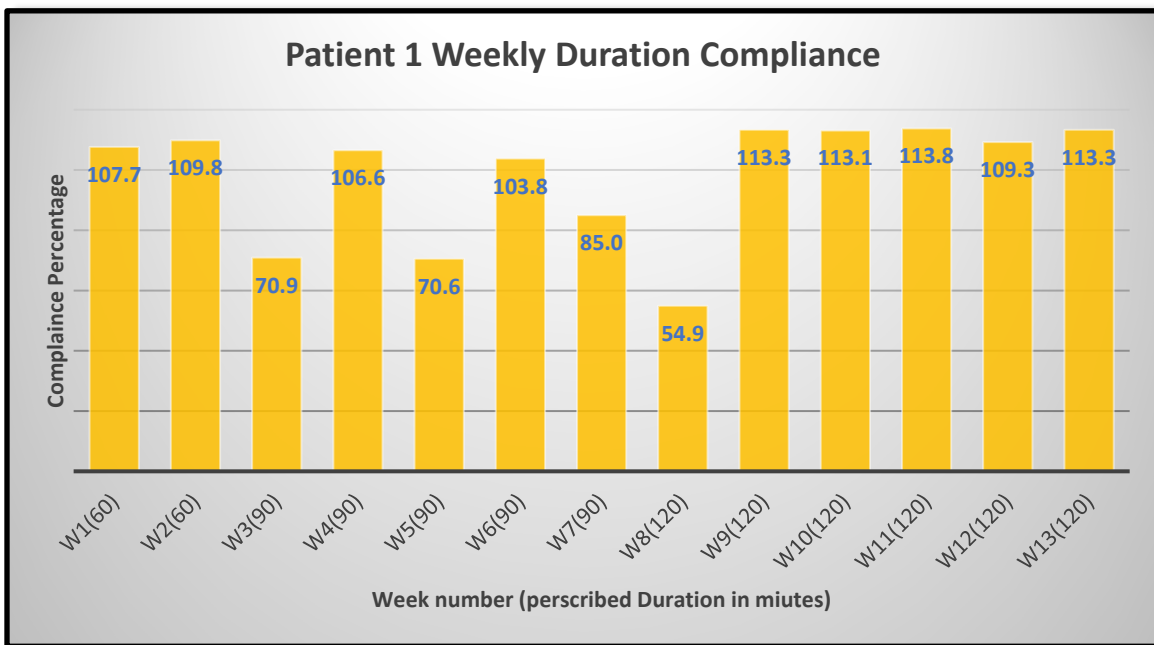


Figure 5.44: Patient#1 Duration Compliance (Highest Compliance among patients), the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed duration for that week.

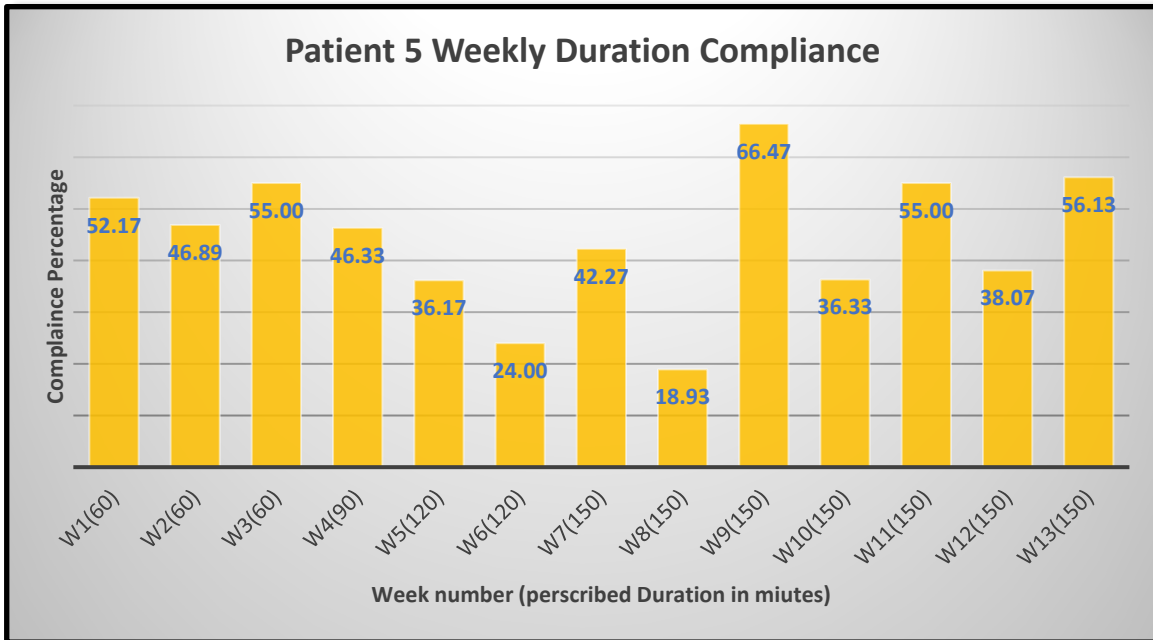


Figure 5.45: Patient#5 Duration Compliance (lowest among patients), the week numbers are shown as W1, W2, etc., and the numbers in the parentheses below that are the prescribed duration for that week

One-way ANOVA ( $\alpha = 0.05$ ) test was applied to the monthly Duration Compliance metric to study the mean differences of average compliance for each month. No statistically significant difference was found for the Duration Compliance over the three months; the p-value was 0.48, which indicates no significant differences.

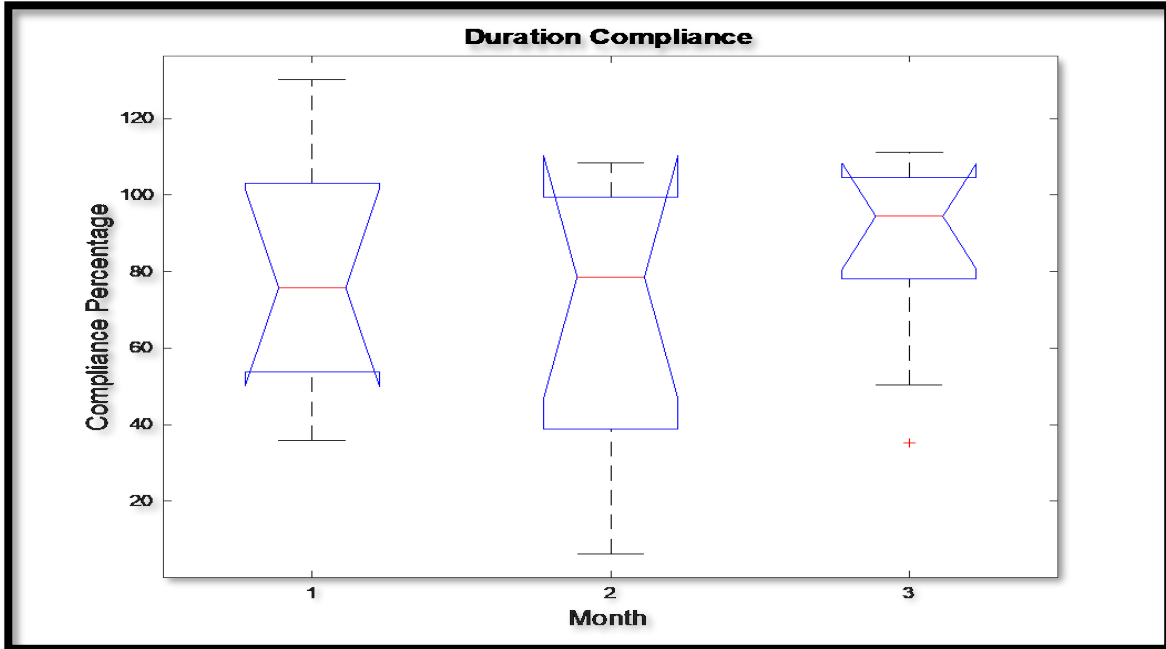


Figure 5.46: Duration Compliance Box Plot for each month, the lowest black bar (lower whisker) represents the most inadequate compliance among all patients. The top black bar (higher whisker) represents the highest compliance value among all patients. The low blue bar represents the 25<sup>th</sup> percentile, and the top blue bar represents the 75<sup>th</sup> percentile, and the medium red bar represents the median compliance value. The red cross in the third month represents the outlier value.

Table 5.9: Duration Compliance Box Plot Values

Duration Compliance Box Plot			
Box Plot Values	1 <sup>st</sup> Month	2 <sup>nd</sup> Month	3 <sup>rd</sup> month
Lowest Compliance (Bottom whisker)	35.75	6.25	35.15
Highest Compliance (Top whisker)	130.15	108.47	111.08
25th Percentile (Lower blue line)	53.80	38.83	78.04
75th Percentile (Upper blue line)	103.03	99.47	104.58
Median (Red line)	75.76	78.56	94.44

**Discussion:** The Average compliance for all the patients over the three months was 80.37%.

Also, by analyzing

Figure 5.43 we observed much patients-maintained compliance higher than 50% in most of the program weeks. Also, following Figure 5.46 we found out that the patient median (94.44%) for the third month was higher than the first and second months (75.76% and 78.56%).

Patient Number 1 achieved the highest duration compliance for the exercise duration with an average of 97%. The highest compliance was in week 11, with a percentage of 113.75% of the 120 minutes prescribed duration for that week (Figure 5.45). The lowest was for week number 8, with compliance of 54.92% of the 120 minutes prescribed duration for that week (Figure 5.45). Patient number 5 had the lowest level for duration compliance with an average of 44.14%. The highest week for patient number 5 was for week number 9 with a compliance percentage of 66.47% for the prescribed duration of 150 minutes and the lowest week was for week number 8 with compliance of 18.93% of the prescribed 150 minutes (Figure 5.46).

Moreover, patient number 2 duration compliance increase over the 3 months. Patients number 3,7 duration compliance decreased throughout the 3 months (Figure 5.44). Patients number 1, 4, 5, 8, and 9 compliances had lower compliances in the second month than the first month, but they managed to increase their compliances in the third month (Figure 5.44). Patient 6 had the highest compliance in the second month, but for this patient, the third-month compliance was higher than the first month (Figure 5.44).

The one-way ANOVA test showed no significant difference across the three months for the patients ( $p=0.48$ ). There were no variations in the first and second months as the lowest compliance was 35.75% and 6.25%, respectively. The highest is 130.15% and 108.47%, respectively. The

median was 75.76% and 78.56%, respectively. The third month's lowest was 35.15% percent, and the highest was 111.08% and the median 94.44% Figure 5.46.

**Conclusion:** The patients showed an average of 80.37% compliance for the entire 3-months of the program. The compliance average decreased from 80.28% for the first month to 68.72% for the second month. However, it increased for the third month to 86.28%.

### ***5.3.5 Exercise Frequency Compliance***

Adherence to the frequency exercise prescription is another critical factor in the integrity of any prescribed physical exercise; the knowledge of its determinants will define the participant adherence to the number of exercises performed to the prescribed number of exercises which that will improve studying physical exercise as a treatment for a health deficiency.

Therefore, we propose to define adherence or compliance to the prescribed exercise based on the number of performed exercises at the prescribed level; Indeed, a third compliance metric we analyzed based on the exercises prescriptions is the frequency of the exercises performed per week. Each patient has been prescribed a different frequency at the beginning of every week thorough out the program. Based on this compliance measure, the average patient adherence to the prescribed frequency was 75.52%. The highest adherence to the prescribed exercise duration was with an average of 102.56%. The lowest adherence was attained, with an average of 51.92%.

**Method:** The Exercises Frequency Compliances metric was calculated by totaling the number of exercise sessions that were performed for 10 minutes or longer and dividing the total number by the total number of prescribed exercise sessions for each week for every patient. For example, if a patient is 80% compliant, the patient performed 80% of the total number of prescribed exercises on the average three months of the program. We calculated each exercise Frequency Compliance based on the prescribed total number of exercises value for each study week. Then, we figured the

average weekly compliances for each patient as the prescription was updated every week. For example, if a patient is prescribed 3 exercises per week, then the patient has to exercise 3 sessions that last 10 minutes or longer in the week to archive 100% of compliance.

Therefore, we examined each week's prescribed number of exercises. We compare the number of exercises the patient performed for each week; by dividing the number of performed sessions over the number of prescribed sessions.

**Results :** (Figure 5.34-Figure 5.48) Represent the patient's overall weekly Exercise Frequency Compliance. Then (Figure 5.49) shows the average Exercise Frequency Compliance overall view for the 3 months period.

The highest Frequency Compliance among patients was with an average of 97%. The lowest exercise Frequency Compliance among the subjects was 44.14%. The highest and lowest patient weekly compliance percentage are demonstrated in (Figure 5.50 and Figure 5.51). For more details of the other patient's data, please see Appendix A.5.

One-way ANOVA ( $\alpha = 0.05$ ) test was applied to the monthly Exercise Frequency Compliance metric to study the mean differences of average compliance for each month. The p-value was 0.49, which indicated no significant differences in the compliances among the three months. No statistically significant difference was found for the Exercise Frequency Compliance over the three months.

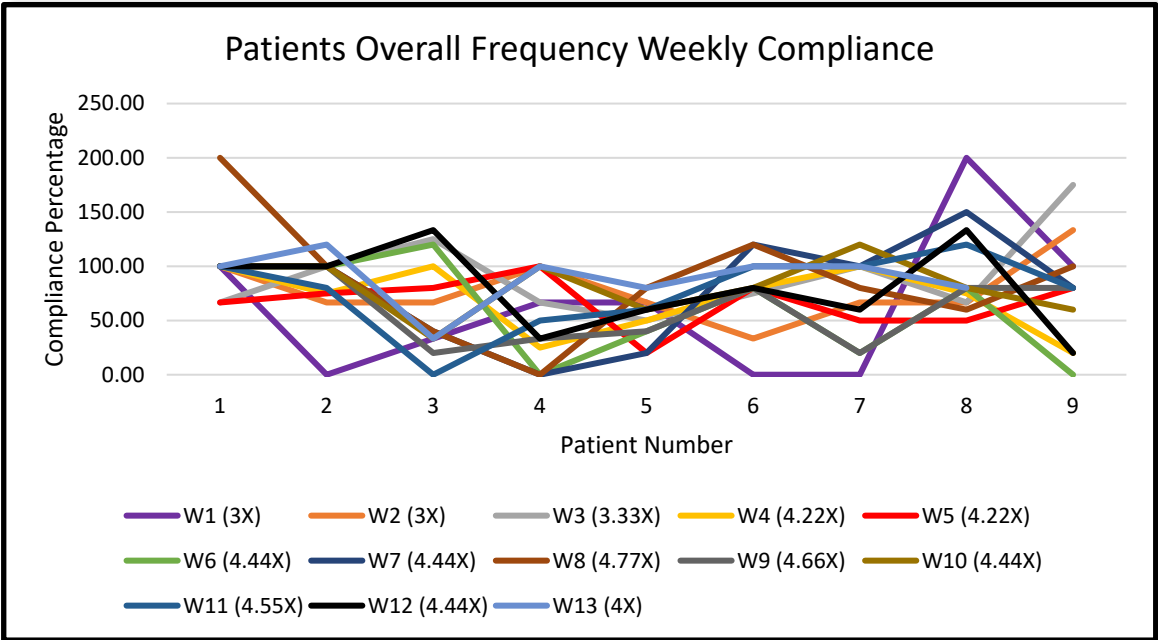


Figure 5.47: Patients Overall Weekly Frequency Compliance, the week numbers are shown as W1, W2, etc., and the numbers in the parentheses next to their average prescribed frequency for that week

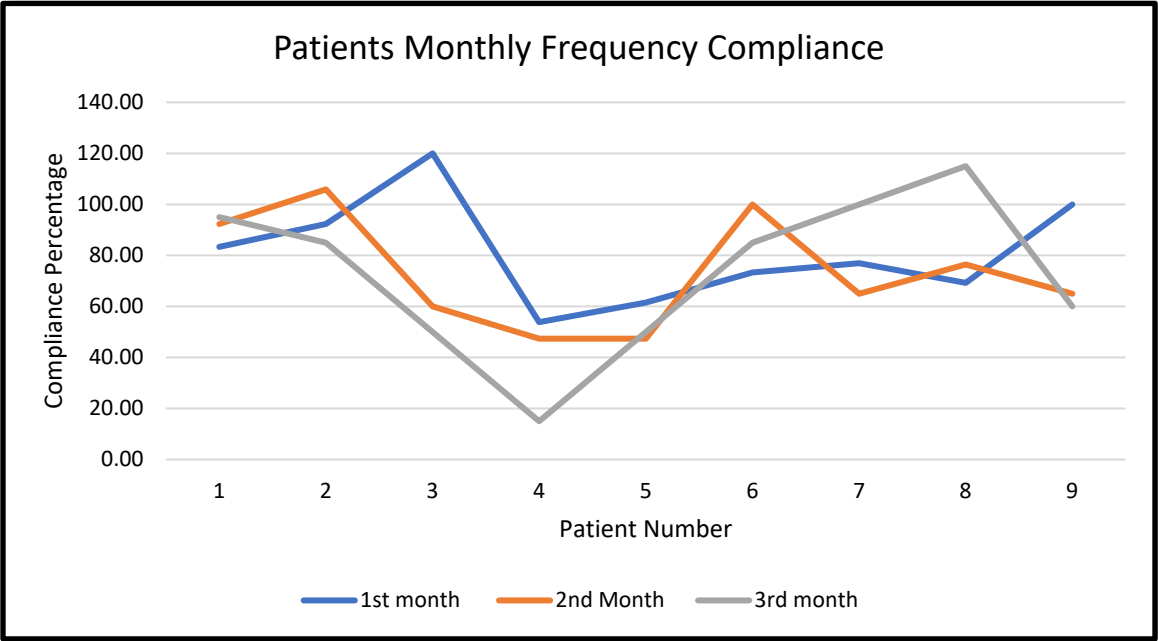


Figure 5.48: Patients Monthly Frequency Compliance

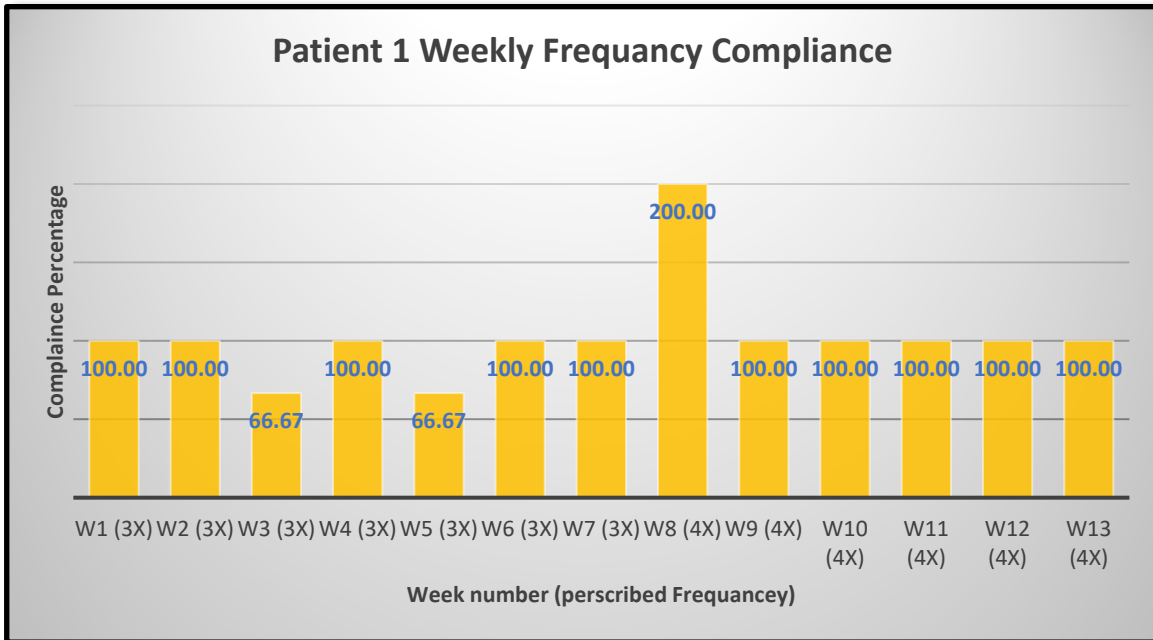


Figure 5.49: Patient#1 Frequency Compliance (Highest Compliance among patients), the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed frequency for that week.

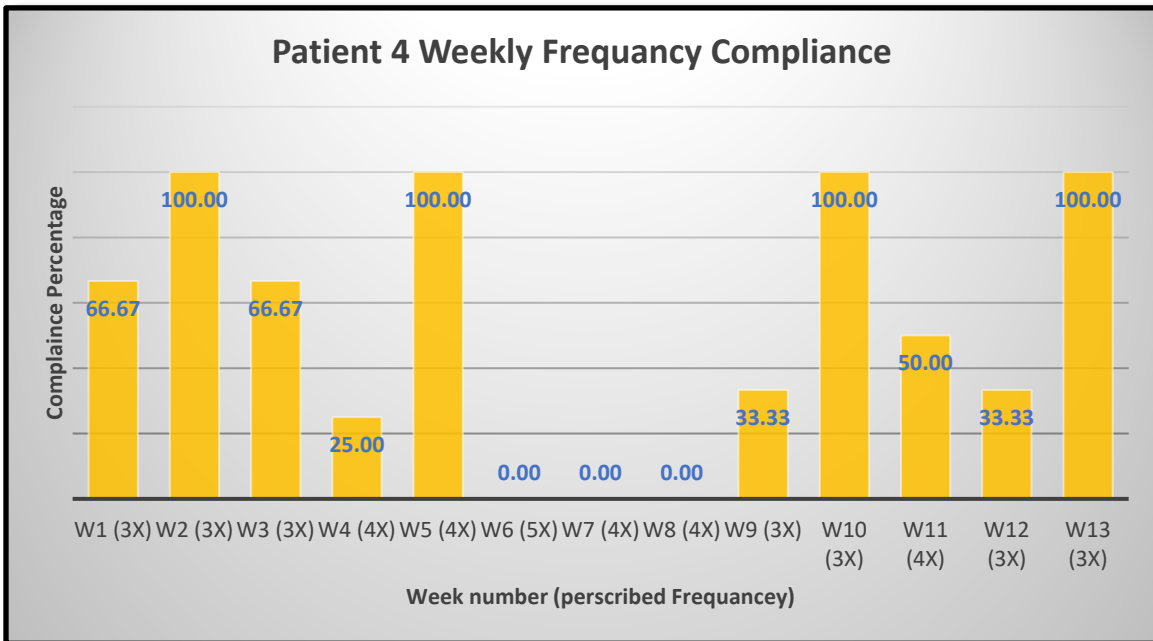


Figure 5.50 Patient#4 Frequency Compliance (lowest among patients), the week numbers are shown as W1, W2, etc. and the numbers in the parentheses below that are the prescribed frequency for that week

Box plots were plotted for the three-month average values for Exercise Frequency Compliance metrics, as it is presented below.



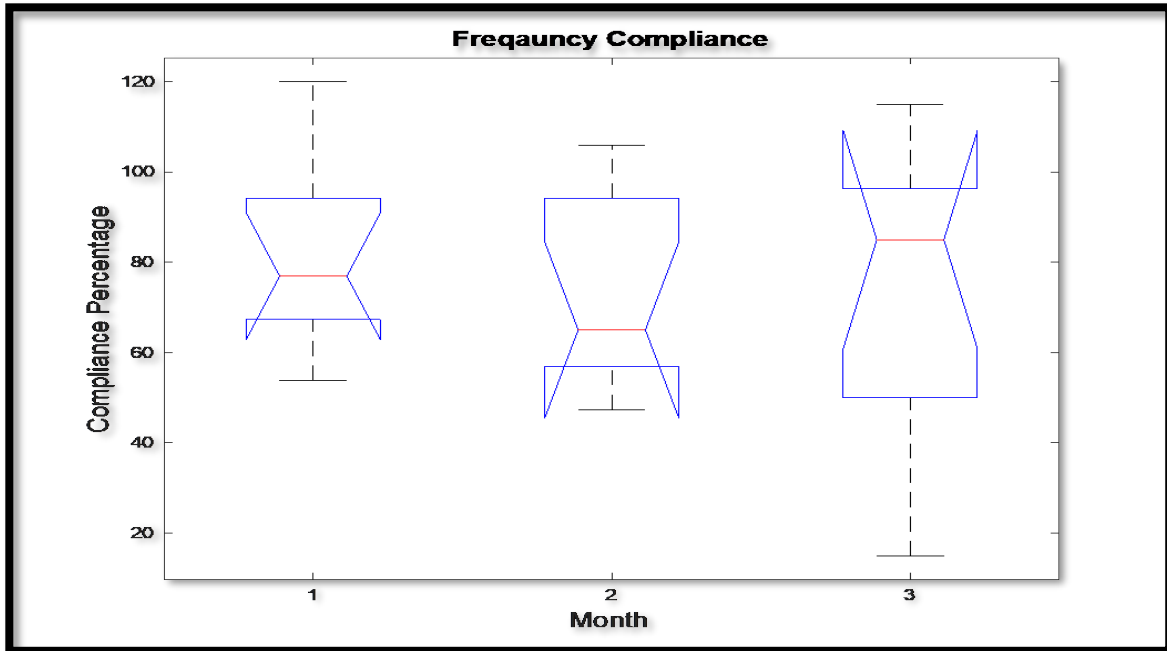


Figure 5.51: Frequency Compliance Box Plot, for each month, the lowest black bar (lower whisker) represents the most insufficient compliance among all patients, top black bar (higher whisker) represents the highest compliance value among all patients. The low blue bar represents the 25<sup>th</sup> percentile, and the top blue bar represents the 75<sup>th</sup> percentile, and the medium red bar represents the median compliance value.

Table 5.10: Frequency Compliance Box Plot Values

Frequency Compliance Box Plot			
Box Plot Values	1 <sup>st</sup> Month	2 <sup>nd</sup> Month	3 <sup>rd</sup> month
Lowest Compliance (bottom whisker)	53.85	4.37	15
Highest Compliance (top whisker)	120	105.88	115
25th Percentile (lower blue line)	67.30	56.84	50
75th Percentile (upper blue line)	94.23	94.23	96.25
Median (Red line)	76.92	65	85

**Discussion:** The average Frequency Compliance for all the patients overall in the 13 weeks of the program was 75.52%. Indeed, 6 out of the 9 patients had Frequency Compliance of more than 60% (Figure 5.49). Figure 5.52 showed that the median of the Frequency Compliance increased from than 1<sup>st</sup> and 2<sup>nd</sup> months to 85% in the 3<sup>rd</sup> month.

Patient number 1 achieved the highest value of the compliance metric. The highest compliance week for patient number 1 was week number 8, where the patient performed double the prescribed frequency, and the lowest was for weeks 3 and 5, where the patient performed 66.7% of the prescribed three exercises for the week (Figure 5.50).

The lowest Frequency Compliance was observed in patient number 4, as the patient had an average of 51.92% weekly compliance. The patient achieved 100% compliance in weeks number 2,5,10, and 13 (Figure 5.51). On the other hand, the patient had 0% compliance in weeks number 6,7, and 8, where the patient was prescribed 5 and 4 times a week, respectively (Figure 5.51).

In addition, for patients number 1, 7, and 8, their monthly frequency compliance increased throughout the three months. Patient number 1 had higher compliances for the second and third months compared to the first month (Figure 5.49). Patient number 8 compliance increased each month (Figure 5.49). Patients number 2,3,4,9 their frequency compliances decreased over the 3 months (Figure 5.49). Patient 5 compliance for the first month was higher than the second and third months. Patient number 6 had the highest compliance in the first month, then it decreased in the second month, but for the third month was more elevated than the second month and lower than the first month (Figure 5.49).

Also, a one-way ANOVA ( $\alpha = 0.05$ ) test was applied to each compliance metric to study the mean differences of average compliance for each month. No statistically significant difference was found for Exercise Frequency Compliance over the three months as all the P values were more significant than 0.05 (0.72). As shown by the box plot (Figure 5.52), no variations were present in the first and second months as the lowest compliance was 53.85% and 4.37%, respectively. The highest is 120% and 105.08% for the first and second months, respectively. (Figure 5.52). The median for the 1<sup>st</sup> and the 2<sup>nd</sup> months were 76.92% and 65%, respectively (Figure 5.52). The third

month's lowest was 15% percent, and the highest was 115%, and the median was 85% (Figure 5.52).

**Conclusion:** The patients showed an average of 75.52% compliance for the entire 3 months of the program. There were no significant differences in the compliance from month to month. However, the compliance averages decreased from the 1<sup>st</sup> to the 3<sup>rd</sup> month. The first month had a compliance average of 81.17%, and it declined to 72.78% for the 3<sup>rd</sup> month.

### ***5.3.2 Compliance of Achieving the Heart Rate Momentarily***

As mentioned in the compliance of the heart rate compliance section, the amount of effort and the body's physiological adaptation can be indicated by heart rate. Also, heart rate monitoring is an essential element in fitness assessment and training programs [90]. Therefore we also analyzed the Momentarily Heart Rate Compliance to investigate if the patients achieved the prescribed heart rate at least once of their exercises attempts that lasted 10 minutes or longer.

**Method:** We calculated if the patients attain a heart rate equal to or above the prescribed heart rate at least once in an exercise session. As indicated earlier, a session would only be considered for this analysis if the patient exercised for at least 10 minutes. We calculated the number of exercises a patient achieved the prescribed heart rate at least once in each attempt in each week. Then we divided that number of exercises over the total performed exercises for that particular week. For example, a patient would have 100% of week compliance if the patient reached the target heart rate in every attempt the patient performed for that week, while if a patient only attained the prescribed heart rate for one of three sessions, they would be 33% compliant.

**Results:** (Figure 5.53) Represent the patient's overall weekly Momentarily Heart Rate Compliance. Then (Figure 5.54) Shows the average Momentarily Heart Rate Compliance overall view for the 3 months period. The compliance values for sample patients using this compliance

metric are presented in (Figure 5.55-Figure 5.58). The patients who reached the highest compliance reached the target heart rate at each attempt throughout the three-month program (Figure 5.55 and Figure 5.56). The highest compliance was 100%, and the lowest compliance in this metric was 69.23%. However, the patient with the most inadequate compliance was number 3 and patient number 4 (Figure 5.57 and Figure 5.58). Patient number 3 did not complete the prescribed hear rate in weeks 9-10 and 12-13 (Figure 5.57). Patient 4 did not reach the prescribed heart rate in weeks 9-10 and 12-13 (Figure 5.57). Patient 4 did not reach the prescribed heart rate in weeks number 6 and weeks 11-13 (Figure 5.58). Patient number 7 compliance also presented here as this patient was on Beta-blocker medication while the patient was in the study (Figure 5.59).

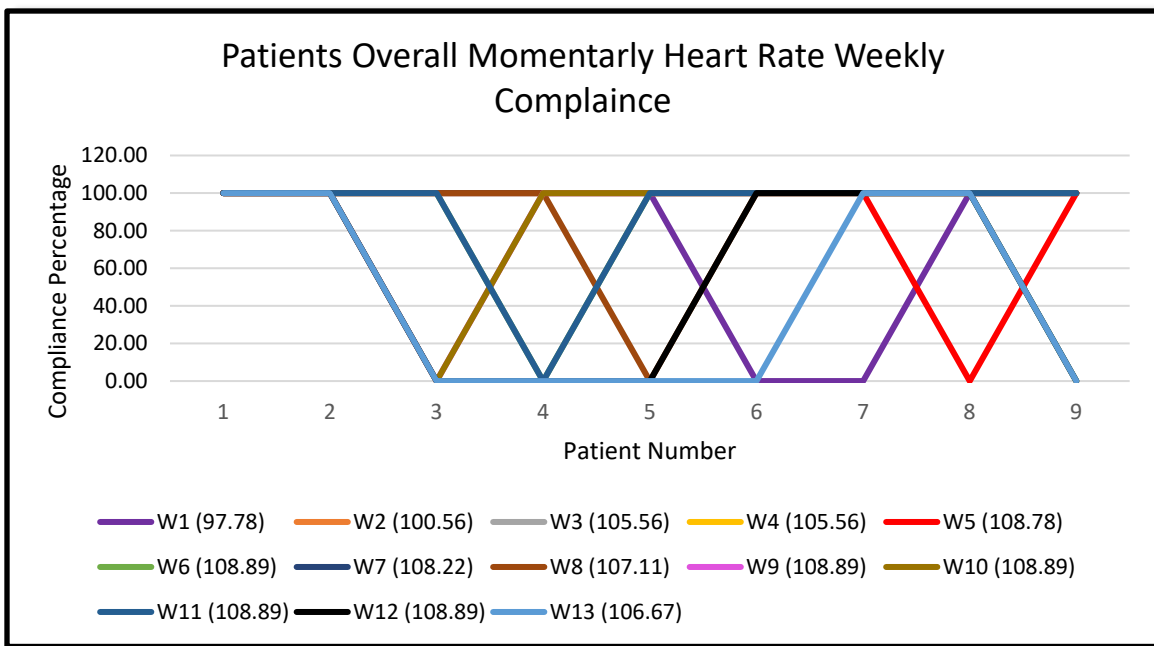


Figure 5.52: Patients Overall Weekly Momentarily Heart Rate Compliance, the week numbers are shown as W1, W2, etc., and the numbers in the parentheses below that are the average prescribed heart rate for that week

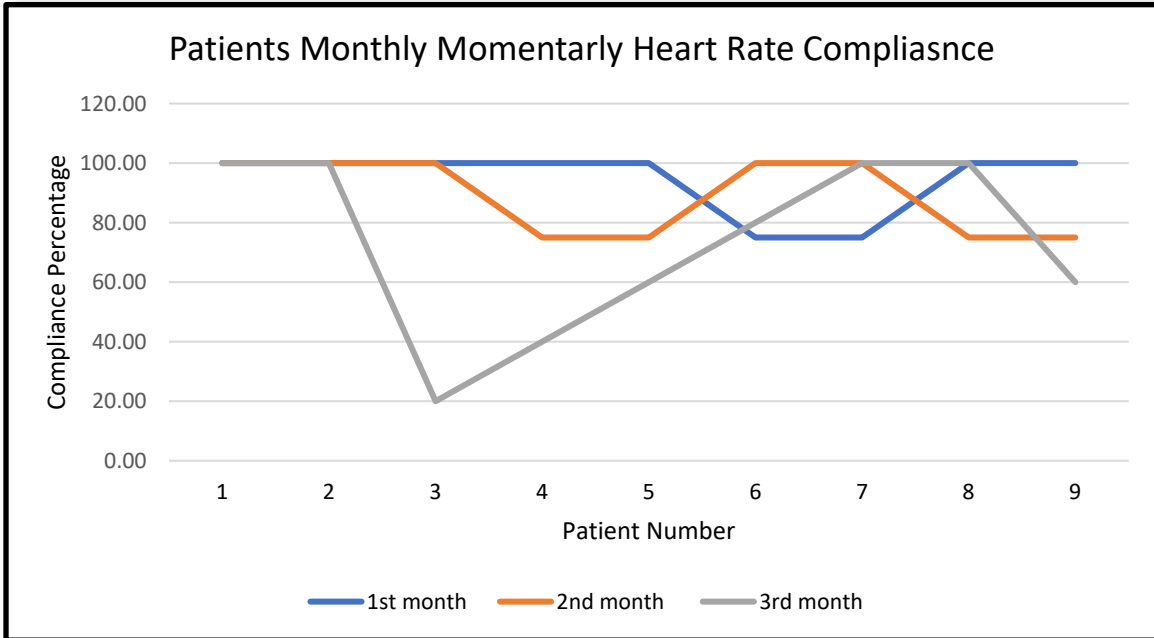


Figure 5.53: Patients Monthly Momentarily Heart Rate Compliance

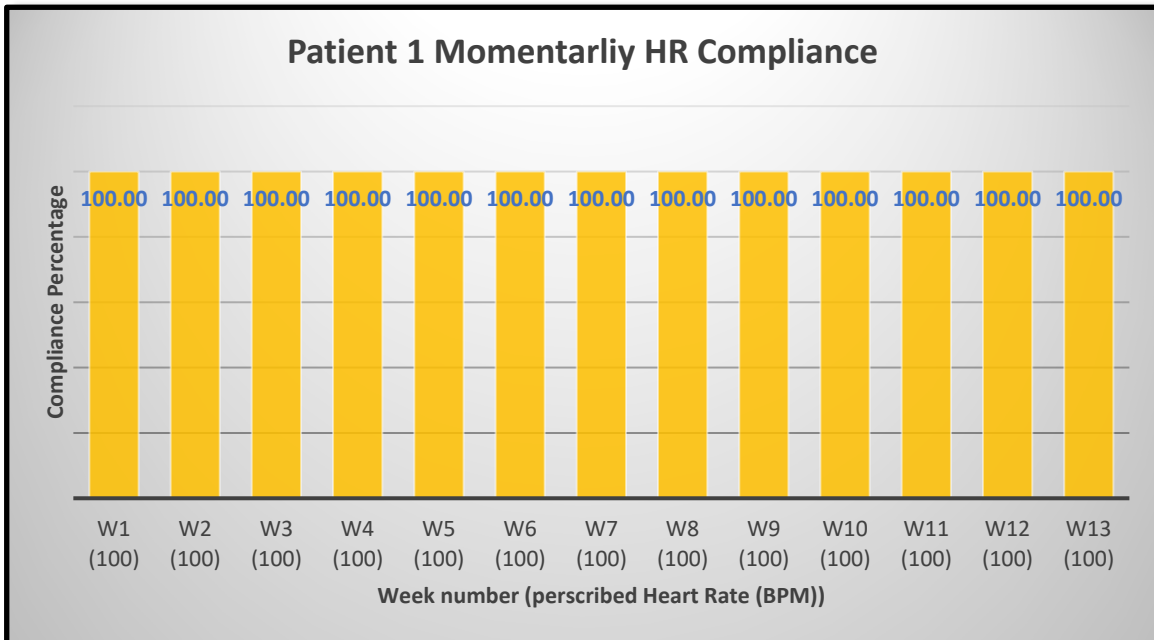


Figure 5.54: Patient#1 Momentarily Heart Rate Weekly Compliance, the week numbers are shown as W1, W2, etc., and the numbers in the parentheses below that are the prescribed heart rate for that week.

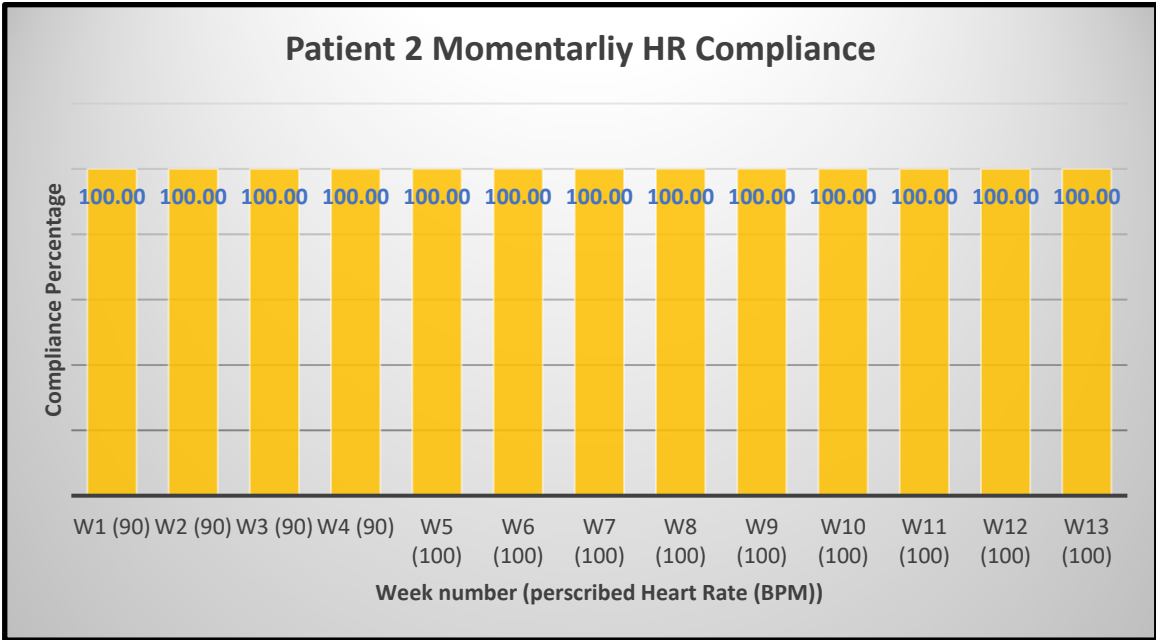


Figure 5.55: Patient#2 Momentariiy Heart Rate Weekly Compliance, the week numbers are shown as W1, W2, etc., and the numbers in the parentheses below that are the perscribed heart rate for that week.

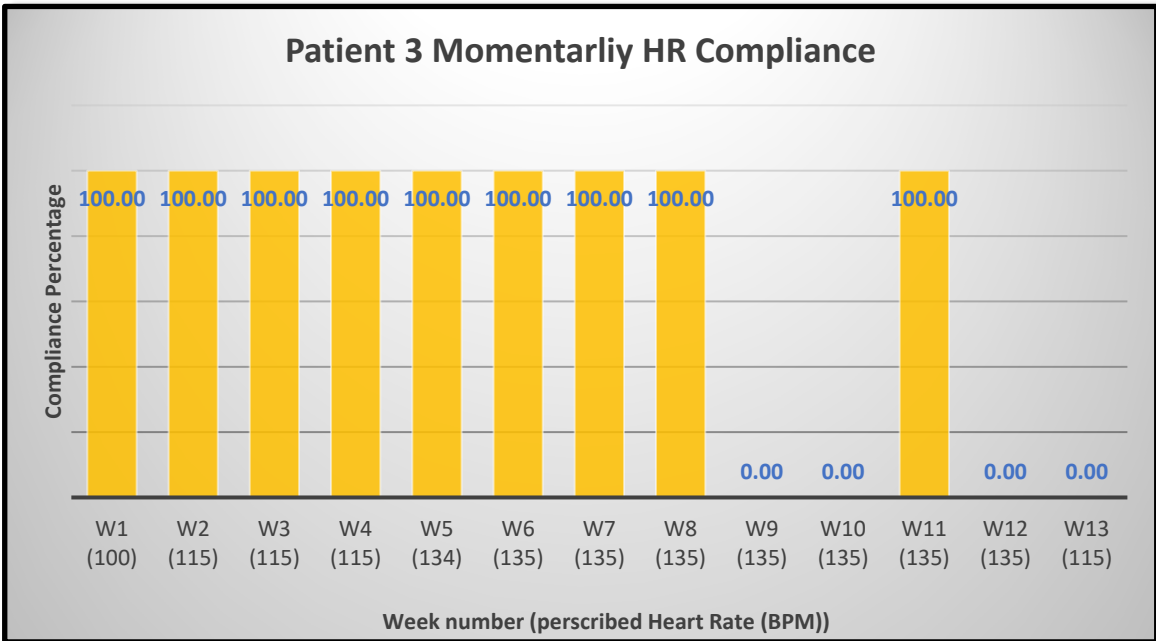


Figure 5.56: Patient#3 Momentariiy Heart Rate Weekly Compliance, the week numbers are shown as W1, W2, etc., and the numbers in the parentheses below that are the perscribed heart rate for that week.

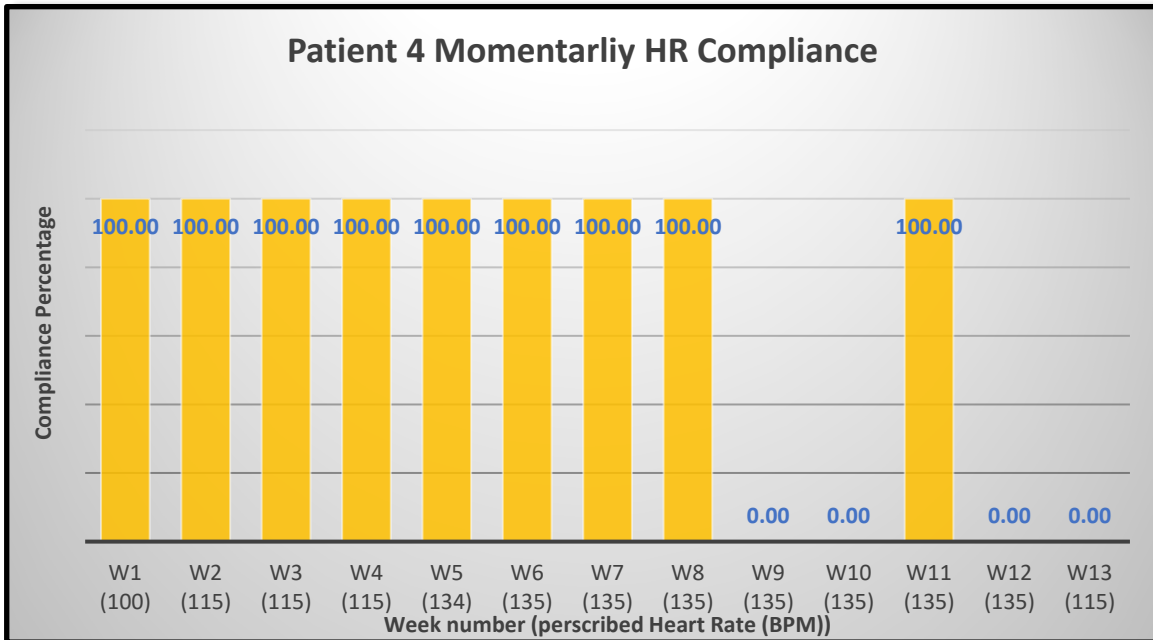


Figure 5.57: Patient#4 Momentarily Heart Rate Weekly Compliance, the week numbers are shown as W1, W2, etc., and the numbers in the parentheses below that are the prescribed heart rate for that week.

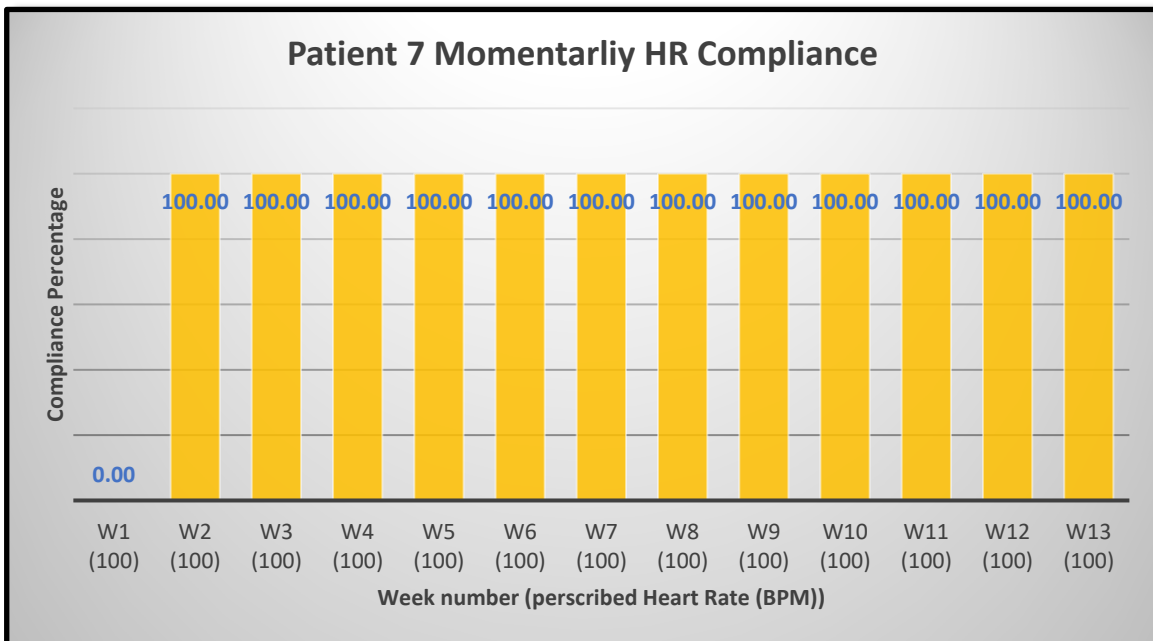


Figure 5.58: Patient#7 Momentarily Heart Rate Weekly Compliance, the week numbers are shown as W1, W2, etc., and the numbers in the parentheses below that are the prescribed heart rate for that week.

One-way ANOVA ( $\alpha = 0.05$ ) test was applied to the monthly Momentarily Heart rate Compliance metric to study the mean differences of average compliance for each month. No

statistically significant difference was found for the heart rate compliance over the three months, as all the p values were more significant than 0.05 (p=0.08).

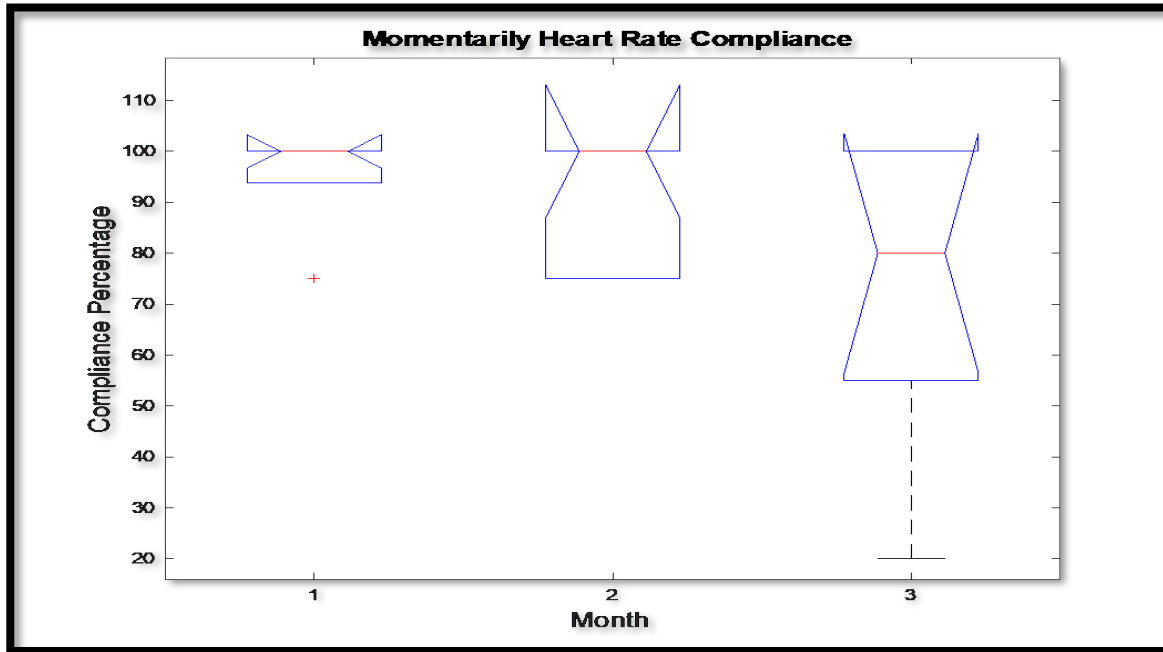


Figure 5.59: The Total Patient Average of Momentarily Heart Rate Compliance Box Plot for each month, the lowest black bar (lower whisker) represents the most insufficient compliance among all patients. The top black bar (higher whisker) represents the highest compliance value among all patients. The low blue bar represents the 25<sup>th</sup> percentile, and the top blue bar represents the 75<sup>th</sup> percent tile, and the medium red bar represents the median compliance value.

Table 5.11: Momentarily Compliance Box Plot Values

Momentarily Compliance Box Plot			
Box Plot Values	1 <sup>st</sup> Month	2 <sup>nd</sup> Month	3 <sup>rd</sup> month
Lowest Compliance (bottom whisker)	75	75	20
Highest Compliance (top whisker)	100	100	100
25th Percentile (lower blue line)	N/A	N/A	55
75th Percentile (upper blue line)	N/A	N/A	75
Median (Red line)	100	100	80

**Discussion:** The patients, in general, gained an average of 84.62% compliance level. That is, they reached the prescribed heart rate 84.62% of the time at least once. Observing the monthly overall



patient compliance, we observed that most of the patients gained Momentarily Heart Rate Compliance more than 70% over the 3-months. Only one patient (Patient number 3) achieved 0% compliance during the third month (Figure 5.54).

The patients with the highest rate for this compliance metric were patients' numbers 1 and 2. Both patients achieved 100% compliance according to this measure in all the exercise sessions that they performed. Patient number 3 and patient number 4 had the lowest compliance level as they both reached 69.23% in achieving the prescribed heart rate once in their performed exercise. However, patient number 7 gained 92.31%, despite being on Beta-blocker medicine.

The one-way ANOVA test showed no significant difference across the three months for the patients ( $p=0.08$ ). The box plot (Figure 5.60) showed no variations in the first and second months as the lowest compliance was 75%, and the highest is 100%. The lowest compliance for the third month was 20% percent, and the highest was 100%, and the median was 80% (Figure 5.60).

**Conclusion:** The patients showed an average of 84.62% compliance for the entire 3 months of the program. There was a decrease in monthly average compliance as it decreased from 94.44% for the 1<sup>st</sup> month to 73.33% for the 3<sup>rd</sup> month.

### ***5.3.3 Proposed Compliance Metrics by the PMT vs. Medical Team Pilot Study Home Exercise Compliance Metric Without the PMT***

Previously, our medical team conducted a pilot study in which the team recruited 9 participants and completed the program for the aerobic exercise training (AET) program. In addition, the team recruited 7 participants for the stretching and toning program (SAT). For the comparison, only results for AET participants are discussed here.

The participants were at least 6 months after their initial injury with mild to severe TBI and self-reported memory and executive impairment [27]. All the participants completed the baseline

assessments for AET [27]. In the study's AET group, each participant performed one in-person training session with a certified trainer at the beginning of the intervention, for the participant could self-confidently exercise by themselves with the appropriate use of HR monitoring at home, where all training activities logged in a specified log [27]. Throughout the study period, the participants were requested to perform the prescribed exercise, plus their regular daily activities, either at a local fitness center or at home [27]. To ensure the completion of the prescribed training programs, a research staff called the participants monthly [27]. When compliance to exercise programs were noticed to be less than the prescribed duration or frequency, additional in-person or telephone meetings were held to remove barriers to exercise and inspire participants to resume the program [27].

The average compliance was 70% for the participants who turned in training logs (7 participants), 40% to 91% (median 76%) for the AET group [27]. This compliance average was calculated by the ratio of the number of completed over prescribed exercise sessions in which participants achieved the target heart rate, even if it was momentarily [27].

The intensity, frequency, and duration of the AET program were constructed on each individual's maximal heart rate (HR) and gradually increased as participants adapted to workloads [27]. Participants were trained to increase progressively exercise intensity (from 50–60% to 70–80% of maximal HR) and duration from 60 minutes in the first week (20 mins x 3 days) to a total of 150 mins a week by the end of the fourth week (30 mins x 5 days or 50 mins x 3 days), then maintain this level for the remaining 8 weeks [27]. Each training session included 5-minute warm-up and 5-minutes cool-down periods [27]. Any aerobic exercise modes were allowed as long as the subject achieved the prescribed training dose [27].

In the present study, by taking the average of each proposed compliance metric for all patients, we compared each proposed compliance metric total average with the medical team pilot study compliance total average (Table 5.5). Also, we compared the lowest, highest and median compliances for each proposed metric with the lowest highest and median of the pilot study compliance lowest, highest, and median (Table 5.5).

*Table 5.12: Duration and Frequency Compliances and their Averages. Each compliance metric compared to the 70% of the average pilot study compliance, 76% median, highest 91%, and lowest 40%*

Patient Number	Heart Rate Compliance%	Duration Compliance%	Frequency Compliance%	Momentarily Heart Rate Compliance%
1	94.32	97.84	102.56	100.00
2	89.15	89.29	85.90	100.00
3	25.18	77.28	63.46	73.33
4	82.69	63.97	51.92	71.67
5	13.87	44.14	53.33	78.33
6	39.85	80.70	79.10	85.00
7	34.06	91.40	70.51	91.67
8	95.28	83.38	95.51	91.67
9	26.71	97.84	102.56	78.33
<b>Median</b>	39.85<76	83.38>76	79.10>76	85>76
<b>Highest</b>	95.28>91	97.84>91	102.56>91	100>91
<b>Lowest</b>	13.87<40	44.14>40	51.92>40	71.67>40
<b>Average</b>	55.68%<70%	80.64%>70%	78.32>70%	84.62%>70%

From Table 5.12 it can be seen that only the Heart Rate Compliance was less than the previous pilot study compliance. As we can observe, the median of the Duration Compliance, Frequency Compliance, and Momentarily Heart Rate Compliance are higher than the median of the pilot study Compliance and the highest, lowest, and average Compliance values.

### 5.7 Discussion

We used the WHO classification to categorize the patient compliance with applying the PMT system. The first category is complying patients, i.e., patients who comply both to the

number of training sessions prescribed and the duration of the prescribed cycle (e.g., the duration of a structured program) by at least 80%. The second category consists of non-compliant patients who comply <20% to the prescribed number of training sessions and their duration [145]. The third category corresponds to the partially compliant patients who perform the prescribed exercises but tend to neglect some of them or do not perform them for the prescribed duration [145].

*Table 5.13: Compliance Classifications for the Proposed compliance Metrics and number of patients at each classification*

Compliance Classification	Heart Rate Compliance (Patients)	Duration Compliance (Patients)	Frequency Compliance (Patients)	Momentarily Heart Rate Compliance (Patients)
Complying Patients ( $\geq 80\%$ )	4	6	4	5
Partially Compliant Patients ( $> 20\%$ )	4	3	5	4
Non-Comply Patients ( $< 20\%$ )	1	0	0	0

In our study, 100% of the participants completed the 3-month program. 3 out of the 4 compliance metrics had a compliance average higher than the pilot study compliance metric average. In Table 5.13, the values of each compliance were compared individually with 80% and 20% levels that WHO recommends. The results are not taking into account both the frequency of doing the exercise and other compliance measures. Based on the WHO classification of compliance, in the present study, 44% of the patients have complied, 44% are partially compiled, and 11% are non-compiled by the Heart Rate Compliance.

By the Duration Compliance, 66% are considered compiled patients, and 33% are partially compiled. Also, 44% are compiled patients, and 55% have partially complied patients for the frequency compliance. Finally, by the Momentarily Heart Rate Compliance, 55% are compiled patients, and 44% have partially complied patients.

Based on the compliance classification table (Table 5.13), the patients complied highly based on the Duration Compliance metric followed by the Momentarily Heart Rate Compliance. The next level was Frequency Compliance. The least level was the Heart Rate Compliance. Similarly, proposed compliance metrics showed higher compliance than the medical team's pilot study except for the Heart Rate compliance.

Based on the compliances metrics results, the PMT system helped the present study's patient group to increase their exercising level and maintain acceptable compliance level with most of the compliances metrics. Momentarily Heart Rate Compliance will always be higher or equal but not less than Heart Rate Compliance. If a patient maintained a high Heart Rate Compliance, they, as a result, would have high Momentarily Heart Rate Compliance.

A combination of compliances metrics results can be considered only if the therapist intent to assess the outcome measures of a treatment based on all the metrics target values. However, compliance combinations can vary based on the final objectives of the exercise interventions.

## **5.8 Conclusion**

In this chapter, we proposed 4 metric compliances applied to the outcome of the PMT system for exercise. Momentarily Heart Rate Compliance showed the highest compliance average, and the Herat Rate Compliance metric showed the least compliance average among all the patients. The compliance metric results showed that the PMT system has the potential to increase TBI patient physical exercise adherence. Some of the proposed compliances metrics can be predicted from one another, such as the Momentarily Heart Rate Compliance can be expected from the Heart Rate Compliance. A combination of the metrics can be considered based on the final objectives of the exercise interventions.

## CHAPTER 6

### PMT Effects on Heart Rate Variability Measurements

#### 6.1 Introduction

Heart rate variability (HRV) is a quantifiable measure of the fluctuations in the time interval between successive heartbeats [106]. HRV echoes neurocardiac function, heart-brain interactions generate it, and the dynamic nonlinear autonomic nervous system (ANS) processes it [106]. Further, HRV reflects the autonomic balance of blood pressure (BP), blood gas exchange, heart, and vascular tone. HRV metrics measure ANS imbalances. For instance, when the variations in the temporal position of the consecutive heartbeats are minor, a person perceives oneself in a fight-or-flight mode. However, when the changes in the temporal position of consecutive heartbeats are significant, a person is emotionally in a more relaxed state [147]. Additionally, some association between low HRV and worsening depression or anxiety has been demonstrated by several studies [147] [148]. A person will have a higher risk of death and cardiovascular disease with low HRV [149]. In the population of interest in this study, traumatic brain injury (TBI) patients, it has been shown that HRV is reduced [150].

This chapter will evaluate Apple Watch in estimating heart rate variability in traumatic brain patients pre and post exercises intervention using the PMT system. Then, we will study the difference in heart rate variability pre and post the exercises therapy interventions in TBI subjects using the PMT system.

## 6.2 Evaluation of Apple Watch in Estimating Heart Rate Variability Measures in Traumatic Brain Injury Patients

Several quantitative measures of HRV have been developed, and they can be categorized as time-domain, frequency-domain, and nonlinear measurements [106]. To compute these measures, the temporal locations of each successive two R peaks of the QRS complex obtained from an electrocardiogram recording (ECG) are identified. Then, the time interval between successive R peaks is measured and referred to as the RR interval. The resulting time series of the RR intervals are used for deriving both time-domain and frequency-domain measures [106]. Nonlinear measurement is usually used to quantify the unpredictability or stochastic nature of the time series [106]. In this study, only the time and frequency domain measures of HRV are considered. The nonlinear measures usually need at least a 24h ECG recording. Our recording was limited to 5 minutes; patient testing constraints would not permit more extended recording.

Apple Watch (AW), manufactured and marketed by Apple corporation in Cupertino, CA USA, can measure near-real-time heart rate. In our previous study of AW's cardiac monitoring capabilities, we had shown that AW has a high level of accuracy in measuring heart rate [6].

Therefore, studying the ability of the AW in measuring heart rate variability is the logical next step. In particular, the study of HRV in TBI patients is of interest because exercise can be beneficial in treating TBI patients [151], and such treatment may improve HRV in TBI patients

*Method-* Three time-domain measures of HRV were assessed by quantifying the variations in inter-beat intervals (IBI). IBI is defined as the elapsed time between consecutive heartbeats [106]. Specifically, the three time-domain measures of HRV that we considered were mean, standard deviation, and coefficient of variation of the IBI over a specified time epoch. We computed the time-domain HRV metrics as follows (Eqs. 1-3).

$$\overline{IBI} = \frac{\sum_{i=1}^N IBI_i}{N} \quad (1)$$

where,  $IBI_i$  is the  $i^{\text{th}}$ , interbeat interval  $\overline{IBI}$  is the mean of recorded IBI's,  $\sum_{i=1}^N IBI_i$  is the sum of the IBI's, and  $N$  is the number of IBI values.

$$\sigma_{IBI} = \sqrt{\frac{\sum_{i=1}^N |IBI_i - \overline{IBI}|^2}{N-1}} \quad (2)$$

where  $\sigma_{IBI}$  is the standard deviation of IBI's over the recording interval. In addition to the mean and standard deviation of IBI, the coefficient of variation of IBI was also computed as:

$$CV_{IBI} = \frac{\sigma_{IBI}}{\overline{IBI}} \quad (3)$$

There are multiple frequency-domain measures of HRV that have been proposed [106]. In this study, we focused on Four frequency-domain measures of HRV. The first considered frequency-domain measure is the sum of the absolute power values of IBI recording at a very low-frequency band range (VLF) of 0.0033–0.04 Hz. Hence, VLF reflects the oscillations in IBI, which have periods between 25 and 300 s. Next, the absolute power of IBI in the LF band range of 0.04–0.15 Hz is considered. This range contains patterns with periods between 7 and 25 s [106]. Finally, the absolute power of IBI in the frequency range of (0.15-0.4 Hz) is considered and referred to as high-frequency power. These bands are proposed by the Task Force of the European Society of Cardiology and by the North American Society of Pacing and Electrophysiology [152]. Using power spectral density (PSD), we computed the absolute power values for very low frequency (0.0033-0.04 Hz), low (0.04-0.15 Hz), and high frequency (0.15-0.4 Hz) range.

In a 5-min recording, there are potentially 12–45 complete periods of oscillation [106]. The HF which sometimes is referred to as respiratory band range, is 0.15–0.40 Hz and is affected by breathing frequency from 9 to 24 bpm [106]. The ratio of LF to HF power (LF/HF ratio) may



approximate the ratio of the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) activities under regulated conditions [106]

The HRV measurements in the frequency domain can be expressed in absolute or relative power [106]. Absolute power is computed as  $\text{ms}^2/\text{Hz}$  [105]. Relative power is approximated as the percentage of total HRV power or in normal units (nu), which is obtained by dividing the absolute power for a specific frequency band by the summed absolute power of the LF and HF bands [101]. The relative power metric allows one to evaluate and compare the frequency-domain HRV metrics for patients despite the wide variations in specific power bands and total power among them [106].

To evaluate the accuracy of AW in computing the HRV, we concurrently measured the heart rate by Apple Watch Series3 (Apple, Cupertino, CA USA), worn on the right wrist, and electrocardiogram (ECG) using Biopac MP 150 ECG system (BIOPAC Systems, Goleta, CA USA). While an internal program of the AW governs the AW the occurrence of the measurement of heart rate, the ECG device produced an analog waveform of ECG, which was sampled using the National Instrument NI-USB-6128 analog-to-digital converter (National Instruments, Austin, TX USA). The sample rate was 256 samples/s, and the ECG data were recorded using a Dell Latitude E640 laptop computer (Dell, Round Rock, TX USA) running a custom-made LabView program (National Instruments, Austin, TX USA) for the data acquisition.

The concurrent ECG and AW measurements were made over 5 minutes in 9 TBI patients with no known disabilities (7 males, 2 females, aged  $55.2 \pm 7.5$  years, BMI  $28.4 \pm 5.0$  lb./in<sup>2</sup>). Our institutional review board (IRB) approved the protocol for the study, and the subjects signed an informed consent form that our IRB also approved. During the measurement, the subjects were resting in a supine position. The data were stored and analyzed offline. The data collected by the AW were collected for offline analysis using our personal mobile trainer (PMT) ecosystem.

The recorded ECG waveform was analyzed to detect the QRS complex using a custom-made MATLAB program (version R2018; MathWorks, Natick, MA USA). Specifically, for each detected QRS complex, the R wave peak was automatically identified using a peak detection algorithm. A sample of the recorded ECG and detected peaks are shown in (Figure 6.61). The elapsed times between successive R peaks of the QRS complexes give the IBI values, and it is also called RR intervals. Since the heartbeats do not occur at regular intervals, the temporal instance of each RR interval value is not equidistant from one another. We interpolated between the recorded instances of heartbeats to obtain a uniform sample representation of RR intervals for further analysis. The interpolation was performed using a cubic spline interpolation method which is available in MATLAB software. The sample rate for the interpolated RR intervals was 256 samples/s.

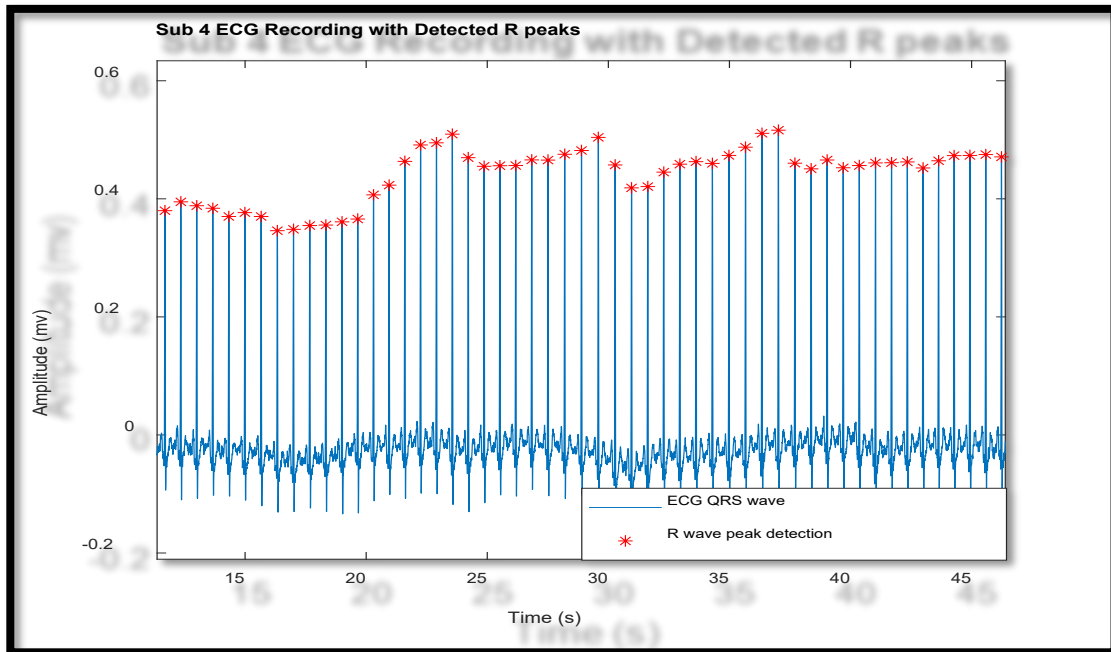


Figure 6.60: Patient 4 ECG recording with R peak detection. The blue waveform is the recorded ECG QRS waveform, and the red stars are the detected R peaks

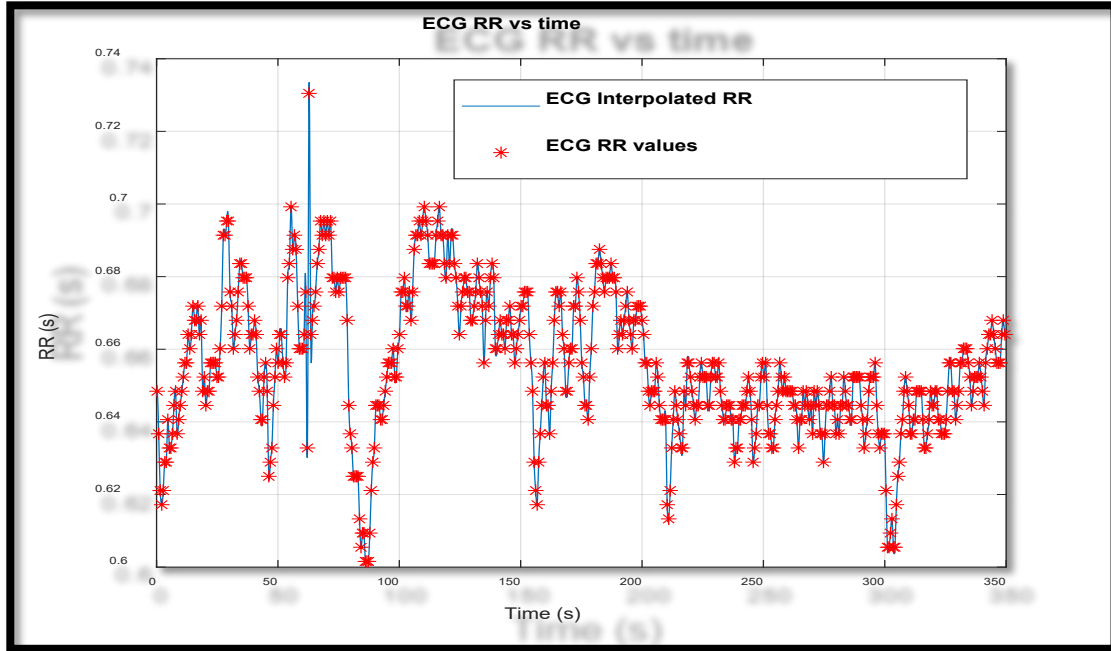


Figure 6.61: Patient 4 ECG RR values and their interpolation, the blue waveform is the ECG interpolated RR values, and red stars are the ECG RR values

Similarly, the heart rates captured by the AW were also recorded at irregular intervals as dictated by the internal algorithm of the AW. To estimate the RR intervals from the recorded AW heartrates, we converted the RR interval associated with each recorded heart rate by the following formula:

$$\text{Apple RR} = \frac{60}{\text{Apple HR}} \quad (4)$$

These values were also interpolated and resampled using the same interpolation method applied to the ECG-derived RR intervals to attain uniform sampling. Examples of interpolation of the RR intervals derived from ECG and estimated from AW are shown in Figure 6.62 and Figure 6.63, respectively.

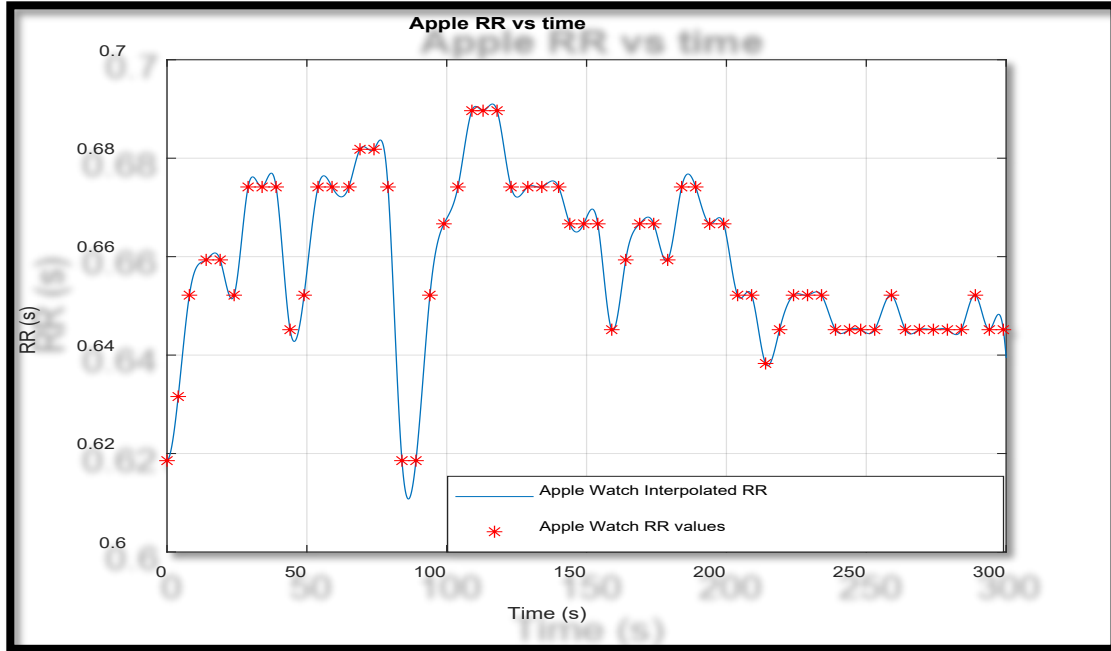


Figure 6.62: Patient 4 Apple RR values and their interpolation

The time-domain and frequency-domain measures of HRV were extracted using the Apple-Watch-recorded heart rate and the concurrently recorded corresponding ECG waveforms. Specifically, we computed the mean, standard deviation, and coefficient variation for the ECG-measured and AW-measured IBI's for the time-domain measures. To calculate the frequency domain measures of HRV, we obtained the power spectral density (PSD) of the interpolated RR intervals extracted from AW and ECG. Next, the magnitude of the power in three frequency bands was considered: 1) very-low-frequency (VLF); 2) low-frequency (LF); 3) high-frequency (HF) bands [152]. Further, we also examined the ratio of the absolute power in LF to the total power in HF.

Using the time-domain and frequency-domain measures of HRV obtained from ECG recording as gold standards, we performed a two-tail Wilcoxon rank-sum test on the mean of metrics to examine the equivalency of these measures. Further, we applied the Bald-Altman (B&A) as mentioned in Ch.2 Section 2.1. Analysis of these HRV metrics to ascertain the

agreement of the HRV metrics derived from the recorded AW heart rates and their corresponding values obtained from the concurrently recorded ECG data.

For B&A plots, the average of each pair's values of Apple HRV and ECG HRV measures is shown on the x-axis and the difference between the pair values on the y-axis. The bias (B) and limits of agreement (LOA) were calculated as mentioned in (Ch.2 Section 2.1 Equation 2 and Equation 3)

*Comparison of HRV Metrics Derived From AW and ECG-* Table 6.14 displays the mean  $\pm$  one standard deviation of the time and frequency-domain metrics obtained from the patients' data pre- and post-intervention. It is noted that the comparisons reported in Table 6.1 reflect the comparison between AW and ECG and not the effect of the exercise on the HRV metrics. The results of the exercise on the HRV metrics are discussed in section 6.3 of this chapter. Figure 6.64 and Figure 6.65 show the B&A plot of the RR interval values obtained from the ECG and those estimated from the AW heart rate measurement pre- and post-intervention. Figure 6.66-Figure 6.71 shows B&A plot for comparison of the pre-intervention for time-domain HRV metrics as obtained from ECG and estimated from the AW measurements. Representative plots of the power spectral density of the RR intervals extracted from ECG and the RR intervals estimated from AW are shown in Figure 6.72 and Figure 6.73, respectively. The B&A plot for assessing the similarity of frequency-domain HRV metrics obtained from pre- and post-intervention ECG recordings and estimated from AW heart rate measurements are shown in Figure 6.74-Figure 6.81.

Table 6.14: 2-tail Wilcoxon rank-sum test ( $\alpha=0.05$ ) results for the mean and standard deviation of HRV metric derived from ECG and AW. The comparison is made for the measurements by these devices at the time of data collection, both for pre and post-intervention.

	<b>HRV Metric</b>	<b>Time</b>	<b>ECG (Mean±SD)</b>	<b>AW (Mean±SD)</b>	<b>P-value</b>
<b>1</b>	SD of RR (ms)	Baseline*	30±10	20±10	0.01
<b>2</b>		Post-Intervention	40±20	30±20	0.34
<b>3</b>	Mean of RR (ms)	Baseline	870±20	880±10	0.80
<b>4</b>		Post-Intervention	880±16	880±16	0.95
<b>5</b>	SDRR Coeff. of Variation %	Baseline*	40±10	30±10	0.03
<b>6</b>		Post-Intervention	5.00±2.00	4.00±2.00	0.30
<b>7</b>	VLF (ms <sup>2</sup> )	Baseline	0.88±0.62	0.71±0.50	0.50
<b>8</b>		Post-Intervention	1.4±1.44	1.4±1.62	0.88
<b>9</b>	LF (ms <sup>2</sup> )	Baseline*	0.53±0.42	0.13±0.12	0.04
<b>10</b>		Post-Intervention*	0.70±0.97	0.1±0.1	0.01
<b>11</b>	HF (ms <sup>2</sup> )	Baseline*	0.16±0.09	0.00±0.00	<0.05
<b>12</b>		Post-Intervention*	0.20±0.26	0.00±0.01	<0.05
<b>13</b>	LF/HF	Baseline*	3.65±2.30	31.7±11.25	<0.05
<b>14</b>		Post-Intervention*	5.21±8.78	32.8±19.8	<0.05

\* The ECG-derived metric is significantly different from the Apple-Watch-derived metric ( $\alpha=0.05$ )

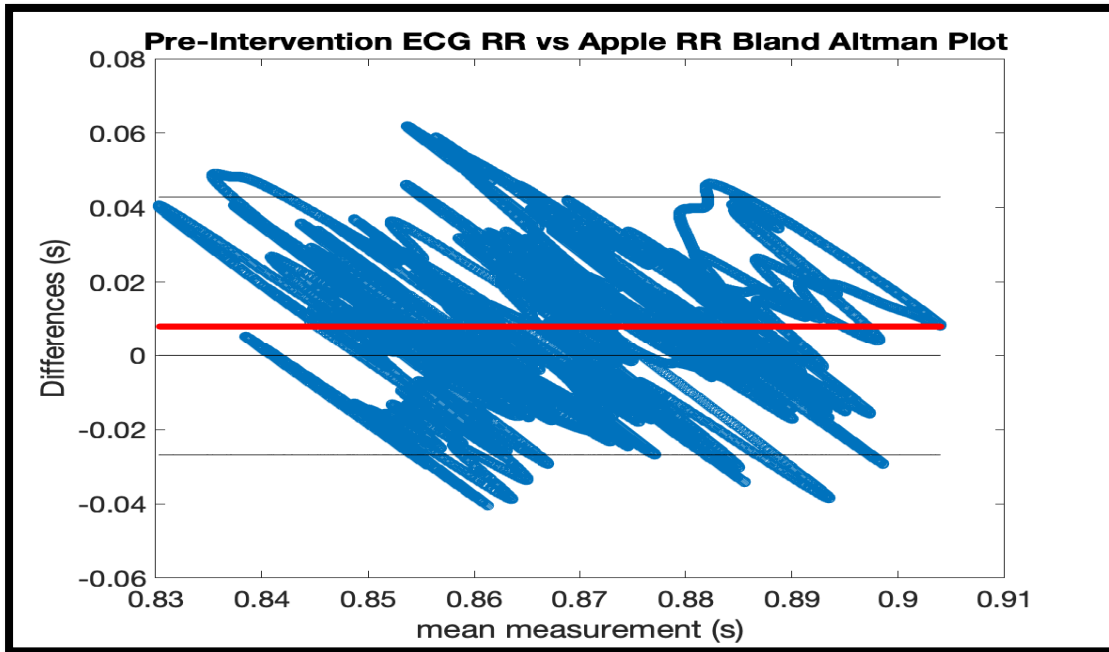


Figure 6.63: ECG-RR and Apple-RR pre-intervention B&A plot for all subjects (values shown are for 77064 sample points from the interpolated data). The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA: Bias  $\pm 1.96SD$  (Ch.2, Eq. 2)

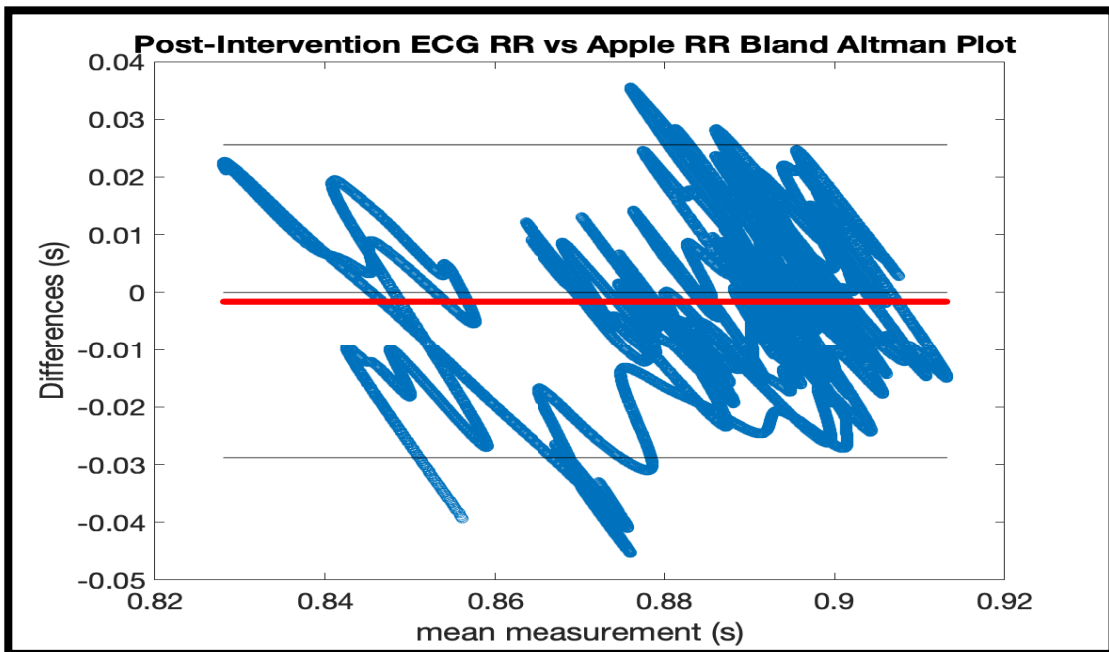


Figure 6.64: ECG-RR and Apple-RR post-intervention B&A plot for all subjects (values shown are for 77064 sample points from the interpolated data). The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA: Bias  $\pm 1.96SD$  (Ch.2, Eq. 2)

***Discussion of the Results of Comparing HRV Metrics Obtained from AW with those Obtained from ECG-*** Examination of the SD of RR intervals for pre- and post-intervention obtained from ECG with the SD of the estimated RR intervals from AW (i.e., rows 1 and 2 in Table 6.14) reveals that the AW estimate is not statistically the same as ECG. It is believed that this is due to infrequent sampling of the heart rate by the AW. The rate of obtaining the RR sample by the AW was  $0.88 \pm 0.01$  s for pre-intervention and  $0.88 \pm 0.16$  s for post-intervention. Indeed, when a subject wearing the watch is experiencing stable heart rate, as is the case for our subjects resting in a supine position during the recording, the watch lowers the frequency of recording the heart rate. However, the mean of RR values obtained from the watch for pre- and post-interventions (i.e., rows 3 and 4 of Table 6.14) is statistically not significantly different from that of the ECG. When these results (rows 1,2,3 and 4 of Table 6.14) are taken together, it indicates that while there are larger oscillations in RR values measured using ECG, the absence of these oscillations in the AW estimate of RR -due to infrequent sampling of the watch – does not lead to a significant difference in the estimate of the heart rate. Consequently, the significant difference observed in the coefficient of variations (rows 5 and 6 of Table 6.14) is expected, as variance values (rows 1 and 2 of Table 6.14) are significantly different even though the means are not.

In many studies, HRV is calculated over 24 hours. Hence, the recording contains short-term high-frequency changes and the lowest-frequency components observed in a 24-hour interval [153]. As the period of monitoring decreases, SDRR estimates shorter and shorter cycle lengths. In addition, the total variance of HRV increases with the length of the analyzed recording [153]. Therefore, ideally, the measures of HRV should be obtained from a 24-hr recording. However, this is not feasible for many clinical applications, including the one reported here. However, it has



been reported that a 5-min recording can be used to obtain reasonable estimates of HRV when the subjects are breathing at a normal breathing rate (11-20 breath/min) [154].

The preliminary results of this study suggest that the mean of the estimate of VLF for pre and post interventions (rows 7 and 8, Table 6.14) obtained from AW are not significantly different from the ones extracted from ECG. However, for LF, HF, and LF/HF (rows 9-14 Table 6.14), the estimates from AW are statistically different from the corresponding values obtained from ECG.

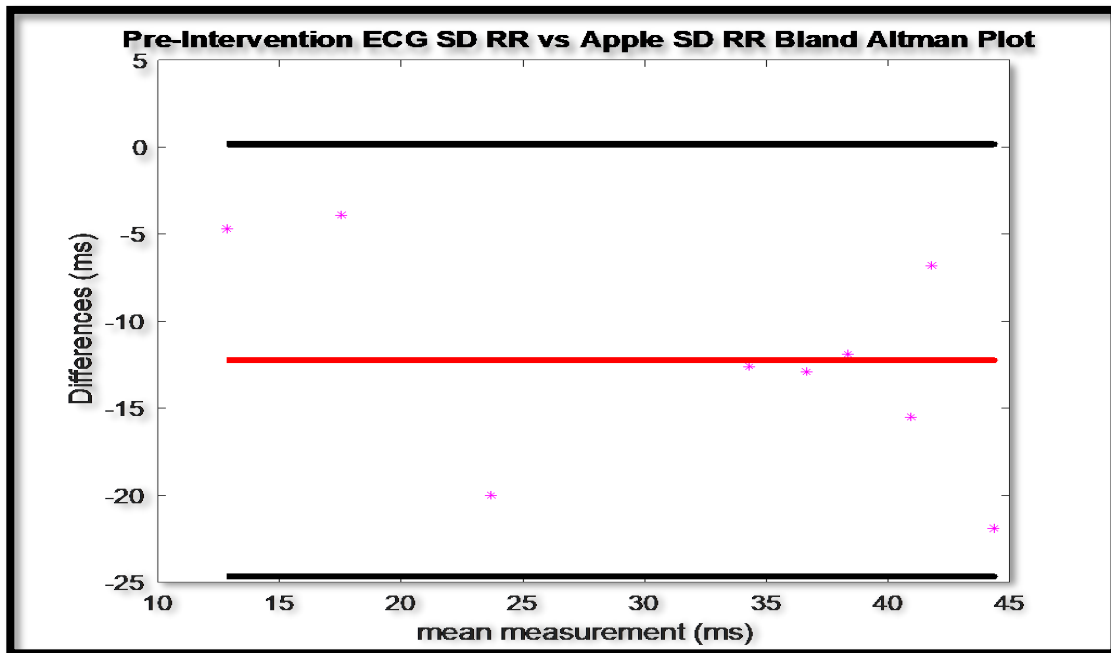


Figure 6.65: Pre-intervention means ECG SDRR and Mean Apple SDRR B&A plot for all subjects. The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA: Bias $\pm$ 1.96SD (Ch.2, Eq. 2)

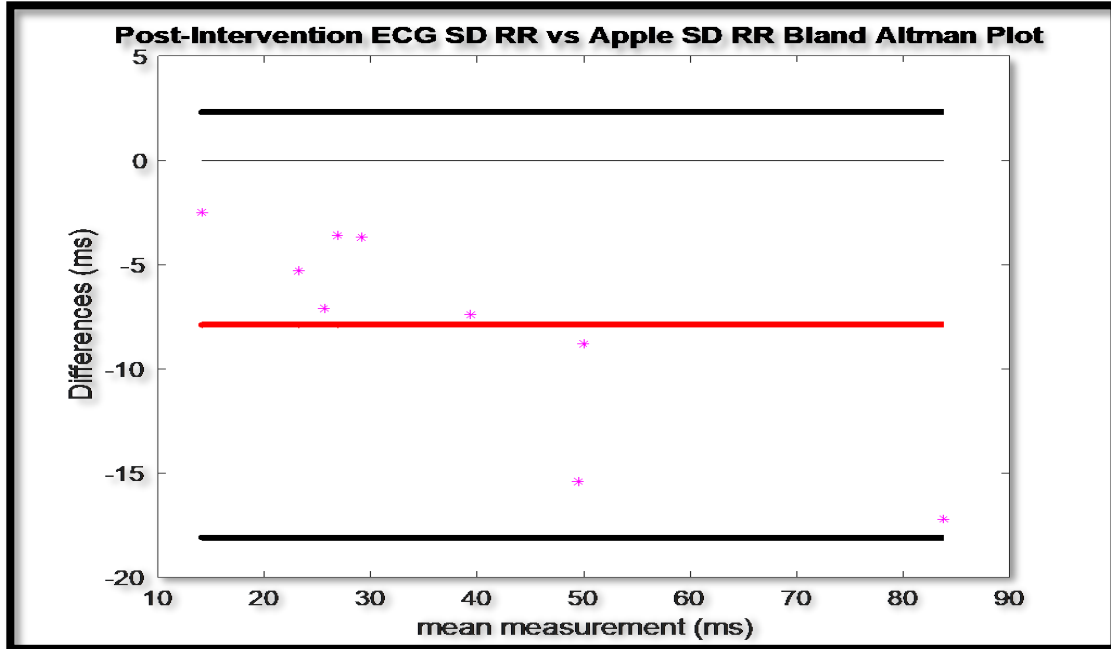


Figure 6.66: post-intervention means ECG SDRR and Mean Apple SDRR B&A plot for all subjects. The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA:  $Bias \pm 1.96SD$  (Ch.2, Eq. 2)

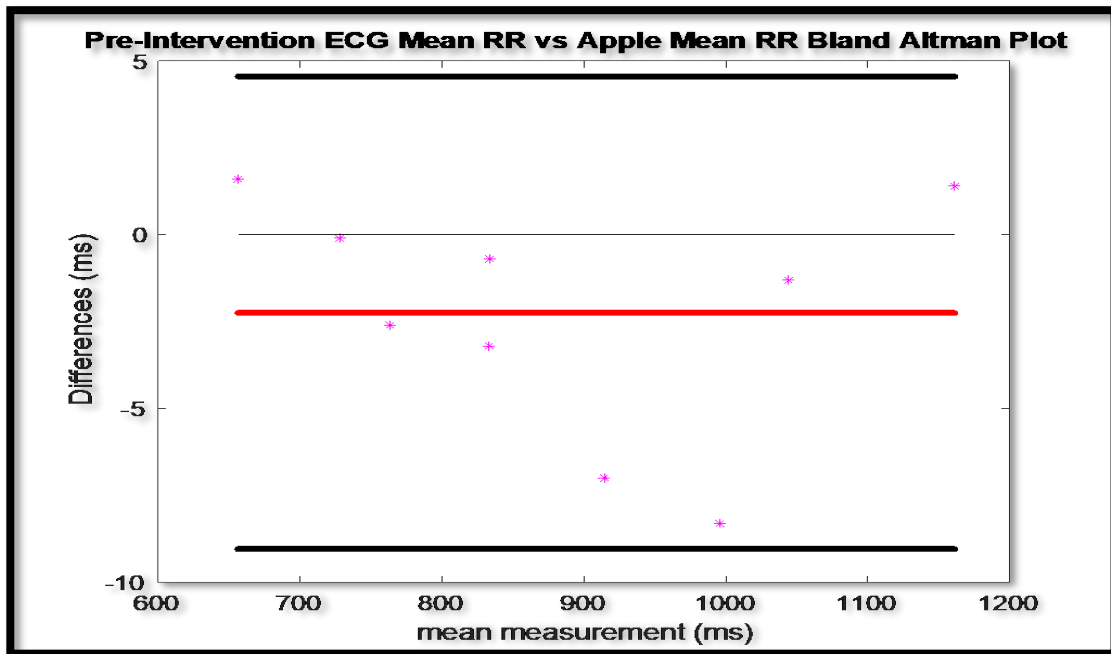


Figure 6.67: pre-intervention means ECG RR and Mean Apple RR B&A plot for all subjects. The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA:  $Bias \pm 1.96SD$  (Ch.2, Eq. 2)

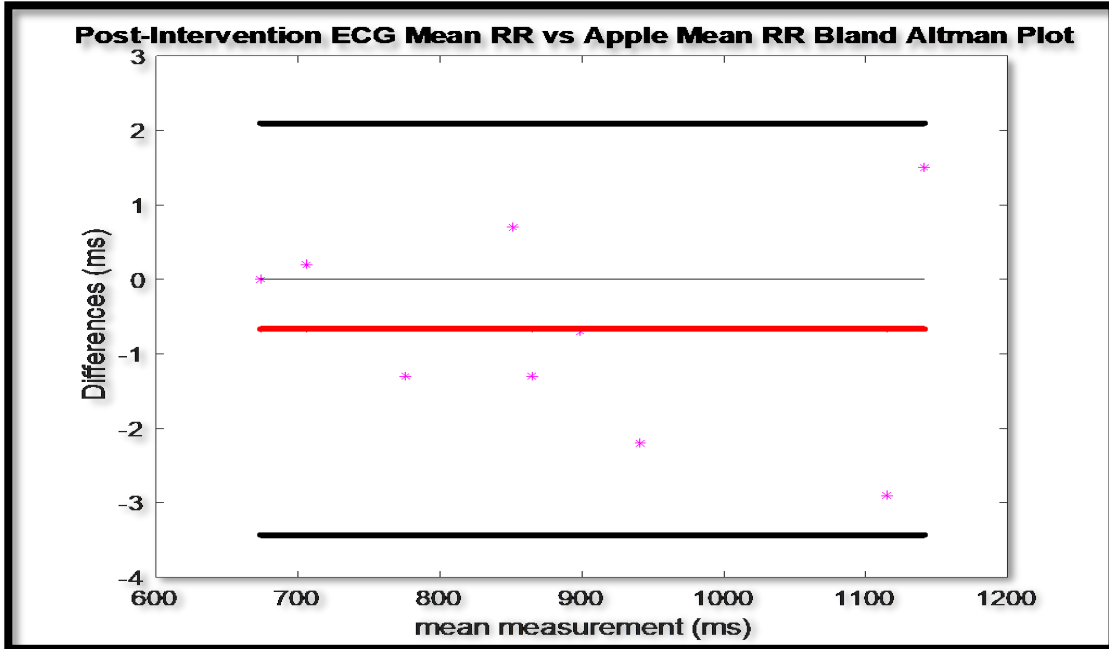


Figure 6.68: Post-intervention means ECG RR and Mean Apple RR B&A plot for all subjects. The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA:  $Bias \pm 1.96SD$  (Ch.2, Eq. 2)

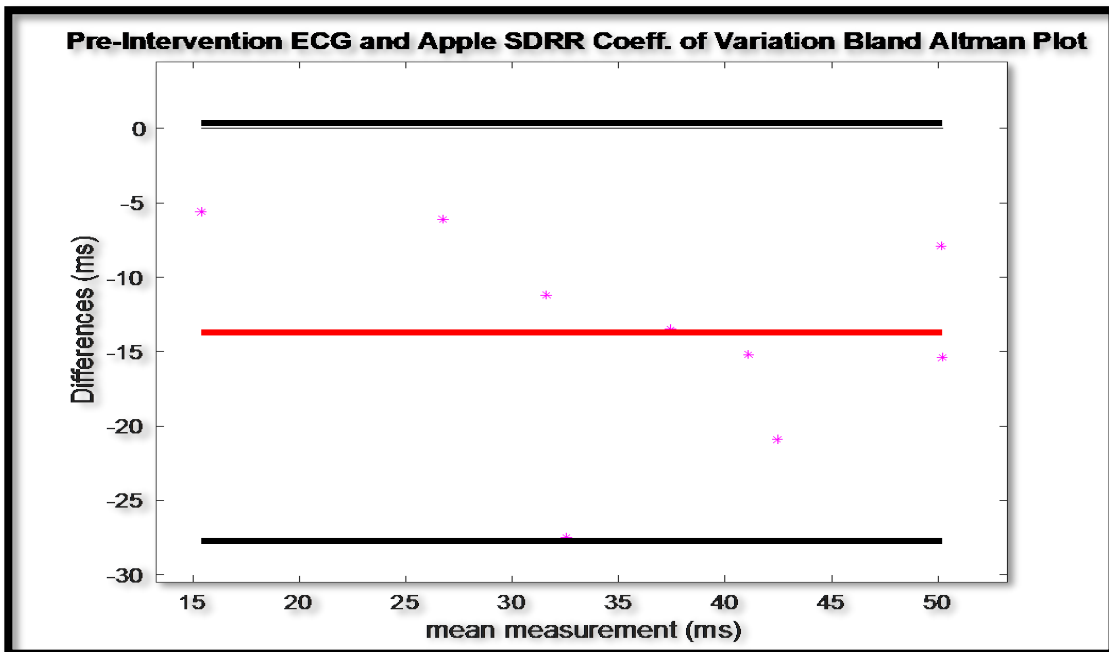


Figure 6.69: Pre-intervention ECG and Apple SDRR coefficient of variation B&A plot for all subjects. The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA:  $Bias \pm 1.96SD$  (Ch.2, Eq. 2)

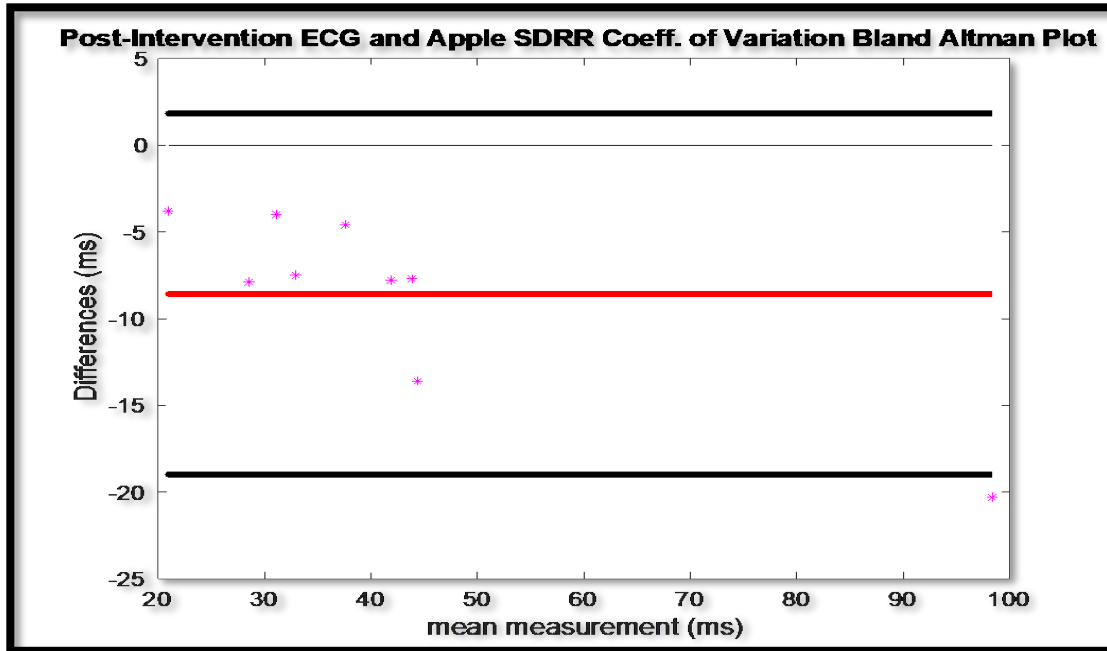


Figure 6.70: Post-intervention ECG and Apple SDRR coefficient of variation B&A plot for all subjects. The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA:  $Bias \pm 1.96SD$  (Ch.2, Eq. 2)

Based on the outcome of comparing the mean of the time-domain and frequency-domain metrics considered in this study (Table 6.14), only the mean of RR (rows 3 and 4 of Table 6.14) and VLF (rows 7 and 8 Table 6.14) can be useful in estimating the HRV from the AW recordings. Referring to B&A plots for these two metrics in Figure 6.68-Figure 6.75, one can observe these metrics exhibit similarity, as they fall within the LOA boundaries. It is likely that the low sample rate of the heart rate by the AW in resting supine position misses capturing higher frequency oscillation in RR interval and creates the disparity between AW measurements and the ECG-derived HRV metrics.

Indeed, in a study of simultaneous recording of ECG and AW in healthy subjects who got seated after walking, a more significant agreement between the ECG recordings and AW-extracted HRV was obtained [154]. In that study, the AW recording of the heart rates was more frequent than in the present study, as the recorded heart rate was more transient than in the supine position.

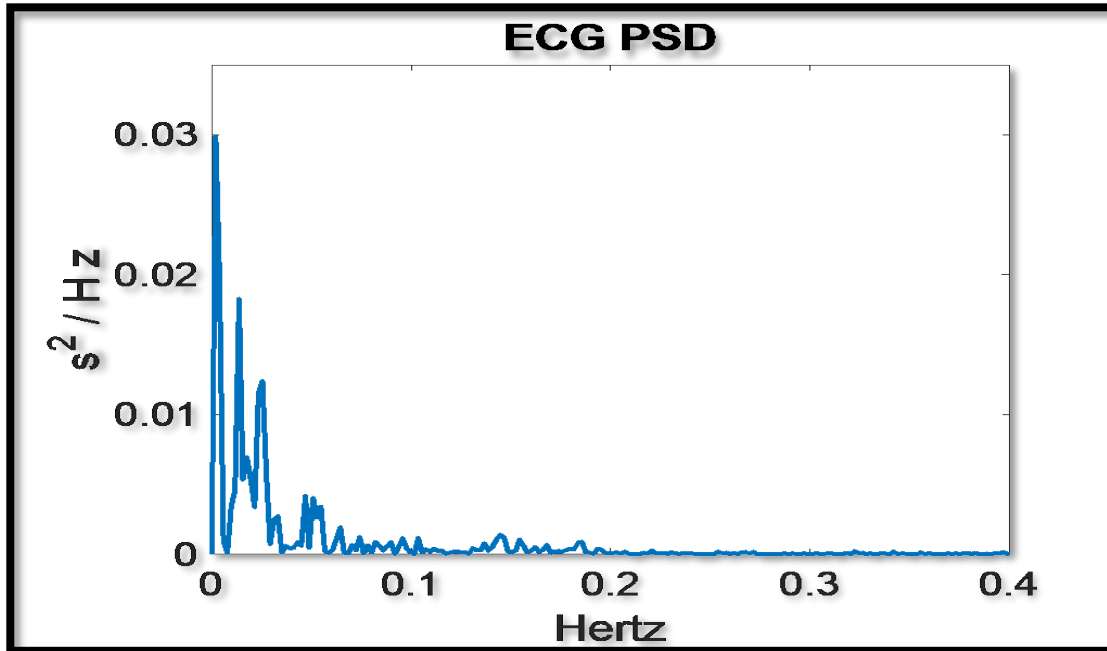


Figure 6.71: Patient No.4 Pre-intervention ECG power spectrum density plot

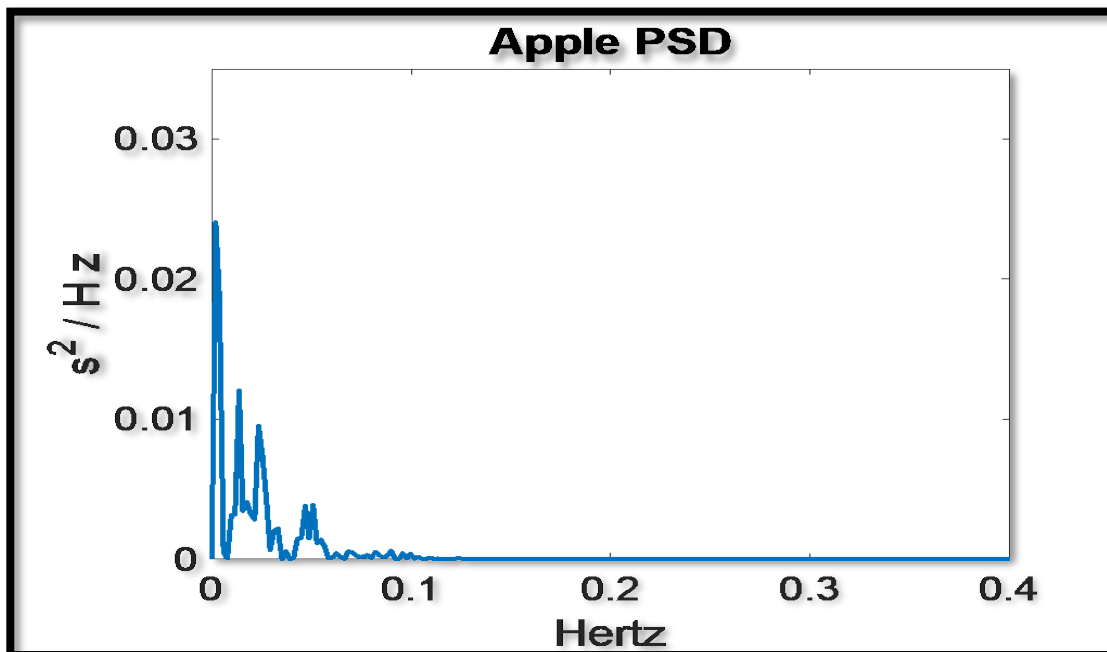


Figure 6.72: Patient No.4 Pre-intervention AW power spectrum density plot

At this time, the frequency of sampling of heart rate by AW is not controllable by the user. Suppose in the future models of AW; it becomes possible to increase the heart rate measurement frequency; in that case, it may be possible to improve the accuracy of estimating AW's HRV metrics.

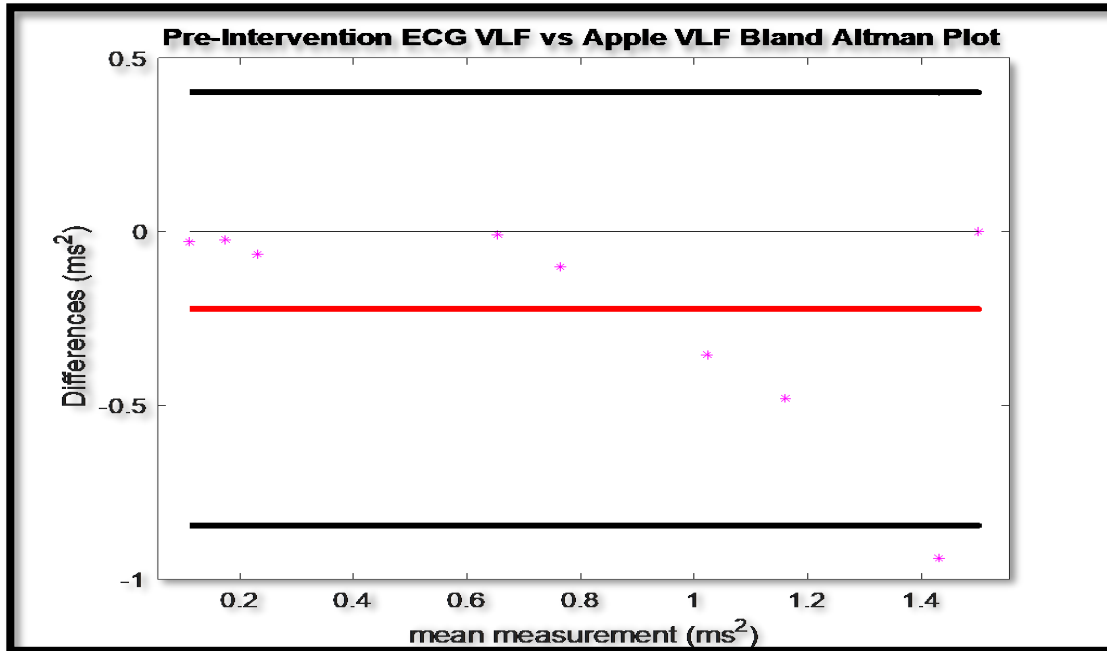


Figure 6.73: Pre-intervention ECG and Apple very-low-frequency HRV B&A plot. The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA: Bias $\pm$ 1.96SD (Ch.2, Eq. 2)

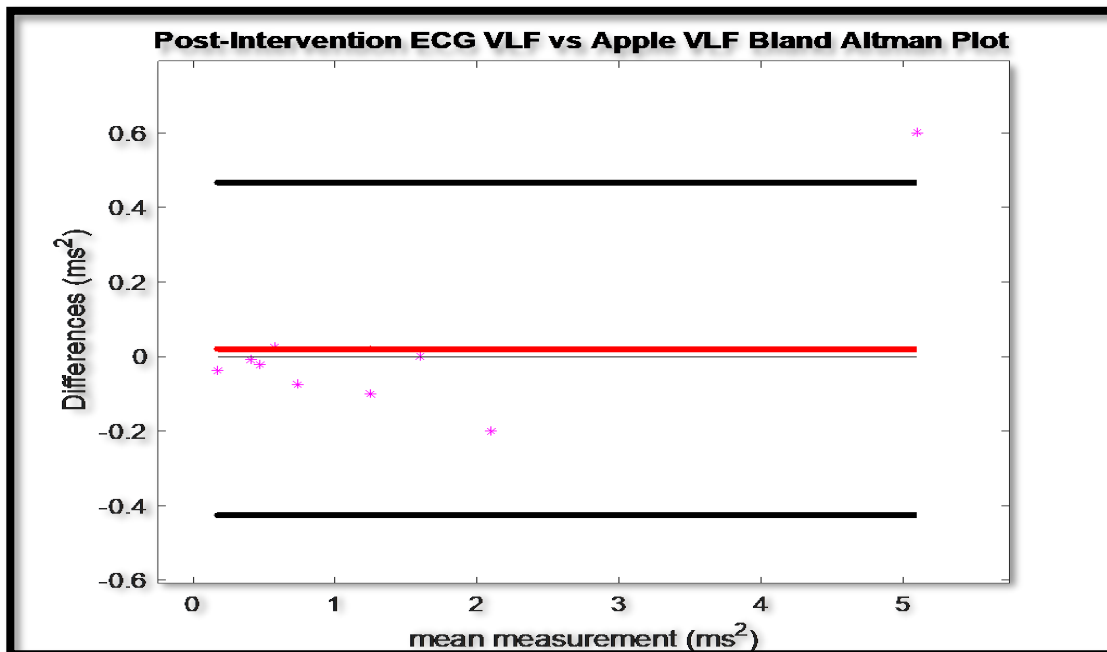


Figure 6.74: Post-intervention ECG and Apple very-low-frequency HRV B&A plot. The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA: Bias $\pm$ 1.96SD (Ch.2, Eq. 2)

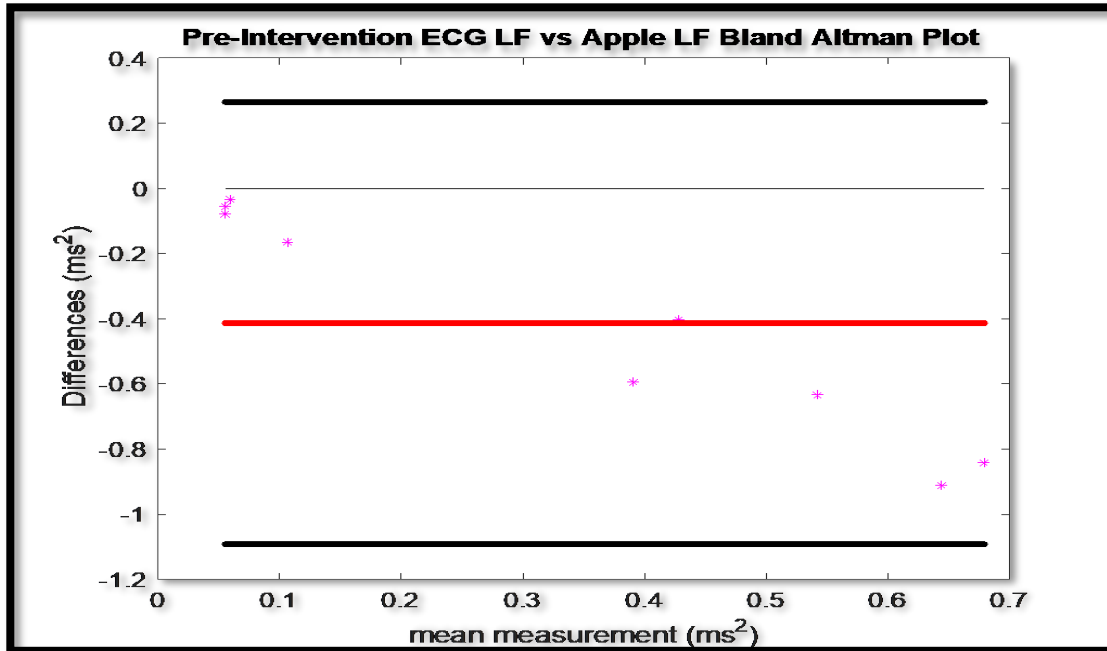


Figure 6.75: Pre-intervention ECG and Apple low-frequency HRV B&A plot. The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA:  $Bias \pm 1.96SD$  (Ch.2, Eq. 2)

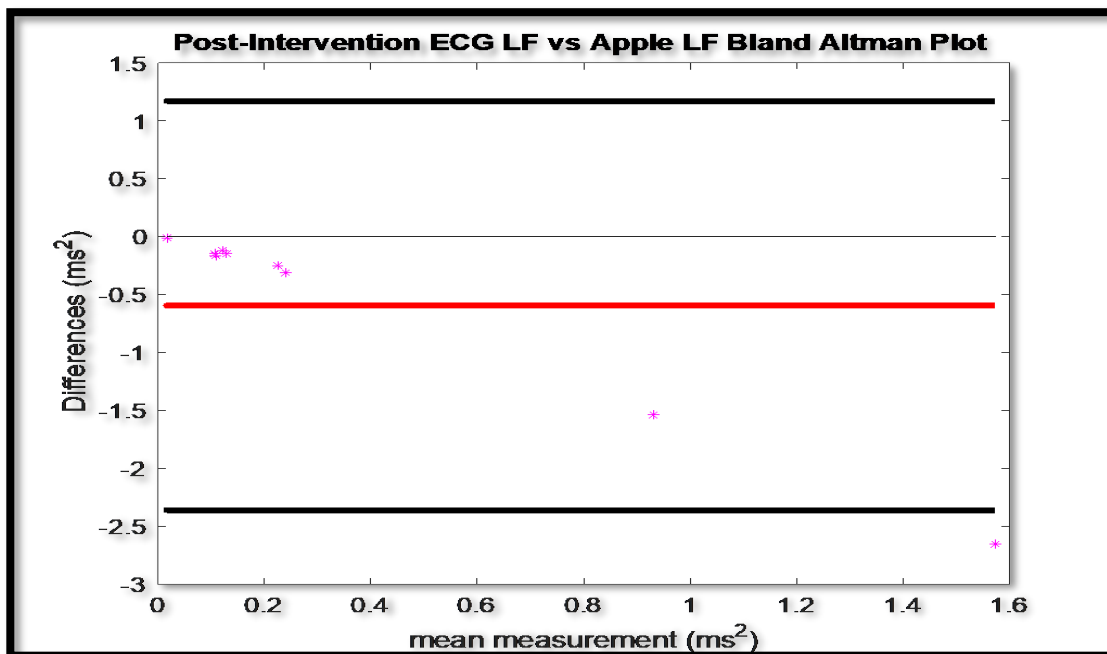


Figure 6.76: Post-intervention ECG and Apple low-frequency HRV B&A plot. The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA:  $Bias \pm 1.96SD$  (Ch.2, Eq. 2)

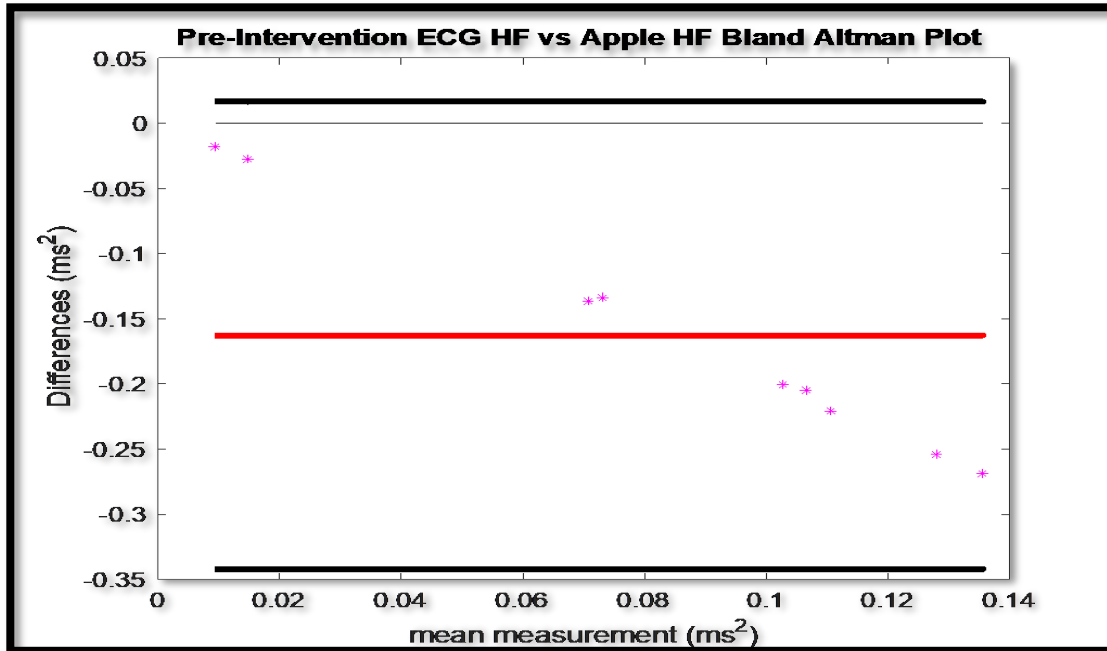


Figure 6.77: Pre-intervention ECG and Apple high-frequency HRV B&A plot. The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA:  $Bias \pm 1.96SD$  (Ch.2, Eq. 2)

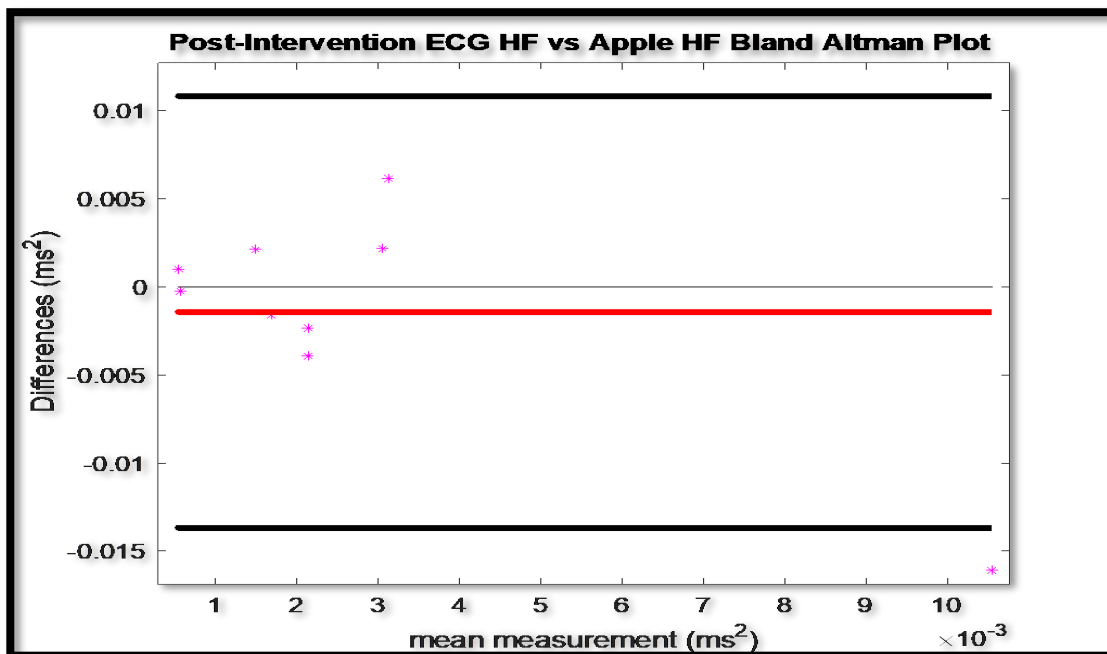


Figure 6.78: Post-intervention ECG and Apple high-frequency HRV B&A plot. The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA:  $Bias \pm 1.96SD$  (Ch.2, Eq. 2)



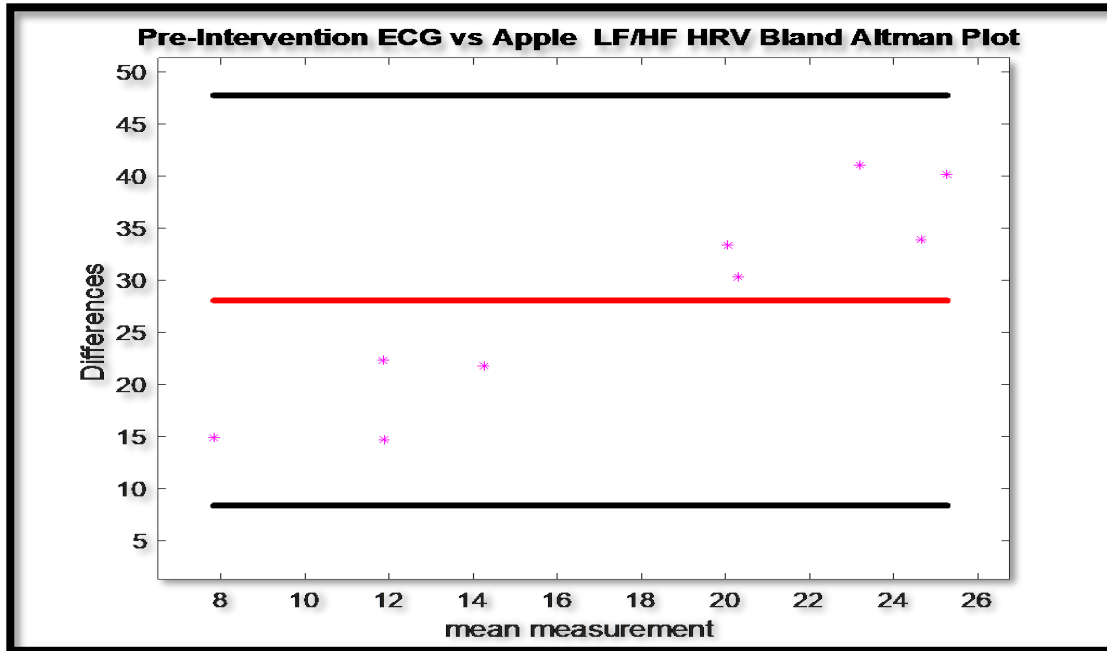


Figure 6.79: Pre-intervention ECG and Apple low-frequency/high-frequency HRV B&A plot. The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA:  $Bias \pm 1.96SD$  (Ch.2, Eq. 2)

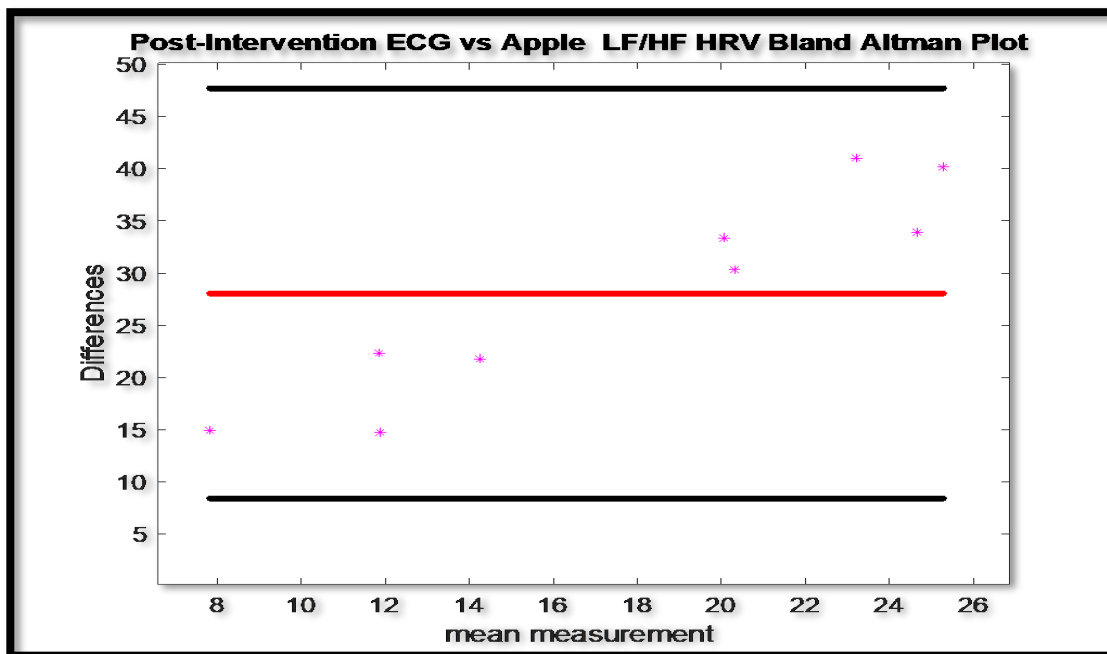


Figure 6.80: Post-intervention ECG and Apple low-frequency/high-frequency HRV B&A plot. The middle red line shows the Bias (Ch.2, Eq. 1), and the top & bottom black lines represent the LOA:  $Bias \pm 1.96SD$  (Ch.2, Eq. 2)

**Conclusion-** Based on the result of this study, the standard deviation of the RR intervals obtained from the AW does not fully predict the measures by the ECG. Additionally, among the four heart

rate variability metrics considered in this study, only the frequency-domain very-low-frequency power (VLF) appears to reasonably estimate the VLF power computed from ECG. The lack of accuracy could be due to the watch's low sampling rate when the user is resting.

### **6.3 Measuring the Changes in HRV, Post Physical Exercise Interventions Using the PMT System, Compared to Baseline**

Several studies have confirmed the existence of an association between higher resting HRV and active inhibitory prefrontal-subcortical circuits [102] [103] [155]. In particular, higher resting-state HRV appears to be related to increased activity in executive brain regions [156], while lower resting HRV seems to be related to hypoactive prefrontal regulation [157] [158]. As A Result, a vagal control of the heart appears to be correlated with the effective functioning of self-regulatory neural circuits, which allow the organism to respond quickly and flexibly to environmental demands [102] [156] [103] [159].

Therefore, with high compliance to physical exercises activities, one may expect that the resting heart rate variability of the participants should increase after the intervention of the prescribed physical exercise.

Method of Measuring the Changes in HRV, Post Physical Exercise Interventions Using the PMT System, Compared to Baseline - We applied a similar approach to that we used in section 6.1 to collect the heart rate variability measurements. The patients had heart rate tests while sitting, pre-physical exercises intervention, and post the exercises intervention.

To observe any change to HRV by performing an exercise, we calculated the mean and standard deviation of the patient's HRV metrics; then, we examined them for any increase in the mean of the measurements between pre-intervention and post-intervention.

***Results of Measuring the Changes in HRV, Post Physical Exercise Interventions Using the PMT System, Compared to Baseline***

2 tail Wilcoxon rank-sum test ( $\alpha=0.05$ ) between HRV metrics for pre and post 3 months of exercise interventions conducted. Table 6.2 illustrate P-value results for the two-tail Wilcoxon rank-sum test between pre and post 3 months of exercise interventions. Then we plotted ECG and Apple standard deviation of the RR for all patients before and after 3-months of exercise intervention, as is represented in Figure 6.82. Then Figure 6.83 shows ECG and Apple mean RR for all patients before and after the exercise intervention for 3-months. After that, Figure 6.84 represent ECG and Apple Watch pre-and post-intervention RRSD coefficient of variation, a time-domain heart rate variability metric, for all patients

*Table 6.15: 2-tail Wilcoxon rank-sum test ( $\alpha=0.05$ ) results for HRV metric derived from ECG pre- vs. post-intervention and AW pre vs. post-intervention.*

HRV Metric	Device	P-Value (Pre vs. Post)
SD of RR	ECG	0.94
	Apple Watch	0.55
Mean of RR	ECG	0.93
	Apple Watch	0.93
SDRR Coeff. of Variation	ECG	0.60
	Apple Watch	0.43
VLF	ECG	0.60
	Apple Watch	0.50
LF	ECG	0.98
	Apple Watch	0.70
HF	ECG	>0.05
	Apple Watch	>0.05
LF/HF	ECG	>0.05
	Apple Watch	>0.05

\* The ECG-derived metric is significantly different from the Apple-Watch-derived metric ( $\alpha=0.05$ )

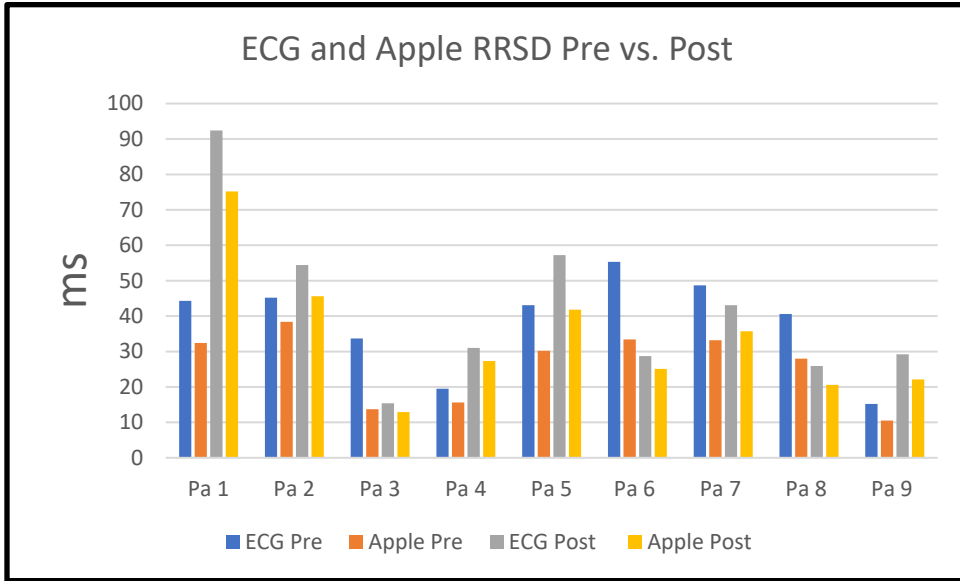


Figure 6.81: ECG and Apple Watch pre-and post-intervention RR standard deviation, a time-domain heart rate variability metric, for all patients

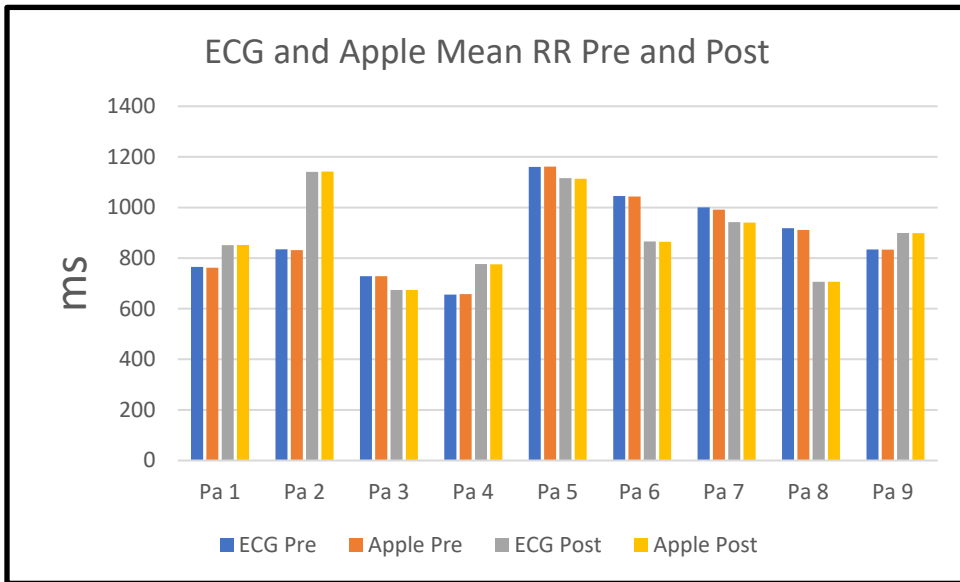


Figure 6.82: ECG and Apple Watch pre-and post-intervention mean RR, a time-domain heart rate variability metric, for all patients

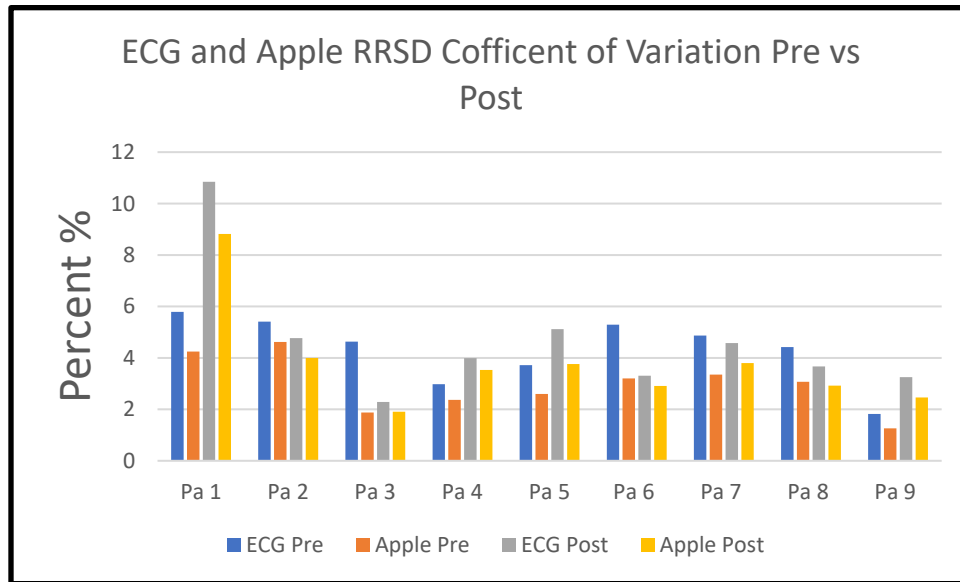


Figure 6.83: ECG and Apple Watch pre-and post-intervention RRSD coefficient of variation, a time-domain heart rate variability metric, for all patients

In addition, we plotted HRV metrics in frequency domain pre and post-intervention for all patients. Figure 6.85 represents the very low-frequency HRV for pre and post-intervention. Furthermore, Figure 6.86 and Figure 6.87 illustrate the low frequency and high frequency respectively for the same time of VLF data collection both for pre-and post-intervention. Finally, Figure 6.88 demonstrate the ratio of the LF/HF HRV for ECG and Apple from all patient pre and post-intervention.

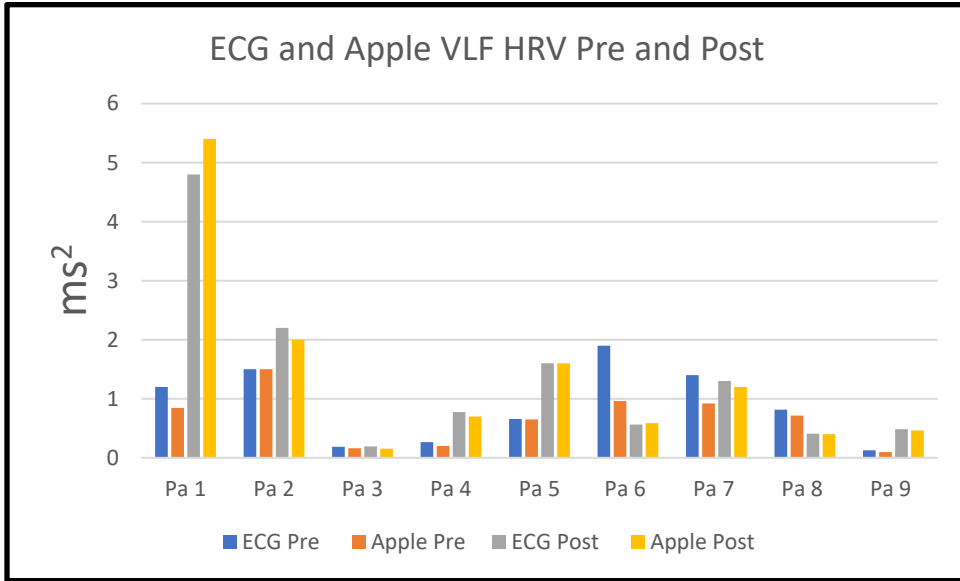


Figure 6.84: ECG and Apple Watch pre-and post-intervention very-low-frequency heart rate variability for all patients

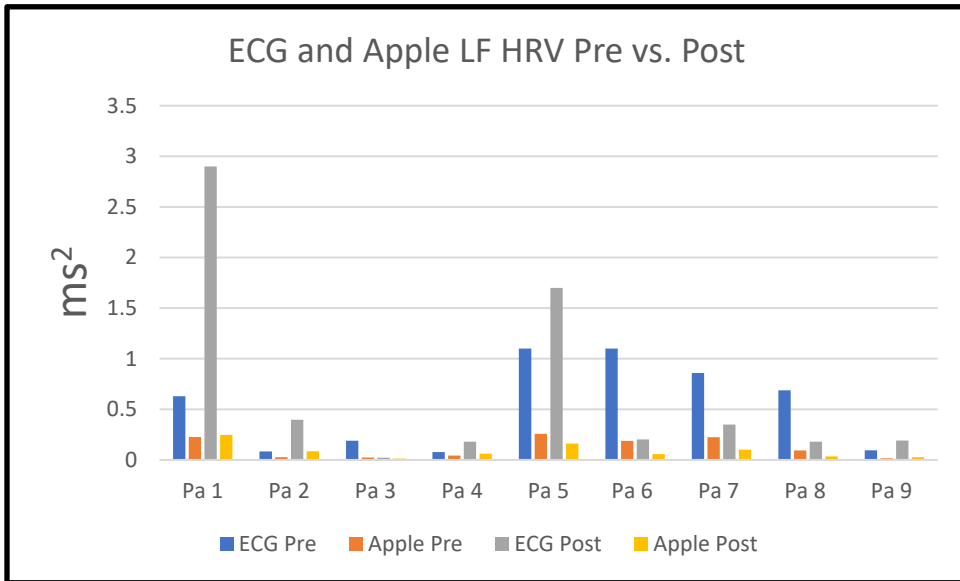


Figure 6.85: ECG and Apple Watch pre-and post-intervention low-frequency heart rate variability for all patients

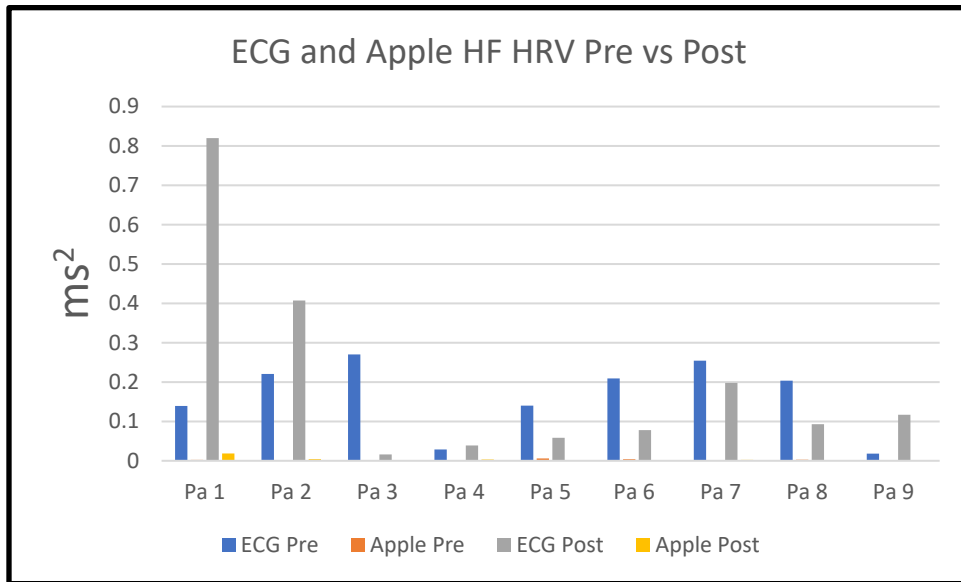


Figure 6.86: ECG and Apple Watch pre-and post-intervention high-frequency heart rate variability for all patients

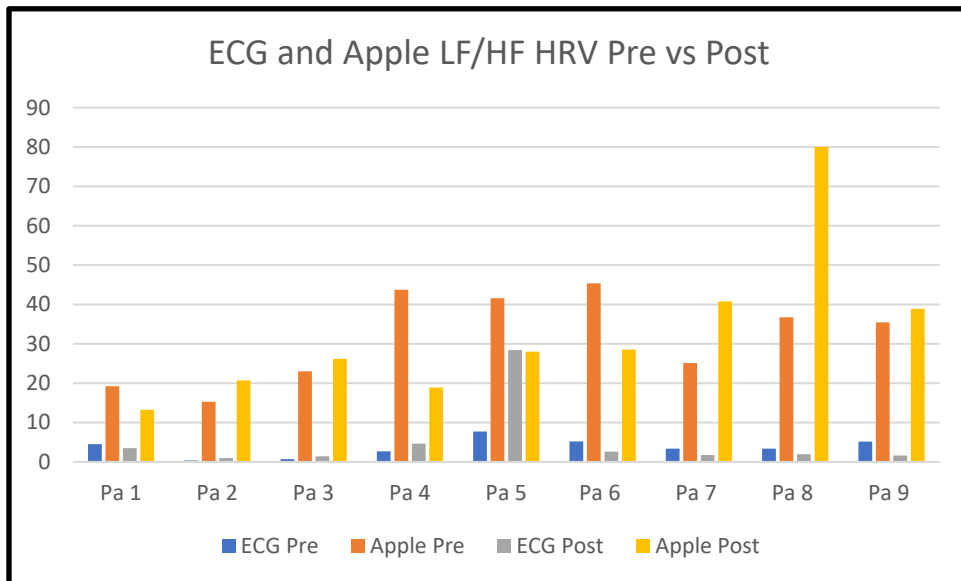


Figure 6.87: ECG and Apple Watch pre-and post-intervention low frequency/high-frequency heart rate variability for all patients

Indeed, to further analyze the differences between pre and post-intervention, we presented in several plots the difference between the mean of every HRV metrics pre and post-intervention. Figure 6.88 and Figure 6.89 represent an increase in mean RRSD HRV between the pre and post-intervention for ECG and Apple, respectively.

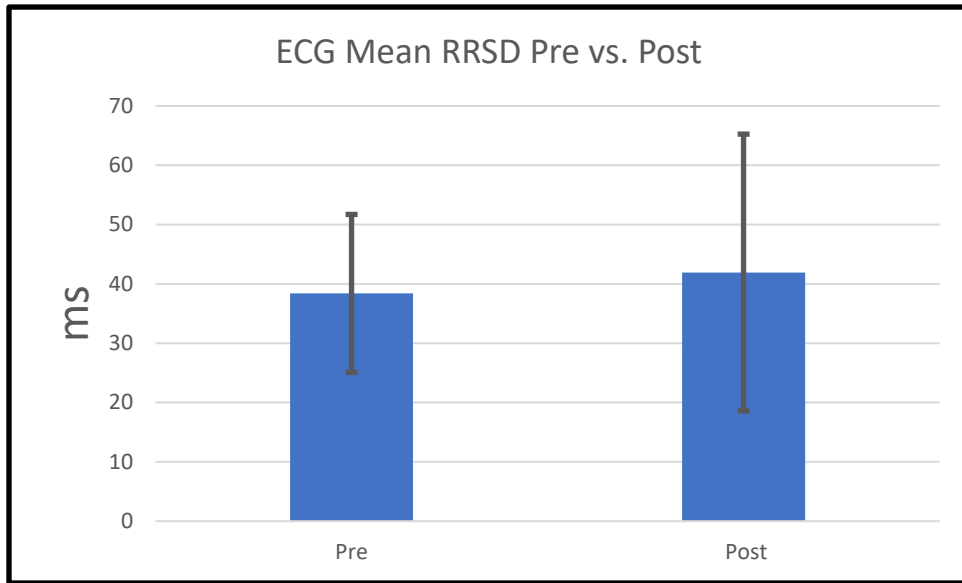


Figure 6.88: ECG Pre- and Post-Intervention RR Standard Deviation Time Domain Mean Heart Rate Variability for all patients. The vertical line represents the mean, standard deviation.

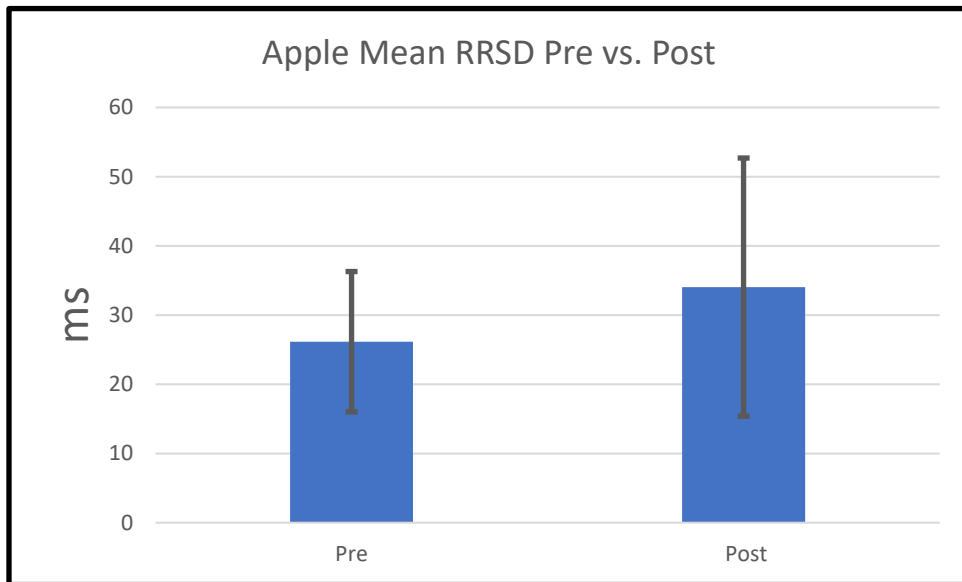


Figure 6.89: Apple Watch Pre- and Post-Intervention RR Standard Deviation Time Domain Mean Heart Rate Variability for all patients. The vertical line represents the mean, standard deviation.



Then we also represented in Figure 6.91 and Figure 6.92 showing a slight difference in mean RR HRV for the pre and post-intervention for ECG and Apple, respectively.

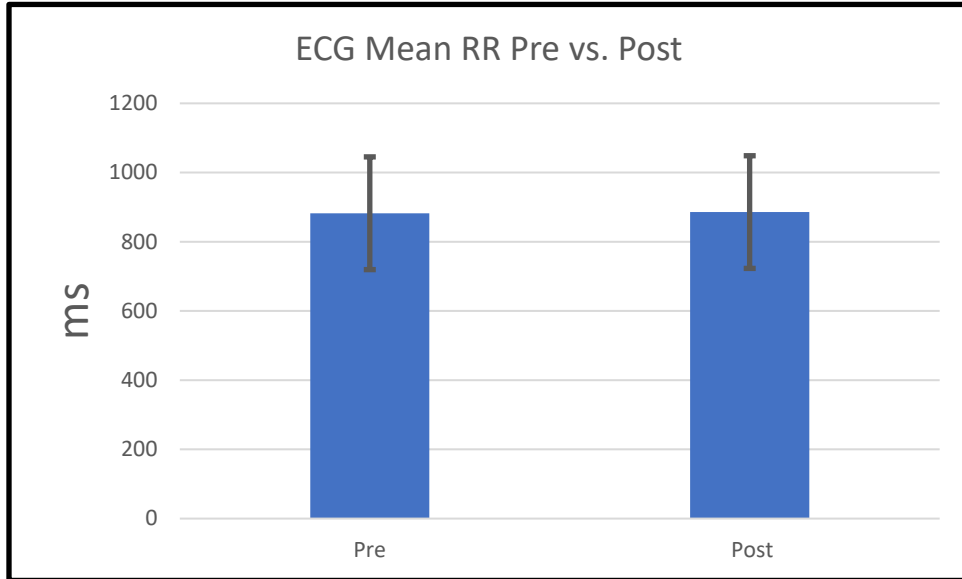


Figure 6.90: ECG pre-and post-intervention mean RR time-domain mean heart rate variability for all patients. the vertical line represents the mean standard deviation.

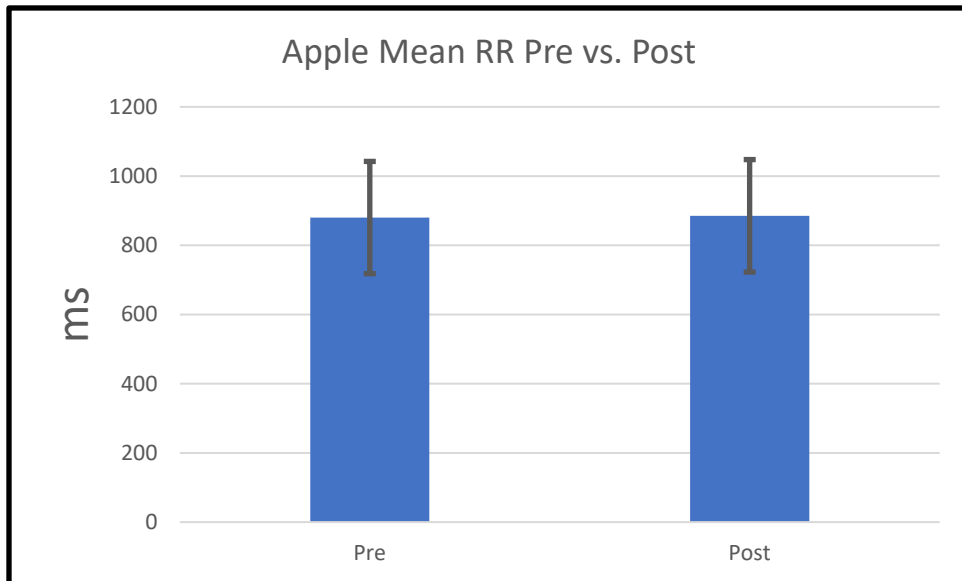


Figure 6.91: Apple pre-and post-intervention mean RR time-domain mean heart rate variability for all patients. the vertical line represents the mean standard deviation.

Furthermore, we presented Figure 6.93 and Figure 6.94 differences pre and post for the RRSD coefficient of variation pre and post-intervention. As it also shows an increase between the post and pre-intervention for ECG and Apple both.

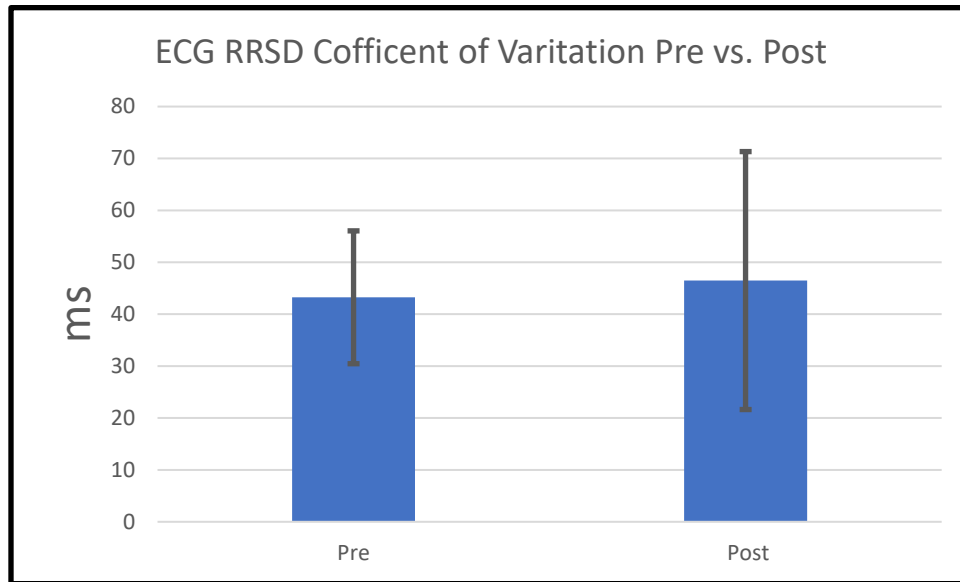


Figure 6.92: ECG pre-and post-intervention RR standard deviation coefficient of variation time-domain mean heart rate variability for all patients. the vertical line represents the mean standard deviation.

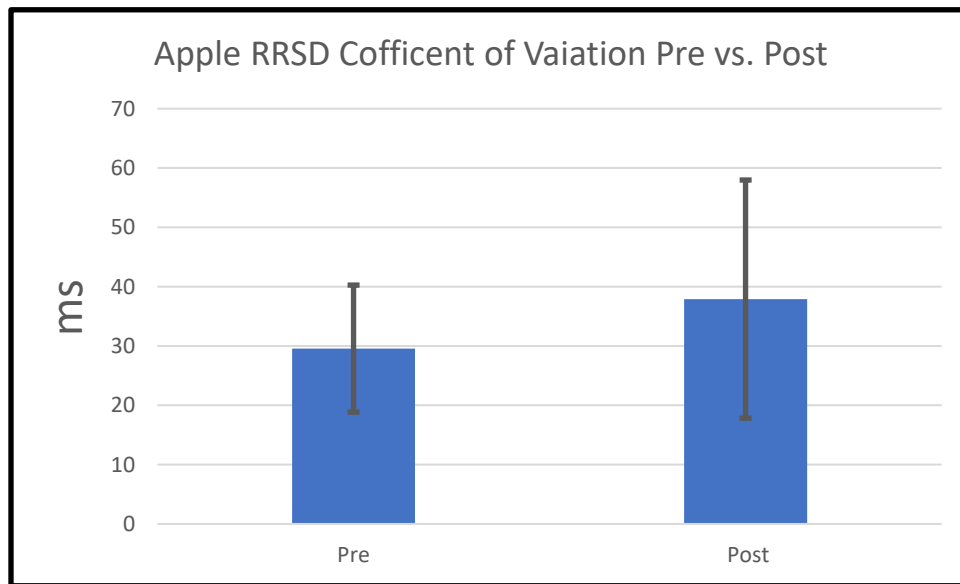


Figure 6.93: Apple pre-and post-intervention RR standard deviation coefficient of variation time-domain mean heart rate variability for all patients. the vertical line represents the mean standard deviation.

In addition, we presented the frequency domain metrics mean from all patients for pre and post-intervention. Figure 6.95 and Figure 6.96 demonstrate the very low frequency for ECG and Apple, respectively. Also, Figure 6.97 and Figure 6.98 illustrate the mean difference between pre and post-intervention for ECG low-frequency HRV and Apple low-frequency HRV. Then Figure

6.99 and Figure 6.100 show the difference between the mean of ECG high-frequency HRV and Apple high-frequency HRV for pre and post-intervention.

Finally, Figure 6.101 and Figure 6.102 illustrate the difference in mean for ECG and Apple LF/HF HRV metrics pre and post-intervention.

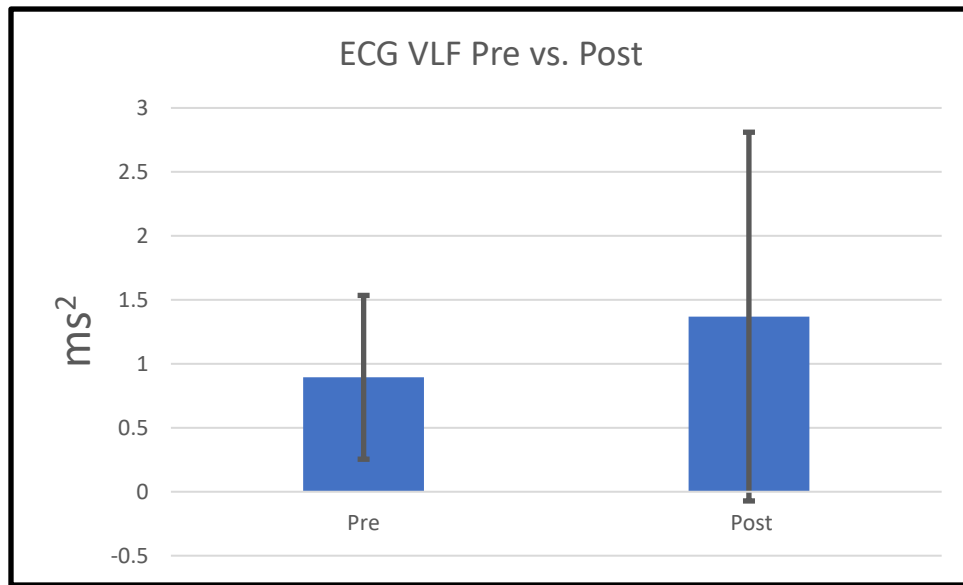


Figure 6.94: ECG pre-and post-intervention very low frequency mean heart rate variability for all patients. the vertical line represents the mean standard deviation.

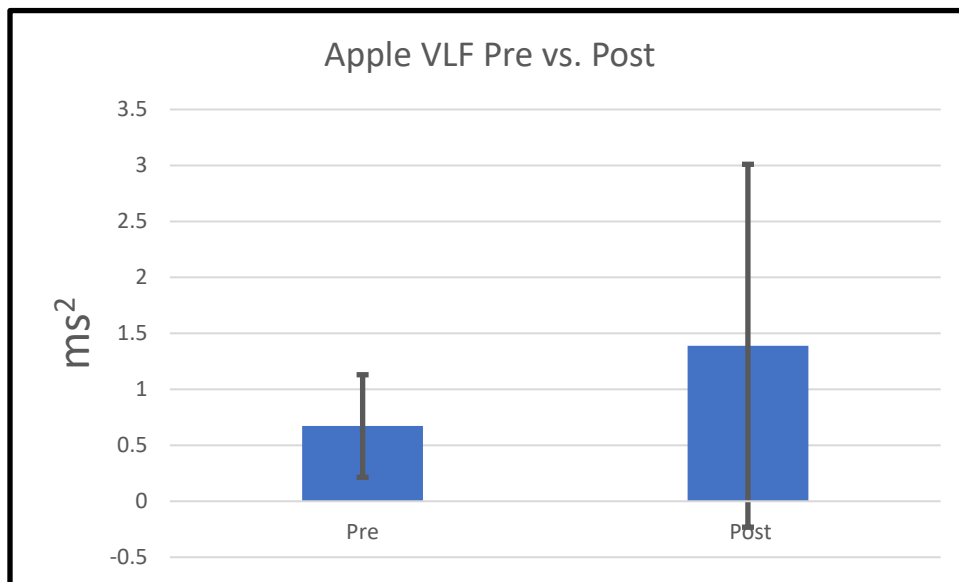


Figure 6.95: Apple Watch pre-and post-intervention very-low-frequency mean heart rate variability for all patients. the vertical line represents the mean, standard deviation.

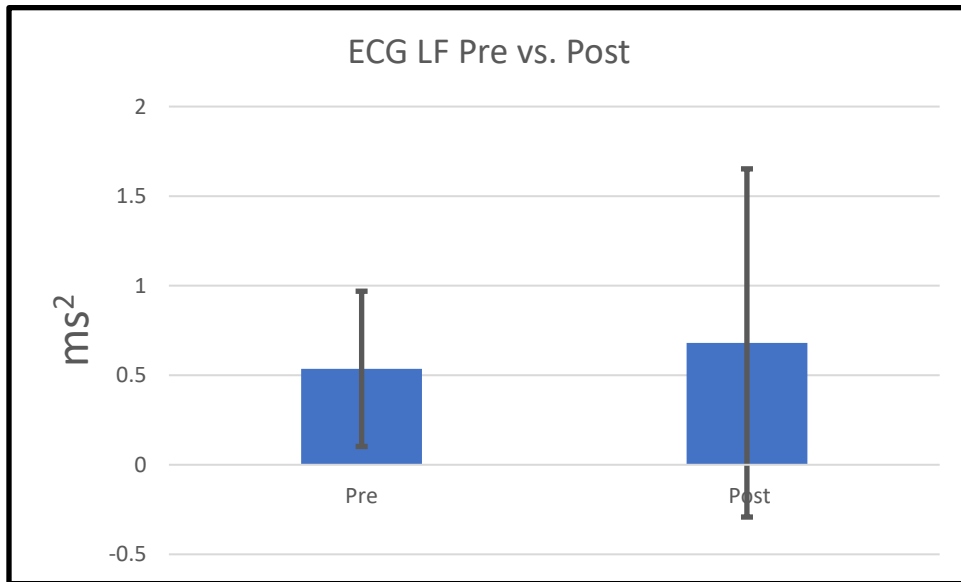


Figure 6.96: ECG pre-and post-intervention low frequency mean heart rate variability for all patients. the vertical line represents the mean standard deviation.

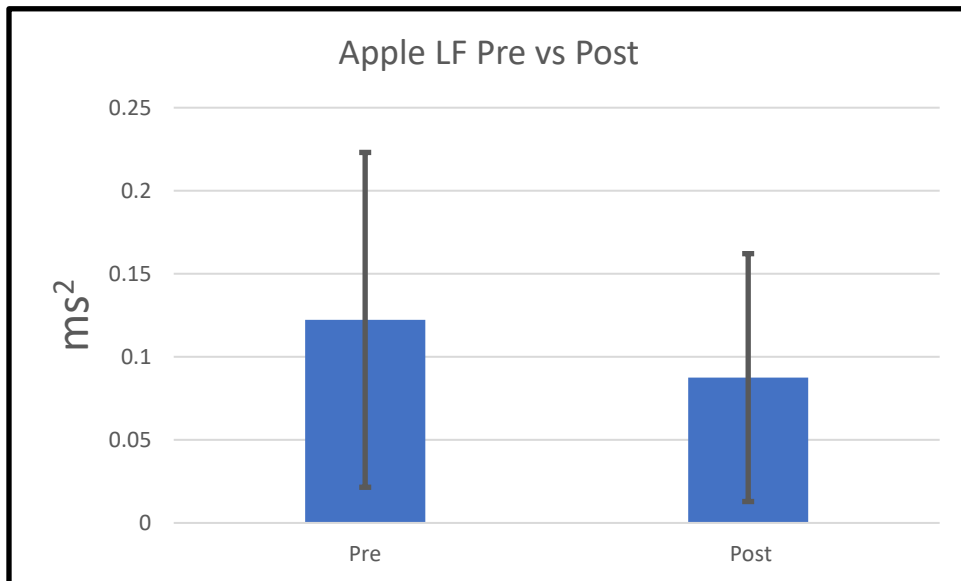


Figure 6.97: ECG pre-and post-intervention low frequency mean heart rate variability for all patients. the vertical line represents the mean standard deviation.

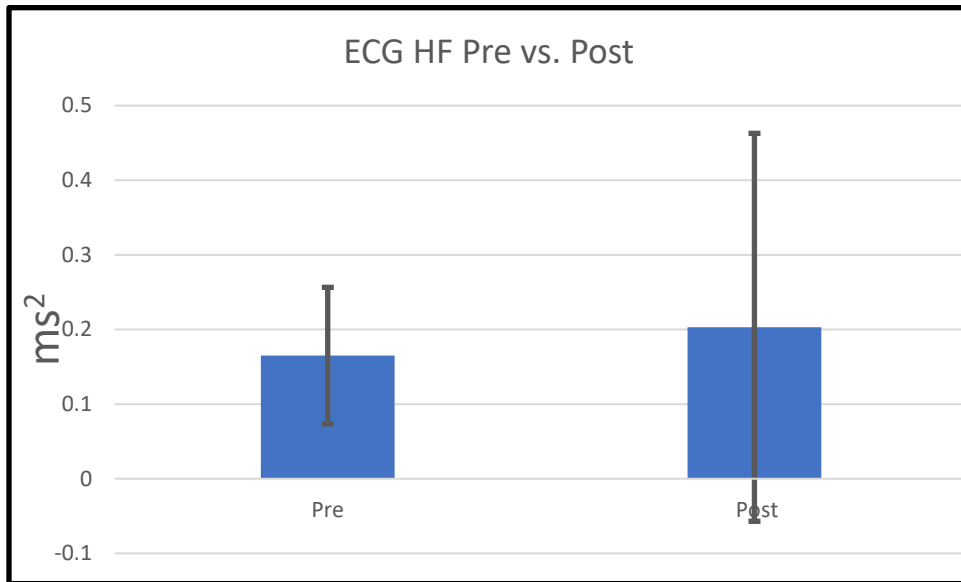


Figure 6.98: ECG pre-and post-intervention high frequency mean heart rate variability for all patients. the vertical line represents the mean, standard deviation.

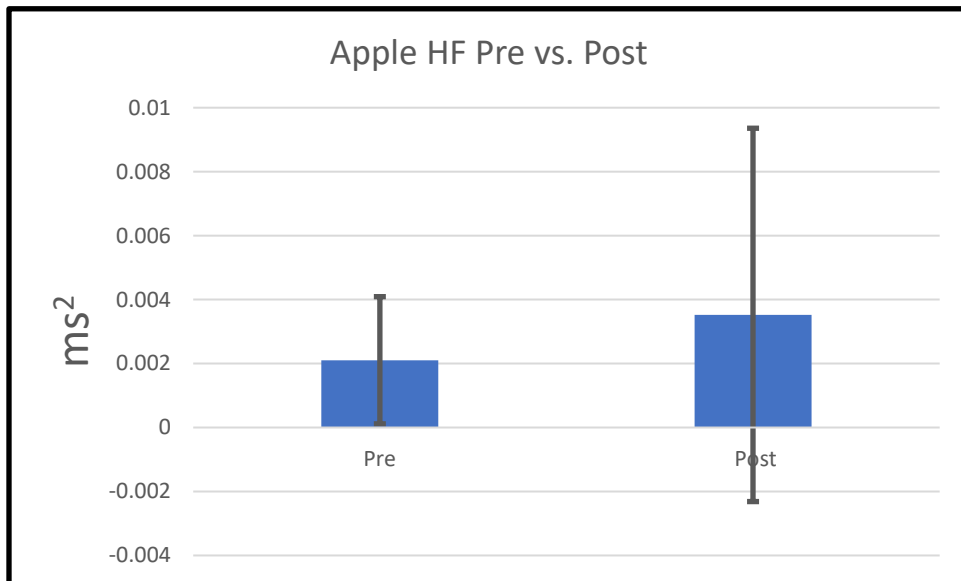


Figure 6.99: Apple pre-and post-intervention high frequency mean heart rate variability for all patients. the vertical line represents the mean standard deviation.

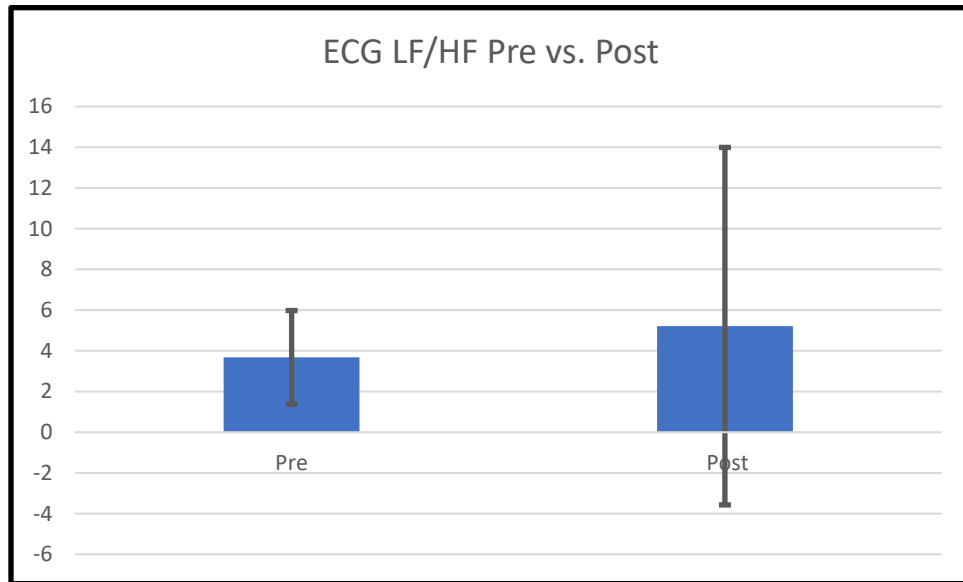


Figure 6.100: ECG pre-and post-intervention low frequency/high frequency mean heart rate variability for all patients. The vertical line represents the mean, standard deviation.

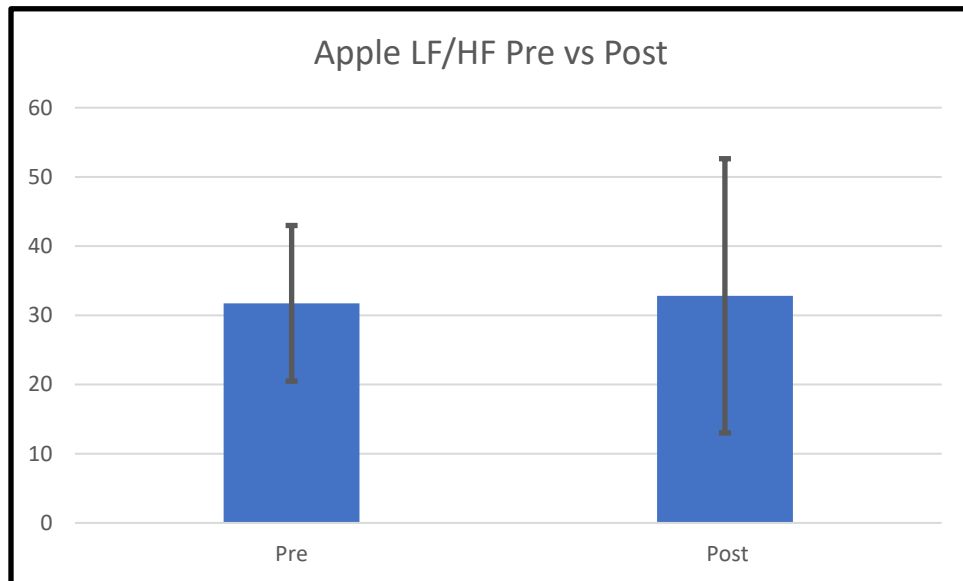


Figure 6.101: Apple pre-and post-intervention low frequency/high frequency mean heart rate variability for all patients. the vertical line represents the mean, standard deviation.

***Discussion of Measuring the Changes in HRV, Post Physical Exercise Interventions Using the PMT System, Compared to Baseline*** - Following Table 6.15 the results of the Wilcoxon rank-sum test revealed that no statical significance differences were observed between the pre and post

interventions for all time domain and frequency domain. All the HRV metrics comparisons resulted in a p-value higher than 0.05.

However, when following the plots of Figure 6.82- Figure 6.88, differences between pre and post interventions HRV metrics measures are noticed, but when following the plots in Figure 6.89- Figure 6.102 we observed differences in standard deviation accompanying the difference in the mean value. This observation can illuminate no significant difference in results from all the HRV metrics pre-intervention and post-intervention tests.

The small sample size [160] and the duration of the exercise intervention [161] could be the reason for the no significant change between the pre and post-intervention HRV metrics measures.

#### **6.4 Conclusion:**

We found that HRV measures derived from Apple Watch do not fully match those derived from the ECG. Additionally, among the four heart rate variability metrics considered in this study, only the frequency-domain very-low-frequency power (VLF) appears to reasonably estimate the VLF power computed from ECG.

Also, we studied the change in the heart rate variability for the TBI patients who participated in the physical exercise intervention using the PMT system. We found no difference in the heart rate variability results collected from ECG and Apple Watch between pre-and post-intervention.

## CHAPTER 7

### Estimation of Energy Expenditure

#### 7.1 Introduction

One of the fundamental theories in exercise science is the overload principle of training. Exercise at a strength above that usually obtained will induce particular adaptations, allowing the body to function more efficiently [162]. The overload principle can be applied by controlling combinations of training frequency, intensity, and duration [162]. Training at the appropriate intensity is an essential element of any successful exercise program [163]. It does not only allow patients to optimize the overload principle safely and effectively correctly, but it also allows them to avoid excessive training outcomes such as fatigue or loss of interest [164].

As it was mentioned in Ch4 section 2 that the aerobic exercise leads to higher oxygen and glucose consumption that can cause increased energy expenditure and lead to a reduction of body fat and increased muscle strength, and better cognitive function [165] [73] [166] [167]. Hence, it is expected that exercise will increase the energy expenditure for TBI patients.

This chapter will present the results of studying the active energy value that Apple Watch reported and transferred to the PMT portal system for each patient. Indeed, we will explore the correlation between the change in the exercise active energy and activity prescribed metrics applied to define the intensity of the exercises, such as exercise duration and heart rates. We will study the correlation by using the average heart rate and duration of the sessions. Even though we have the Frequency Compliance values available, but we believe that the Frequency Compliance



will not have a meaningful correlation as the compliance has discrete values. Therefore, we will not consider Frequency Compliance in the analysis

To study the linear correlation between the exercise active energy and activity prescribed metrics from a different perspective, we computed different sets of linear correlation coefficients, as the following

- The total duration of weekly exercise vs. Weekly Total Active Energy
- Duration of every session that the patient has performed (39-45 sessions) vs. the active energy expenditure for the session.
- Total Weekly Compliance vs. Weekly Active Energy
- Weekly Duration Compliance for every exercise session for All Patients vs. Corresponding Active Energy of the sessions
- Weekly Mean of Average Heart Rate vs. Weekly Total Active Energy
- All Average Heart Rate Sessions vs. All Active Energy recorded for the corresponding Sessions
- Weekly Heart Rate Compliance vs. Weekly Total Active Energy
- All Patients Heart Rate Compliances vs. Corresponding Active Energy Sessions

## **7.2 Method:**

We analyzed the active energy values measured by the Apple Watch during each exercise session performed by the TBI patient. Specifically, we collected all registered active energy values in the PMT system's portal from each patient's exercise attempt that at least lasted for 10 minutes. Next, we explored the linear correlation for the comparisons mentioned above.

The linear correlation analysis was based on the Pearson's Linear Correlation coefficient of determination R. The Linear correlation R-value measures the strength and direction of a linear relationship between two variables on a scatterplot. R-value is between +1 and -1.

While no universally accepted levels for assessing the computed R values exists, the R-value for the two variables can be interpreted based on the following:

- Exactly -1. A perfect downslope (negative) linear relationship
- -0.70. A strong downslope (negative) linear relationship
- -0.50. A moderate downslope (negative) relationship
- -0.30. A weak downslope (negative) linear relationship
- 0. No linear relationship
- +0.30. A weak upslope (positive) linear relationship
- +0.50. A moderate upslope (positive) relationship
- +0.70. A strong upslope (positive) linear relationship
- Exactly +1. A perfect upslope (positive) linear relationship

We calculated the R-value as the following:

$$R(a, b) = \frac{\sum_{i=1}^n (X_{a,i} - \bar{X}_a)(Y_{b,i} - \bar{Y}_b)}{\sqrt{\sum_{i=1}^n (X_{a,i} - \bar{X}_a)^2 \sum_{j=1}^n (Y_{b,j} - \bar{Y}_b)^2}} \quad (1)$$

where  $R(a, b)$  is the linear correlation R-value, the  $X_{a,i}$  is the exercise intensity metric value (e.g., exercise heart rates or duration), and  $Y_{b,i}$  is the active energy value,  $\bar{X}_a$  is the exercise intensity metric mean, and  $\bar{Y}_b$  is the active energy value.

Furthermore, we calculated the linear regression coefficient of determination.

$R^2$  determines the proportion of variation in the dependent variable that the independent variable can describe. Notably, R-squared demonstrates how well the data fit a linear regression model (the goodness of fit).

The average R-value is calculated by taking the square root of the average R-squared value. That is since correlation coefficients are not additive [168].

### **7.3 Results:**

Below, the tables for the linear correlation coefficients R and regression coefficient of determination  $R^2$  are presented. In addition, the linear correlation coefficients of determination (i.e., R's) are shown in bar plots to illustrate the highest and lowest linear correlation coefficients between the patient at every comparison. Then, representative plots demonstrate the highest and lowest linear correlation scatter plots and their linear fit line. Furthermore, in Appendix 4, we show the scatter plots for the rest of the comparison's linear correlation scatterplots with their fitted line for the data from each comparison we conducted for every patient.

Table 7.16 shows the weekly total duration and weekly total active energy linear correlation coefficients R and the regression coefficient of determination R-squared values for each patient. Figure 7.103 illustrates the weekly total duration and weekly total active energy linear correlation coefficients R-value. Figure 7.104 and Figure 7.105 show the highest and lowest linear correlation among patients for the weekly total duration and weekly total active energy linear correlation.

Table 7.16: Patients Weekly total exercise duration vs. Weekly Total Active Energy, linear correlation coefficient (R), and linear regression coefficient (R<sup>2</sup>). The last row represents the Average R-value and Average R<sup>2</sup>-value

Total Weekly Duration vs. Total Weekly Active Energy		
Patient #	R	R <sup>2</sup>
Patient 1	0.98	0.96
Patient 2	0.97	0.95
Patient 3	0.98	0.96
Patient 4	0.96	0.91
Patient 5	0.98	0.97
Patient 6	0.98	0.96
Patient 7	0.75	0.56
Patient 8	0.95	0.91
Patient 9	0.92	0.85
Average	0.94	0.89
All Duration Session vs. Active Energy	0.61	0.40

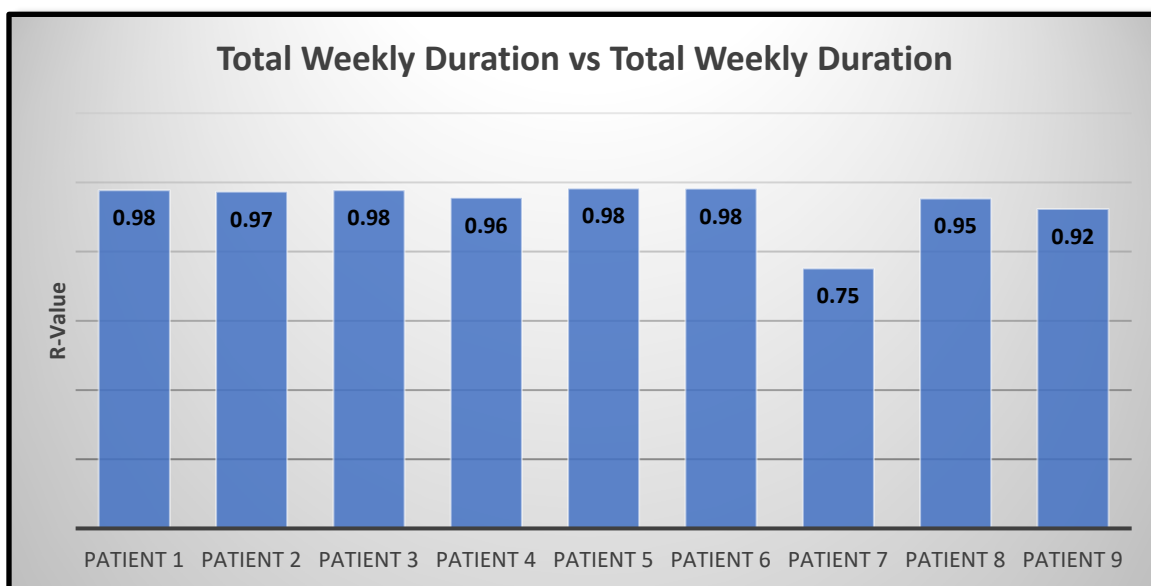


Figure 7.102: Weekly Total Energy vs. Total Weekly Duration Linear Correlation Coefficient R-value for each patient

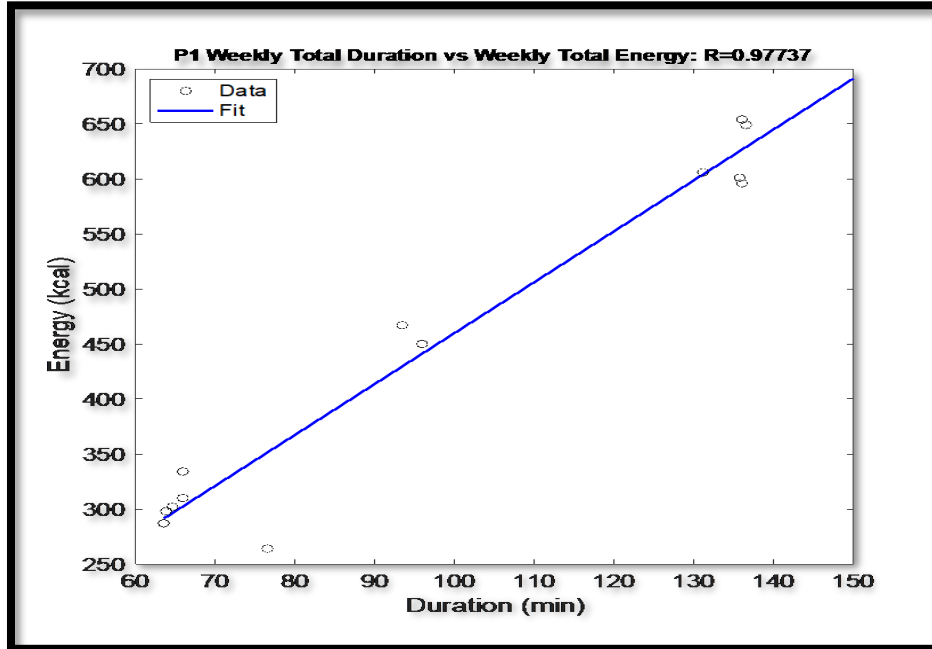


Figure 7.103: Weekly Total Duration vs. Weekly Total Active Energy linear correlation for patient#1 (highest linear correlation coefficient among patients)

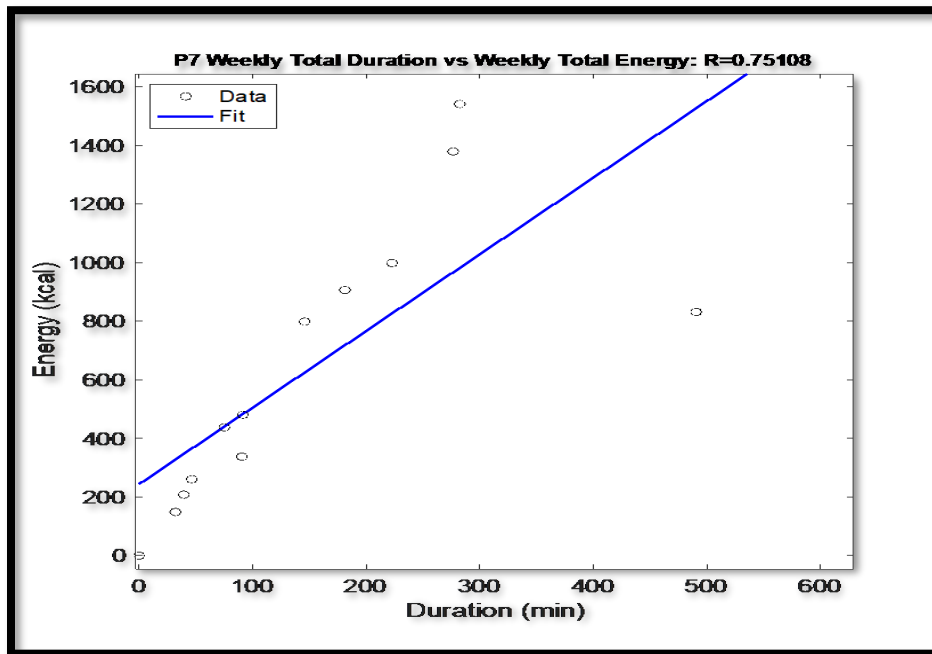


Figure 7.104: Weekly Total Duration vs. Weekly Total Active Energy linear correlation for patient#1 (lowest linear correlation coefficient among patients)

Table 7.17 shows all duration sessions and all active energy sessions linear correlation coefficients R and the regression coefficient of determination R-squared values for each patient.

Then Figure 7.106 illustrates the weekly total duration and weekly total active energy linear correlation coefficients R-value. Figure 7.107 and Figure 7.108 shows the highest and lowest linear correlation among patient for all duration sessions and all active energy sessions linear correlation.

Table 7.17: Patients All Duration Sessions vs. All Active Energy Sessions, linear correlation coefficient (R), and linear regression coefficient (R2). The last row represents the Average R-value and Average R2-value

All Duration Sessions vs. All Active Energy Sessions		
Patient #	R	R-squared
Patient 1	0.80	0.64
Patient 2	0.87	0.76
Patient 3	0.85	0.73
Patient 4	0.97	0.94
Patient 5	0.95	0.90
Patient 6	0.94	0.88
Patient 7	0.95	0.90
Patient 8	0.83	0.69
Patient 9	0.67	0.45
Average	0.87	0.77
All Duration Session vs. Active Energy	0.61	0.40

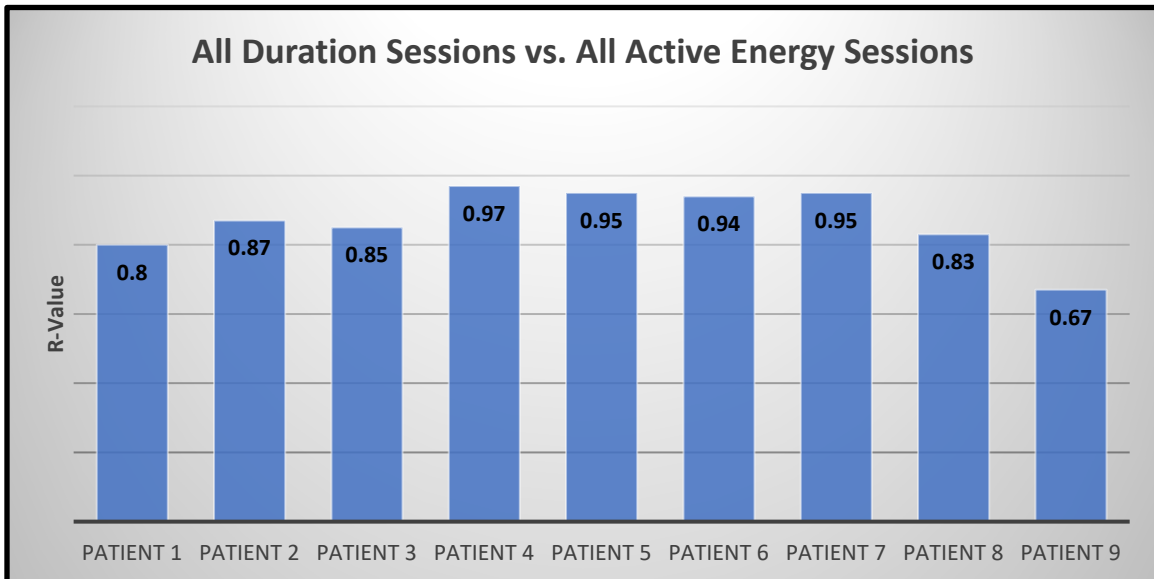


Figure 7.105: All Duration Sessions vs. All Active Energy Sessions Linear Correlation Coefficient R-value for each patient

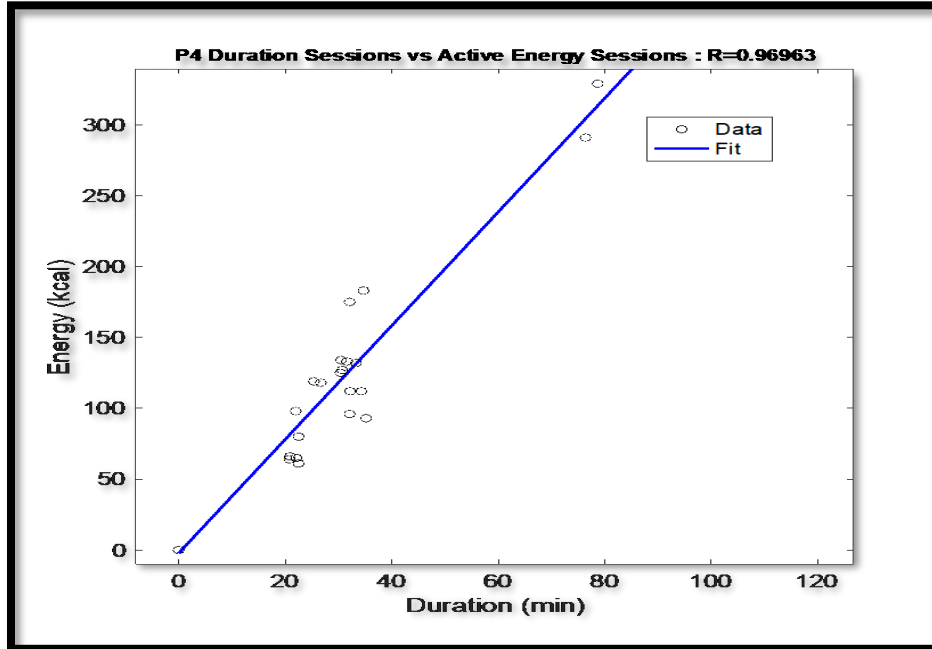


Figure 7.106: Duration Sessions vs. Active Energy Sessions linear correlation for patient#4 (highest linear correlation coefficient among patients)

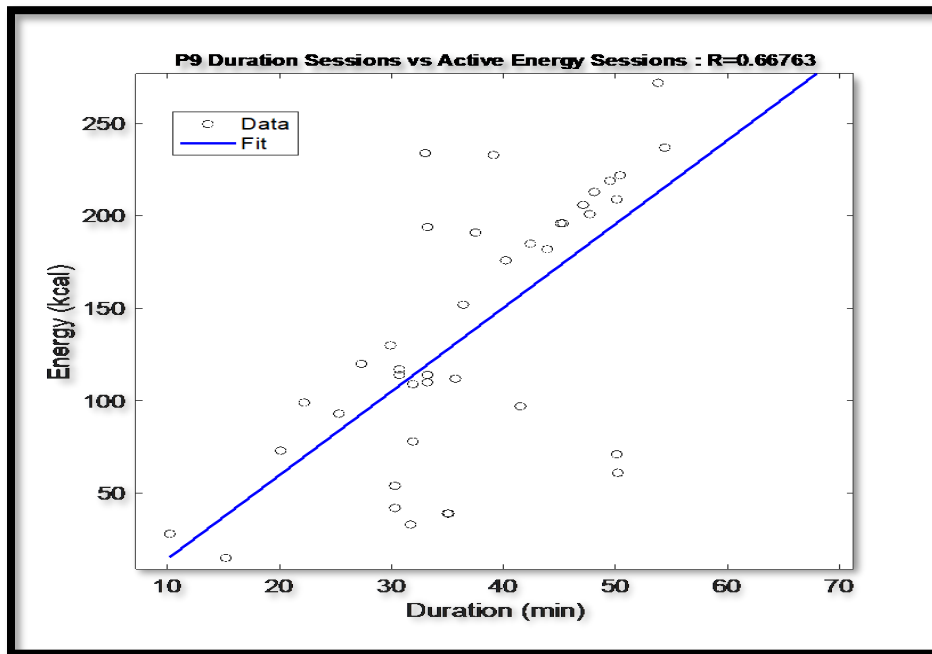


Figure 7.107: Duration Sessions vs. Active Energy Sessions linear correlation for patient#9 (lowest linear correlation coefficient among patients)

Figure 7.109 illustrates all duration sessions and their corresponding active energy values linear correlation for all 9 patients. The linear correlation R-value for this comparison is 0.62.

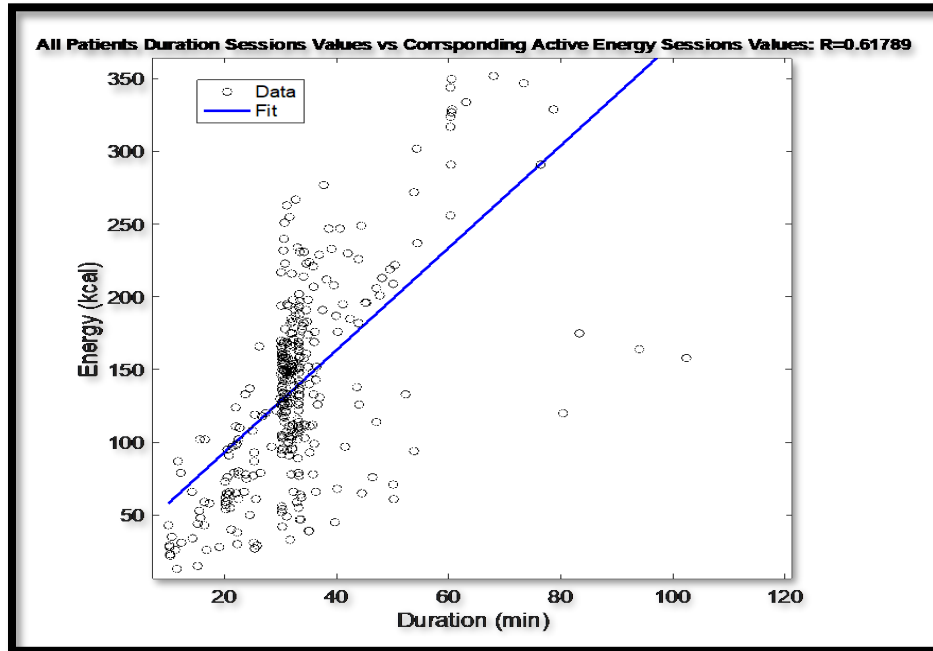


Figure 7.108: All 9 Patients Duration Sessions vs. Corresponding Active Energy Sessions linear correlation

Table 7.18 shows weekly Duration Compliance and weekly total active energy linear correlation coefficients R and the regression coefficient of determination R-squared values for each patient. Then, Figure 7.110 illustrates the weekly Duration Compliance and weekly total active energy linear correlation coefficients R-value bar plot. Figure 7.111 and Figure 7.112 shows the highest and lowest linear correlation among patient for weekly Duration Compliance and weekly total active energy linear correlation.



Table 7.18: Patient's Weekly Duration Compliance vs. Weekly Total Active Energy, linear correlation coefficient (R), and linear regression coefficient (R2). The last row represents the Average R-value and Average R2-value

Weekly Duration Compliance vs. Weekly Total Active Energy		
Patient #	R	R-squared
Patient 1	0.68	0.46
Patient 2	0.97	0.94
Patient 3	0.91	0.82
Patient 4	0.89	0.78
Patient 5	0.84	0.70
Patient 6	0.98	0.96
Patient 7	0.96	0.92
Patient 8	0.62	0.39
Patient 9	0.78	0.62
Average	0.86	0.73
All Duration Session vs. Active Energy	0.61	0.40

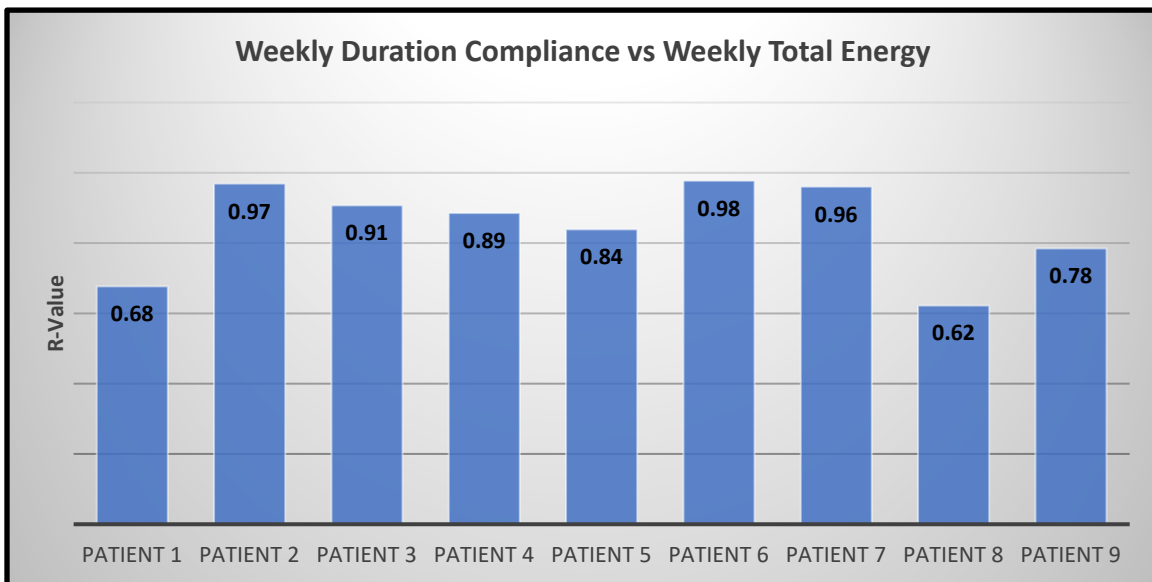


Figure 7.109: Weekly Duration Compliance vs. Weekly Total Active Energy Linear Correlation Coefficient R-value for each patient

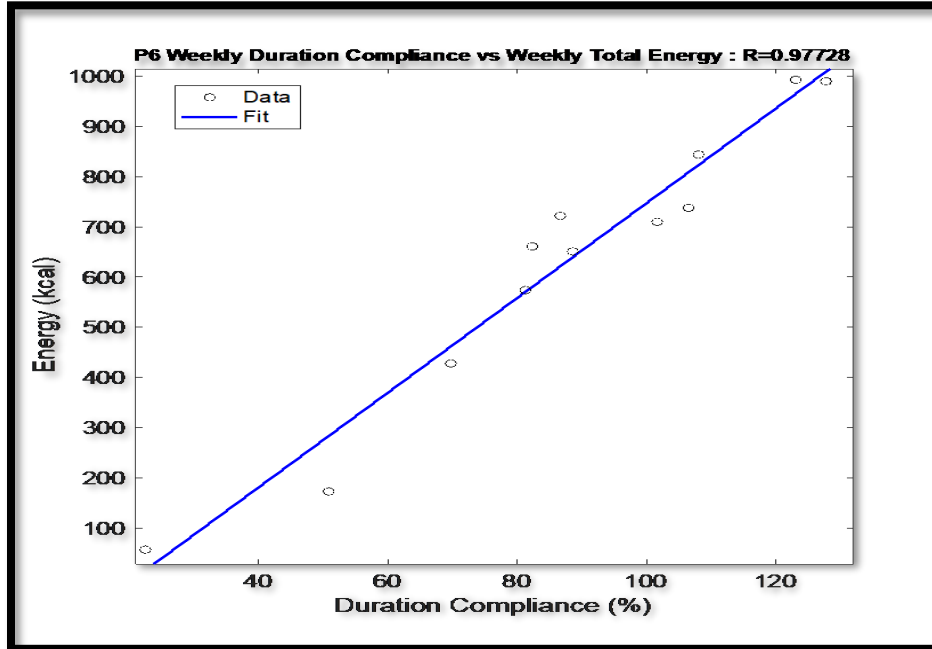


Figure 7.110: Weekly Duration Compliance vs. Weekly Total Active Energy linear correlation for patient#6 (highest linear correlation coefficient among patients)

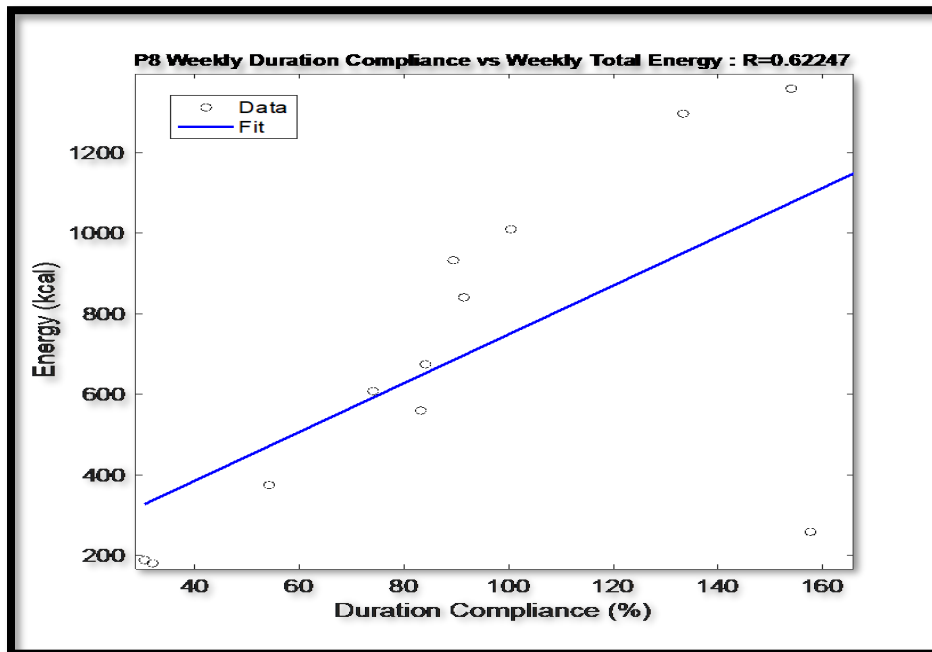


Figure 7.111: Weekly Duration Compliance vs. Weekly Total Active Energy linear correlation for patient#8 (lowest linear correlation coefficient among patients)

Figure 7.113 illustrates all 13-weeks Duration Compliances and their corresponding active energy values linear correlation for all 9 patients. The linear correlation R-value for this comparison is 0.75.

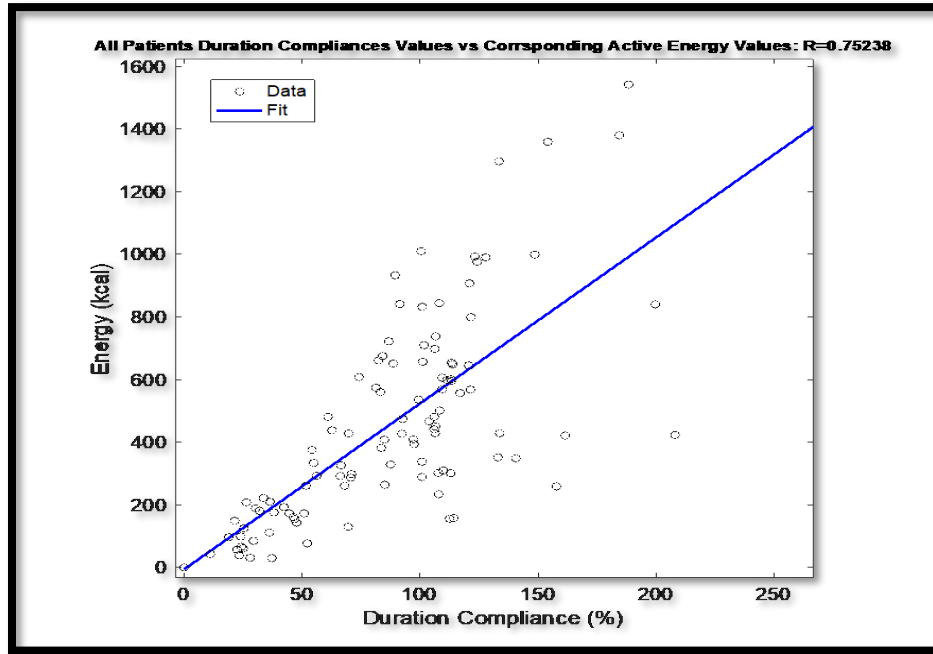


Figure 7.112: All 9 Patients Duration Compliances vs. Corresponding Active Energy Sessions linear correlation

Table 7.19 shows the weekly mean of average heart rate and weekly total active energy linear correlation coefficients R and the R-squared values for each patient. Figure 7.114 illustrates the weekly mean average heart rate and weekly total active energy linear correlation coefficients R-value bar plot. Figure 7.115 and Figure 7.116 shows the highest and lowest linear correlation among patient for the weekly mean of average heart rate and weekly total active energy linear correlation.

Table 7.19: Patients Weekly Mean of Average Heart Rate vs. Weekly Total Active Energy, linear correlation coefficient (R), and linear regression coefficient (R<sup>2</sup>). The last row represents the Average R-value and Average R<sup>2</sup>-value

Weekly Mean of Average Heart Rate vs. Weekly Total Active Energy		
Patient #	R	R-squared
Patient 1	0.28	0.08
Patient 2	0.75	0.56
Patient 3	0.26	0.07
Patient 4	0.78	0.61
Patient 5	0.70	0.50
Patient 6	0.91	0.83
Patient 7	0.40	0.16
Patient 8	0.42	0.18
Patient 9	0.51	0.26
<b>Average</b>	<b>0.60</b>	<b>0.36</b>
<b>All Patient Sessions</b>		
<b>Average Heart Rate vs. Active Energy Sessions</b>	<b>0.19</b>	<b>0.04</b>

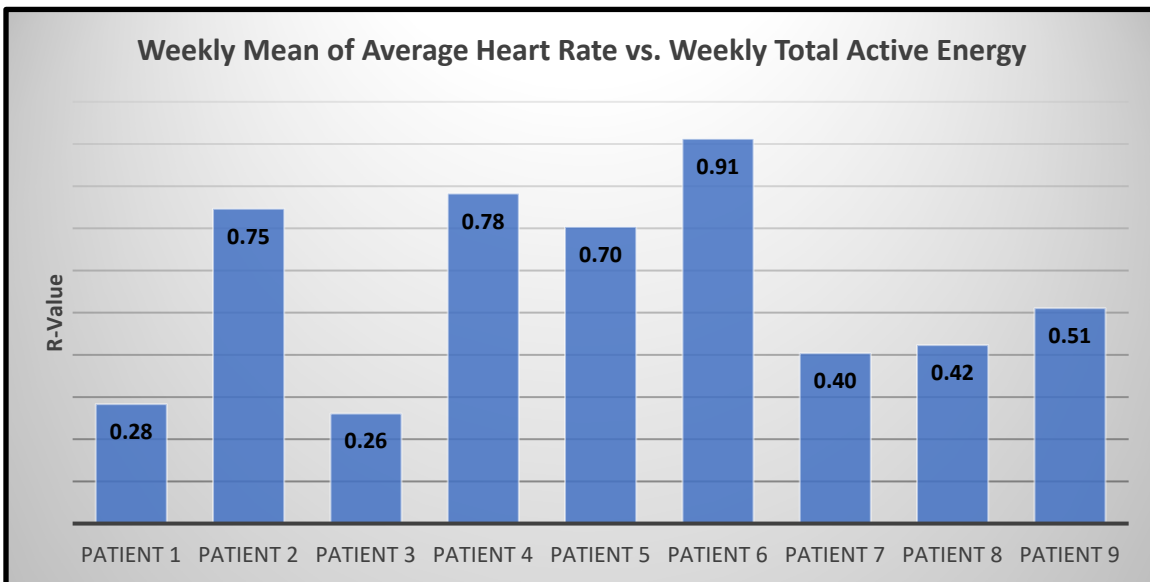


Figure 7.113: Weekly Mean of Average Heart Rate vs. Weekly Total Active Energy Linear Correlation Coefficient R-value for each patient

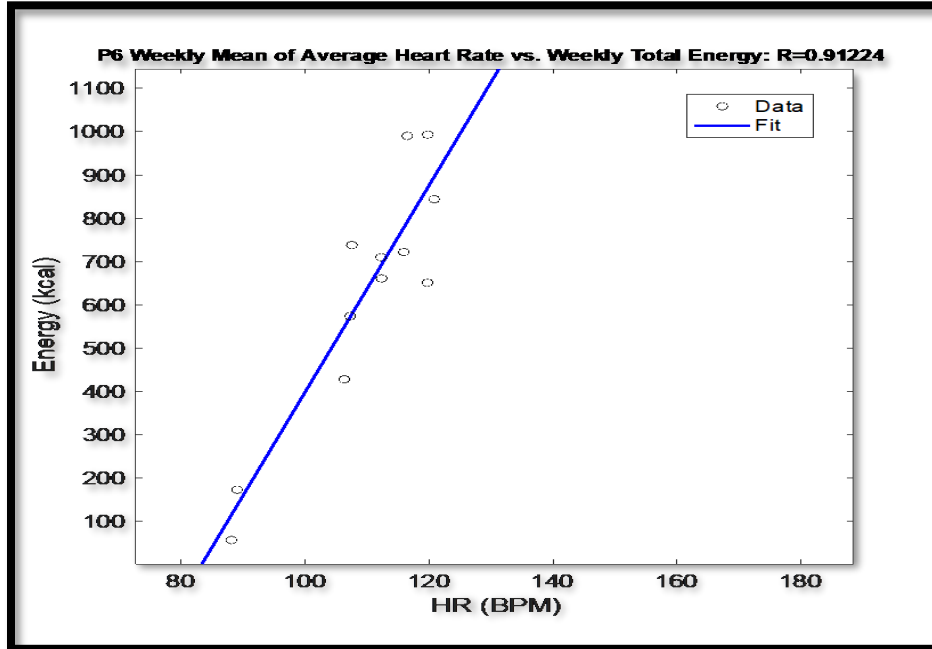


Figure 7.114: Weekly Mean of Average Heart Rate vs. Weekly Total Active Energy linear correlation for patient#6 (highest linear correlation coefficient among patients)

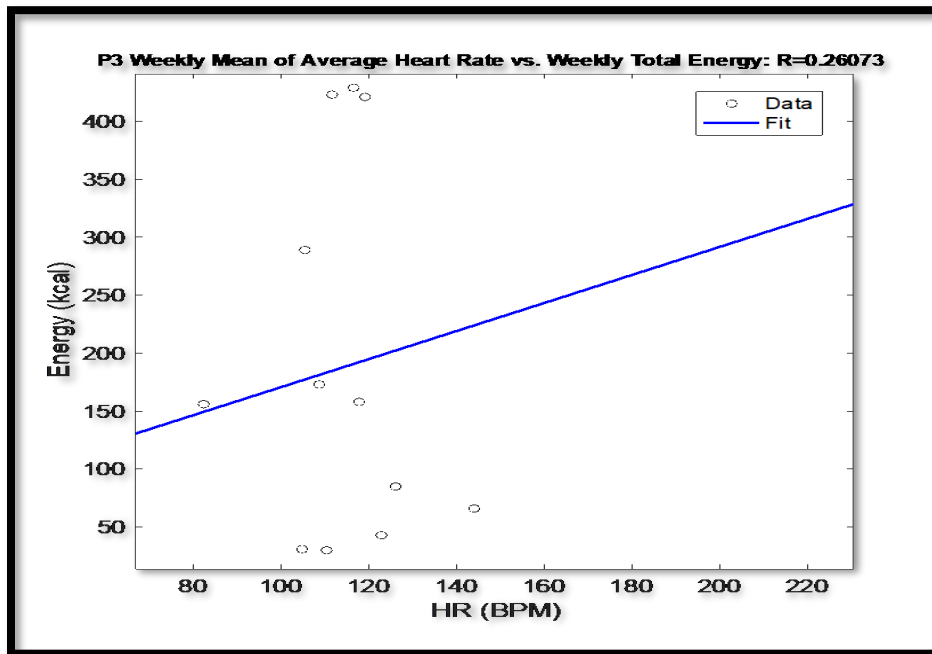


Figure 7.115: Weekly Mean of Average Heart Rate vs. Weekly Total Active Energy linear correlation for patient#3 (lowest linear correlation coefficient among patients)

Figure 7.117 illustrates all session's average heart rates and their corresponding active energy values linear correlation for all 9 patients. The linear correlation R-value for this comparison is 0.19.

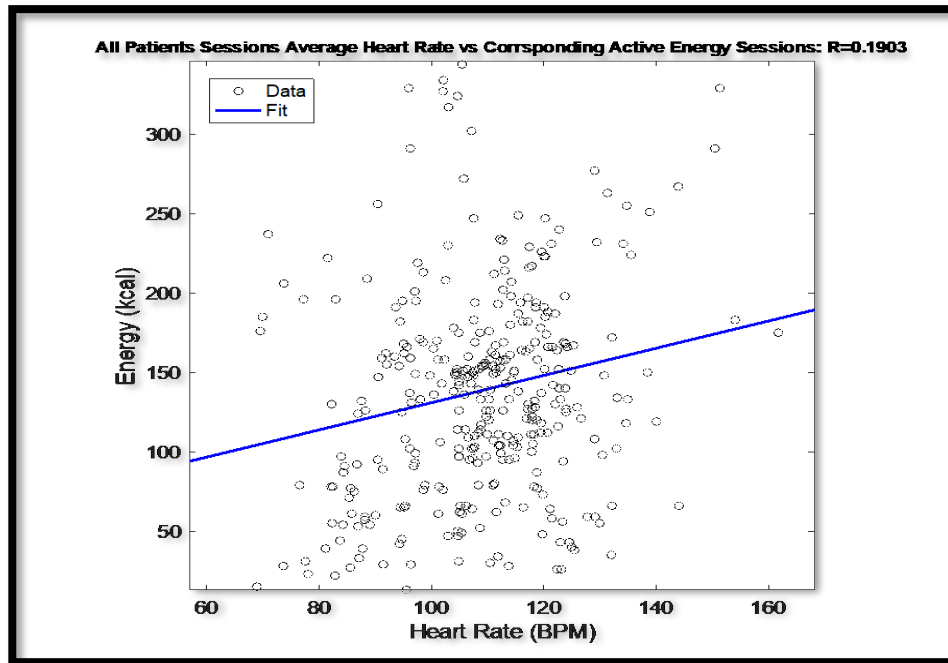


Figure 7.116: All 9 Patients Average Heart Rate Sessions Values vs. Corresponding Active Energy Sessions linear correlation

Table 7.20 shows weekly Heart Rate Compliance and weekly total active energy linear correlation coefficients R and the R-squared values for each patient. Then Figure 7.118 illustrates the weekly Heart Rate Compliance and weekly total active energy linear correlation coefficients R-value bar plot. Figure 7.119 and Figure 7.120 shows the highest and lowest linear correlation among patient for weekly Heart Rate Compliance and weekly total active energy linear correlation.

Table 7.20: Patient's Weekly Heart Rate Compliance vs. Weekly Total Active Energy, linear correlation coefficient (R), and linear regression coefficient (R2). The last row represents the Average R-value and Average R2-value

Weekly Heart Rate Compliance vs. Weekly Total Active Energy		
Patient #	R	R-squared
Patient 1	0.46	0.21
Patient 2	-0.52	0.30
Patient 3	0.13	0.02
Patient 4	0.22	0.05
Patient 5	0.36	0.13
Patient 6	0.57	0.33
Patient 7	0.03	0.00
Patient 8	-0.02	0.00
Patient 9	0.16	0.03
Average	0.42	0.18
All Patient Sessions Average Heart Rate vs. Active Energy Sessions	0.19	0.04

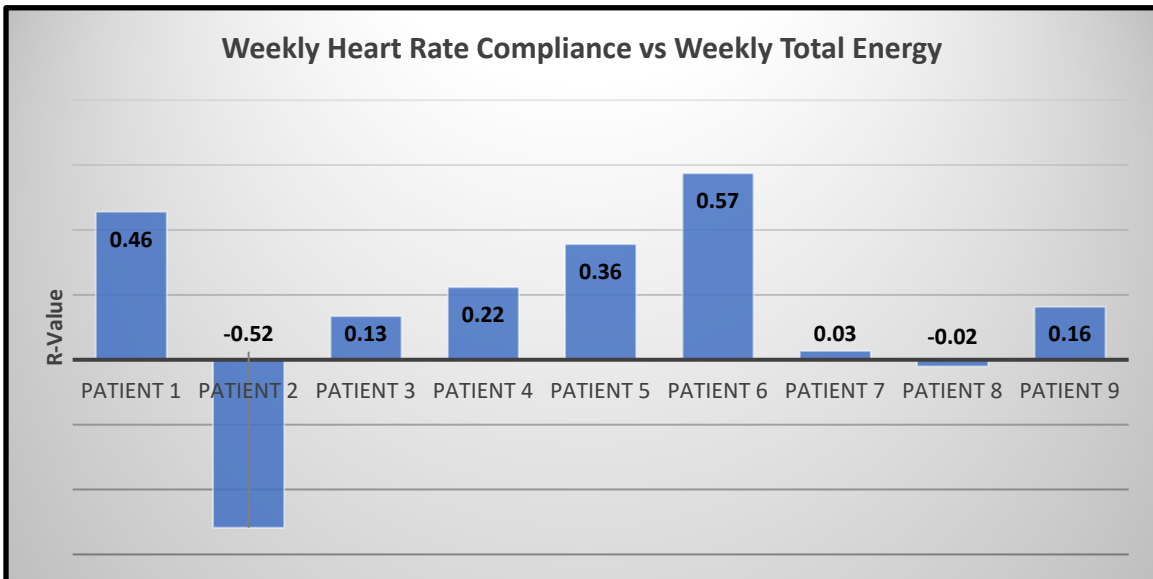


Figure 7.117: Weekly Heart Rate Compliance vs. Weekly Total Energy Linear Correlation Coefficient R-value for each patient

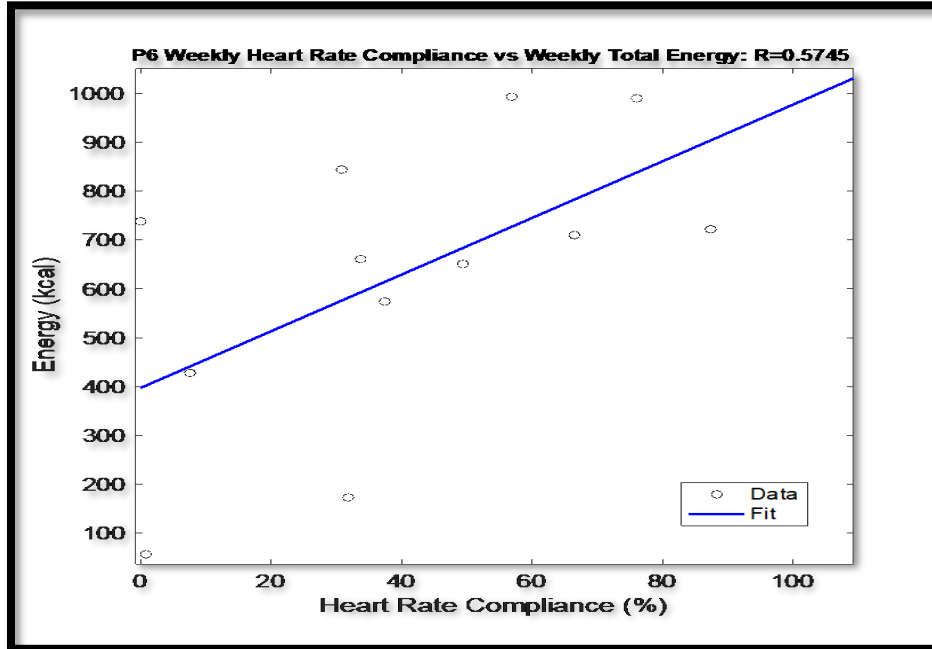


Figure 7.118: Weekly Heart Rate Compliance vs. Weekly Total Active Energy linear correlation for patient#6 (highest linear correlation coefficient among patients)

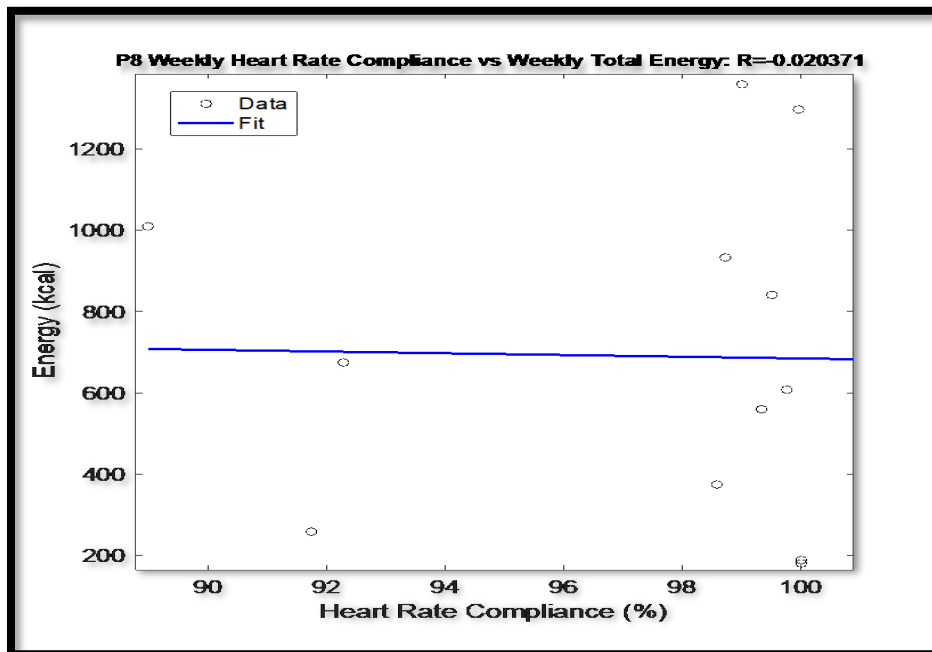


Figure 7.119: Weekly Heart Rate Compliance vs. Weekly Total Active Energy linear correlation for patient#8 (lowest linear correlation coefficient among patients)



Figure 7.121 illustrates all Heart Rates Compliances for 13 weeks and their corresponding active energy values linear correlation for all 9 patients. The linear correlation R-value for this comparison is 0.25.

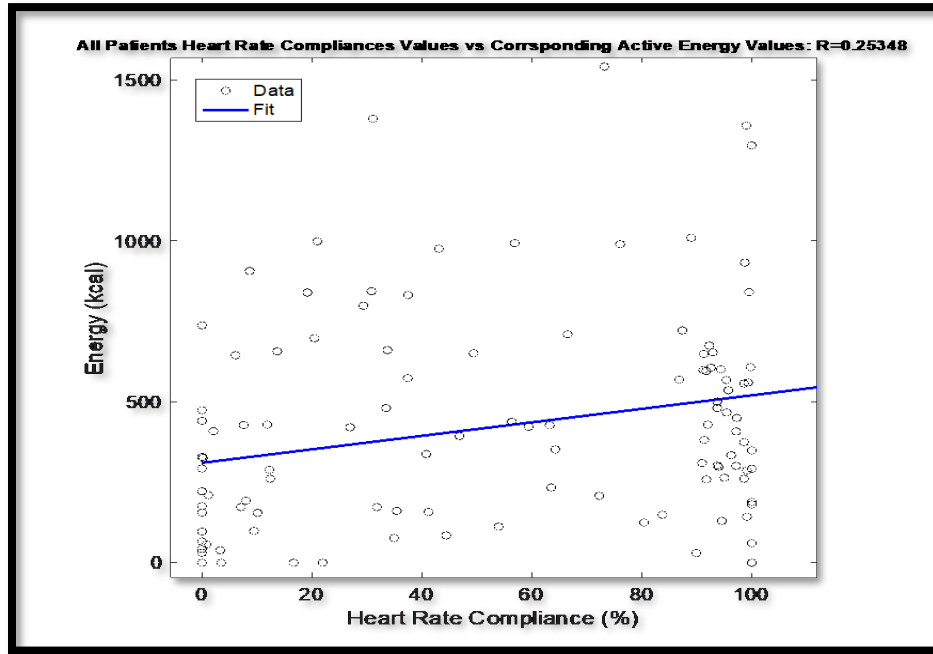


Figure 7.120: All 9 Patients Heart Rate Compliances vs. Corresponding Active Energy Sessions linear correlation

Table 7.21 shows all sessions' average heart rate and corresponding active energy linear correlation coefficients R and the  $R^2$  values for each patient. Further, Figure 7.122 illustrates all sessions' average heart rate and corresponding active energy linear correlation coefficients R-value bar plot. Finally, Figure 7.123 and Figure 7.124 shows the highest and lowest linear correlation among patient for all sessions average heart rate and their corresponding active energy.

Table 7.21: Patients Average Heart Rate Sessions vs. Active Energy Sessions, linear correlation coefficient (R), and linear regression coefficient (R2). The last row represents the Average R-value and Average R2-value

All Average Heart Rate Sessions vs. All Active Energy Sessions		
Patient #	R	R-squared
Patient 1	0.36	0.13
Patient 2	0.88	0.78
Patient 3	0.78	0.62
Patient 4	0.83	0.70
Patient 5	0.43	0.19
Patient 6	0.89	0.79
Patient 7	0.61	0.37
Patient 8	0.83	0.69
Patient 9	0.06	0.00
Average	0.69	0.57
All Patient Sessions Average Heart Rate vs. Active Energy Sessions	0.19	0.04

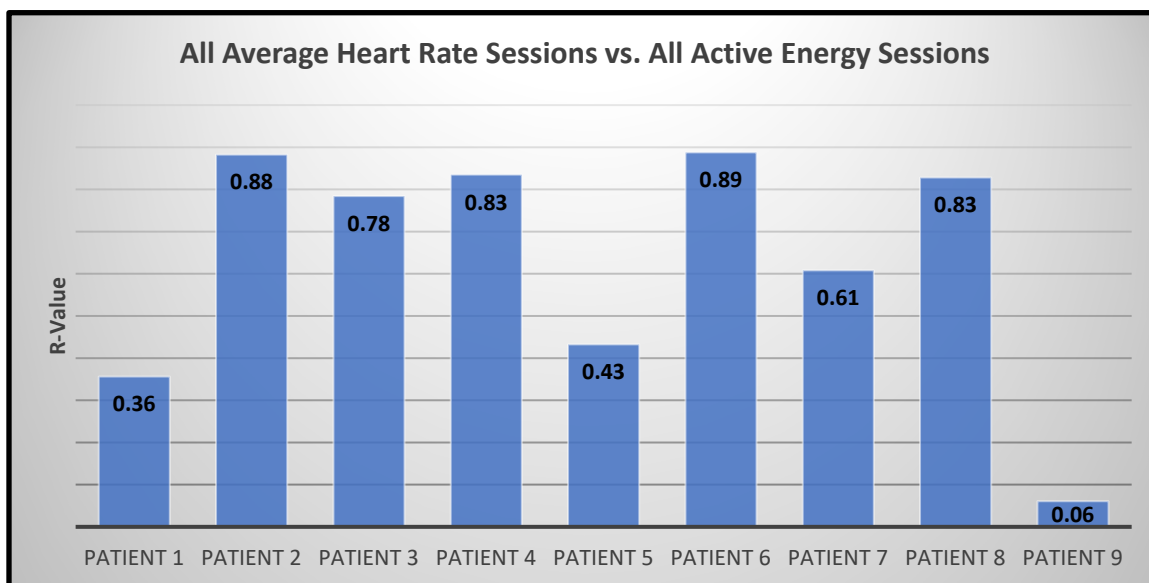


Figure 7.121: All Average Heart Rate Sessions vs. All Active Energy Sessions Linear Correlation Coefficient R-value for each patient

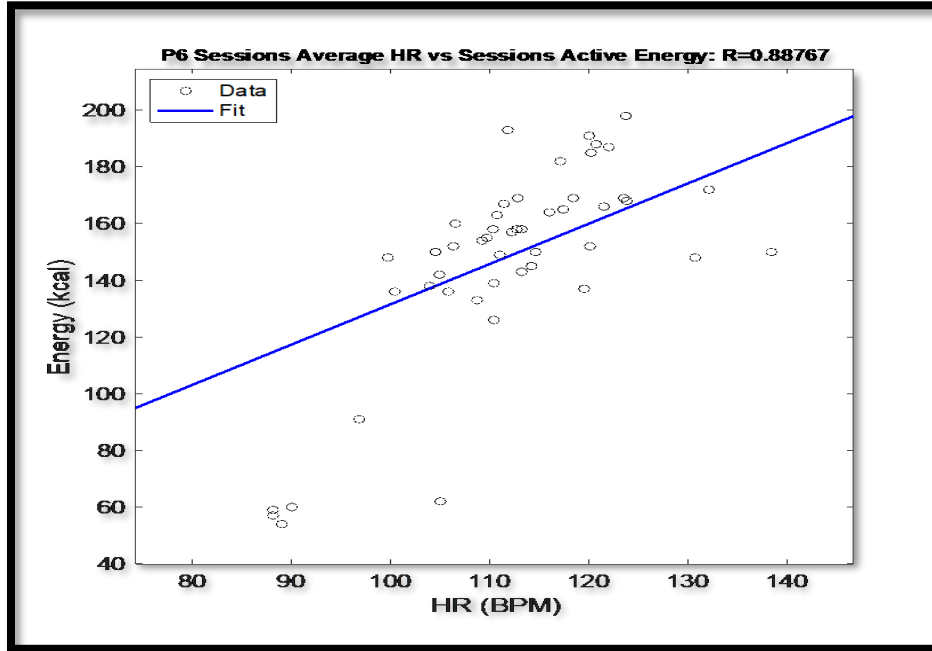


Figure 7.122: All Heart Rate Sessions vs. All Active Energy Sessions linear correlation for patient#6 (highest linear correlation coefficient among patients)

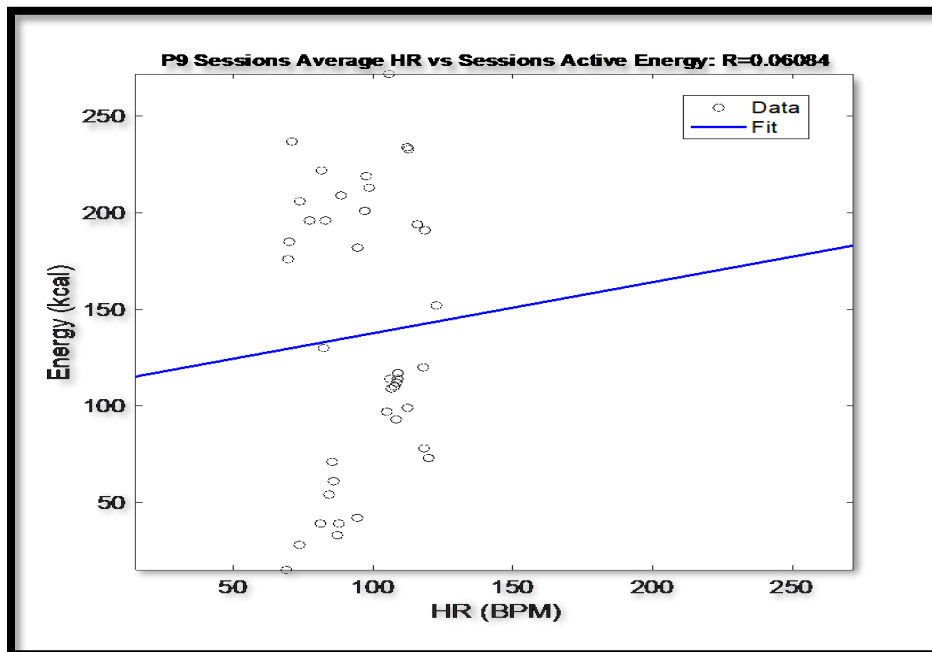


Figure 7.123: All Heart Rate Sessions vs. All Active Energy Sessions linear correlation for patient#9 (lowest linear correlation coefficient among patients)

#### 7.4 Discussion:

In general, exercise duration and Duration Compliance metrics showed a significant linear correlation with active energy. The highest linear correlation between exercise's weekly total duration and weekly total active energy as the correlation average R-value was 0.94, which indicates a strong positive linear relationship. The highest R-value was for Patient 1 data as it was 0.98, and the lowest was for Patient 7 as the R-value was 0.75. Both the highest and lowest R-values indicated a strong positive linear correlation. The average regression coefficient of determination  $R^2$  value is 0.89, which tells 89% of the data will fit the linear regression model.

The average R-value for the linear correlation between all duration sessions and all active energy sessions was 0.87, showing a strong positive linear relationship. The highest R-value was for Patient 4 data as it was 0.96, and the lowest was for Patient 9 as the R-value was 0.66. The highest R-value indicated a strong positive linear correlation, but the lowest R-value showed a moderate positive linear relationship. The average regression coefficient of determination  $R^2$  value is 0.77, which tells 77% of the data will fit the linear regression model.

Weekly Duration Compliance linear correlation with active energy also showed a strong positive linear relationship, and the R-value average was 0.86. The highest R-value was for Patient 6 data, as it was 0.97, and the lowest was for Patient 8, as the corresponding R-value was 0.62. the highest R-value indicated a strong positive linear correlation, and the lowest R-value showed a moderate positive linear relationship. However, the average regression coefficient of determination  $R^2$  value is 0.73, which shows a strong upslope and indicates that 73% of the data may fit the linear regression model. Furthermore, we tested linear correlation for all patients' durations sessions value with their corresponding active energy values. The resulting R-value was 0.61, showing a moderate positive linear relationship between them.

With further analysis, we found a moderate linear correlation between the weekly mean of average heart rate and total weekly energy. The linear correlation R-value average was 0.6, indicating a moderate positive linear relationship. However, the  $R^2$  value was 0.36, suggesting that only 36% of the data will fit a linear regression model. The highest R-value was for Patient 6 data as it was 0.91, and the lowest was for Patient 3, as that R-value was 0.26.

We found a weak linear relationship between the weekly Heart Rate Compliance and the weekly total active energy as the linear correlation average R-value was 0.42. The highest R-value was for Patient 6 data as it was 0.57, which indicates a moderate positive linear correlation. The lowest R-value was for Patient 2, as it was -0.02, which indicates no linear correlation existed.

Furthermore, we found a moderate linear relationship between the session's average heart rates and the corresponding session's active energy as the linear correlation R-value average was 0.69. The highest R-value was for Patient 6 data as it was 0.88, which indicates a strong positive linear correlation. The lowest R-value was for Patient 9, as it was 0.06. The lowest R-value showed no linear relationship. The average regression coefficient of determination  $R^2$  value is 0.57, which tells that 57% of the data will fit the linear regression model.

Also, as we gathered all the average heart rate sessions values from all 9 patients and analyzed their correlation with the corresponding active energy values. We found no linear relationship between the data as the correlation coefficient R-value was 0.2.

We believe the low linear relation between the Heart Rate Compliance and the active energy is because the patients can accumulate active energy value even when they do not achieve the prescribed target heart rate. Indeed, that can explain how patients who achieved high compliance through the 3-month exercise program did not show a high linear relationship with active energy throughout the same period.

The linear correlation coefficient average for all patient's correlation results of All Average Heart Rate Sessions vs. All Active Energy Sessions (Table 7.21) showed a moderate positive linear correlation (Average  $R=0.69$ ). However, we did not find a linear correlation when we combined all the patient's data and study the correlation between the sessions average heart rate and corresponding active energy values as the R-value was 0.19 (Figure 7.117)

We believe this discrepancy in linear correlation coefficient R-values is because it is possible to have a linear relationship between heart rate value and active energy for each patient. Still, that linear relationship could be different from one patient to other. Therefore, when all values are tested for linear relationships, the result showed no linear relationship.

Observing that the highest linear relationship was obtained for regressing the exercised session duration and the active energy for that session indicates that the Apple Watch might be giving higher weight to the duration of exercise when estimating the active energy measurements. Based on publicly available information from Apple Inc., the Apple Watch uses other data from various sensors (i.e., accelerometer and gyroscope) to calculate active energy [169]. Therefore, it is reasonable to expect that the data from plethysmography (heart rate sensor), accelerometer (motion speed sensor), and gyroscope (direction sensor) altogether have a factor in the active energy estimation. However, our results suggest that the heart rate is not prominent as the duration.

## **7.5 Conclusion**

We found a strong positive linear relationship between the exercise duration and active energy measurements and between the Duration Compliance and the active energy measurements.

Also, we found an average moderate positive linear regression between the heart rate measurements and the active energy measurements. However, we did not find a linear relationship between the Heart Rate Compliance and the active energy measurements.

## CHAPTER 8

### PMT User Rating

#### 8.1 Introduction

The System Usability Scale (SUS) offers a reliable tool for measuring software usability [170]. It comprises a ten-item questionnaire with five response options for respondents, from Strongly Agree to Disagree Strongly. Initially created by John Brooke in 1986 [170], over 1300 articles and publications have referred to the SUS, which has made this method somewhat of an industry standard. Using SUS, the observed benefits include simplicity of administering to participants, providing reliable results with a small sample size, and differentiating between usable and unusable systems effectively [170].

SUS is a Likert scale with a rating scale found on survey forms that measure how people feel about a system [171]. SUS comprises a series of questions that can be asked from a system's users to answer, ideally, 5 balanced responses that users can select. Also, it often comes with a neutral midpoint [171].

Furthermore, the scale measurements of usability have several different aspects such as effectiveness (can patients accomplish their goals), efficiency (how much effort and resource are expended in achieving those objectives), and satisfaction (was the experience satisfactory) [170]. This chapter will study the result of the SUS surveys that the patients filled at the end of their three months of exercise intervention and were asked to assess their experience with the iPhone and Apple Watch application apps (*TBIcare*) of the PMT ecosystem.



## 8.2 Method

The SUS has ten items questioner with five response options for respondents, from Strongly Agree to Disagree Strongly, without any wording between them. The questions are presented to the patients were as follows:

1. I think that I would like to use this system frequently.
2. I found the system unnecessarily complex.
3. I thought the system was easy to use.
4. I think that I would need the support of a technical person to be able to use this system.
5. I found the various functions in this system were well integrated.
6. I thought there was too much inconsistency in this system.
7. I would imagine that most people would learn to use this system very quickly.
8. I found the system very cumbersome to use.
9. I felt very confident using the system.
10. I needed to learn a lot of things before I could get going with this system.

After each patient completes the 3-months prescribed physical exercise intervention using the TBicare app, they participated in an in-clinic exit visit. At the end of each patient's visit, the patient was asked to fill a SUS survey uploaded on a website link.

To calculate each patient's SUS score, we will subtract 1 from every odd question's score [170]. For example, if a patient answered for question number 5 was the second response after Strongly Agree, which is number 2, then the score for that question will be 1, as  $2-1=1$ . Moreover, for each of the even-numbered questions, we will subtract their value from 5 [170]. For example, if a patient answered for question number 8, the mid response between Strongly Agree and Strongly Disagree, which is number 3, then the score for that question will be 2, as  $5-3=2$ .

Finally, to calculate the SUS score, we will sum the score inputs from each item [170]. Then we will multiply the sum of the scores by 2.5 to obtain the overall value of SUS. SUS scores have a range of 0 to 100 [170]. From the literature, the average SUS score is 68 [171]. Therefore, the literature suggests that a score value of 80.3 or higher is considered an A score [170]. This score indicates the patient highly accepts the applications [170]. A score around 68 gets the applications a C [170], and it is interpreted that the applications are acceptable but could improve [170]. A score value of 51 or under means that the applications failed and did not meet patient satisfaction [170].

Once we collected and calculated the user's scores, the correlation between users' compliance and user satisfaction on the PMT system was studied.

### 8.3 Results

Table 8.22 shows the average weekly heart rate compliance, weekly duration compliance, weekly frequency compliance, and weekly momentarily heart rate compliance metrics and sus scores for each patient. In addition, the table also presents each metric median, highest, lowest, and average values for the sample population are also given. Also, we are showing in Table 8.23 the Pearson linear correlation coefficients R-value for the comparison for each of the patient's compliance metrics with the patient's SUS score. The frequency compliance metric showed a negative moderate linear relationship with the patient's SUS scores.

*Table 8.22: Average of Weekly Heart Rate Compliance, Duration Compliance, Frequency Compliance, and Momentarily Heart Rate Compliance metrics and SUS Scores for each patient. Each metric median, highest, lowest, and average values for the sample population are also presented.*

Patient Number	Heart Rate Compliance%	Duration Compliance%	Frequency Compliance%	Momentarily Heart Rate Compliance%	SUS Score
1	94.32	97.84	102.56	100.00	57.50
2	89.15	89.29	85.90	100.00	50.00
3	25.18	77.28	63.46	73.33	85.00
4	82.69	63.97	51.92	71.67	67.50
5	13.87	44.14	53.33	78.33	87.50
6	39.85	80.70	79.10	85.00	92.50
7	34.06	91.40	70.51	91.67	77.50
8	95.28	83.38	95.51	91.67	95.00
9	26.71	97.84	102.56	78.33	32.50
Median	39.85	83.38	79.10	85	77.50
Highest	95.28	97.84	102.56	100	95.00
Lowest	13.87	44.14	51.92	71.67	32.50
Average	55.68	80.64	78.32	84.62	71.67

Table 8.23: SUS scores and each Compliance Metric Pearson Linear Correlation Determination Coefficients (R-Values)

Compliance Metric	Pearson Linear Correlation R-Value
Heart Rate Compliance	-0.15
Duration Compliance	-0.51
Frequency Compliance	-0.5
Momentarily Heart Rate Compliance	-0.16

#### 8.4 Discussion:

SUS score results had an average of 71.67 and a median of 77.5. The average and the median scores indicate that the patients felt that the combined Apple Watch and iPhone application is acceptable, but they need some improvements. A Pearson Linear Correlation determination coefficient was calculated between each average compliance metric and the SUS score for each patient. The highest correlation was for the Duration Compliance then Frequency Compliance. The linear correlation R-values for these two compliances indicated that the Duration Compliance and the Frequency Compliance have a moderate negative linear relationship.

However, The Linear Correlation R-values for the Heart Rate Compliance and the Momentarily Herat Rate Compliance showed no linear correlation between them and the SUS scores.

Furthermore, all the linear correlation coefficients were negative. That indicates the higher the compliance from the patient, the lower SUS scores the applications received. This finding suggests that the more experience the patient has with the application, the more area of improvement the patient will notice in the application.

## **8.5 Conclusion:**

The SUS average score for the PMT's iPhone and Apple Watch applications indicates that the patients believe that the applications are acceptable but need some improvements. A moderate negative correlation was found between the SUS scores and the Duration Compliance and between the SUS scores and the Frequency Compliance. That indicates the more the patients used the phone and the watch applications more points of improvement were discovered by the patients.

## CHAPTER 9

### CONCLUSIONS AND FUTURE WORK

#### 9.1 Conclusions

The main impact of this study has shown the feasibility of developing a mobile-based PMT system to:

- Help TBI patients to increase their compliance to prescribed exercise treatment
- Objectively track the level of the exercise that they perform
- Enable the clinicians to monitor at all times the compliance of the patients with the prescribed exercise treatment
- Objectively measure the effect of the prescription on the patient on heart rate for each exercise session
- Provide encouragement and feedback to the patient using a multimodal communication approach
- Obtain input from the patient about the perception of the difficulty of the exercise (using Borg survey) by the clinicians; so that they can take that into account such perceptions in adjusting the prescription and improving the patient compliance.

This study developed and tested a home health care system for enhancing exercise therapy for traumatic brain injury patients. A Personal Mobile Trainer system (PMT) was created aiming to aid traumatic brain injury patients to maintain their prescribed physical exercises by eliminating barriers that can face TBI patients to achieve exercise goals, thus increasing their exercises adherence. Furthermore, the designed system provided the medical care team the facility to

instantly monitor and, if need, provide input to the patients regarding their physical exercise progress. Such access to patient progress also aids the medical care team in modifying or adjust the physical exercises prescription for each patient, as needed.

The study was started by defining the platform that the system was built on. Therefore, the study was initiated by assessing the accuracy of heart rate measurements by four wrist-worn fitness tracking devices during slow walking, fast walking, sitting, slow biking, and fast biking in five healthy subjects. The Apple watch showed the highest agreement, followed by the Polar watch compared to ECG. Apple Watch successfully pursues the dynamic changes in ECG.

Based on the WFT assessments results, the PMT system was designed and built by utilizing Apple Watch as the WFT device in conjunction with the Apple iPhone. Then to complete the PMT design, a cloud-based server was incorporated in the PMT hardware design structure that allows a convenient and highly flexible means of accessing patient's exercise activities at any place and point in time that internet access is available. The proposed PMT system was built and tested successfully with the research team members prior to using it with TBI patients.

The PMT was issued to the TBI volunteer subjects who participated in a 3-month exercise therapy study to evaluate the feasibility of this technology monitoring patient compliance and its potential efficacy in increasing compliance. Four metric compliances were proposed and applied to the outcome of the PMT system for exercise. The compliance metrics were Heart Rate Compliance, Duration Compliance, Frequency Compliance, and Heart Rate Momentarily Compliance. Momentarily Heart Rate Compliance showed the highest compliance average ( $84.62\% \pm 12.16\%$ ), and the Herat Rate Compliance metric showed the least compliance average among all the patients ( $55.68\% \pm 33.8$ ). Duration Compliance also resulted in an acceptable average of ( $80.64\% \pm 17.23$ ), which is considered above the medical team pilot study threshold.

These results showed that the PMT system could increase TBI patient's adherence to prescribed physical exercises.

Also, the difference in heart rate variability pre and post the exercises therapy interventions in TBI subjects was studied using the PMT system. No change was found in the heart rate variability results collected from ECG and Apple Watch between pre- and post-intervention. In addition, the possibility of using the Apple Watch in estimating heart rate variability in traumatic brain patients pre and post exercises intervention was assessed using the PMT system. It was found that HRV measures derived from Apple Watch do not fully match those derived from the ECG. However, the Apple Watch showed feasibility in estimating HRV from apple watch and using it as an index of exercise effectiveness.

Additionally, among the four heart rate variability metrics considered in this study, only the frequency-domain very-low-frequency power (VLF) appears to reasonably estimate the VLF power computed from ECG.

The correlation between the change in the exercise active energy and activity prescribed metrics was applied to define the exercise intensity, such as exercise duration and heart rates. It was found that there is a strong positive linear correlation between the exercise duration and active energy measurements and between the Duration Compliance and the active energy measurements. Alternatively, the correlation coefficient between the Heart Rate Compliance and the active energy measurements was low. Nevertheless, it was found an average moderate positive linear correlation between heart rate and active energy measurements.

Finally, the SUS average score for the PMT's iPhone and Apple Watch applications indicated that the patients believed that the applications are acceptable but needed some improvements.



## 9.2 Future Work

The PMT system's feasibility for tracking compliance can be further investigated to monitor the system's efficacy on larger patient groups. Also, evaluating active energy estimation by the Apple Watch in healthy subjects compared to actigraph to verify the Apple watch energy estimation accuracy should be considered. In addition, studying the active energy estimation by the Apple Watch on TBI patient need to be made to determine the accuracy of the energy expenditure during exercise for the TBI patients.

Furthermore, the Apple Watch's accuracy in estimating the heart rate measurements should be verified on more healthy subjects to define the accuracy of estimated heart rate variability.

Moreover, studying the heart rate variability on more extended exercise interventions to test the efficacy of the exercise interventions on the heart rate variability metrics should be considered in future studies. Also, studying the accuracy of the Apple Watch in estimating HRV on a more extended period (e.g., 24 hrs) may be helpful. Additionally, as the new versions of the Apple Watch can estimate oxygen saturation (SpO<sub>2</sub>), studying the accuracy of the Apple Watch in assessing oxygen the accuracy of saturation (SpO<sub>2</sub>) measurements compared to medical oxygen oximetry could be valuable. Likewise, it would be beneficial if the WFT manufacturers would provide enhancements that can be accessed by the PMT designers, such as more instantaneous heart rate measurements, calorie expenditure as a function of time that is not limited to exercise periods or exercise type.

metrics. We will also study the accuracy of the Apple Watch in estimating oxygen saturation (SpO<sub>2</sub>) comparing to medical oxygen oximetry.

## Appendices

### A.2 CHAPTER 2 APPENDIX:

#### A.2.1: ECG and WFT Heart Rate Measurements Comparison

##### *Slow Walk Mode*

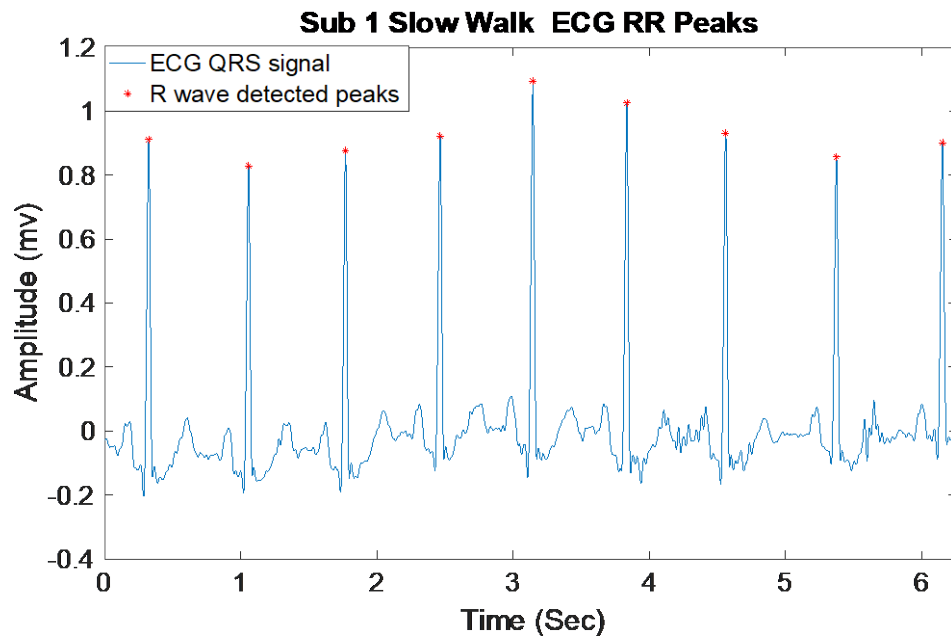


Figure A2.124: Subject No.1 slow walk ECG RR peak detection

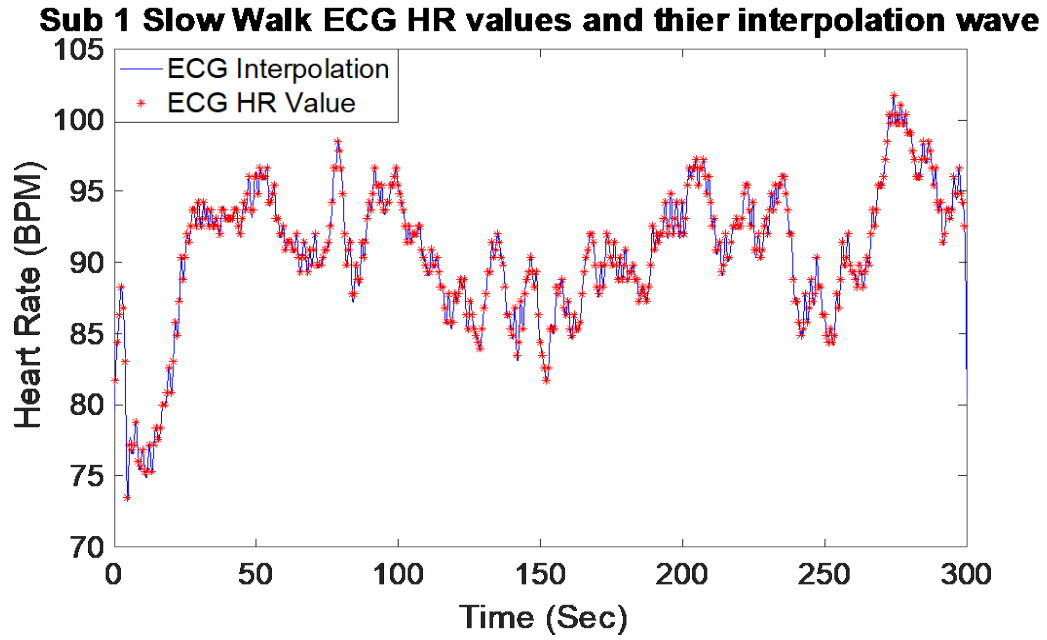


Figure A2.125: Subject No.1 ECG HR Slow Walk interpolation

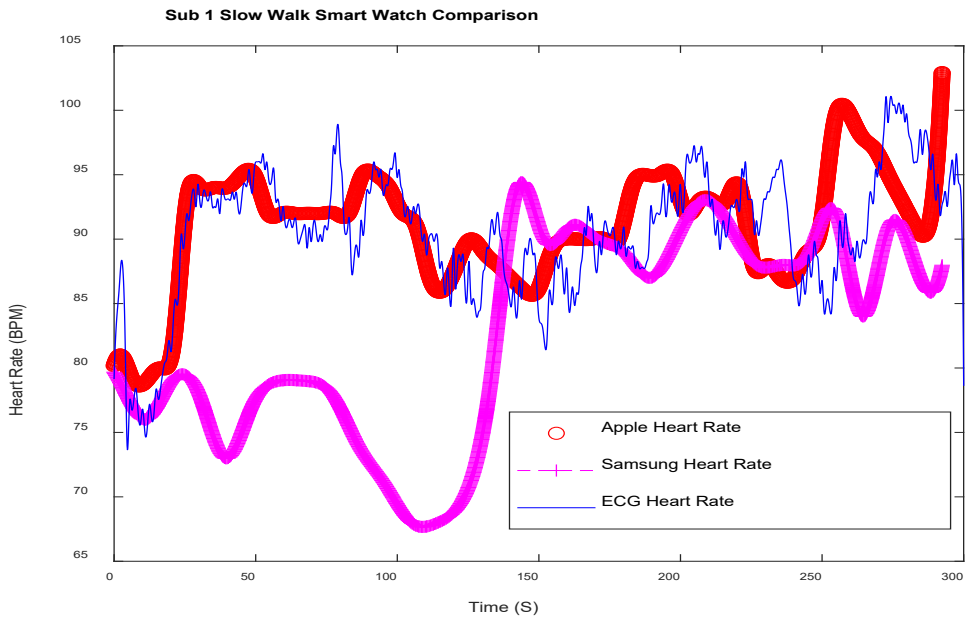


Figure A2.126: Subject No1 Slow Walk WFT Comparison

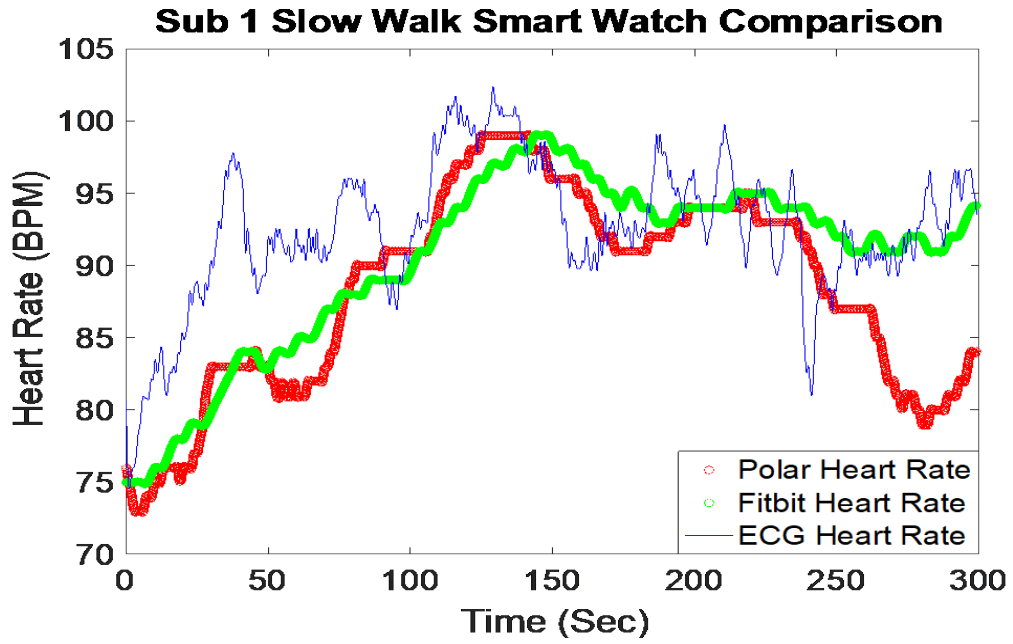


Figure A2.127: Subject No1 Slow Walk WFT Comparison

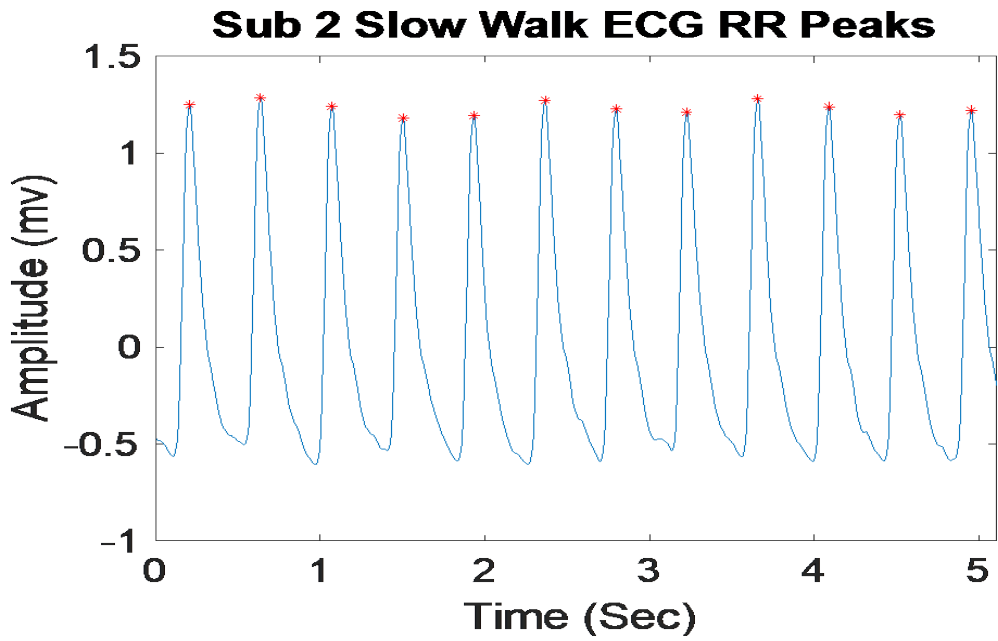


Figure A2.128: Subject No. 2 Slow Walk ECG RR Peaks detection

### Sub 2 Slow Walk ECG HR values and thier interpolation wave

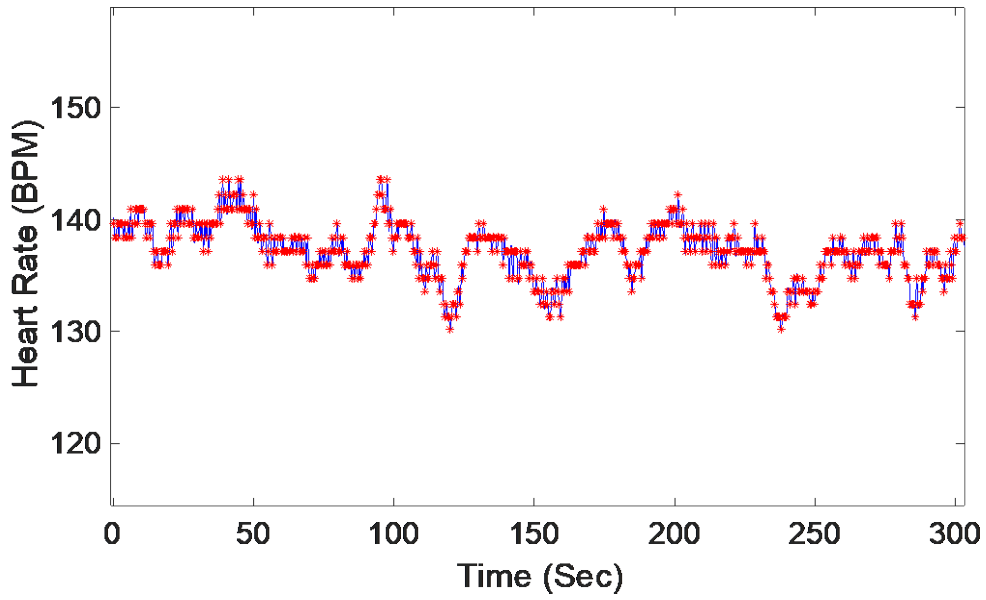


Figure A2.129: Subject No.2 Slow walk exercise ECG interpolation

### Sub 2 Slow Walk Smart Watch Comparison

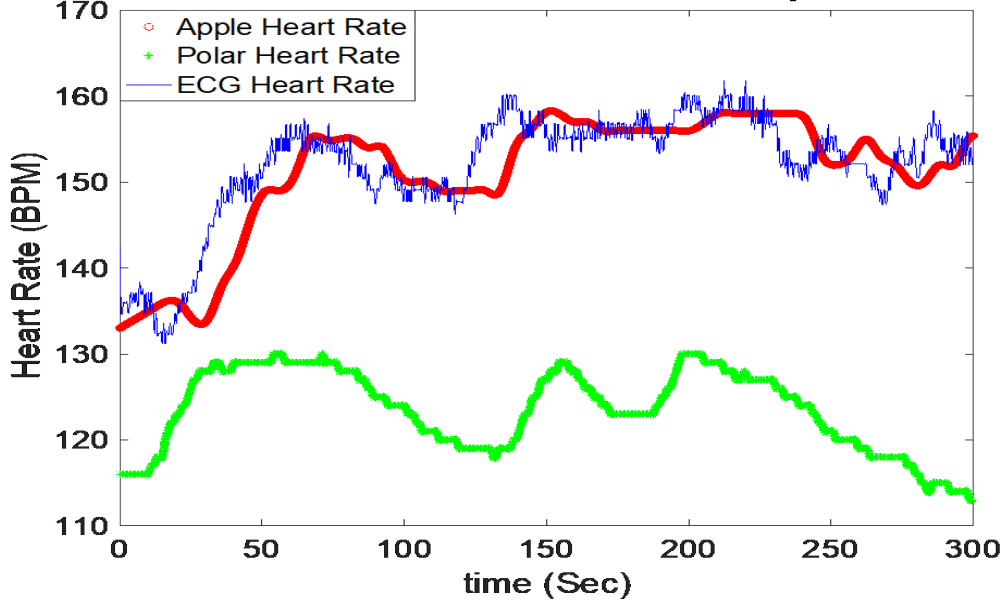


Figure A2.130: Subject No.2 Slow Walk Apple and Polar WFT compared to ECG

### Sub 2 Slow Walk Smart Watch Comparison

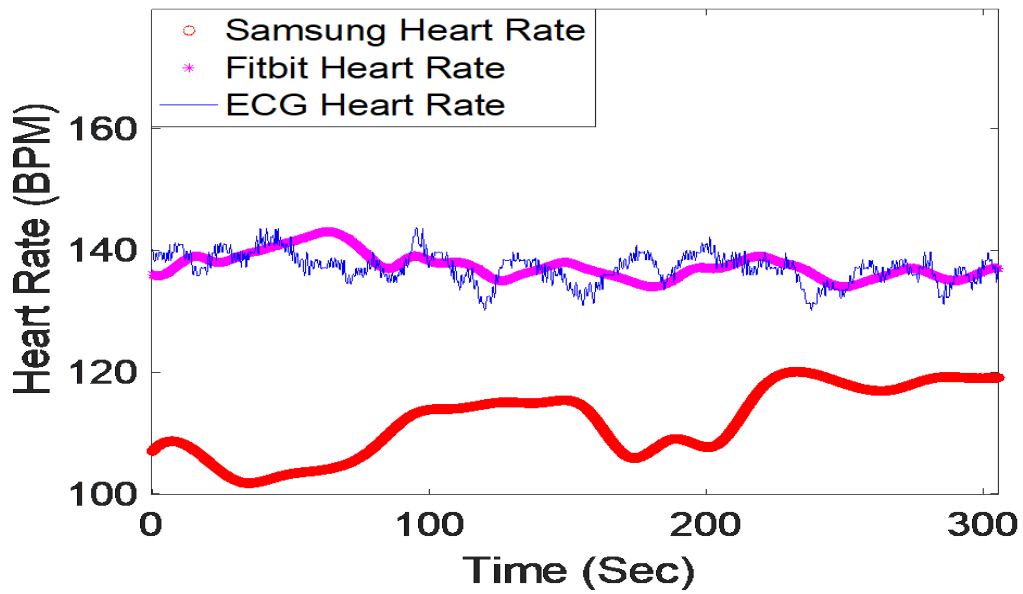


Figure A2.131: Subject No.2 Slow Walk Samsung and Fitbit WFT's compared to ECG

### Sub 3 Slow Walk ECG RR Peaks

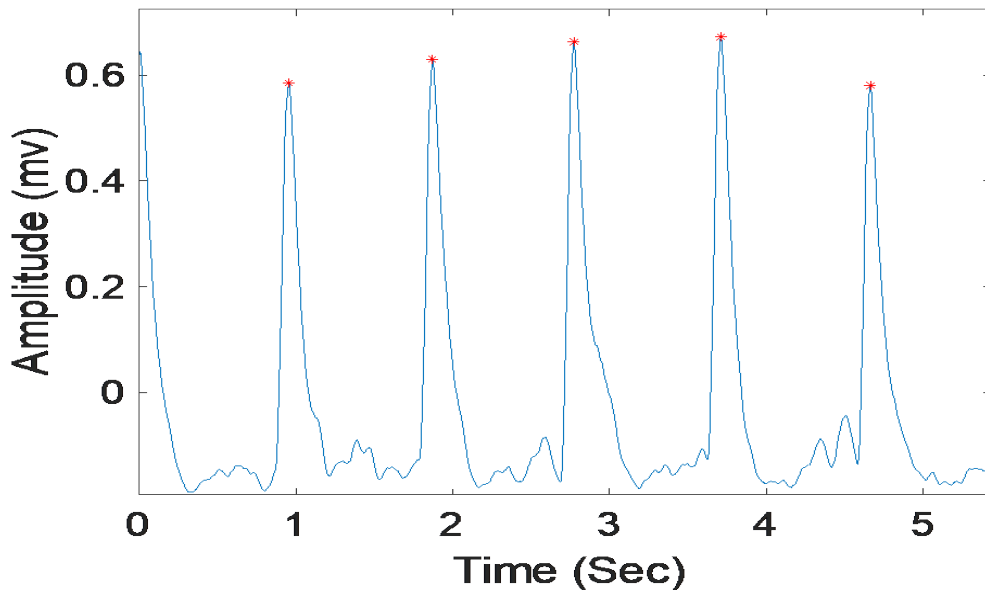


Figure A2.132: Subject No. 3 slow walk ECG RR Peaks detection (Amplified R wave)

### Sub 3 Slow Walk ECG HR values and thier interpolation wave

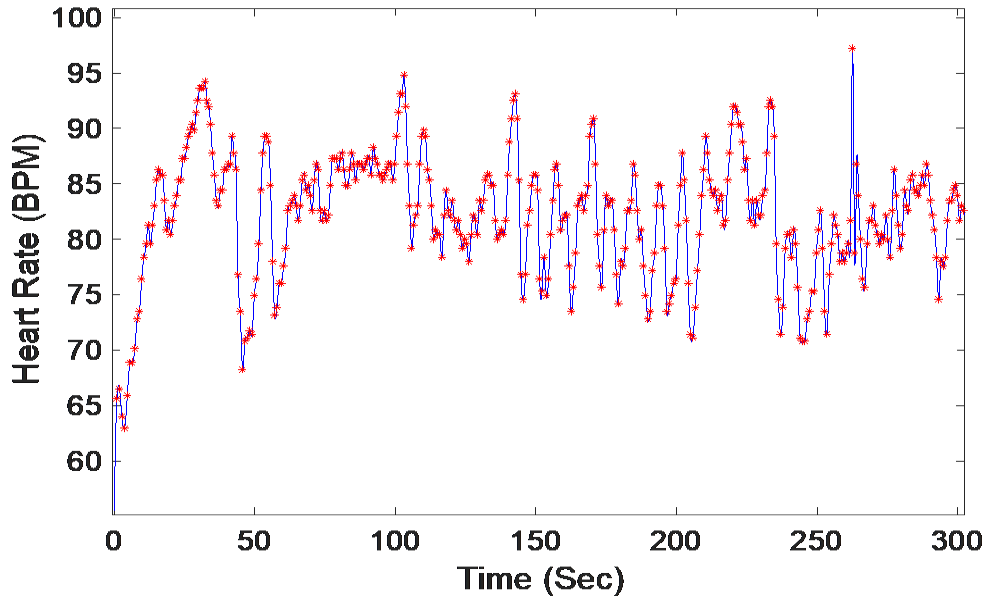


Figure A2.133: Subject No.3 slow walk exercise ECG HR interpolation

### Sub 3 Slow Walk Smart Watch Comparison

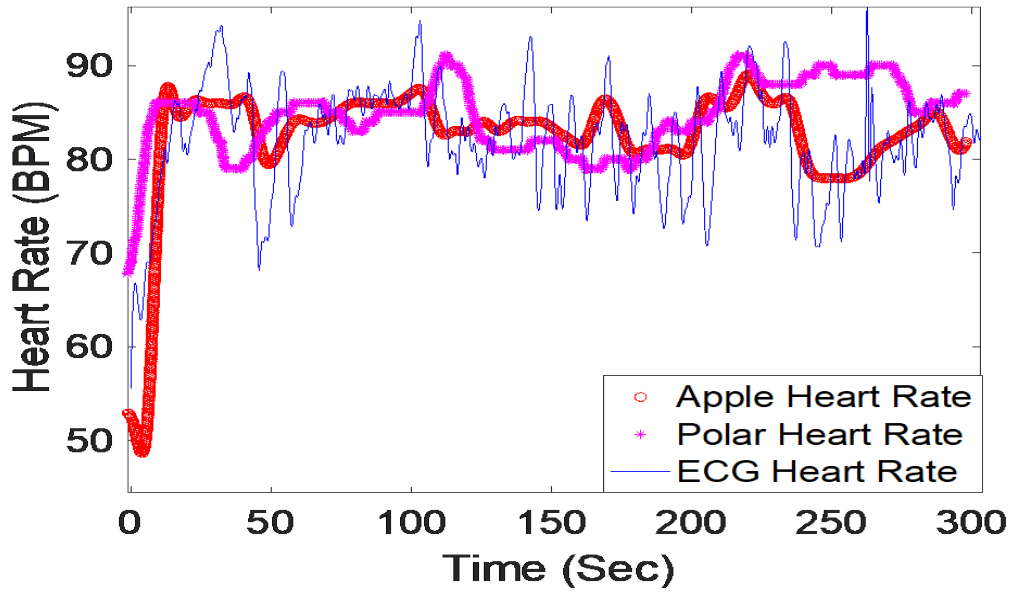


Figure A2.134: Subject No.3 slow walk Apple and Polar WFT compared to ECG

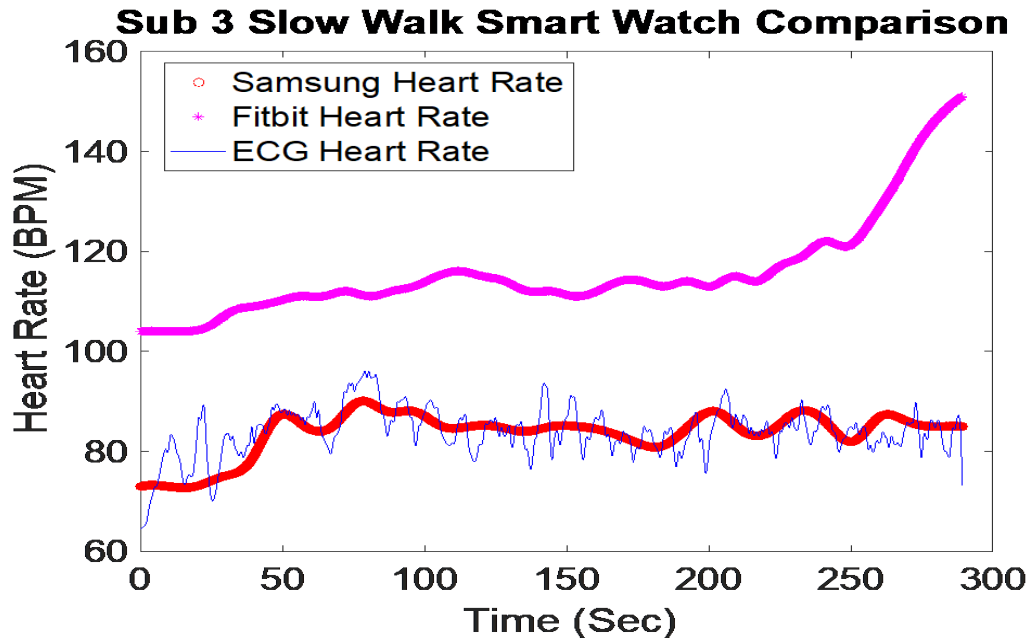


Figure A2.135: Subject No.3 slow walk Samsung and Fitbit WFT compared to ECG

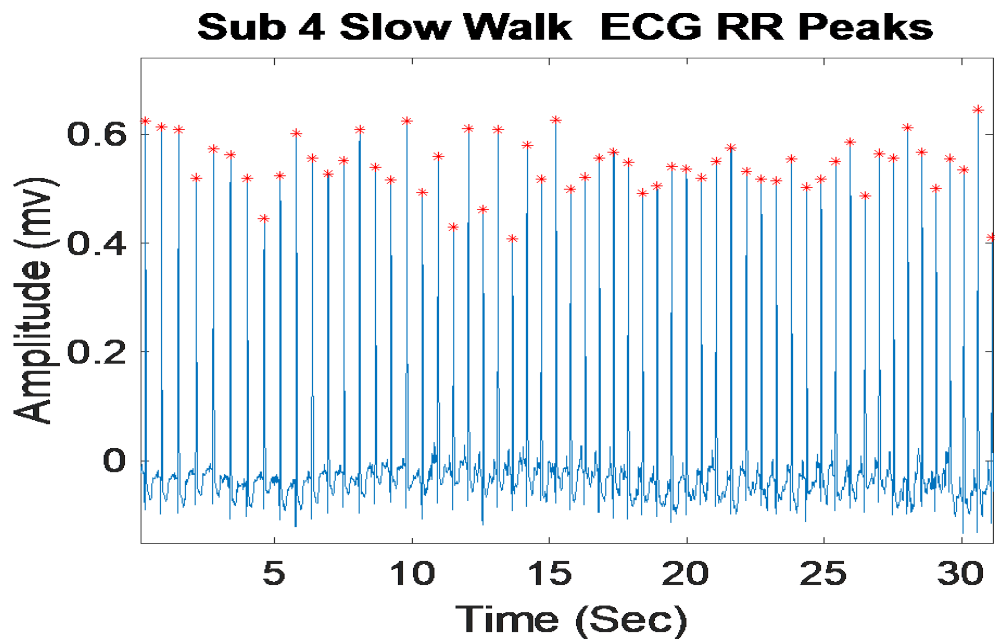


Figure A2.136: Subject No. 4 slow walk ECG RR Peaks detection



### Sub 4 Slow Walk ECG HR values and their interpolation wave

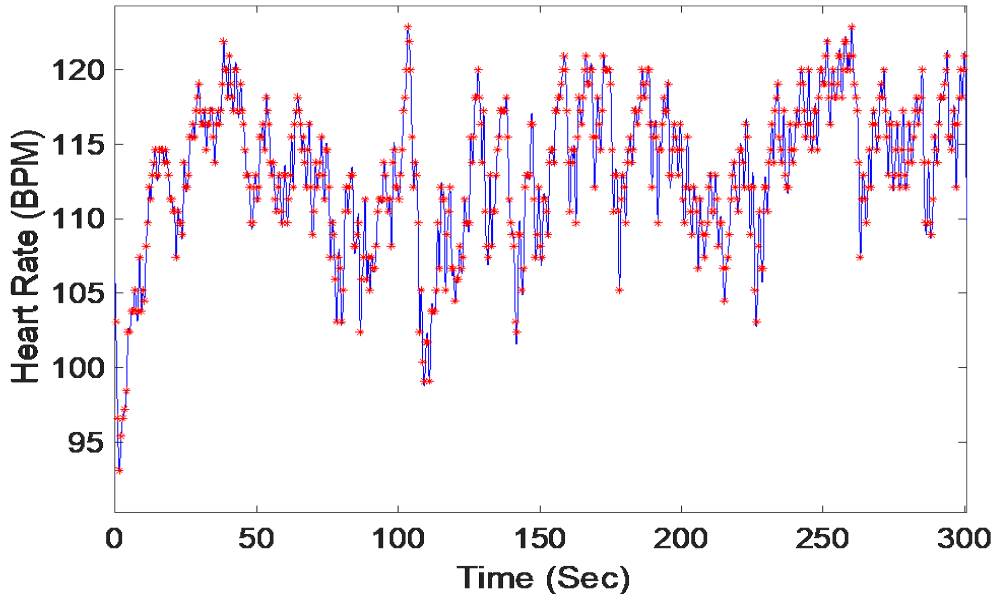


Figure A2.137: Subject No.4 slow walk exercise ECG HR interpolation

### Sub 4 Slow Walk Smart Watch Comparison

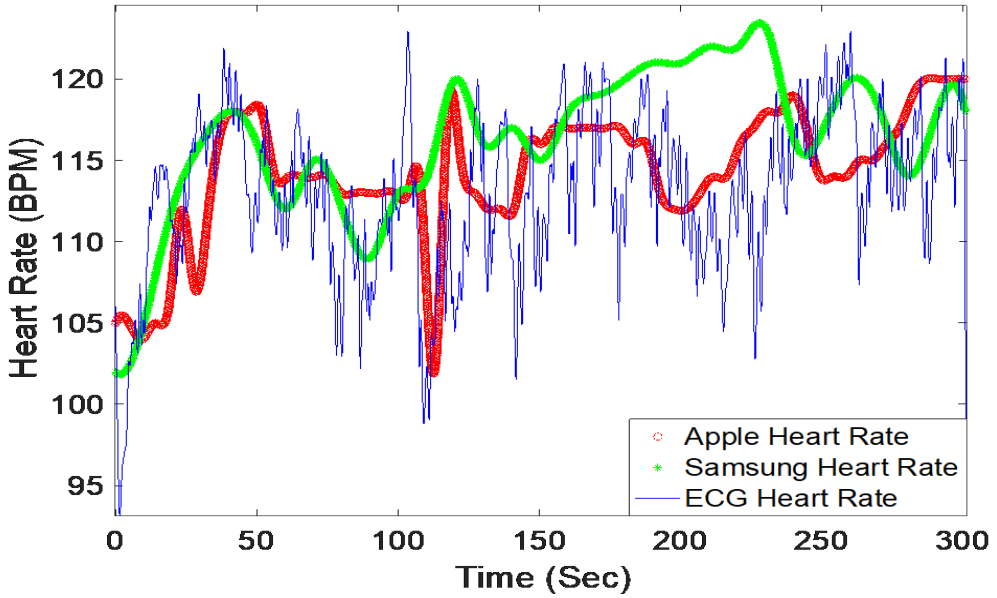


Figure A2.138: Subject No.4 slow walk Apple and Samsung WFT compared to ECG

### Sub 4 Slow Walk Smart Watch Comparison

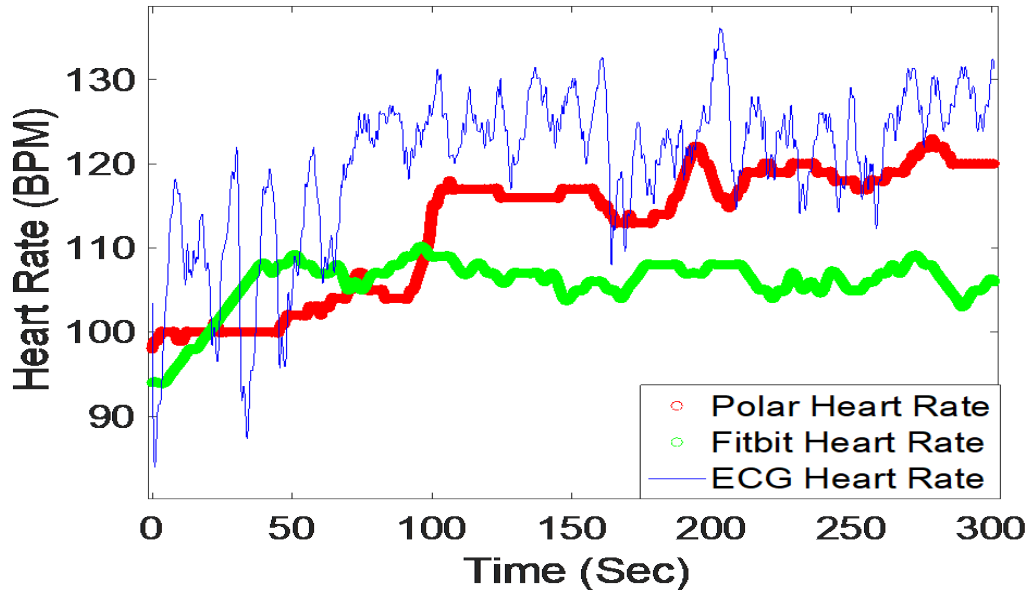


Figure A2.139: Subject No.4 slow walk Polar and Fitbit WFT compared to ECG

### Sub 5 Slow Walk ECG RR Peaks

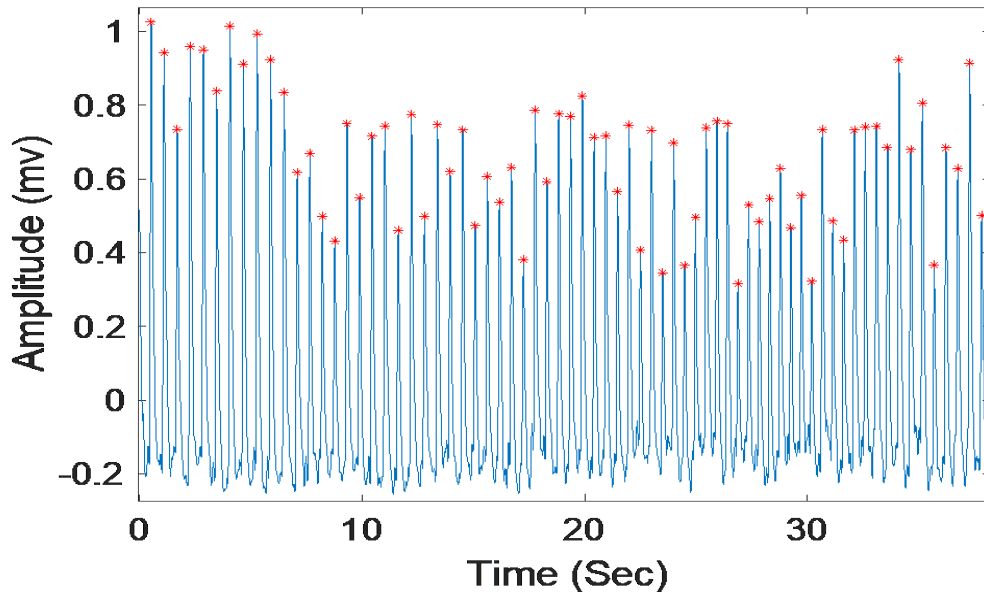


Figure A2.140: Subject No. 5 slow walk ECG RR Peaks detection (Amplified R wave)

### Sub 5 Slow Walk ECG HR values and thier interpolation wave

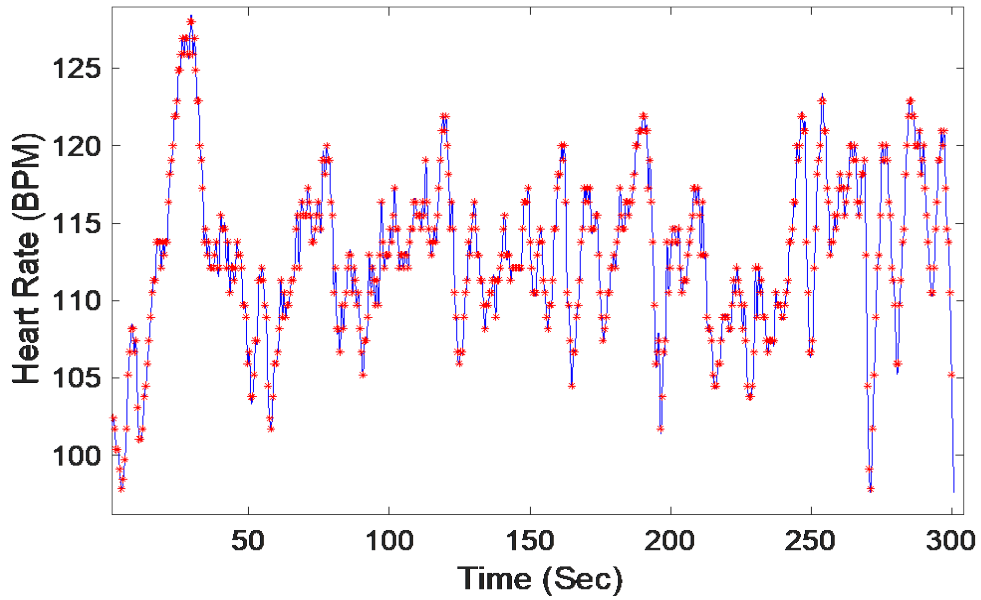


Figure A2.141: Subject No.5 slow walk exercise ECG HR interpolation

### Sub 5 Slow Walk Smart Watch Comparison

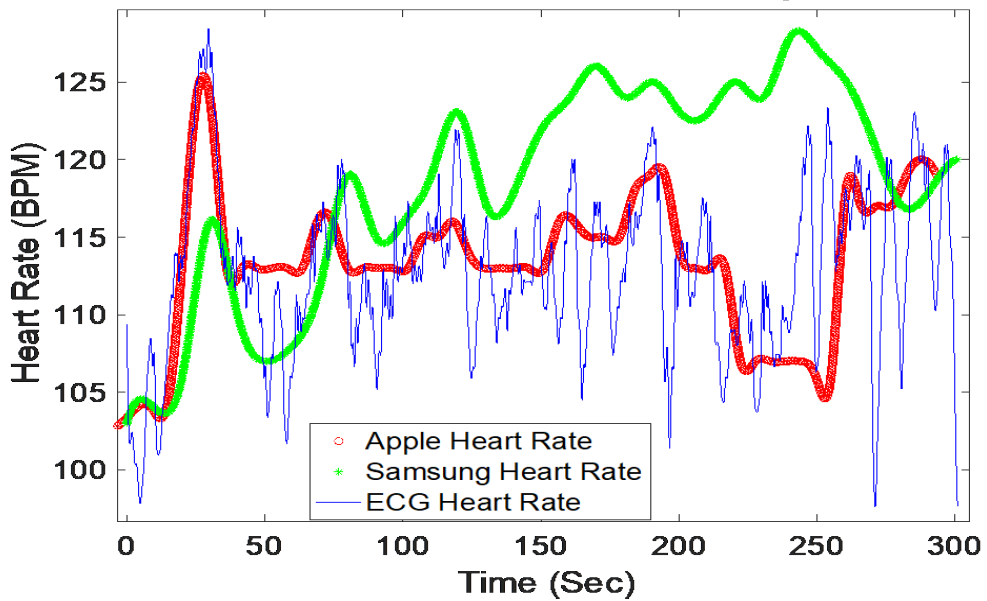


Figure A2.142: Subject No.5 slow walk Apple and Samsung WFT compared to ECG

### Sub 5 Slow Walk Smart Watch Comparison

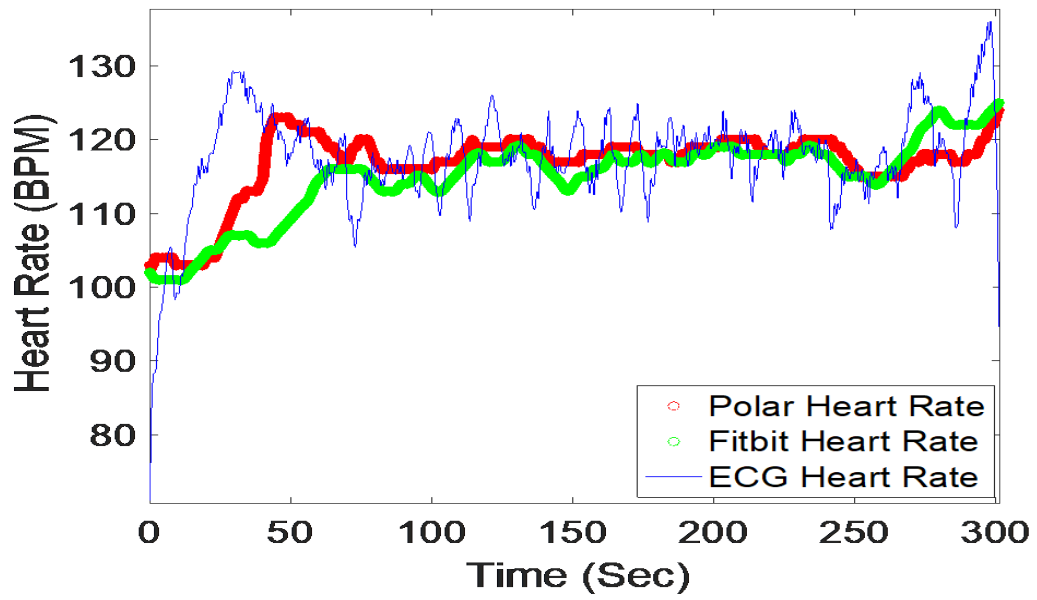
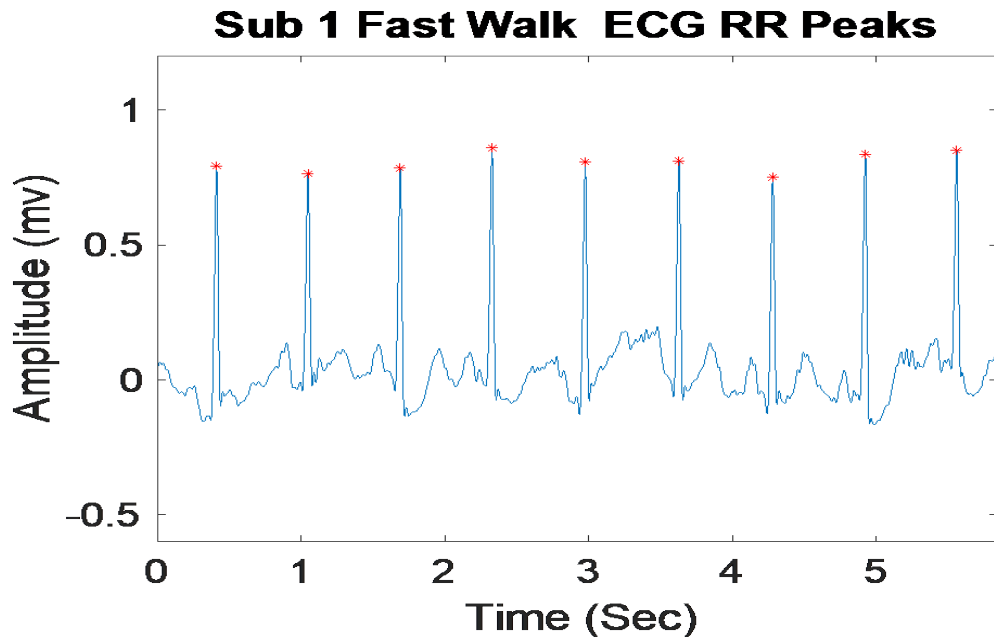
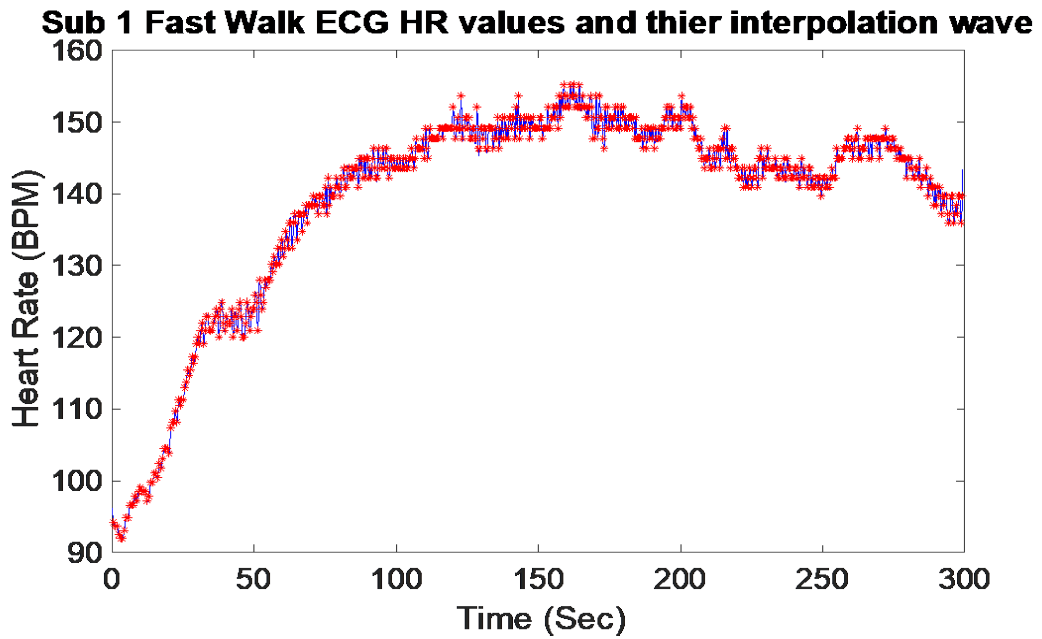


Figure A2.143: Subject No.5 slow walk Polar and Fitbit WFT compared to ECG

*Fast Walk Mode*



*Figure A2.144: NO.1 Fast walk ECG RR peak detection*



*Figure A2.145: Subject No.1 ECG HR Fast Walk interpolation*

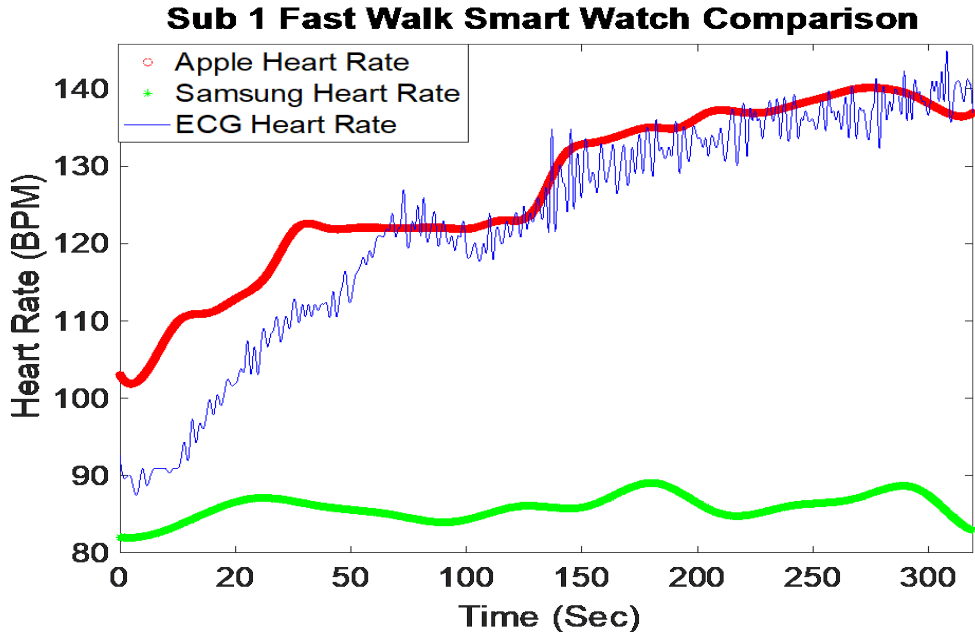


Figure A2.146: Subject No1 Fast Walk WFT Comparison

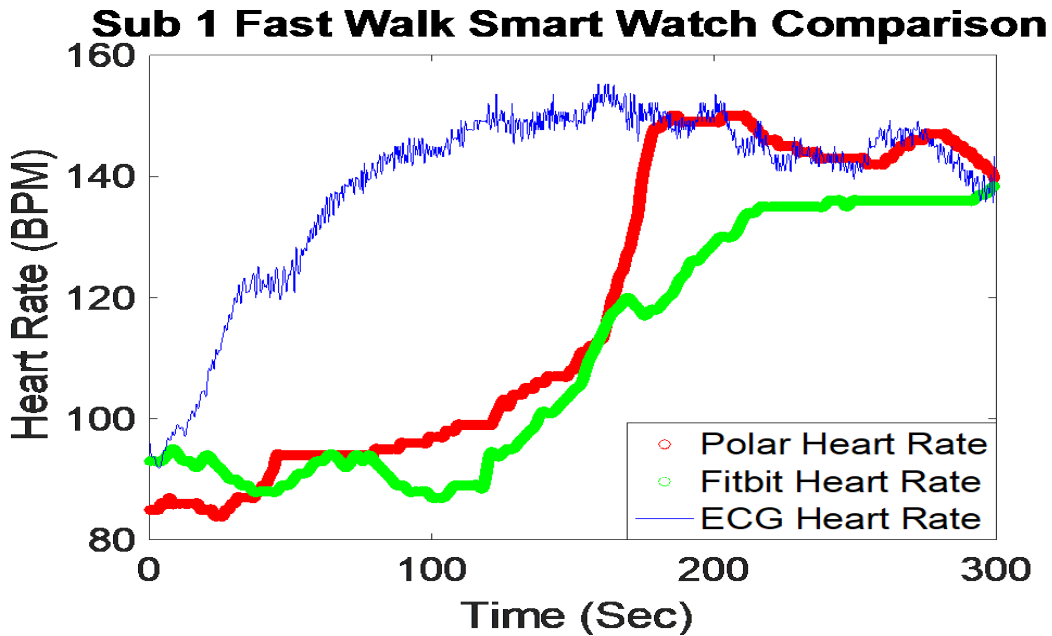


Figure A2.147: Subject No.1 Fast Walk WFT comparison

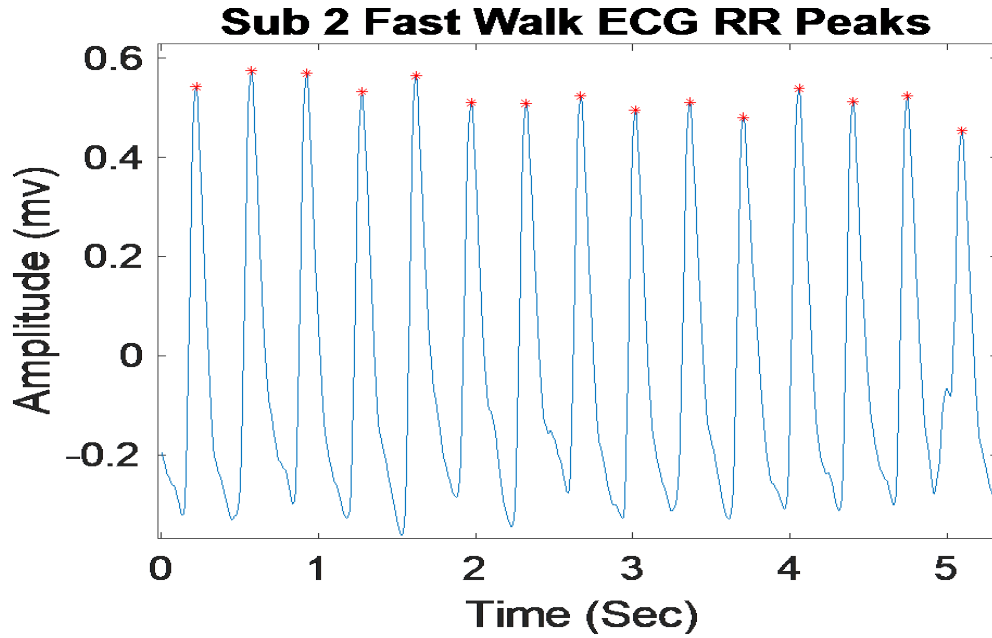


Figure A2.148: Subject No. 2 Fast Walk ECG RR Peaks detection (Amplified R wave)

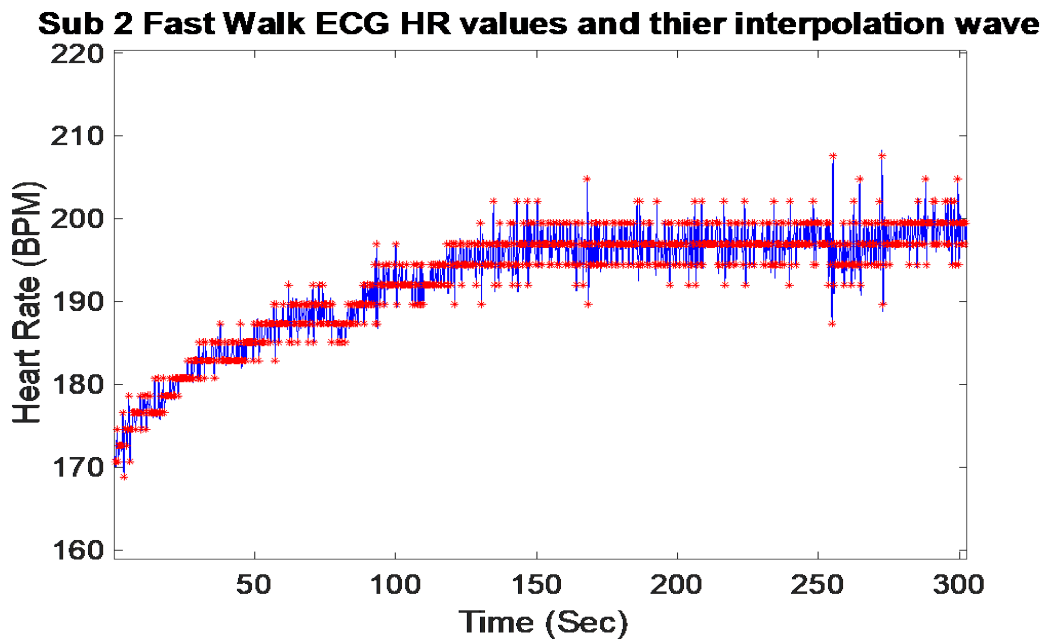


Figure A2.149: Subject No.2 fast walk exercise ECG interpolation

### Sub 2 Fast Walk Smart Watch Comparison

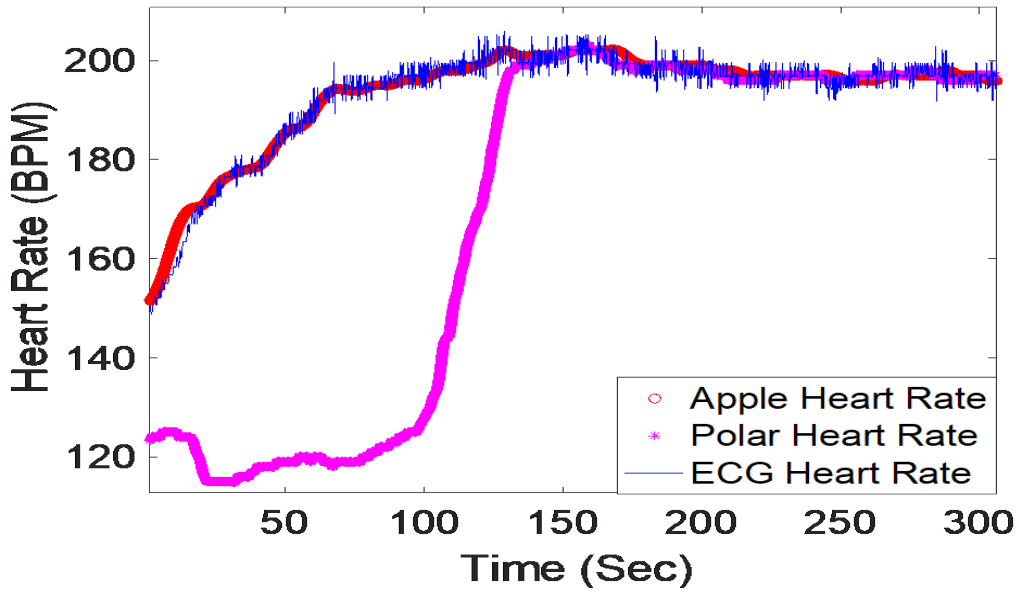


Figure A2.150: Subject No.2 Fast Walk Apple and Polar WFT compared to ECG

### Sub 2 Fast Walk Smart Watch Comparison

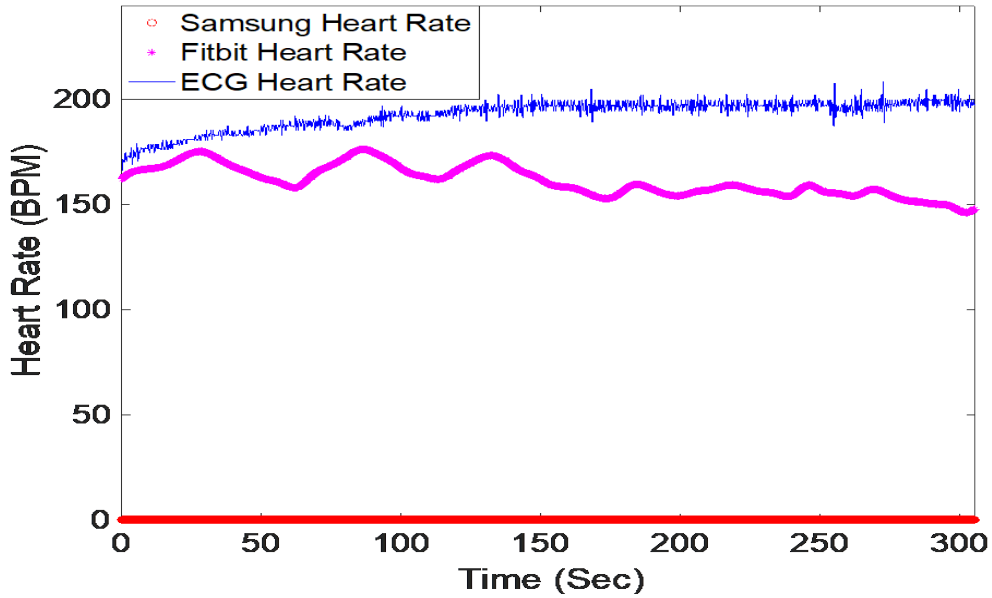


Figure A2.151: Subject No.2 Fast Walk Samsung and Fitbit WFT compared to ECG



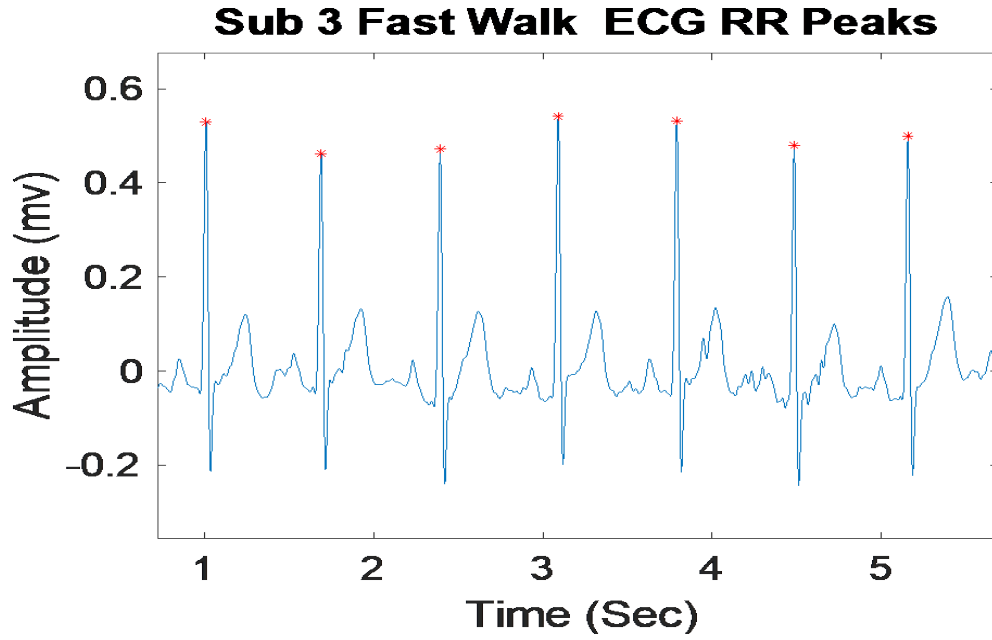


Figure A2.152: Subject No. 3 fast walk ECG RR Peaks detection

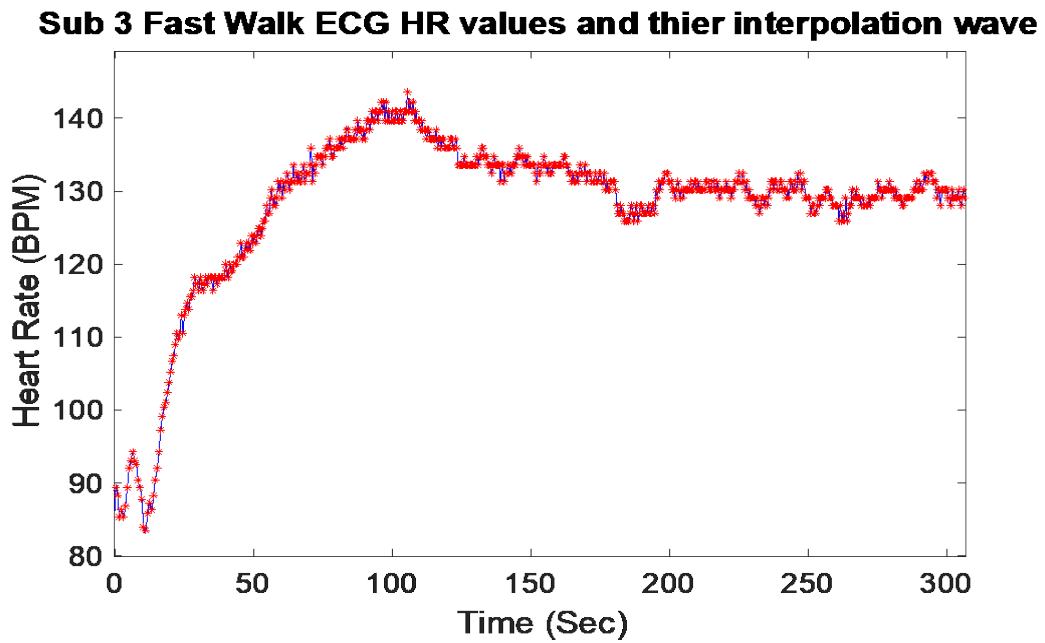


Figure A2.153: Subject No.3 fast walk exercise ECG HR interpolation

### Sub 3 Fast Walk Smart Watch Comparison

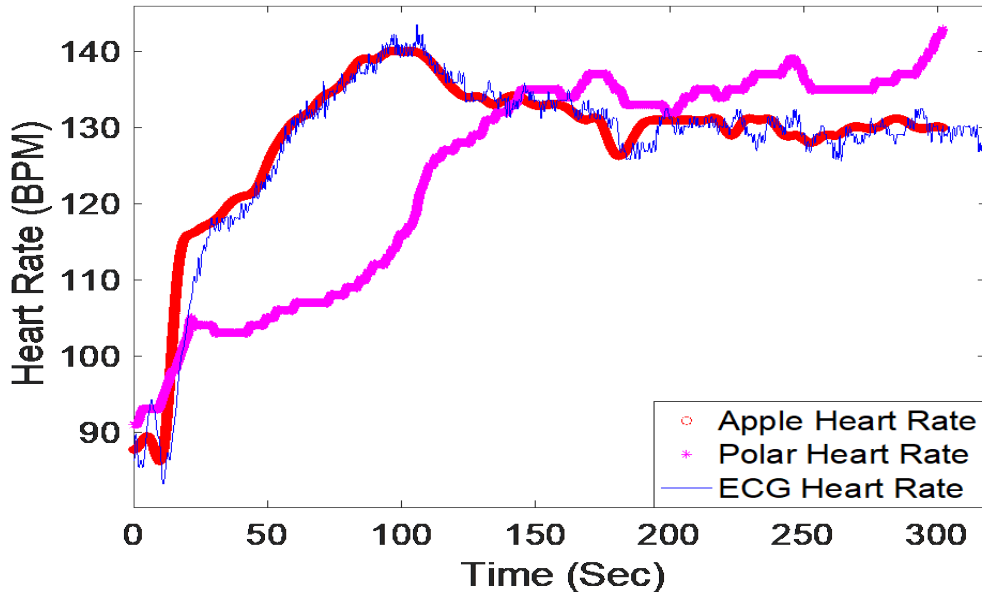


Figure A2.154: Subject No.3 fast walk Apple and Polar WFT compared to ECG

### Sub 3 Fast Walk Smart Watch Comparison

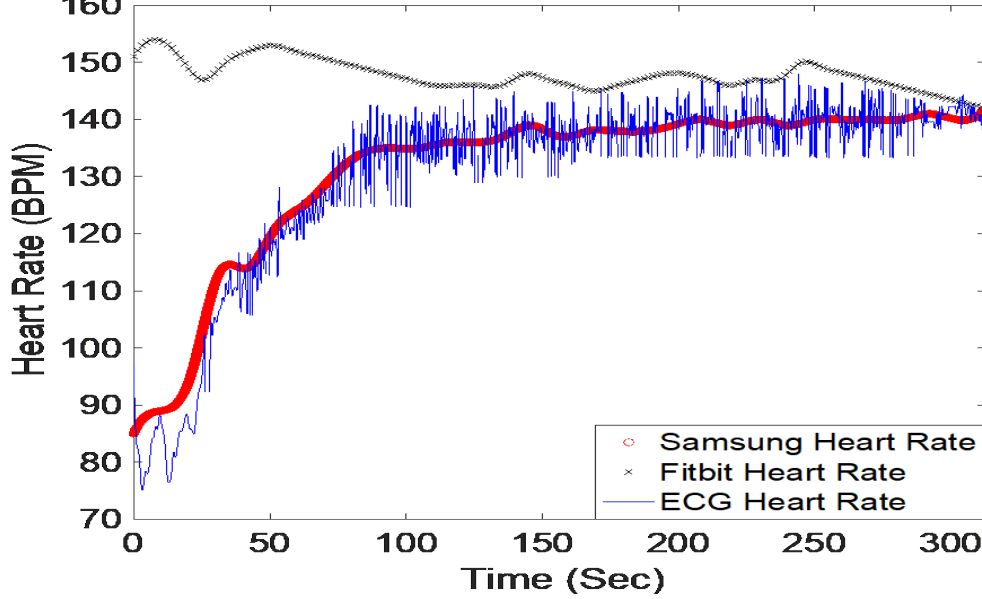


Figure A2.155: Subject No.3 fast walk Samsung and Fitbit WFT compared to ECG

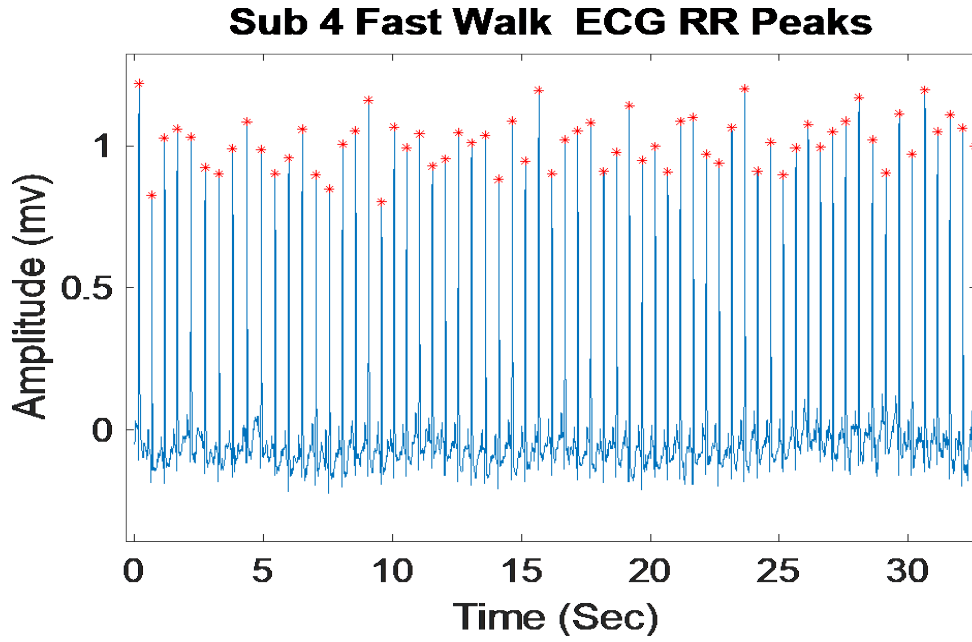


Figure A2.156: Subject No. 4 fast walk ECG RR Peaks detection

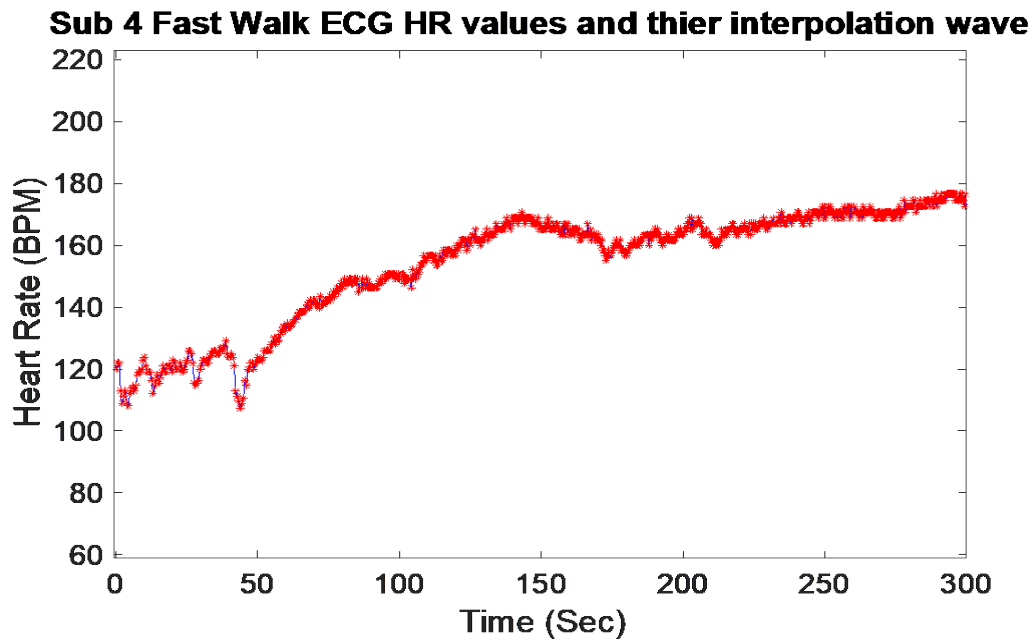


Figure A2.157: Subject No.4 fast walk exercise ECG HR interpolation

### Sub 4 Fast Walk Smart Watch Comparison

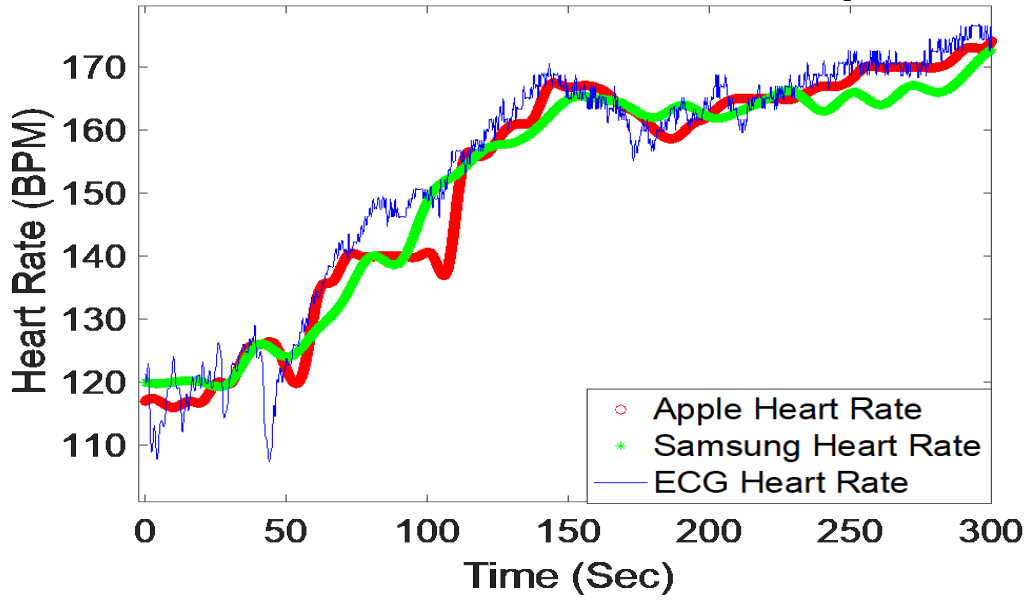


Figure A2.158: Subject No.4 fast walk Apple and Samsung WFT compared to ECG

### Sub 4 Fast Walk Smart Watch Comparison

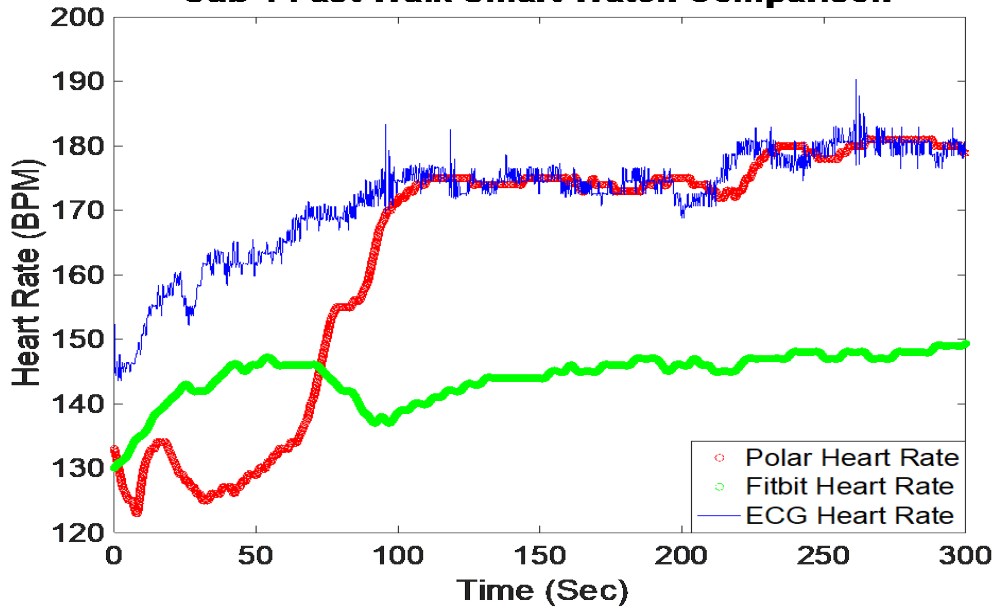


Figure A2.159: Subject No.4 fast walk Polar and Fitbit WFT compared to ECG

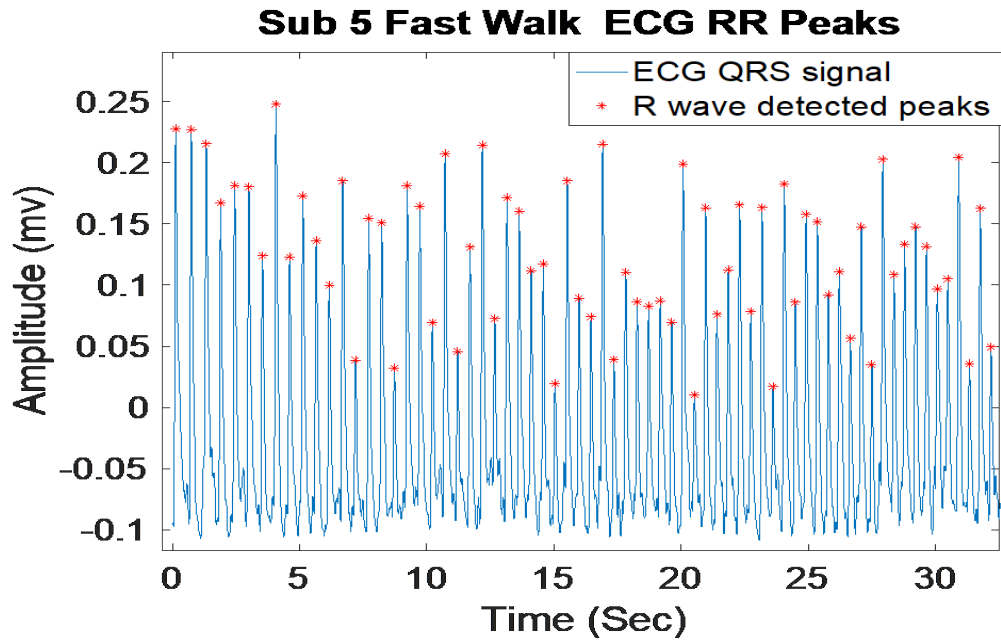


Figure A2.160: Subject No. 5 fast walk ECG RR Peaks detection (Amplified R wave)

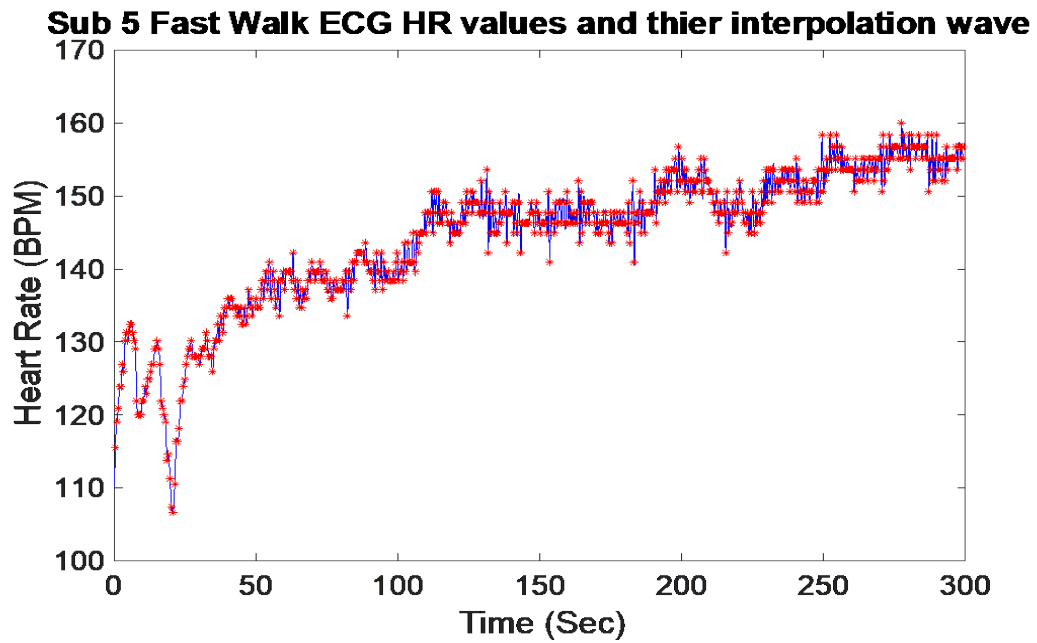


Figure A2.161: Subject No.5 fast walk exercise ECG interpolation

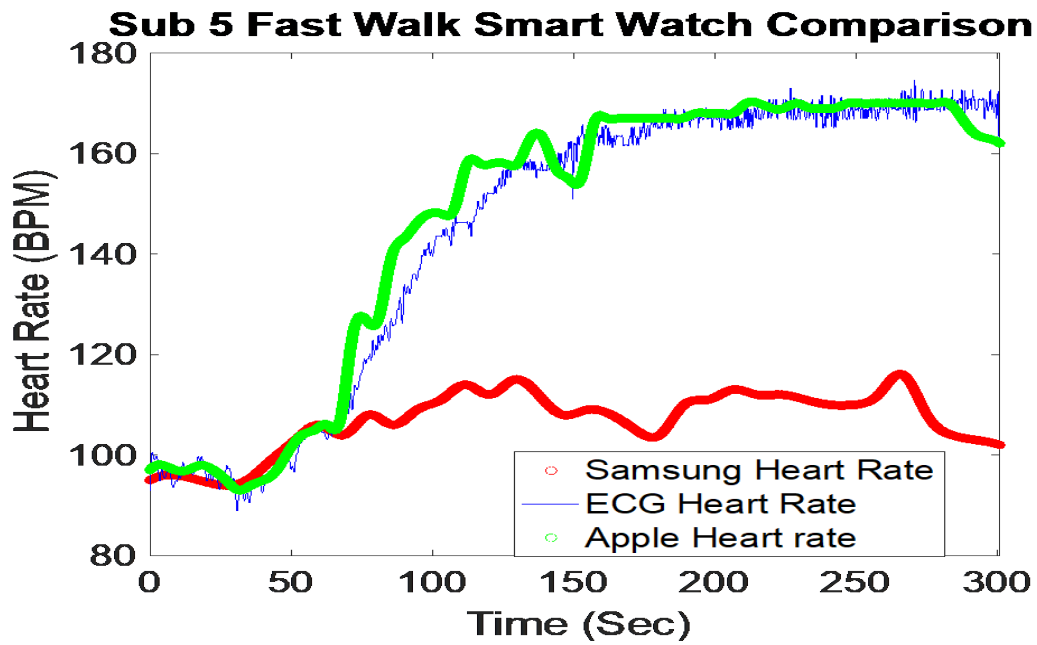


Figure A2.162: Subject No.5 fast walk Apple and Samsung WFT compared to ECG

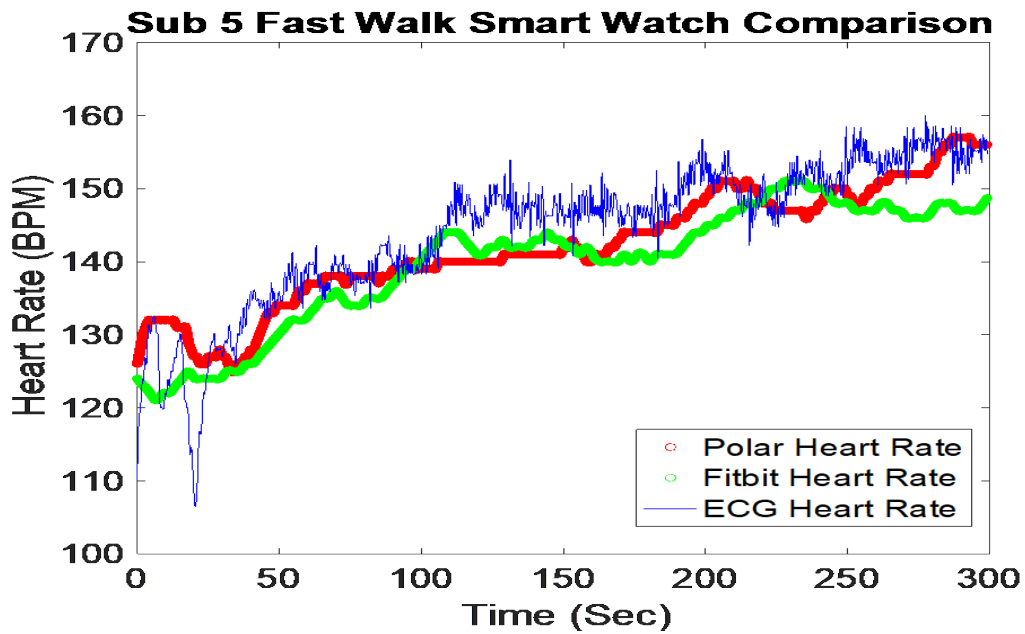
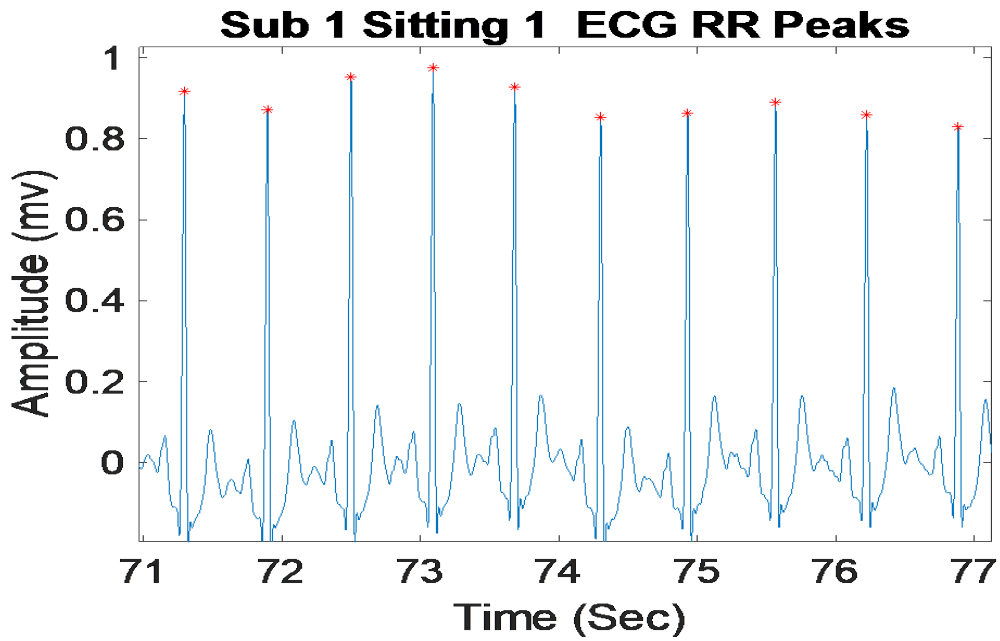
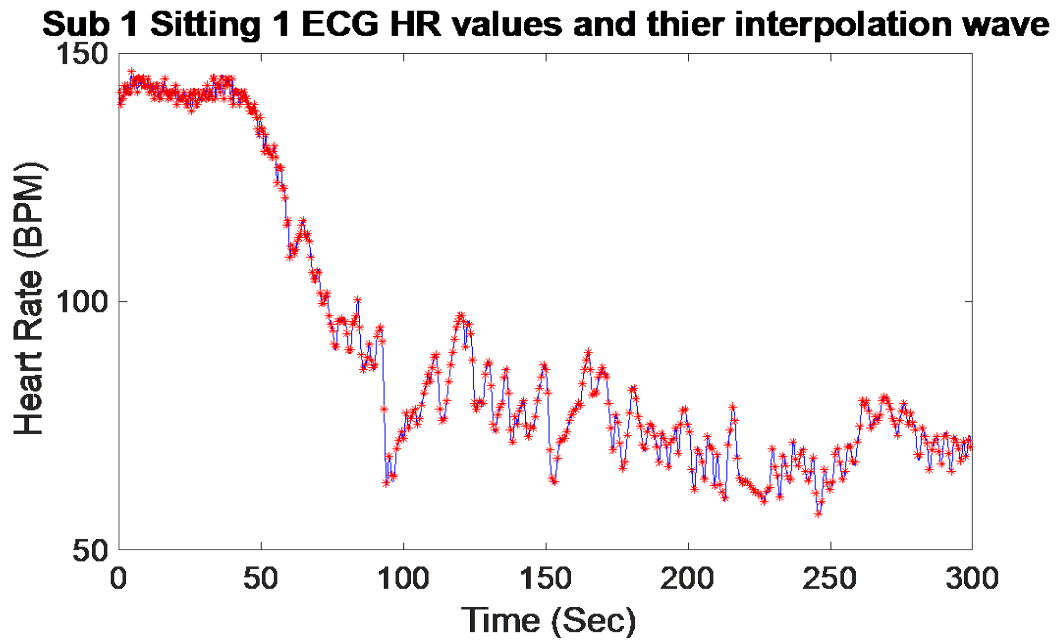


Figure A2.163: Subject No.5 fast walk Polar, and Fitbit WFT compared to ECG

*Sitting Mode*



*Figure A2.164: Subject No.1 Sitting ECG RR Peaks dedication*



*Figure A2 165: Subject No.1 Sitting exercise ECG interpolation*

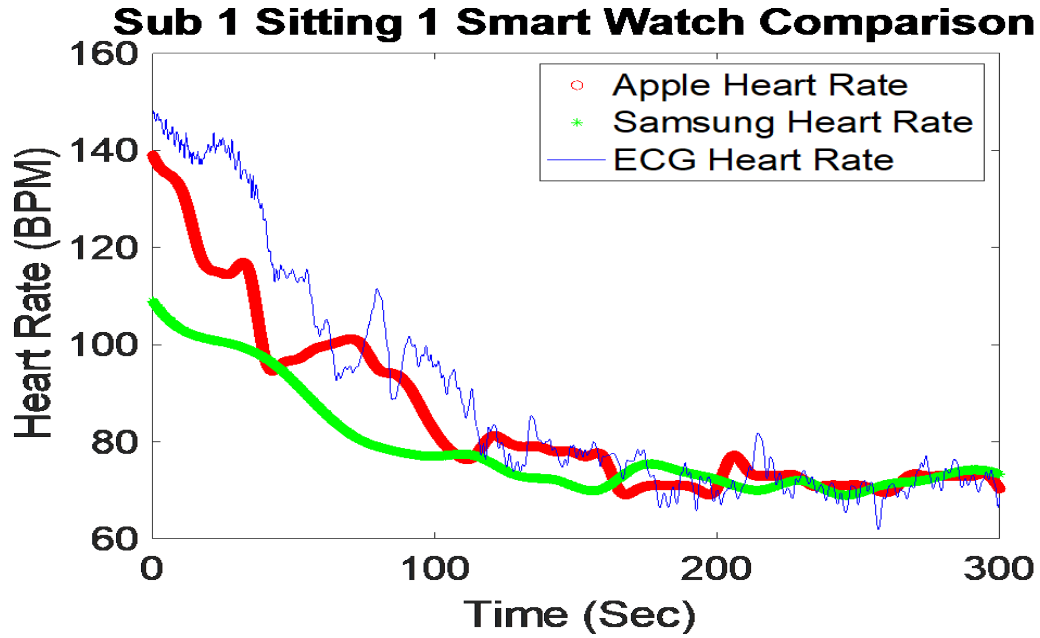


Figure A2.166: Subject No.1 Sitting Apple and Samsung WFT compared to ECG

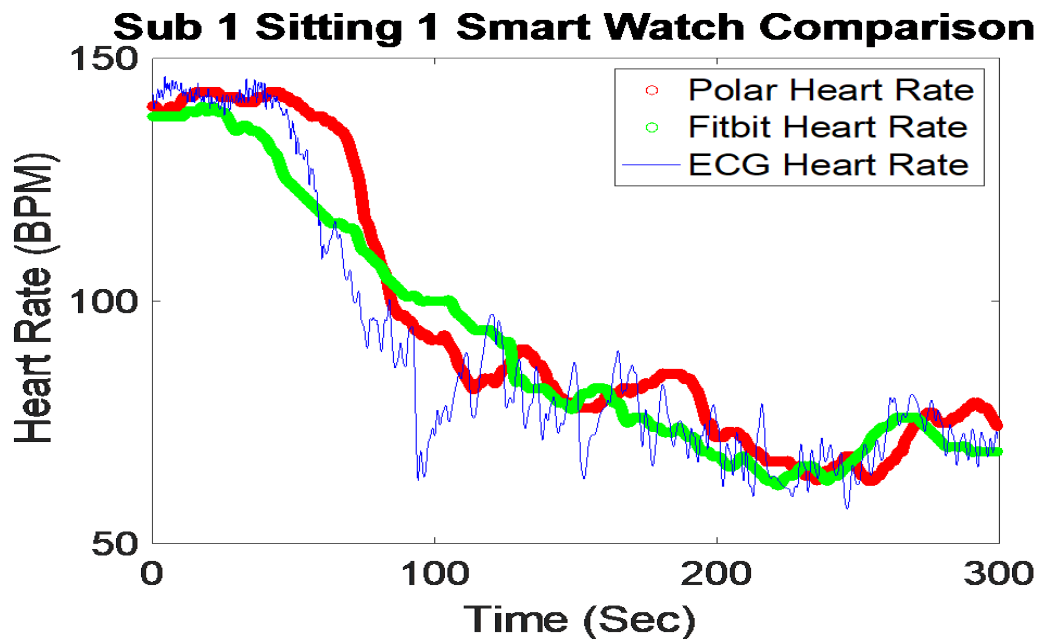


Figure A2.167: Subject No.1 Sitting Polar and Fitbit WFT compared to ECG



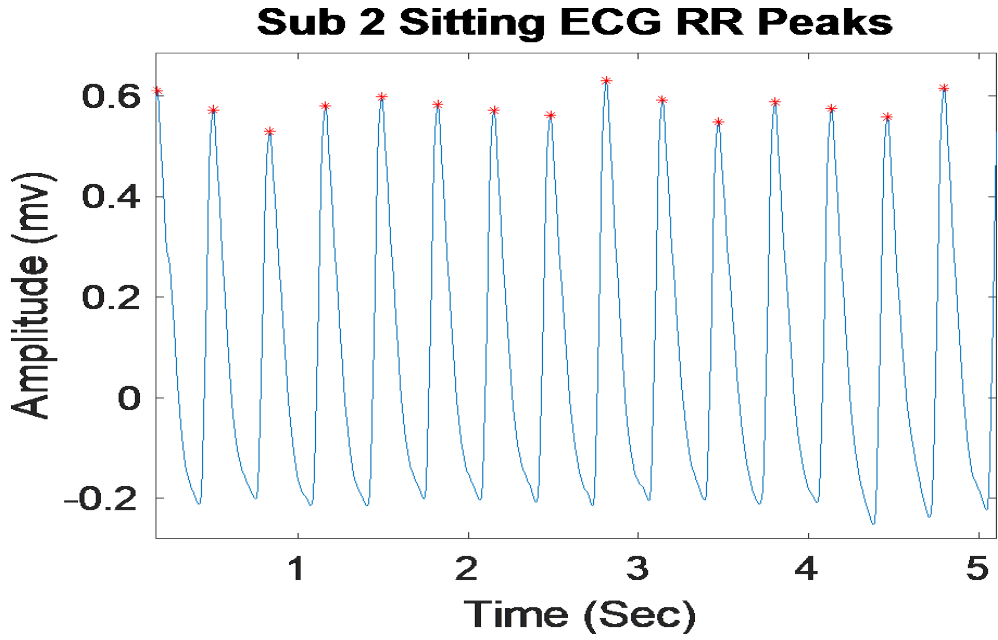


Figure A2.168: Subject No. 2 Sitting ECG RR Peaks detection (Amplified R wave)

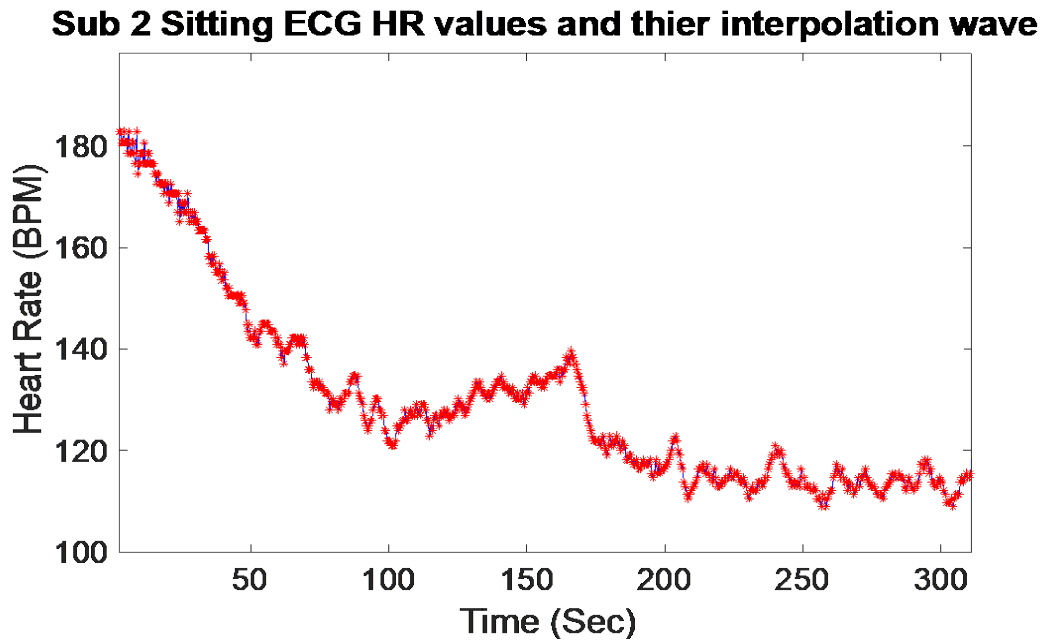


Figure A2.169: Subject No.2 Sitting exercise ECG HR interpolation

### Sub 2 Sitting Smart Watch Comparison

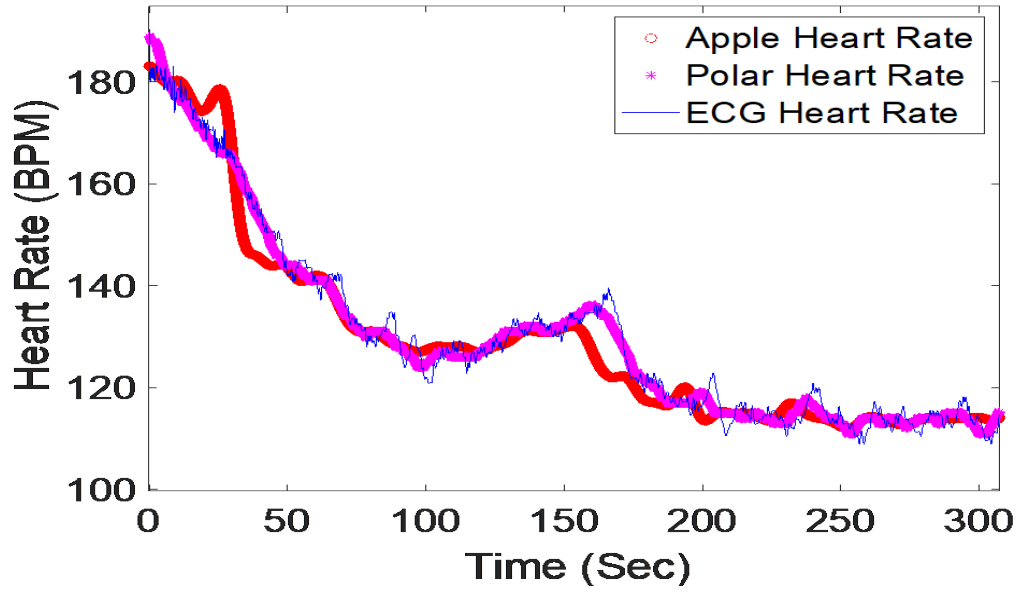


Figure A2.170: Subject No.2 Sitting Apple and Polar WFT compared to ECG

### Sub 2 Sitting Smart Watch Comparison

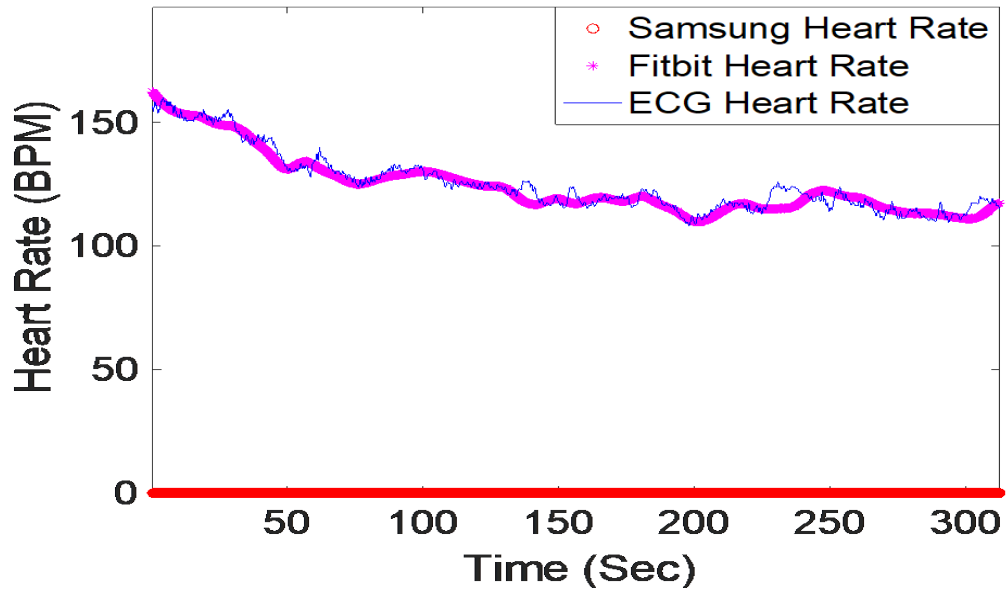


Figure A2.171: Subject No.2 Sitting Samsung and Fitbit WFT compared to ECG

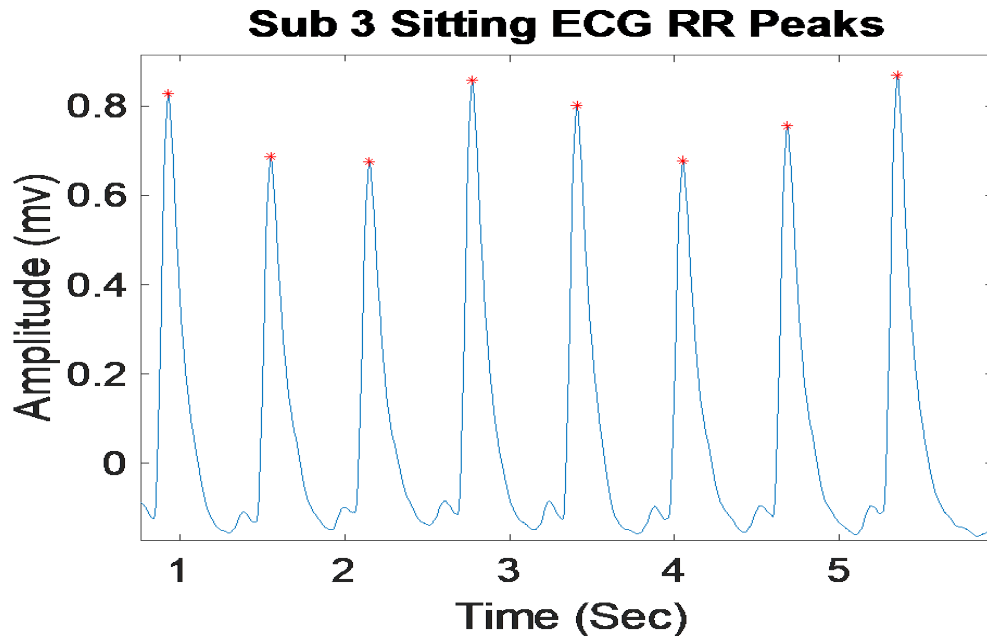


Figure A2.172: Subject No. 3 sitting ECG RR Peaks detection (Amplified R wave)

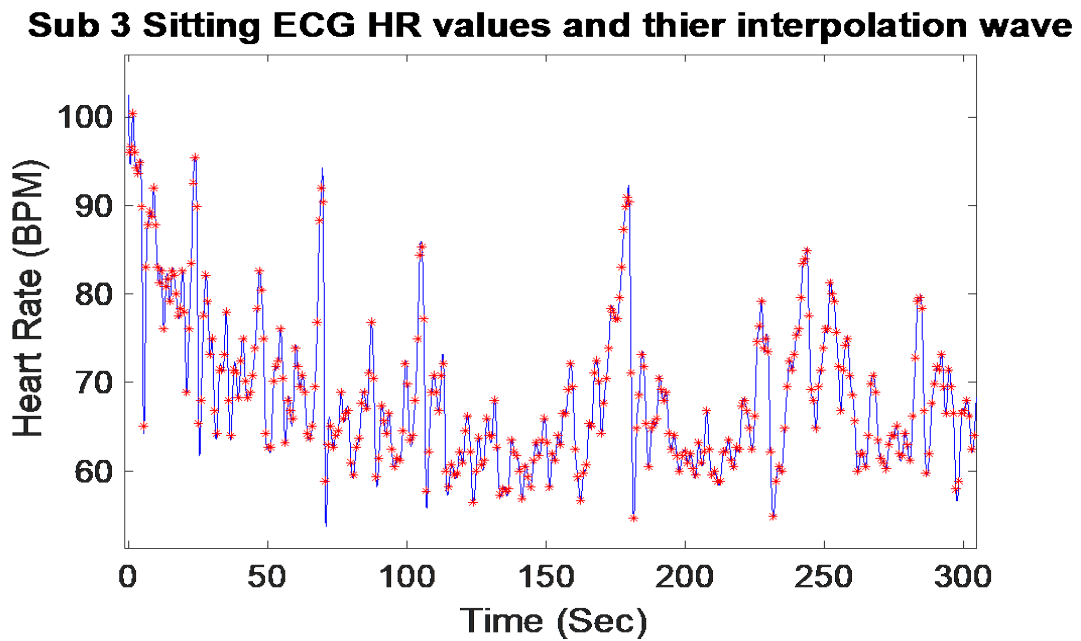


Figure A2.173: Subject No.3 sitting exercise ECG HR interpolation

### Sub 3 Sitting Smart Watch Comparison

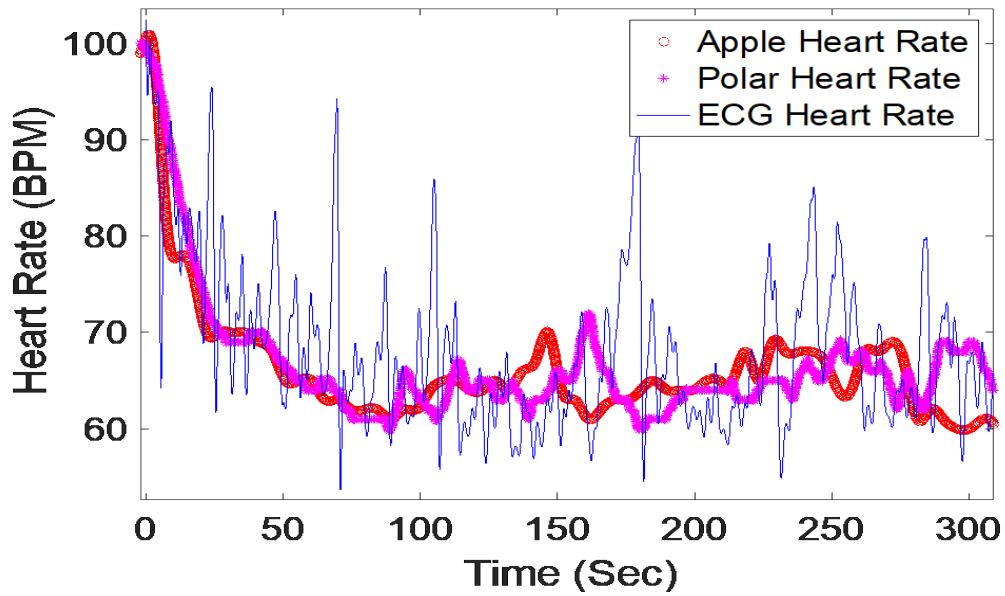


Figure A2.174: Subject No.3 sitting Apple and Polar WFT compared to ECG

### Sub 3 Sitting Smart Watch Comparison

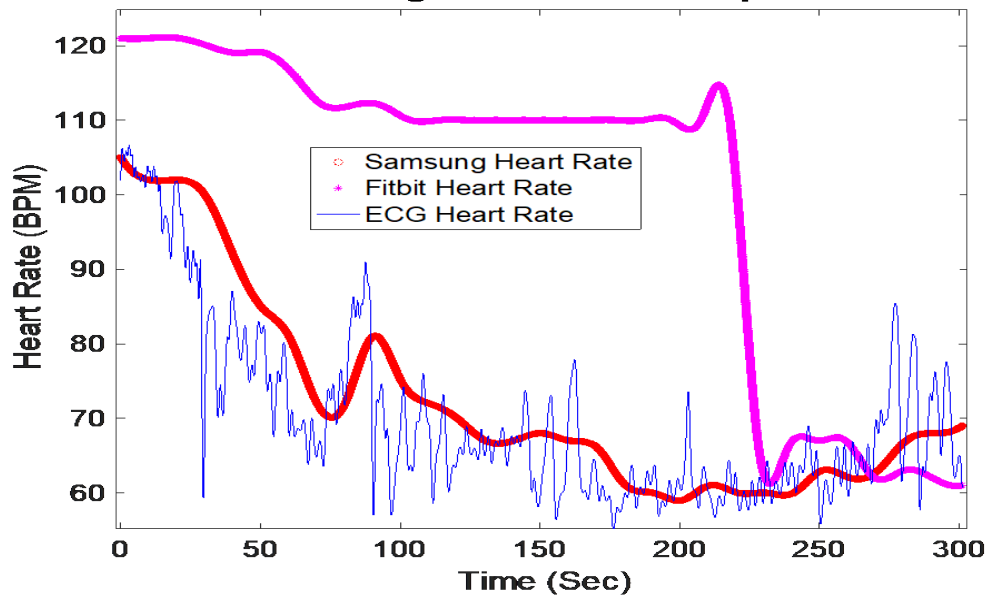


Figure A2.175: Subject No.3 sitting Samsung and Fitbit WFT compared to ECG

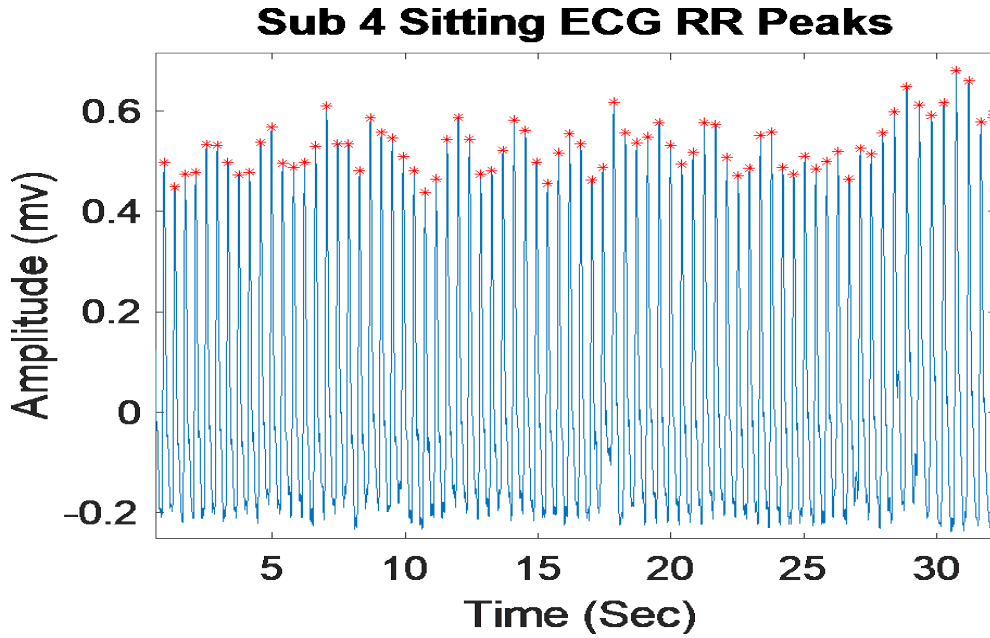


Figure A2.176: Subject No. 4 sitting ECG RR Peaks detection (Amplified R wave)

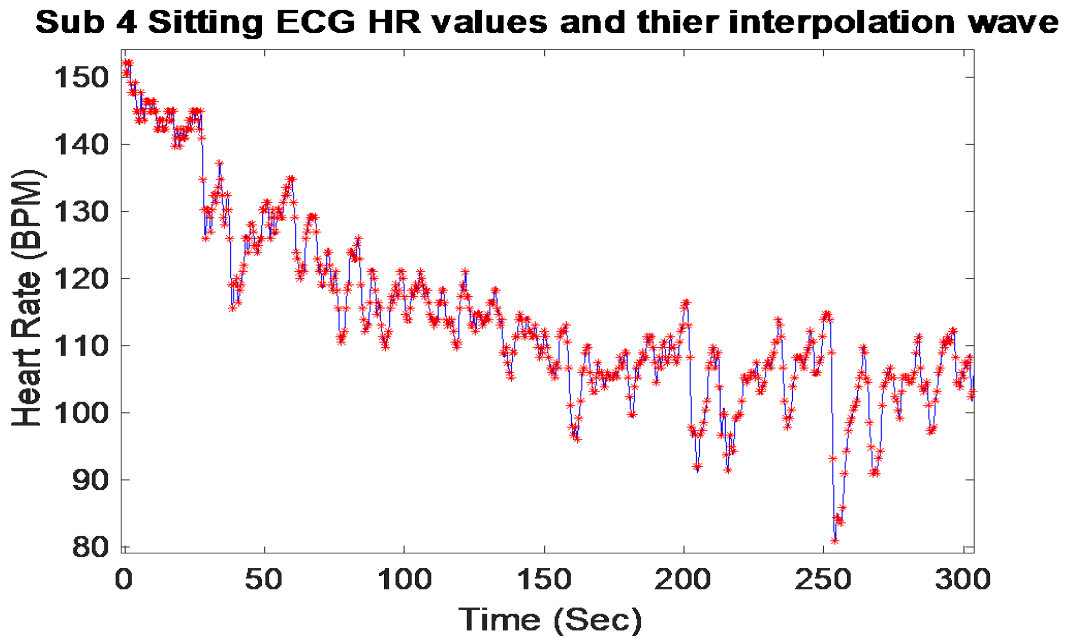


Figure A2.177: Subject No.4 sitting exercise ECG HR interpolation

### Sub 4 Sitting Smart Watch Comparison

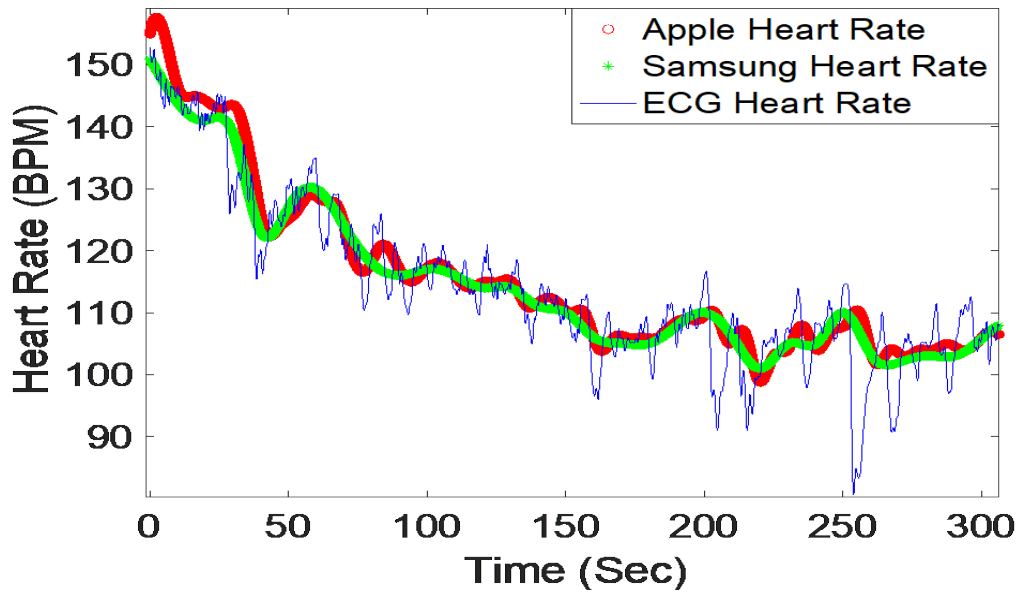


Figure A2.178: Subject No.4 fast sitting Apple and Samsung WFT compared to ECG

### Sub 4 Sitting Smart Watch Comparison

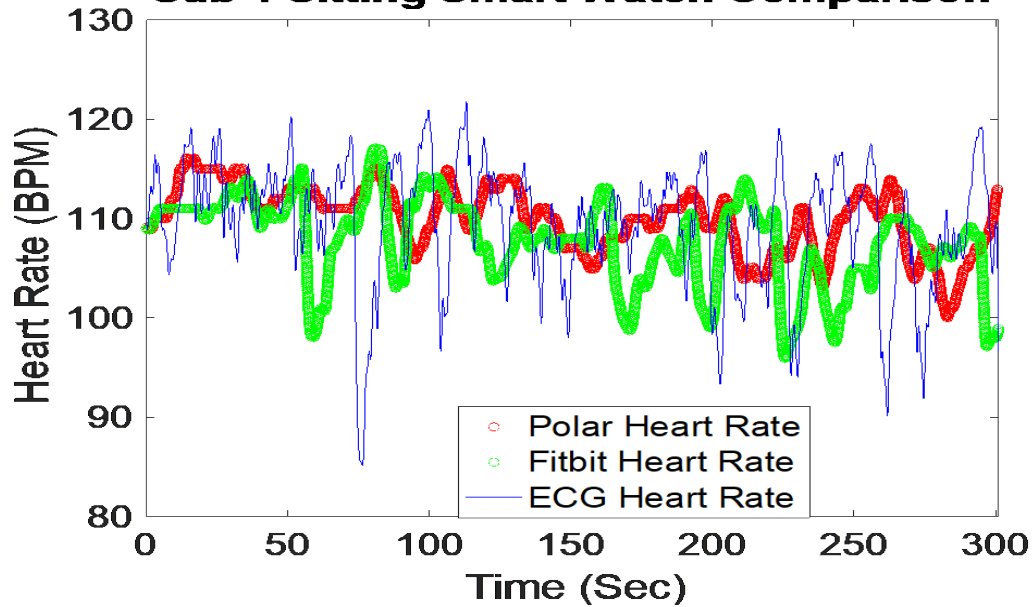


Figure A2.179: Subject No.4 sitting Polar, and Fitbit WFT compared to ECG

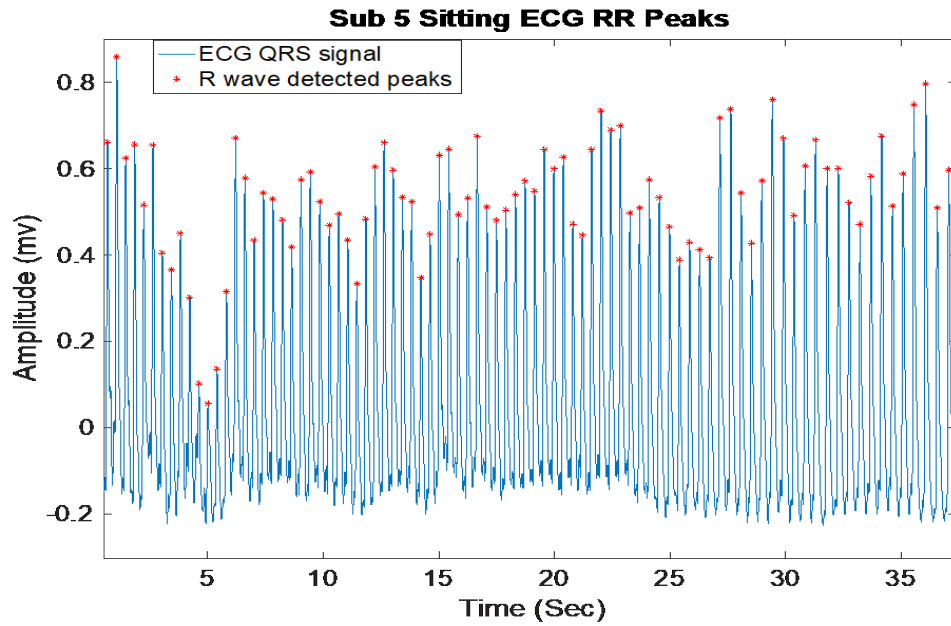


Figure A2.180: Subject No. 5 sitting ECG RR Peaks detection (Amplified R wave)

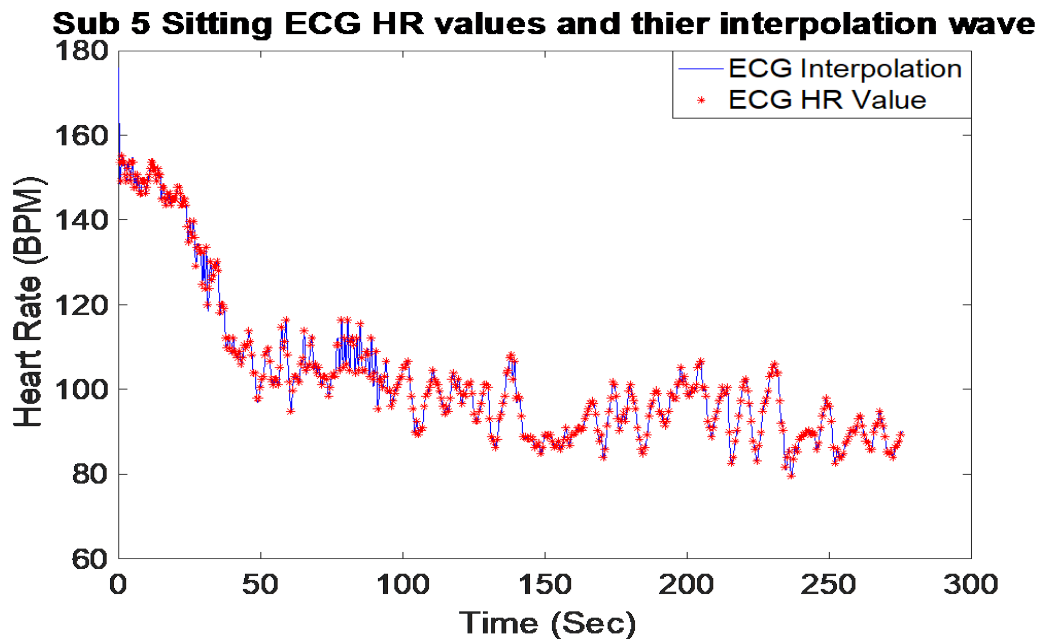


Figure A2.181: Subject No.5 sitting exercise ECG HR interpolation

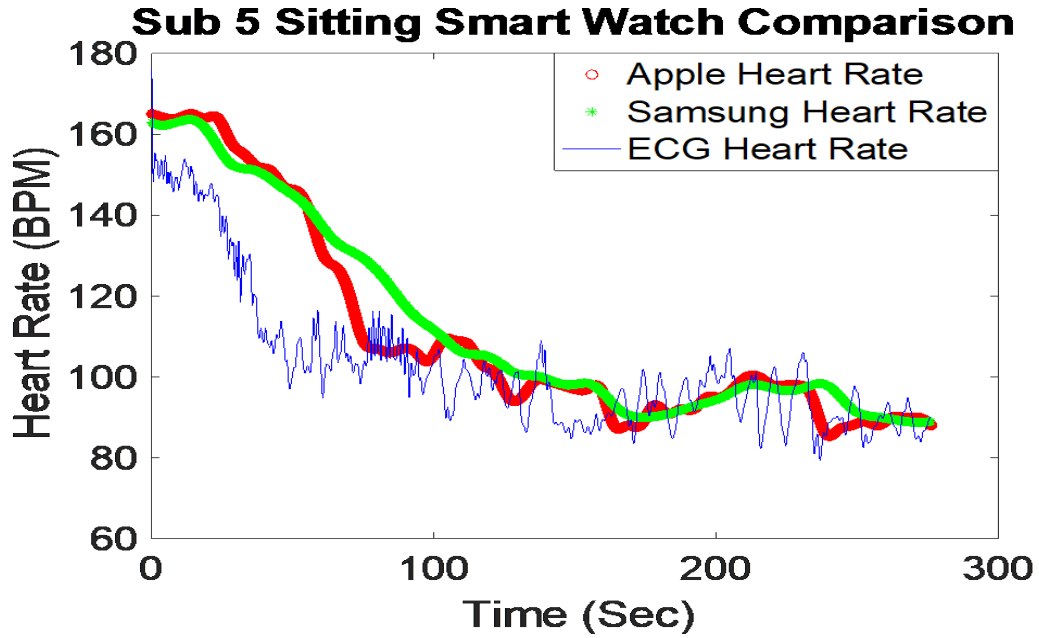


Figure A2.182: Subject No.5 sitting Apple and Samsung WFT compared to ECG

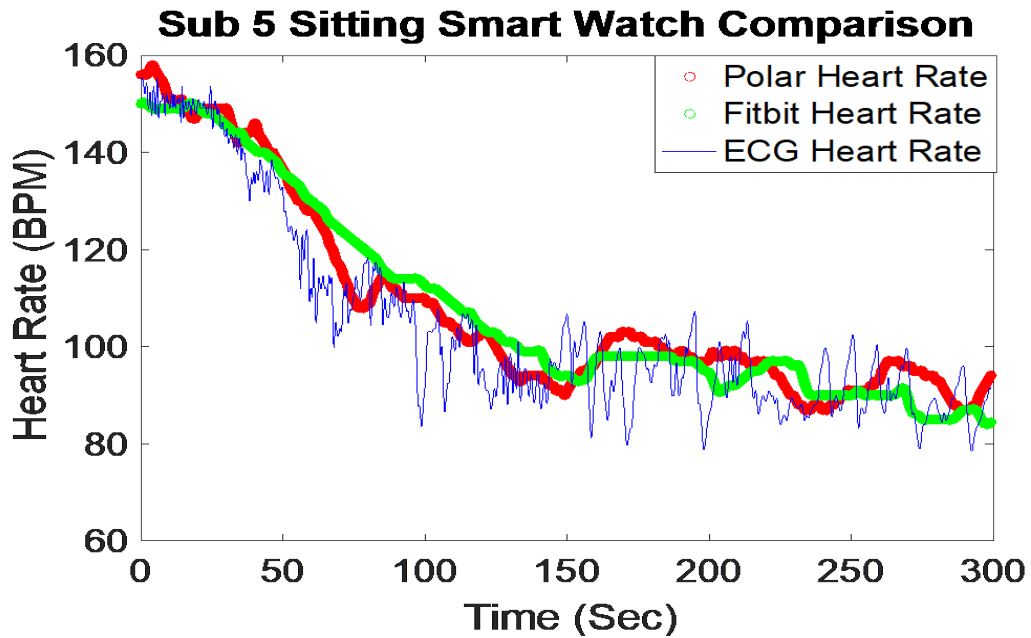


Figure A2.183: Subject No.5 sitting Polar and Fitbit WFT compared to ECG



*Slow Bike Mode*

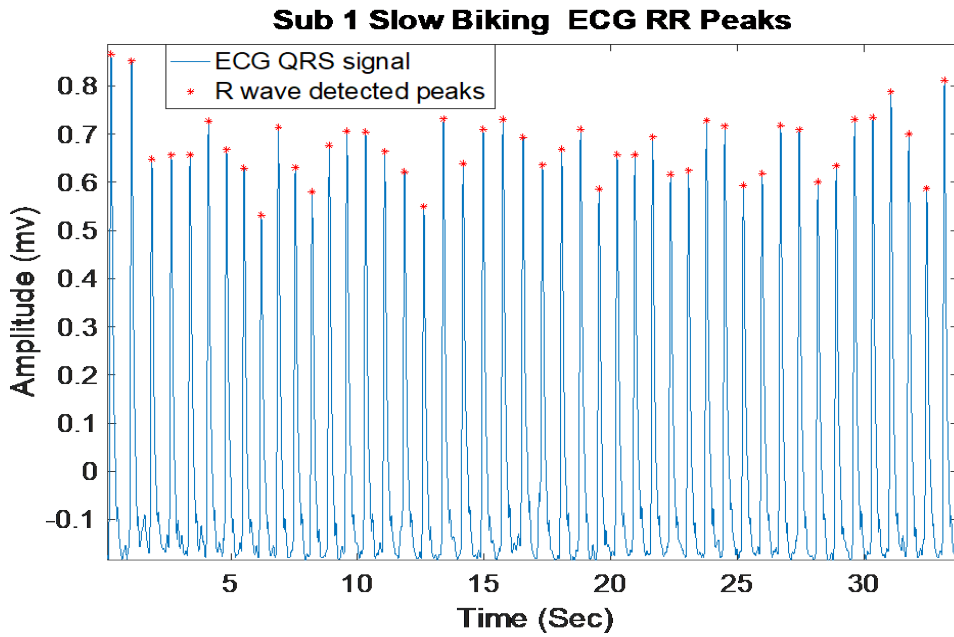


Figure A2.184: Subject No. 1 Slow Biking ECG RR peaks detection

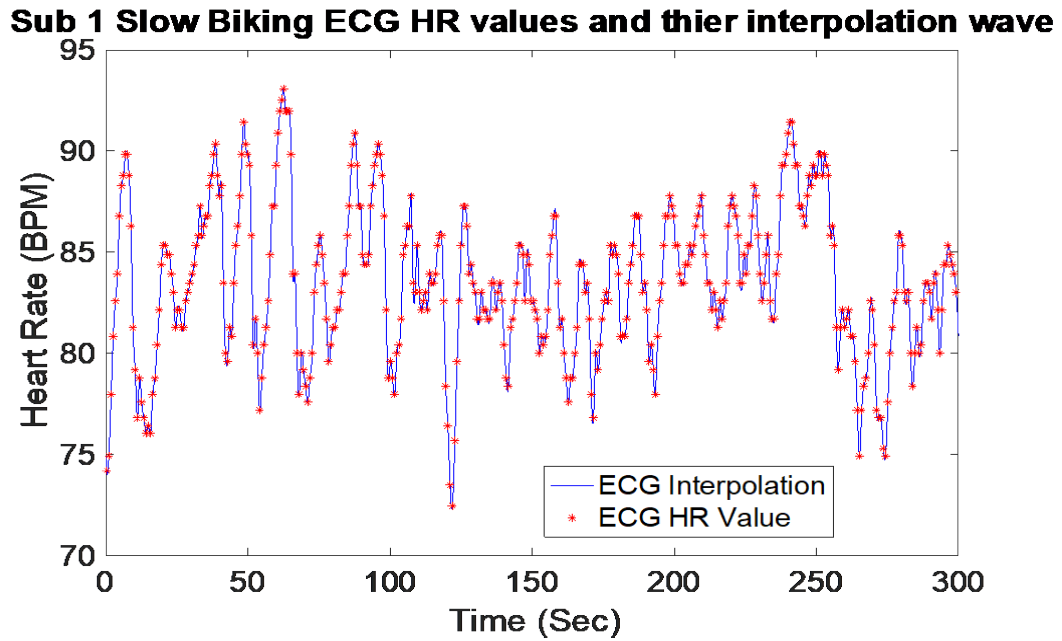


Figure A2.185: Subject No. 1 Slow Biking exercise ECG interpolation

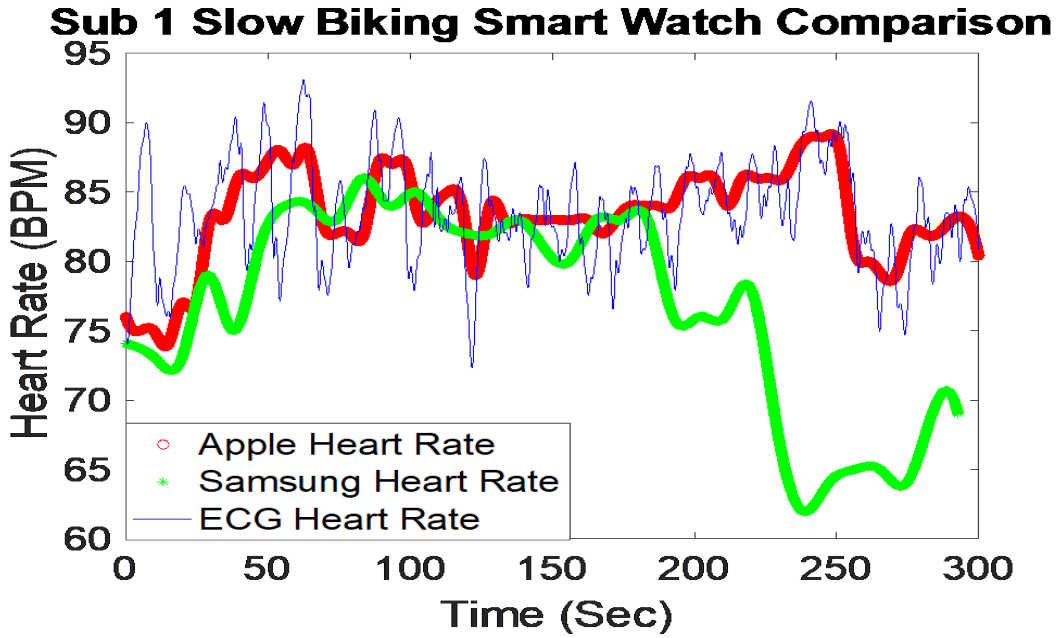


Figure A2.186: Subject No.1 Slow Biking Apple and Samsung WFT compared to ECG

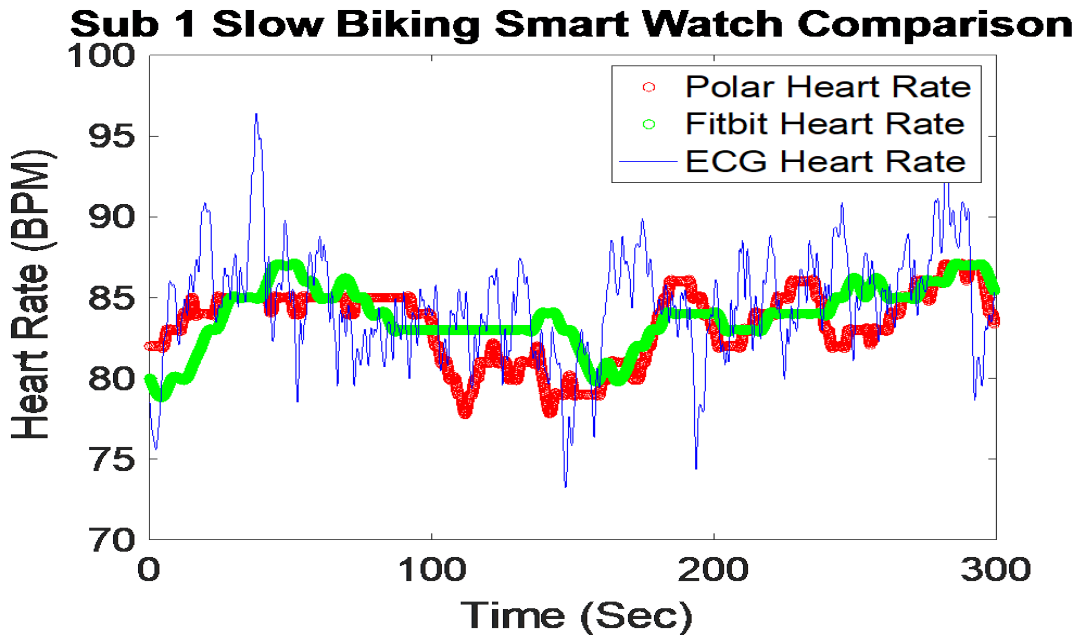


Figure A2.187: Subject No.1 Slow Biking Polar and Fitbit WFT's compared to ECG

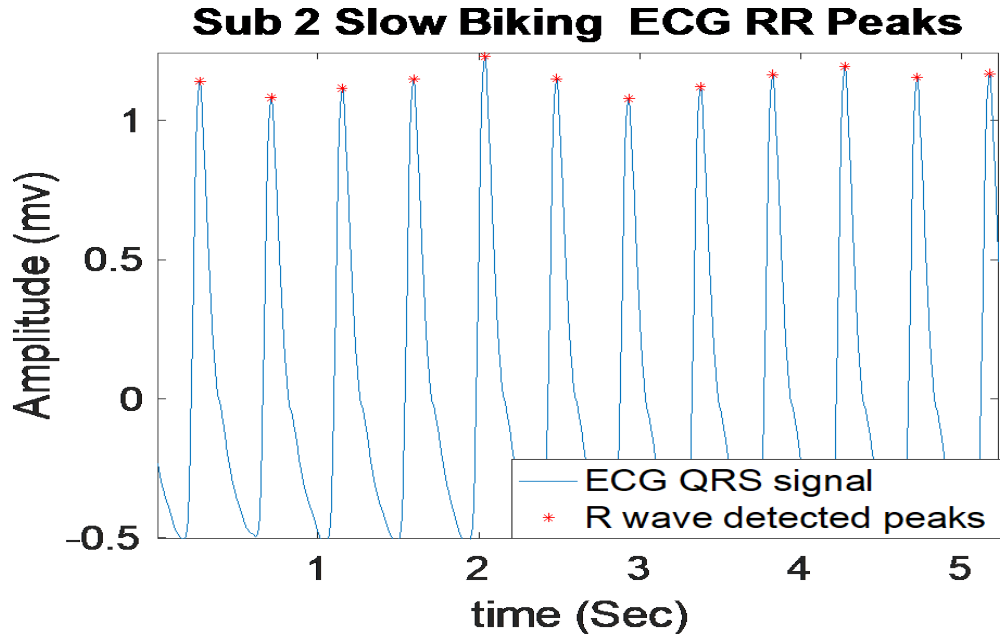


Figure A2.188: Subject No. 2 Slow Biking ECG RR peaks detection

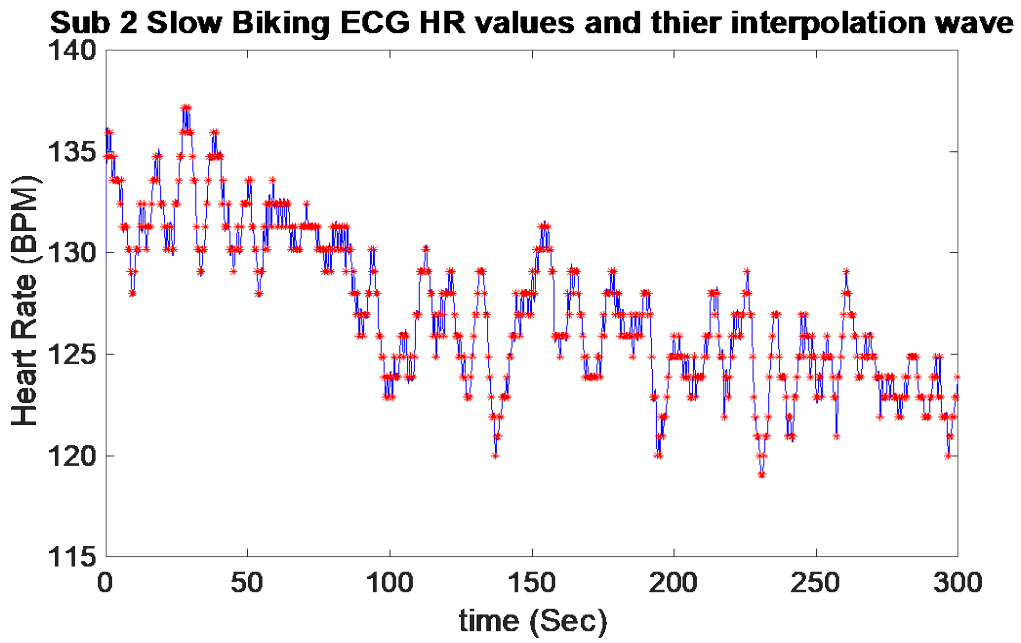


Figure A2.189: Subject No.2 Slow Biking exercise ECG interpolation

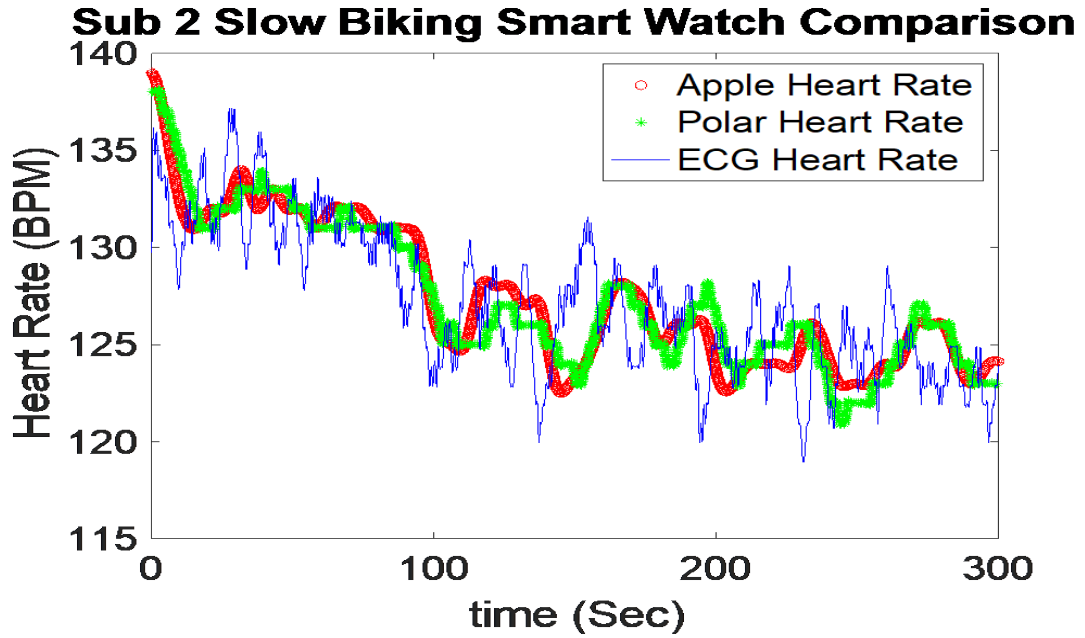


Figure A2.190: Subject No.2 Slow Biking Apple and Polar WFT compared to ECG

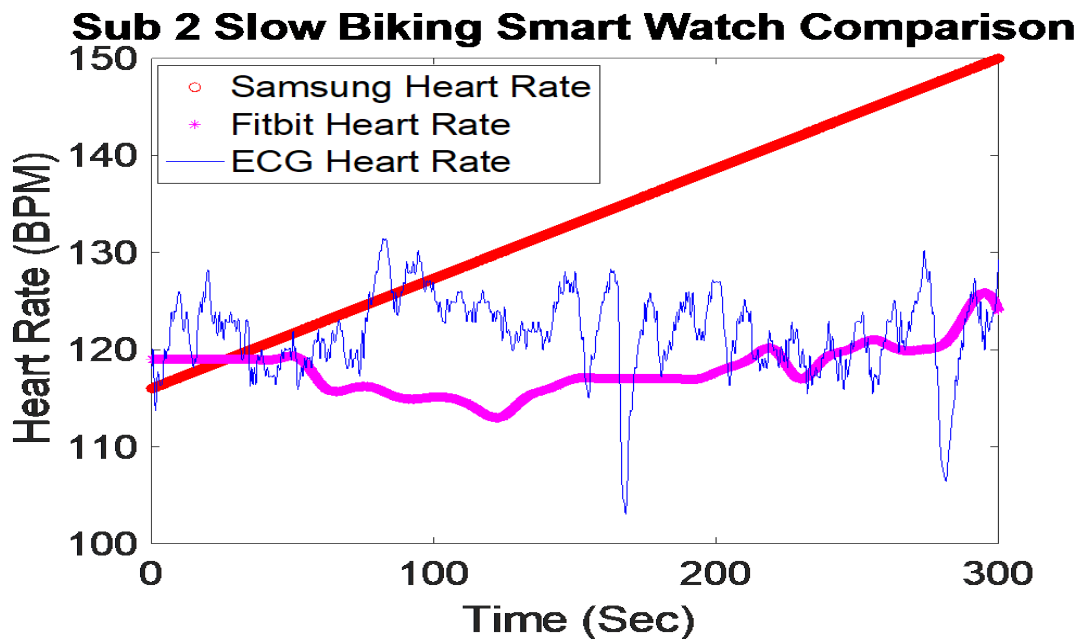


Figure A2.191: Subject No.2 Slow Biking Samsung and Fitbit WFT compared to ECG

### Sub 3 Slow Biking ECG RR Peaks

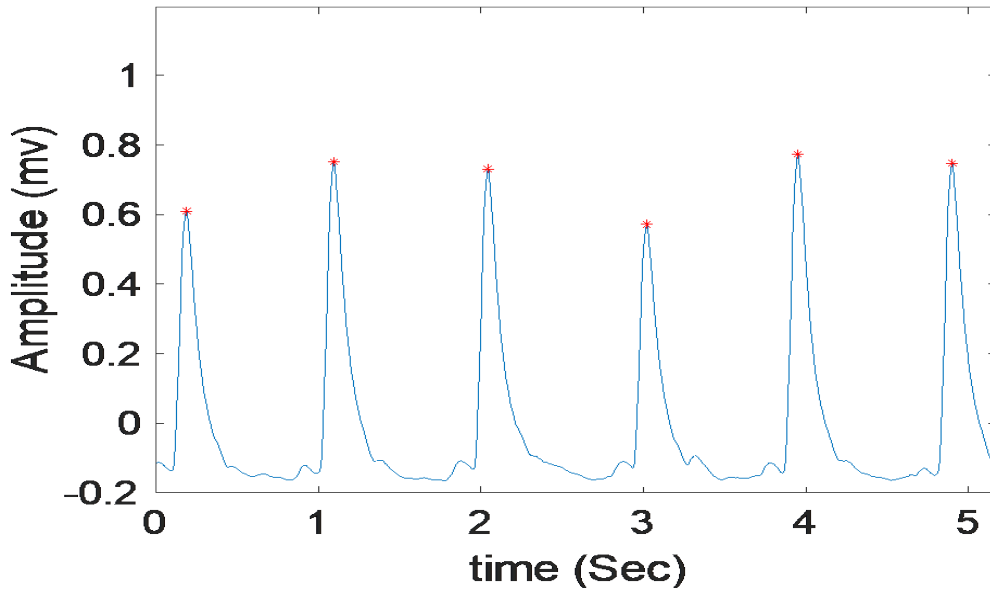


Figure A2.192: Subject No. 3 slow biking ECG RR Peaks detection (Amplified R wave)

### Sub 3 Slow Biking ECG HR values and thier interpolation wave

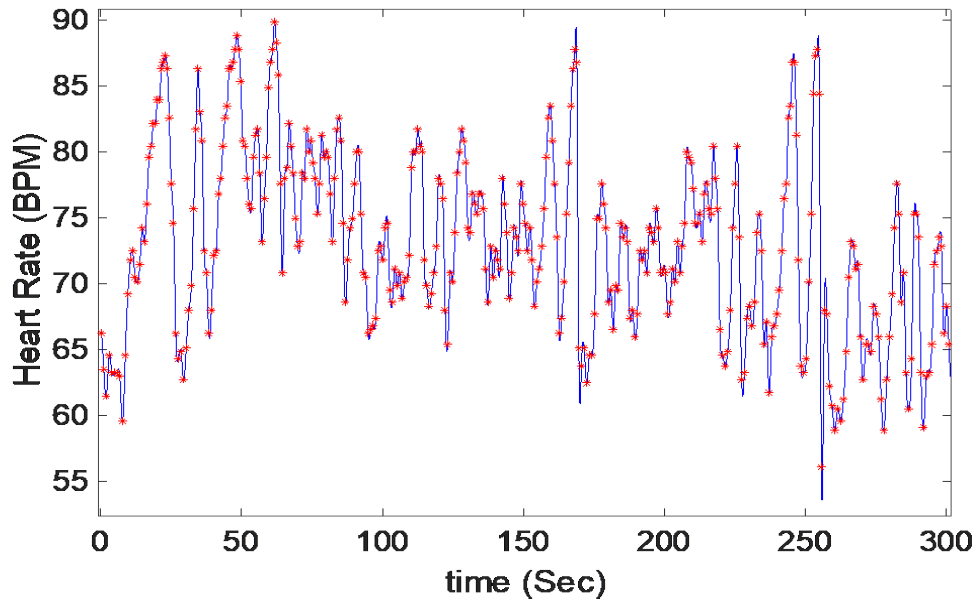


Figure A2.193: Subject No.3 slow biking exercise ECG HR interpolation

### Sub 3 Slow Biking Smart Watch Comparison

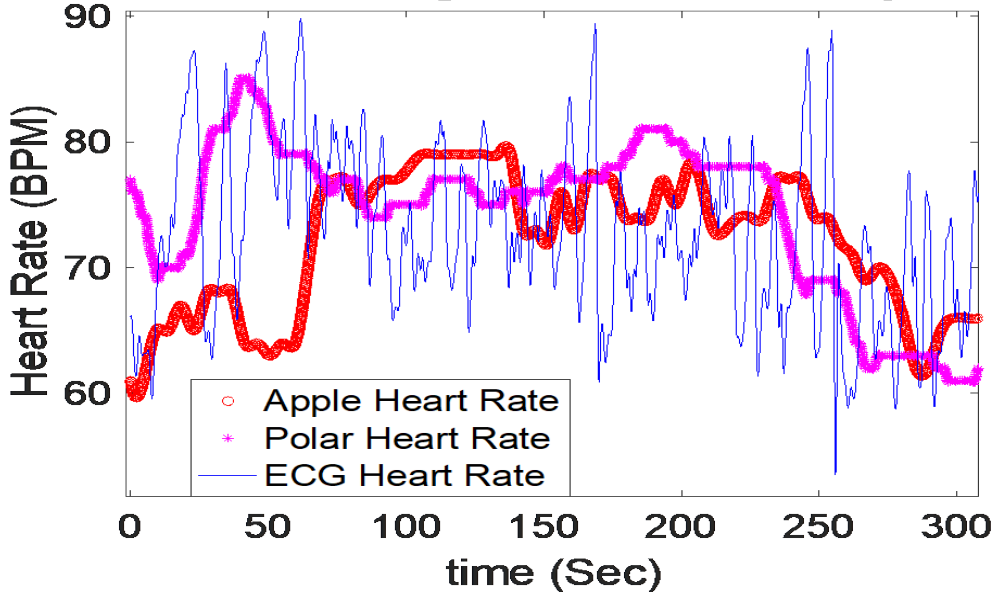


Figure A2.194: Subject No.3 slow biking Apple and Polar WFT compared to ECG

### Sub 3 Slow Biking Smart Watch Comparison

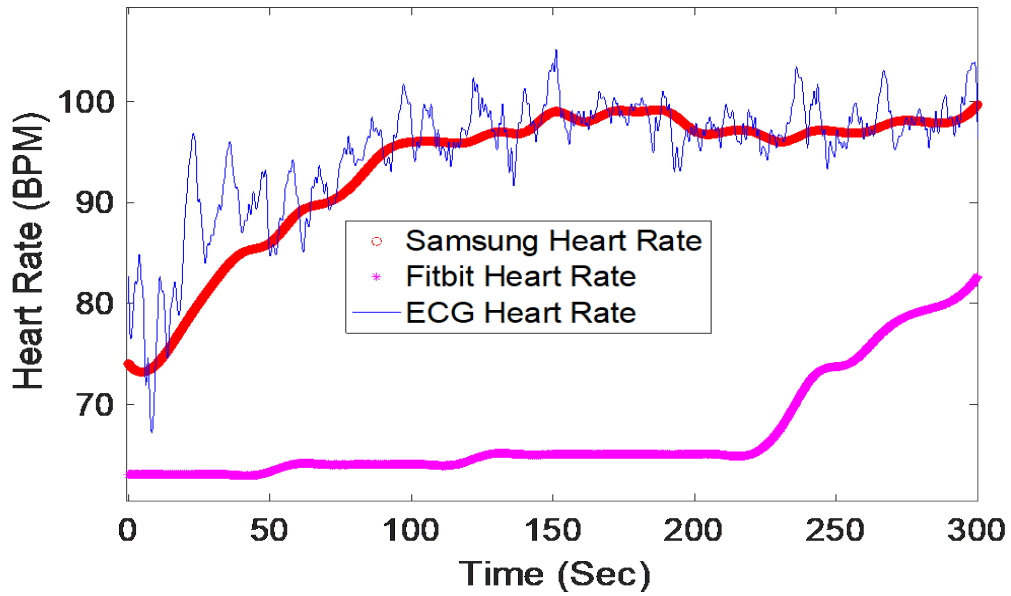


Figure A2.195: Subject No.3 slow biking Samsung and Fitbit WFT compared to ECG

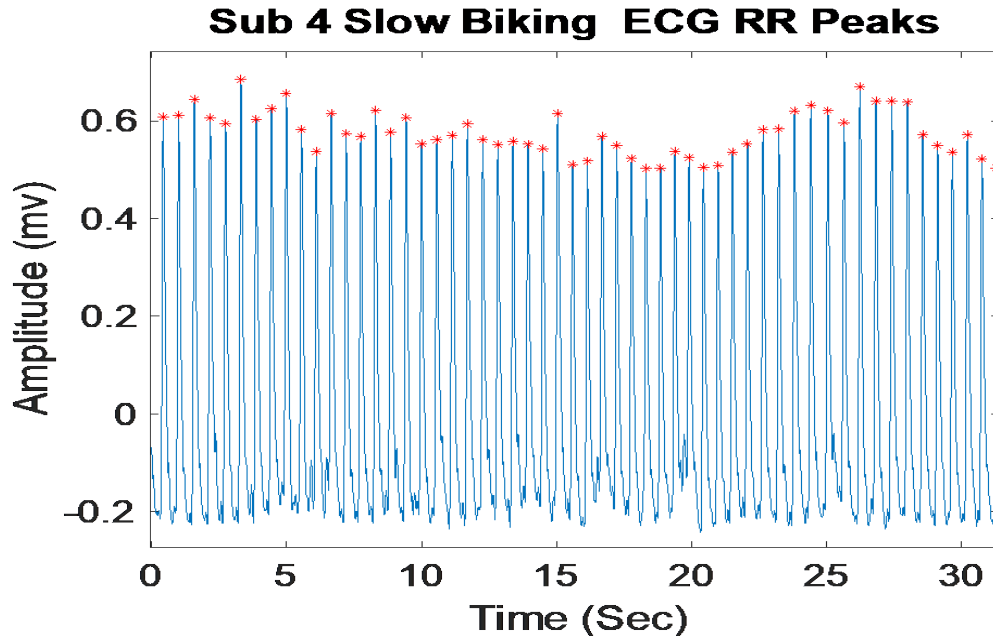


Figure A2.196: Subject No. 4 slow biking ECG RR Peaks detection (Amplified R wave)

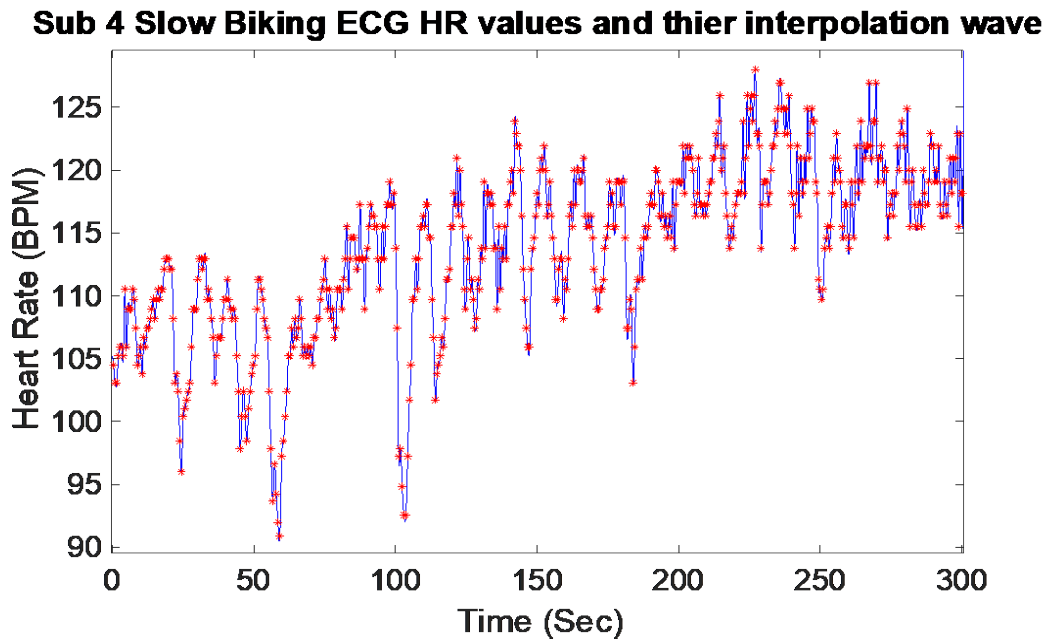


Figure A2.197: Subject No.4 slow biking exercise ECG HR interpolation

### Sub 4 Slow Biking Smart Watch Comparison

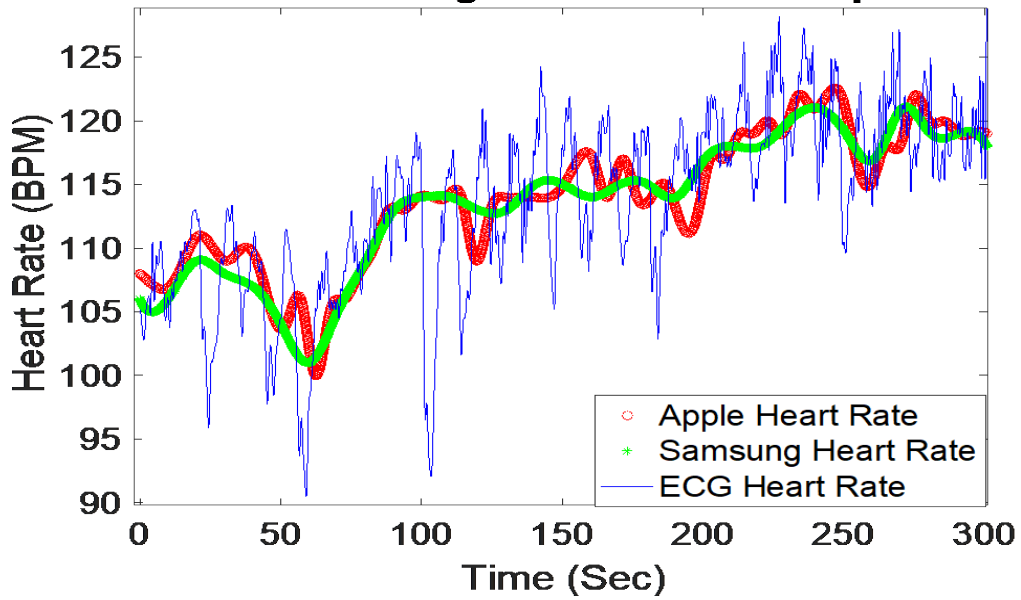


Figure A2.198: Subject No.4 slow biking Apple and Samsung WFT compared to ECG

### Sub 4 Slow Biking Smart Watch Comparison

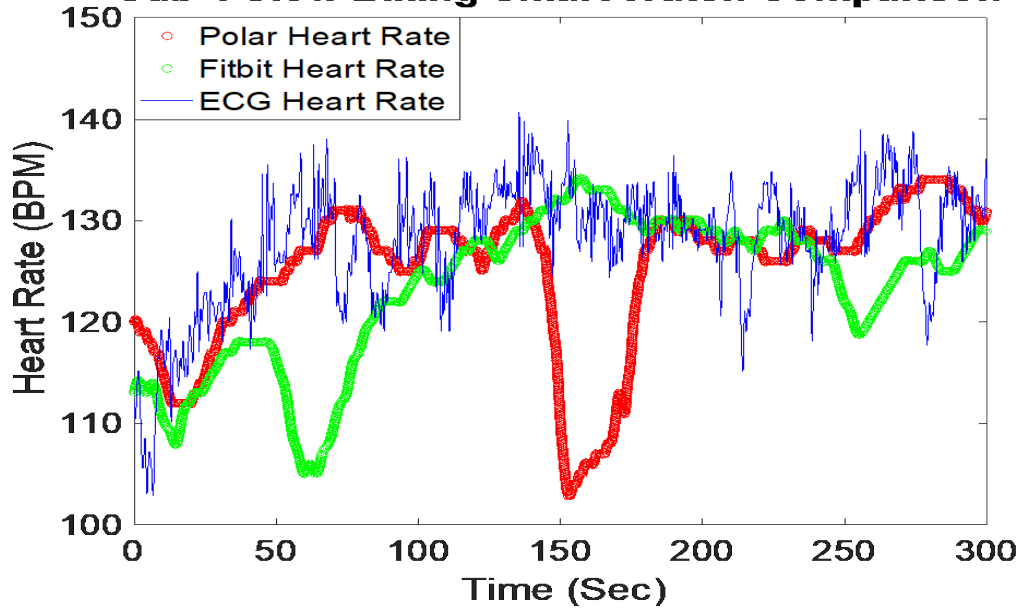


Figure A2.199: Subject No.4 slow biking Polar and Fitbit WFT compared to ECG



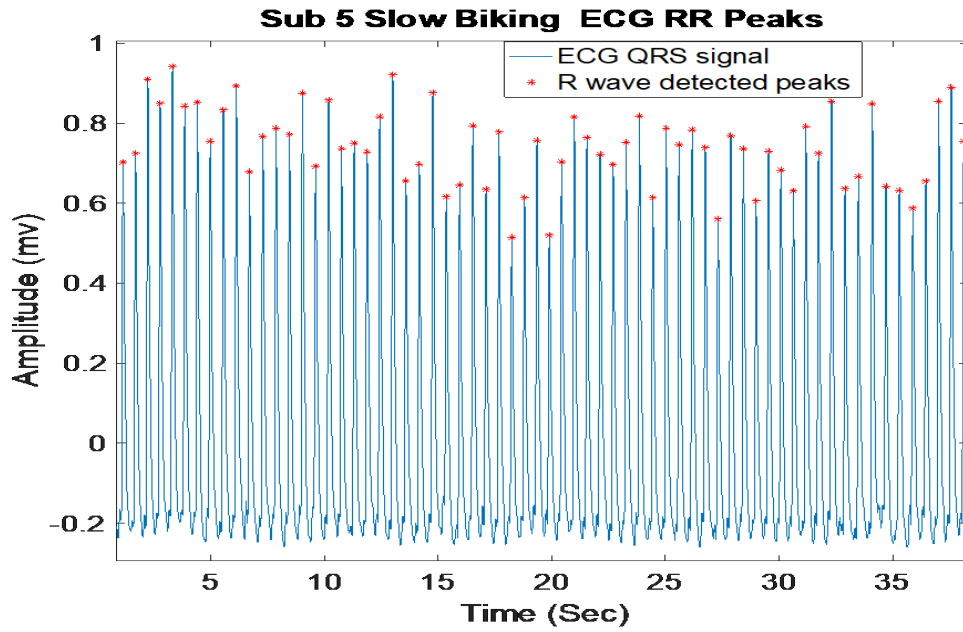


Figure A2.200: Subject No. 5 slow biking ECG RR Peaks detection (Amplified R wave)

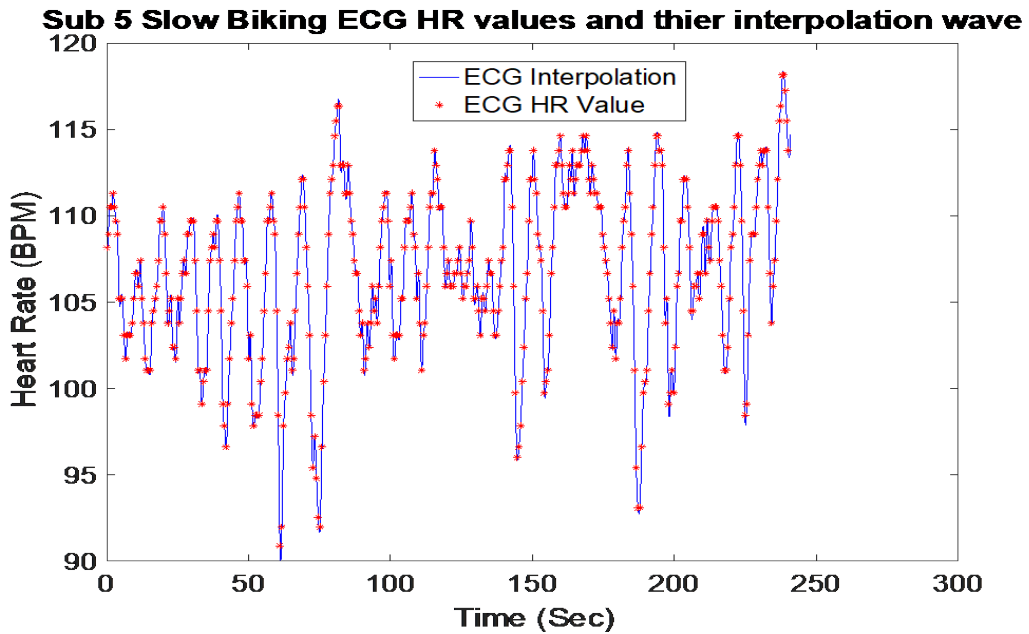


Figure A2.201: Subject No.5 slow biking exercise ECG HR interpolation

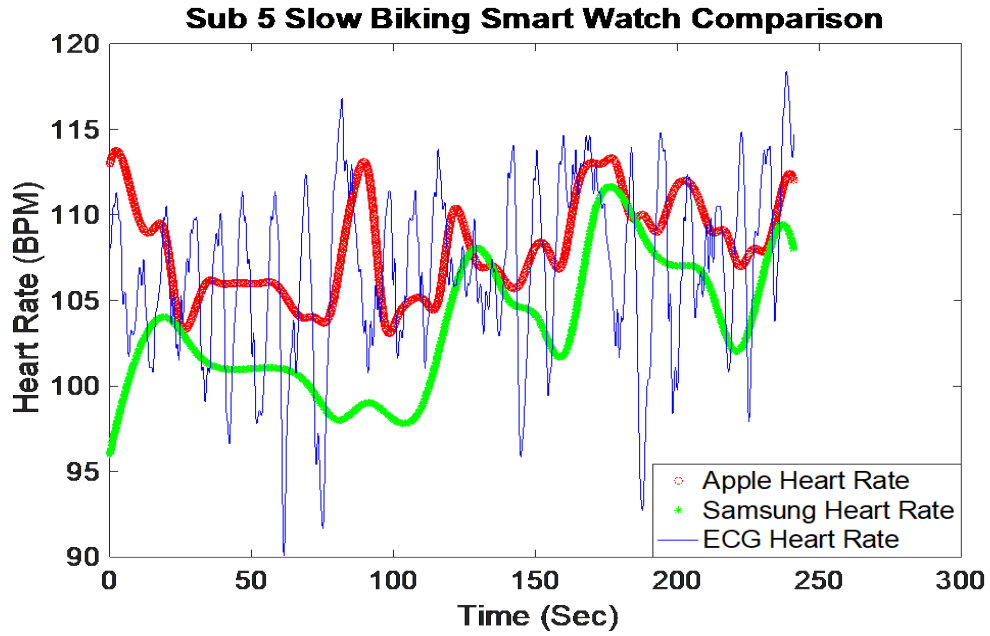


Figure A2.202: Subject No.5 slow biking Apple and Samsung WFT compared to ECG

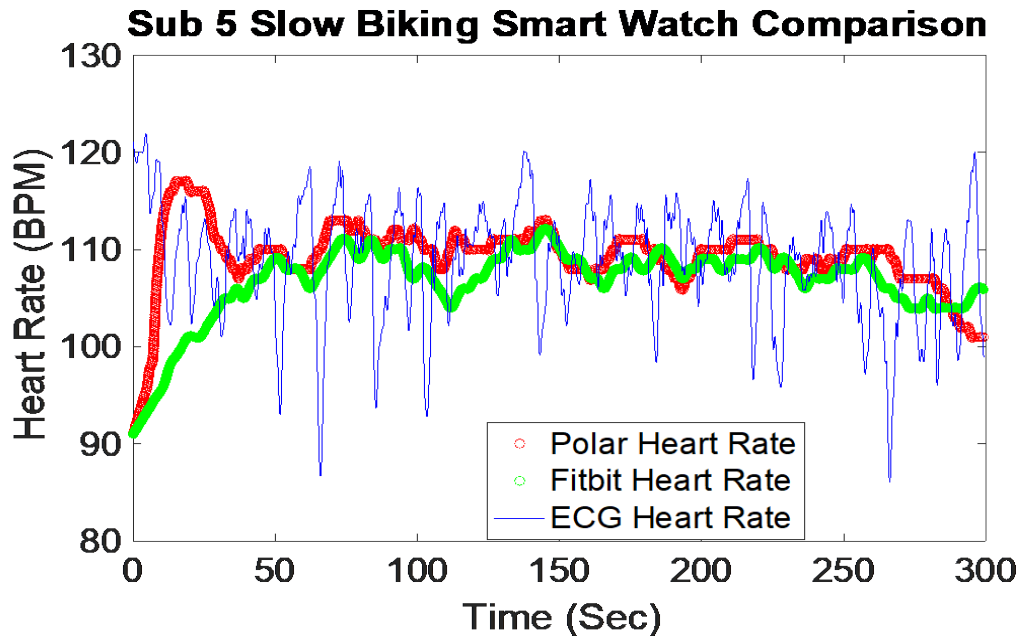
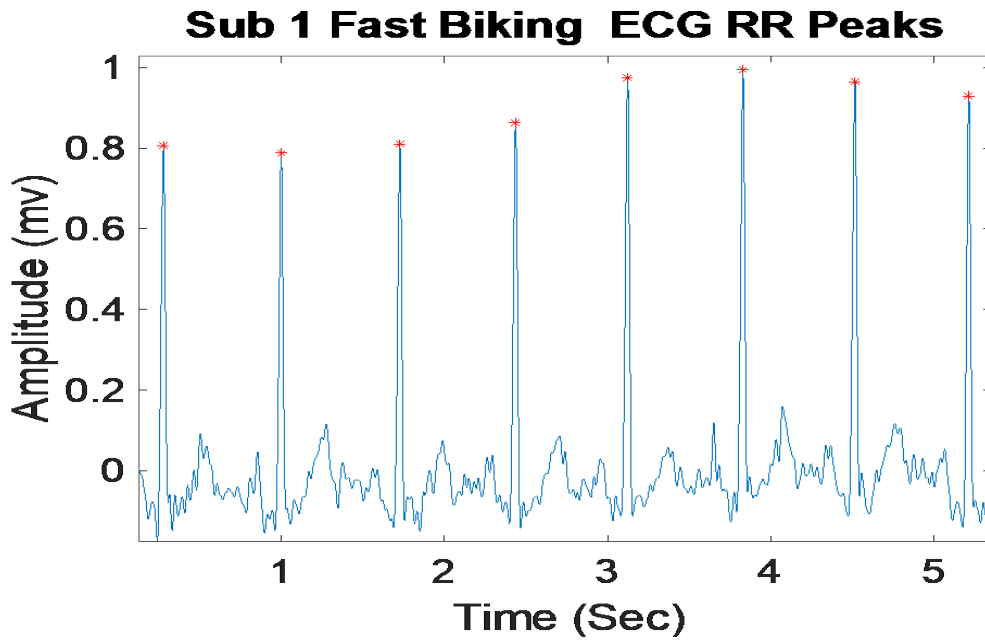
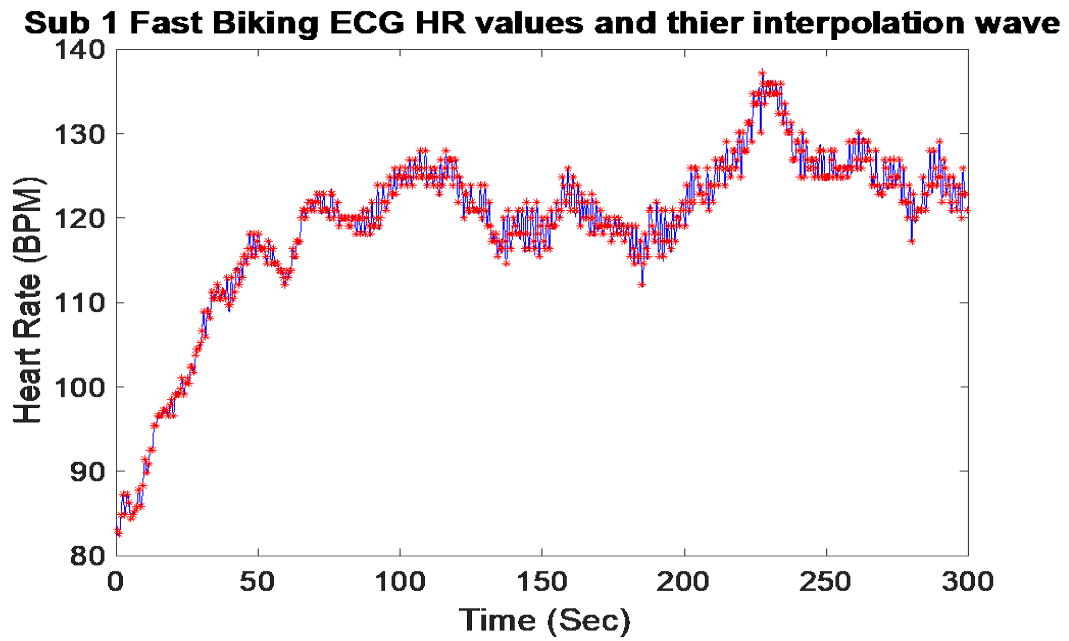


Figure A2.203: Subject No.5 slow biking Polar and Fitbit WFT compared to ECG

*Fast Bike Mode*



*Figure A2.204: Subject No. 1 fast biking ECG RR Peaks detection*



*Figure A2.205: Subject No.1 fast biking exercise ECG interpolation*

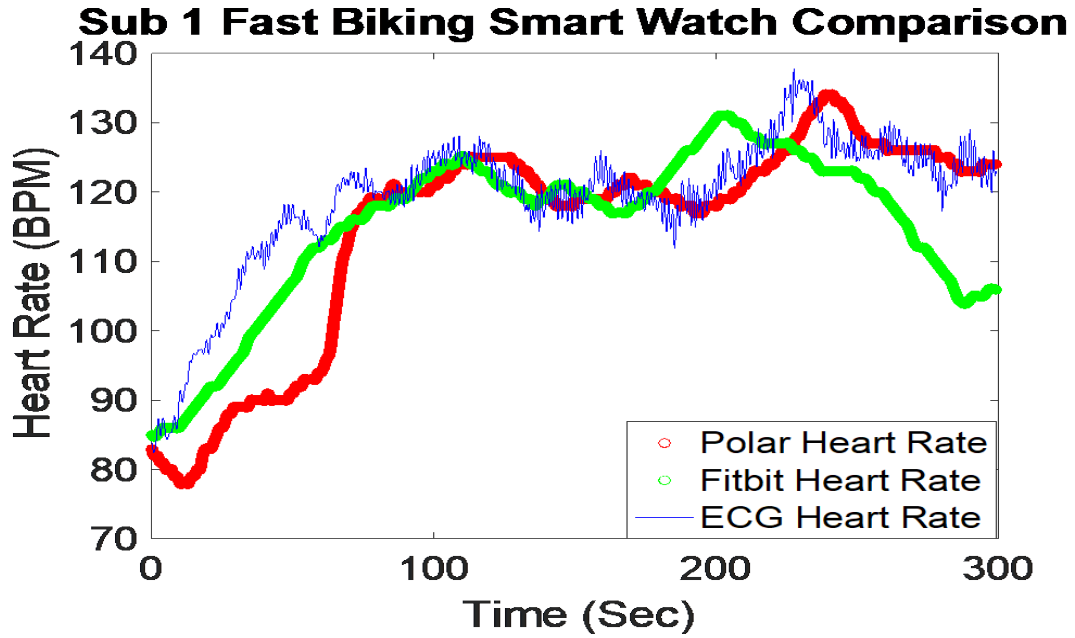


Figure A2.206: Subject No.1 Fast Biking Polar and Fitbit WFT compared to ECG

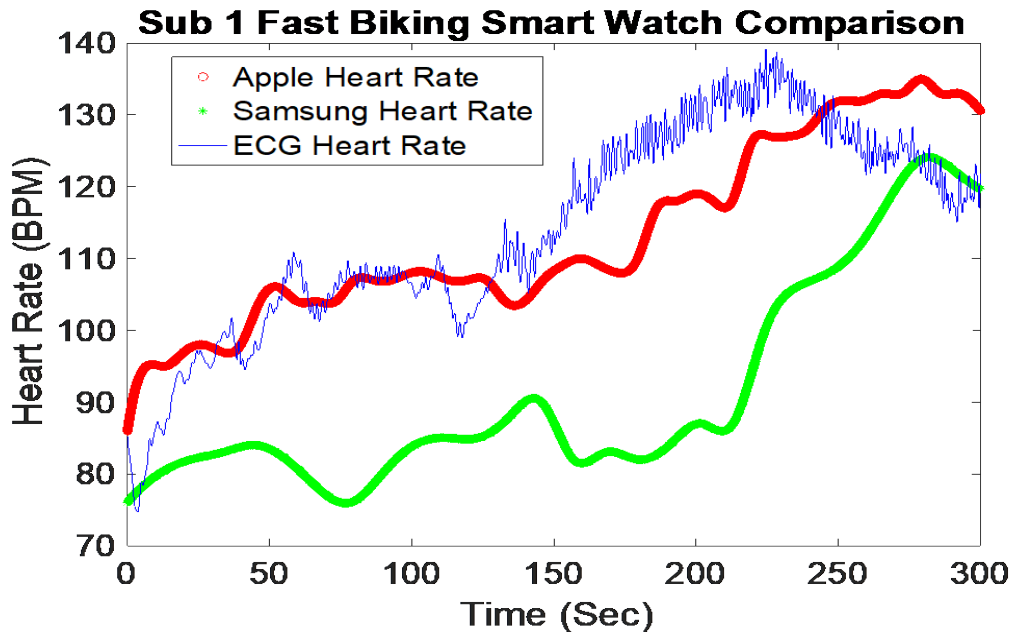


Figure A2.207: Subject No.1 Fast Biking Apple and Samsung WFT compared to ECG

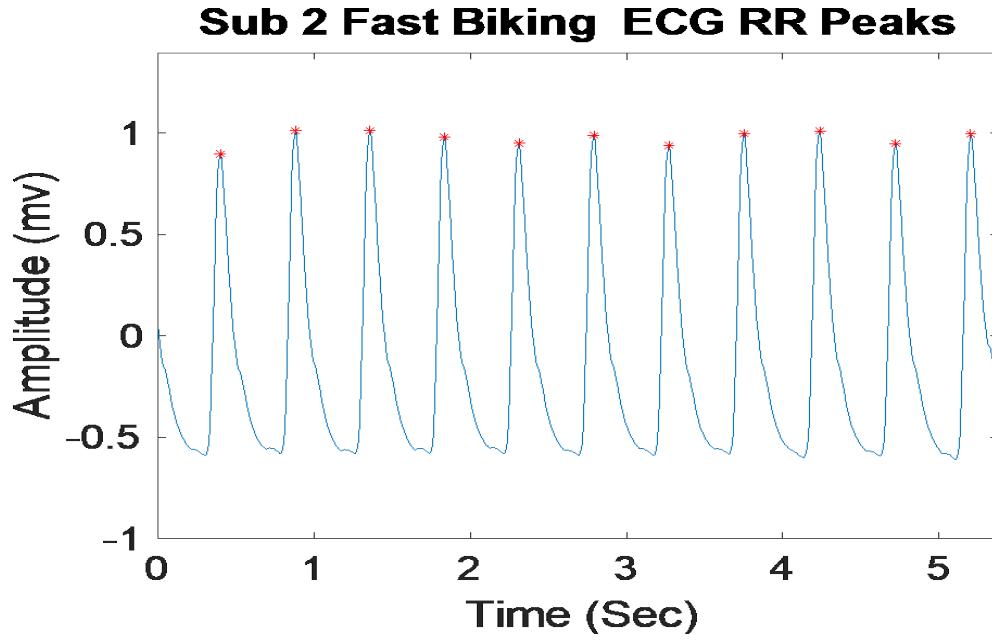


Figure A2.208: Subject No. 2 Fast Biking ECG RR Peaks detection (Amplified R wave)

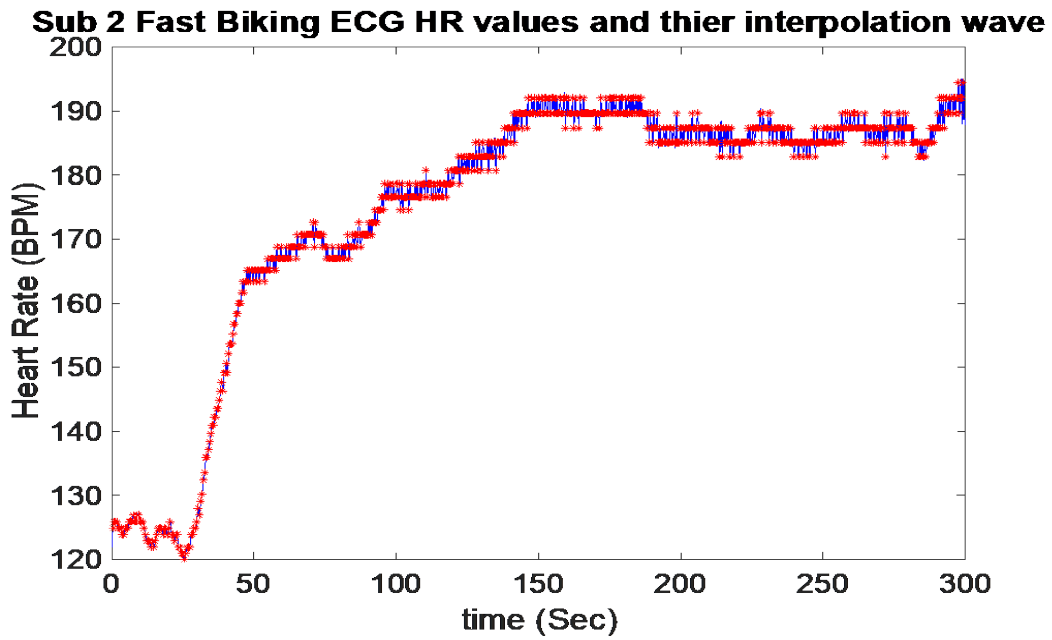


Figure A2.209: Subject No.2 Fast biking exercise ECG HR interpolation

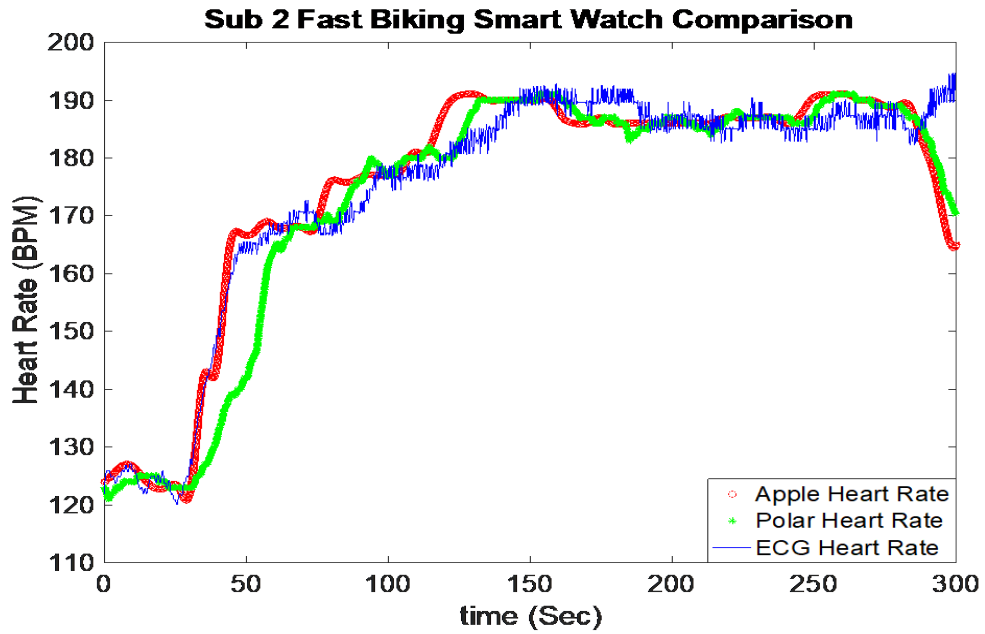


Figure A2.210: Subject No.2 Fast Biking Apple and Polar WFT compared to ECG

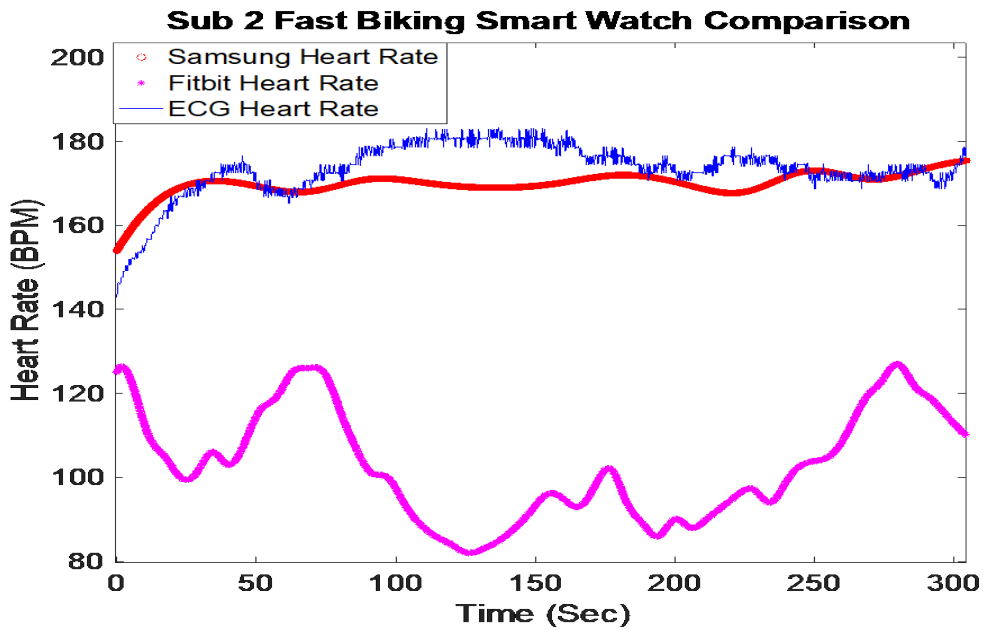


Figure A2.211: Subject No.2 fast biking Samsung and Fitbit WFT compared to ECG

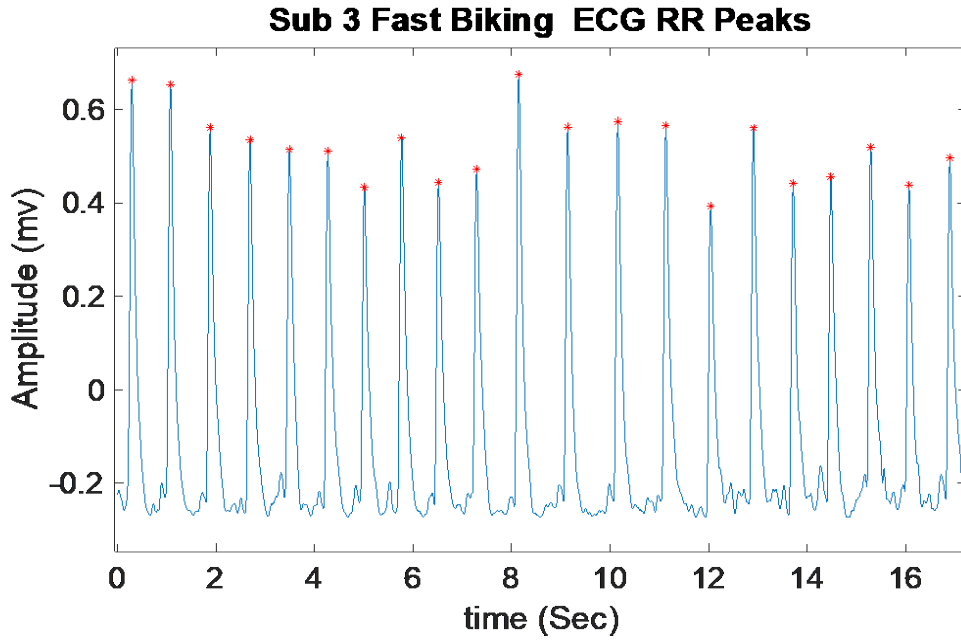


Figure A2.212: Subject No. 3 fast biking ECG RR Peaks detection (Amplified R wave)

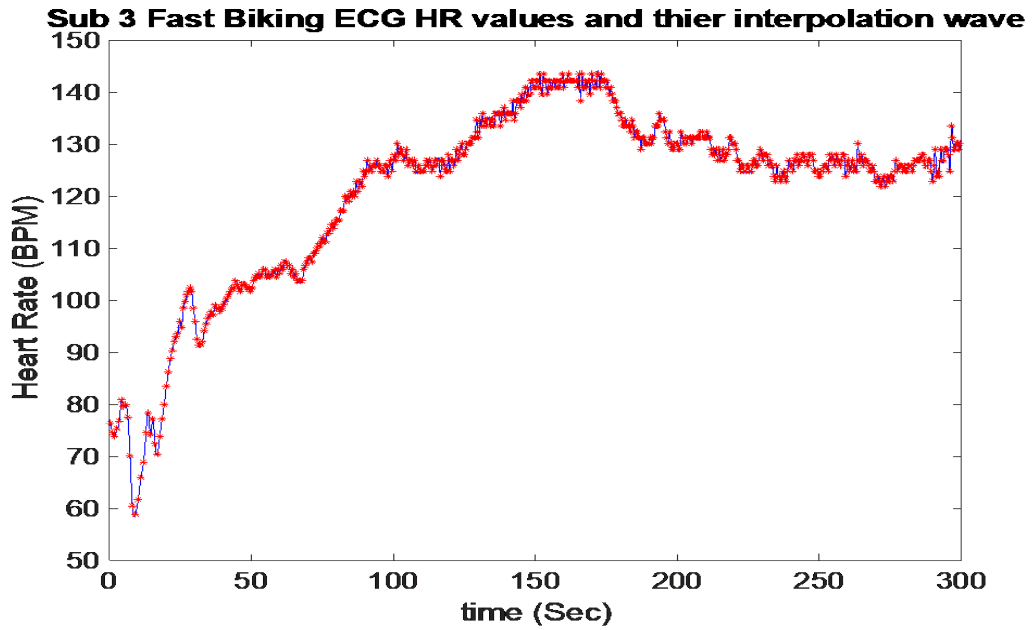


Figure A2.213: Subject No.3 fast biking exercise ECG HR interpolation

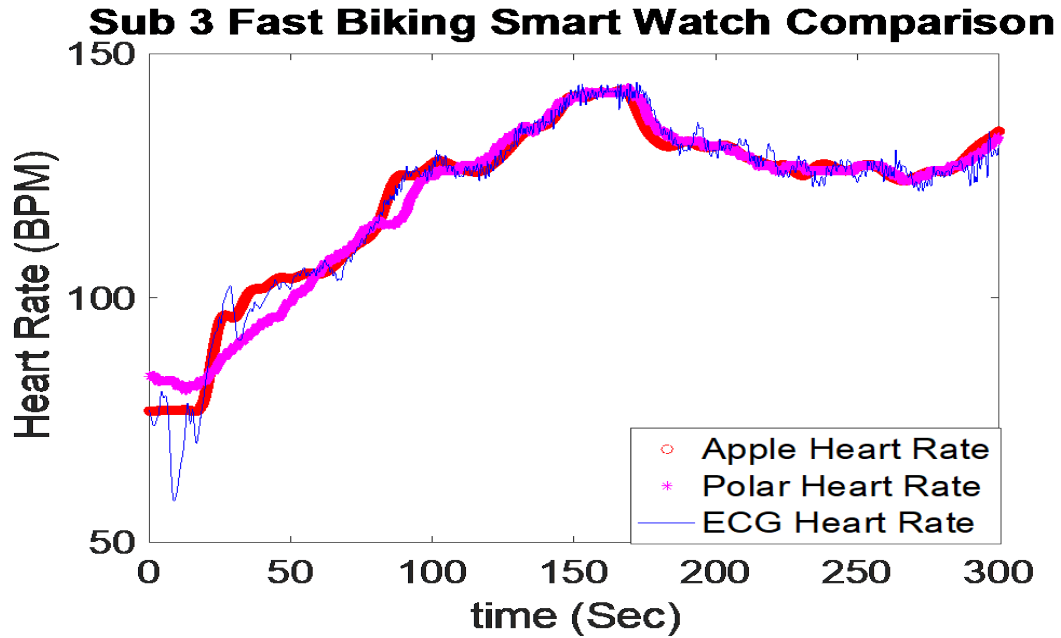


Figure A2.214: Subject No.3 fast biking Apple and Polar WFT compared to ECG

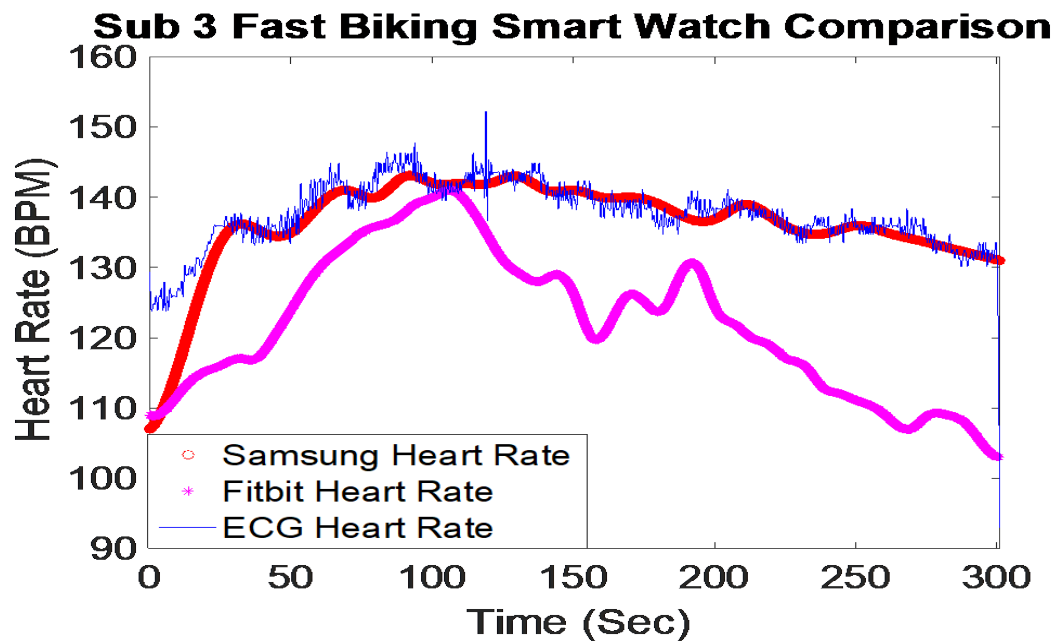


Figure A2.215: Subject No.3 fast biking Samsung and Fitbit WFT compared to ECG



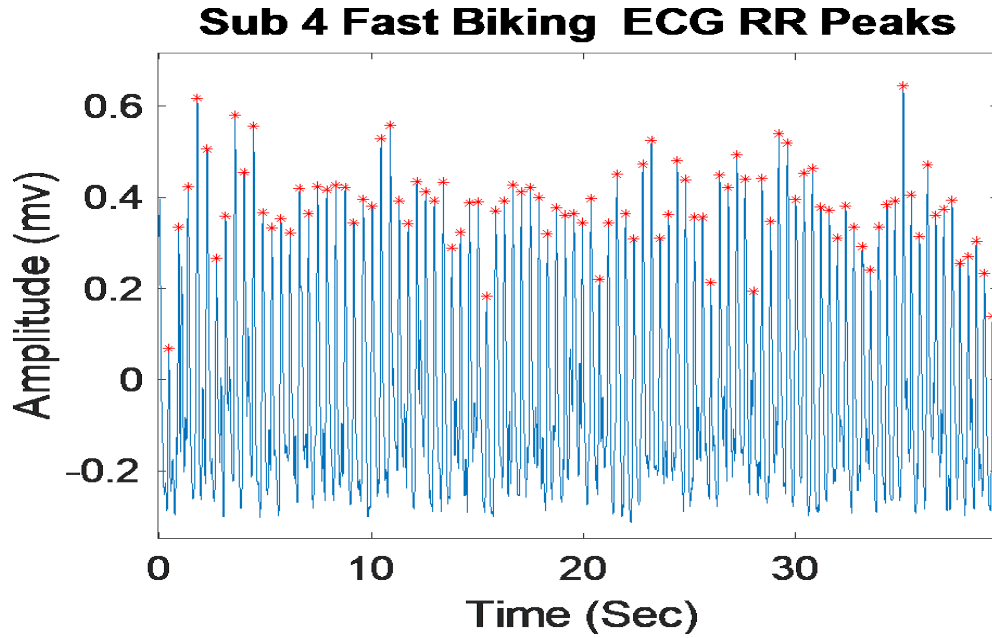


Figure A2.216: Subject No. 4 fast biking ECG RR Peaks detection (Amplified R wave)

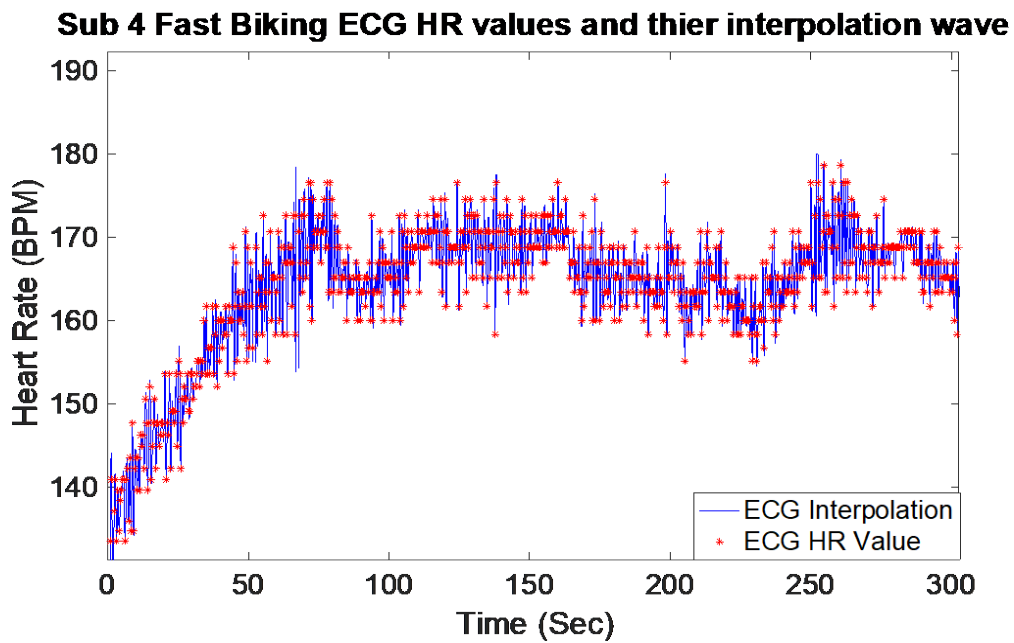


Figure A2.217: Subject No.4 fast biking exercise ECG HR interpolation

### Sub 4 Fast Biking Smart Watch Comparison

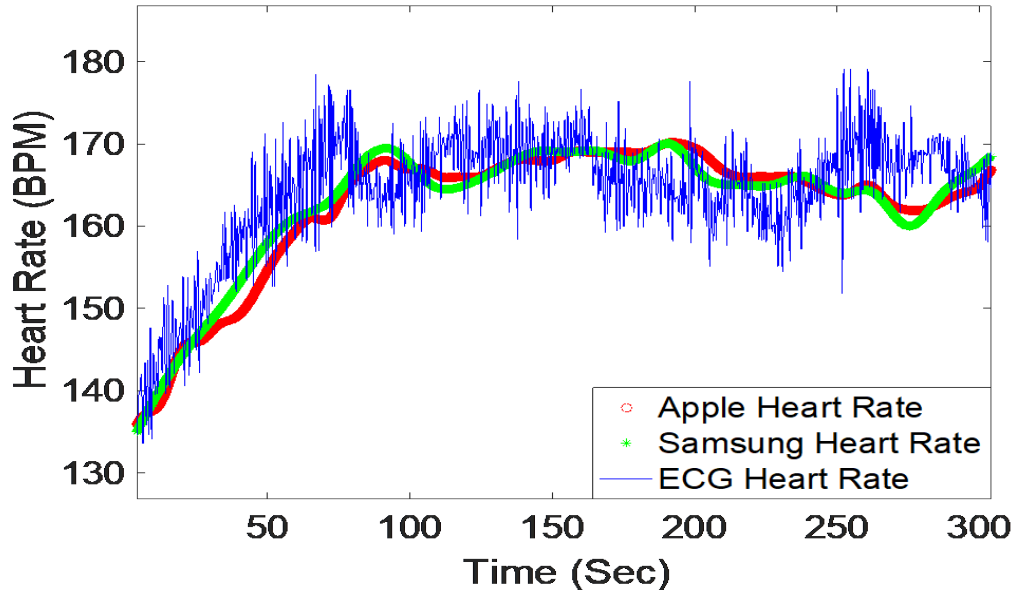


Figure A2.218: Subject No.4 fast biking Apple and Samsung WFT compared to ECG

### Sub 4 Fast Biking Smart Watch Comparison

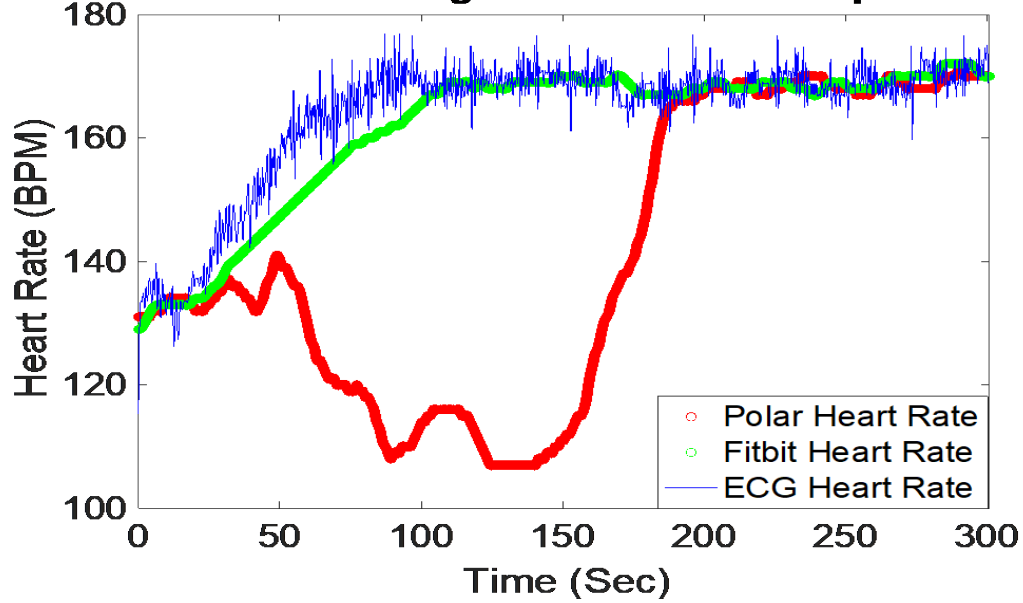


Figure A2.219: Subject No.4 fast biking Polar and Fitbit WFT compared to ECG

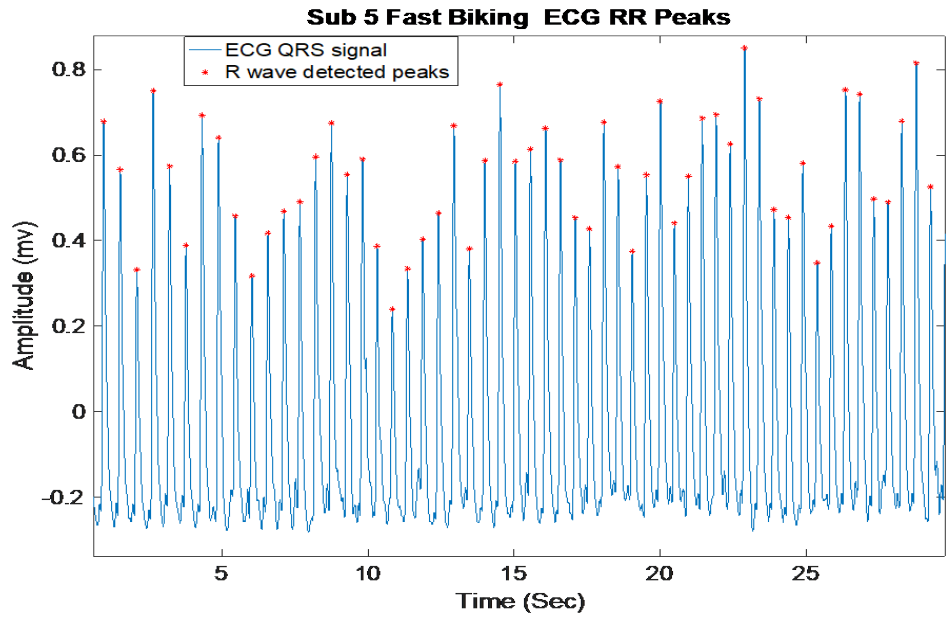


Figure A2.220: Subject No. 5 fast biking ECG RR Peaks detection (Amplified R wave)

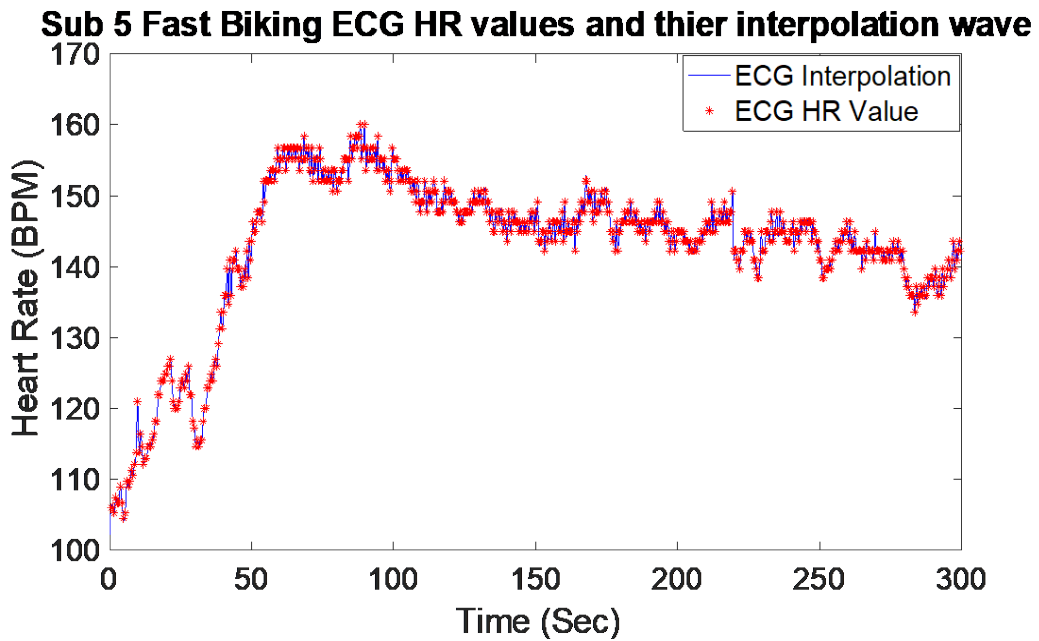


Figure A2.221: Subject No.5 fast biking exercise ECG HR interpolation

### Sub 5 Fast Biking Smart Watch Comparison

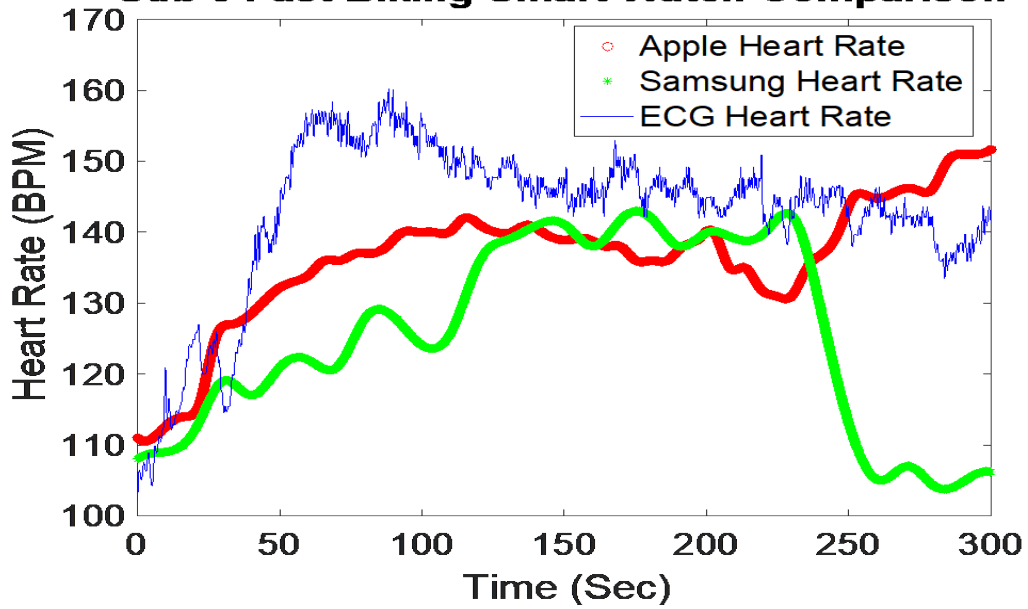


Figure A2.222: Subject No.5 fast biking Apple and Samsung WFT compared to ECG

### Sub 5 Fast Biking Smart Watch Comparison

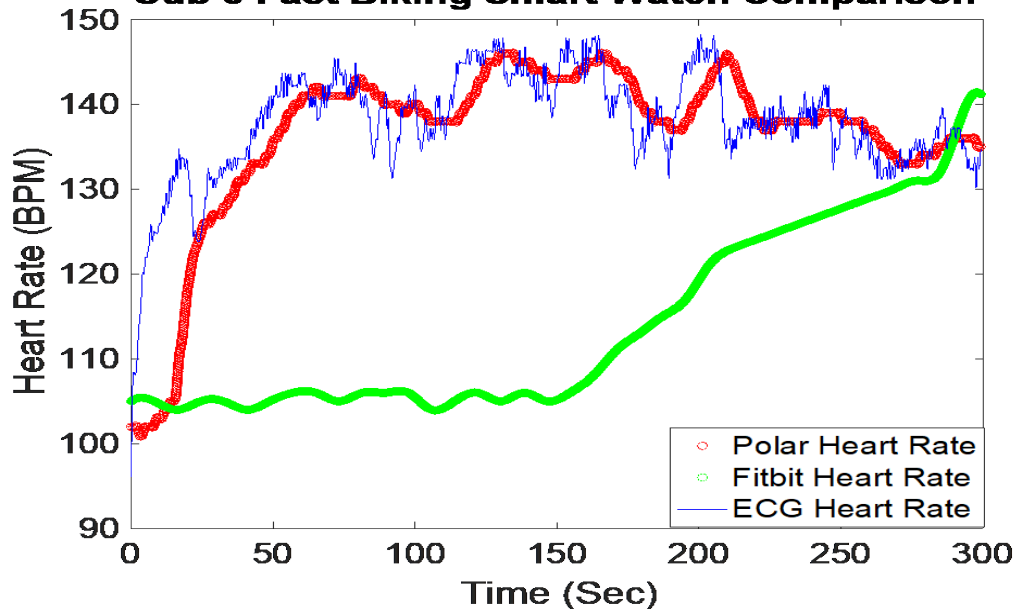


Figure A2.223: Subject No.5 fast biking Polar and Fitbit WFT compared to ECG

## A.2.2: WFTs Bland and Altman Plots:

### *APPLE WFT Bland and Altman Plots*

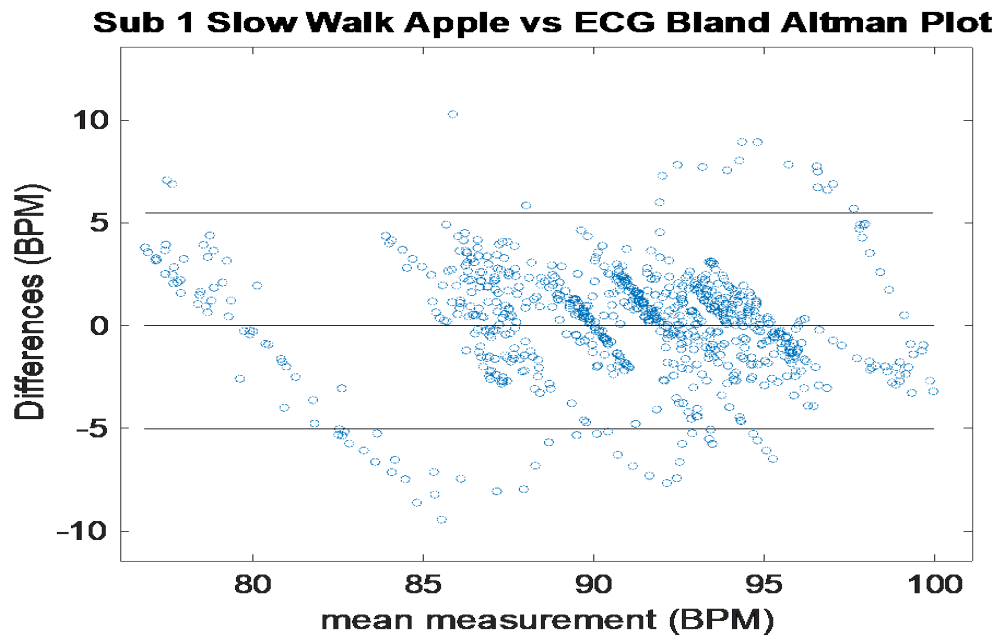


Figure A2.224: Subject No. 1 Apple's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 2 Slow Walk Apple vs ECG Bland Altman Plot

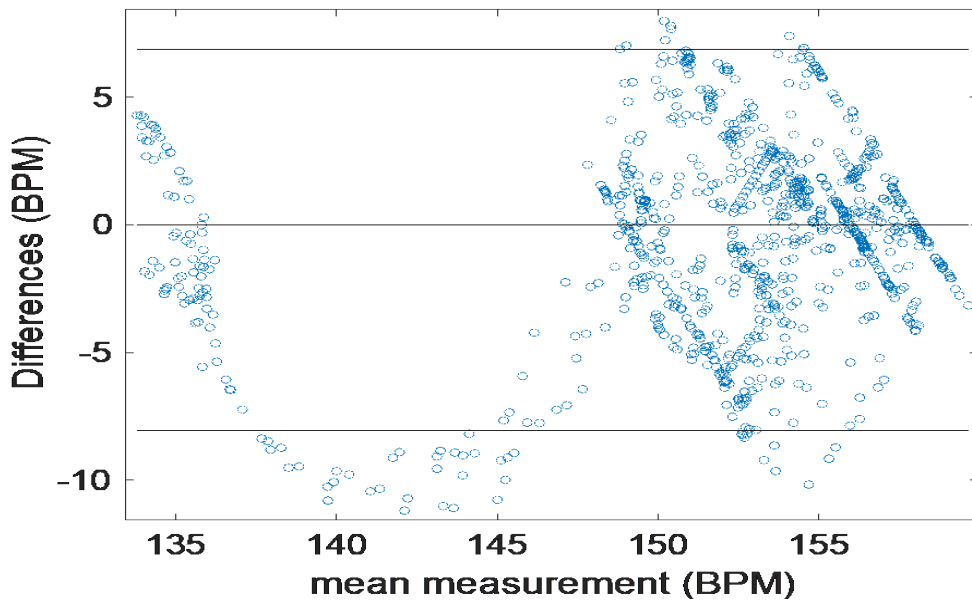


Figure A2.225: Subject No. 2 Apple's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 3 Slow Walk Apple vs ECG Bland Altman Plot

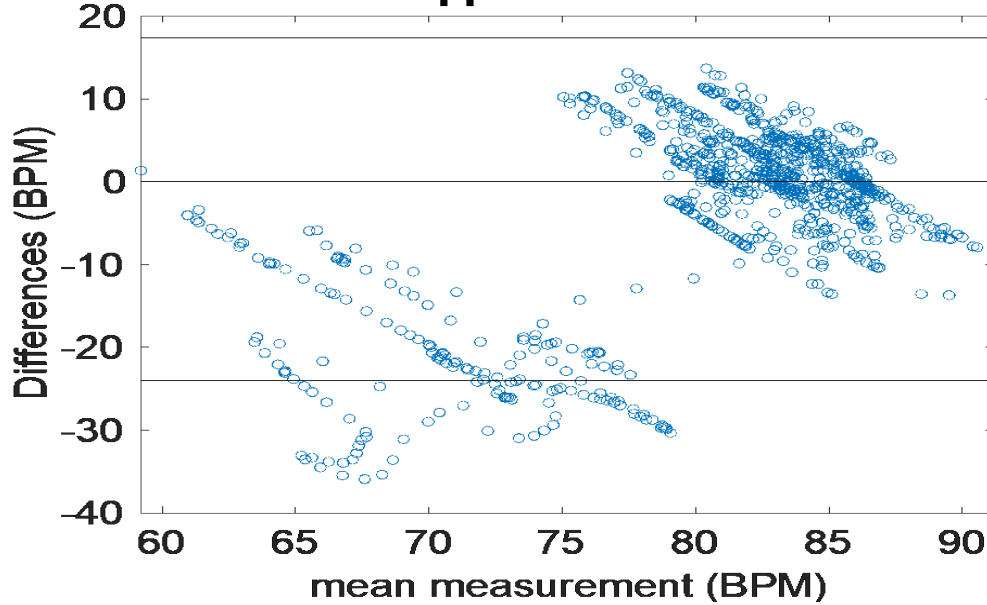


Figure A2.226: Subject No. 3 Apple's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

**Sub 4 Slow Walk Apple vs ECG Bland Altman Plot**

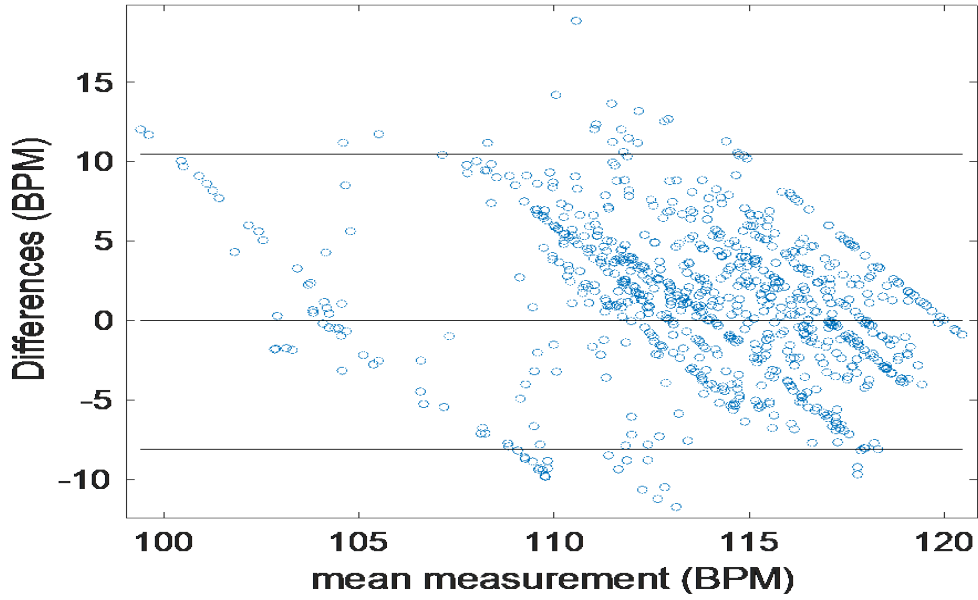


Figure A2.227: Subject No. 4 Apple's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

**Sub 5 Slow Walk Apple vs ECG Bland Altman Plot**

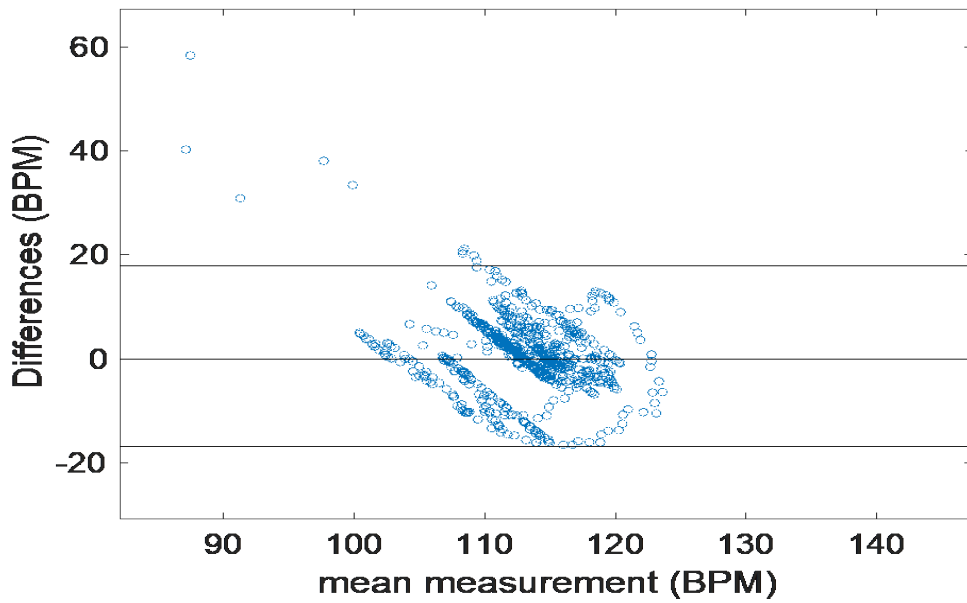


Figure A2.228: Subject No. 5 Apple's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

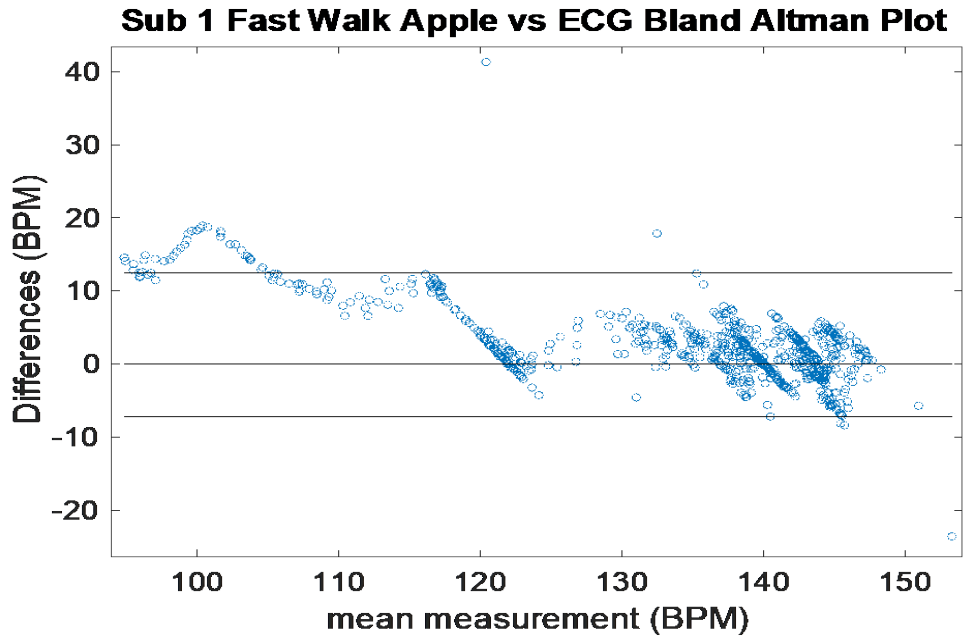


Figure A2.229: Subject No. 1 Apple's B&A for fast walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

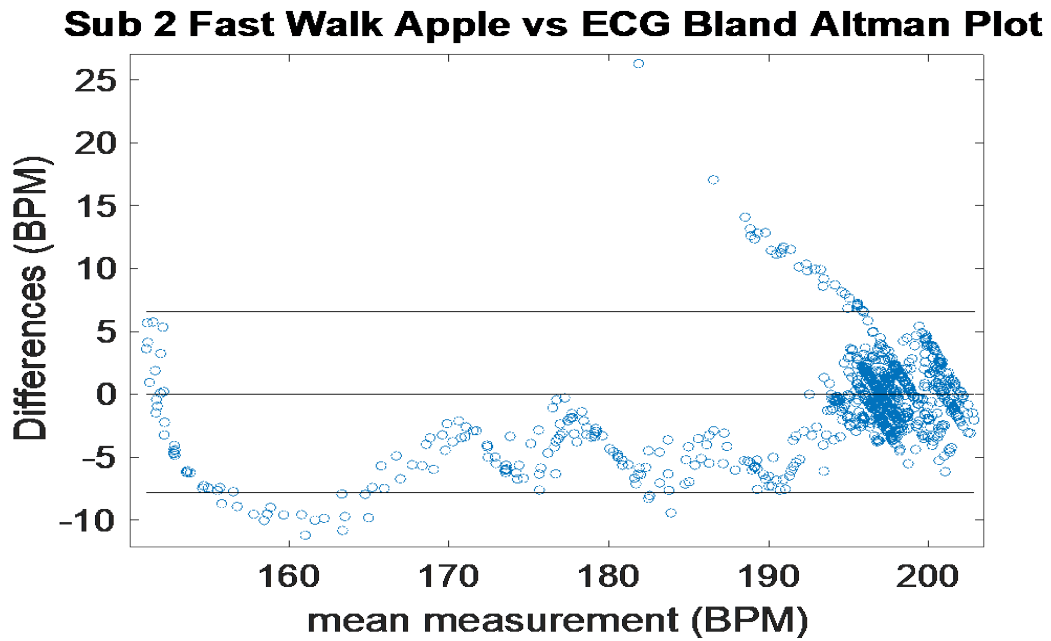


Figure A2.230: Subject No. 2 Apple's B&A for fast walking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)



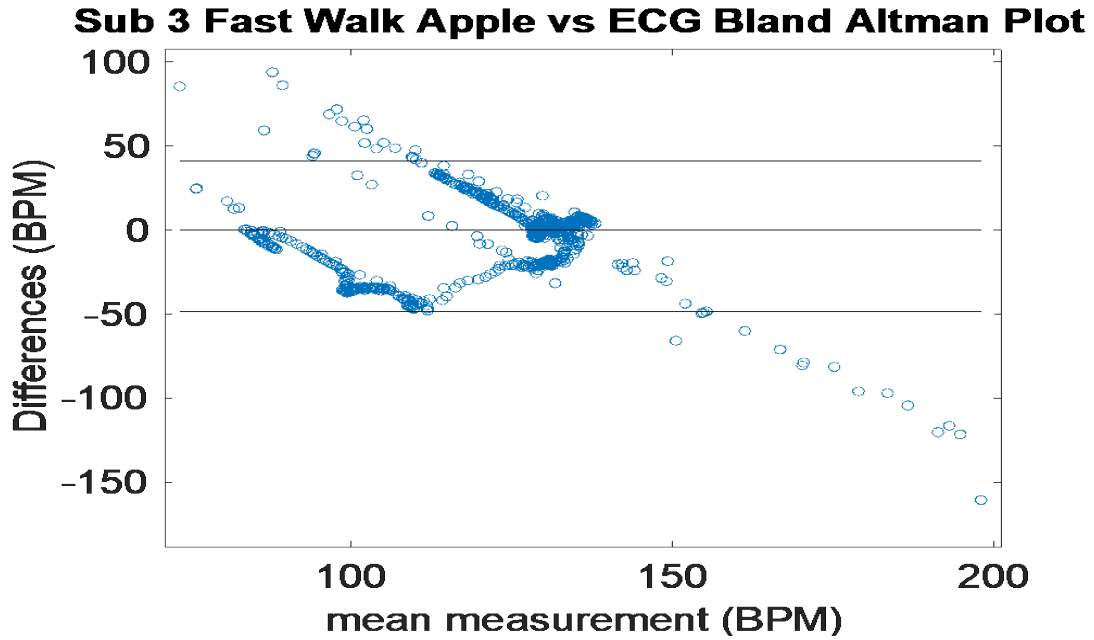


Figure A2.231: Subject No. 3 Apple's B&A for fast walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

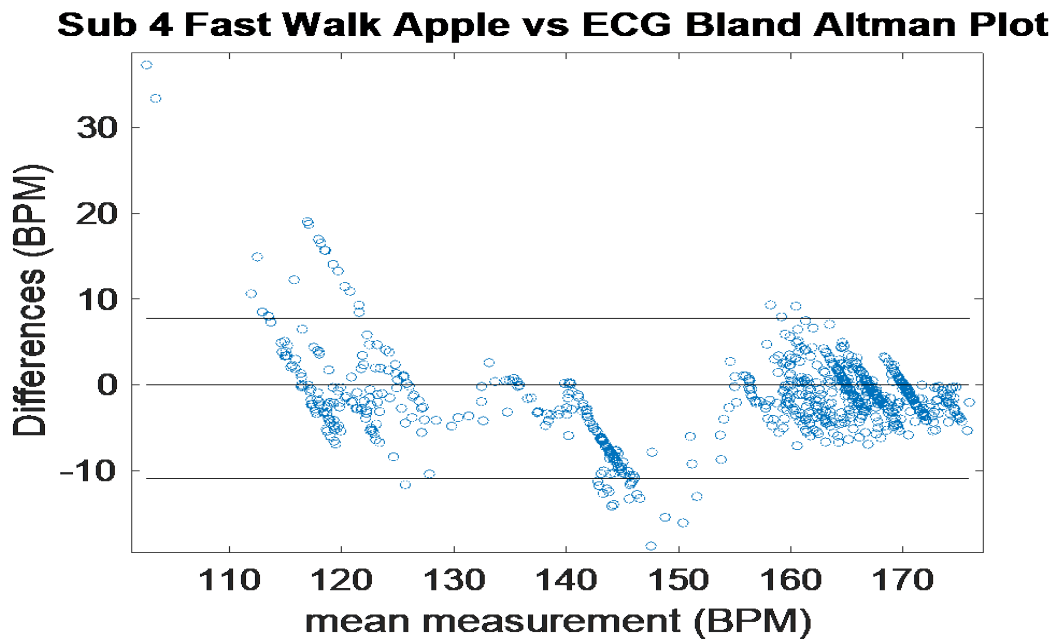


Figure A2.232: Subject No. 4 Apple's B&A for fast walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 5 Fast Walk Apple vs ECG Bland Altman Plot

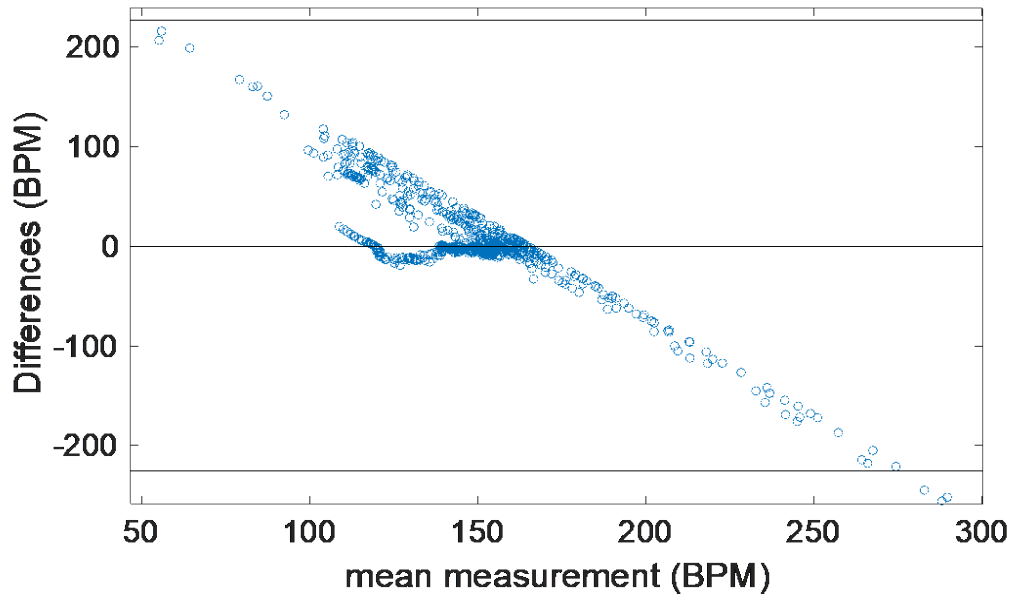


Figure A2.233: Subject No. 5 Apple's B&A for fast walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 1 Sitting Apple vs ECG Bland Altman Plot

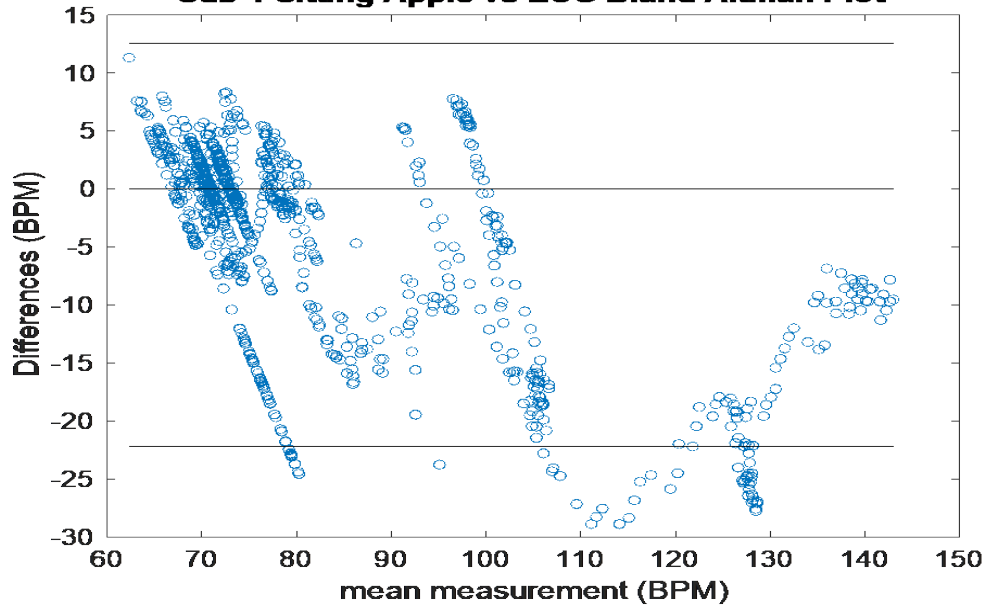


Figure A2.234: Subject No. 1 Apple's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 2 Sitting Apple vs ECG Bland Altman Plot

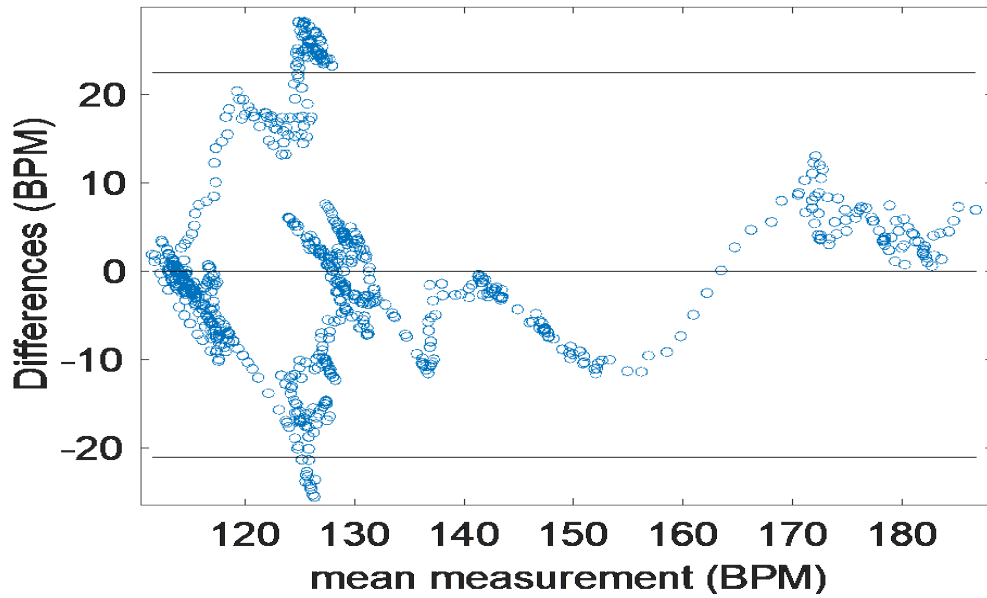


Figure A2.235: Subject No. 2 Apple's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 3 Sitting Apple vs ECG Bland Altman Plot

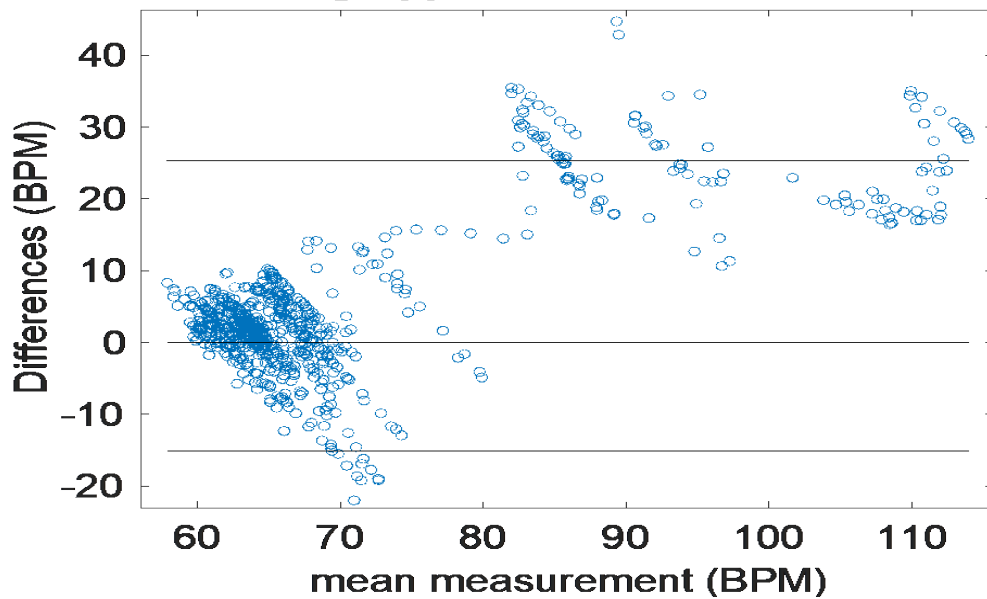


Figure A2.236: Subject No. 3 Apple's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 4 Sitting Apple vs ECG Bland Altman Plot

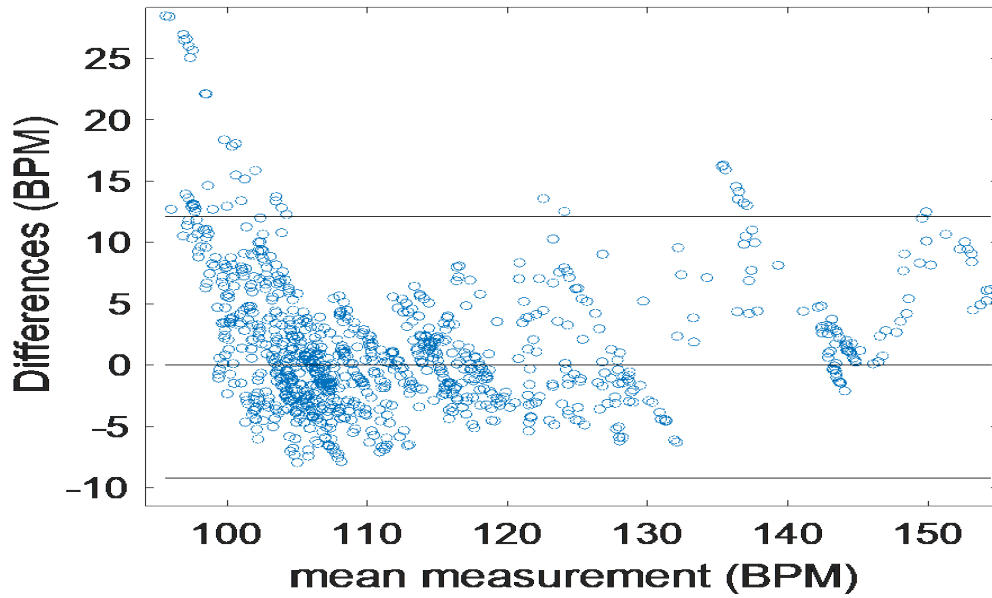


Figure A2.237: Subject No. 4 Apple's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 5 Sitting Apple vs ECG Bland Altman Plot

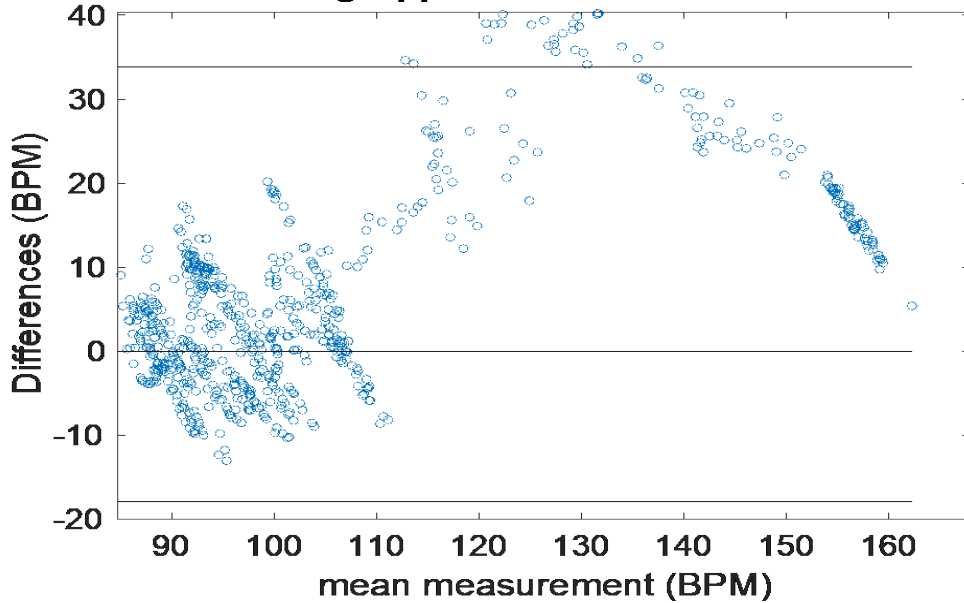


Figure A2.238: Subject No. 5 Apple's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 1 Slow Biking Apple vs ECG Bland Altman Plot

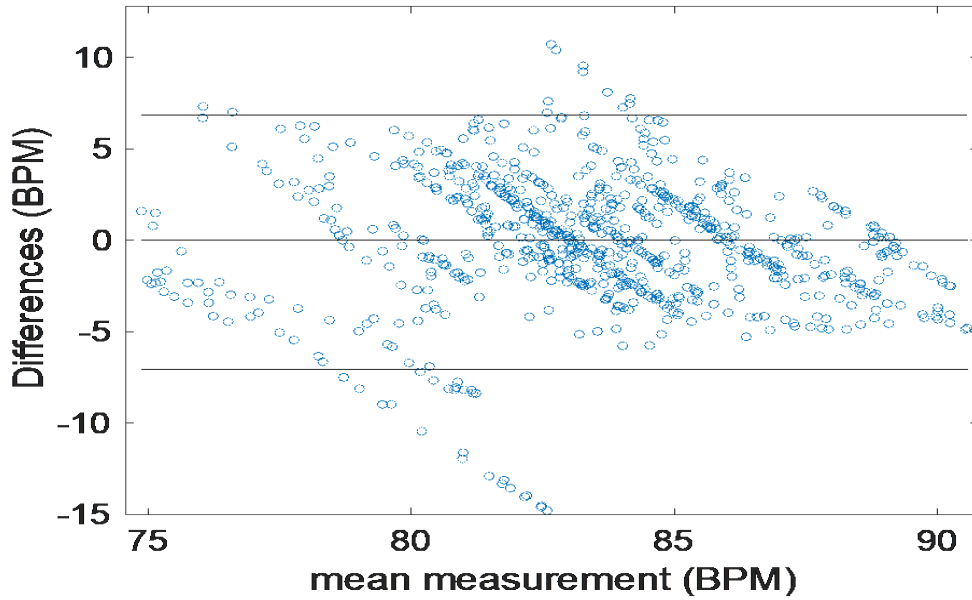


Figure A2.239: Subject No. 1 Apple's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 2 Slow Biking Apple vs ECG Bland Altman Plot

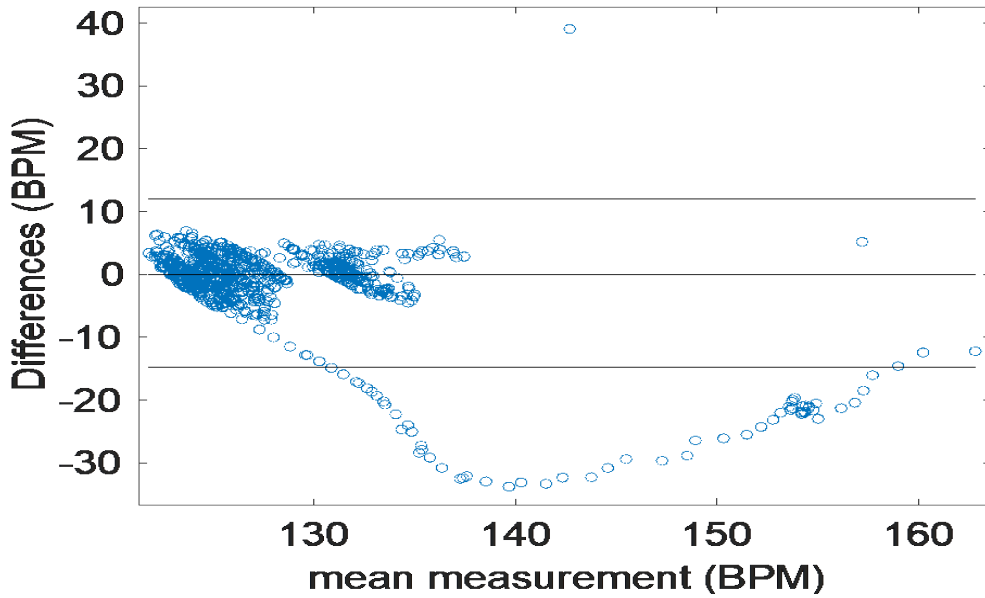


Figure A2.240: Subject No. 2 Apple's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 3 Slow Biking Apple vs ECG Bland Altman Plot

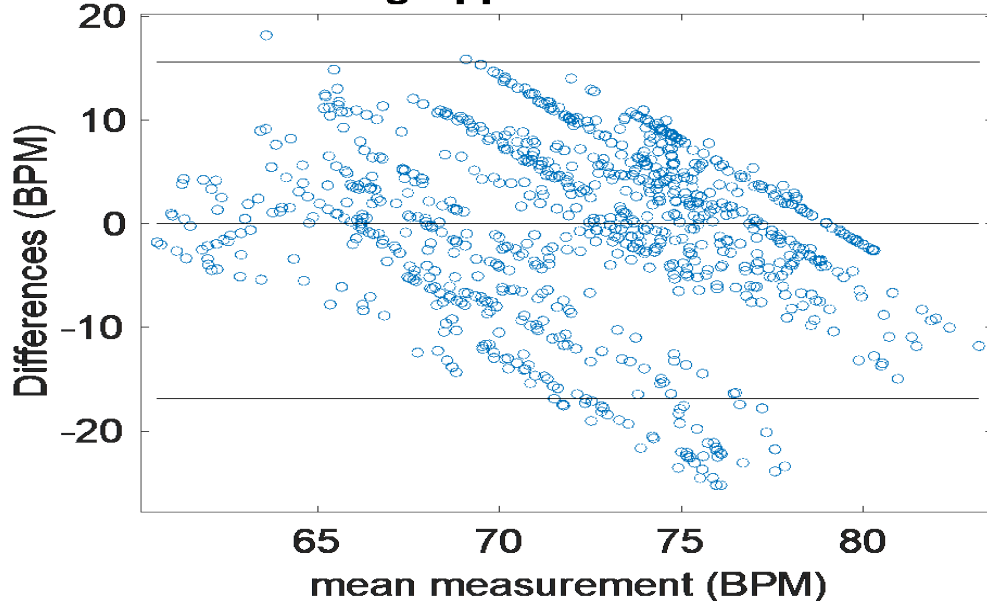


Figure A2.241: Subject No. 3 Apple's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 4 Slow Biking Apple vs ECG Bland Altman Plot

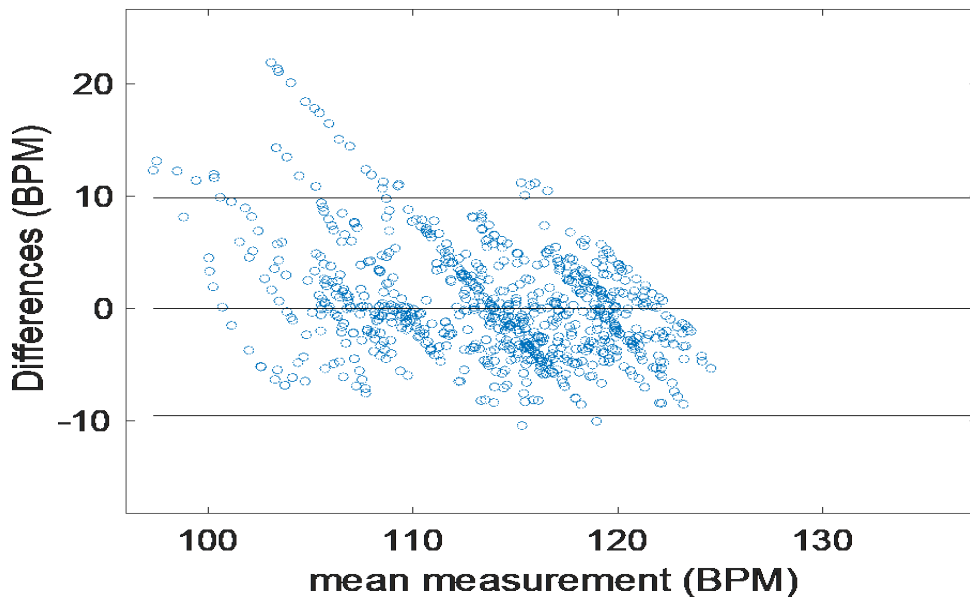


Figure A2.242: Subject No. 4 Apple's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 5 Slow Biking Apple vs ECG Bland Altman Plot

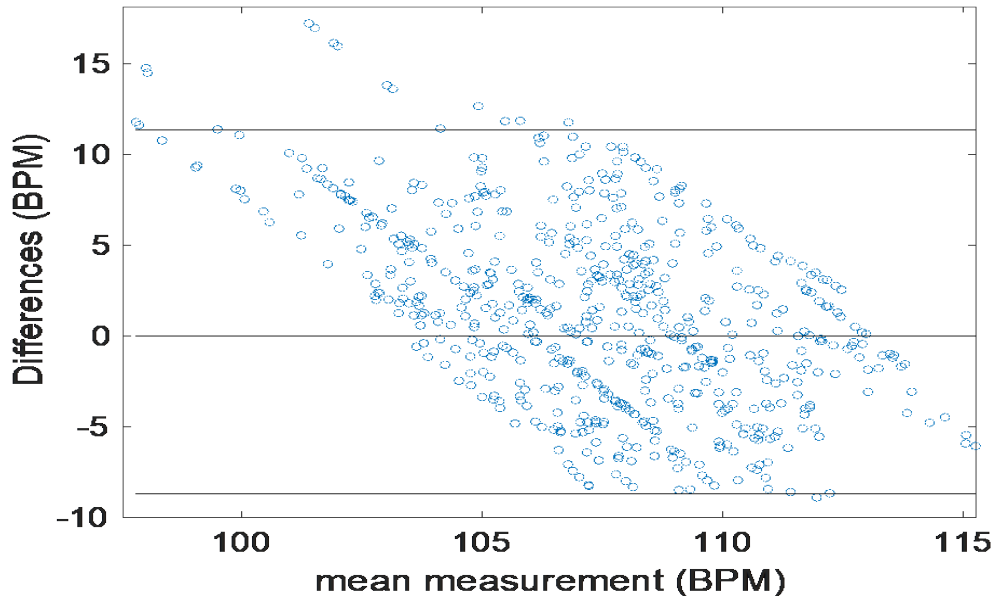


Figure A2.243: Subject No. 5 Apple's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 1 Fast Biking Apple vs ECG Bland Altman Plot

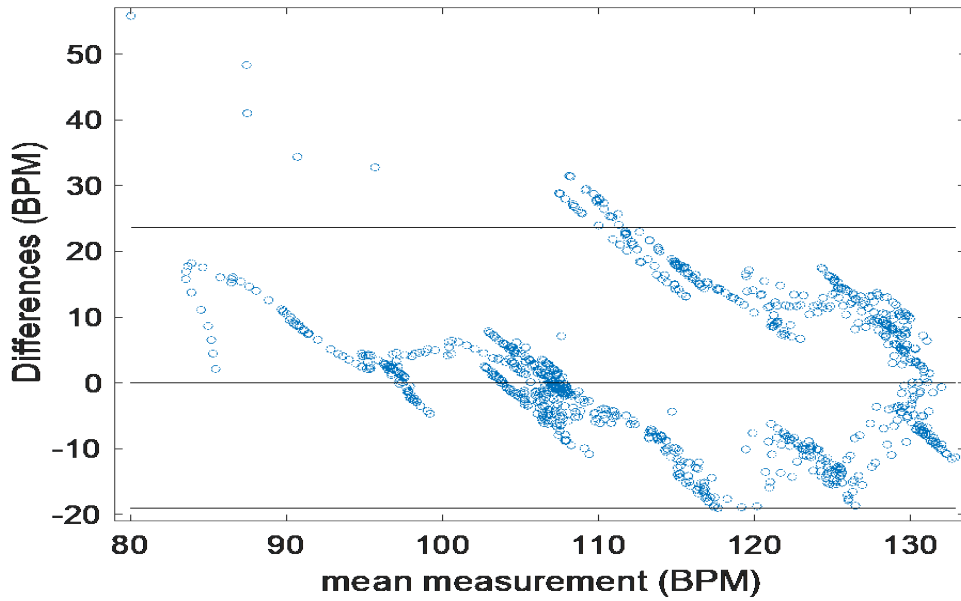


Figure A2.244: Subject No. 1 Apple's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 2 Fast Biking Apple vs ECG Bland Altman Plot

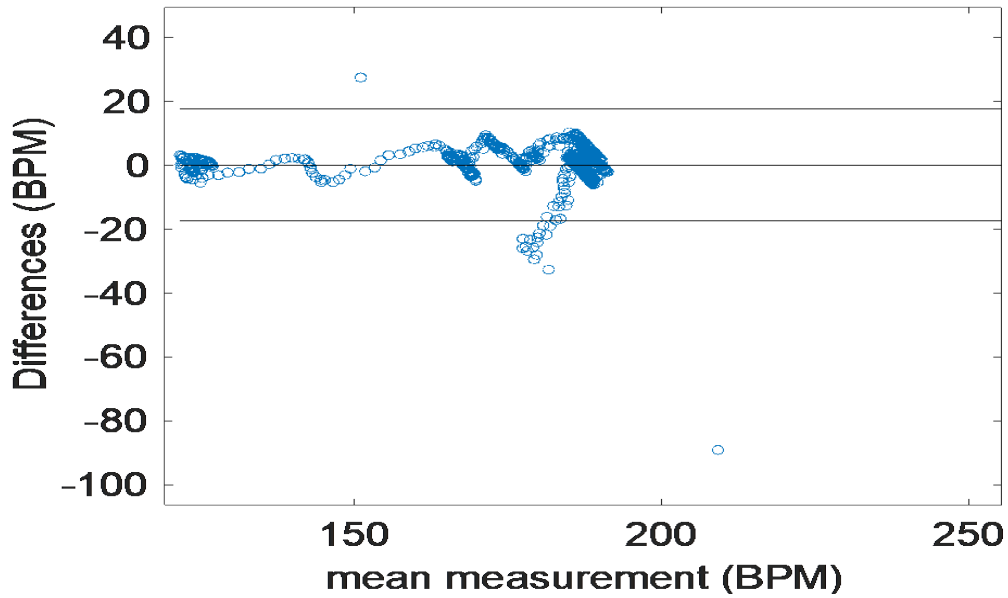


Figure A2.245: Subject No. 2 Apple's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 3 Fast Biking Apple vs ECG Bland Altman Plot

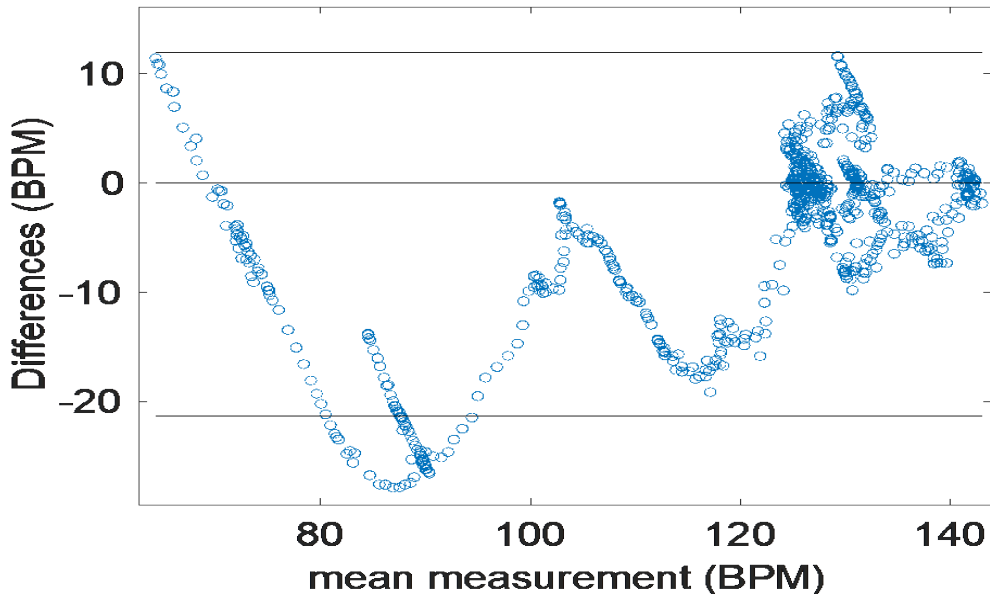


Figure A2.246: Subject No. 3 Apple's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)



### Sub 4 Fast Biking Apple vs ECG Bland Altman Plot

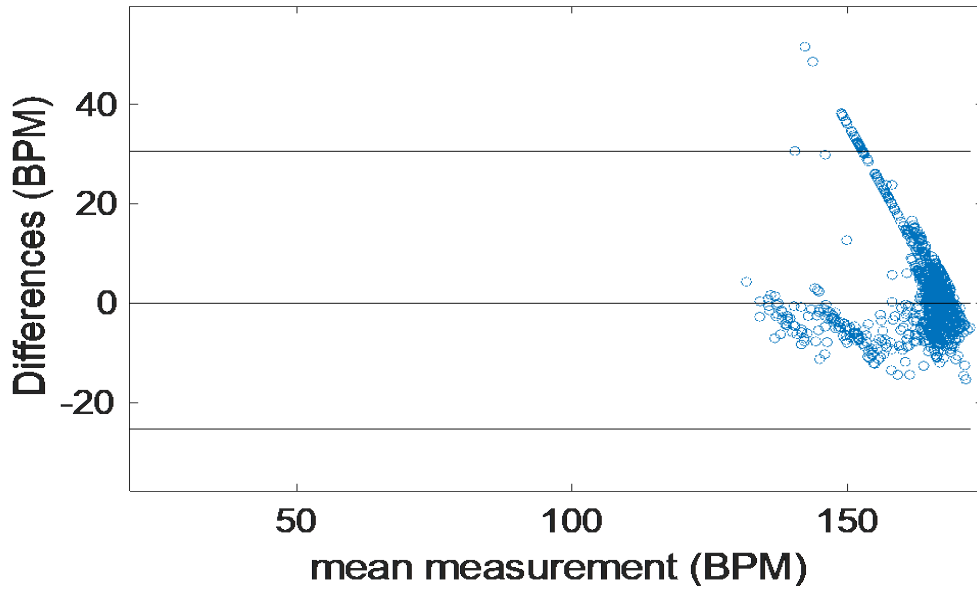


Figure A2.247: Subject No. 4 Apple's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 5 Fast Biking Apple vs ECG Bland Altman Plot

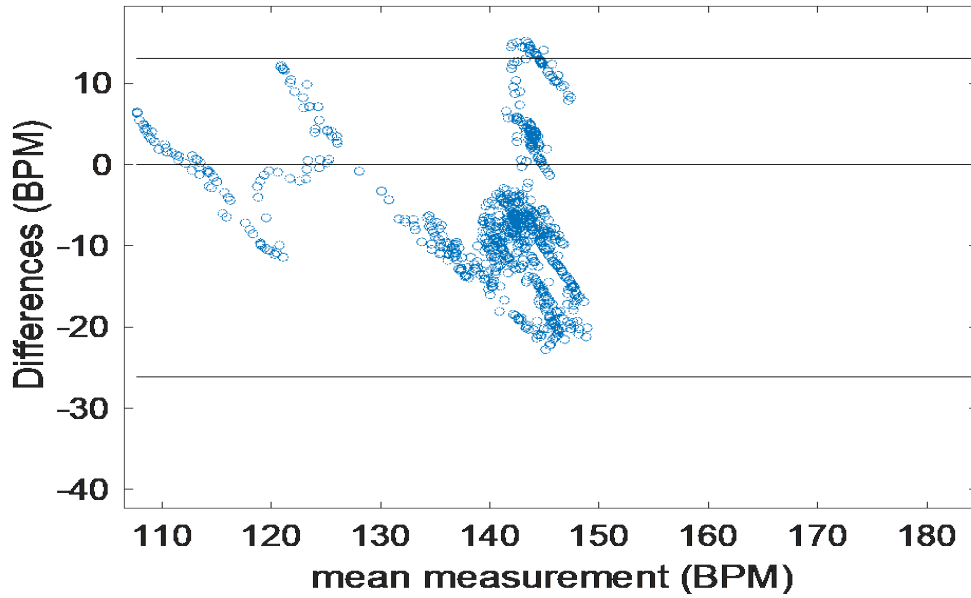


Figure A2.248: Subject No. 5 Apple's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

*Polar WFT Bland and Altman Plots*

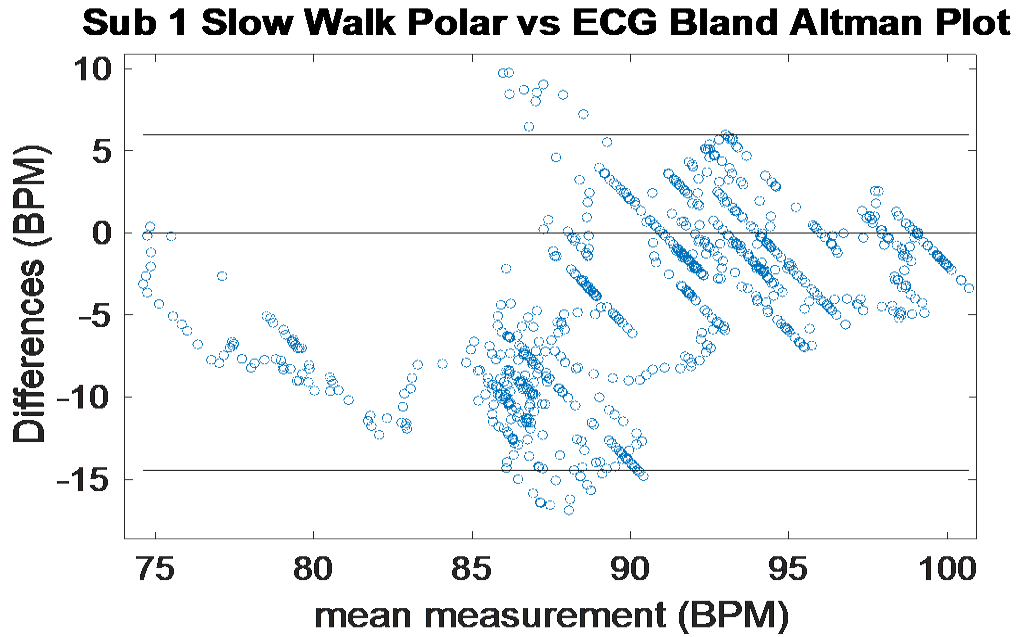


Figure A2.249: Subject No 1 Polar's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

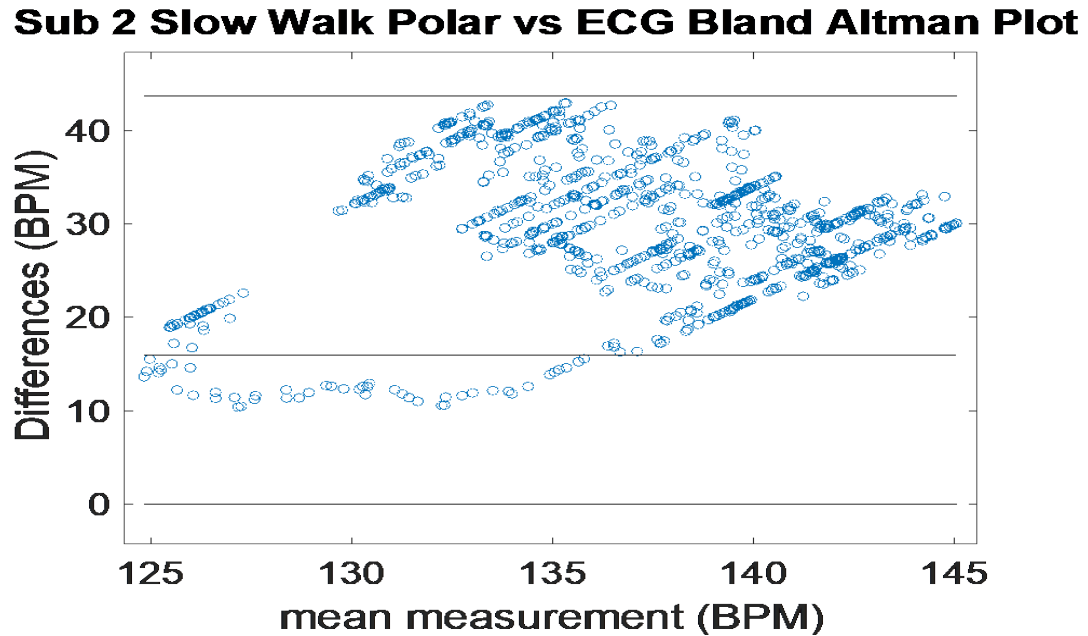


Figure A2.250: Subject No. 2 Polar's B&A for slow walking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 3 Slow Walk Polar vs ECG Bland Altman Plot

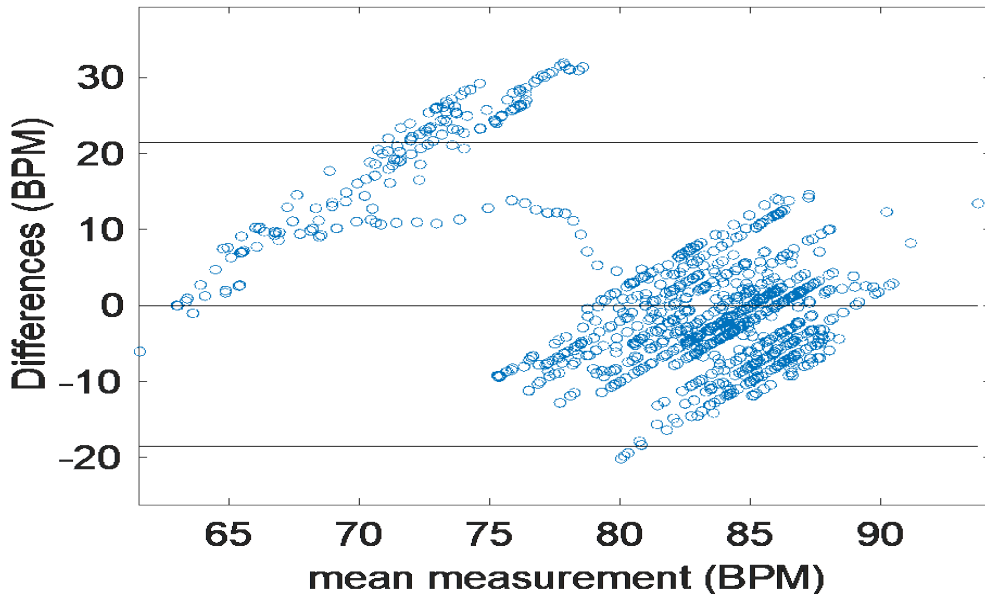


Figure A2.251: Subject No. 3 Polar's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 4 Slow Walk Polar vs ECG Bland Altman Plot

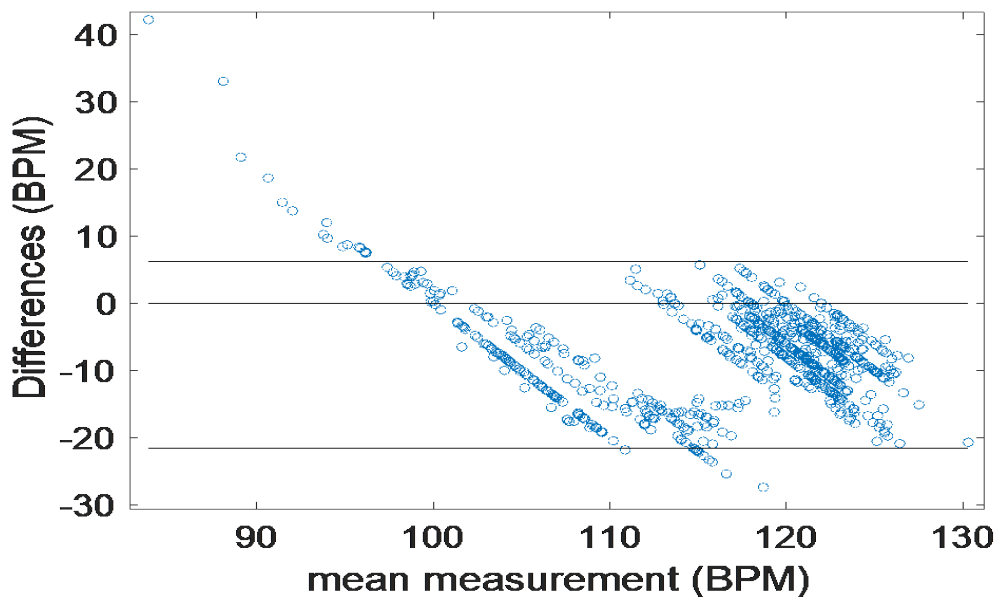


Figure A2.252: Subject No. 4 Polar's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 5 Slow Walk Polar vs ECG Bland Altman Plot

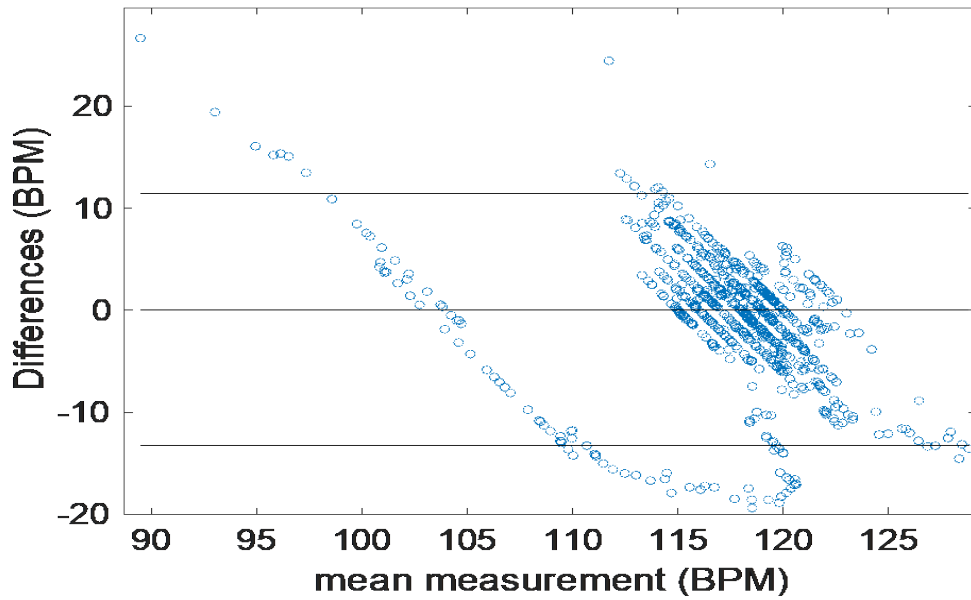


Figure A2.253: Subject No. 5 Polar's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 1 Fast Walk Polar vs ECG Bland Altman Plot

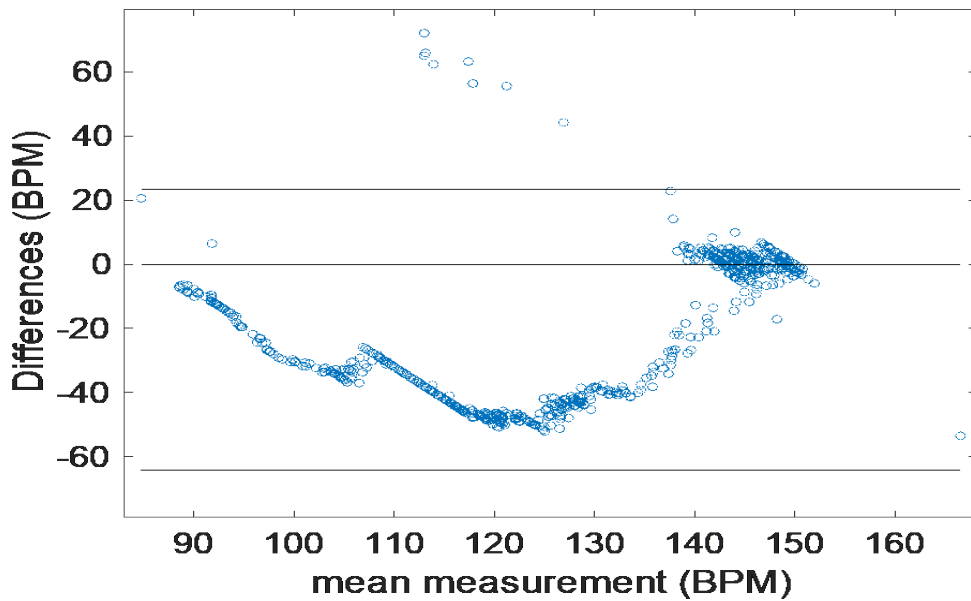


Figure A2.254: Subject No. 1 Polar's B&A for fast walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 2 Fast Walk Polar vs ECG Bland Altman Plot

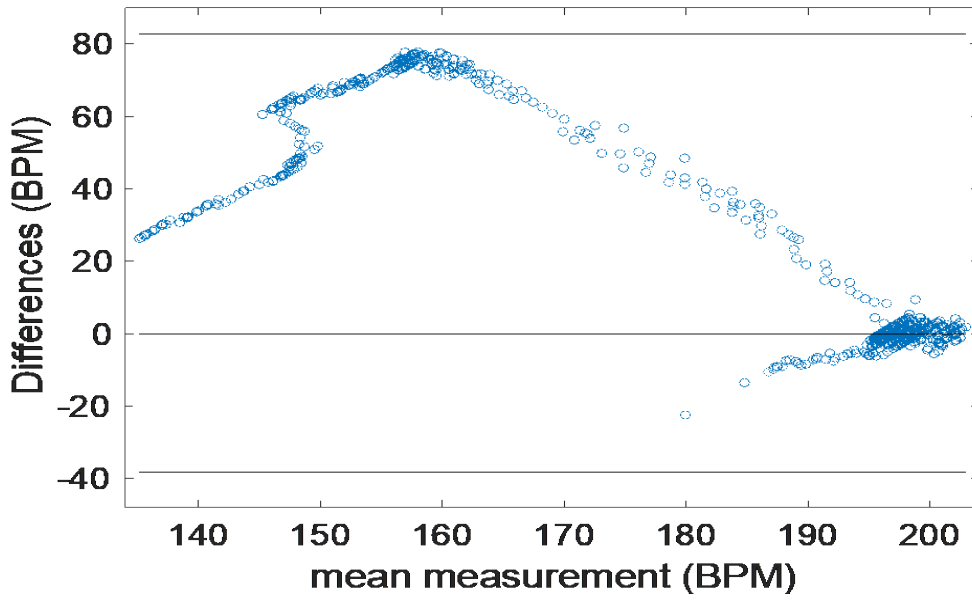


Figure A2.255: Subject No. 2 Polar's B&A for fast walking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 3 Fast Walk Polar vs ECG Bland Altman Plot

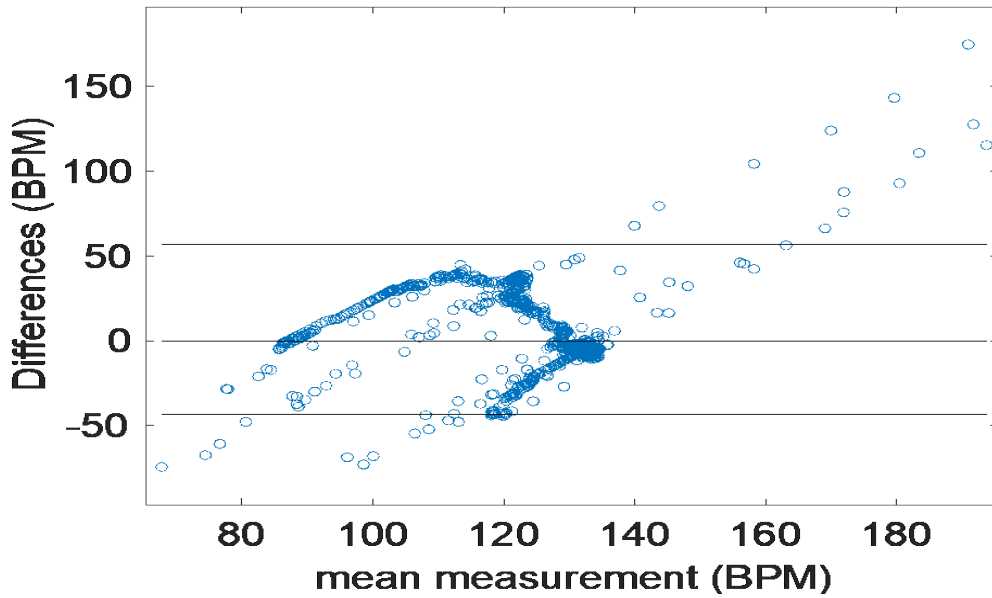


Figure A2.256: Subject No. 3 Polar's B&A for fast walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 4 Fast Walk Polar vs ECG Bland Altman Plot

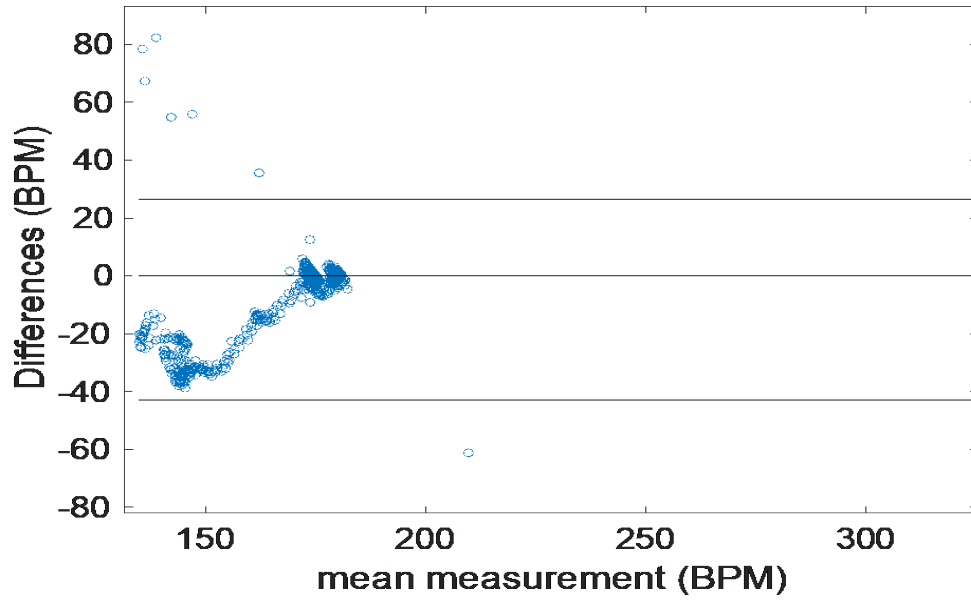


Figure A2.257: Subject No. 4 Polar's B&A for fast walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 5 Fast Walk Polar vs ECG Bland Altman Plot

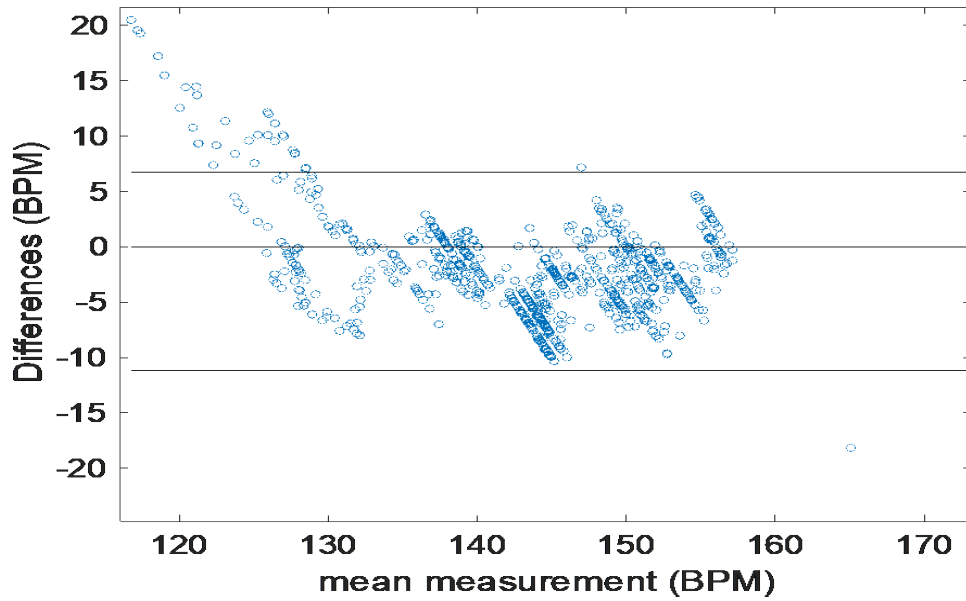


Figure A2.258: Subject No. 5 Polar's B&A for fast walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 1 Sitting Polar vs ECG Bland Altman Plot

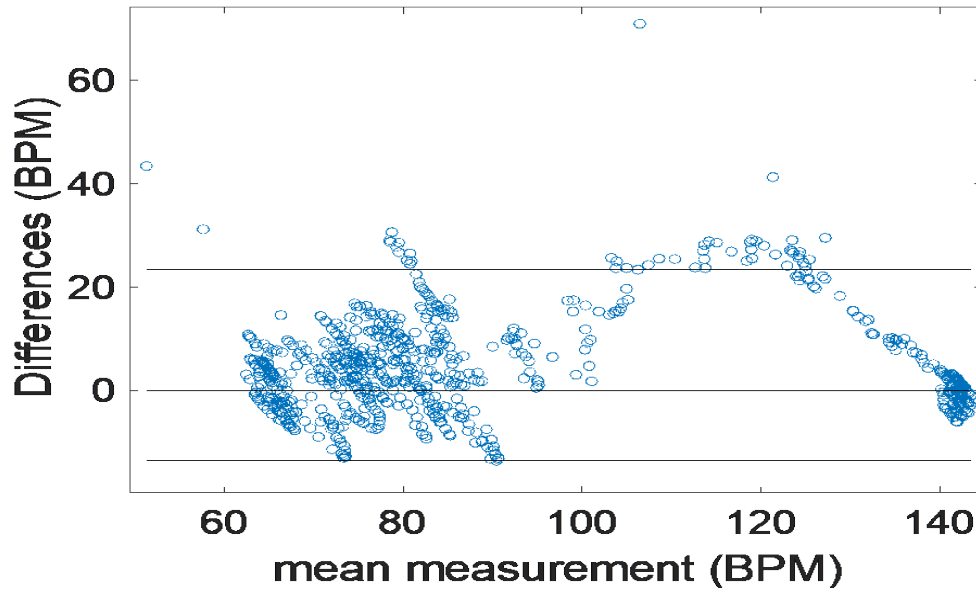


Figure A2.259: Subject No. 1 Polar's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 2 Sitting Polar vs ECG Bland Altman Plot

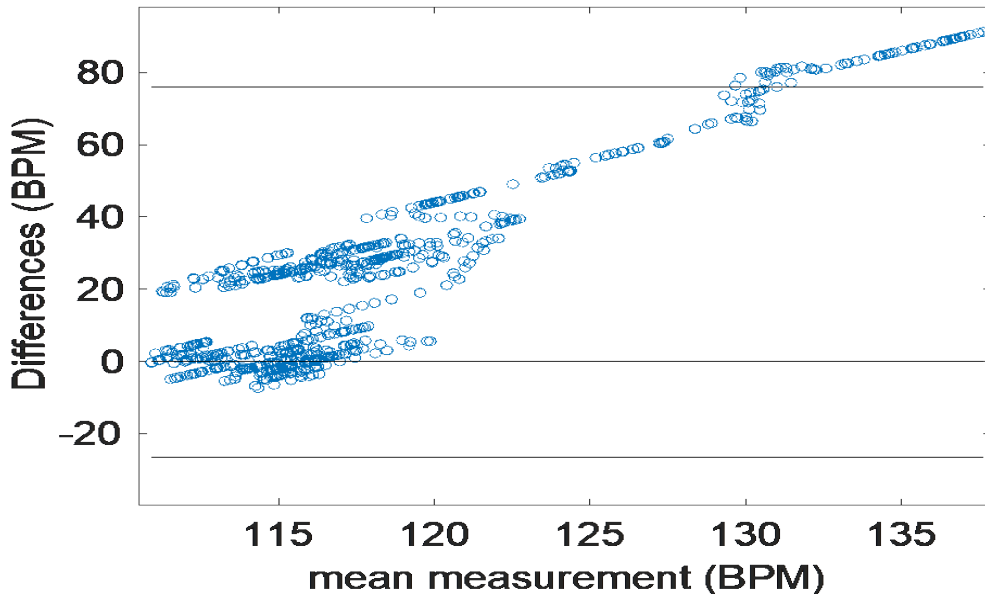


Figure A2.260: Subject No. 2 Polar's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 3 Sitting Polar vs ECG Bland Altman Plot

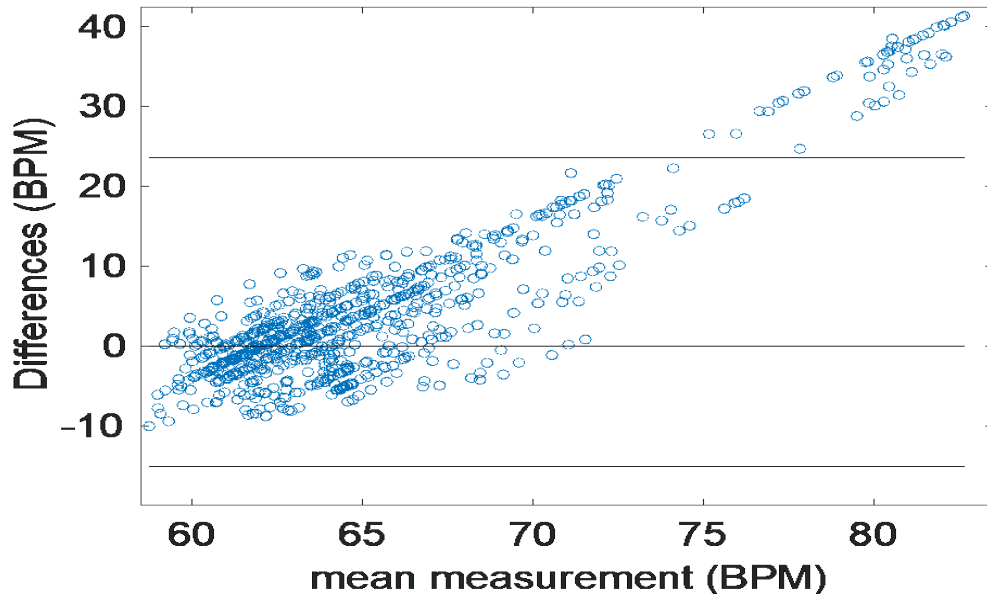


Figure A2.261: Subject No. 3 Polar's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 4 Sitting Polar vs ECG Bland Altman Plot

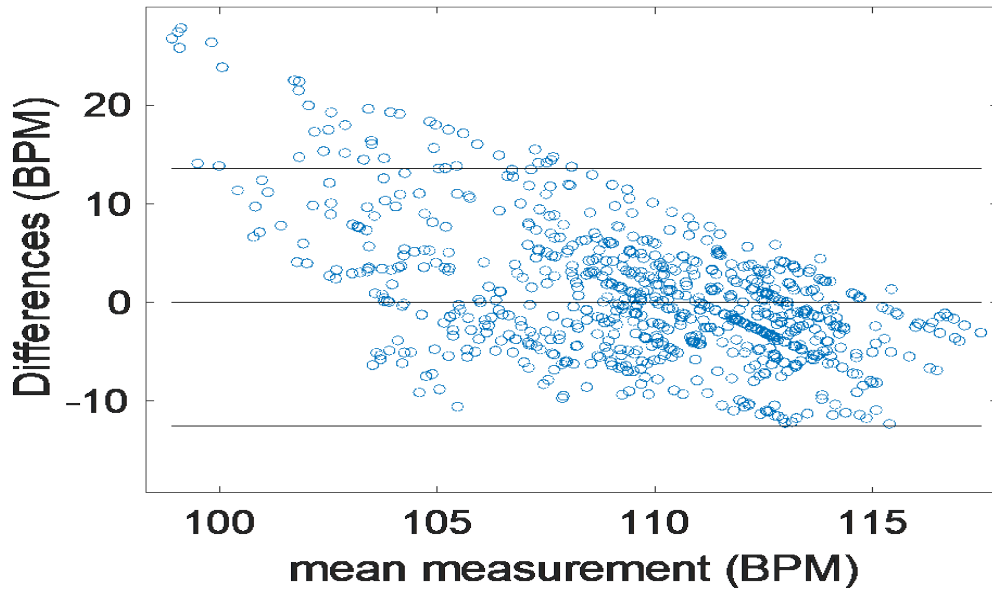


Figure A2.262: Subject No. 4 Polar's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)



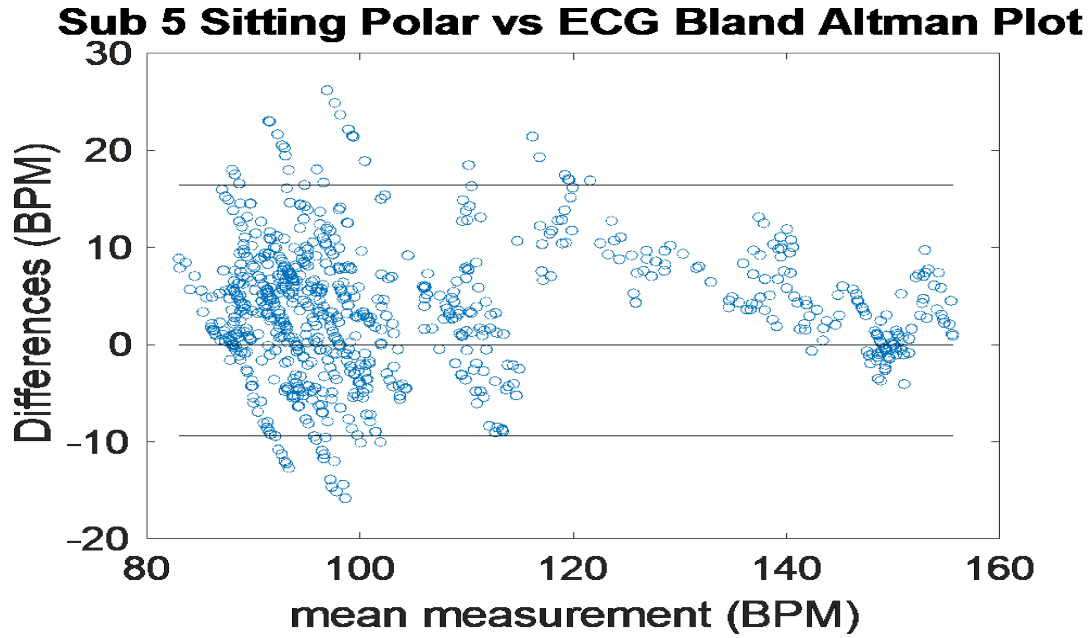


Figure A2.263: Subject No. 5 Polar's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

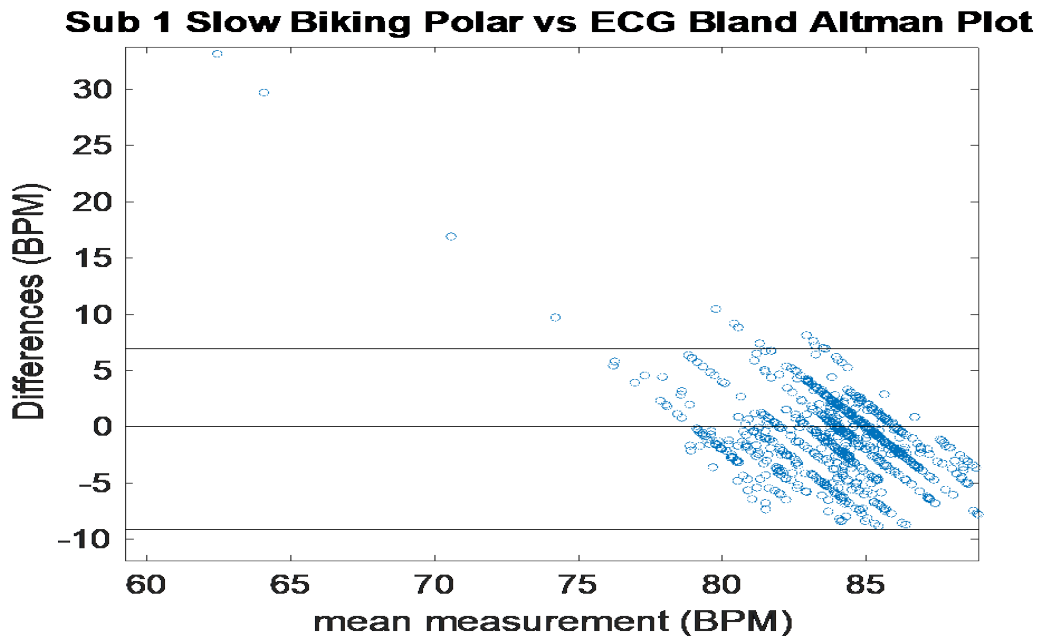


Figure A2.264: Subject No. 1 Polars's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 2 Slow Biking Polar vs ECG Bland Altman Plot

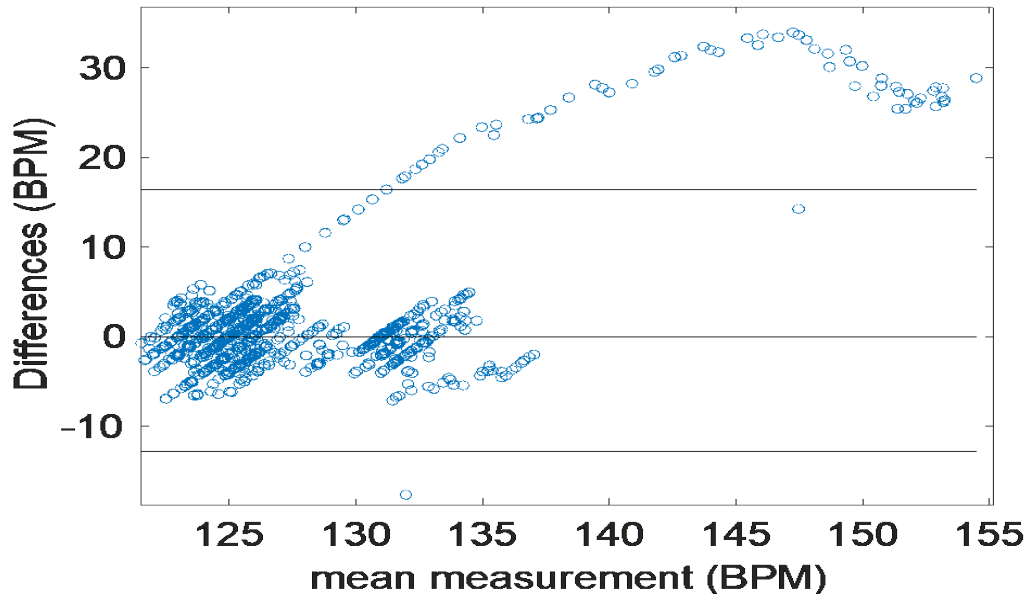


Figure A2.265: Subject No. 2 Polar's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 3 Slow Biking Polar vs ECG Bland Altman Plot

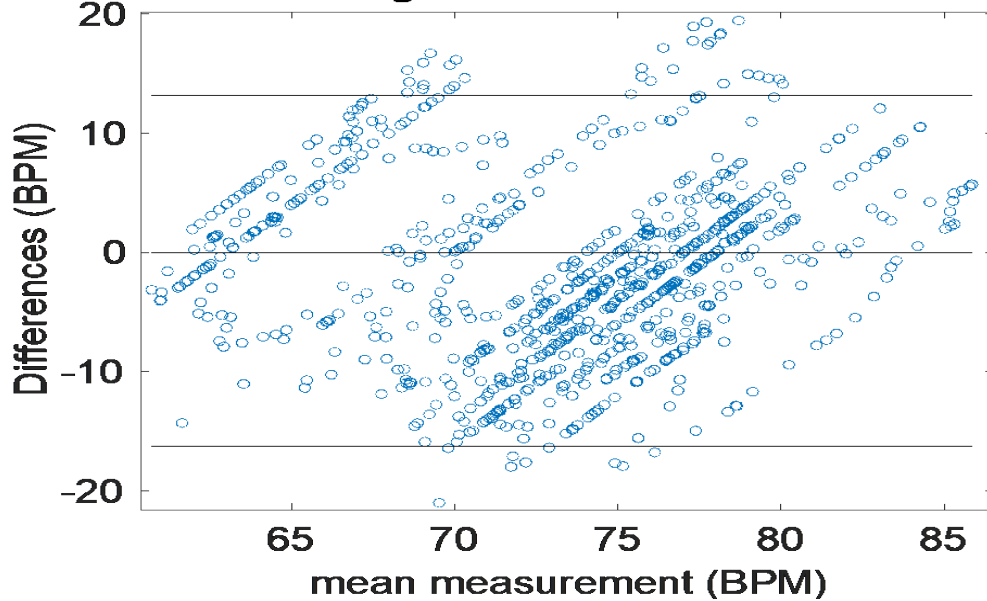


Figure A2.266: Subject No. 3 Polar's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 4 Slow Biking Polar vs ECG Bland Altman Plot

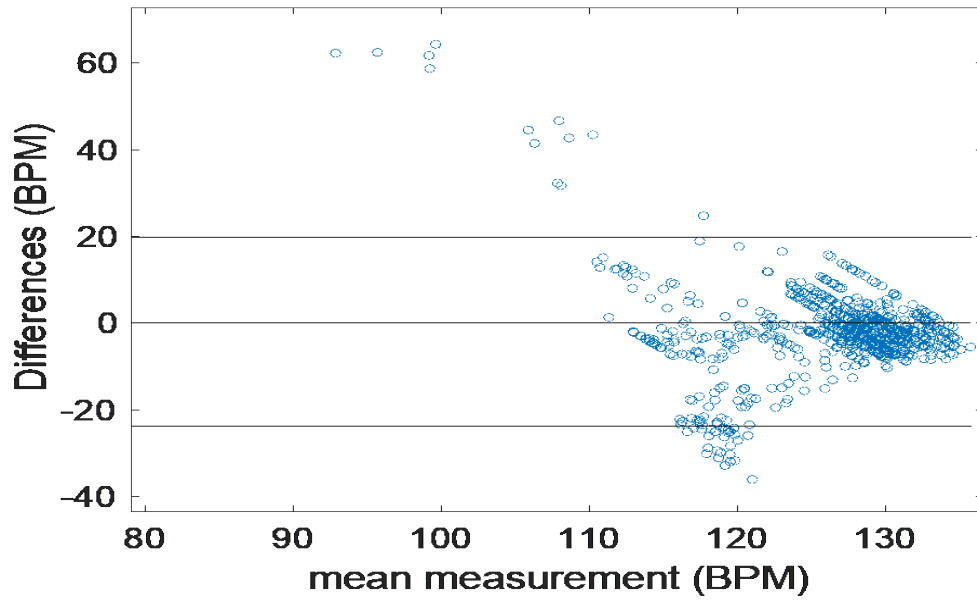


Figure A2.267: Subject No. 4 Polar's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 5 Slow Biking Polar vs ECG Bland Altman Plot

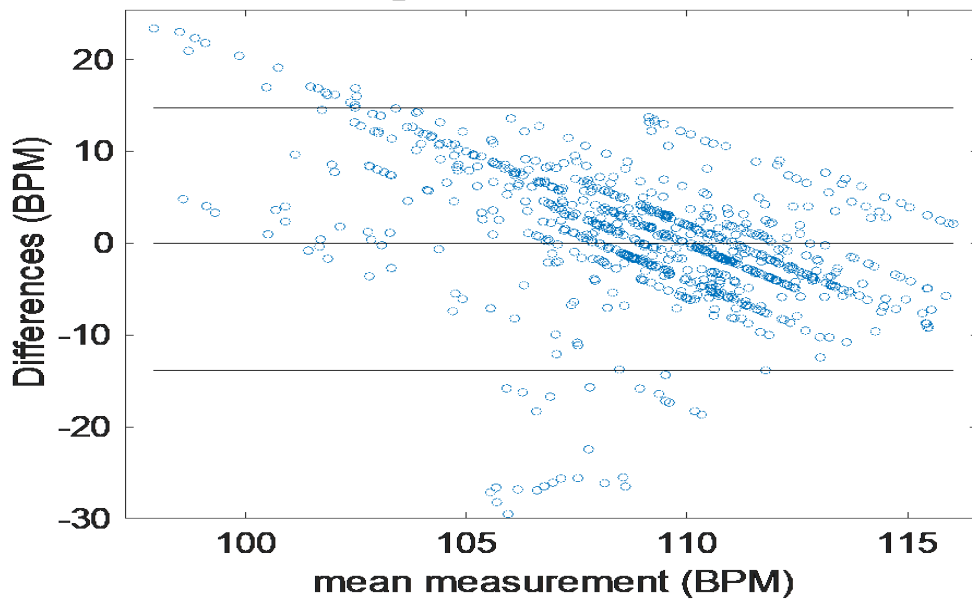


Figure A2.268: Subject No. 5 Polar's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

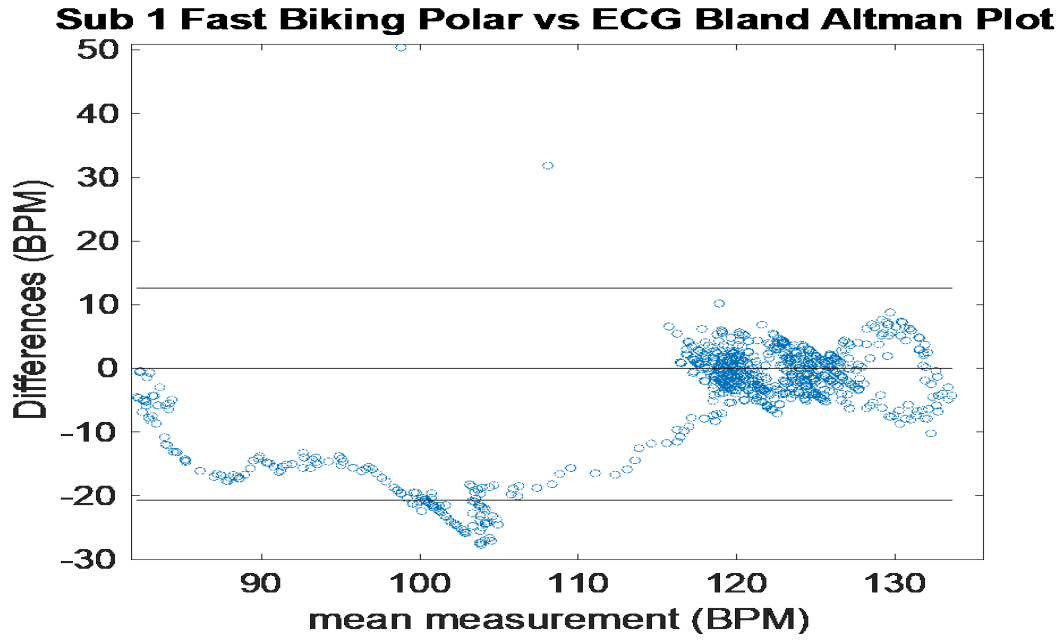


Figure A2.269: Subject No. 1 Polar's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

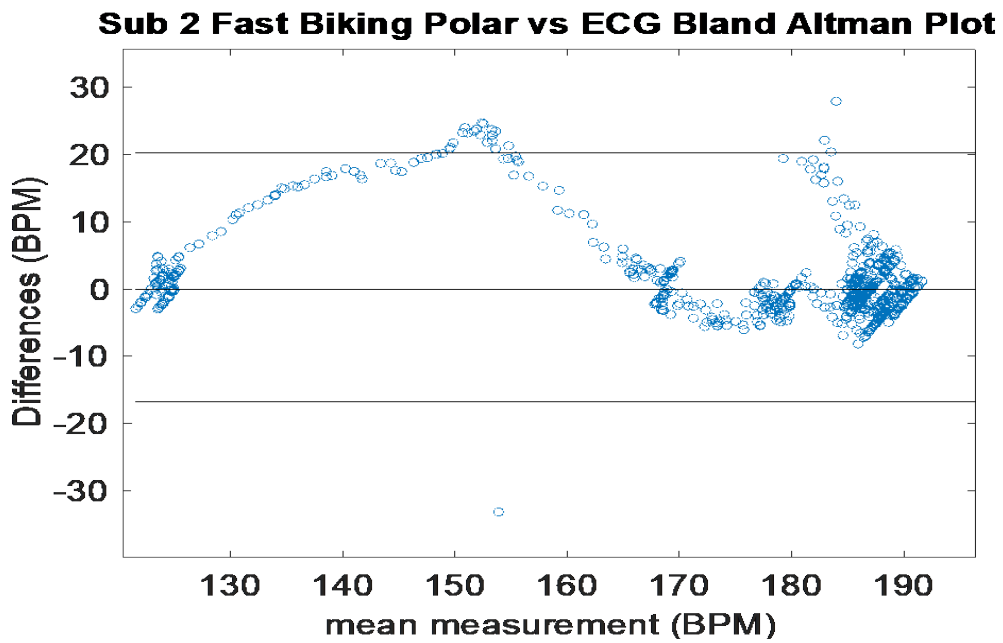


Figure A2.270: Subject No. 2 Polar's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 3 Fast Biking Polar vs ECG Bland Altman Plot

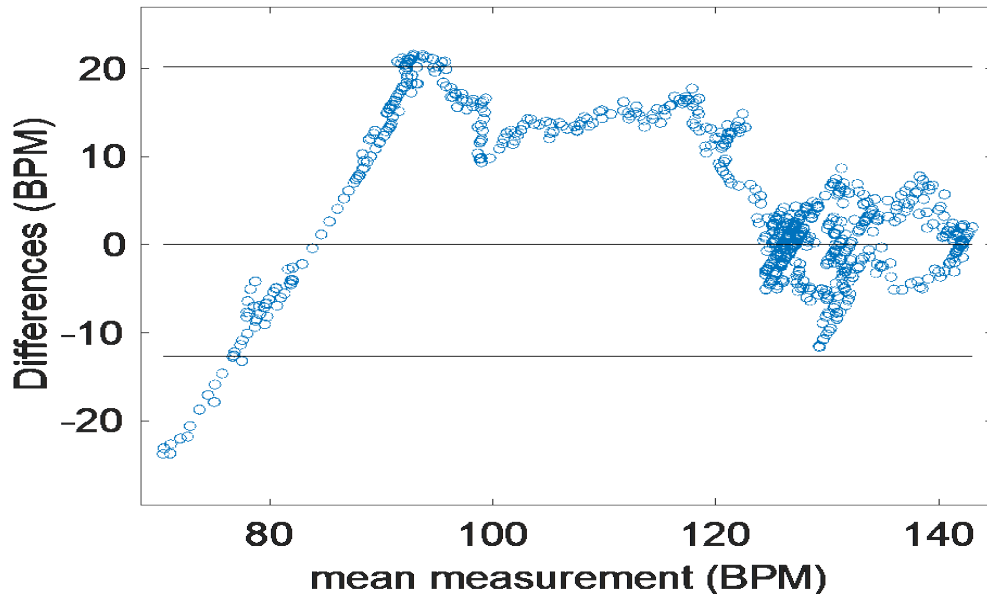


Figure A2.271: Subject No. 3 Polar's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 4 Fast Biking Polar vs ECG Bland Altman Plot

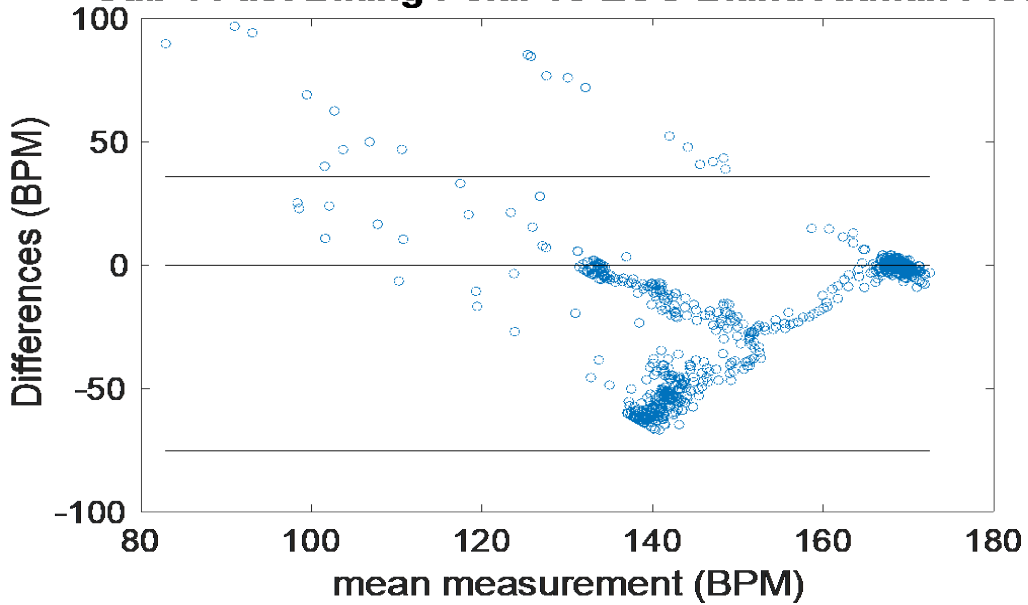


Figure A2.272: Subject No. 4 Polar's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 5 Fast Biking Polar vs ECG Bland Altman Plot

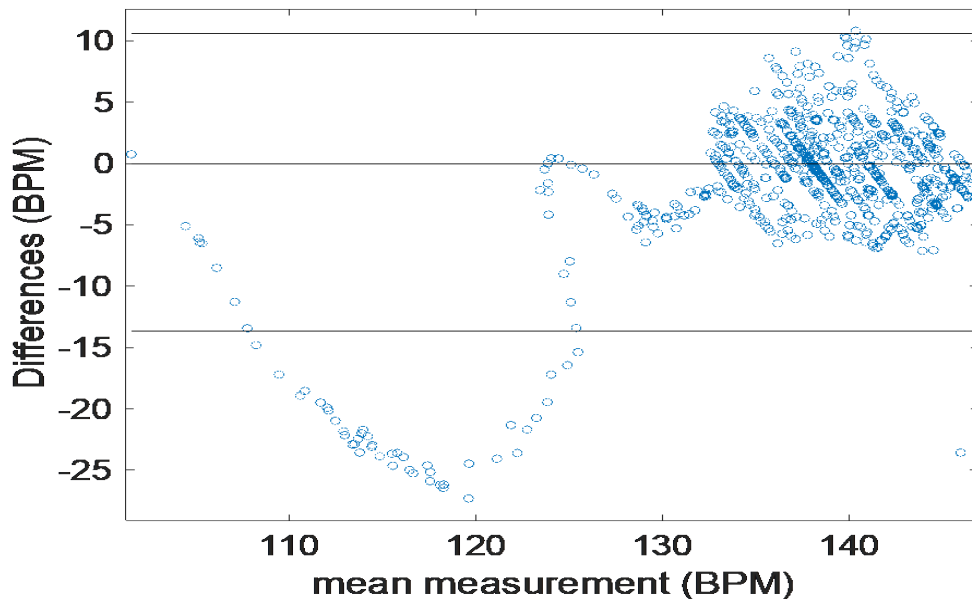


Figure A2.273: Subject No. 5 Polar's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

*Fitbit WFT Bland and Altman Plots*

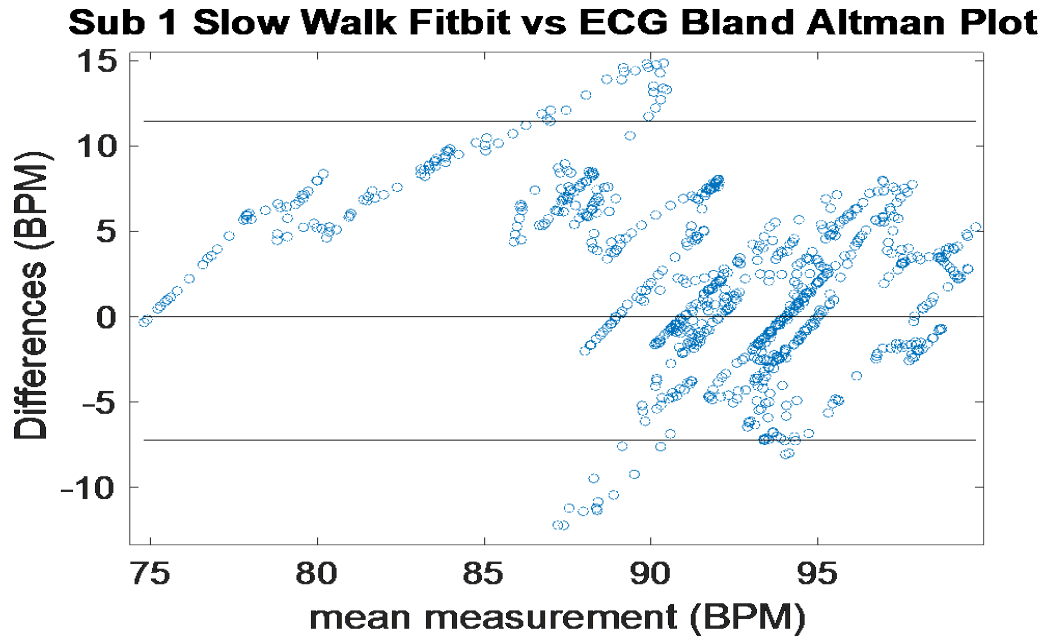


Figure A2.274: Subject No 1 Fitbit's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

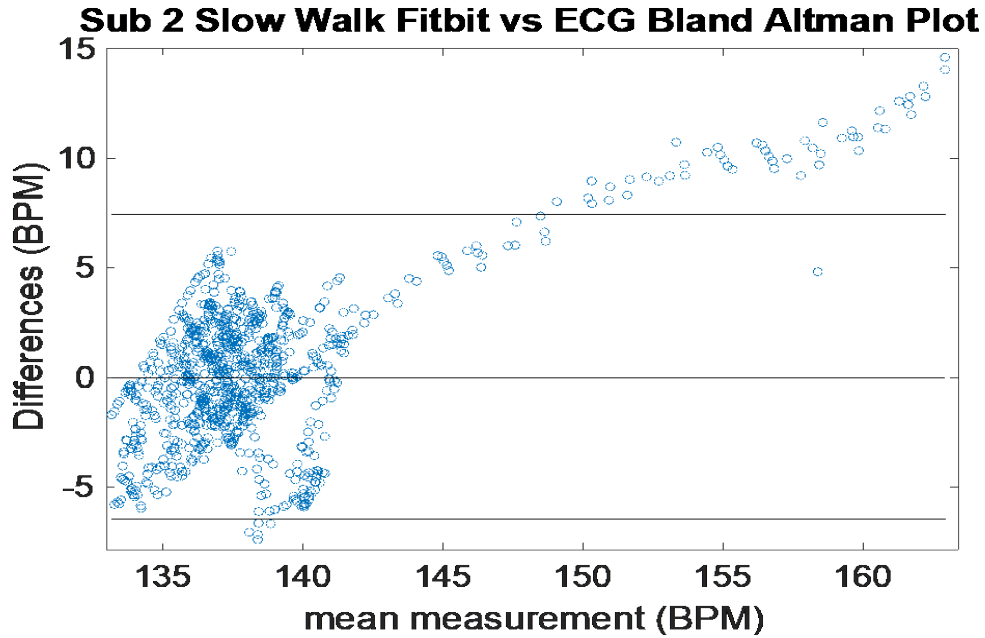


Figure A2.275: Subject No. 2 Fitbit's B&A for slow walking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 3 Slow Walk Fitbit vs ECG Bland Altman Plot

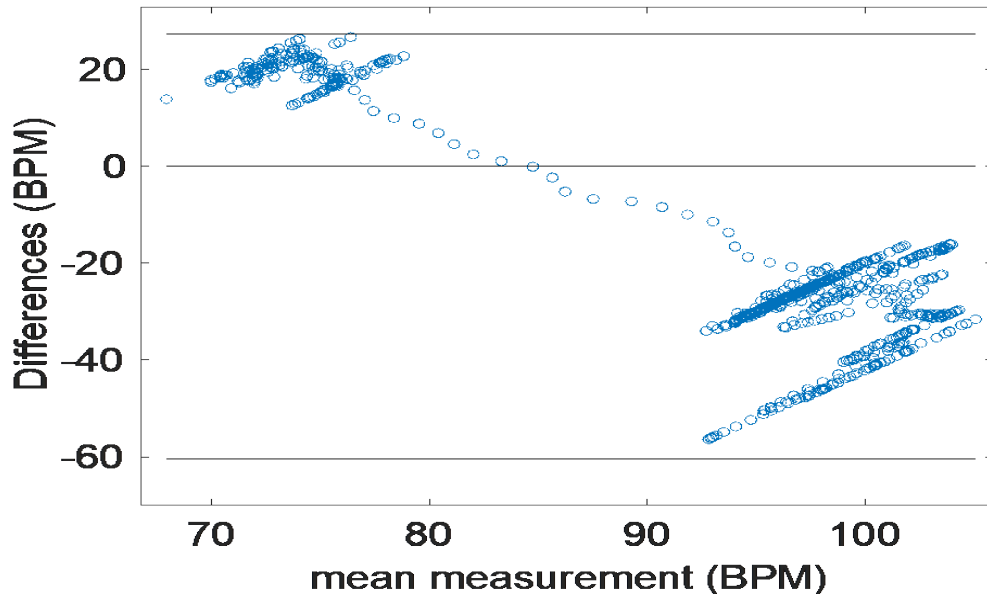


Figure A2.276: Subject No. 3 Fitbit's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 4 Slow Walk Fitbit vs ECG Bland Altman Plot

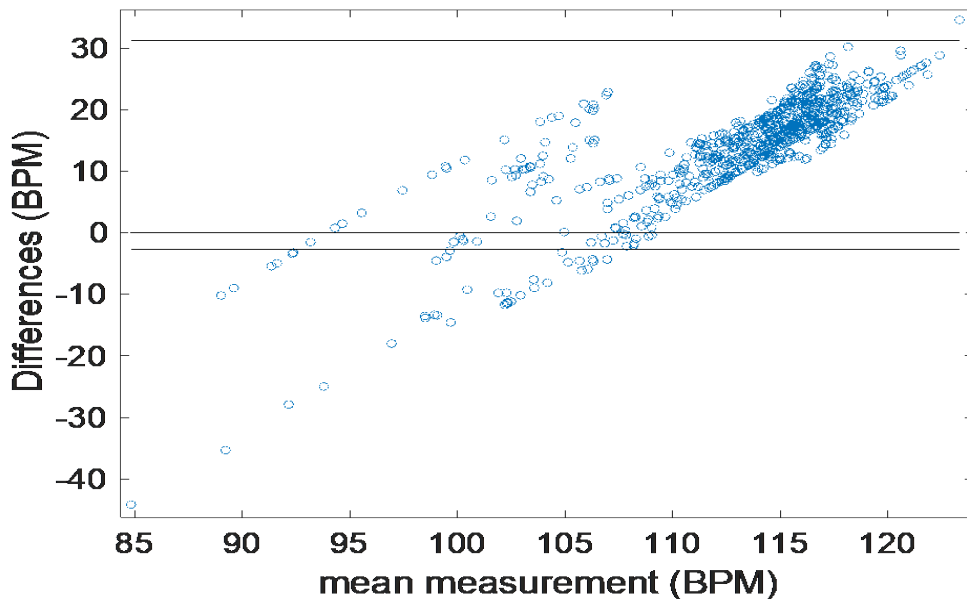


Figure A2.277: Subject No. 4 Fitbit's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)



### Sub 5 Slow Walk Fitbit vs ECG Bland Altman Plot

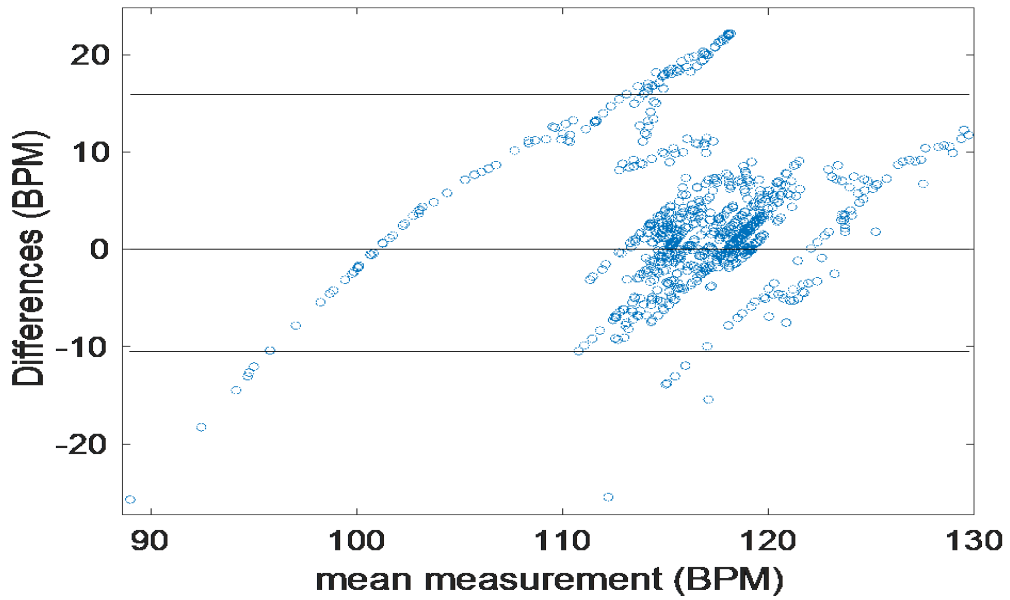


Figure A2.278: Subject No. 5 Fitbit's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 1 Fast Walk Fitbit vs ECG Bland Altman Plot

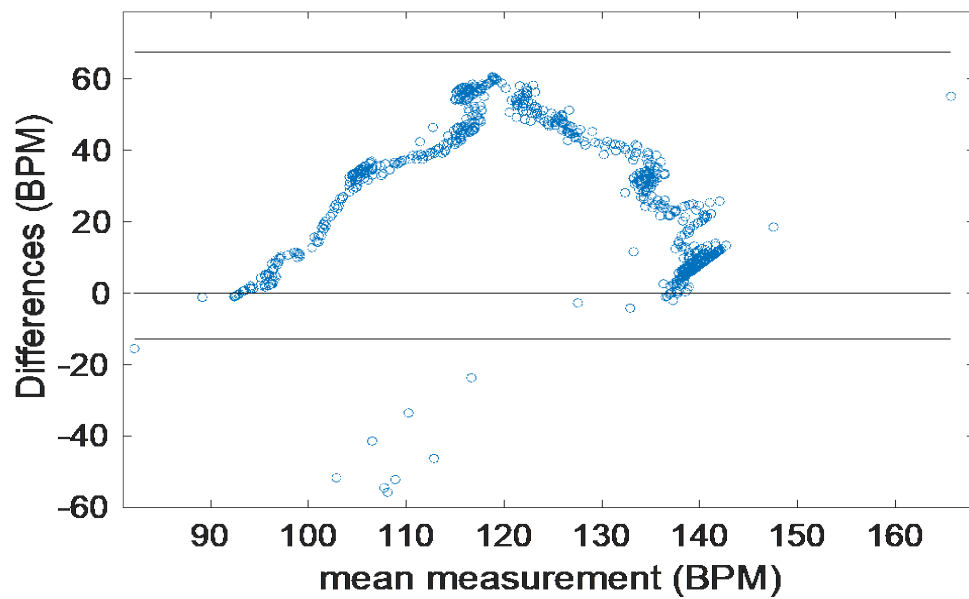


Figure A2.279: Subject No. 1 Samsung's B&A for fast walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

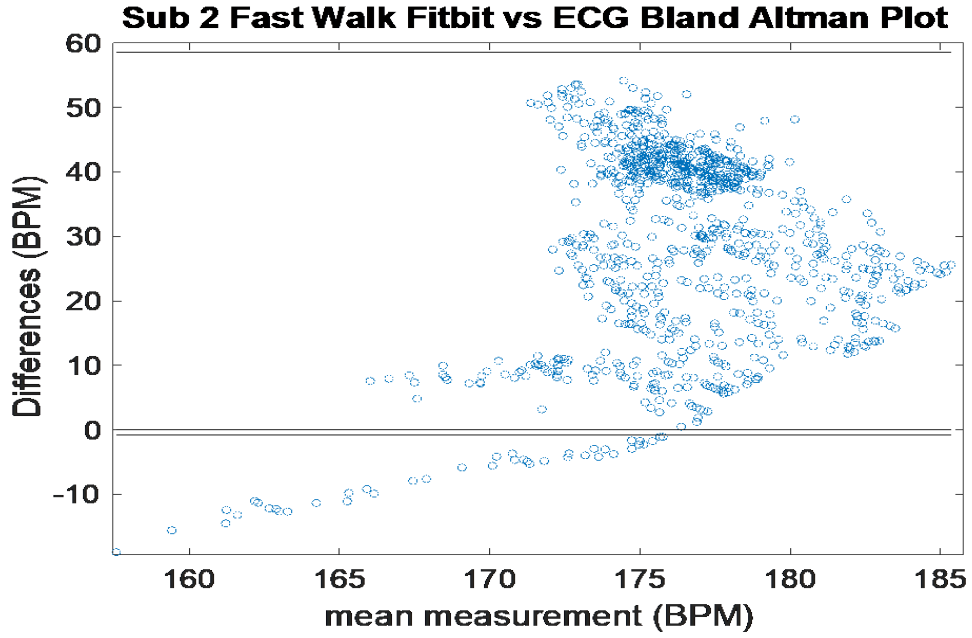


Figure A2.280: Subject No. 2 Fitbit's B&A for fast walking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

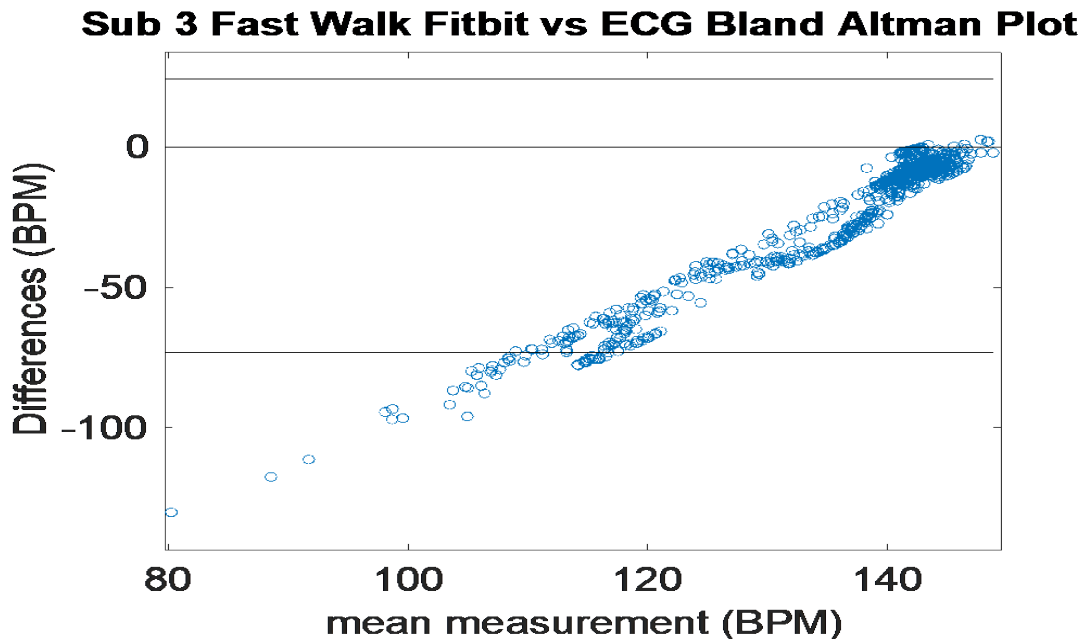


Figure A2.281: Subject No. 3 Fitbit's B&A for fast walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 4 Fast Walk Fitbit vs ECG Bland Altman Plot

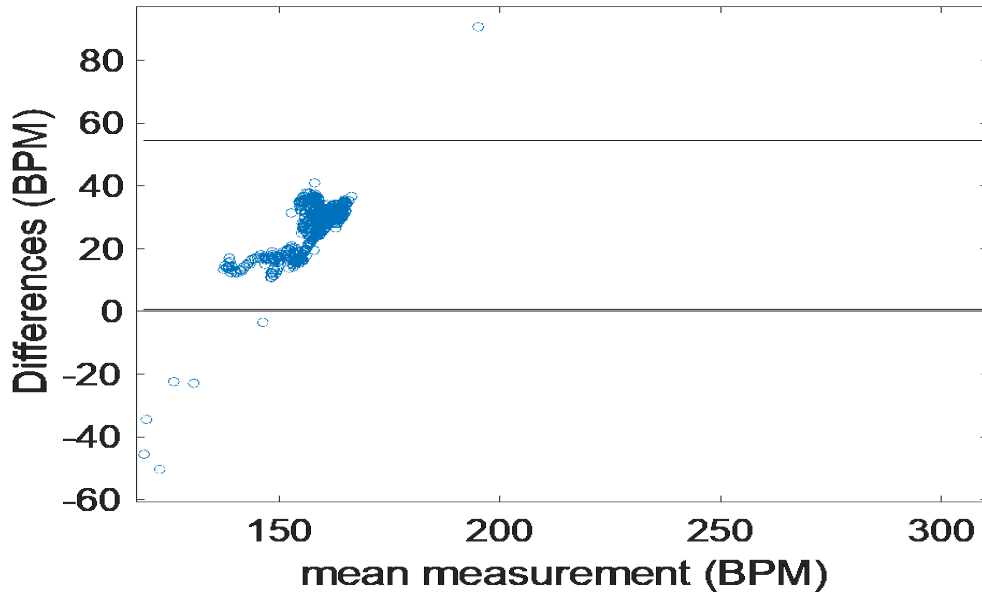


Figure A2.282: Subject No. 4 Fitbit's B&A for fast walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 5 Fast Walk Fitbit vs ECG Bland Altman Plot

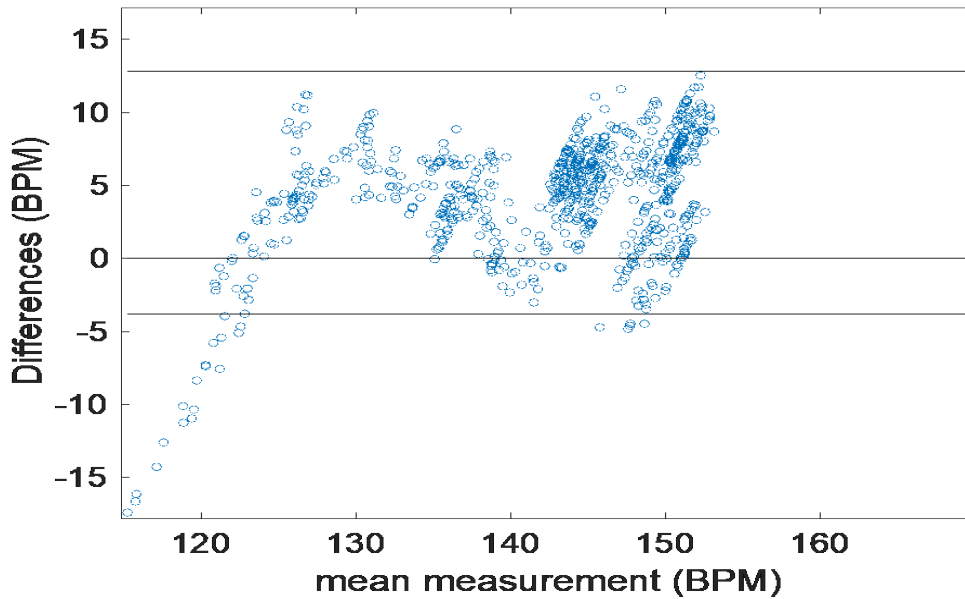


Figure A2.283: Subject No. 5 Fitbit's B&A for fast walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 1 Sitting Fitbit vs ECG Bland Altman Plot

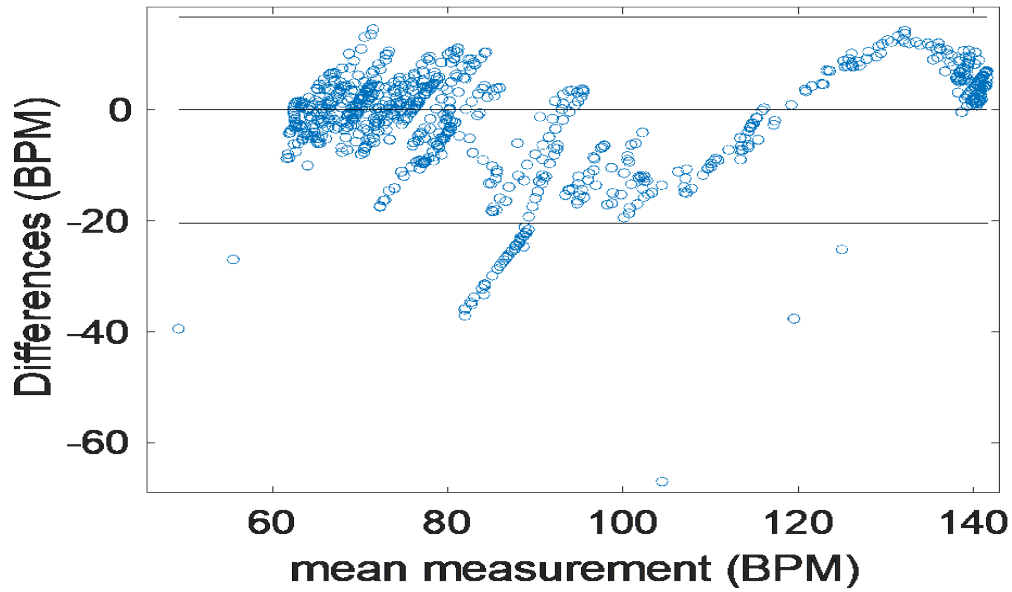


Figure A2.284: Subject No. 1 Fitbit's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 2 Sitting Fitbit vs ECG Bland Altman Plot

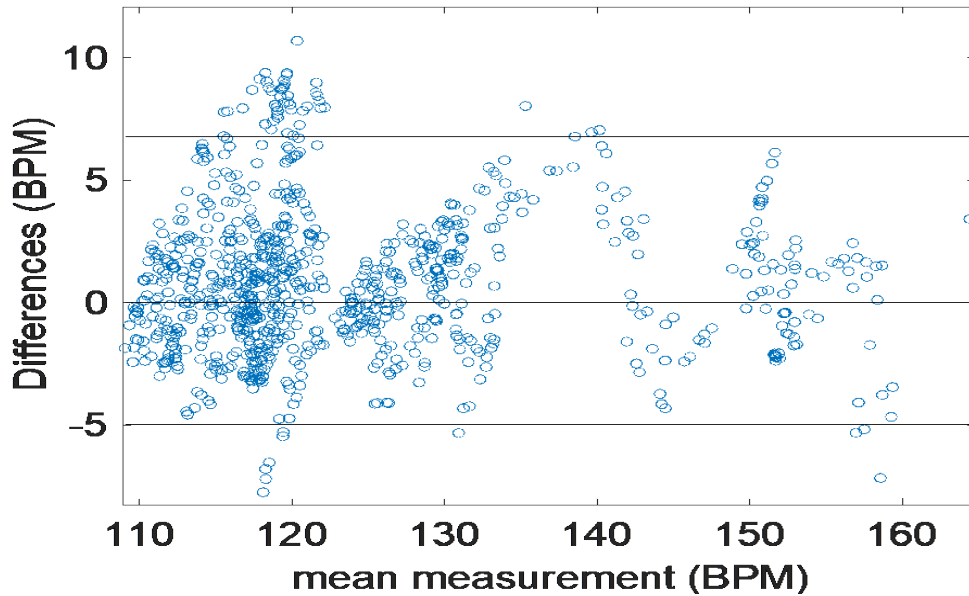


Figure A2.285: Subject No. 2 Fitbit's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 3 Sitting Fitbit vs ECG Bland Altman Plot

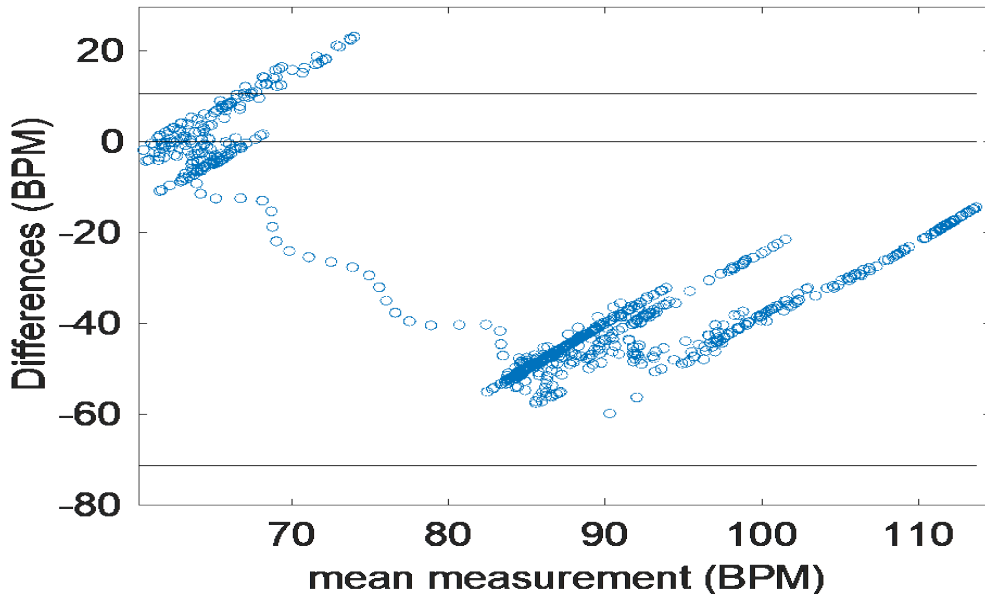


Figure A2.286: Subject No. 3 Fitbit's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 4 Sitting Fitbit vs ECG Bland Altman Plot

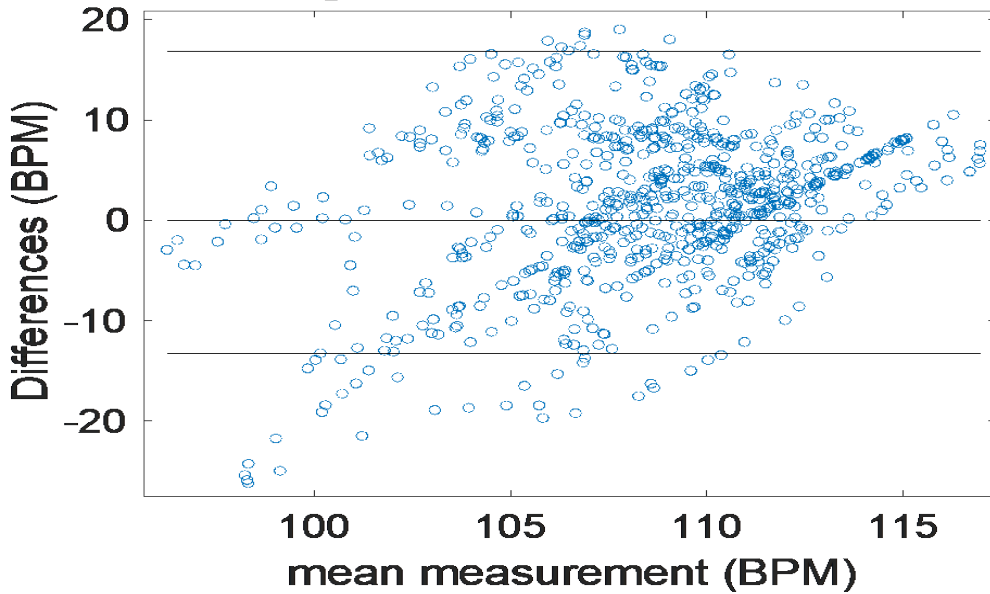


Figure A2.287: Subject No. 4 Fitbit's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

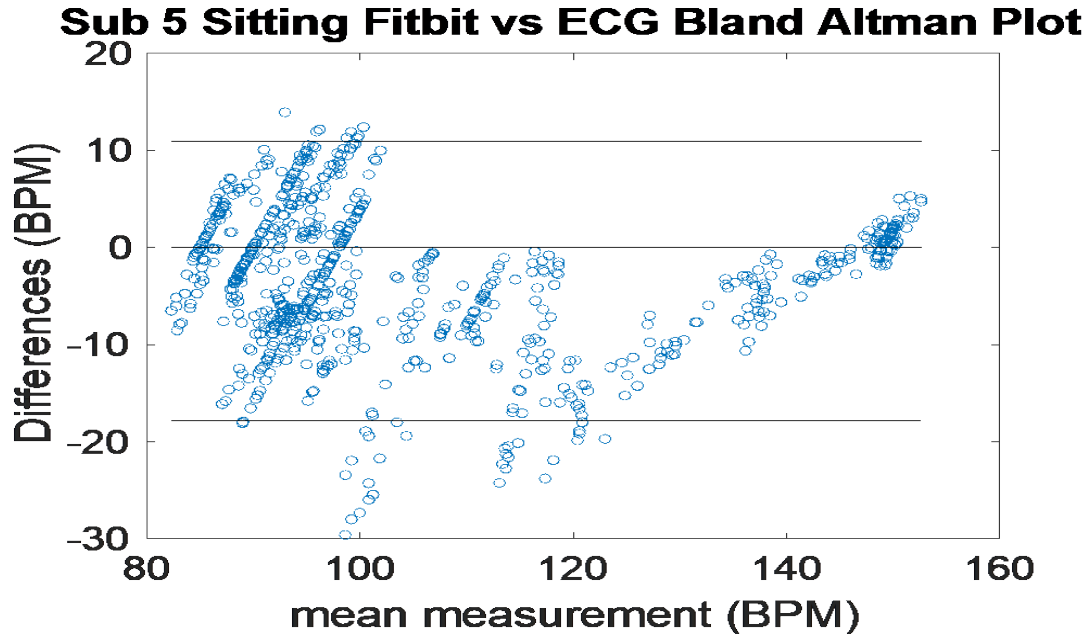


Figure A2.288: Subject No. 5 Fitbit's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

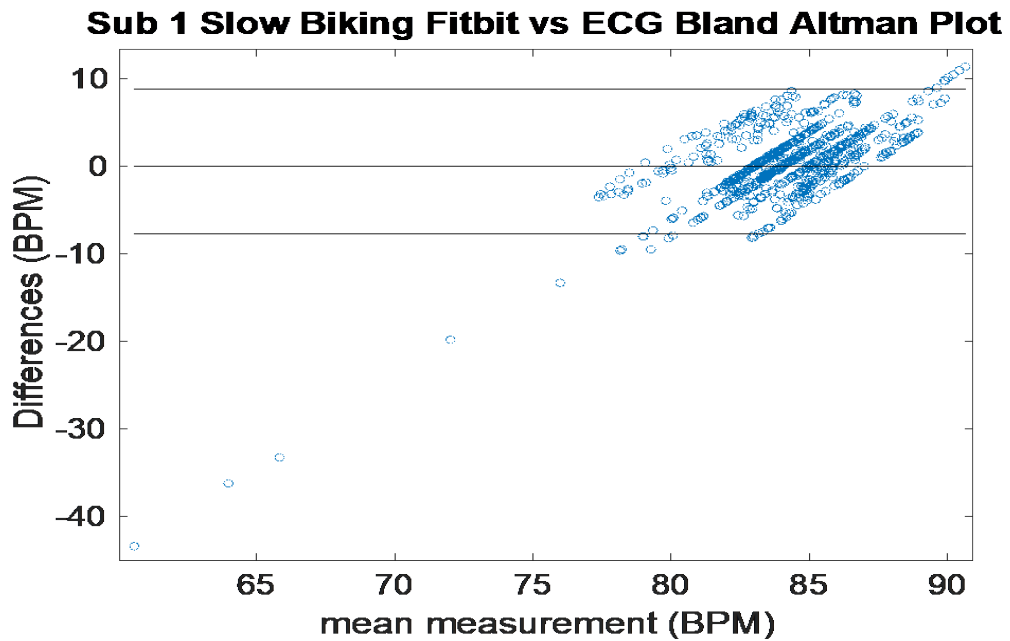


Figure A2.289: Subject No. 1 Fitbit's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

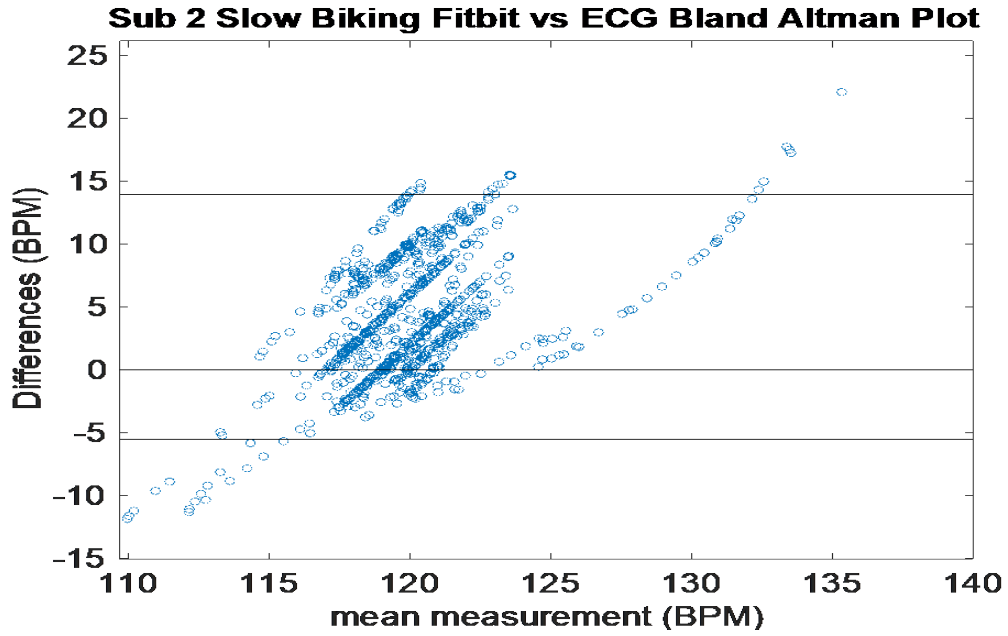


Figure A2.290: Subject No. 2 Fitbit's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

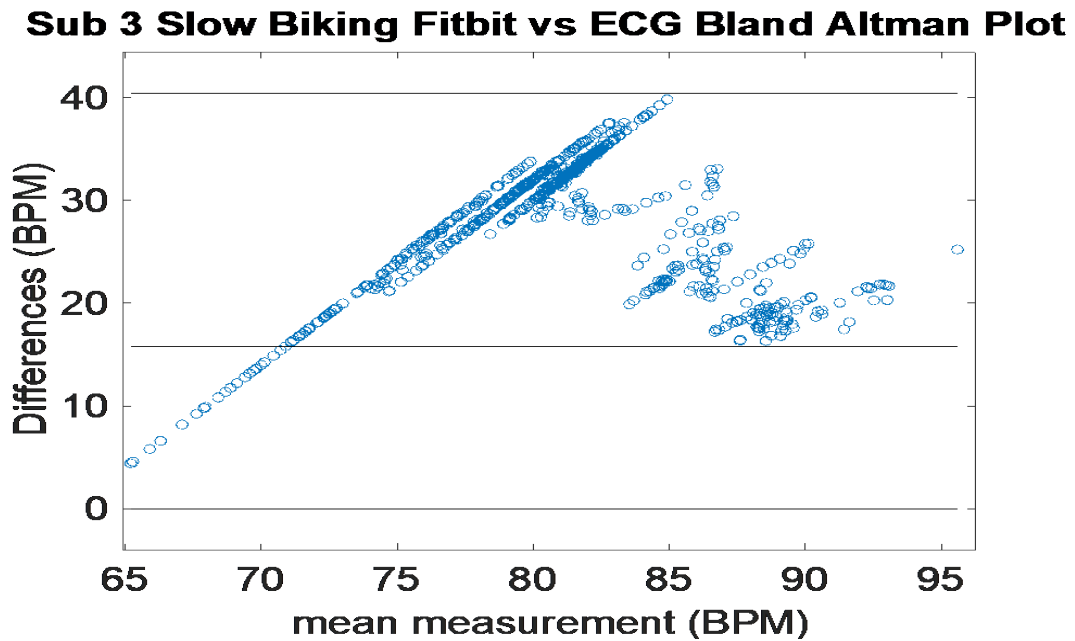


Figure A2.291: Subject No. 3 Fitbit's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 4 Slow Biking Fitbit vs ECG Bland Altman Plot

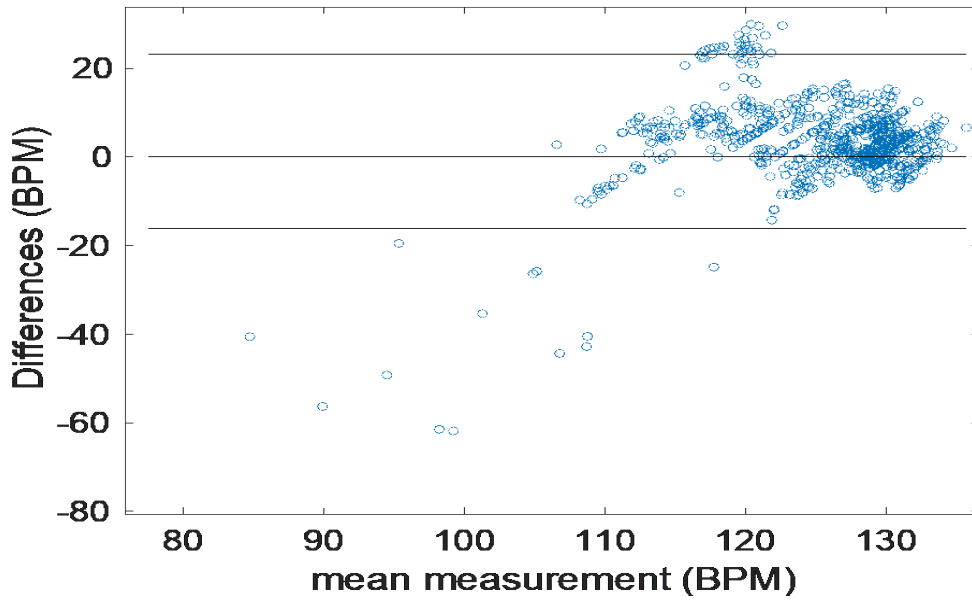


Figure A2.292: Subject No. 4 Fitbit's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 5 Slow Biking Fitbit vs ECG Bland Altman Plot

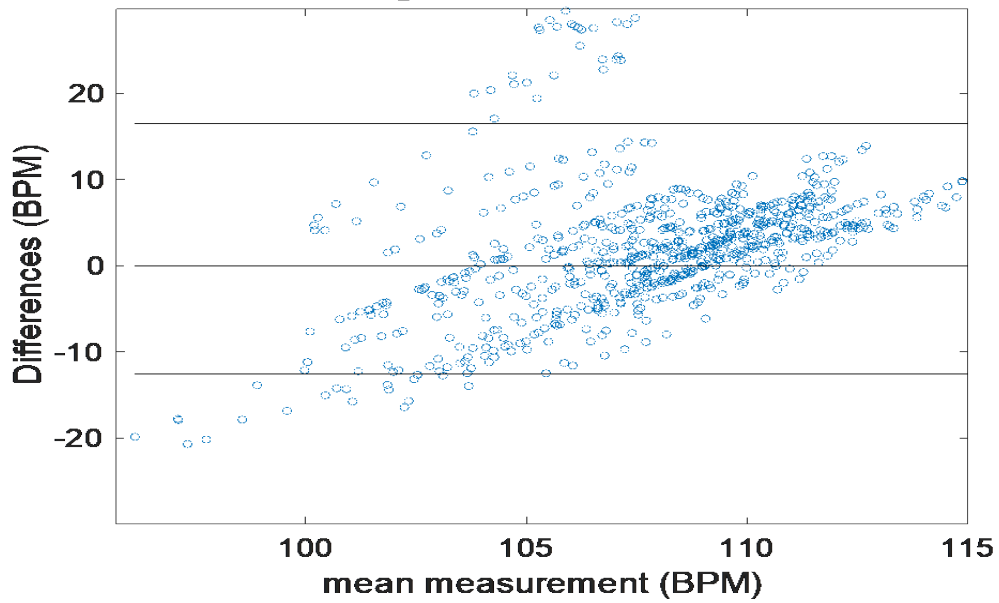


Figure A2.293: Subject No. 5 Fitbit B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)



### Sub 1 Fast Biking Fitbit vs ECG Bland Altman Plot

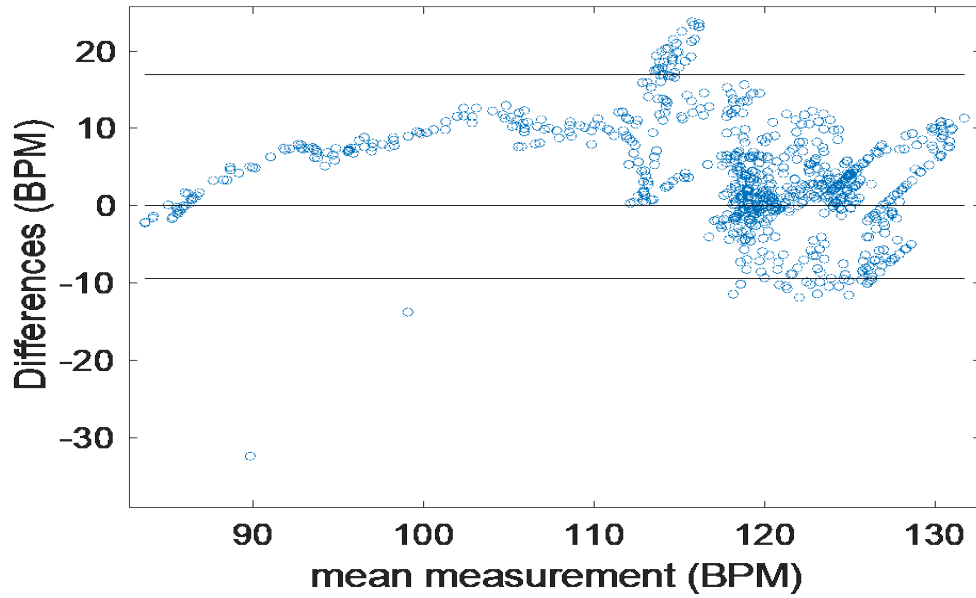


Figure A2.294: Subject No. 1 Fitbit's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 2 Fast Biking Fitbit vs ECG Bland Altman Plot

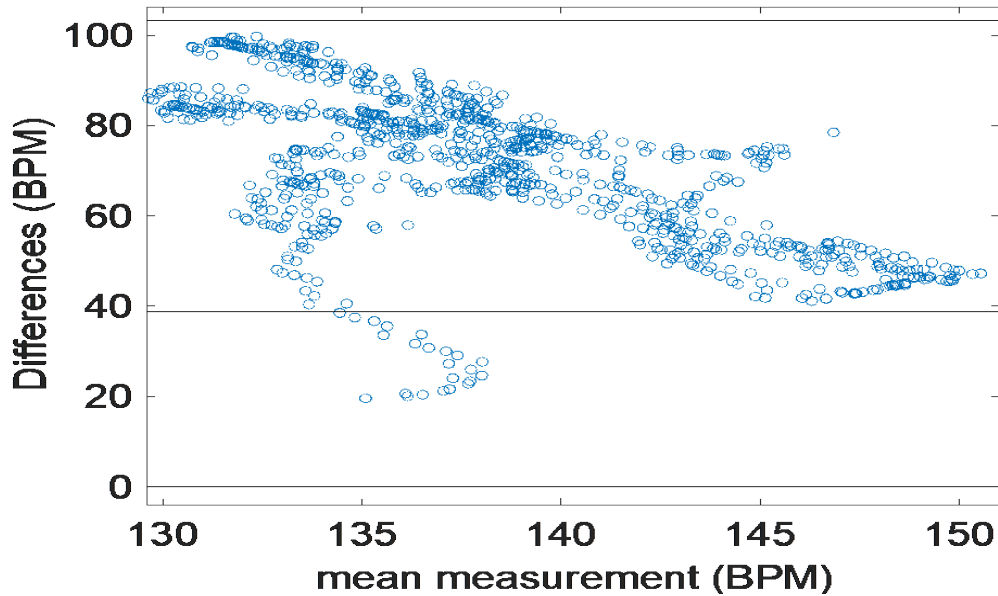


Figure A2.295: Subject No. 2 Fitbit's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

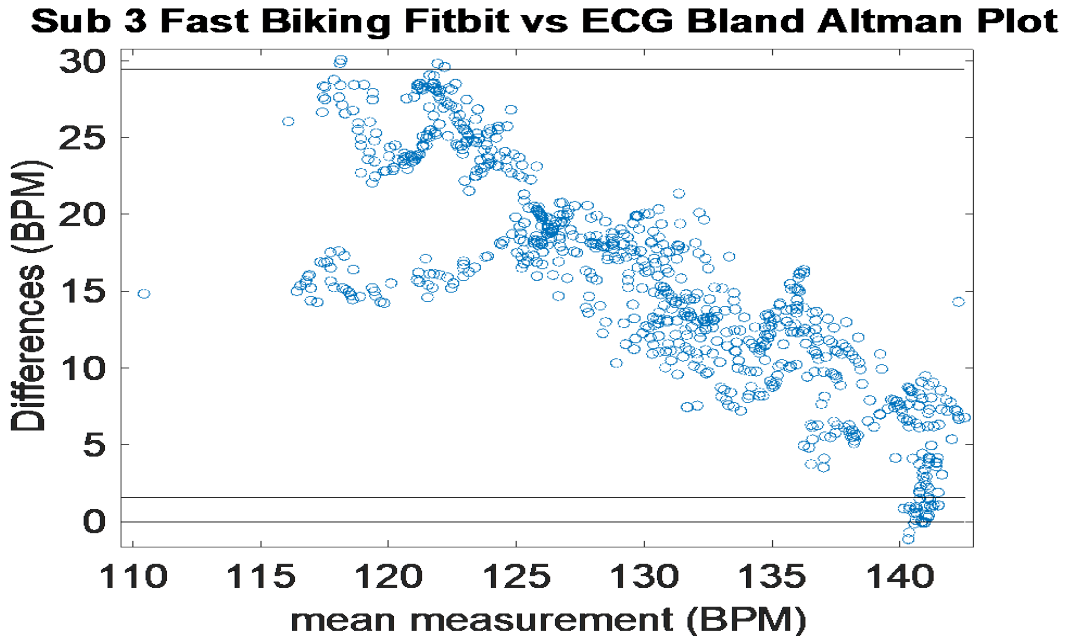


Figure A2.296: Subject No. 3 Fitbit's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

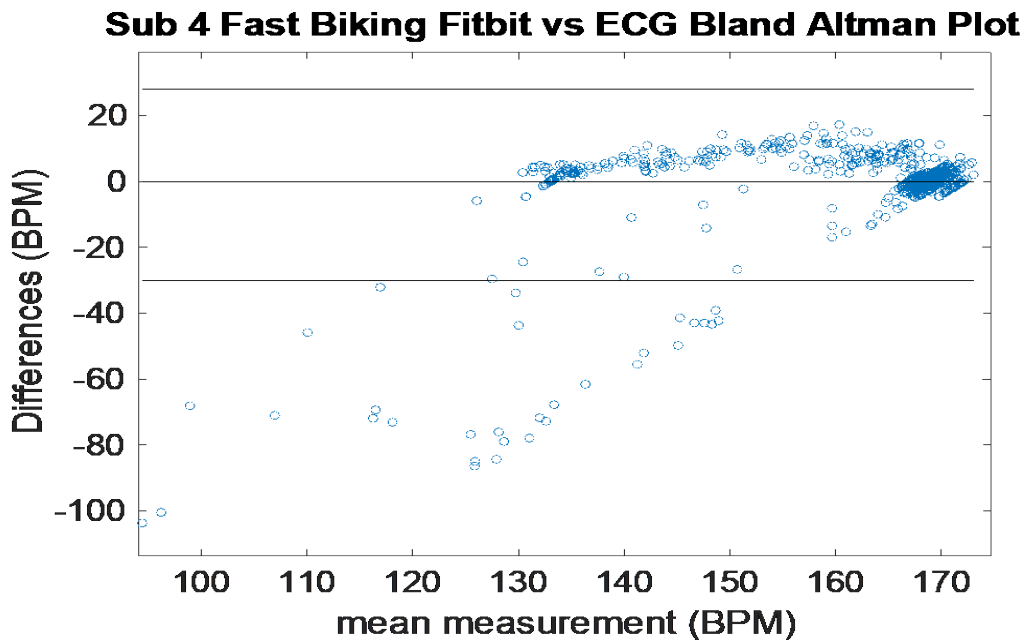


Figure A2.297: Subject No. 4 Fitbit's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 5 Fast Biking Fitbit vs ECG Bland Altman Plot

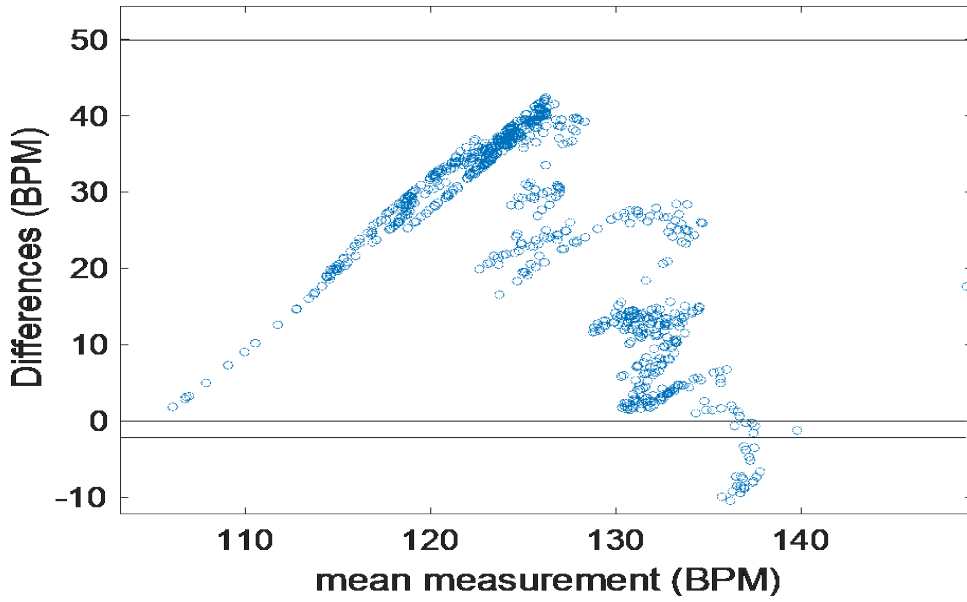


Figure A2.298: Subject No. 5 Fitbit's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Samsung WFT Bland and Altman Plots

#### Sub 1 Slow Walk Samsung vs ECG Bland Altman Plot

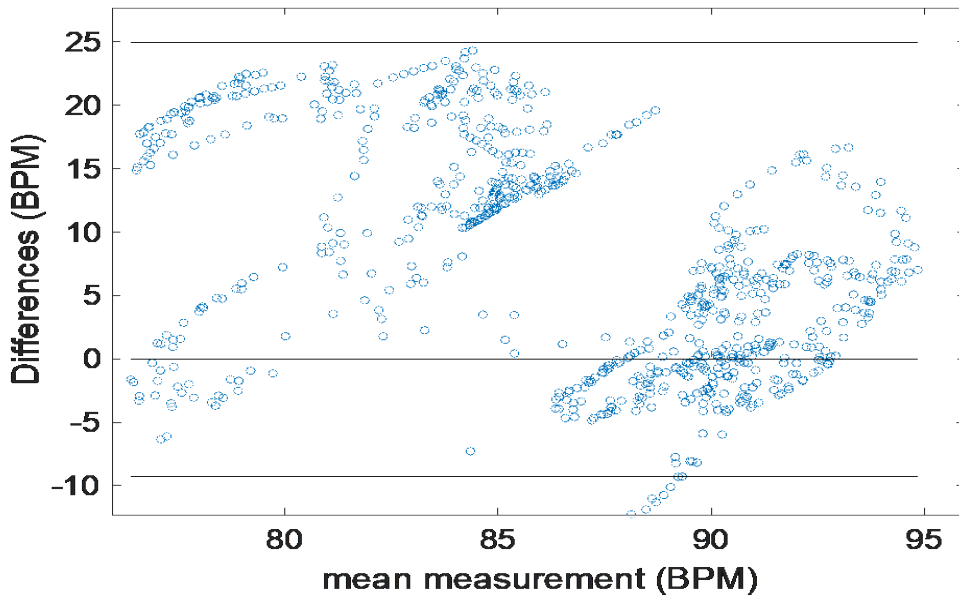


Figure A2.299: Subject No 1 Samsung's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

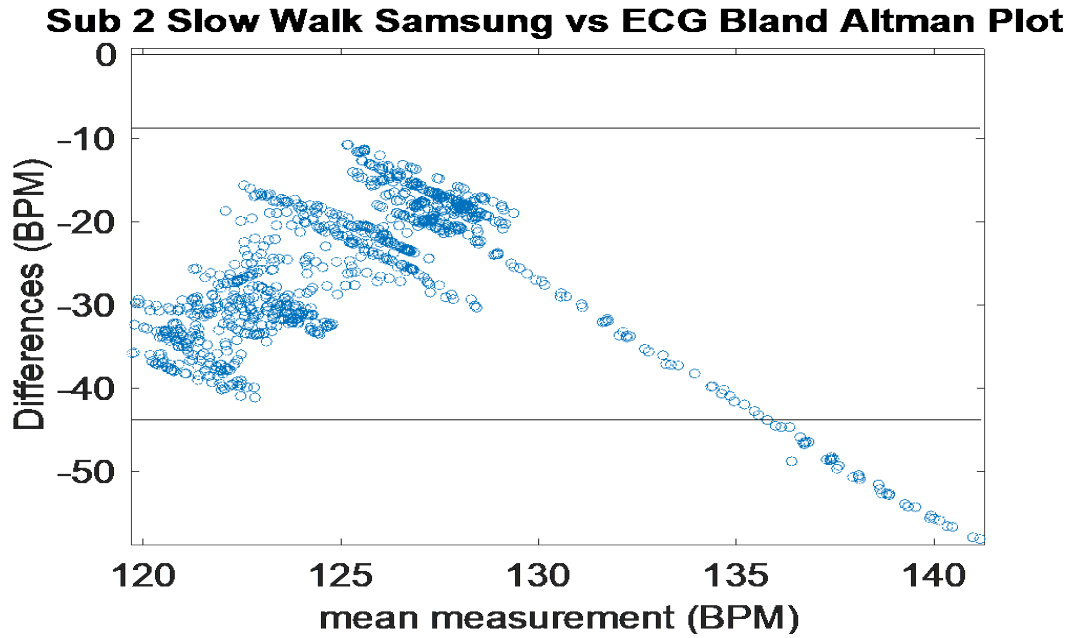


Figure A2.300: Subject No. 2 Samsung's B&A for slow walking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

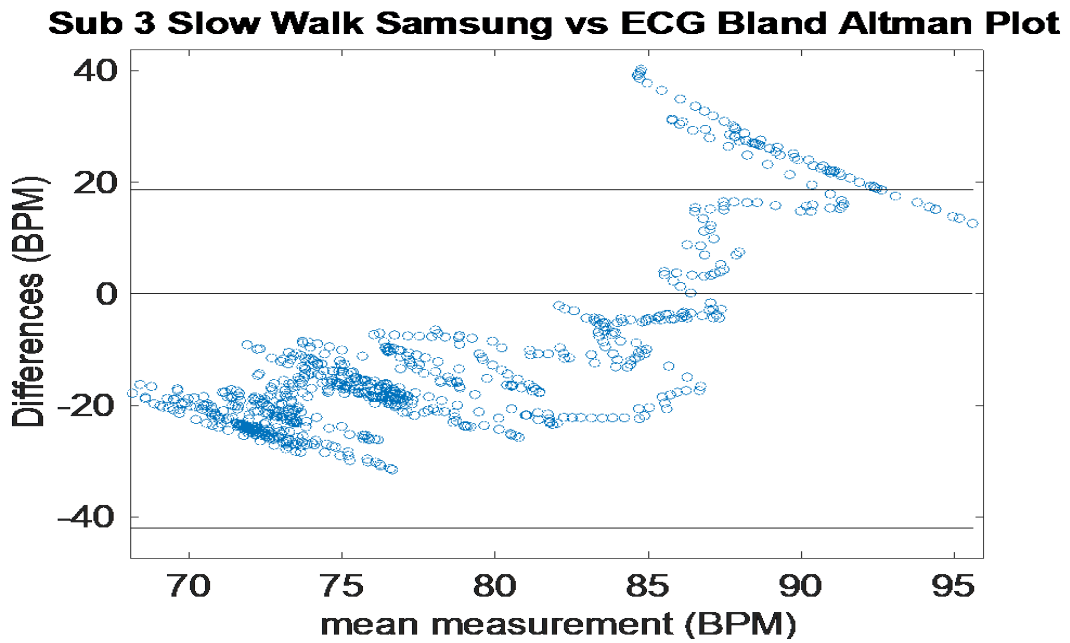


Figure A2.301: Subject No. 3 Samsung's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

**Sub 4 Slow Walk Samsung vs ECG Bland Altman Plot**

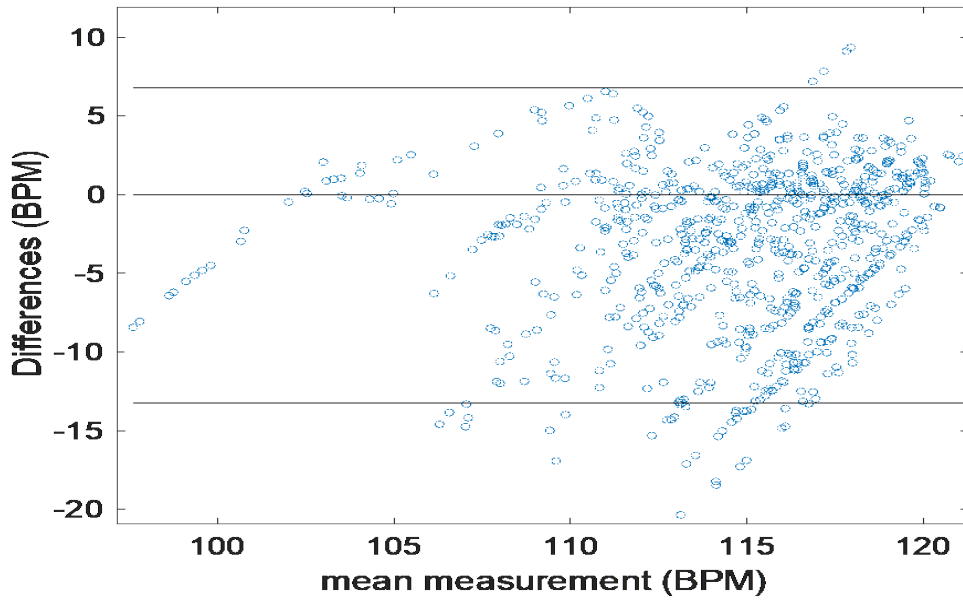


Figure A2.302: Subject No. 4 Samsung's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

**Sub 5 Slow Walk Samsung vs ECG Bland Altman Plot**

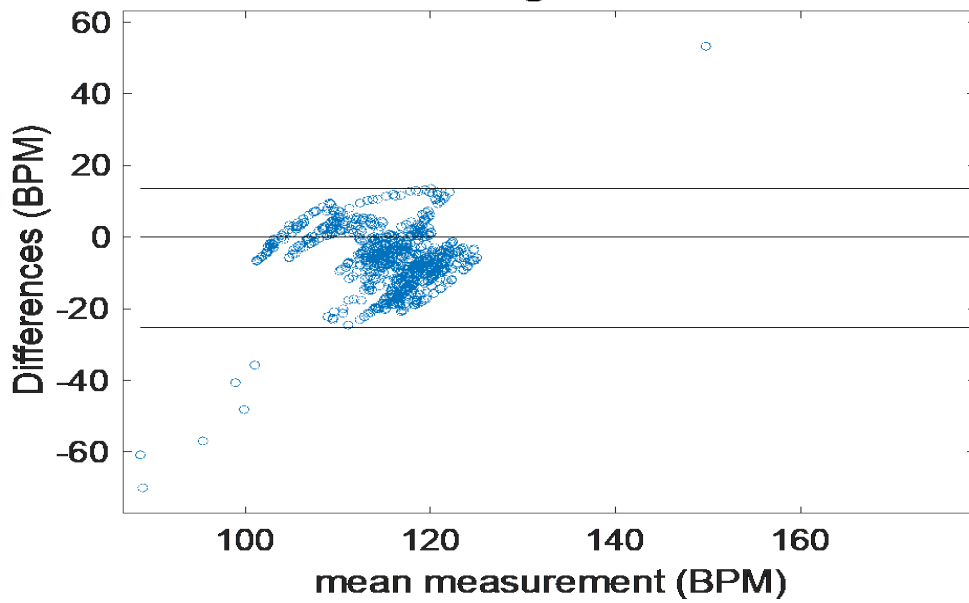


Figure A2.303: Subject No. 5 Samsung's B&A for slow walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

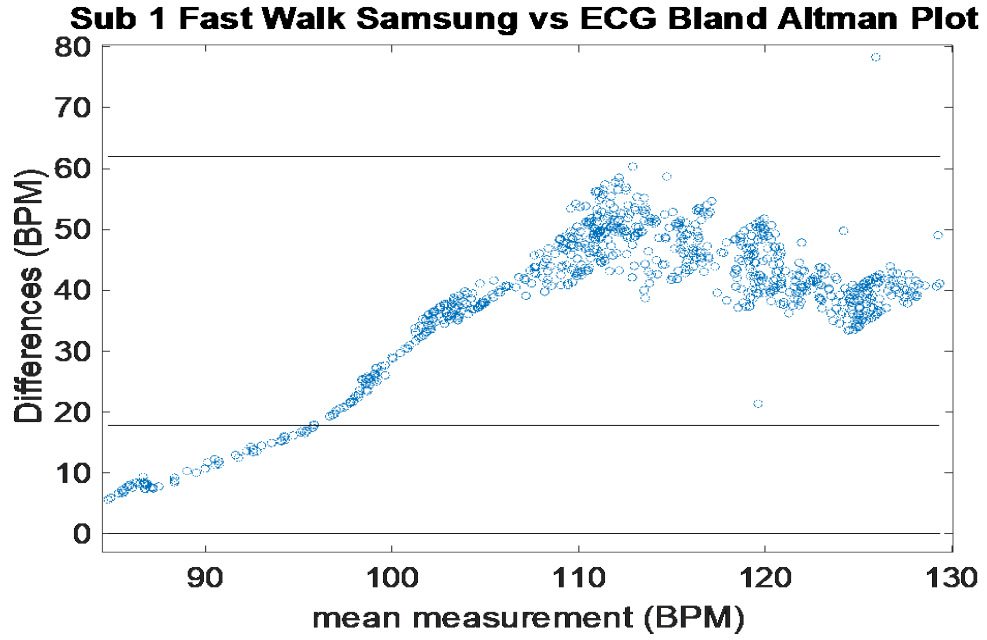


Figure A2.0304: Subject No.1 Fast Walk Samsung's B&A, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

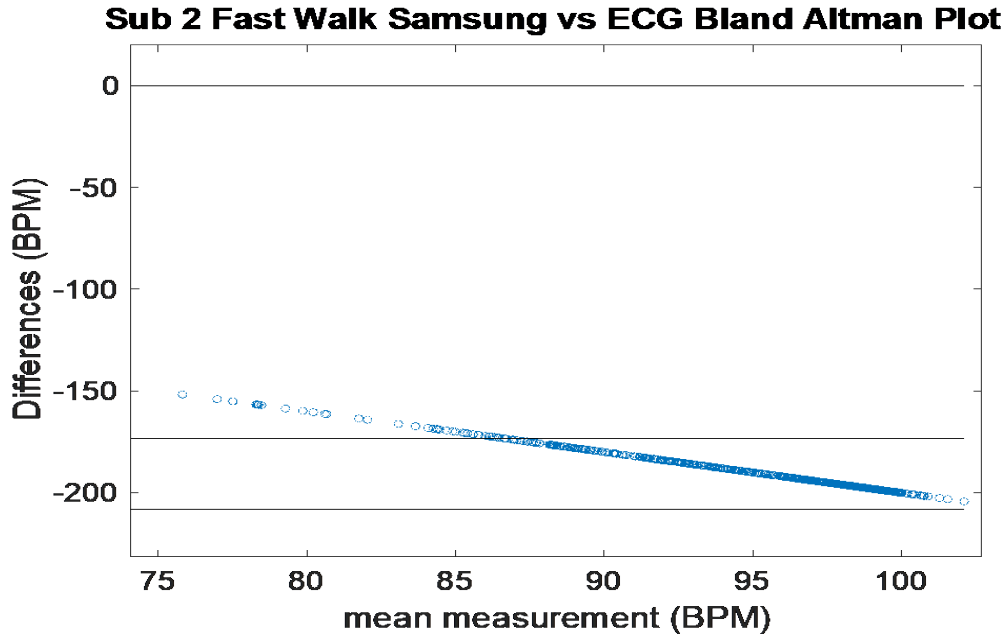


Figure A2.305: Subject No. 2 Samsung's B&A for fast walking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 3 Fast Walk Samsung vs ECG Bland Altman Plot

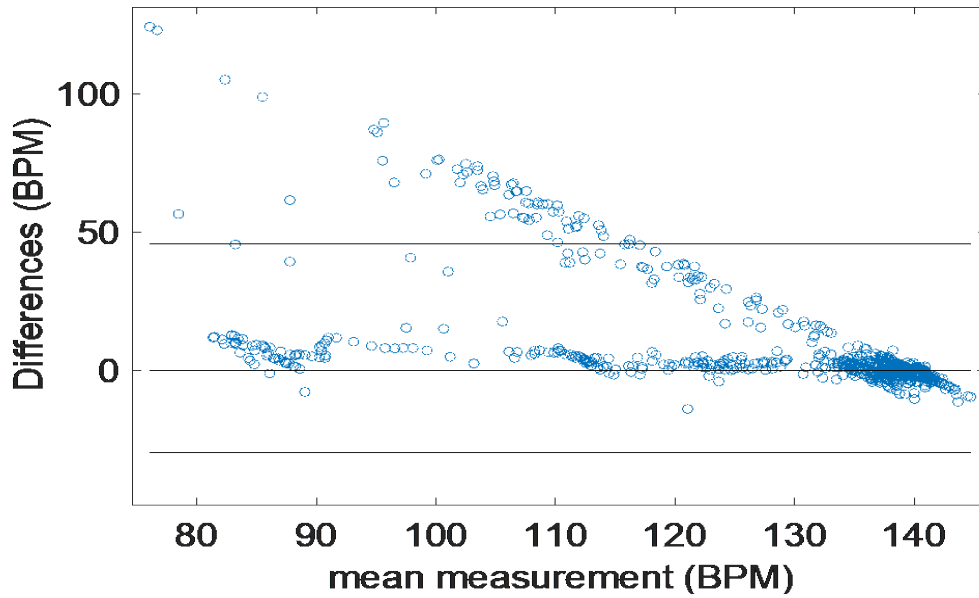


Figure A2.306: Subject No. 3 Samsung's B&A for fast walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 4 Fast Walk Samsung vs ECG Bland Altman Plot

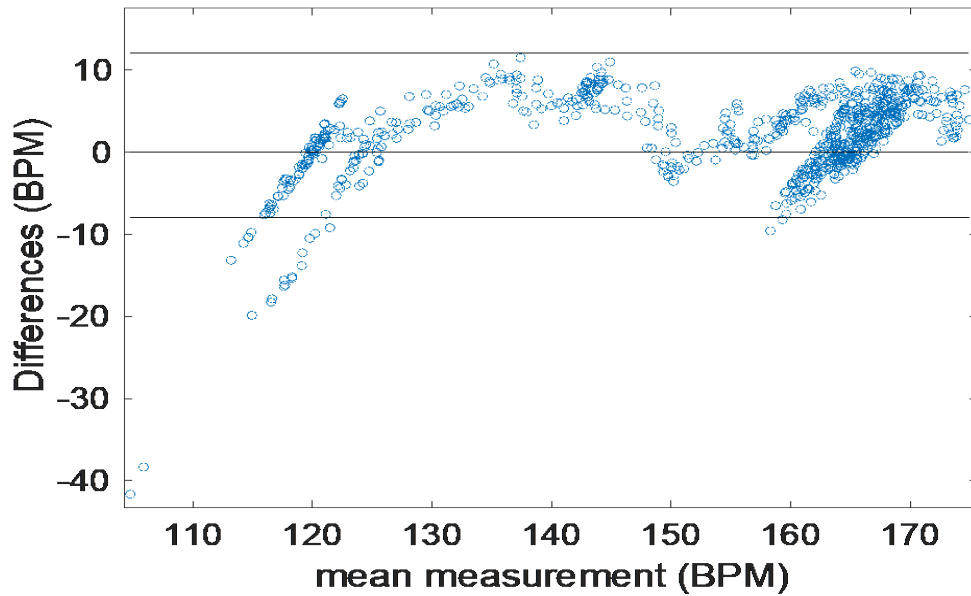


Figure A2.307: Subject No. 4 Samsung's B&A for fast walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 5 Fast Walk Samsung vs ECG Bland Altman Plot

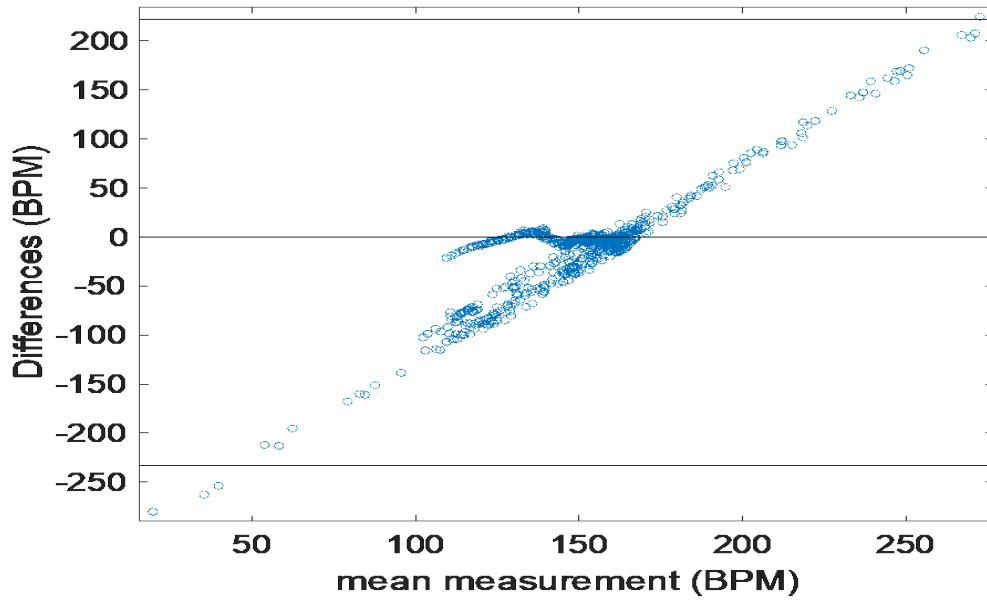


Figure A2.308: Subject No. 5 Samsung's B&A for fast walk, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 1 Sitting Samsung vs ECG Bland Altman Plot

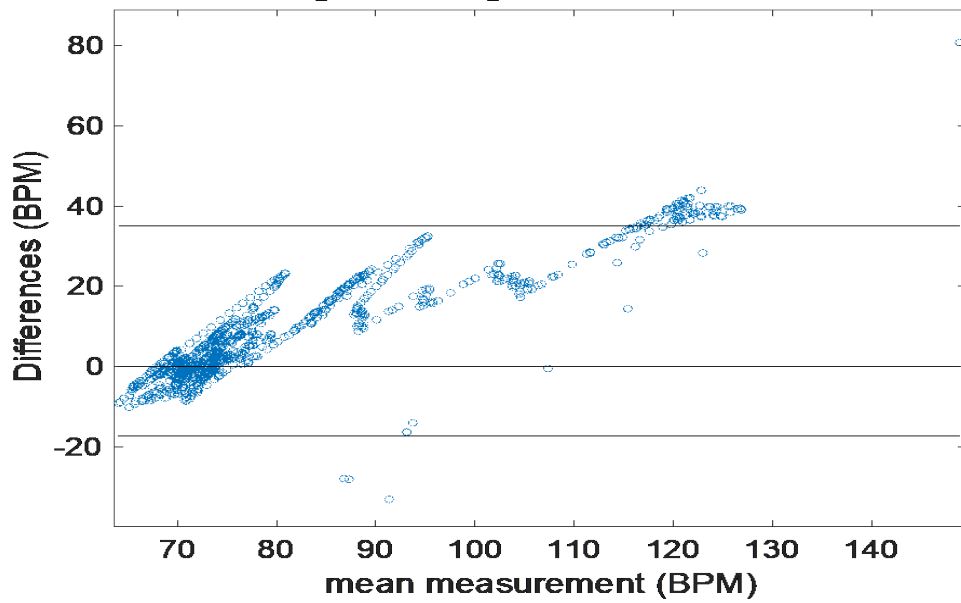


Figure A2.309: Subject No. 1 Samsung's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)



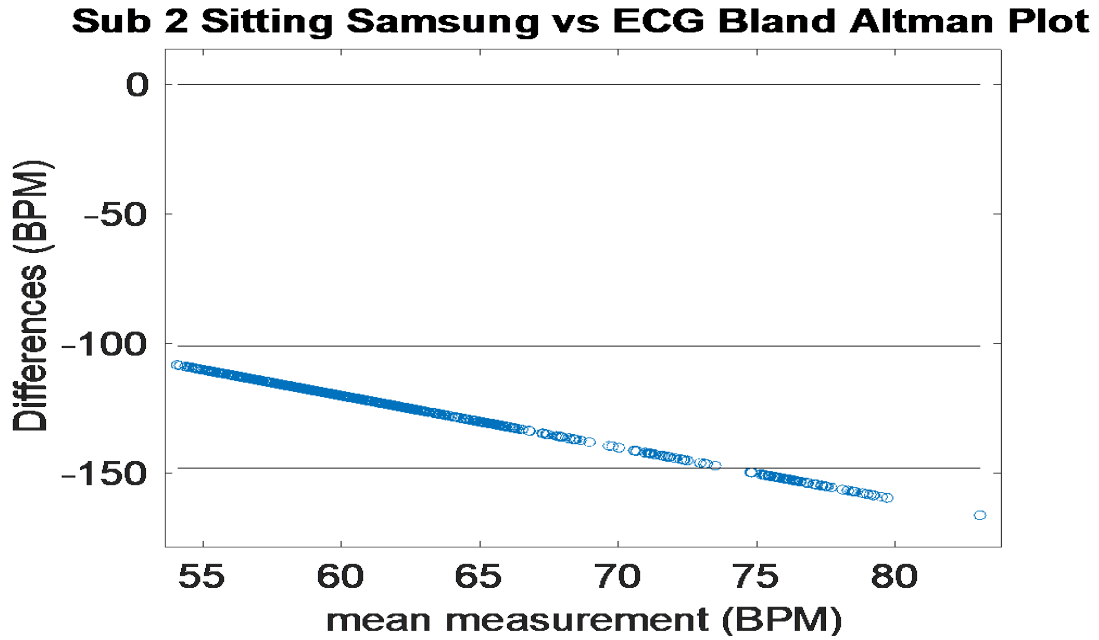


Figure A2.310: Subject No. 2 Samsung's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

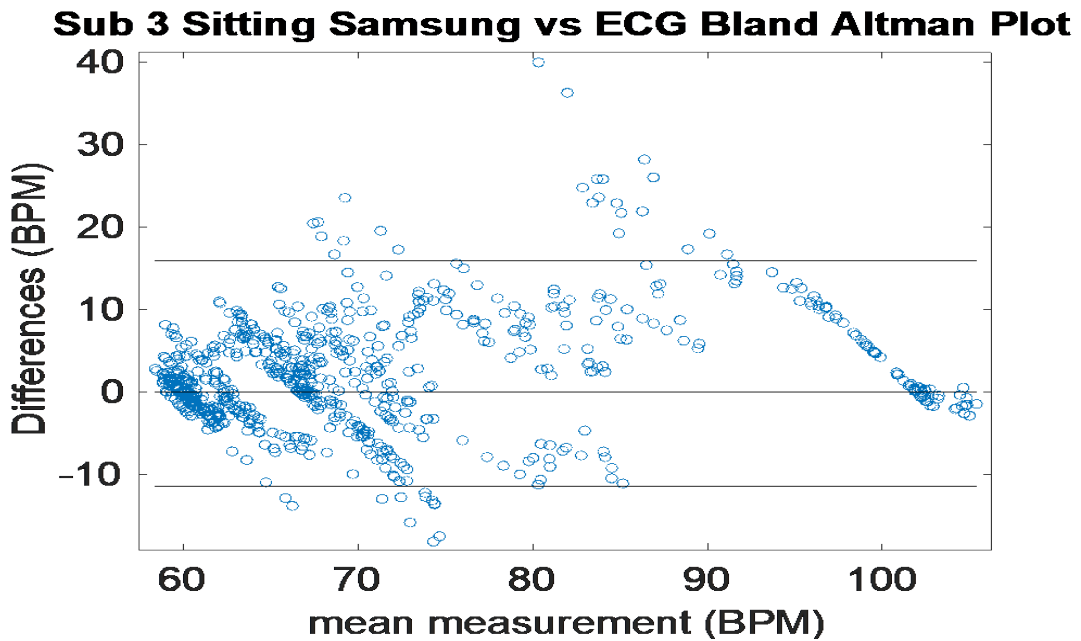


Figure A2.311: Subject No. 3 Samsung's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 4 Sitting Samsung vs ECG Bland Altman Plot

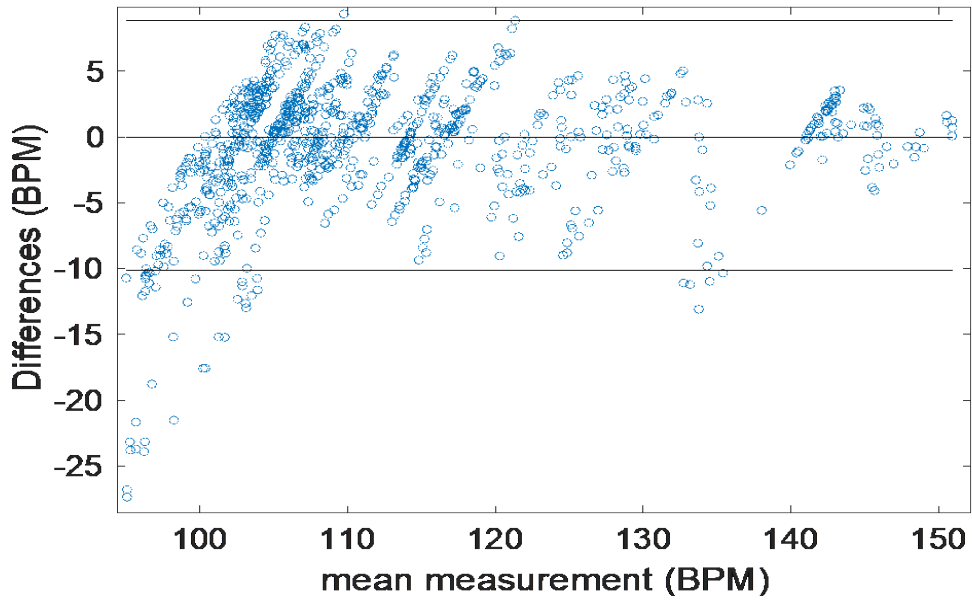


Figure A2.312: Subject No. 4 Samsung's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 5 Sitting Samsung vs ECG Bland Altman Plot

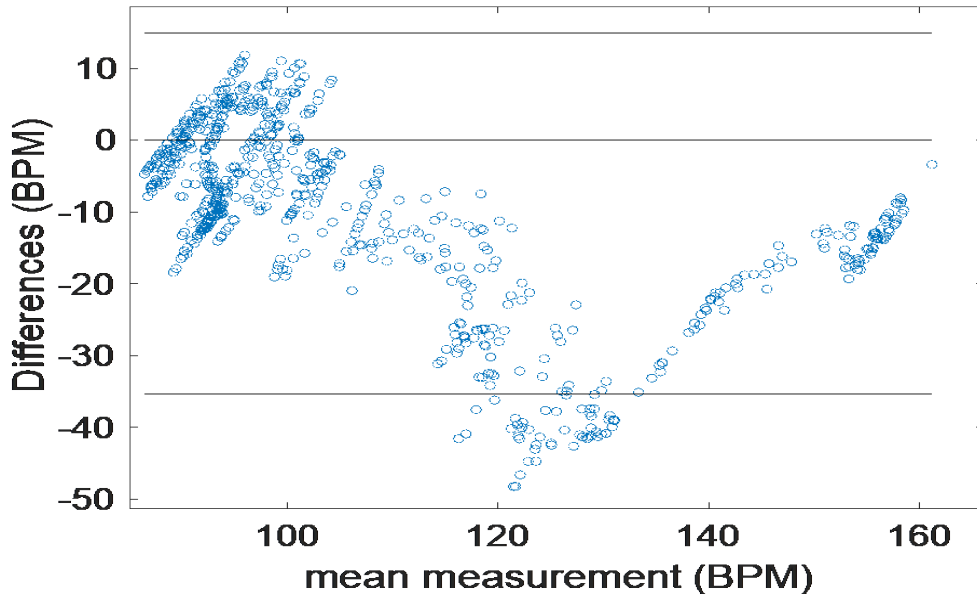


Figure A2.313: Subject No. 5 Samsung's B&A for sitting, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 1 Slow Biking Samsung vs ECG Bland Altman Plot

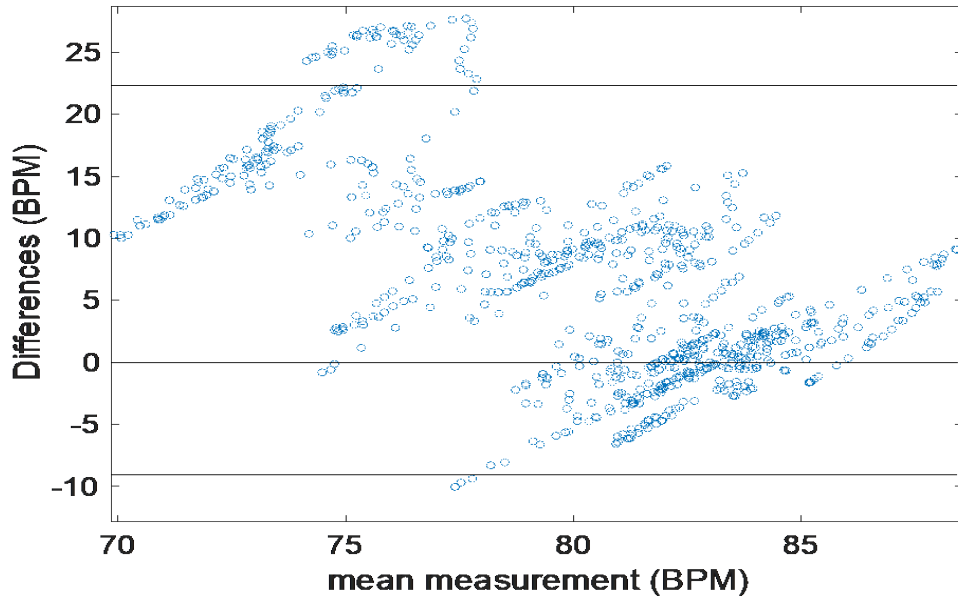


Figure A2.314: Subject No. 1 Samsung's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 2 Slow Biking Samsung vs ECG Bland Altman Plot

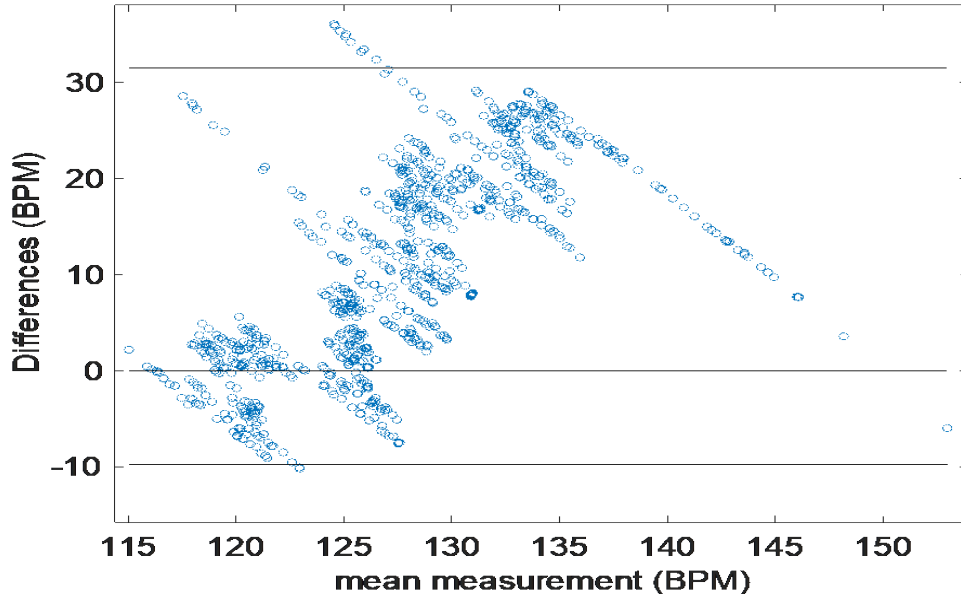


Figure A2.315: Subject No. 2 Samsung's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 3 Slow Biking Samsung vs ECG Bland Altman Plot

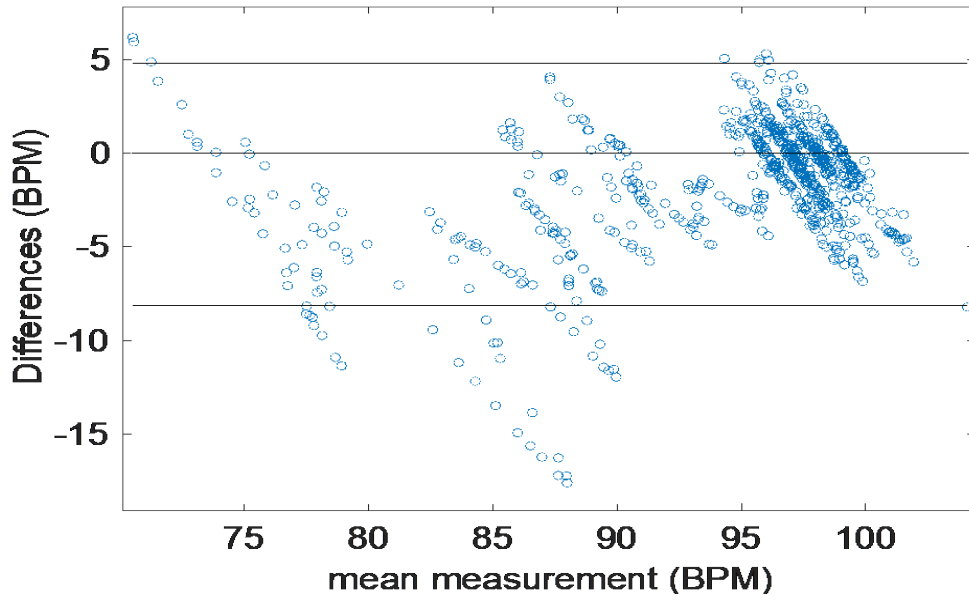


Figure A2.316: Subject No. 3 Samsung's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 4 Slow Biking Samsung vs ECG Bland Altman Plot

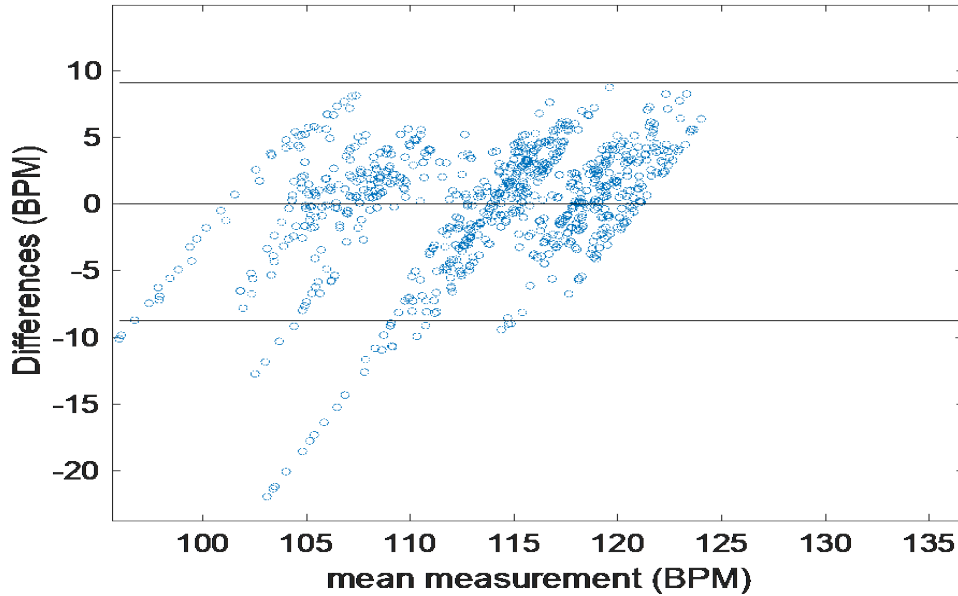


Figure A2.317: Subject No. 4 Samsung's B&A for slow biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 1 Fast Biking Samsung vs ECG Bland Altman Plot

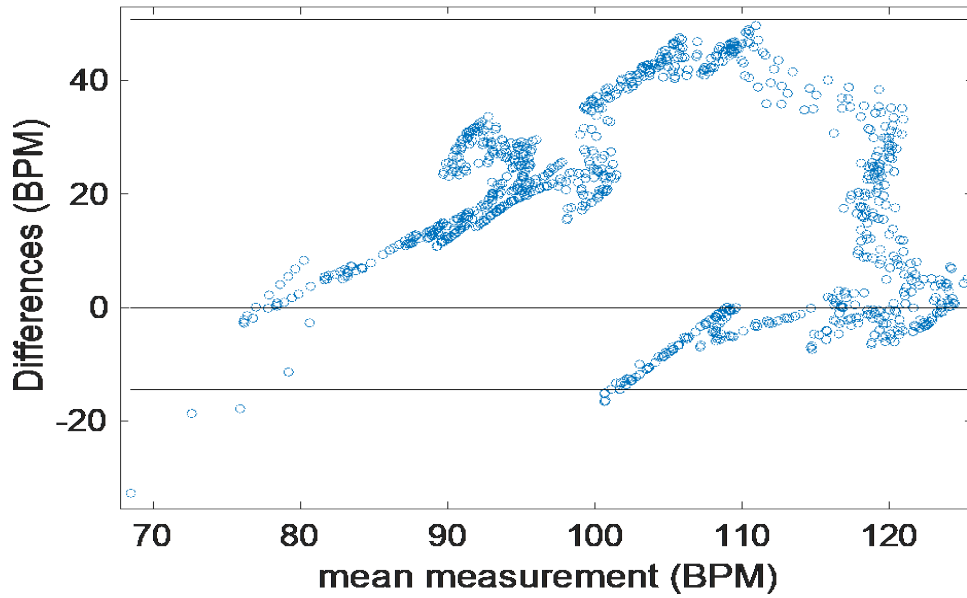


Figure A2.318: Subject No. 1 Samsung's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 2 Fast Biking Samsung vs ECG Bland Altman Plot

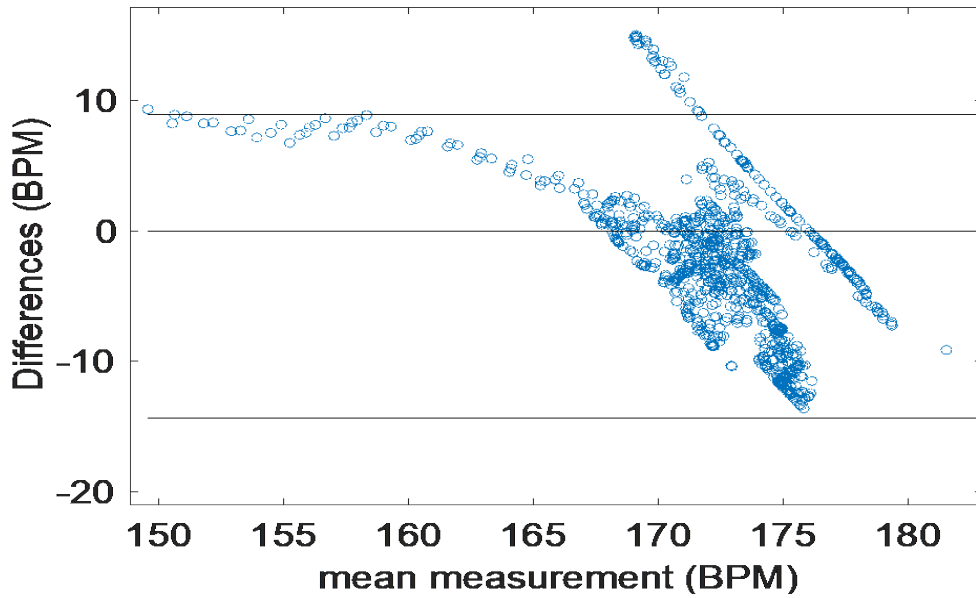


Figure A2.319: Subject No. 2 Samsung's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 3 Fast Biking Samsung vs ECG Bland Altman Plot

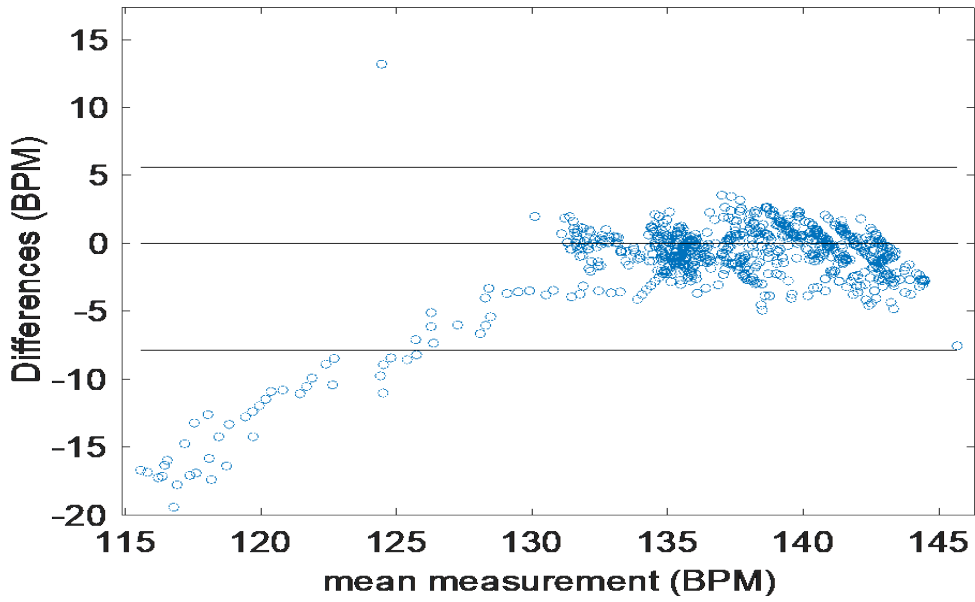


Figure A2.320: Subject No. 3 Samsung's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

### Sub 4 Fast Biking Samsung vs ECG Bland Altman Plot

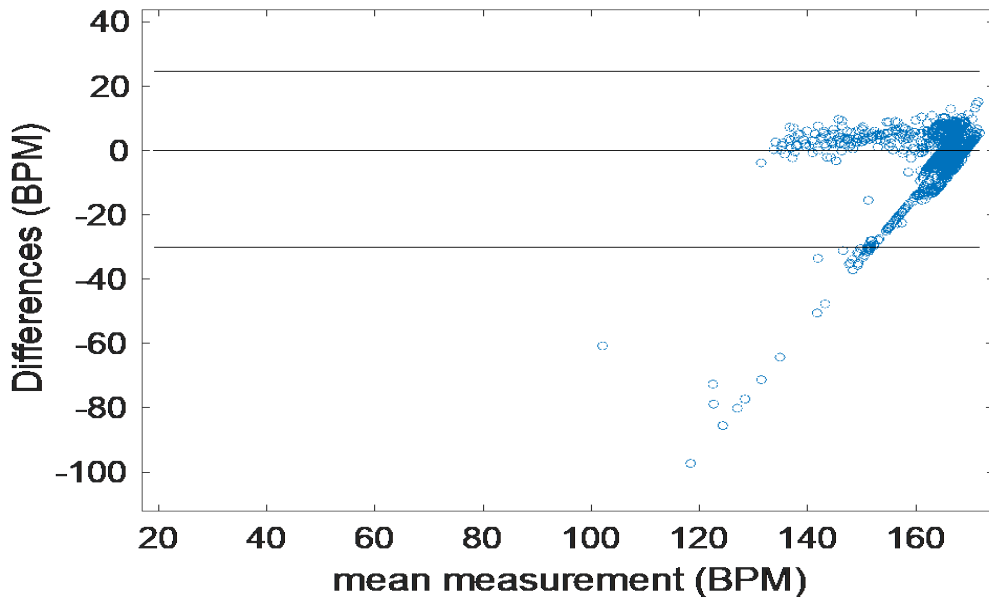


Figure A2.321: Subject No. 4 Samsung's B&A for fast biking, the top & bottom lines represent the LOA:  $\pm 1.96SD$  (Ch2.Eq.2)

## A.2.3: WFTs Error Plots

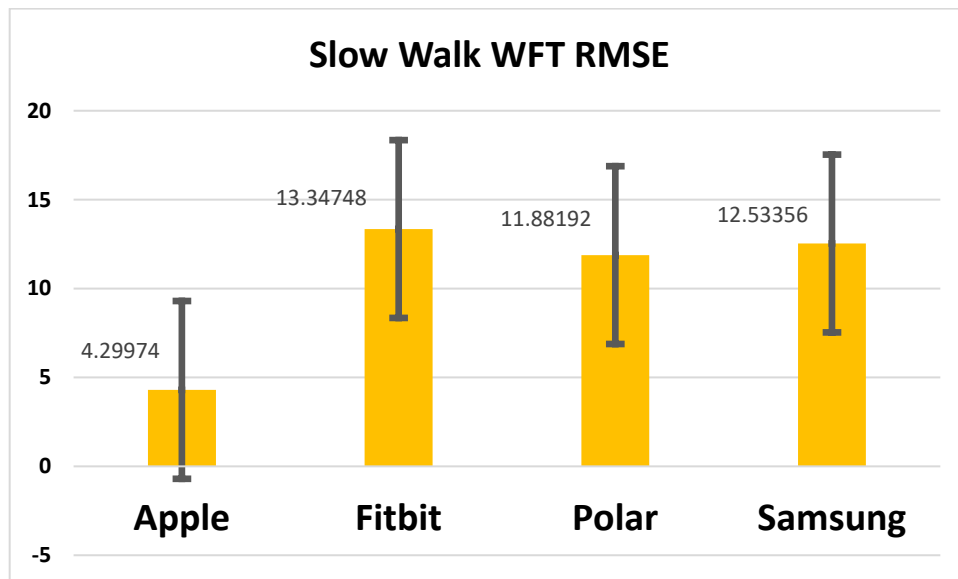


Figure A2.322: Slow Walk Mean of Root Square Error

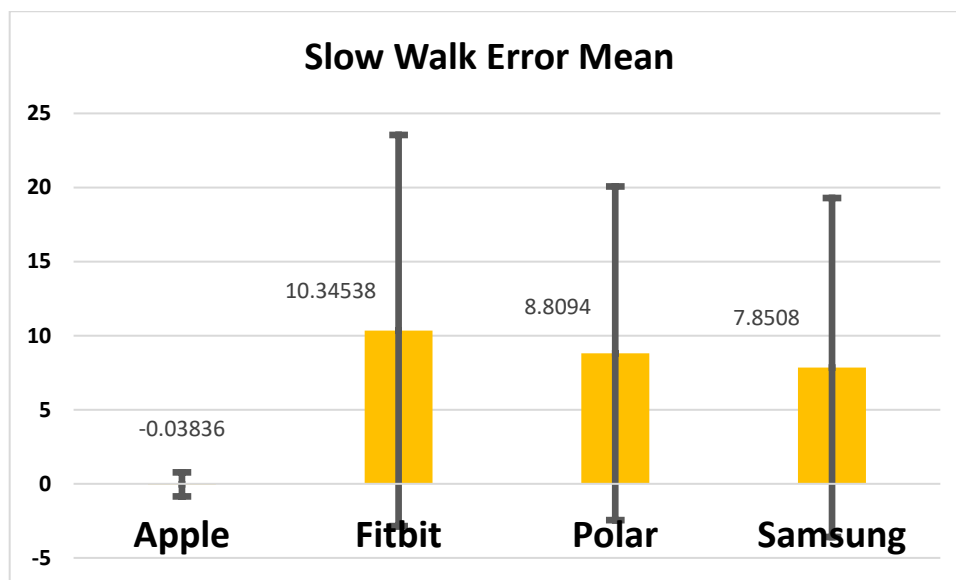


Figure A2.323: Slow Walk Mean of Error Mean

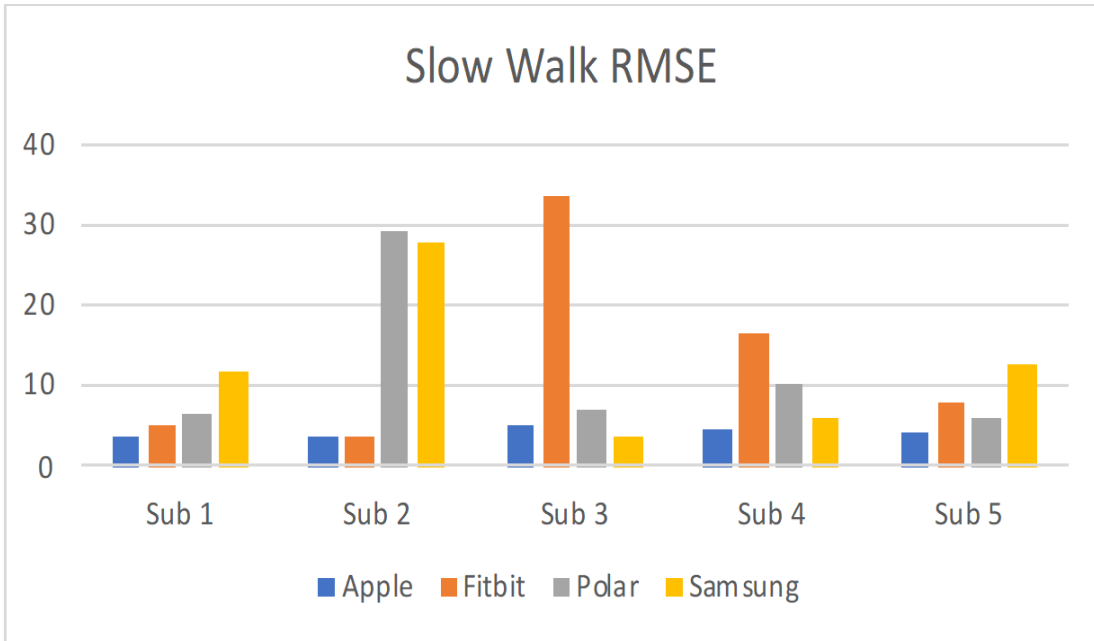


Figure A2.324: Slow Walk Root Mean Square Error

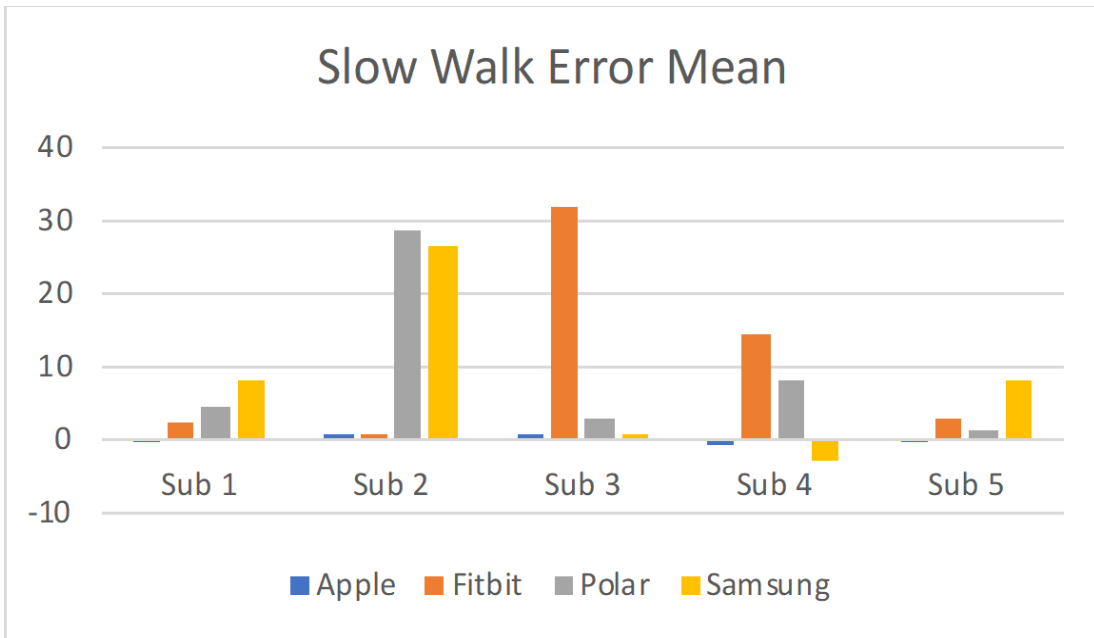


Figure A2.325: Slow Walk Error Mean



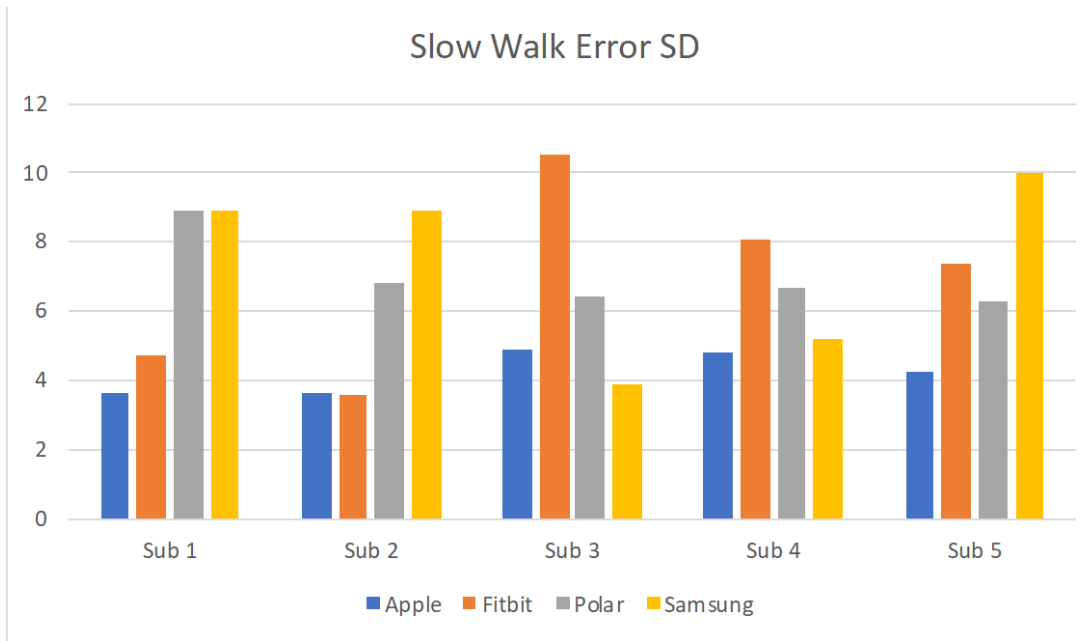


Figure A2.326: Slow Walk Error Standard Deviation

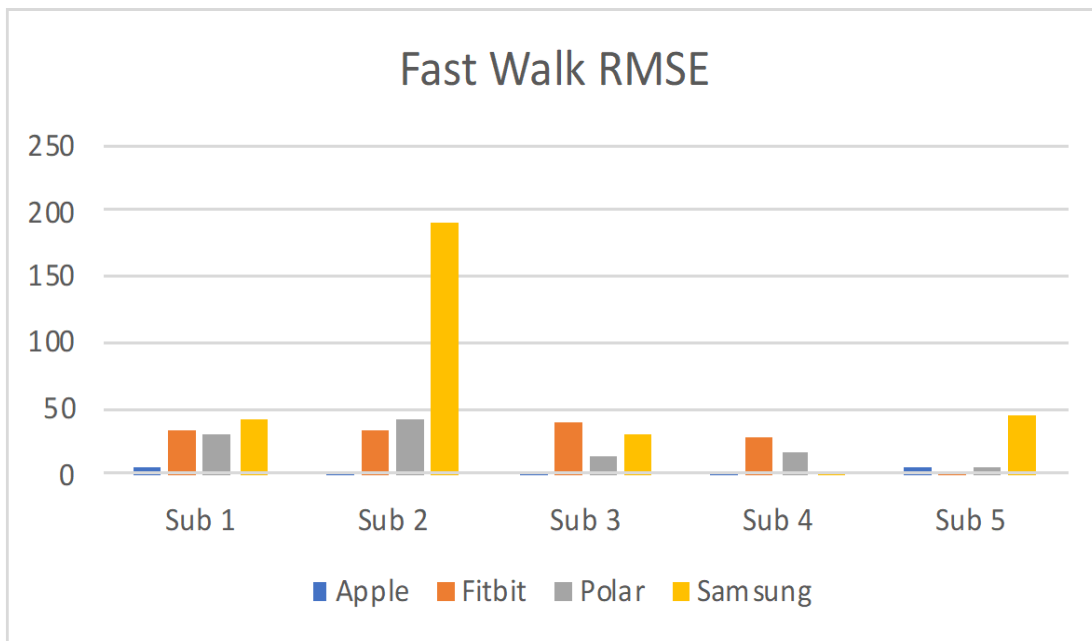


Figure A2.327: Fast Walk Root Mean Square Error

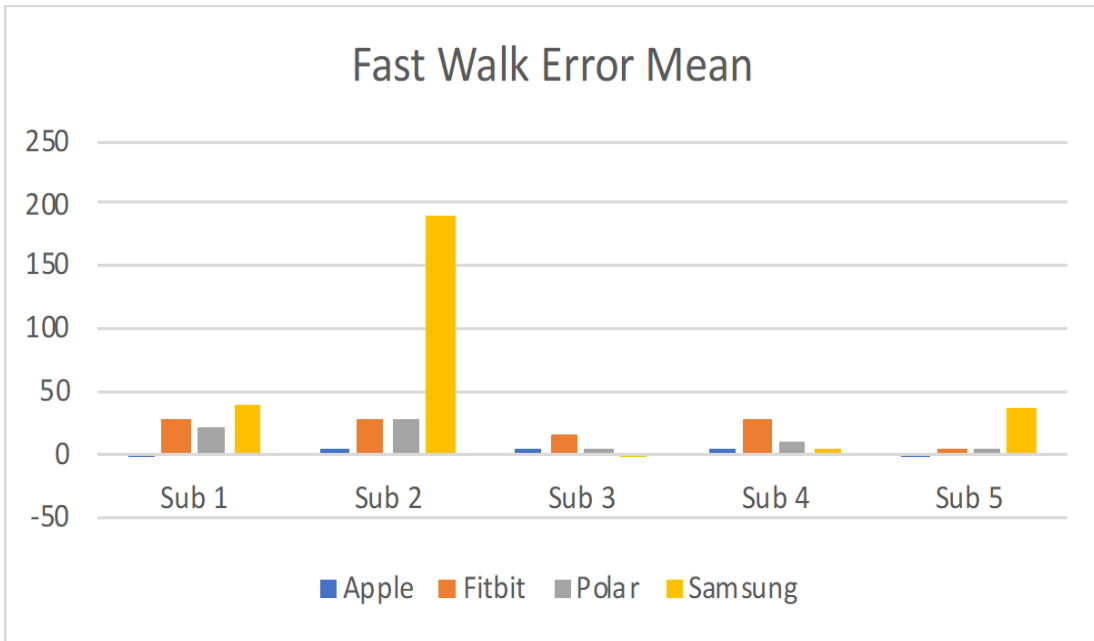


Figure A2.328: Fast Walk Error Mean

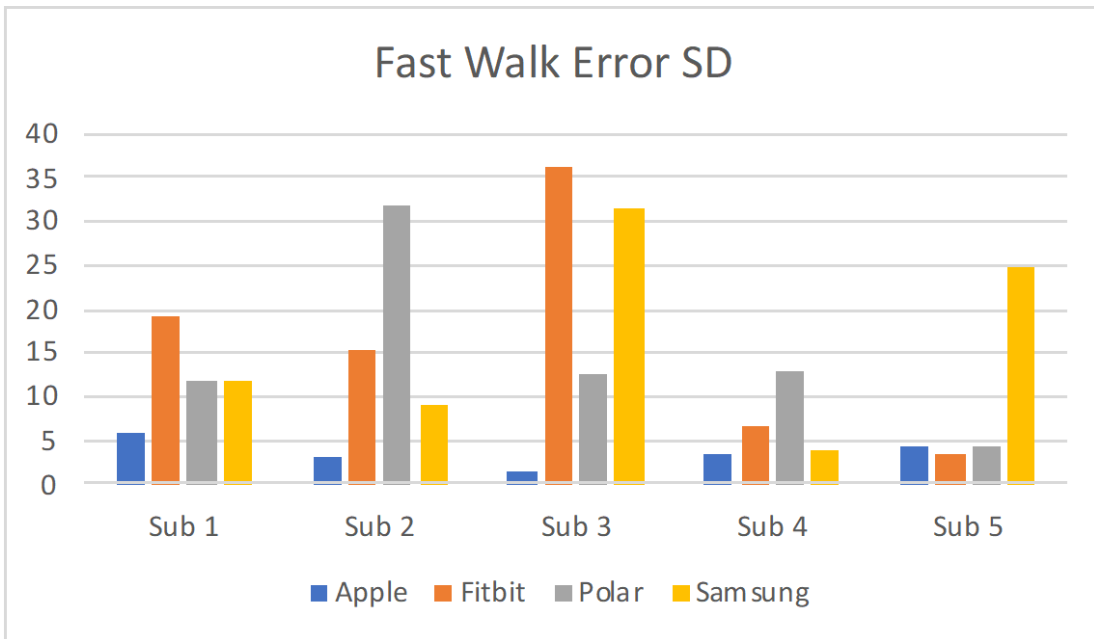


Figure A2. 329:Fast Walk Error Standard Deviation

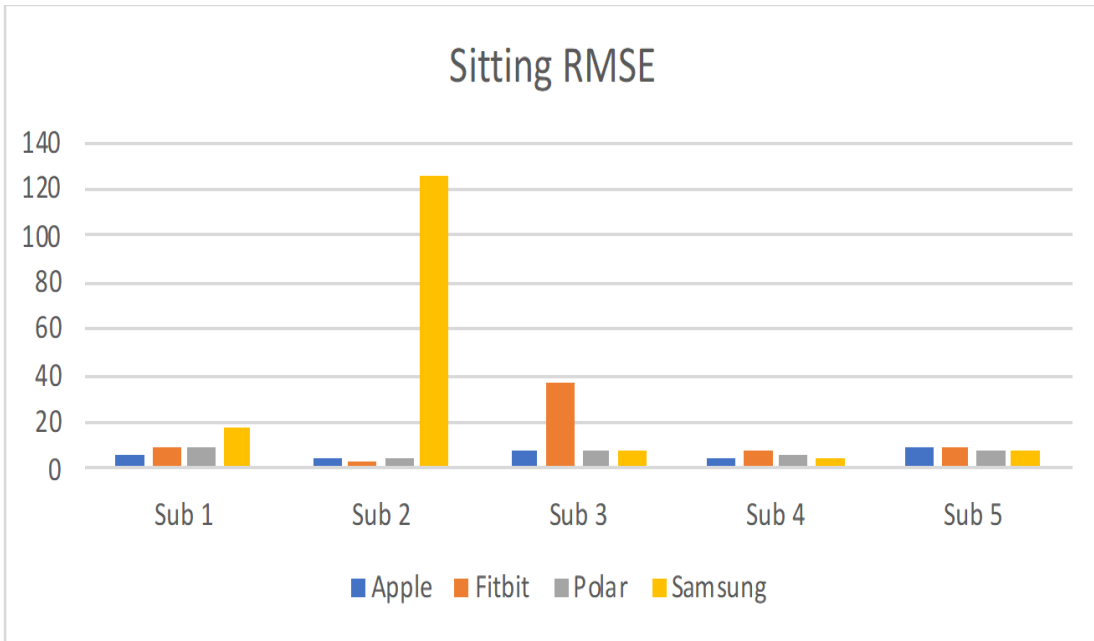


Figure A2.330: Sitting Root Mean Square Error

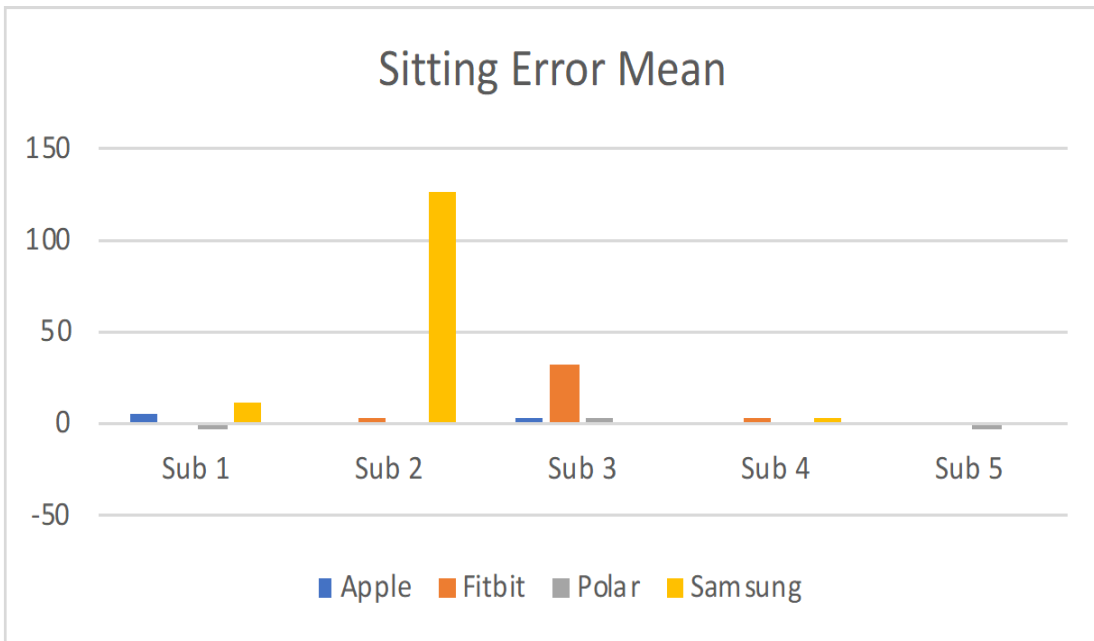


Figure A2.331: Sitting Error Mean

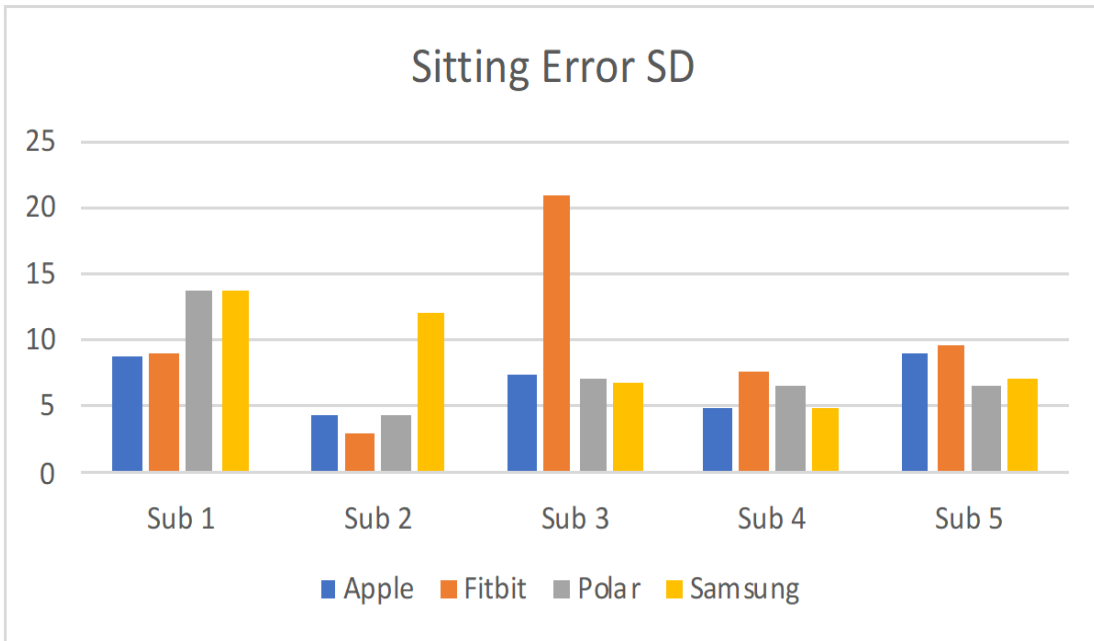


Figure A2.332: Sitting Error Standard Deviation

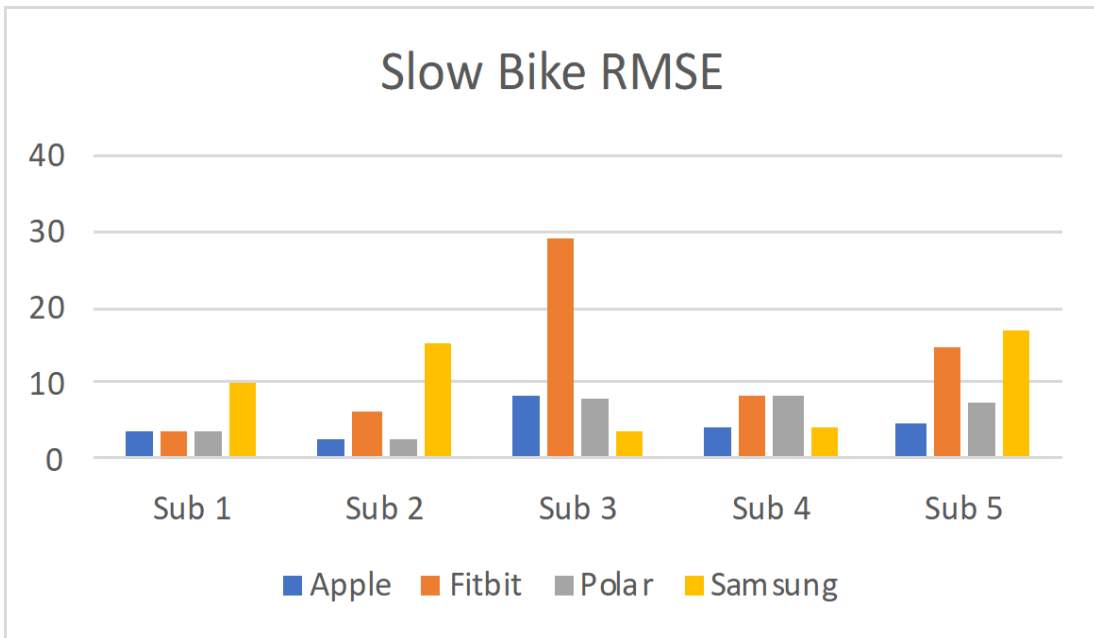


Figure A2.333: Slow Bike Root Mean Square Error

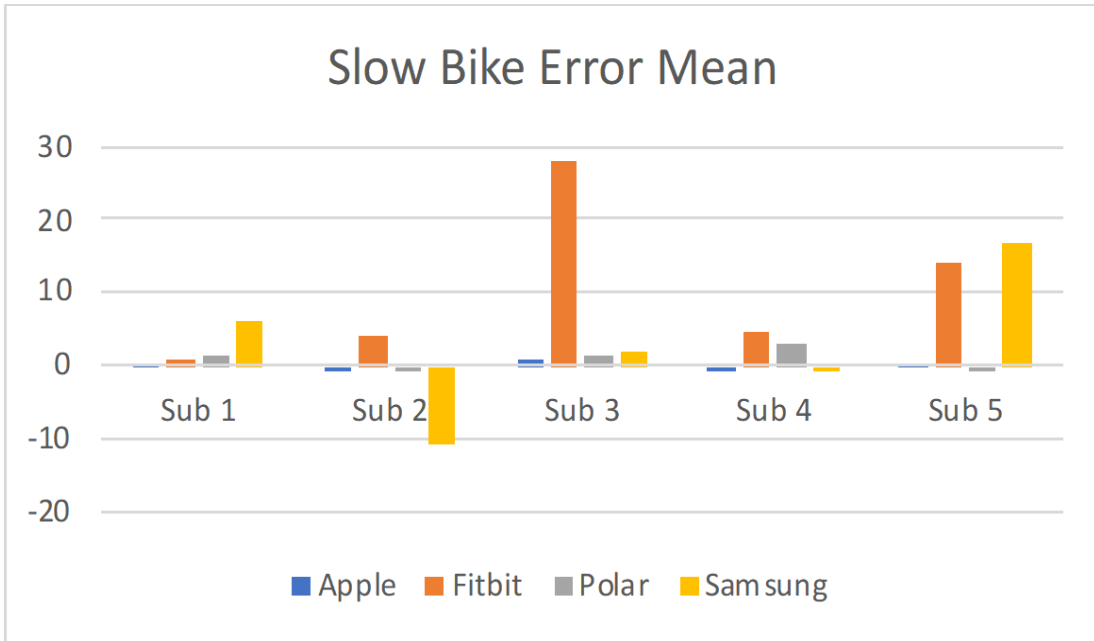


Figure A2.334: Slow Bike Error Mean

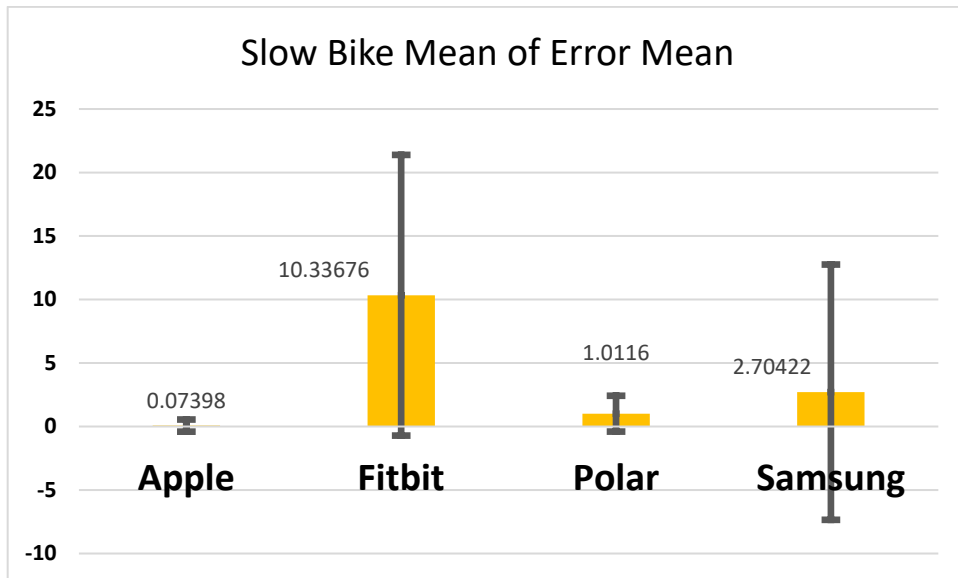


Figure A2.335: Slow Bike Mean of Error Mean

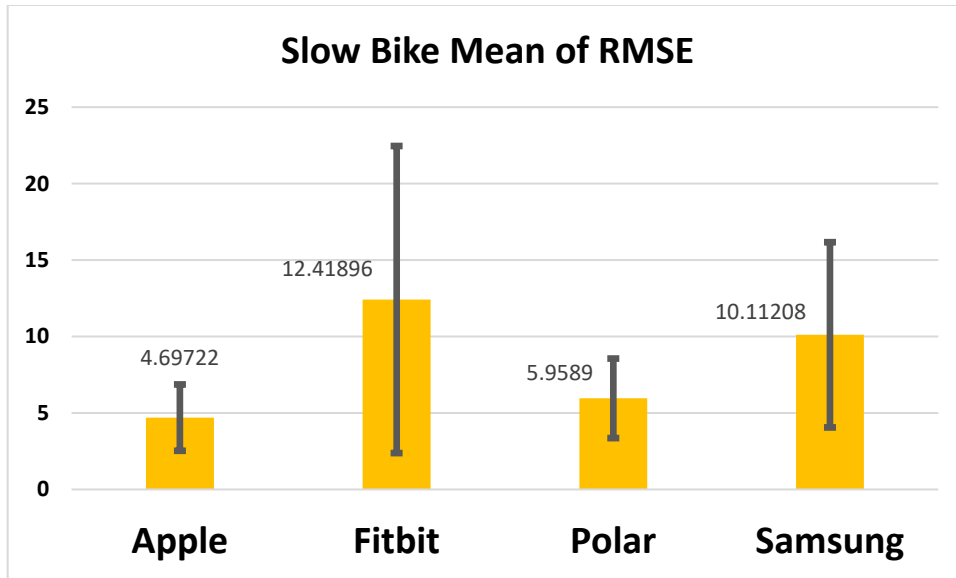


Figure A2.336: Slow Bike Mean of Root Mean Square Error

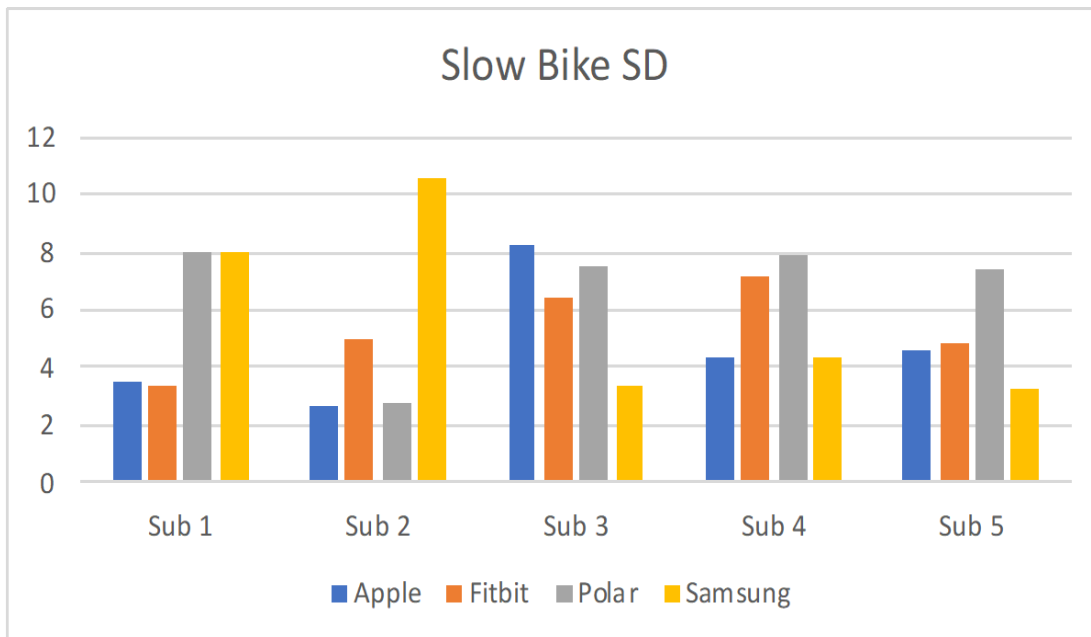


Figure A2.337: Slow Bike Error Standard Deviation

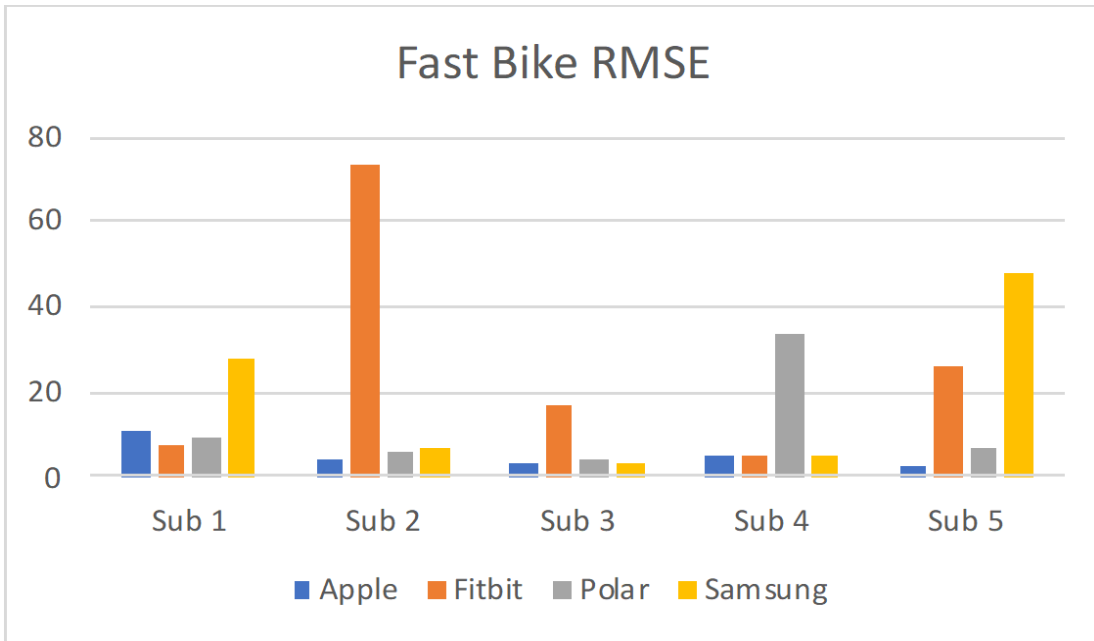


Figure A2.338: Fast Bike Root Mean Square Error

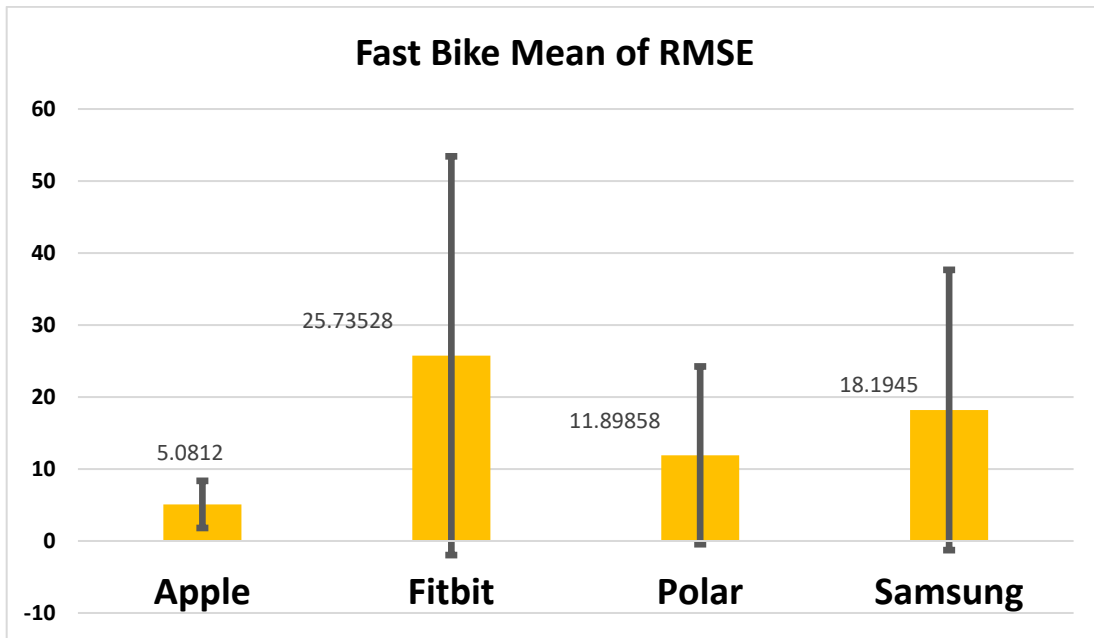


Figure A2.339: Fast Bike Mean of Root Mean Square Error

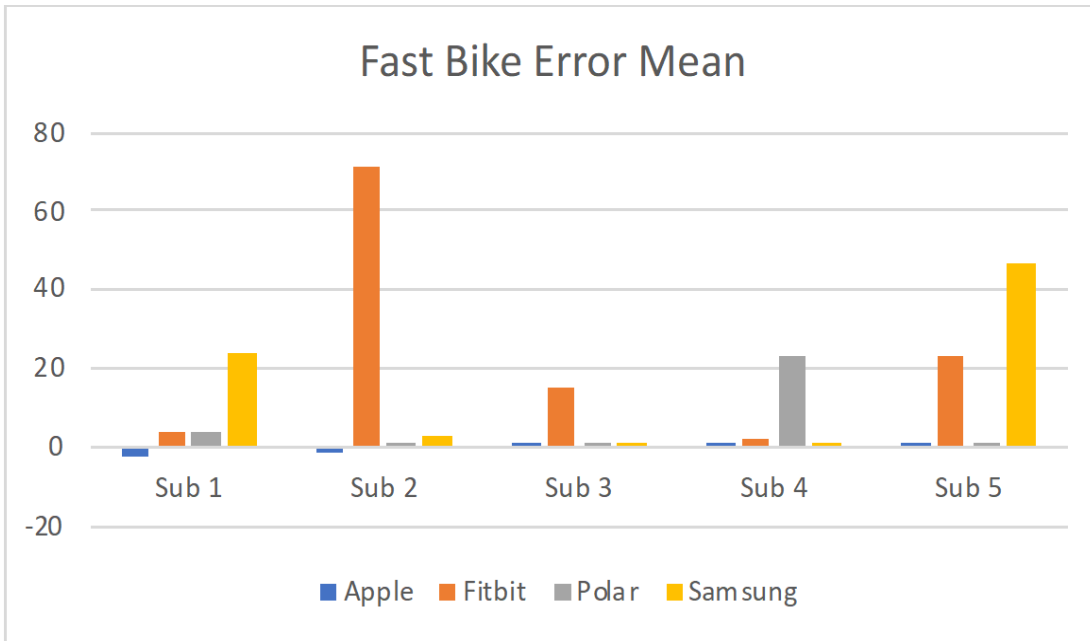


Figure A2.340: Fast Bike Error Mean

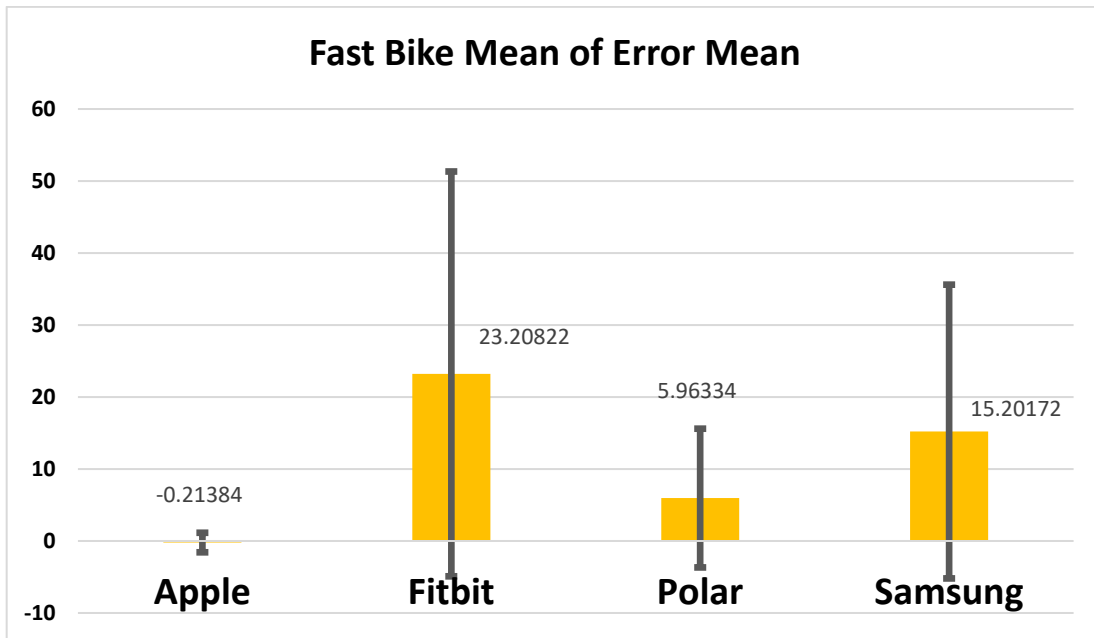


Figure A2.341: Fast Bike Mean of Error Mean



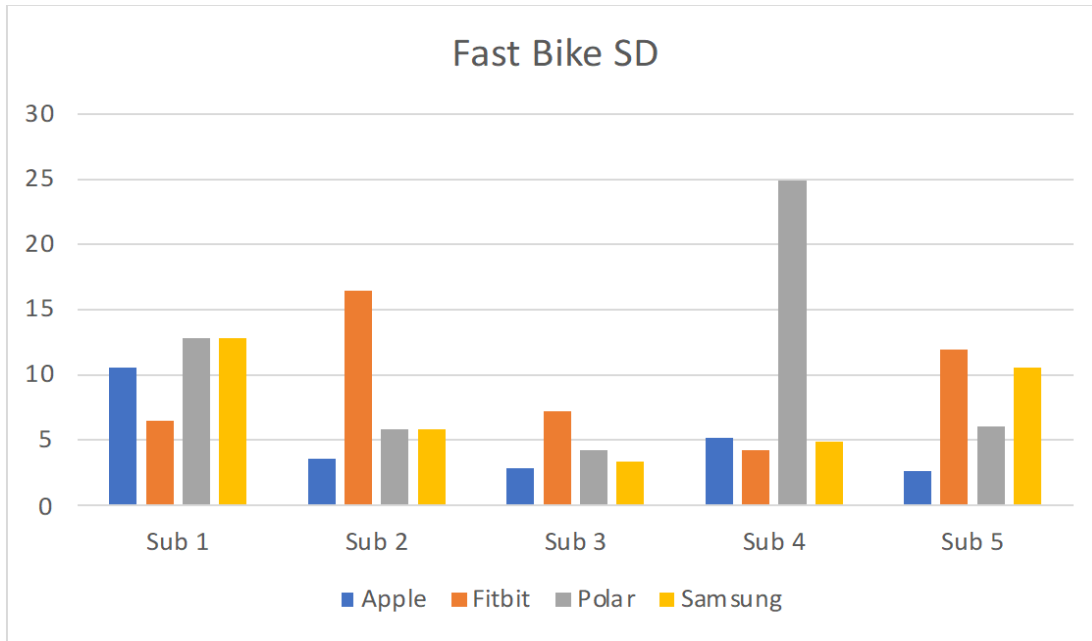


Figure A2.342: Fast Bike Error Standard Deviation

#### A.2.4: Statistical Tests Results Tables

Table A2. 24: Slow Walk T-Test Results for ECG vs WFT HRs

T-Test P Value	Sub 1	Sub 2	Sub 3	Sub 4	Sub 5
Apple	0.881	0.327	<0.05	0.062	0.862
Fitbit	<0.05	0.731	<0.05	<0.05	<0.05
Polar	<0.05	<0.05	<0.05	<0.05	<0.05
Samsung	<0.05	<0.05	<0.05	<0.05	<0.05

Means no significant difference ( $\alpha = 0.05$ )

Table A2. 25: Fast Walk T-Test Results

T-Test P Value	Sub 1	Sub 2	Sub 3	Sub 4	Sub 5
Apple	0.196	0.483	0.0029	0.501	0.897
Fitbit	<0.05	<0.05	<0.05	<0.05	<0.05
Polar	<0.05	<0.05	<0.05	<0.05	<0.05
Samsung	<0.05	<0.05	0.082	0.521	0.756


 Means no significant difference ( $\alpha = 0.05$ )

Table A2. 26: Sitting T-Test Results

T-Test P Value	Sub 1	Sub 2	Sub 3	Sub 4	Sub 5
Apple	0.115	0.605	<0.05	0.299	<0.05
Fitbit	0.425	0.676	<0.05	<0.05	<0.05
Polar	0.002	<0.05	<0.05	0.146	<0.05
Samsung	0.052	<0.05	0.206	0.653	<0.05


 Means no significant difference ( $\alpha = 0.05$ )

Table A2. 27: Slow Bike T-Test Results

T-Test P Value	Sub 1	Sub 2	Sub 3	Sub 4	Sub 5
Apple	0.700	0.357	0.359	0.854	0.042
Fitbit	0.015	<0.05	<0.05	<0.05	<0.05
Polar	<0.05	<0.05	<0.05	<0.05	<0.05
Samsung	<0.05	<0.05	0.083	0.865	<0.05


 Means no significant difference ( $\alpha = 0.05$ )

Table A2. 28: Fast Bike T-Test Results

T-Test P value	Sub 1	Sub 2	Sub 3	Sub 4	Sub 5
Apple	0.280	0.985	0.020	0.266	<0.05
Fitbit	<0.05	<0.05	<0.05	0.014	<0.05
Polar	<0.05	0.113	<0.05	<0.05	<0.05
Samsung	<0.05	0.052	0.035	0.433	<0.05


 Means no significant difference ( $\alpha = 0.05$ )

Table A2. 29: Slow Walk KruskalWallis Test

Source	SS	df	MS	Chi-sq	Prob>Chi-sq
Columns	237	3	79	6.77	0.079
Error	428	16	26.75		
Total	665	19			

Table A2. 30: Slow Bike KruskalWallis Test

Source	SS	df	MS	Chi-sq	Prob>Chi-sq
Columns	143.4	3	47.8	4.0971	0.251
Error	521.6	16	32.6		
Total	665	19			

Table A2. 31:Fast Bike KruskalWallis Test

Source	SS	df	MS	Chi-sq	Prob>Chi-sq
Columns	170.2	3	56.733	4.8629	0.182
Error	494.8	16	30.9250		
Total	665	19			

A5 CHAPTER 5 APPENDIX

Patient 1 Attempts

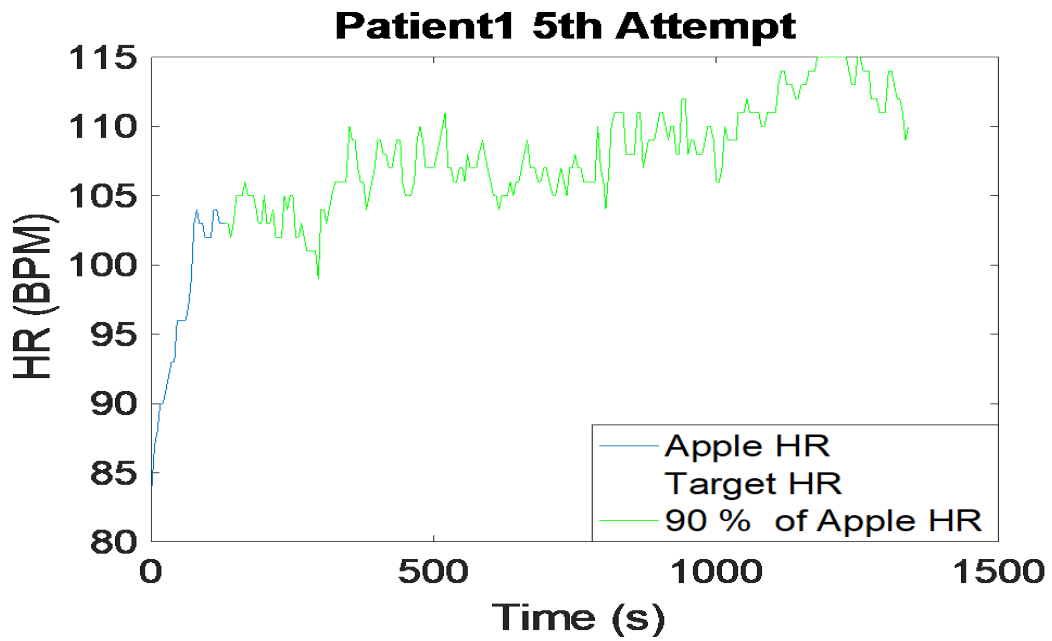


Figure A5.343: Patient No. 1 Week 1 1st Attempt

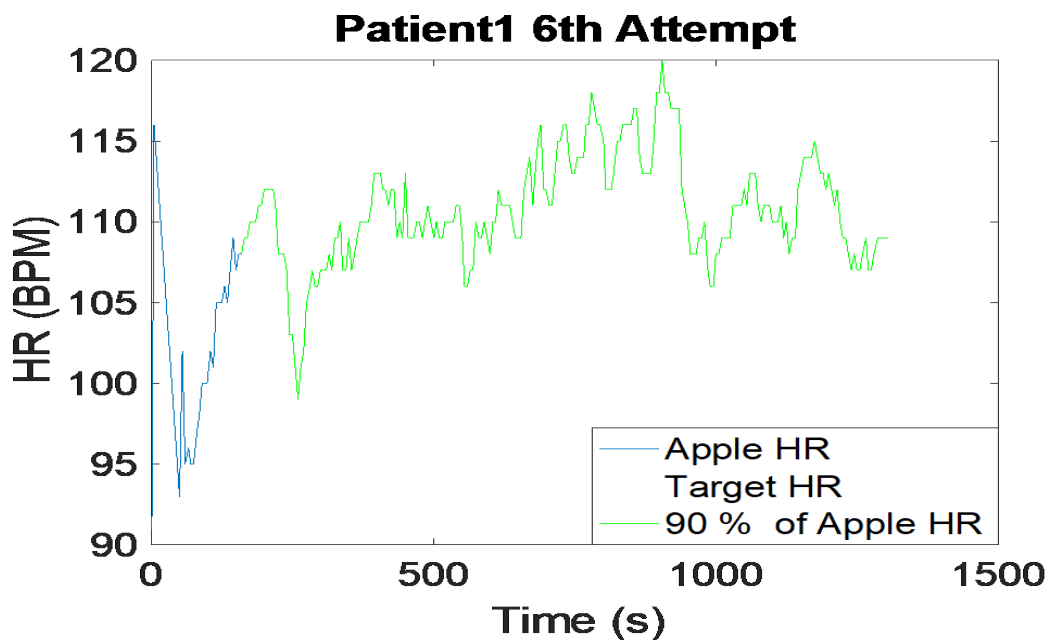


Figure A5.344: Patient No. 1 Week 1 2nd Attempt

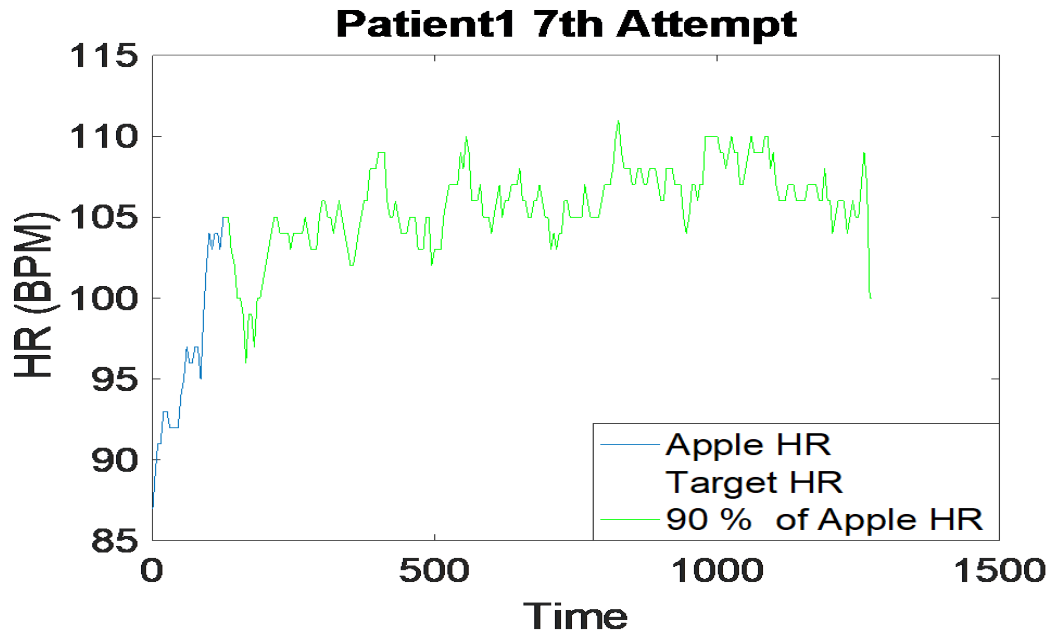


Figure A5.345: Patient No. 1 Week 1 3rd Attempt

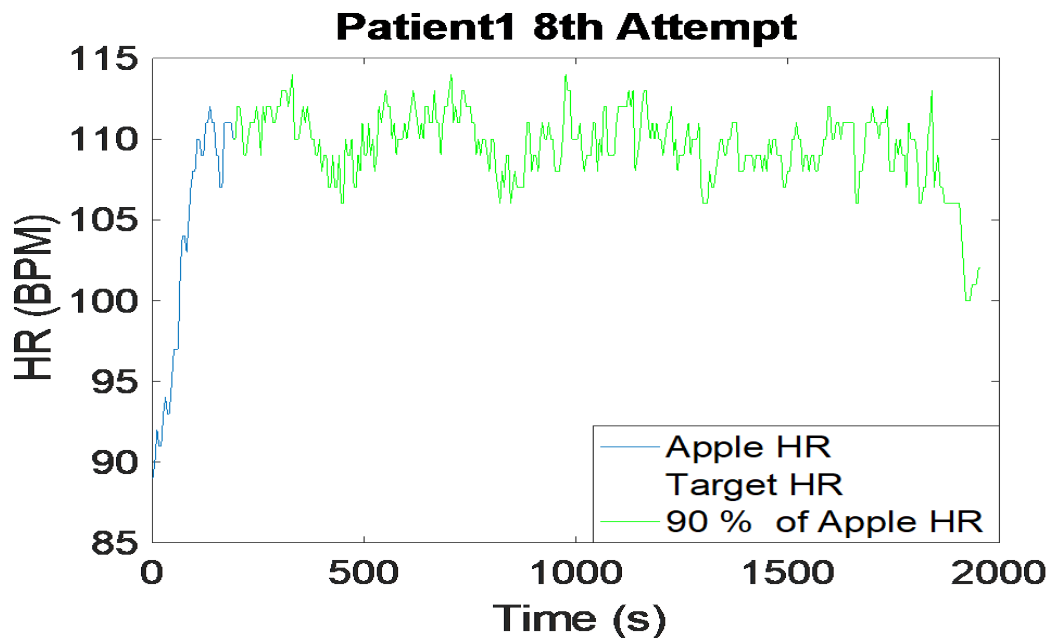


Figure A5.346: Patient No. 1 Week 2 1st Attempt

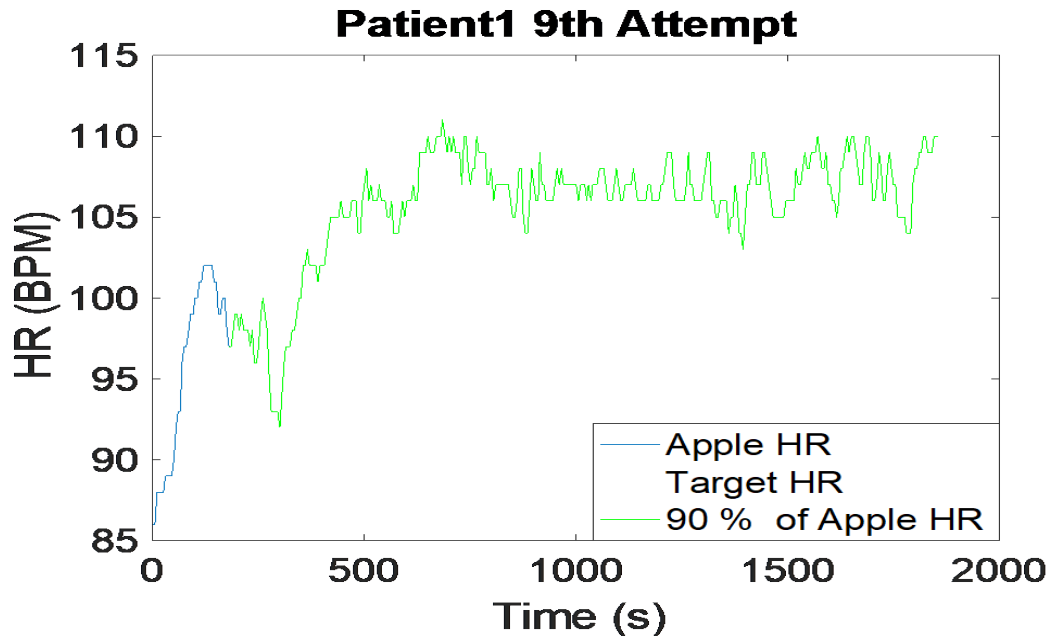


Figure A5.347: Patient No. 1 Week 2 2nd Attempt

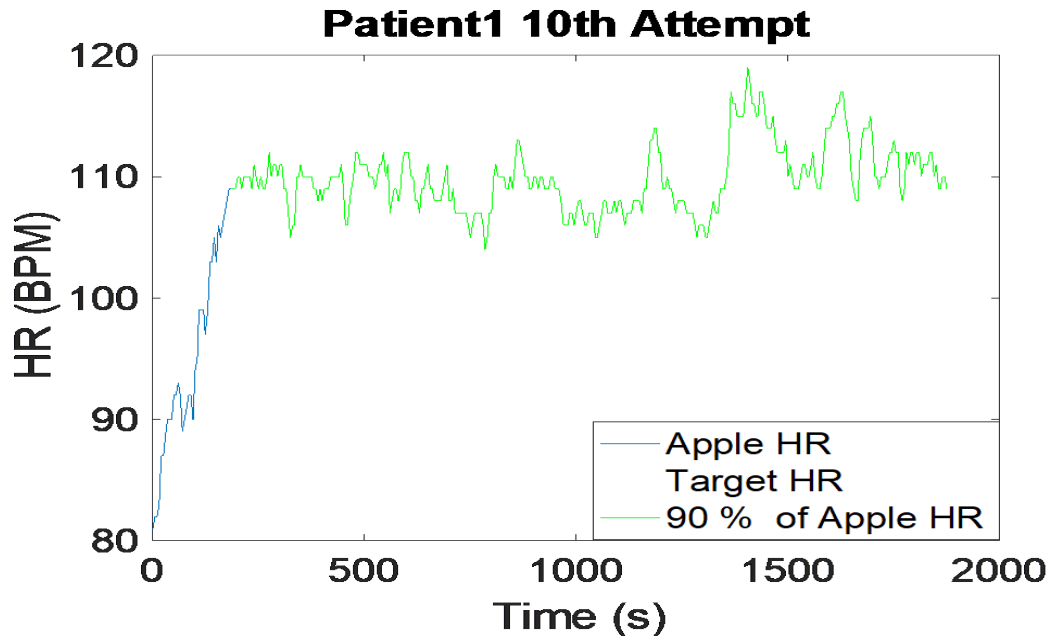


Figure A5.348: Patient No. 1 Week 3 Attempt 1

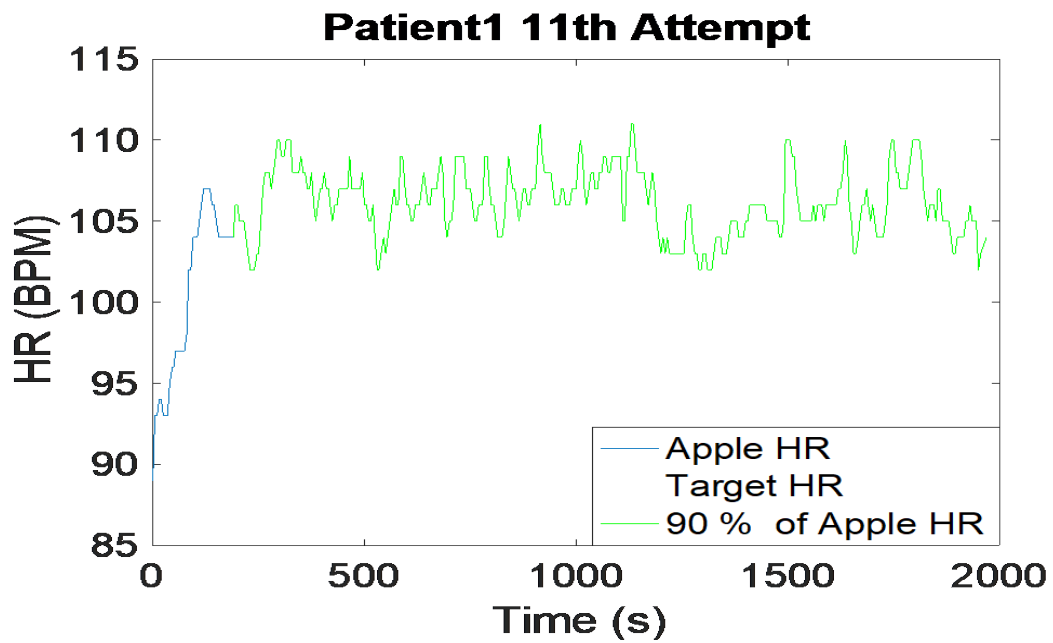
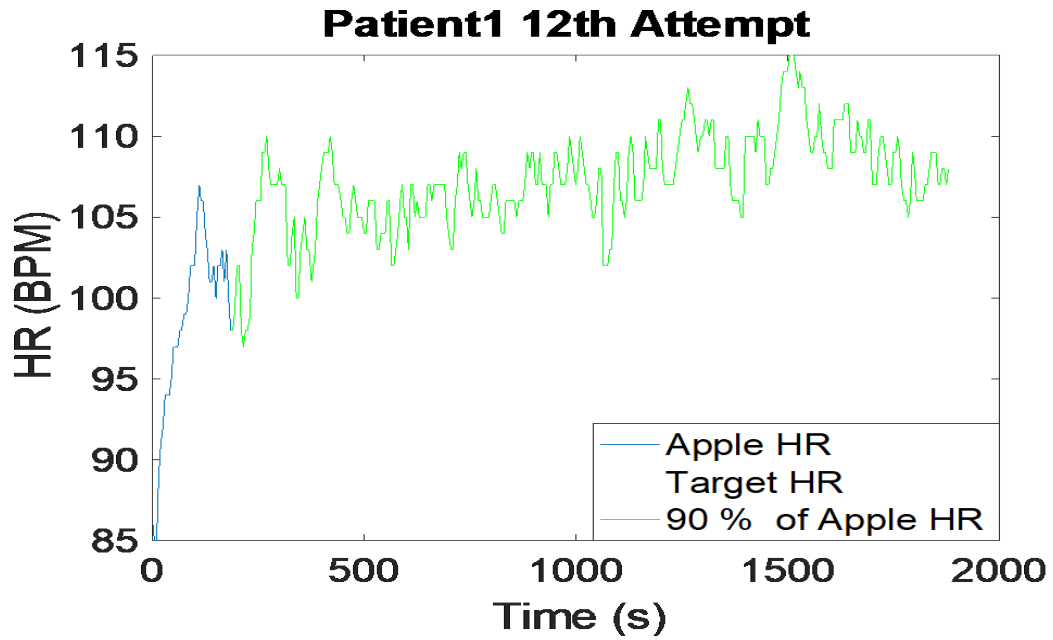
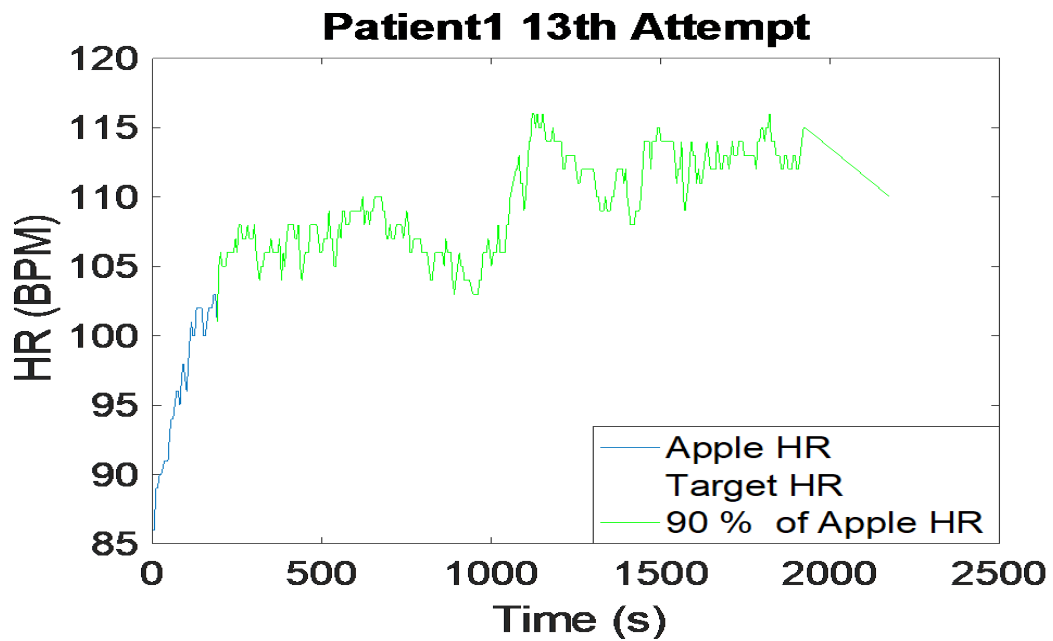


Figure A5.349: Patient No. 1 Week 3 Attempt 2

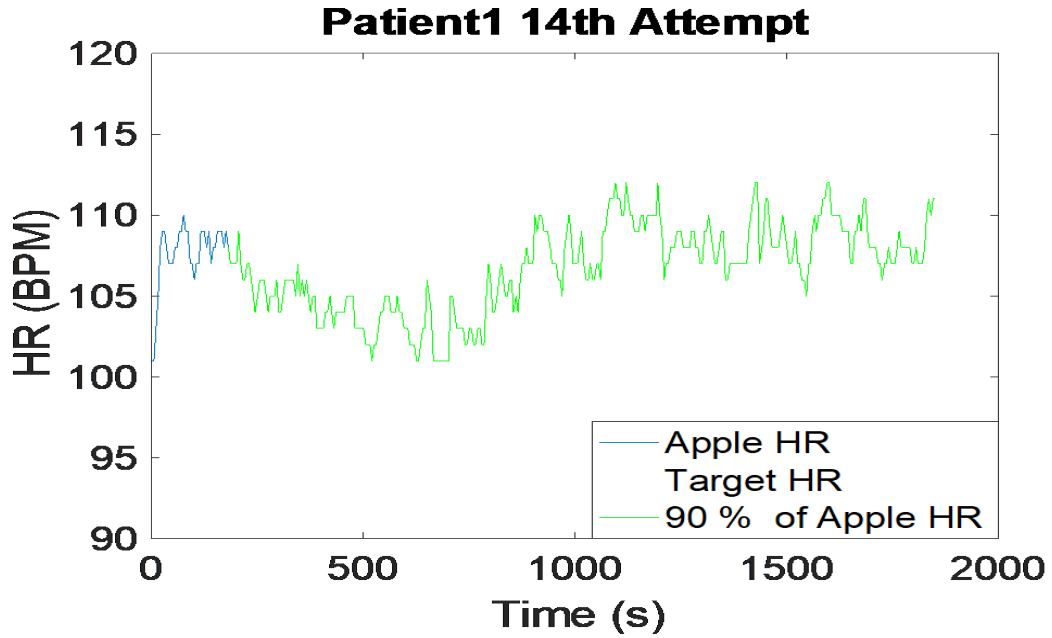




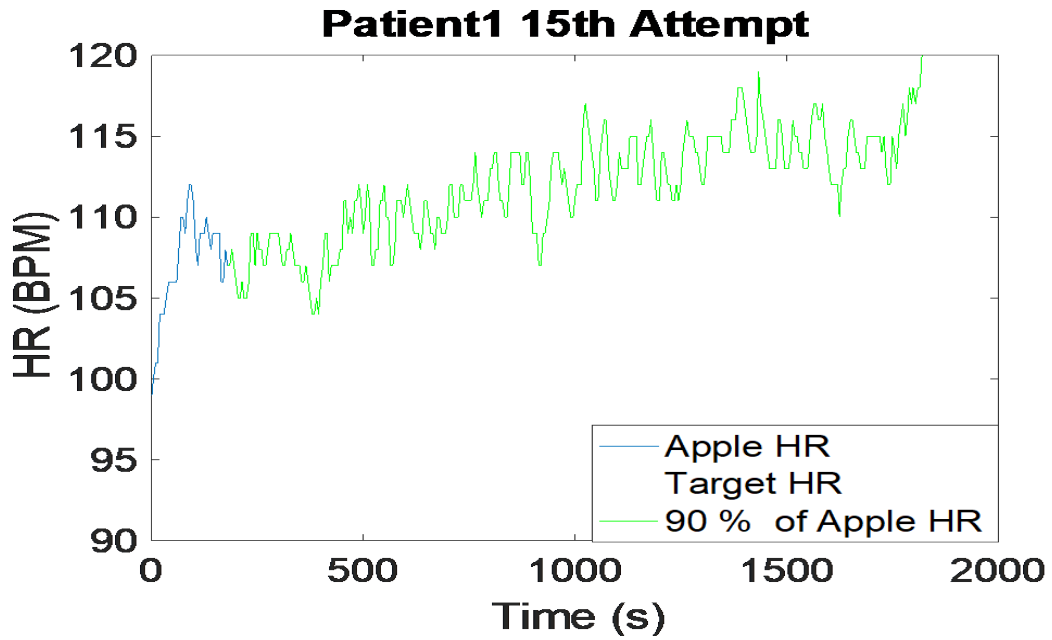
*Figure A5.350: Patient No. 1 Week 3 Attempt 3*



*Figure A5.351: Patient No. 1 Week 4 Attempt 1*



*Figure A5.352: Patient No. 1 Week 4 Attempt 2*



*Figure A5.353: Patient No. 1 Week 5 Attempt 1*

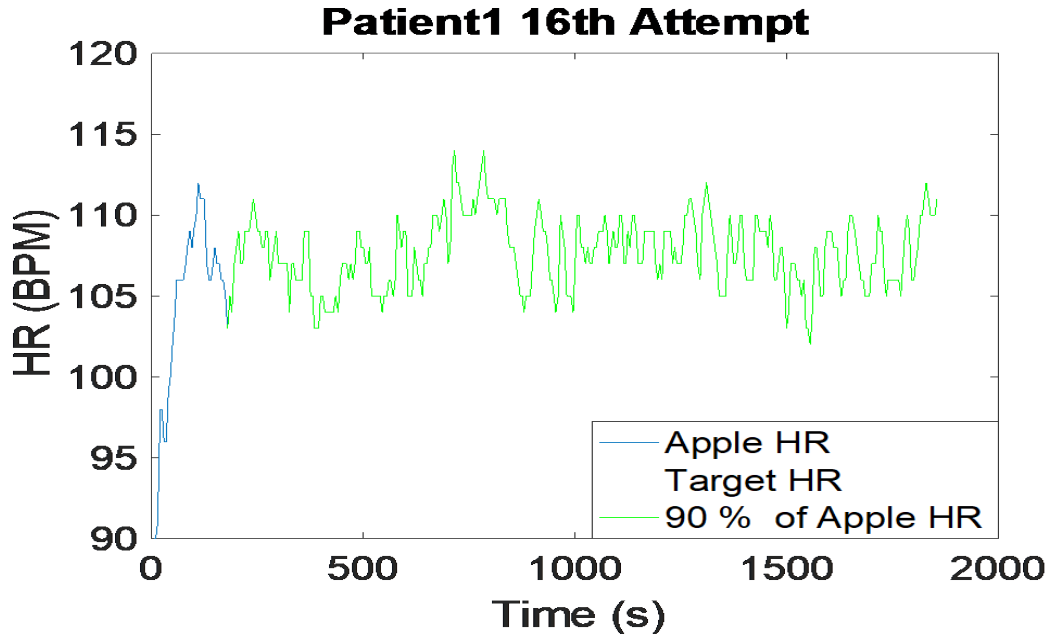


Figure A5.354: Patient No. 1 Week 5 Attempt 2

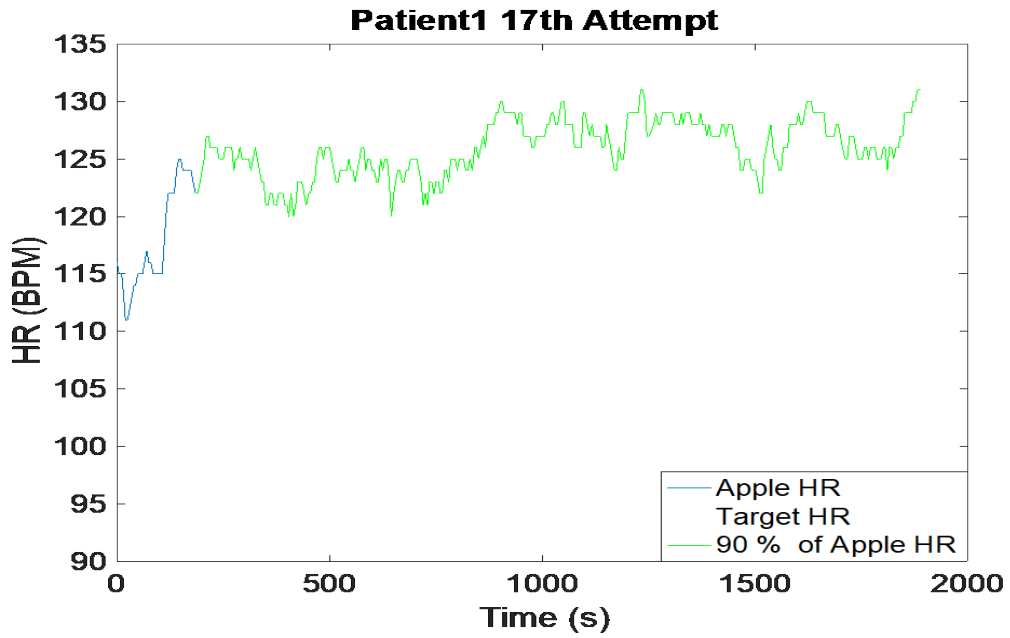


Figure A5.355: Patient No. 1 Week 5 Attempt 3

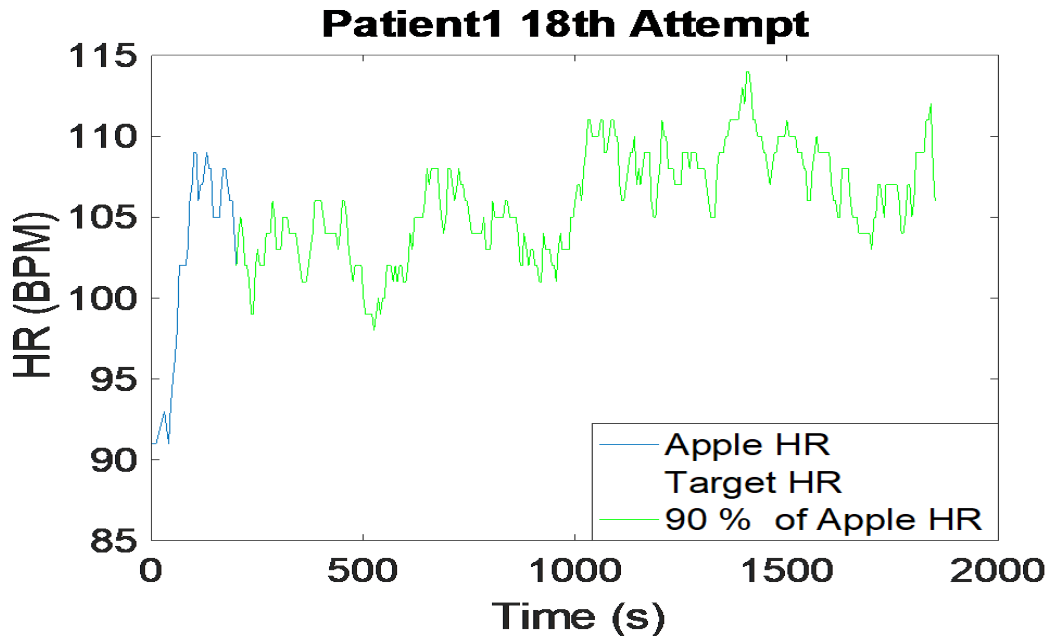


Figure A5.356: Patient No. 1 Week 6 Attempt 1

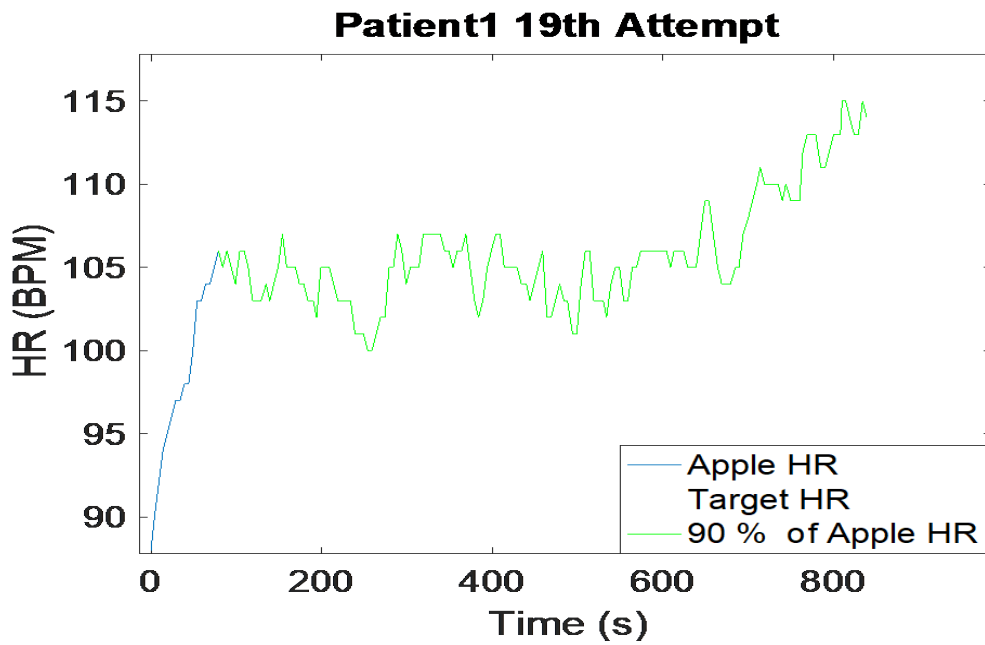


Figure A5.357: Patient No. 1 Week 6 Attempt 2

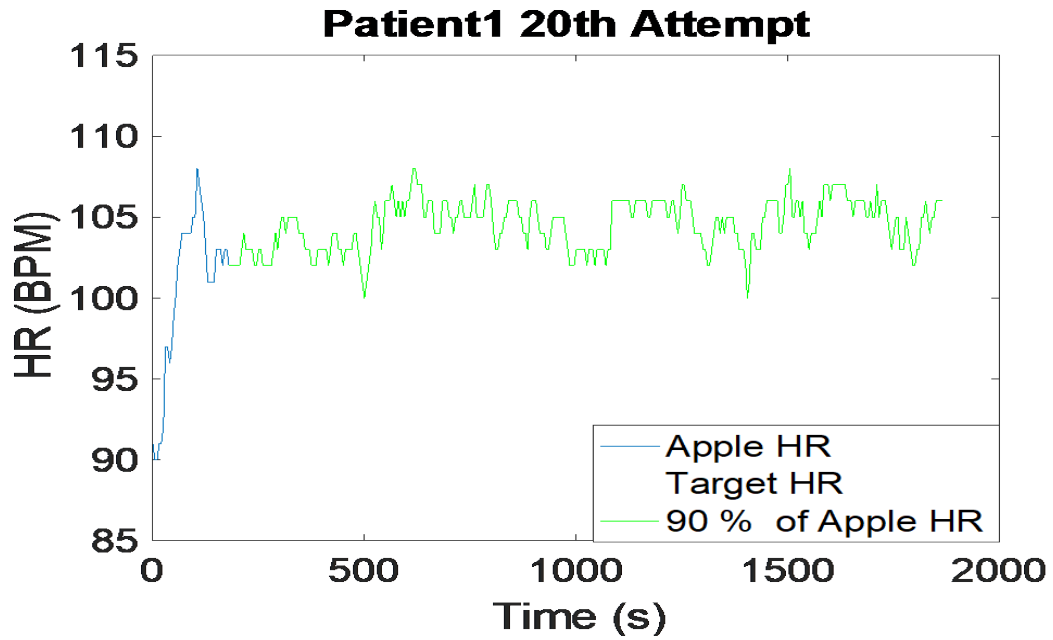


Figure A5.358: Patient No. 1 Week 6 Attempt 3

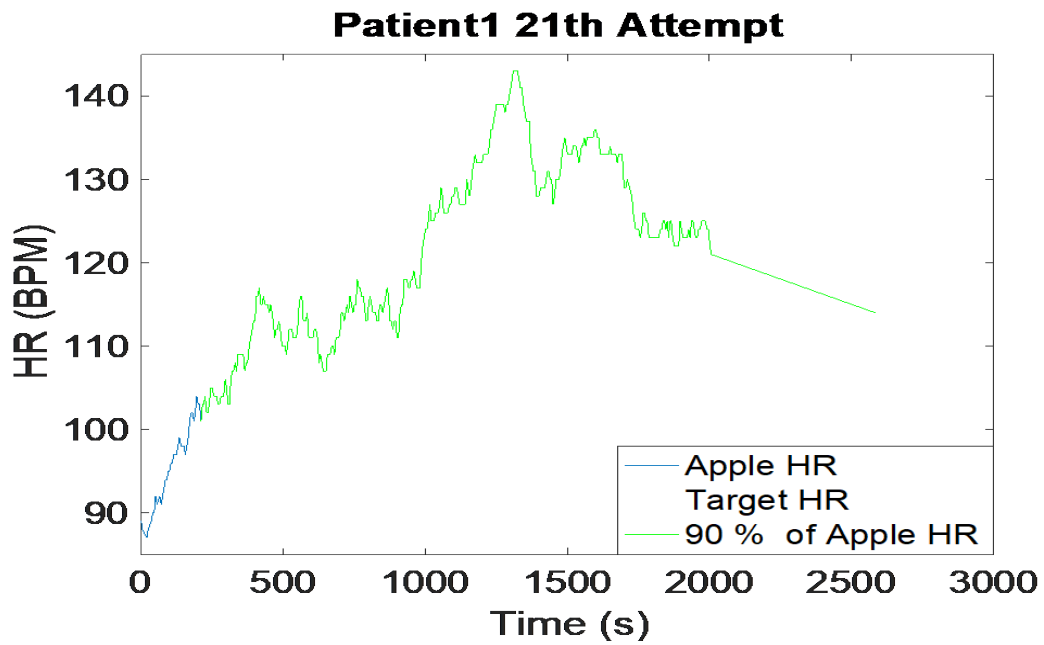


Figure A5.359: Patient No. 1 Week 7 Attempt 1

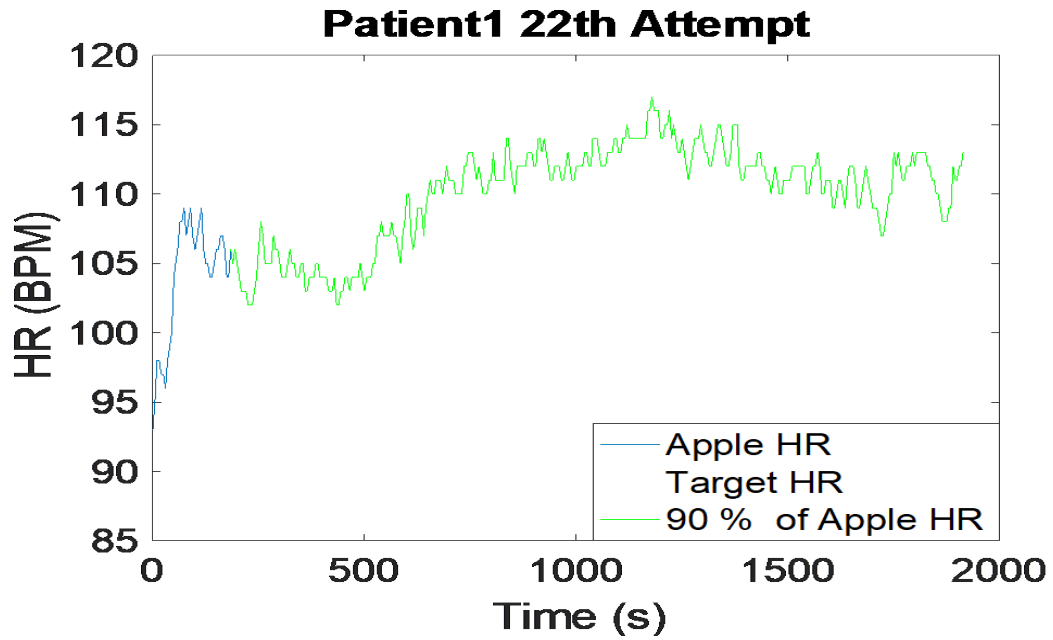


Figure A5.360: Patient No. 1 Week 7 Attempt 2

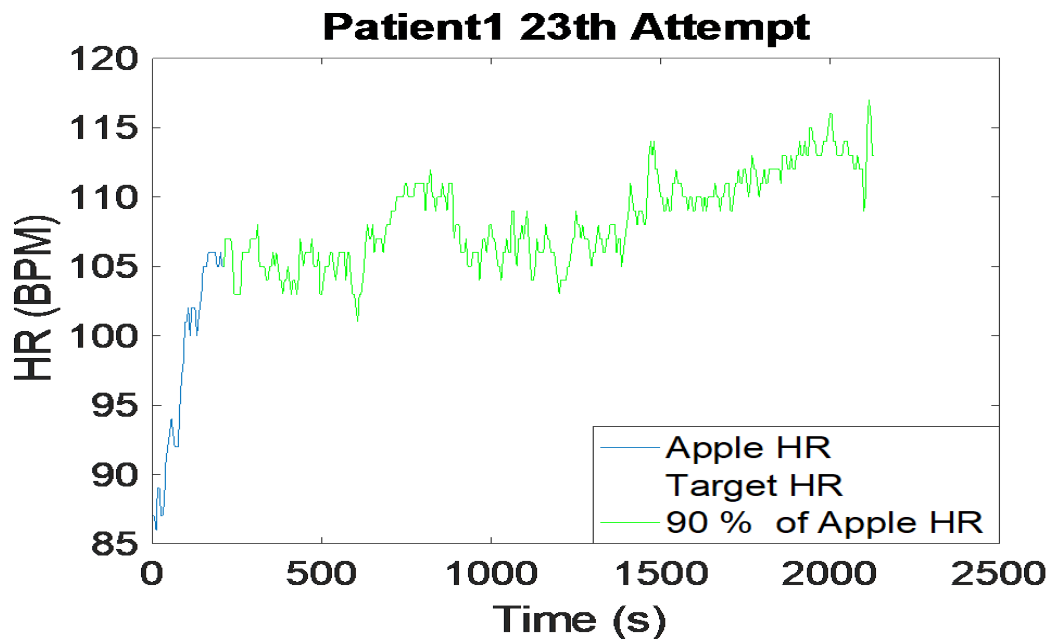


Figure A5.361: Patient No. 1 Week 8 Attempt 1

### Patient1 24th Attempt

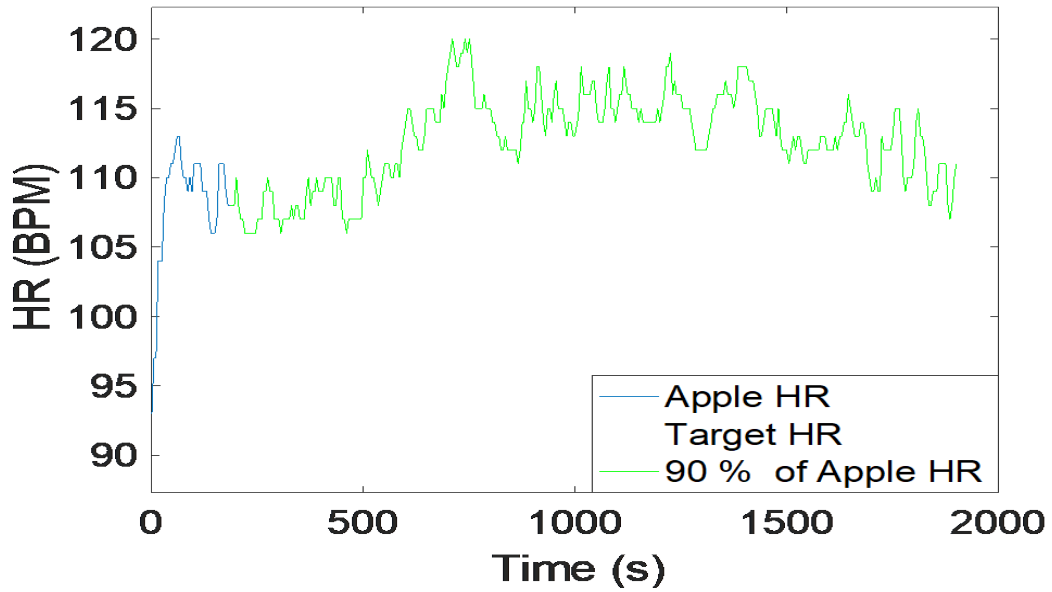


Figure A5.362: Patient No. 1 Week 8 Attempt 2

### Patient1 25th Attempt

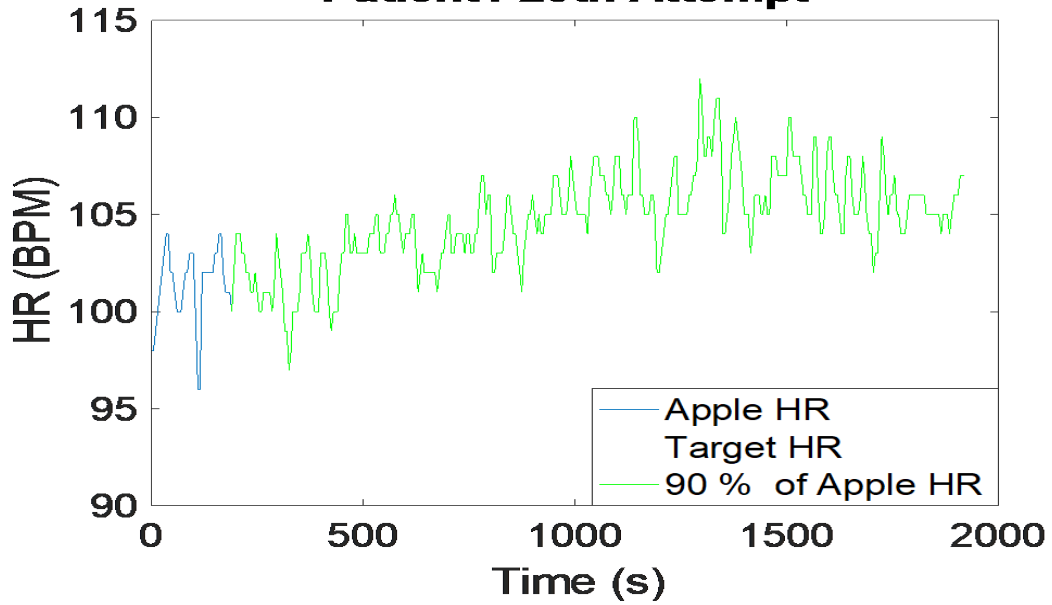


Figure A5.363: Patient No. 1 Week 8 Attempt 3

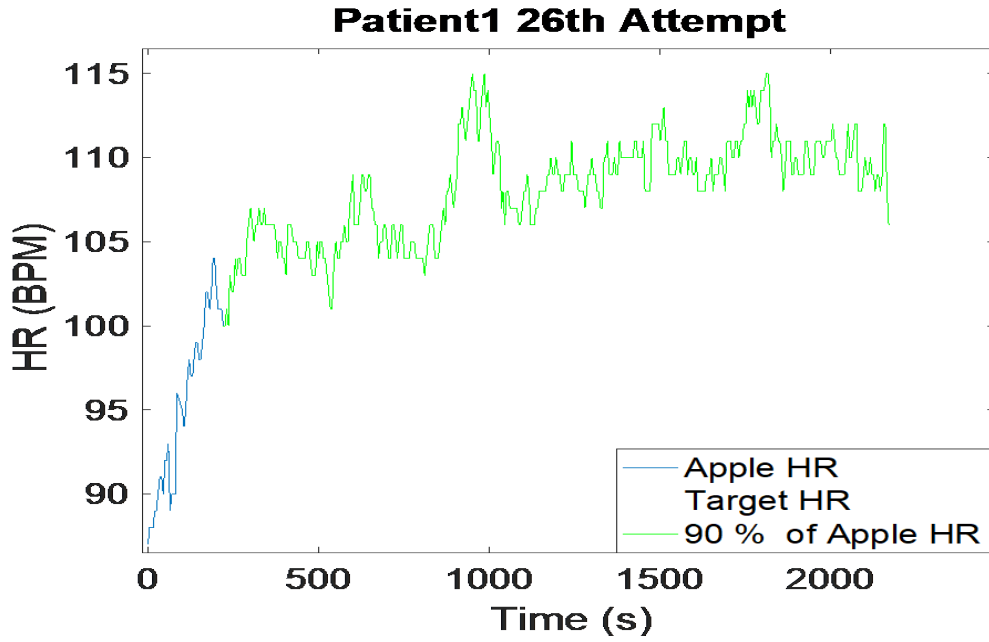


Figure A5.364: Patient No. 1 Week 8 Attempt 4

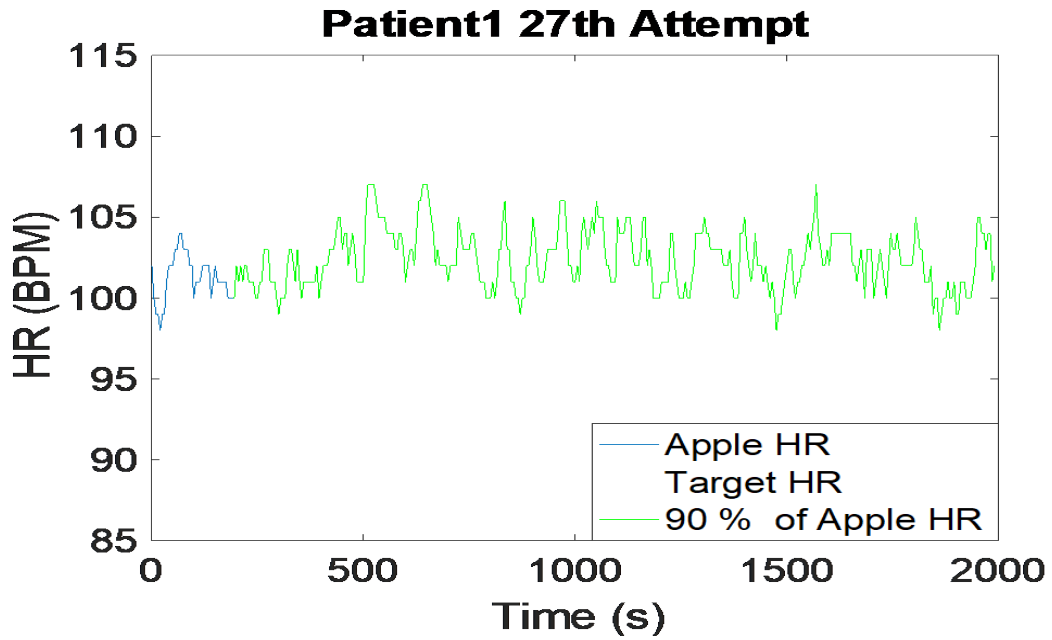


Figure A5.365: Patient No. 1 Week 9 Attempt 1



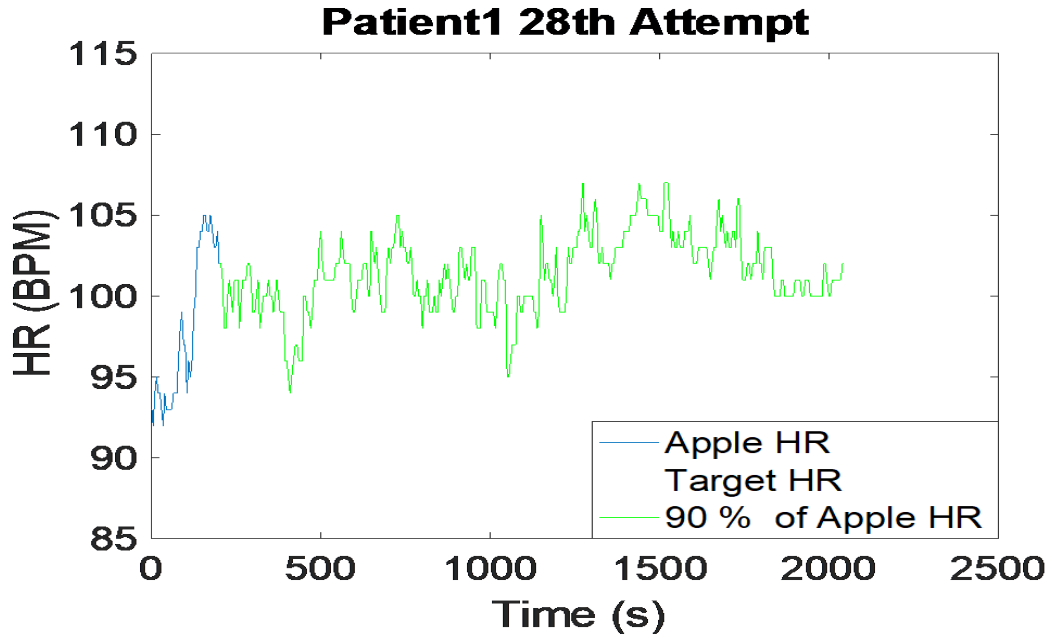


Figure A5.366: Patient No. 1 Week 9 Attempt 2

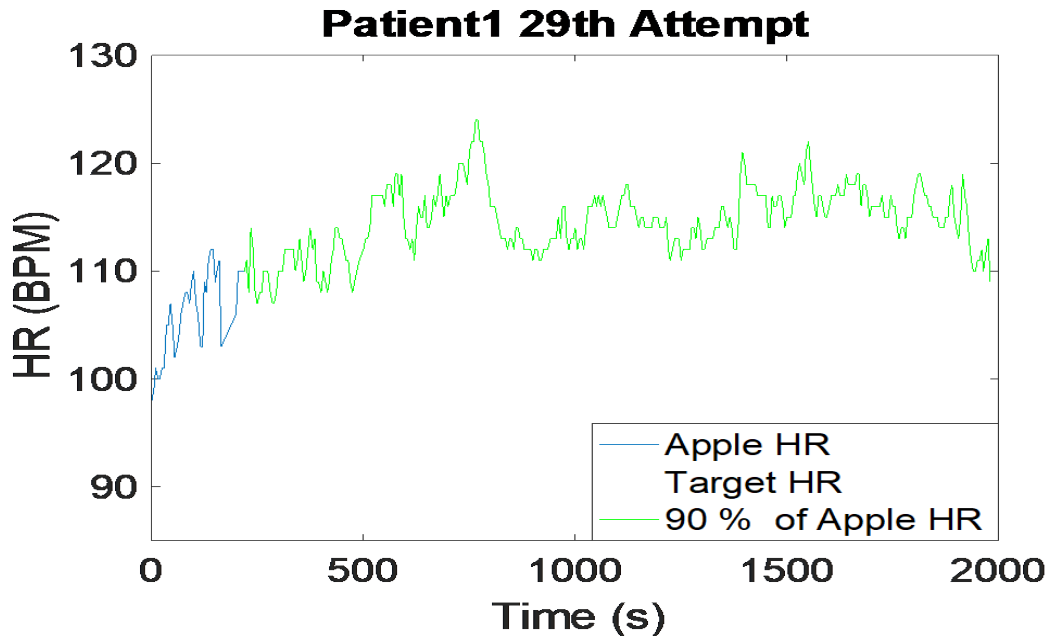
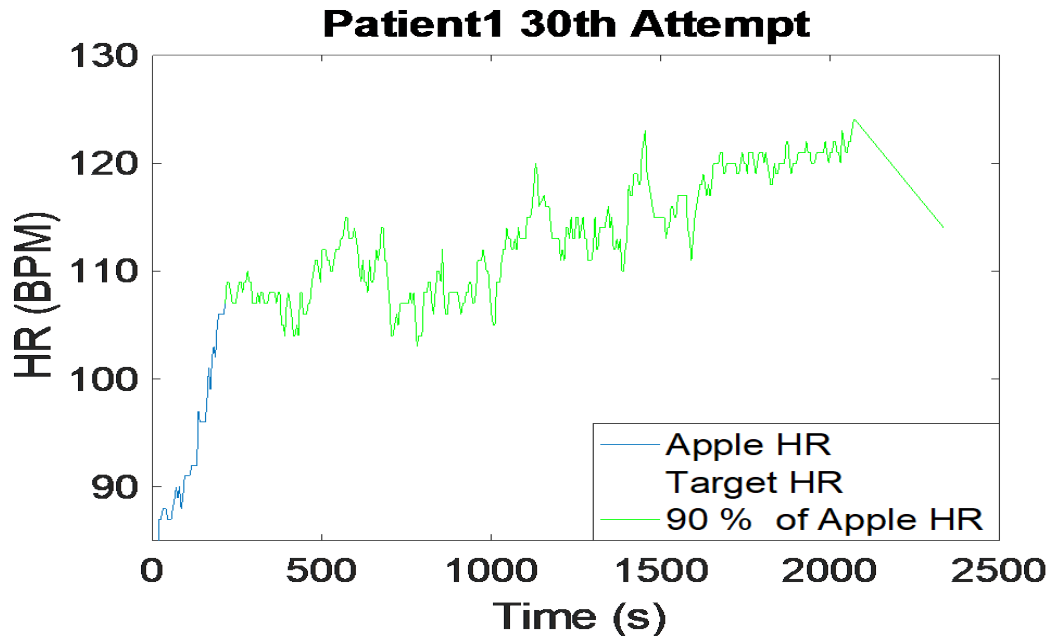
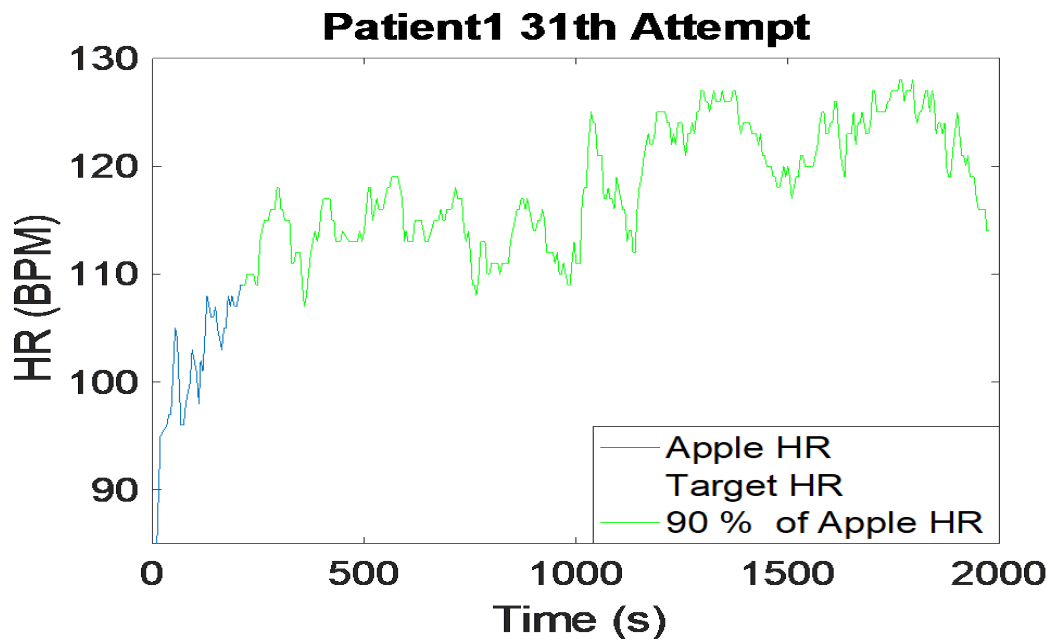


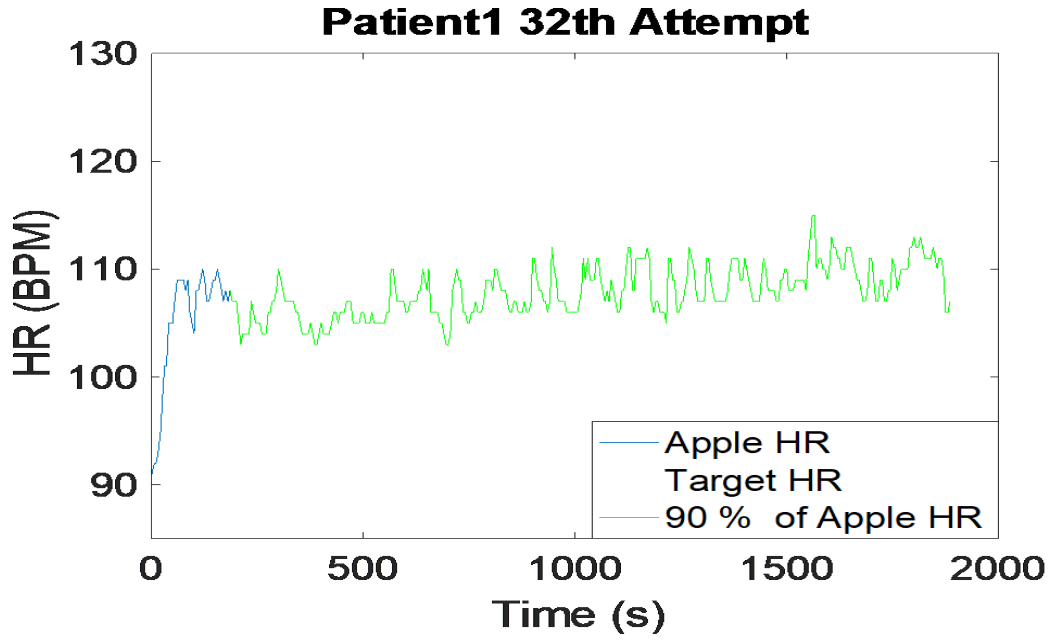
Figure A5.367: Patient No. 1 Week 9 Attempt 3



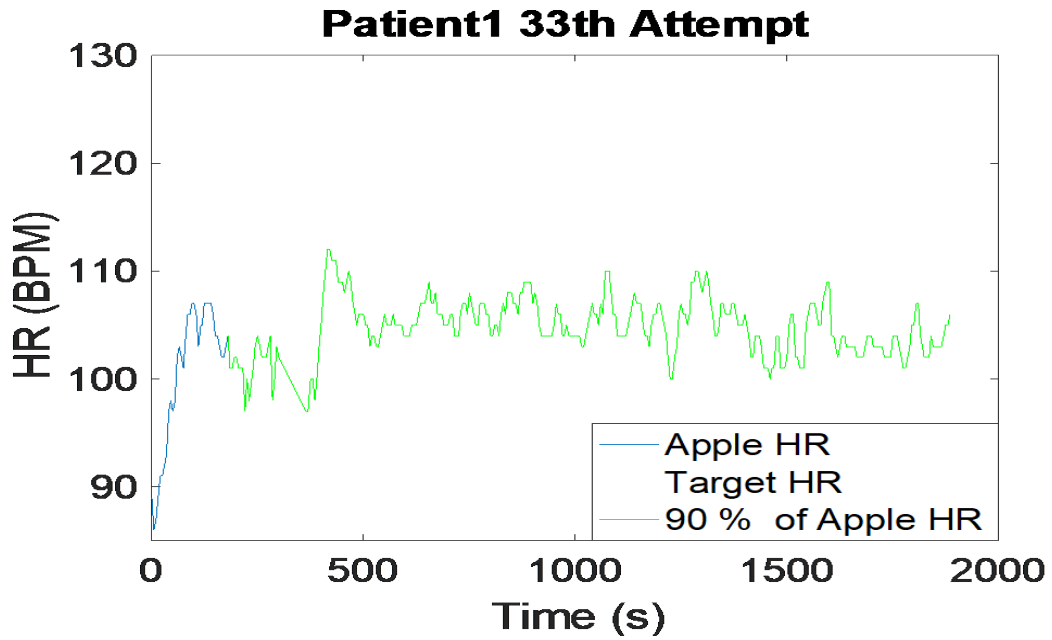
*Figure A5.368: Patient No. 1 Week 9 Attempt 4*



*Figure A5.369: Patient No. 1 Week 10 Attempt 1*



*Figure A5.370: Patient No. 1 Week 10 Attempt 2*



*Figure A5.371: Patient No. 1 Week 10 Attempt 3*

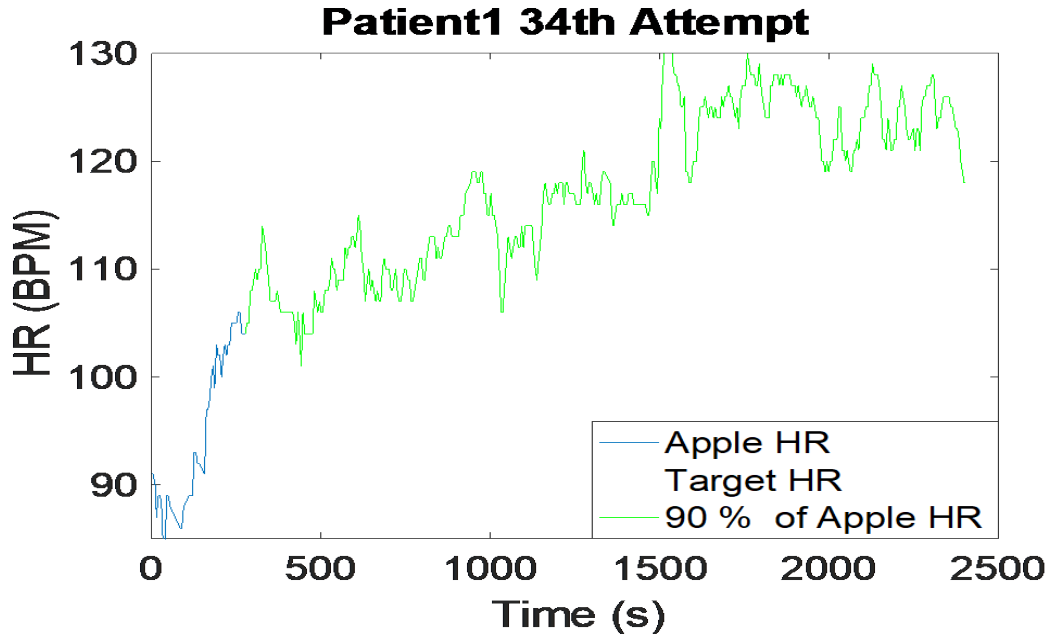


Figure A5.372: Patient No. 1 Week 10 Attempt 4

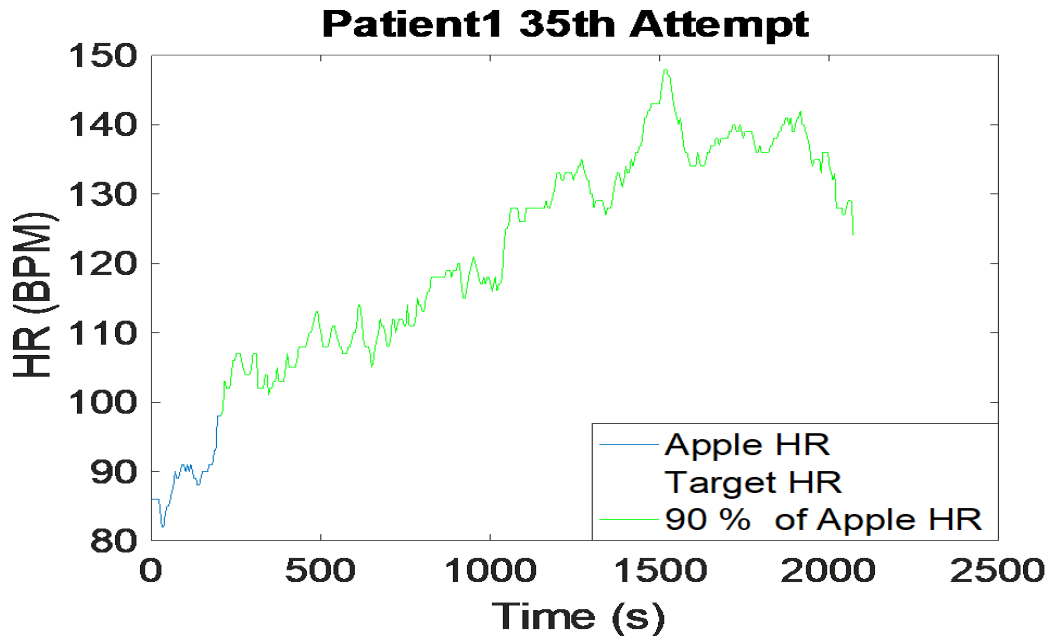


Figure A5.373: Patient No. 1 Week 11 Attempt 1

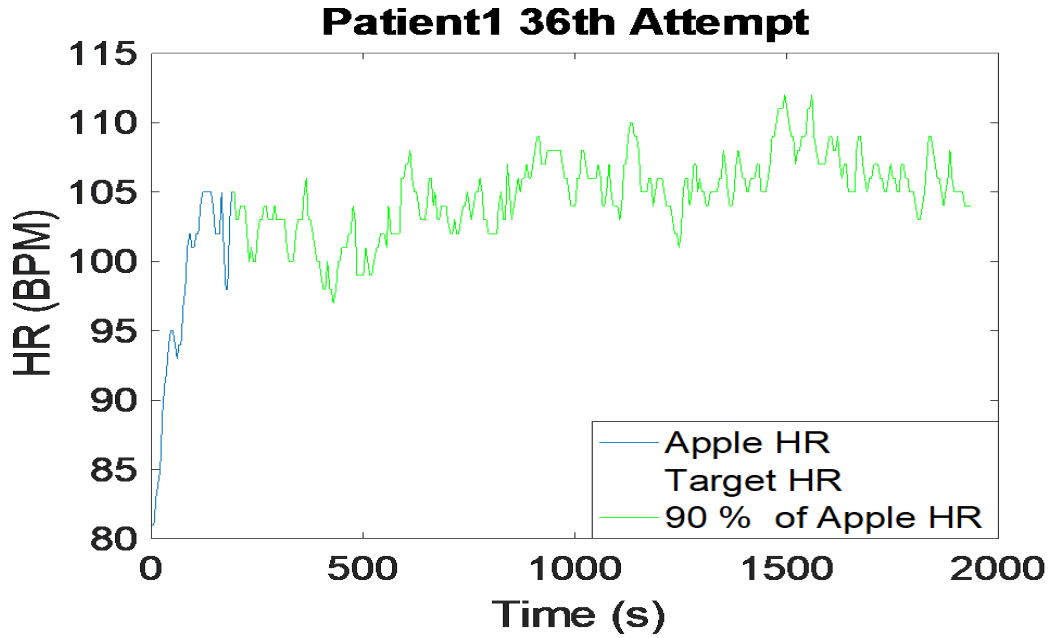


Figure A5.374: Patient No. 1 Week 11 Attempt 2

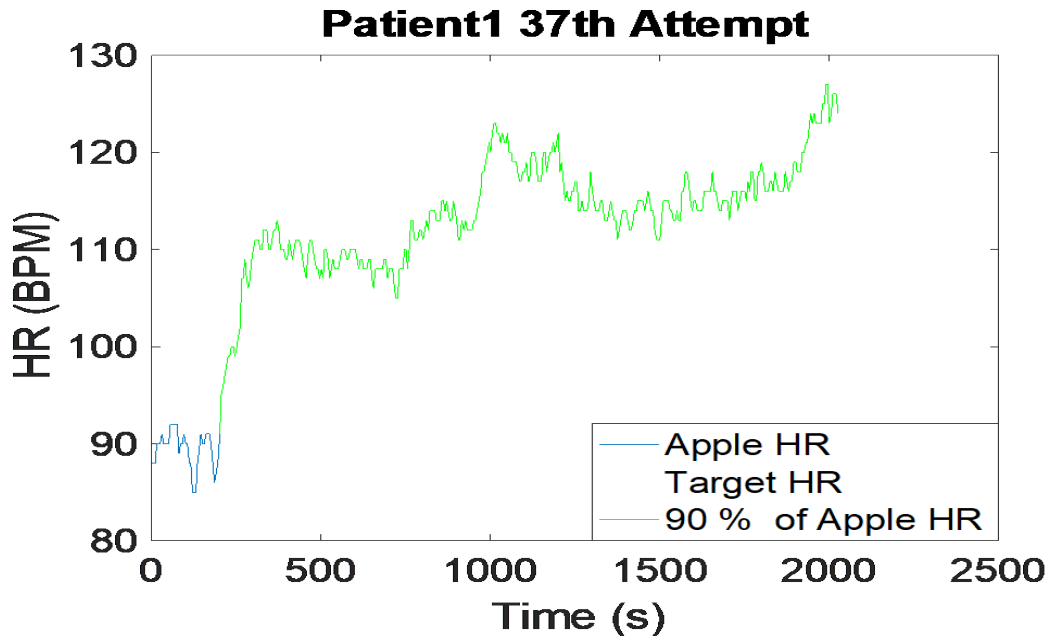
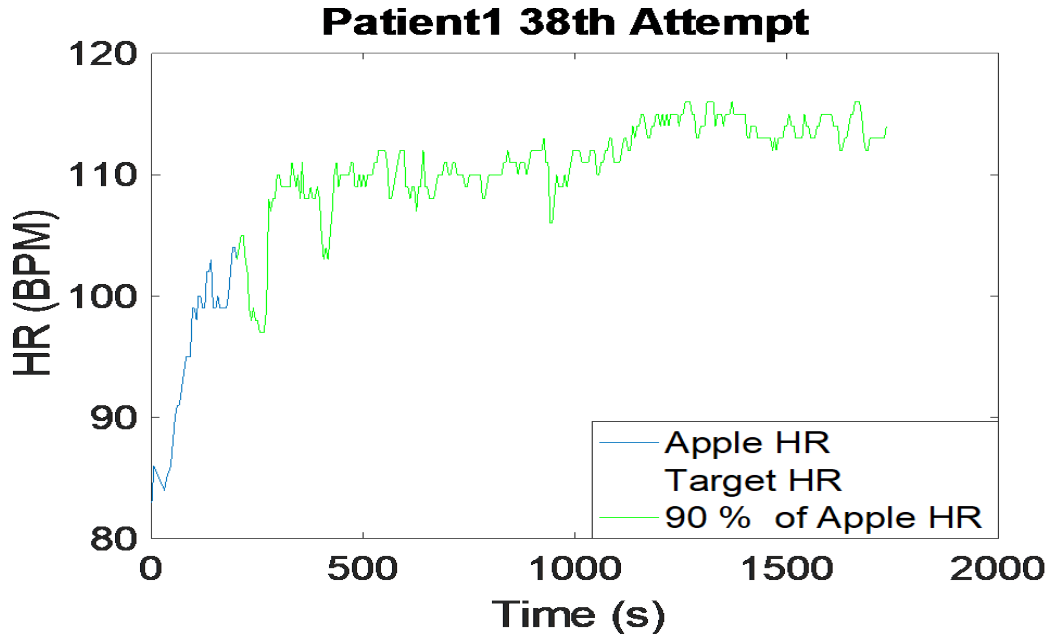
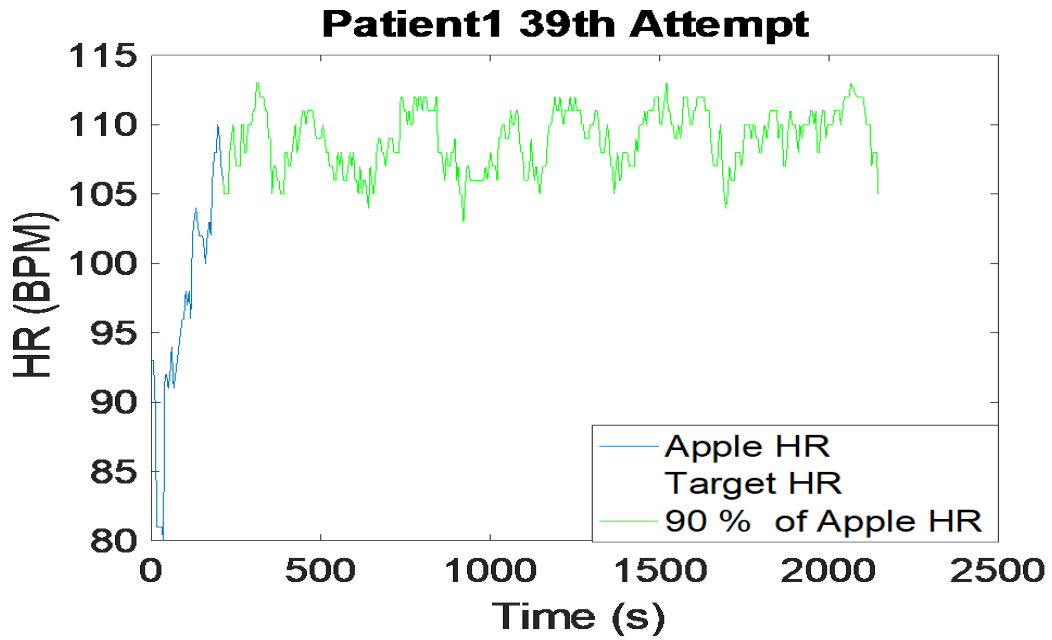


Figure A5.375: Patient No. 1 Week 11 Attempt 3



*Figure A5.376: Patient No. 1 Week 11 Attempt 4*



*Figure A5.377: Patient No. 1 Week 12 Attempt 1*

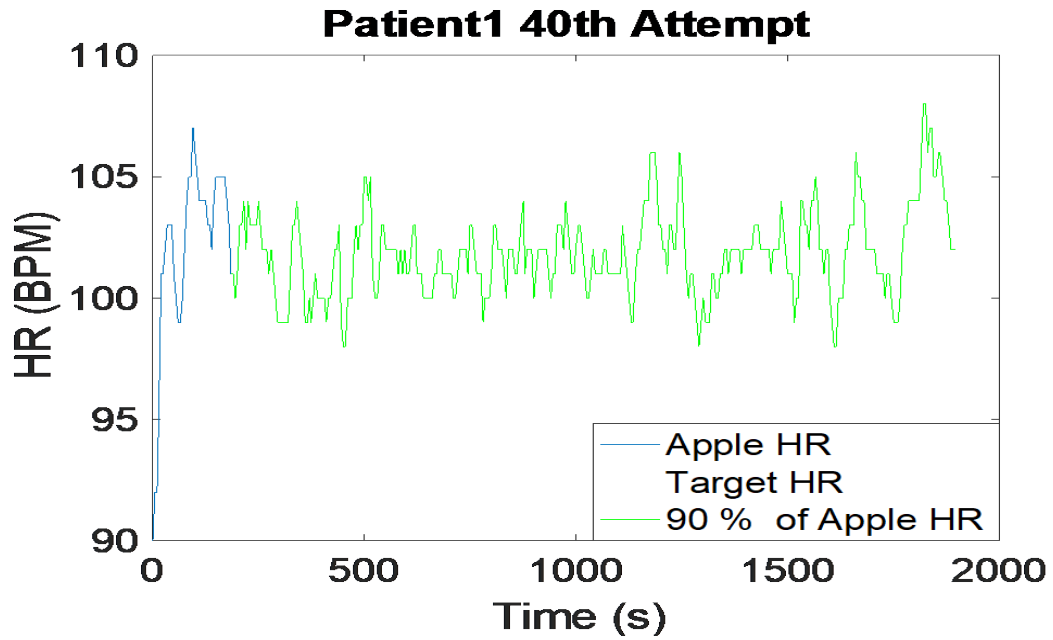


Figure A5.378: Patient No. 1 Week 12 Attempt 2

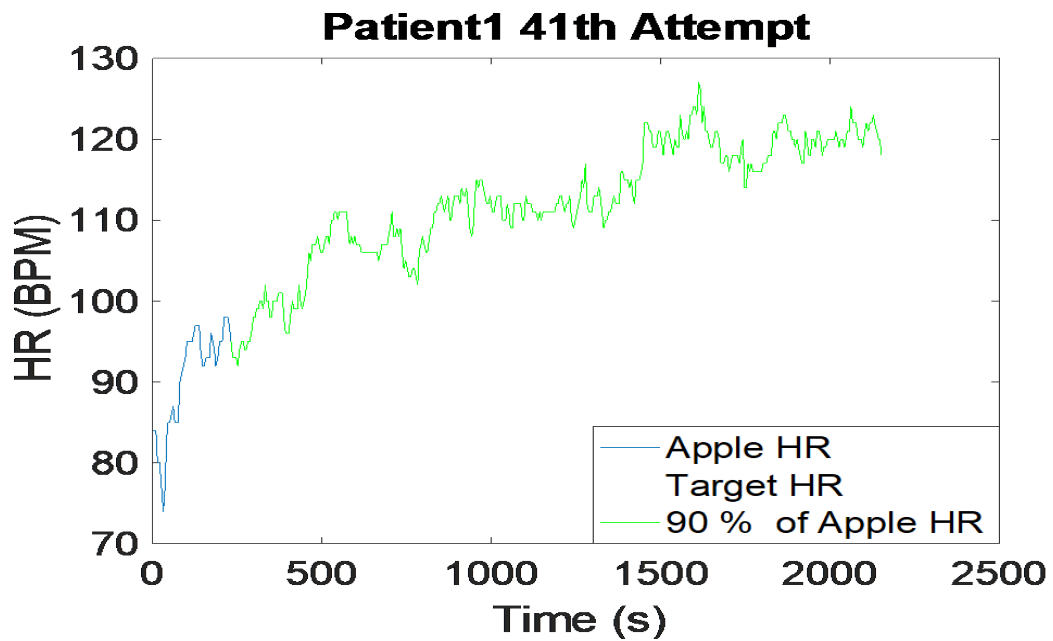


Figure A5.379: Patient No. 1 Week 12 Attempt 3

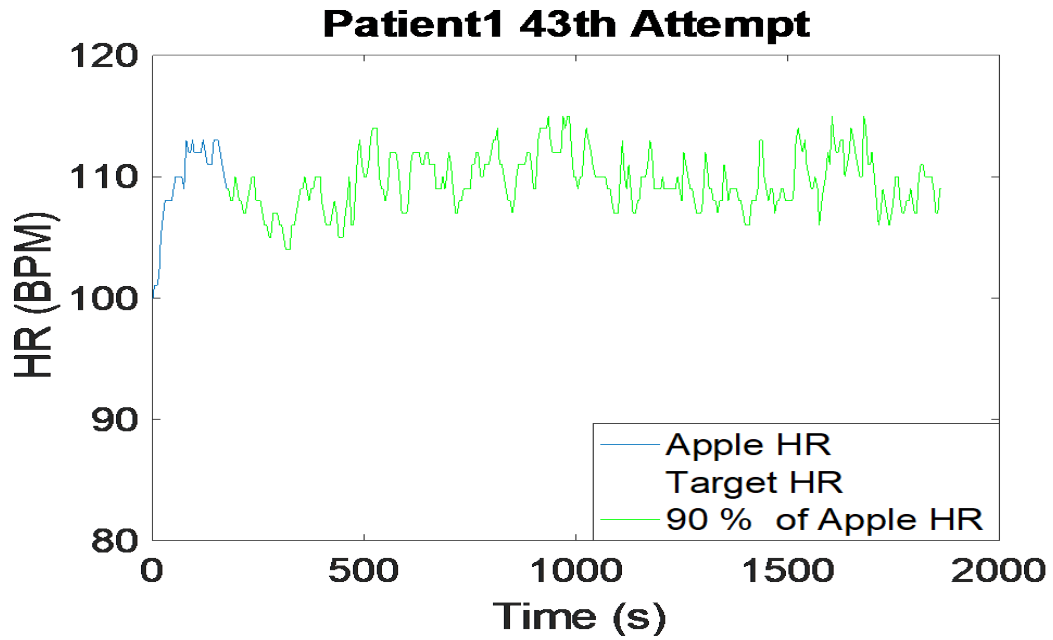


Figure A5.380: Patient No. 1 Week 13 Attempt 1

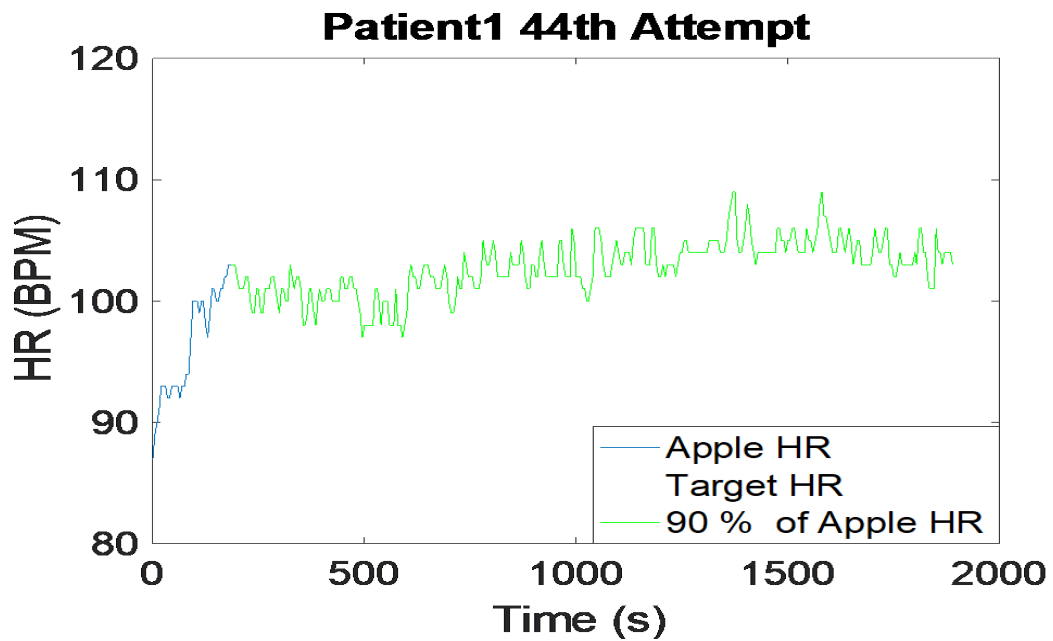


Figure A5.381: Patient No. 1 Week 13 Attempt 2



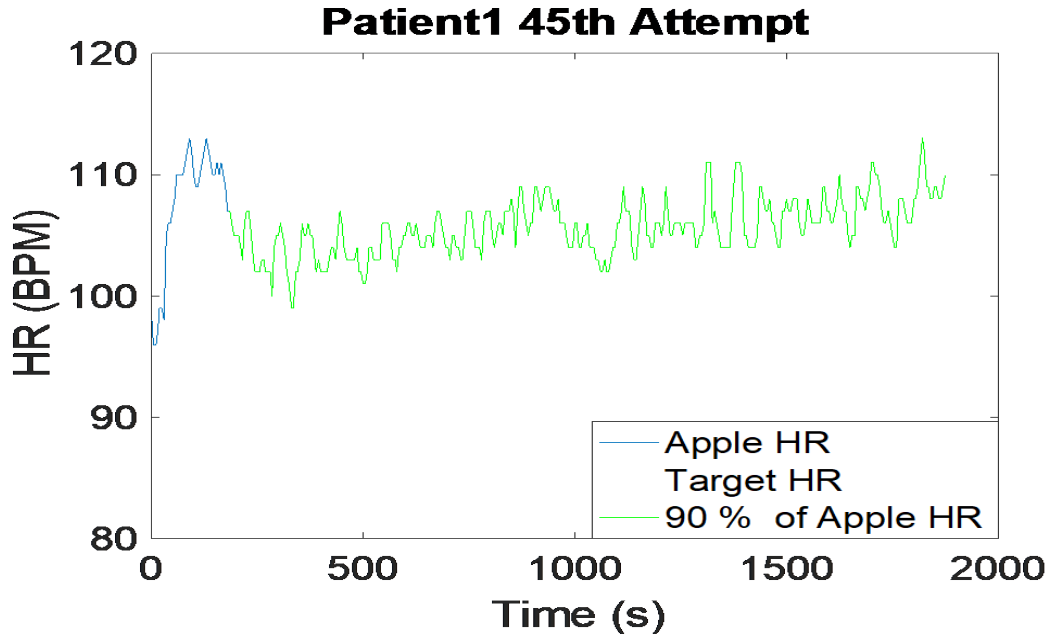


Figure A5.382: Patient No. 1 Week 13 Attempt 3

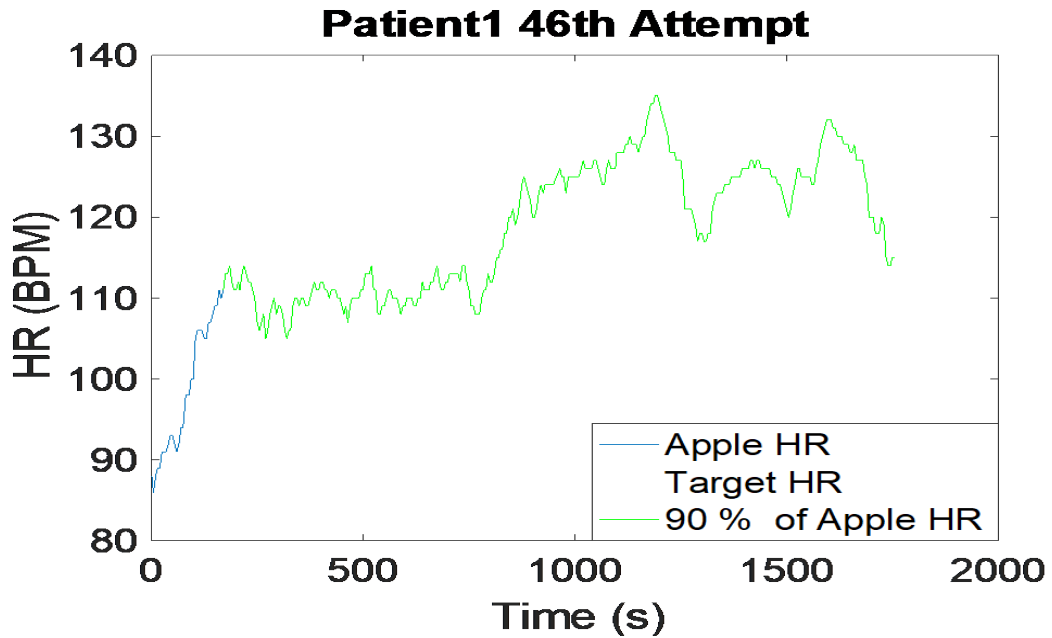
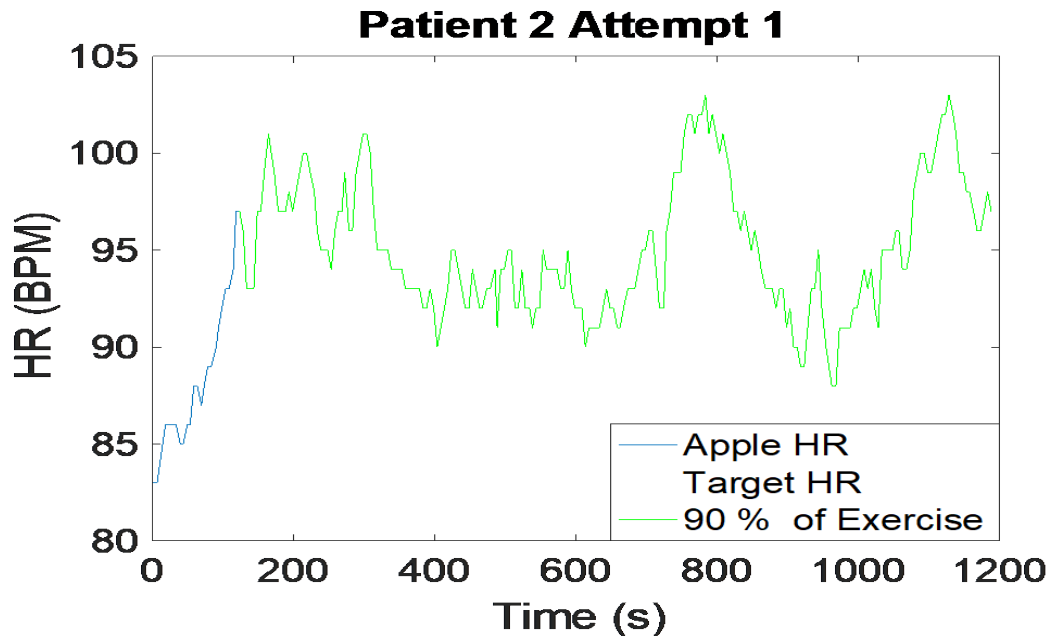
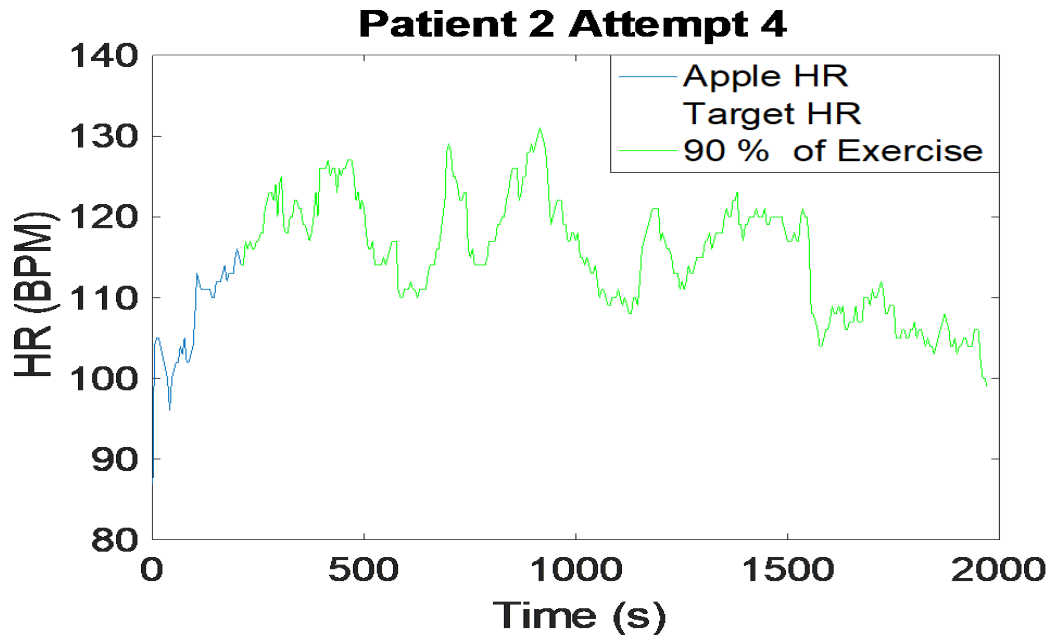


Figure A5.383: Patient No. 1 Week 13 Attempt 4

**Patient 2 Attempts:**



*Figure A5.384: Patient No. 2 Week 1 Attempt 1*



*Figure A5.385: Patient No. 2 Week 2 Attempt 1*

### Patient 2 Attempt 5

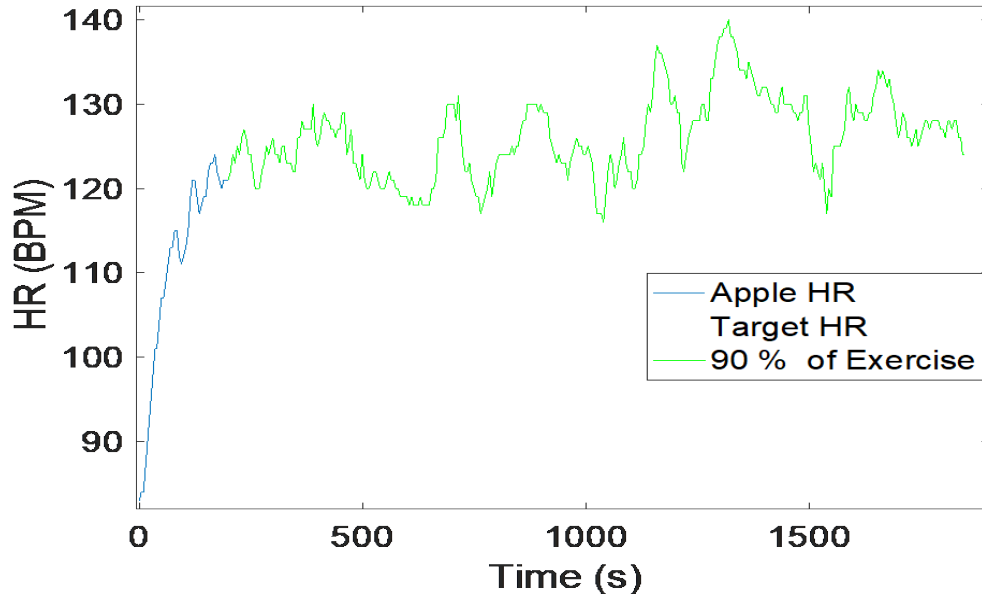


Figure A5.386: Patient No. 2 Week 2 Attempt 2

### Patient 2 Attempt 6

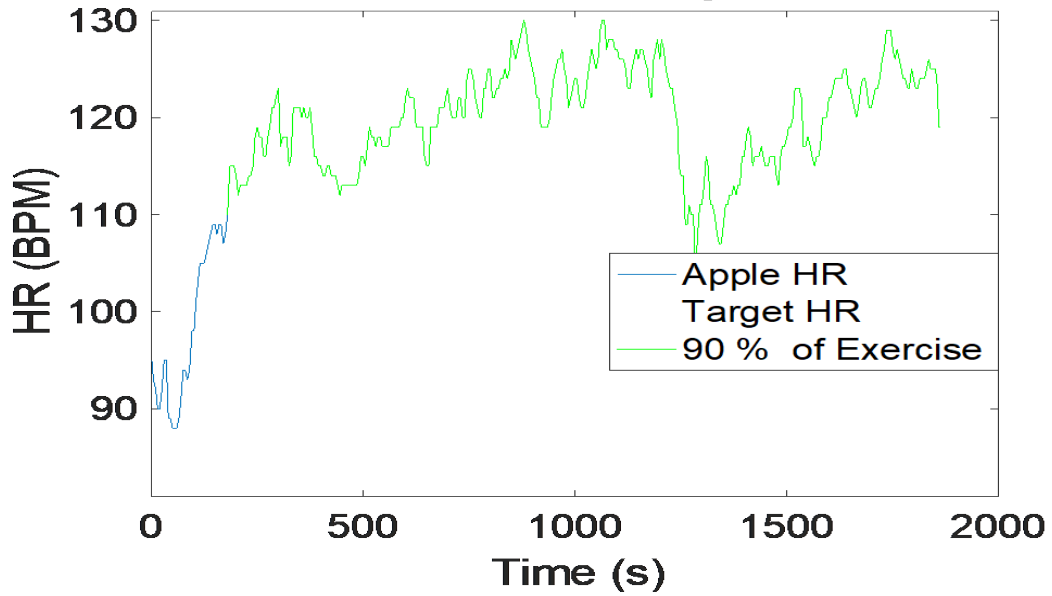


Figure A5.387: Patient No. 2 Week 2 Attempt 3

### Patient 2 Attempt 7

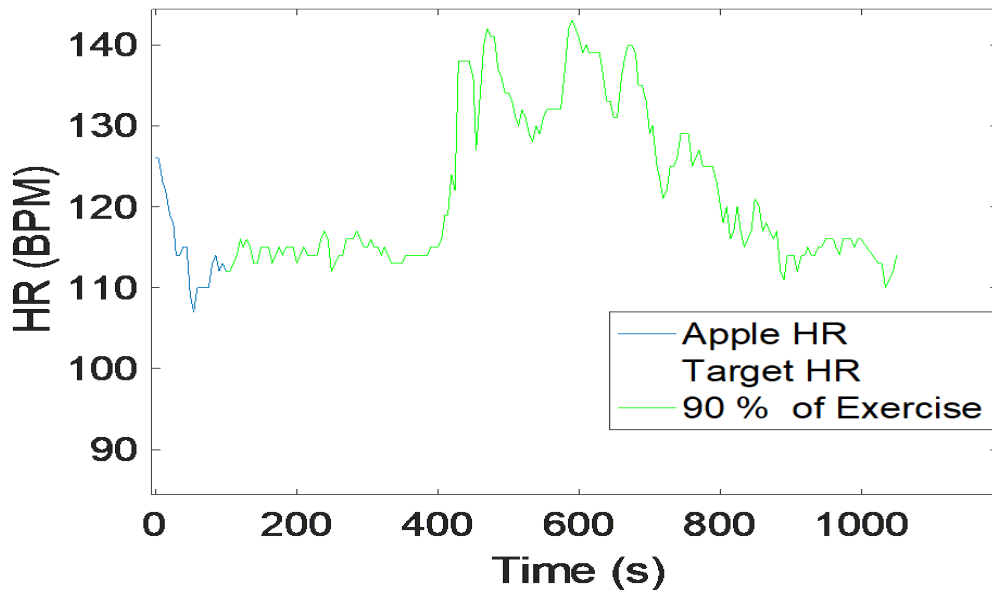


Figure A5.388: Patient No. 2 Week 3 Attempt 1

### Patient 2 Attempt 8

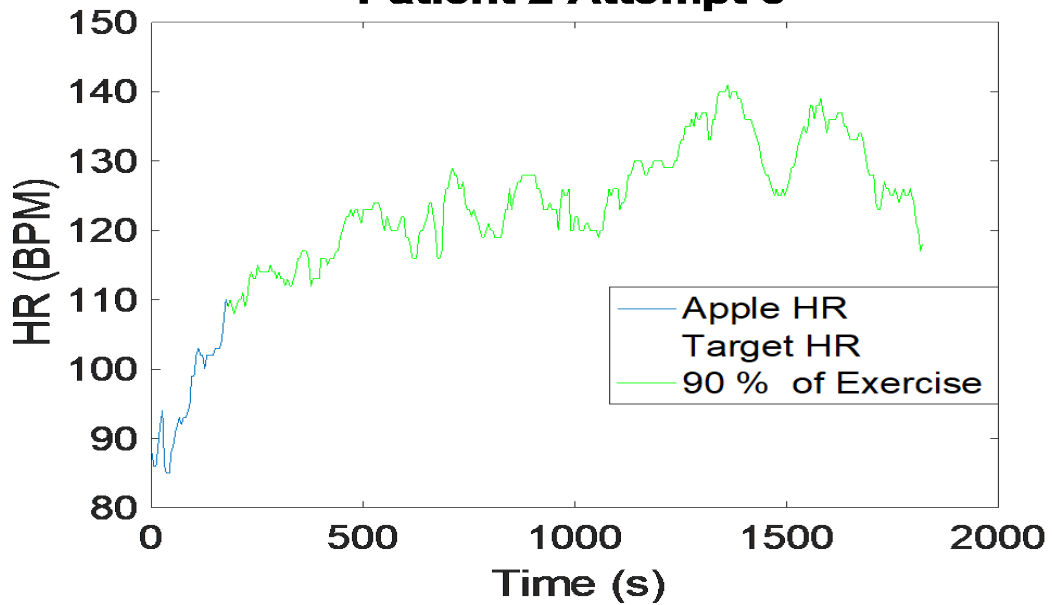


Figure A5.389: Patient No. 2 Week 3 Attempt 2

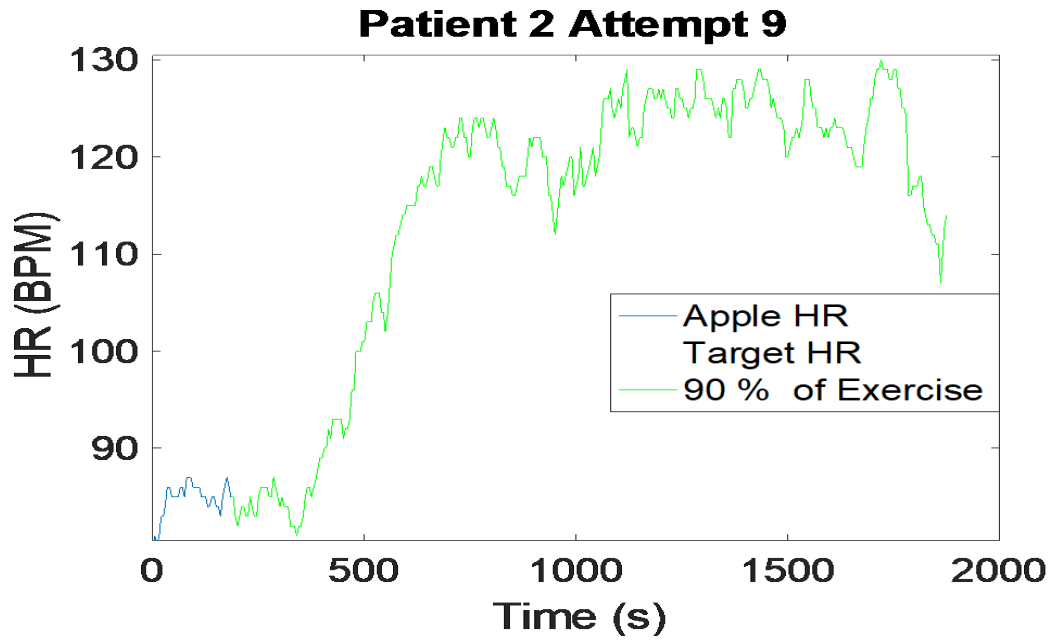


Figure A5.390: Patient No. 2 Week 3 Attempt 3

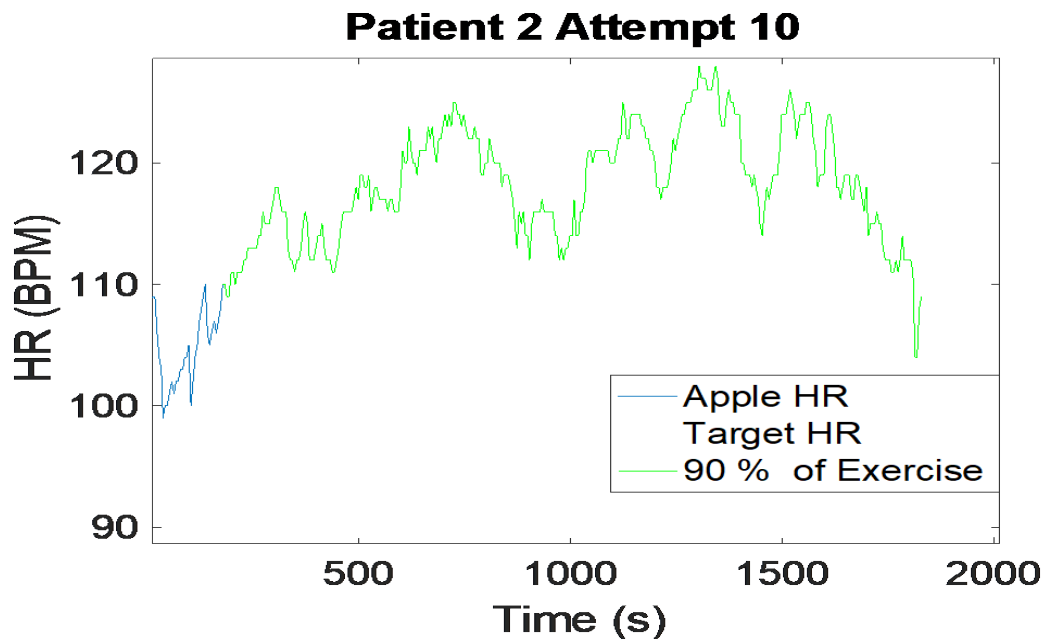


Figure A5.391: Patient No. 2 Week 4 Attempt 1

### Patient 2 Attempt 11

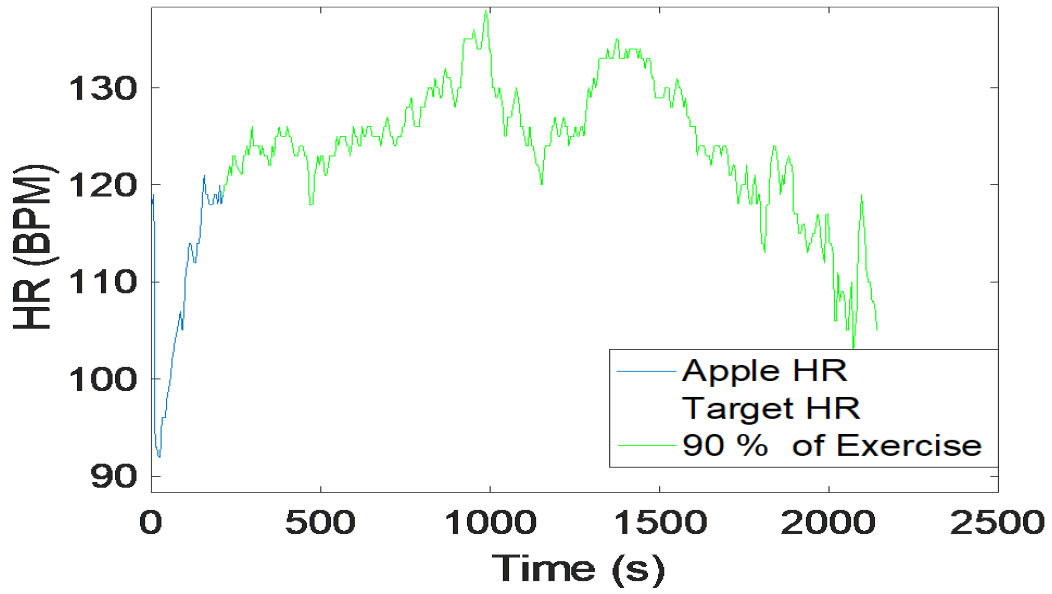


Figure A5.392: Patient No. 2 Week 4 Attempt 2

### Patient 2 Attempt 12

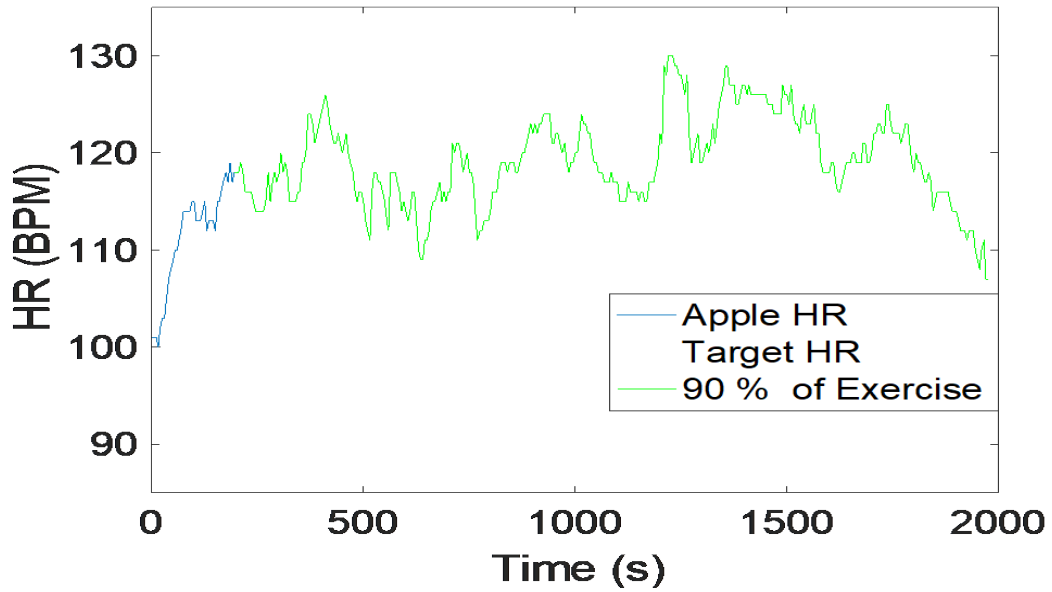
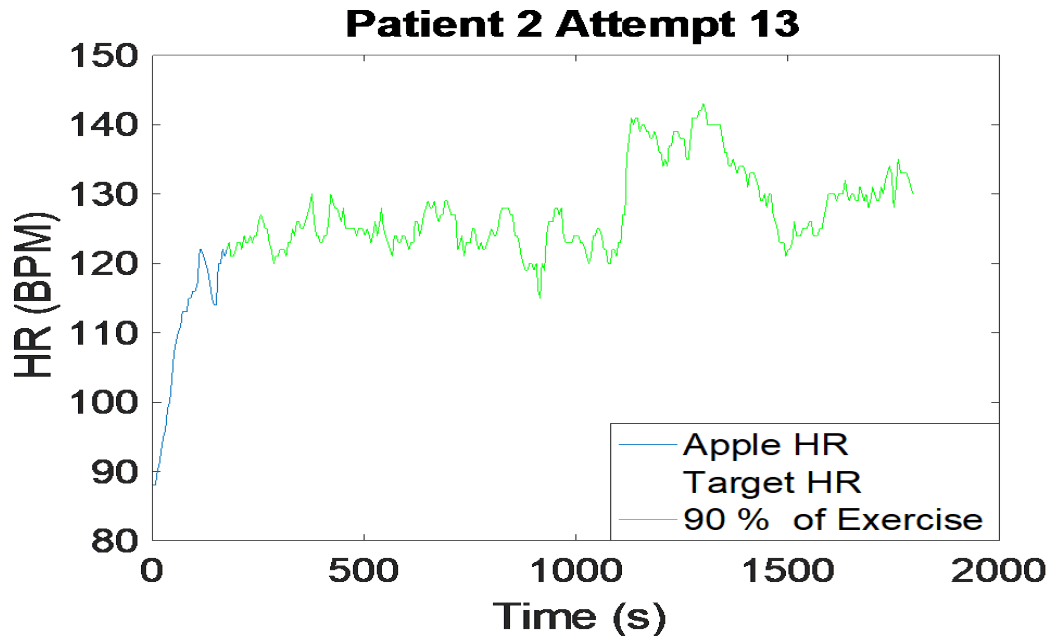
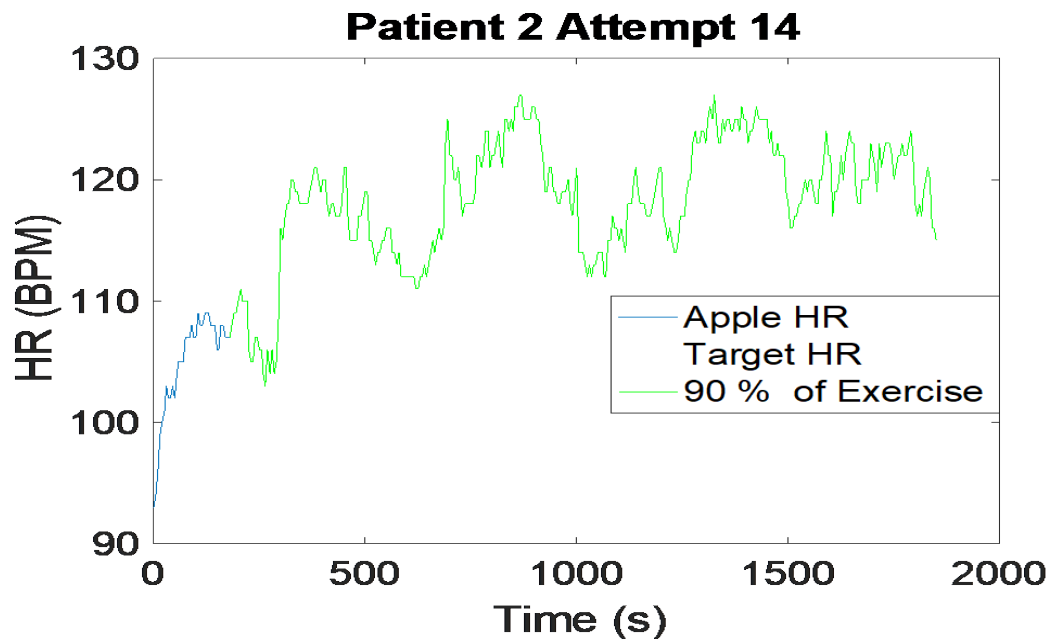


Figure A5.393: Patient No. 2 Week 4 Attempt 3



*Figure A5.394: Patient No. 2 Week 5 Attempt 1*



*Figure A5.395: Patient No. 2 Week 5 Attempt 2*

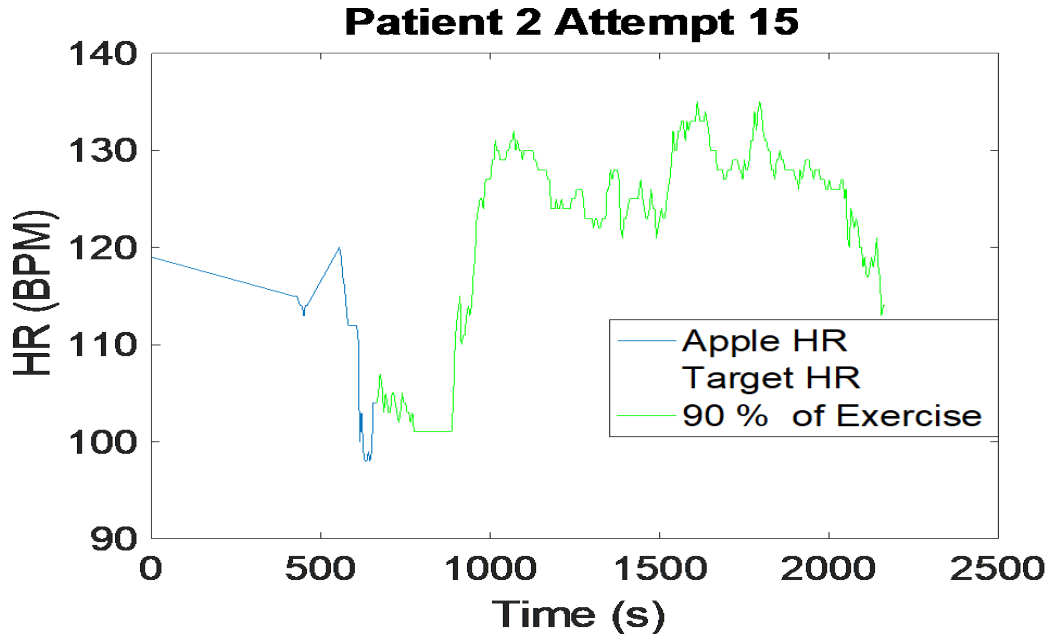


Figure A5.396: Patient No. 2 Week 5 Attempt 3

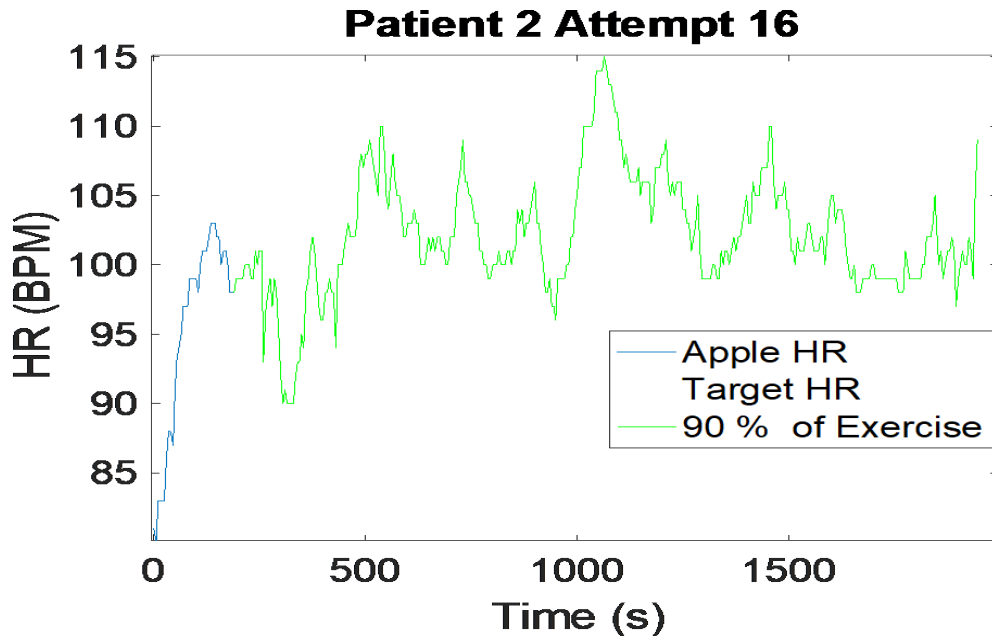


Figure A5.397: Patient No. 2 Week 5 Attempt 4



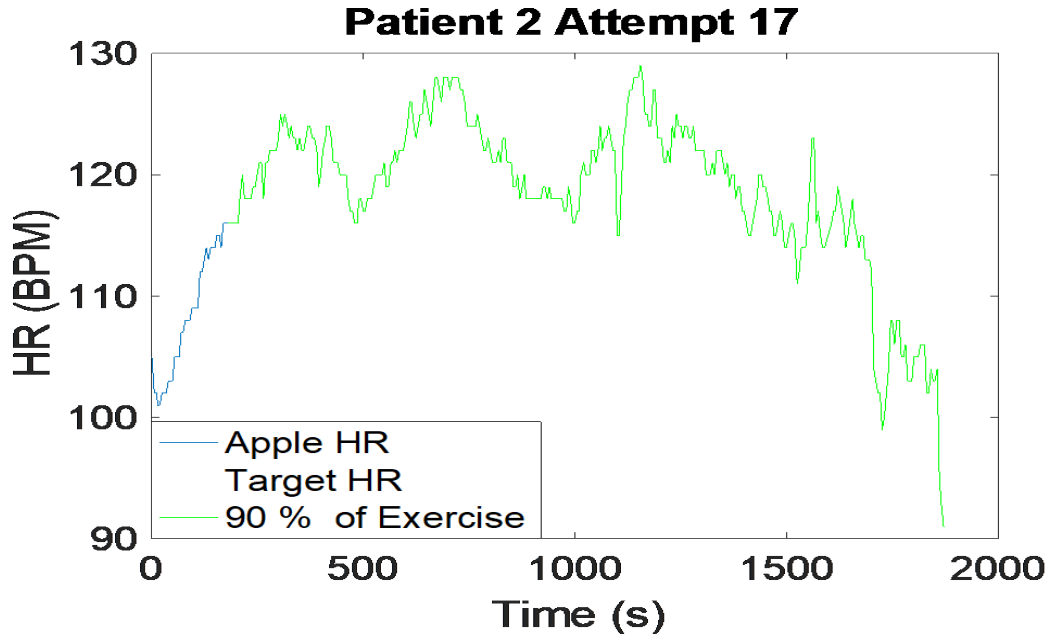


Figure A5.398: Patient No. 2 Week 6 Attempt 1

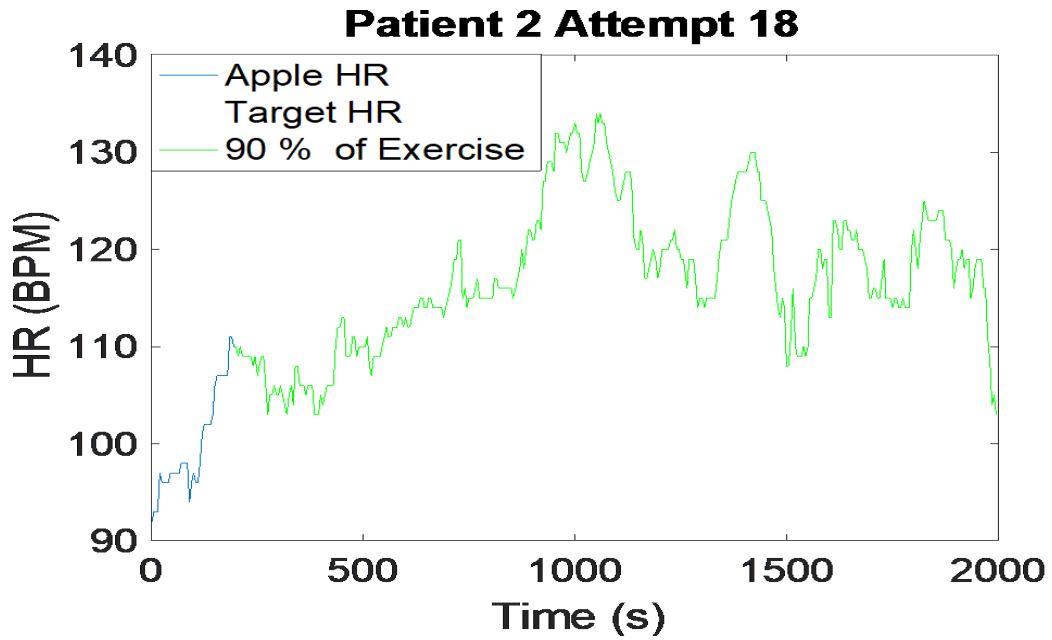
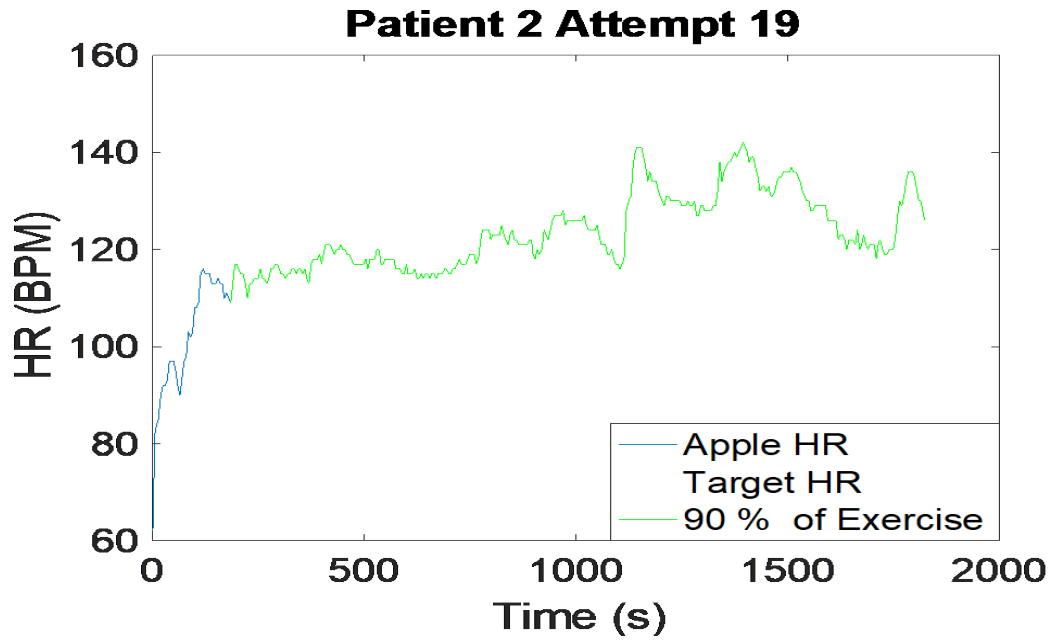
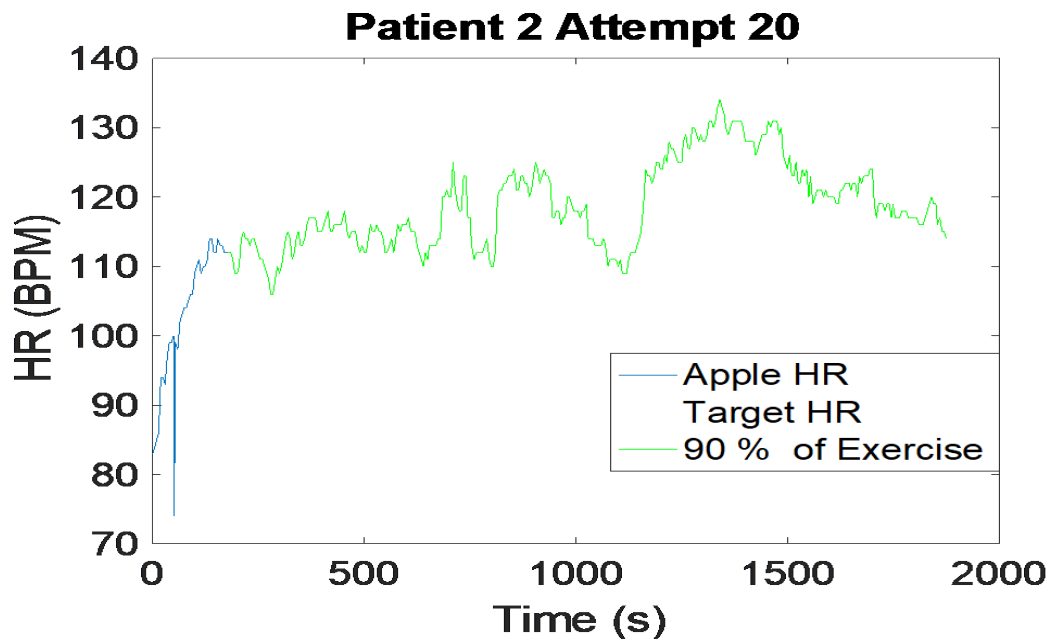


Figure A5.399: Patient No. 2 Week 6 Attempt 2



*Figure A5.400: Patient No. 2 Week 6 Attempt 3*



*Figure A5.401: Patient No. 2 Week 6 Attempt 4*

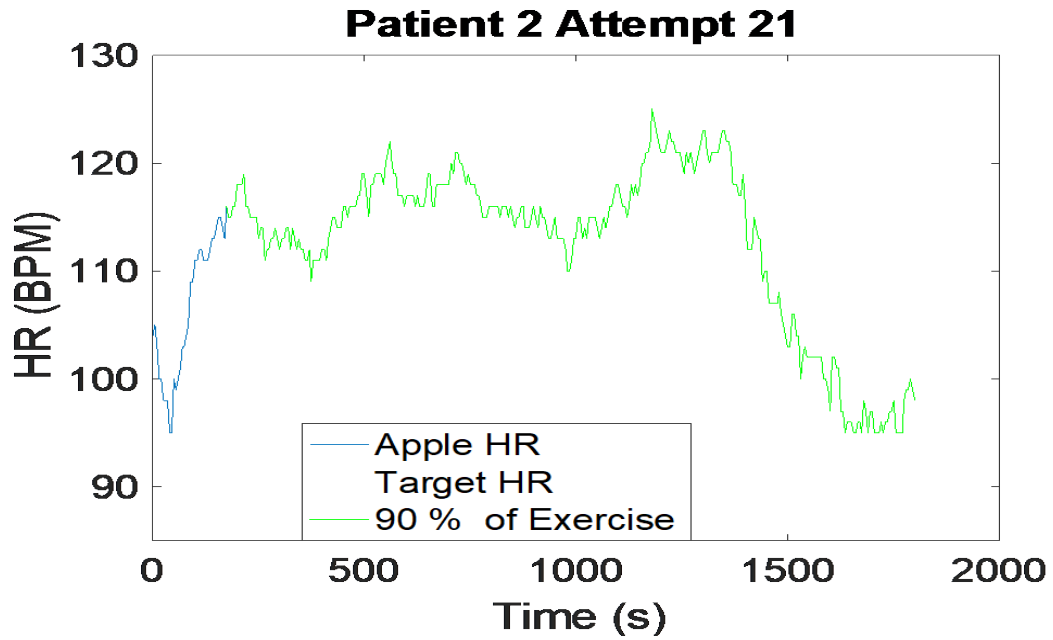


Figure A5.402: Patient No. 2 Week 7 Attempt 1

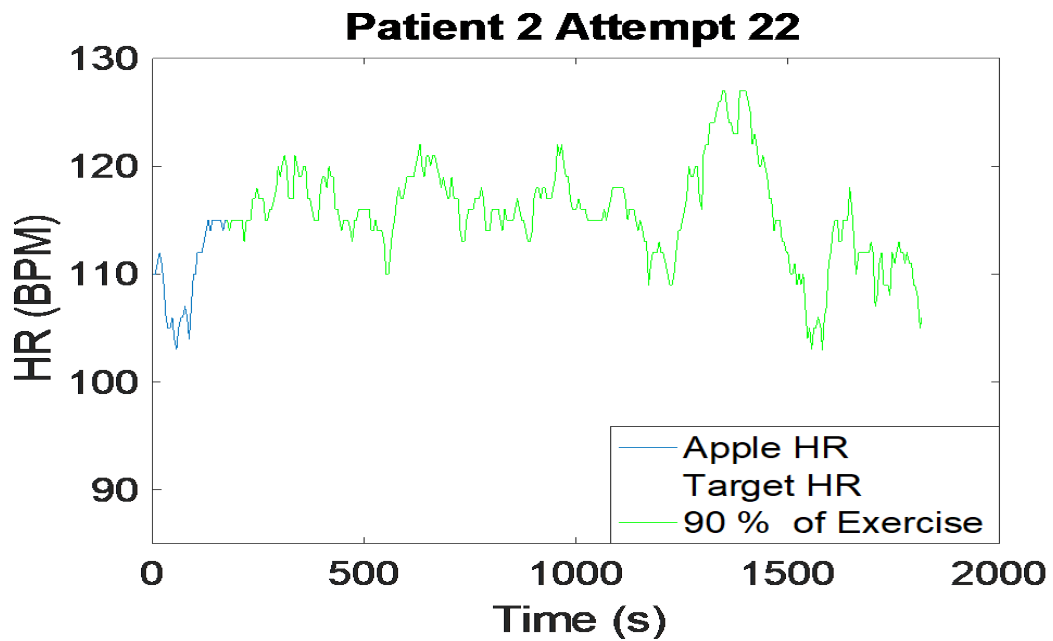


Figure A5.403: Patient No. 2 Week 7 Attempt 2

### Patient 2 Attempt 23

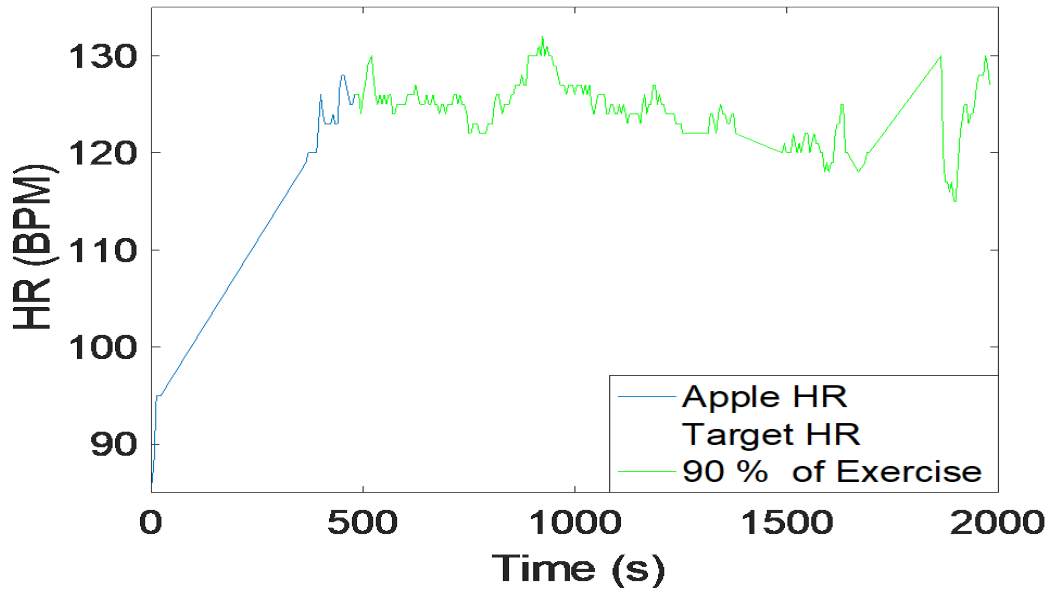


Figure A5.404: Patient No. 2 Week 7 Attempt 3

### Patient 2 Attempt 24

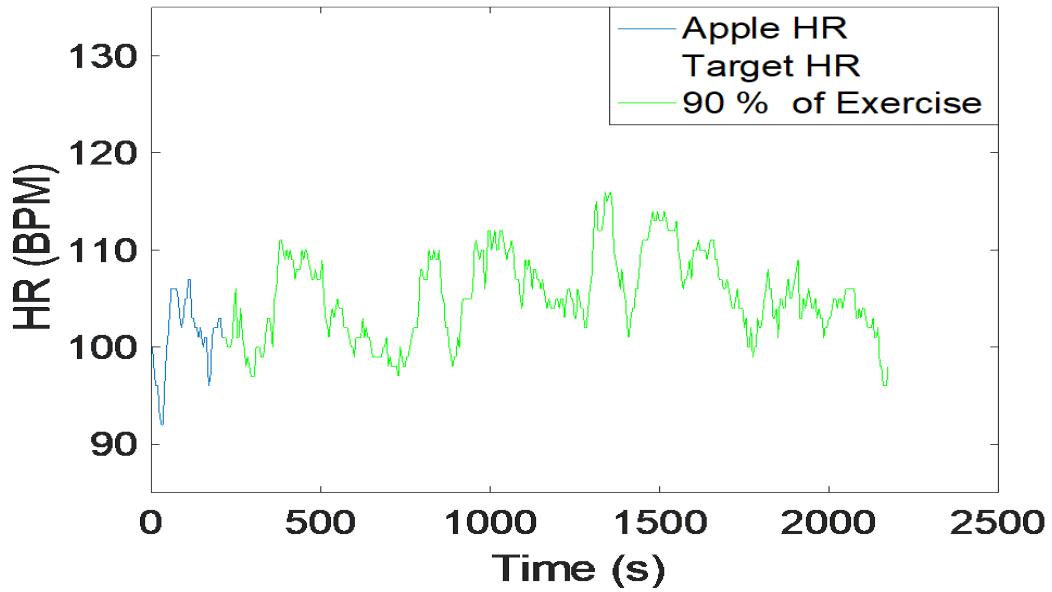


Figure A5.405: Patient No. 2 Week 7 Attempt 4

### Patient 2 Attempt 25

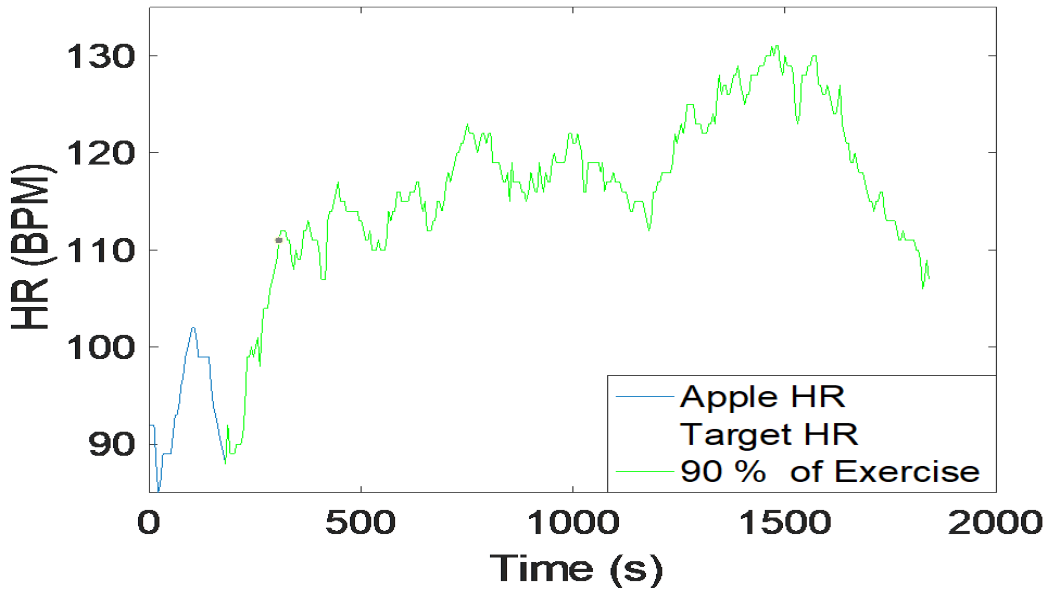


Figure A5.406: Patient No. 2 Week 8 Attempt 1

### Patient 2 Attempt 26

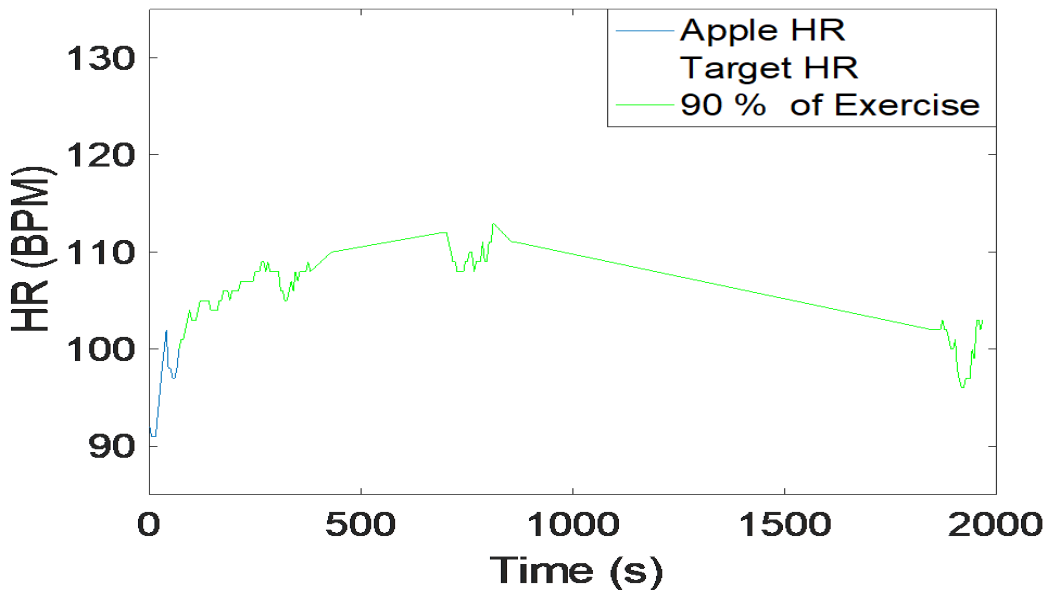


Figure A5.407: Patient No. 2 Week 8 Attempt 2

### Patient 2 Attempt 27

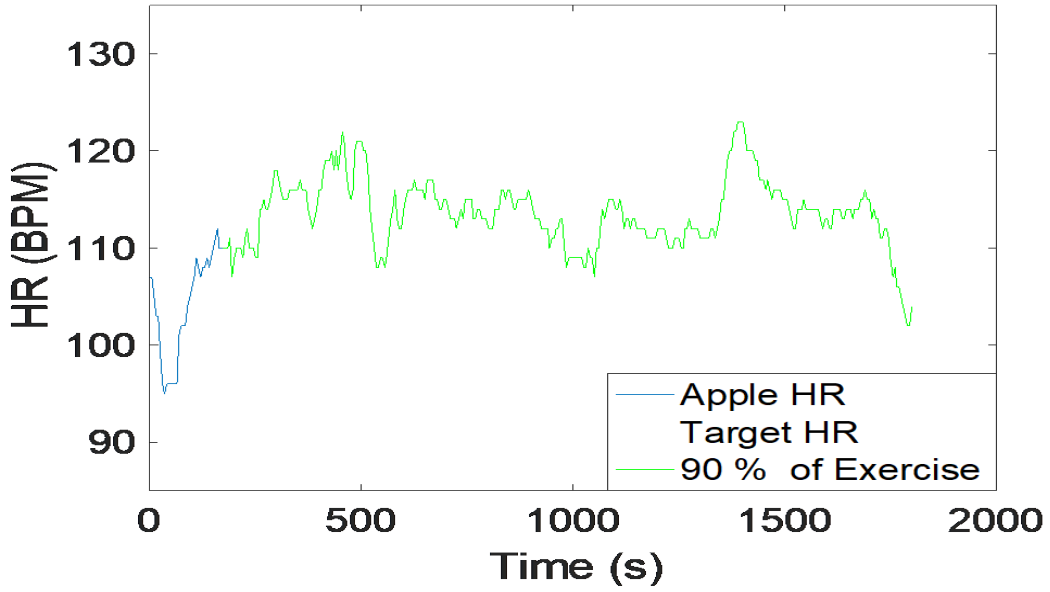


Figure A5.408: Patient No. 2 Week 8 Attempt 3

### Patient 2 Attempt 28



Figure A5.409: Patient No. 2 Week 8 Attempt 4

### Patient 2 Attempt 29

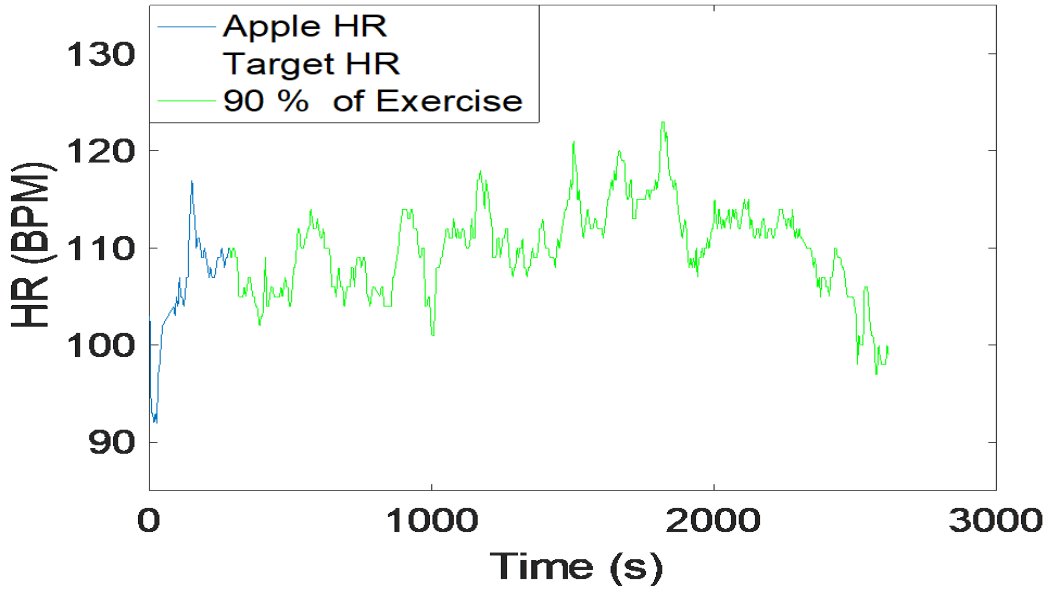


Figure A5.410: Patient No. 2 Week 8 Attempt 5

### Patient 2 Attempt 30

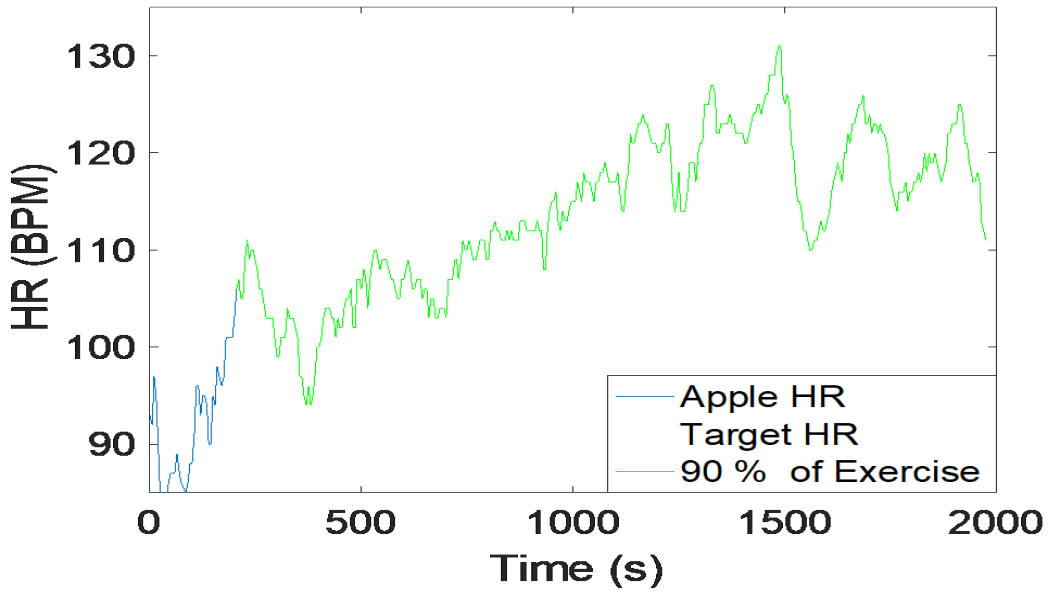
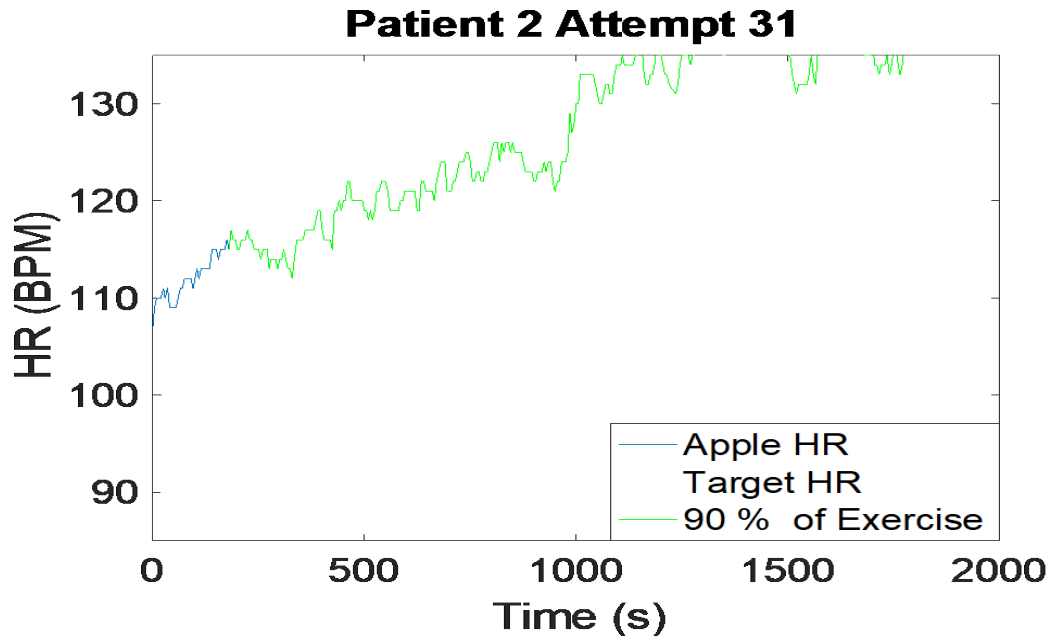
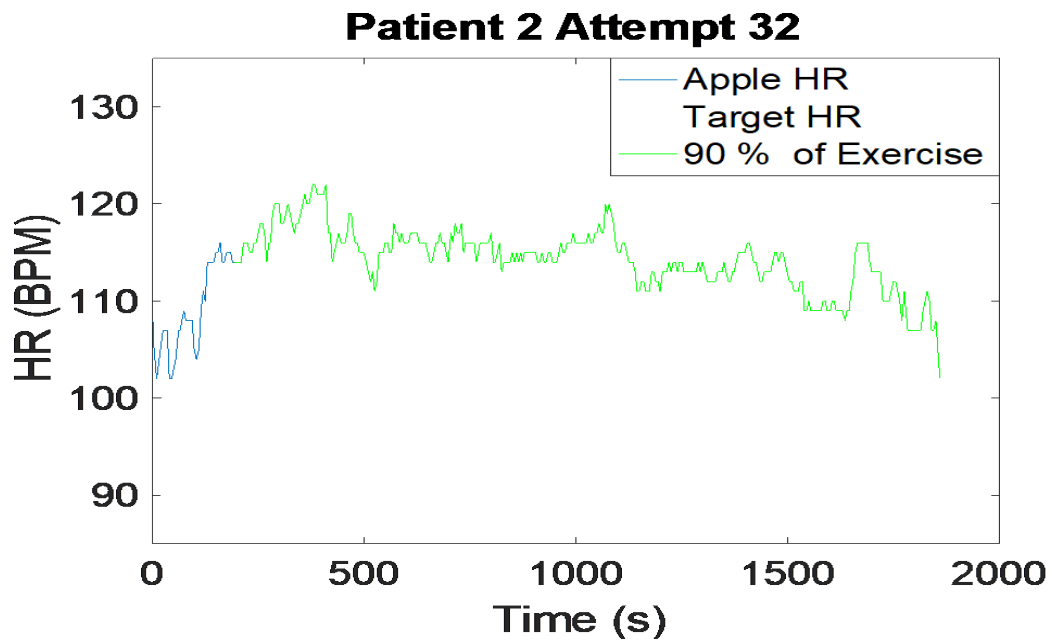


Figure A5.411: Patient No. 2 Week 9 Attempt 1



*Figure A5.412: Patient No. 2 Week 9 Attempt 2*



*Figure A5.413: Patient No. 2 Week 9 Attempt 3*



### Patient 2 Attempt 33



Figure A5.414: Patient No. 2 Week 9 Attempt 4

### Patient 2 Attempt 34

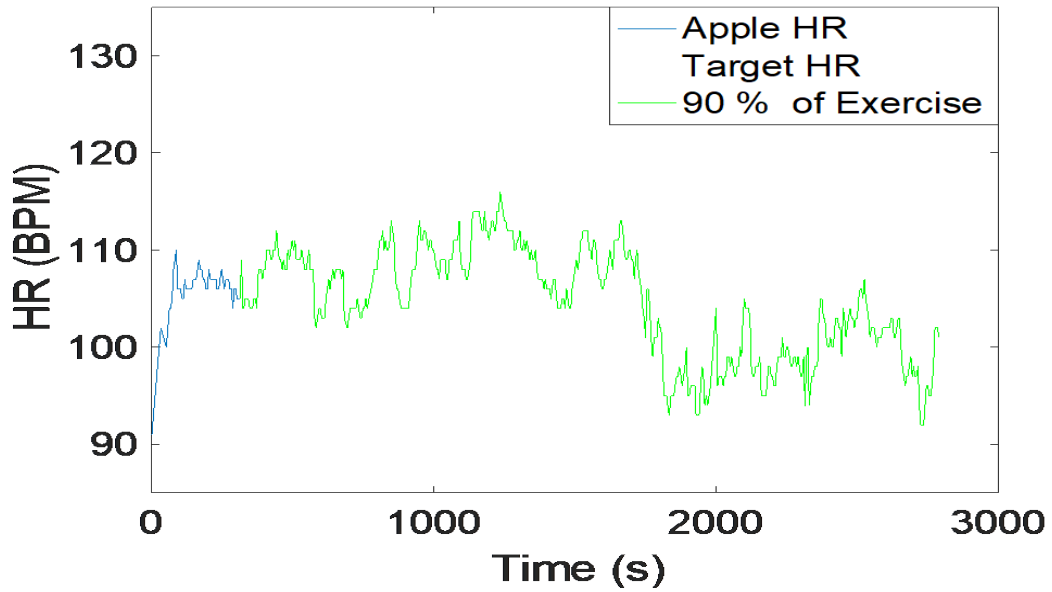


Figure A5.415: Patient No. 2 Week 9 Attempt 5

### Patient 2 Attempt 35

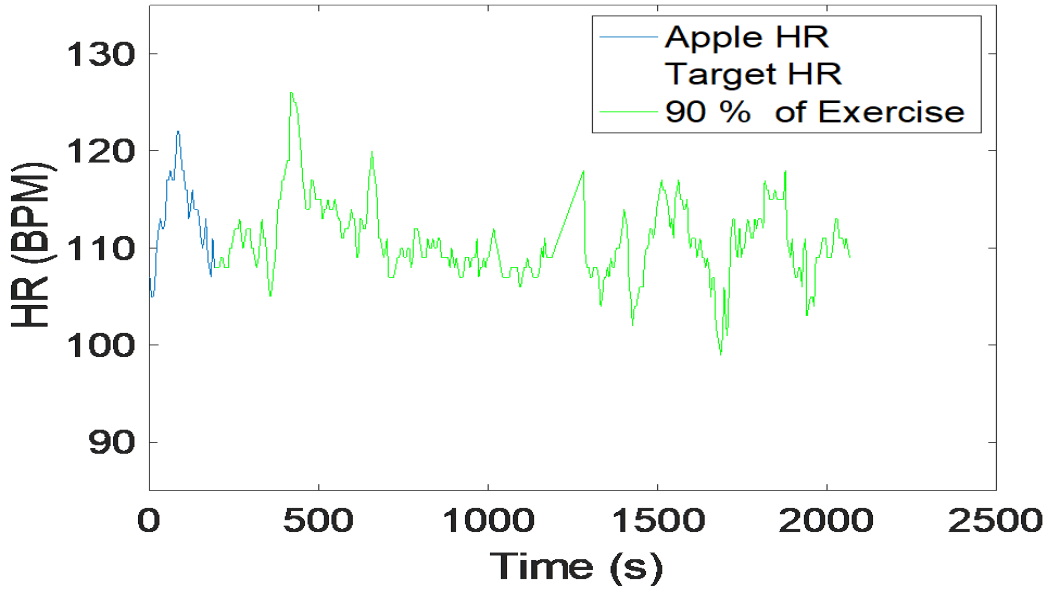


Figure A5.416: Patient No. 2 Week 10 Attempt 1

### Patient 2 Attempt 36

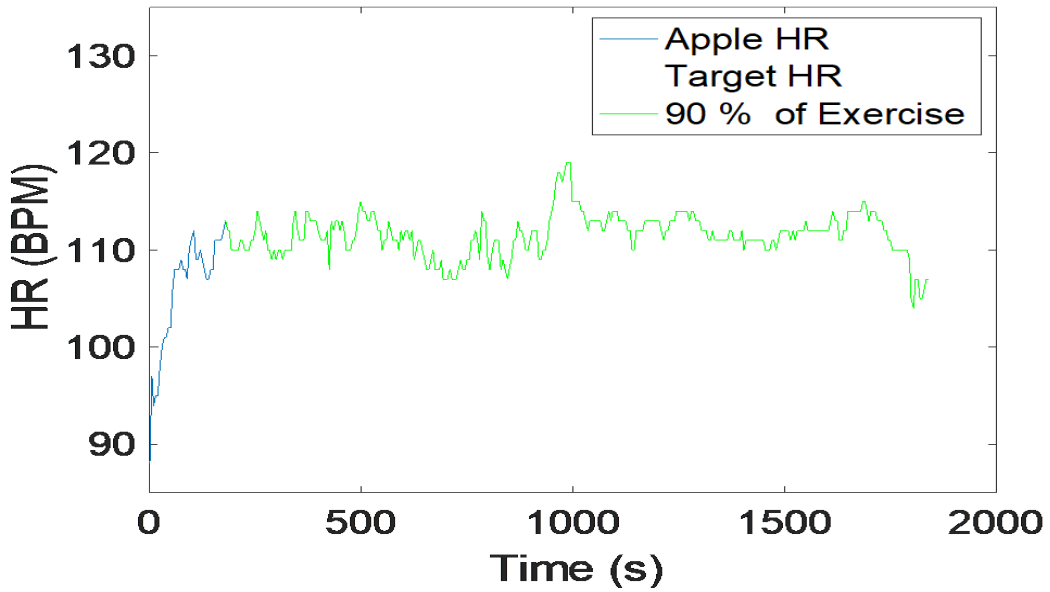


Figure A5.417: Patient No. 2 Week 10 Attempt 2

### Patient 2 Attempt 37



Figure A5.418: Patient No. 2 Week 10 Attempt 3

### Patient 2 Attempt 38



Figure A5.419: Patient No. 2 Week 11 Attempt 1

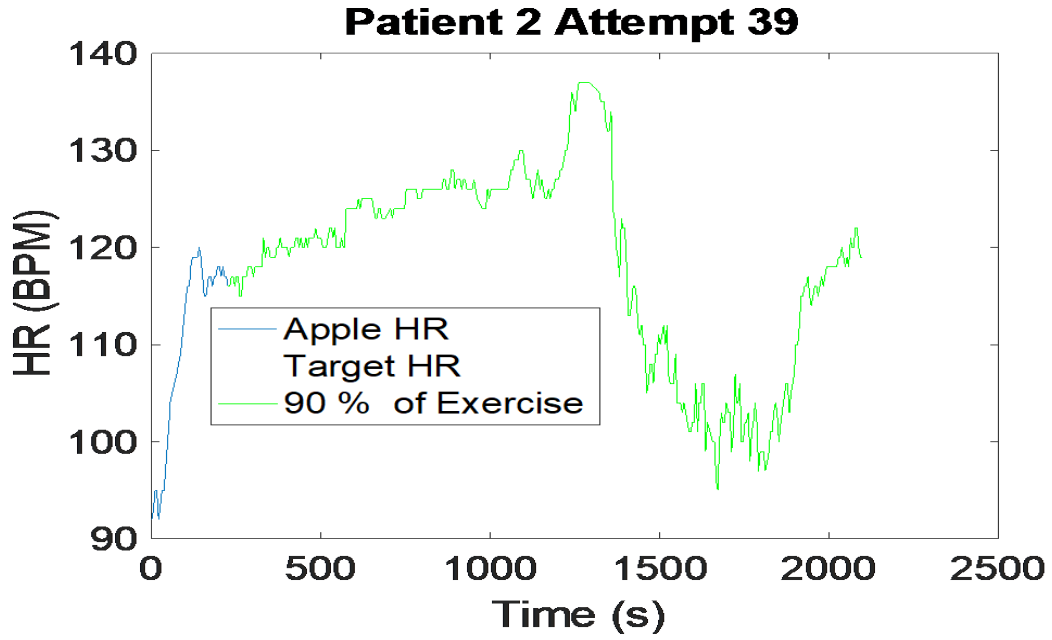


Figure A5.420: Patient No. 2 Week 11 Attempt 2

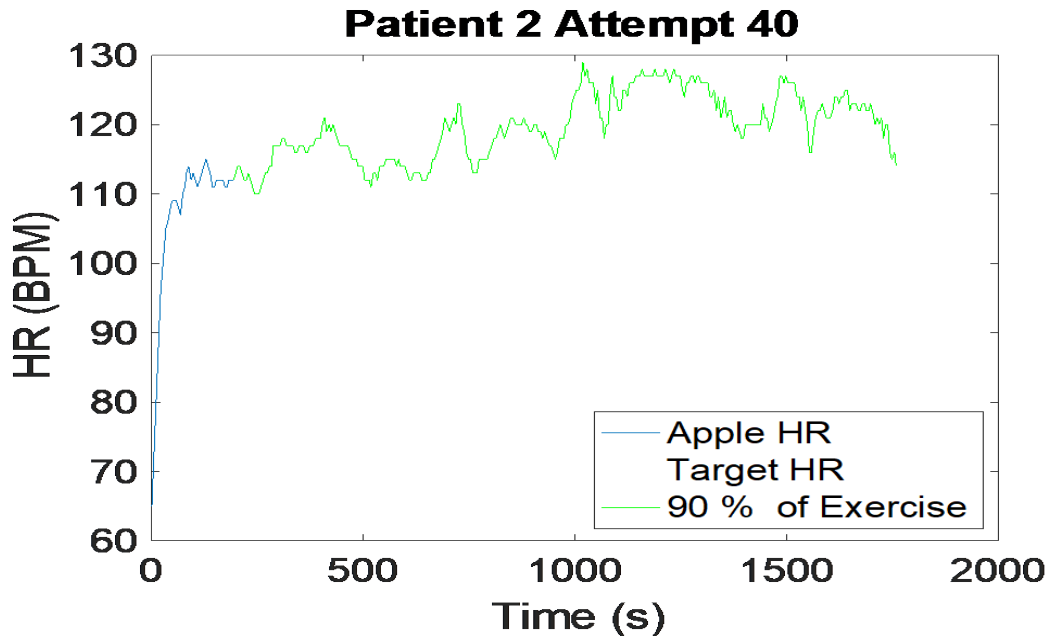


Figure A5.421: Patient No. 2 Week 11 Attempt 3

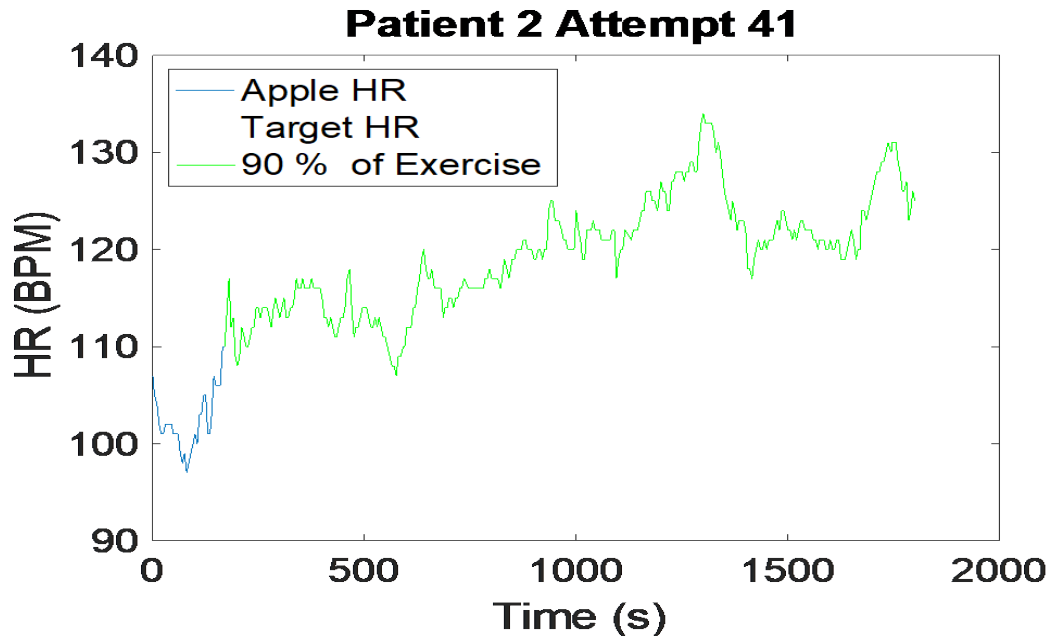


Figure A5.422: Patient No. 2 Week 11 Attempt 4

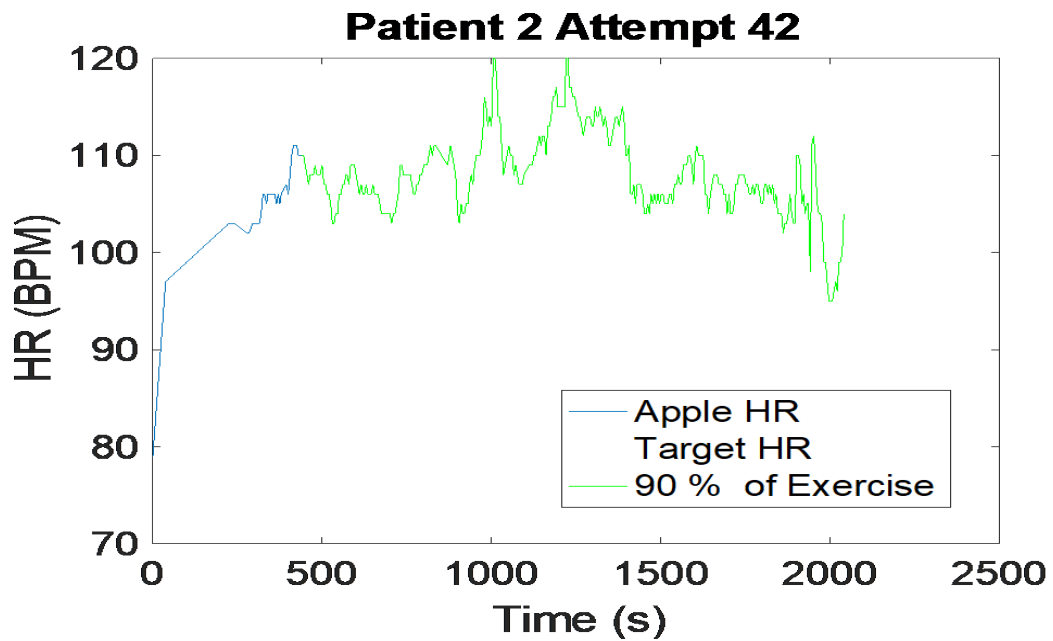


Figure A5.423: Patient No. 2 Week 12 Attempt 1



Figure A5.424: Patient No. 2 Week 12 Attempt 2

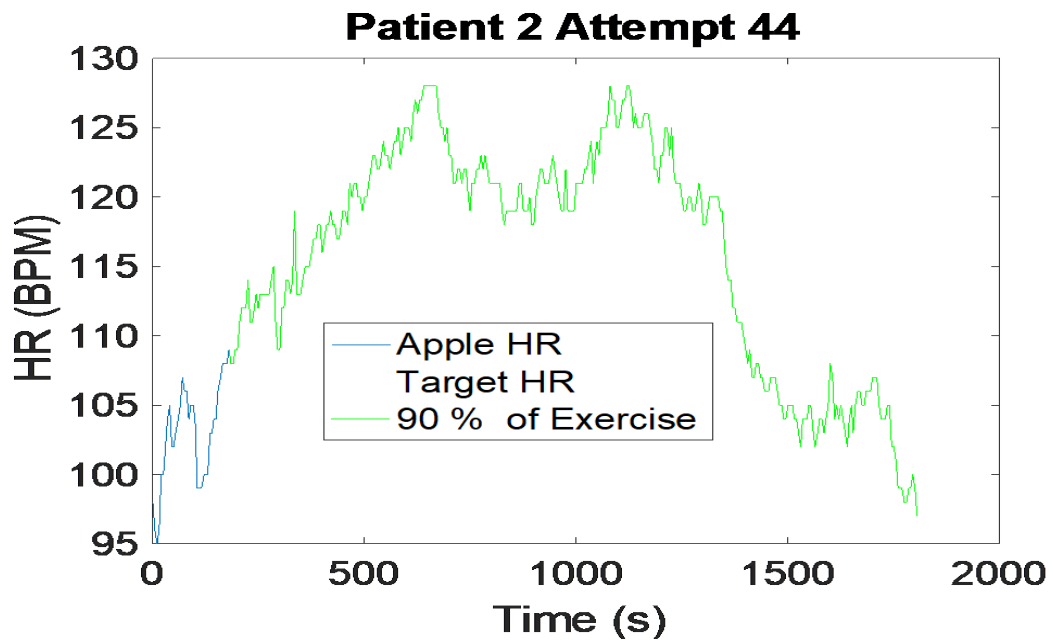


Figure A5.425: Patient No. 2 Week 12 Attempt 3

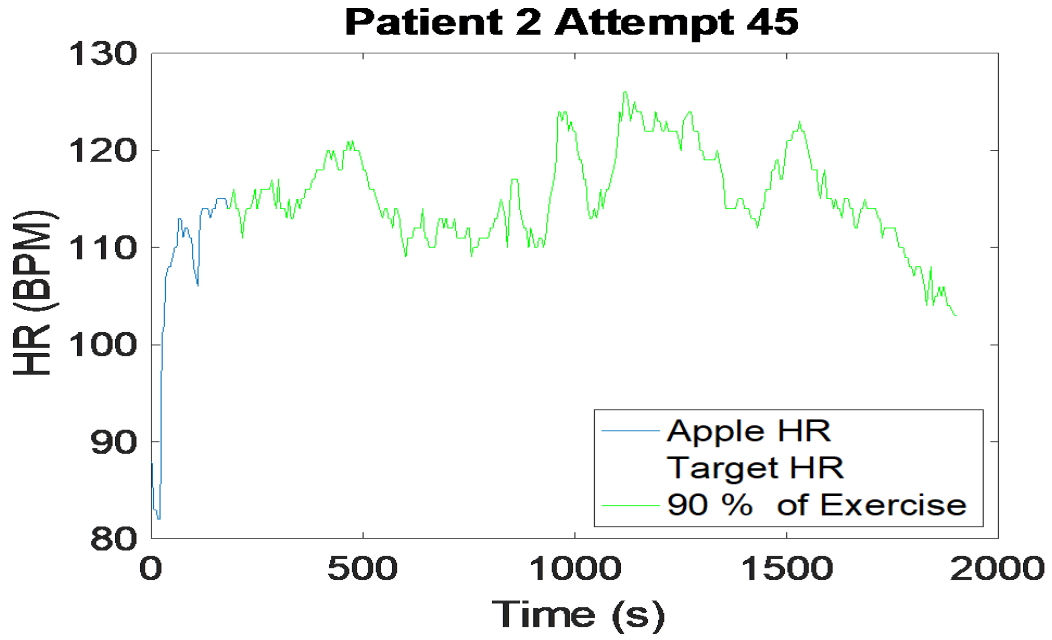


Figure A5.426: Patient No. 2 Week 12 Attempt 4

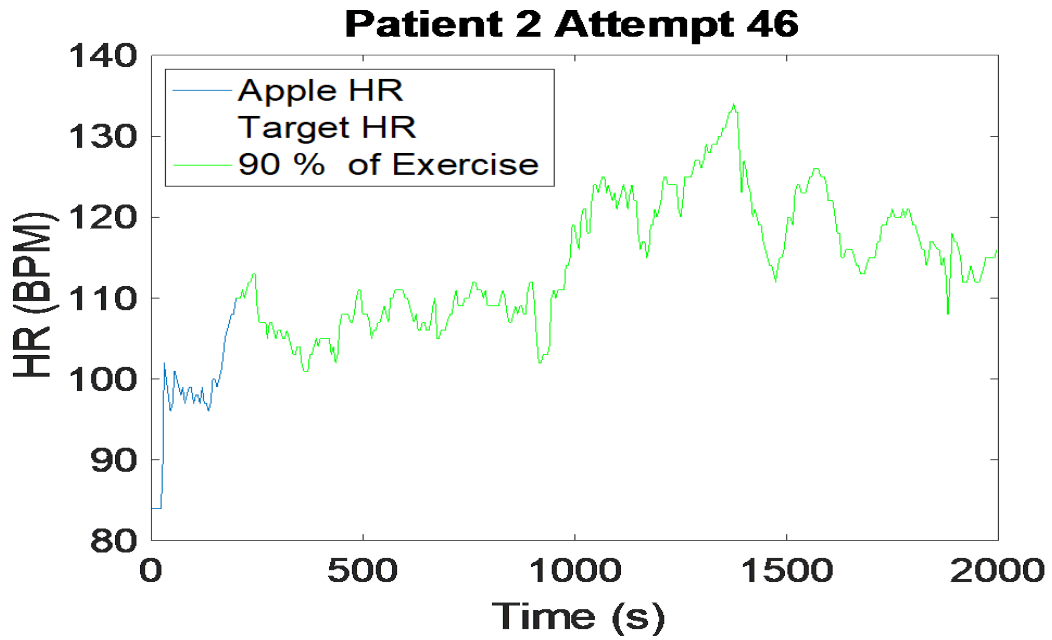


Figure A5.427: Patient No. 2 Week 13 Attempt 1

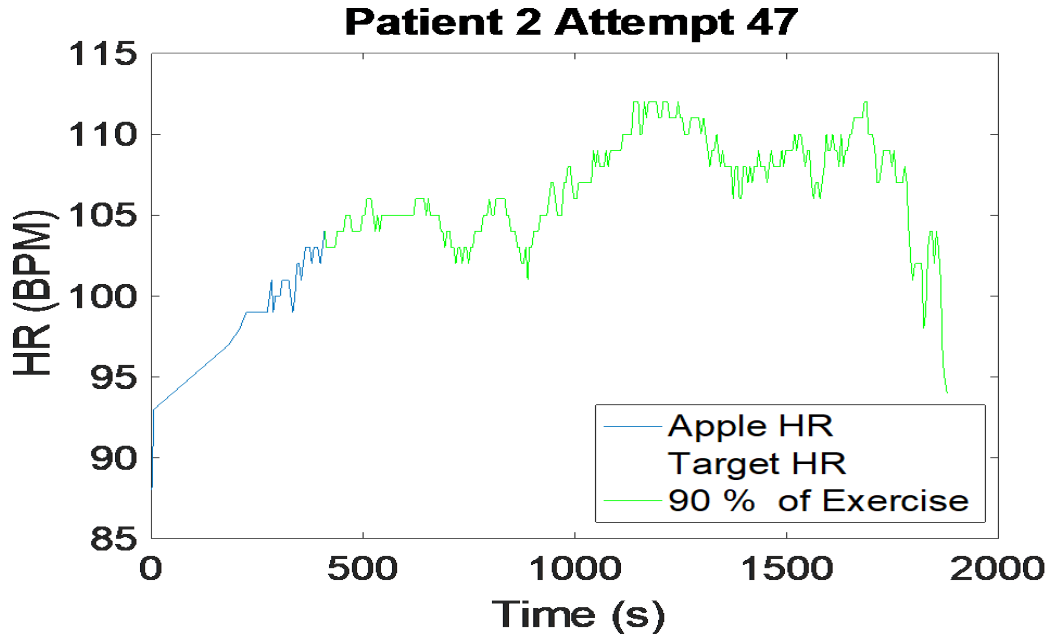


Figure A5.428: Patient No. 2 Week 13 Attempt 2

Patient 3 Attempts:

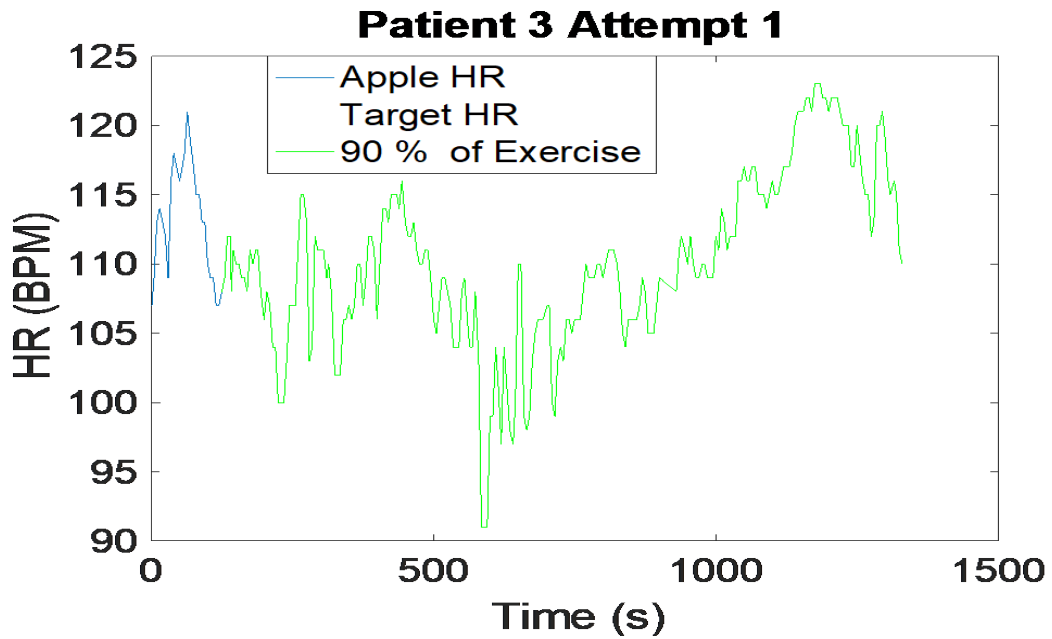


Figure A5.429: Patient No. 3 Week 1 Attempt 1



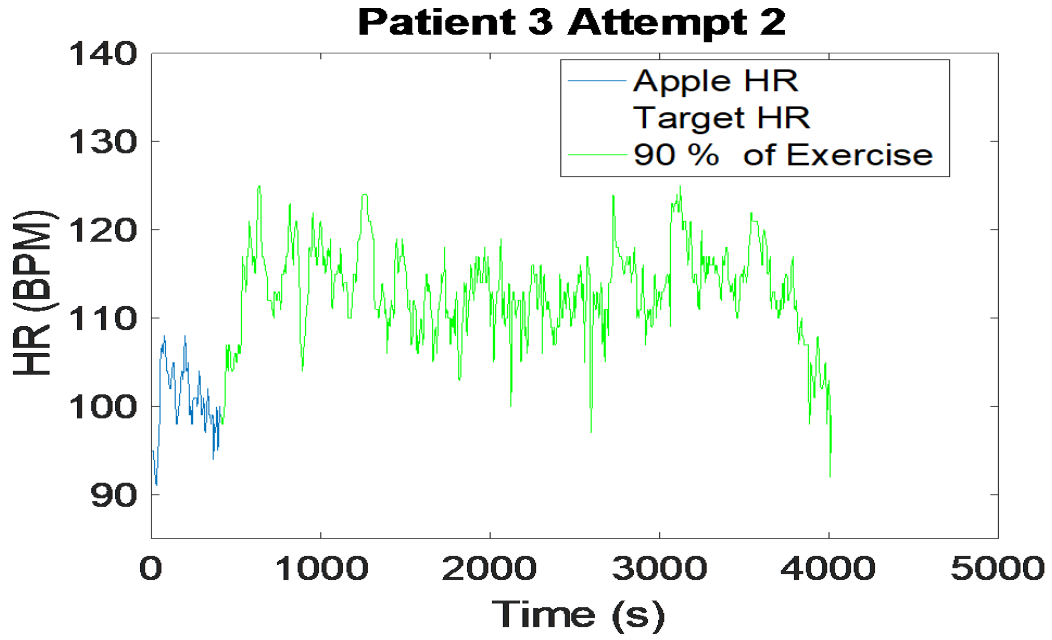


Figure A5.430: Patient No. 3 Week 1 Attempt 2

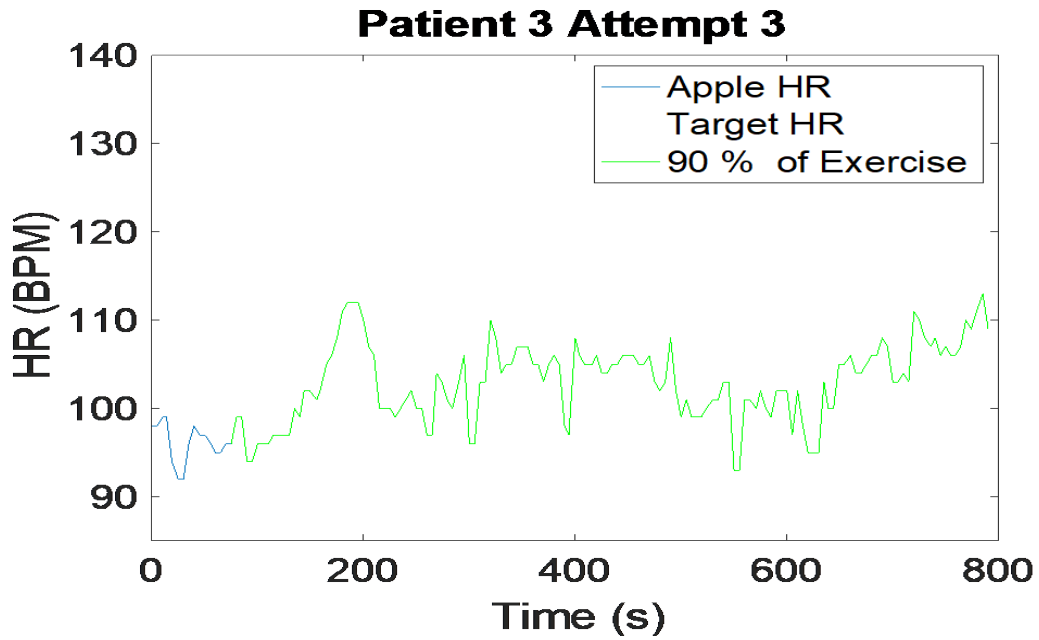


Figure A5.431: Patient No. 3 Week 1 Attempt 3

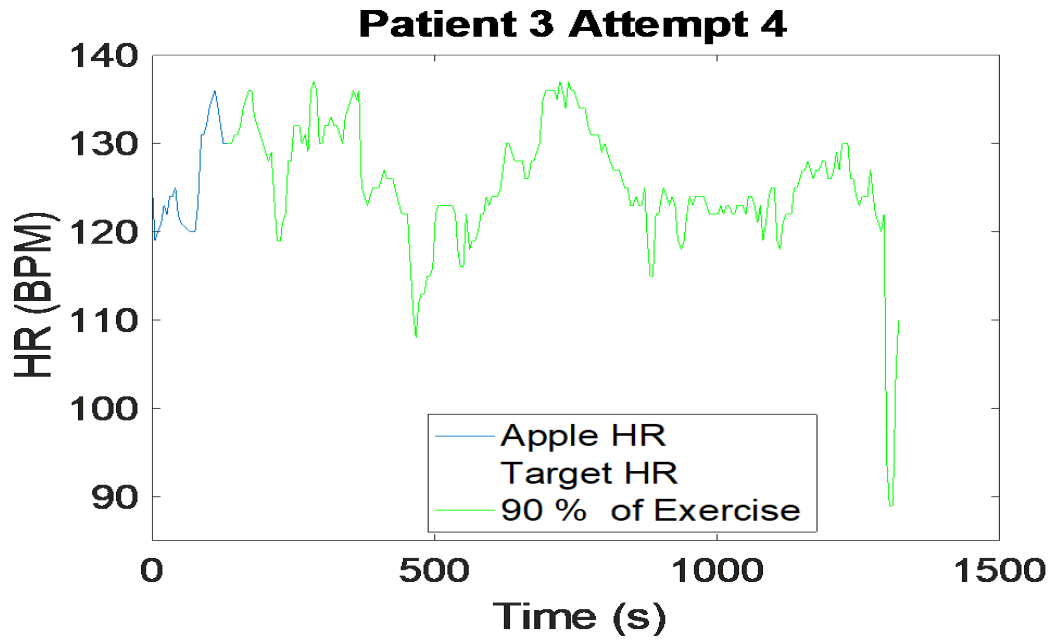


Figure A5.432: Patient No. 3 Week 1 Attempt 4

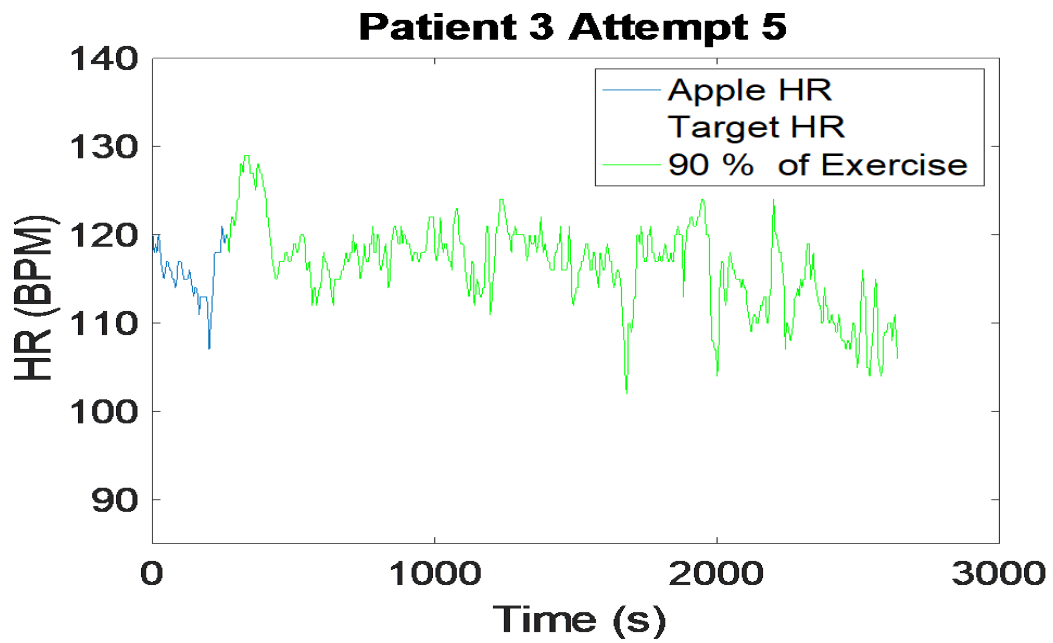


Figure A5.433: Patient No. 3 Week 2 Attempt 1

### Patient 3 Attempt 6

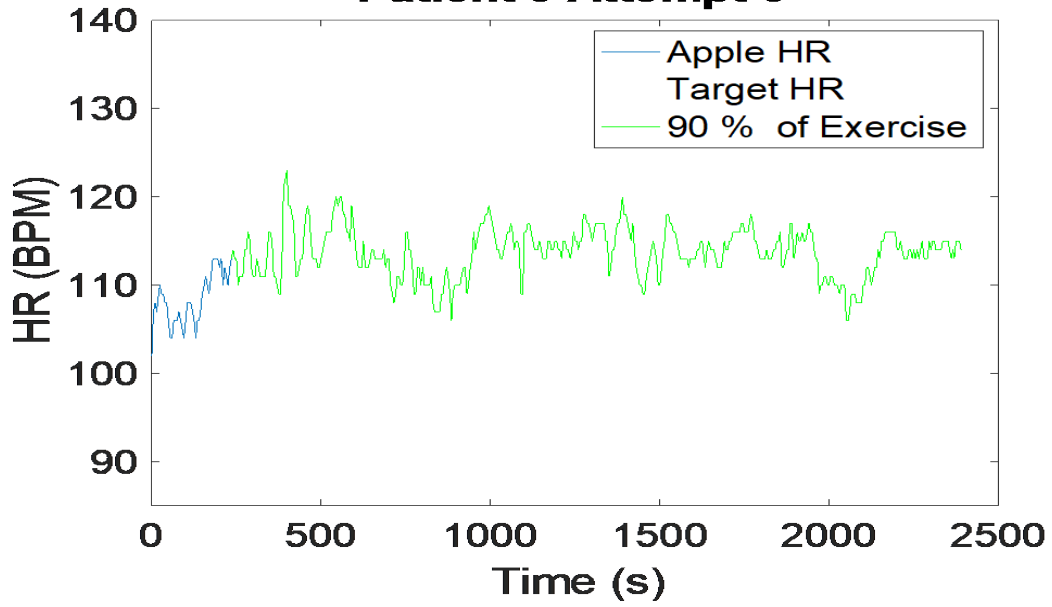


Figure A5.434: Patient No. 3 Week 2 Attempt 2

### Patient 3 Attempt 7



Figure A5.435: Patient No. 3 Week 2 Attempt 3

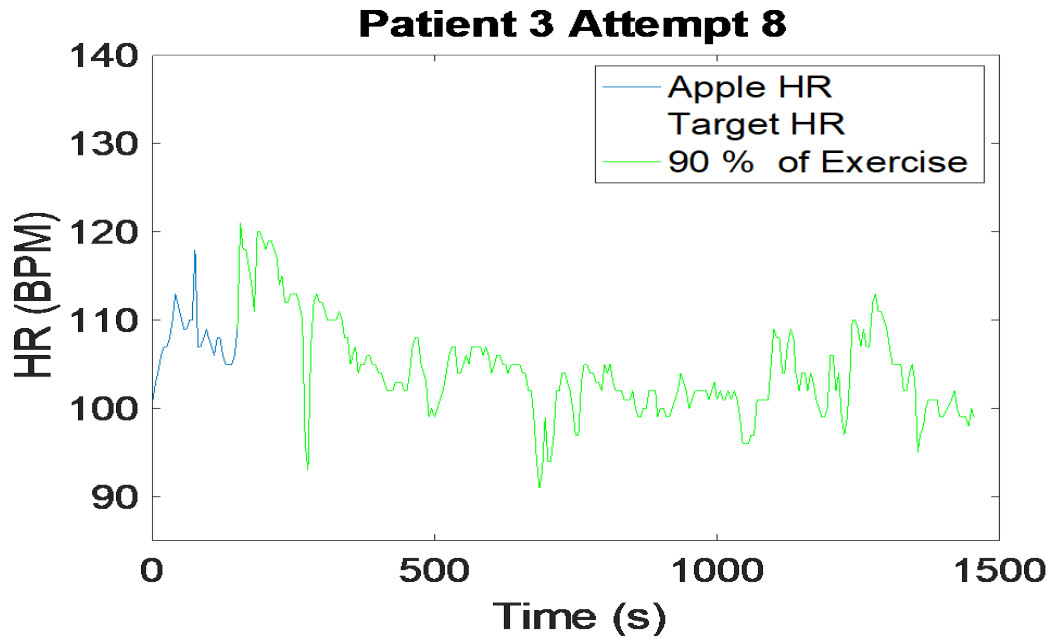


Figure A5.436: Patient No. 3 Week 2 Attempt 4

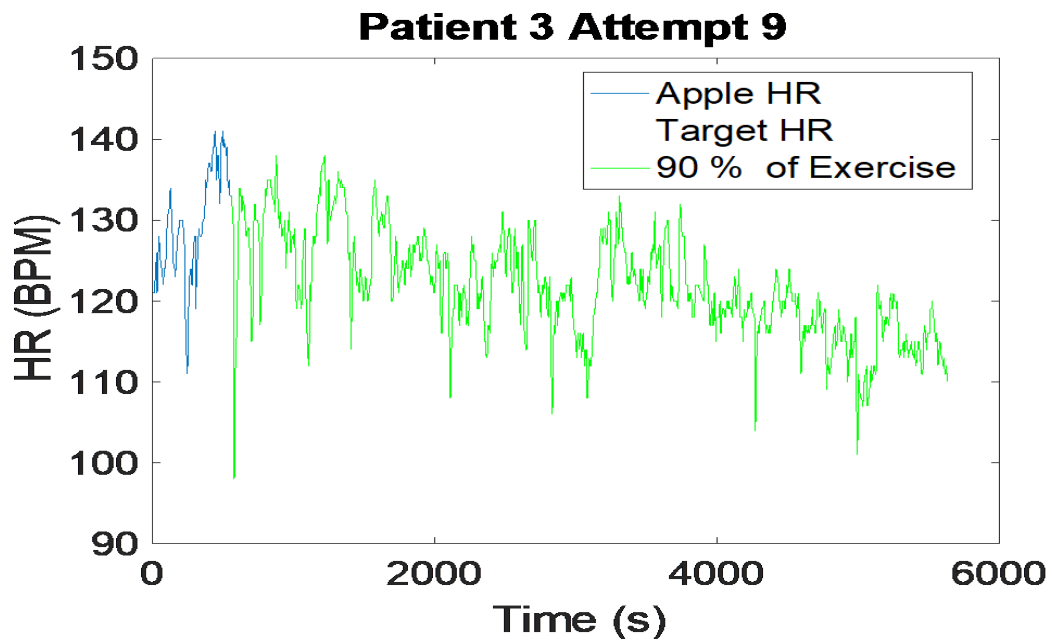


Figure A5.437: Patient No. 3 Week 2 Attempt 5

### Patient 3 Attempt 10

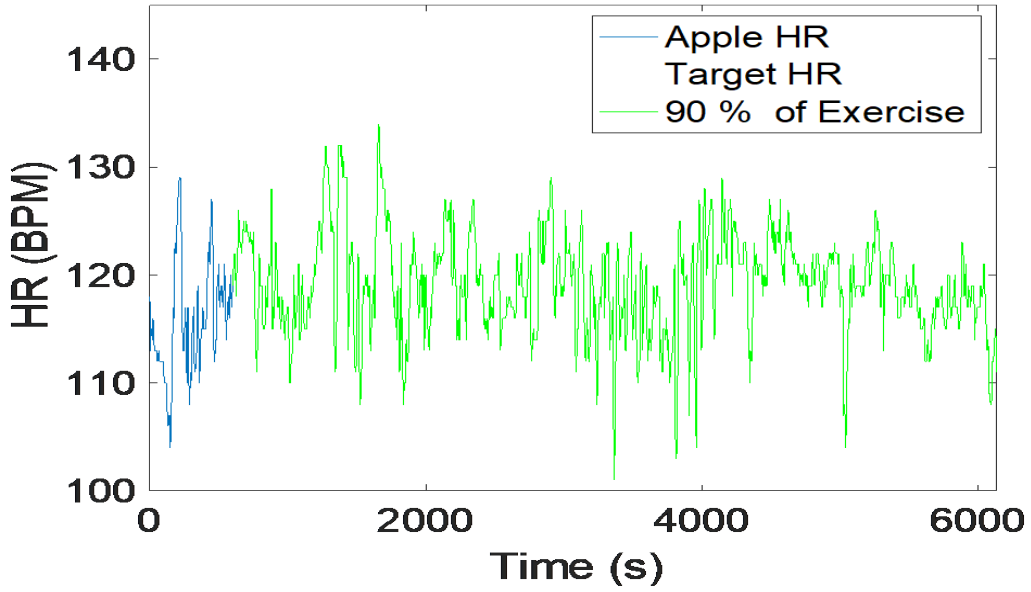


Figure A5.438: Patient No. 3 Week 3 Attempt 1

### Patient 3 Attempt 11

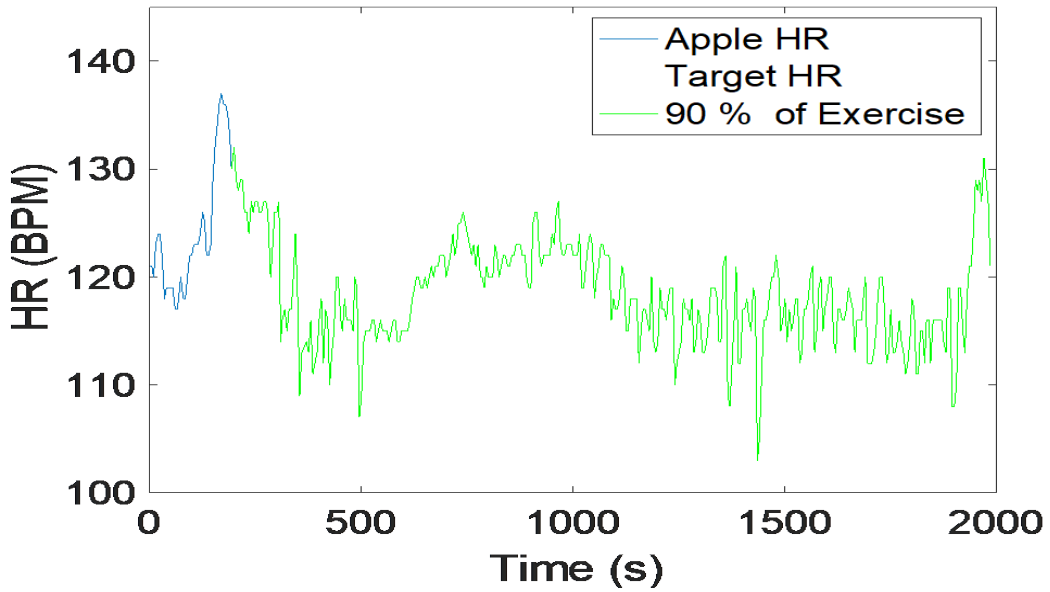


Figure A5.439: Patient No. 3 Week 3 Attempt 2

### Patient 3 Attempt 12

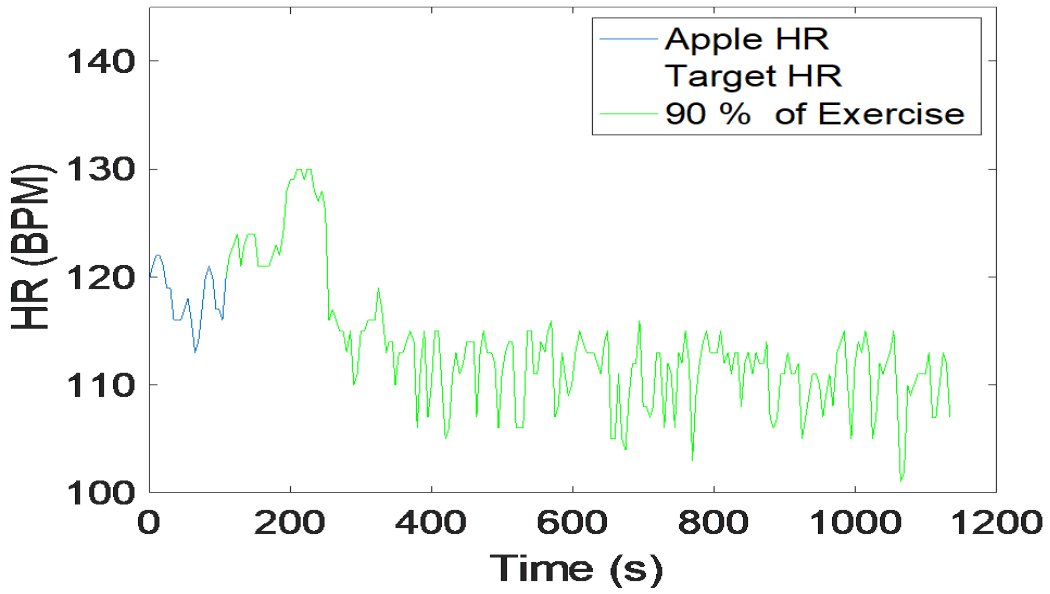


Figure A5.440: Patient No. 3 Week 3 Attempt 3

### Patient 3 Attempt 13

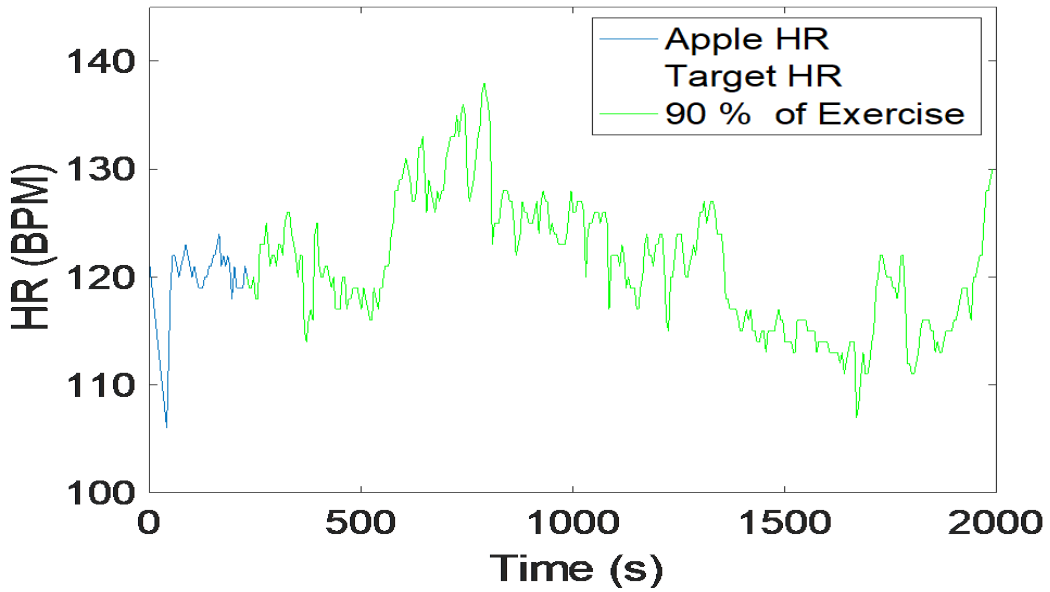


Figure A5.441: Patient No. 3 Week 3 Attempt 4

### Patient 3 Attempt 14

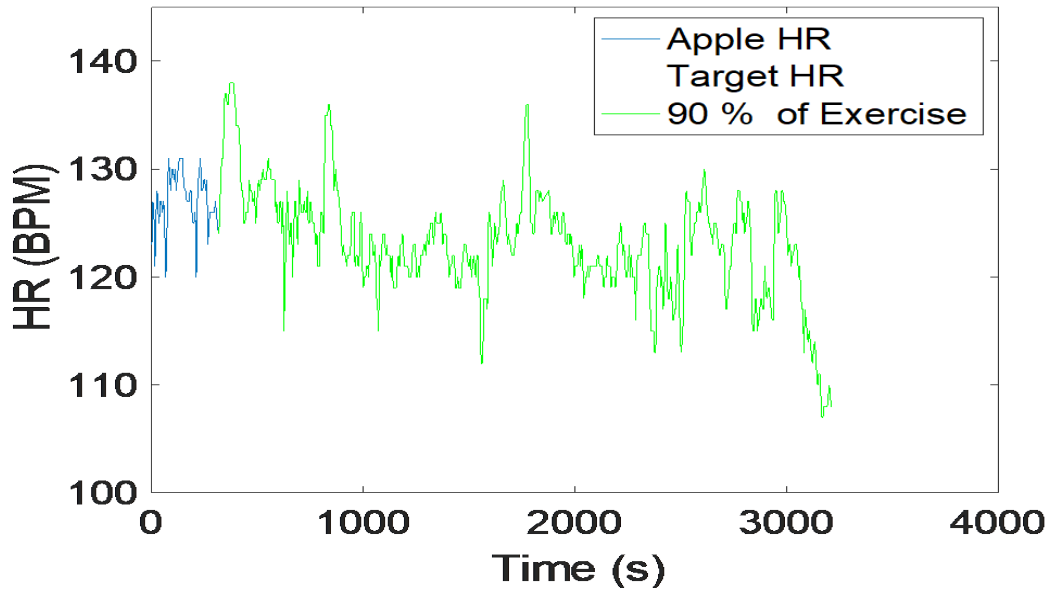


Figure A5.442: Patient No. 3 Week 3 Attempt 5

### Patient 3 Attempt 15

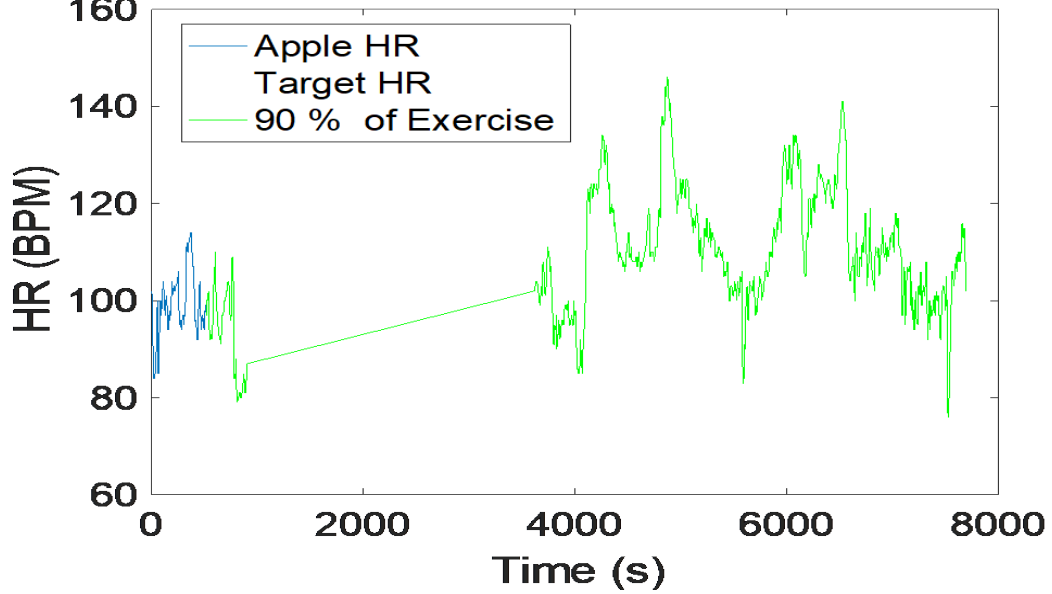


Figure A5.443: Patient No. 3 Week 4 Attempt 1

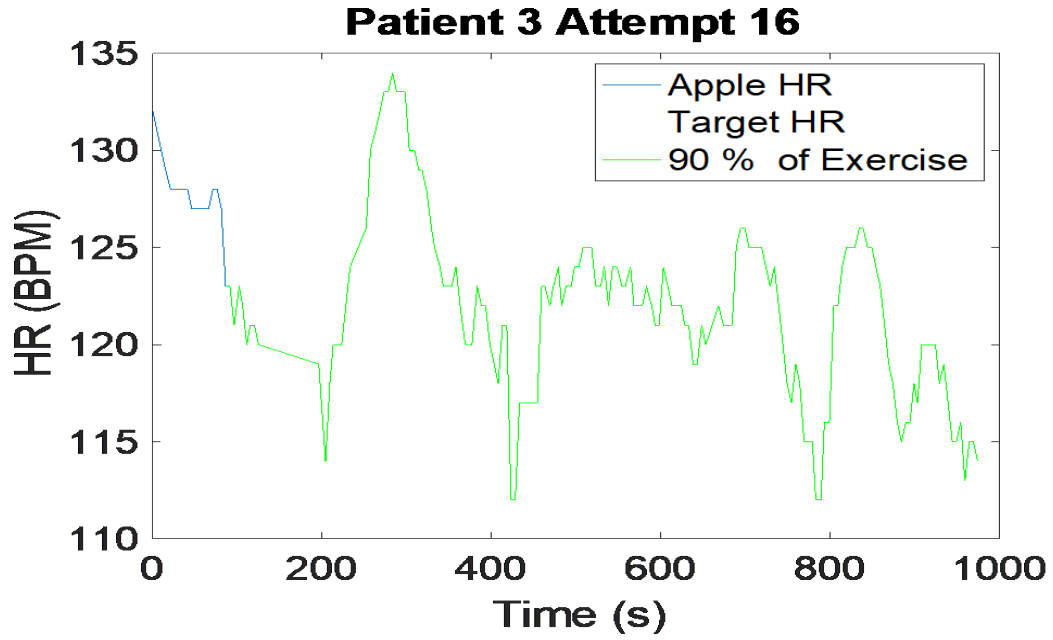


Figure A5.444: Patient No. 3 Week 4 Attempt 2

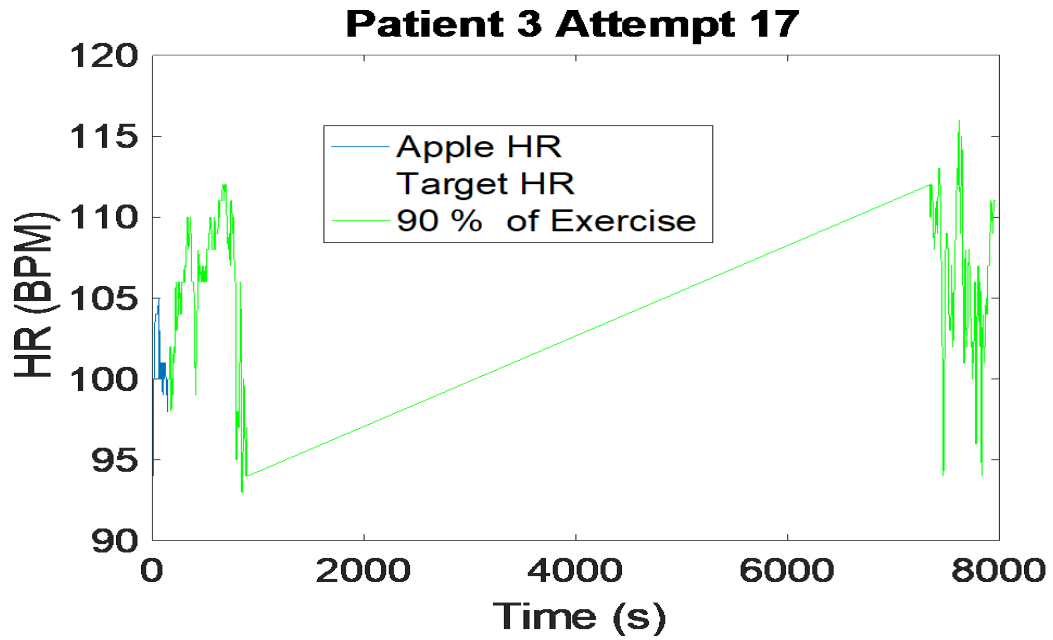


Figure A5.445: Patient No. 3 Week 4 Attempt 3



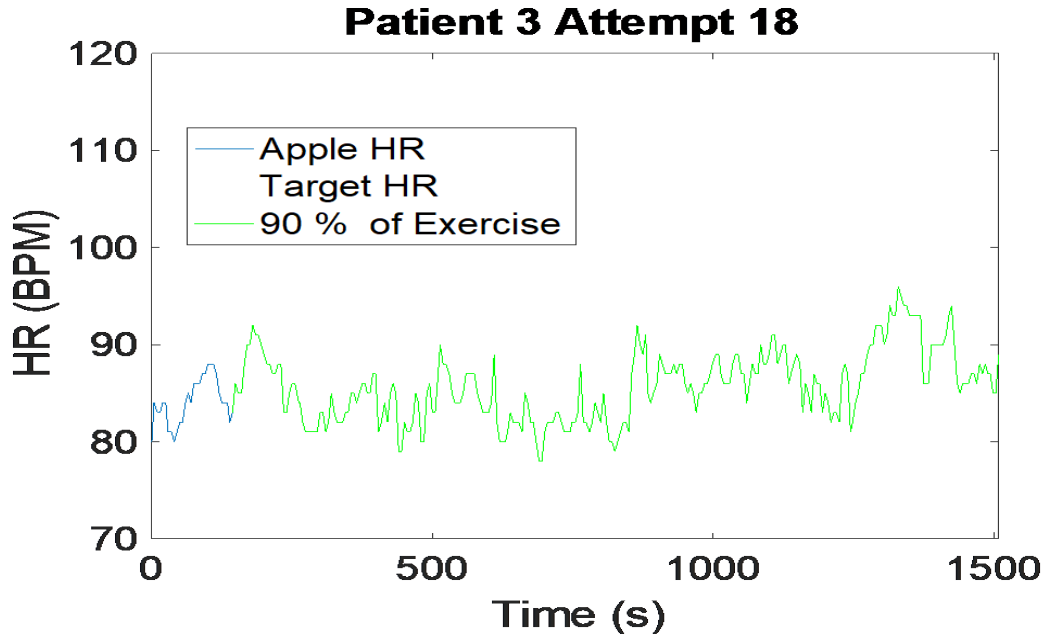


Figure A5.446: Patient No. 3 Week 4 Attempt 4

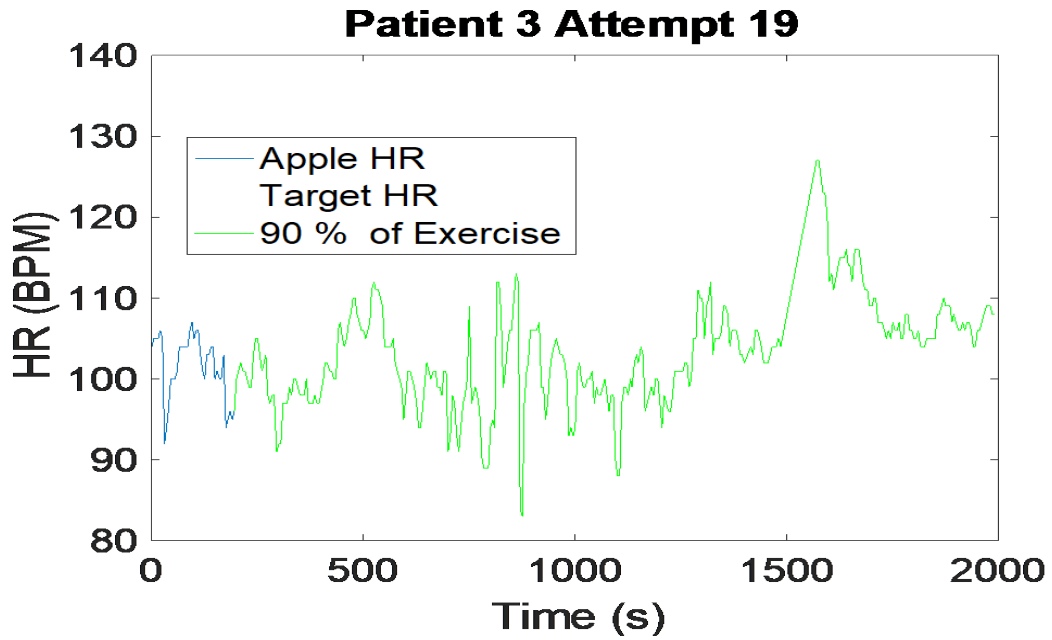
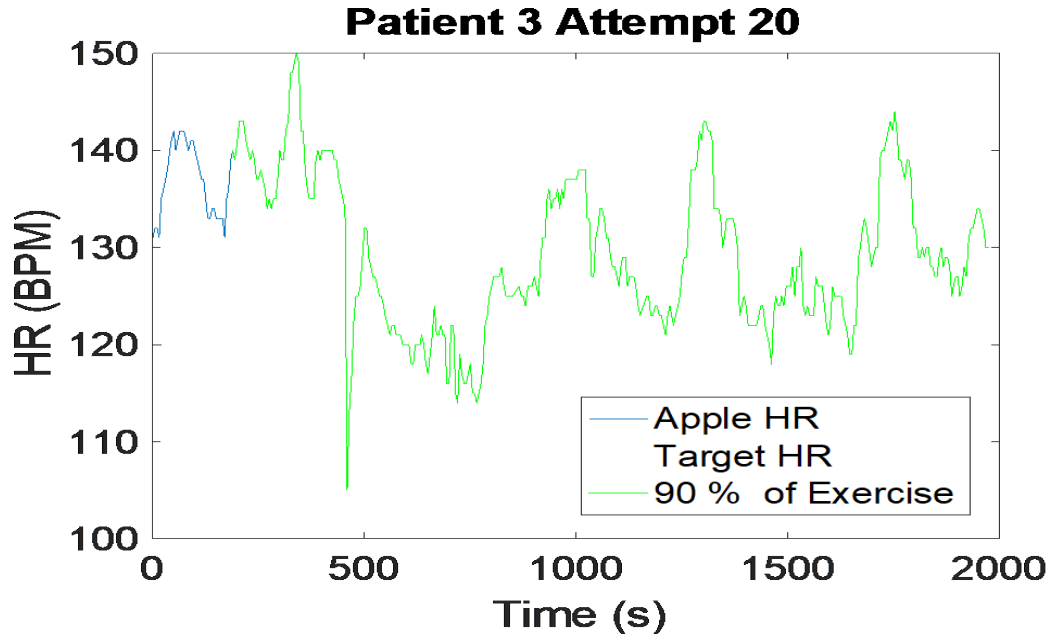
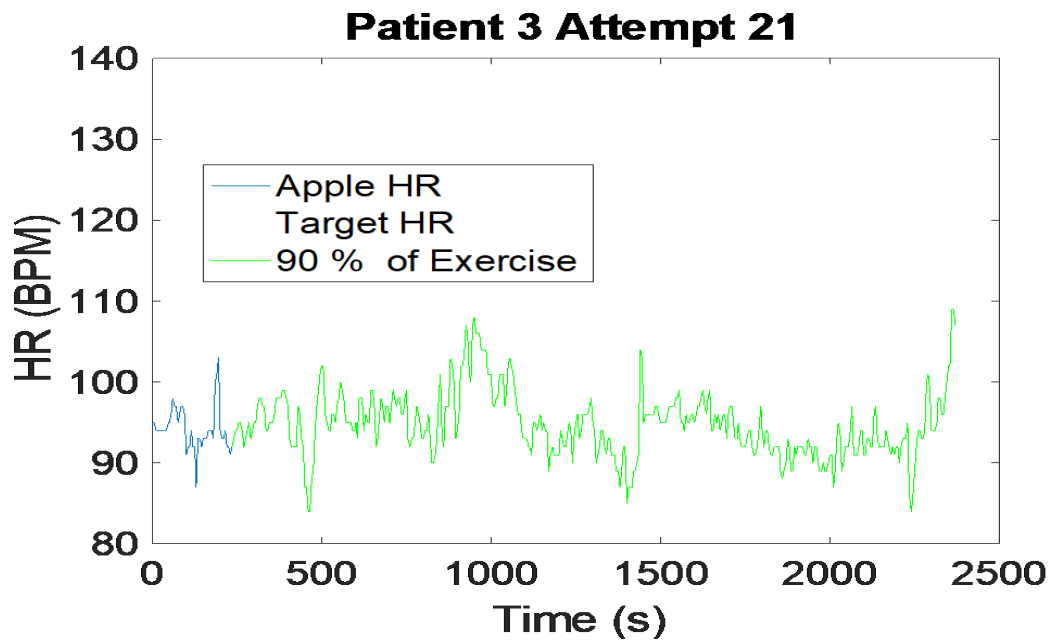


Figure A5.447: Patient No. 3 Week 5 Attempt 1



*Figure A5.448: Patient No. 3 Week 5 Attempt 2*



*Figure A5.449: Patient No. 3 Week 5 Attempt 3*

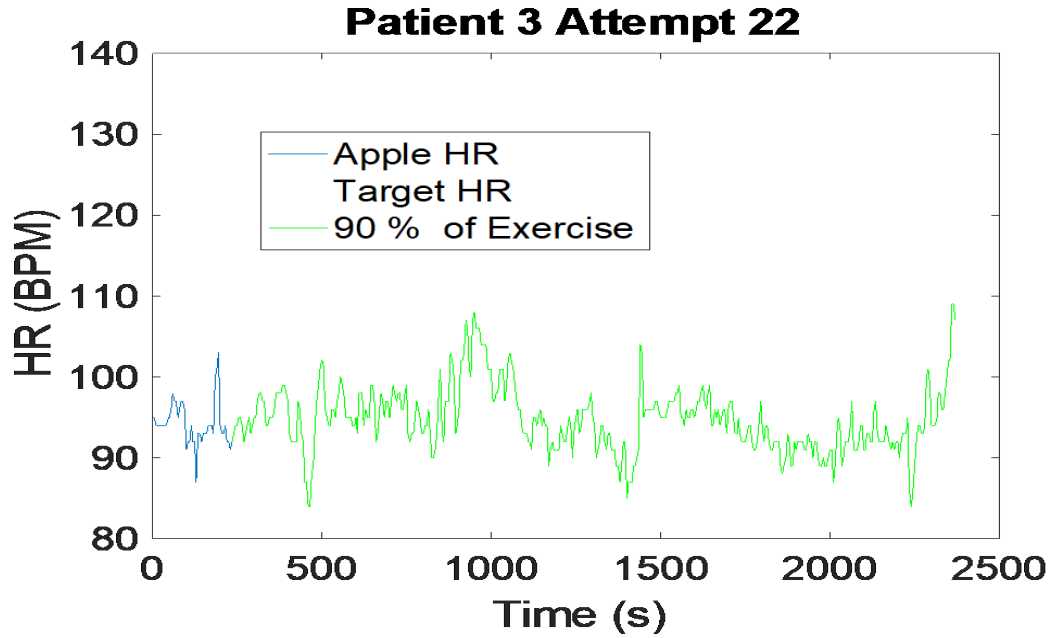


Figure A5.450: Patient No. 3 Week 5 Attempt 4

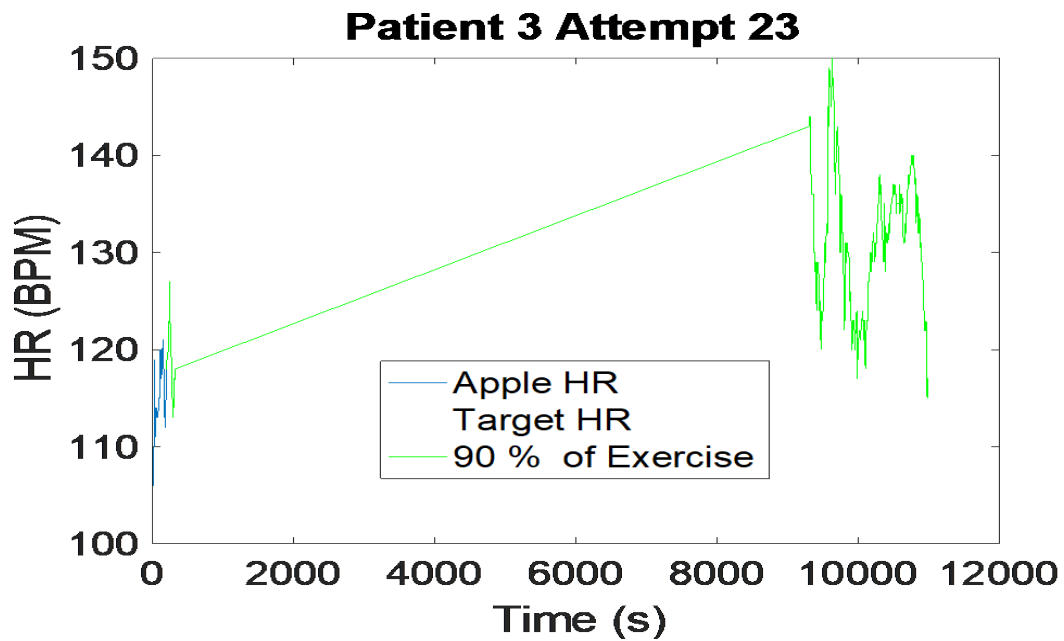


Figure A5.451: Patient No. 3 Week 5 Attempt 5

### Patient 3 Attempt 24

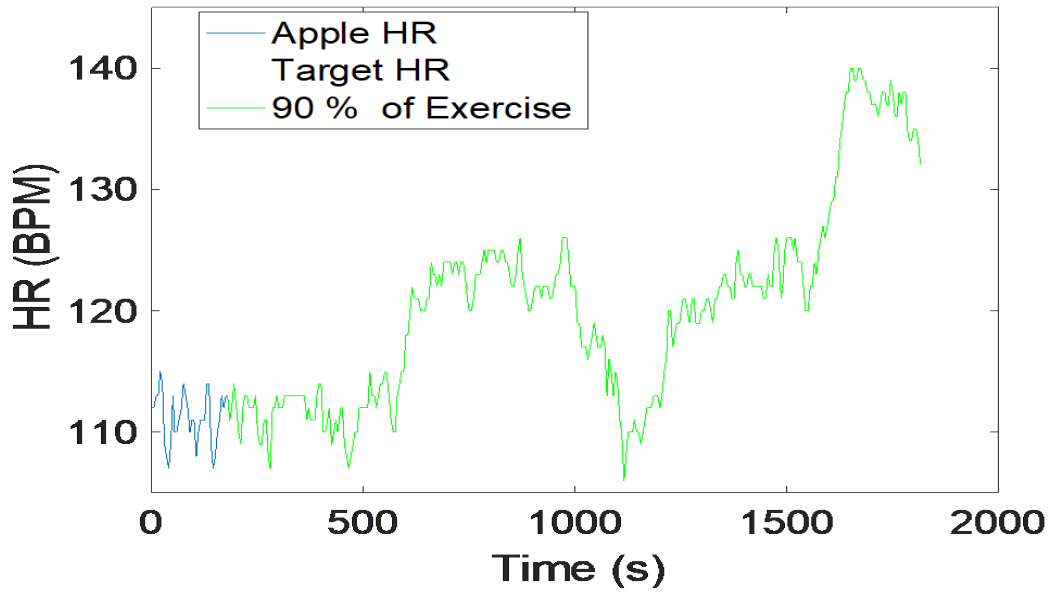


Figure A5.452: Patient No. 3 Week 5 Attempt 6

### Patient 3 Attempt 25

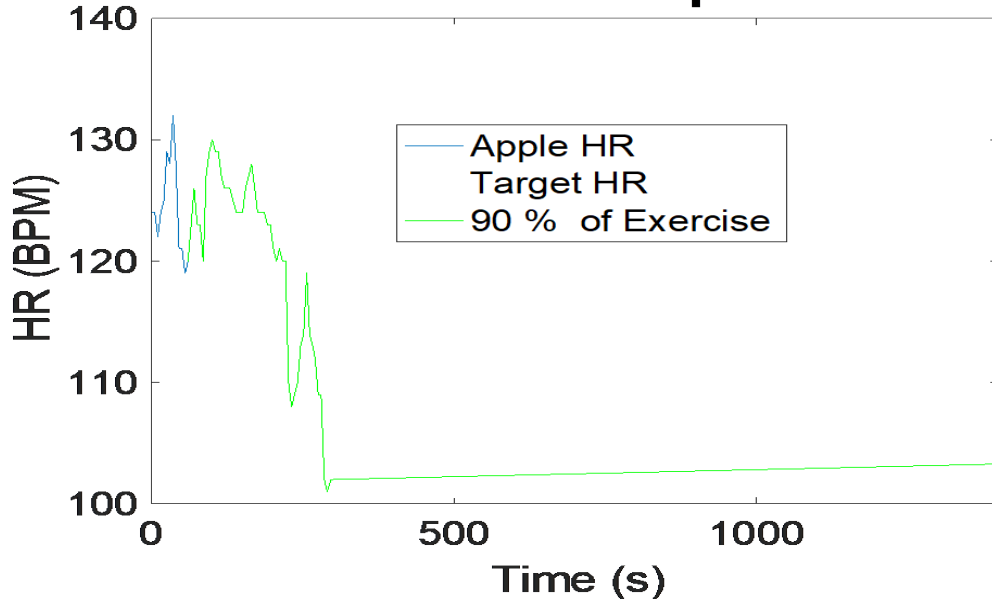


Figure A5.453: Patient No. 3 Week 6 Attempt 1

### Patient 3 Attempt 26

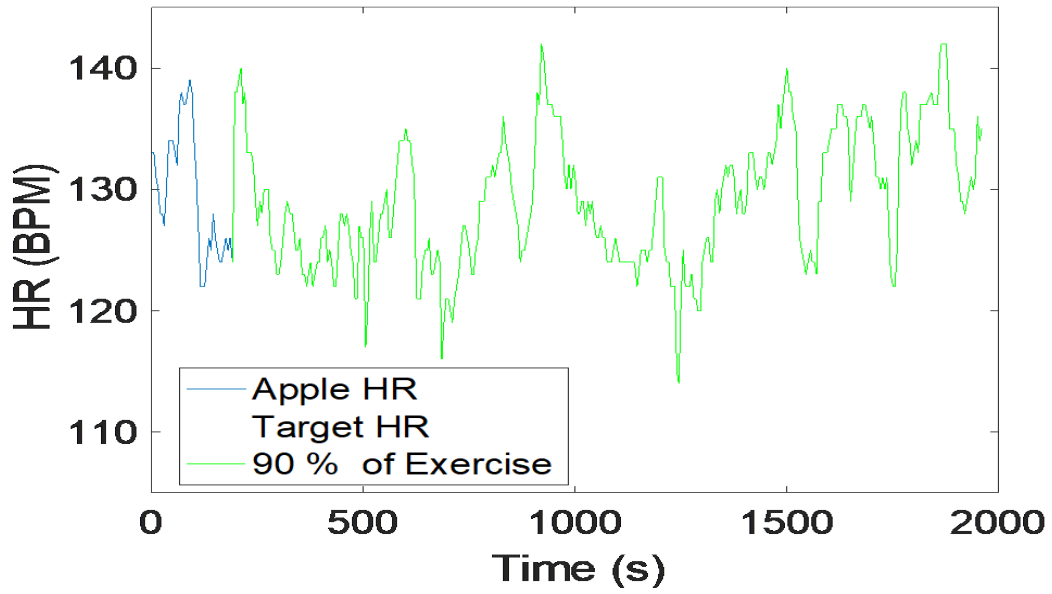


Figure A5.454: Patient No. 3 Week 6 Attempt 2

### Patient 3 Attempt 27

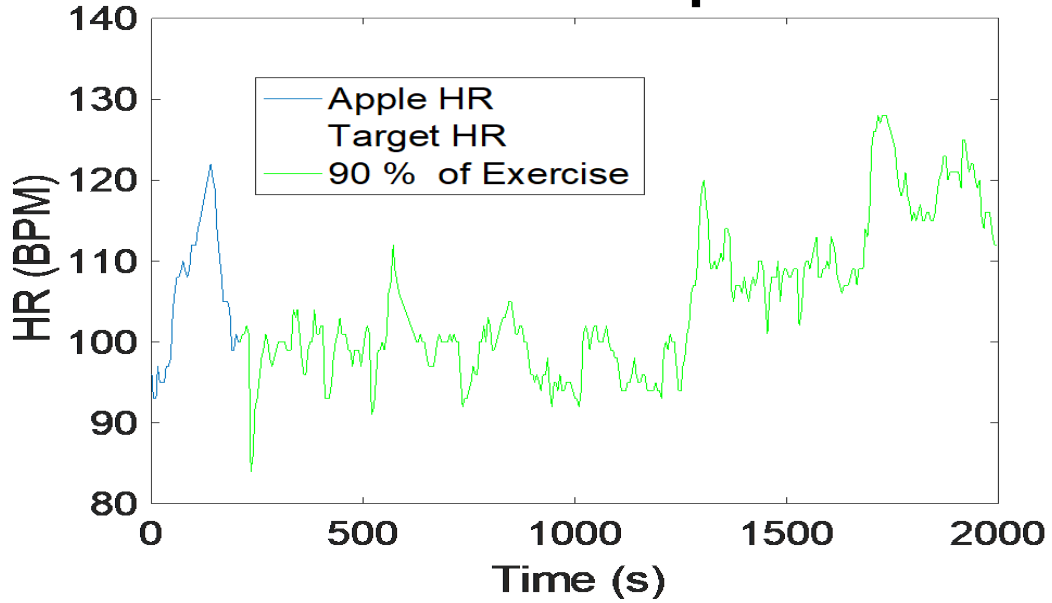


Figure A5.455: Patient No. 3 Week 7 Attempt 1

### Patient 3 Attempt 28

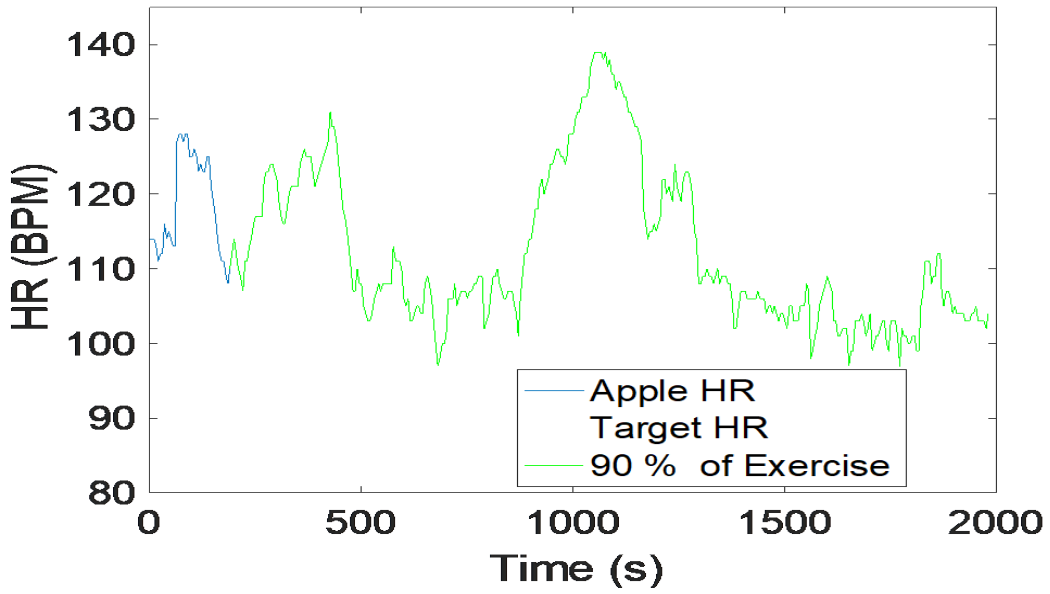


Figure A5.456: Patient No. 3 Week 7 Attempt 2

### Patient 3 Attempt 29

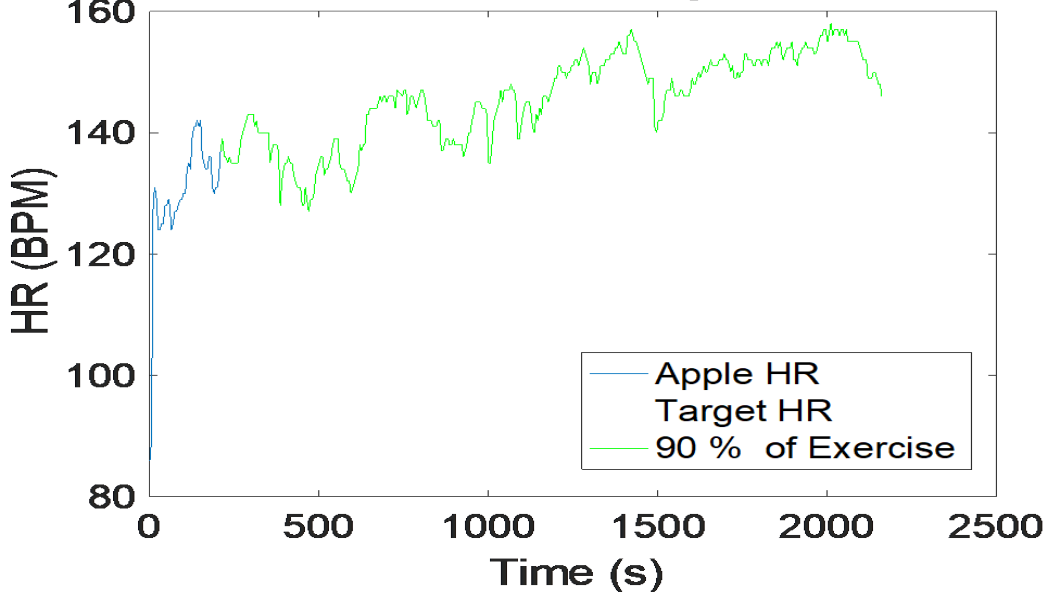


Figure A5.457: Patient No. 3 Week 8 Attempt 1

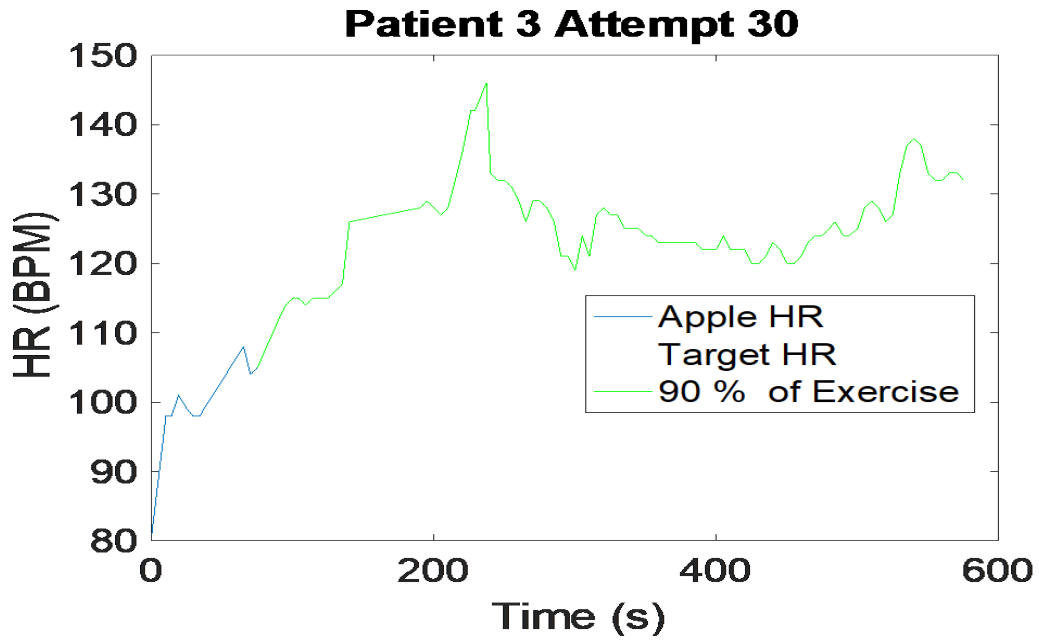


Figure A5.458: Patient No. 3 Week 9 Attempt 1

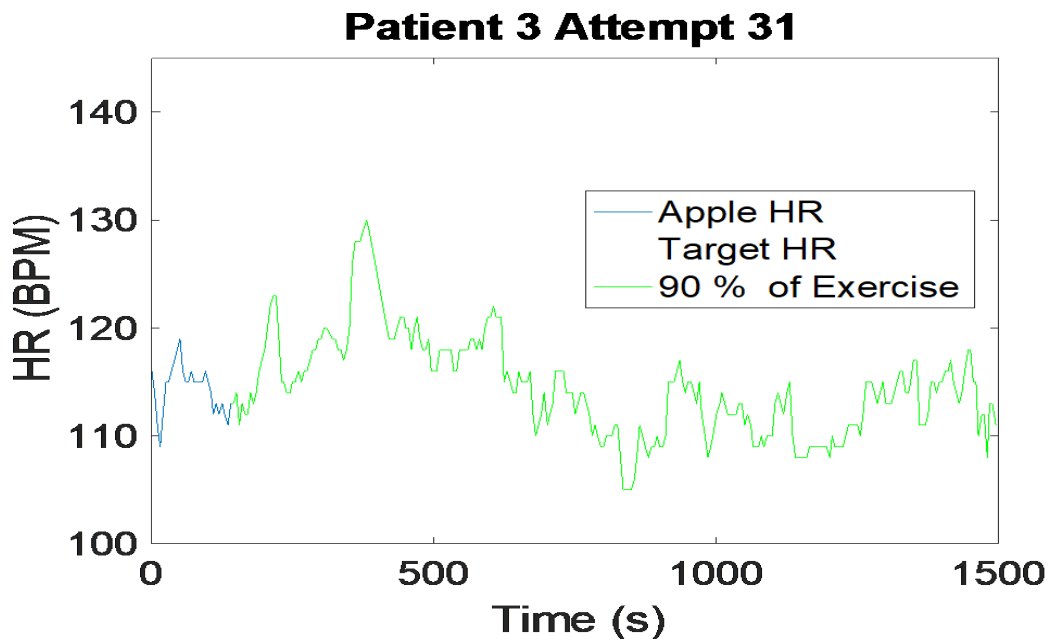


Figure A5.459: Patient No. 3 Week 11 Attempt 1

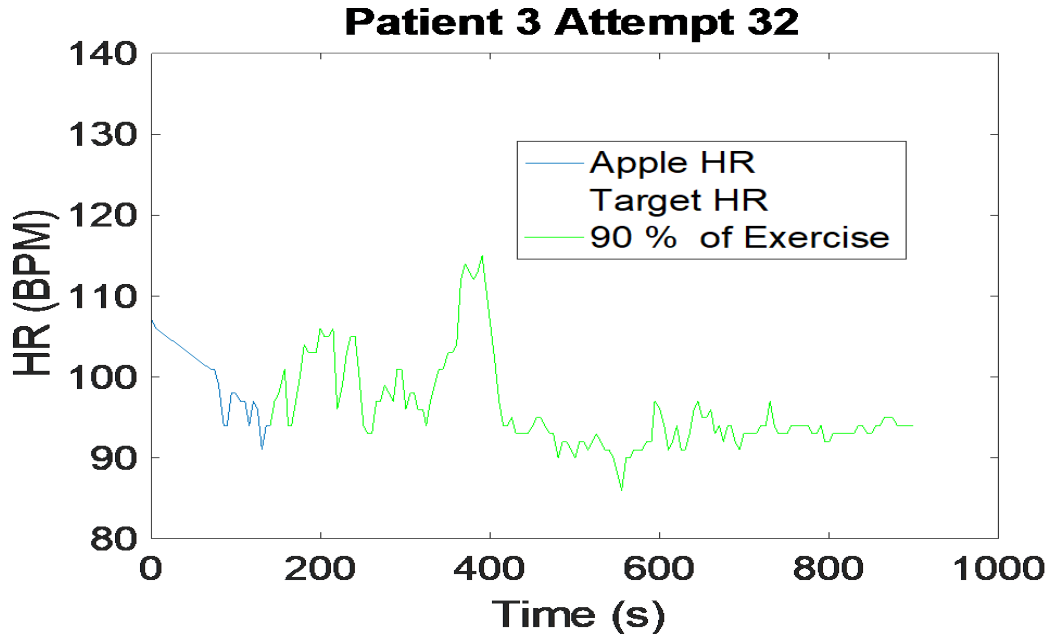


Figure A5.460: Patient No. 3 Week 11 Attempt 2

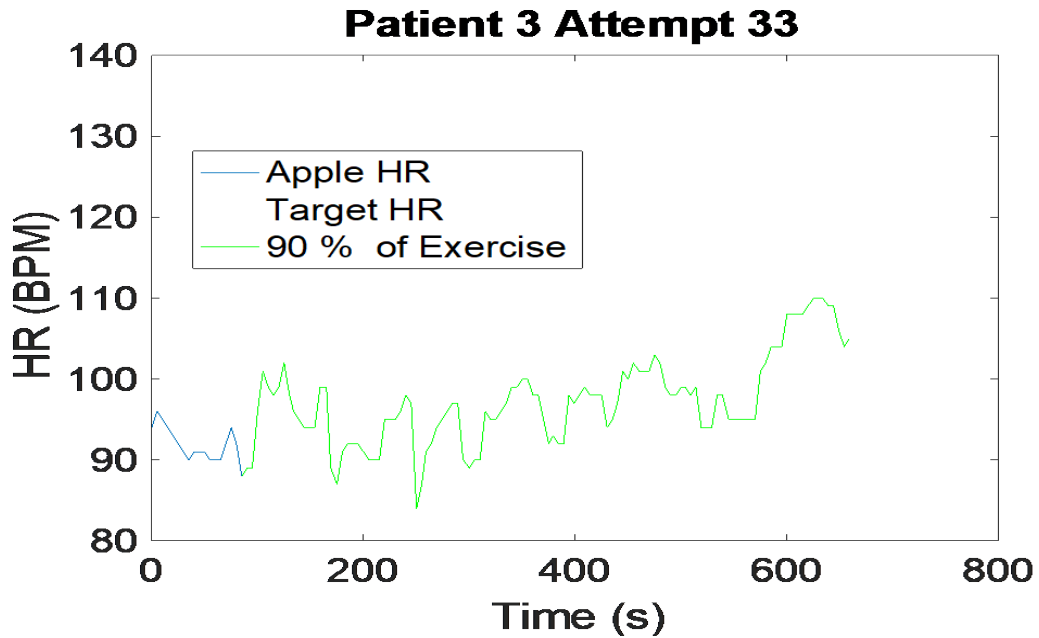


Figure A5. 461

Figure A5.462: Patient No. 3 Week 11 Attempt 3



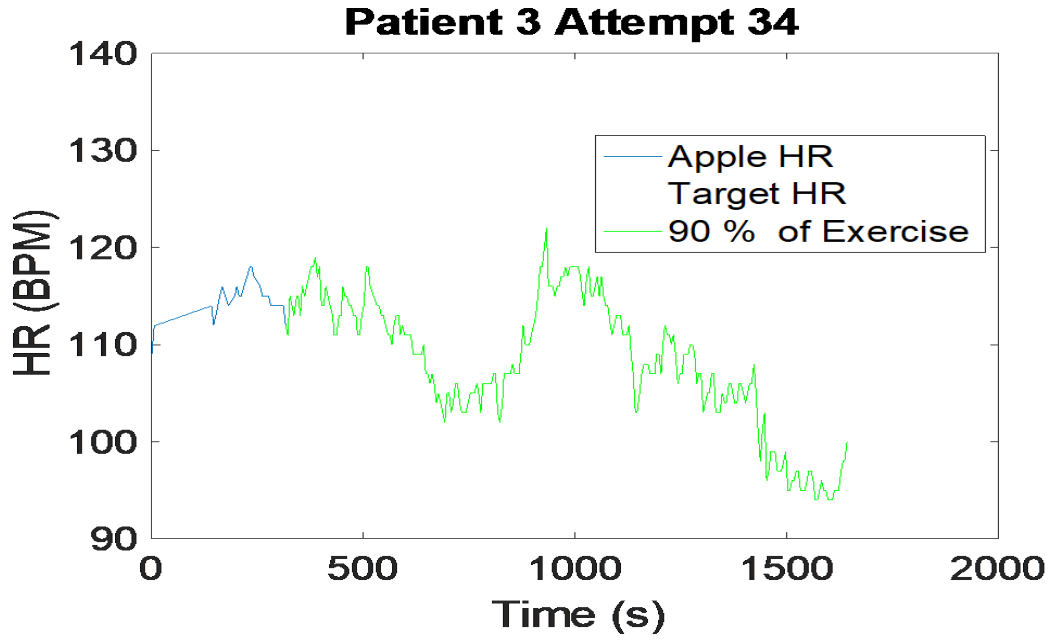


Figure A5.463: Patient No. 3 Week 11 Attempt 4

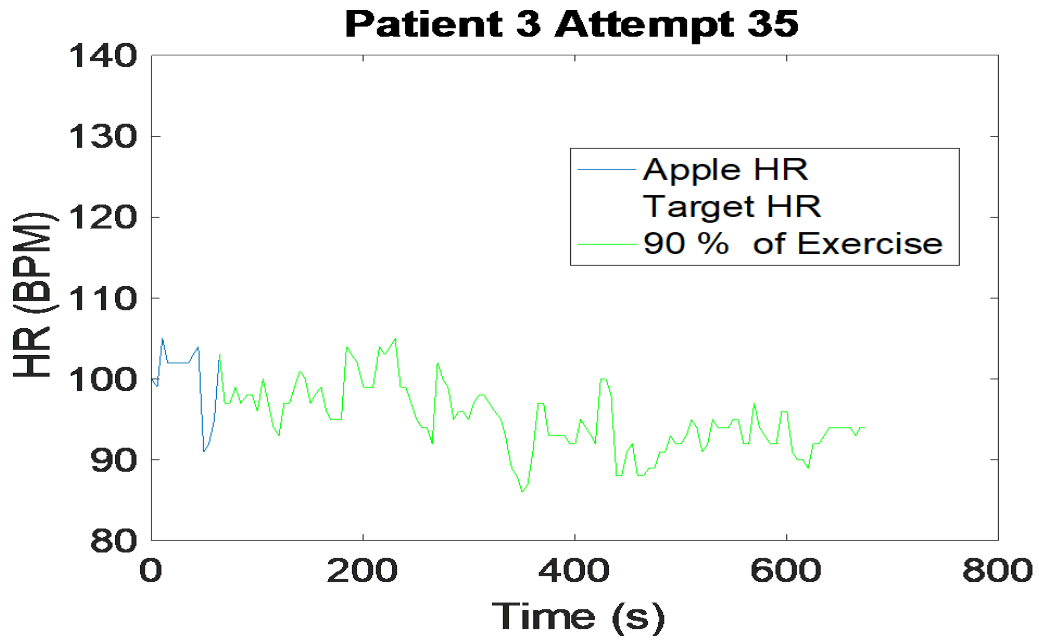
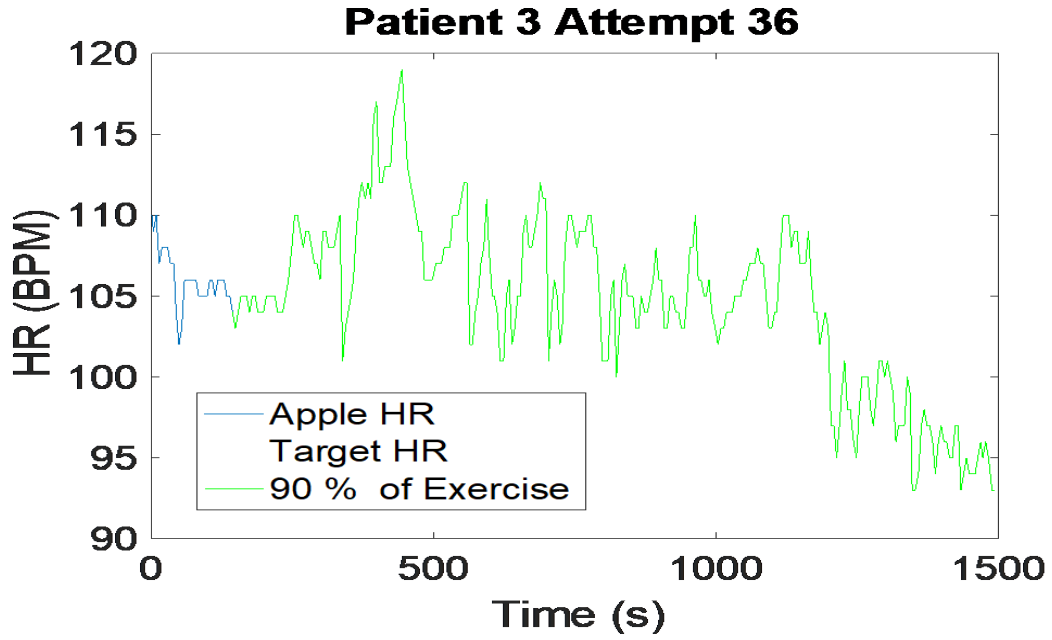
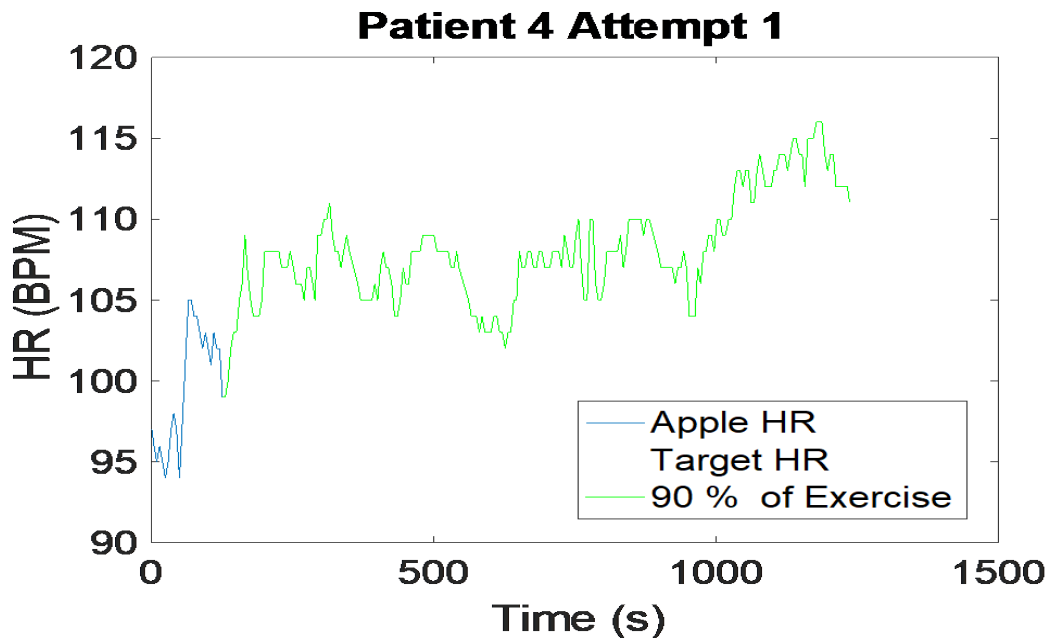


Figure A5.464: Patient No. 3 Week 11 Attempt 5



*Figure A5.465: Patient No. 3 Week 12 Attempt 1*

**Patient 4 Attempts:**



*Figure A5.466: Patient No. 4 Week 1 Attempt 1*

### Patient 4 Attempt 2

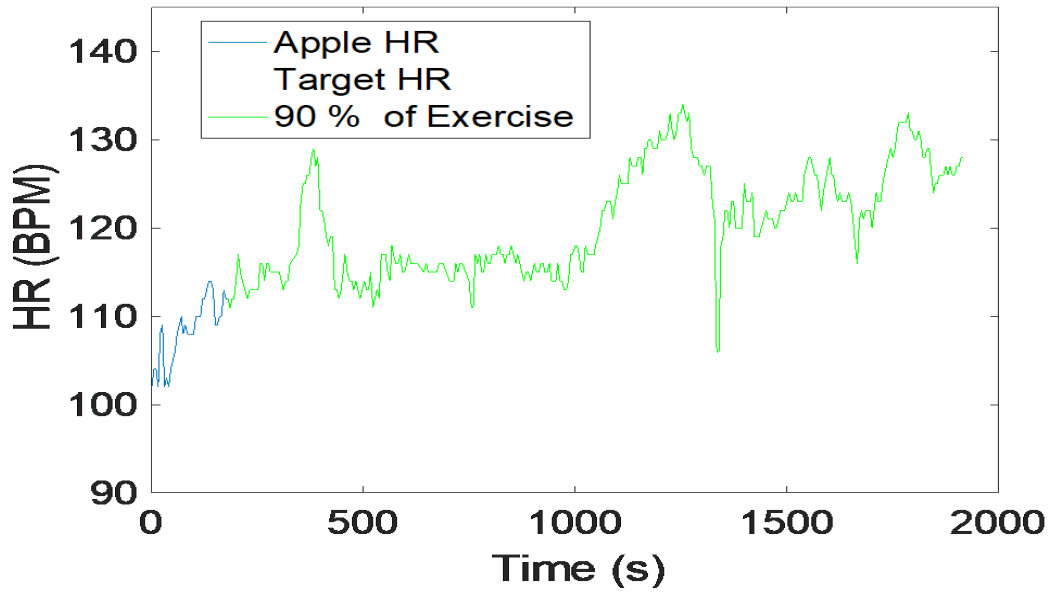


Figure A5.467: Patient No. 4 Week 2 Attempt 1

### Patient 4 Attempt 3

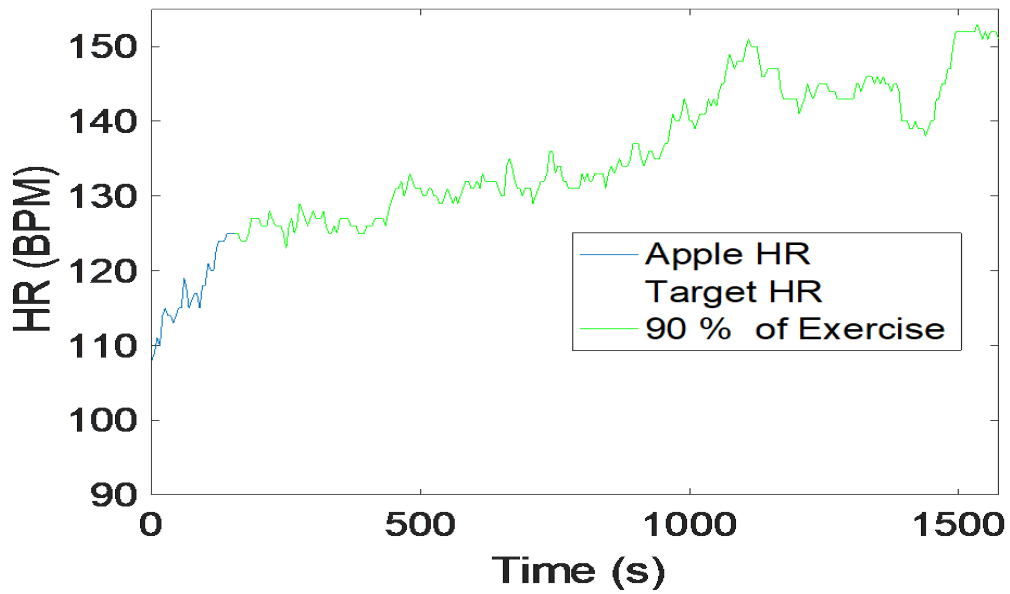


Figure A5.468: Patient No. 4 Week 2 Attempt 2

### Patient 4 Attempt 4

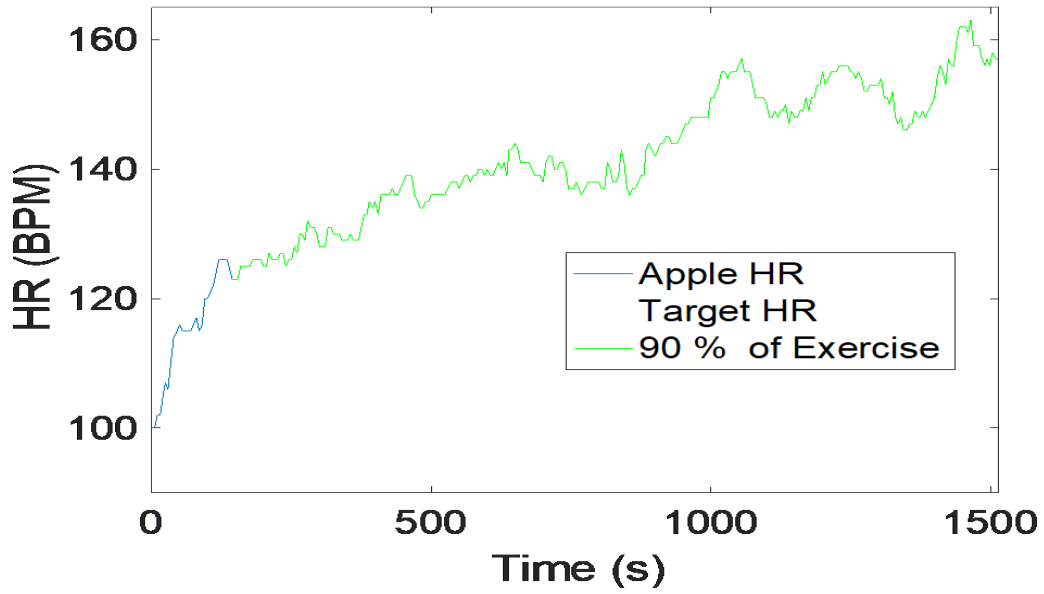


Figure A5.469: Patient No. 4 Week 2 Attempt 3

### Patient 4 Attempt 5

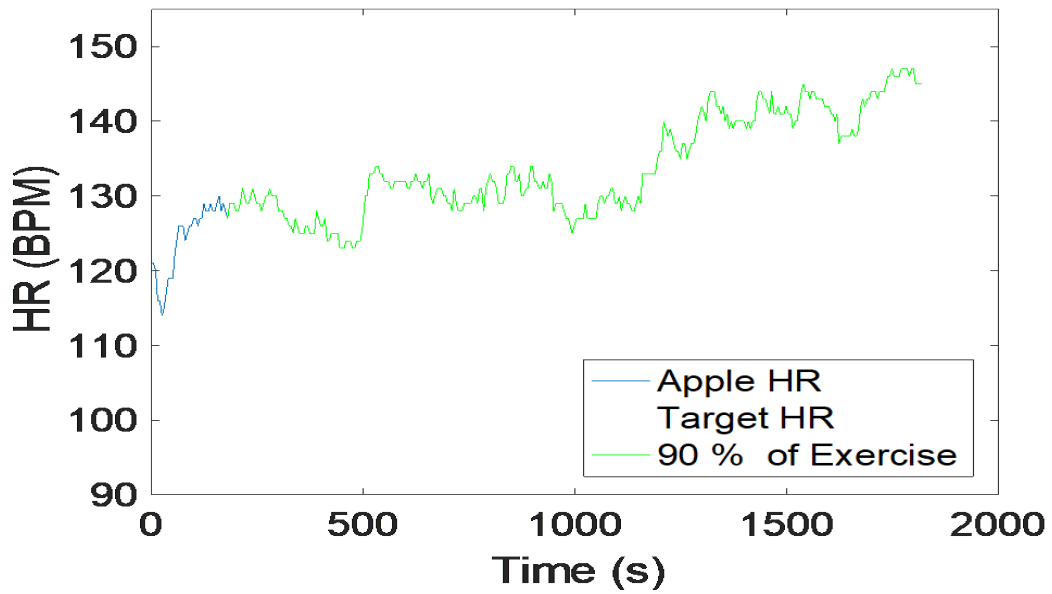


Figure A5.470: Patient No. 4 Week 3 Attempt 1

### Patient 4 Attempt 6

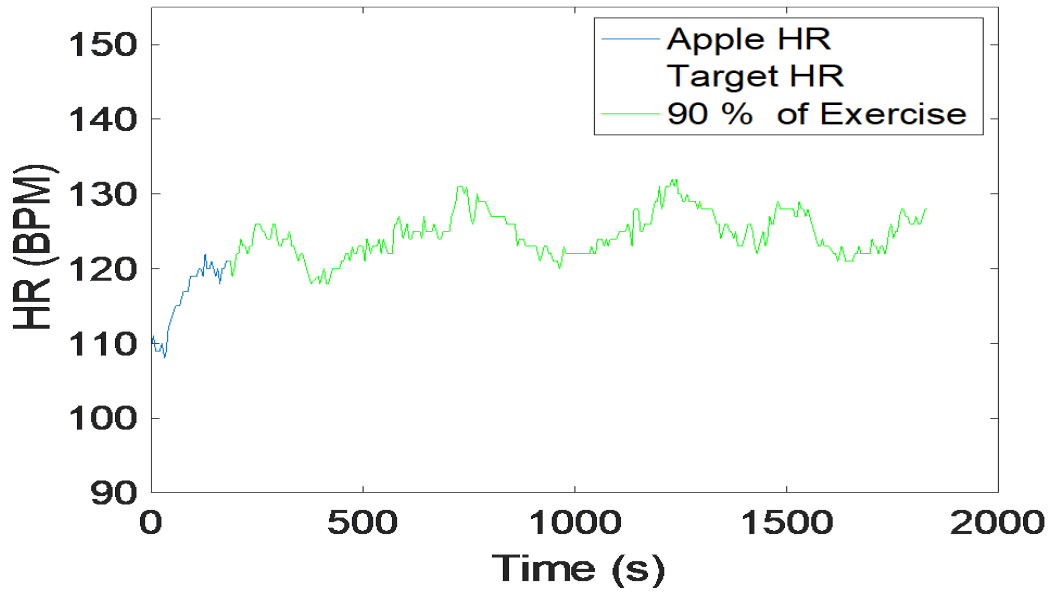


Figure A5.471: Patient No. 4 Week 3 Attempt 2

### Patient 4 Attempt 7



Figure A5.472: Patient No. 4 Week 4 Attempt 1

### Patient 4 Attempt 8

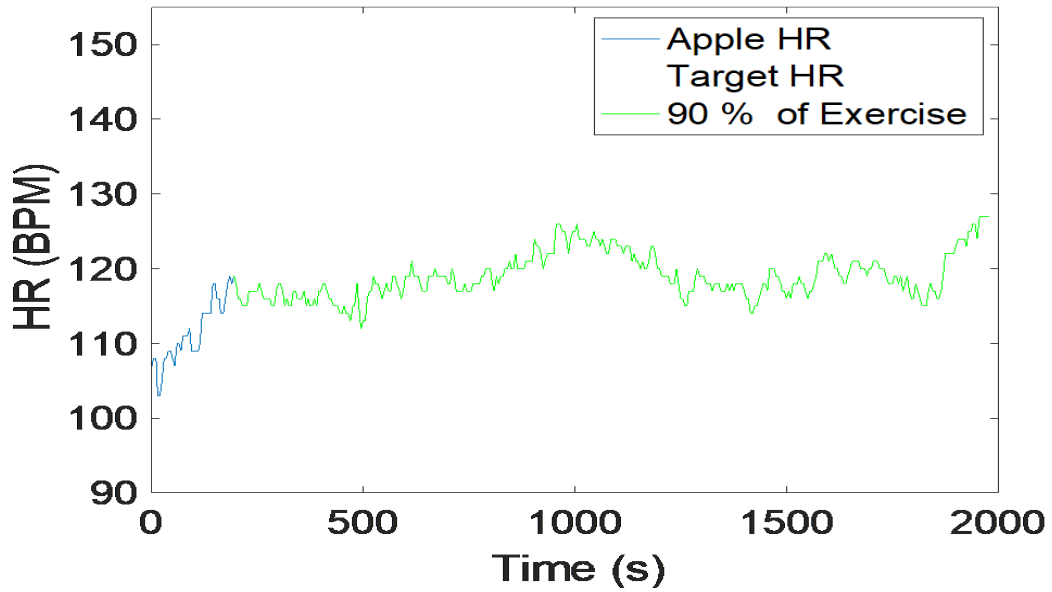


Figure A5.473: Patient No. 4 Week 5 Attempt 1

### Patient 4 Attempt 9



Figure A5.474: Patient No. 4 Week 5 Attempt 2

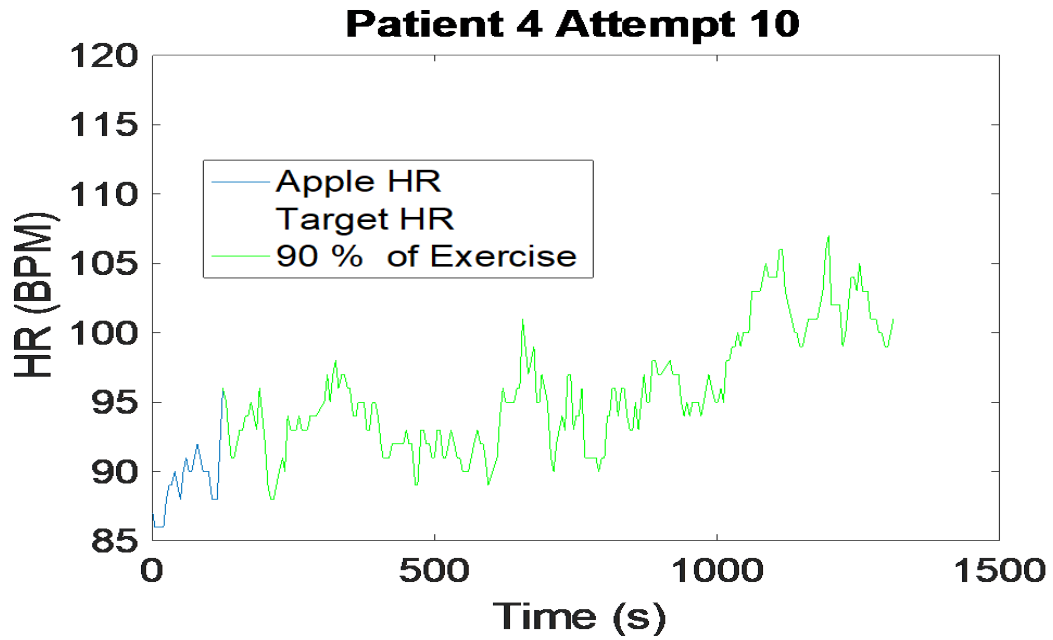


Figure A5.475: Patient No. 4 Week 5 Attempt 3

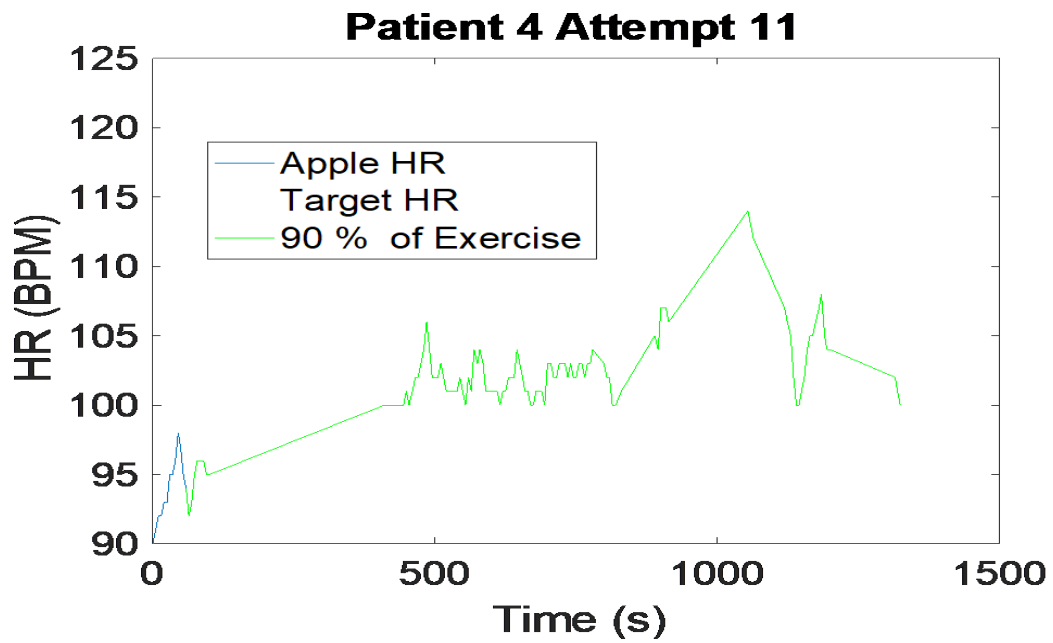


Figure A5.476: Patient No. 4 Week 6 Attempt 1

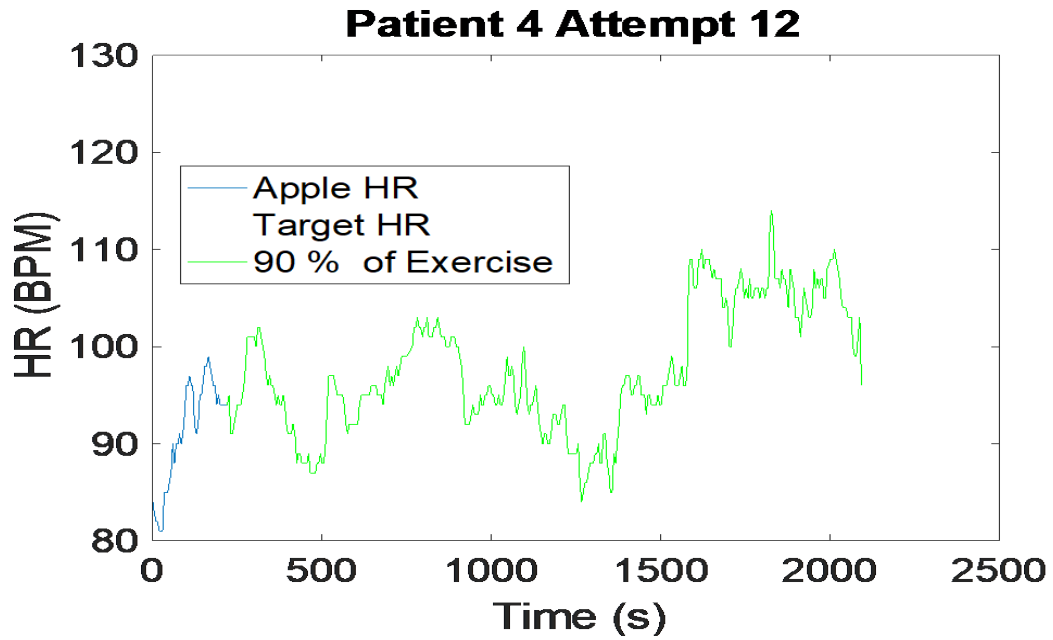


Figure A5. 477: Patient No. 4 Week 7 Attempt 1

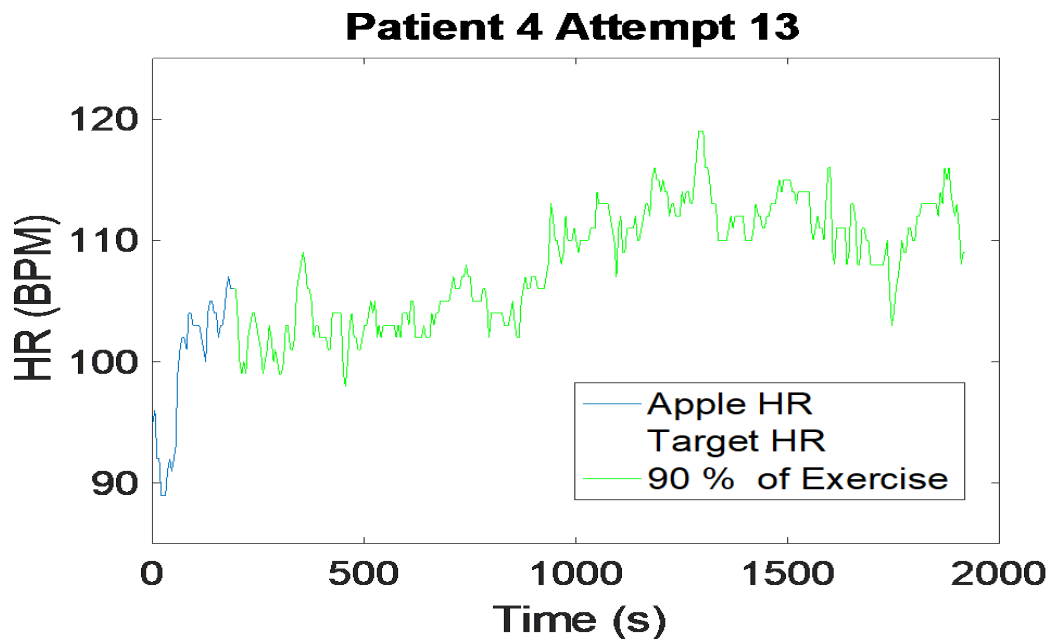


Figure A5. 478: Patient No. 4 Week 7 Attempt 2



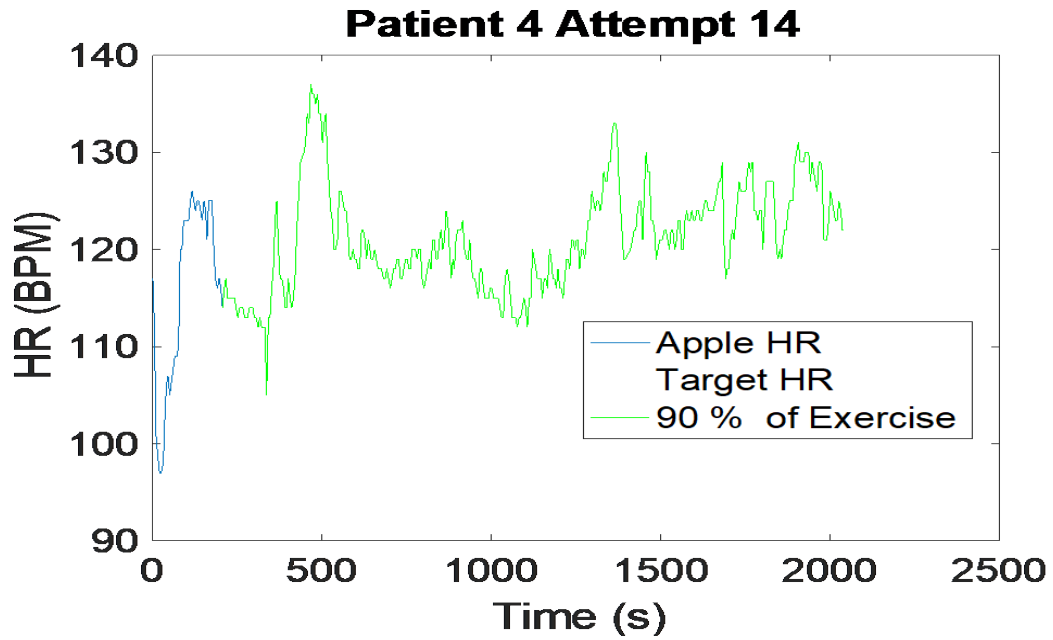


Figure A5. 479: Patient No. 4 Week 7 Attempt 3

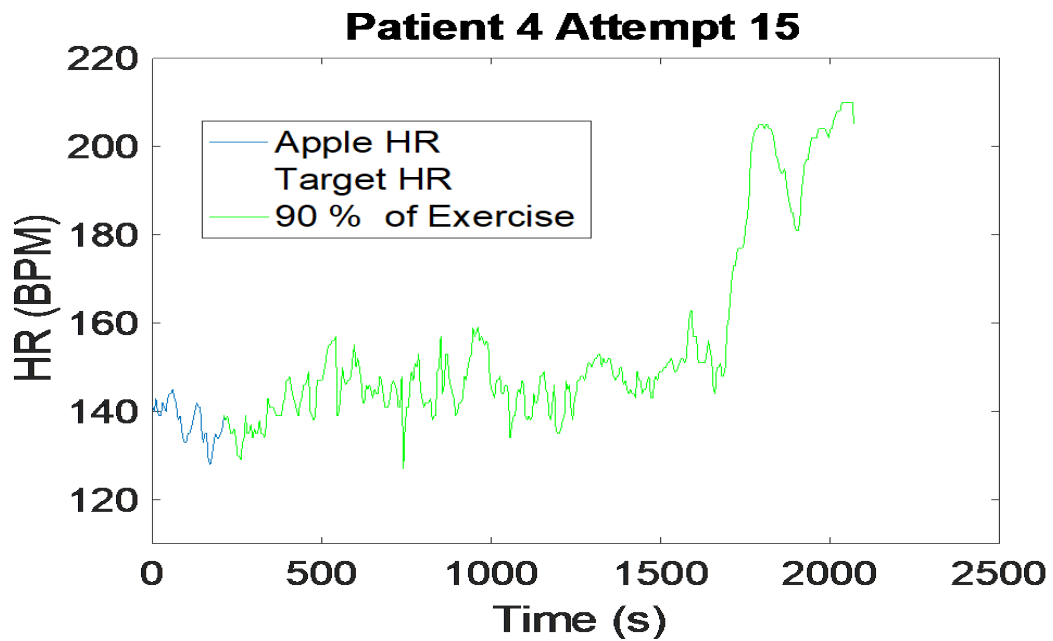


Figure A5. 480: Patient No. 4 Week 8 Attempt 1

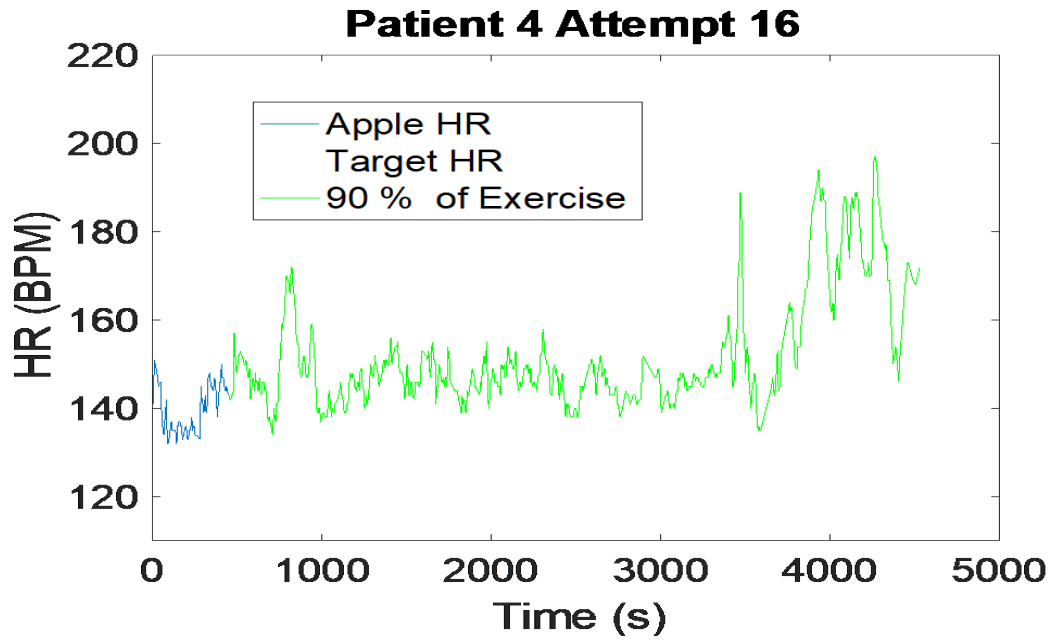


Figure A5.481: Patient No. 4 Week 8 Attempt 2

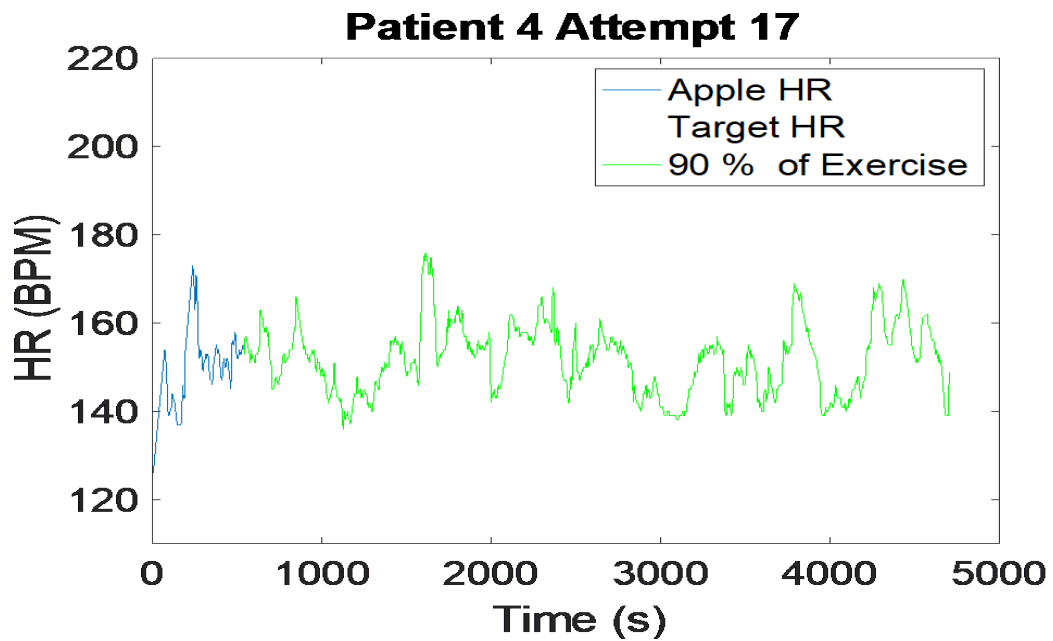


Figure A5.482: Patient No. 4 Week 9 Attempt 1

### Patient 4 Attempt 18

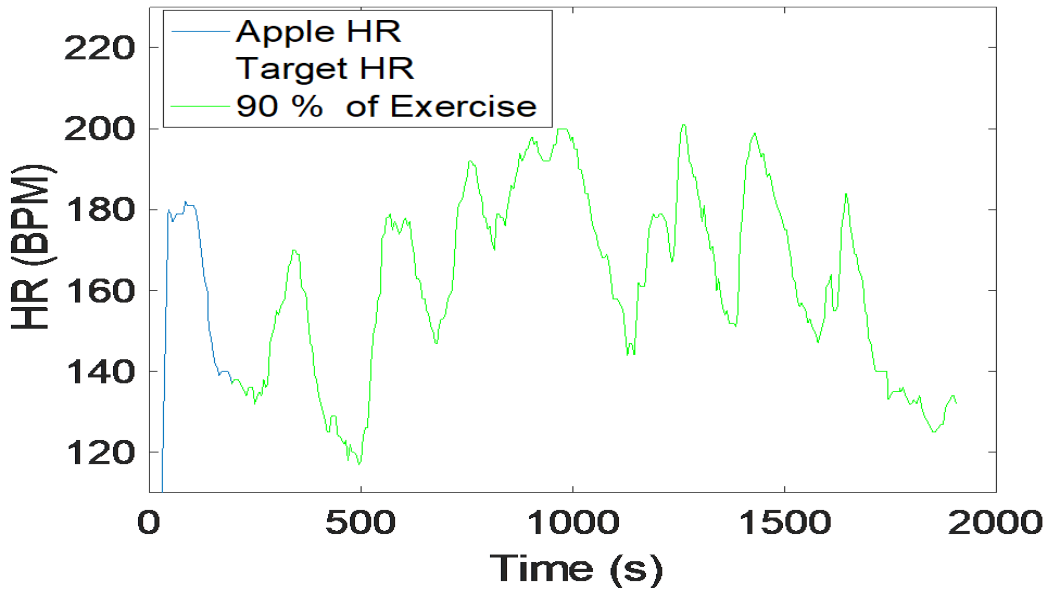


Figure A5.483: Patient No. 4 Week 10 Attempt 1

### Patient 4 Attempt 19

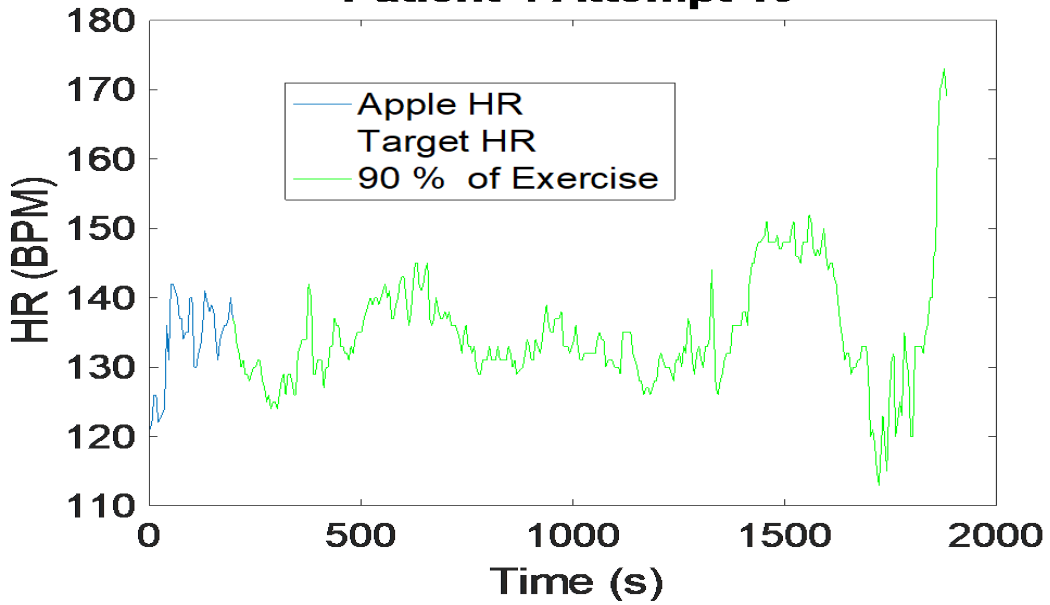
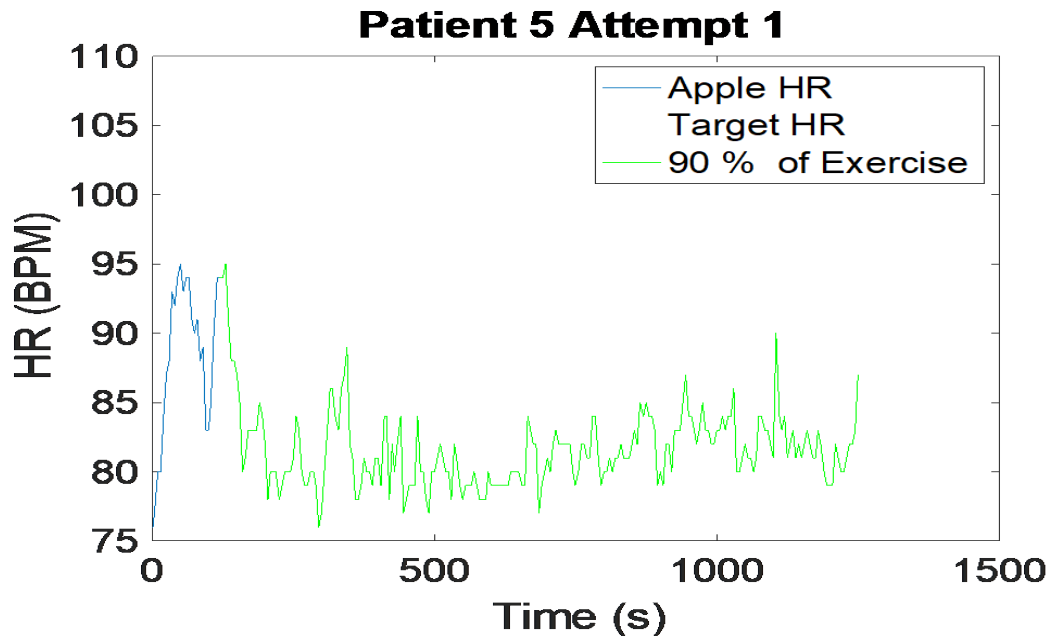
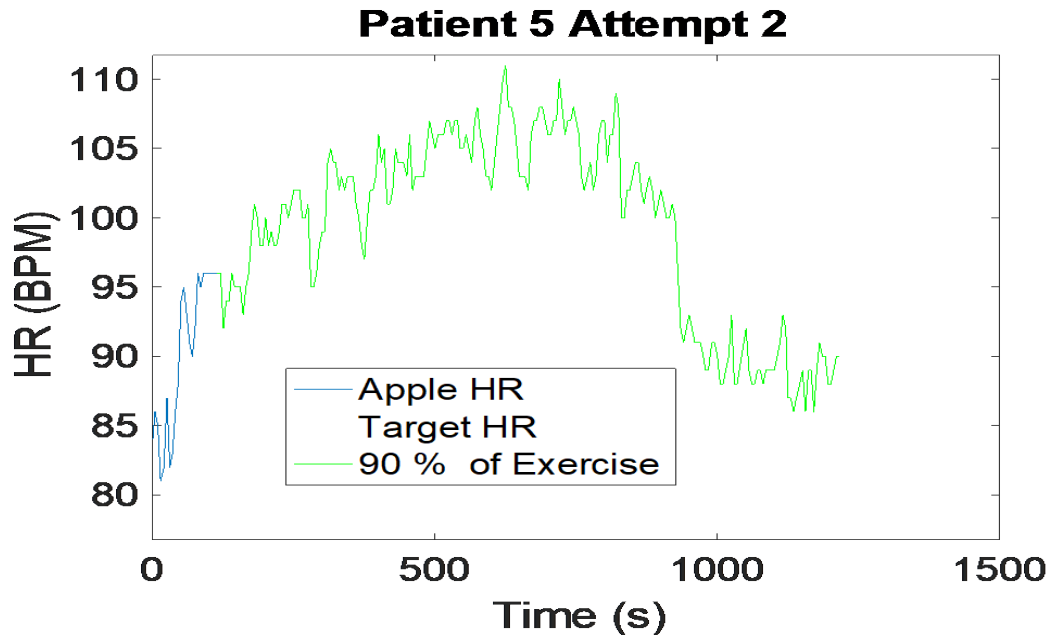


Figure A5.484: Patient No. 4 Week 10 Attempt 2

**Patient 5 Attempts:**



*Figure A5.485: Patient No. 5 Week 1 Attempt 1*



*Figure A5.486: Patient No. 5 Week 1 Attempt 2*

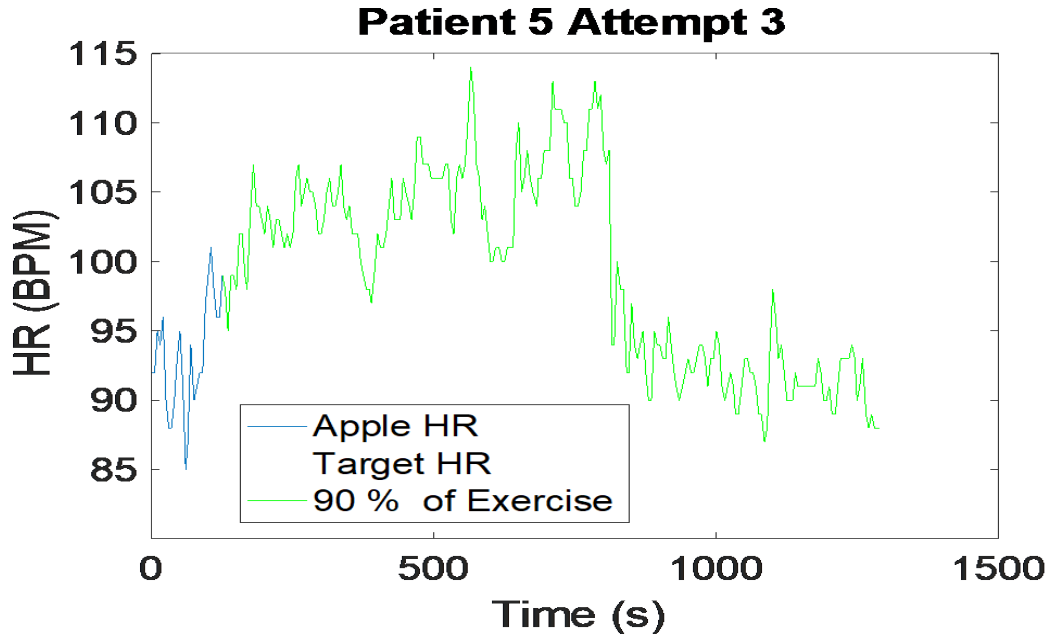


Figure A5.487: Patient No. 5 Week 1 Attempt 3

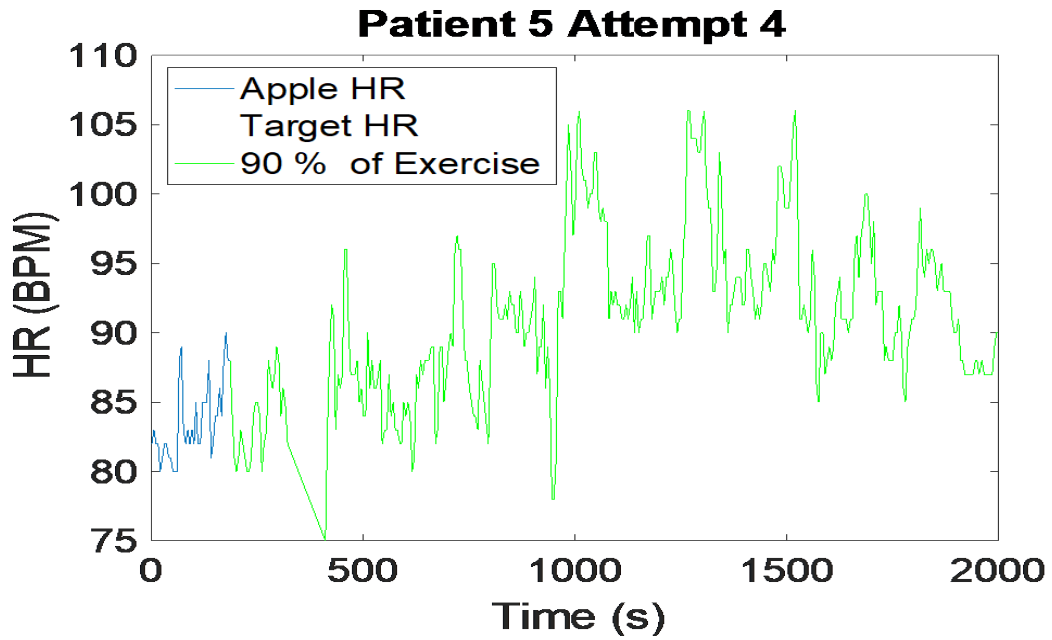


Figure A5.488: Patient No. 5 Week 2 Attempt 1

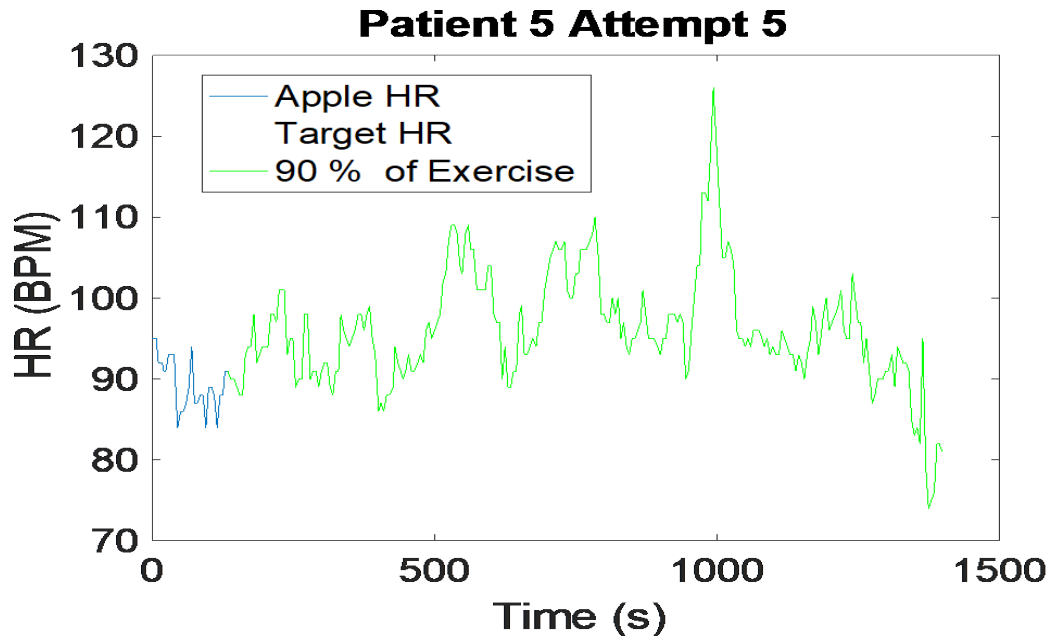


Figure A5.489: Patient No. 5 Week 2 Attempt 2

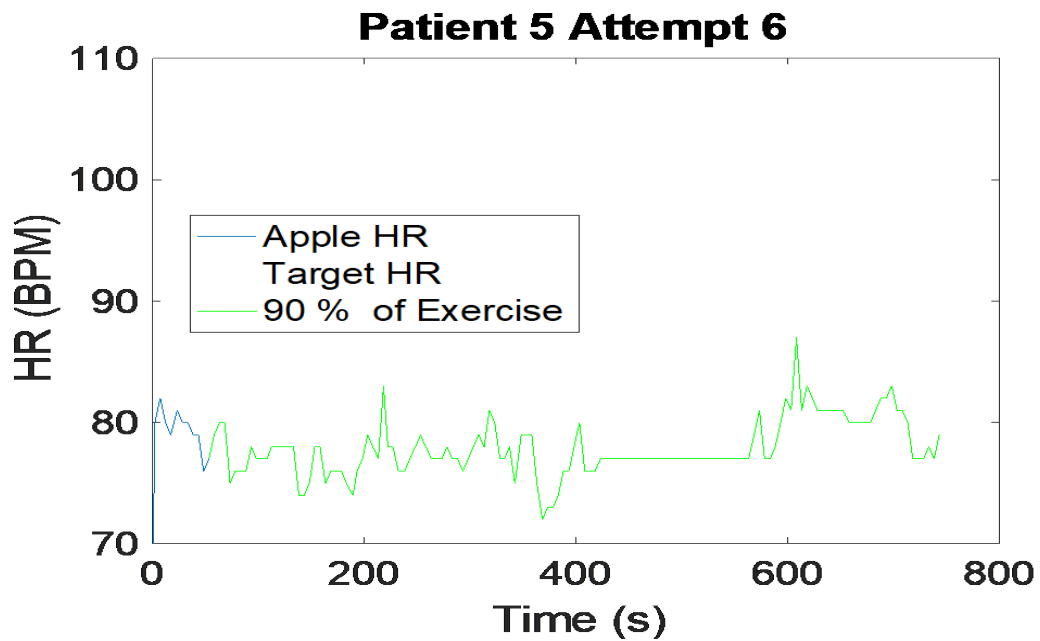


Figure A5.490: Patient No. 5 Week 2 Attempt 3

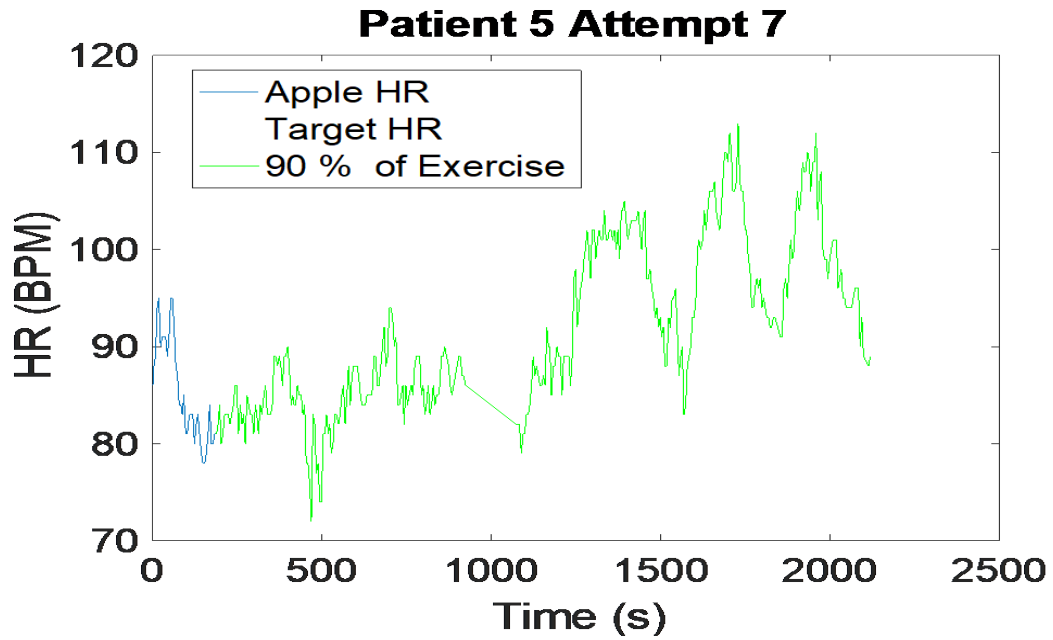


Figure A5.491: Patient No. 5 Week 3 Attempt 1

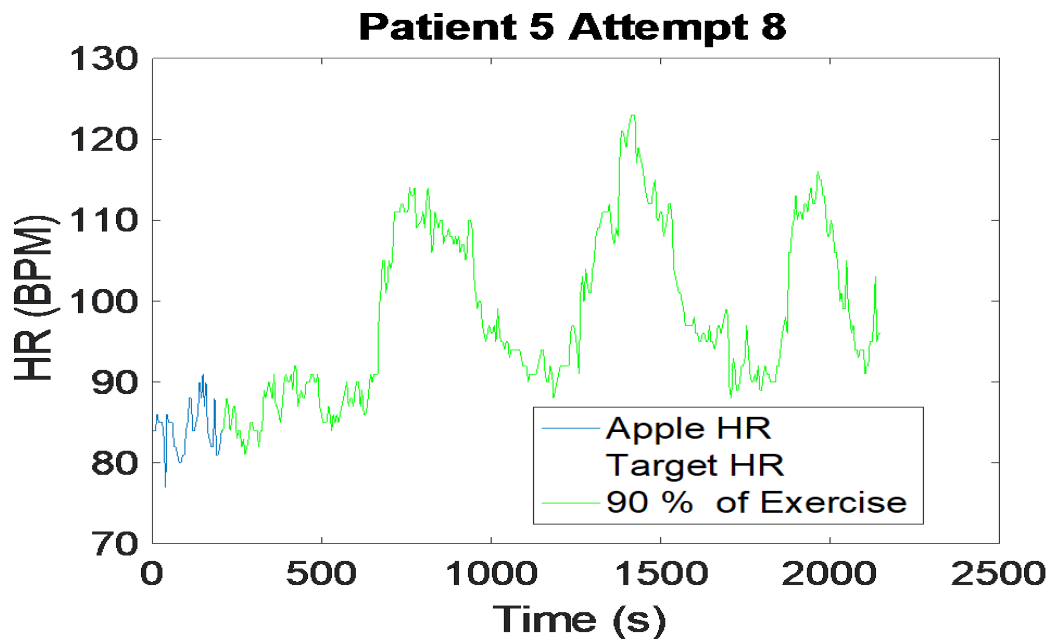


Figure A5.492: Patient No. 5 Week 4 Attempt 1

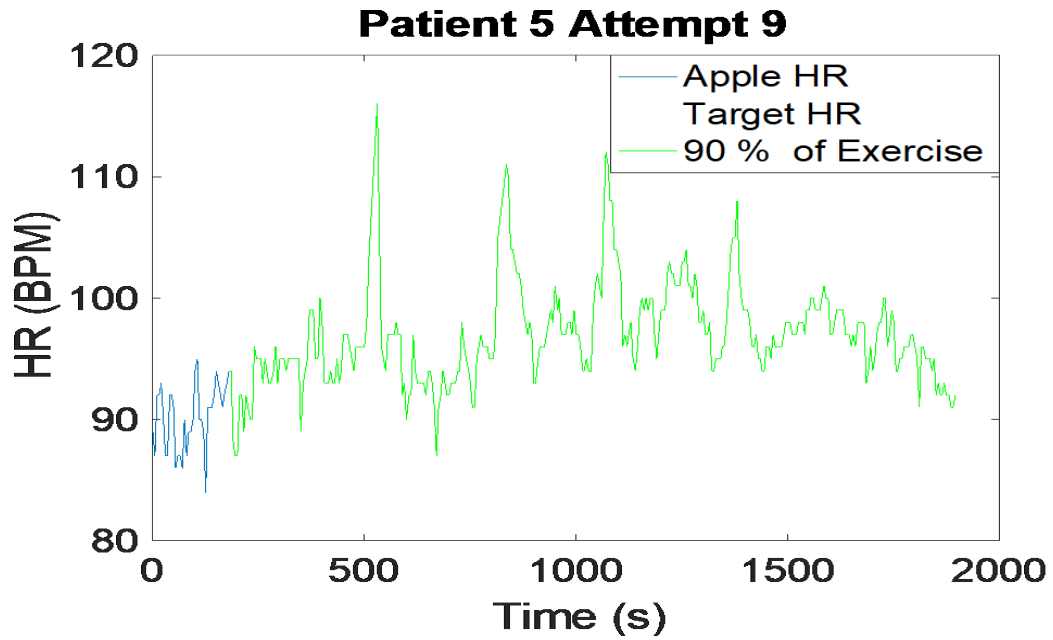


Figure A5.493: Patient No. 5 Week 5 Attempt 1

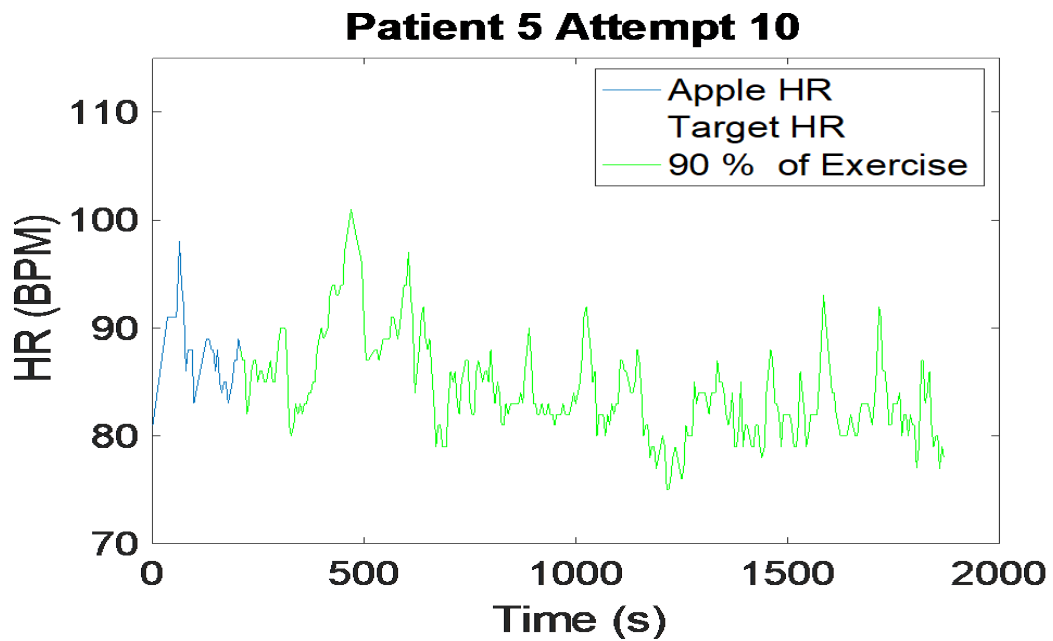


Figure A5.494: Patient No. 5 Week 5 Attempt 2



### Patient 5 Attempt 11

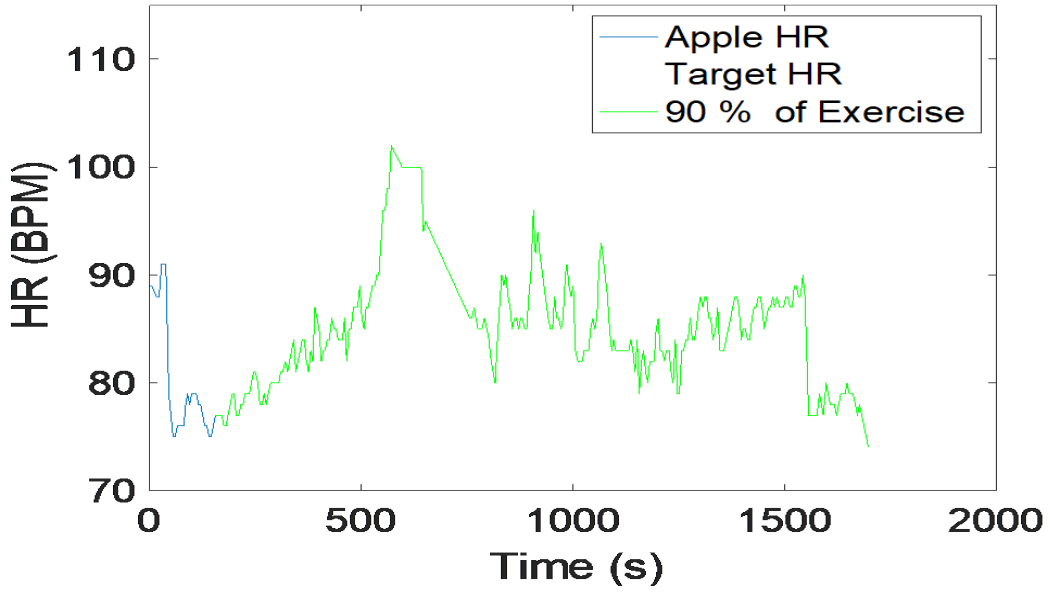


Figure A5.495: Patient No. 5 Week 6 Attempt 1

### Patient 5 Attempt 12

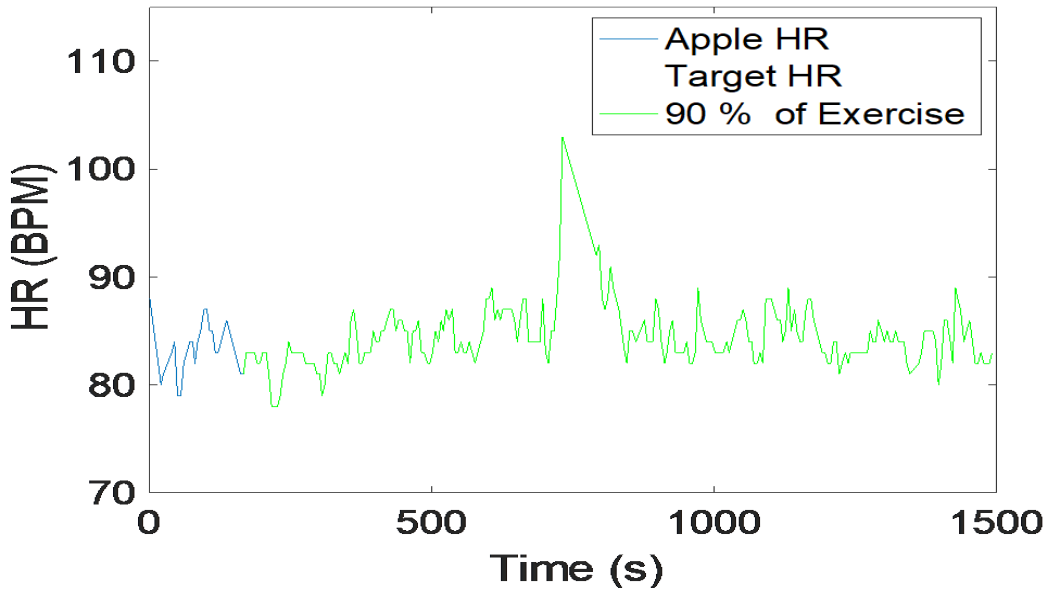


Figure A5.496: Patient No. 5 Week 7 Attempt 1

### Patient 5 Attempt 13

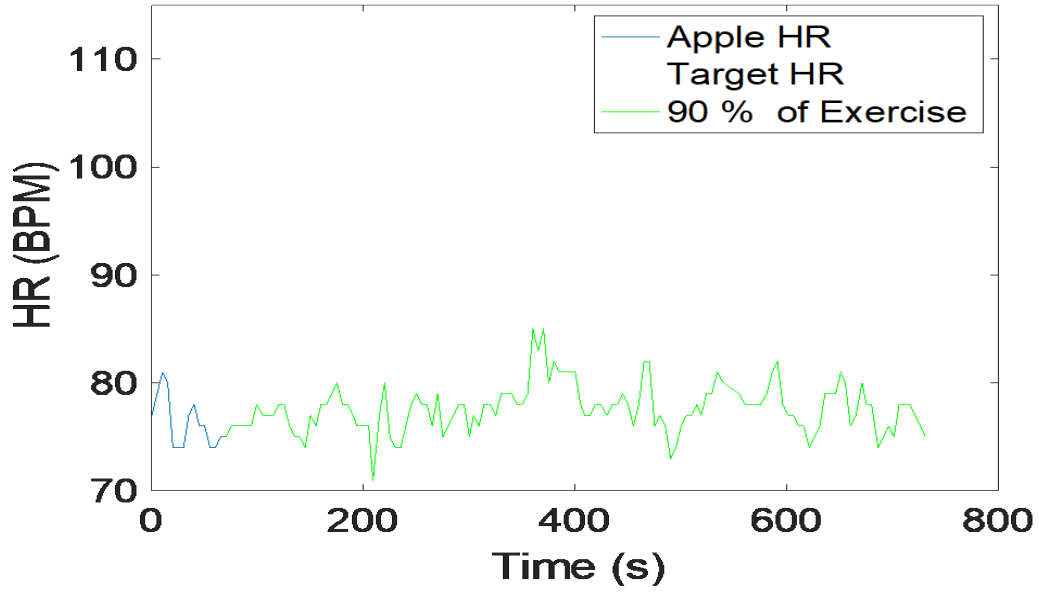


Figure A5.497: Patient No. 5 Week 7 Attempt 2

### Patient 5 Attempt 14

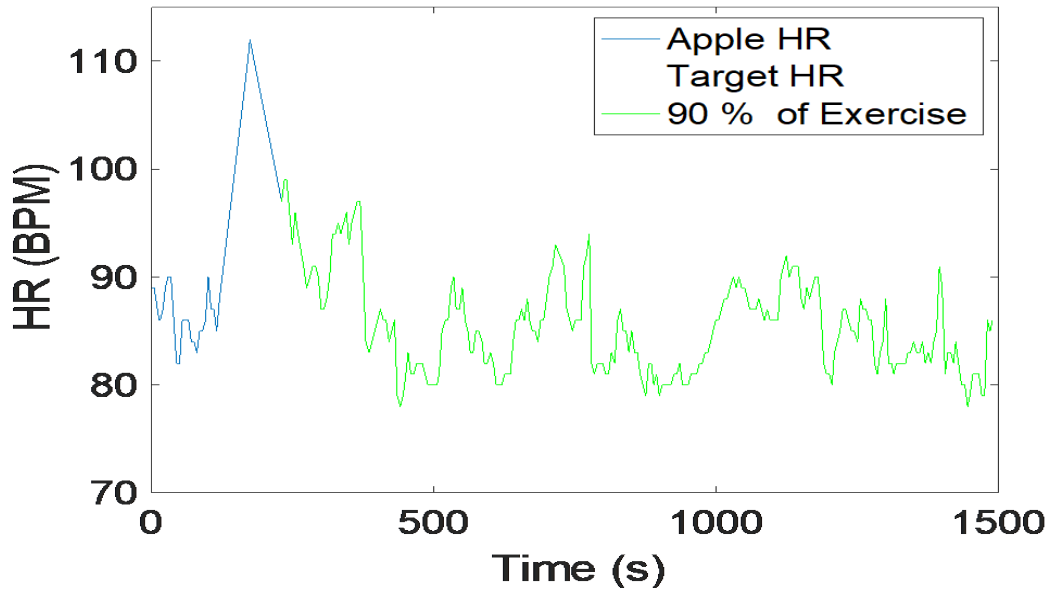


Figure A5.498: Patient No. 5 Week 7 Attempt 3

### Patient 5 Attempt 15



Figure A5.499: Patient No. 5 Week 7 Attempt 4

### Patient 5 Attempt 16

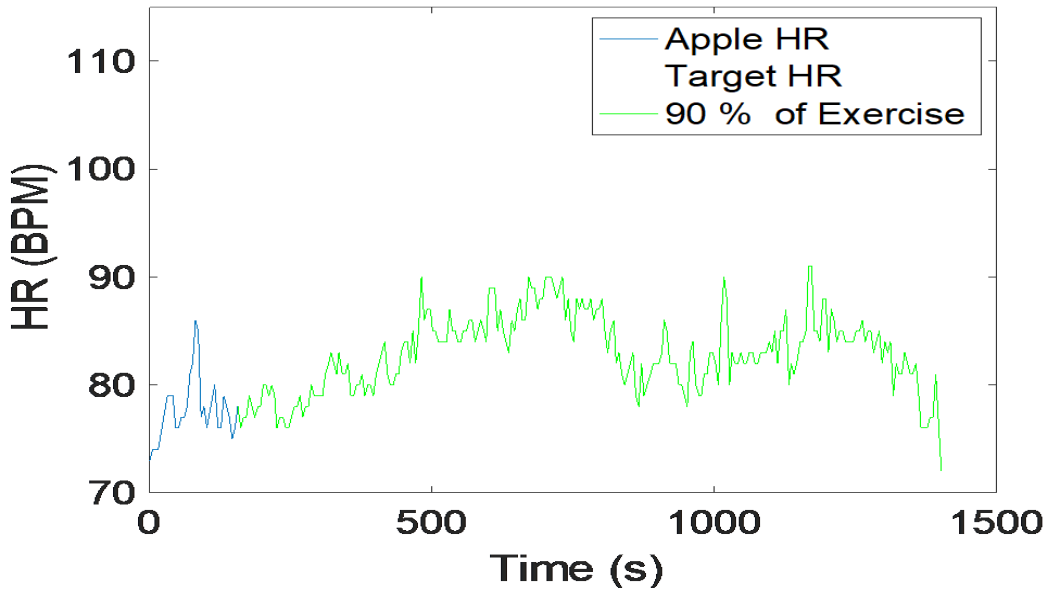


Figure A5.500: Patient No. 5 Week 8 Attempt 1

### Patient 5 Attempt 17

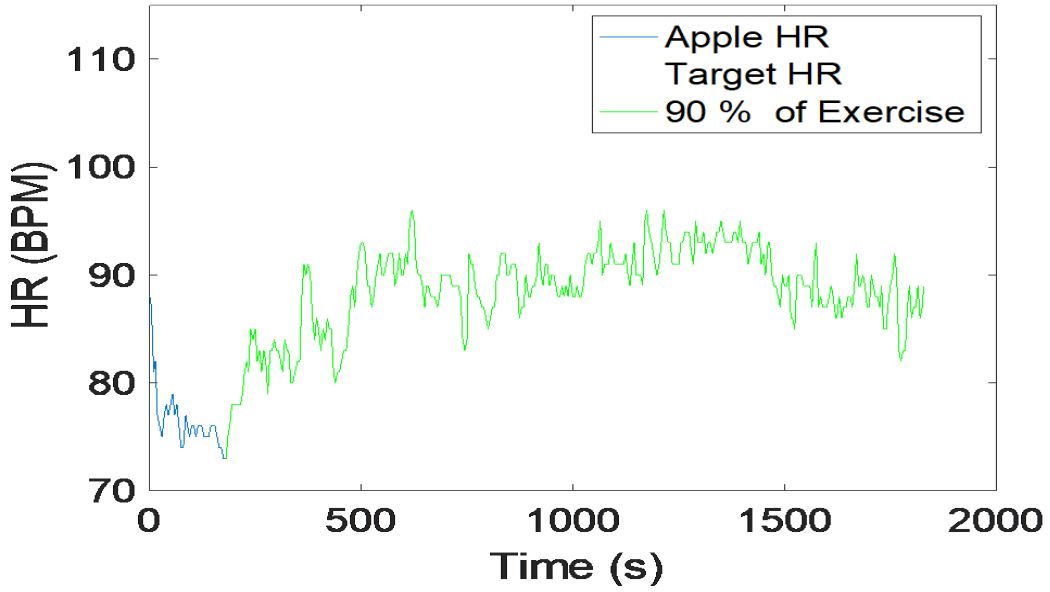


Figure A5.501: Patient No. 5 Week 8 Attempt 2

### Patient 5 Attempt 18

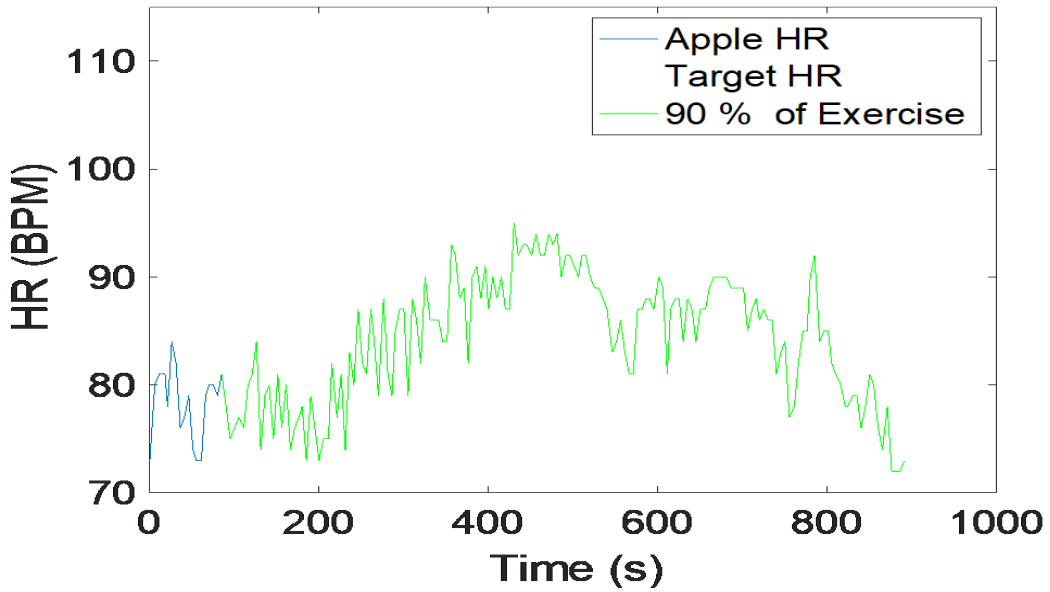


Figure A5.502: Patient No. 5 Week 9 Attempt 1

### Patient 5 Attempt 19

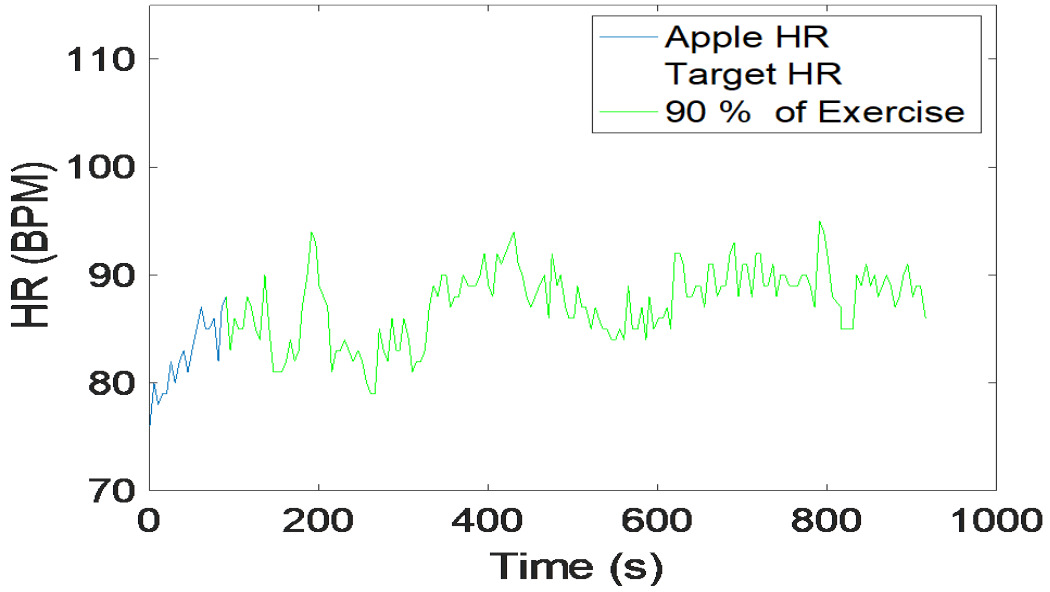


Figure A5.503: Patient No. 5 Week 9 Attempt 2

### Patient 5 Attempt 20

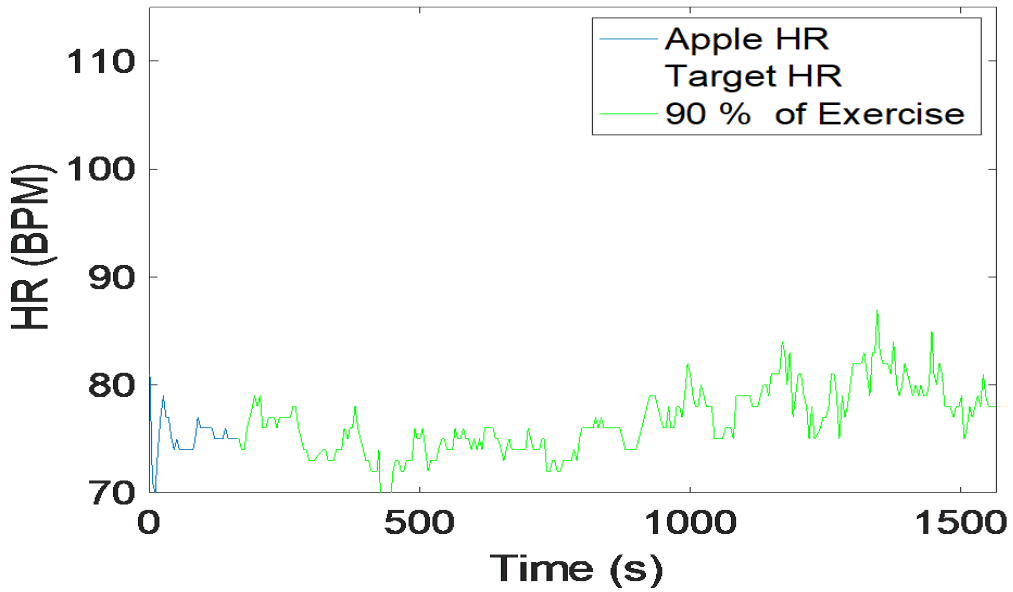


Figure A5.504: Patient No. 5 Week 9 Attempt 3

### Patient 5 Attempt 21

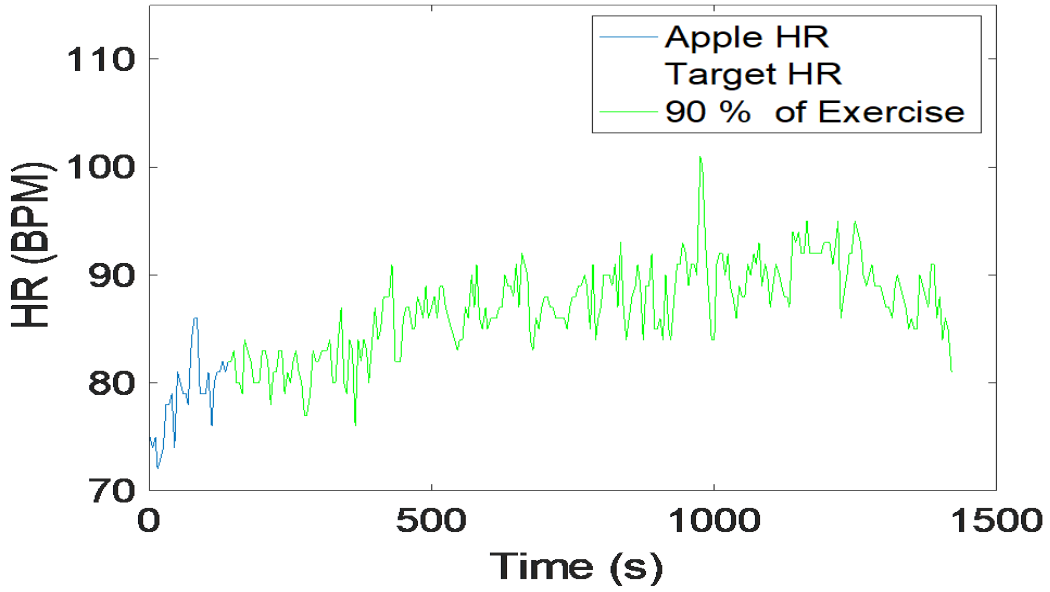


Figure A5.505: Patient No. 5 Week 10 Attempt 1

### Patient 5 Attempt 22

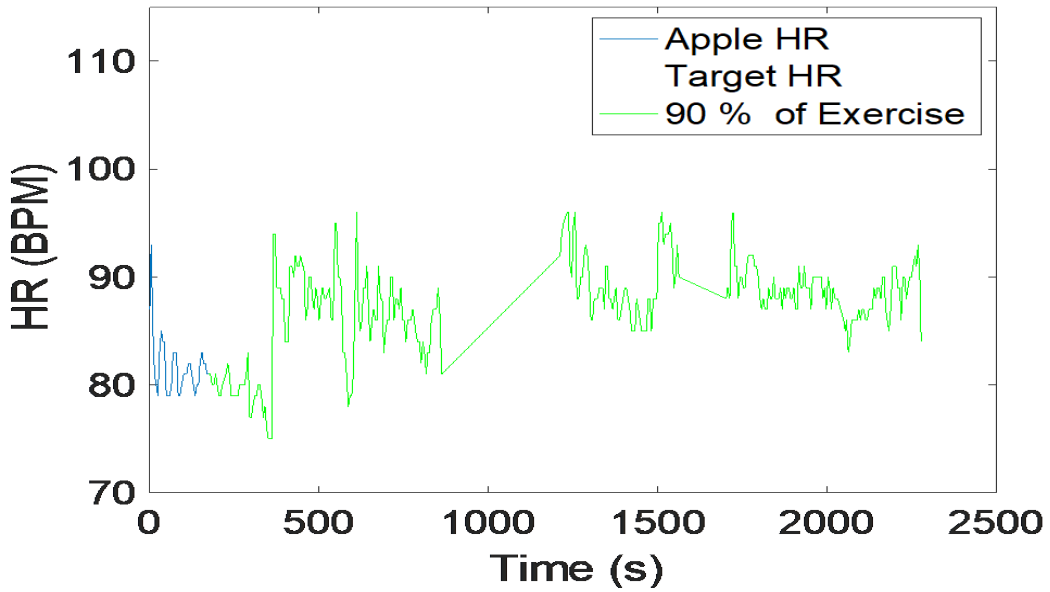


Figure A5.506: Patient No. 5 Week 10 Attempt 2

### Patient 5 Attempt 23



Figure A5.507: Patient No. 5 Week 10 Attempt 3

### Patient 5 Attempt 24

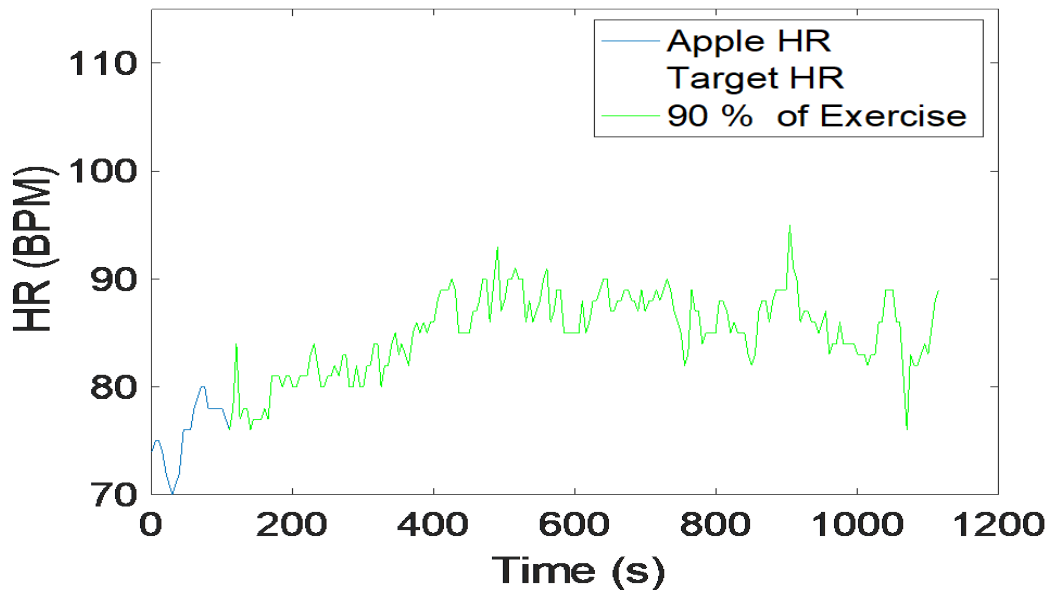


Figure A5.508: Patient No. 5 Week 11 Attempt 1

### Patient 5 Attempt 25

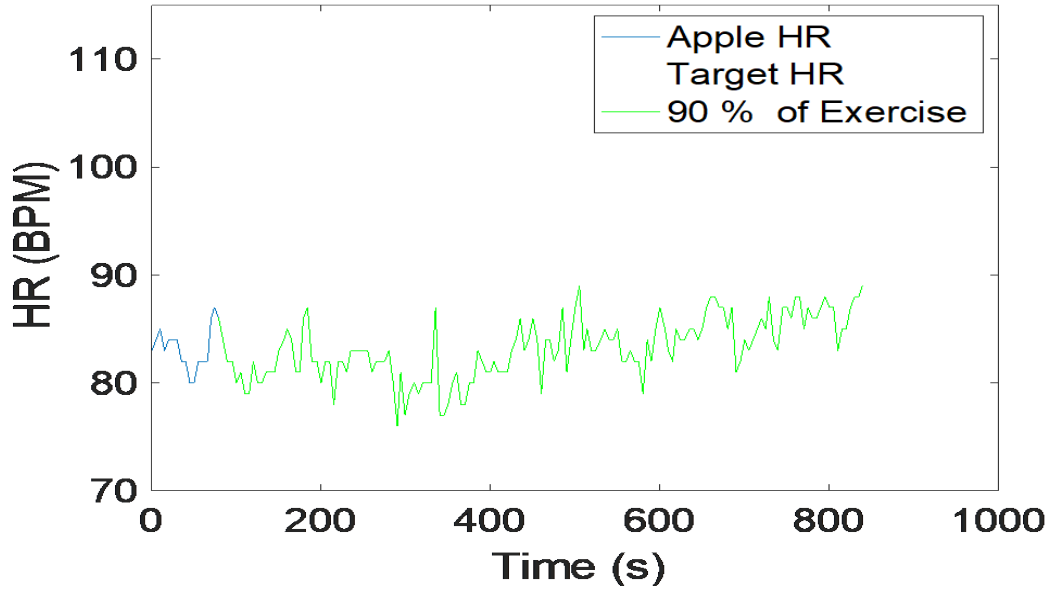


Figure A5.509: Patient No. 5 Week 11 Attempt 2

### Patient 5 Attempt 26

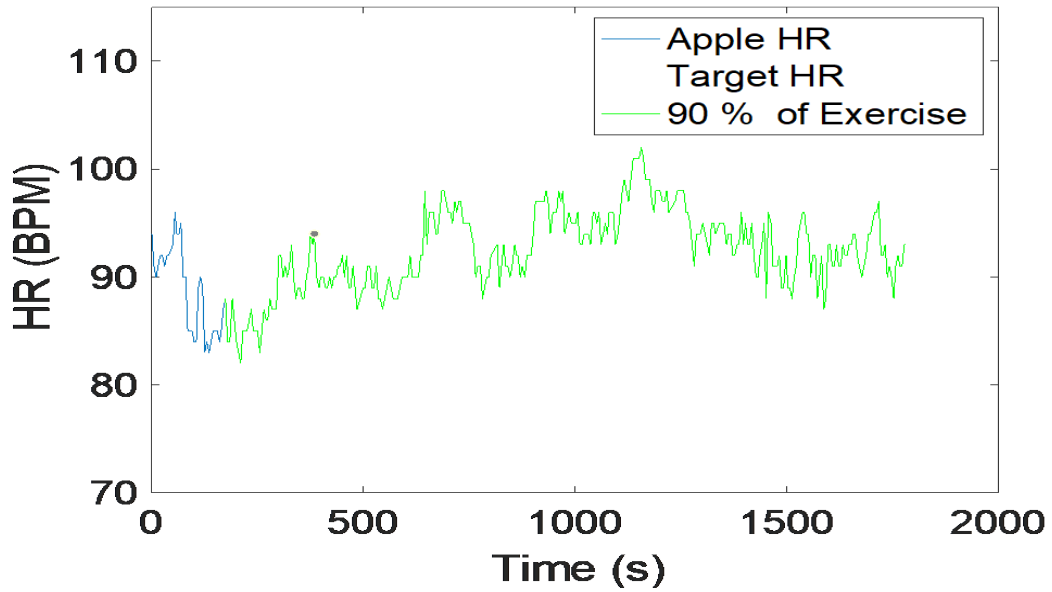


Figure A5.510: Patient No. 5 Week 11 Attempt 3



### Patient 5 Attempt 27

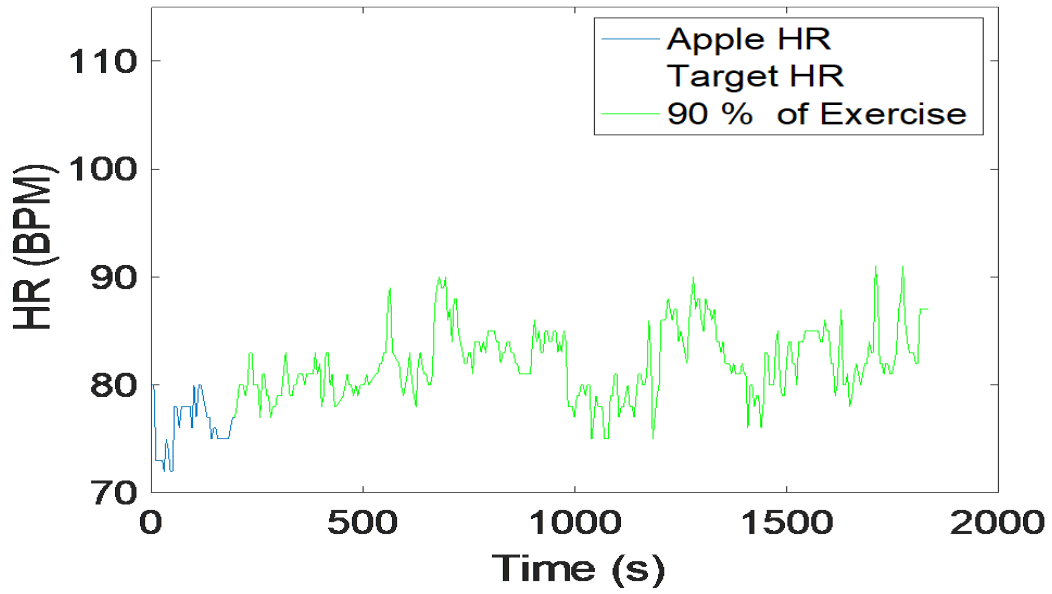


Figure A5.511: Patient No. 5 Week 11 Attempt 4

### Patient 5 Attempt 28

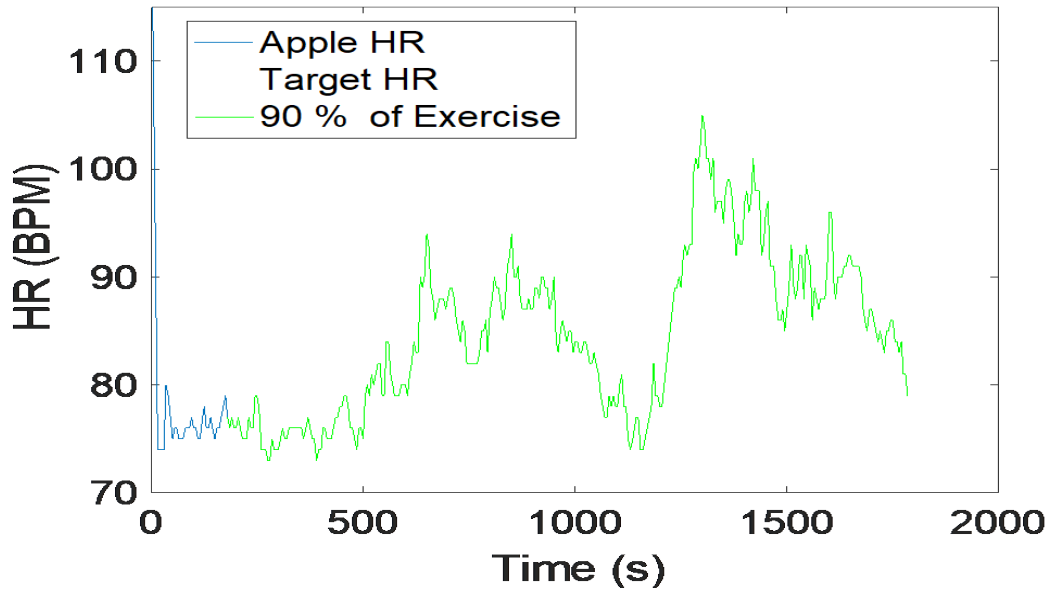
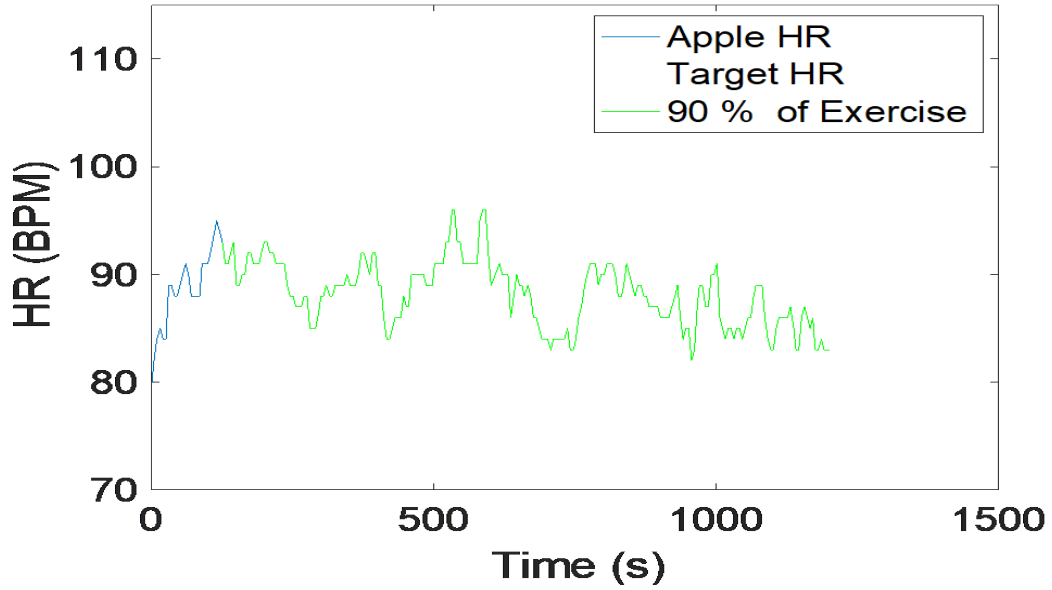


Figure A5.512: Patient No. 5 Week 11 Attempt 5

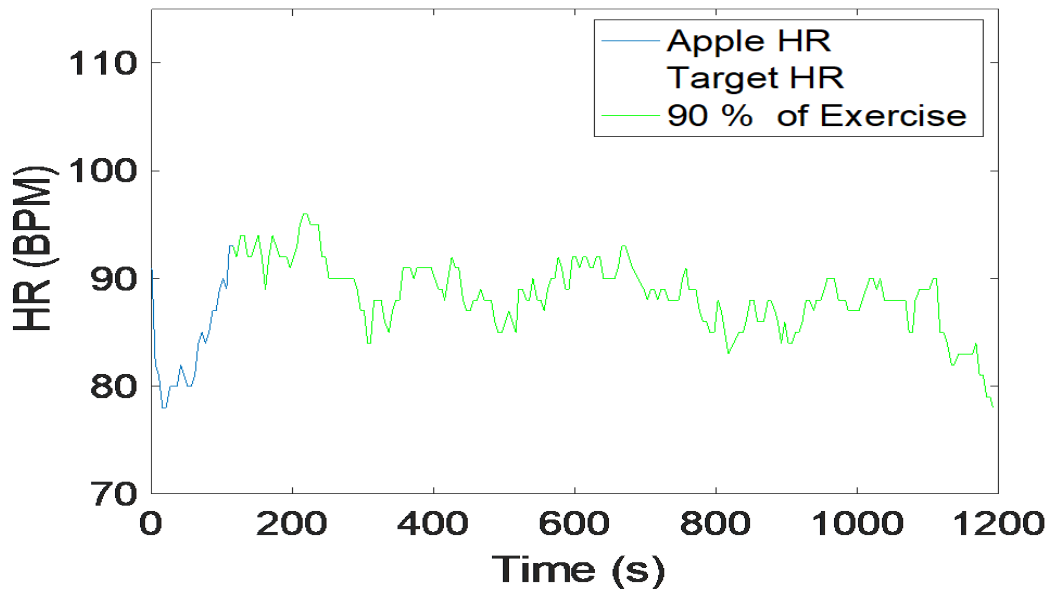
**Patient 6 Attempts:**

**Patient 6 Attempt 1**



*Figure A5.513: Patient No. 6 Week 1 Attempt 1*

**Patient 6 Attempt 2**



*Figure A5.514: Patient No. 6 Week 2 Attempt 1*

### Patient 6 Attempt 3



Figure A5.515: Patient No. 6 Week 2 Attempt 2

### Patient 6 Attempt 4

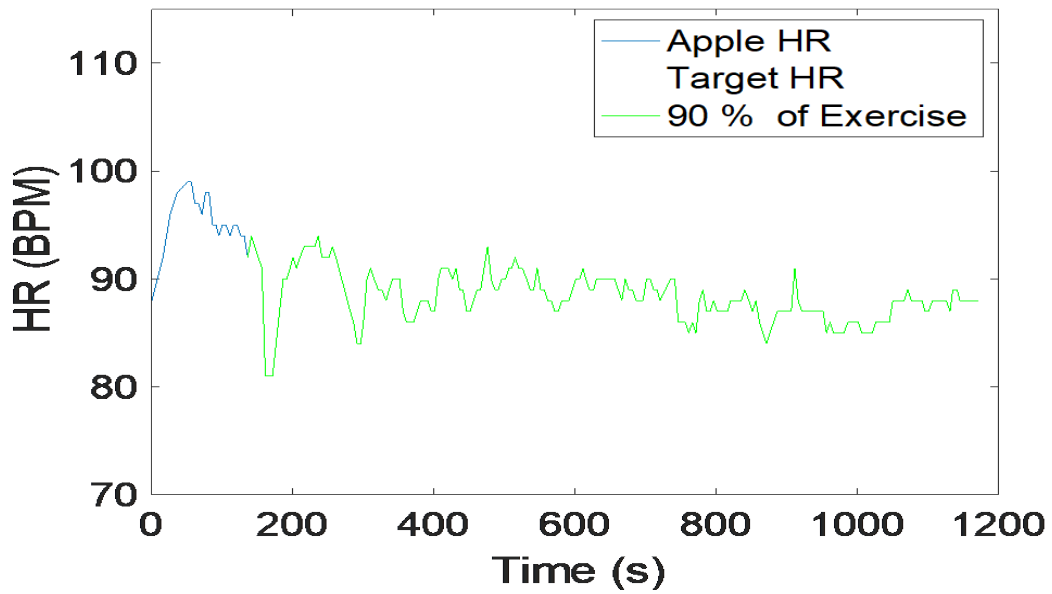


Figure A5.516: Patient No. 6 Week 2 Attempt 3

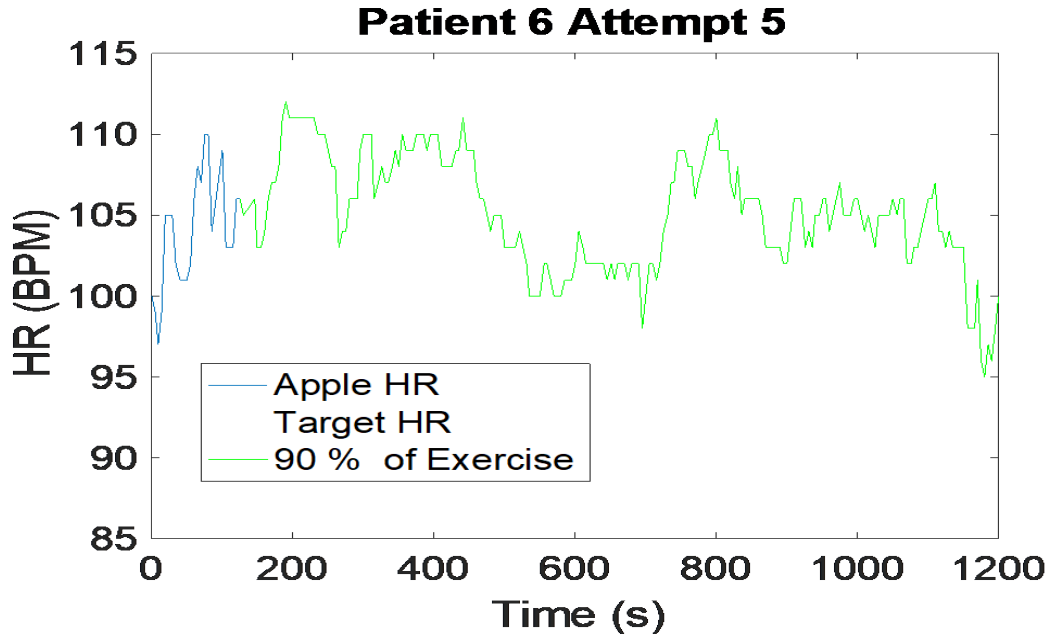


Figure A5.517: Patient No. 6 Week 3 Attempt 1

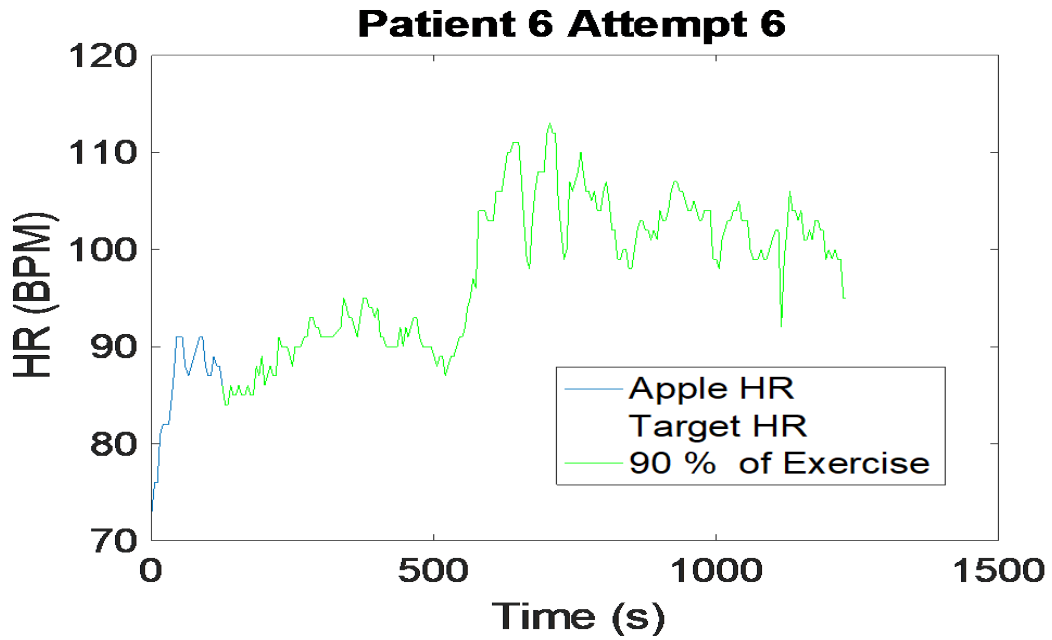


Figure A5.518: Patient No. 6 Week 3 Attempt 2

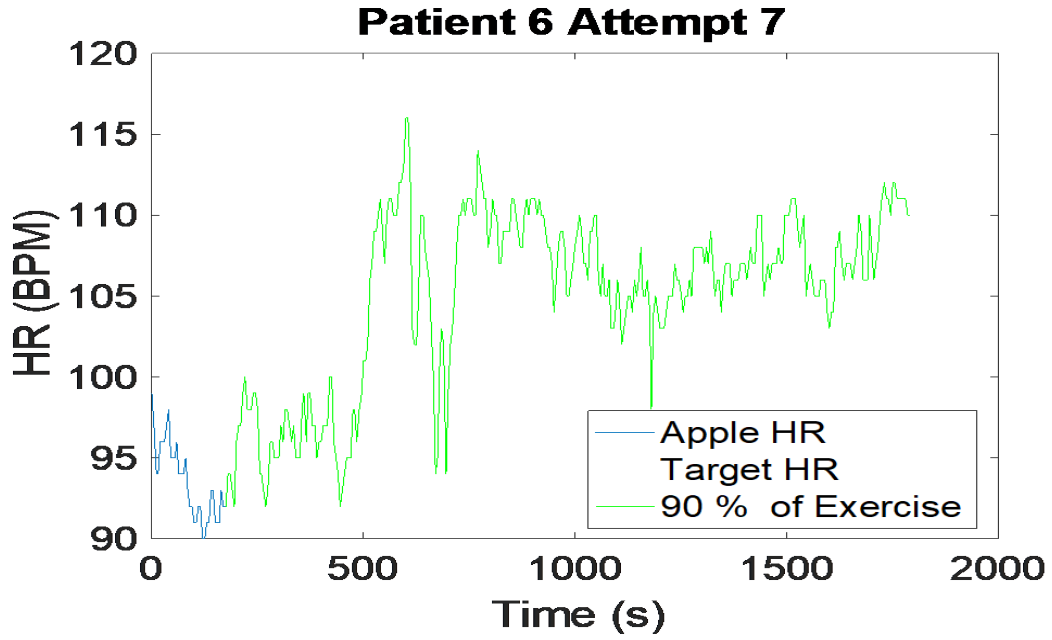


Figure A5.519: Patient No. 6 Week 3 Attempt 3

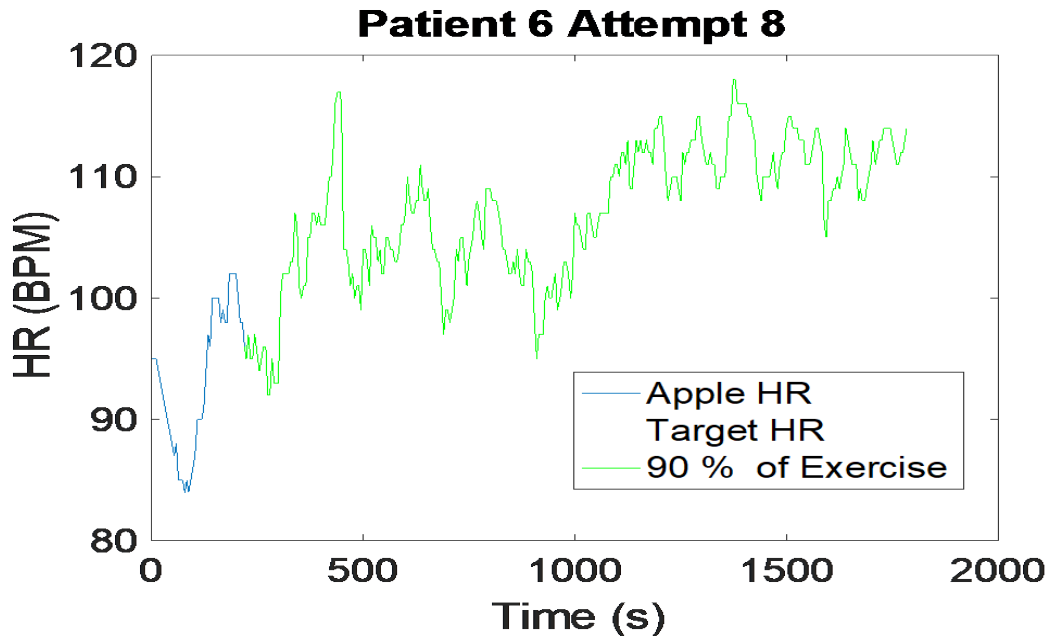


Figure A5.520: Patient No. 6 Week 4 Attempt 1

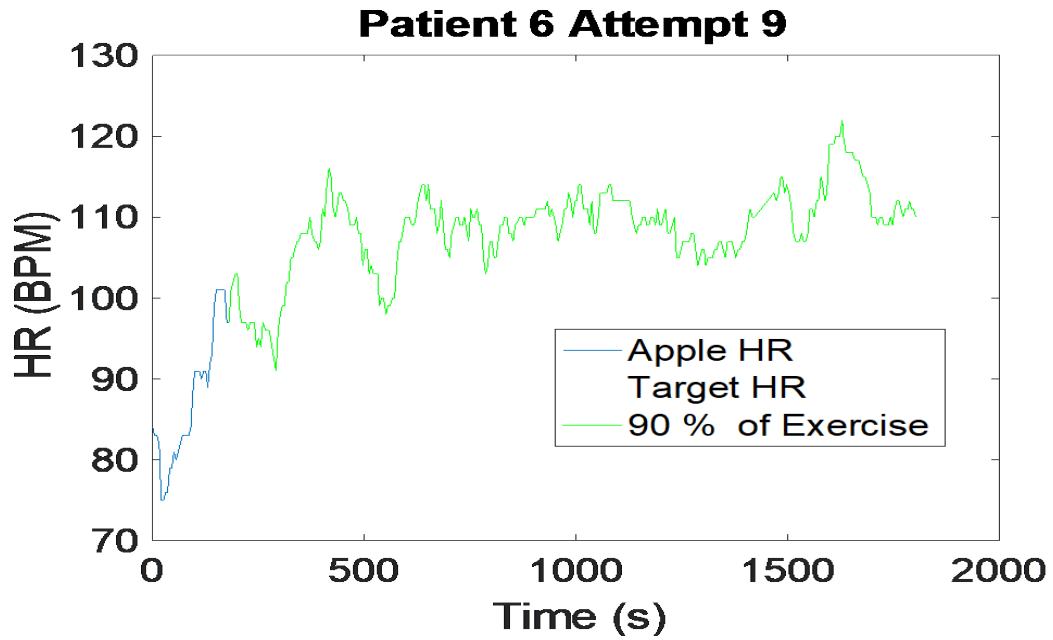


Figure A5.521: Patient No. 6 Week 4 Attempt 2

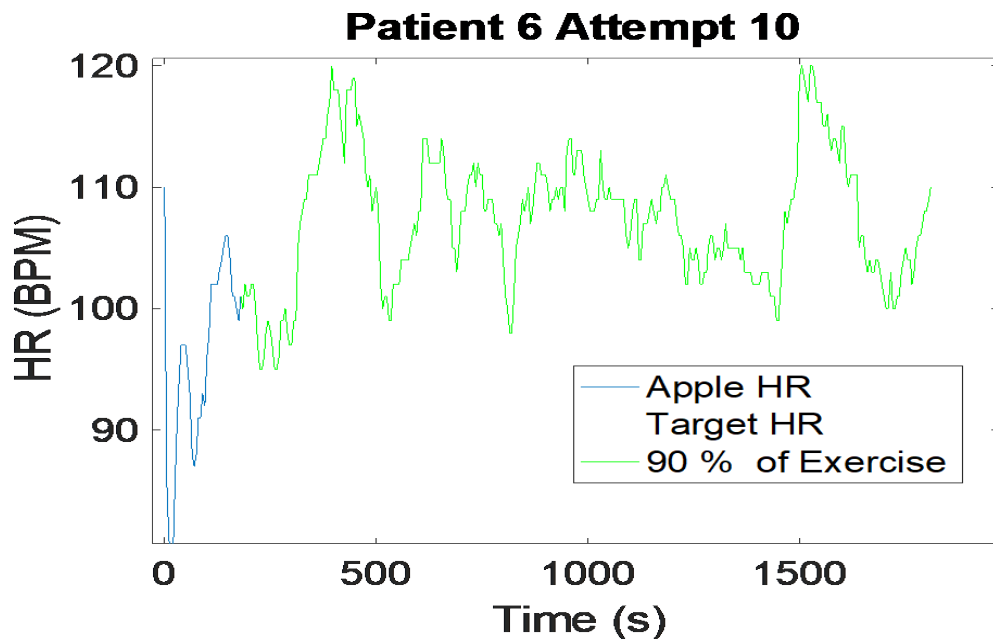


Figure A5.522: Patient No. 6 Week 4 Attempt 3

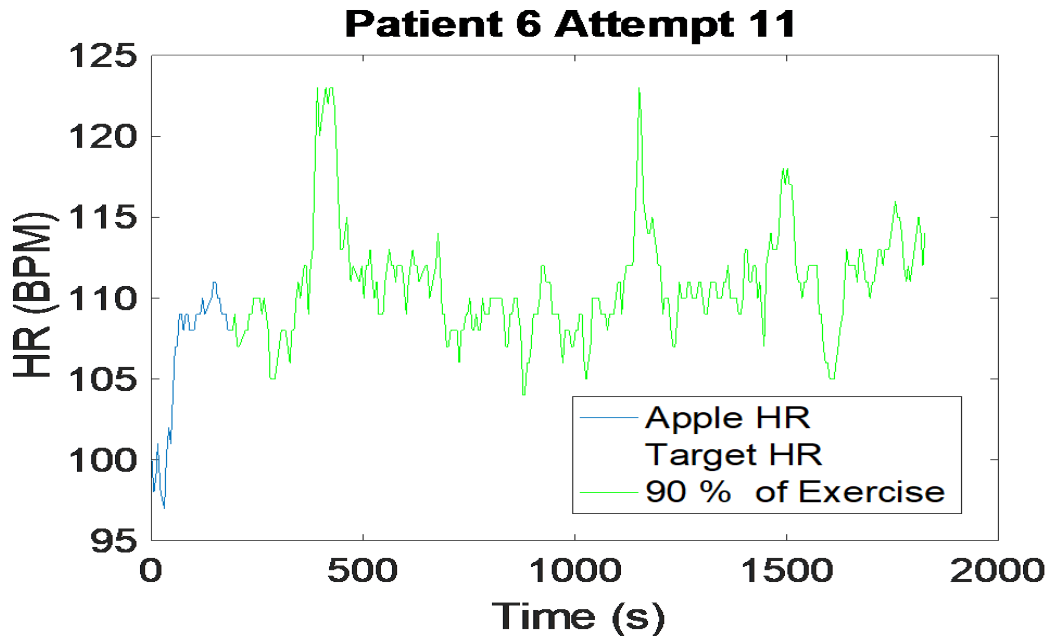


Figure A5.523: Patient No. 6 Week 4 Attempt 4

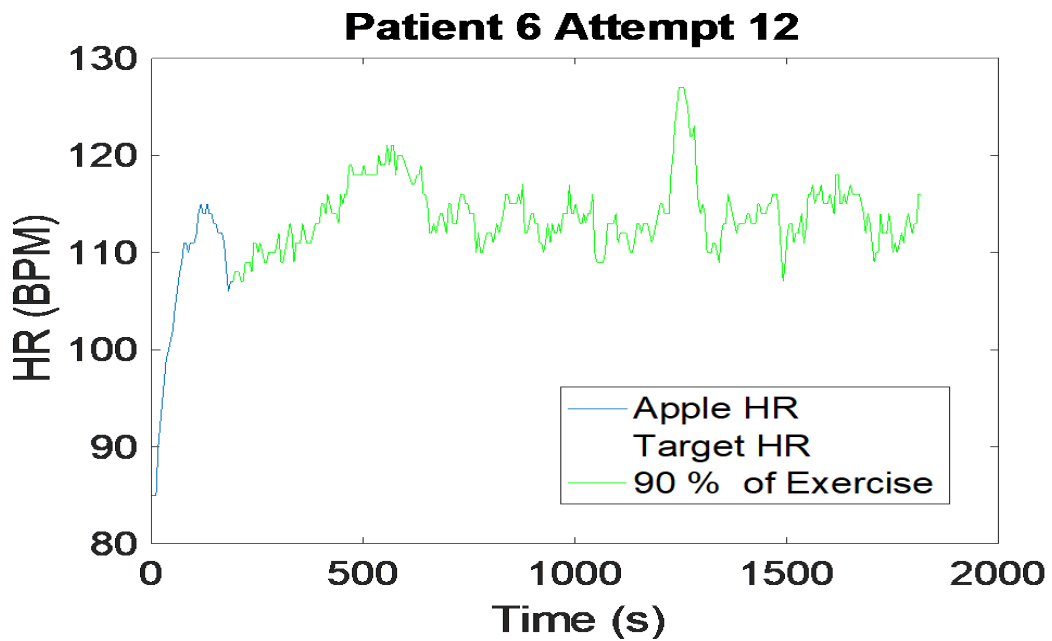
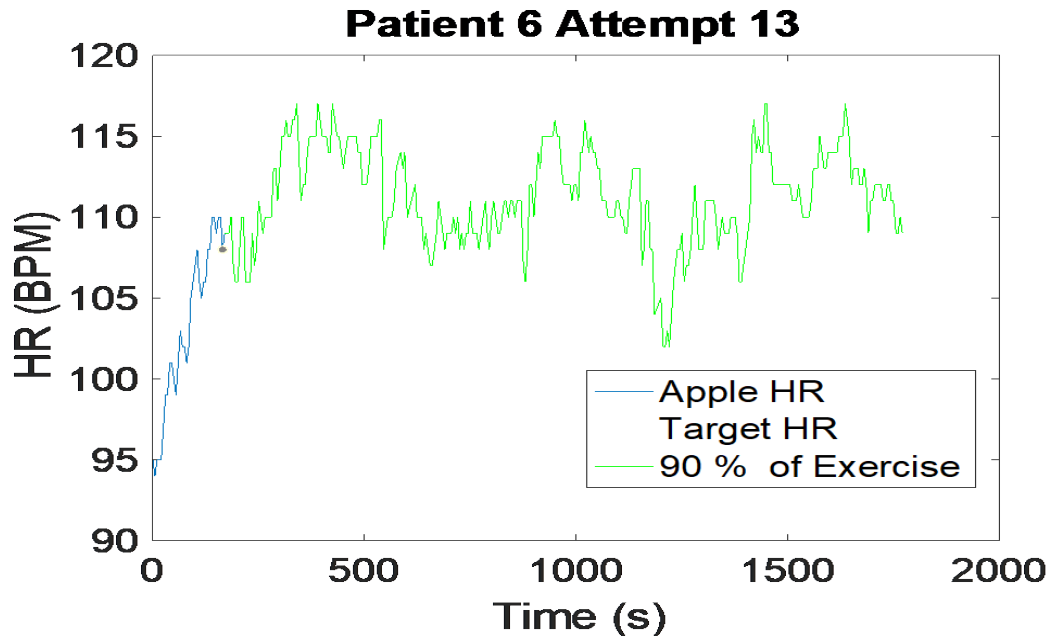
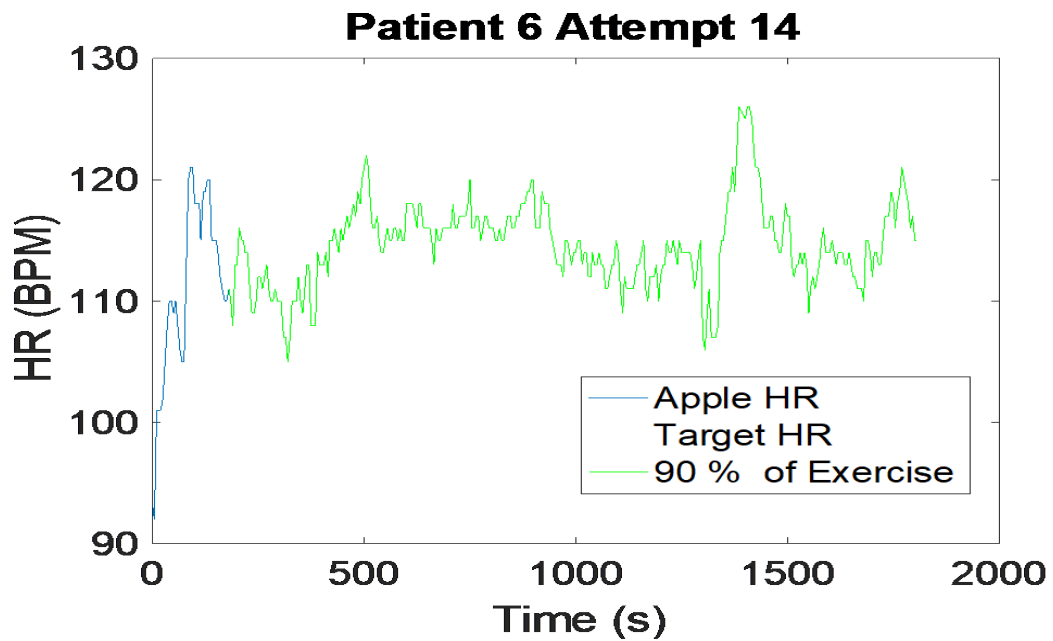


Figure A5.524: Patient No. 6 Week 5 Attempt 1

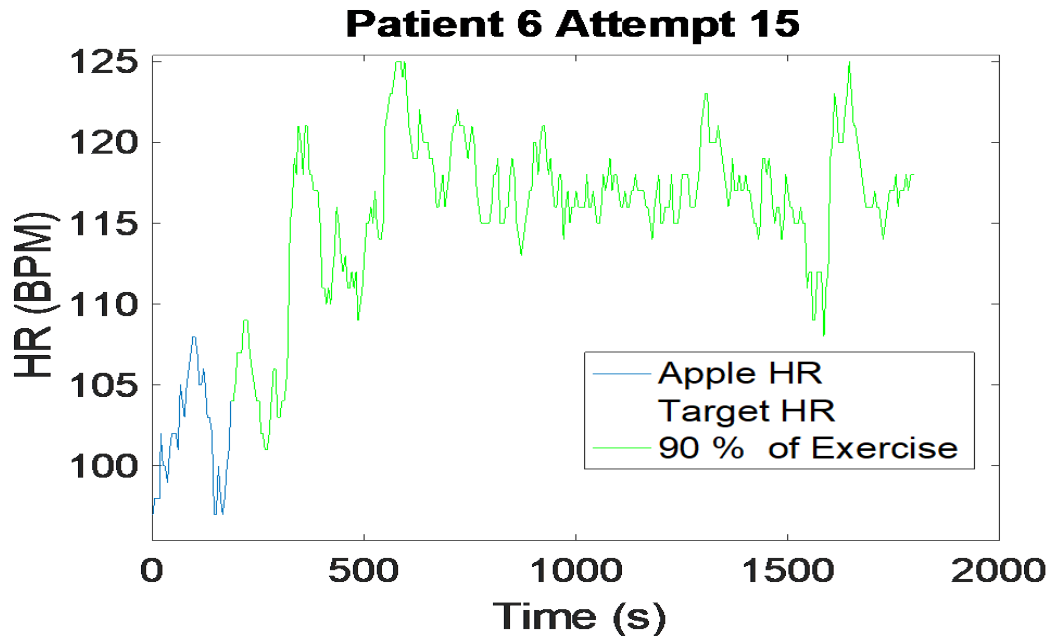


*Figure A5.525: Patient No. 6 Week 5 Attempt 2*

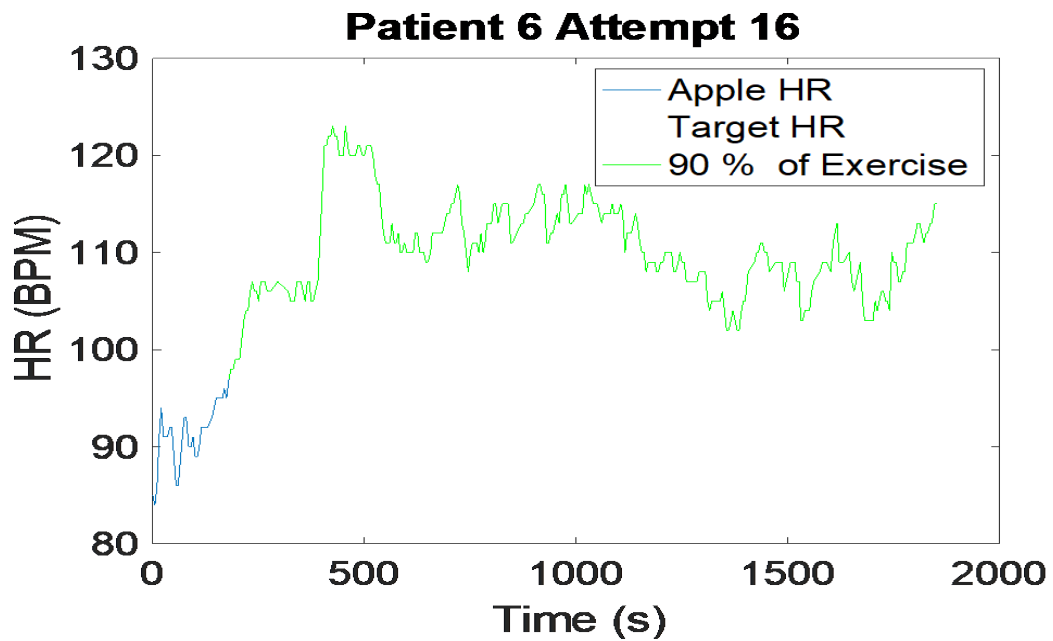


*Figure A5.526: Patient No. 6 Week 5 Attempt 3*





*Figure A5.527: Patient No. 6 Week 5 Attempt 4*



*Figure A5.528: Patient No. 6 Week 5 Attempt 5*

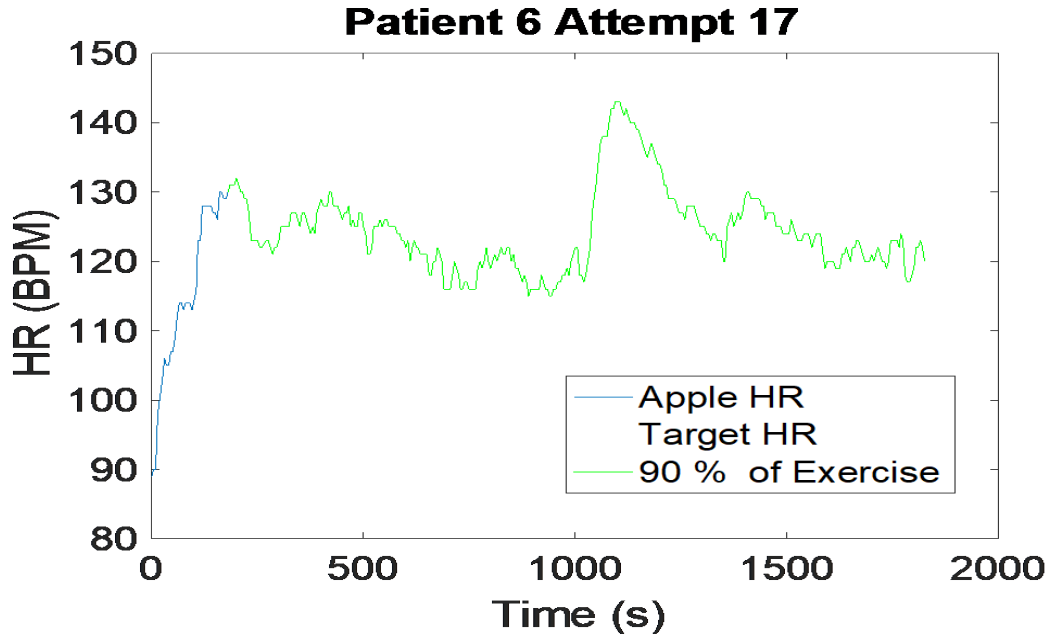


Figure A5.529: Patient No. 6 Week 6 Attempt 1

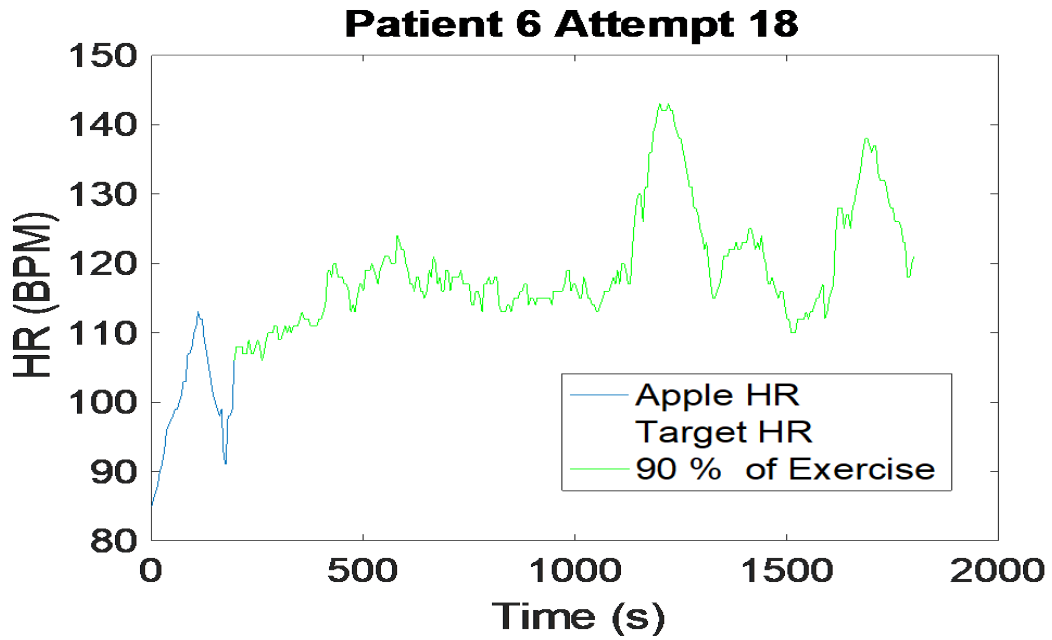


Figure A5.530: Patient No. 6 Week 6 Attempt 2

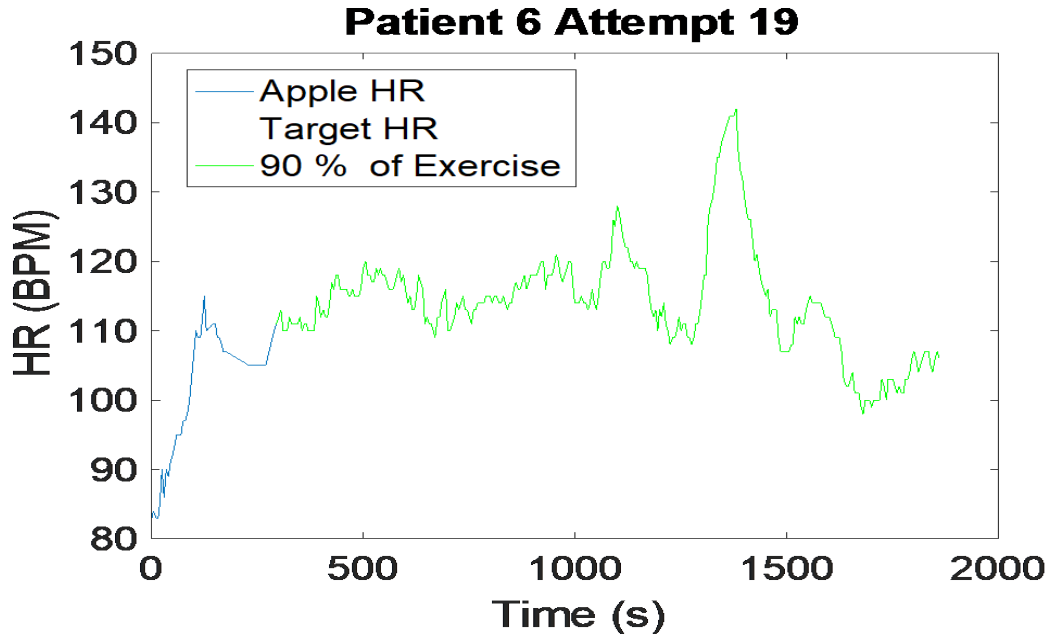


Figure A5.531: Patient No. 6 Week 6 Attempt 3

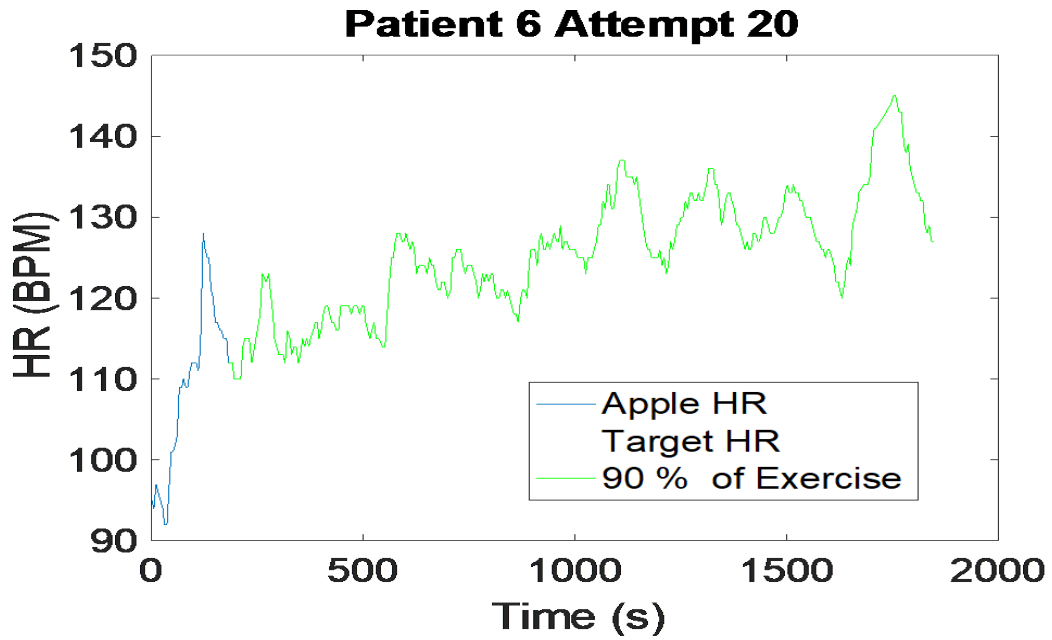


Figure A5.532: Patient No. 6 Week 6 Attempt 4

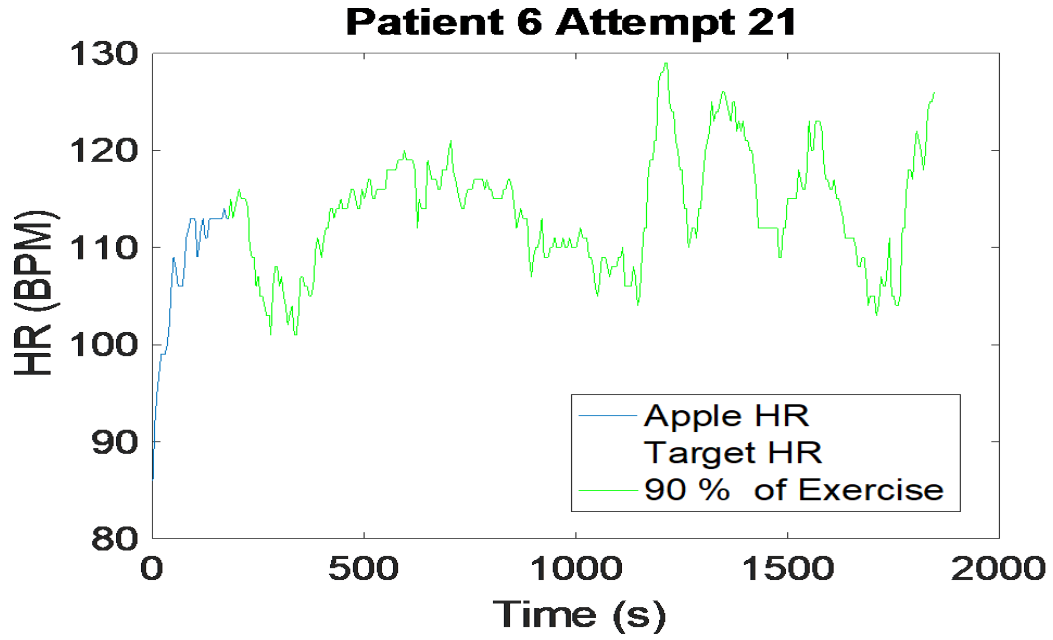


Figure A5.533: Patient No. 6 Week 7 Attempt 1

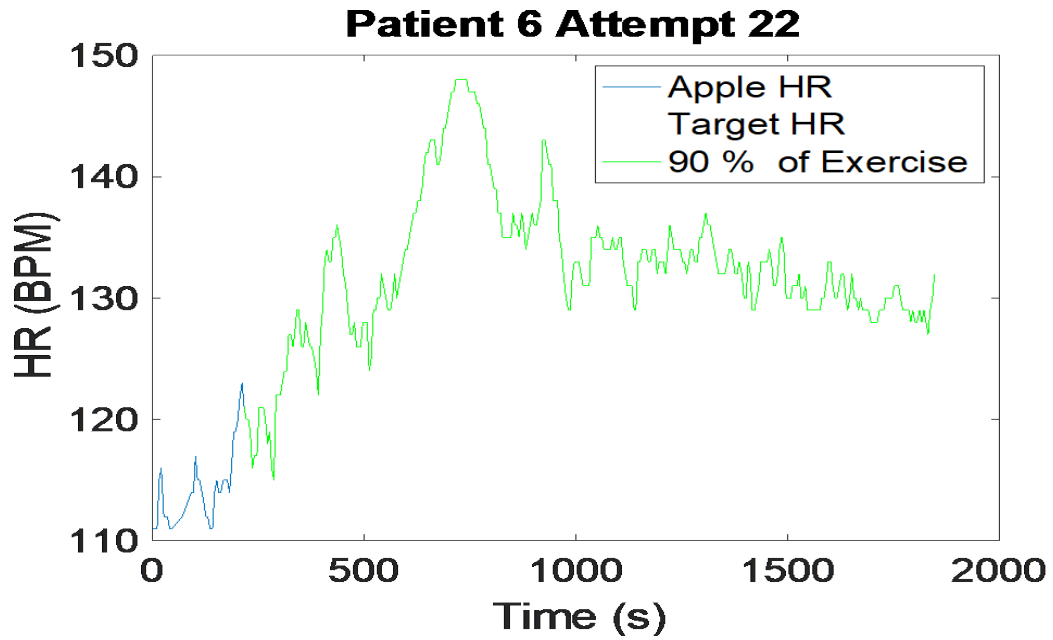


Figure A5.534: Patient No. 6 Week 7 Attempt 2

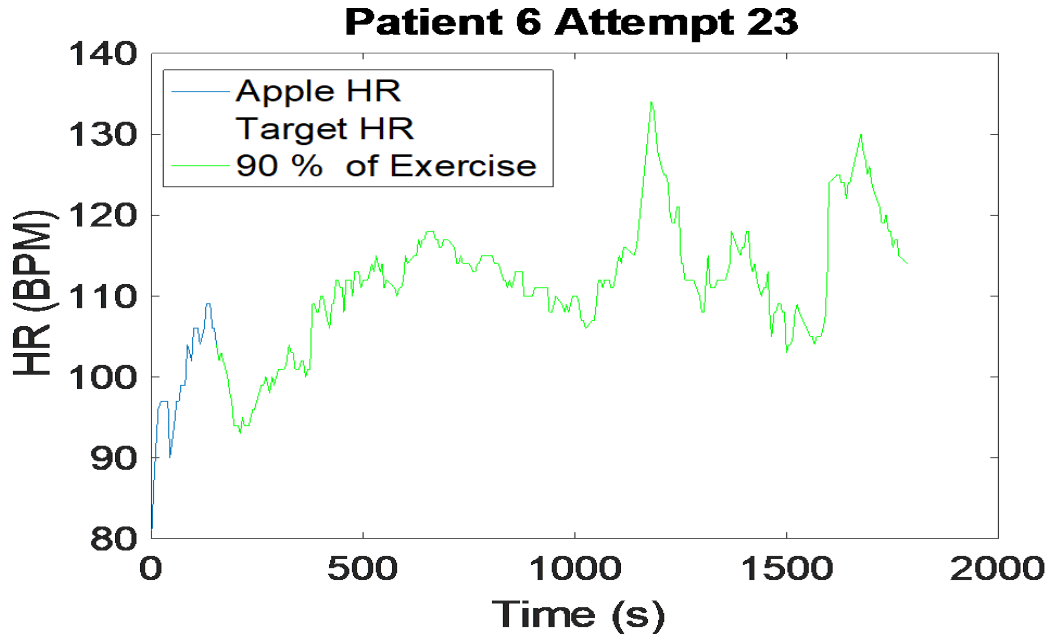


Figure A5.535: Patient No. 6 Week 7 Attempt 3

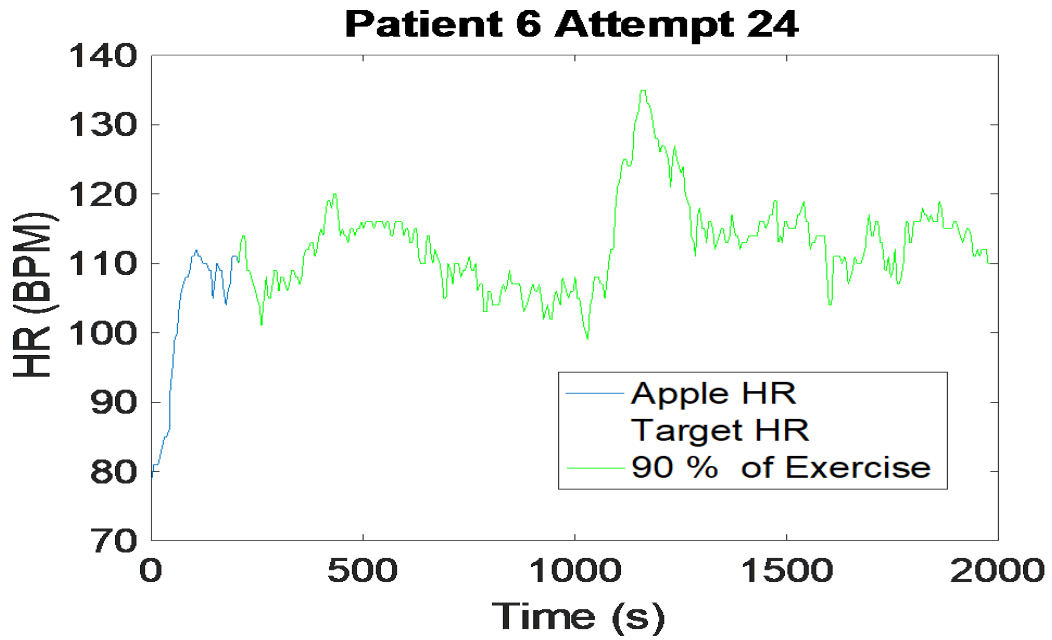


Figure A5.536: Patient No. 6 Week 7 Attempt 4

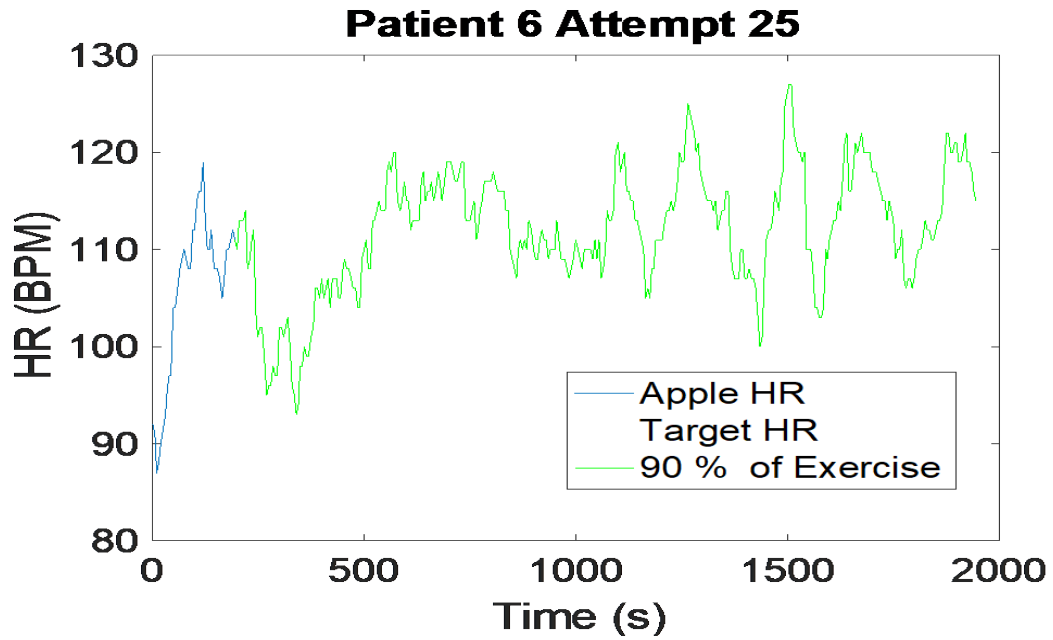


Figure A5.537: Patient No. 6 Week 7 Attempt 5

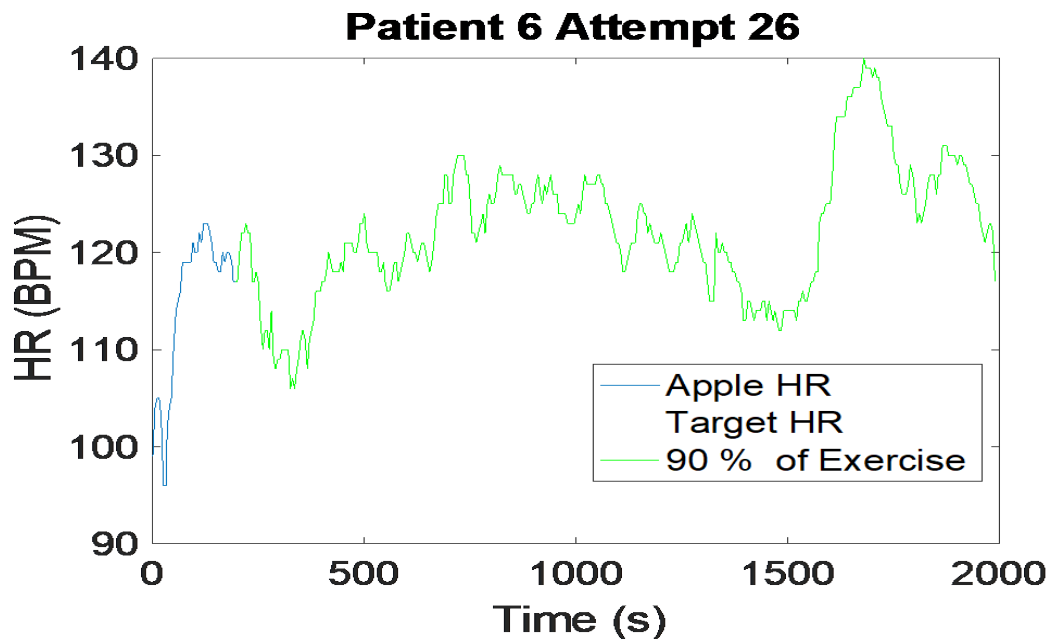


Figure A5.538: Patient No. 6 Week 7 Attempt 6

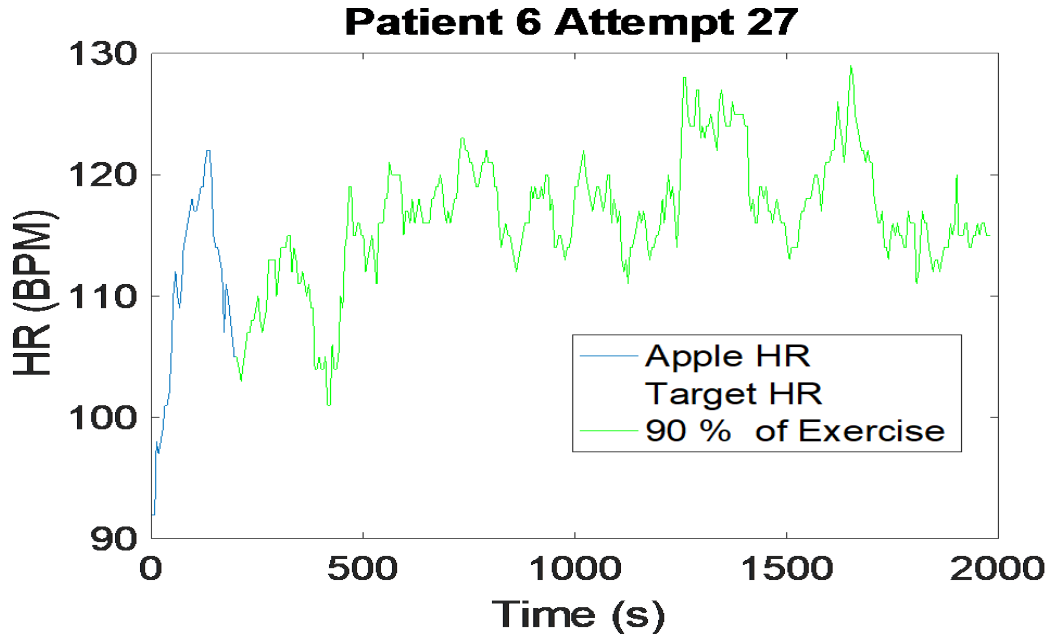


Figure A5.539: Patient No. 6 Week 8 Attempt 1

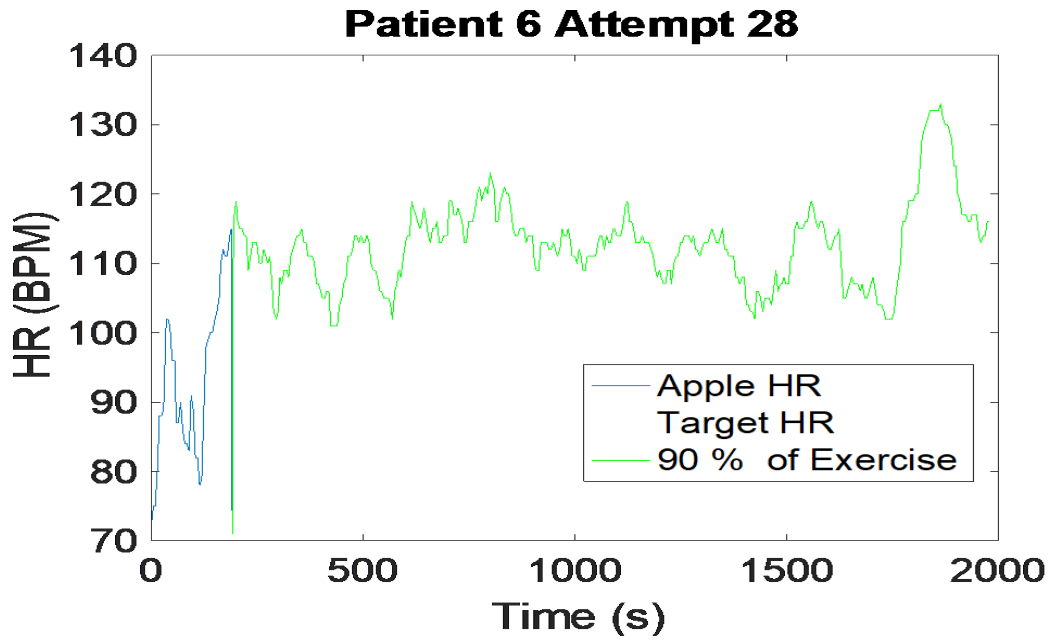


Figure A5.540: Patient No. 6 Week 8 Attempt 2

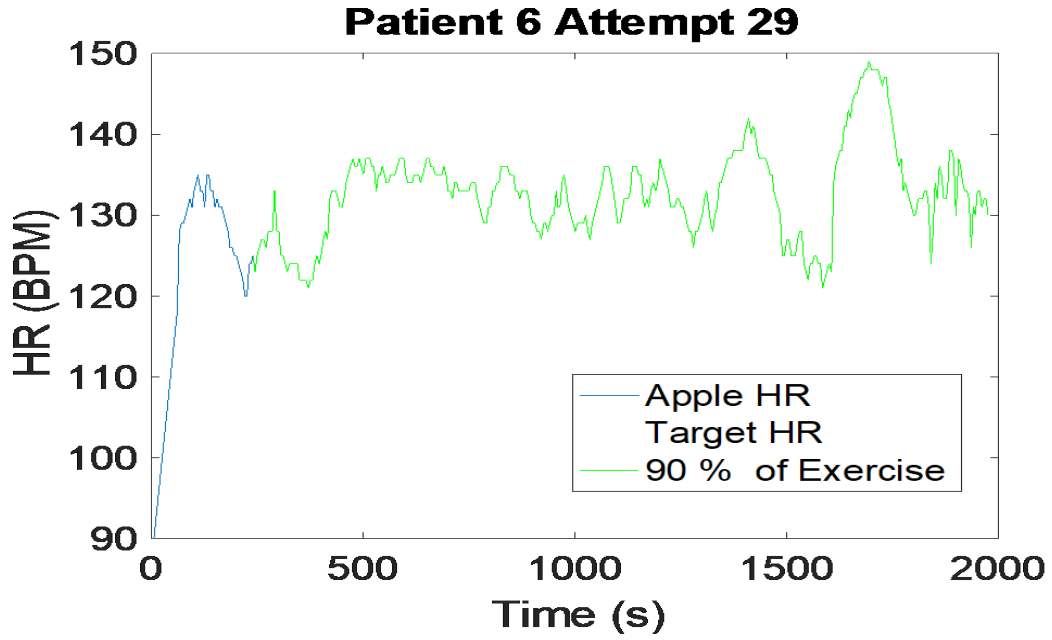


Figure A5.541: Patient No. 6 Week 8 Attempt 3

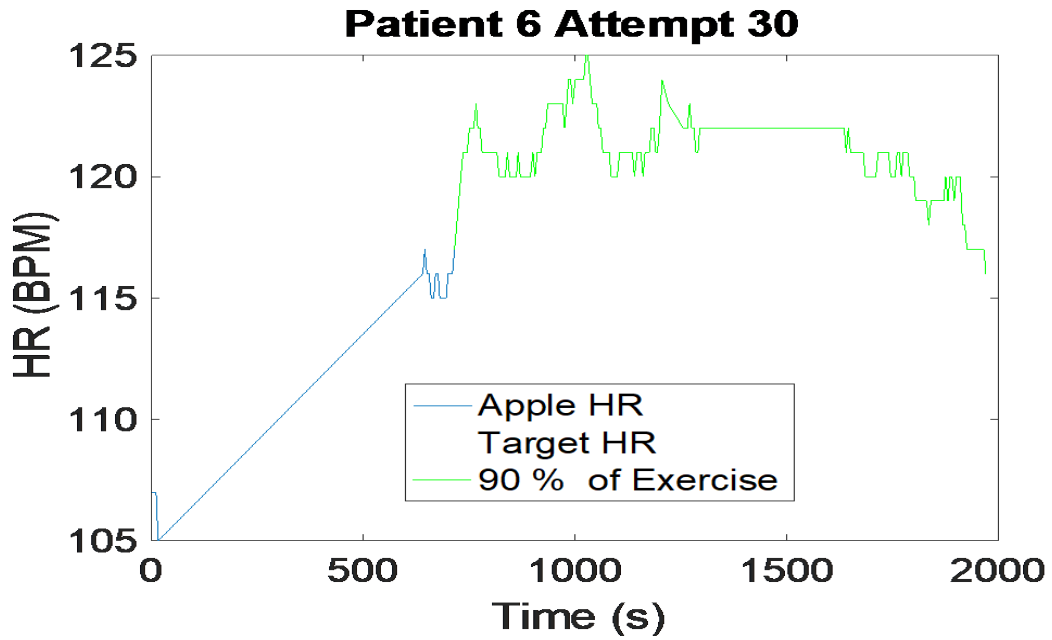


Figure A5.542: Patient No. 6 Week 8 Attempt 4



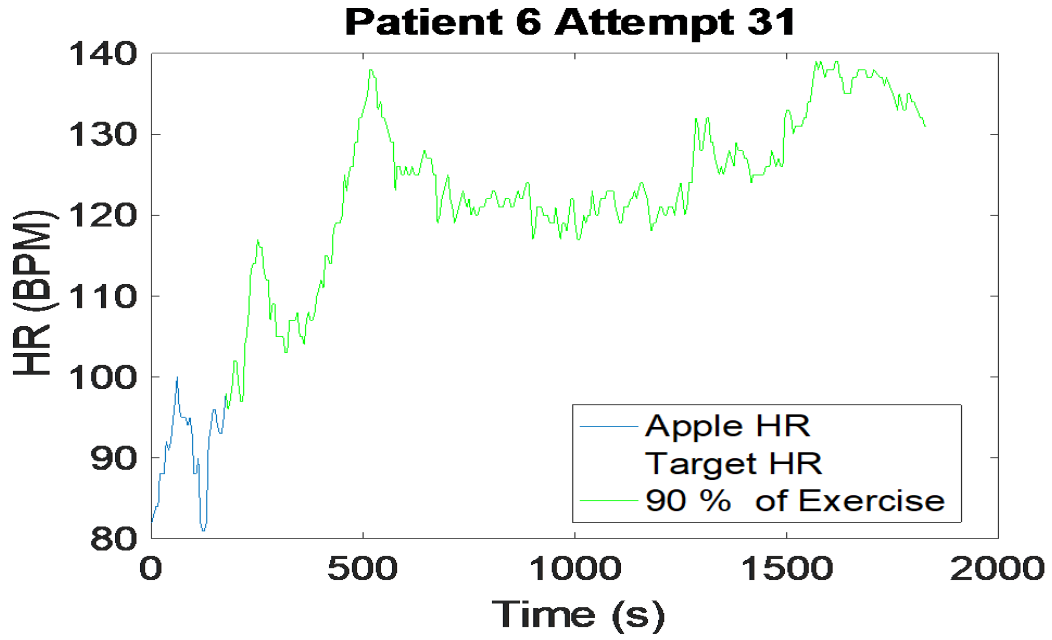


Figure A5.543: Patient No. 6 Week 9 Attempt 1

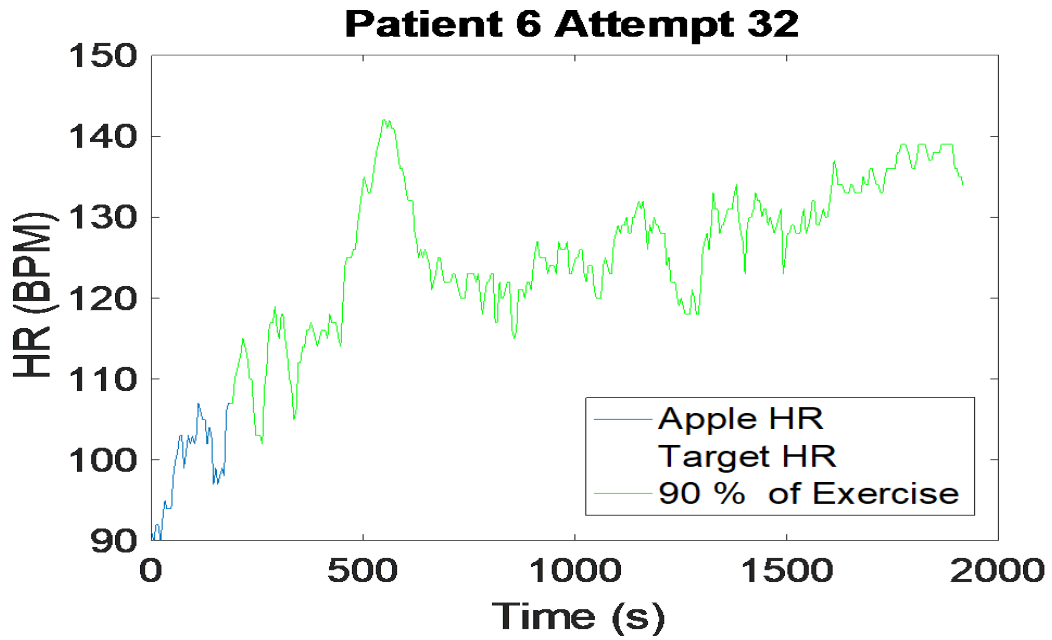


Figure A5.544: Patient No. 6 Week 9 Attempt 2

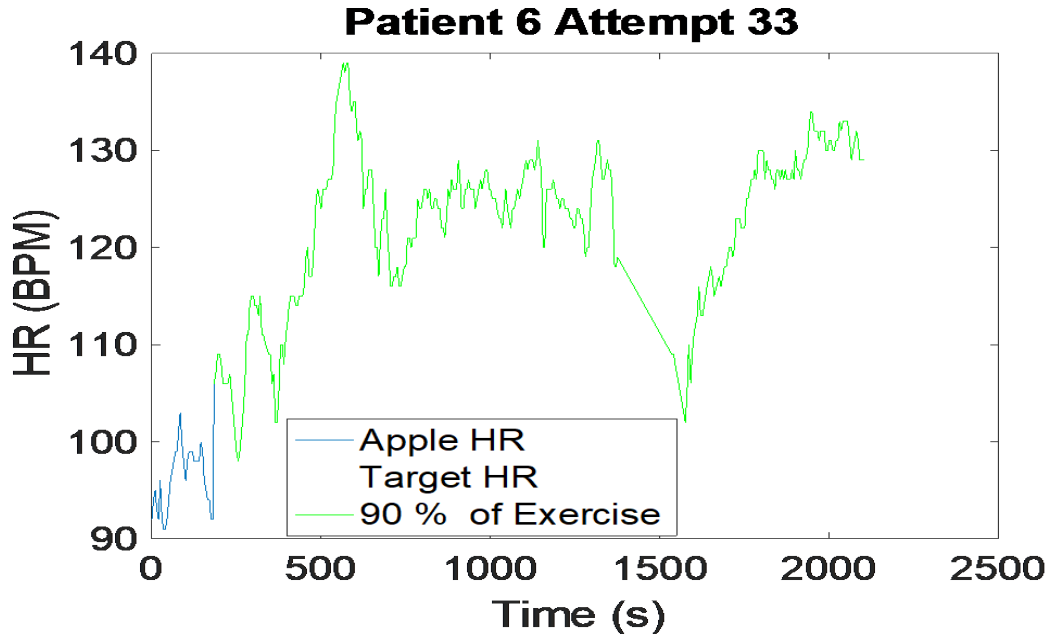


Figure A5.545: Patient No. 6 Week 9 Attempt 3

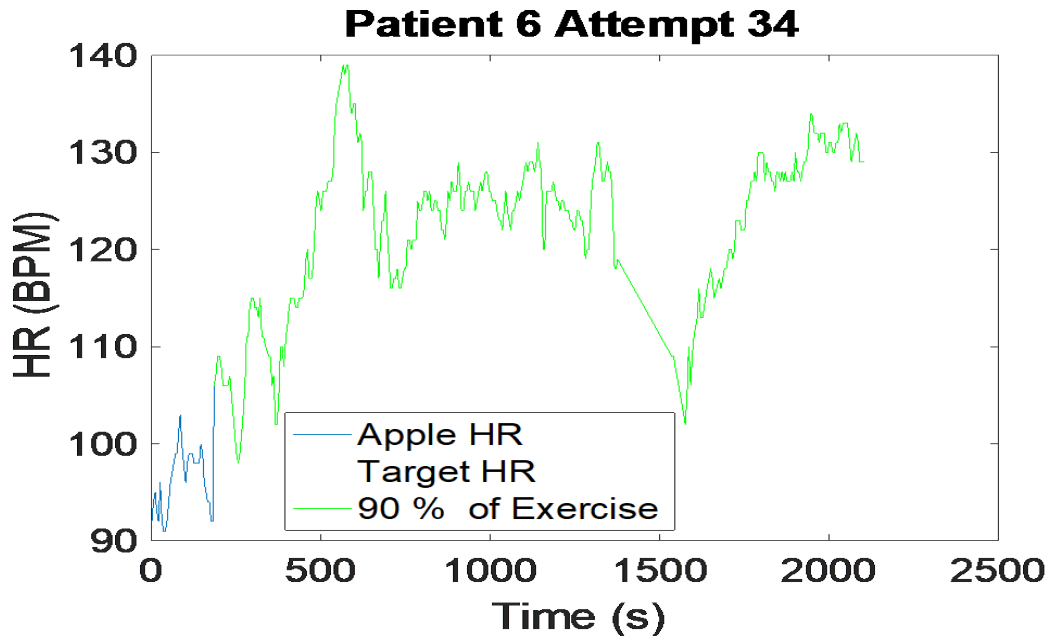


Figure A5.546: Patient No. 6 Week 9 Attempt 4

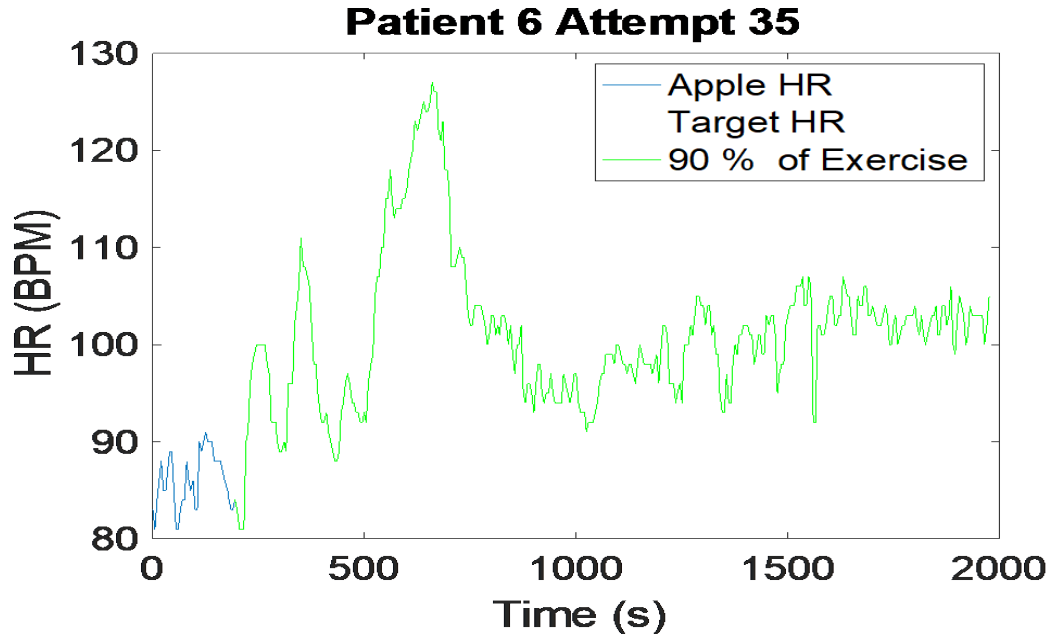


Figure A5.547: Patient No. 6 Week 9 Attempt 5

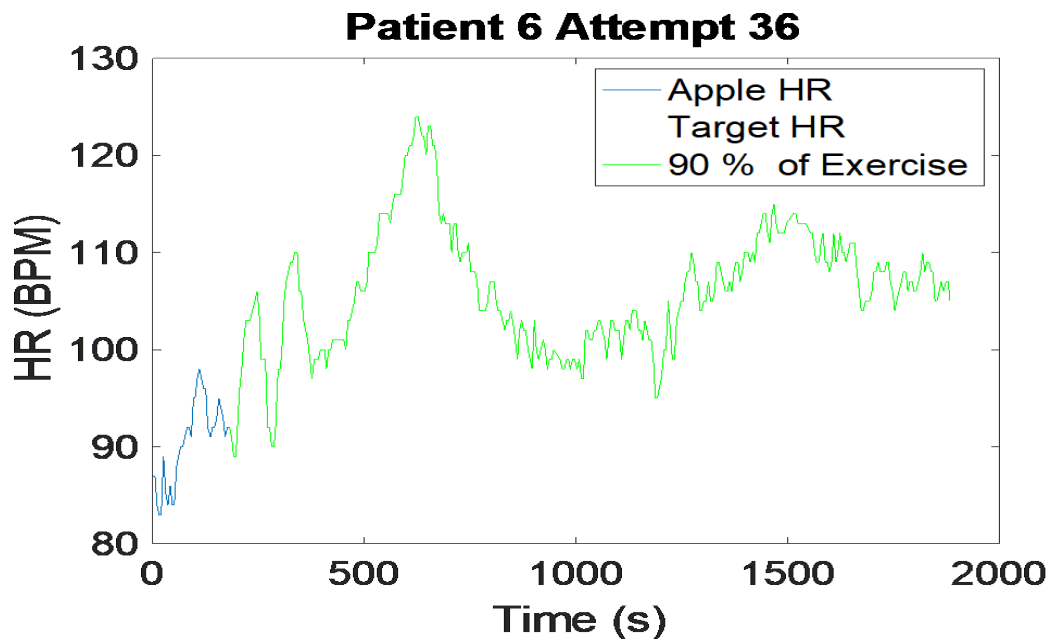


Figure A5.548: Patient No. 6 Week 10 Attempt 1

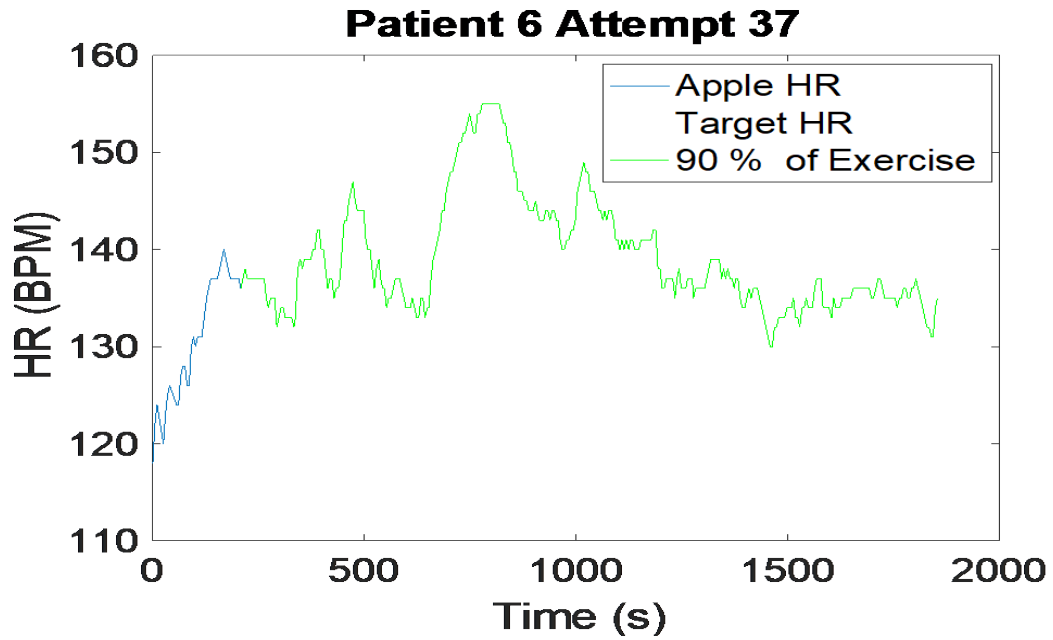


Figure A5.549: Patient No. 6 Week 10 Attempt 2

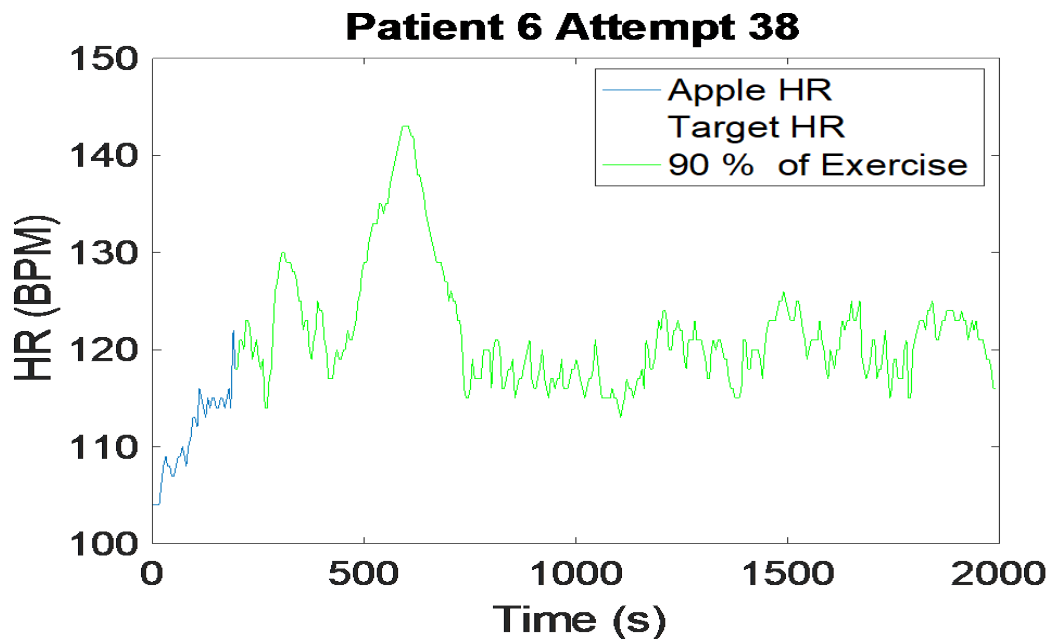


Figure A5.550: Patient No. 6 Week 10 Attempt 3

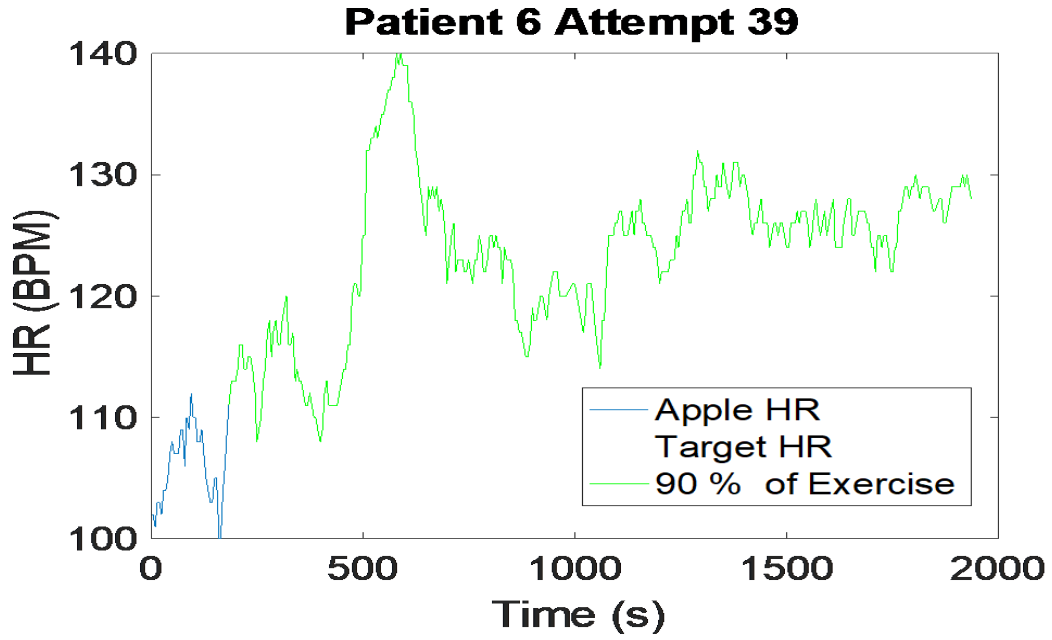


Figure A5.551: Patient No. 6 Week 10 Attempt 4

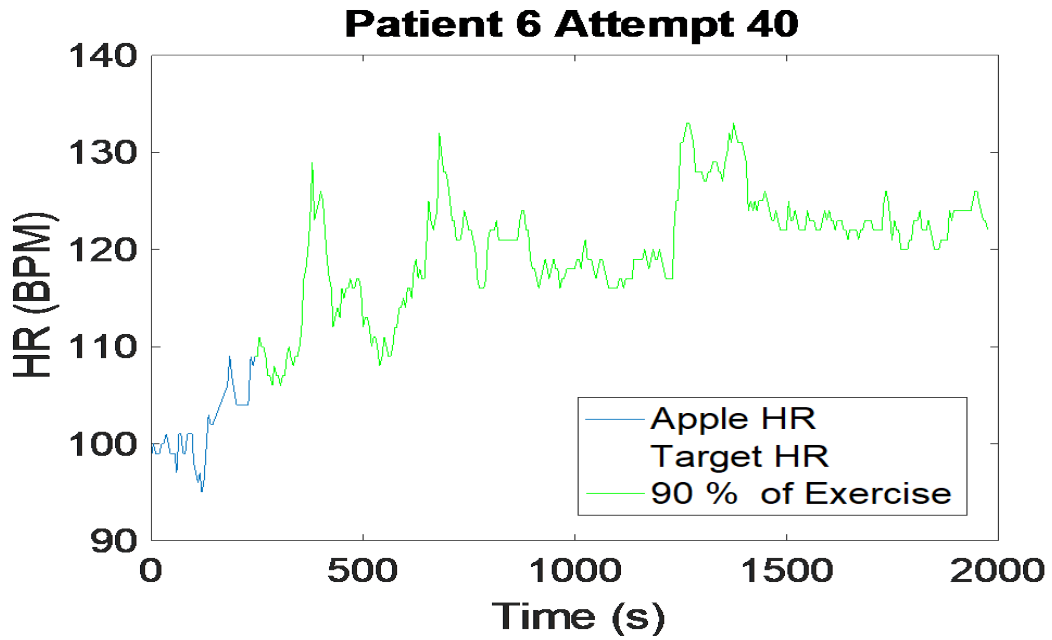


Figure A5.552: Patient No. 6 Week 10 Attempt 5

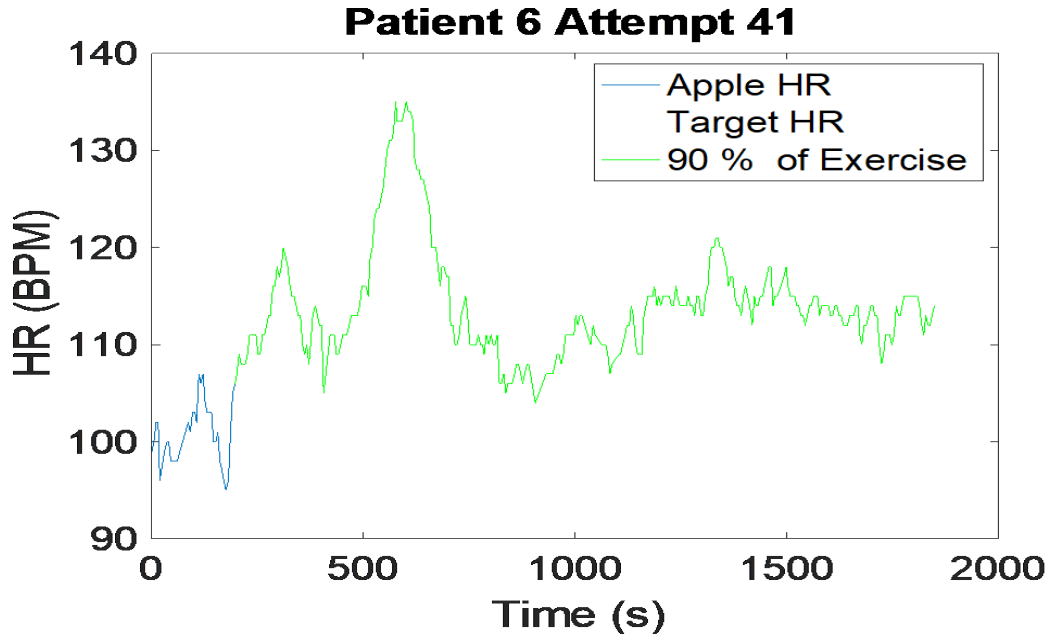


Figure A5.553: Patient No. 6 Week 11 Attempt 1

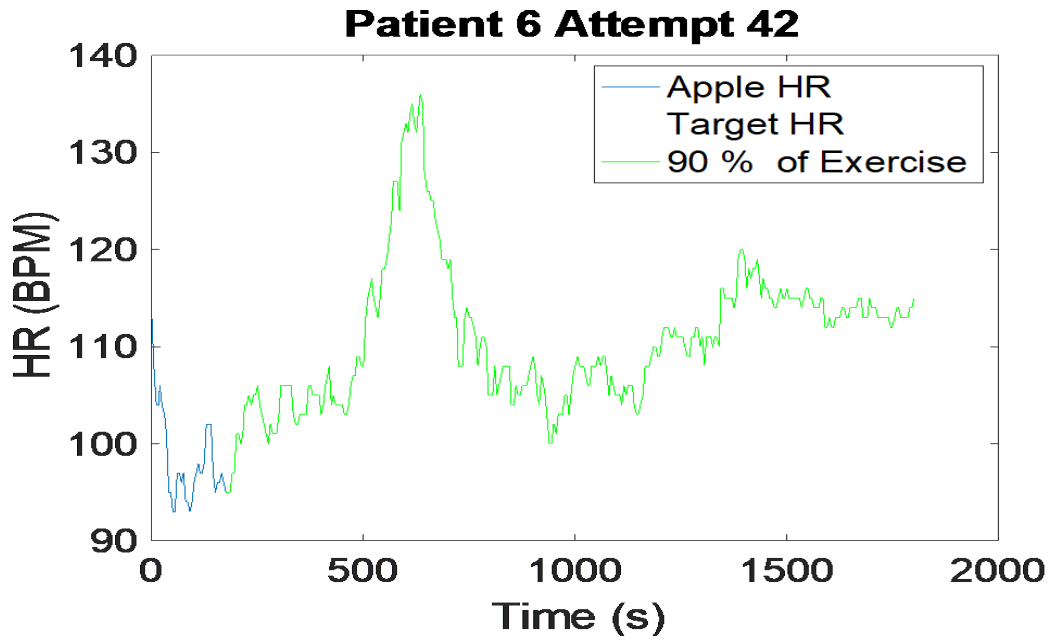


Figure A5.554: Patient No. 6 Week 11 Attempt 2

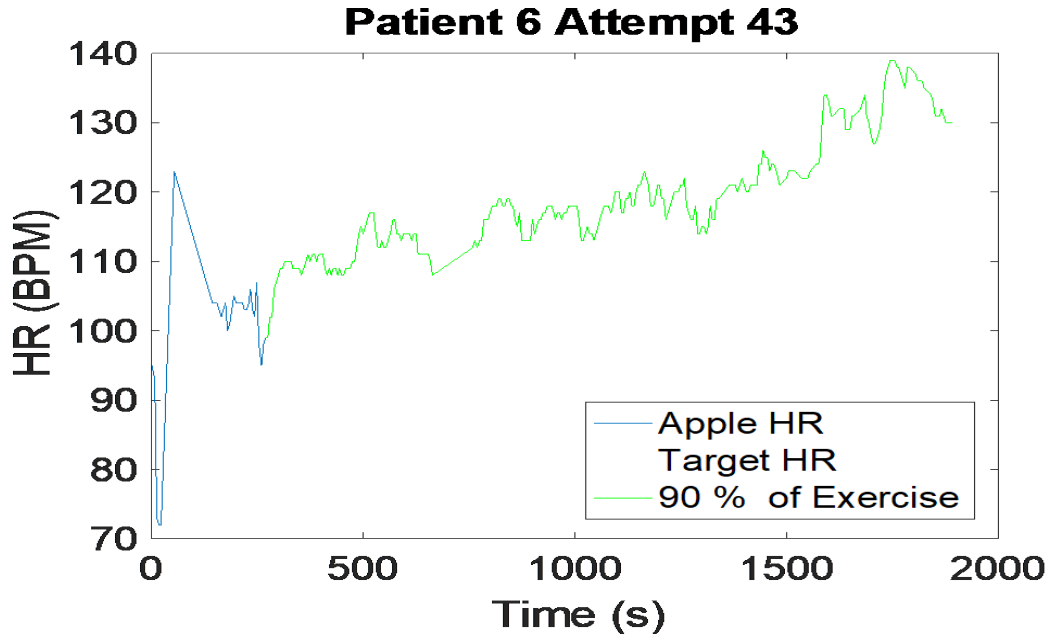


Figure A5.555: Patient No. 6 Week 11 Attempt 3

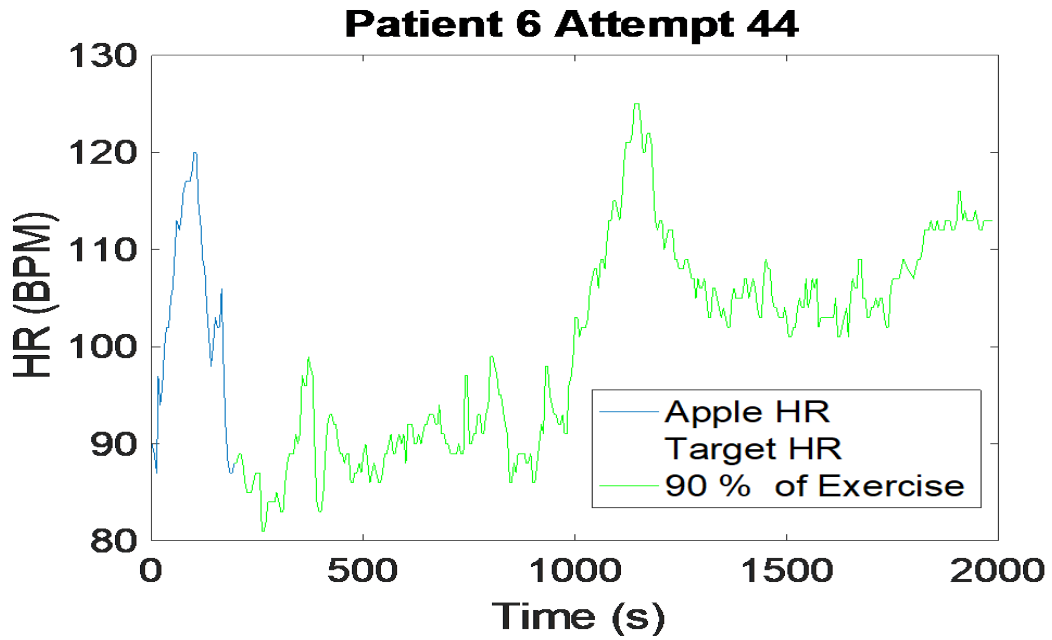


Figure A5.556: Patient No. 6 Week 12 Attempt 1

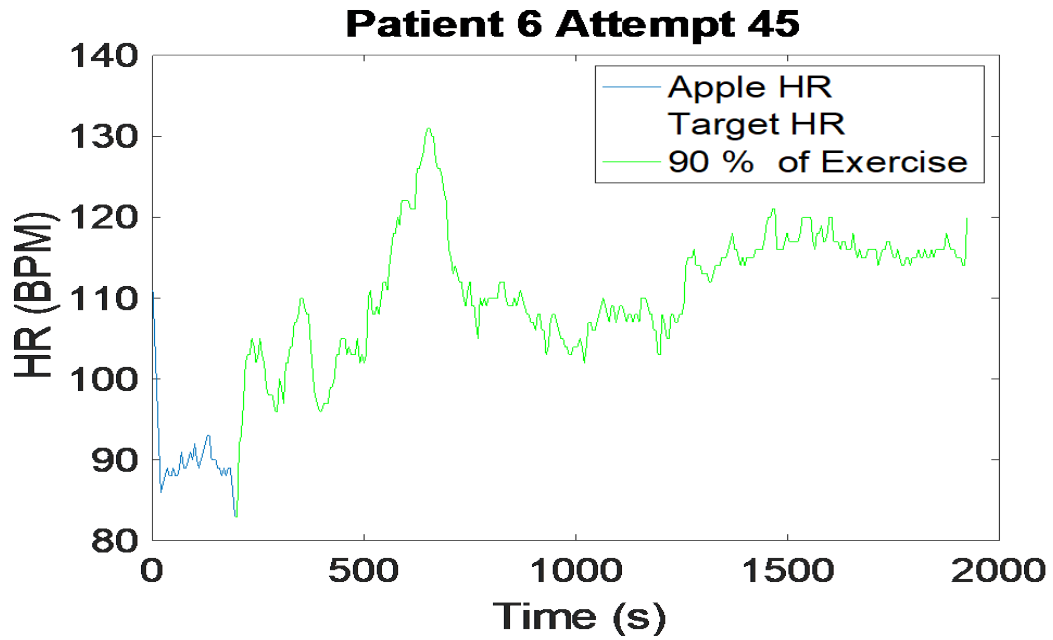


Figure A5.557: Patient No. 6 Week 12 Attempt 2

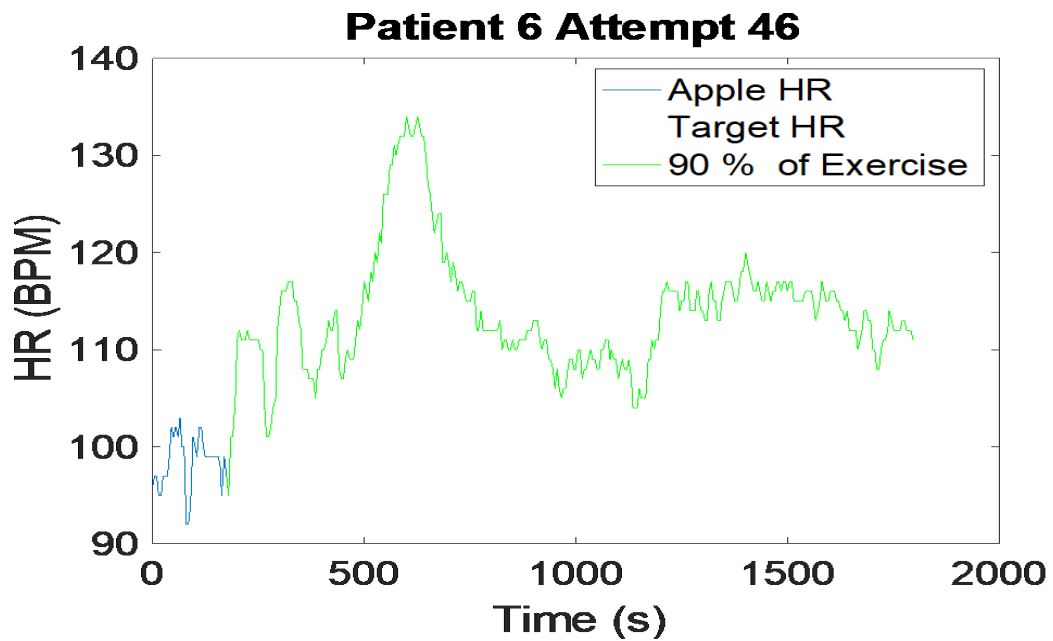


Figure A5.558: Patient No. 6 Week 12 Attempt 3



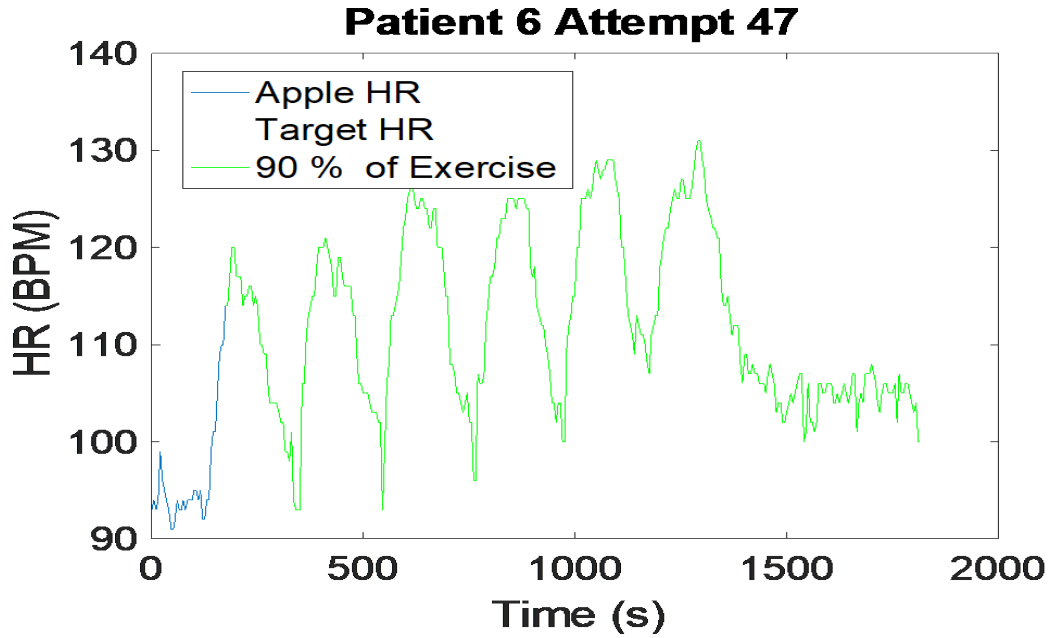


Figure A5.559: Patient No. 6 Week 12 Attempt 4

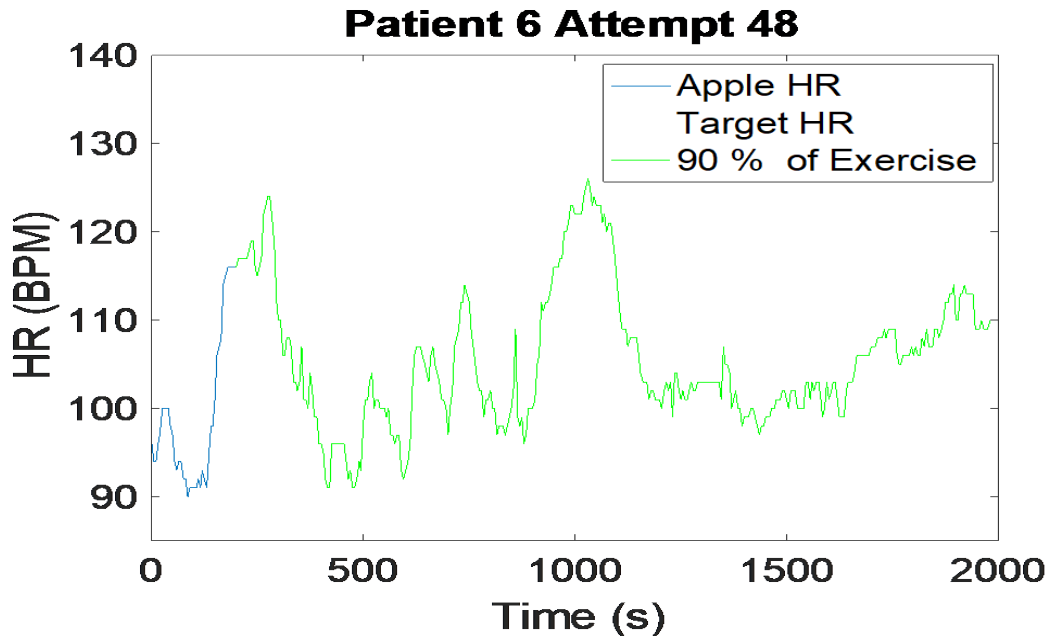


Figure A5.560: Patient No. 6 Week 12 Attempt 5

**Patient 7 Attempts :**

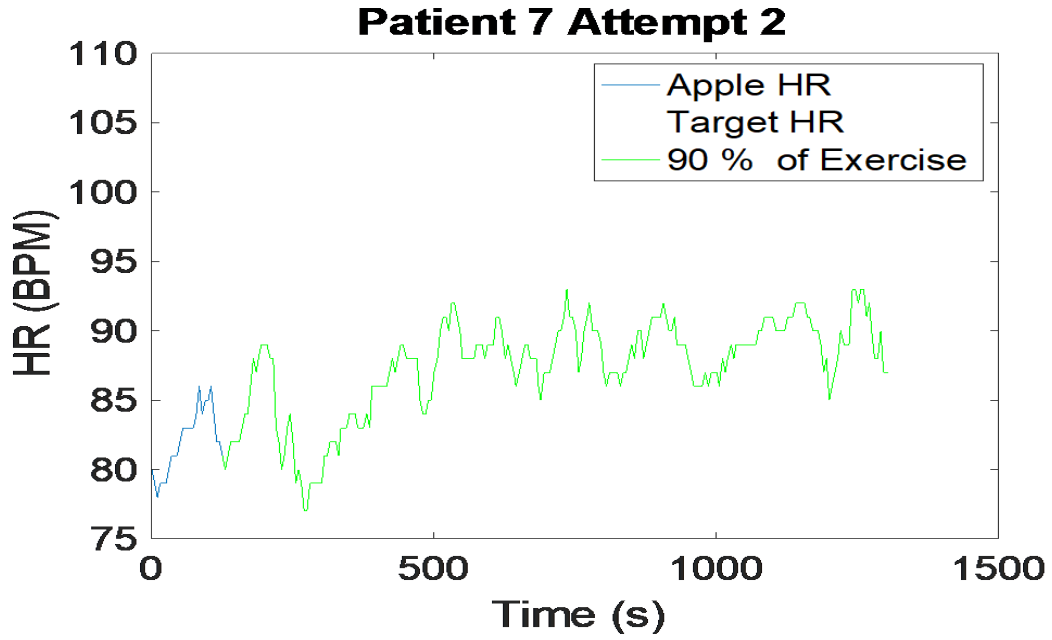


Figure A5.561: Patient No. 7 Week 2 Attempt 1

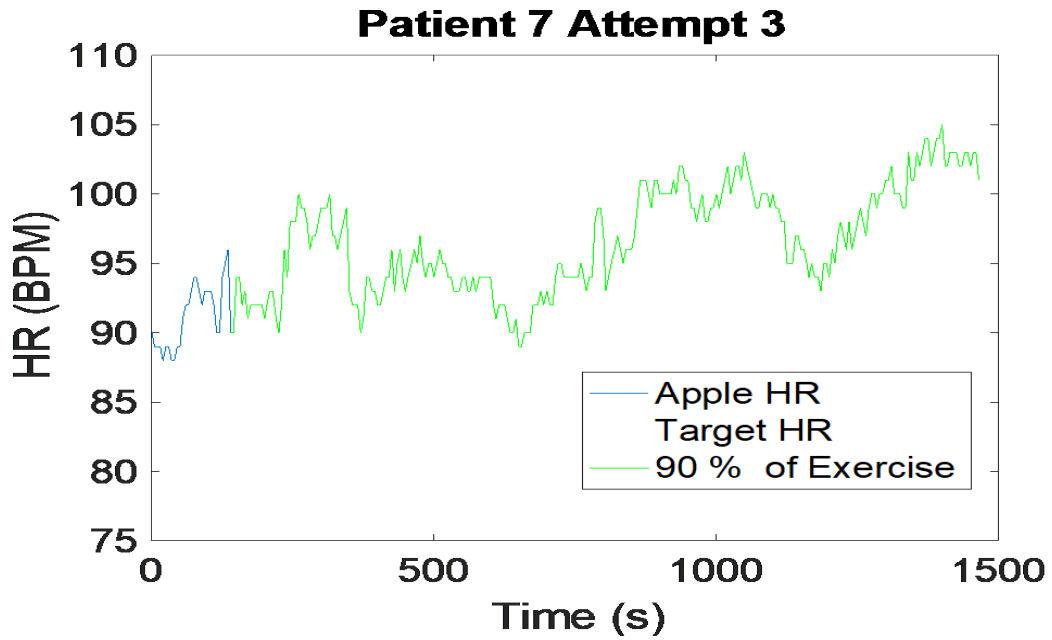


Figure A5.562: Patient No. 7 Week 2 Attempt 2

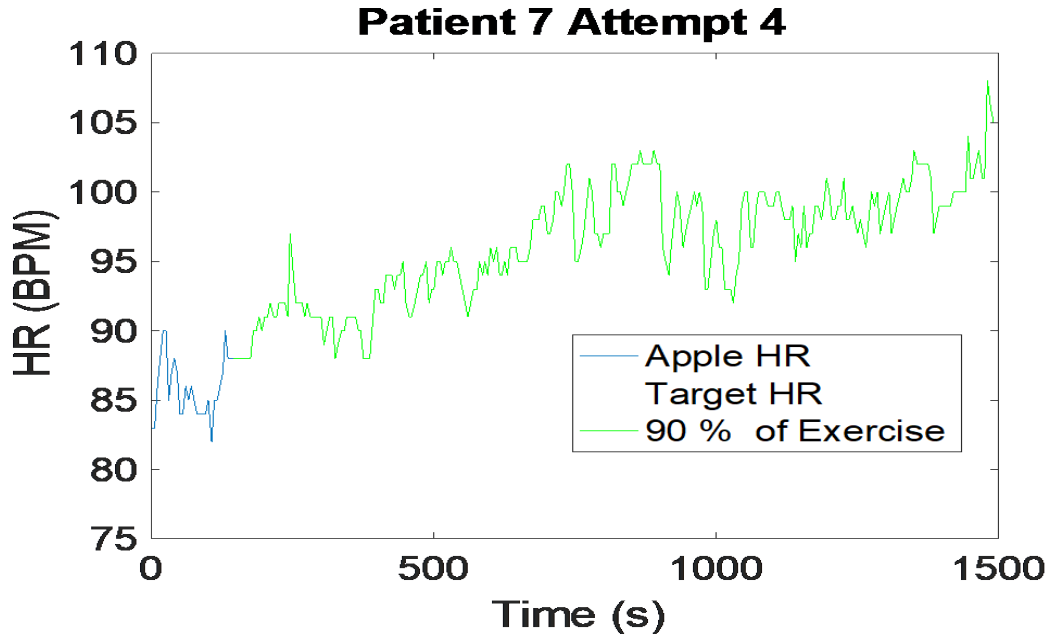


Figure A5.563: Patient No. 7 Week 3 Attempt 1

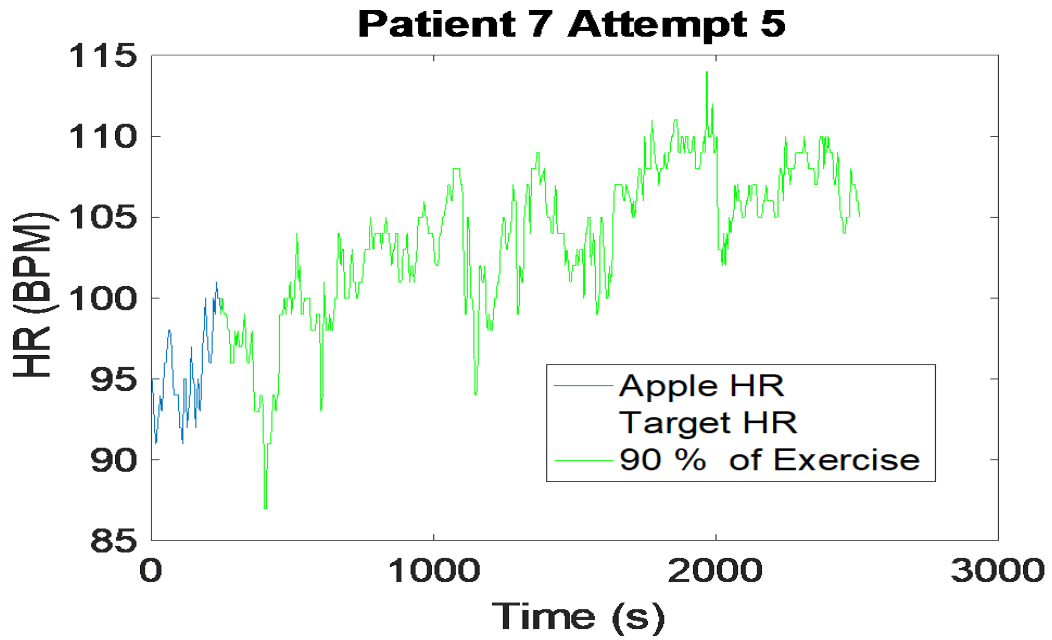


Figure A5.564: Patient No. 7 Week 3 Attempt 2

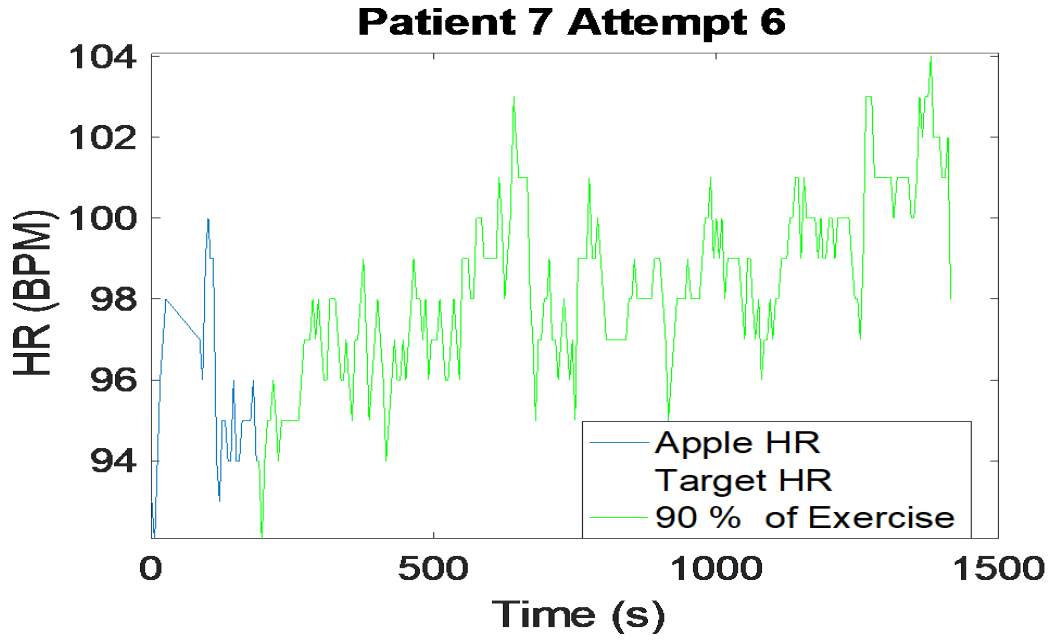


Figure A5.565: Patient No. 7 Week 3 Attempt 3

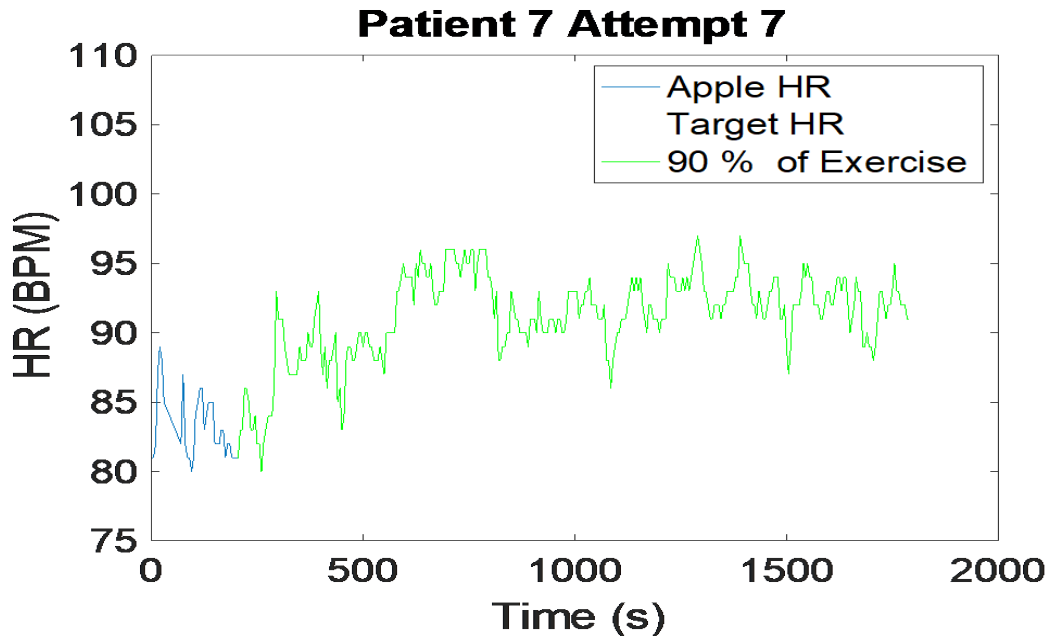


Figure A5.566: Patient No. 7 Week 4 Attempt 1

### Patient 7 Attempt 8

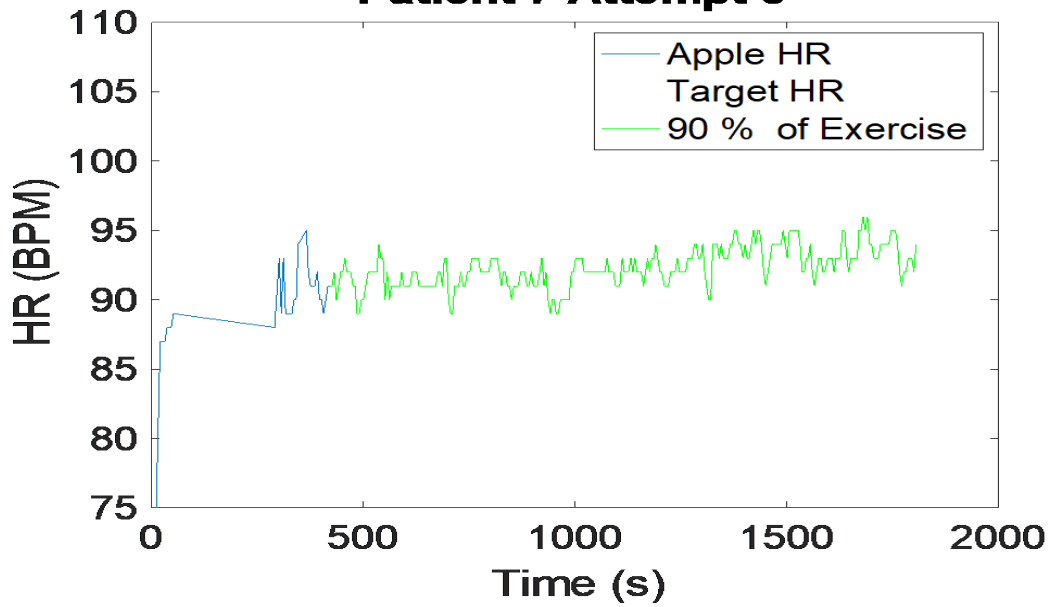


Figure A5.567: Patient No. 7 Week 4 Attempt 2

### Patient 7 Attempt 9

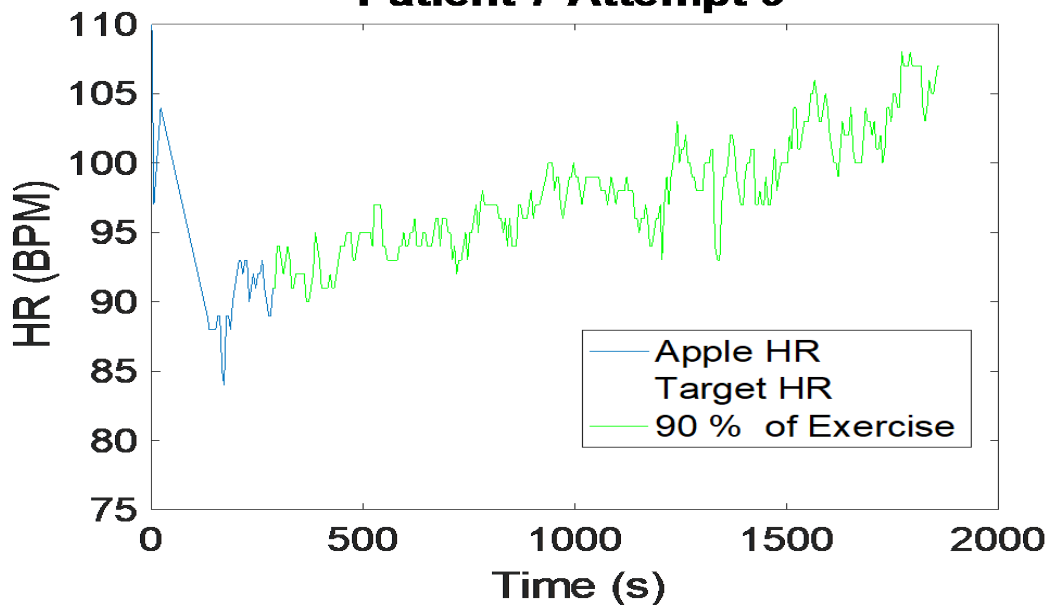


Figure A5.568: Patient No. 7 Week 4 Attempt 3

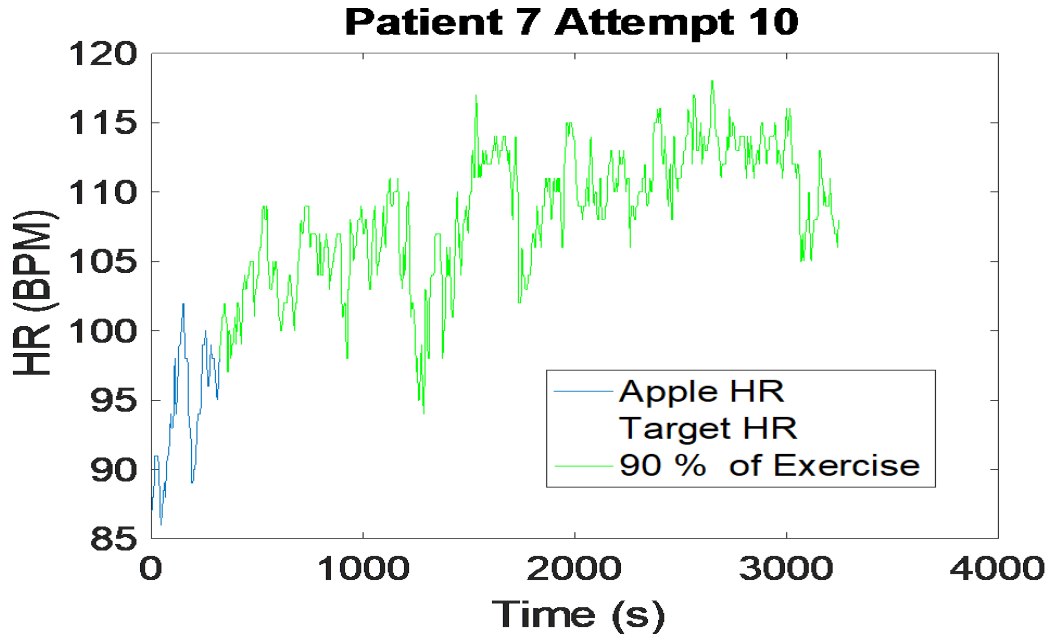


Figure A5.569: Patient No. 7 Week 4 Attempt 4

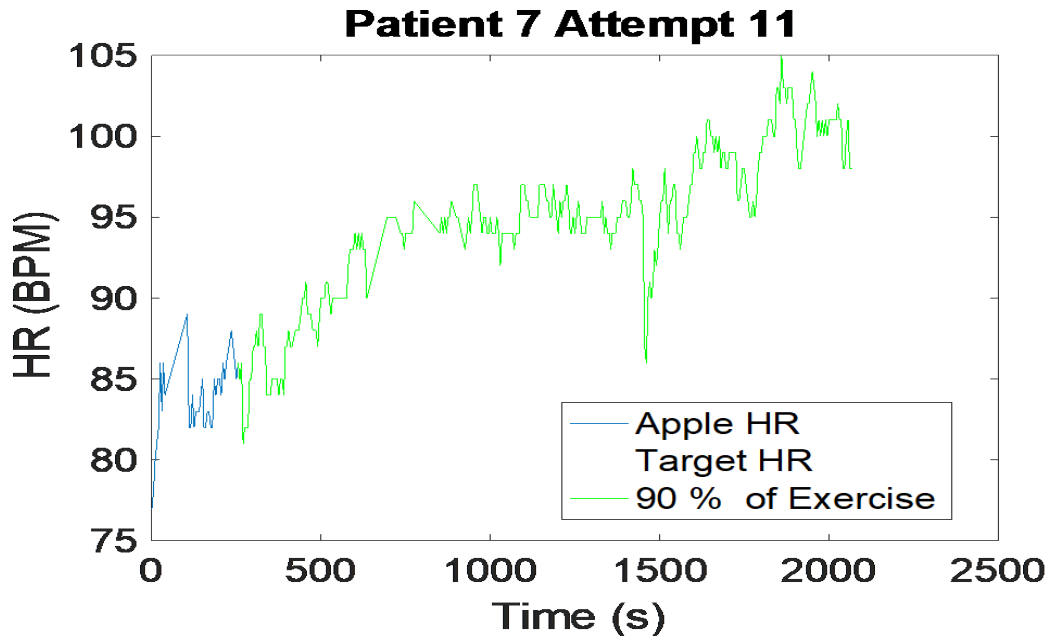


Figure A5.570: Patient No. 7 Week 5 Attempt 1

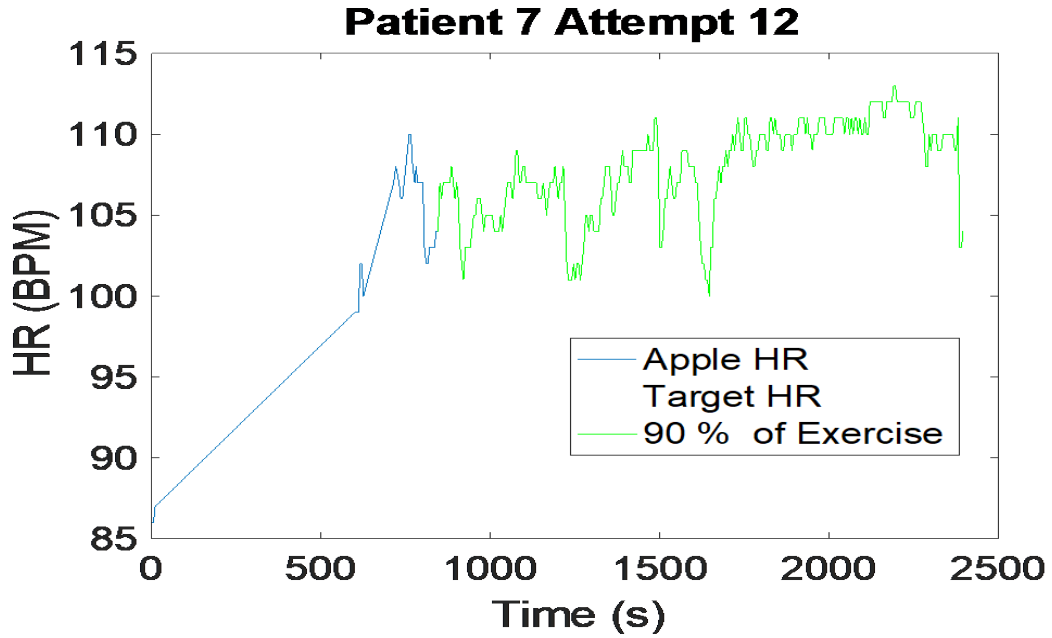


Figure A5.571: Patient No. 7 Week 5 Attempt 2

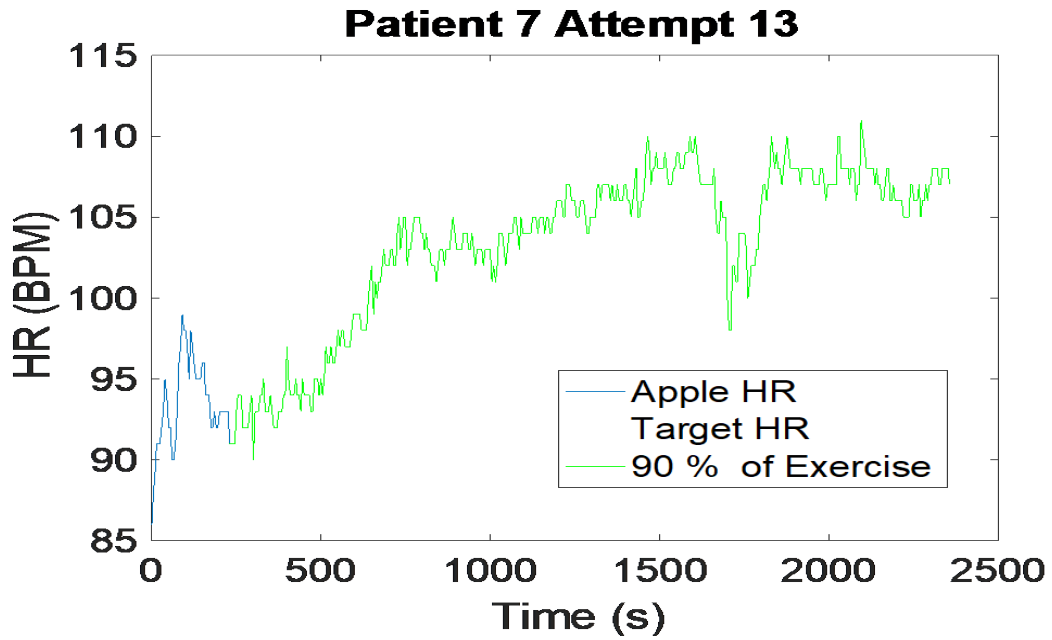


Figure A5.572: Patient No. 7 Week 6 Attempt 1

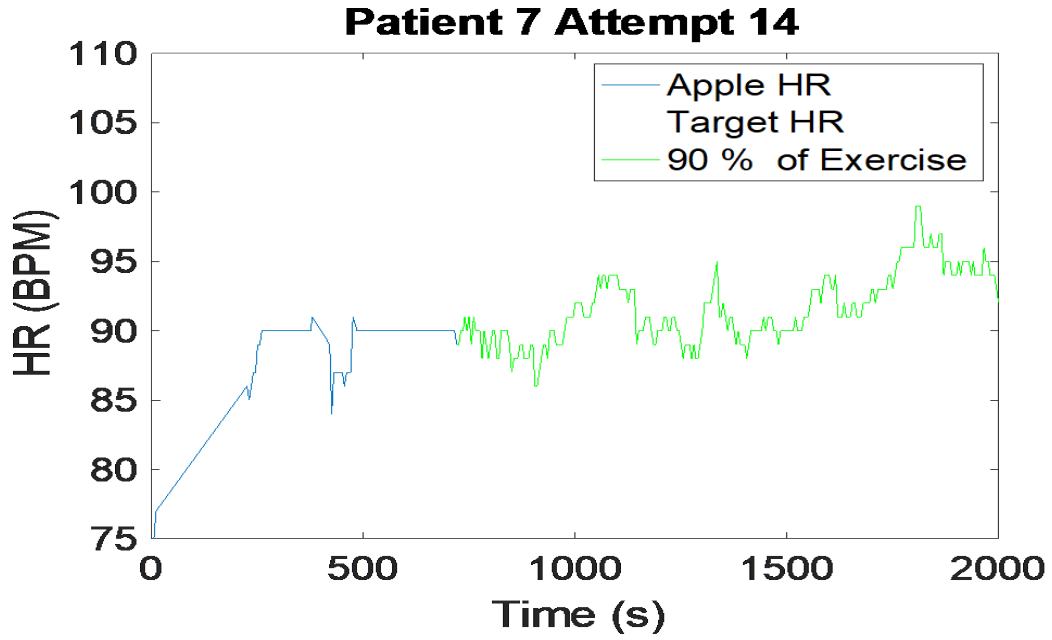


Figure A5.573: Patient No. 7 Week 7 Attempt 1

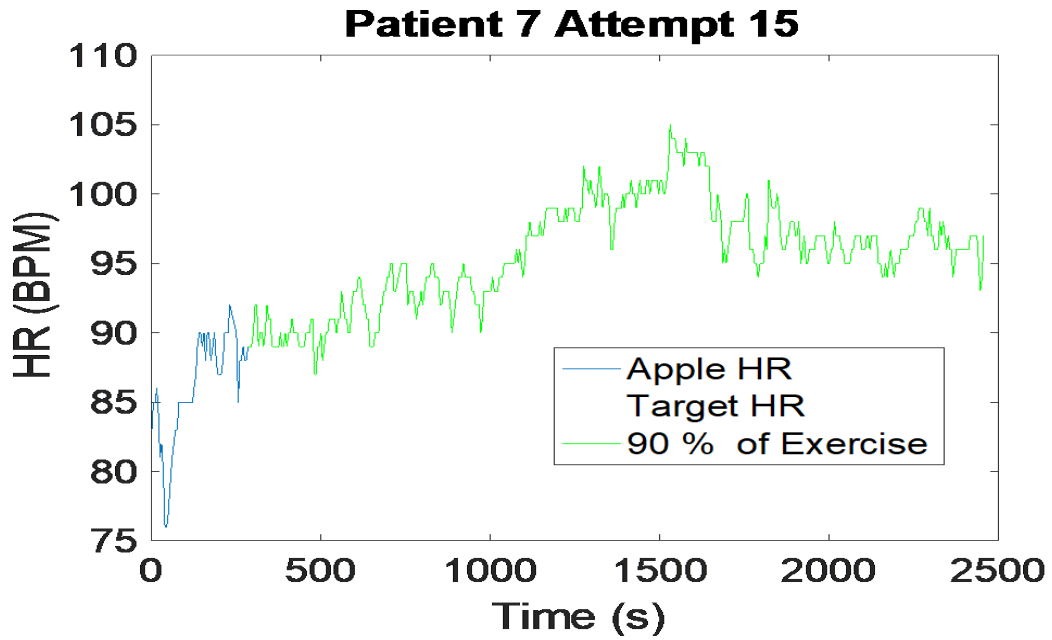


Figure A5.574: Patient No. 7 Week 7 Attempt 2



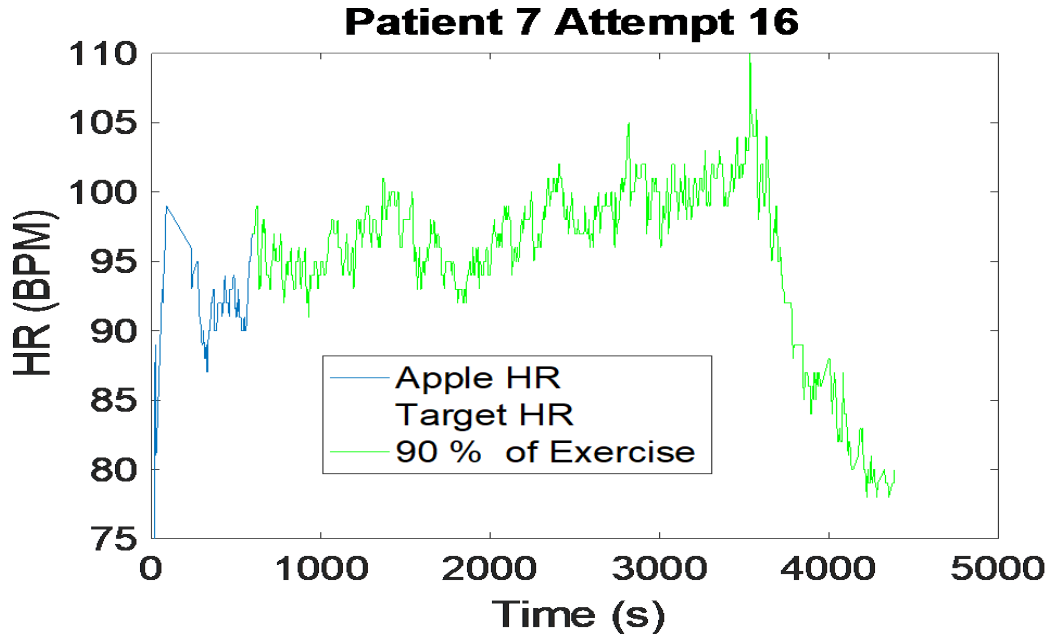


Figure A5.575: Patient No. 7 Week 7 Attempt 3

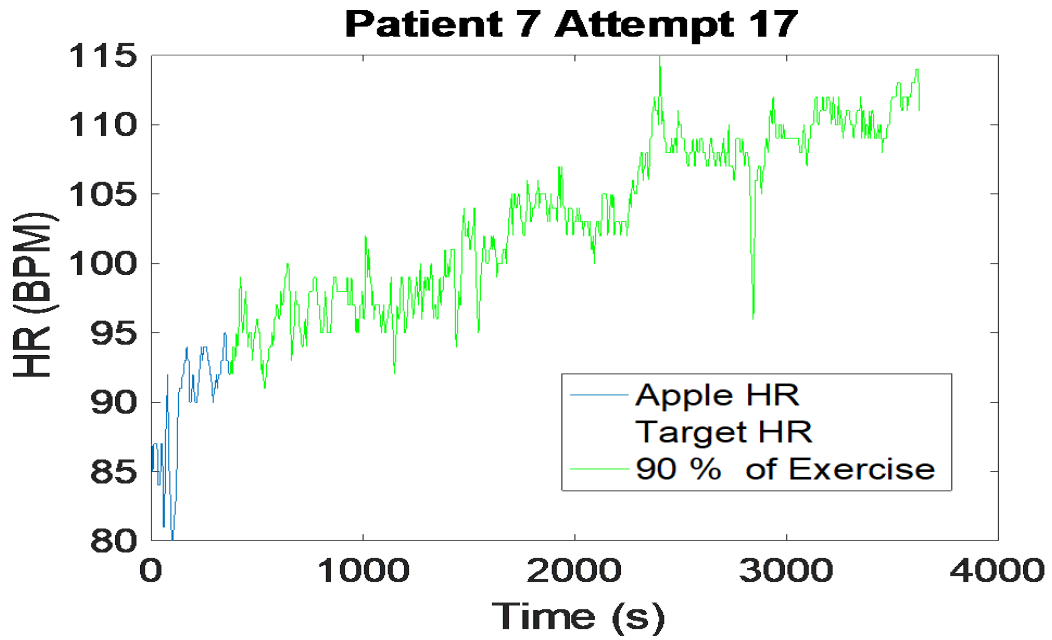
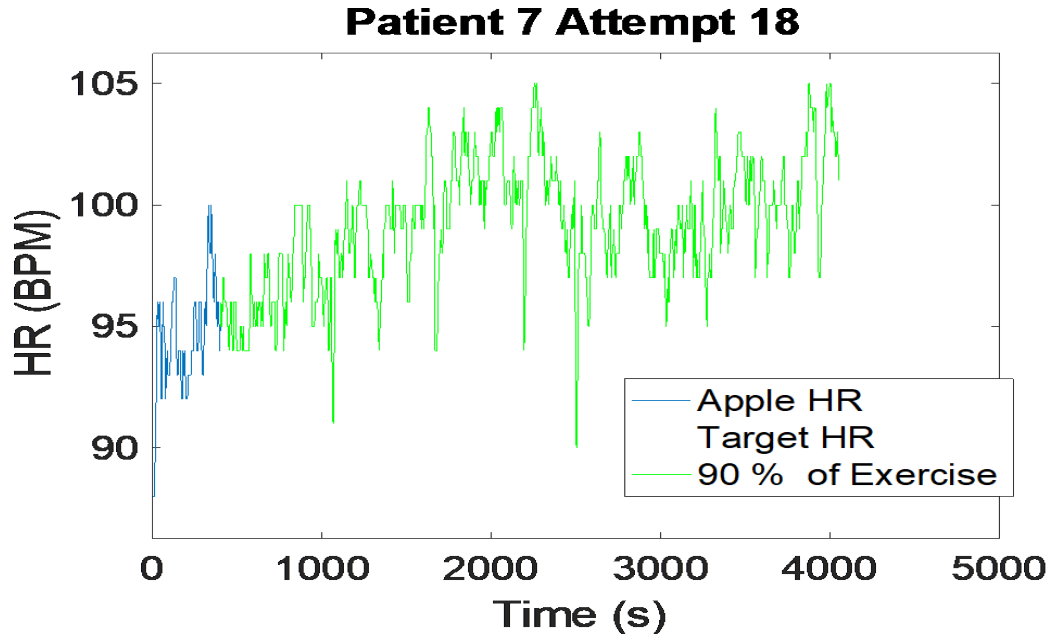
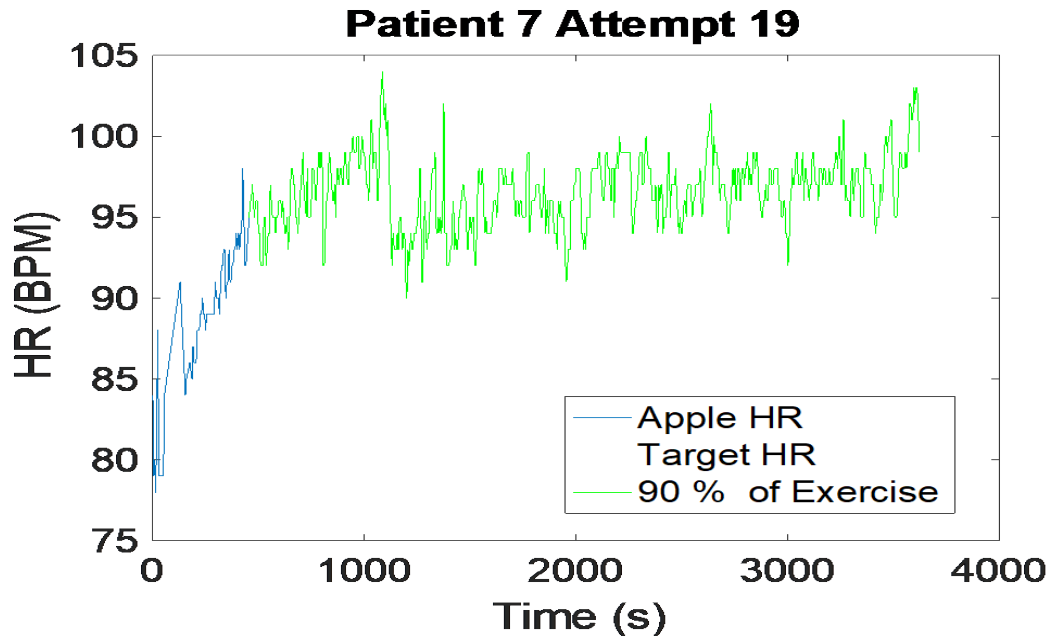


Figure A5.576: Patient No. 7 Week 7 Attempt 4



*Figure A5.577: Patient No. 7 Week 7 Attempt 5*



*Figure A5.578: Patient No. 7 Week 8 Attempt 1*

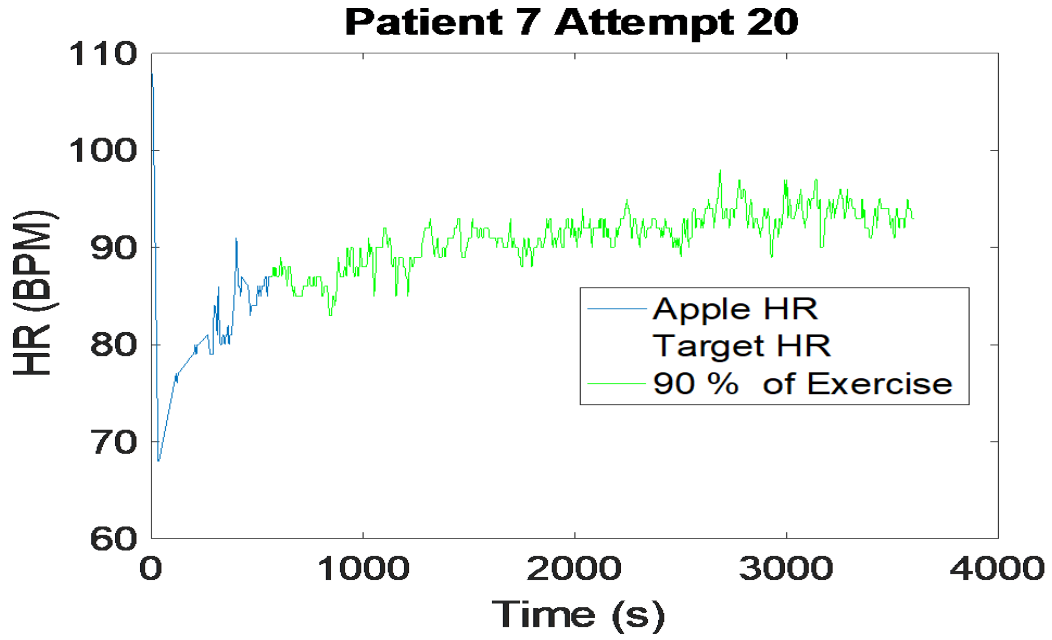


Figure A5.579: Patient No. 7 Week 8 Attempt 2

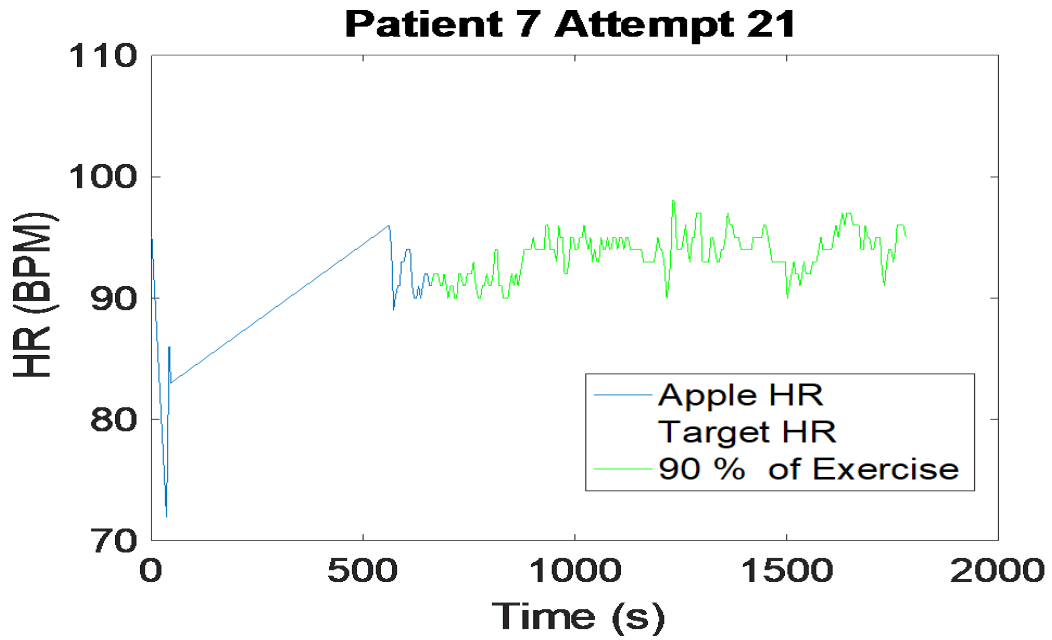


Figure A5.580: Patient No. 7 Week 8 Attempt 3

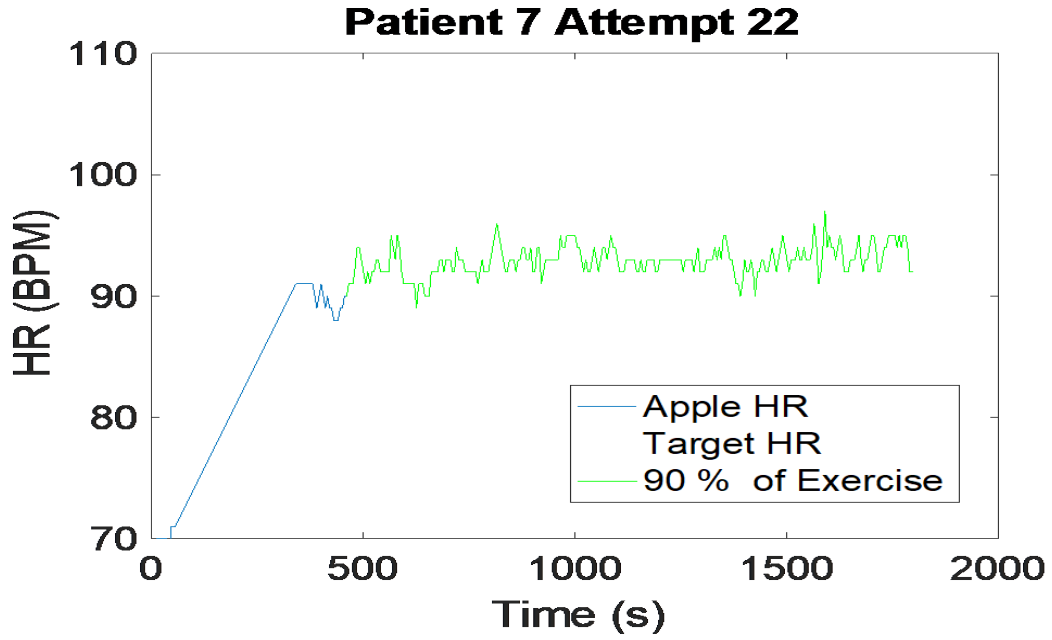


Figure A5.581: Patient No. 7 Week 8 Attempt 4

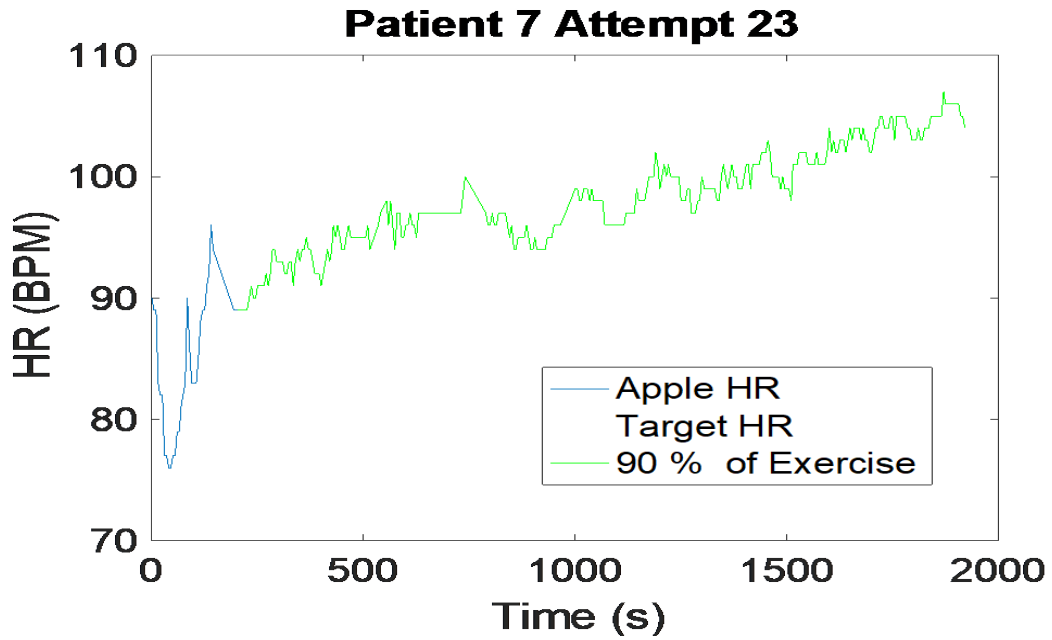
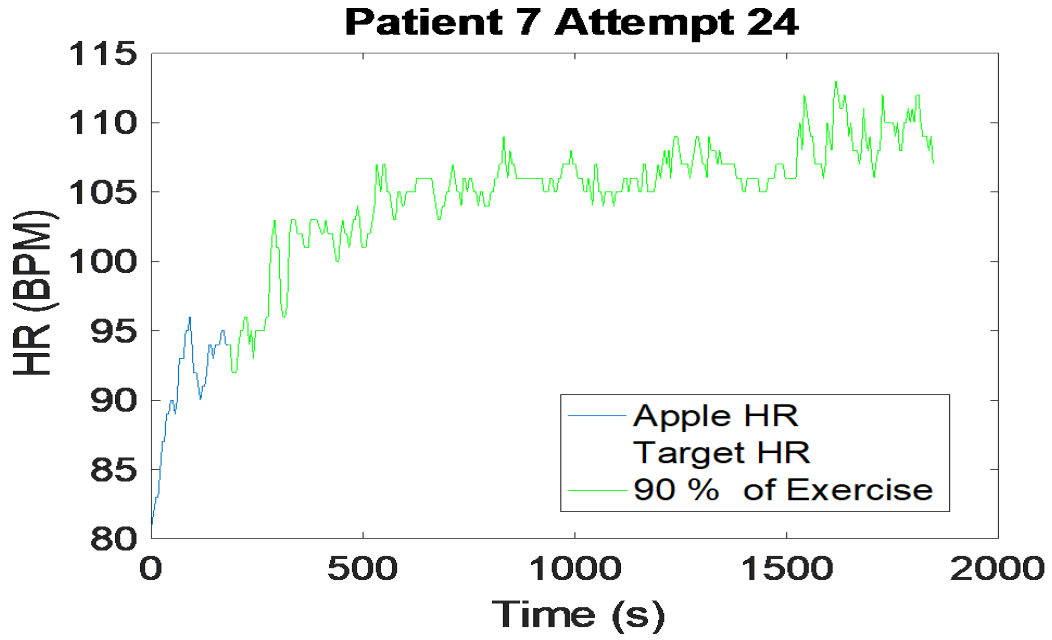
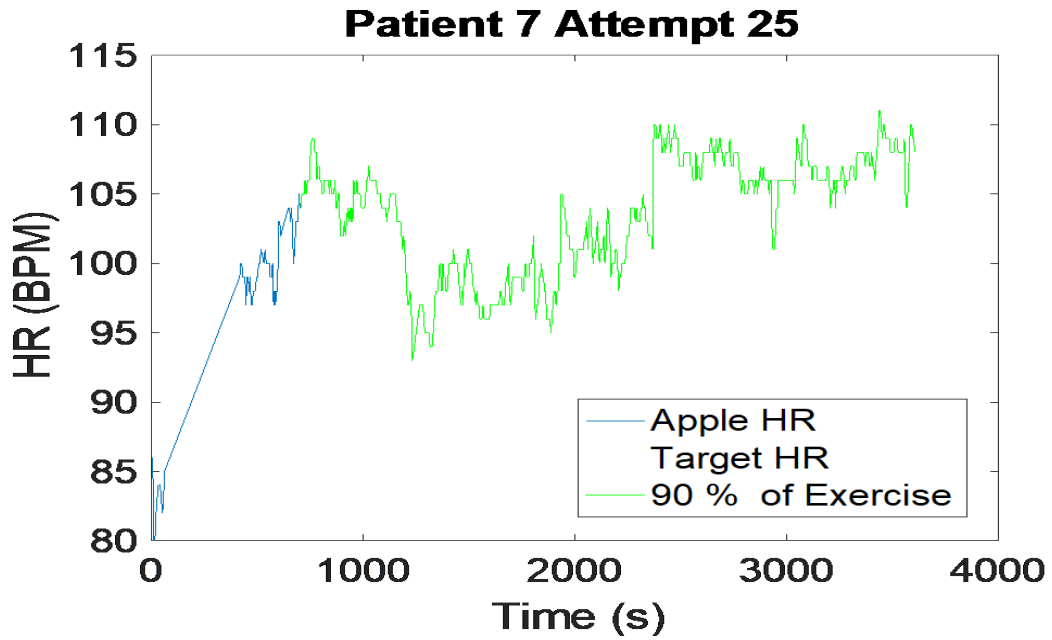


Figure A5.582: Patient No. 7 Week 9 Attempt 1



*Figure A5.583: Patient No. 7 Week 10 Attempt 1*



*Figure A5.584: Patient No. 7 Week 10 Attempt 2*

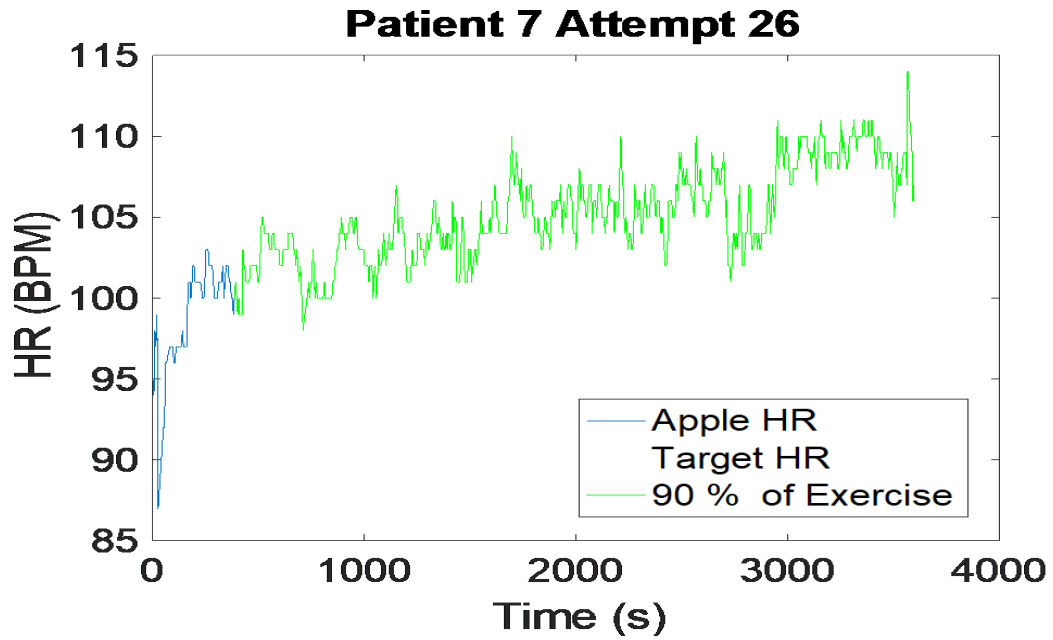


Figure A5.585: Patient No. 7 Week 10 Attempt 3

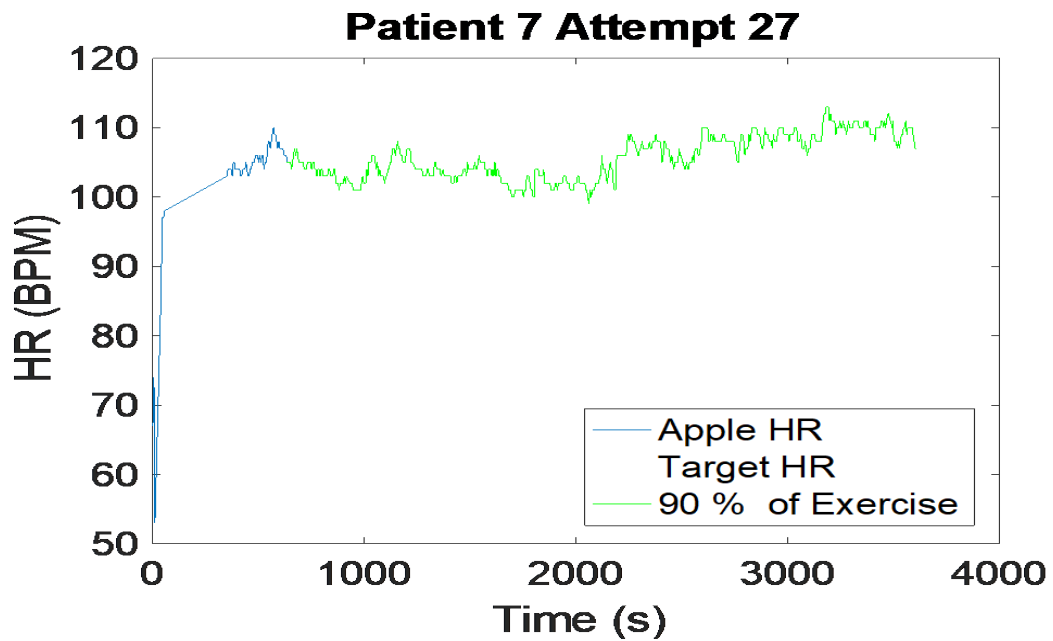


Figure A5.586: Patient No. 7 Week 10 Attempt 4

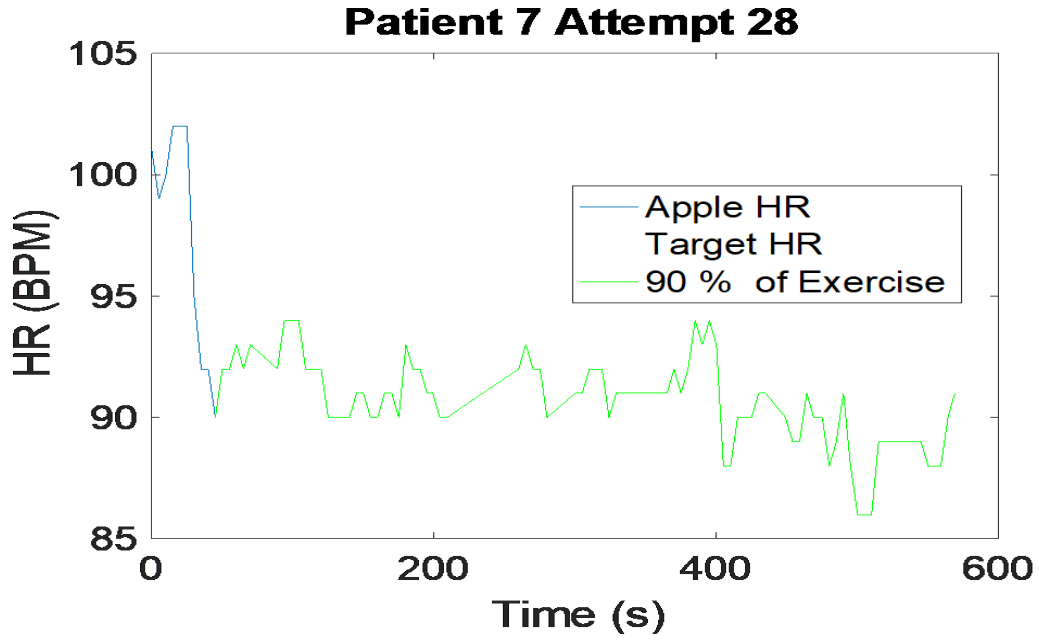


Figure A5.587: Patient No. 7 Week 10 Attempt 5

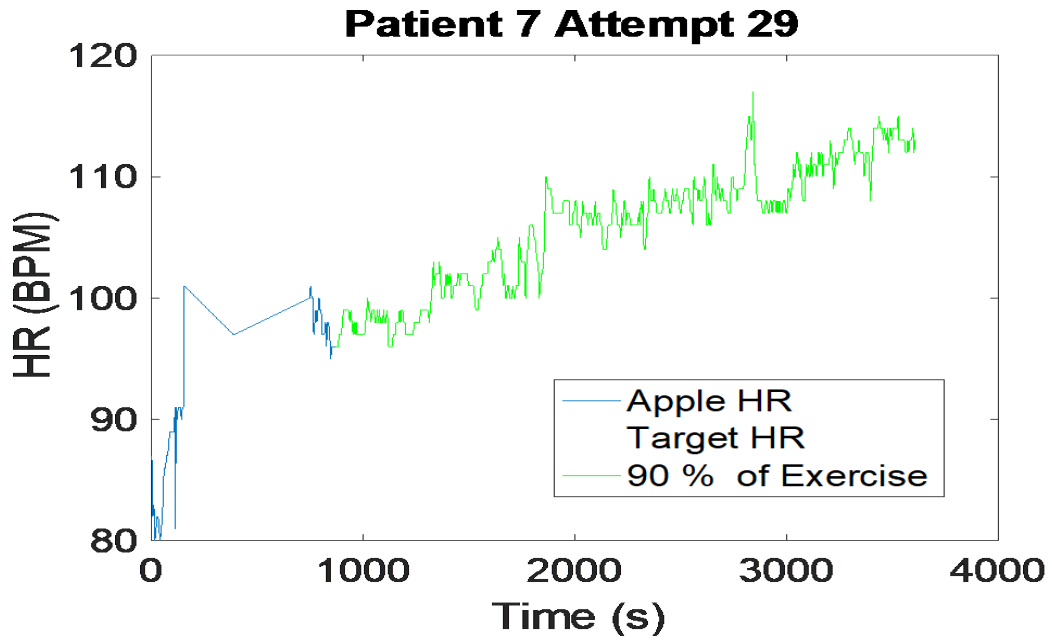
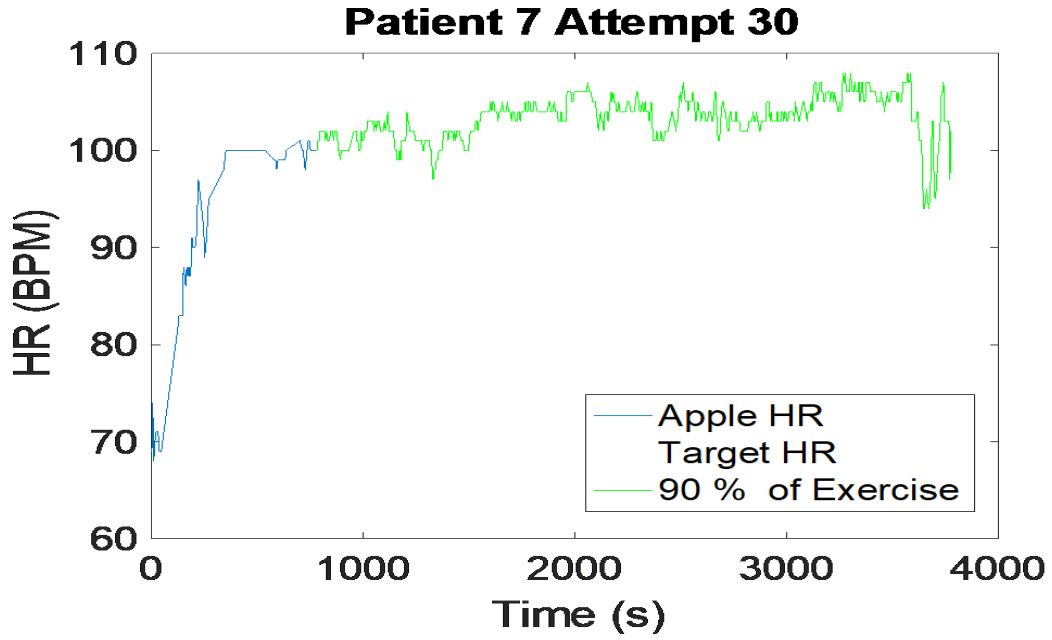
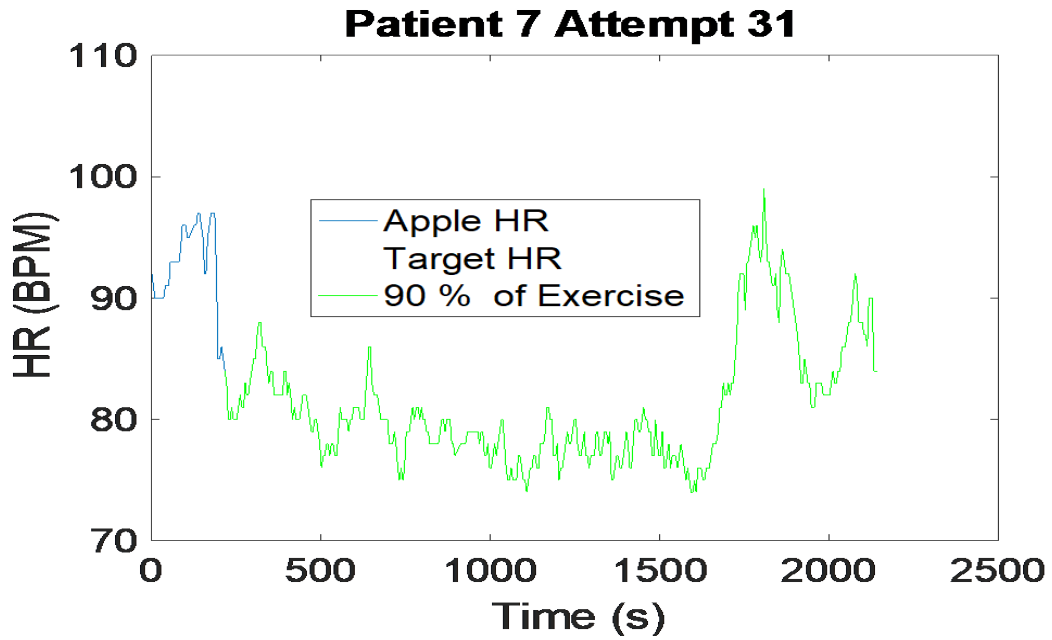


Figure A5.588: Patient No. 7 Week 10 Attempt 6



*Figure A5.589: Patient No. 7 Week 11 Attempt 1*



*Figure A5.590: Patient No. 7 Week 11 Attempt 2*



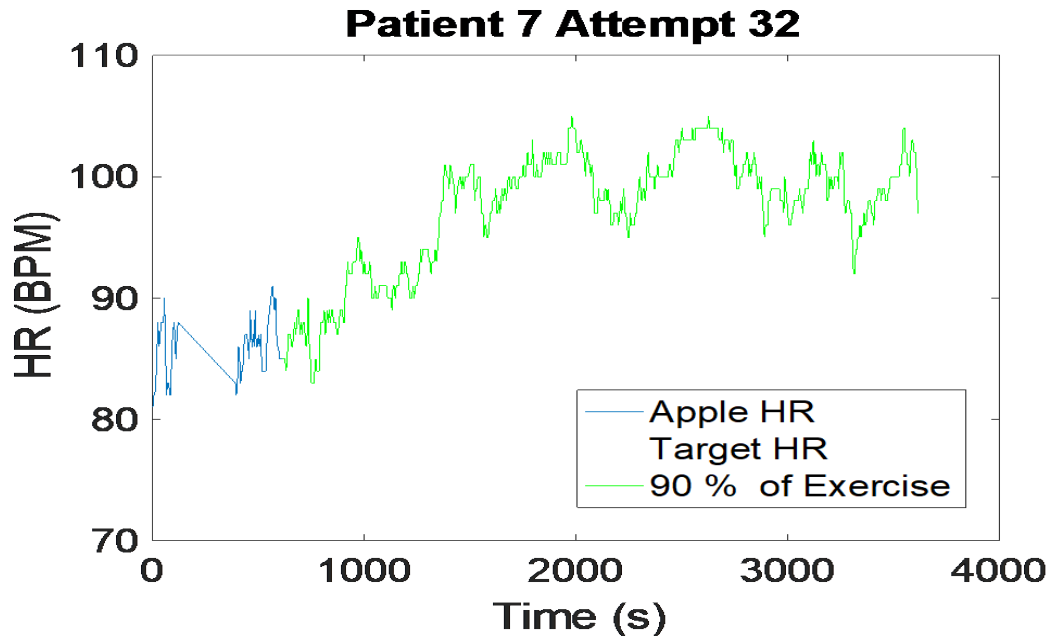


Figure A5.591: Patient No. 7 Week 11 Attempt 3

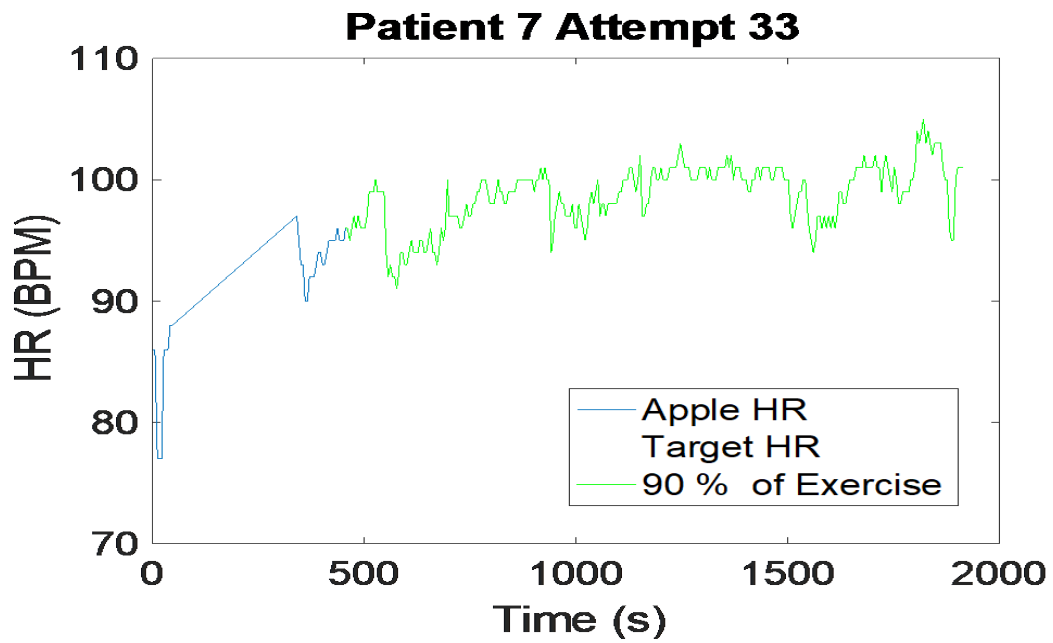
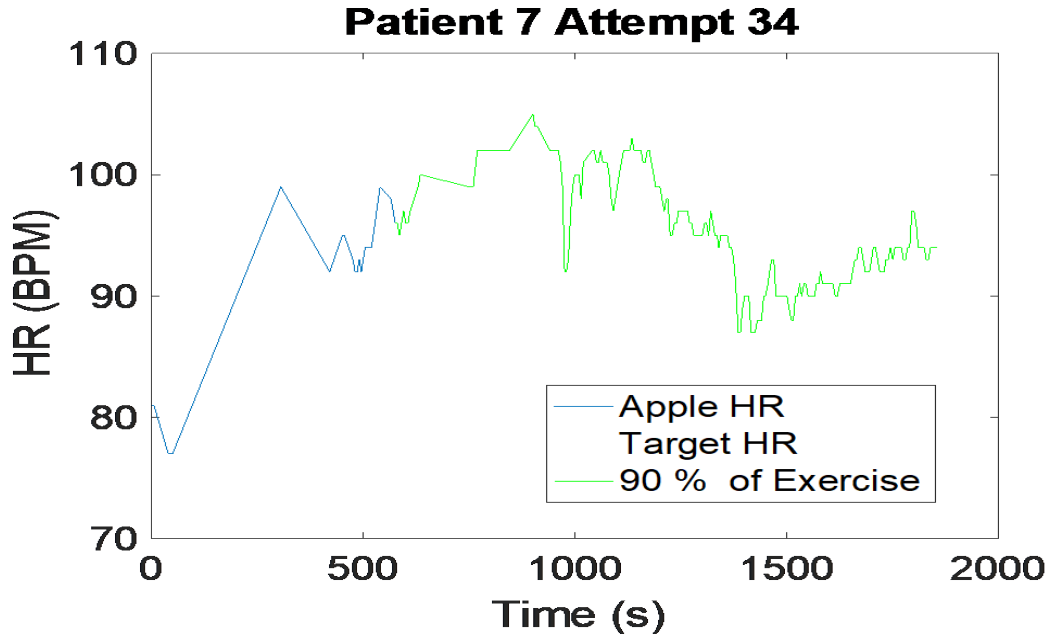
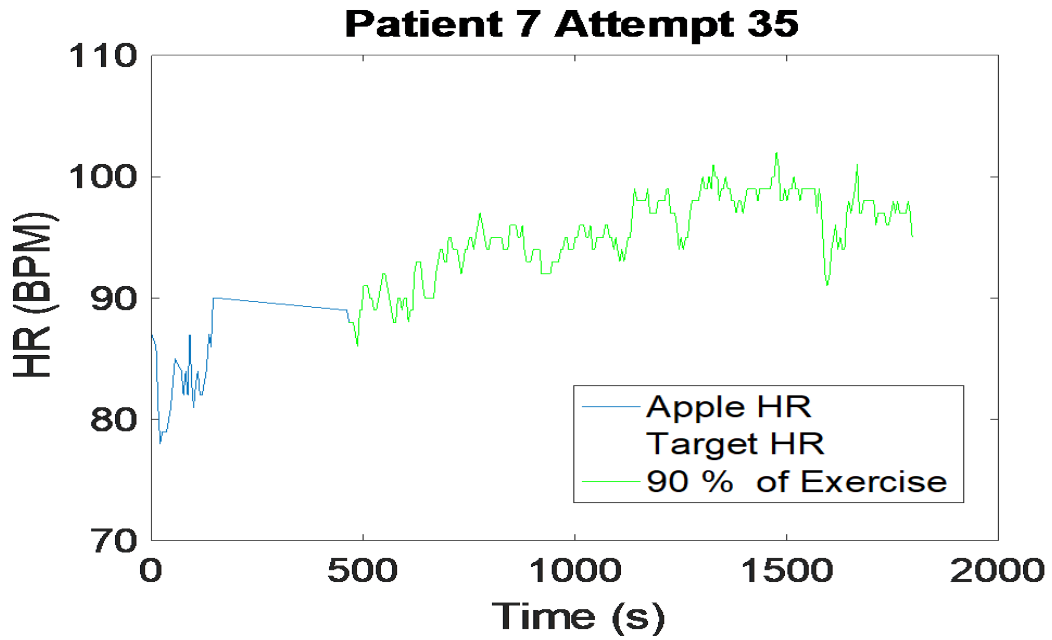


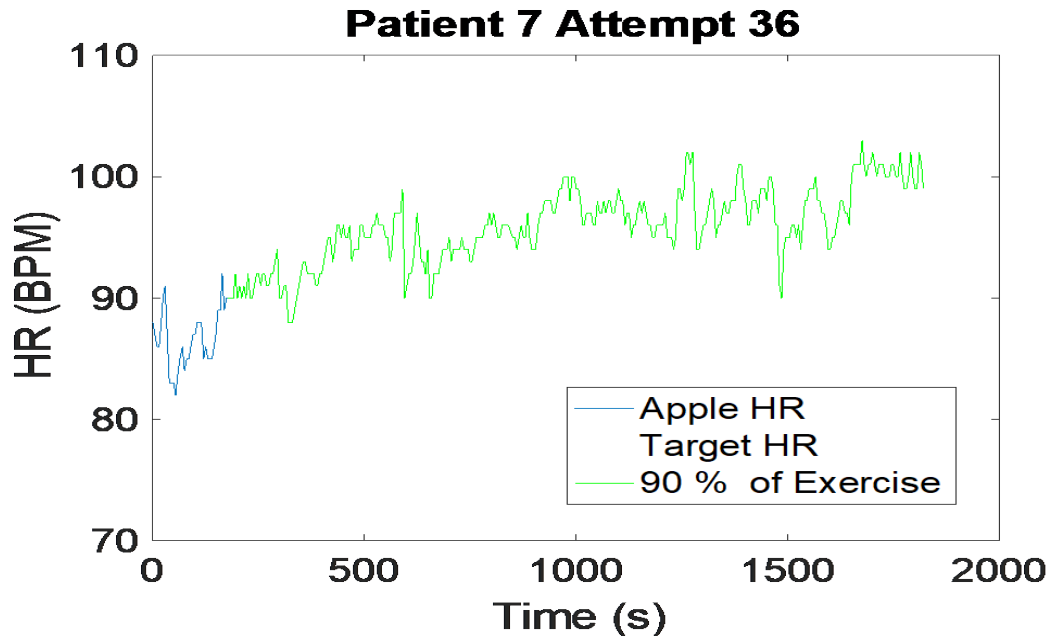
Figure A5.592: Patient No. 7 Week 11 Attempt 4



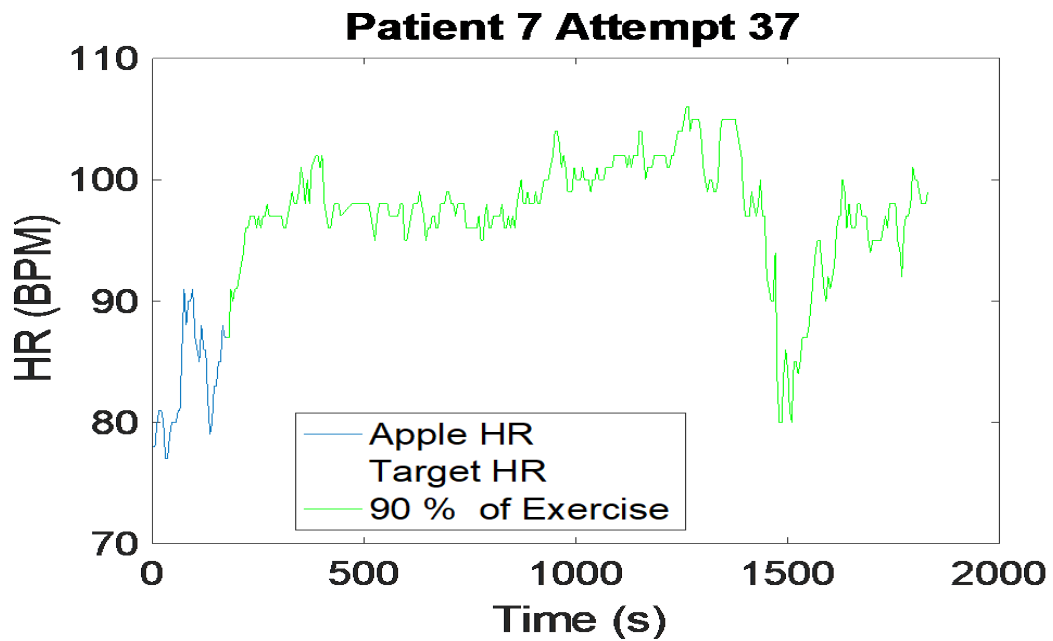
*Figure A5.593: Patient No. 7 Week 11 Attempt 5*



*Figure A5.594: Patient No. 7 Week 12 Attempt 1*



*Figure A5.595: Patient No. 7 Week 12 Attempt 2*



*Figure A5.596: Patient No. 7 Week 12 Attempt 3*

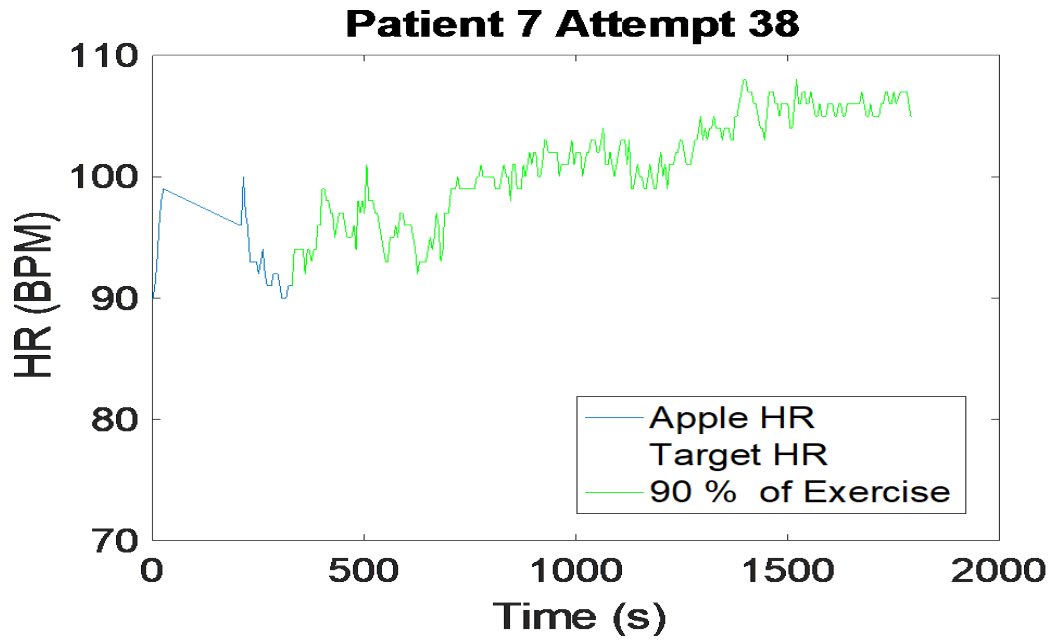


Figure A5.597: Patient No. 7 Week 13 Attempt 1

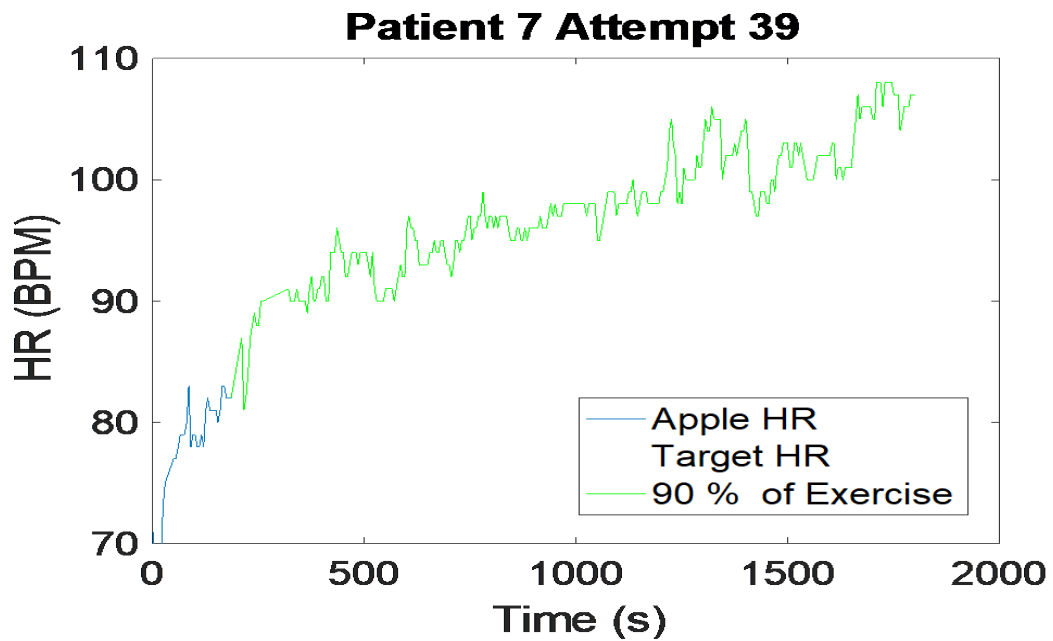


Figure A5.598: Patient No. 7 Week 13 Attempt 2

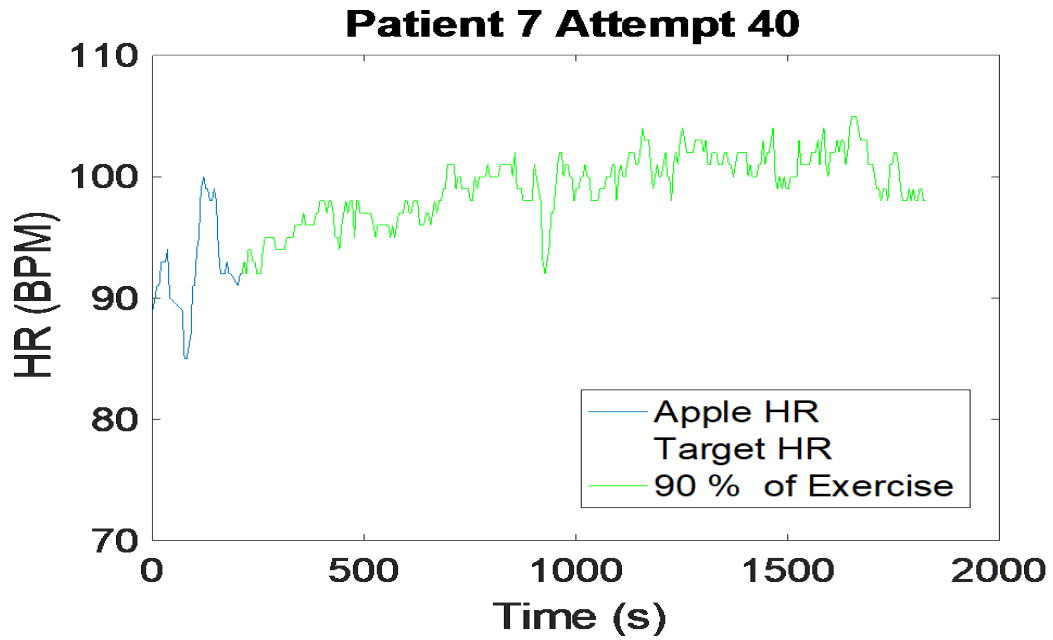


Figure A5.599: Patient No. 7 Week 13 Attempt 3

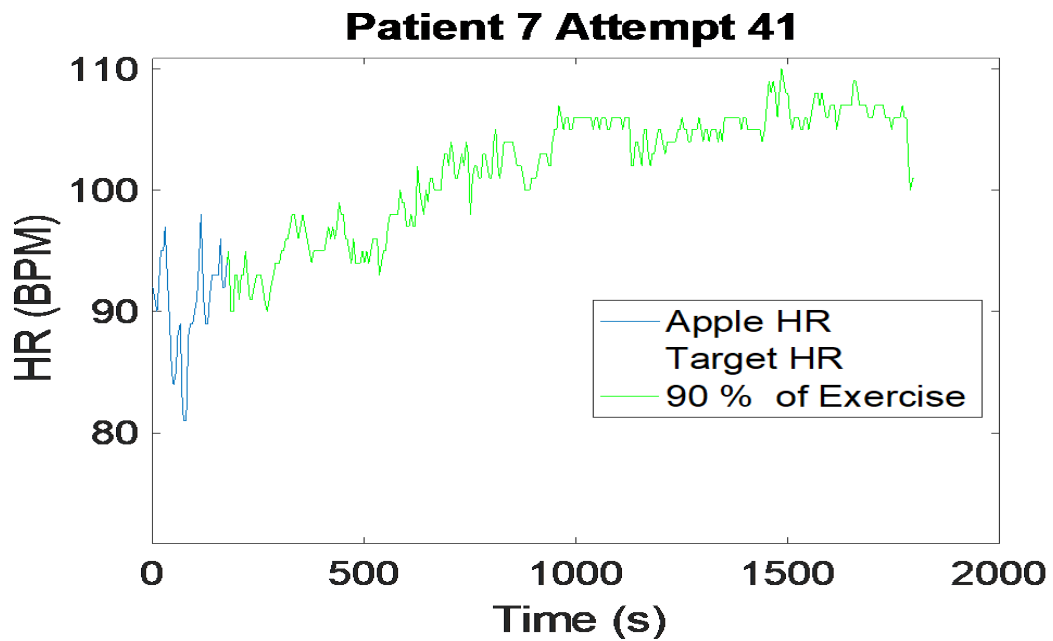


Figure A5.600: Patient No. 7 Week 13 Attempt 4

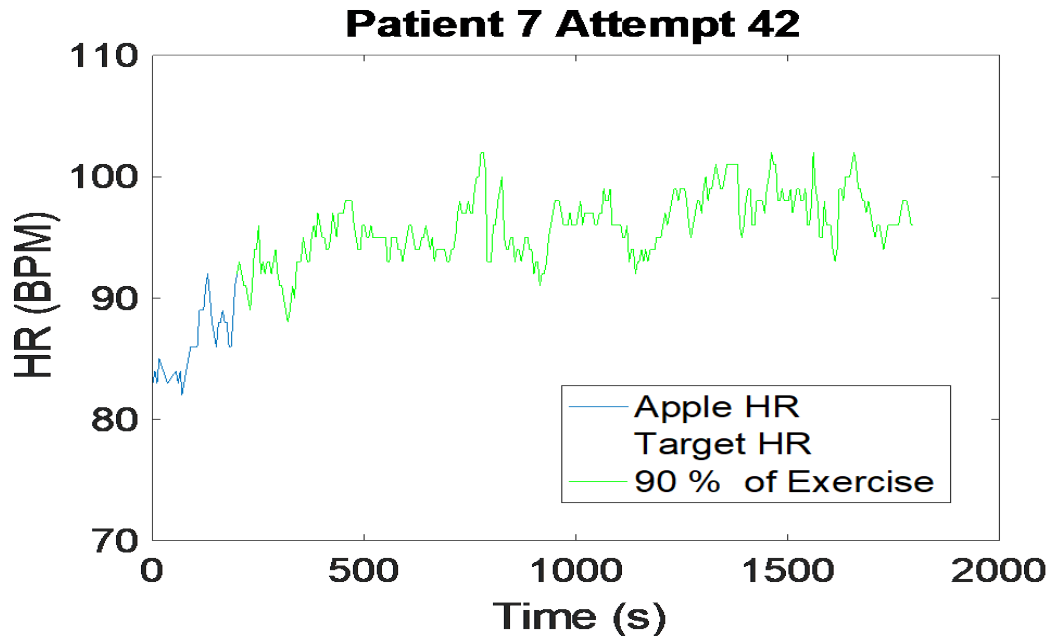
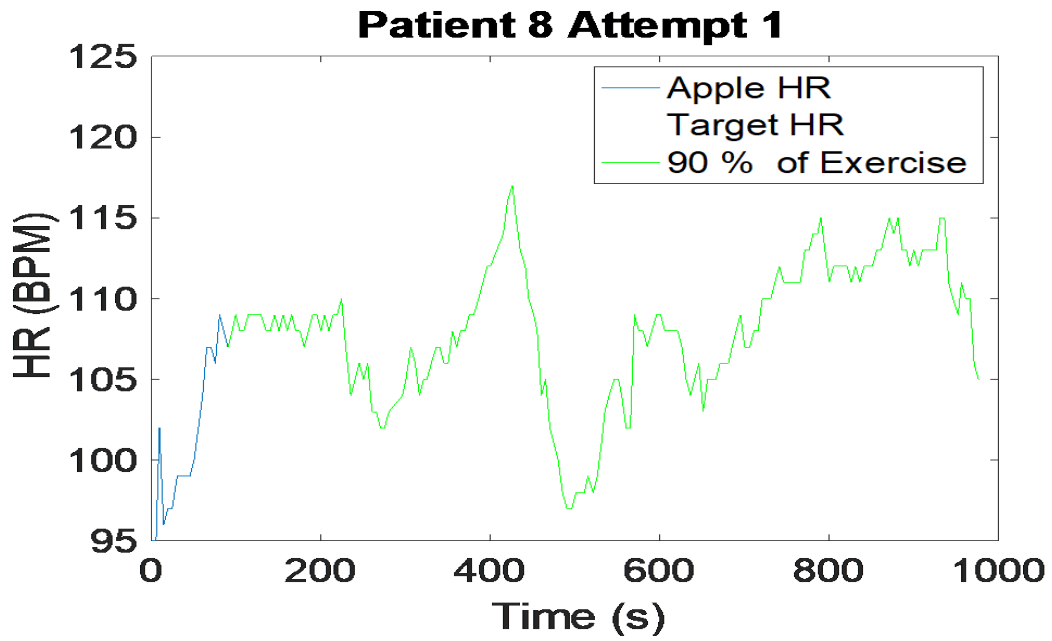
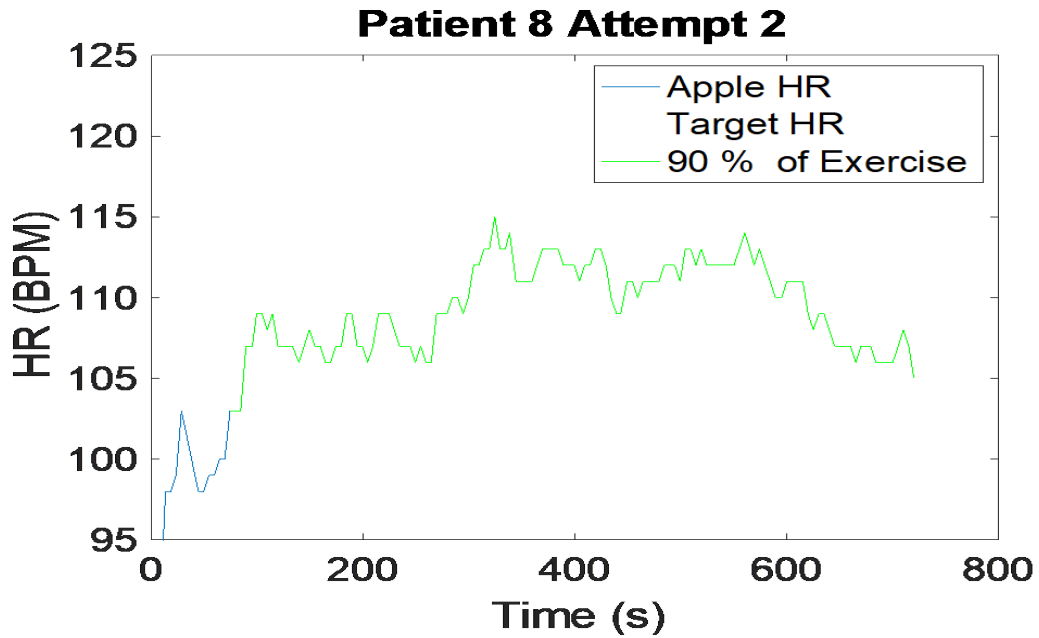


Figure A5.601: Patient No. 7 Week 13 Attempt 5

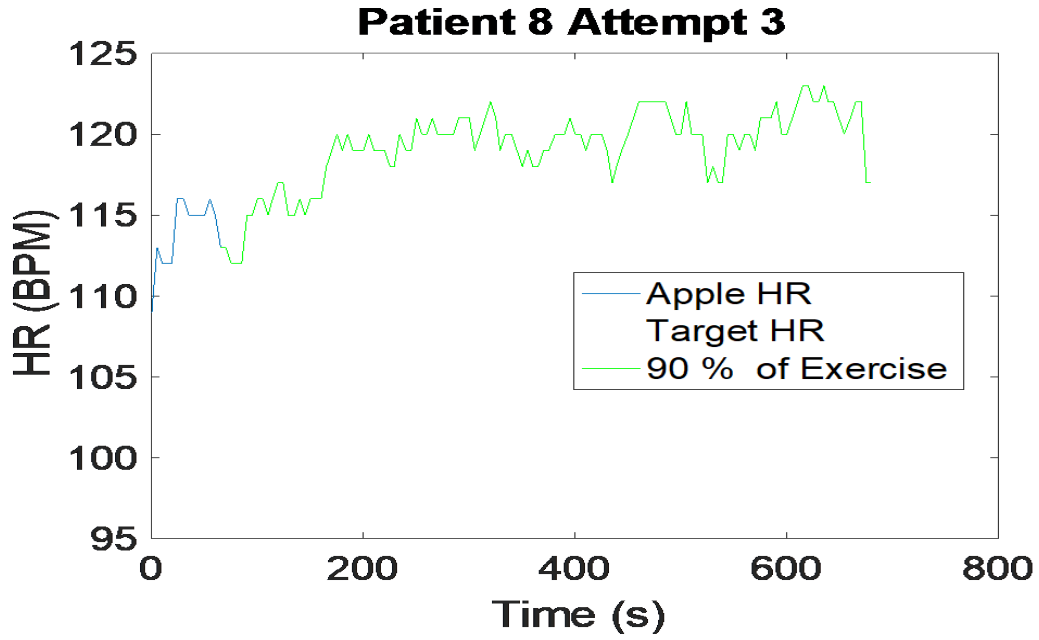
**Patient 8 Attempts:**



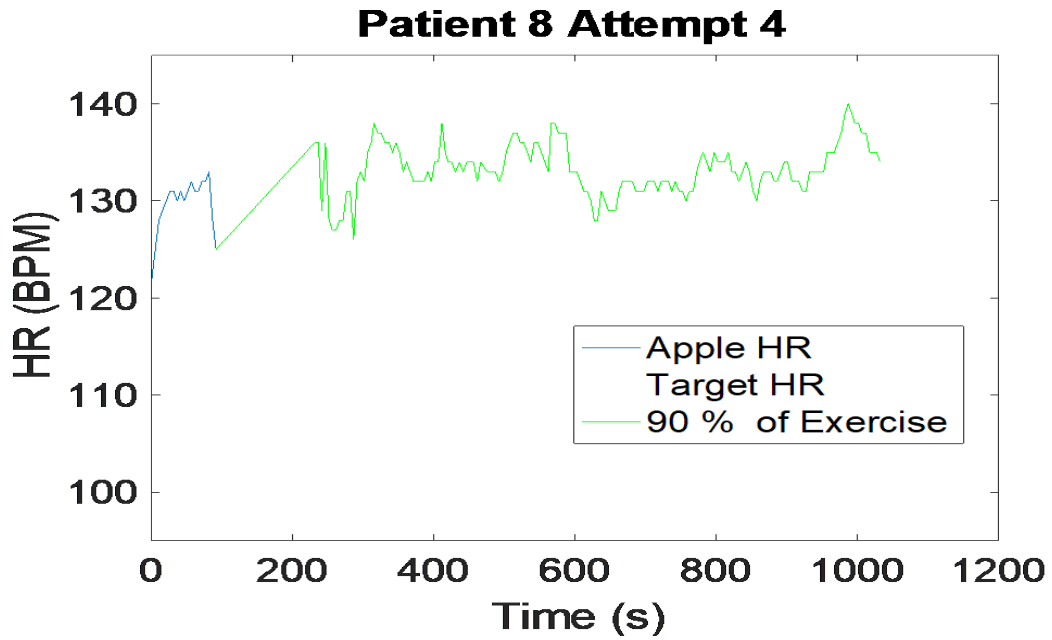
*Figure A5.602: Patient No.8 Week 1 Attempt 1*



*Figure A5.603: Patient No.8 Week 1 Attempt 2*



*Figure A5.604: Patient No.8 Week 2 Attempt 1*



*Figure A5.605: Patient No.8 Week 2 Attempt 2*



### Patient 8 Attempt 5

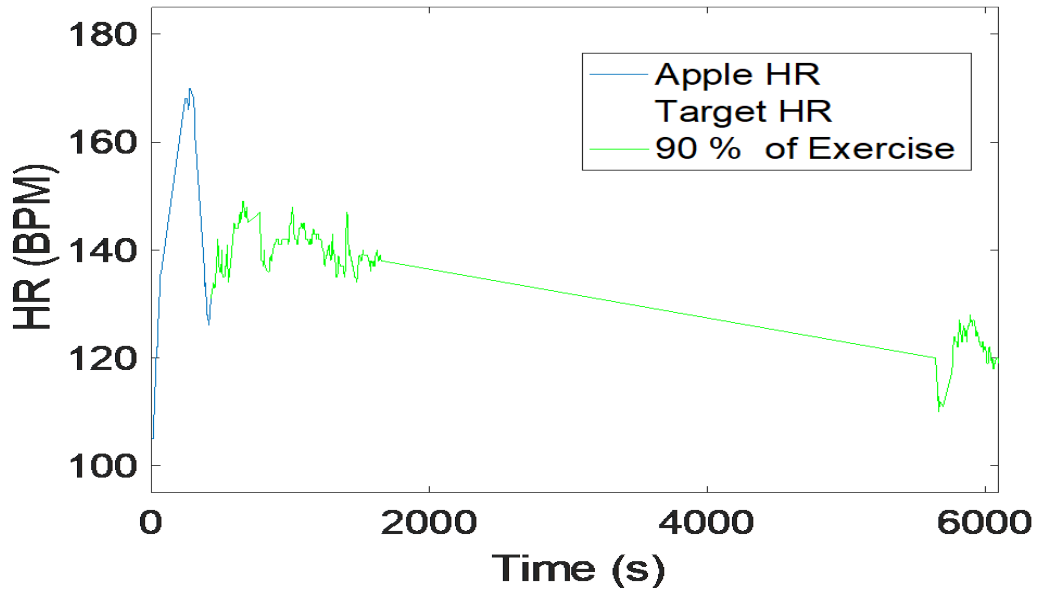


Figure A5.606: Patient No.8 Week 3 Attempt 1

### Patient 8 Attempt 6

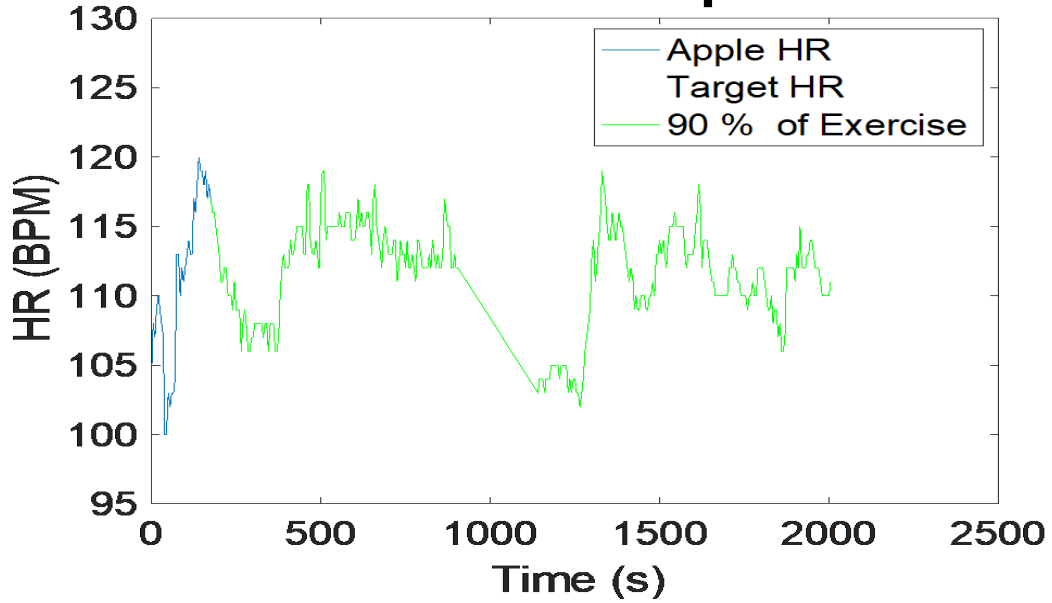


Figure A5.607: Patient No.8 Week 3 Attempt 2

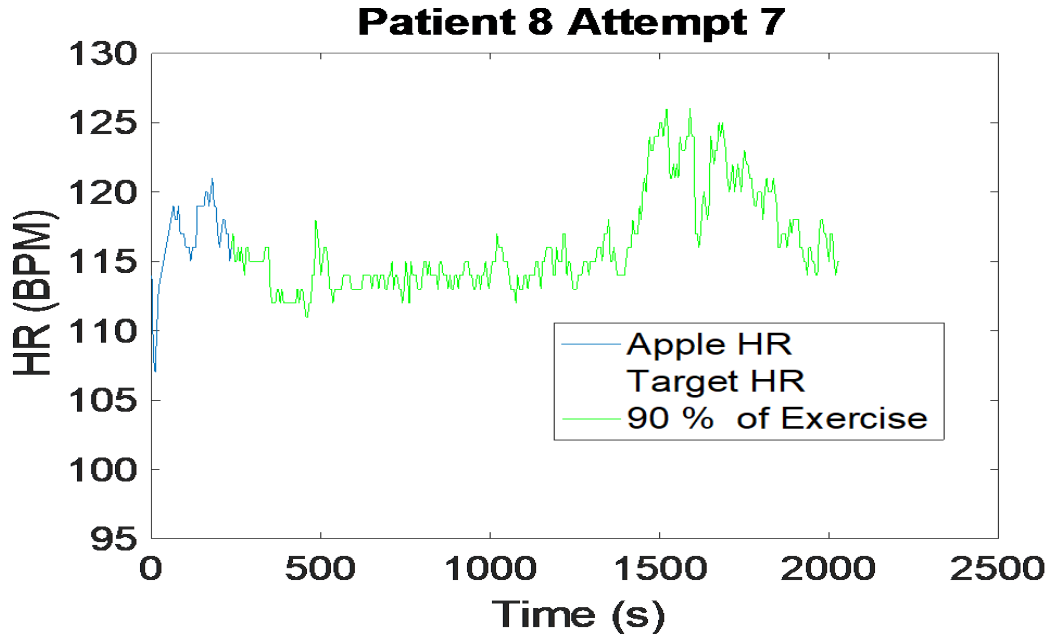


Figure A5.608: Patient No.8 Week 3 Attempt 3

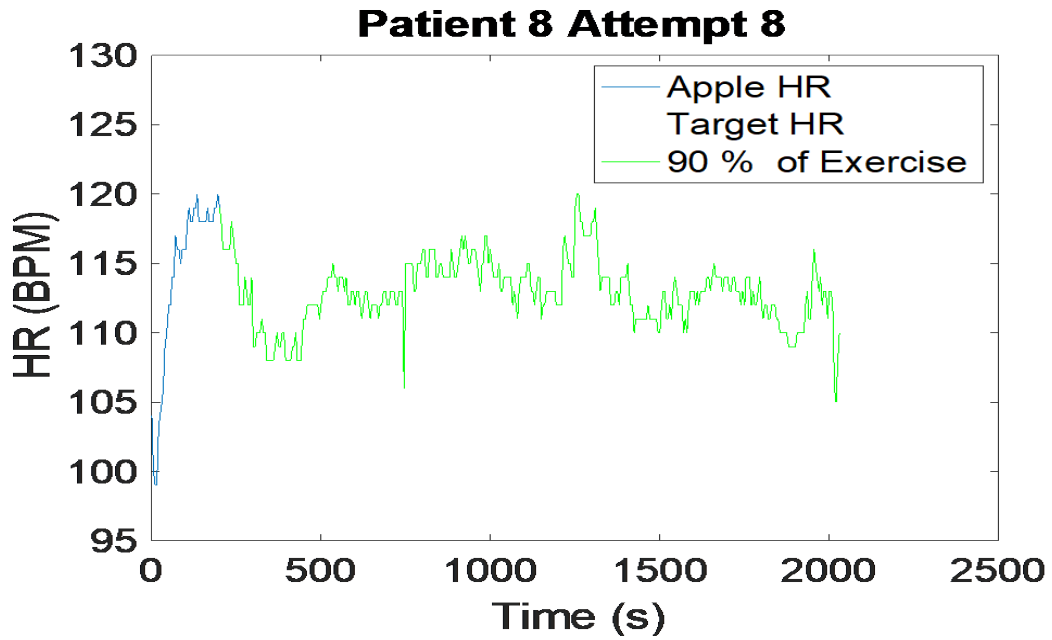


Figure A5.609: Patient No.8 Week 4 Attempt 1

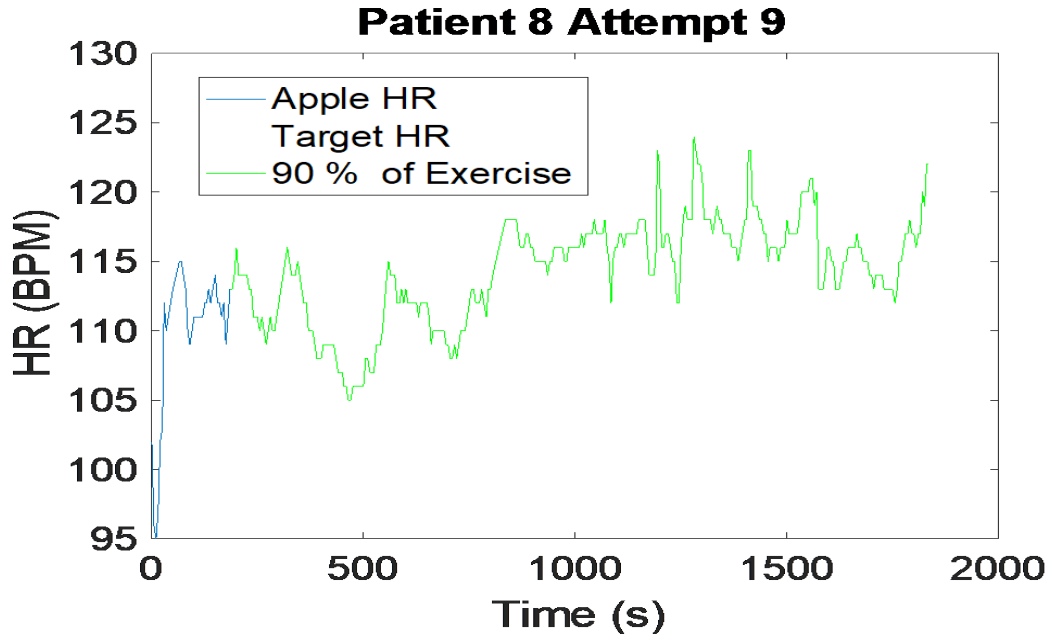


Figure A5.610: Patient No.8 Week 4 Attempt 2

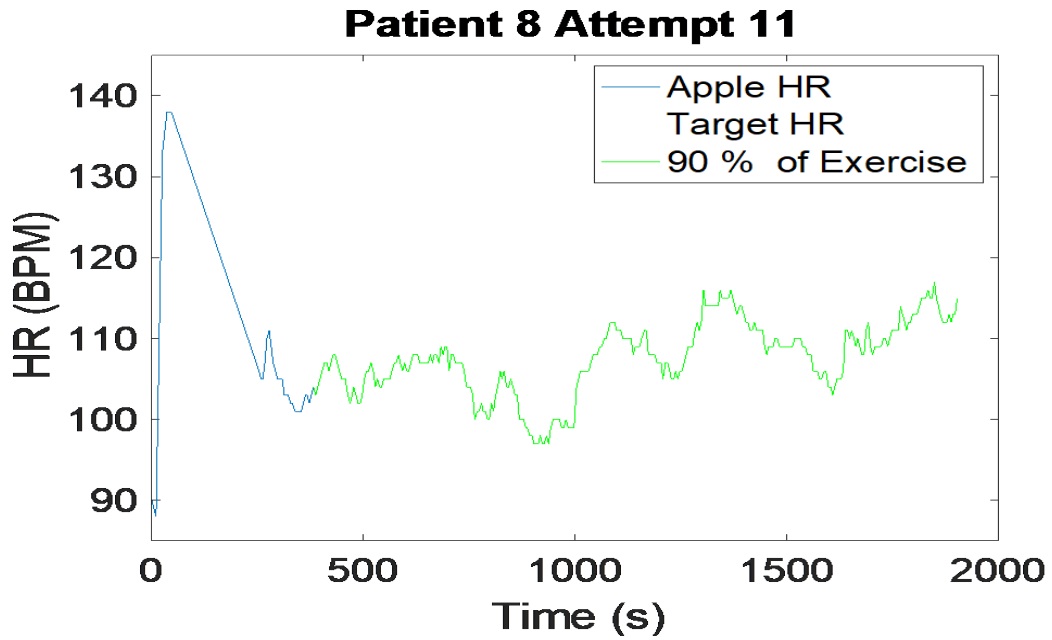


Figure A5.611: Patient No.8 Week 6 Attempt 1

### Patient 8 Attempt 12

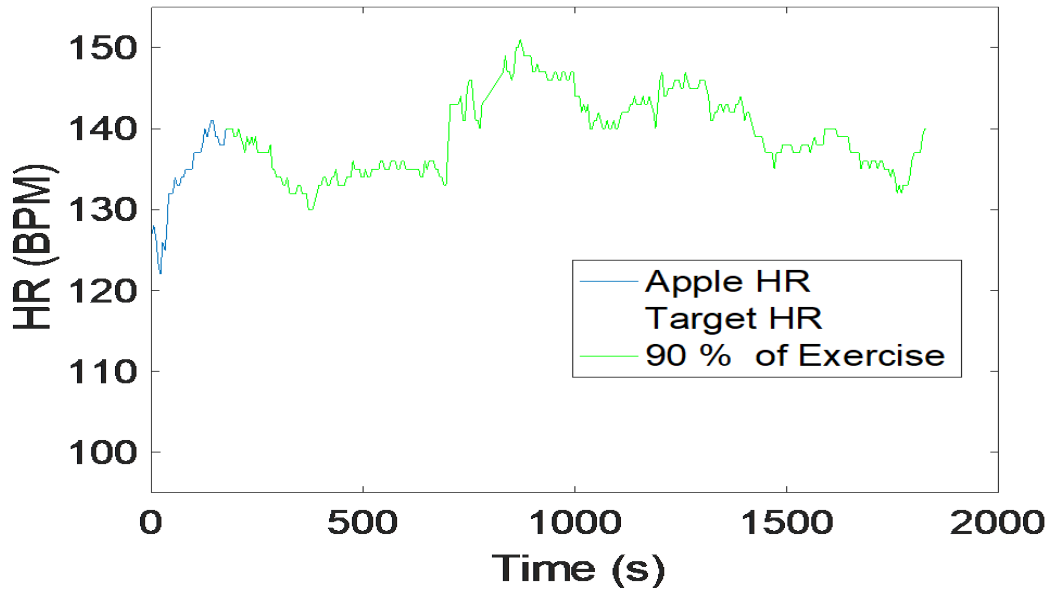


Figure A5.612: Patient No.8 Week 6 Attempt 2

### Patient 8 Attempt 13

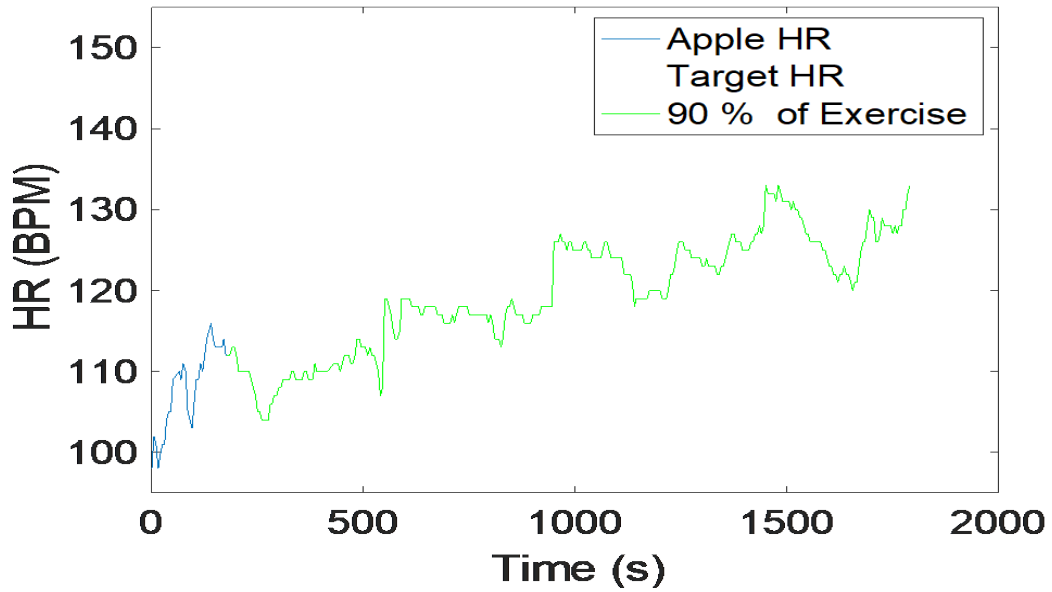


Figure A5.613: Patient No.8 Week 6 Attempt 3

### Patient 8 Attempt 14

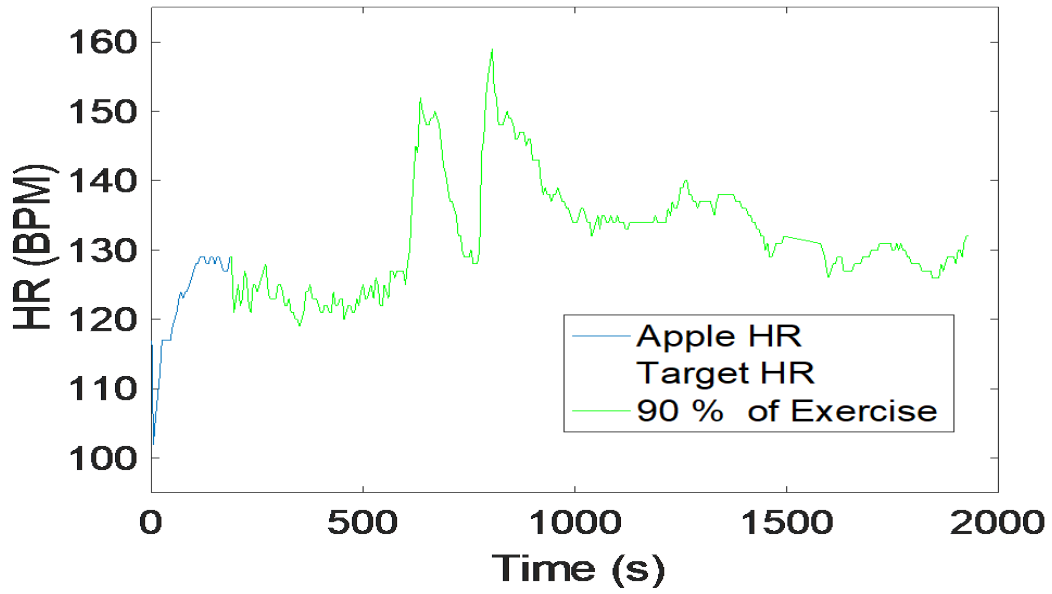


Figure A5.614: Patient No.8 Week 6 Attempt 4

### Patient 8 Attempt 15

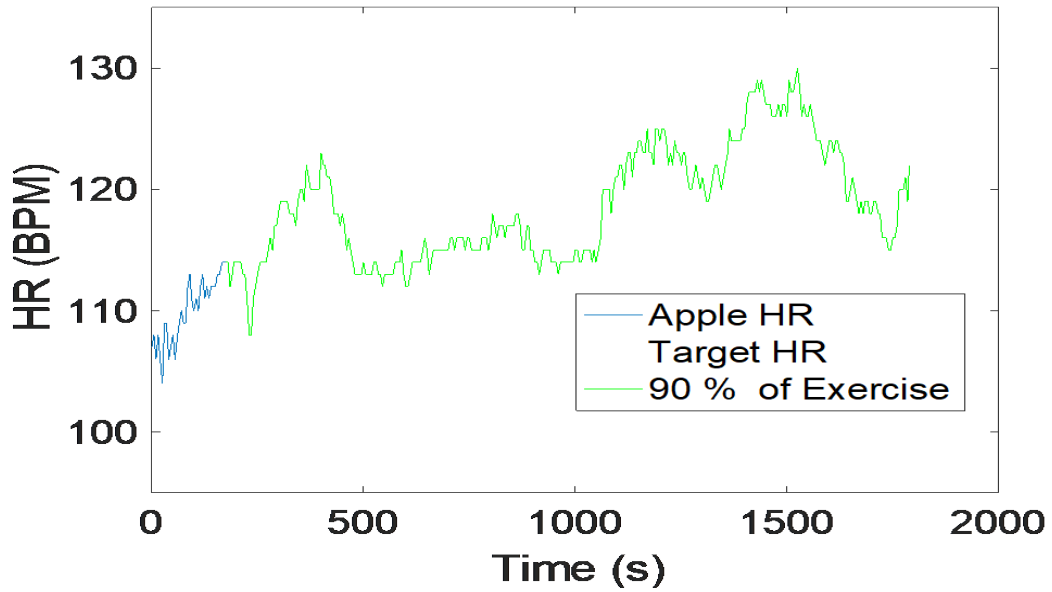


Figure A5.615: Patient No.8 Week 6 Attempt 5

### Patient 8 Attempt 16

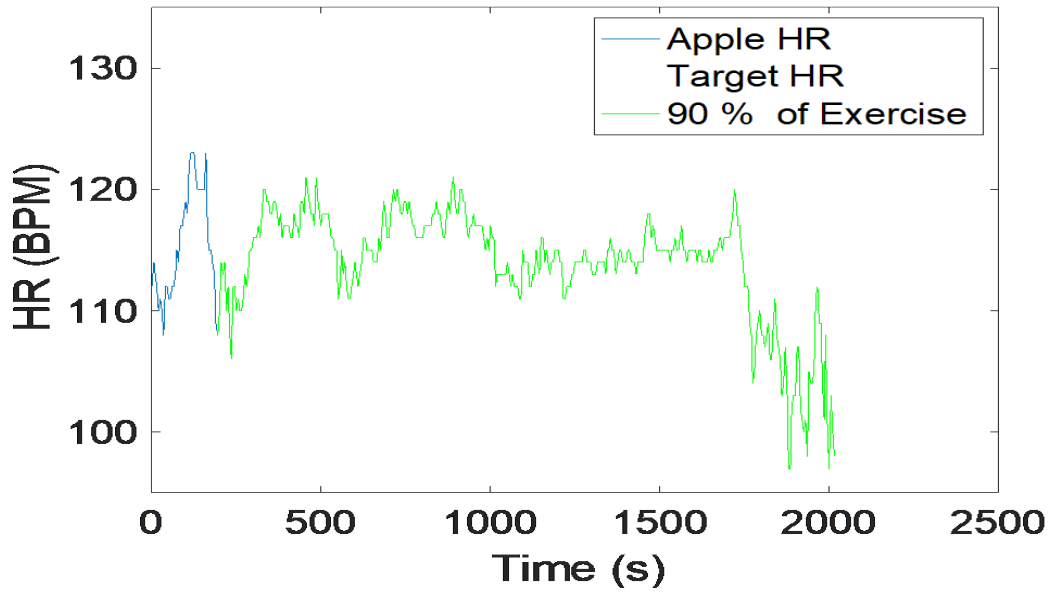


Figure A5.616: Patient No.8 Week 7 Attempt 1

### Patient 8 Attempt 17

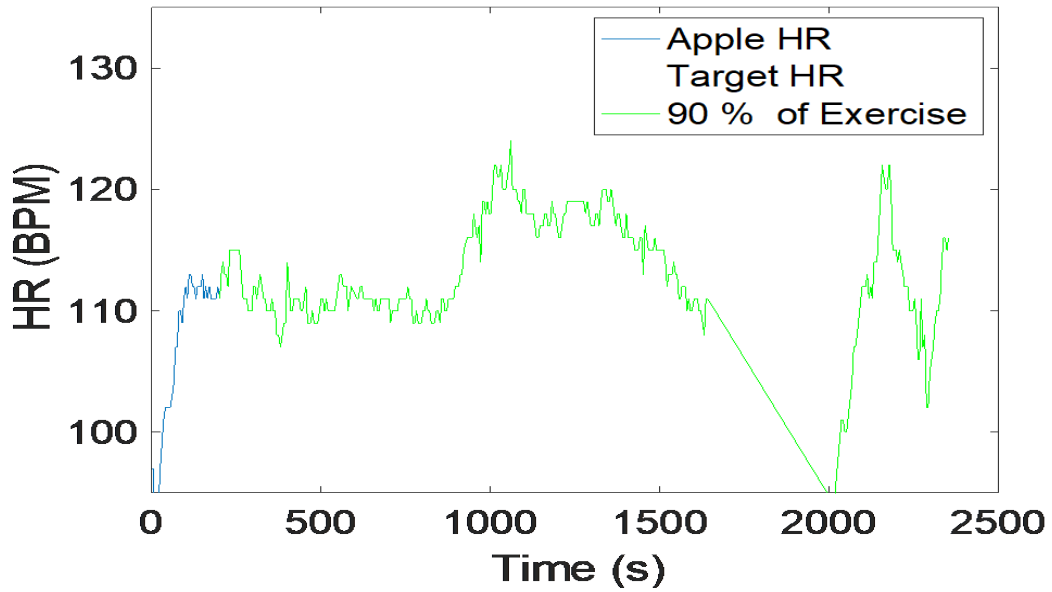


Figure A5.617: Patient No.8 Week 7 Attempt 2

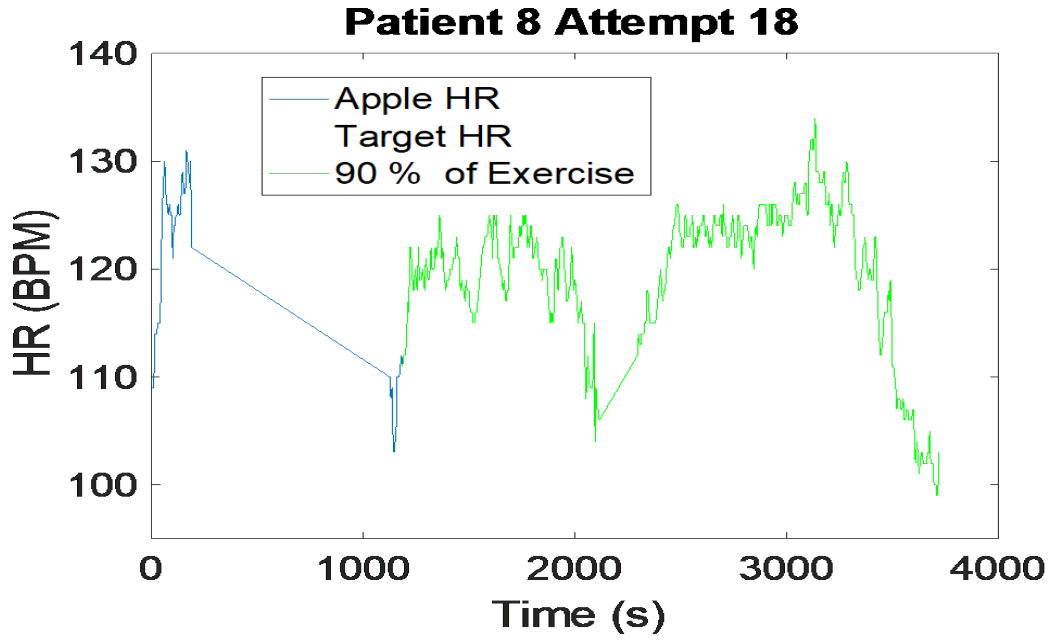


Figure A5.618: Patient No.8 Week 7 Attempt 3

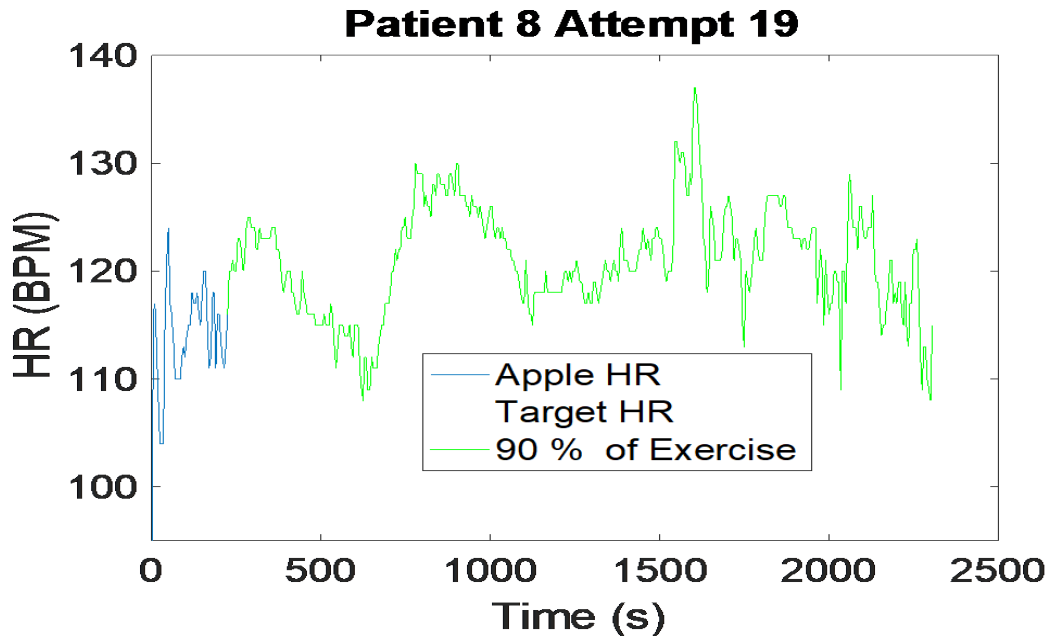


Figure A5.619: Patient No.8 Week 8 Attempt 1

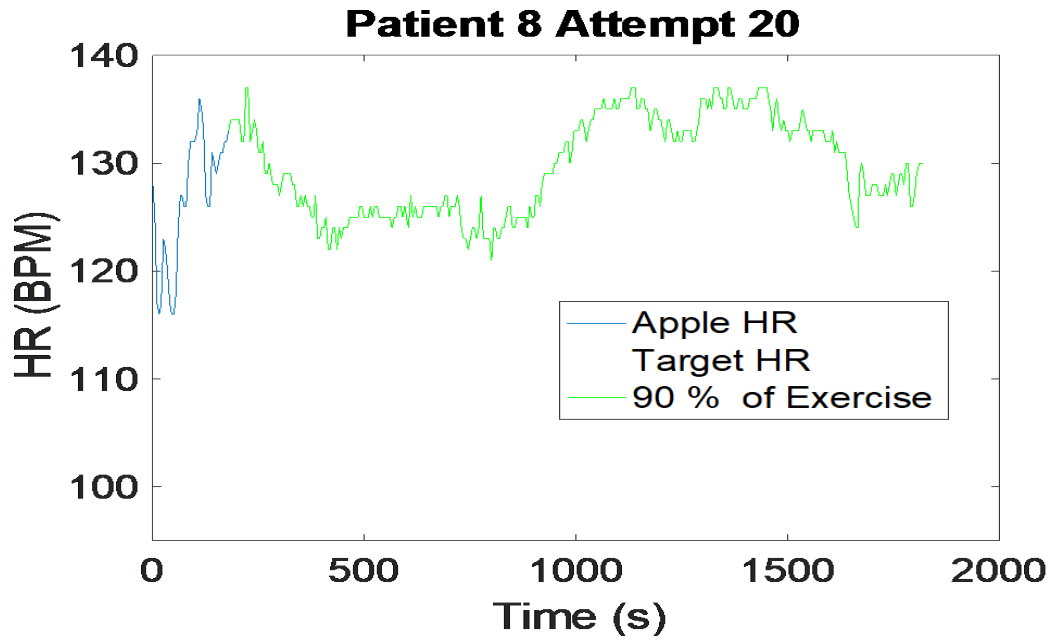


Figure A5.620: Patient No.8 Week 8 Attempt 2

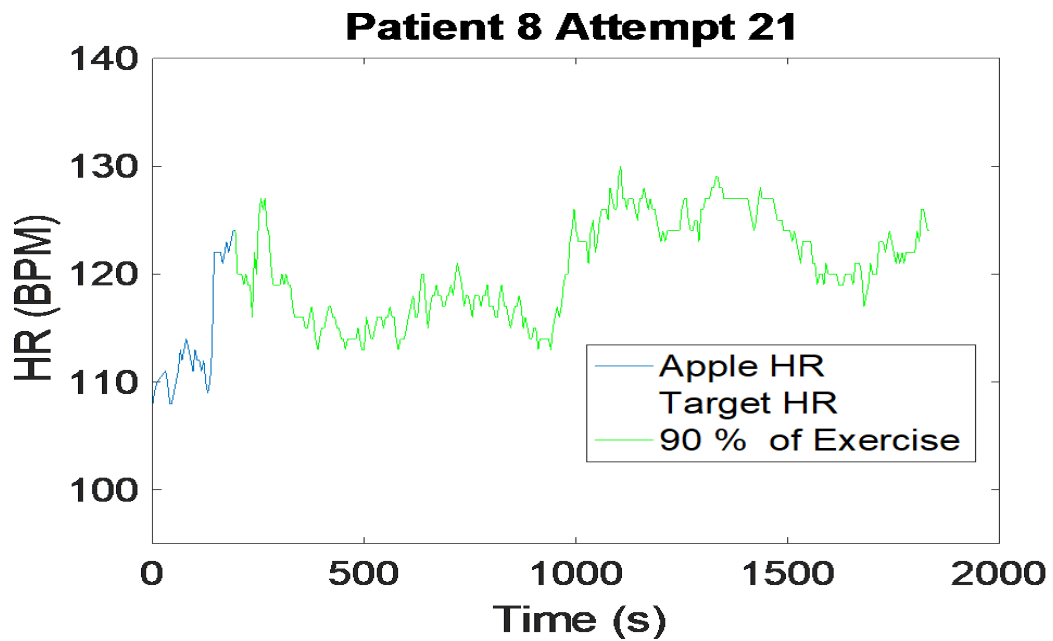


Figure A5.621: Patient No.8 Week 8 Attempt 3



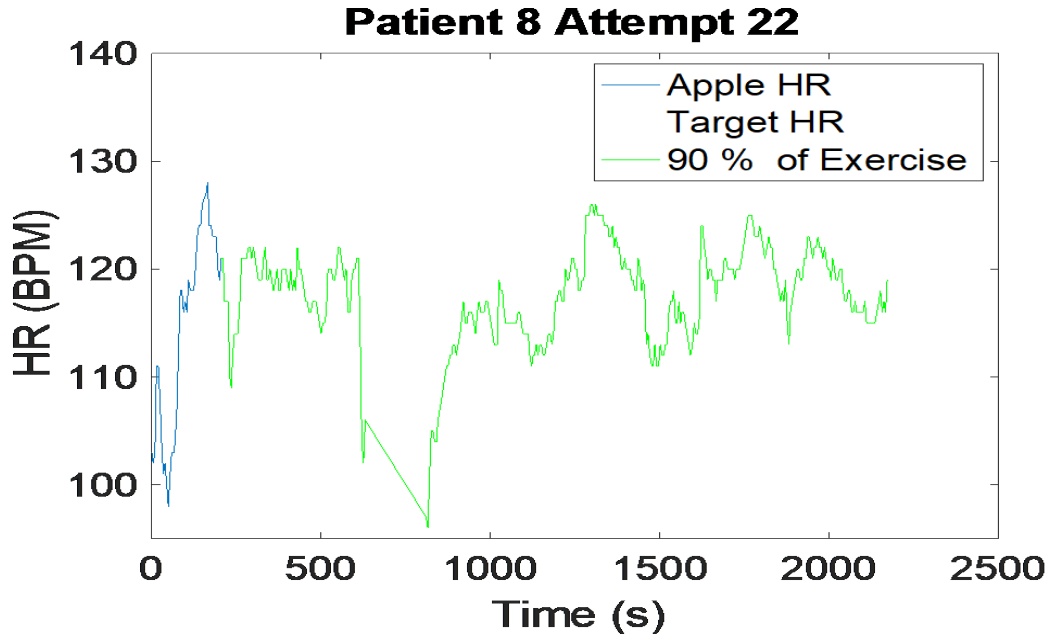


Figure A5.622: Patient No.8 Week 9 Attempt 1

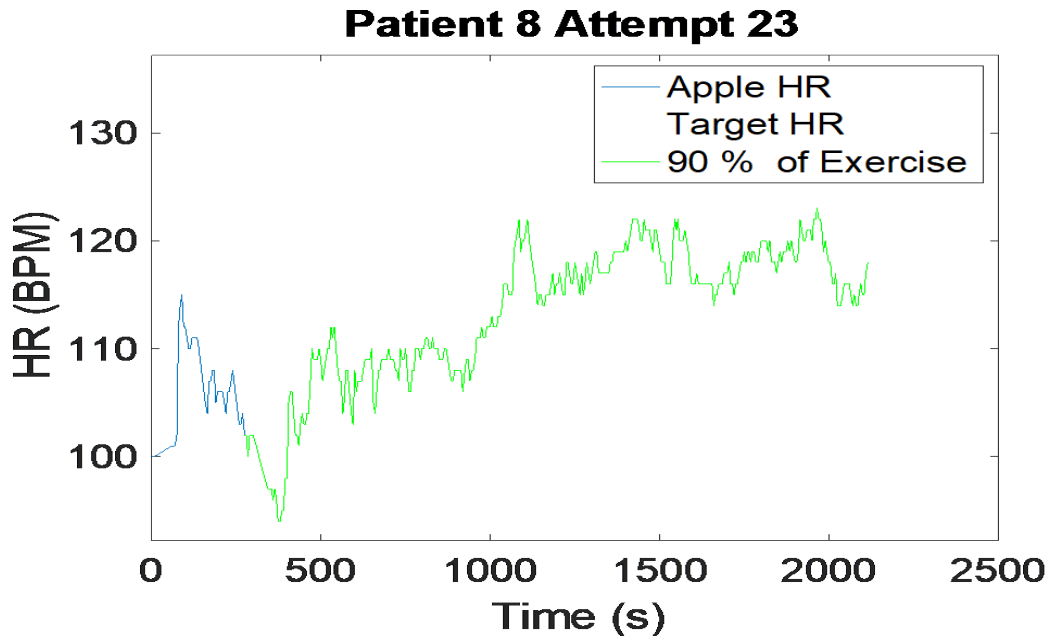


Figure A5.623: Patient No.8 Week 9 Attempt 2

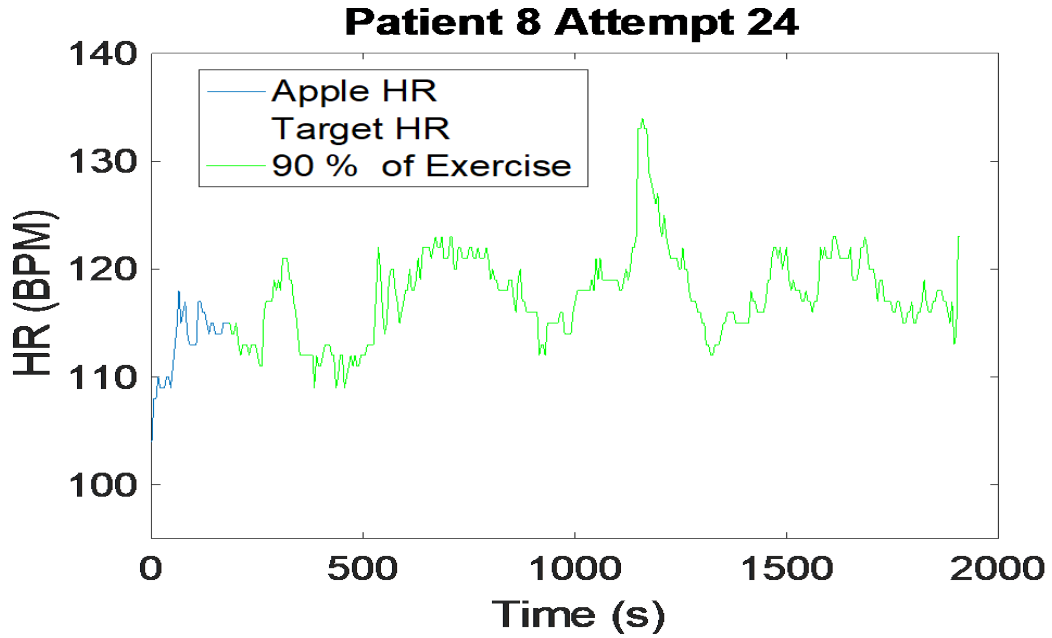


Figure A5.624: Patient No.8 Week 9 Attempt 3

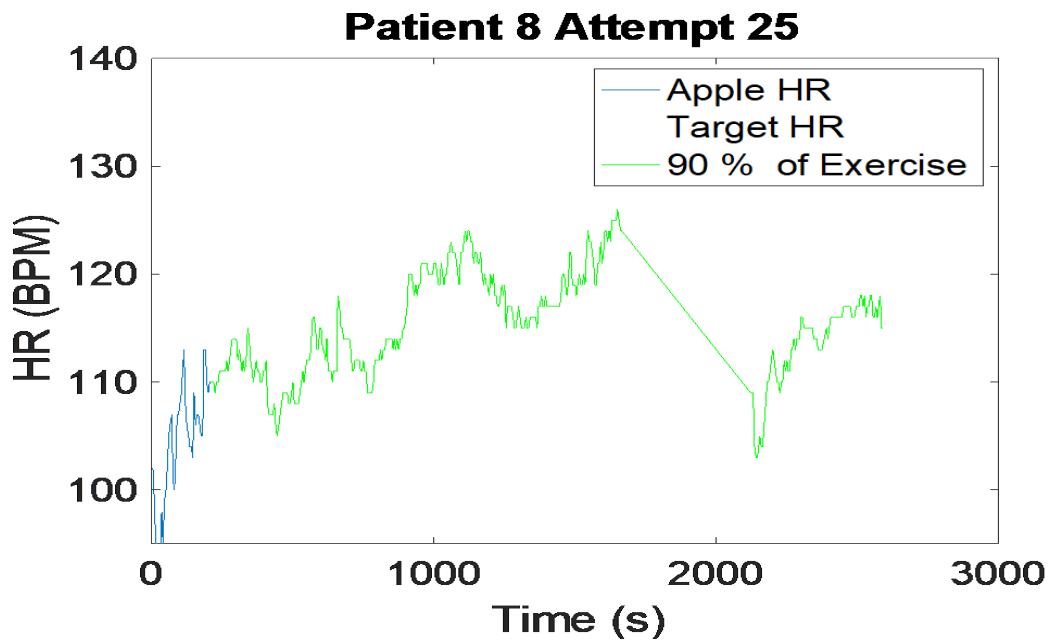


Figure A5.625: Patient No.8 Week 9 Attempt 4

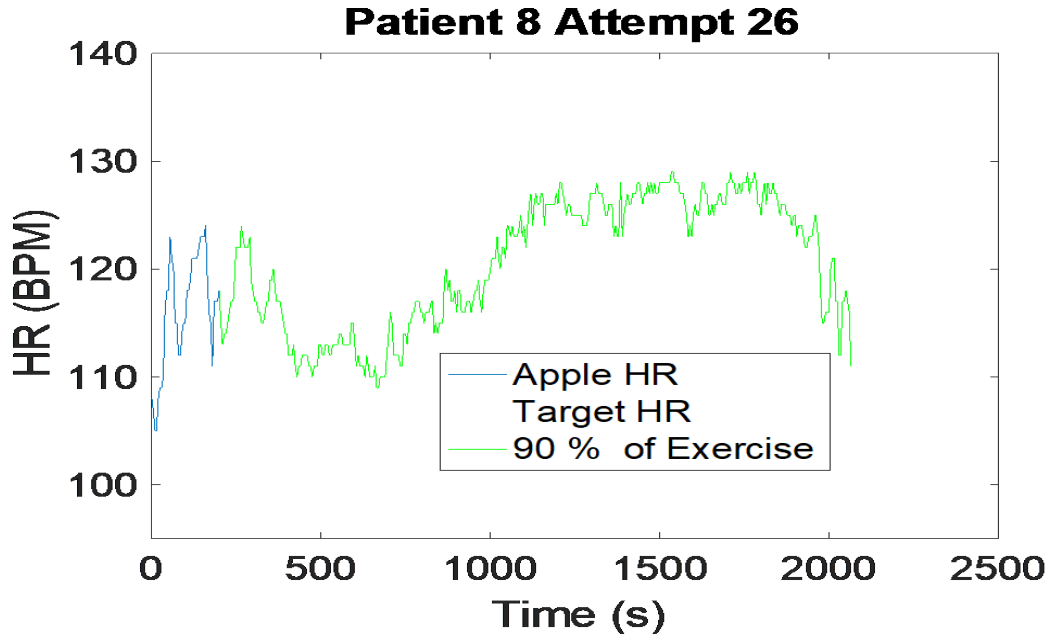


Figure A5.626: Patient No.8 Week 10 Attempt 1

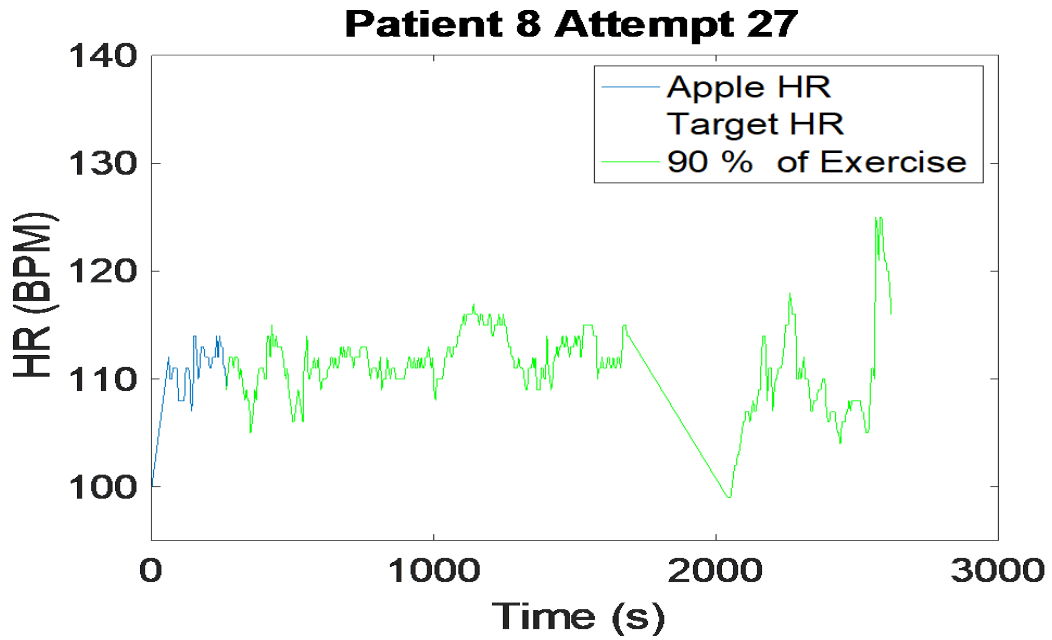


Figure A5.627: Patient No.8 Week 10 Attempt 2

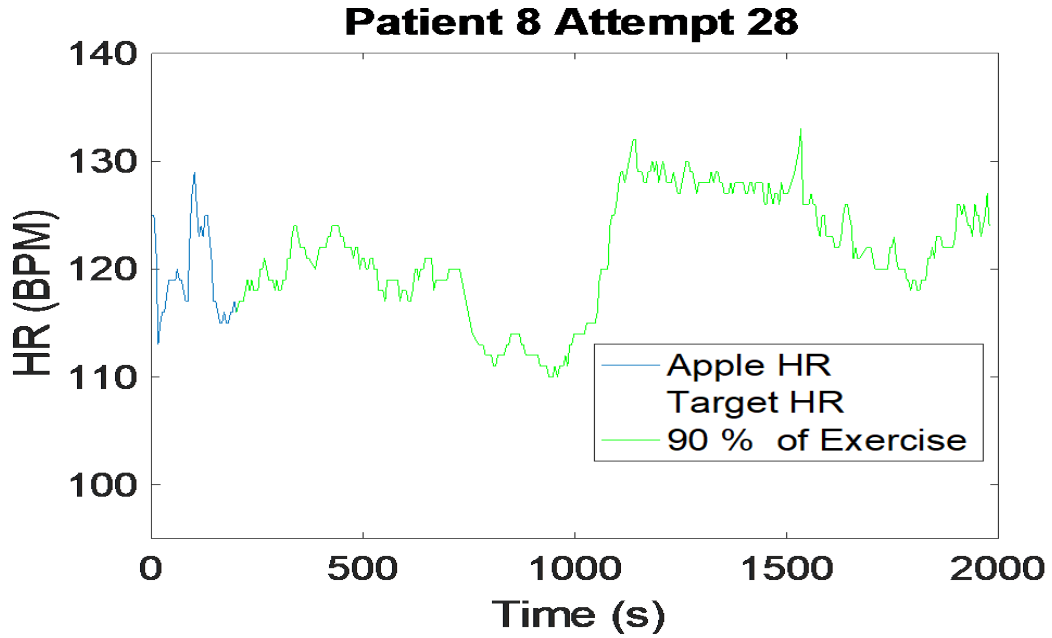


Figure A5.628: Patient No.8 Week 10 Attempt 3

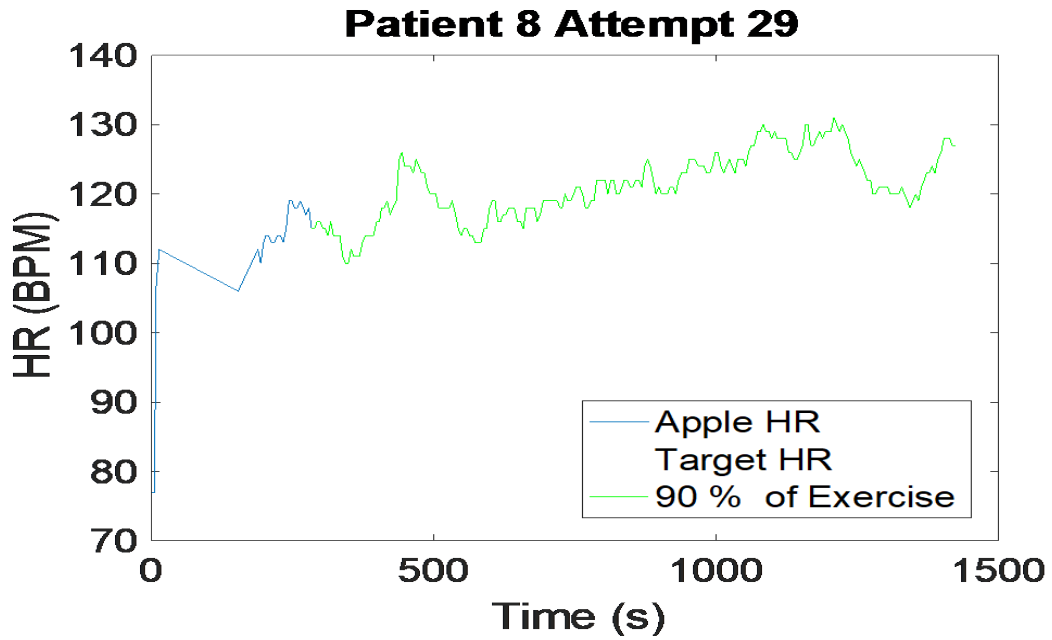


Figure A5.629: Patient No.8 Week 10 Attempt 4

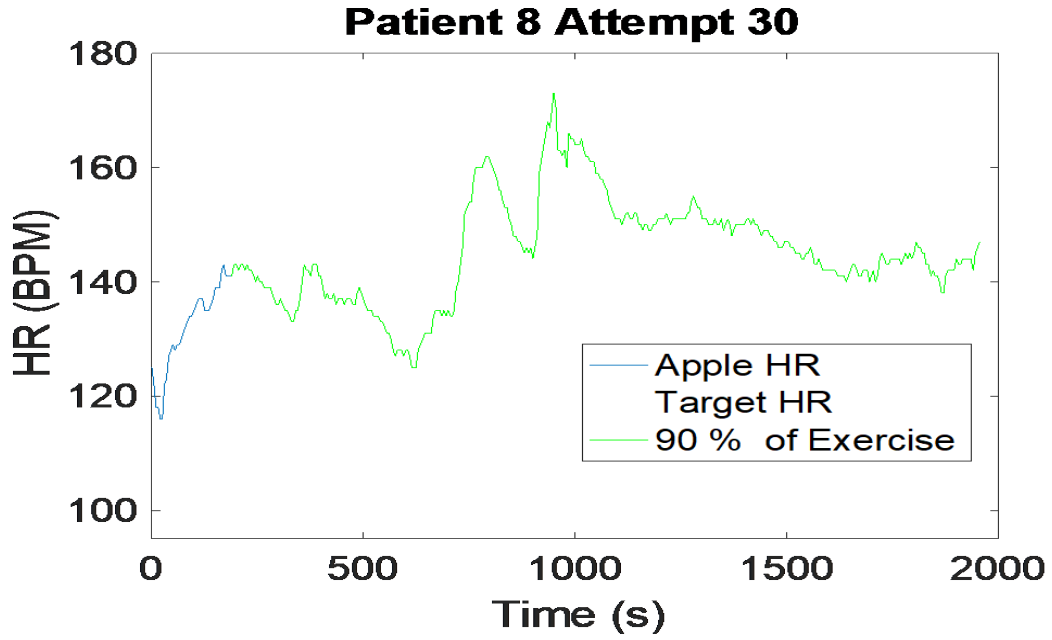


Figure A5.630: Patient No.8 Week 10 Attempt 5

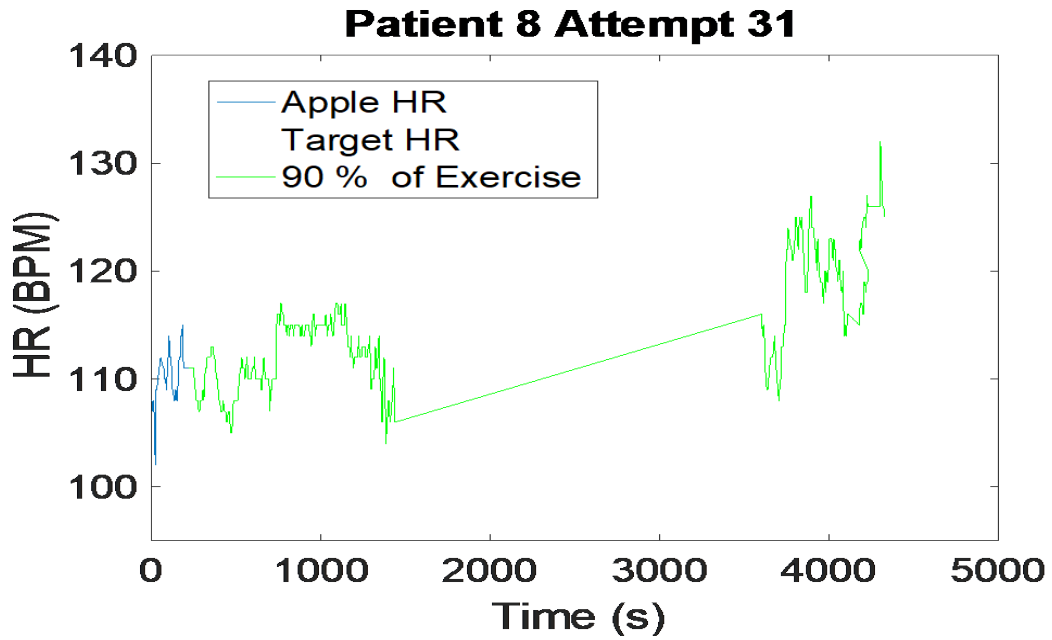


Figure A5.631: Patient No.8 Week 10 Attempt 6

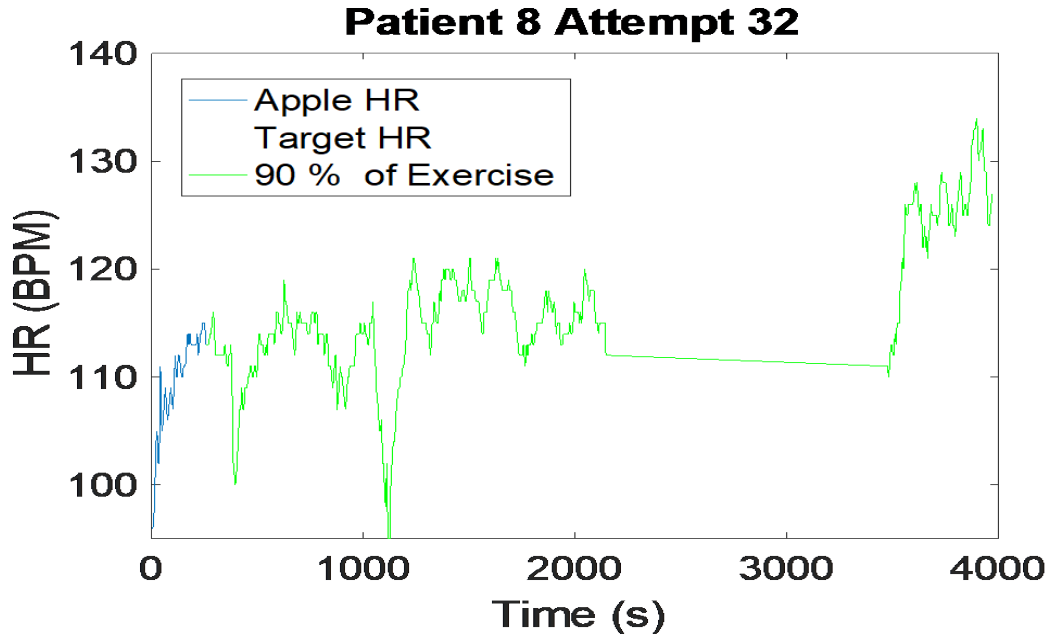


Figure A5.632: Patient No.8 Week 11 Attempt 1

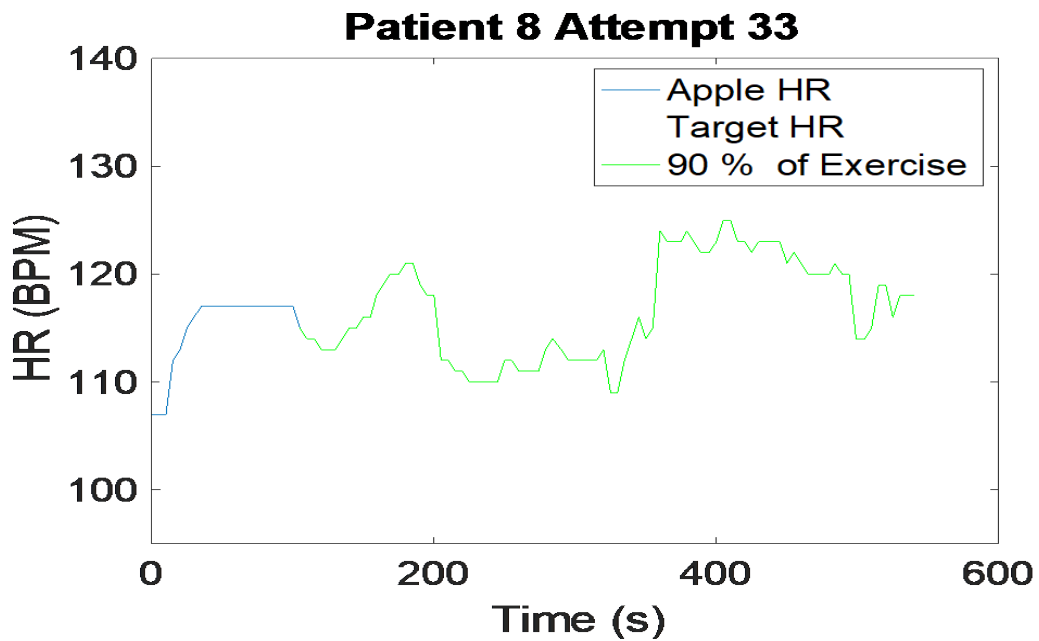


Figure A5.633: Patient No.8 Week 11 Attempt 2

### Patient 8 Attempt 34

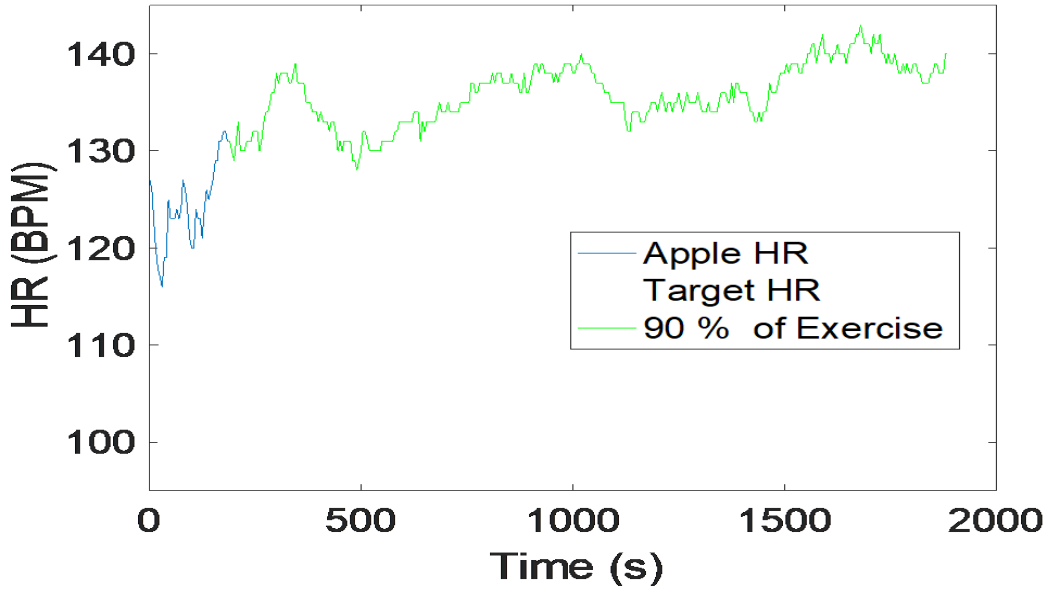


Figure A5.634: Patient No.8 Week 11 Attempt 3

### Patient 8 Attempt 35



Figure A5.635: Patient No.8 Week 11 Attempt 4

### Patient 8 Attempt 36

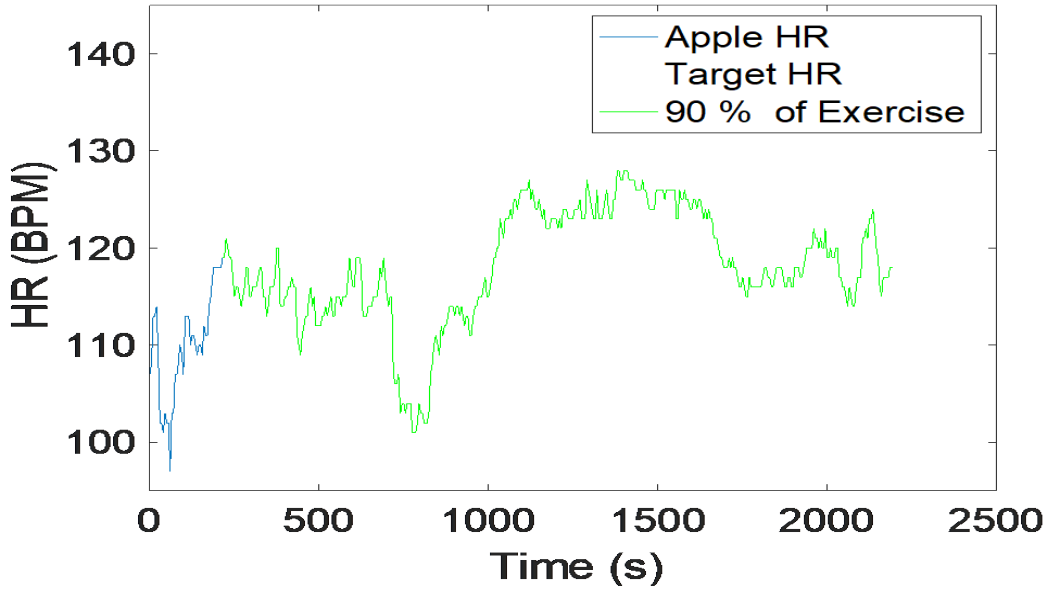


Figure A5.636: Patient No.8 Week 11 Attempt 5

### Patient 8 Attempt 37

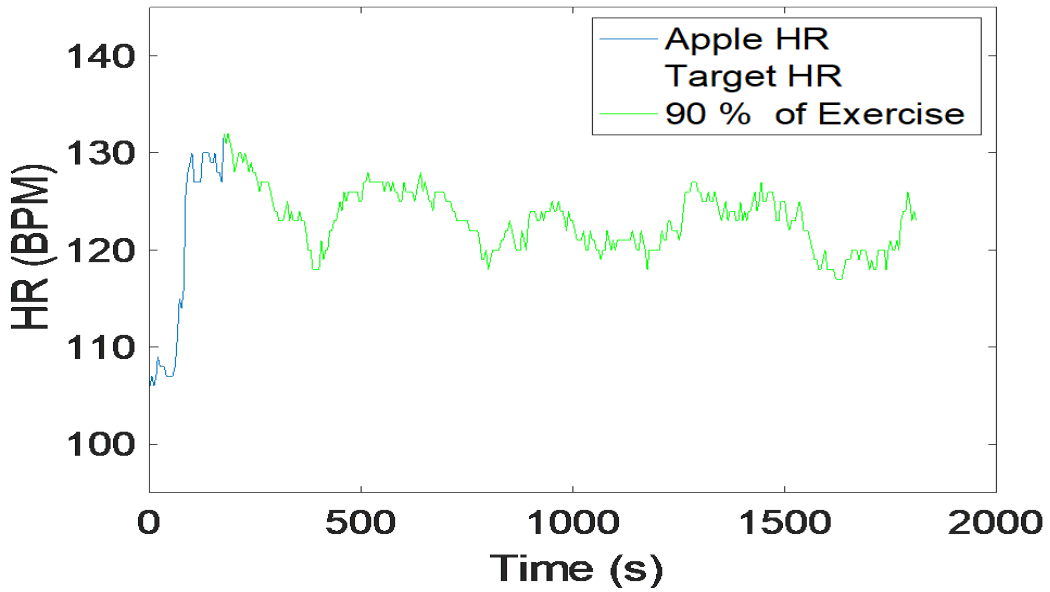


Figure A5.637: Patient No.8 Week 12 Attempt 1



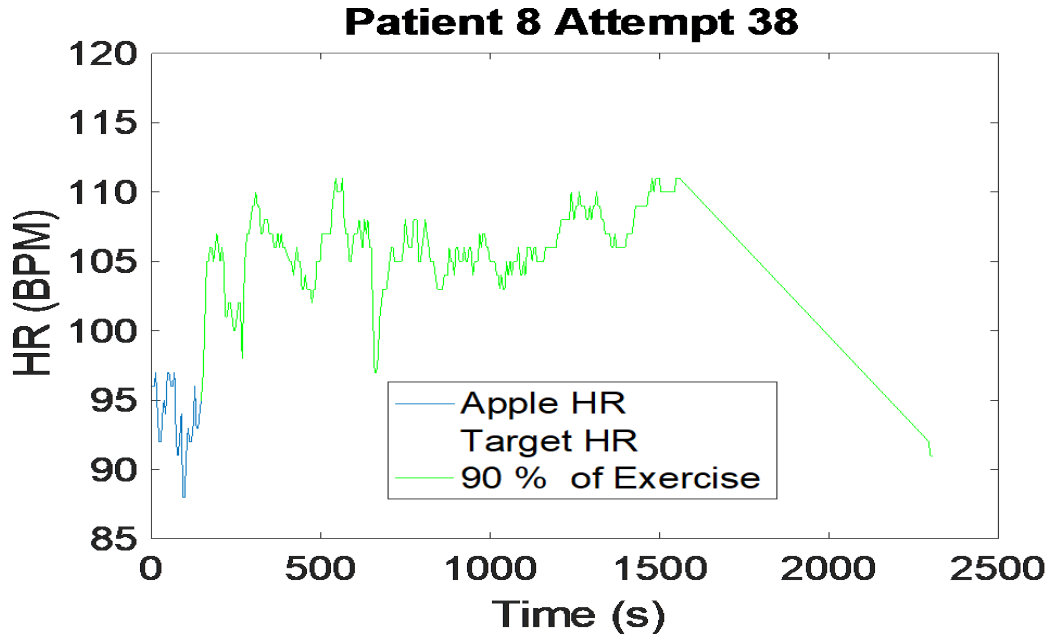


Figure A5.638: Patient No.8 Week 12 Attempt 2

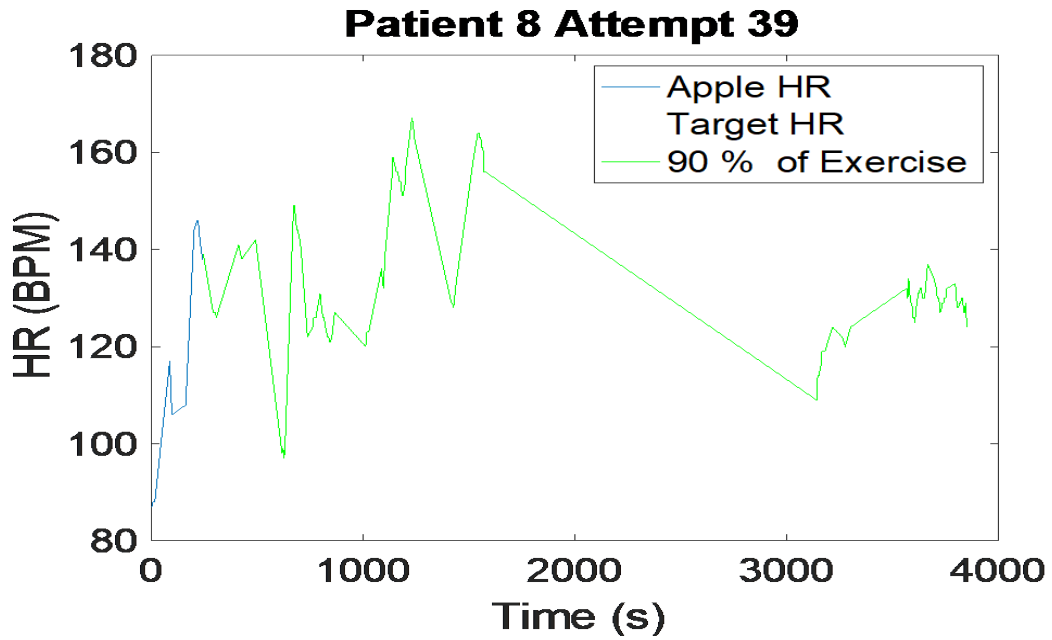
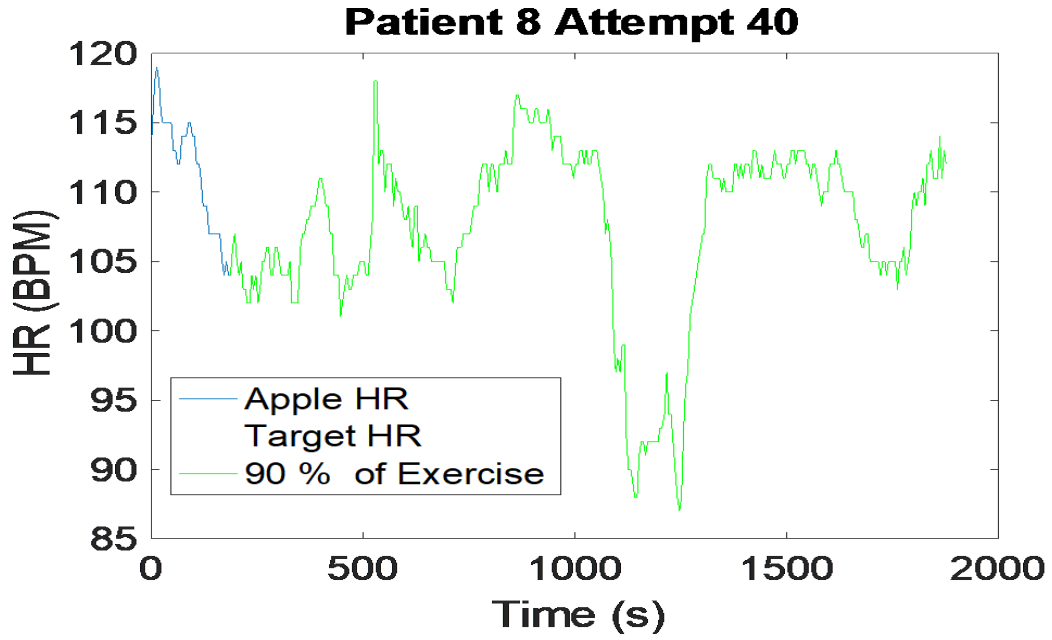
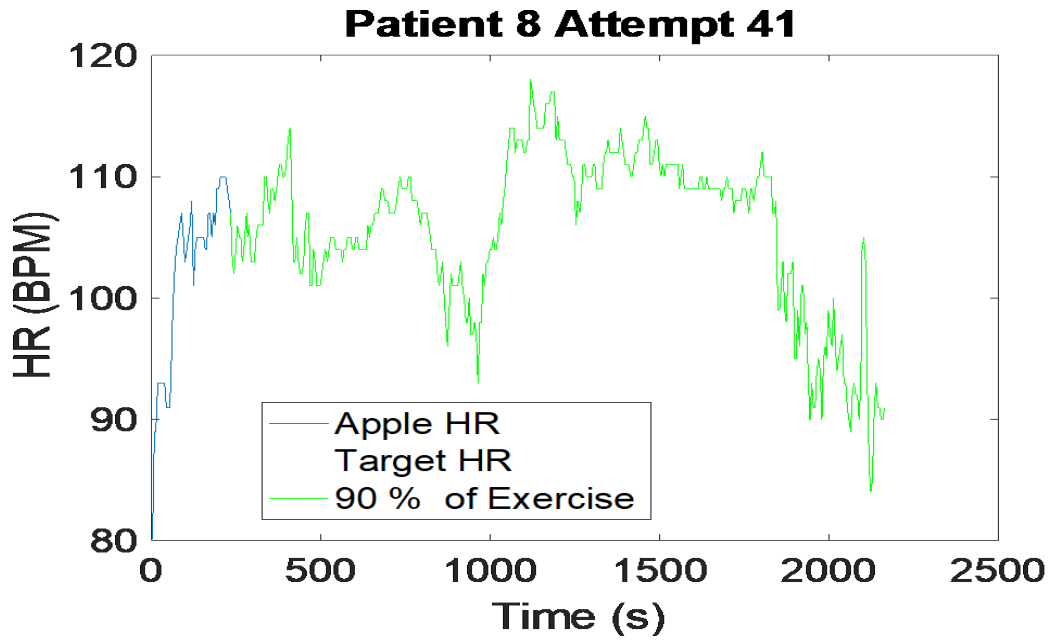


Figure A5.639: Patient No.8 Week 12 Attempt 3



*Figure A5.640: Patient No.8 Week 12 Attempt 4*



*Figure A5.641: Patient No.8 Week 13 Attempt 1*

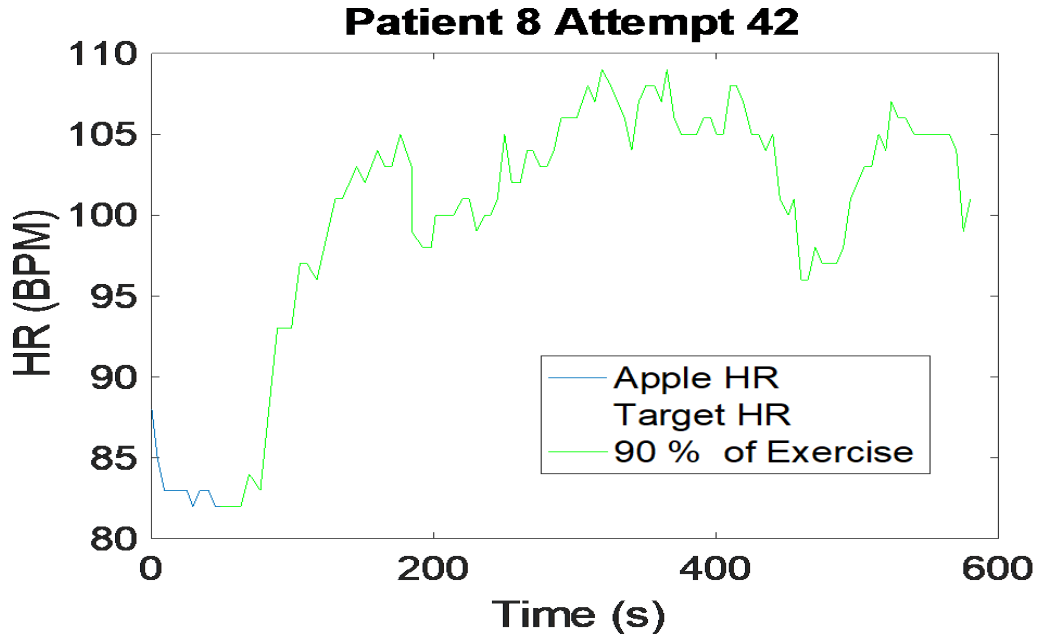


Figure A5.642: Patient No.8 Week 13 Attempt 2

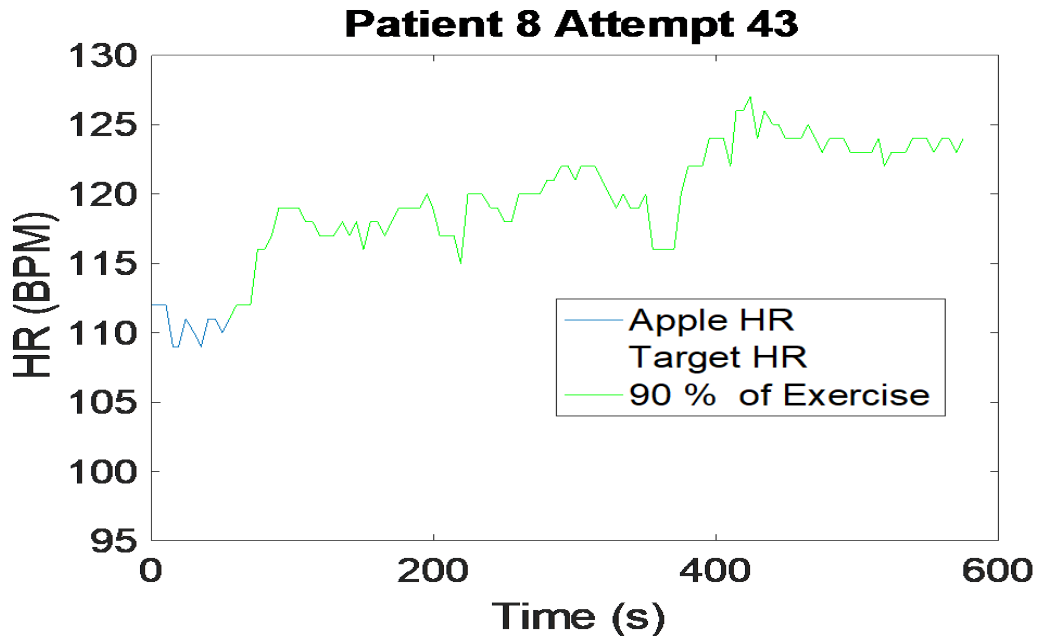


Figure A5.643: Patient No.8 Week 13 Attempt 3

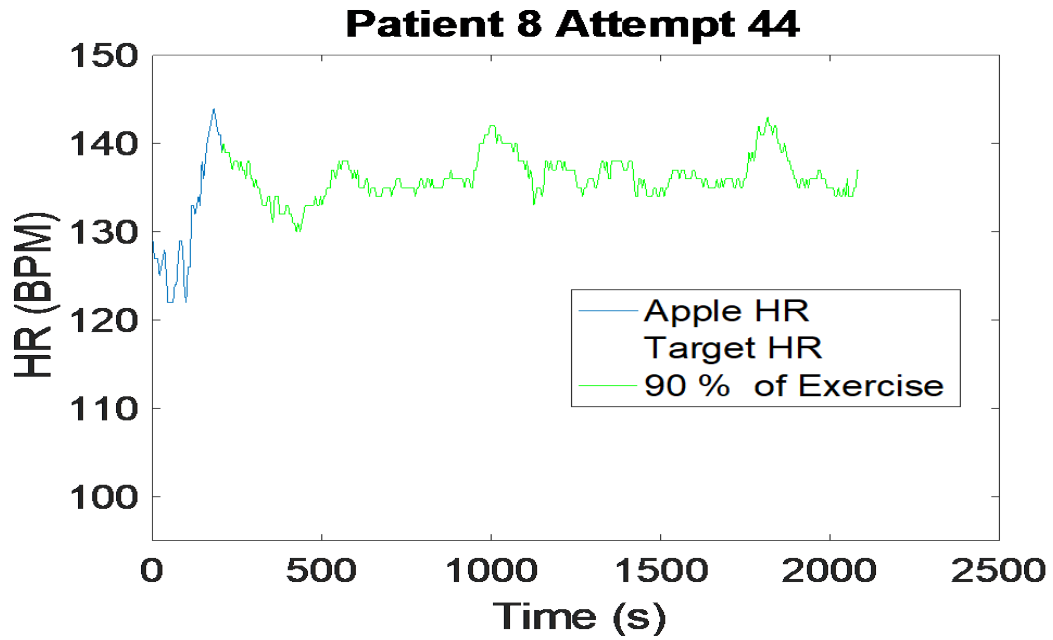


Figure A5.644: Patient No.8 Week 13 Attempt 4

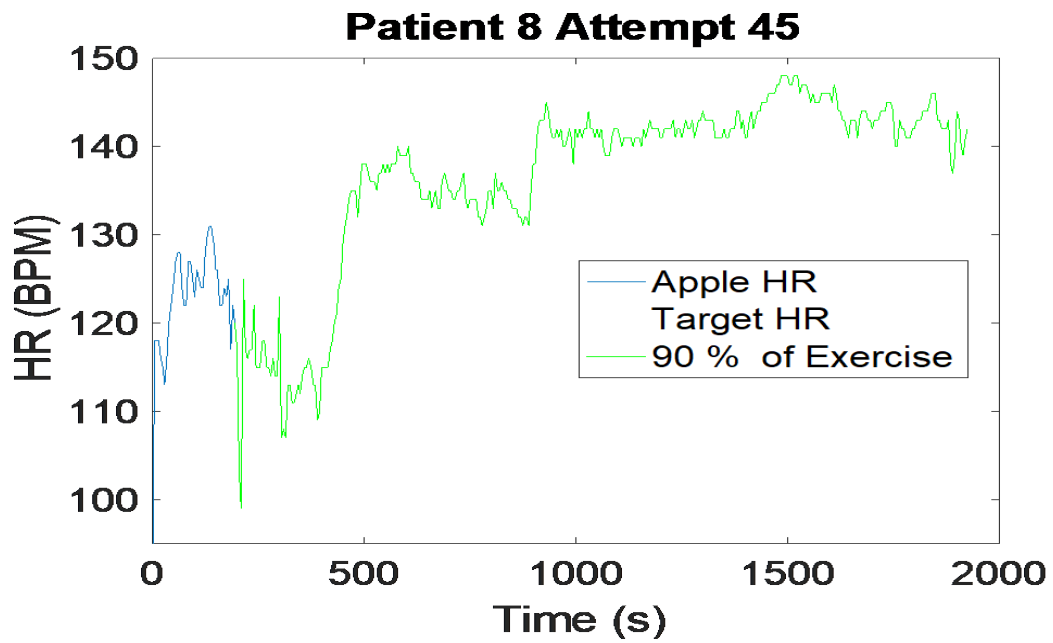


Figure A5.645: Patient No.8 Week 13 Attempt 5

## Patient 9 Attempts

### Patient 9 Attempt 1

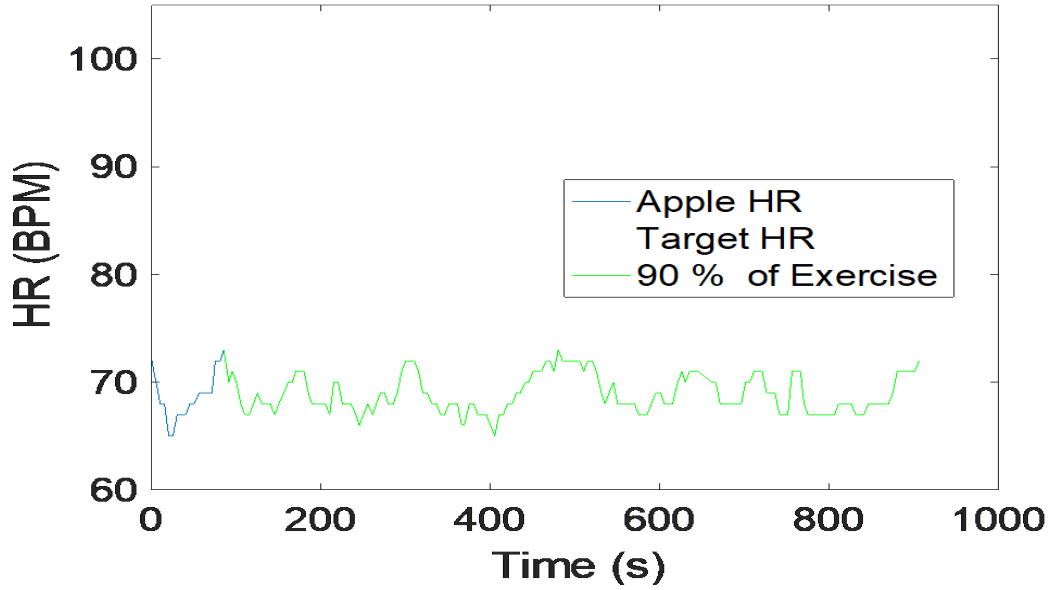


Figure A5.646: Patient No.9 Week 1 Attempt 1

### Patient 9 Attempt 2

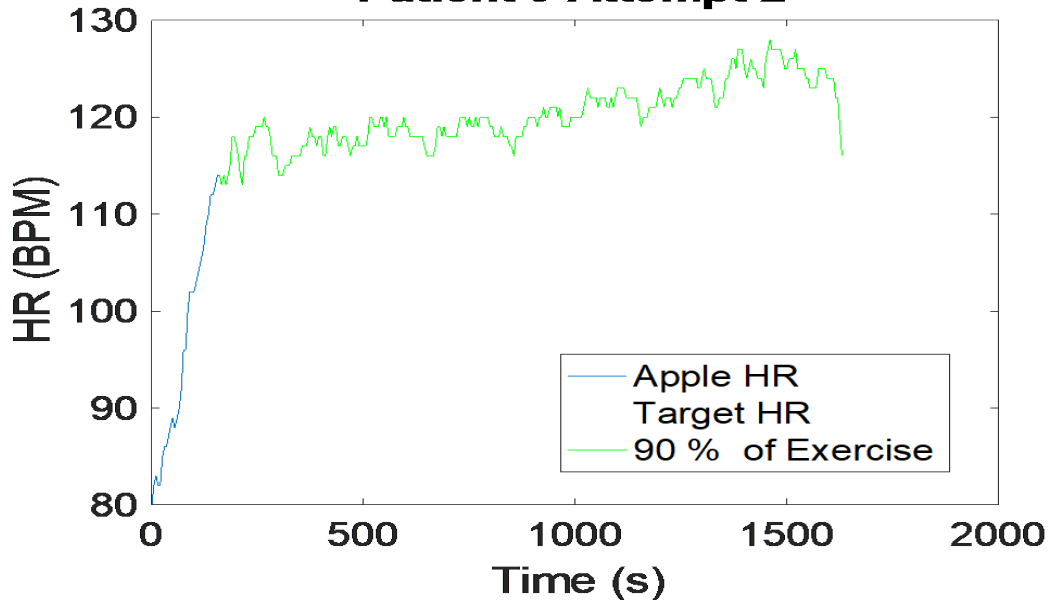


Figure A5.647: Patient No.9 Week 1 Attempt 2

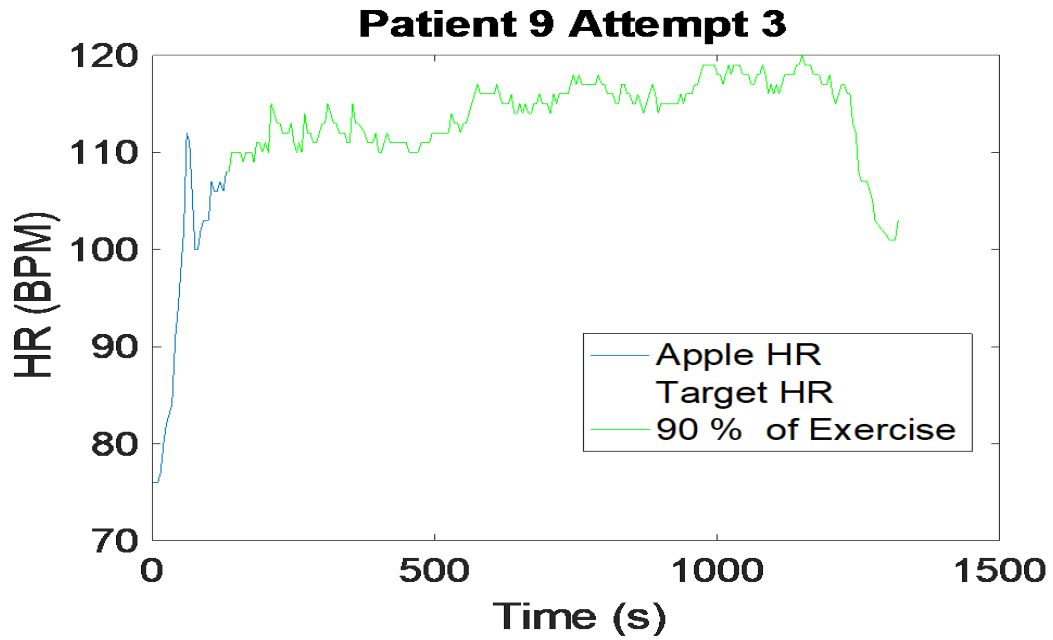


Figure A5.648: Patient No.9 Week 1 Attempt 3

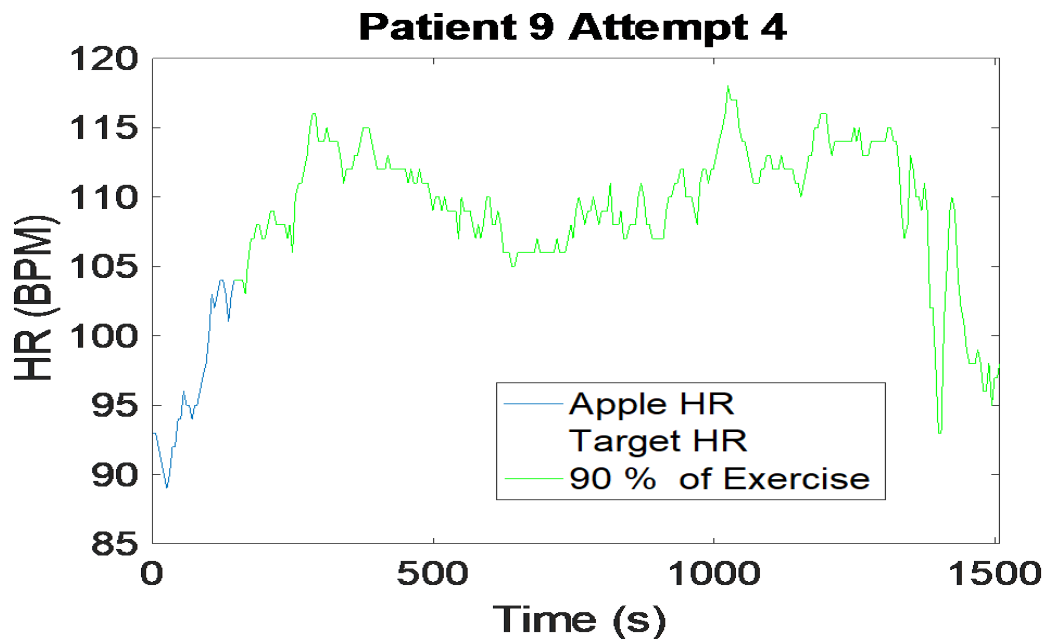
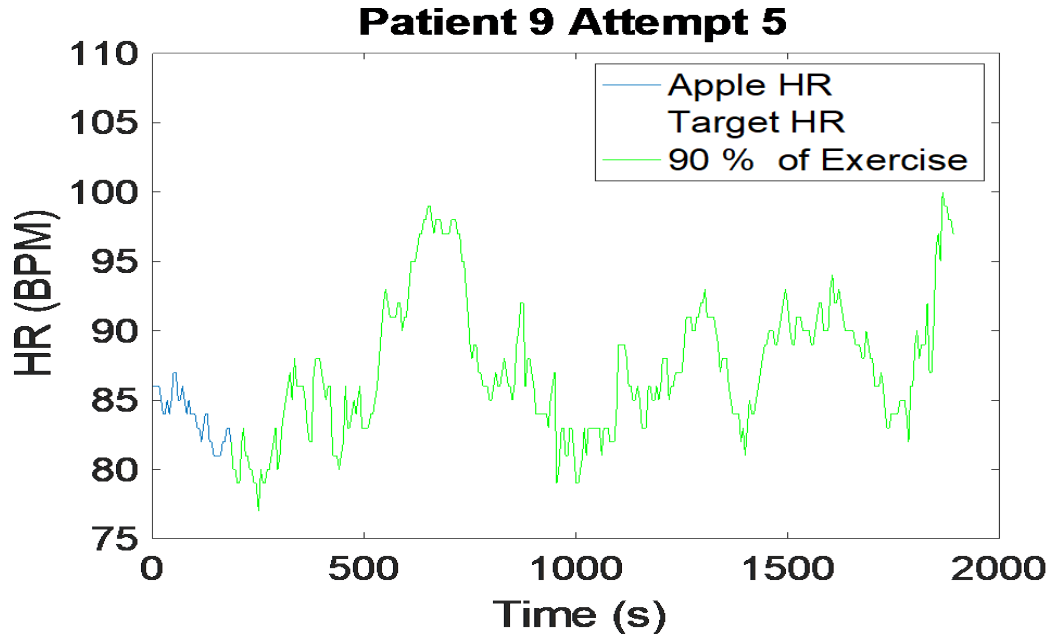
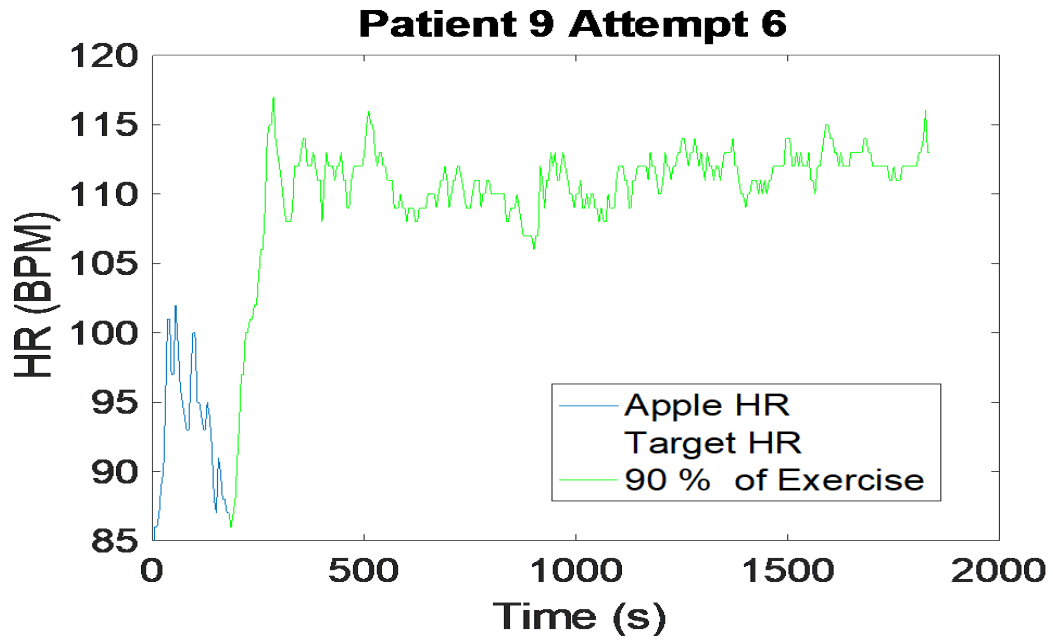


Figure A5.649: Patient No.9 Week 2 Attempt 1



*Figure A5.650: Patient No.9 Week 2 Attempt 2*



*Figure A5.651: Patient No.9 Week 2 Attempt 3*

### Patient 9 Attempt 7

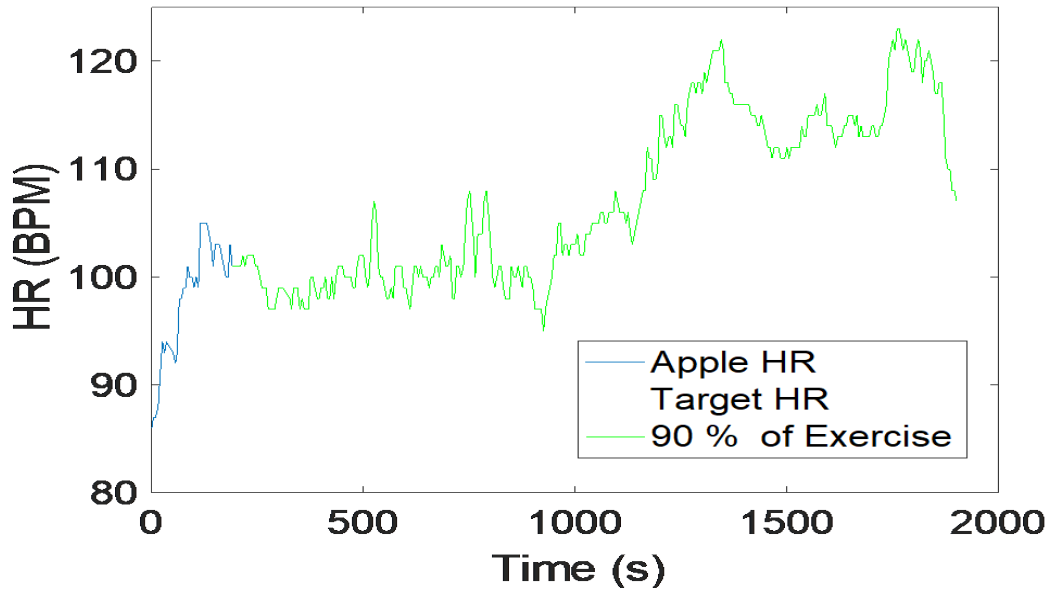


Figure A5.652: Patient No.9 Week 2 Attempt 4

### Patient 9 Attempt 8

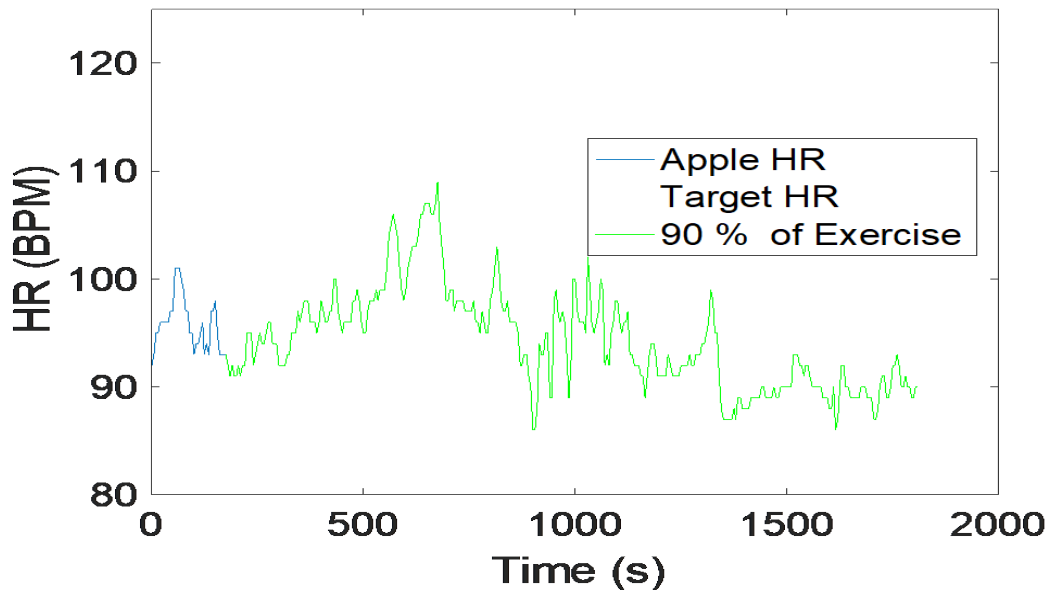


Figure A5.653: Patient No.9 Week 3 Attempt 1



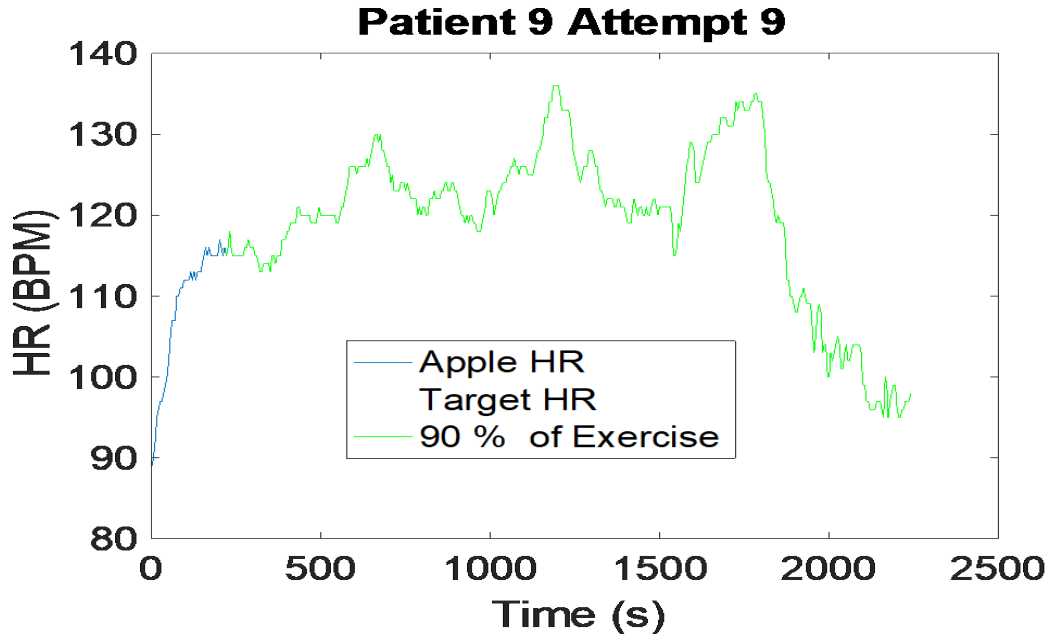


Figure A5.654: Patient No.9 Week 3 Attempt 2

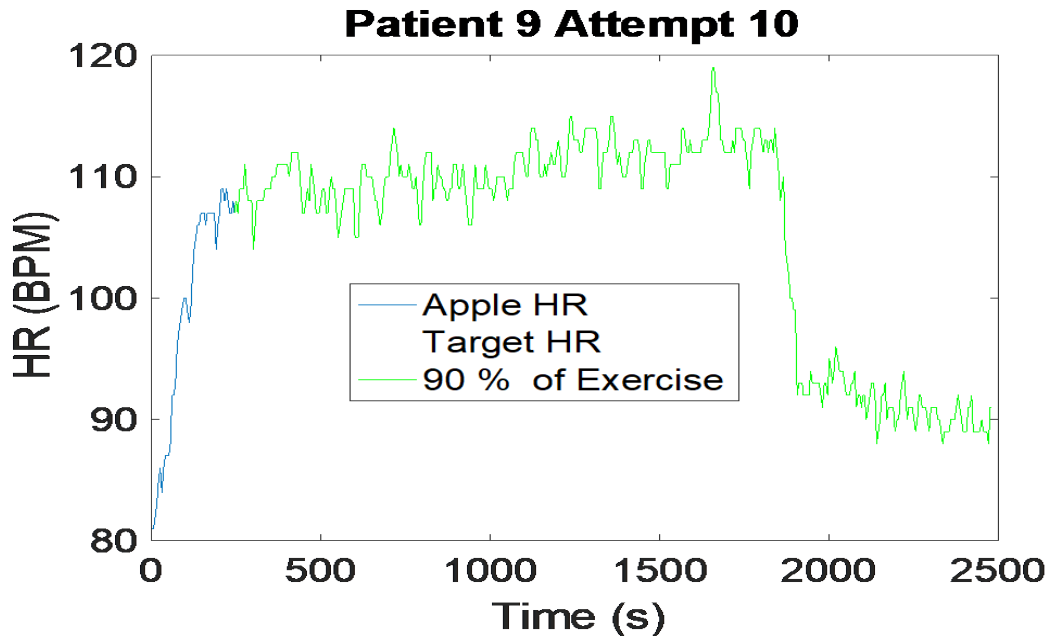


Figure A5.655: Patient No.9 Week 3 Attempt 3

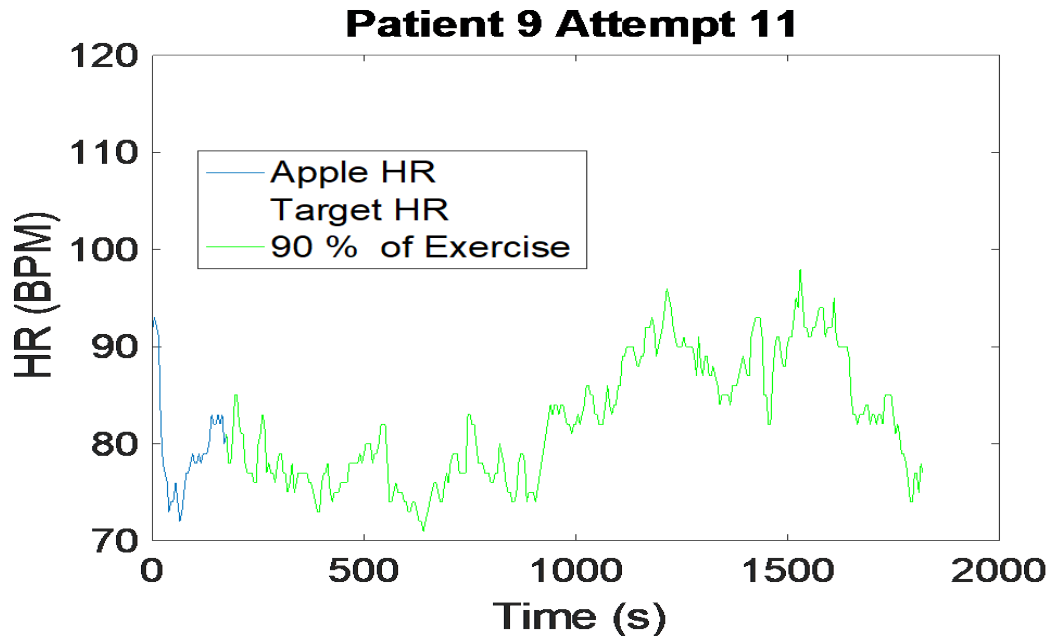


Figure A5.656: Patient No.9 Week 3 Attempt 4

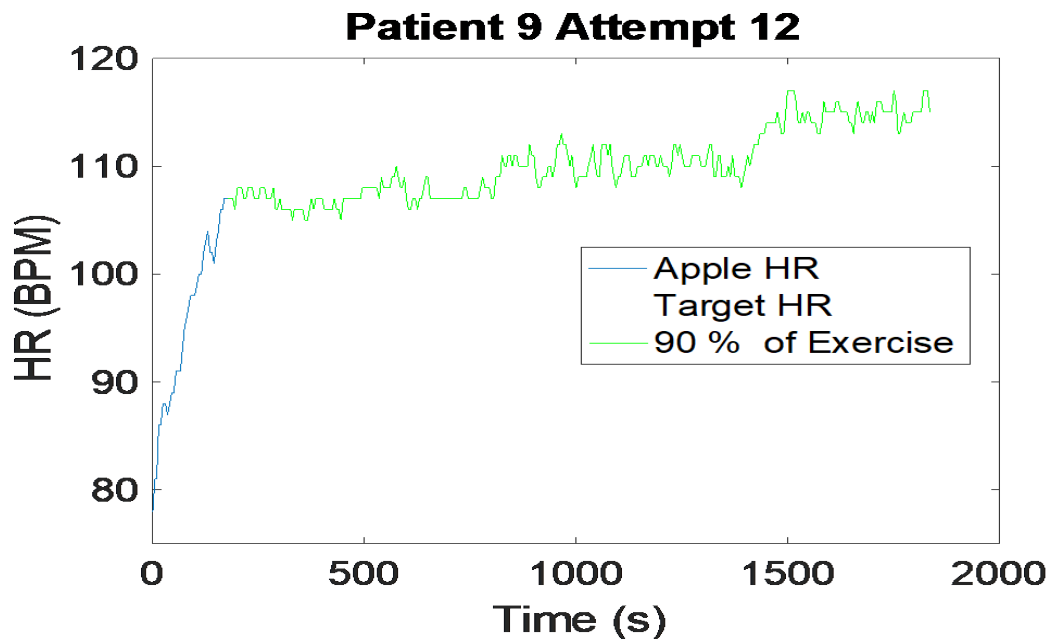


Figure A5.657: Patient No.9 Week 4 Attempt 1

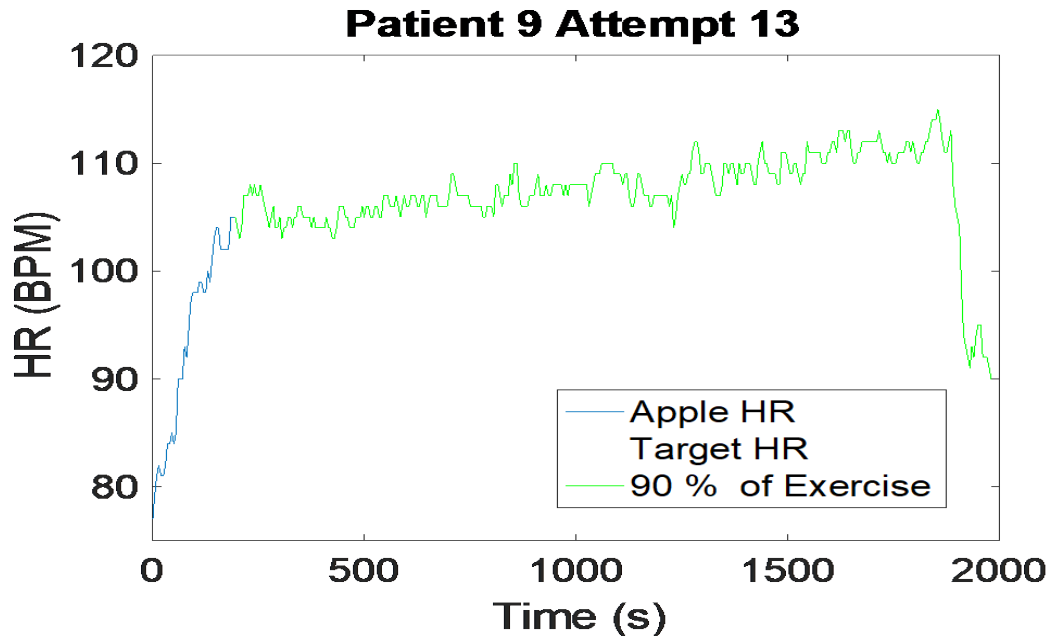


Figure A5.658: Patient No.9 Week 4 Attempt 2

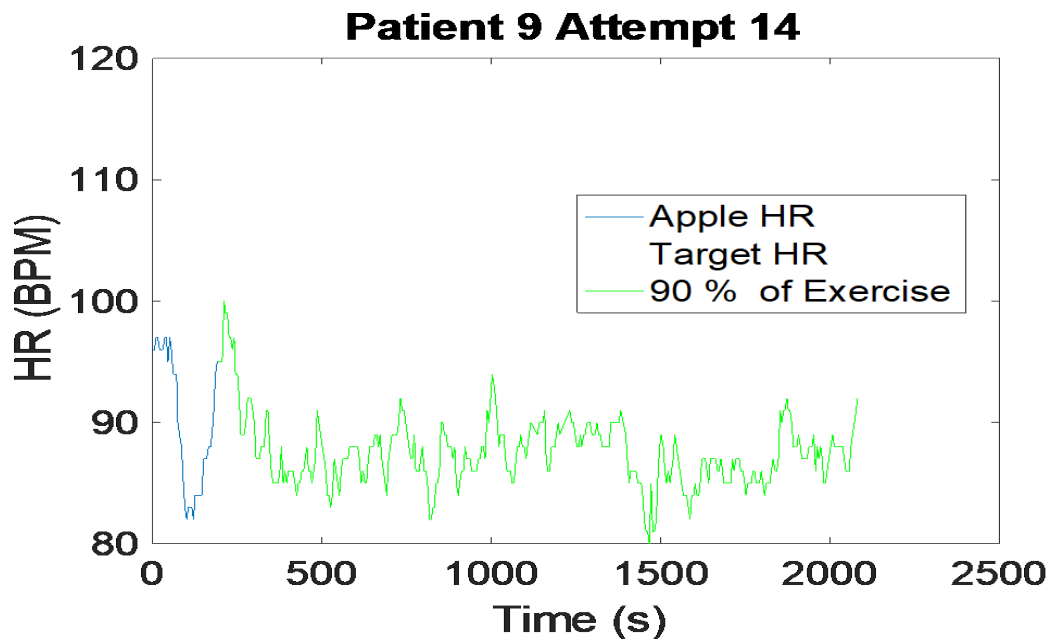


Figure A5.659: Patient No.9 Week 4 Attempt 3

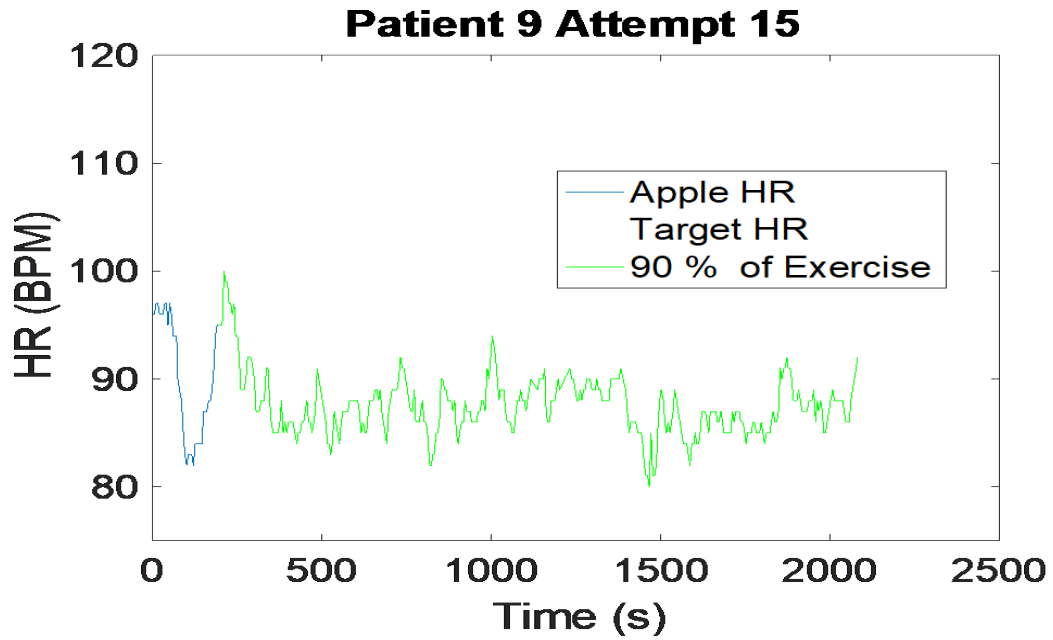


Figure A5.660: Patient No.9 Week 4 Attempt 4

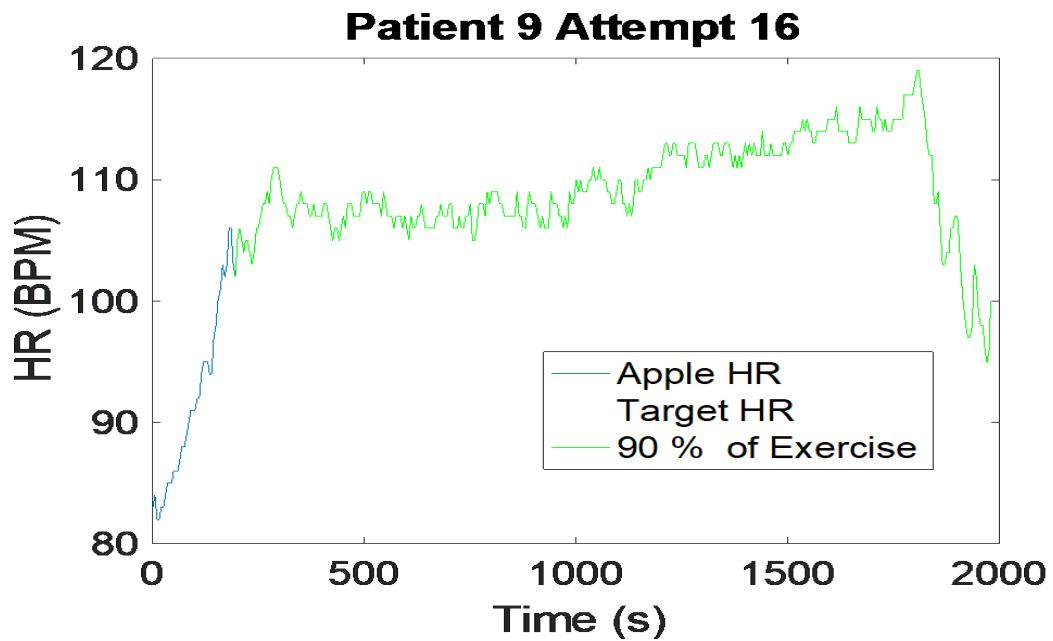


Figure A5.661: Patient No.9 Week 5 Attempt 1

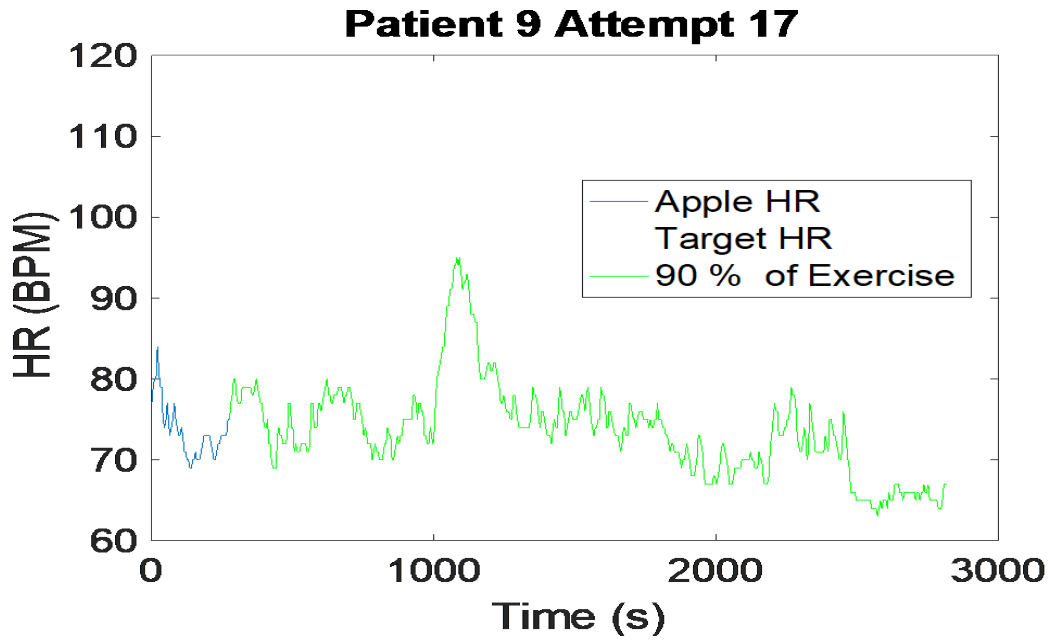


Figure A5.662: Patient No.9 Week 5 Attempt 2

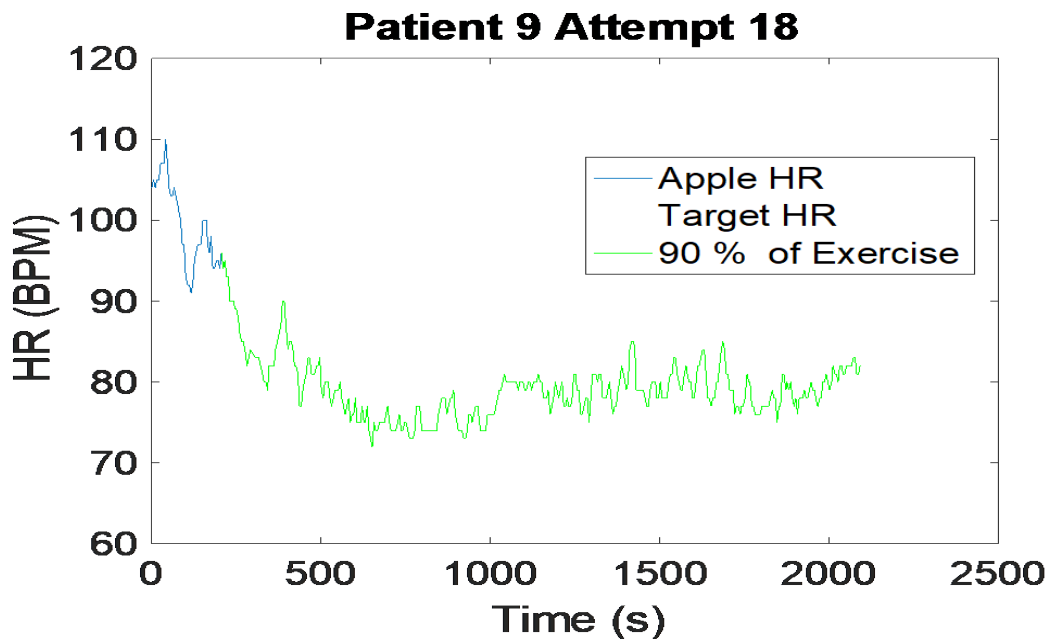


Figure A5.663: Patient No.9 Week 5 Attempt 3

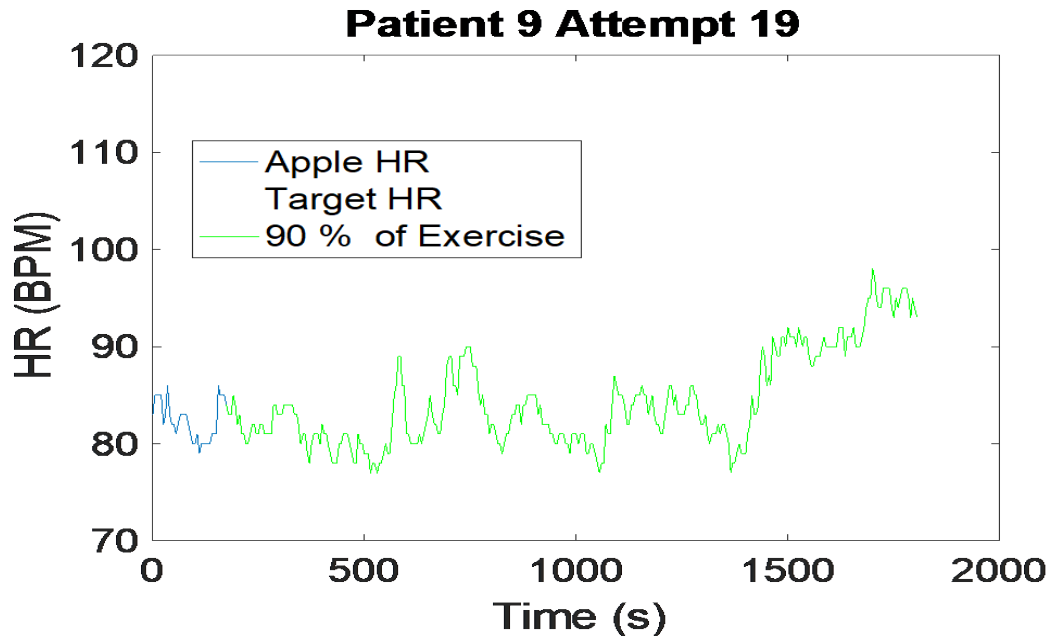


Figure A5.664: Patient No.9 Week 5 Attempt 4

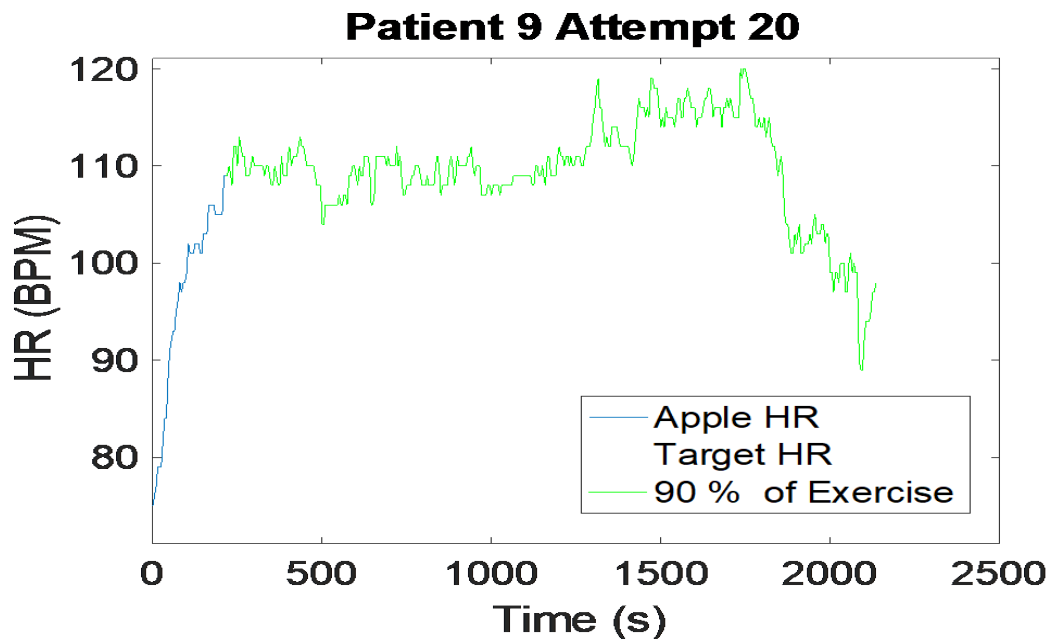


Figure A5.665: Patient No.9 Week 7 Attempt 1

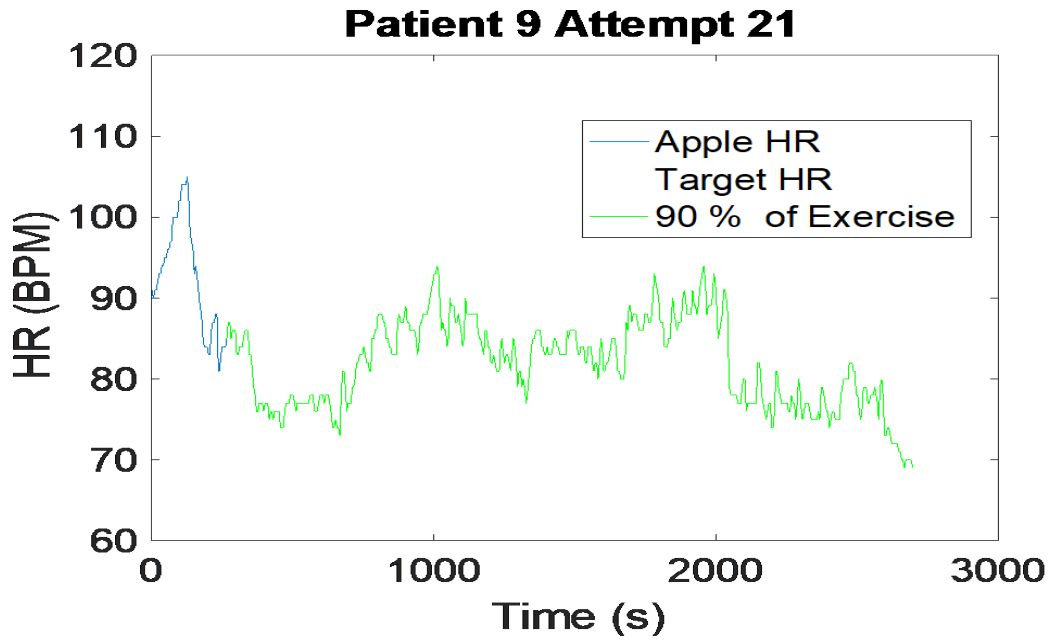


Figure A5.666: Patient No.9 Week 7 Attempt 2

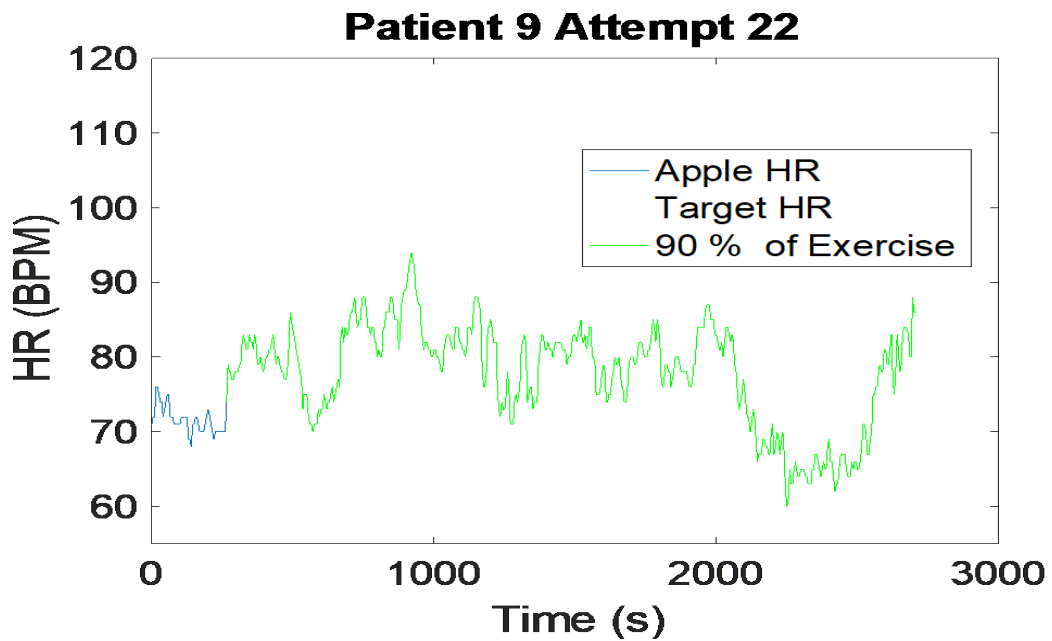
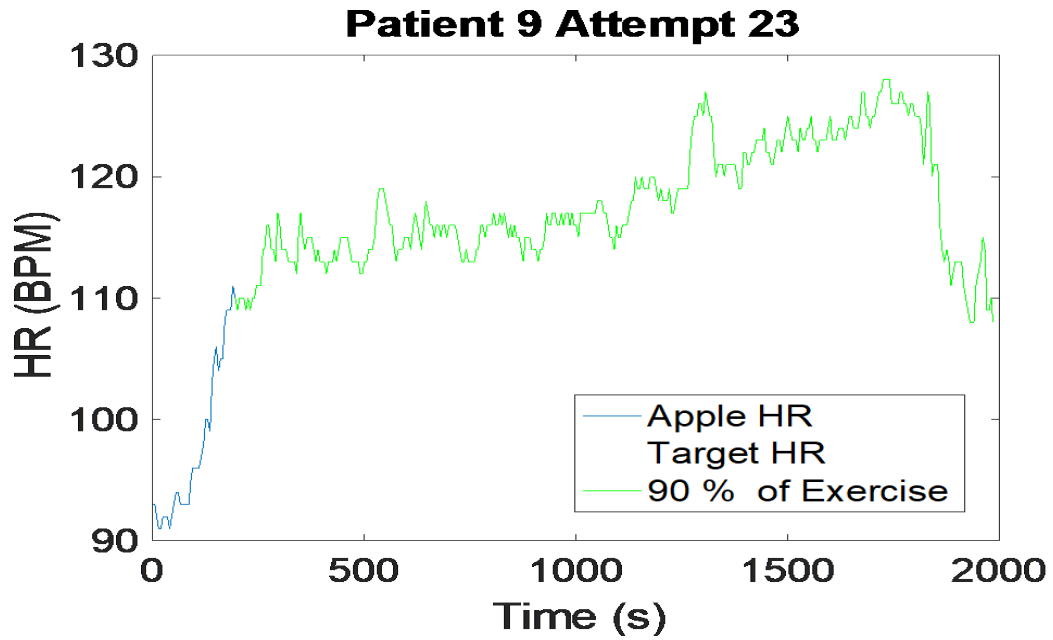
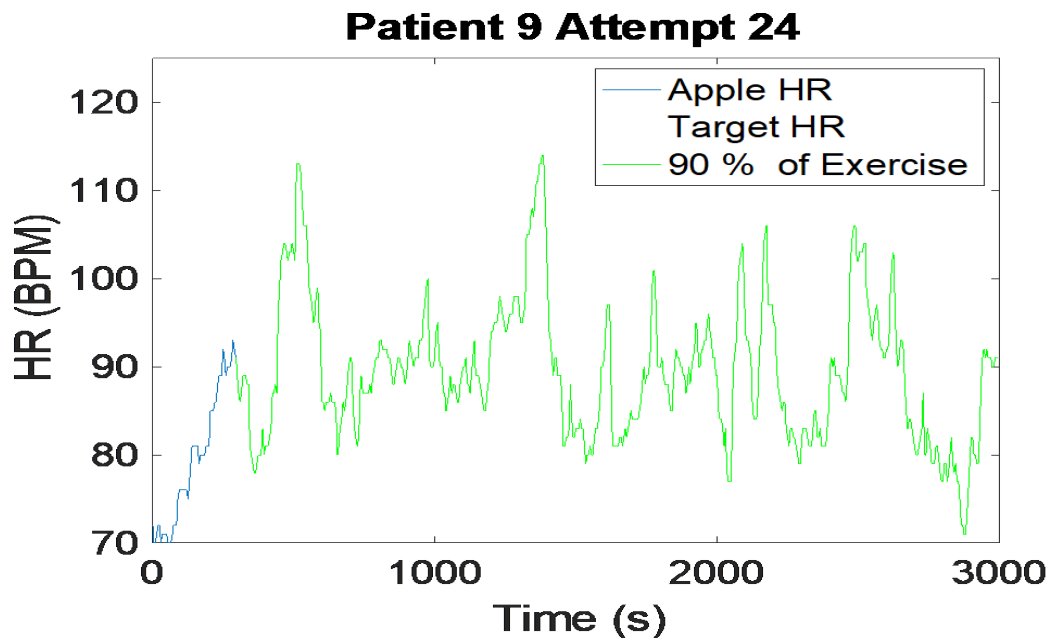


Figure A5.667: Patient No.9 Week 7 Attempt 3



*Figure A5.668: Patient No.9 Week 7 Attempt 4*



*Figure A5.669: Patient No.9 Week 8 Attempt 1*



### Patient 9 Attempt 25

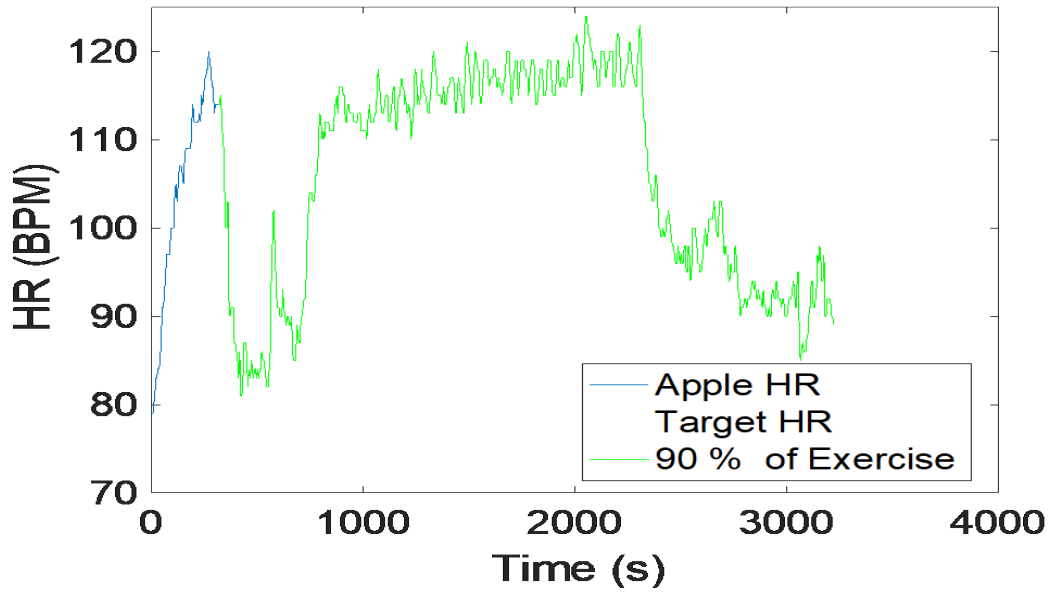


Figure A5.670: Patient No.9 Week 8 Attempt 2

### Patient 9 Attempt 26

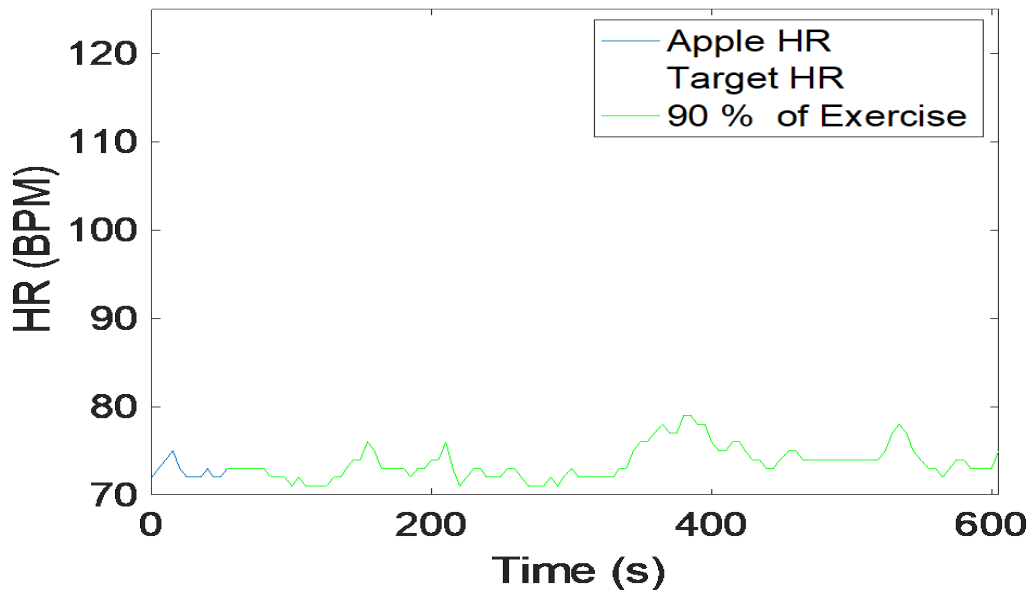
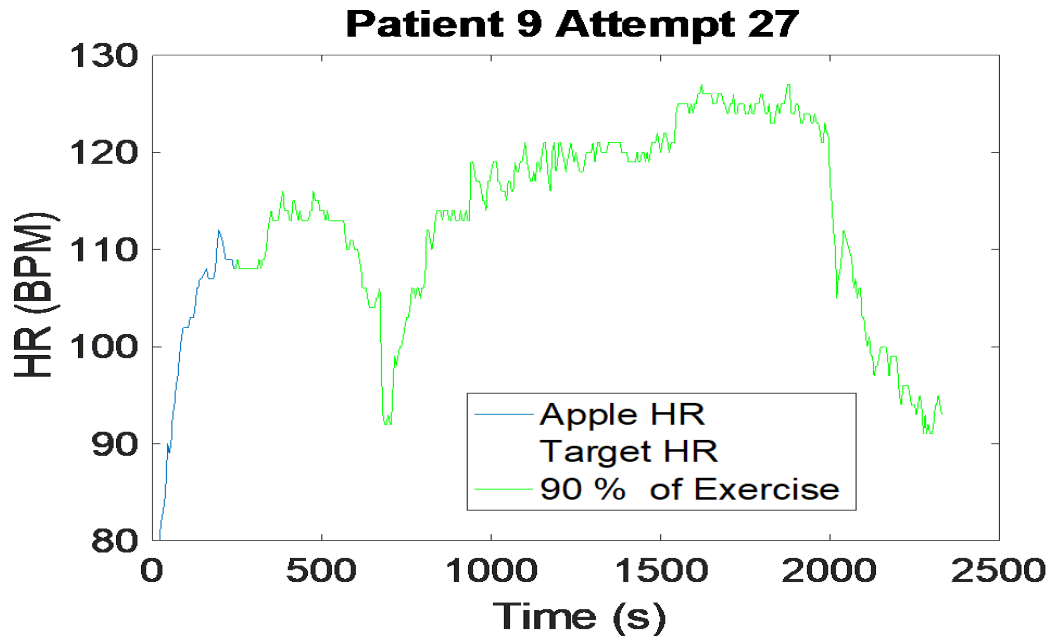
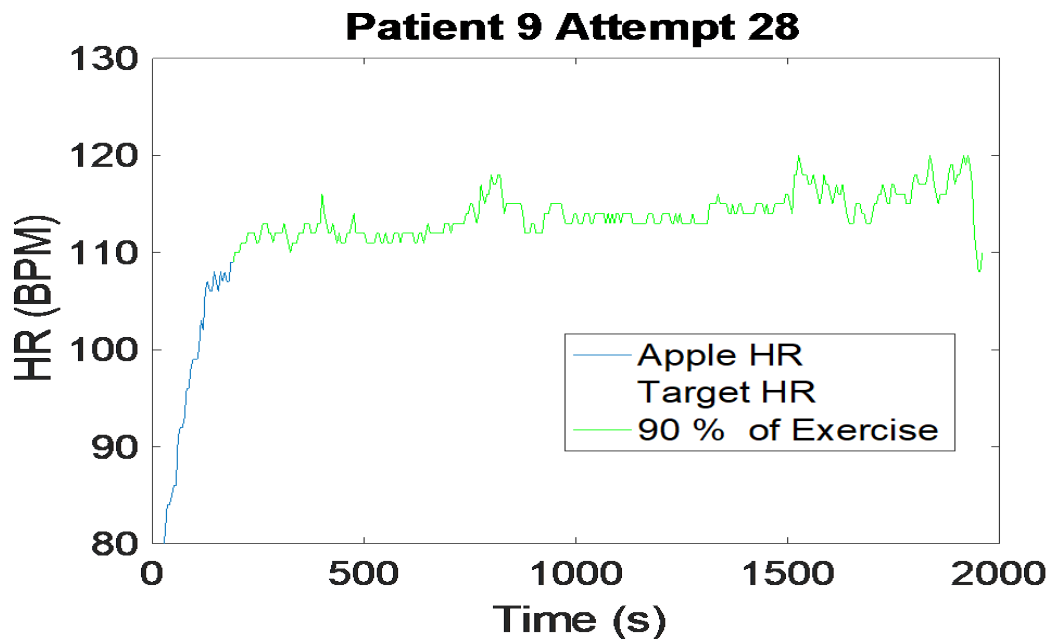


Figure A5.671: Patient No.9 Week 8 Attempt 3



*Figure A5.672: Patient No.9 Week 8 Attempt 4*



*Figure A5.673: Patient No.9 Week 8 Attempt 5*

### Patient 9 Attempt 29

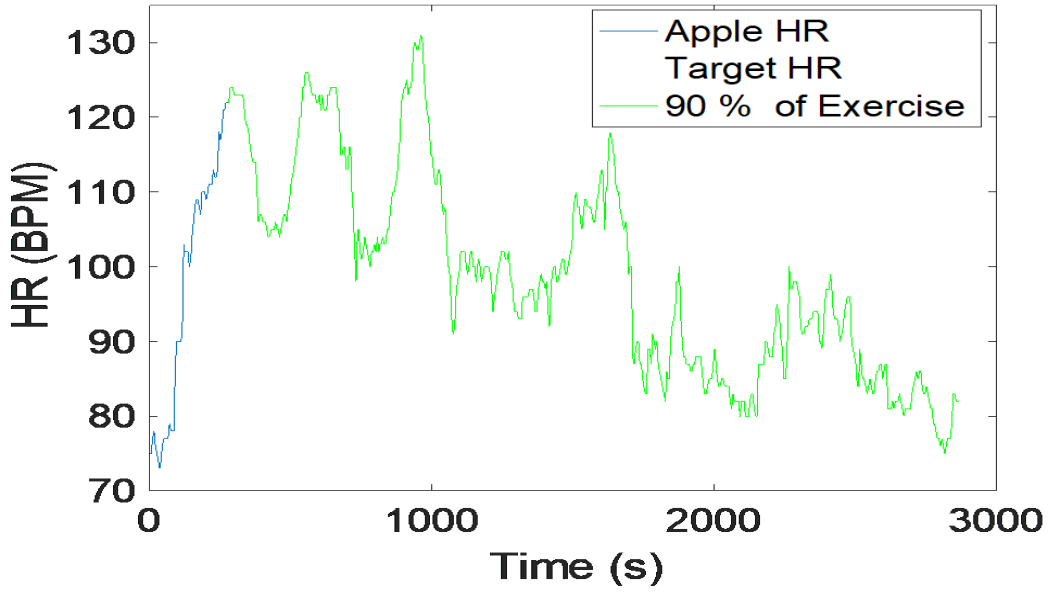


Figure A5.674: Patient No.9 Week 9 Attempt 1

### Patient 9 Attempt 30

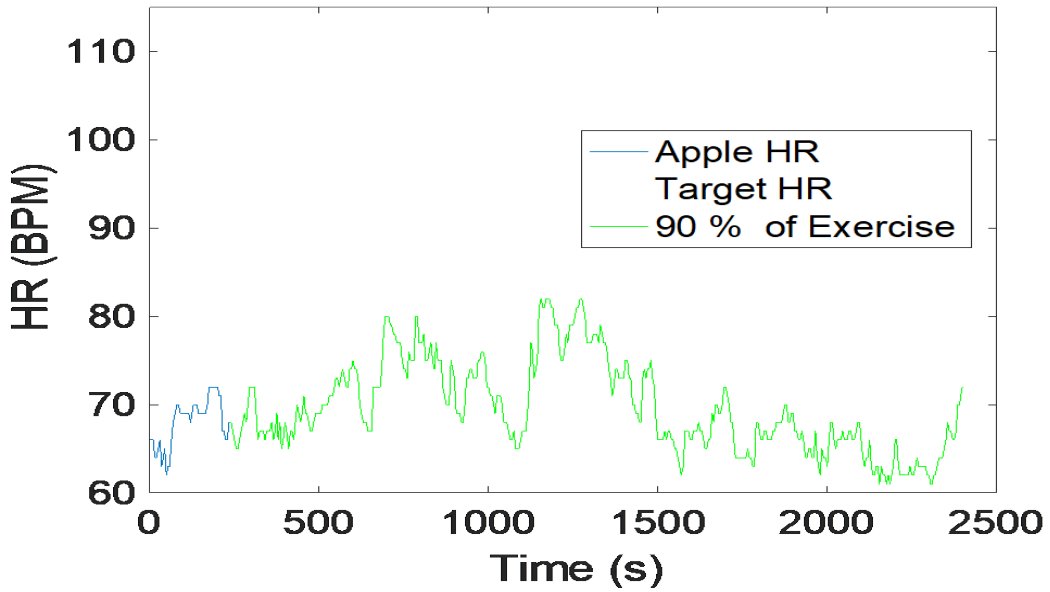


Figure A5.675: Patient No.9 Week 9 Attempt 2

### Patient 9 Attempt 31



Figure A5.676: Patient No.9 Week 9 Attempt 3

### Patient 9 Attempt 32

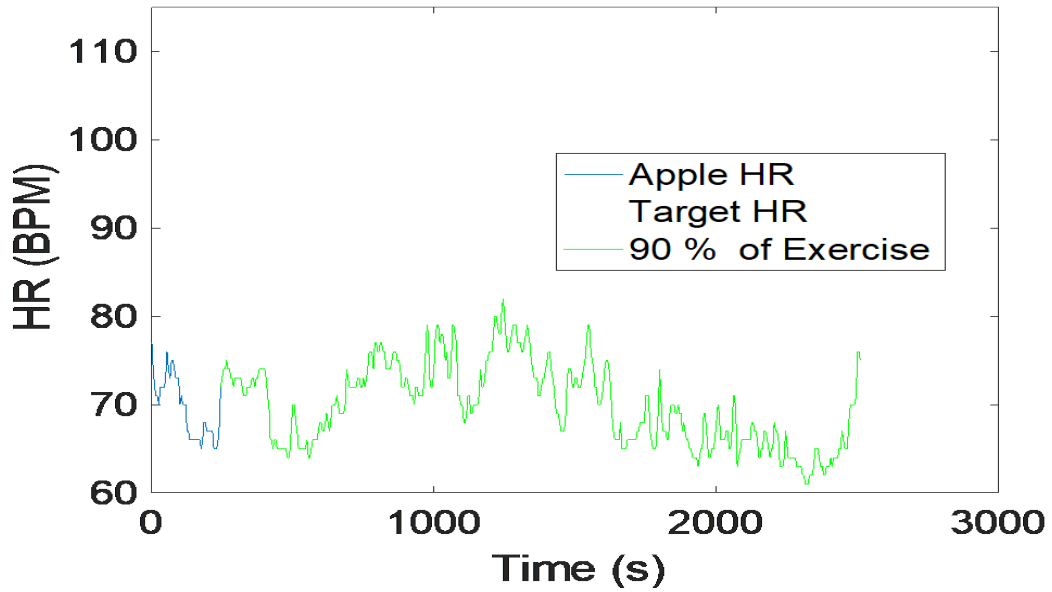


Figure A5.677: Patient No.9 Week 9 Attempt 4

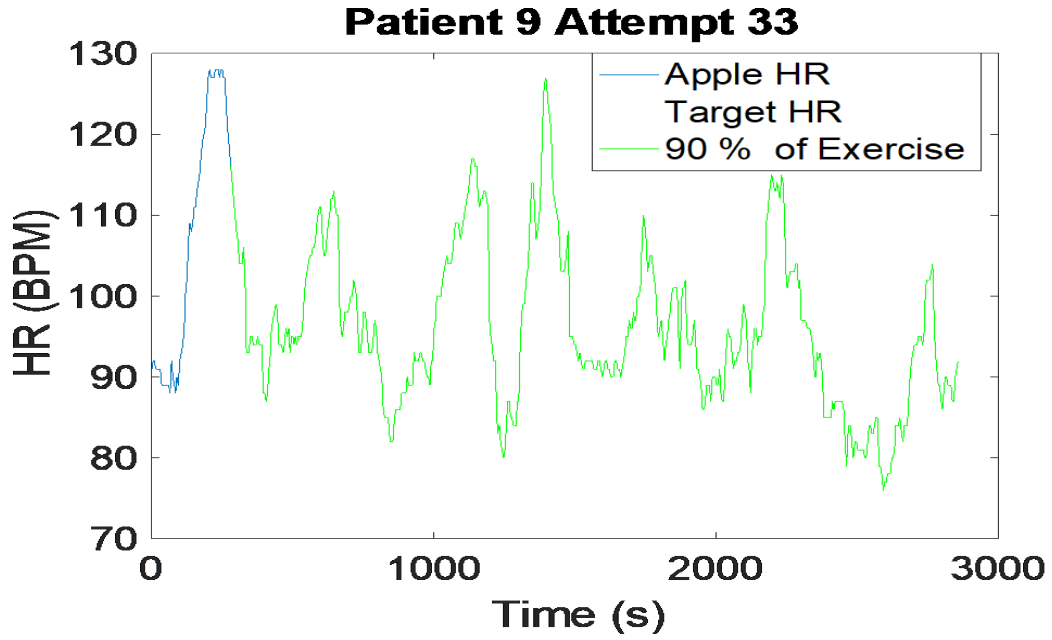


Figure A5.678: Patient No.9 Week 10 Attempt 1

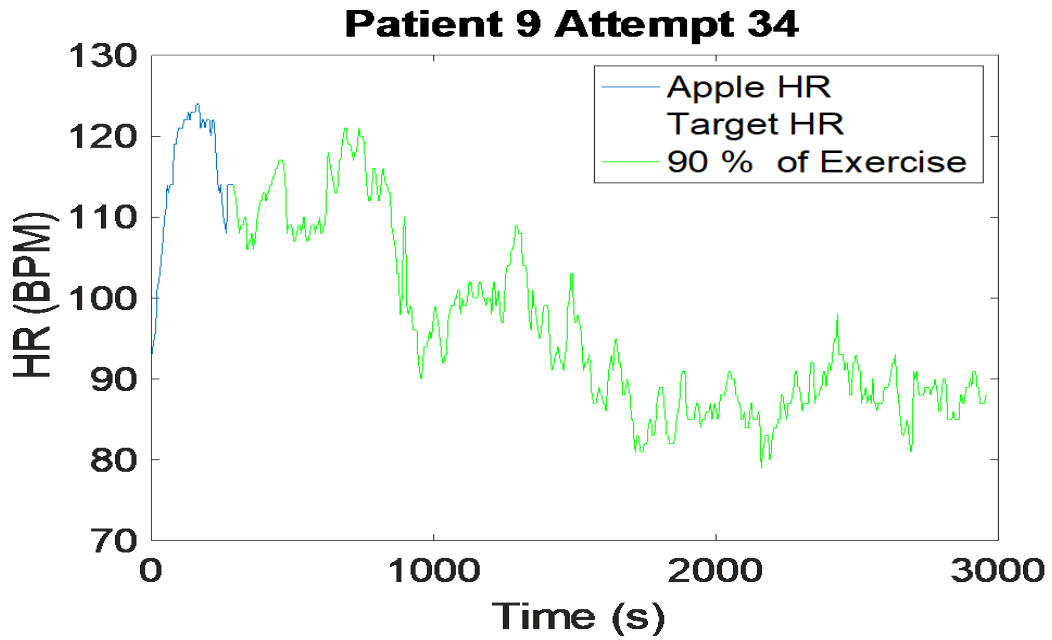


Figure A5.679: Patient No.9 Week 10 Attempt 2

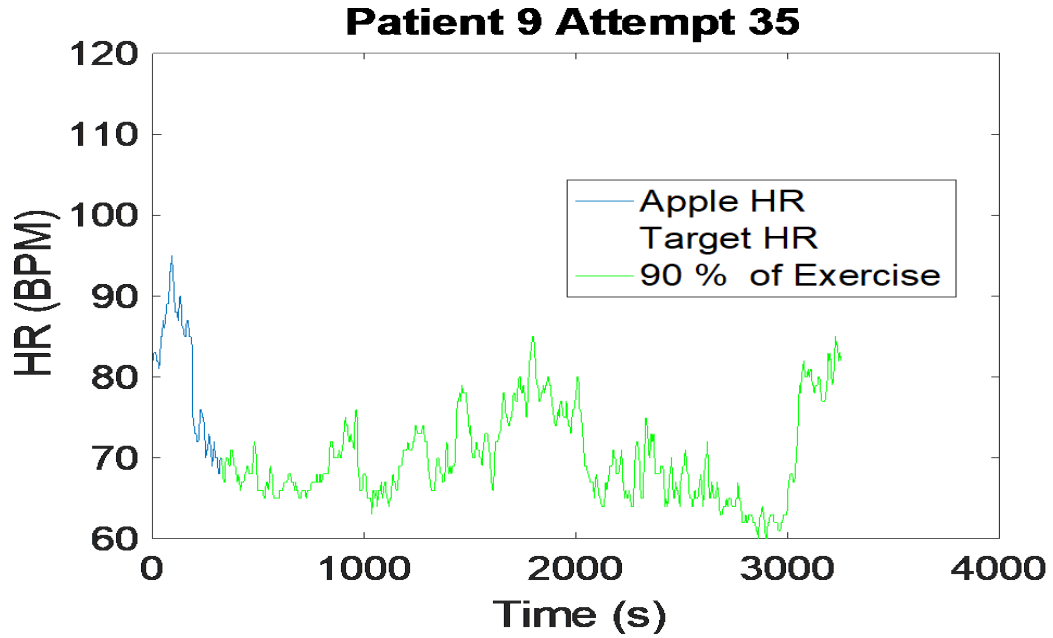


Figure A5.680: Patient No.9 Week 10 Attempt 3

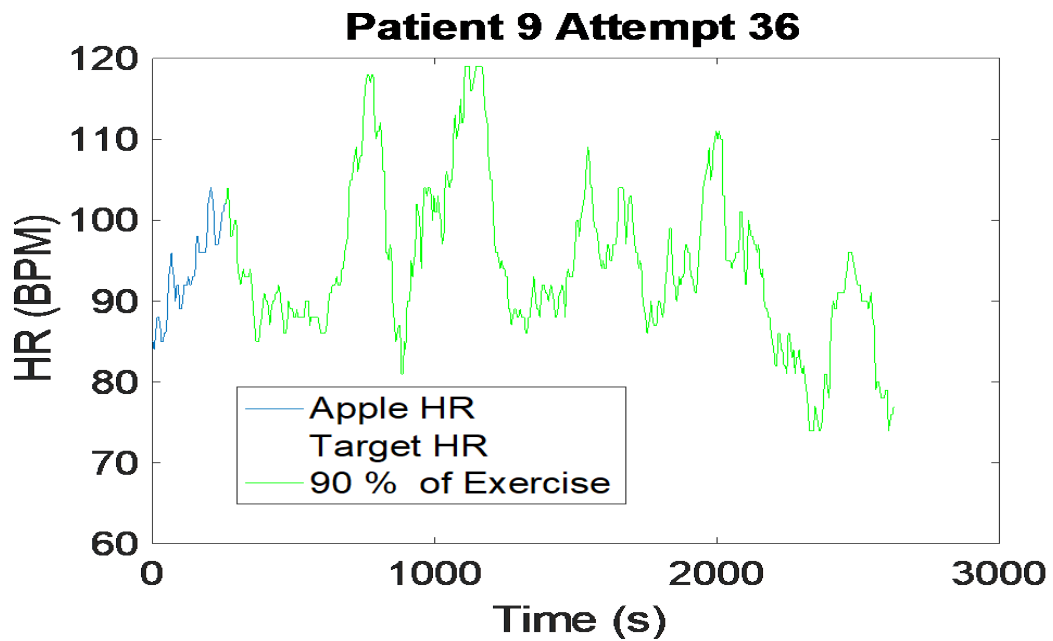


Figure A5.681: Patient No.9 Week 11 Attempt 1

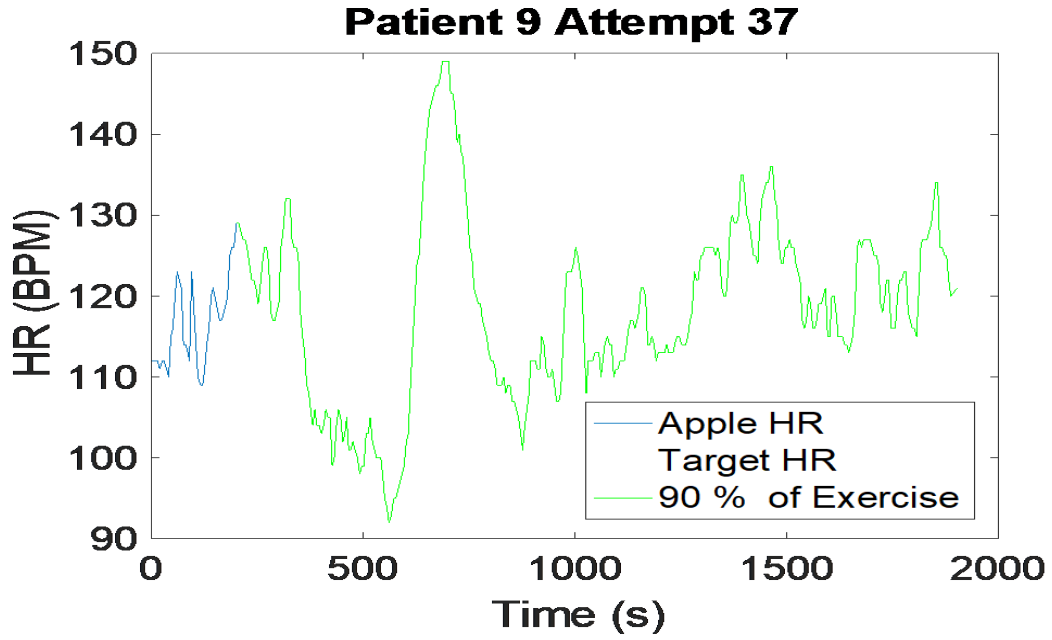


Figure A5.682: Patient No.9 Week 11 Attempt 2

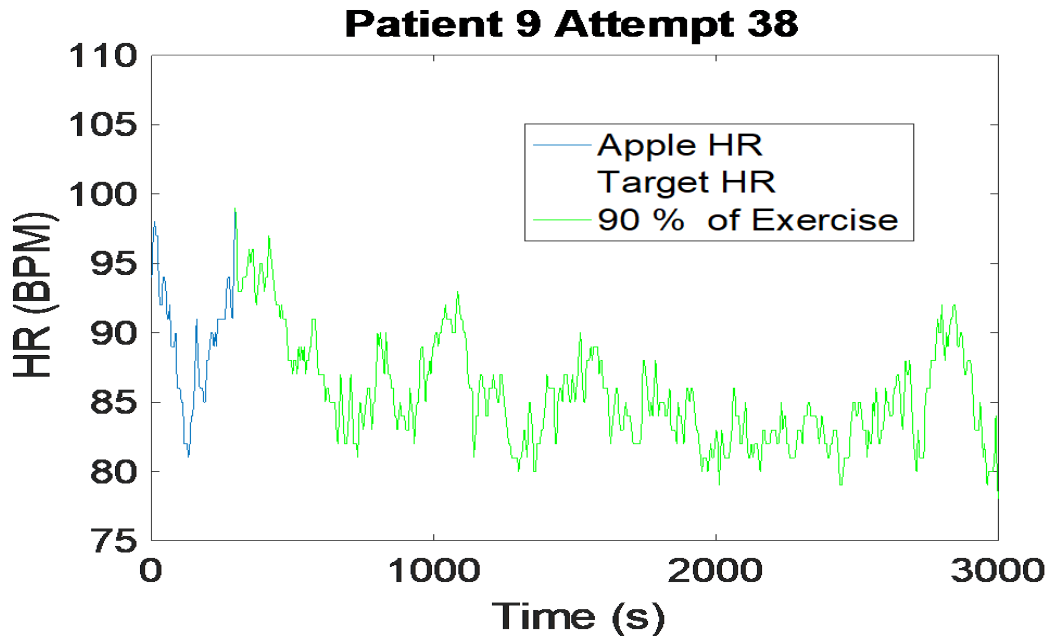


Figure A5.683: Patient No.9 Week 11 Attempt 3

### Patient 9 Attempt 39

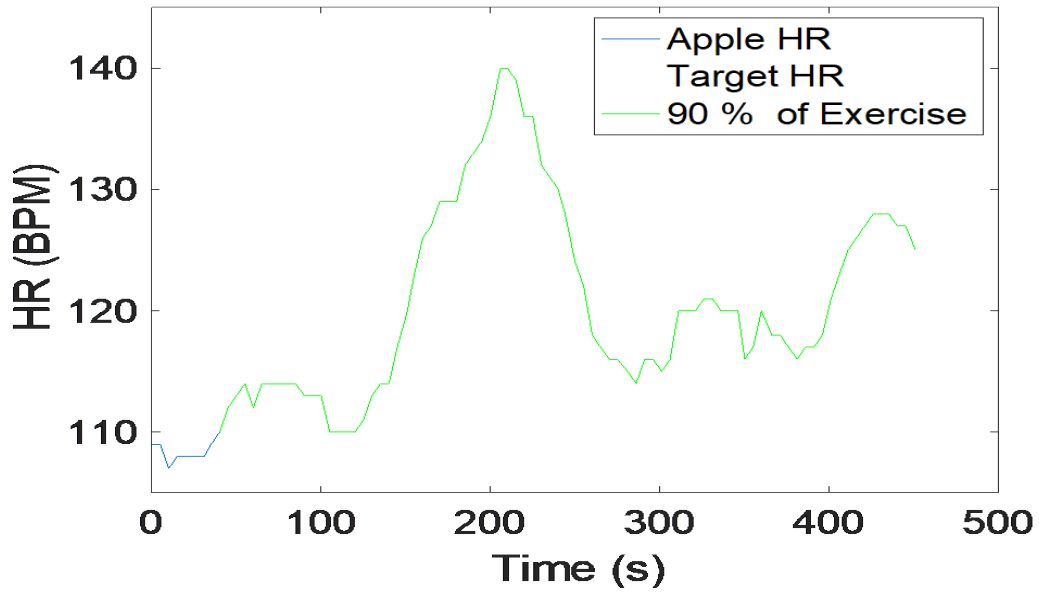


Figure A5.684: Patient No.9 Week 11 Attempt 4

### Patient 9 Attempt 40

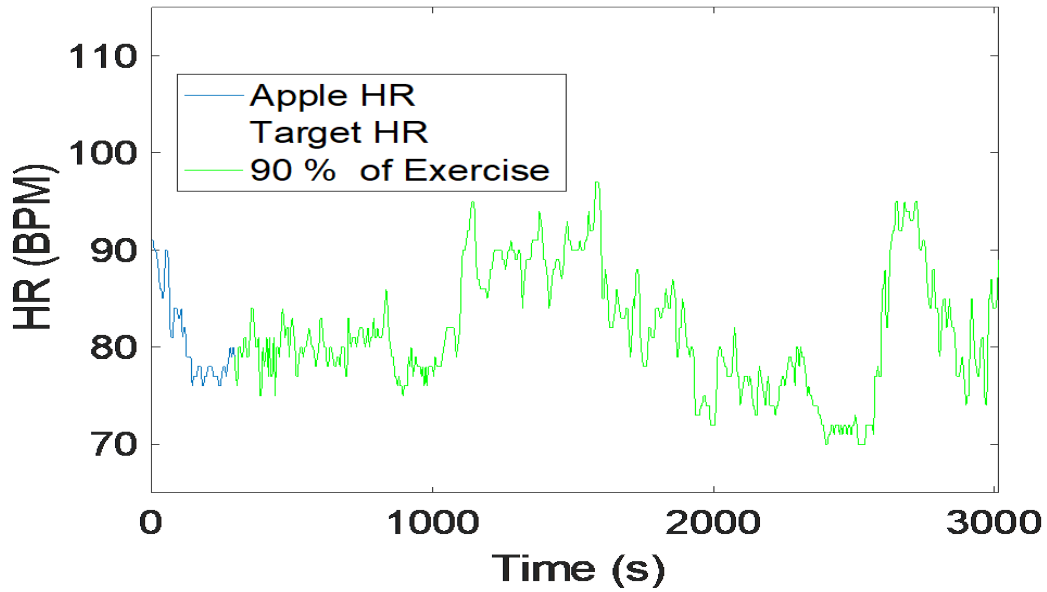


Figure A5.685: Patient No.9 Week 12 Attempt 1



### Patients Heart Rate Compliance Figures:

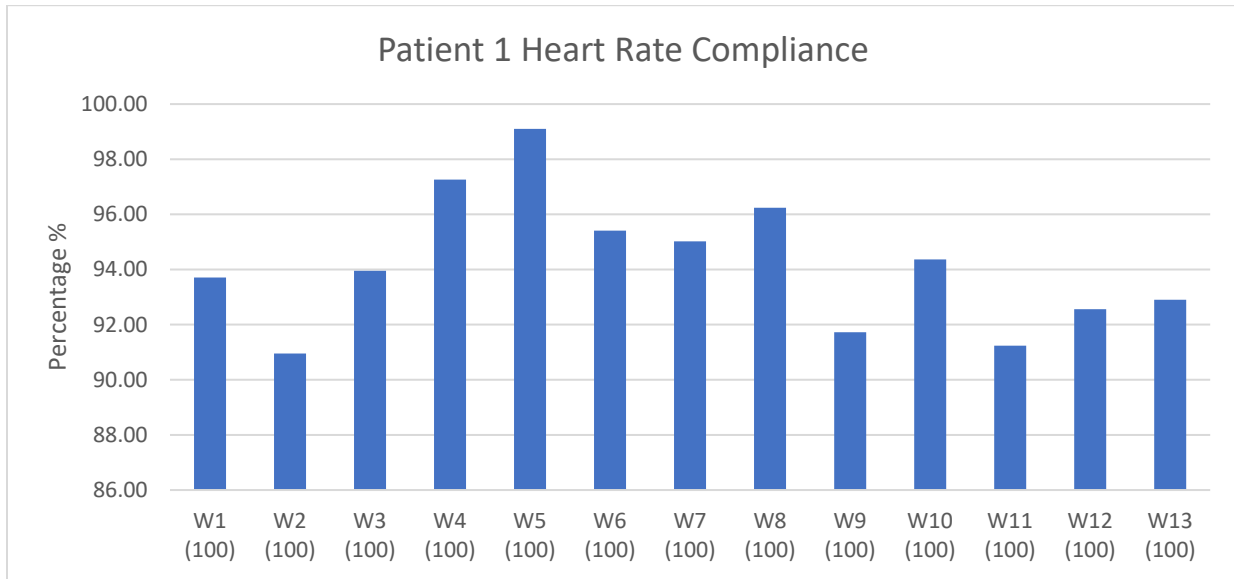


Figure A5.686: Patient#1 Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.

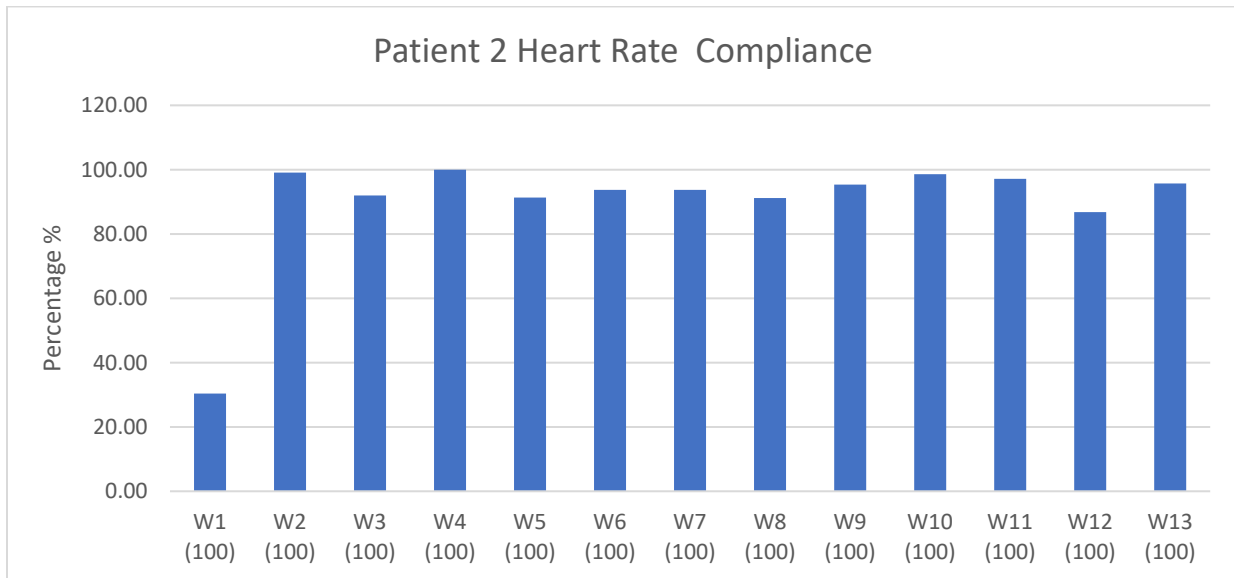


Figure A5.687: Patient#2 Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.

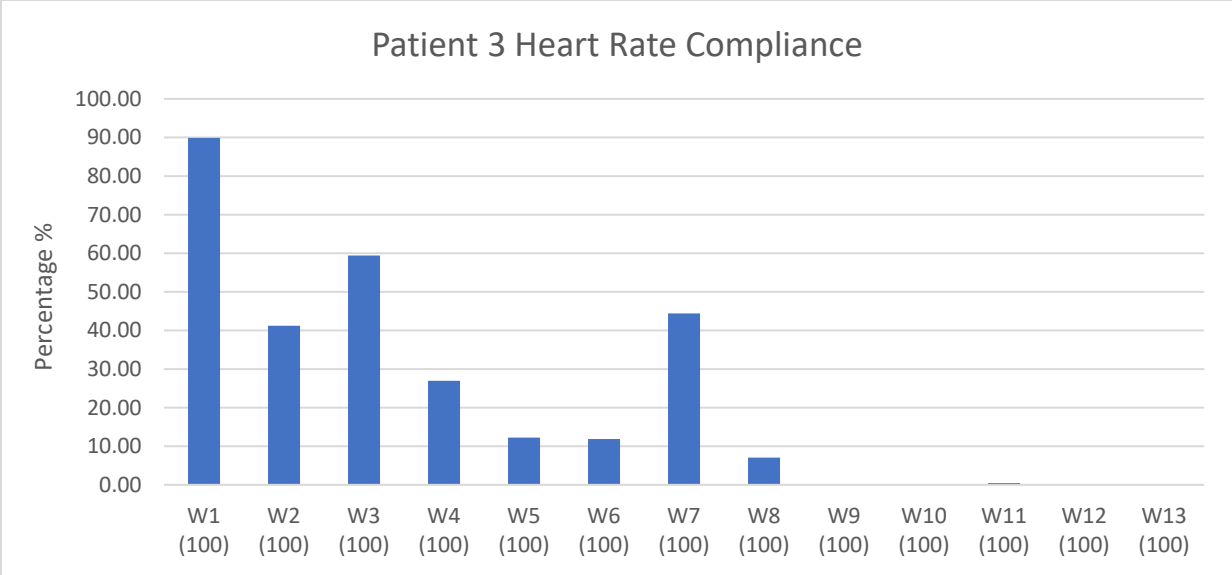


Figure A5.688: Patient#3 Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.

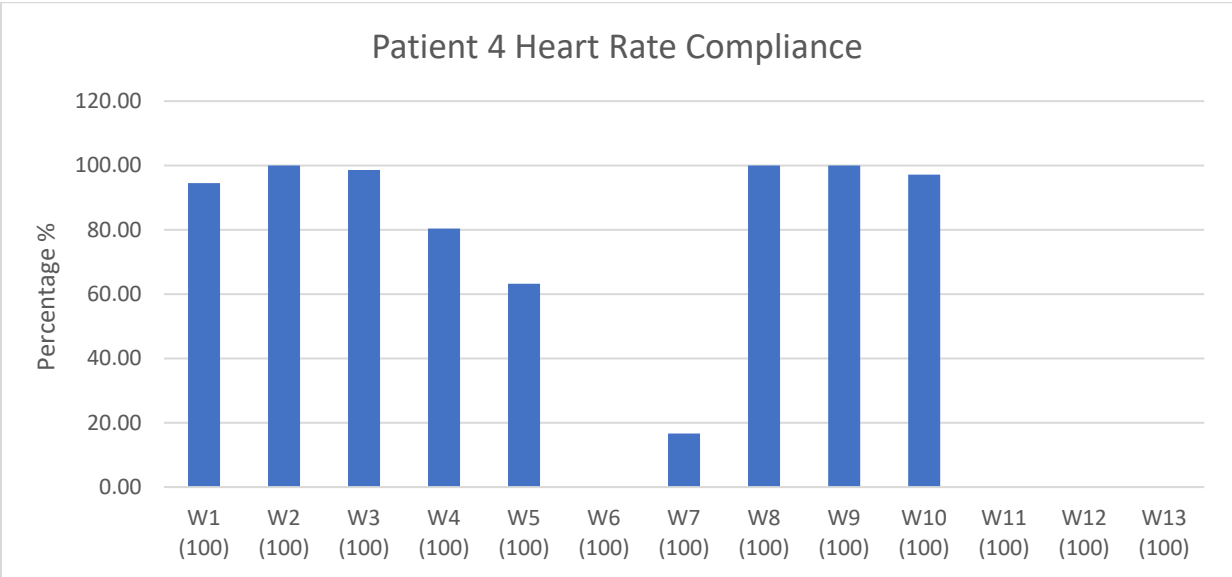


Figure A5.689: Patient#4 Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.

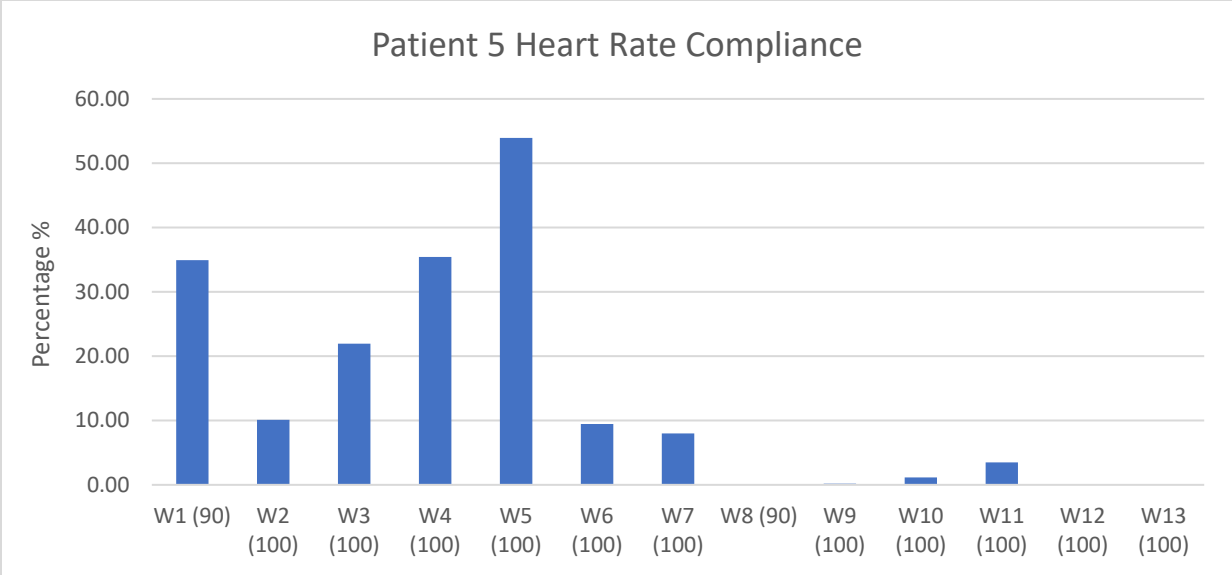


Figure A5.690: Patient#5 Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.

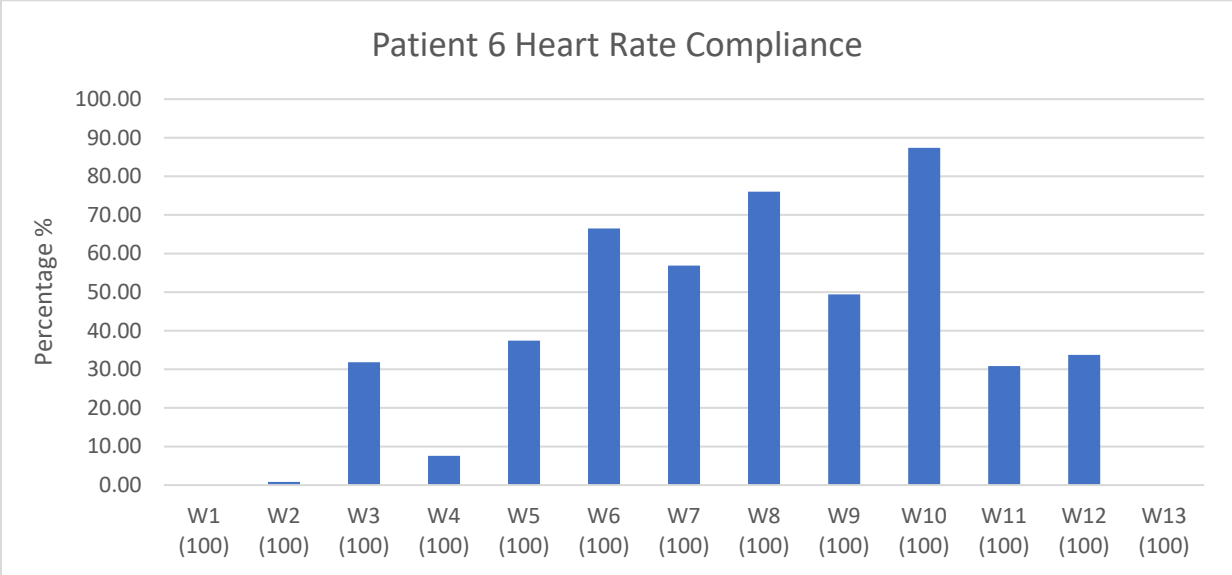


Figure A5.691: Patient#6 Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.

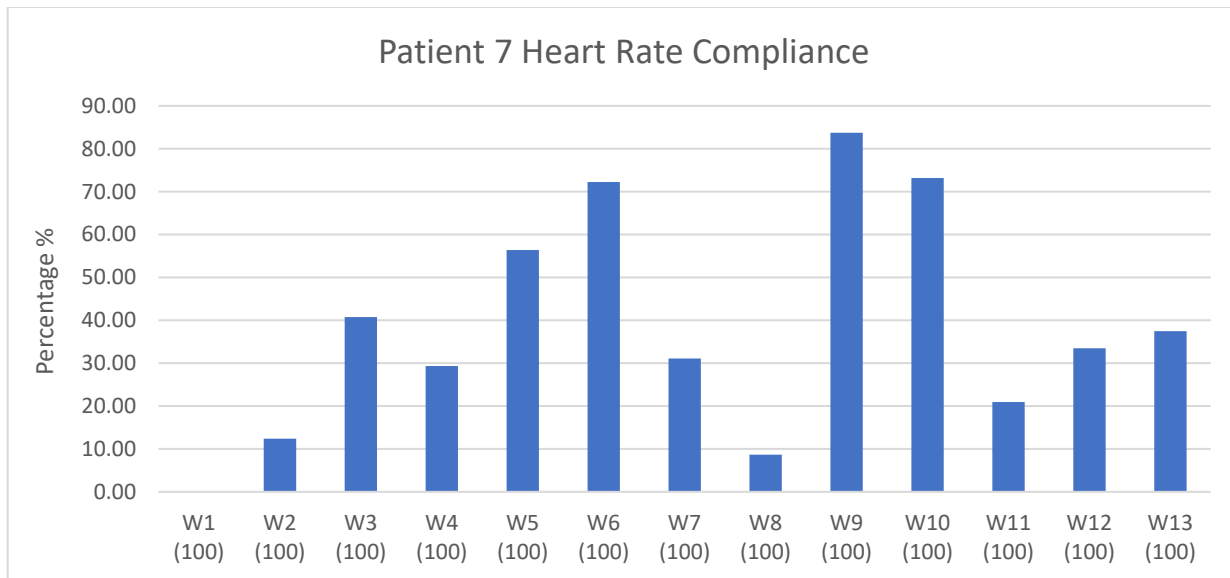


Figure A5.692: Patient#7 Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.

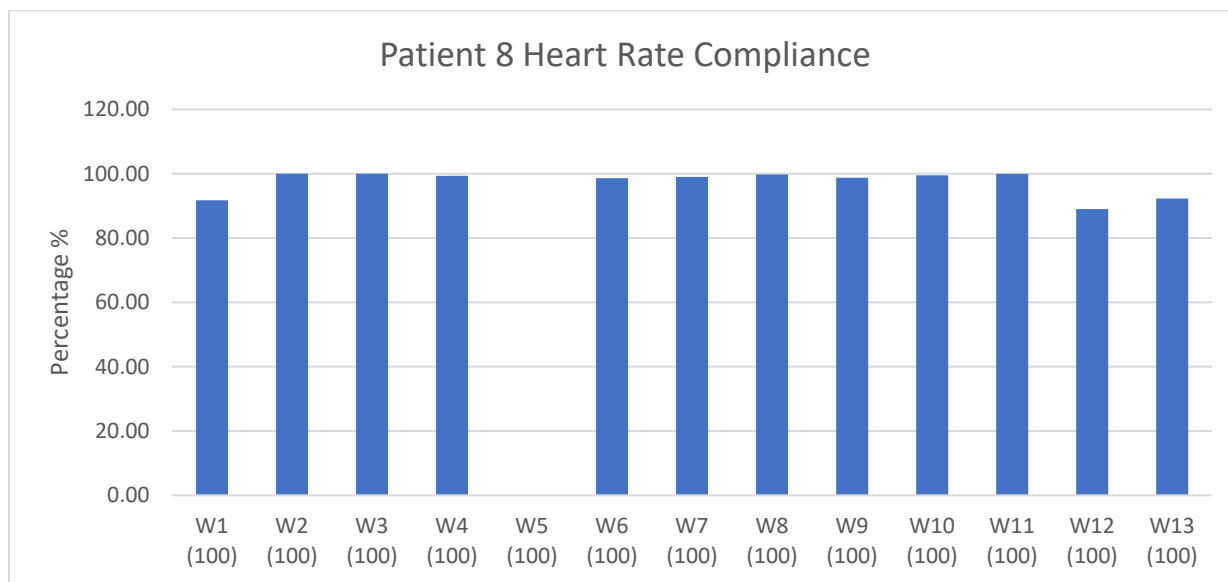


Figure A5.693: Patient#8 Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.

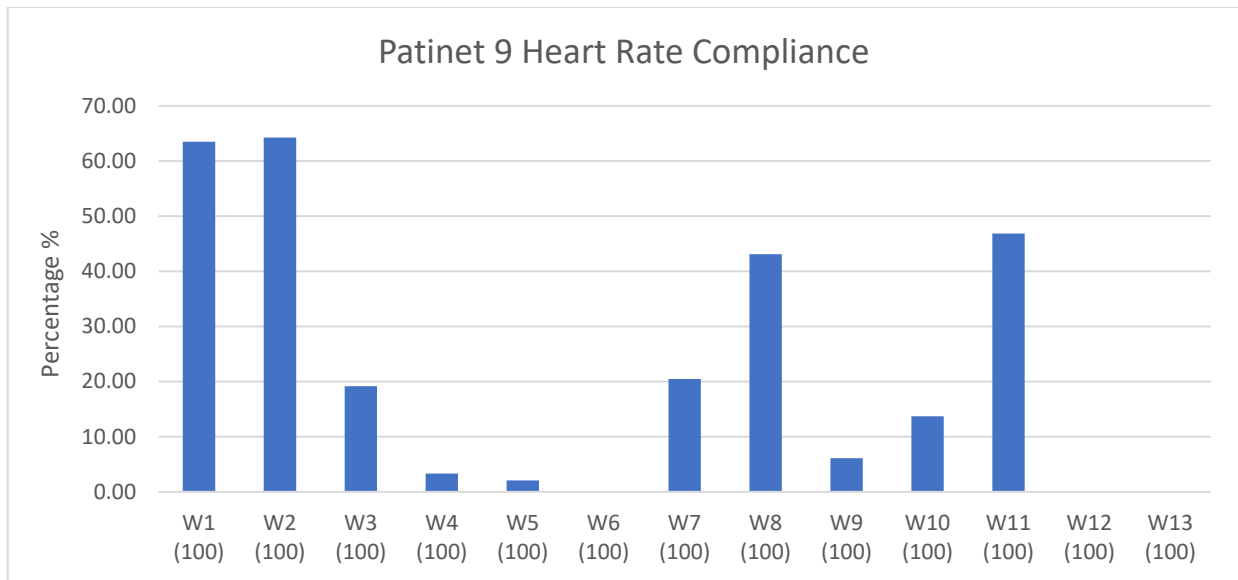


Figure A5.694: Patient#9 Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.

**Patients Duration Compliance Figures:**

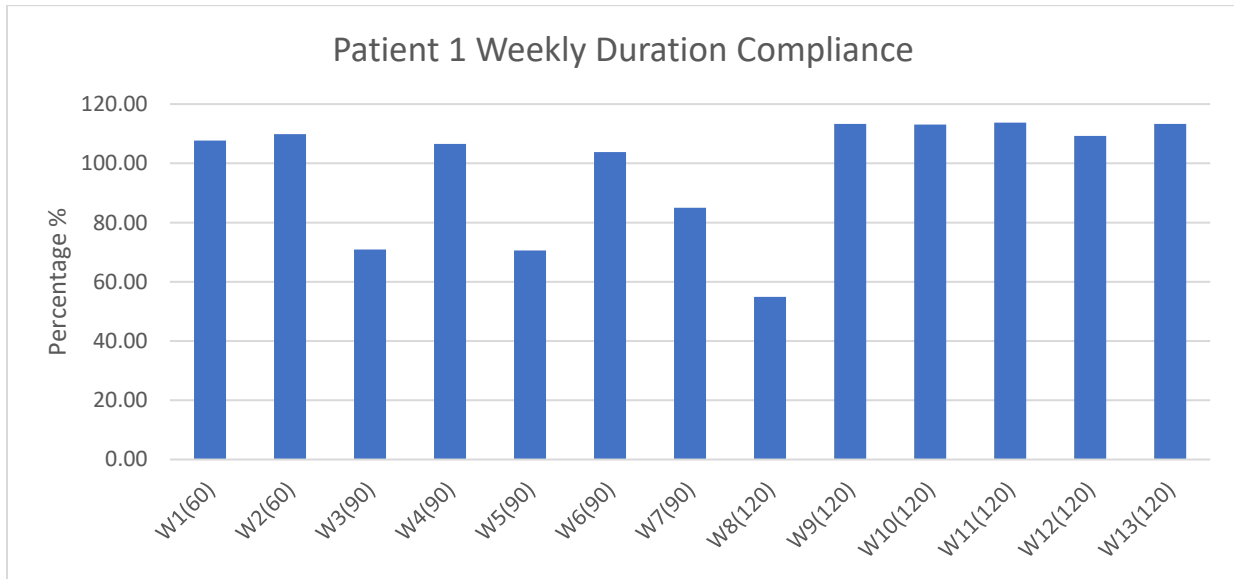


Figure A5.695: Patient#1 Duration Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed duration for that week.

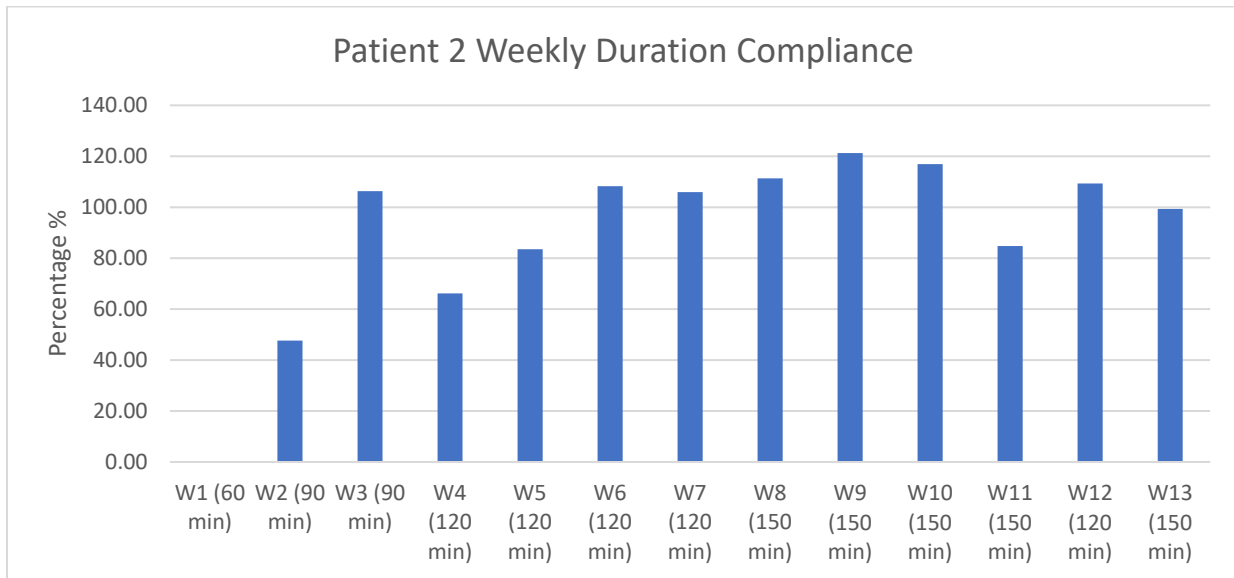


Figure A5.696: Patient#2 Duration Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed duration for that week.

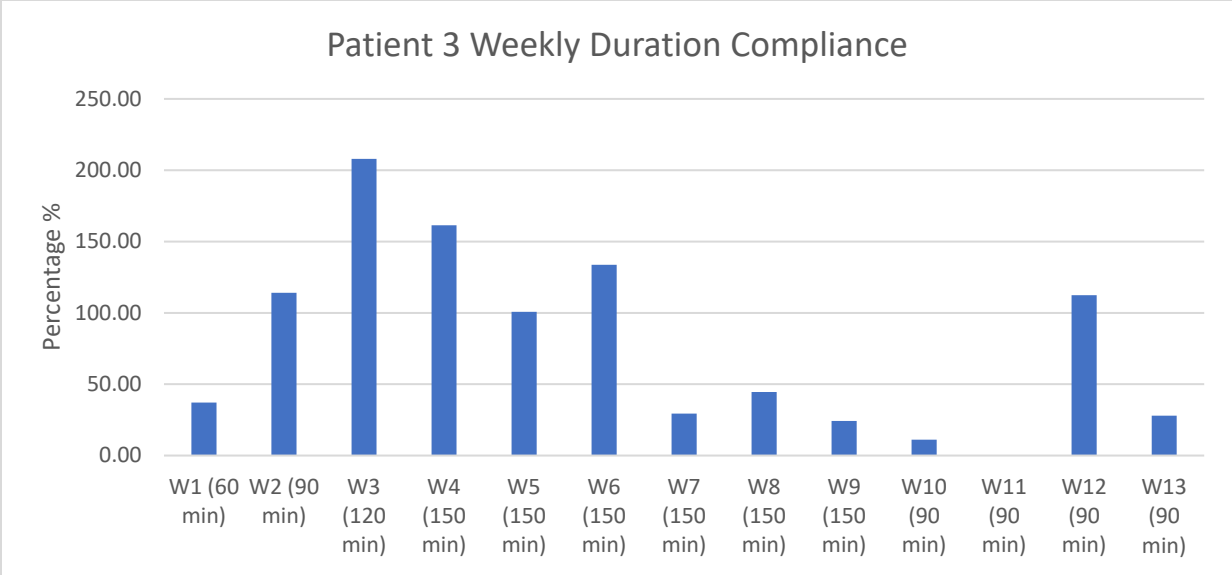


Figure A5.697: Patient#3 Duration Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed duration for that week.

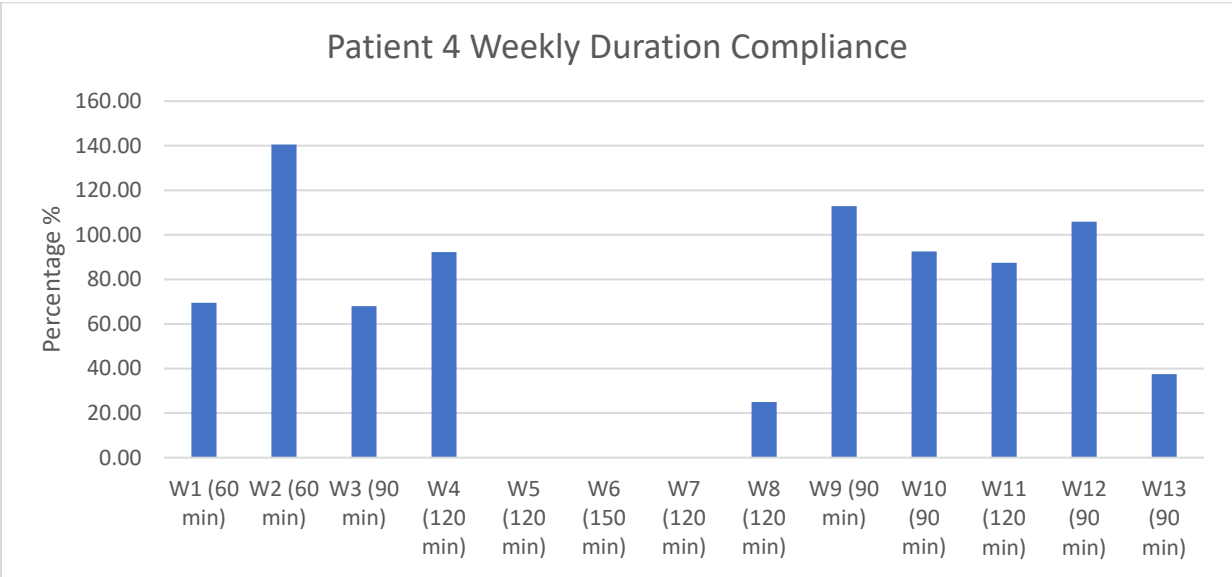


Figure A5.698: Patient#4 Duration Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed duration for that week.

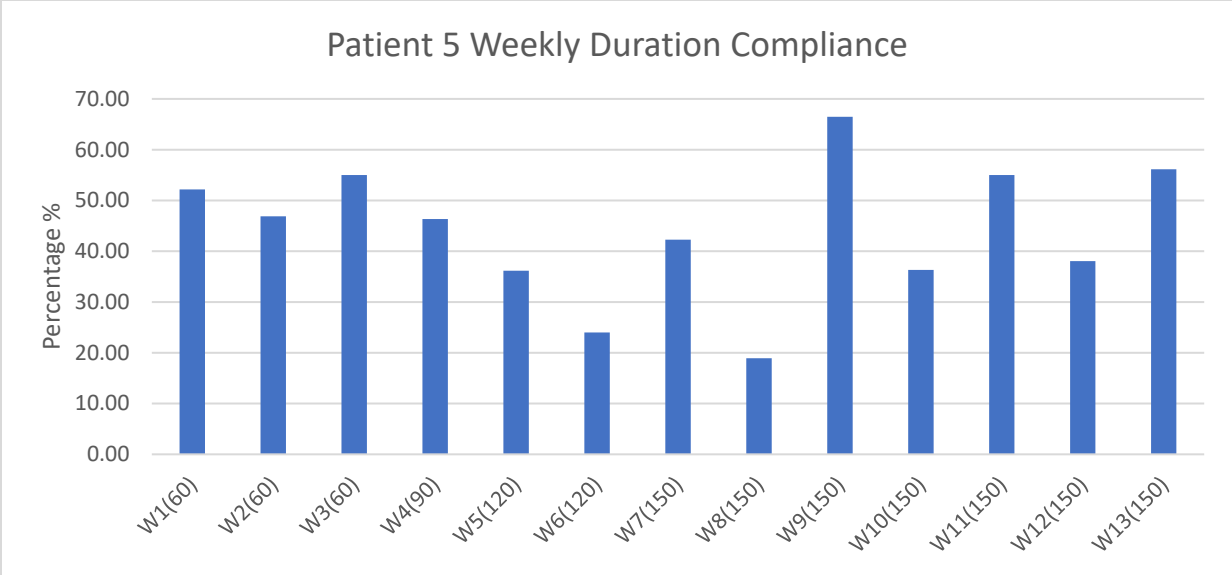


Figure A5.699: Patient#5 Duration Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed duration for that week.

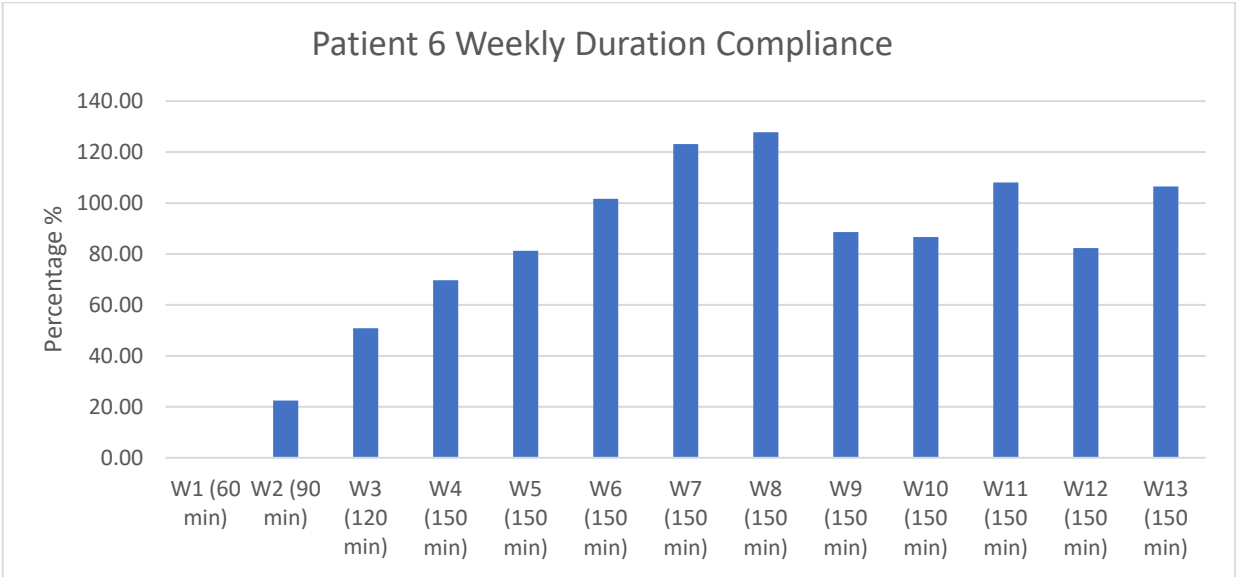


Figure A5.700: Patient#6 Duration Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed duration for that week.



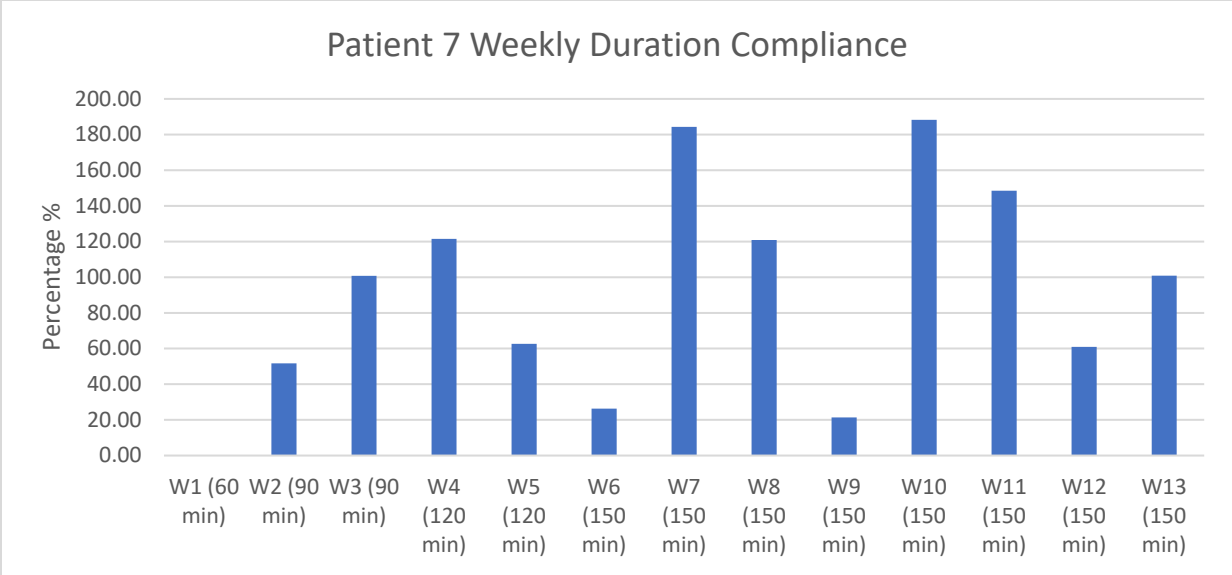


Figure A5.701: Patient#7 Duration Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed duration for that week.

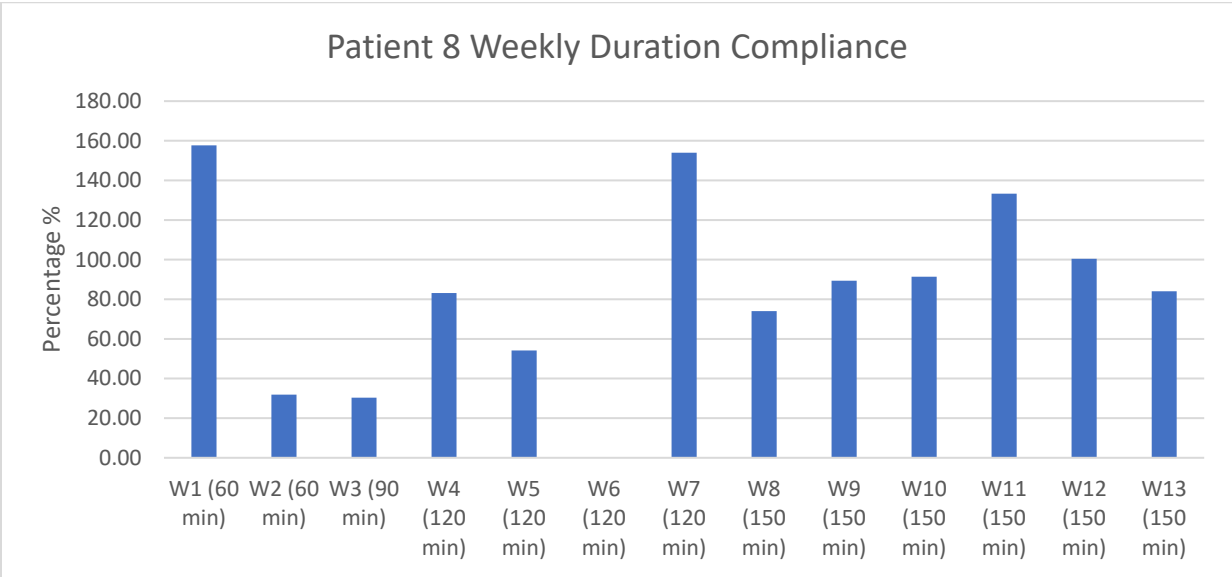
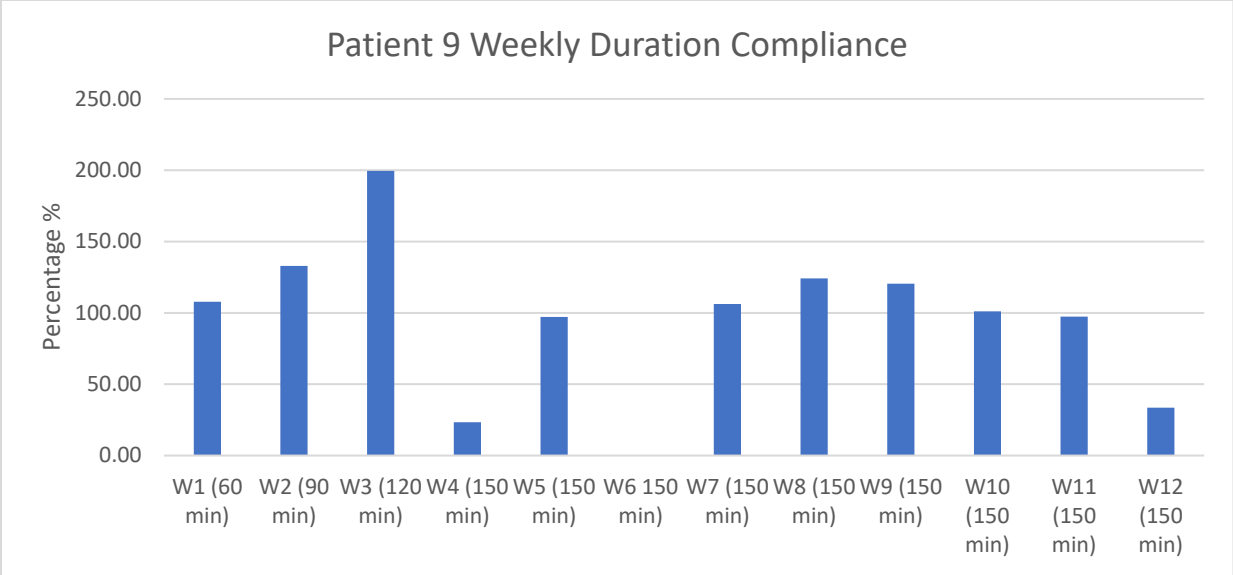


Figure A5.702: Patient#8 Duration Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed duration for that week.



*Figure A5.703: Patient#9 Duration Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed duration for that week.*

**Patients Frequency Compliance Figures:**

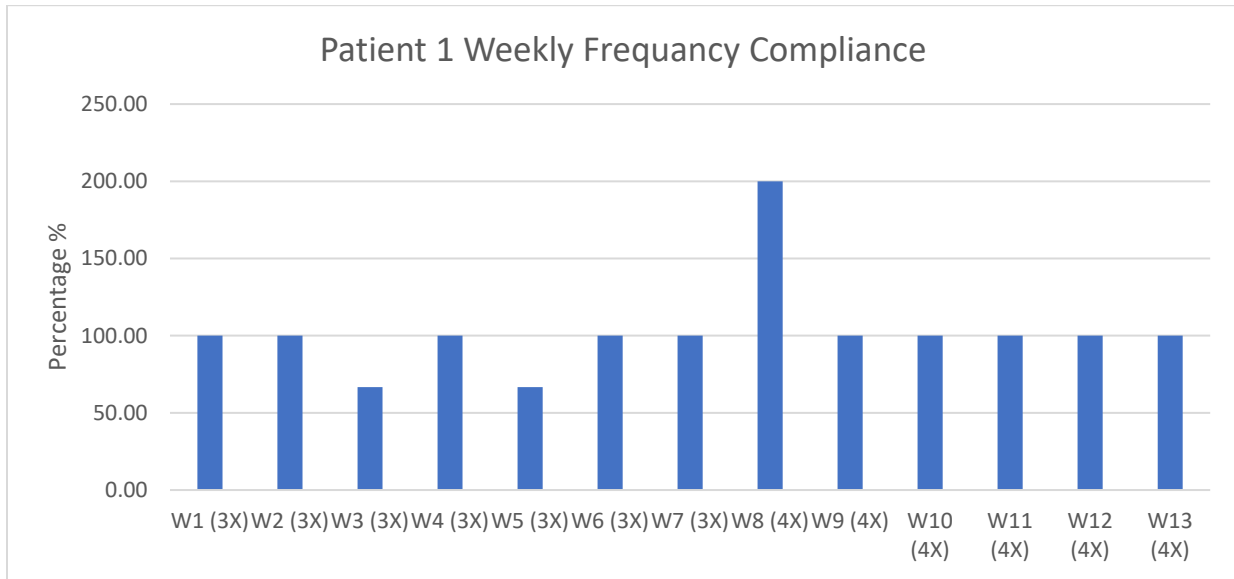


Figure A5.704: Patient#1 Frequency Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed frequency for that week.

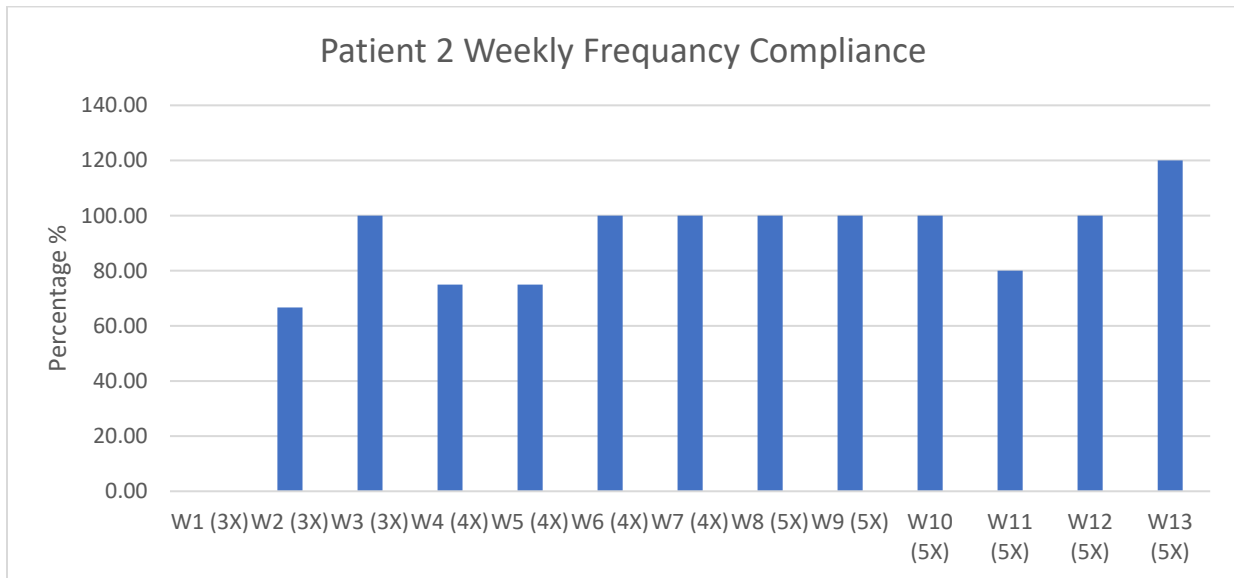


Figure A5.705: Patient#2 Frequency Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed frequency for that week.

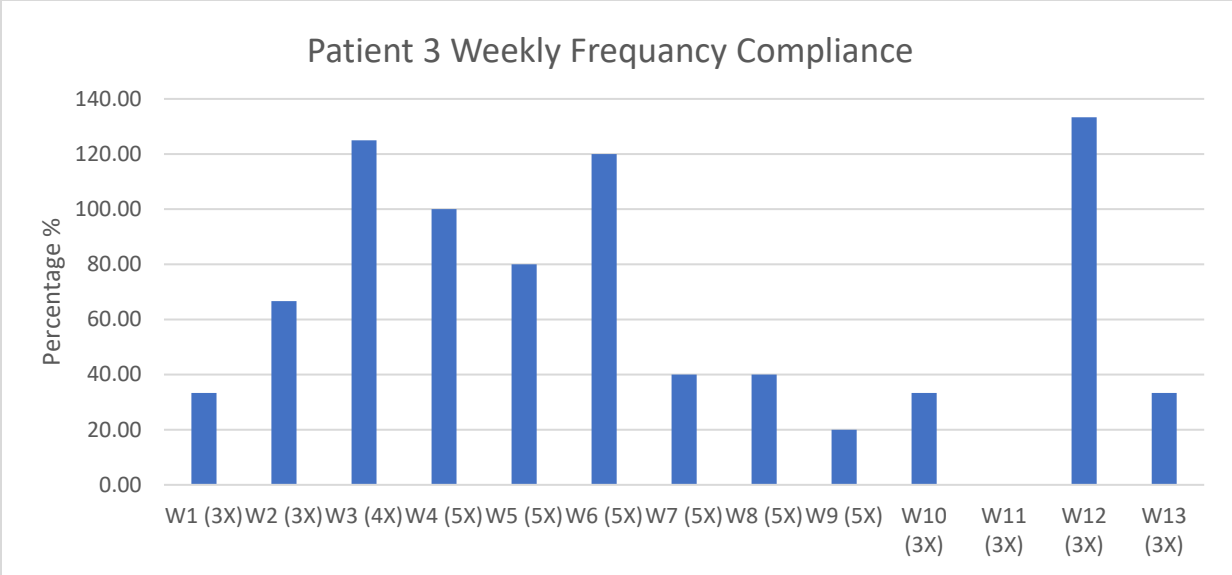


Figure A5.706: Patient#3 Frequency Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed frequency for that week.

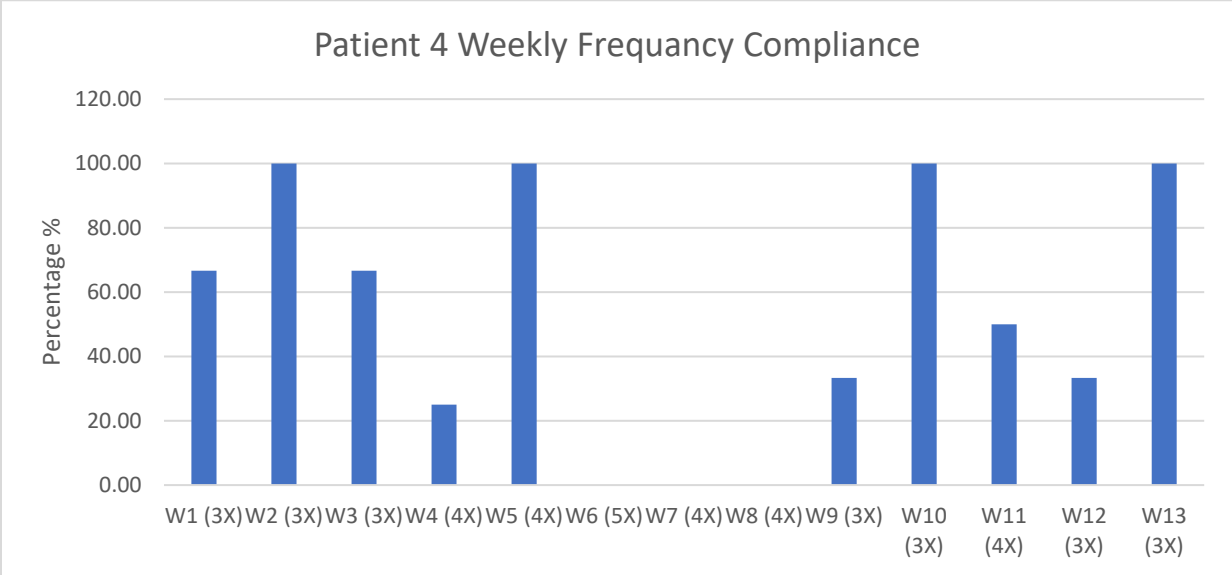


Figure A5.707: Patient#4 Frequency Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed frequency for that week.

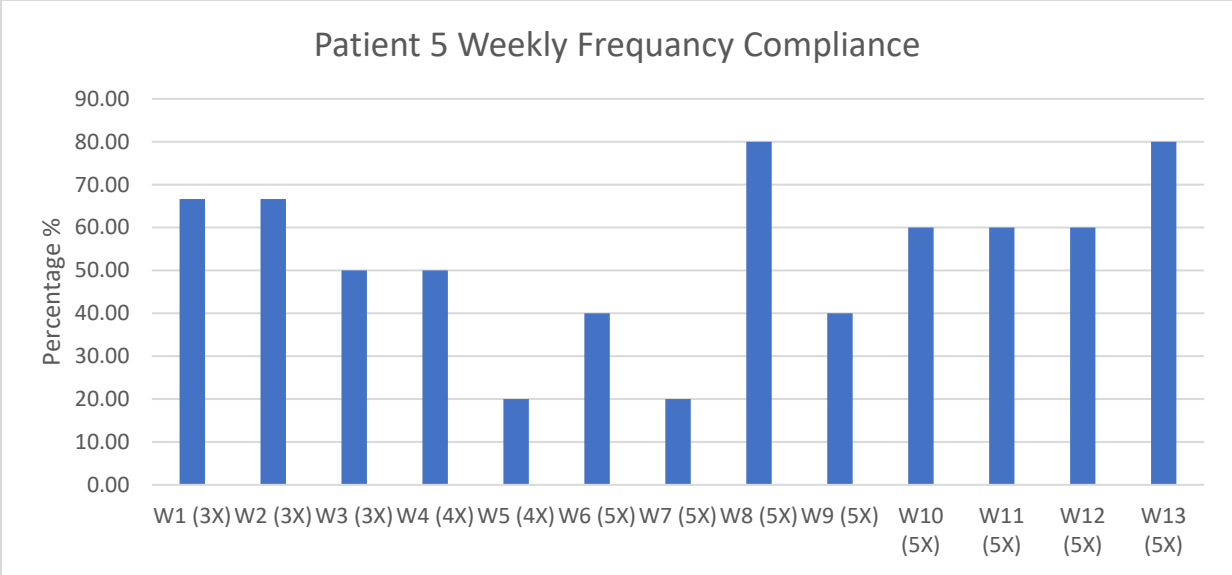


Figure A5.708: Patient#5 Frequency Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed frequency for that week.

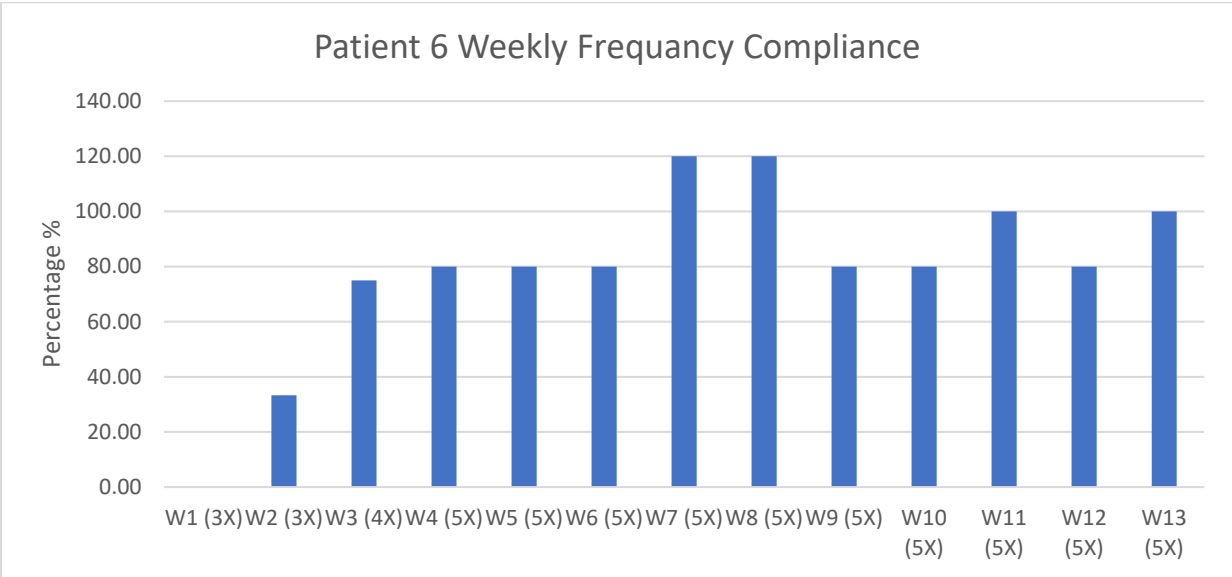


Figure A5.709: Patient#6 Frequency Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed frequency for that week.

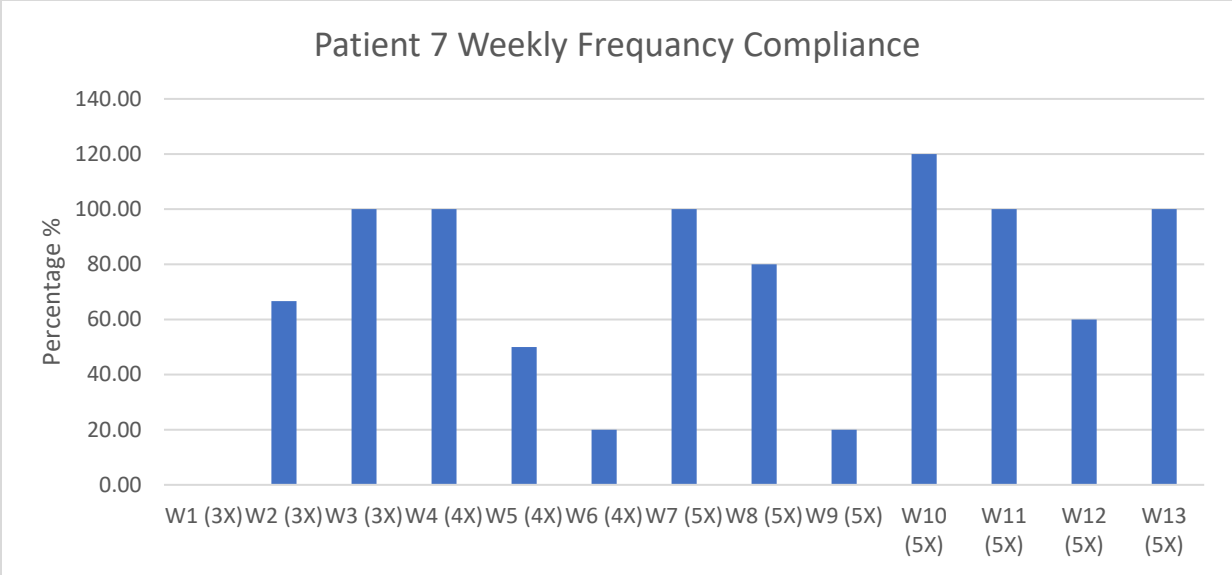


Figure A5.710: Patient#7 Frequency Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed frequency for that week.

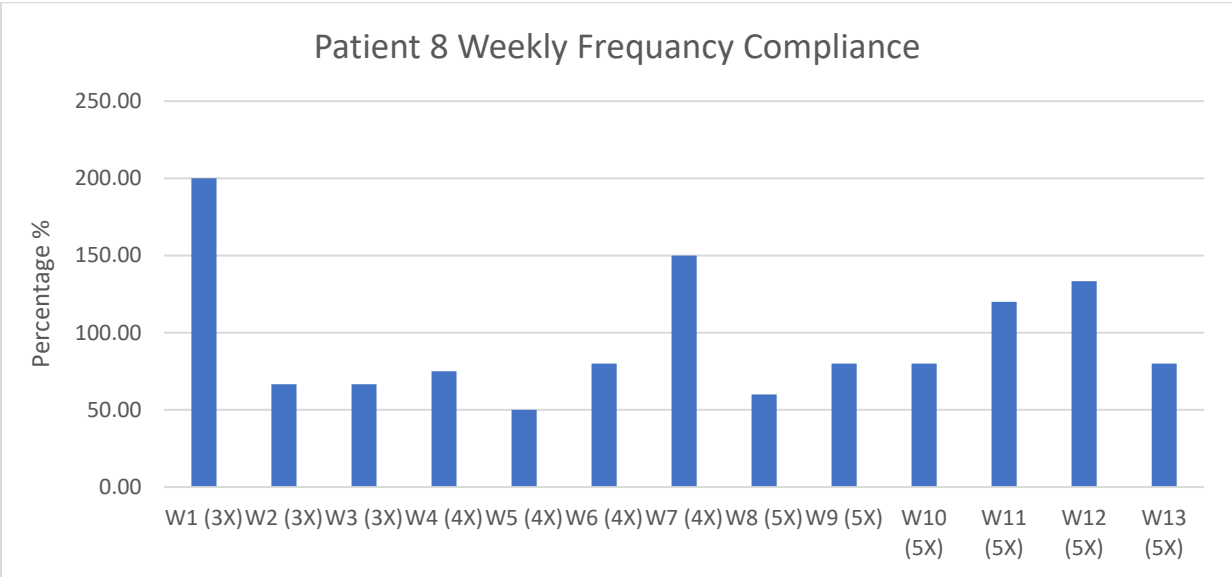


Figure A5.711: Patient#8 Frequency Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed frequency for that week.

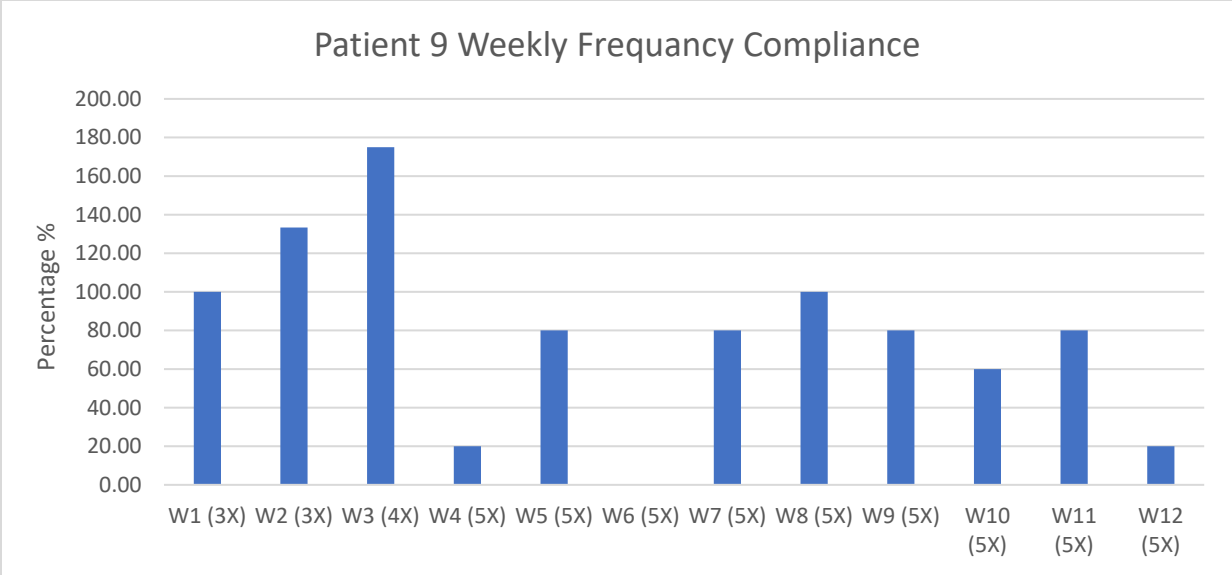


Figure A5.712: Patient#9 Frequency Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed frequency for that week.

### Patients Momentarily Heart Rate Compliance Figures:

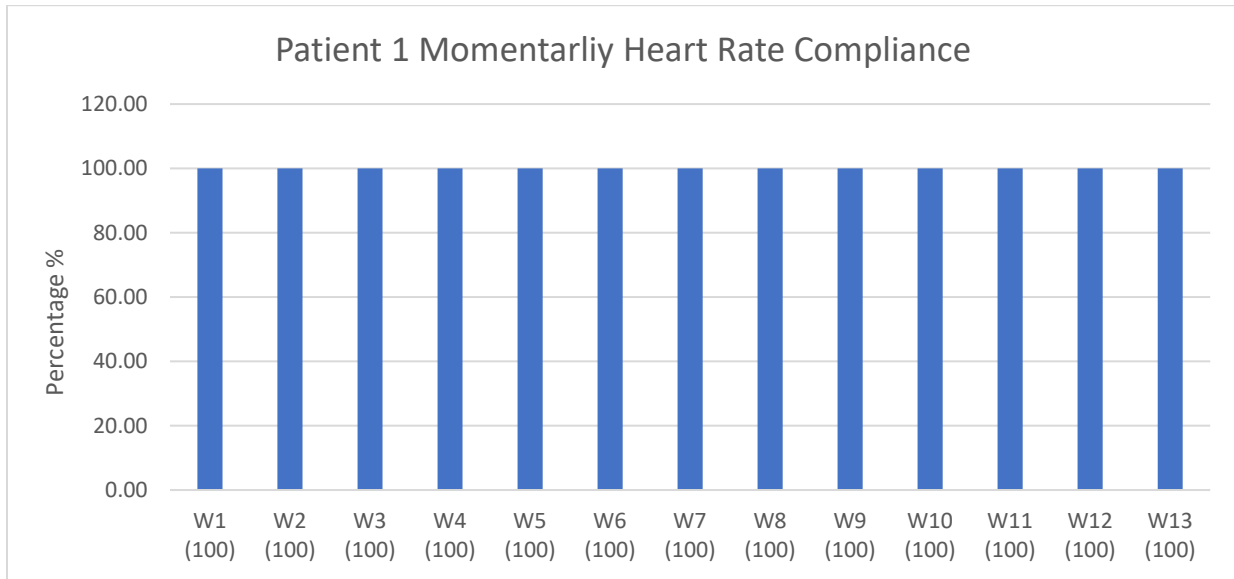


Figure A5.713: Patient#1 Momentarily Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.

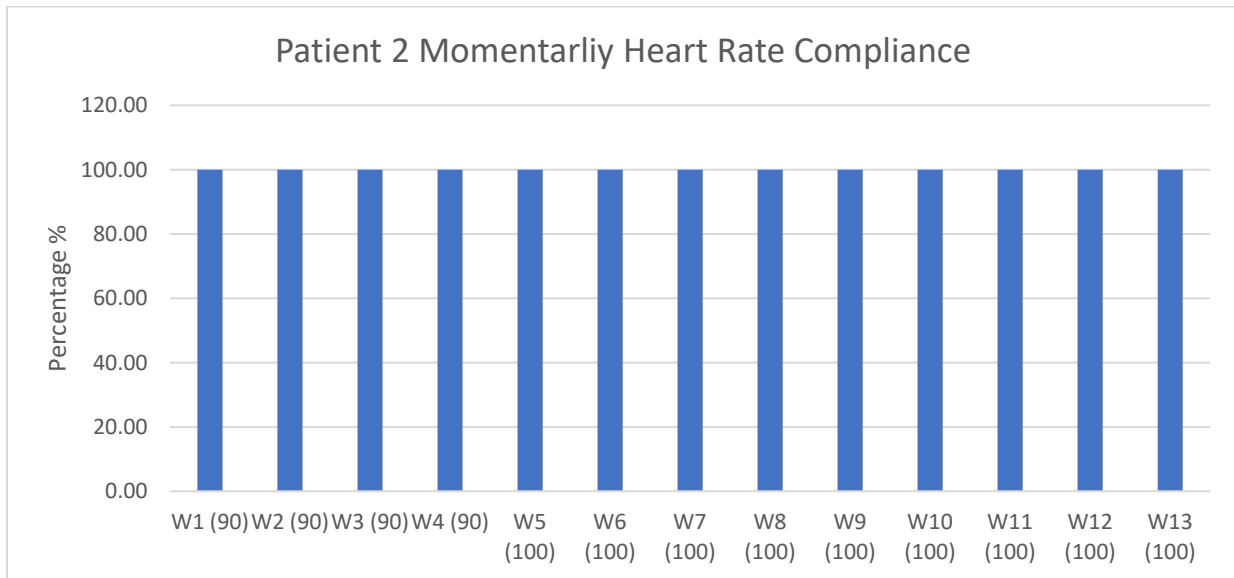


Figure A5.714: Patient#2 Momentarily Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.



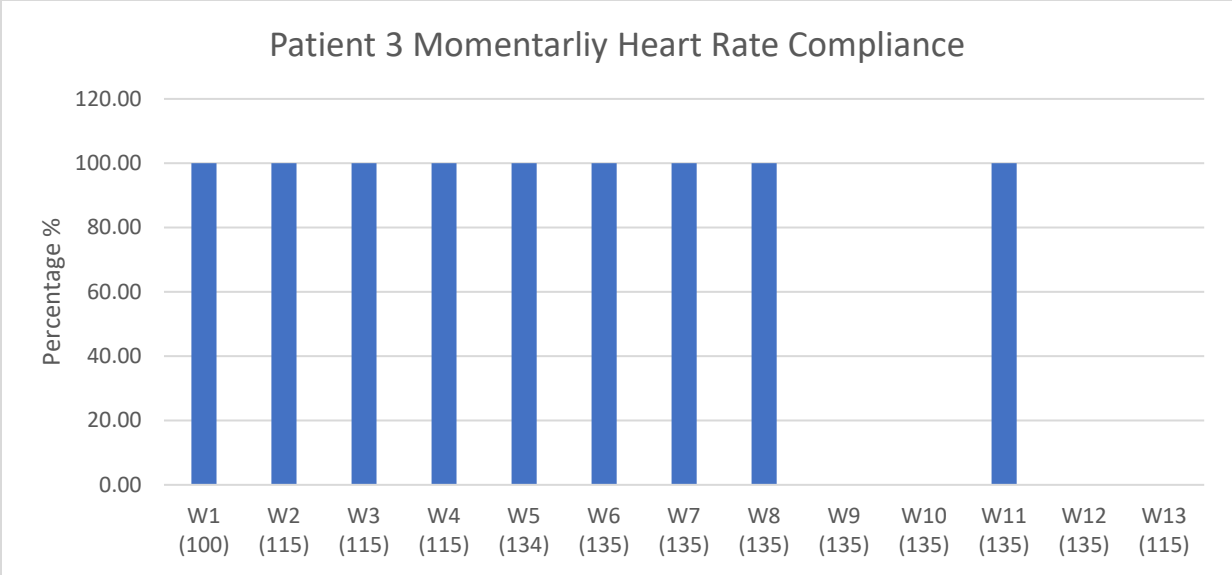


Figure A5.715: Patient#3 Momentarily Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.

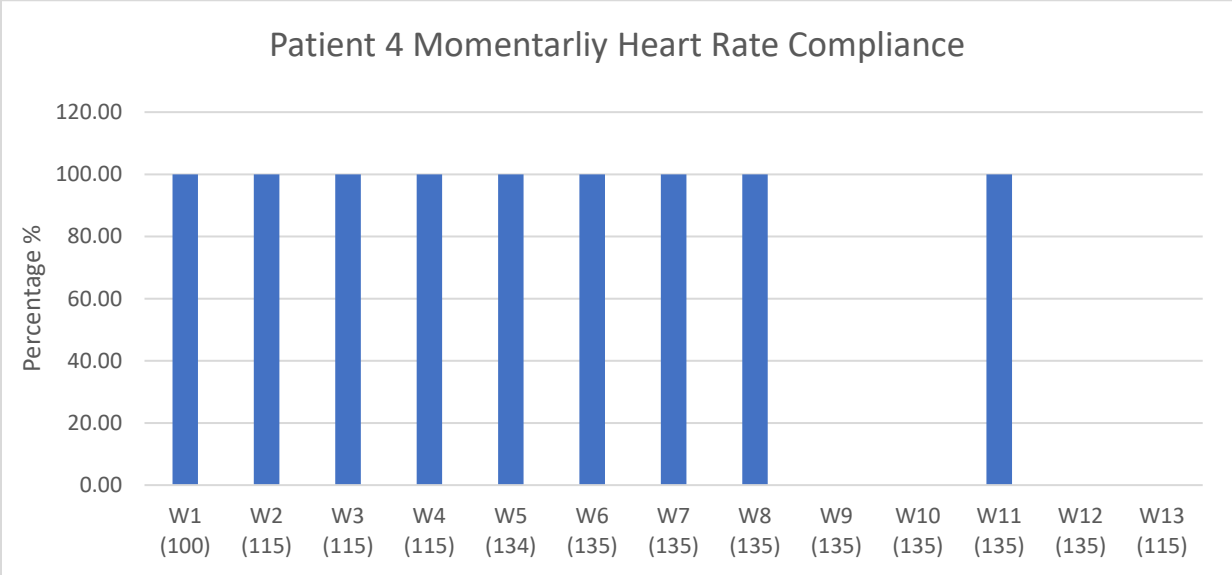


Figure A5.716: Patient#4 Momentarily Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.

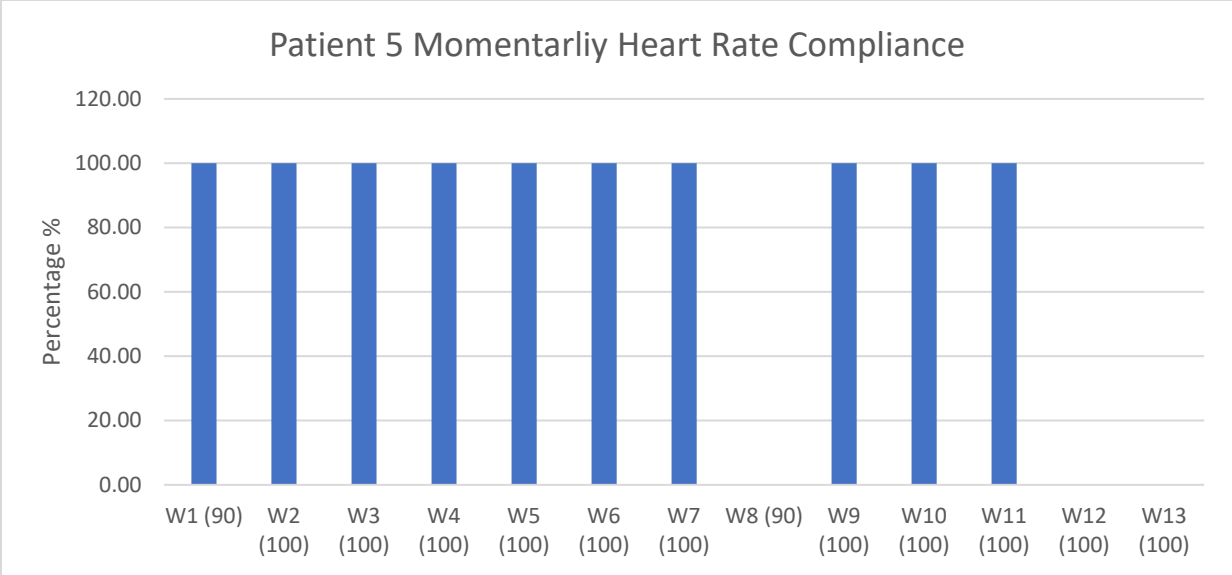


Figure A5.717: Patient#5 Momentarily Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.

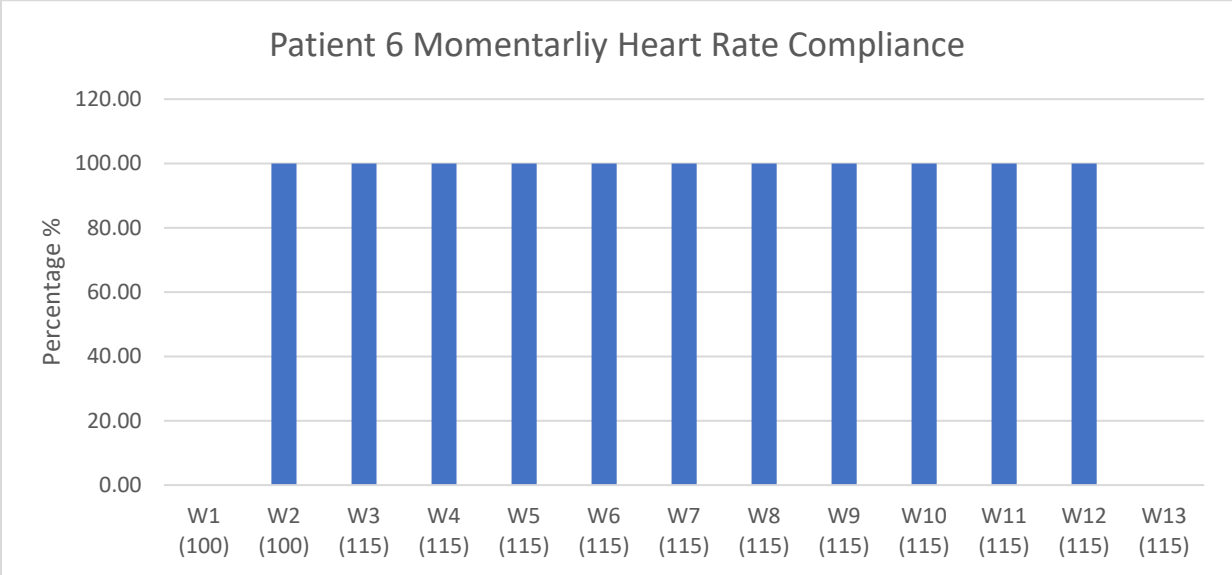


Figure A5.718: Patient#6 Momentarily Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.

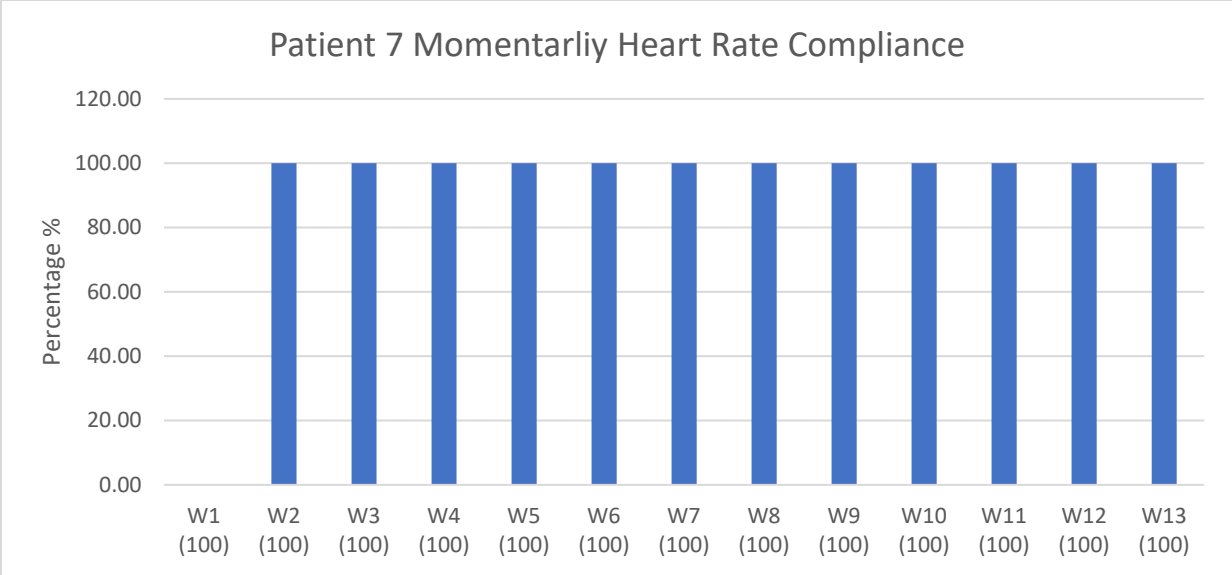


Figure A5.719: Patient#7 Momentarily Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.

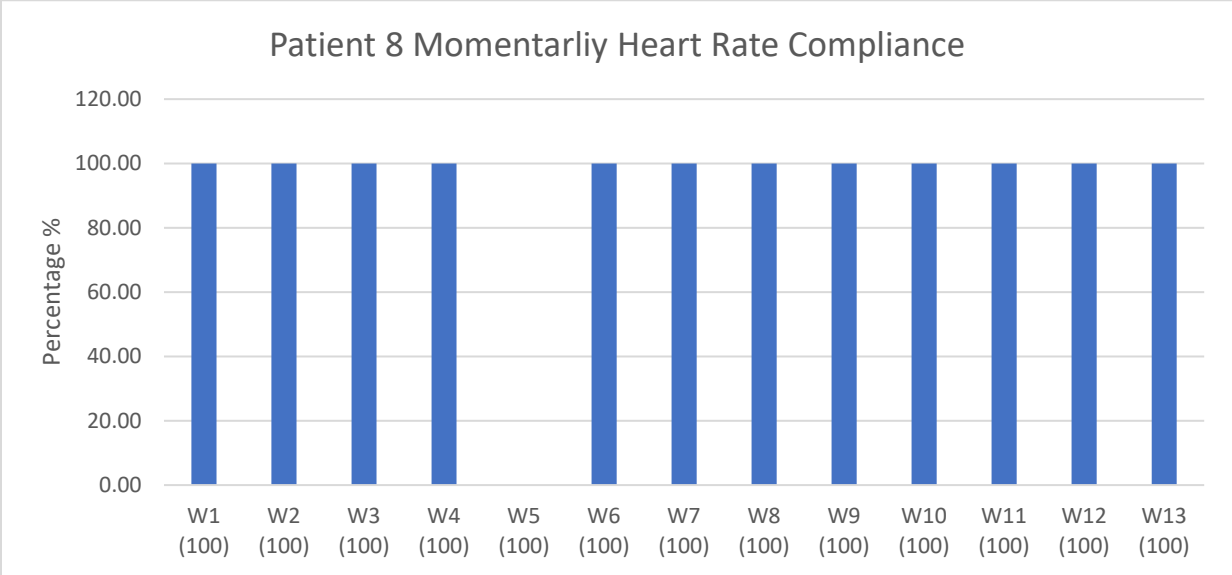
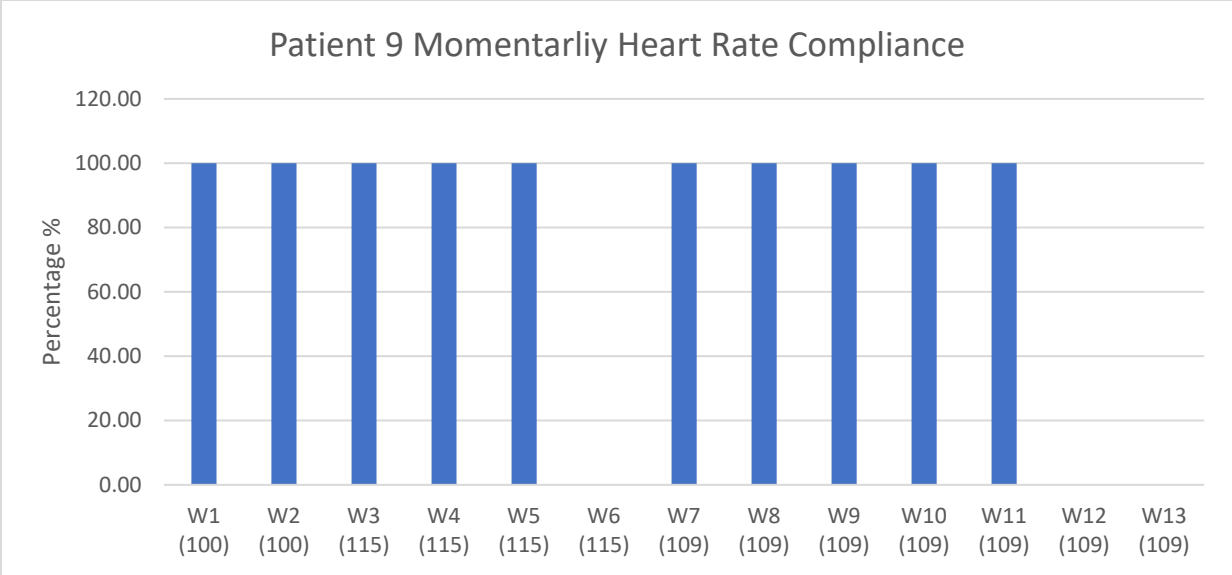


Figure A5.720: Patient#8 Momentarily Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.



*Figure A5.721: Patient#9 Momentarily Heart Rate Compliance, the week numbers are shown as W1, W2, etc. The numbers in the parentheses below that are the prescribed target heart rate for that week.*

## A.6 Chapter 6 Appendix

### Patients Initial and Exit Visits Readings

#### Patient 1 Initial Visit Readings

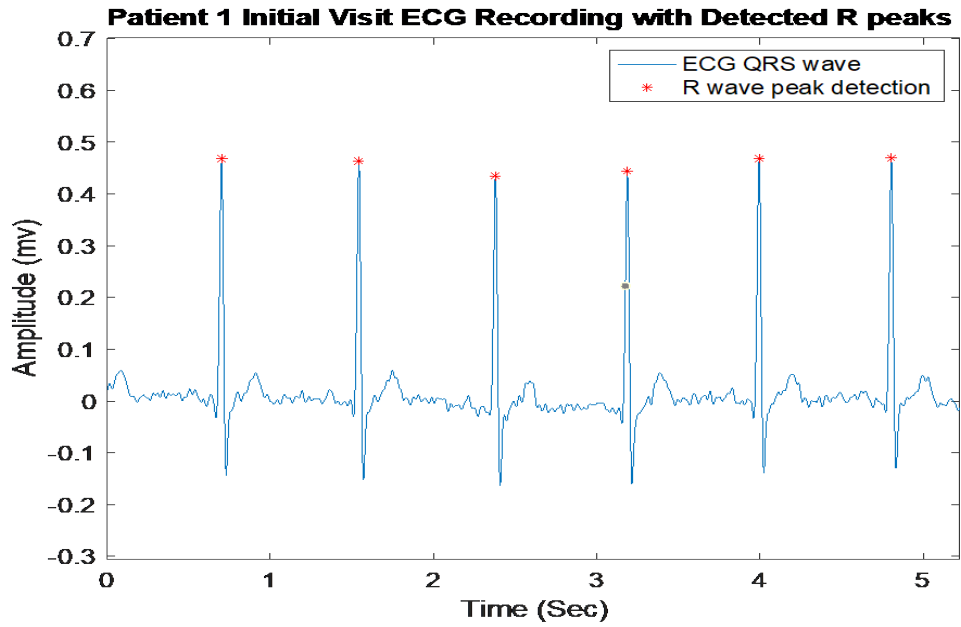


Figure A6. 722: Patient 1 Initial Visit ECG, with detected R peaks

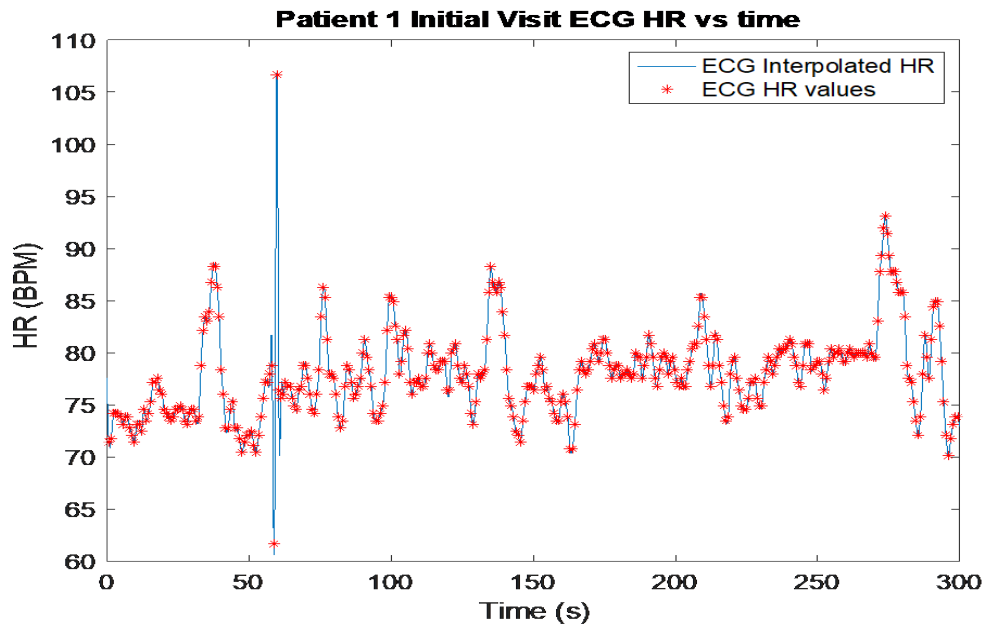


Figure A6. 723: Patient 1 Initial Visit Interpolated ECG HR

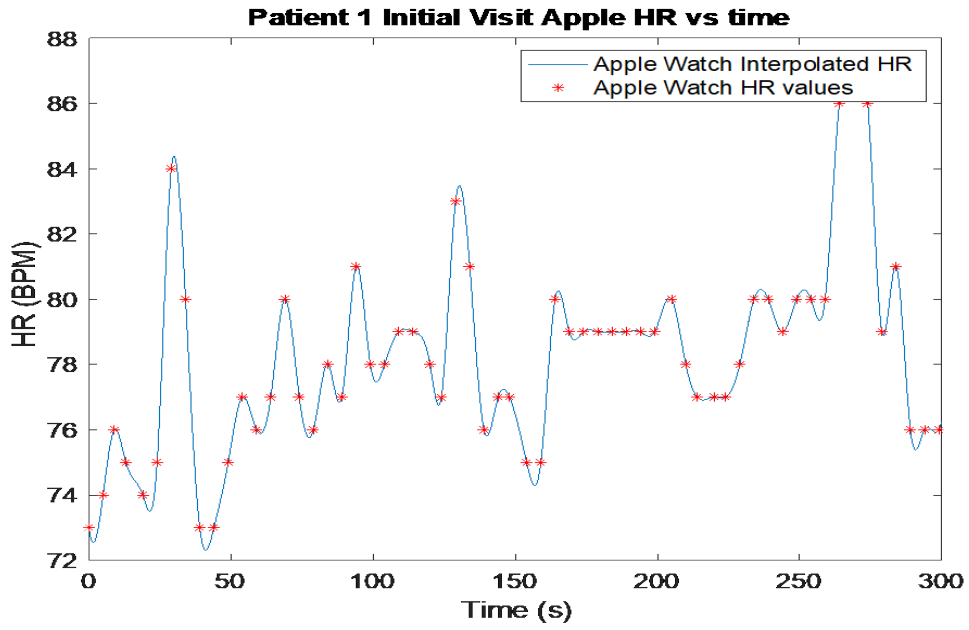


Figure A6. 724: Patient 1 Initial Visit Apple Interpolated HR

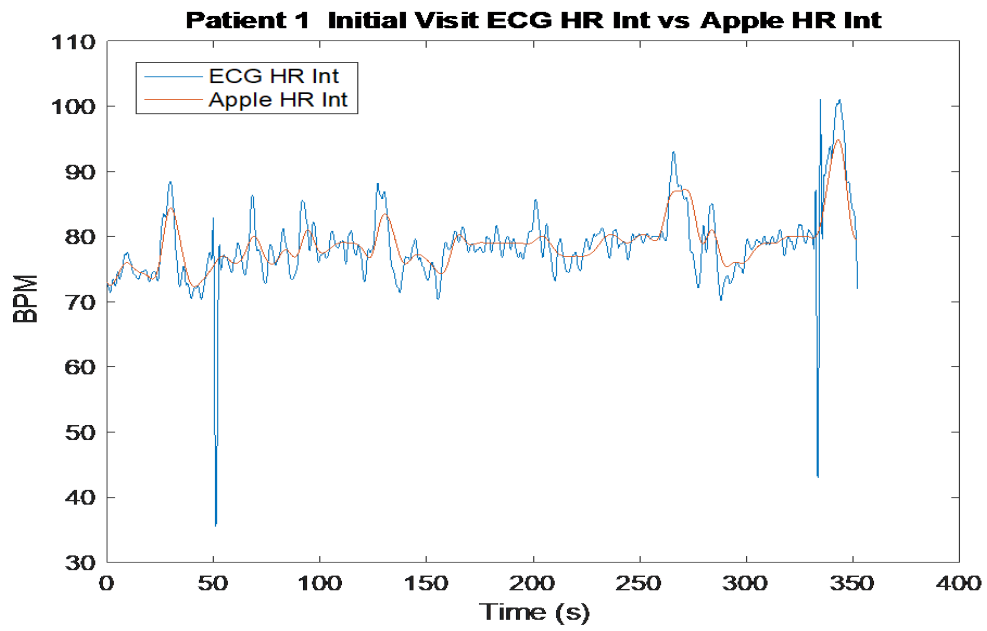


Figure A6. 725: Patient 1 Initial Visit Interpolated ECG and Apple HRs

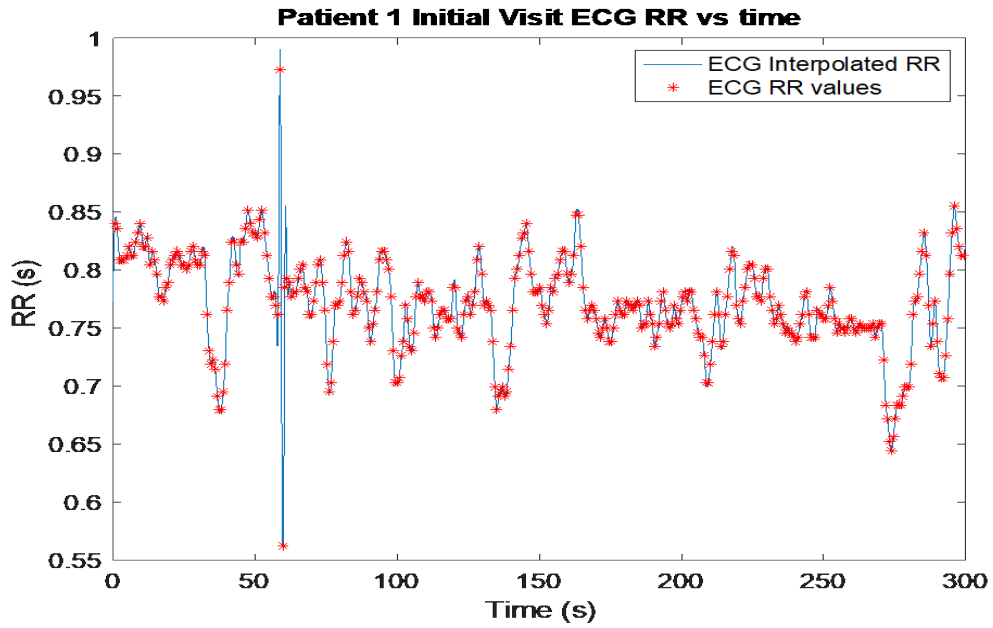


Figure A6. 726: Patient 1 Initial Visit Interpolated ECG RR values

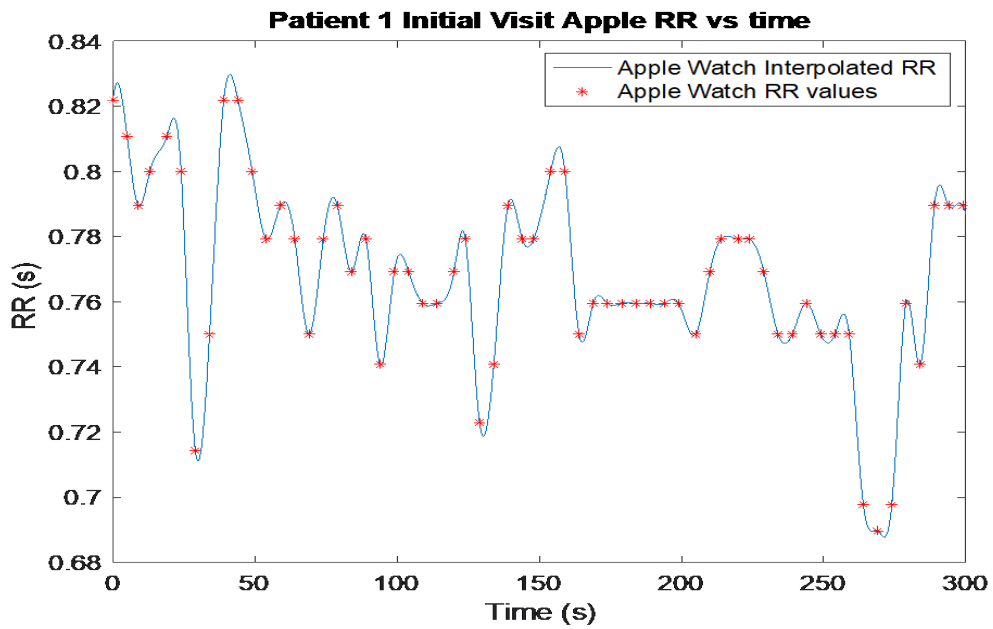


Figure A6. 727: Patient 1 Initial Visit Interpolated RR values

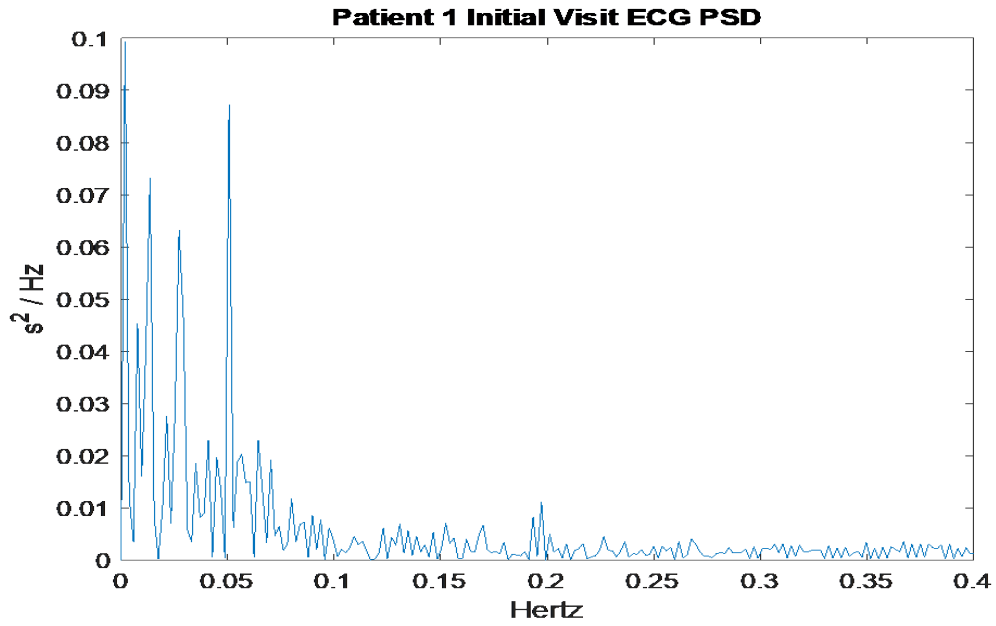


Figure A6. 728: Patient 1 Initial Visit ECG Power Spectral Density

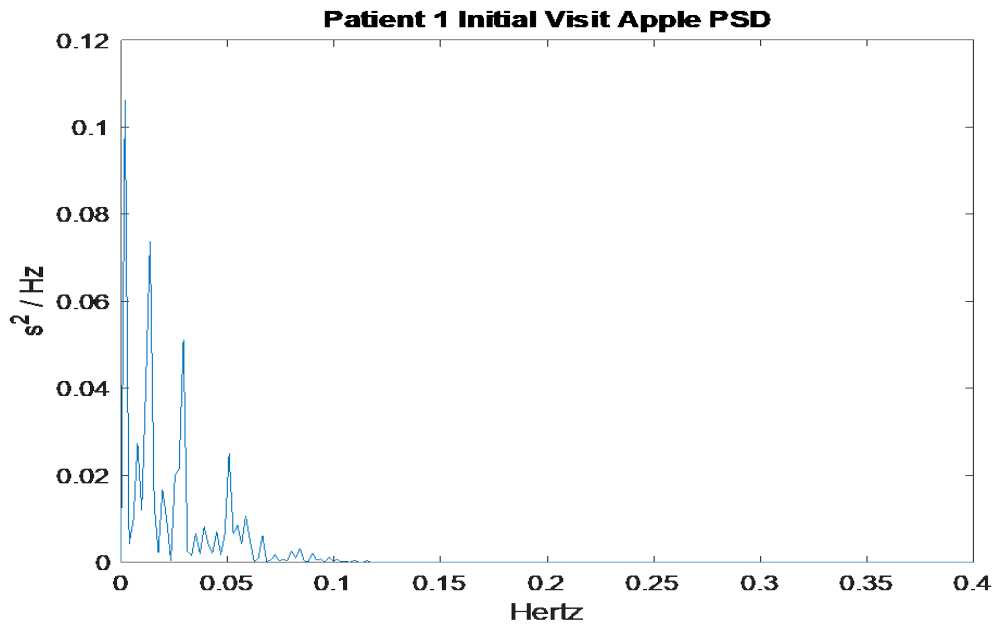


Figure A6. 729: Patient 1 Initial Visit Apple Power Spectral Density



## Patient 1 Exit Visit Readings

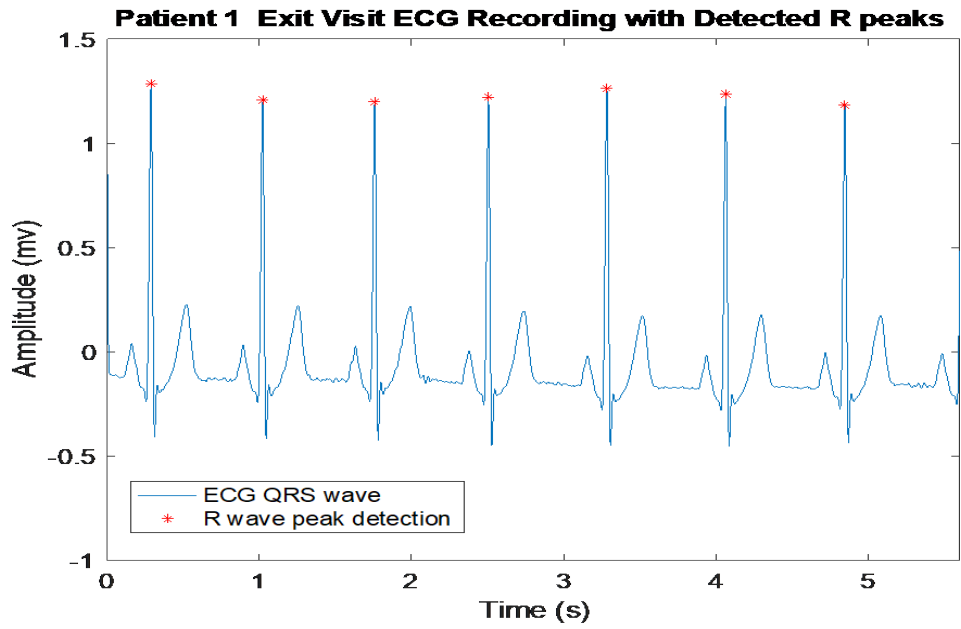


Figure A6. 730: Patient 1 Exit Visit ECG, with detected R peaks

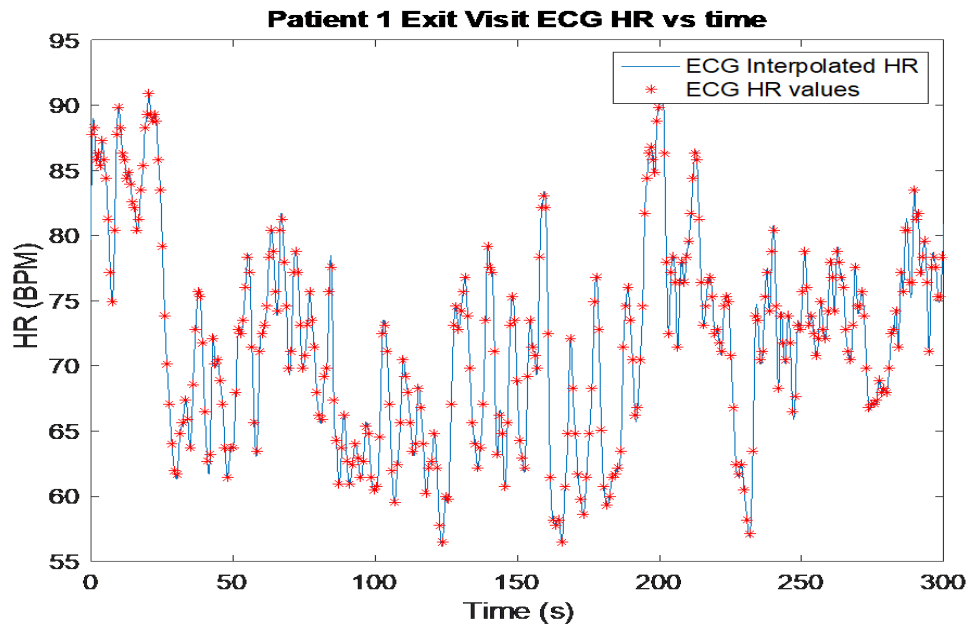


Figure A6. 731: Patient 1 Exit Visit Interpolated ECG HR

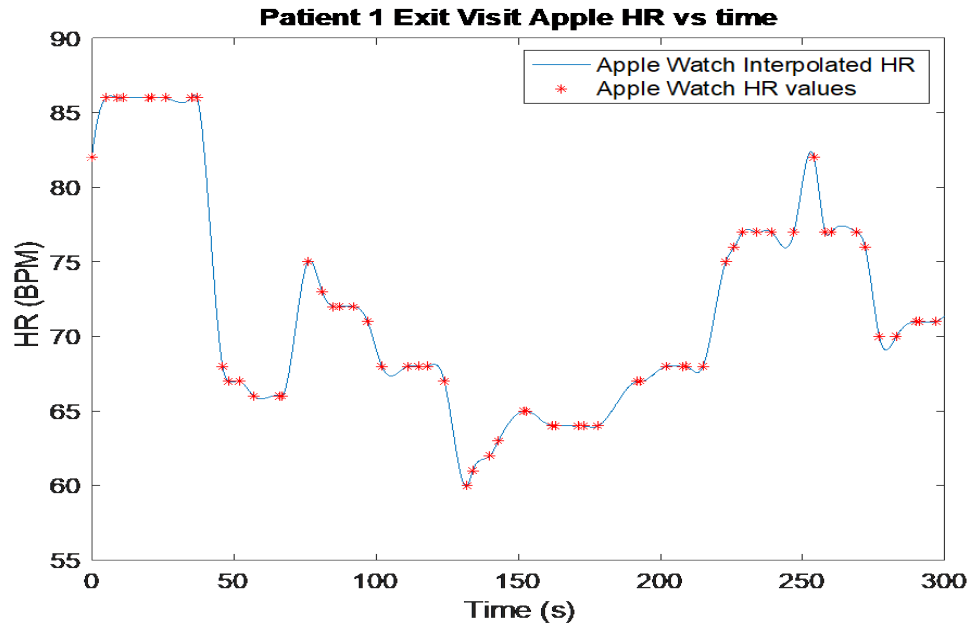


Figure A6. 732: Patient 1 Exit Visit Apple Interpolated HR

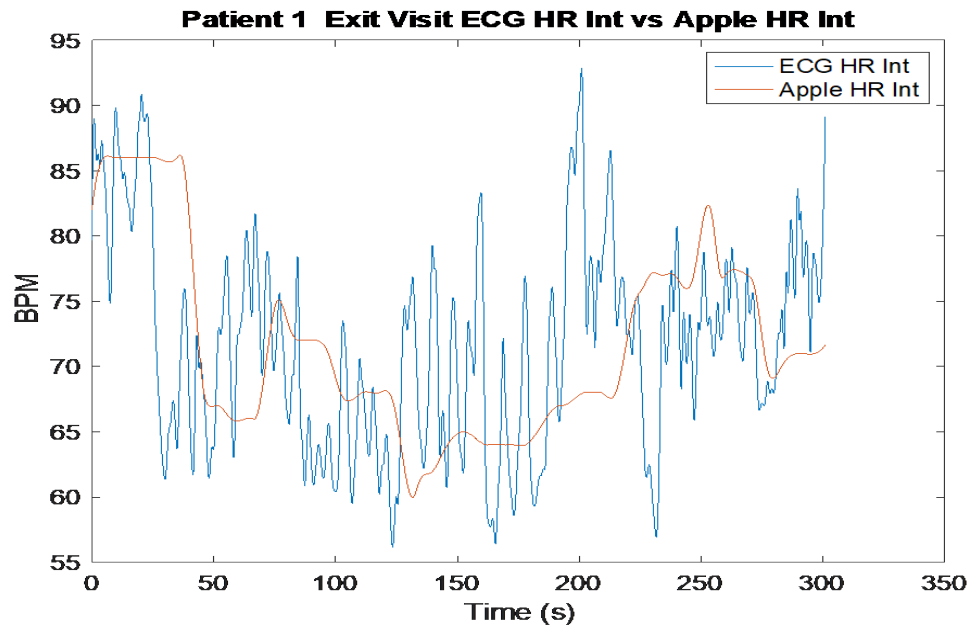


Figure A6. 733: Patient 1 Exit Visit Interpolated ECG and Apple HRs

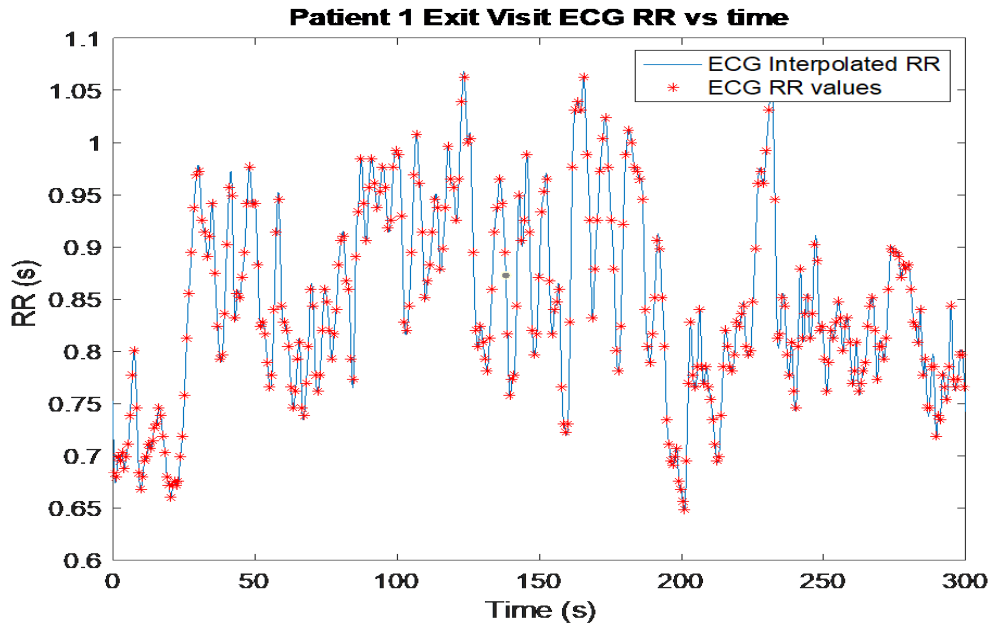


Figure A6. 734: Patient 1 Exit Visit Interpolated ECG RR values

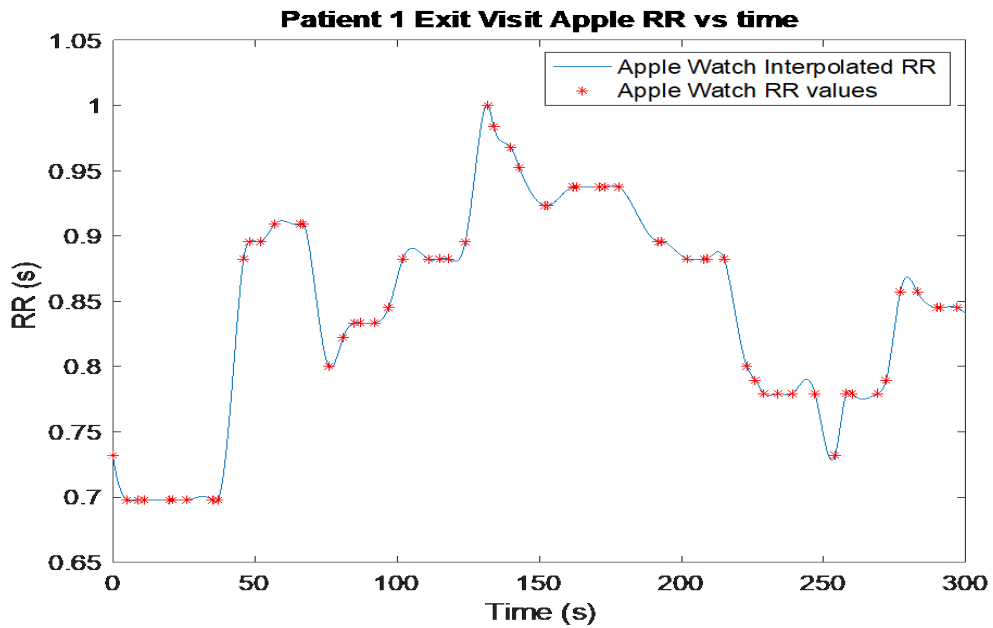


Figure A6. 735: Patient 1 Exit Visit Interpolated RR values

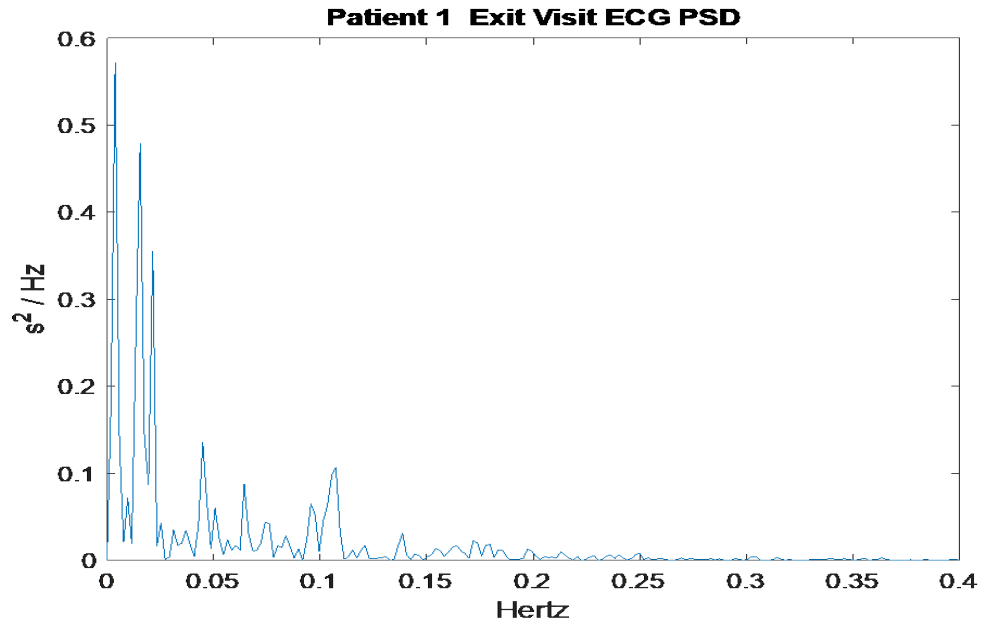


Figure A6. 736: Patient 1 Exit Visit ECG Power Spectral Density

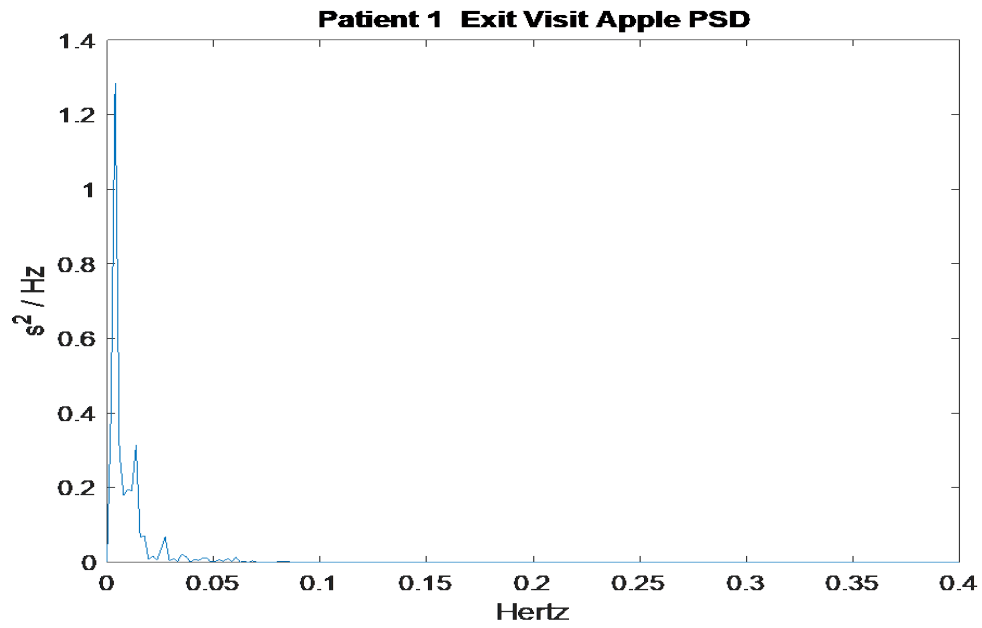


Figure A6. 737: Patient 1 Exit Visit Apple Power Spectral Density

## Patient 2 Initial Visit Readings

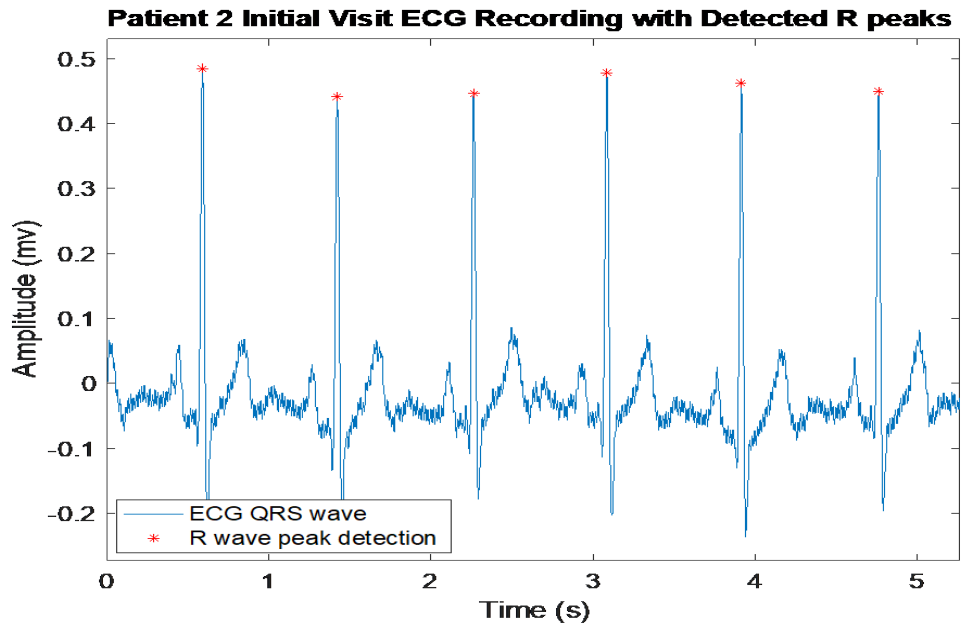


Figure A6. 738: Patient 2 Initial Visit ECG, with detected R peaks

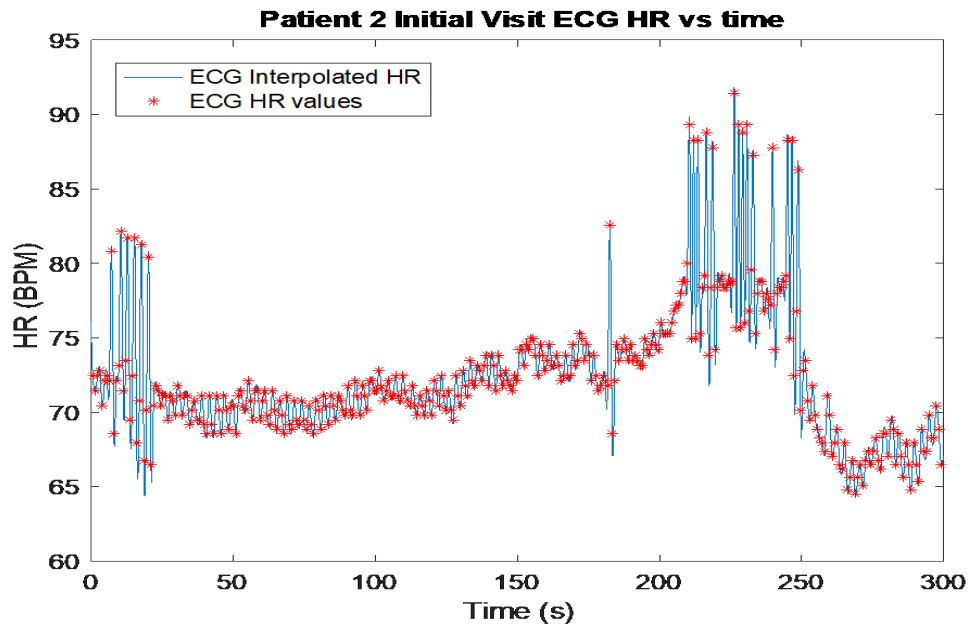


Figure A6. 739: Patient 2 Initial Visit Interpolated ECG HR

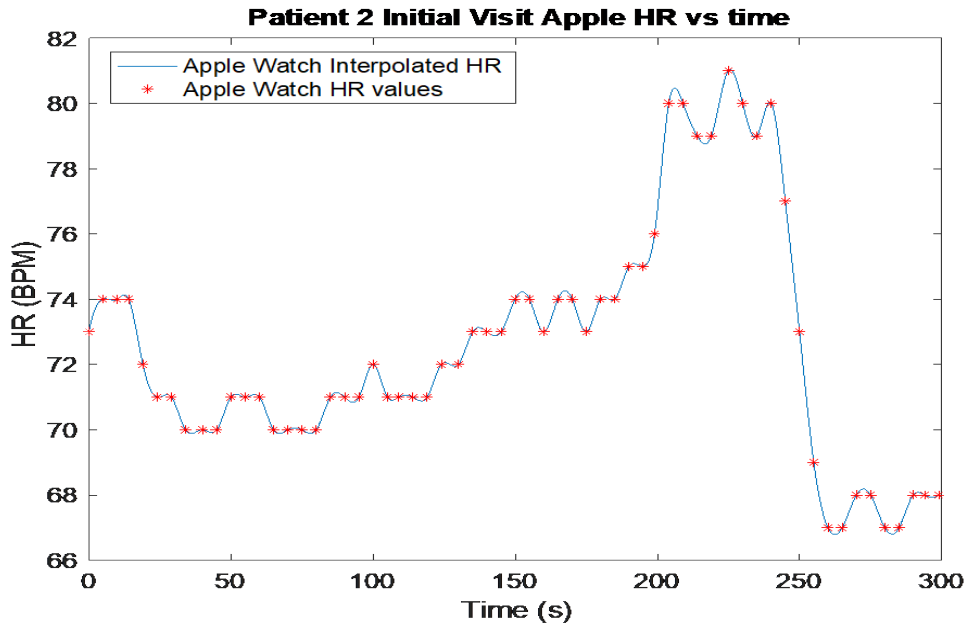


Figure A6. 740: Patient 2 Initial Visit Apple Interpolated HR

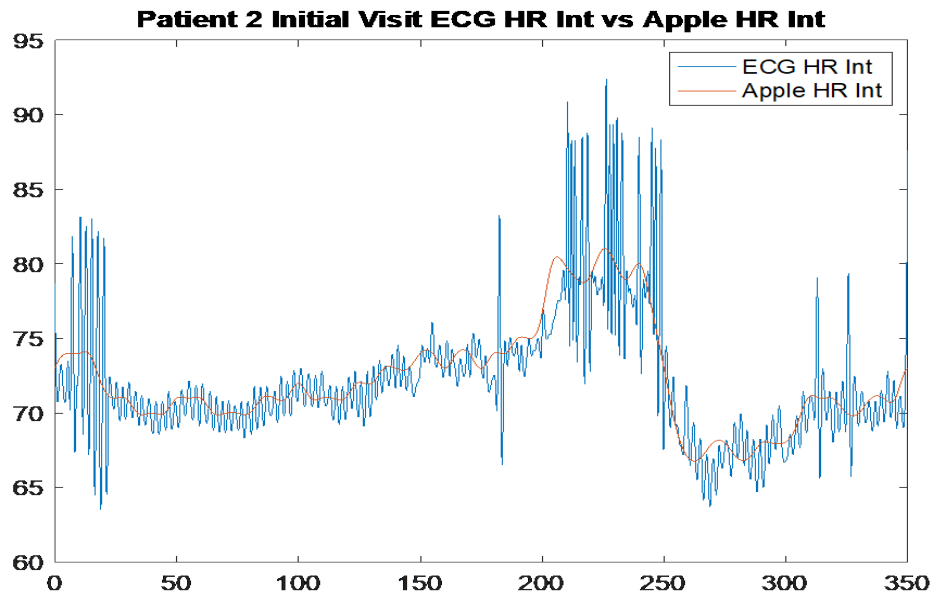


Figure A6. 741: Patient 2 Initial Visit Interpolated ECG and Apple HRs

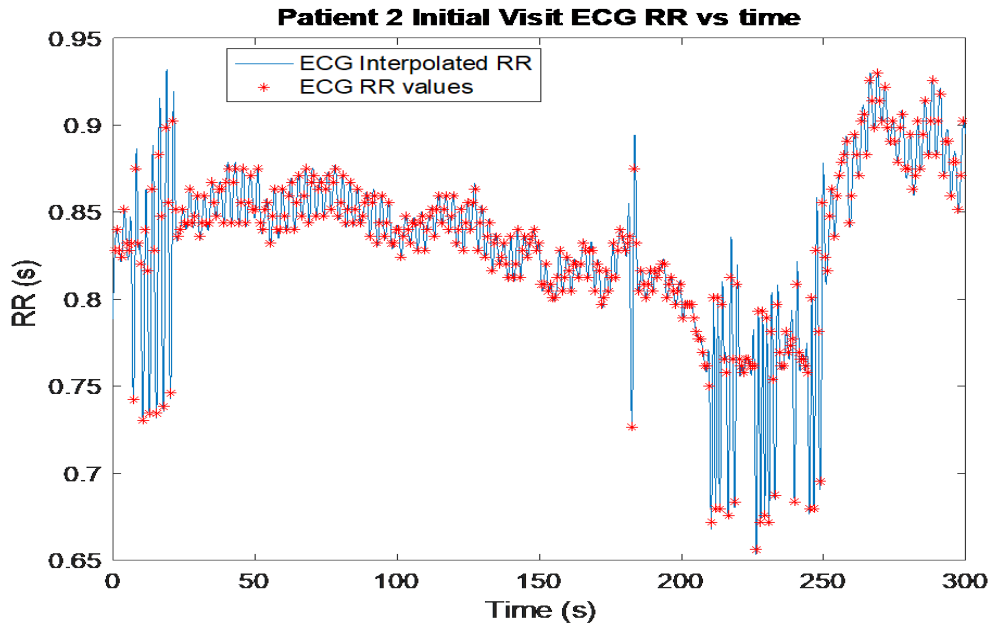


Figure A6. 742: Patient 2 Initial Visit Interpolated ECG RR values

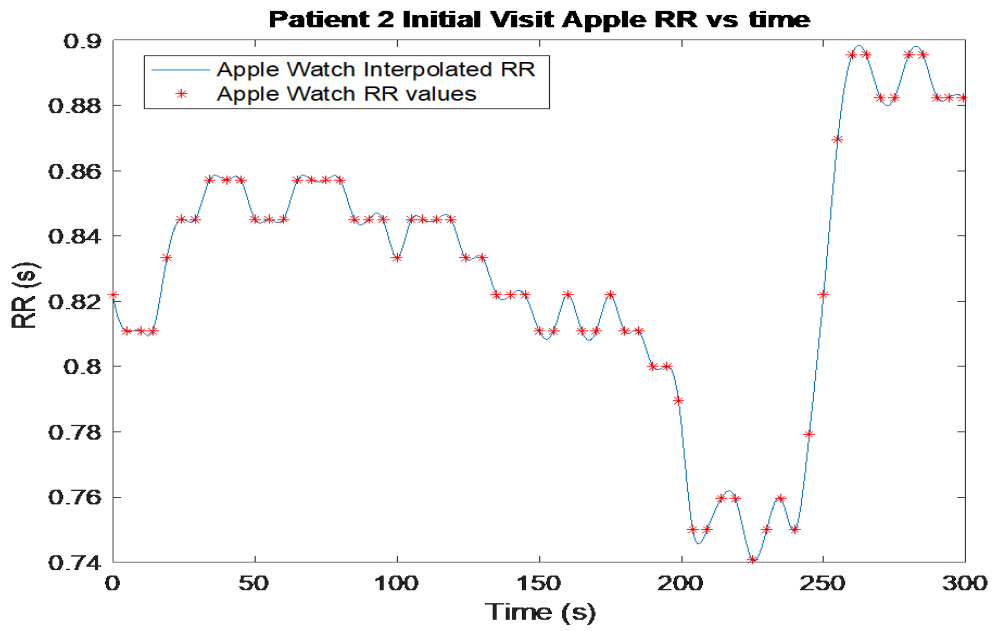


Figure A6. 743: Patient 2 Initial Visit Interpolated Apple RR values

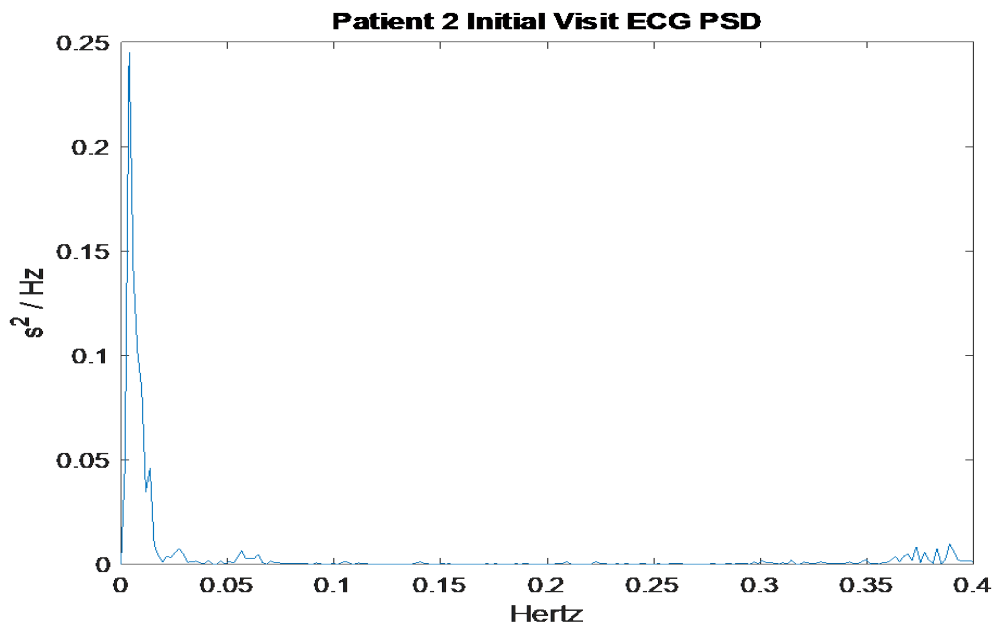


Figure A6. 744: Patient 2 Initial Visit ECG Power Spectral Density

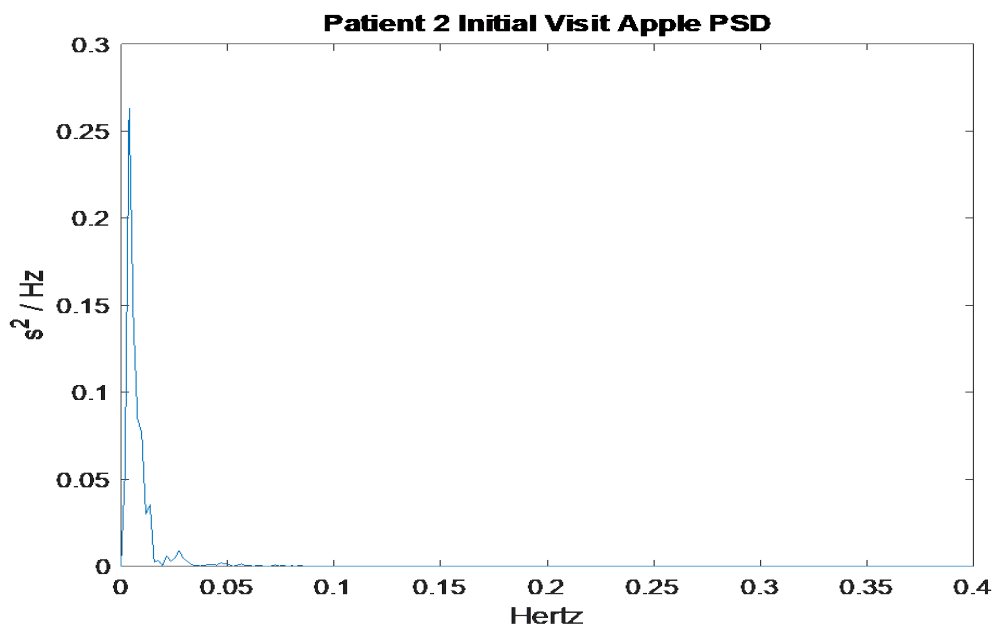


Figure A6. 745: Patient 2 Initial Visit Apple Power Spectral Density



## Patient 2 Exit Visit Readings

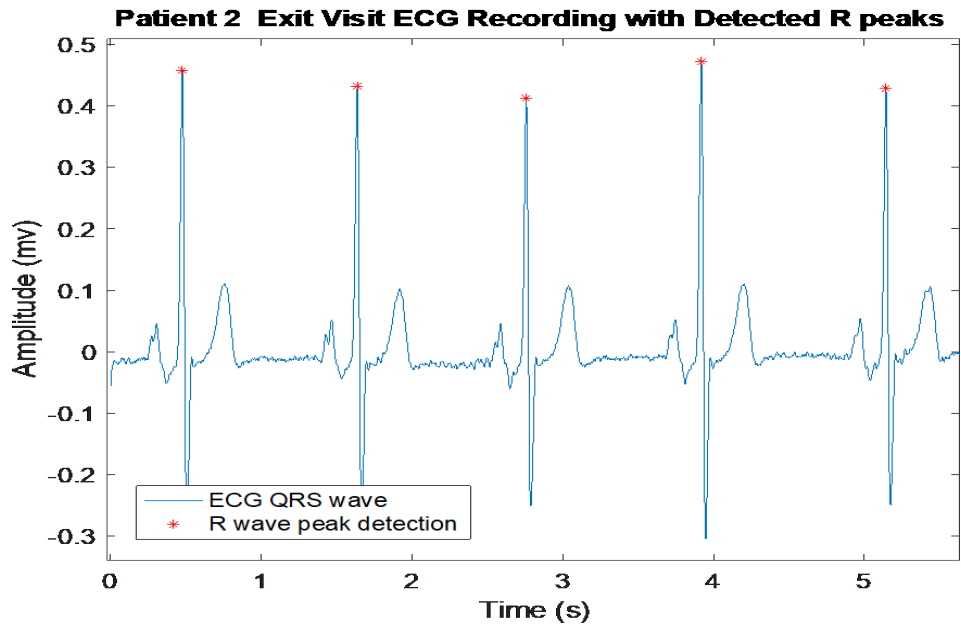


Figure A6. 746: Patient 2 Exit Visit ECG, with detected R peaks

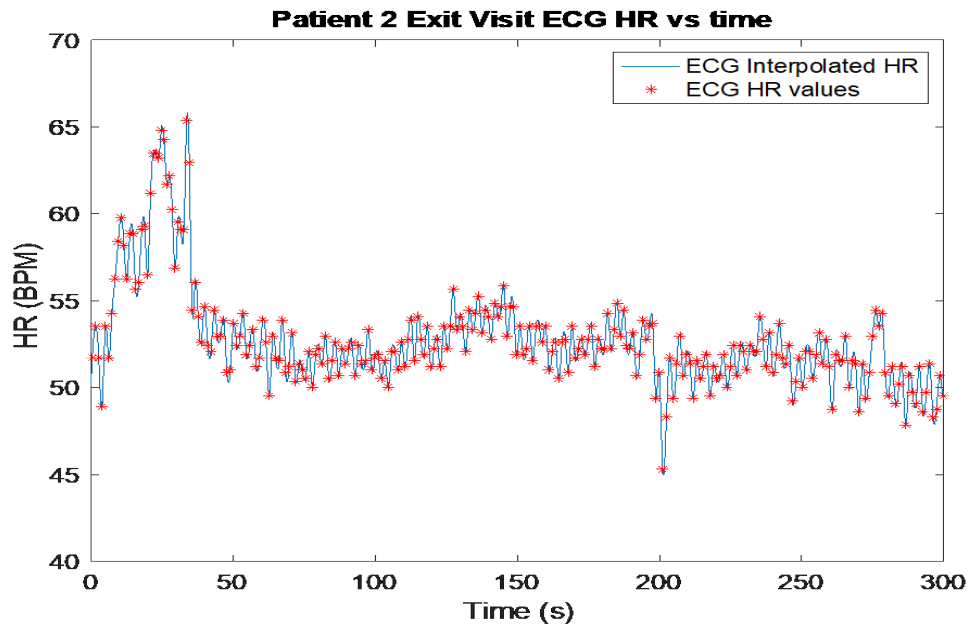


Figure A6. 747: Patient 2 Exit Visit Interpolated ECG HR

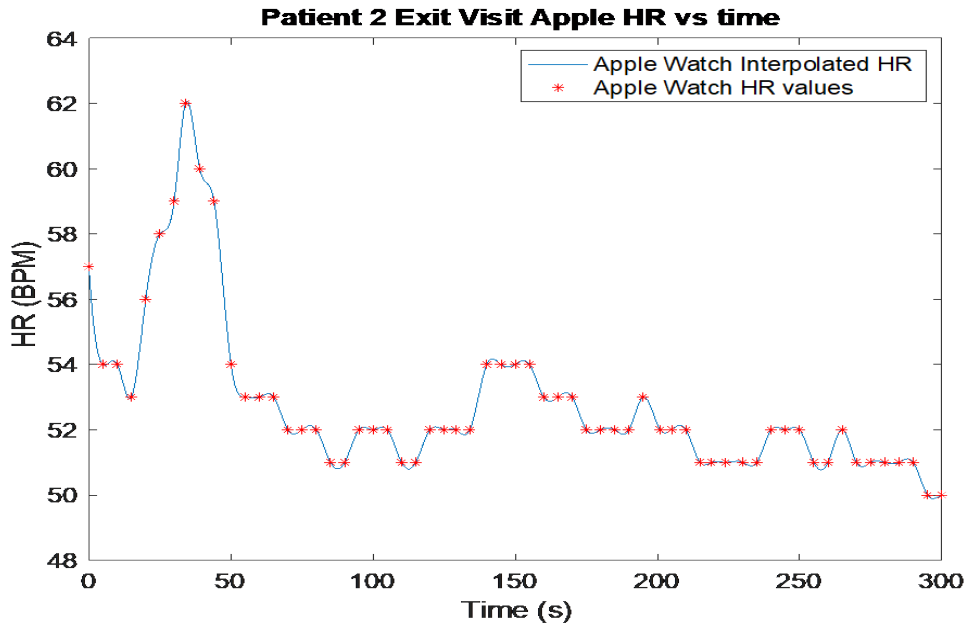


Figure A6. 748: Patient 2 Exit Visit Apple Interpolated HR

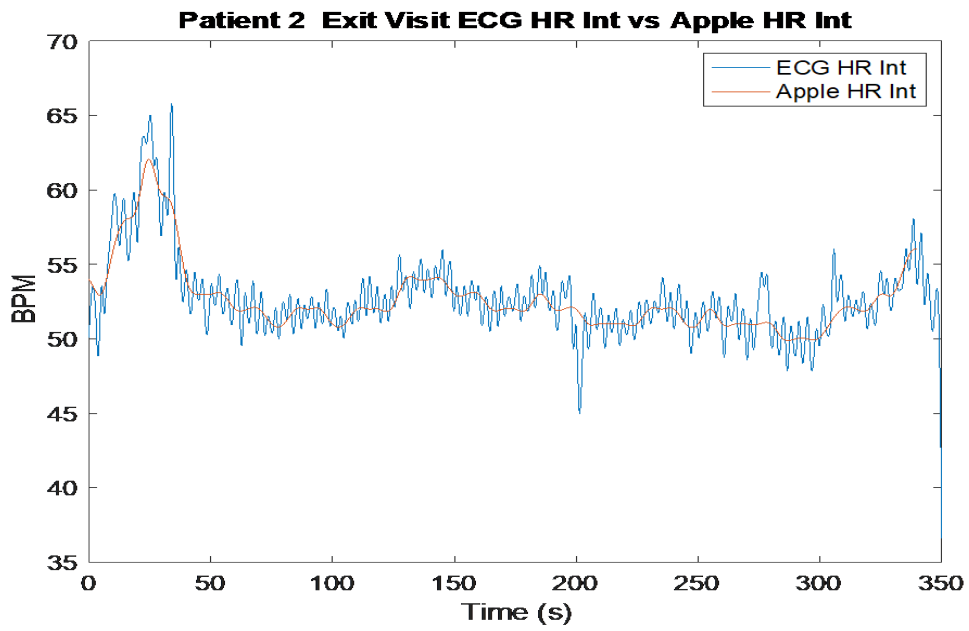


Figure A6. 749: Patient 2 Exit Visit Interpolated ECG and Apple HRs

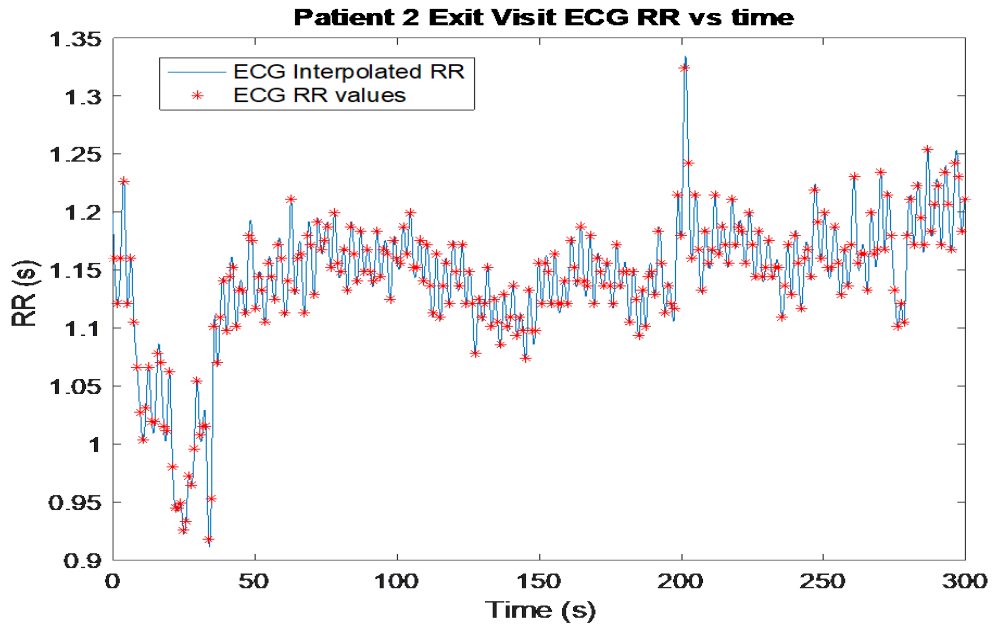


Figure A6. 750: Patient 2 Exit Visit Interpolated ECG RR values

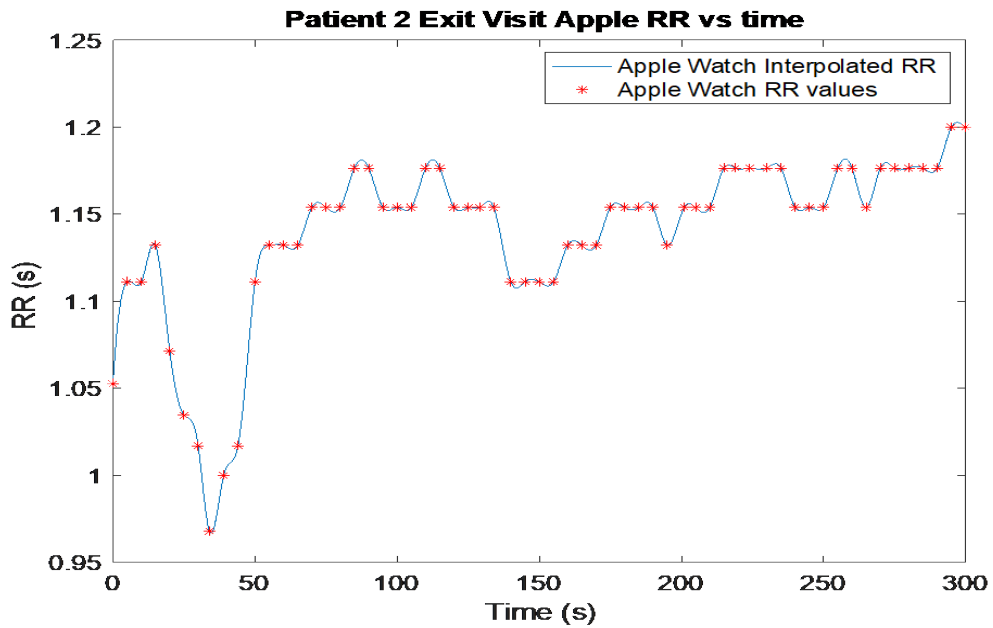


Figure A6. 751: Patient 2 Exit Visit Interpolated Apple RR values

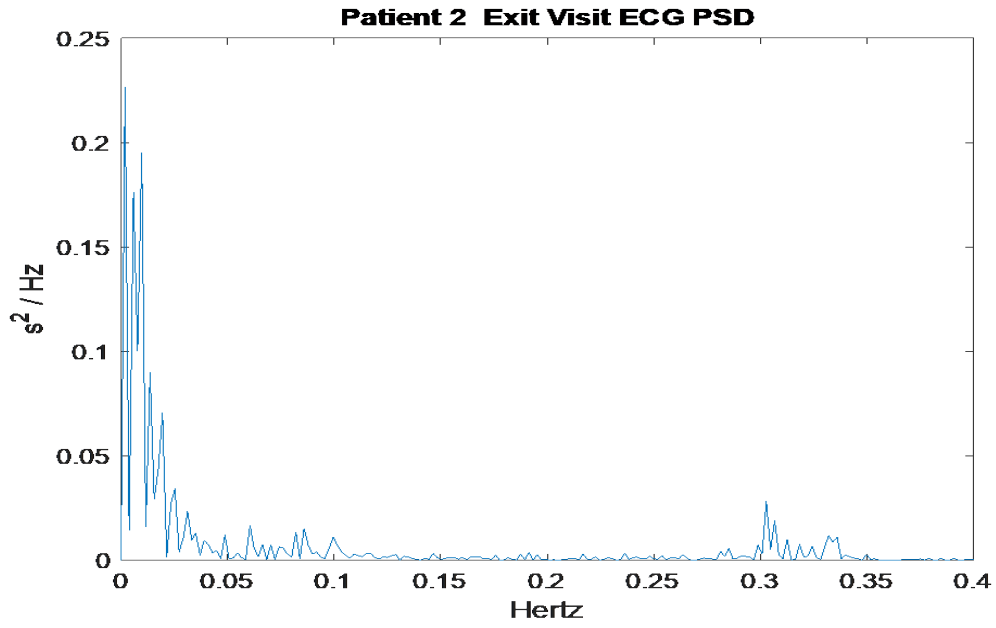


Figure A6. 752: Patient 2 Exit Visit ECG Power Spectral Density

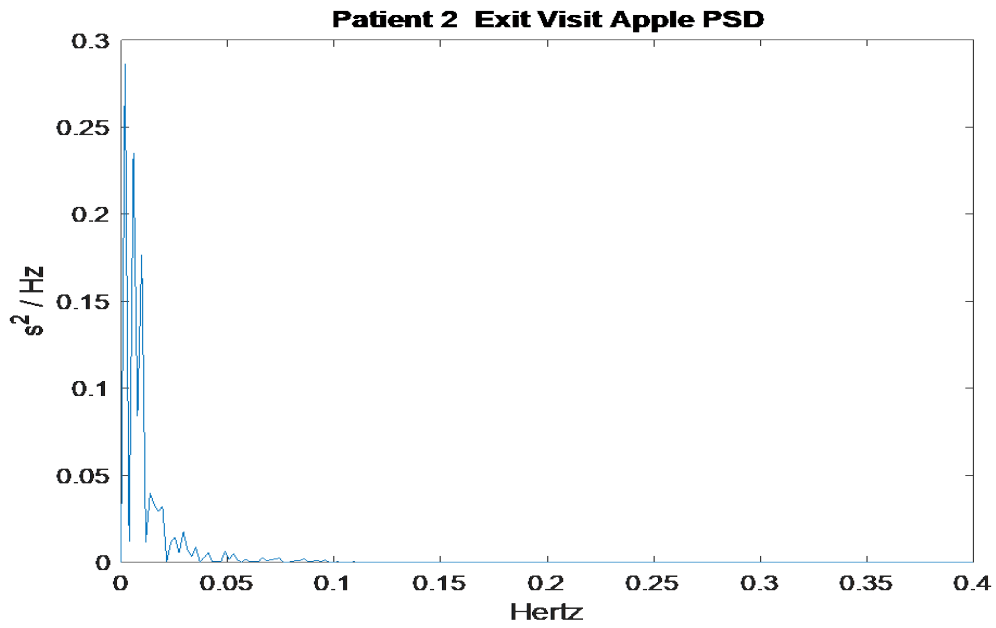


Figure A6. 753: Patient 2 Exit Visit Apple Power Spectral Density

## Patient 3 Initial Visit Readings

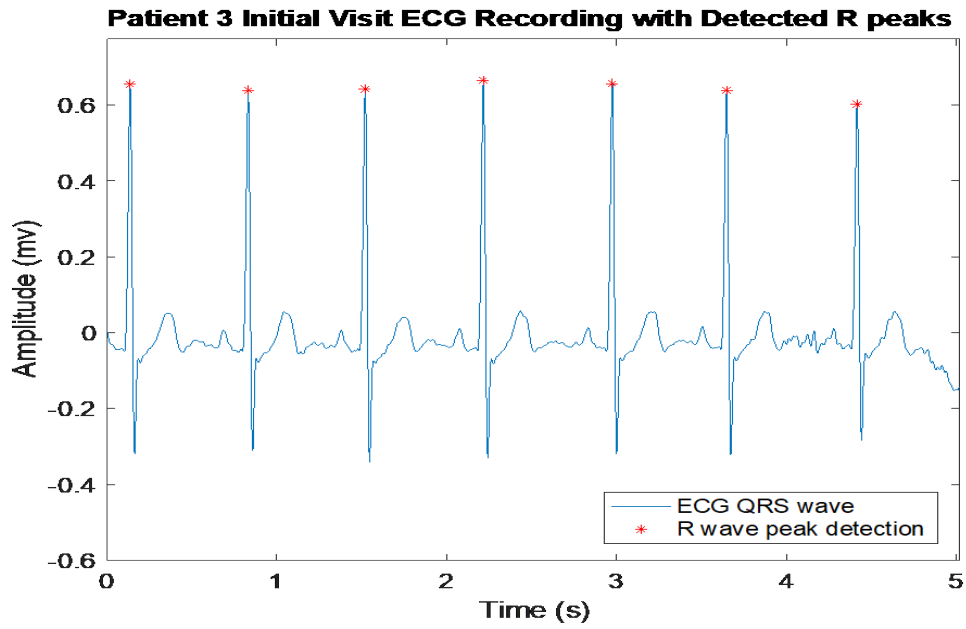


Figure A6. 754: Patient 3 Initial Visit ECG, with detected R peaks

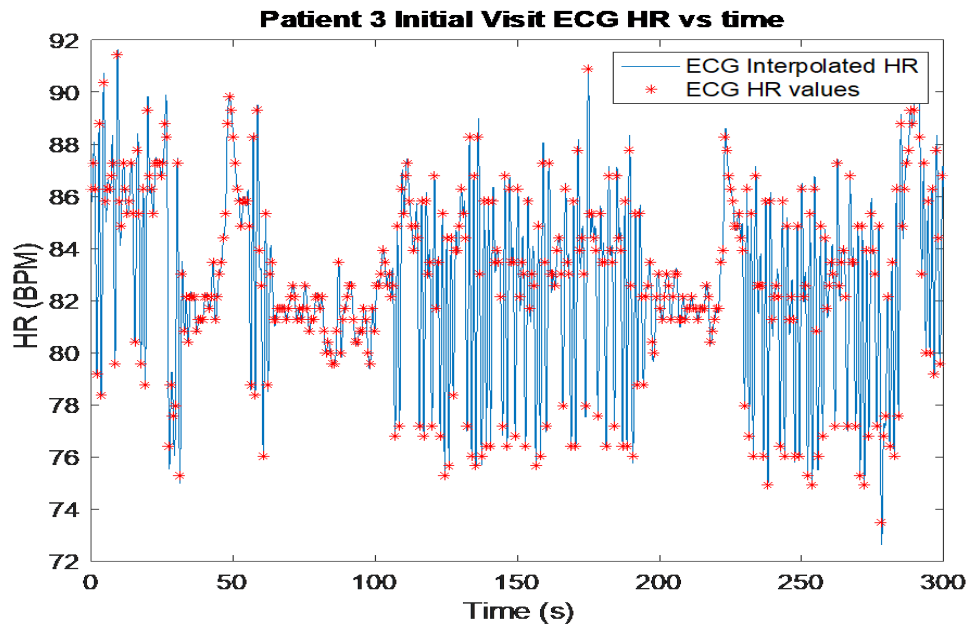


Figure A6. 755: Patient 3 Initial Visit Interpolated ECG HR

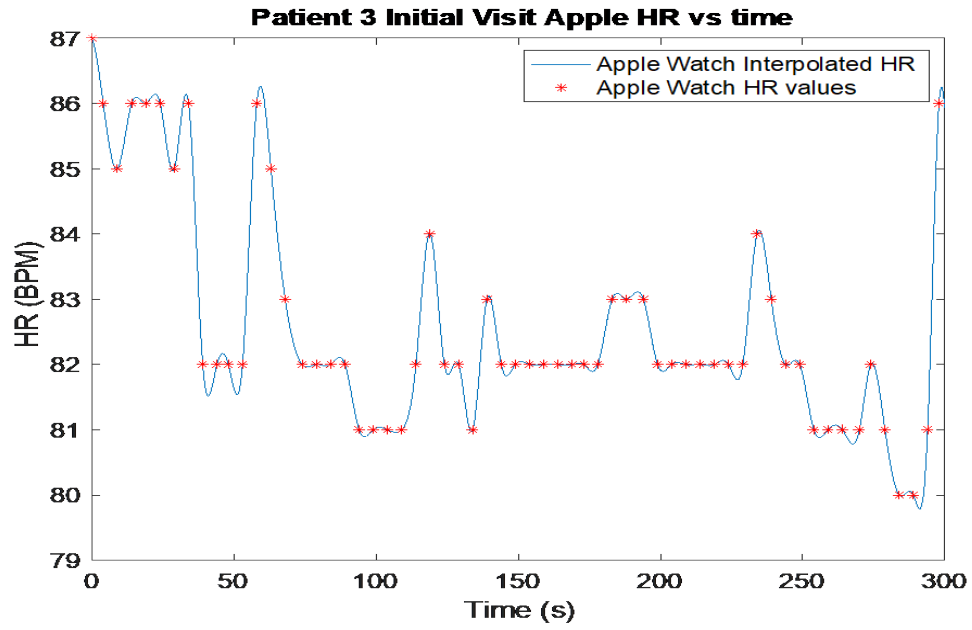


Figure A6. 756: Patient 3 Initial Visit Apple Interpolated HR

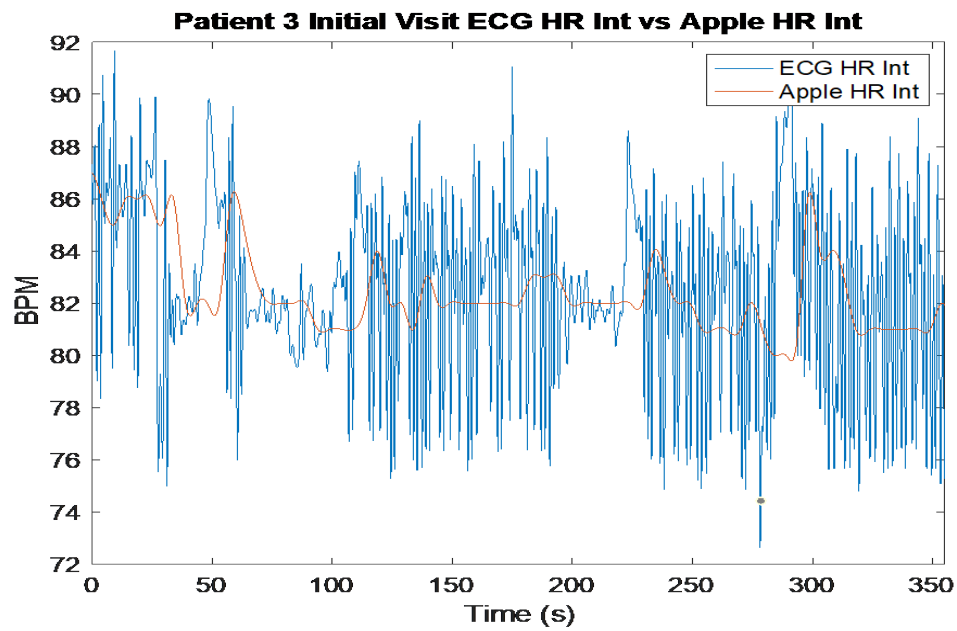


Figure A6. 757: Patient 3 Initial Visit Interpolated ECG and Apple HRs

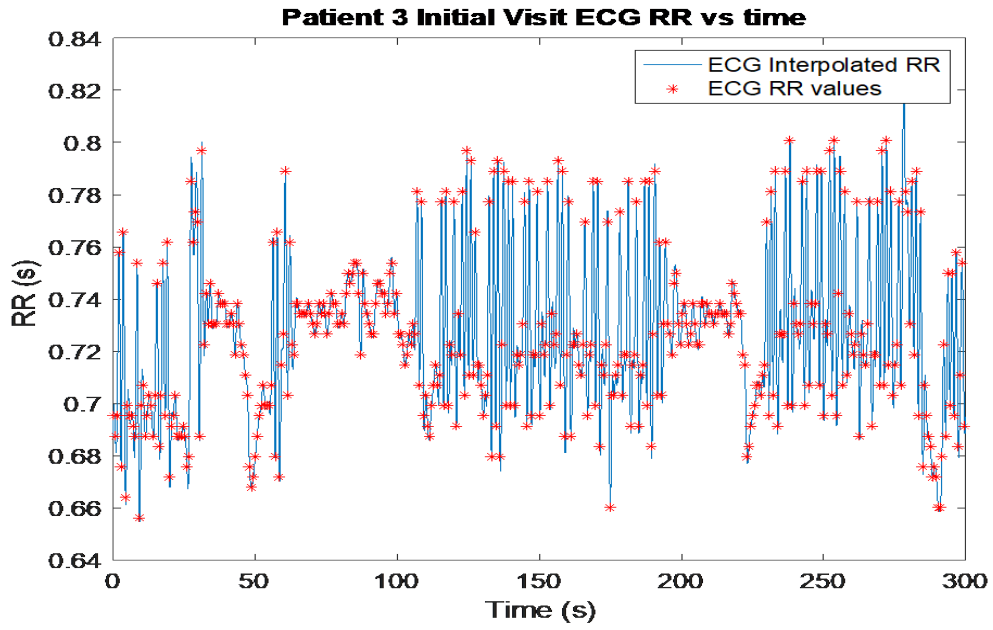


Figure A6. 758: Patient 3 Initial Visit Interpolated ECG RR values

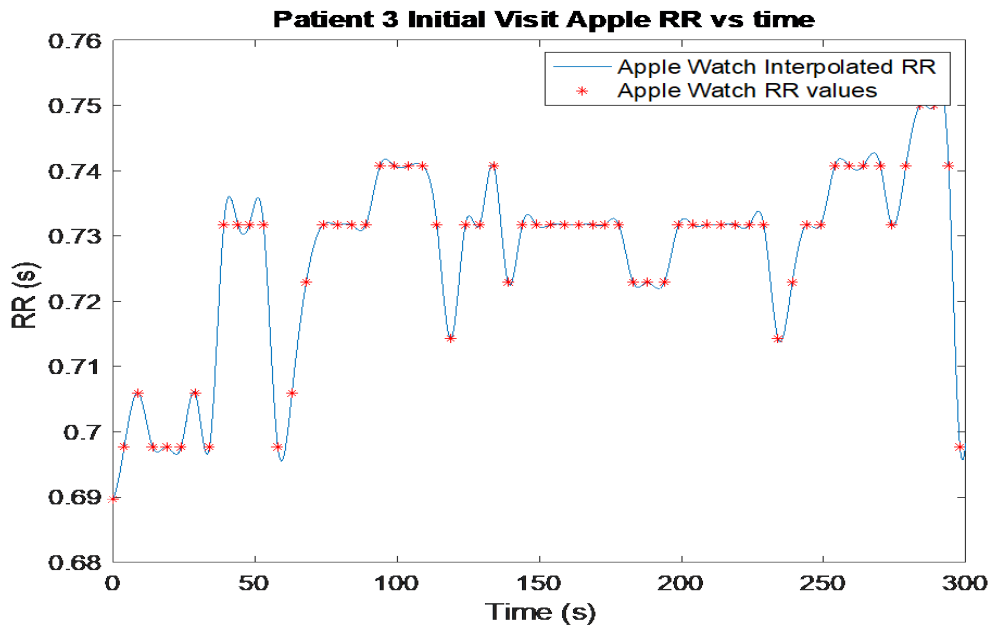


Figure A6. 759: Patient 3 Initial Visit Interpolated Apple RR values

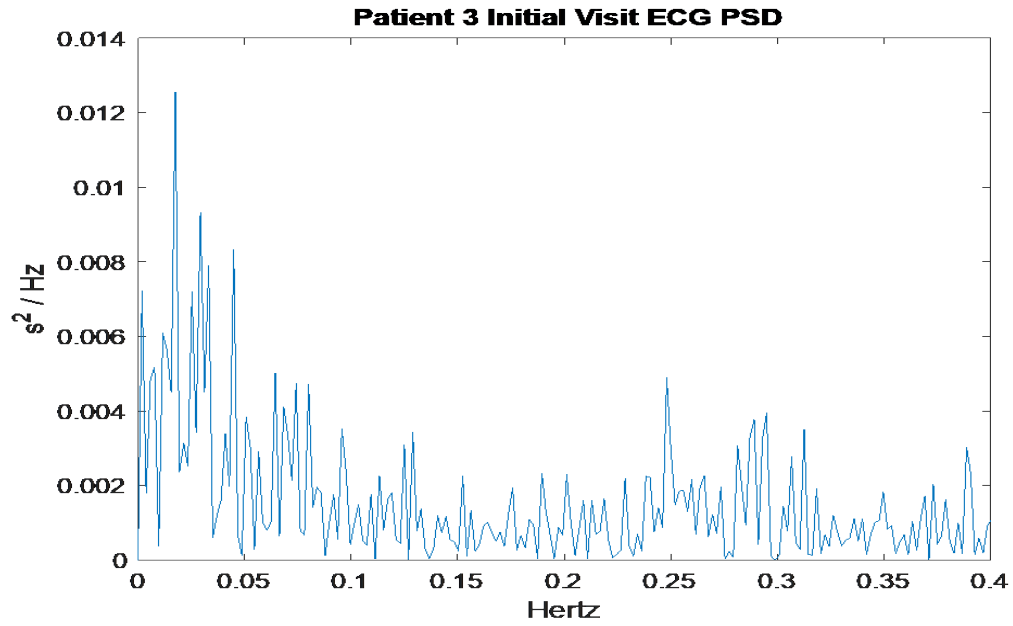


Figure A6. 760: Patient 3 Initial Visit ECG Power Spectral Density

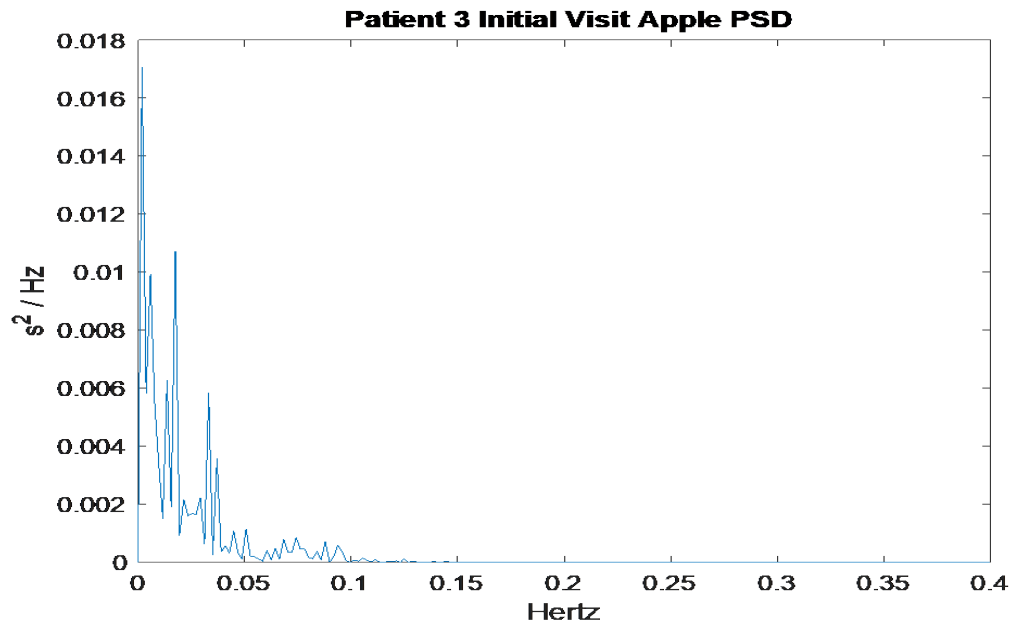


Figure A6. 761: Patient 3 Initial Visit Apple Power Spectral Density



## Patient 3 Exit Visit Readings

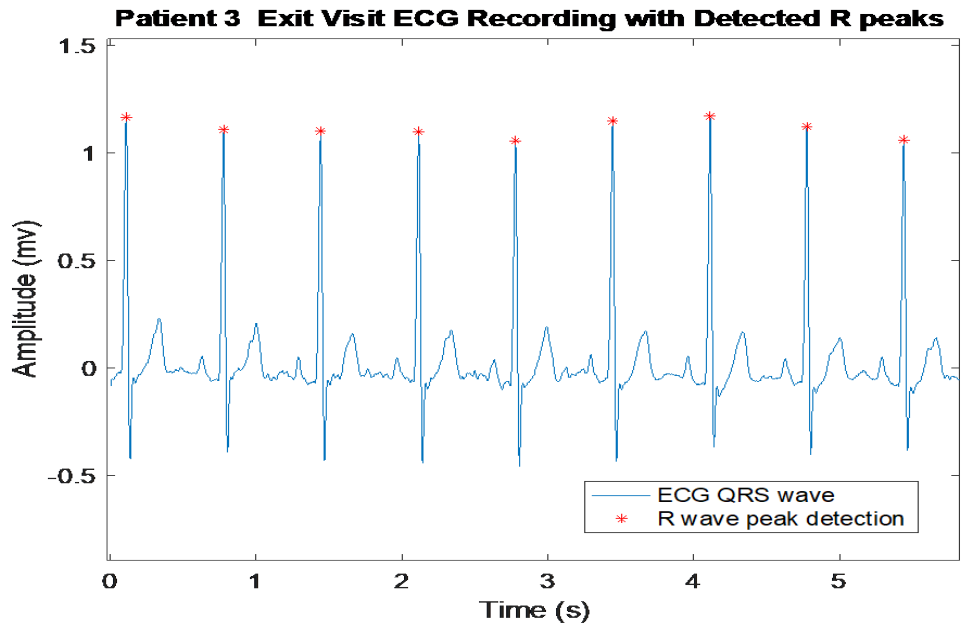


Figure A6. 762: Patient 3 Exit Visit ECG, with detected R peaks

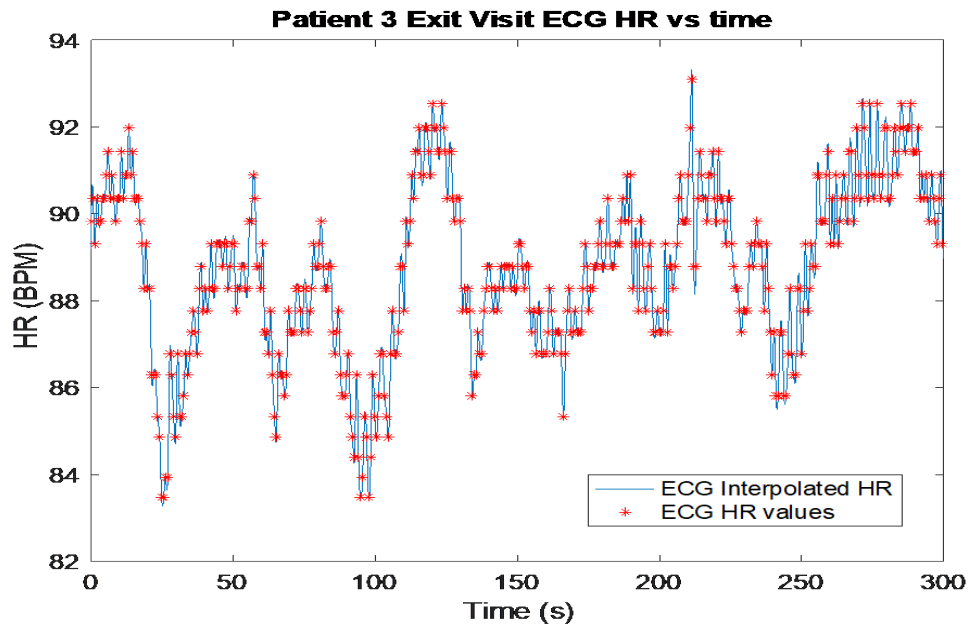


Figure A6. 763: Patient 3 Exit Visit Interpolated ECG HR

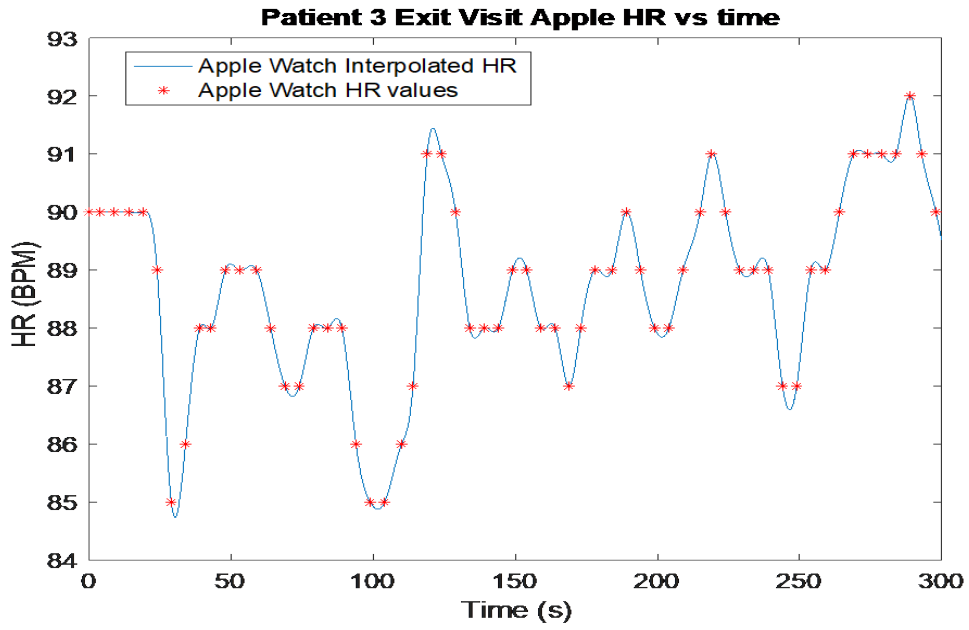


Figure A6. 764: Patient 3 Exit Visit Apple Interpolated HR

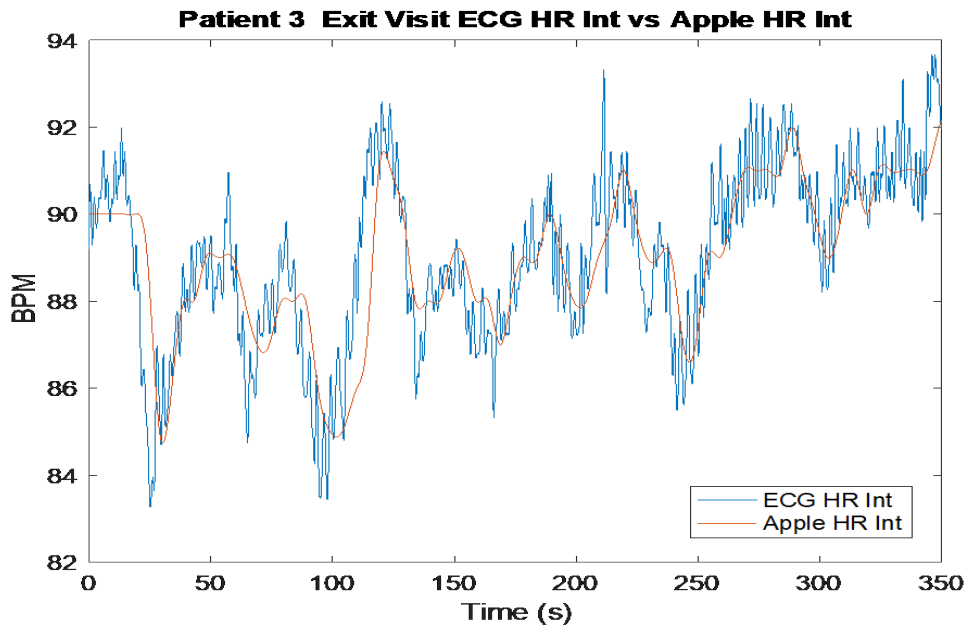


Figure A6. 765: Patient 3 Exit Visit Interpolated ECG and Apple HRs

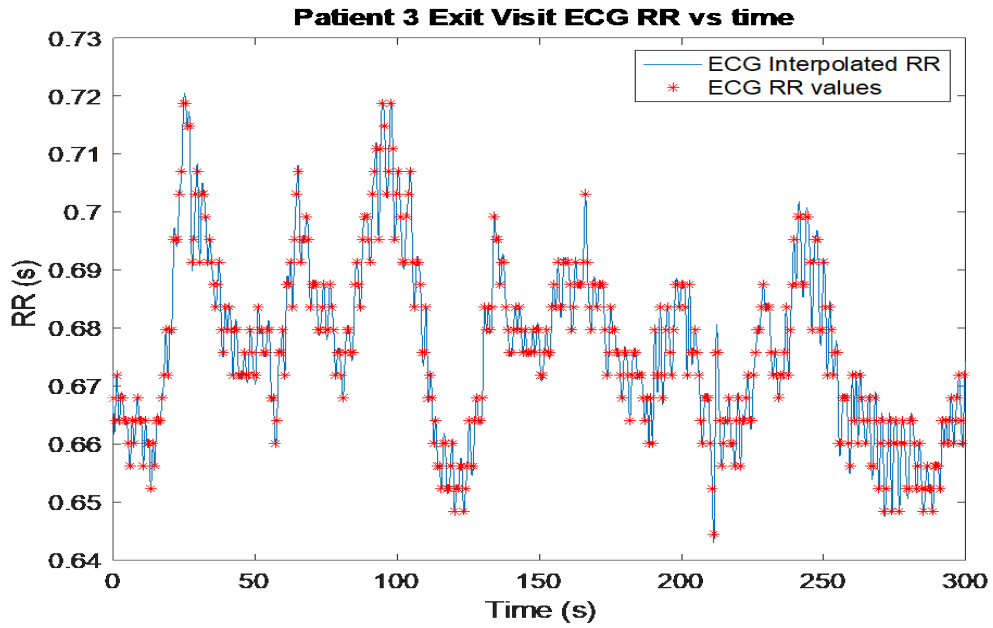


Figure A6. 766: Patient 3 Exit Visit Interpolated ECG RR values

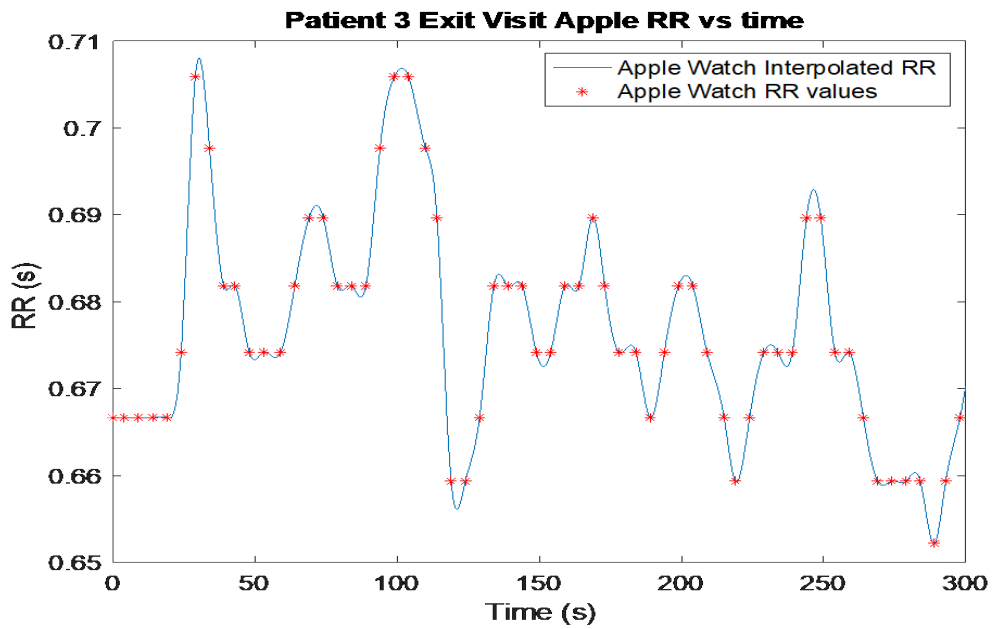


Figure A6. 767: Patient 3 Exit Visit Interpolated Apple RR values

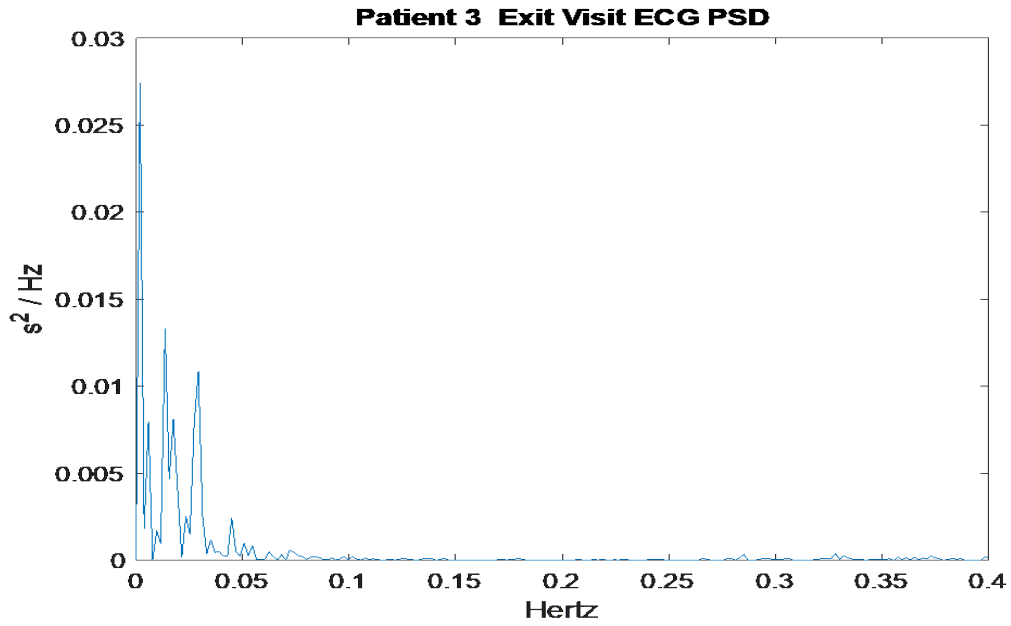


Figure A6. 768: Patient 3 Exit Visit ECG Power Spectral Density

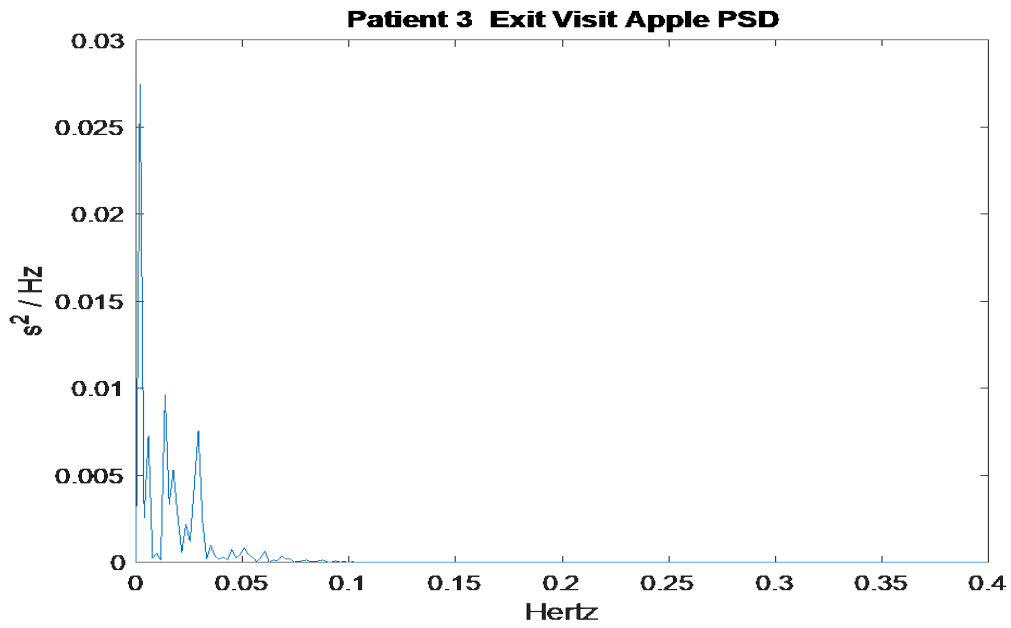


Figure A6. 769: Patient 3 Exit Visit Apple Power Spectral Density

## Patient 4 Initial Visit Readings

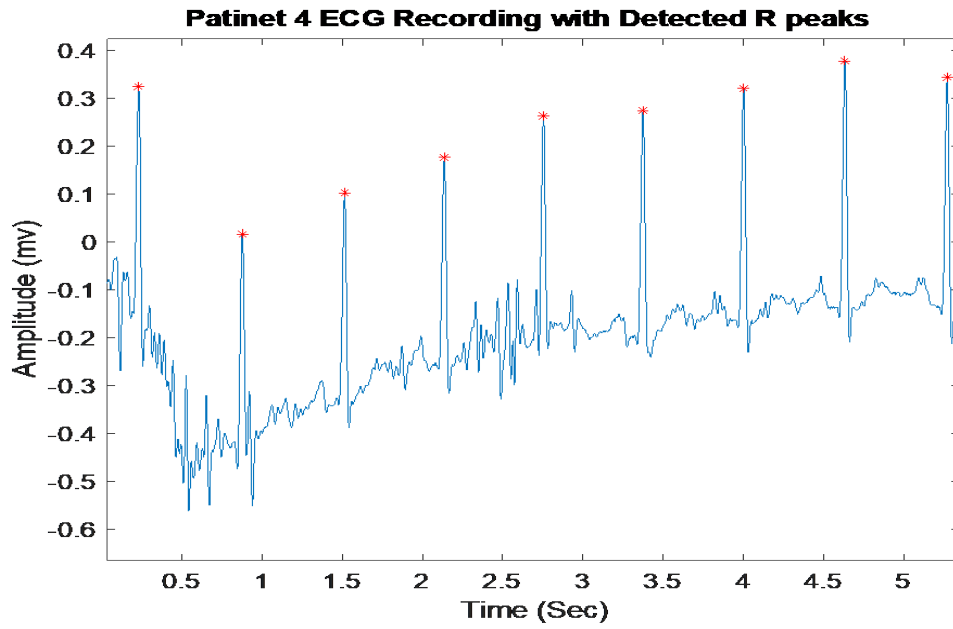


Figure A6. 770: Patient 4 Initial Visit ECG, with detected R peaks

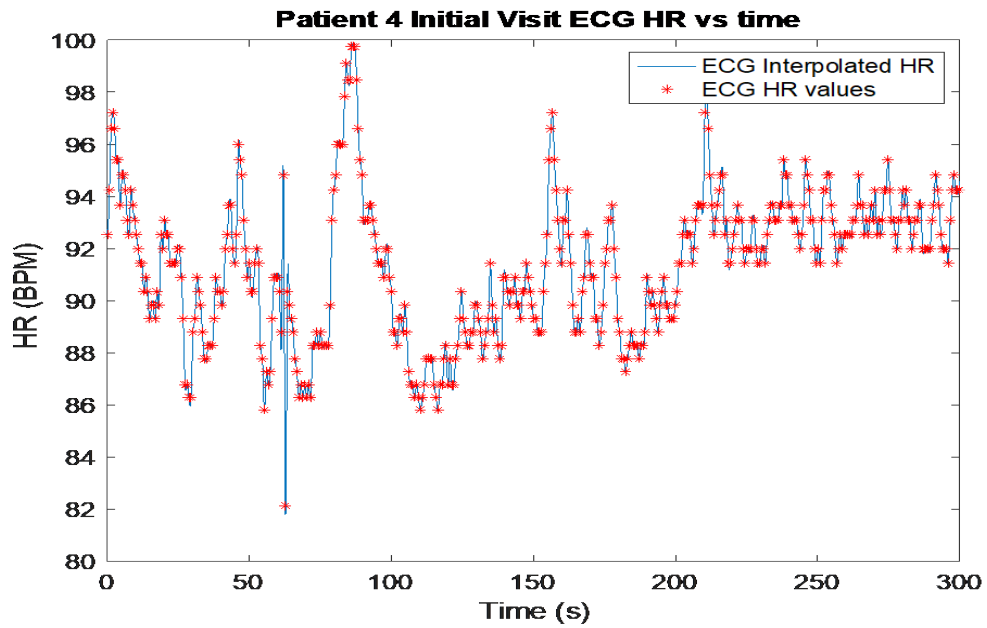


Figure A6. 771: Patient 4 Initial Visit Interpolated ECG HR

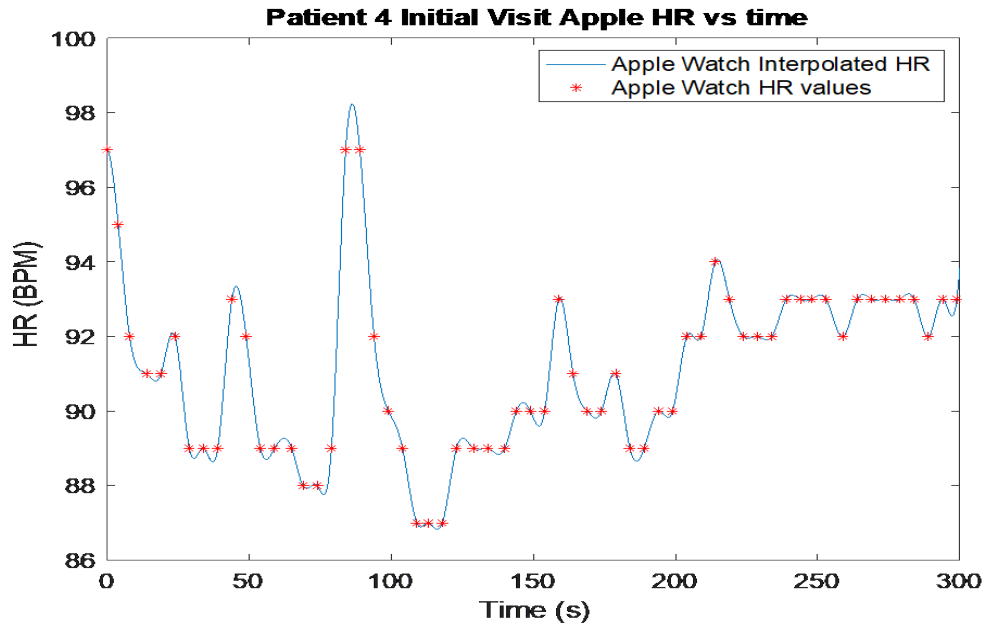


Figure A6. 772: Patient 4 Initial Visit Apple Interpolated HR

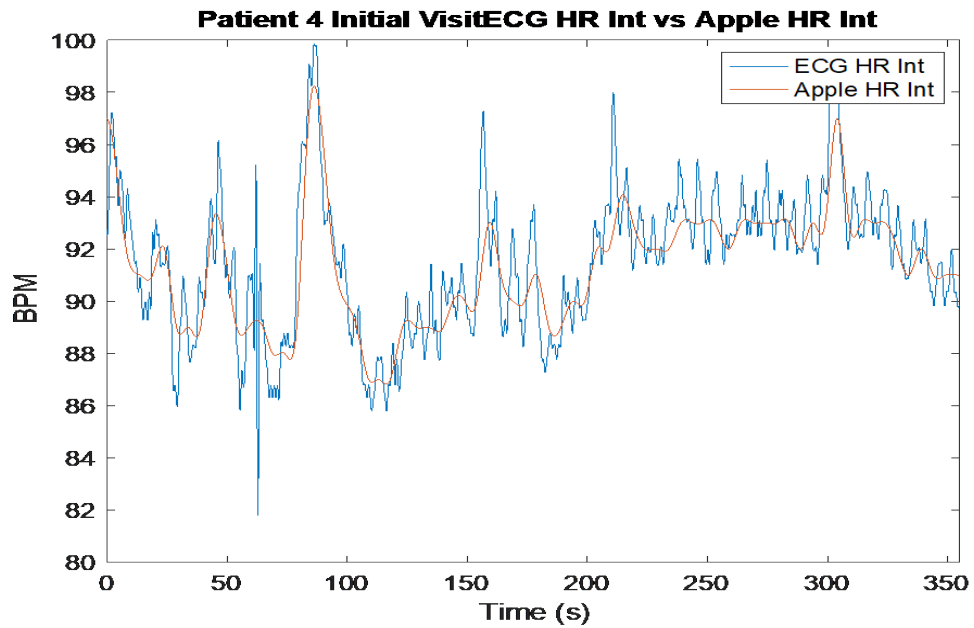


Figure A6. 773: Patient 4 Initial Visit Interpolated ECG and Apple HRs

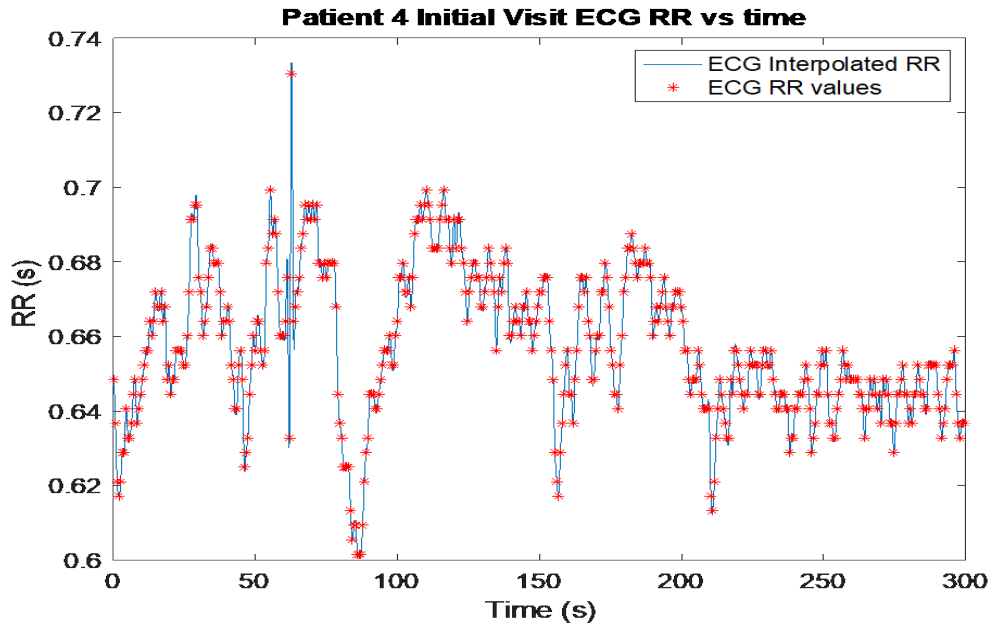


Figure A6. 774: Patient 4 Initial Visit Interpolated ECG RR values

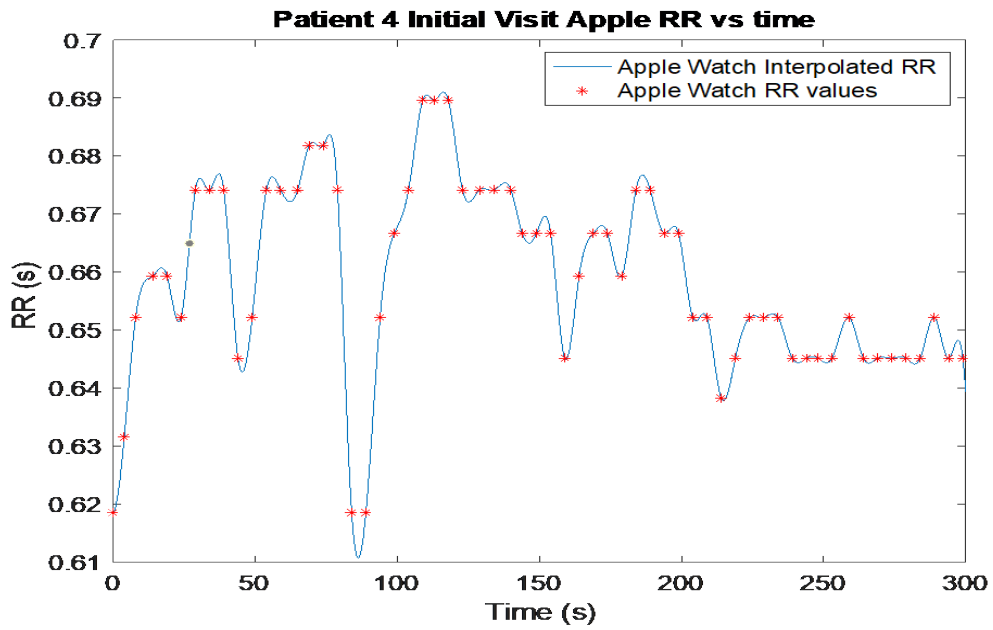


Figure A6. 775: Patient 4 Initial Visit Interpolated Apple RR values

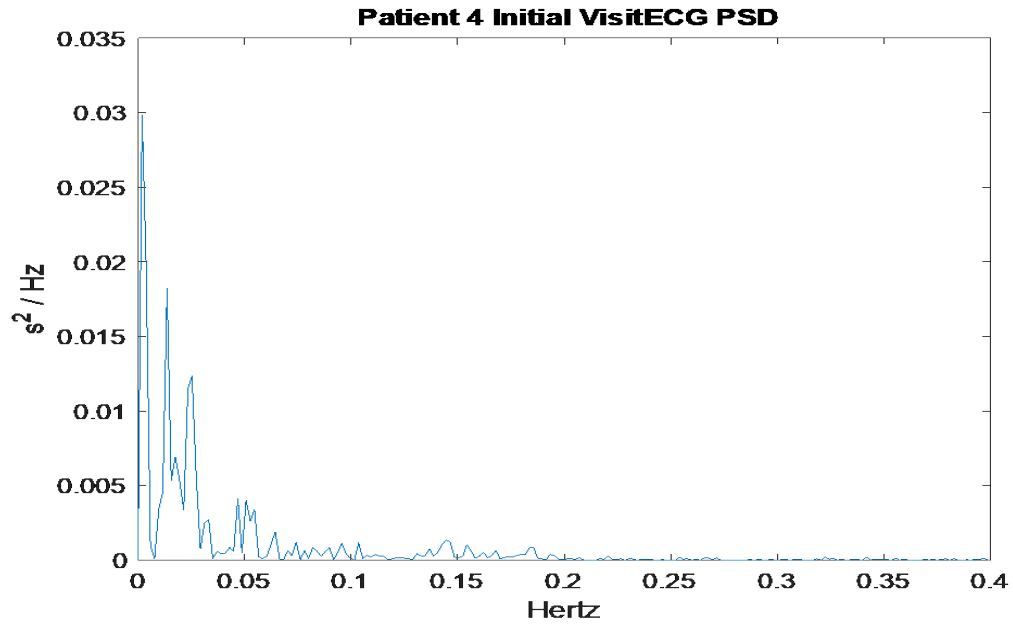


Figure A6. 776: Patient 4 Initial Visit ECG Power Spectral Density

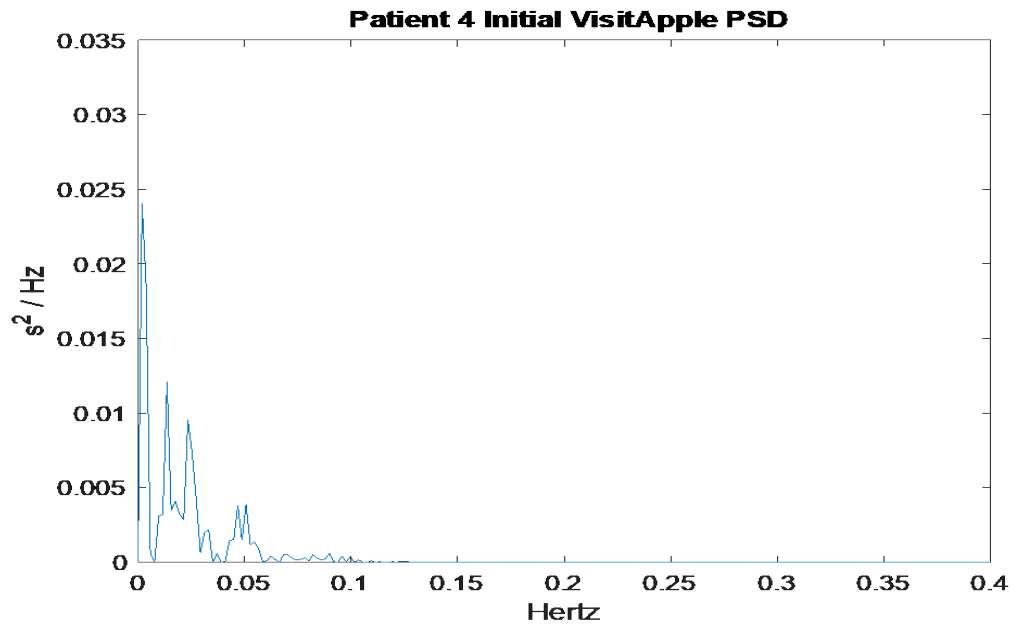


Figure A6. 777: Patient 4 Initial Visit Apple Power Spectral Density



## Patient 5 Exit Visit Readings

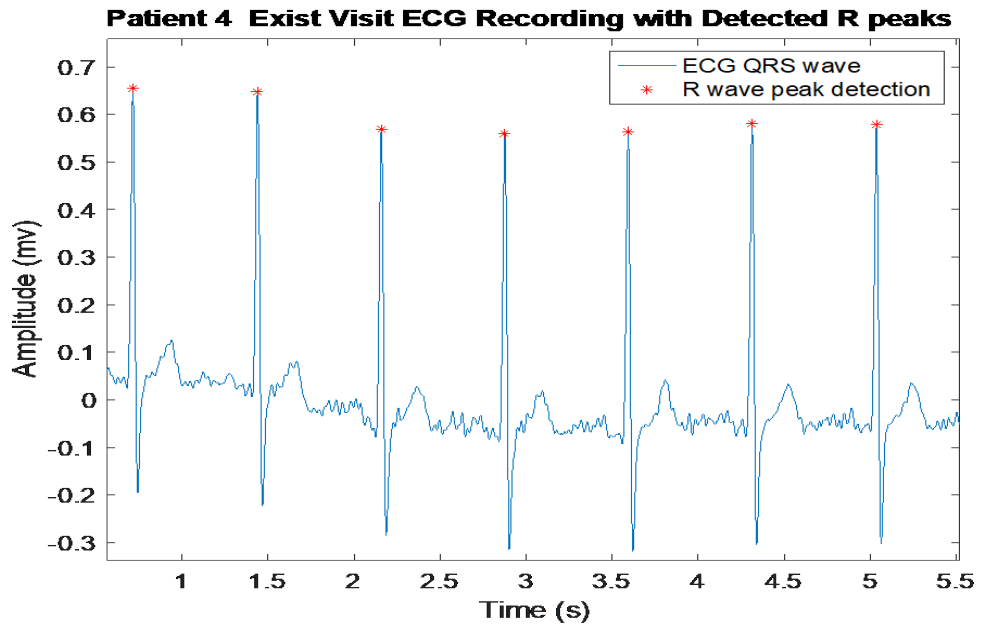


Figure A6. 778: Patient 4 Exit Visit ECG, with detected R peaks

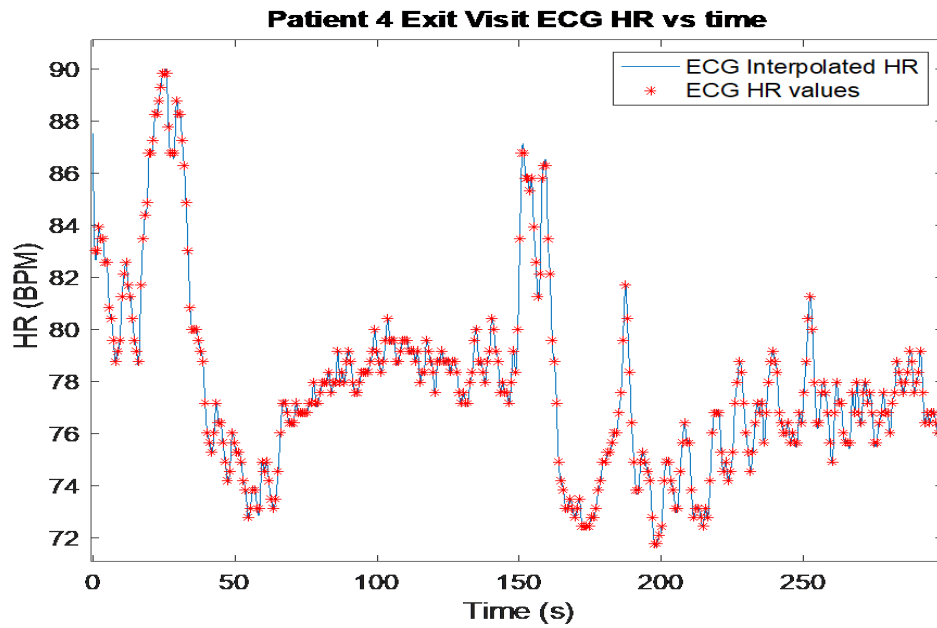


Figure A6. 779: Patient 4 Exit Visit Interpolated ECG HR



Figure A6. 780: Patient 4 Exit Visit Apple Interpolated HR

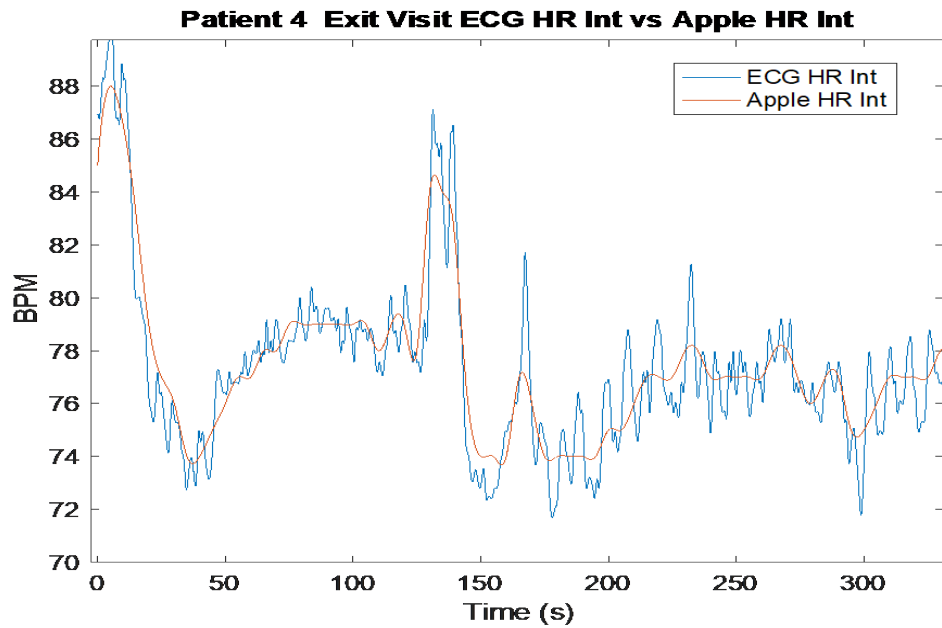


Figure A6. 781: Patient 4 Exit Visit Interpolated ECG and Apple HRs

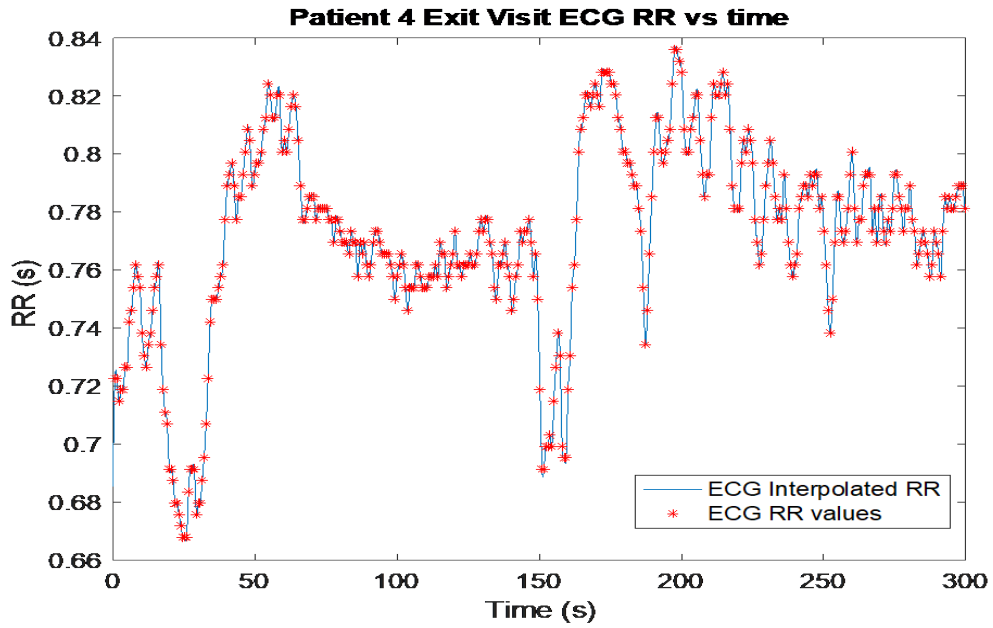


Figure A6. 782: Patient 4 Exit Visit Interpolated ECG RR values

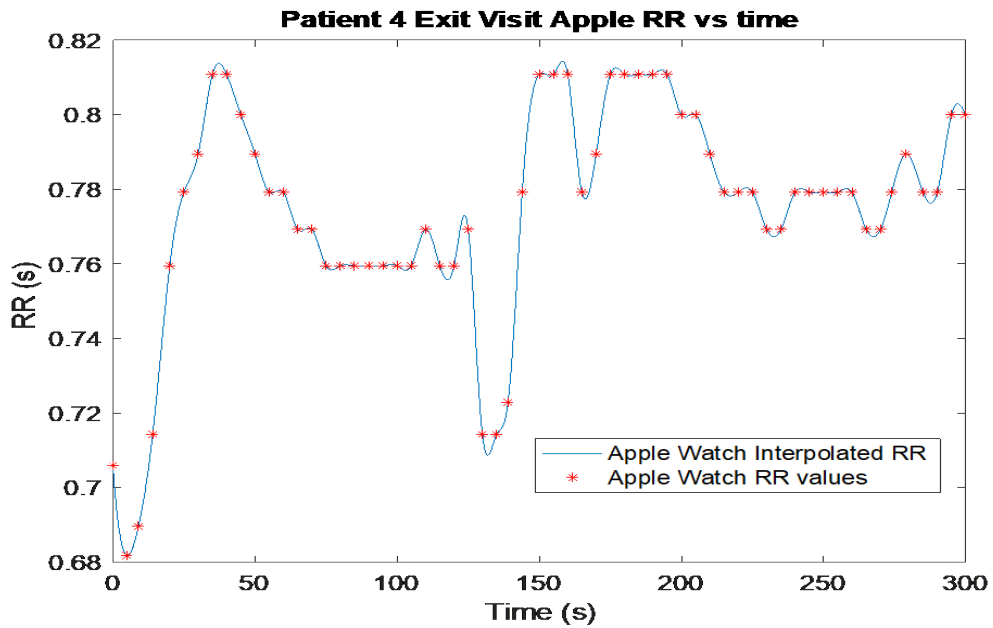


Figure A6. 783: Patient 4 Exit Visit Interpolated Apple RR values

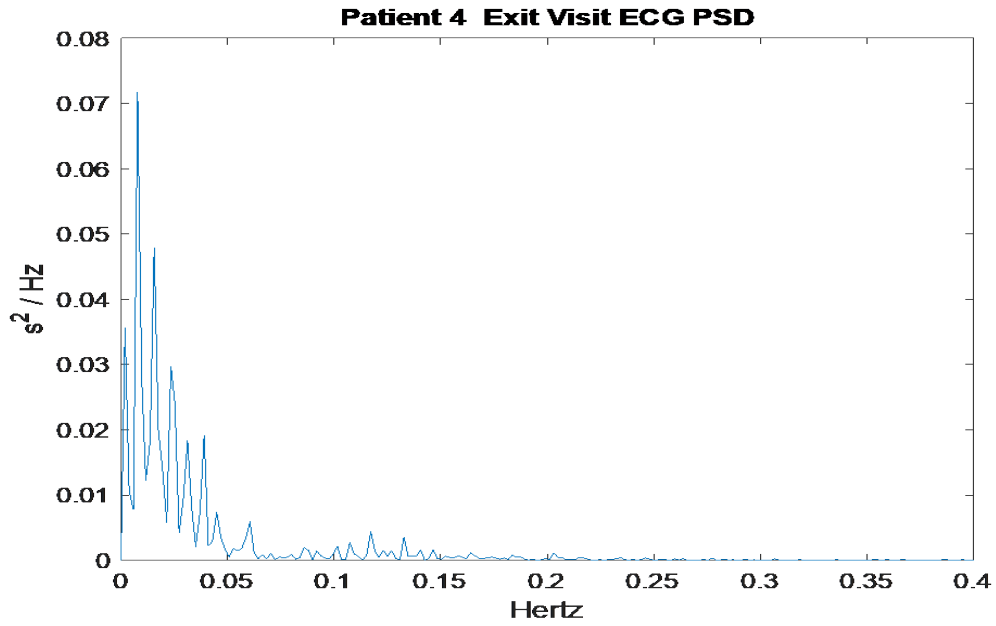


Figure A6. 784: Patient 4 Exit Visit ECG Power Spectral Density

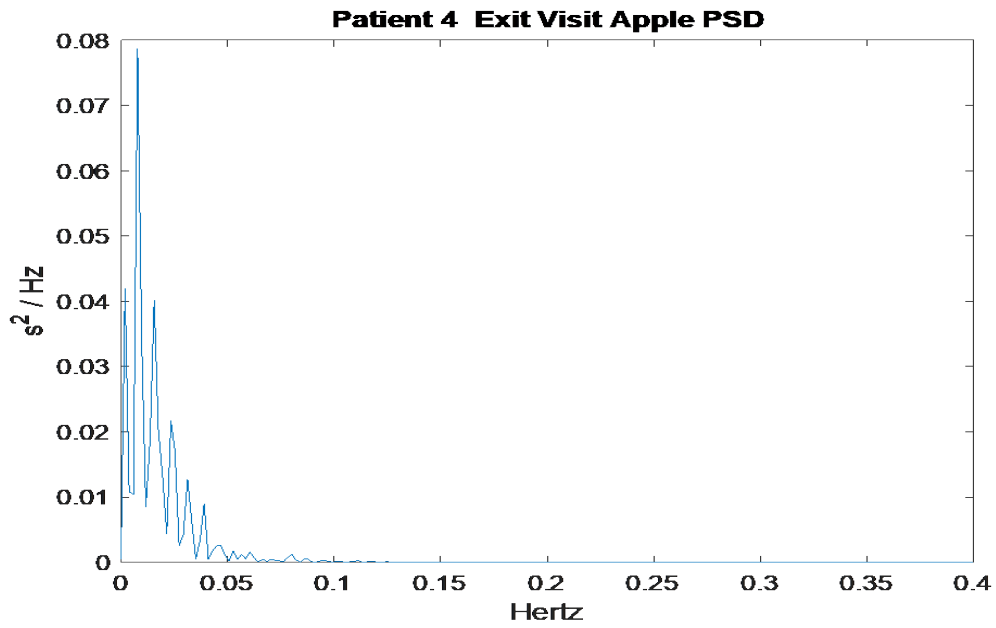


Figure A6. 785: Patient 4 Exit Visit Apple Power Spectral Density

## Patient 5 Initial Visit Readings

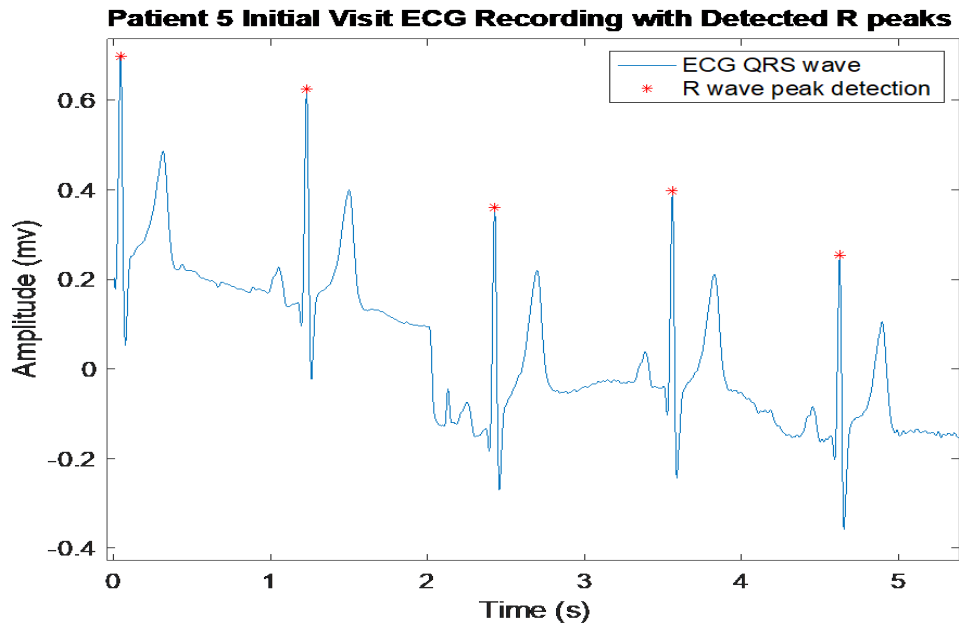


Figure A6. 786: Patient 5 Initial Visit ECG, with detected R peaks

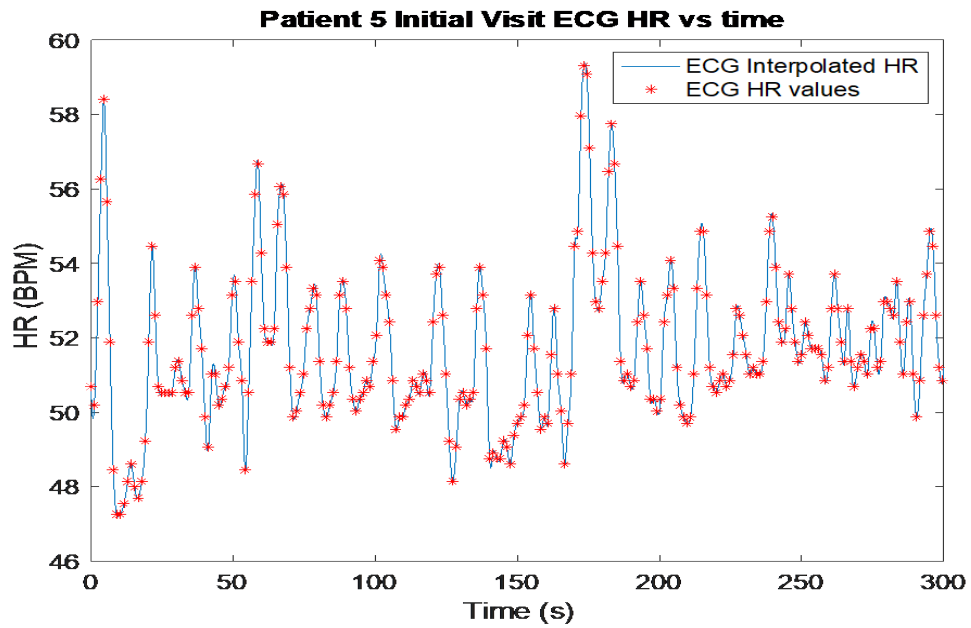


Figure A6. 787: Patient 5 Initial Visit Interpolated ECG HR

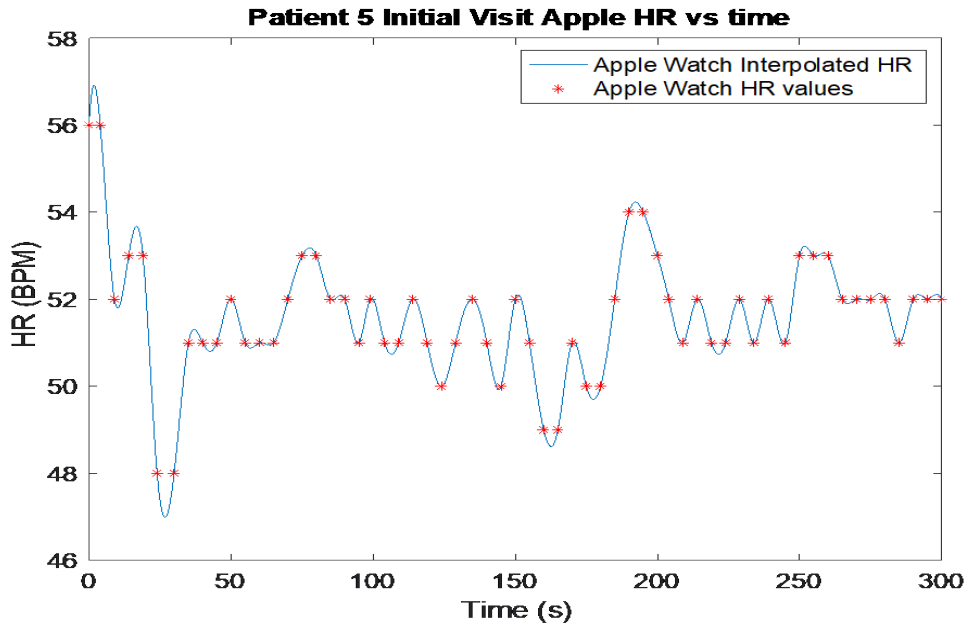


Figure A6.788: Patient 5 Initial Visit Interpolated Apple HR

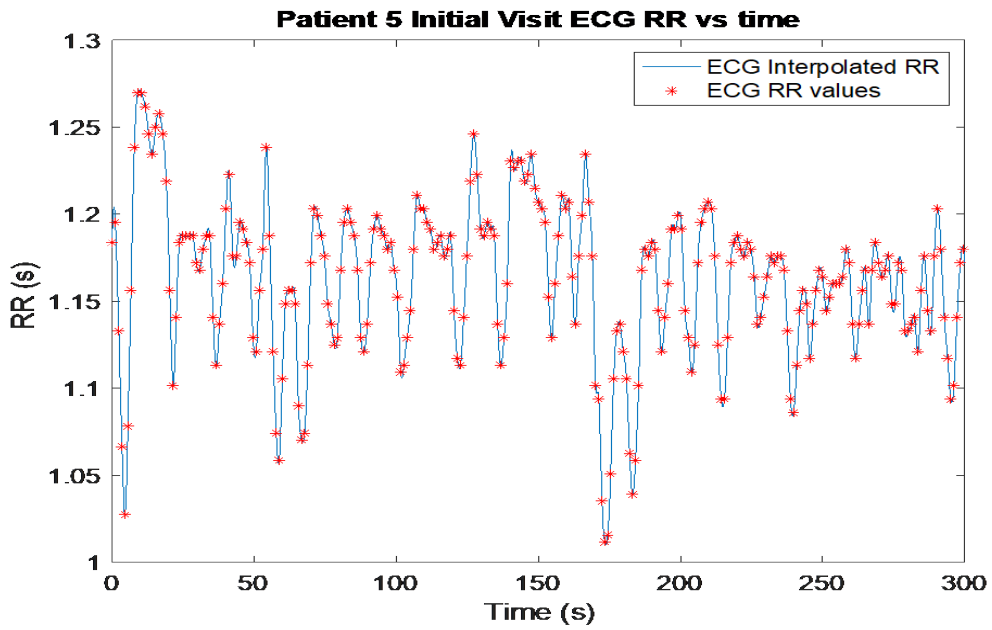


Figure A6.789: Patient 5 Initial Visit Interpolated ECG RR

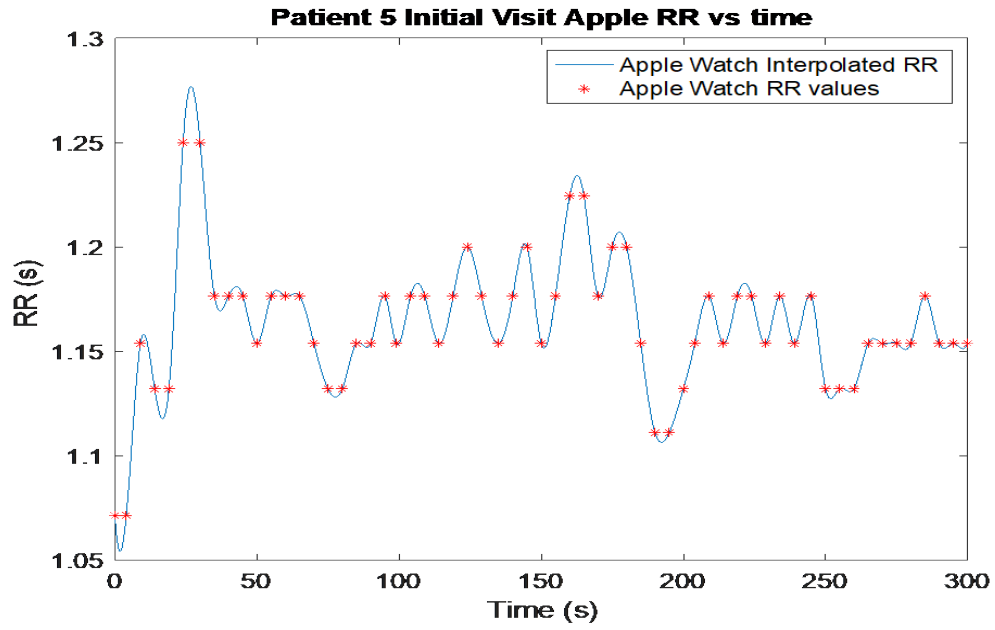


Figure A6. 790: Patient 5 Initial Visit Interpolated Apple RR

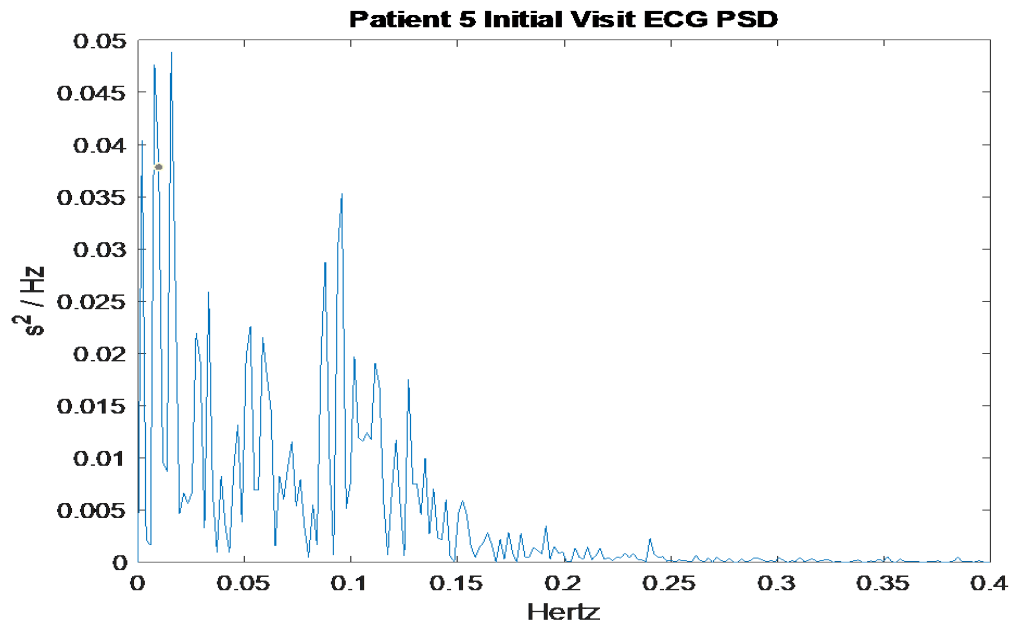


Figure A6. 791: Patient 5 Initial Visit ECG Power Spectral Density

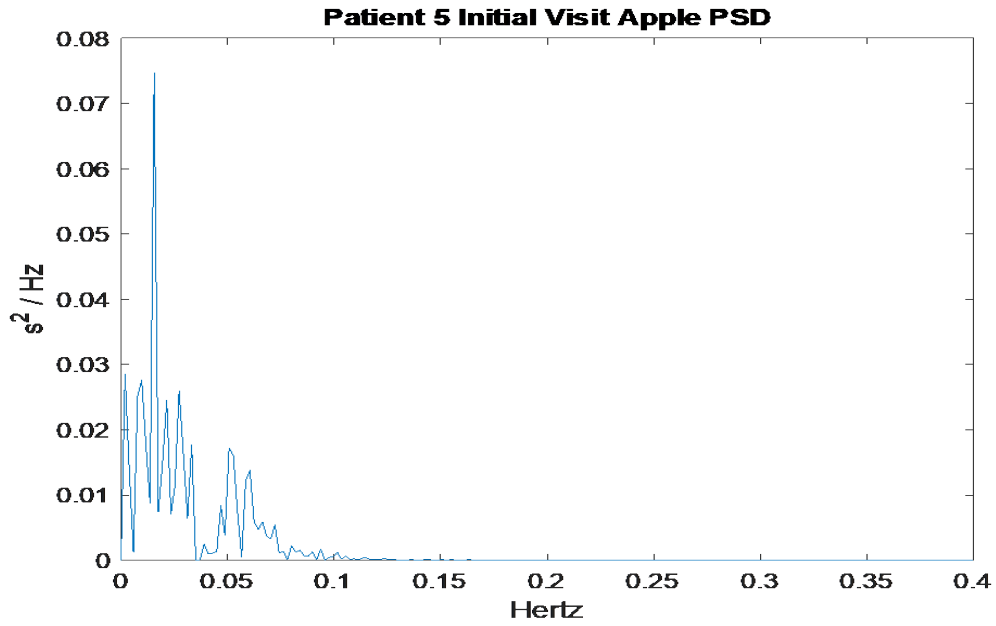


Figure A6. 792: Patient 5 Initial Visit Apple Power Spectral Density

### Patient 5 Exit Visit Readings

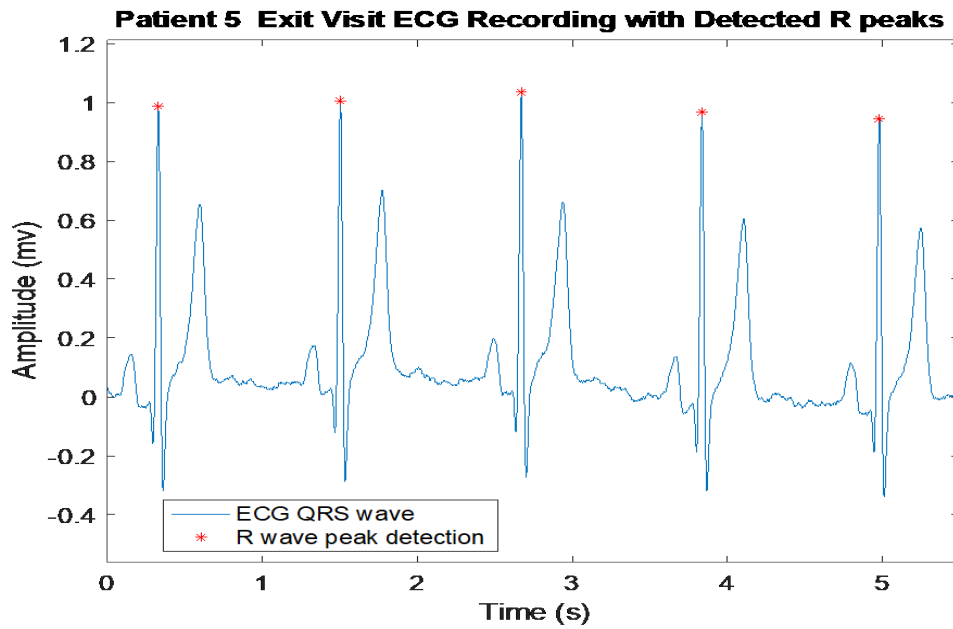


Figure A6. 793: Patient 5 Exit Visit ECG, with detected R peaks



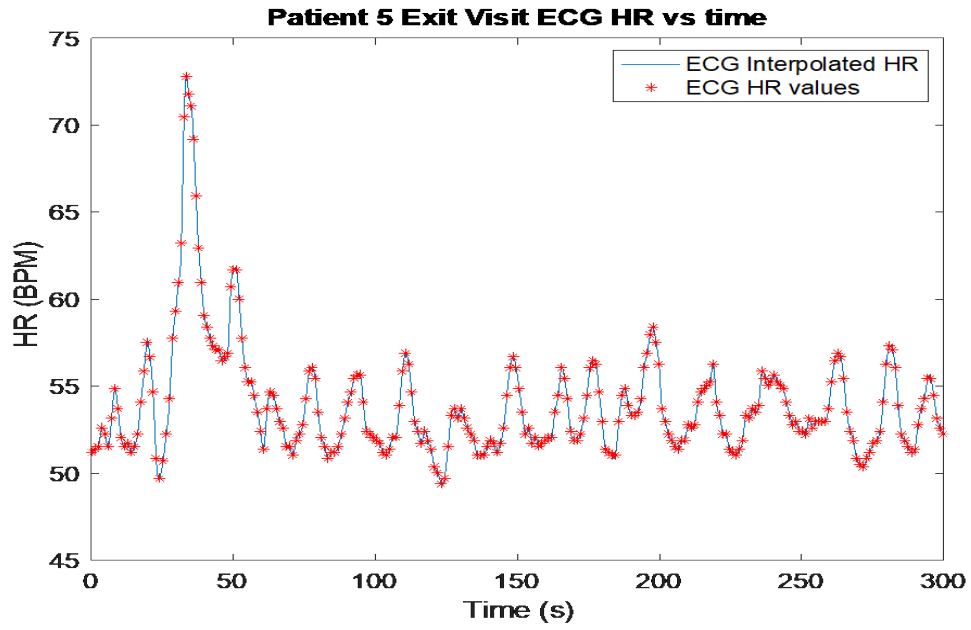


Figure A6. 794: Patient 5 Exit Visit Interpolated ECG HR



Figure A6. 795: Patient 5 Exit Visit Interpolated Apple HR

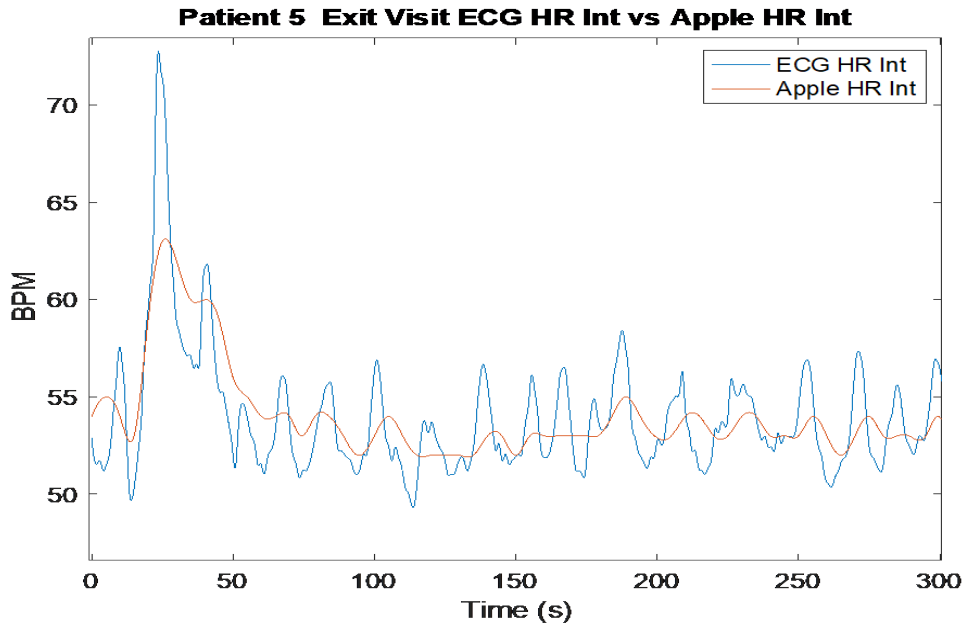


Figure A6. 796: Patient 5 Exit Visit Interpolated ECG and Apple HRs

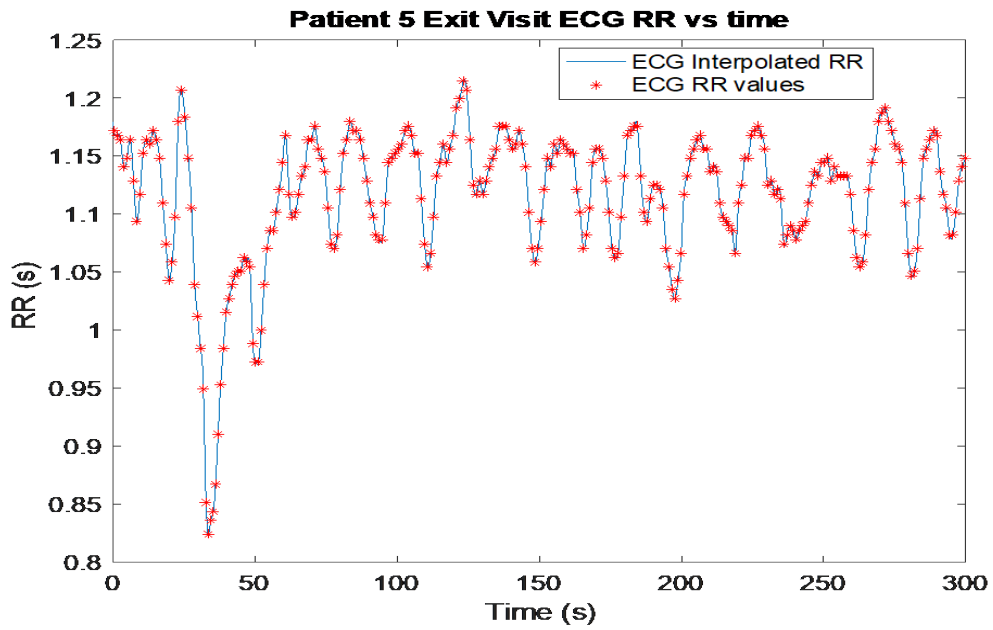


Figure A6. 797: Patient 5 Exit Visit Interpolated ECG RR

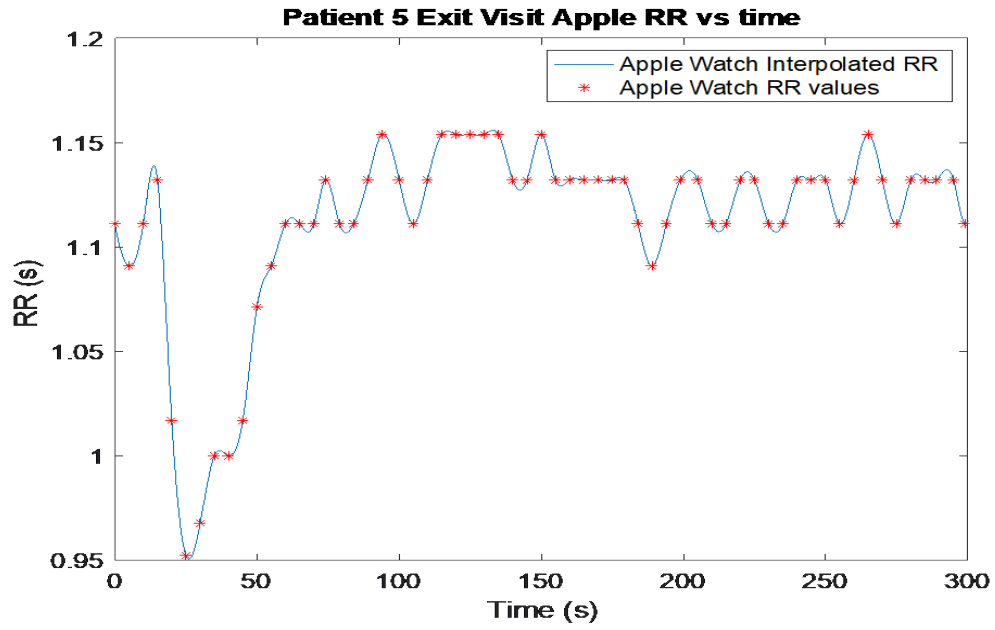


Figure A6. 798: Patient 5 Exit Visit Interpolated Apple RR

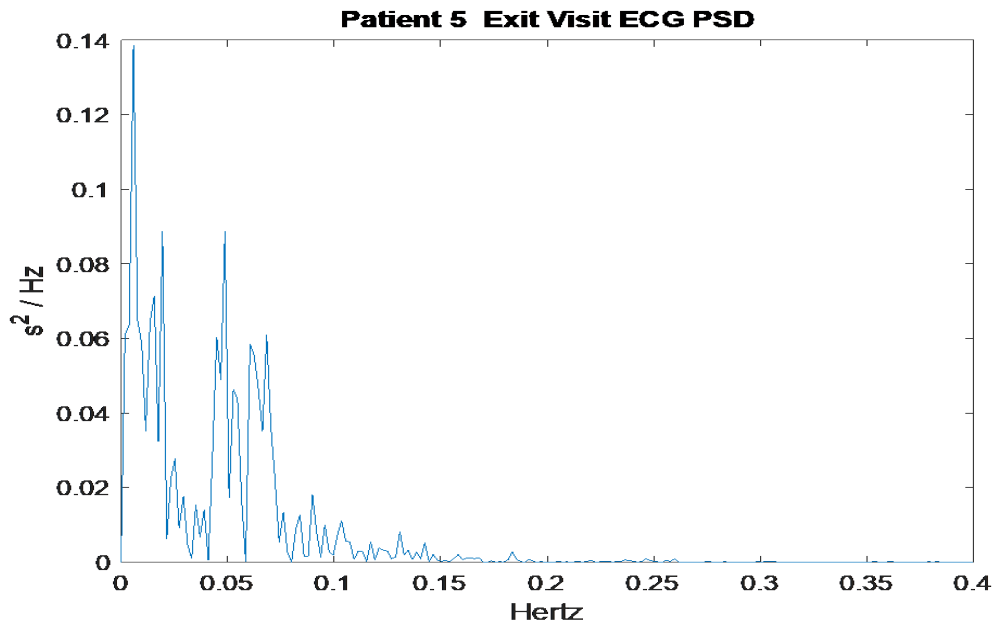


Figure A6. 799: Patient 5 Exit Visit ECG Power Spectral Density

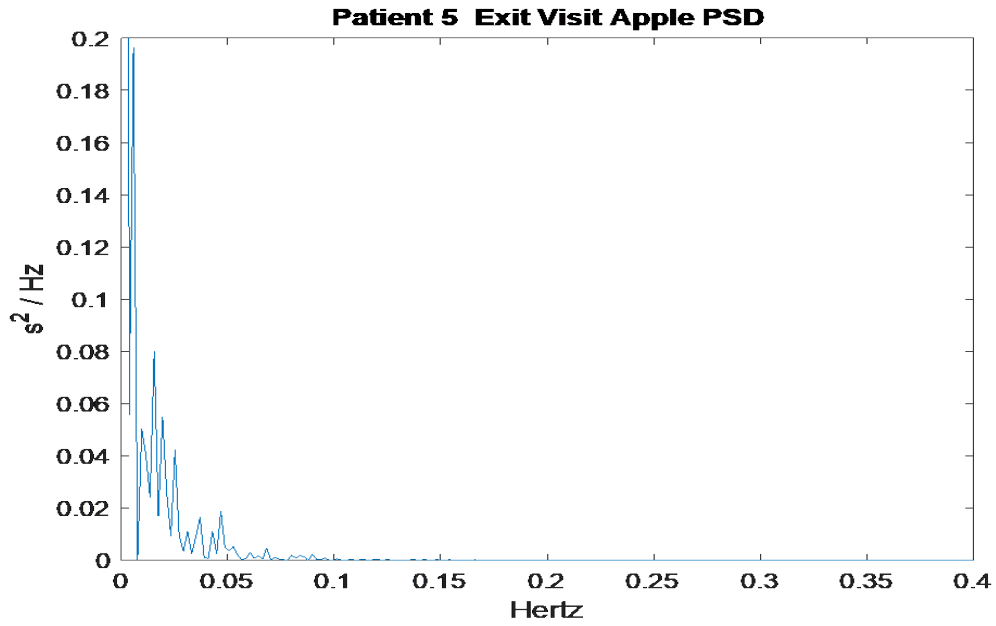


Figure A6. 800: Patient 5 Exit Visit Apple Power Spectral Density

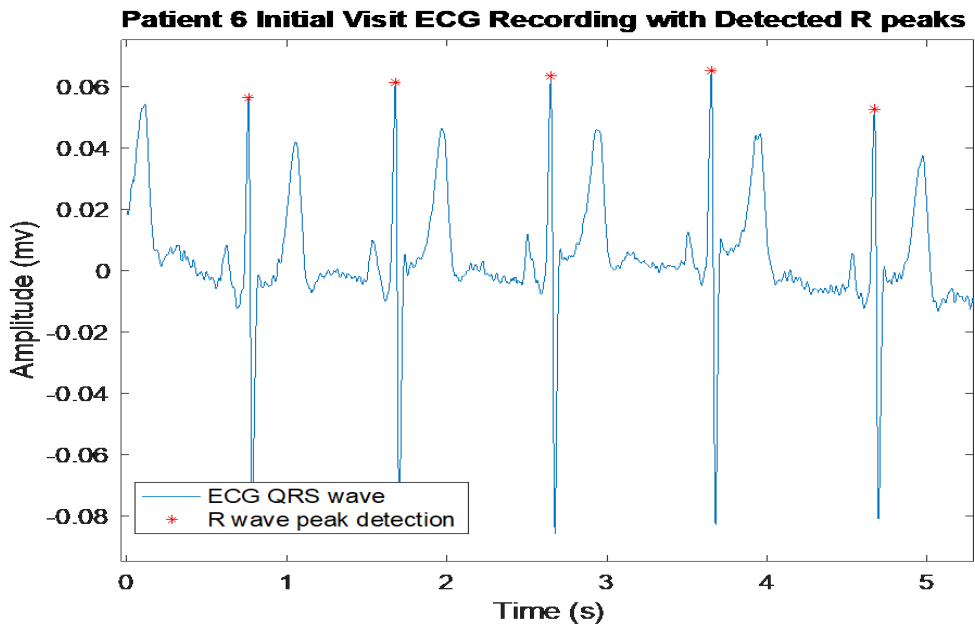


Figure A6. 801: Patient 6 Initial Visit ECG, with detected R peaks

## Patient 6 Initial Visit Readings

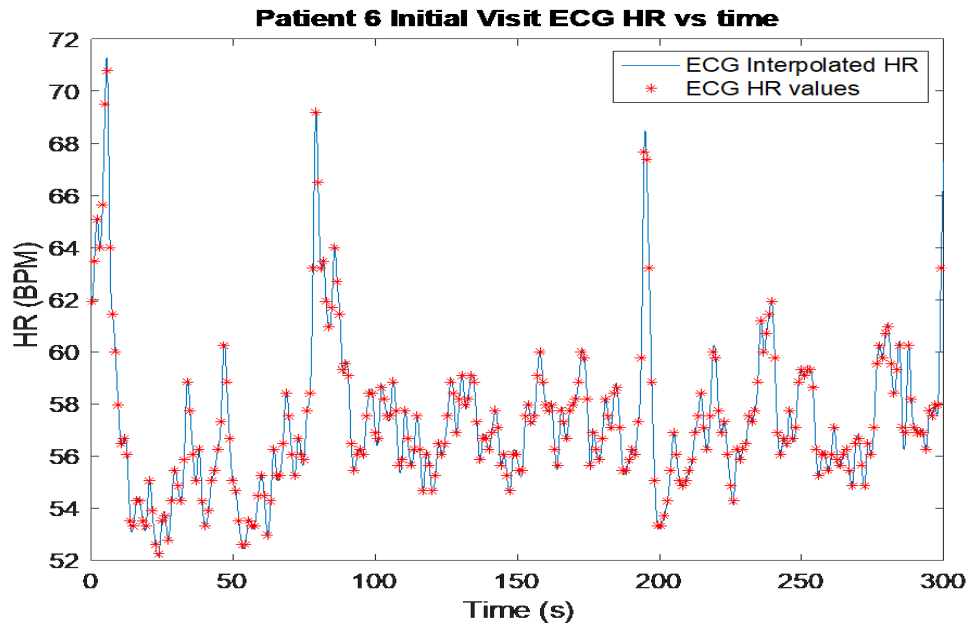


Figure A6. 802: Patient 6 Initial Visit Interpolated ECG HR

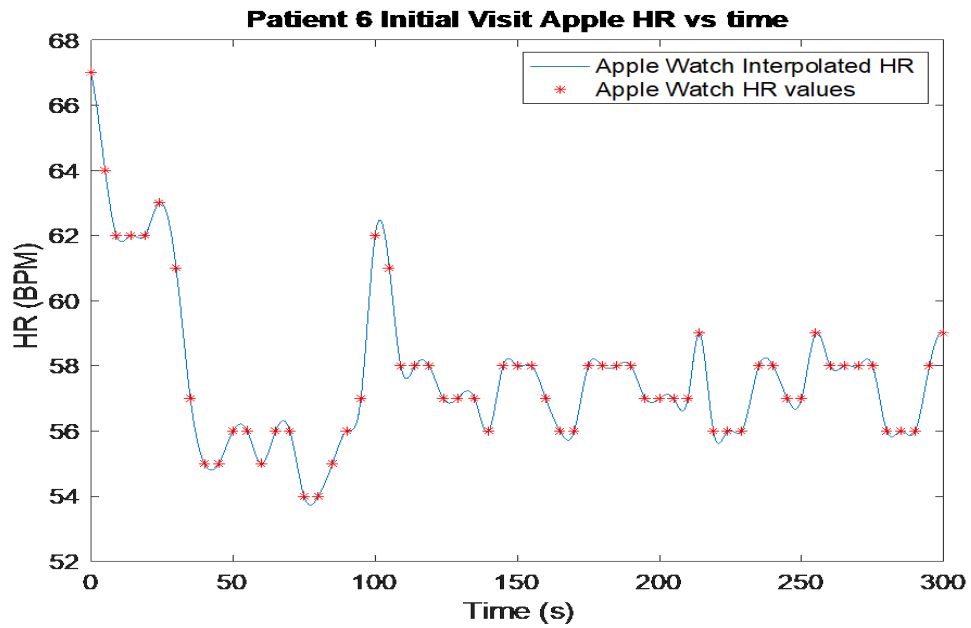


Figure A6. 803: Patient 6 Initial Visit Interpolated Apple HR

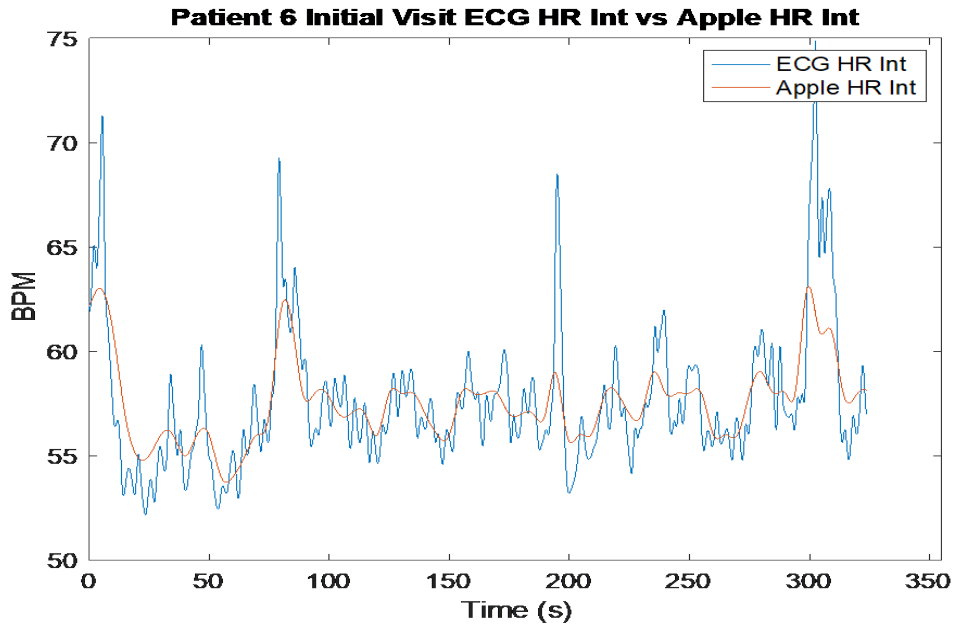


Figure A6. 804: Patient 6 Initial Visit Interpolated ECG and Apple HRs

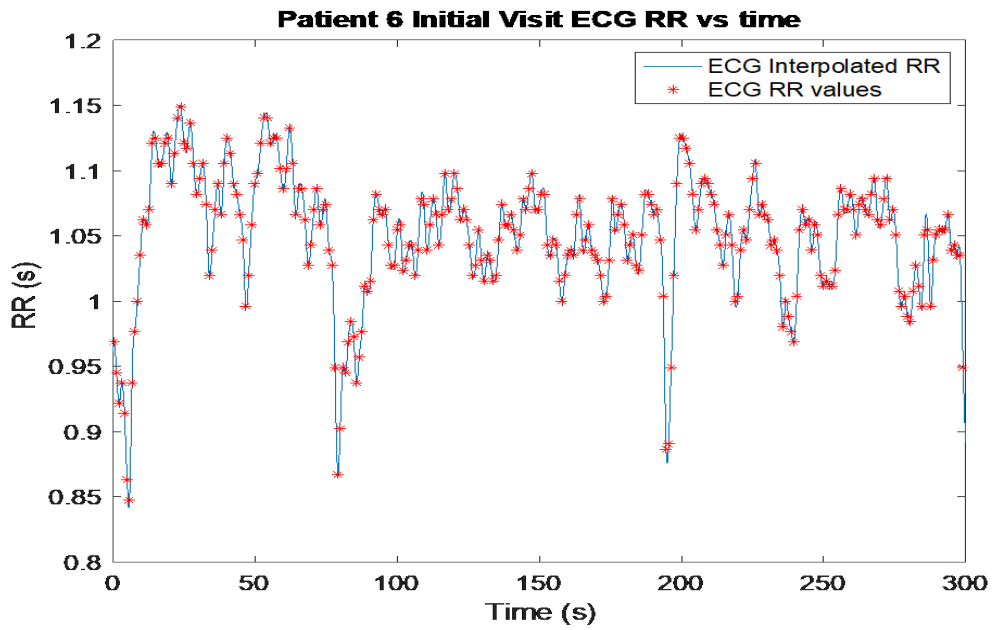


Figure A6. 805: Patient 6 Initial Visit Interpolated ECG RR

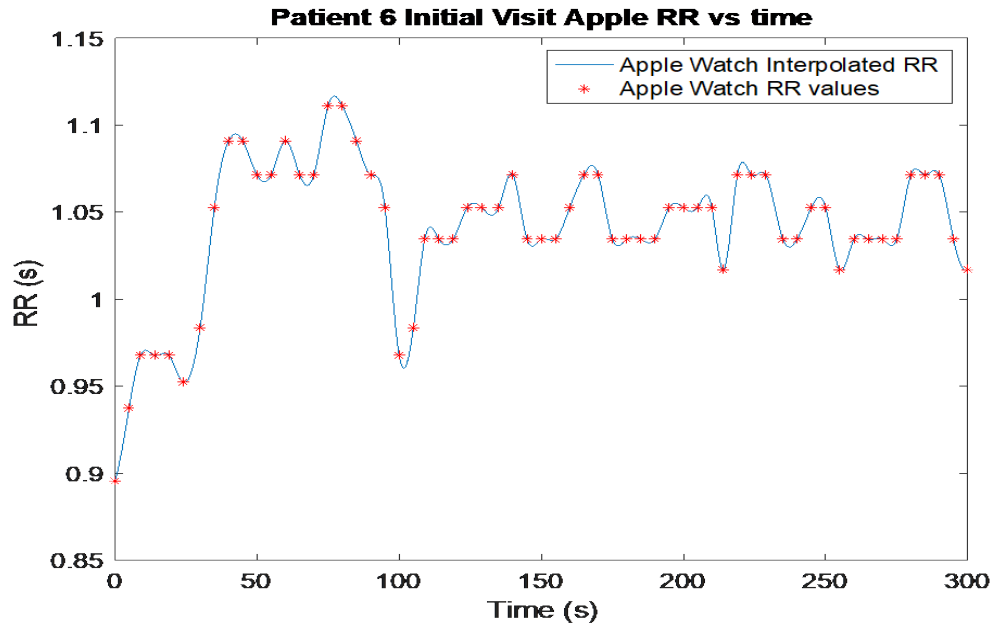


Figure A6. 806: Patient 6 Initial Visit Interpolated Apple RR

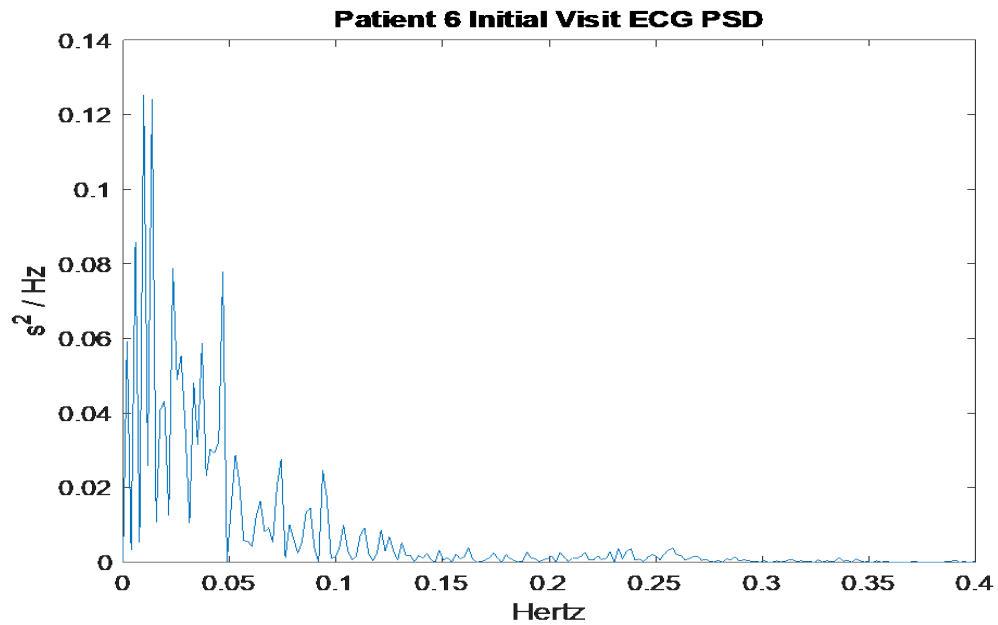


Figure A6. 807: Patient 6 Initial Visit ECG Power Spectral Density

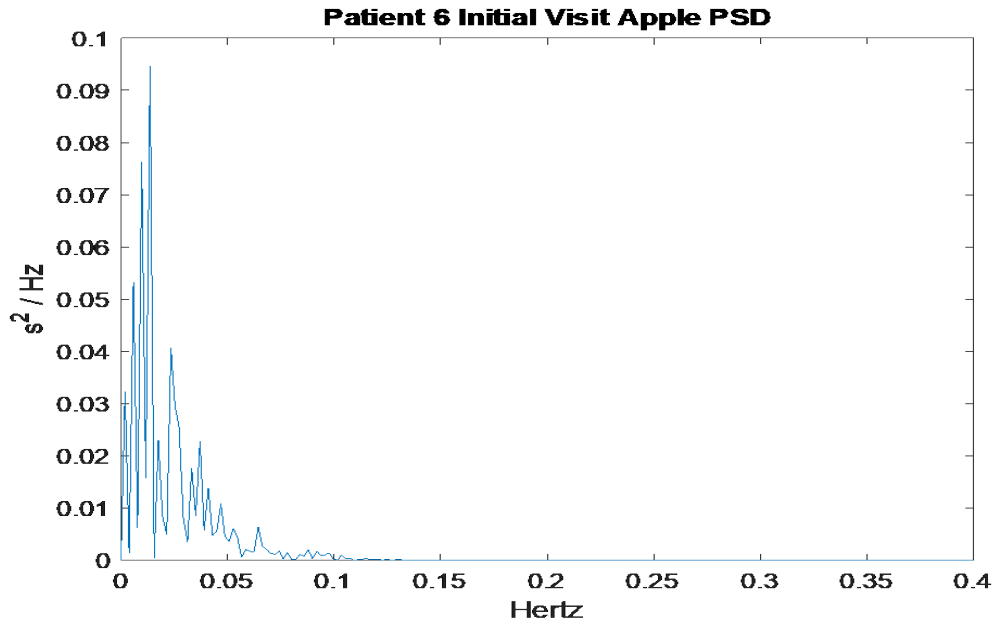


Figure A6. 808: Patient 6 Initial Visit Apple Power Spectral Density



## Patient 6 Exit Visit Readings

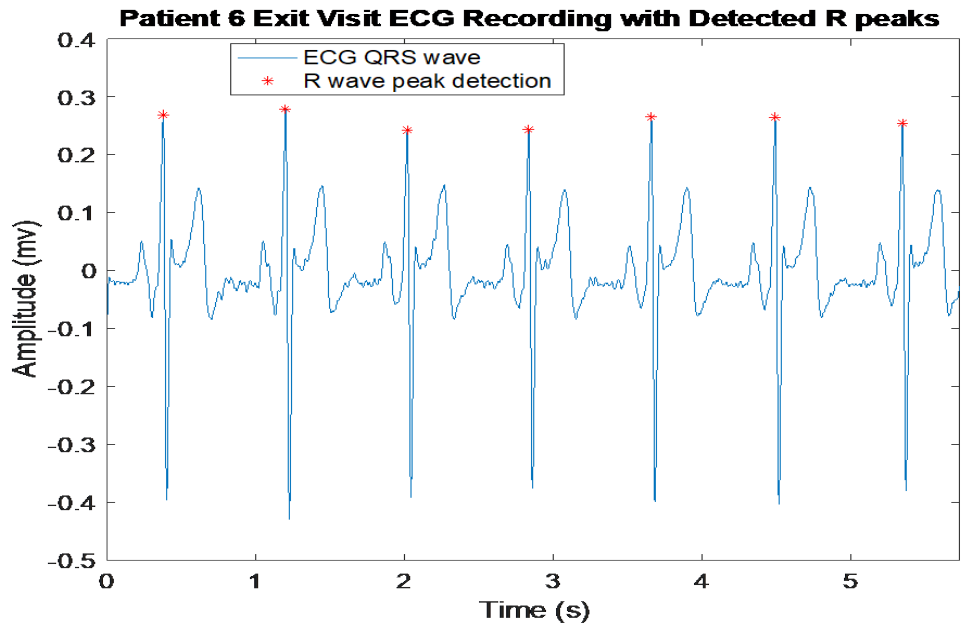


Figure A6. 809: Patient 6 Exit Visit ECG, with detected R peaks

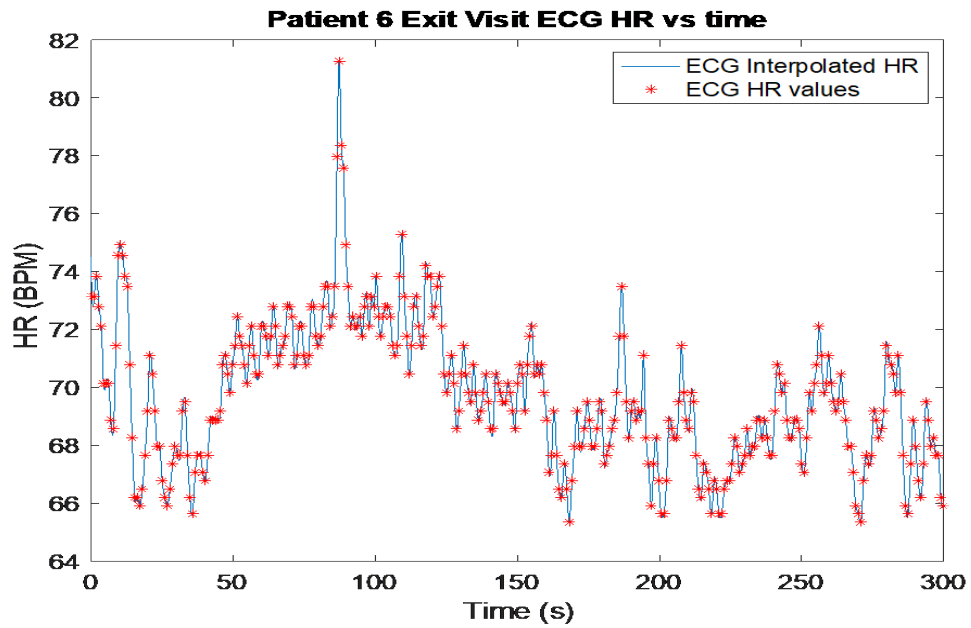


Figure A6. 810: Patient 6 Exit Visit Interpolated ECG RR

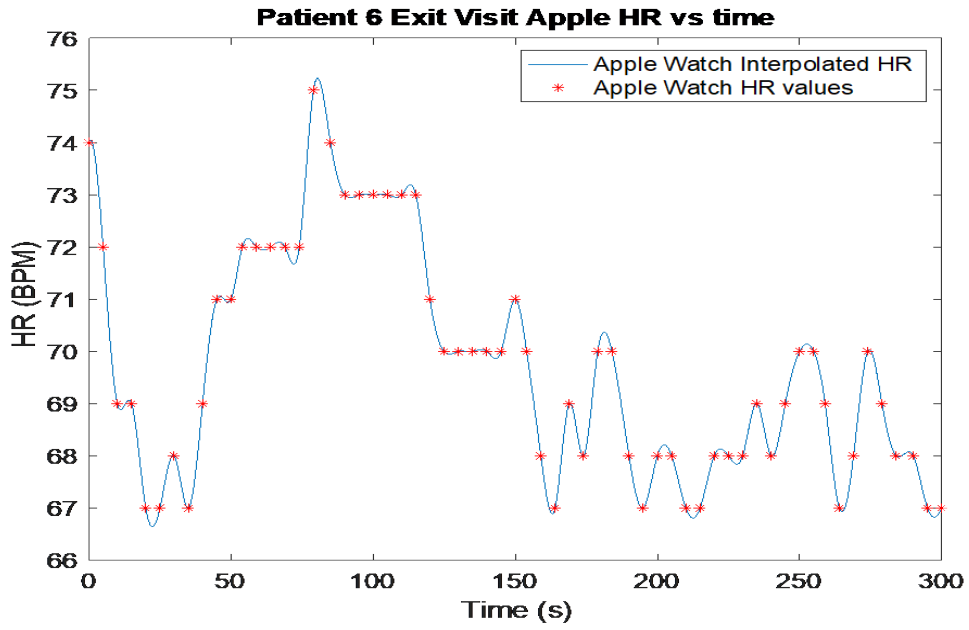


Figure A6. 811: Patient 6 Exit Visit Interpolated Apple RR

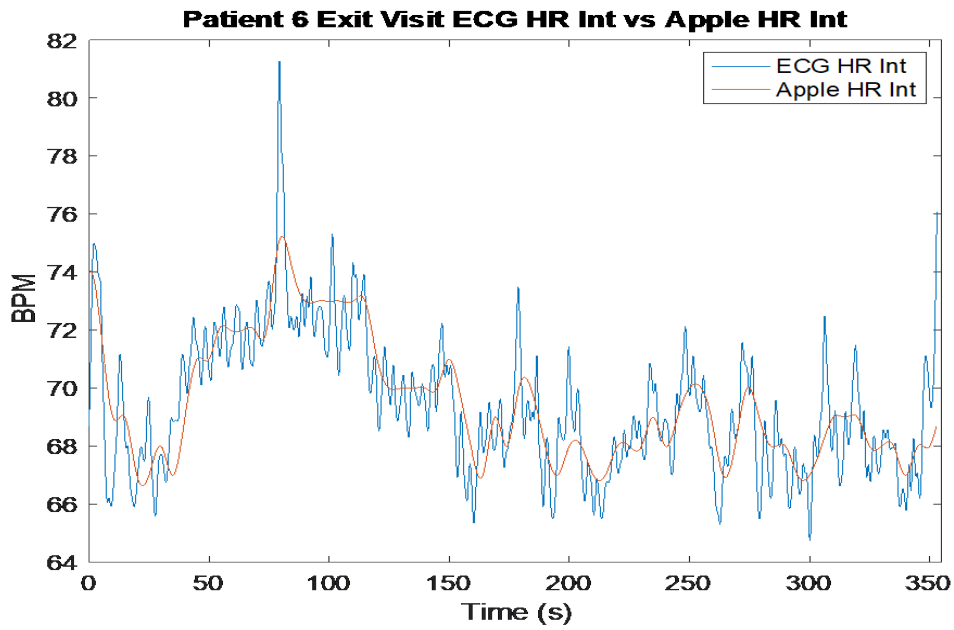


Figure A6. 812: Patient 6 Exit Visit Interpolated ECG and Apple HRs

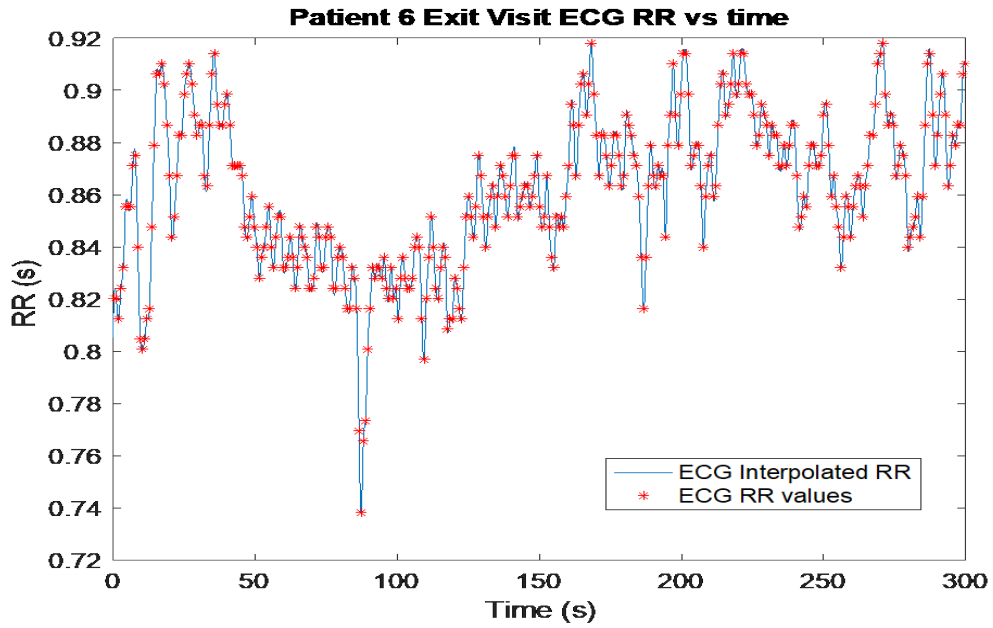


Figure A6. 813: Patient 6 Exit Visit Interpolated ECG RR

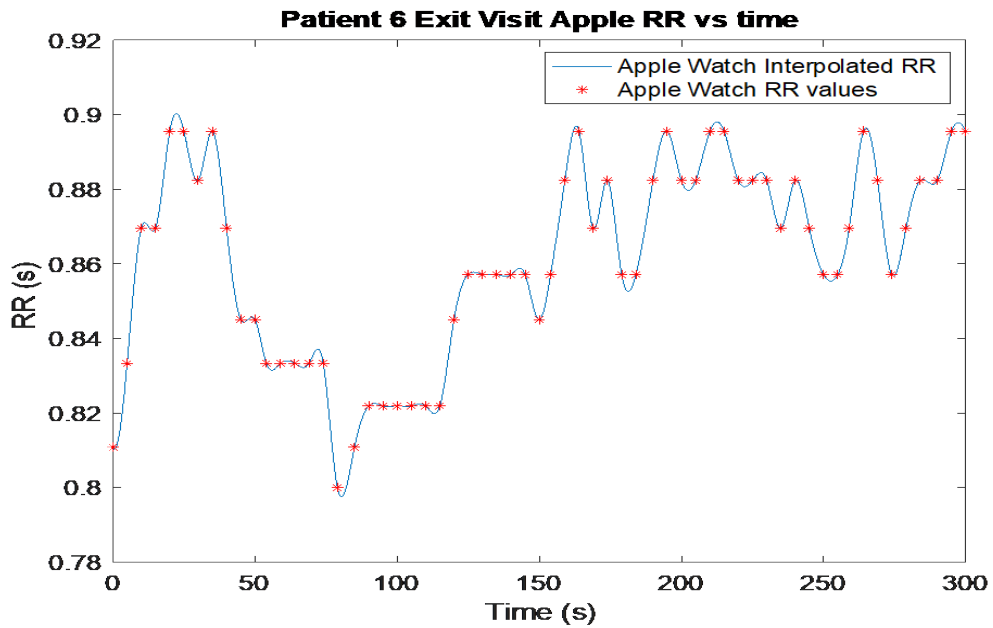


Figure A6. 814: Patient 6 Exit Visit Interpolated Apple RR

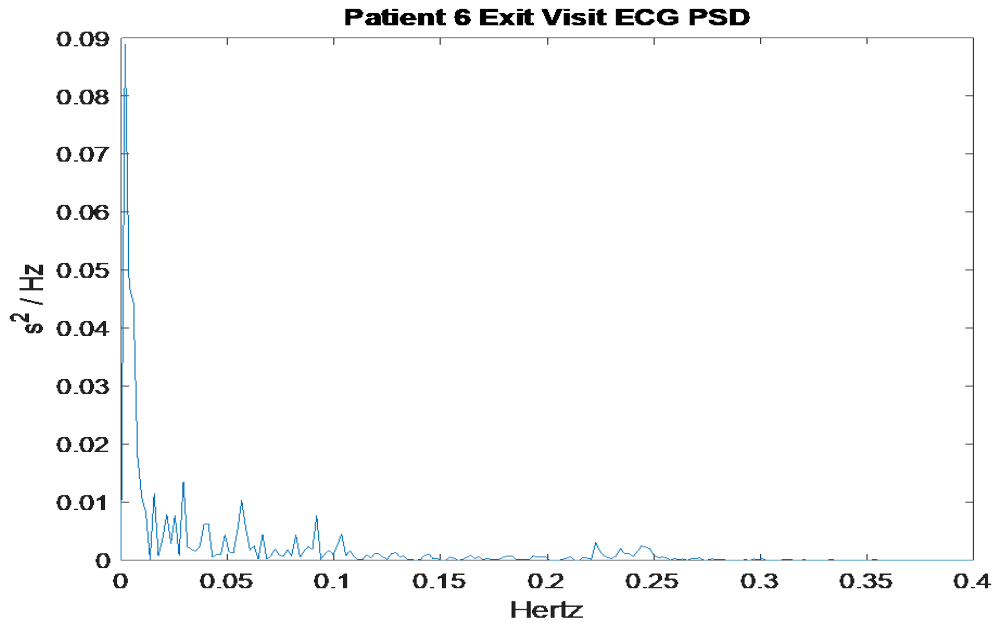


Figure A6. 815: Patient 6 Exit Visit ECG Power Spectral Density

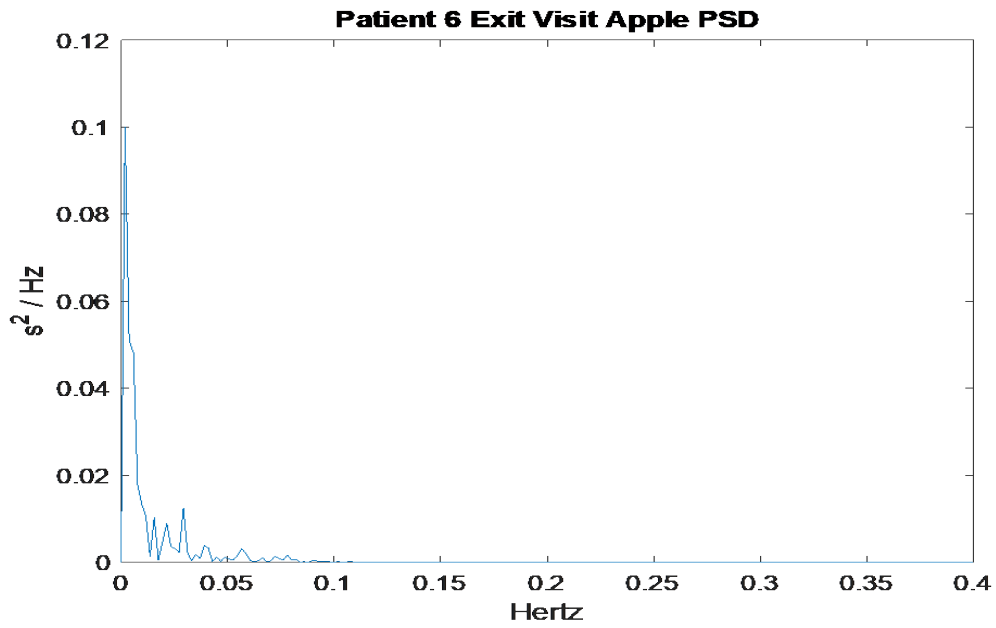


Figure A6. 816: Patient 6 Exit Visit Apple Power Spectral Density

## Patient 7 Initial Visit Readings

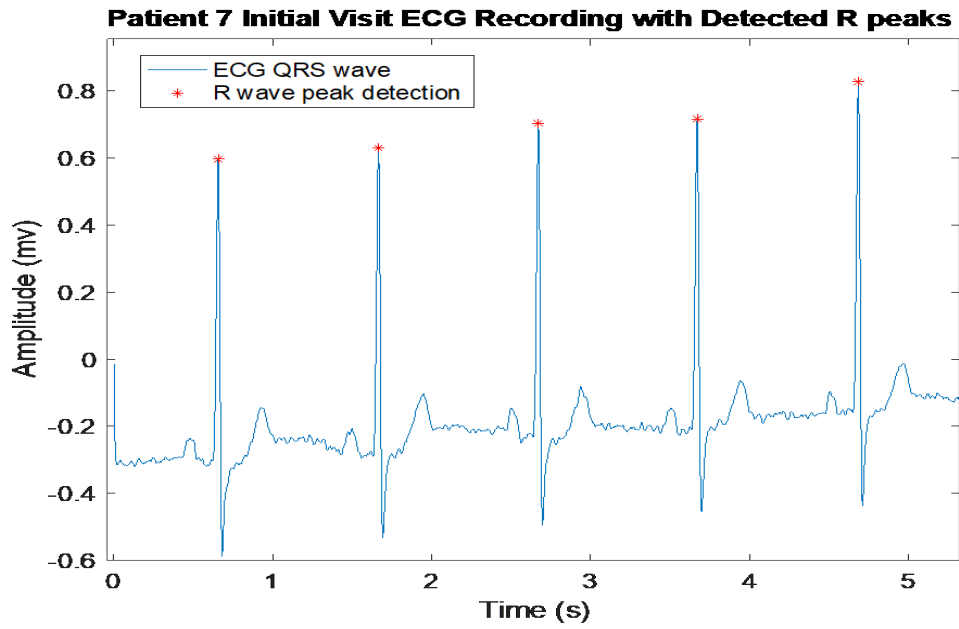


Figure A6. 817: Patient 7 Initial Visit ECG, with detected R peaks

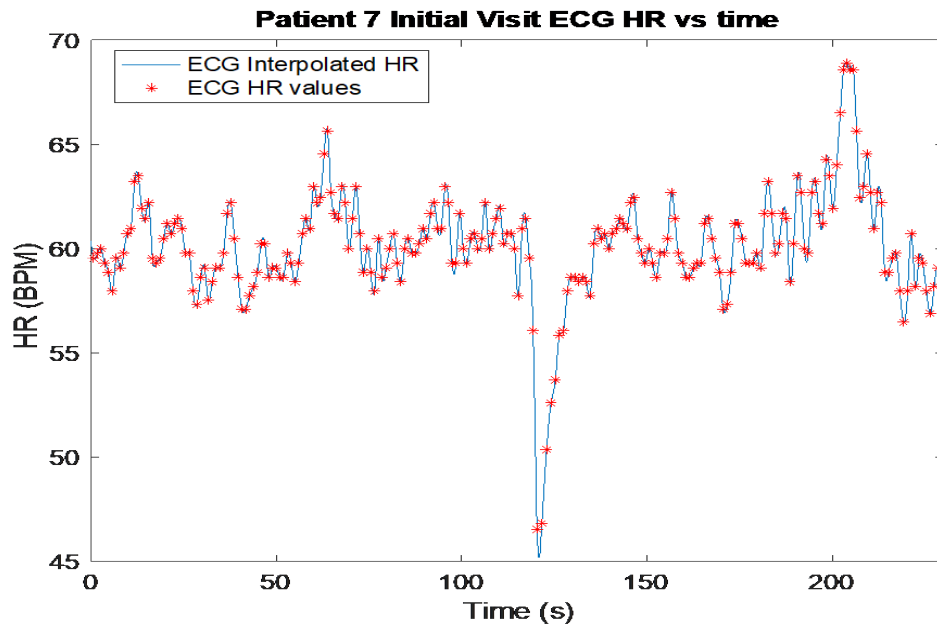


Figure A6. 818: Patient 7 Initial Visit Interpolated ECG HR

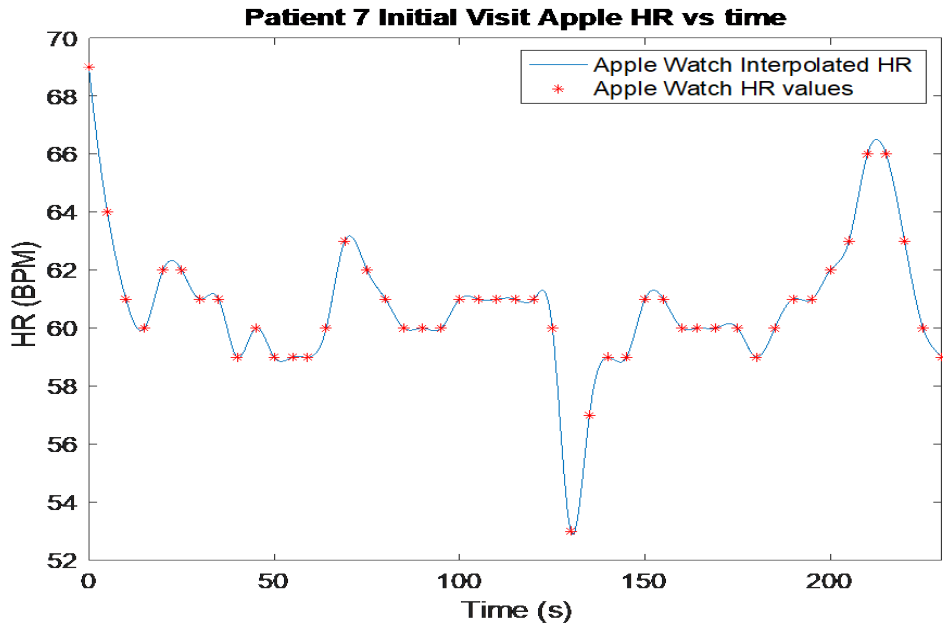


Figure A6. 819: Patient 7 Initial Visit Interpolated Apple HR

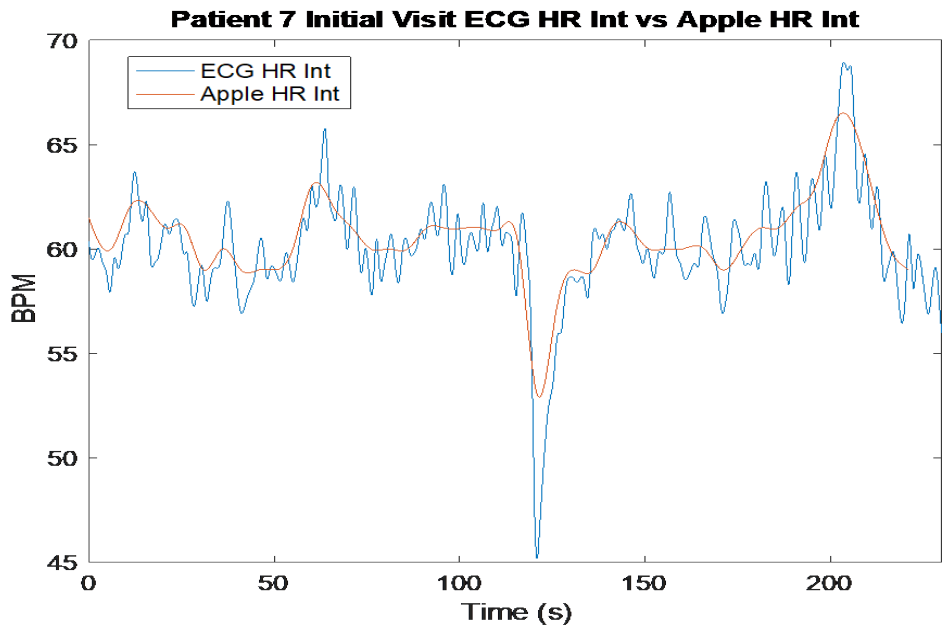


Figure A6. 820: Patient 7 Initial Visit Interpolated ECG and Apple HRs

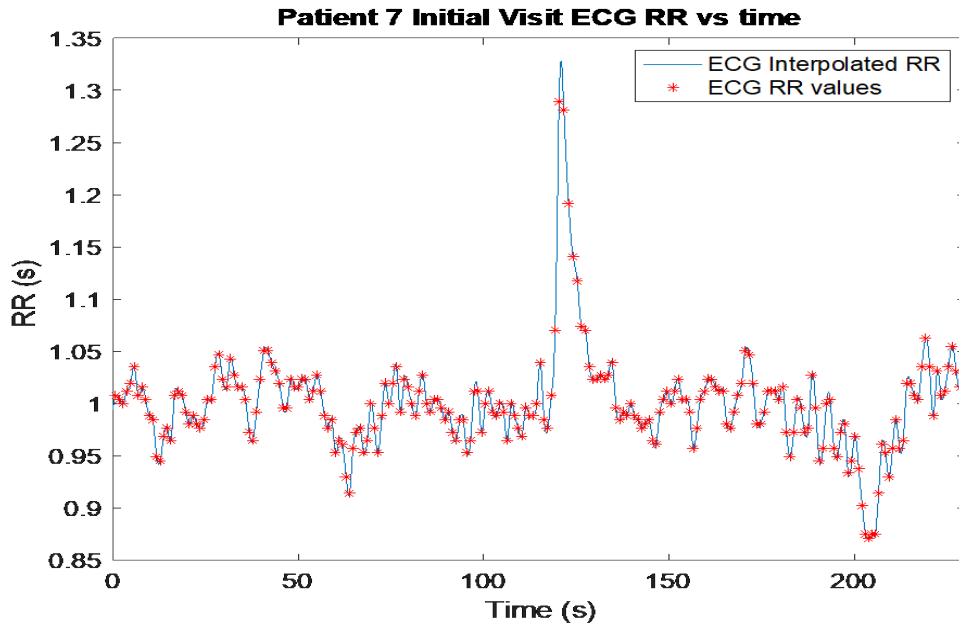


Figure A6. 821: Patient 7 Initial Visit Interpolated ECG RR

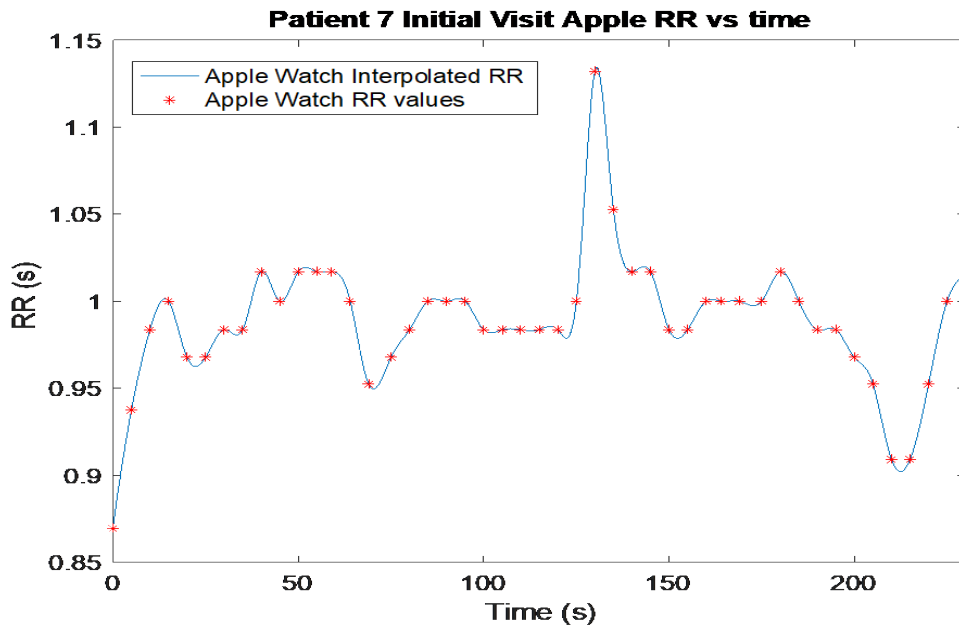


Figure A6. 822: Patient 7 Initial Visit Interpolated Apple RR

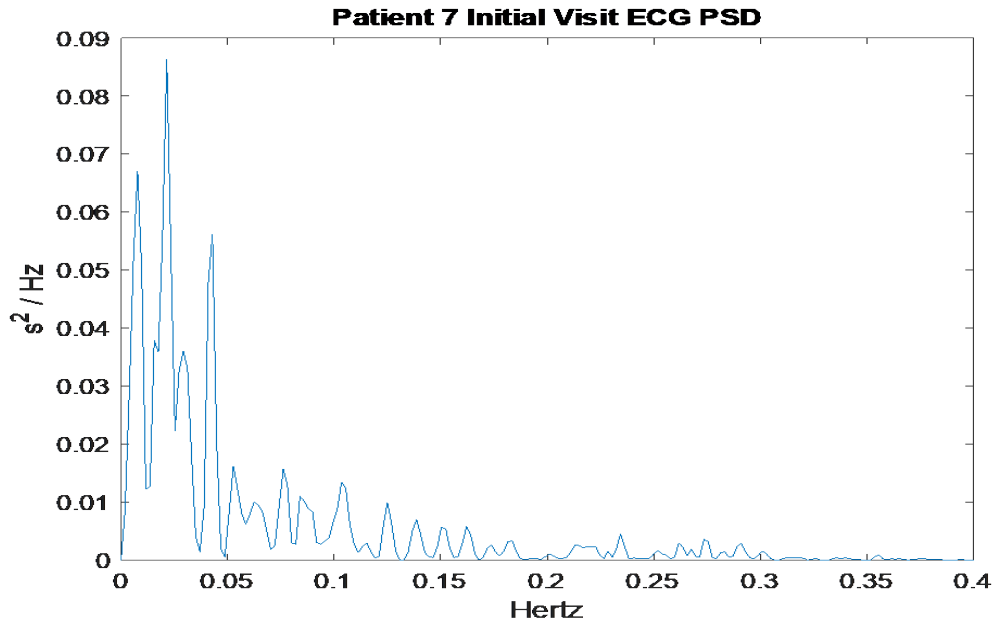


Figure A6. 823: Patient 7 Initial Visit ECG Power Spectral Density

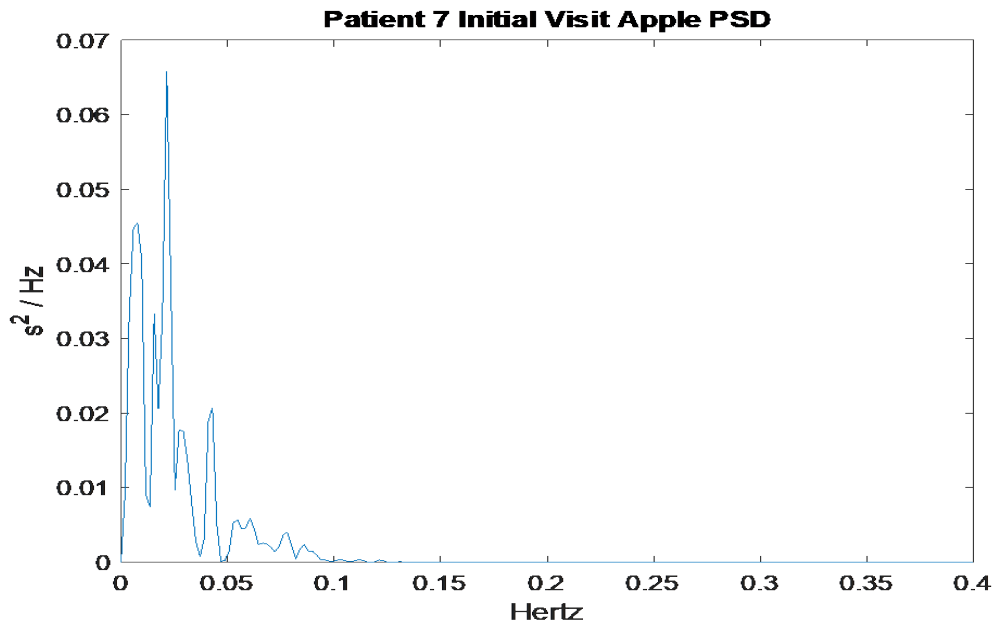


Figure A6. 824: Patient 7 Initial Visit Apple Power Spectral Density



## Patient 7 Exit Visit Readings

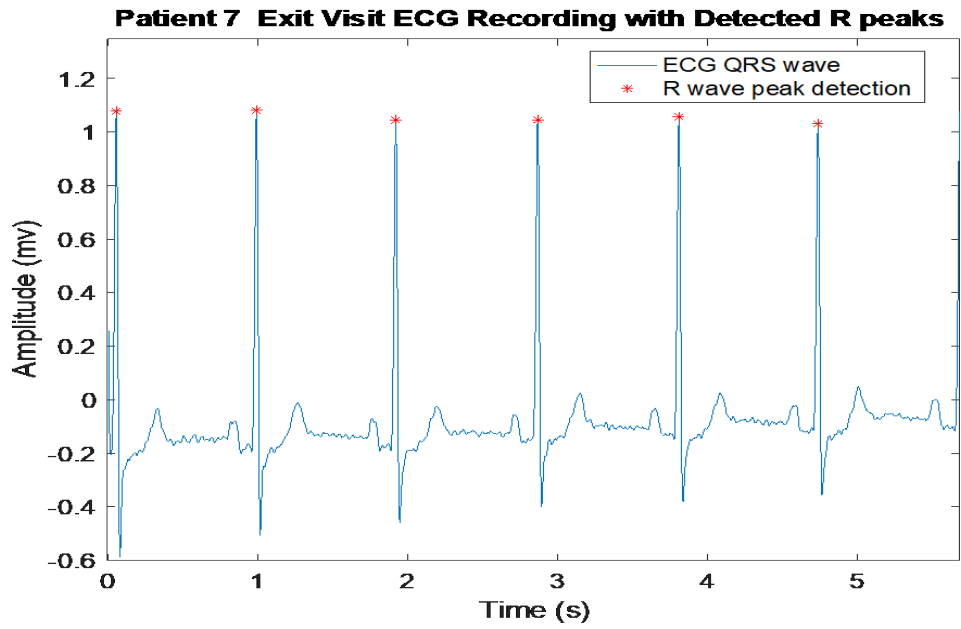


Figure A6. 825: Patient 7 Exit Visit ECG, with detected R peaks

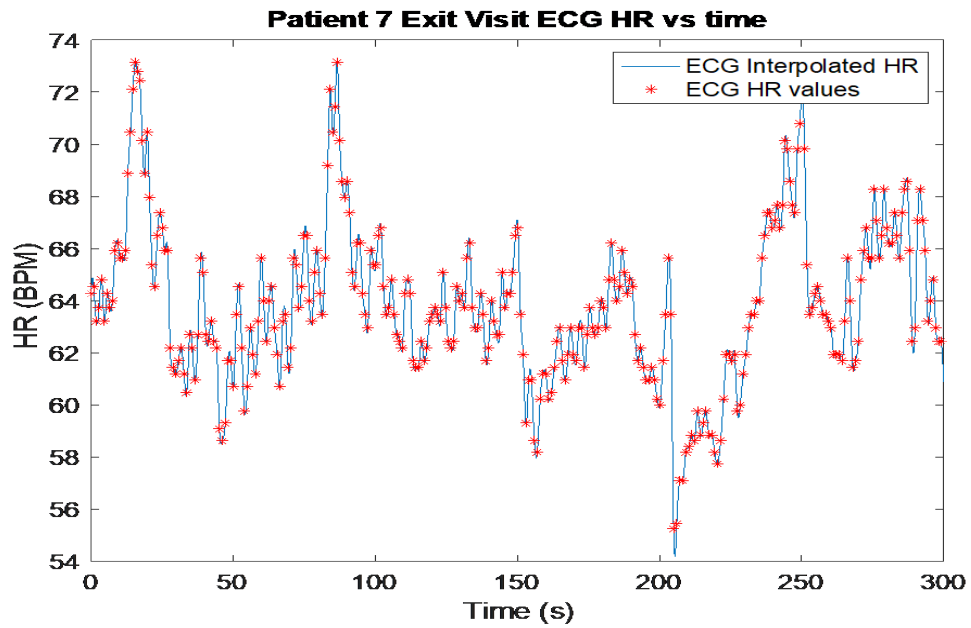


Figure A6. 826: Patient 7 Exit Visit Interpolated ECG HR

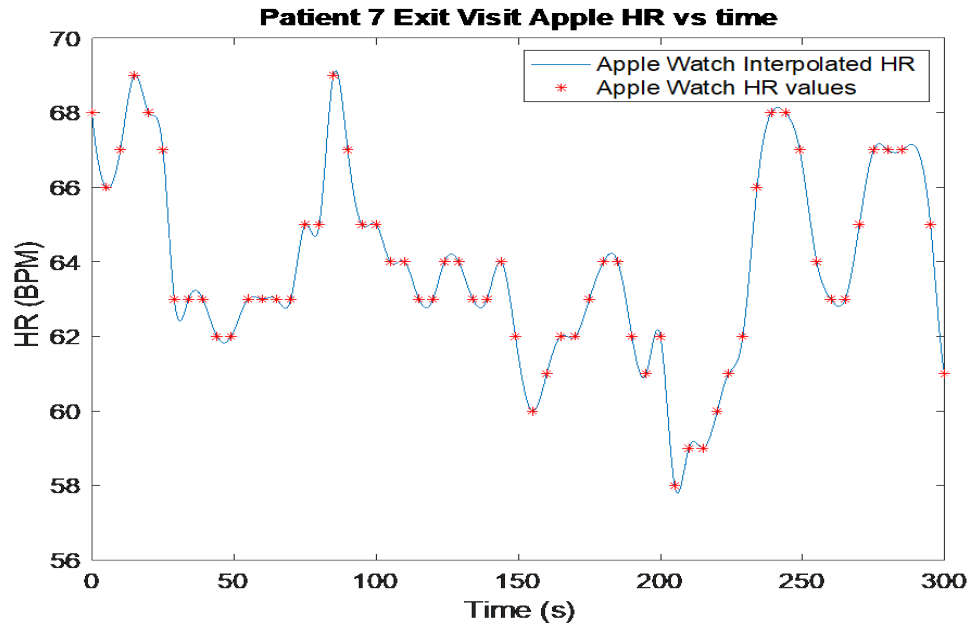


Figure A6. 827: Patient 7 Exit Visit Interpolated Apple HR

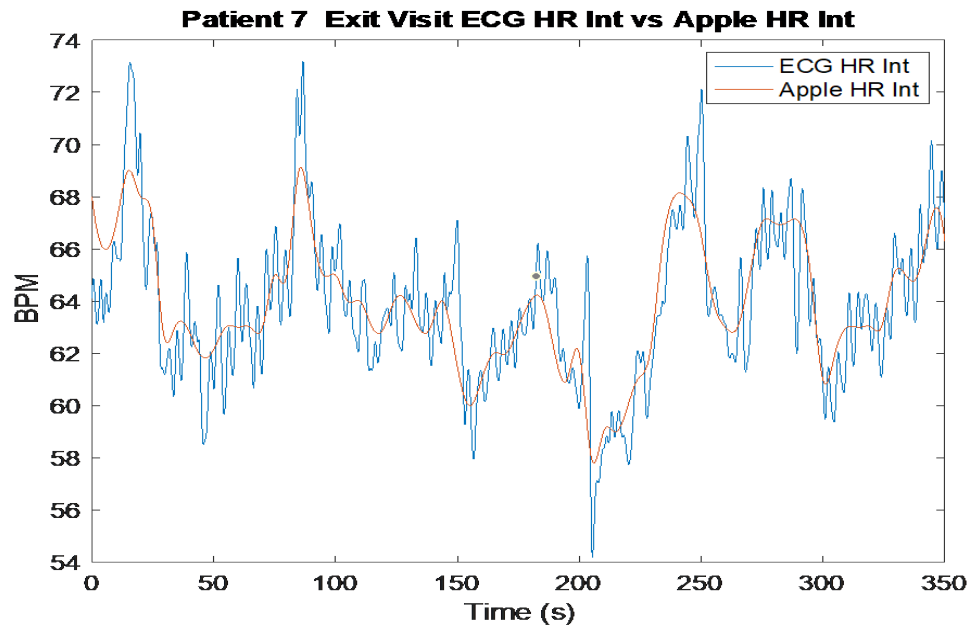


Figure A6. 828: Patient 7 Exit Visit Interpolated ECG and Apple HRs

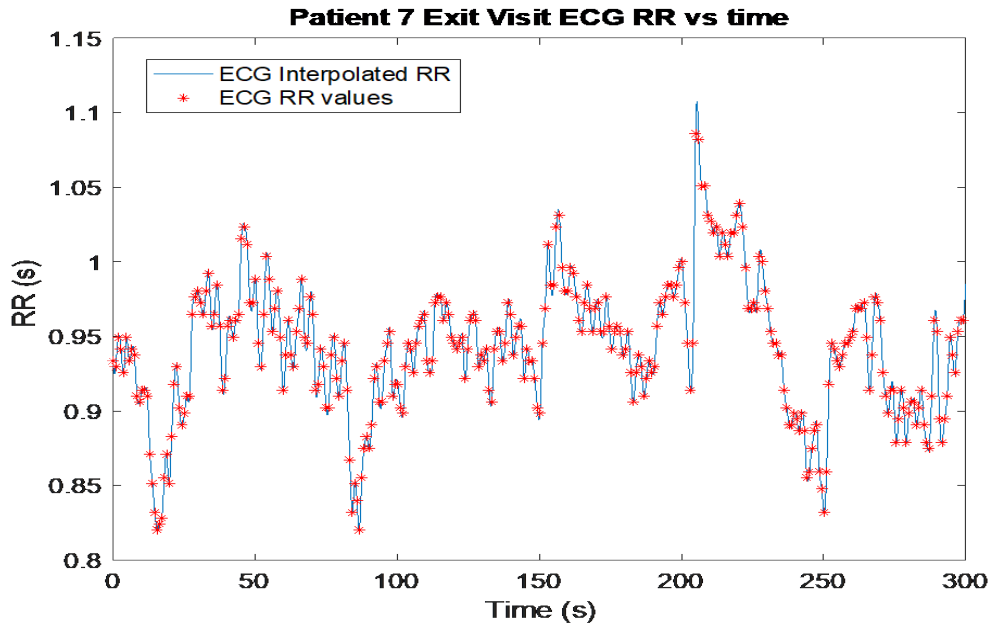


Figure A6. 829: Patient 7 Exit Visit Interpolated ECG RR

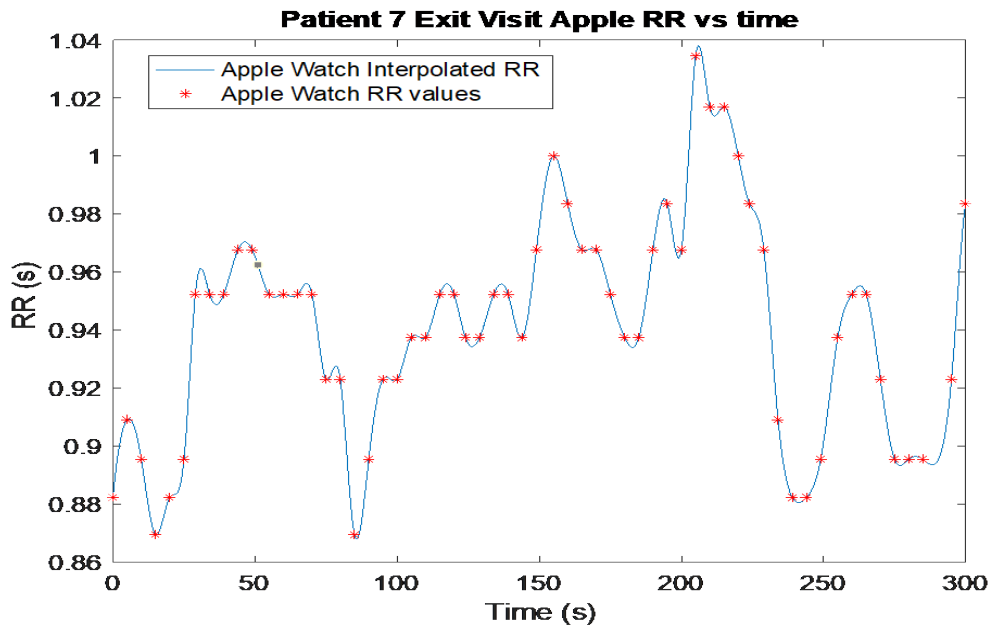


Figure A6. 830: Patient 7 Exit Visit Interpolated Apple RR

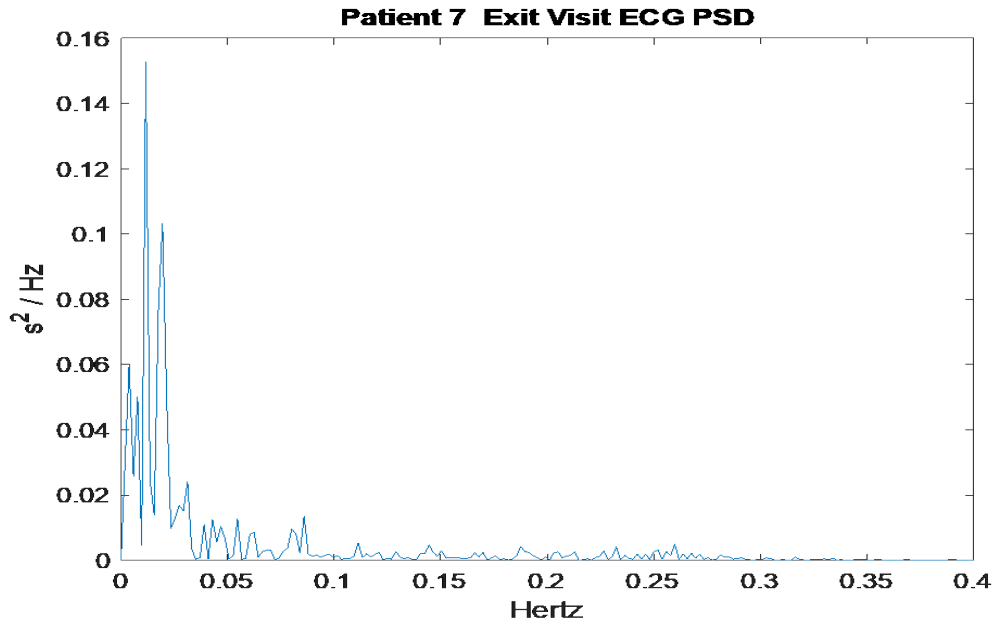


Figure A6. 831: Patient 7 Exit Visit ECG Power Spectral Density

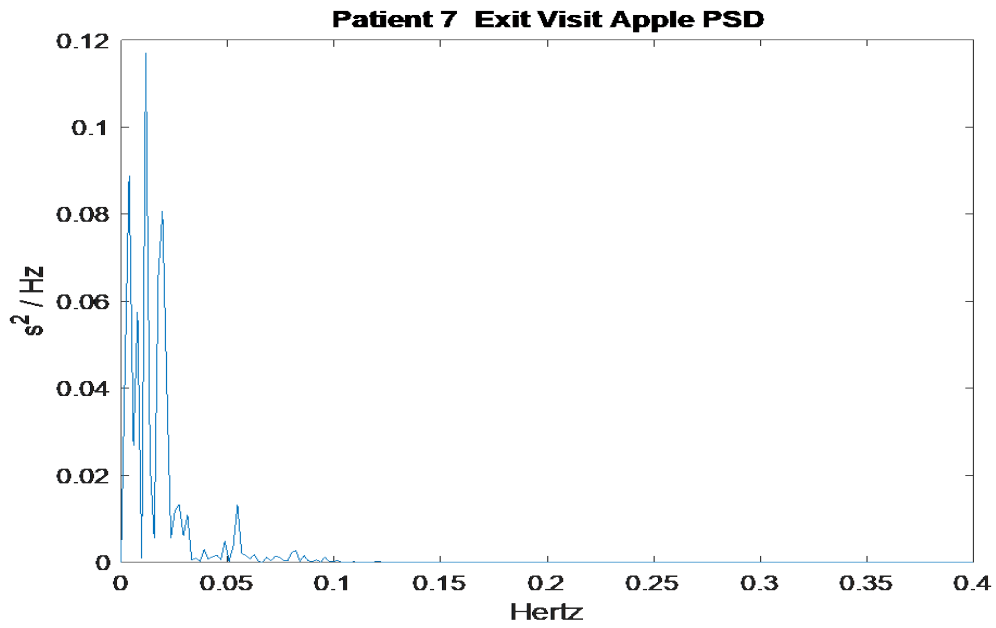


Figure A6. 832: Patient 7 Exit Visit Apple Power Spectral Density

## Patient 8 Initial Visit Readings

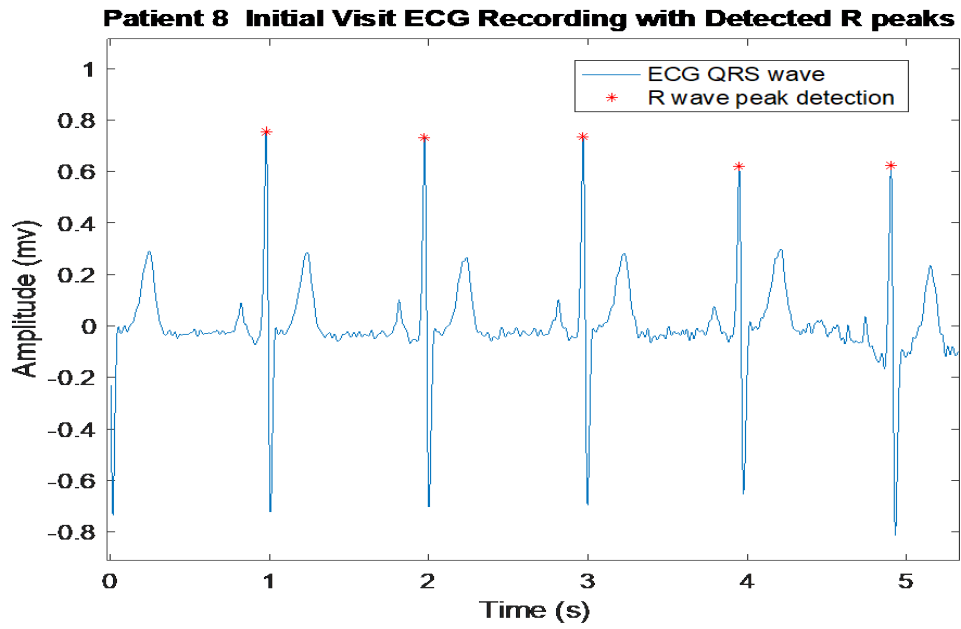


Figure A6. 833: Patient 8 Initial Visit ECG, with detected R peaks

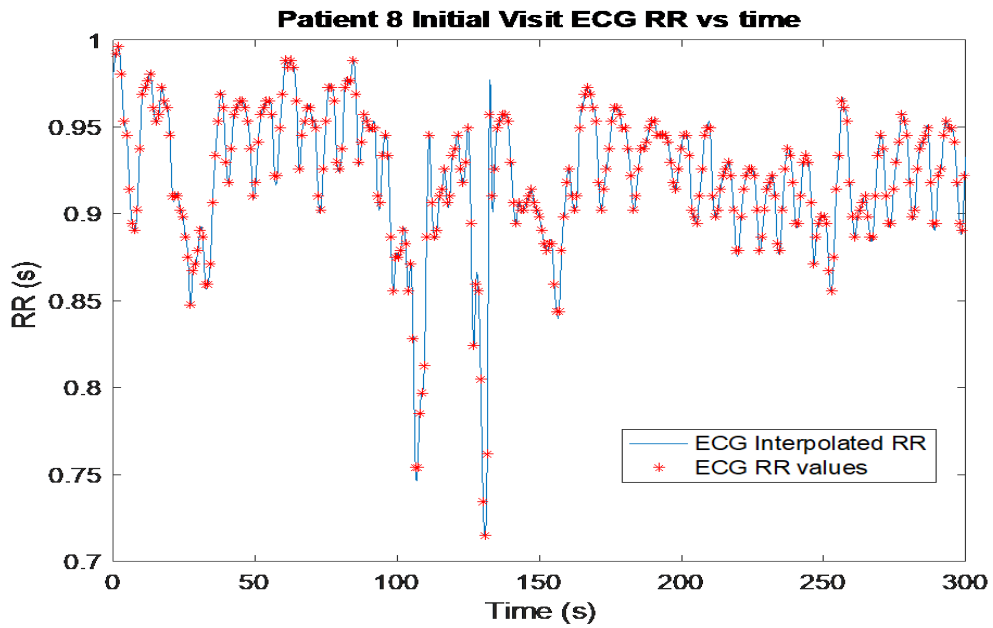


Figure A6. 834: Patient 8 Initial Visit Interpolated ECG HR

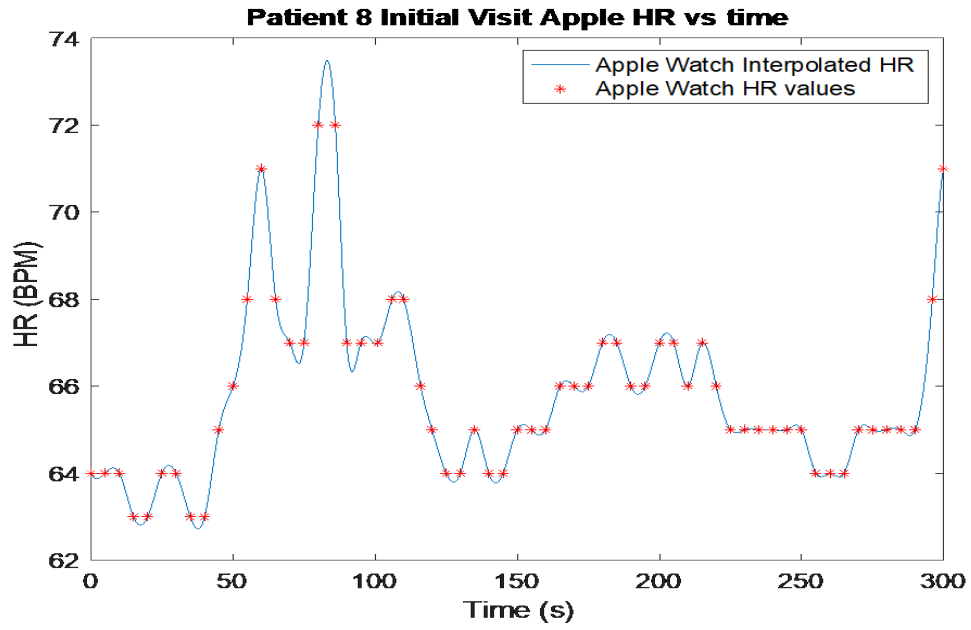


Figure A6. 835: Patient 8 Initial Visit Interpolated Apple HR

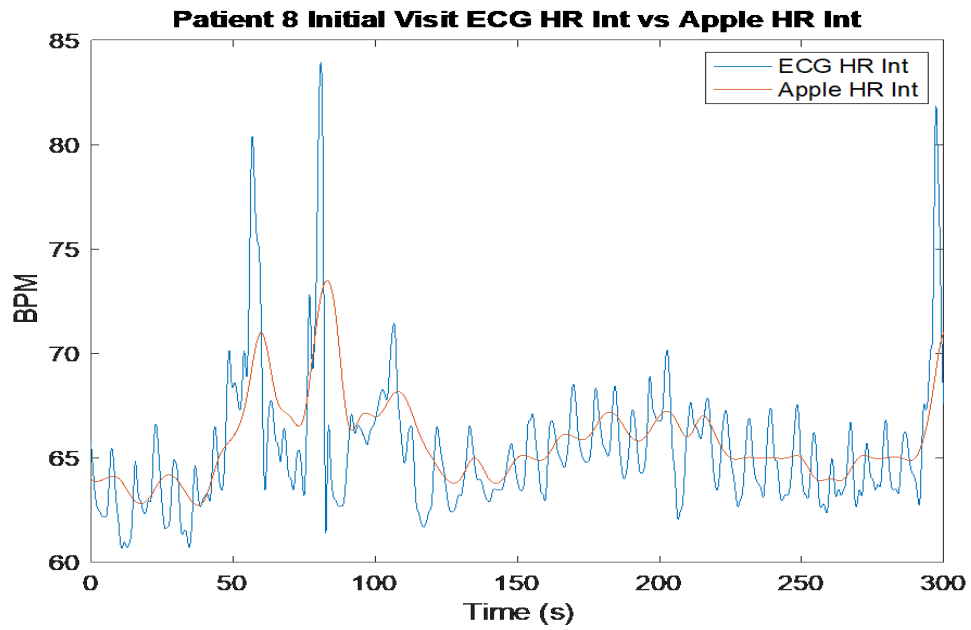


Figure A6. 836: Patient 8 Initial Visit Interpolated ECG and Apple HRs

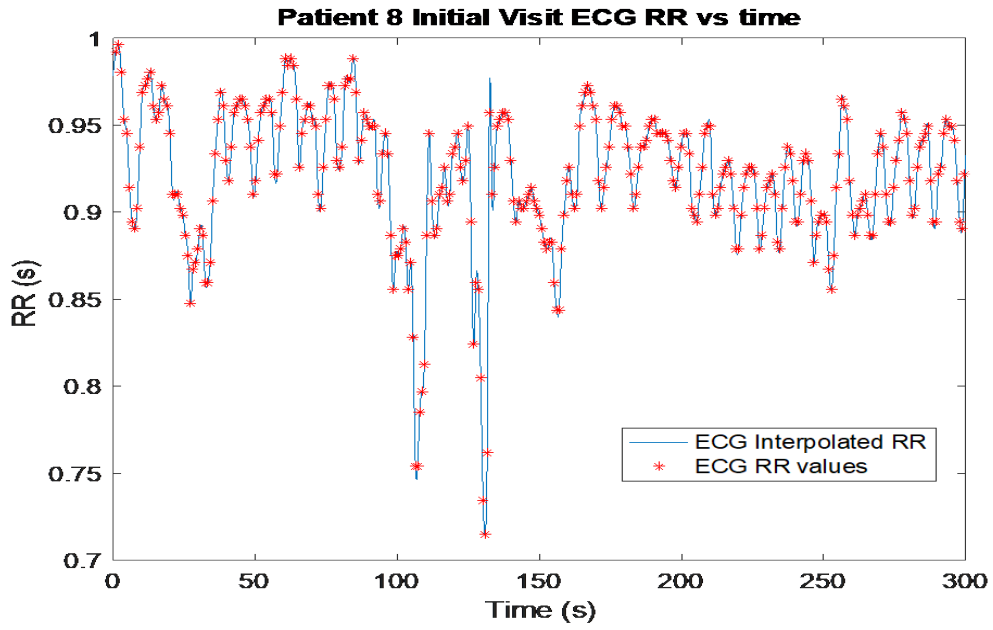


Figure A6. 837: Patient 8 Initial Visit Interpolated ECG RR

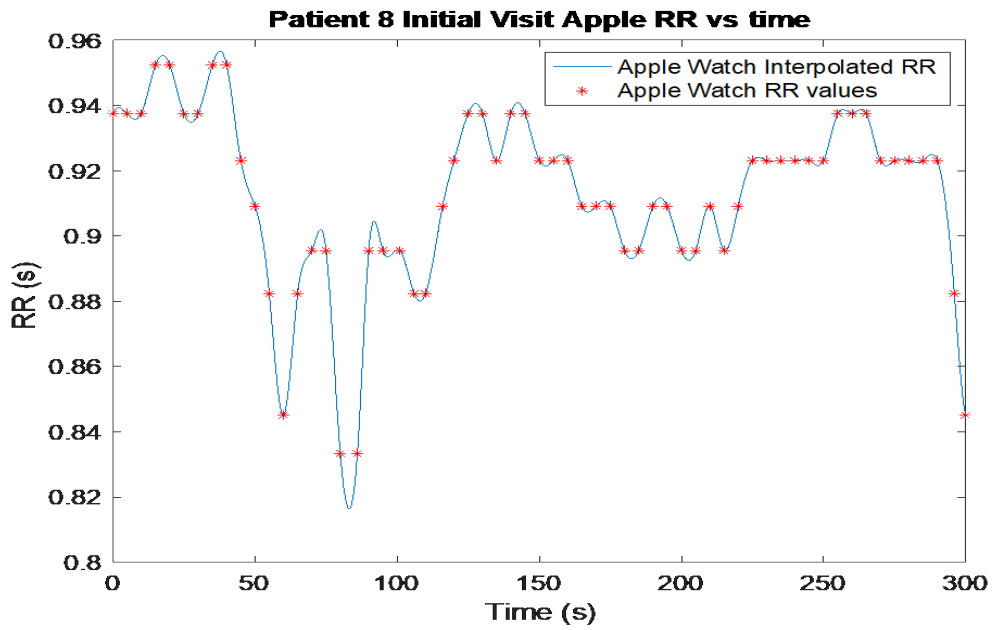


Figure A6. 838: Patient 8 Initial Visit Interpolated Apple RR

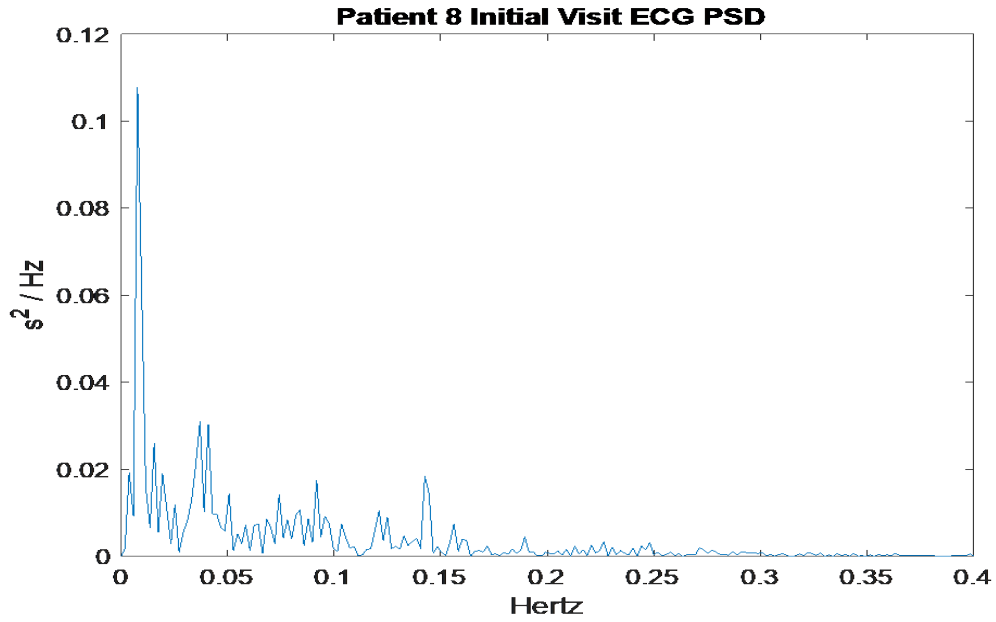


Figure A6. 839: Patient 8 Initial Visit ECG Power Spectral Density

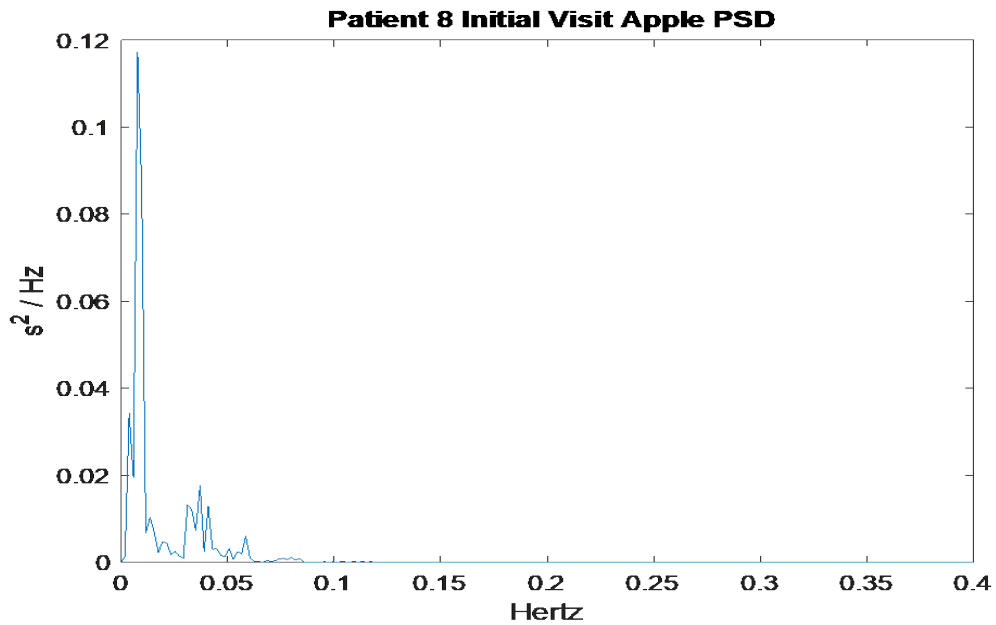


Figure A6. 840: Patient 8 Initial Visit Apple Power Spectral Density



## Patient 8 Exit Visit Readings

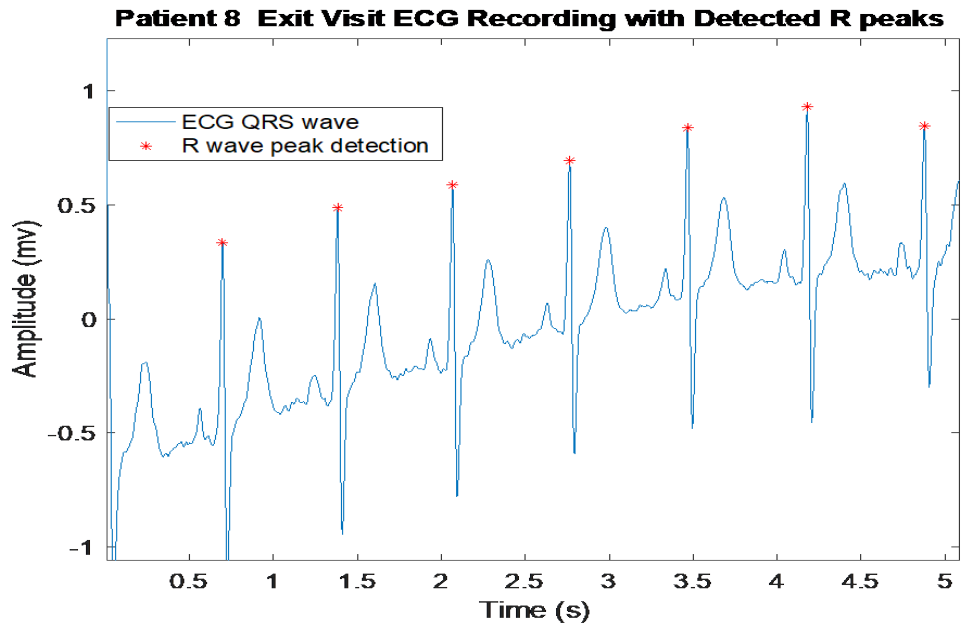


Figure A6. 841: Patient 8 Exit Visit ECG, with detected R peaks

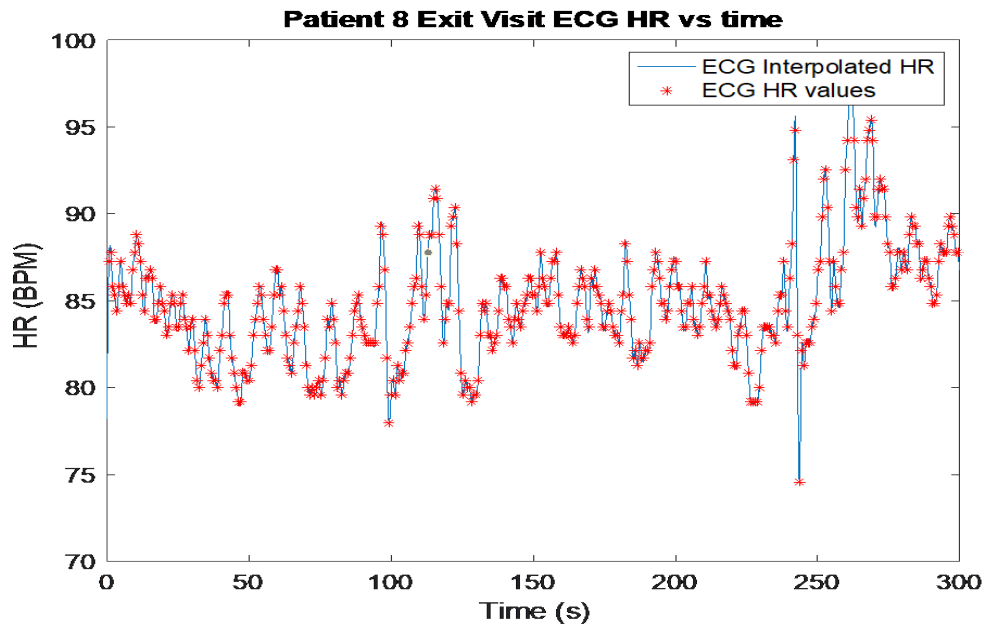


Figure A6. 842: Patient 8 Exit Visit Interpolated ECG HR

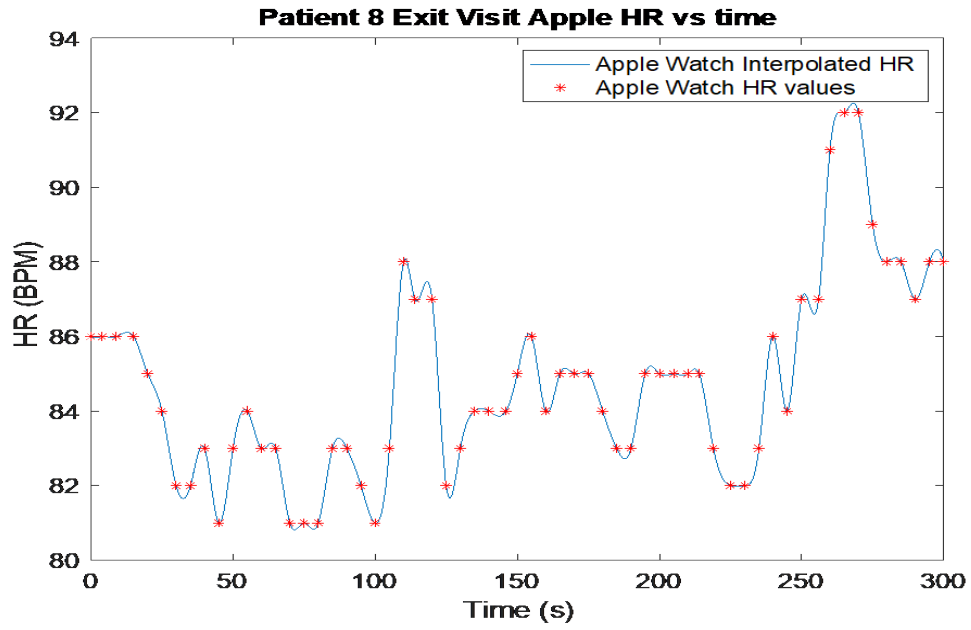


Figure A6. 843: Patient 8 Exit Visit Interpolated Apple HR

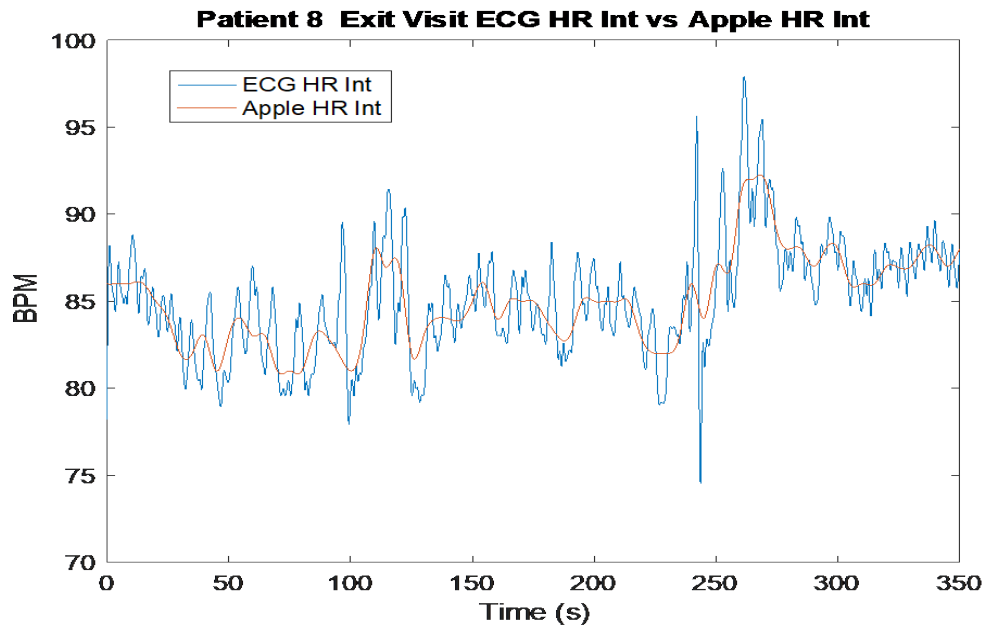


Figure A6. 844: Patient 8 Exit Visit Interpolated ECG and Apple HRs

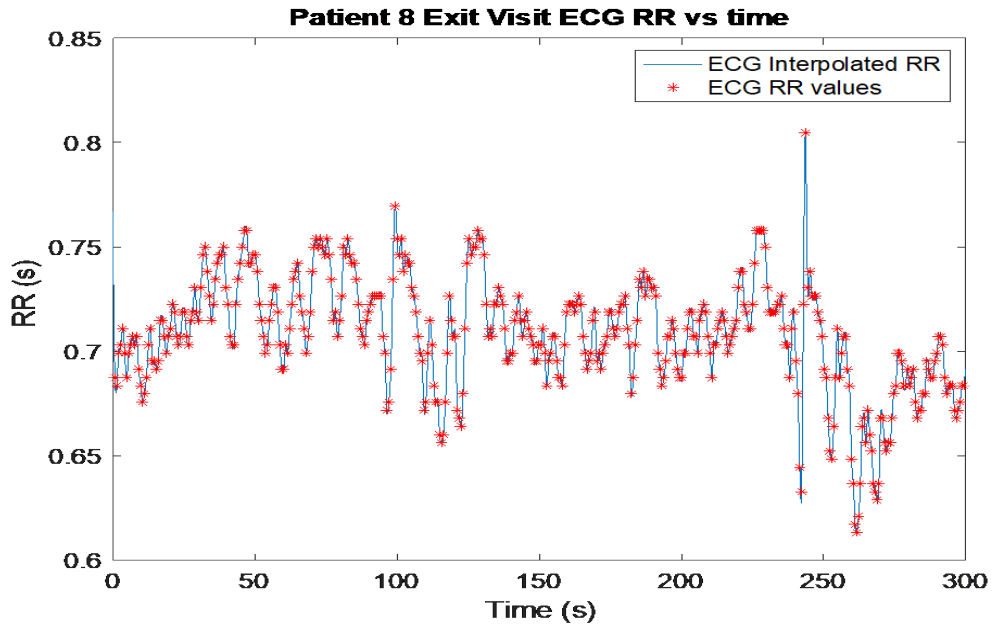


Figure A6. 845: Patient 8 Exit Visit Interpolated ECG RR

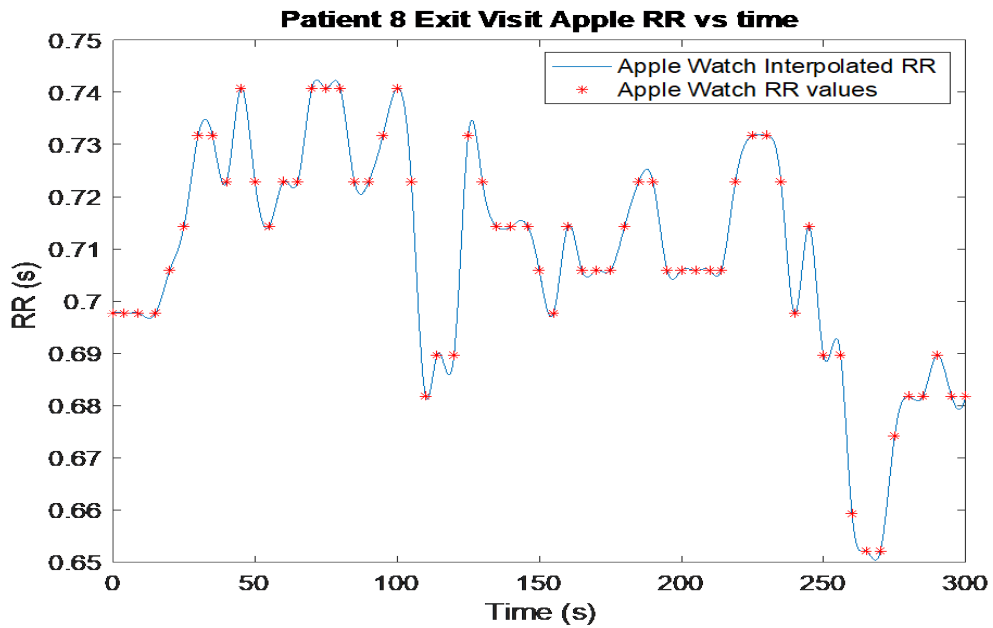


Figure A6. 846: Patient 8 Exit Visit Interpolated Apple RR

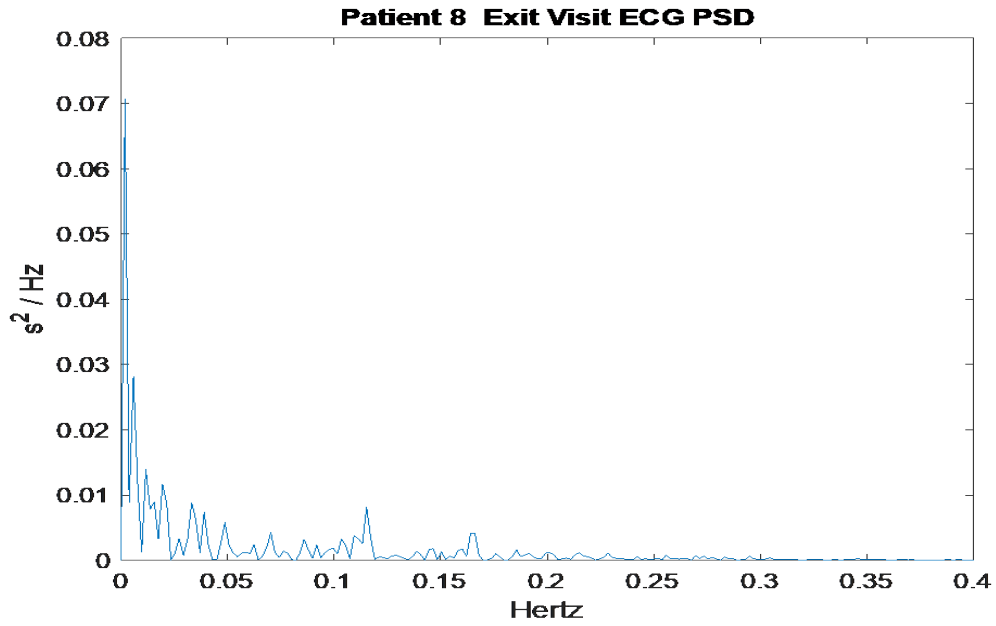


Figure A6. 847: Patient 8 Exit Visit ECG Power Spectral Density

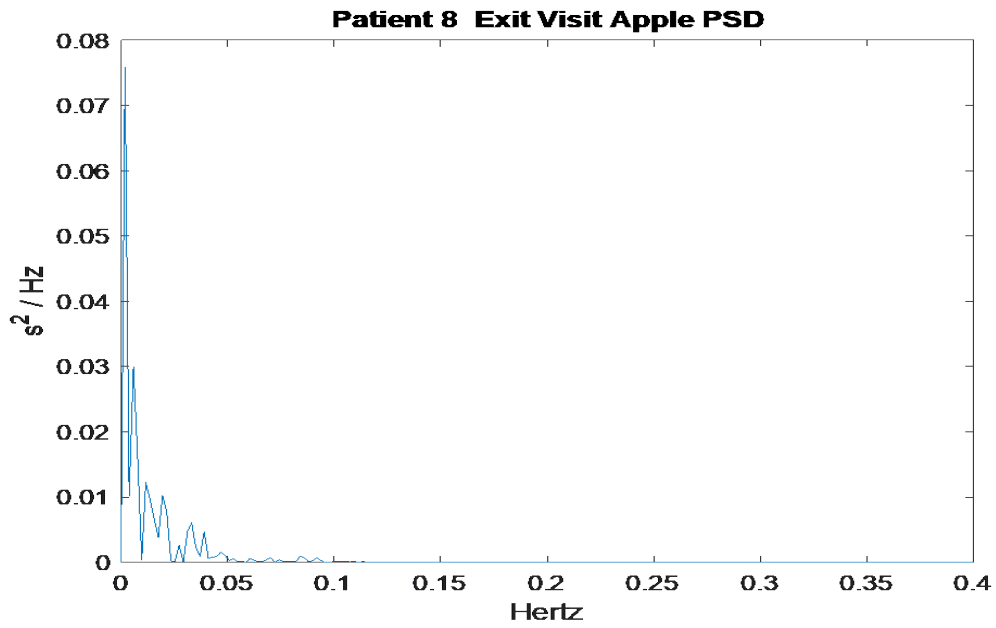


Figure A6. 848: Patient 8 Exit Visit Apple Power Spectral Density

## Patient 9 Initial Visit Readings

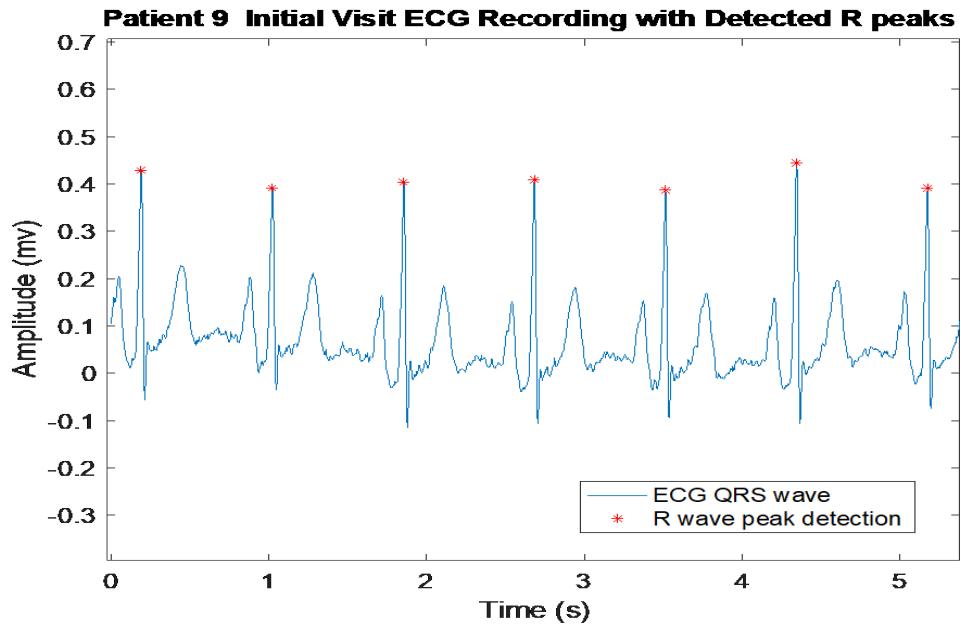


Figure A6. 849: Patient 9 Initial Visit ECG, with detected R peaks

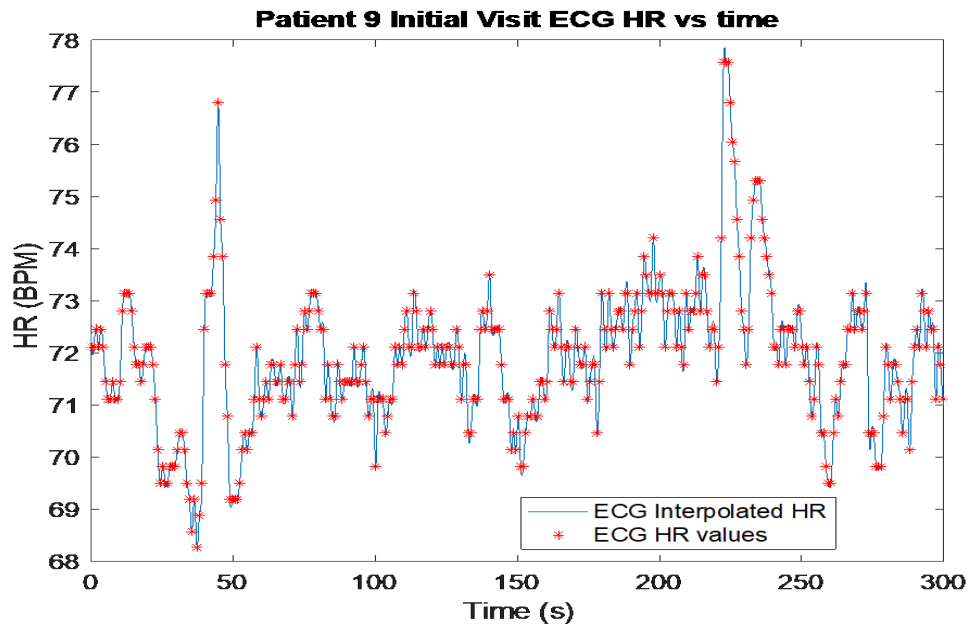


Figure A6. 850: Patient 9 Initial Visit Interpolated ECG HR

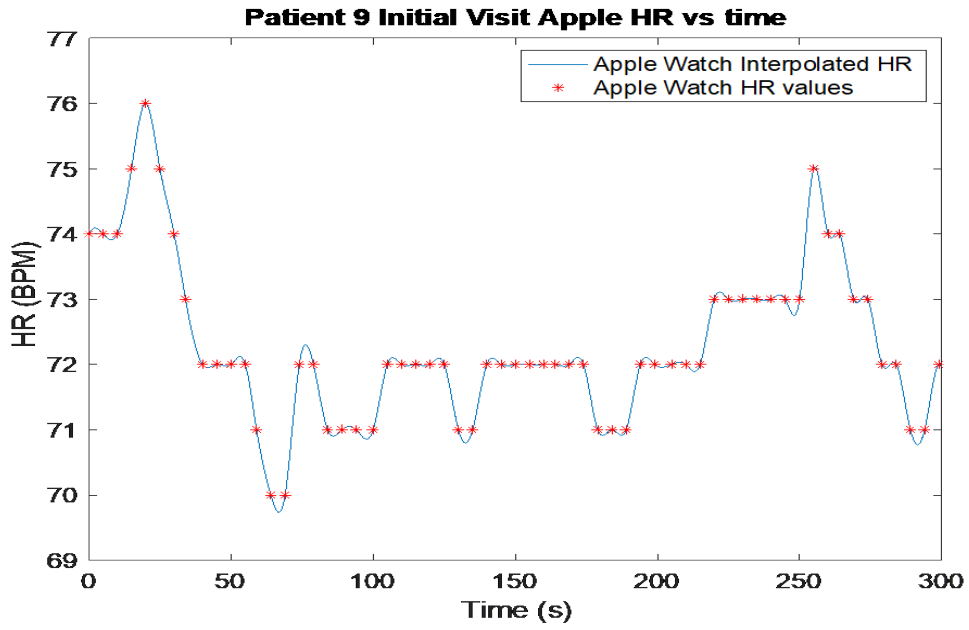


Figure A6. 851: Patient 9 Initial Visit Interpolated Apple HR

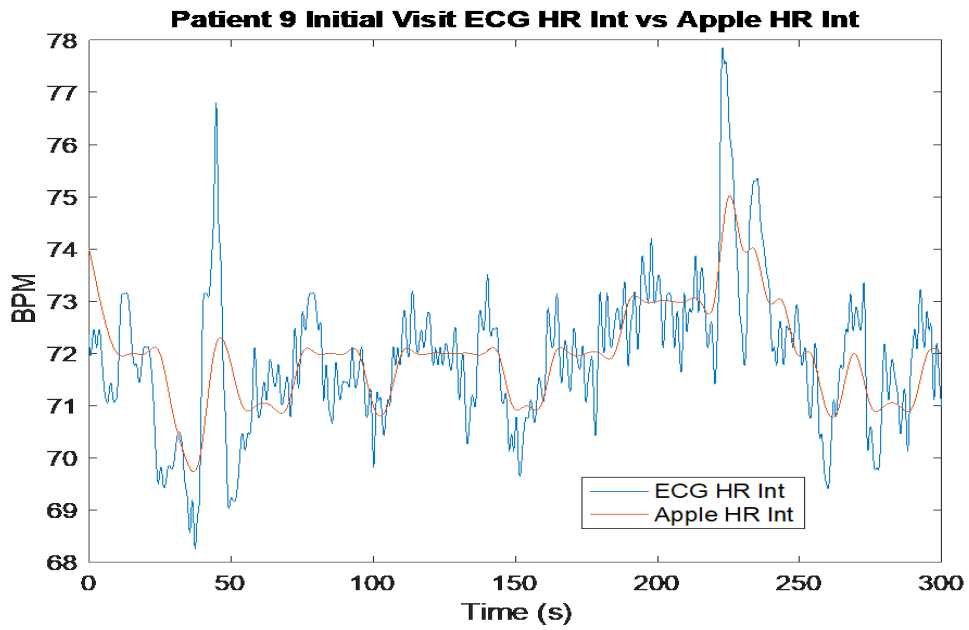


Figure A6. 852: Patient 9 Initial Visit Interpolated ECG and Apple HRs

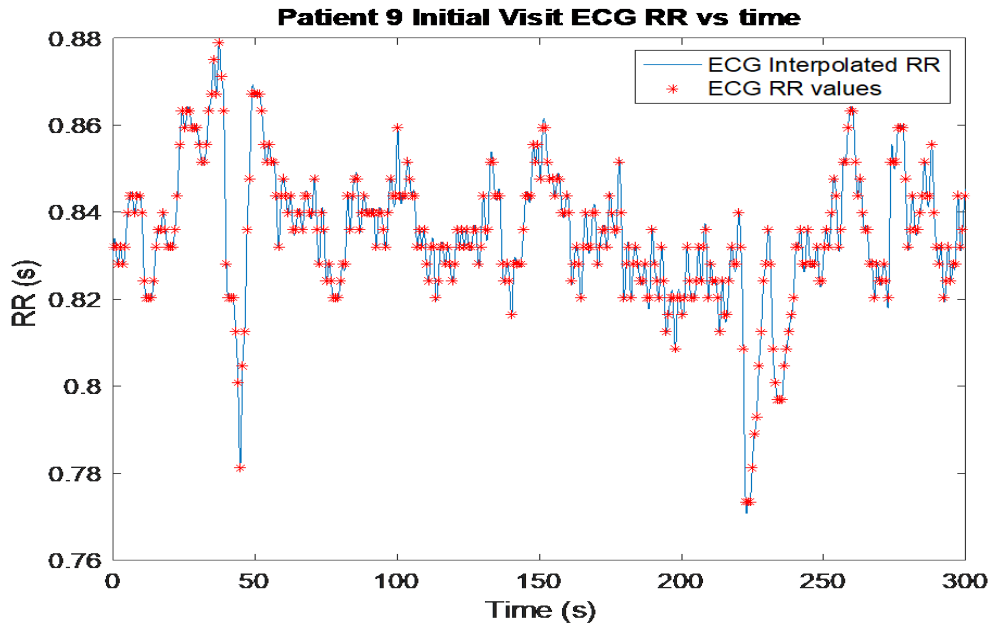


Figure A6. 853: Patient 9 Initial Visit Interpolated ECG RR

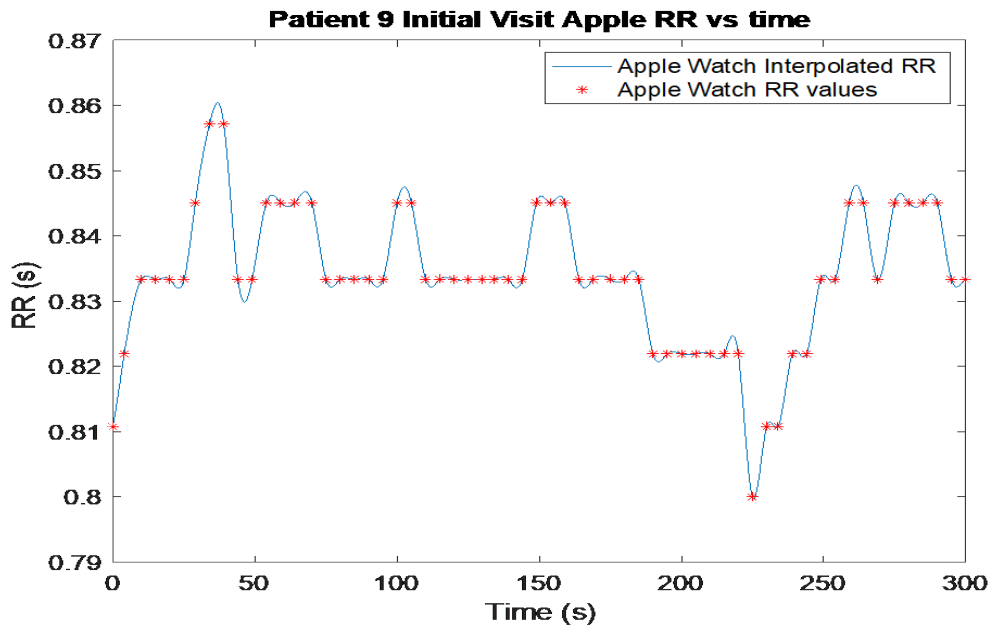


Figure A6. 854: Patient 9 Initial Visit Interpolated Apple RR

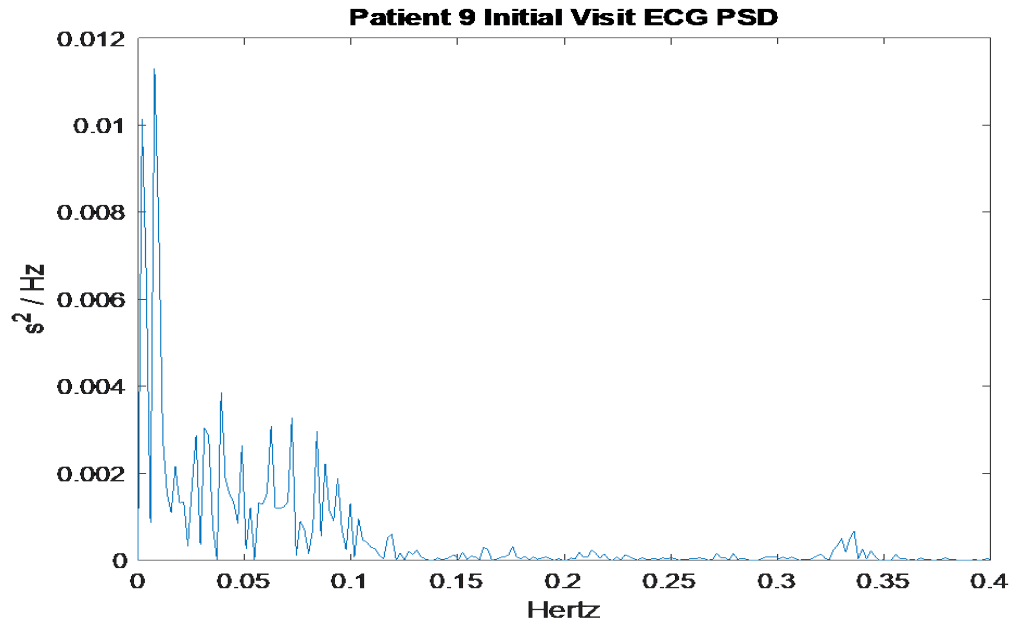


Figure A6. 855: Patient 9 Initial Visit ECG Power Spectral Density

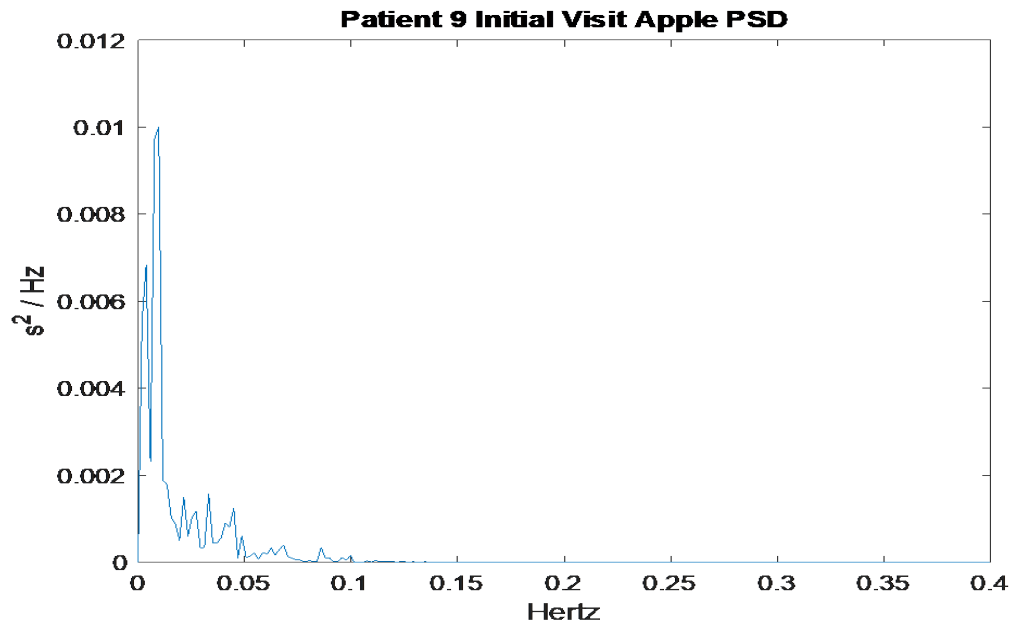


Figure A6. 856: Patient 9 Initial Visit Apple Power Spectral Density



## Patient 9 Exit Visit Readings

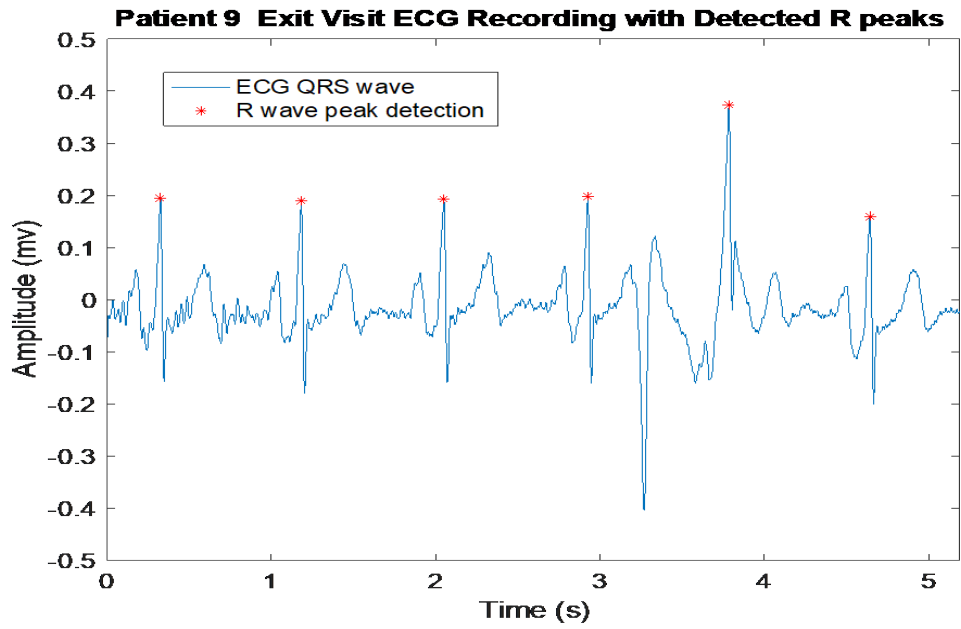


Figure A6. 857: Patient 9 Exit Visit ECG, with detected R peaks

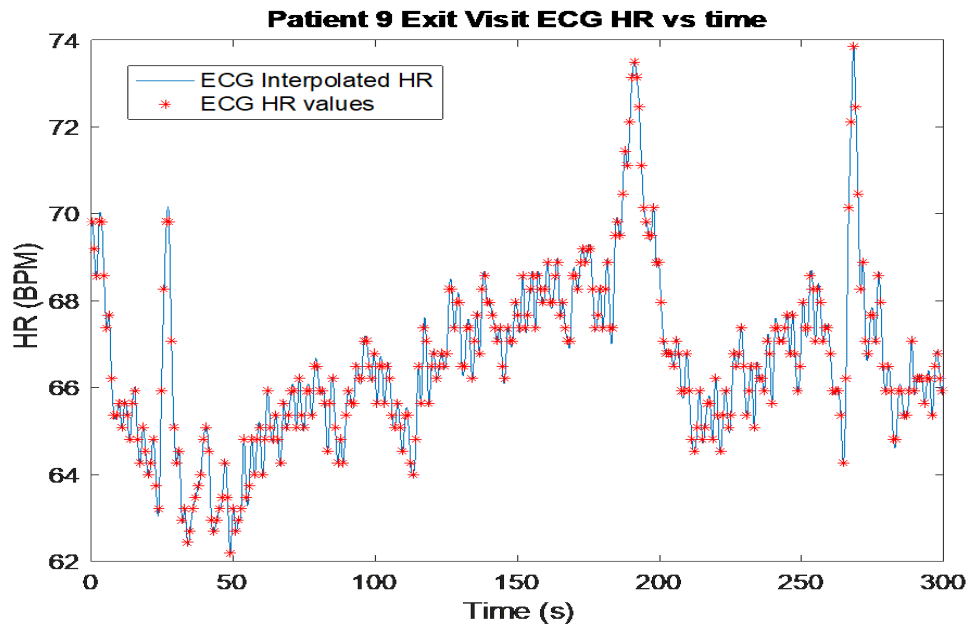


Figure A6. 858: Patient 9 Exit Visit Interpolated ECG HR

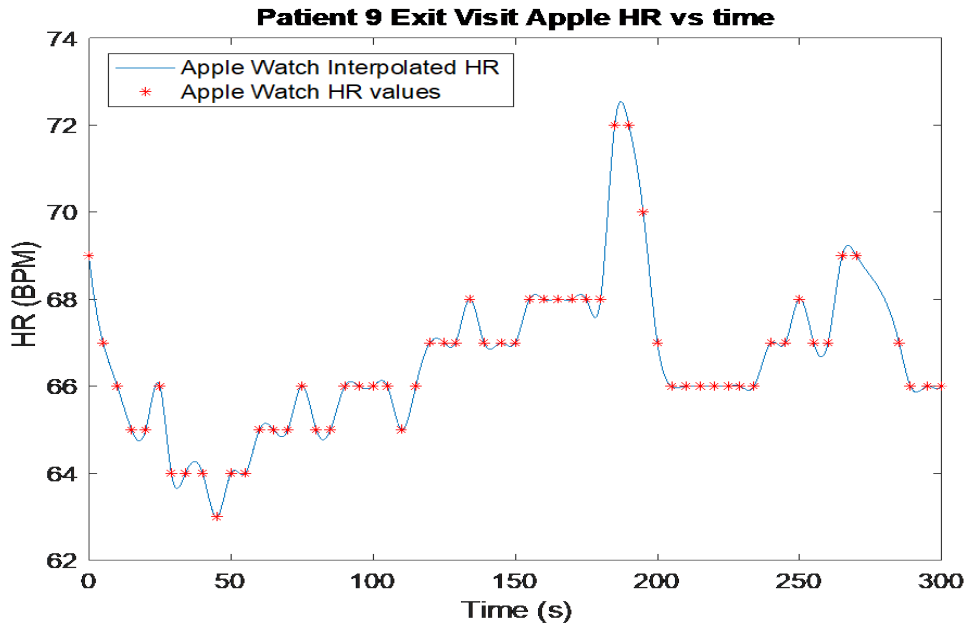


Figure A6. 859: Patient 9 Exit Visit Interpolated Apple HR

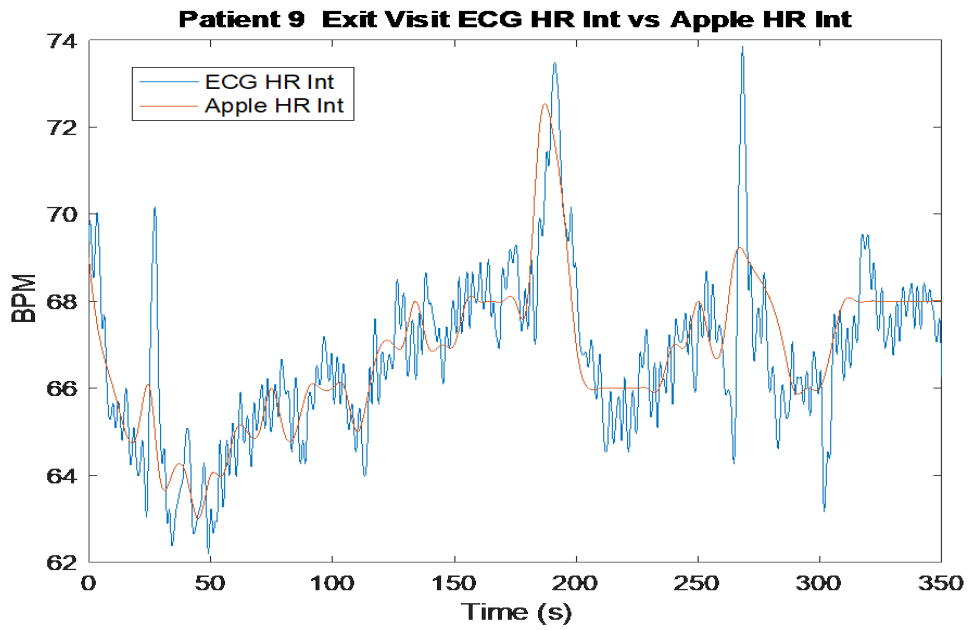


Figure A6. 860: Patient 9 Exit Visit Interpolated ECG and Apple HRs

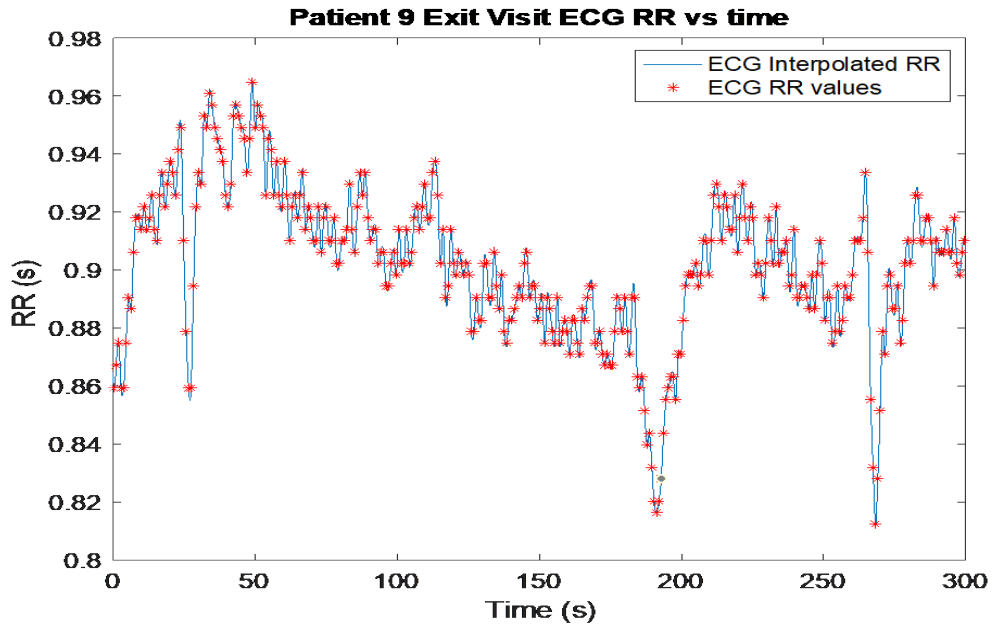


Figure A6. 861: Patient 9 Exit Visit Interpolated ECG RR

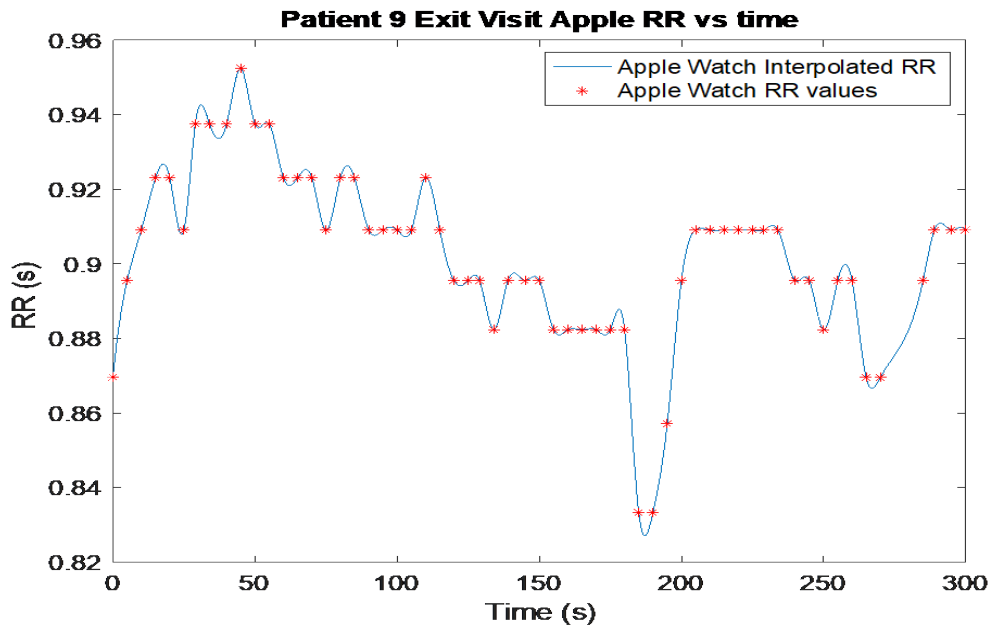


Figure A6. 862: Patient 9 Exit Visit Interpolated Apple RR

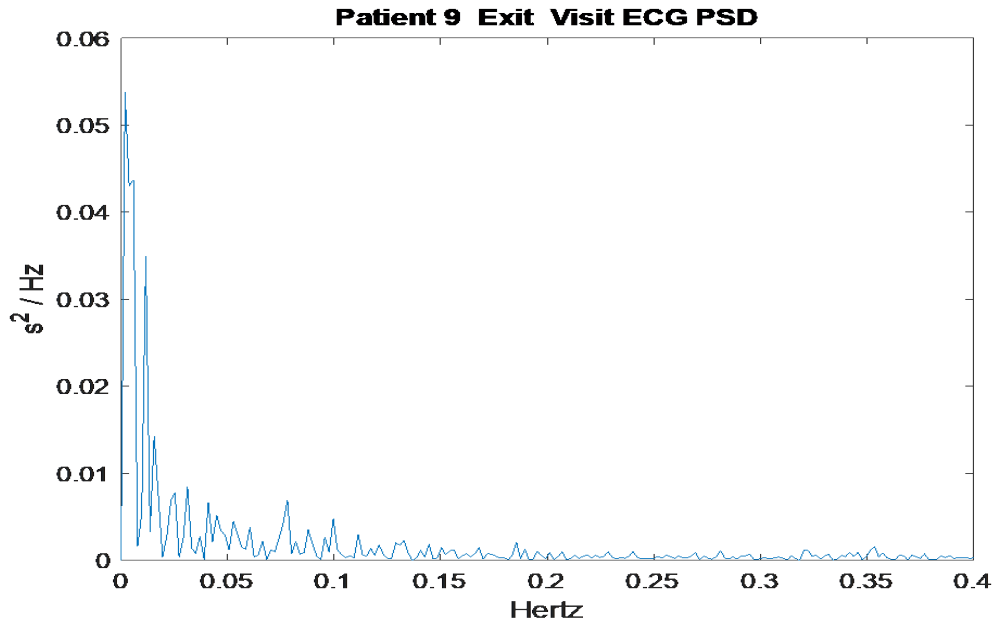


Figure A6. 863: Patient 9 Exit Visit ECG Power Spectral Density

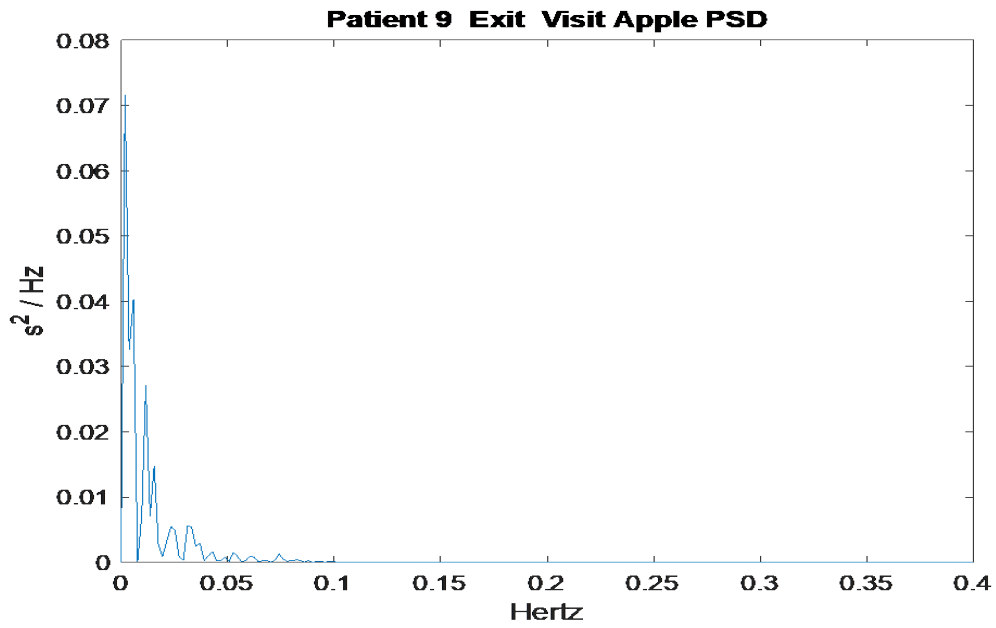


Figure A6. 864: Patient 9 Exit Visit Apple Power Spectral Density

## A.7 Chapter 7 Appendix

### Patient 1 Active Energy:

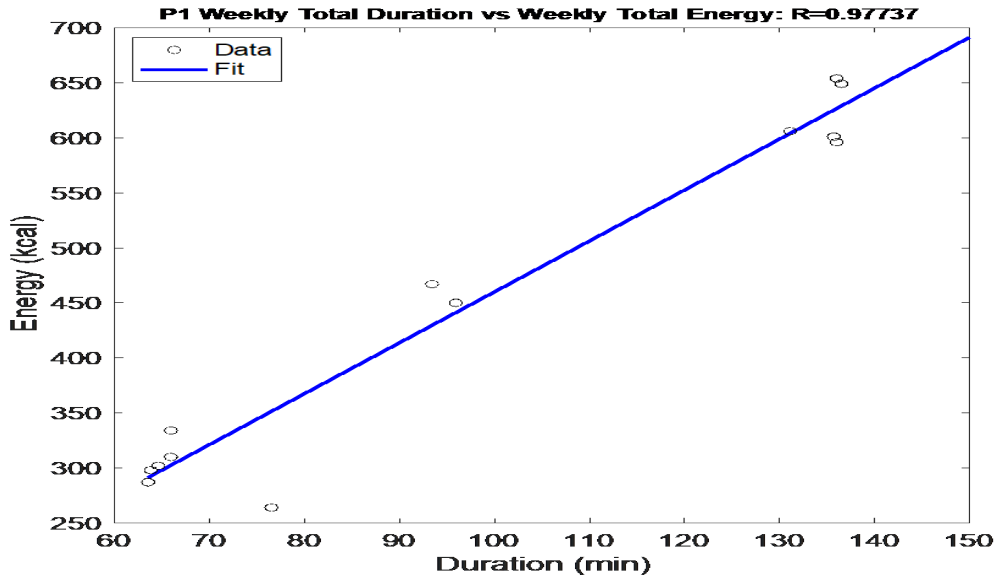


Figure A4.865: Weekly Total duration vs. weekly total active energy linear correlation for patient#1

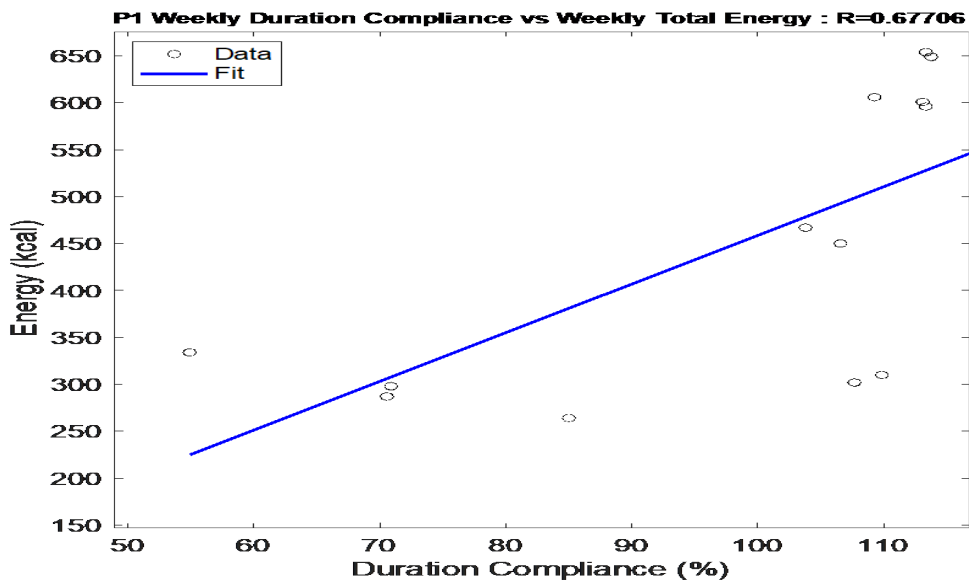


Figure A4.866: Weekly Duration Compliance vs. weekly total active energy linear correlation for patient#1

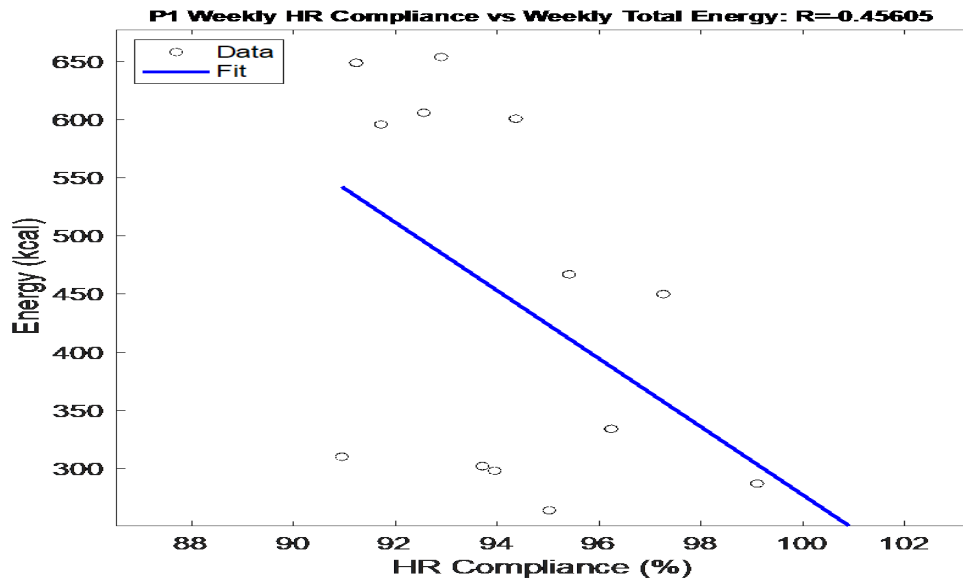


Figure A4.867: Weekly heart rate compliance vs. weekly total active energy linear correlation for patient#1

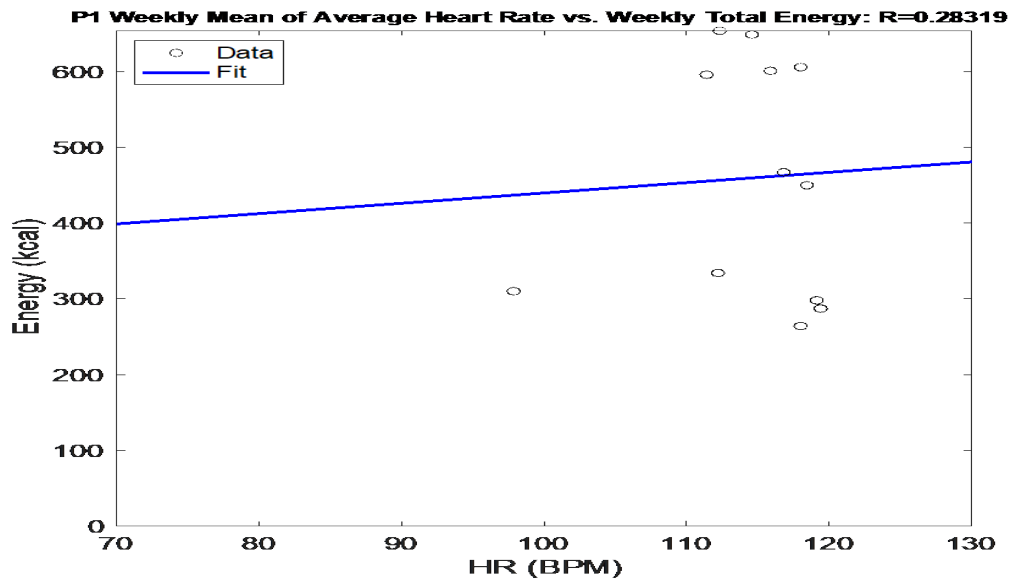


Figure A4.868: Weekly mean of average heart rate vs. weekly total active energy linear correlation for patient#1

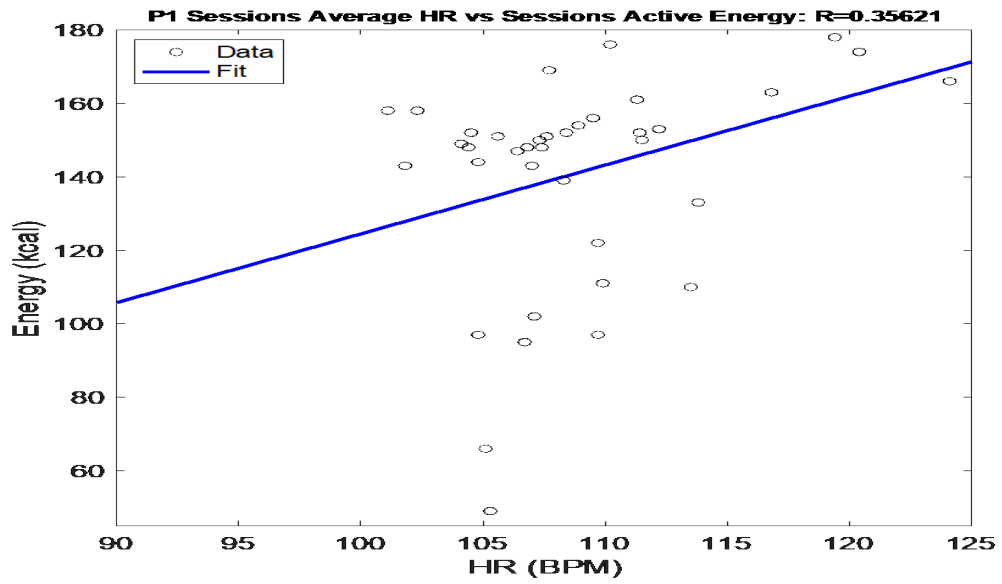


Figure A4.869: Sessions average heart rate vs. sessions active energy linear correlation for patient#1

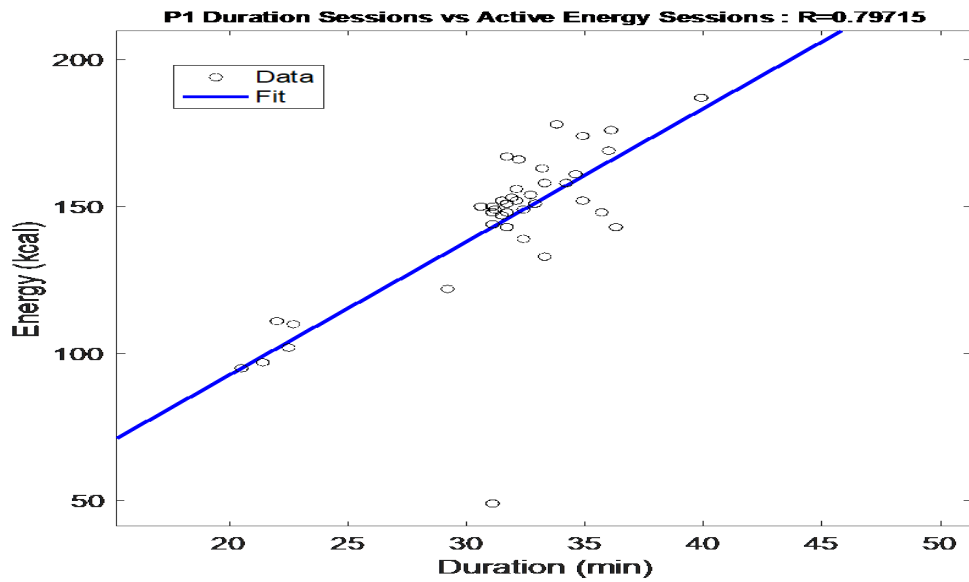
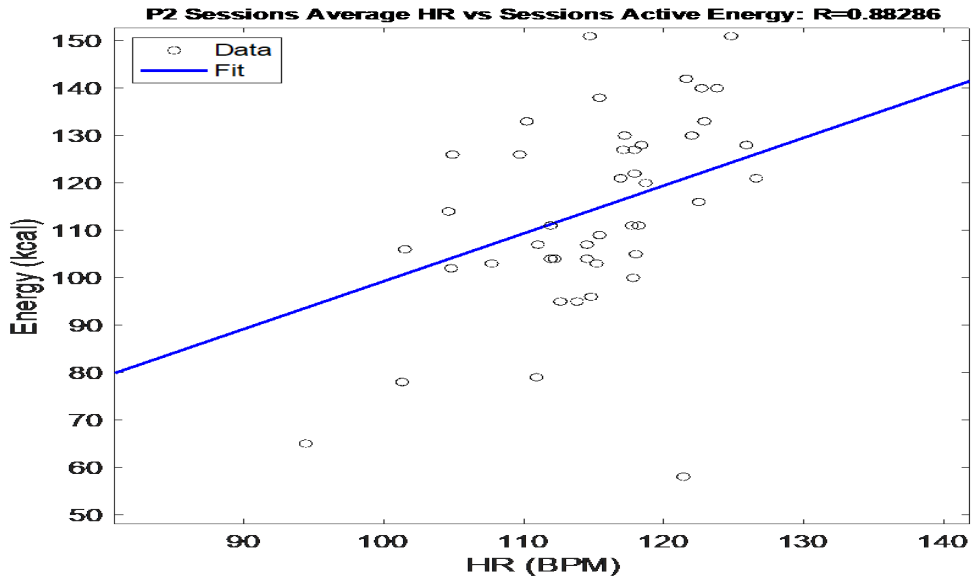
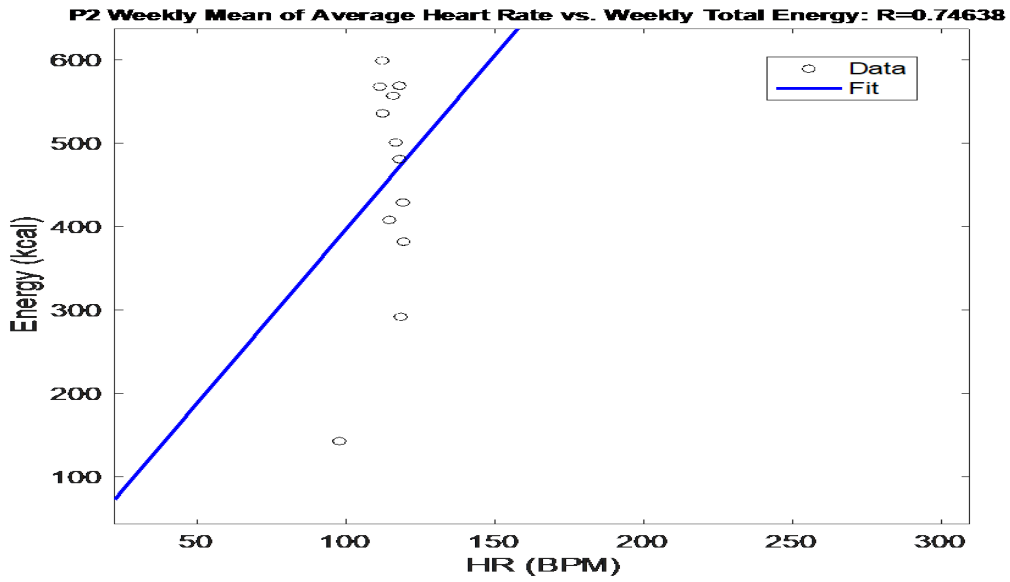


Figure A4.870: Duration Sessions vs. sessions active energy linear correlation for patient#1

**Patient 2 Active Energy:**



*Figure A4.871: Sessions average heart rate vs. sessions active energy linear correlation for patient#2*



*Figure A4.872: Weekly mean of average heart rate vs. weekly total active energy linear correlation for patient#2*



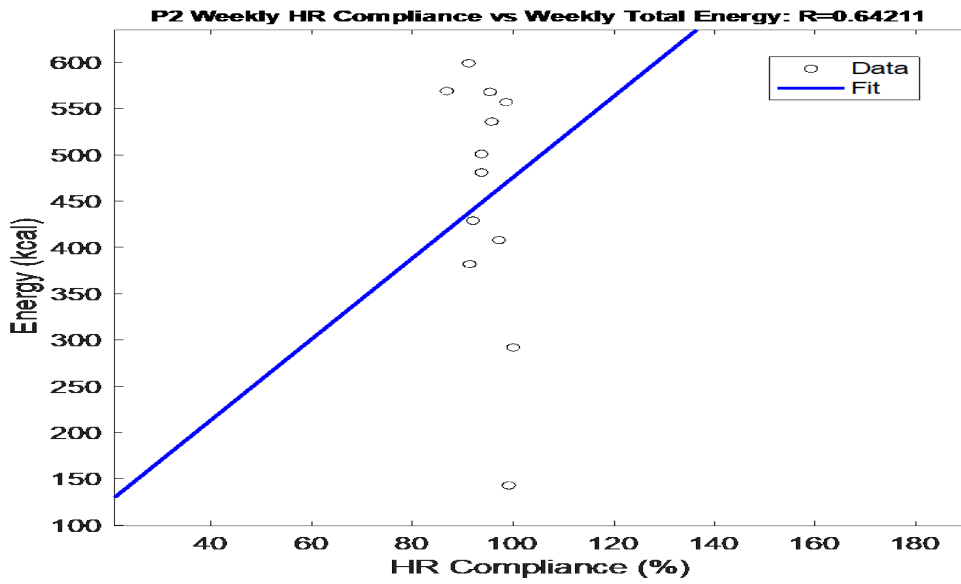


Figure A4.873: Weekly heart rate compliance vs. weekly total active energy linear correlation for patient#2

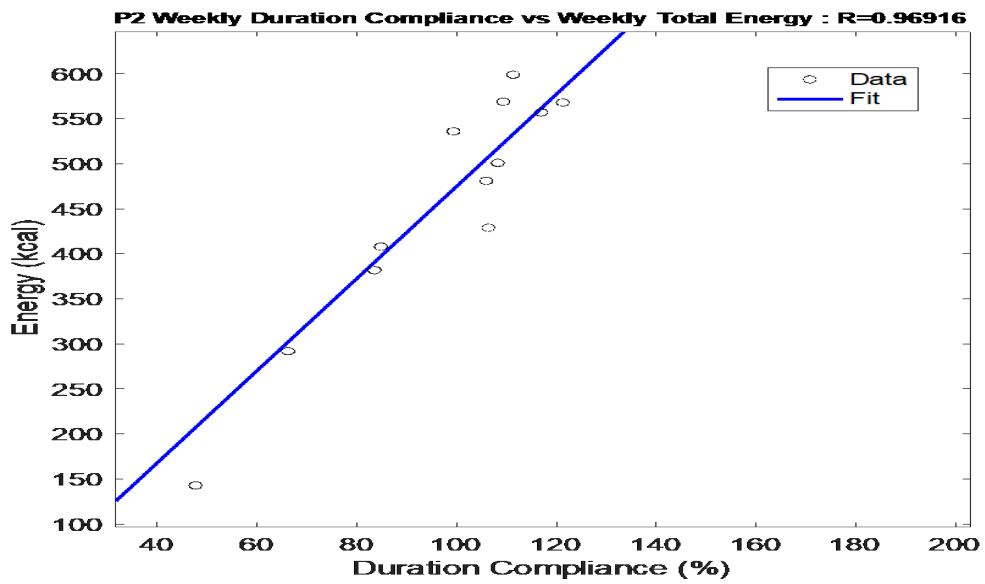
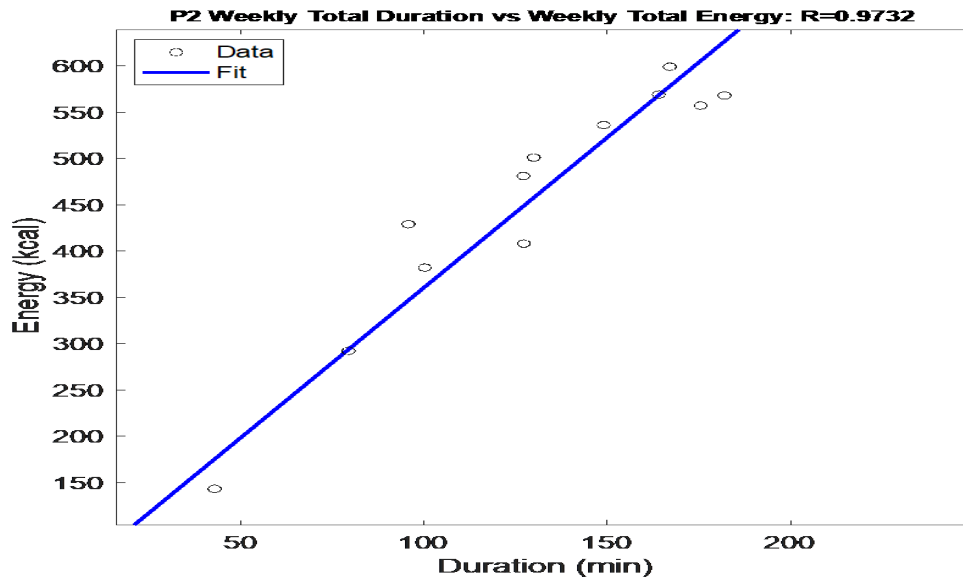


Figure A4.874: Weekly Duration Compliance vs. weekly total active energy linear correlation for patient#2



*Figure A4.875: Weekly Total duration vs. weekly total active energy linear correlation for patient#2*

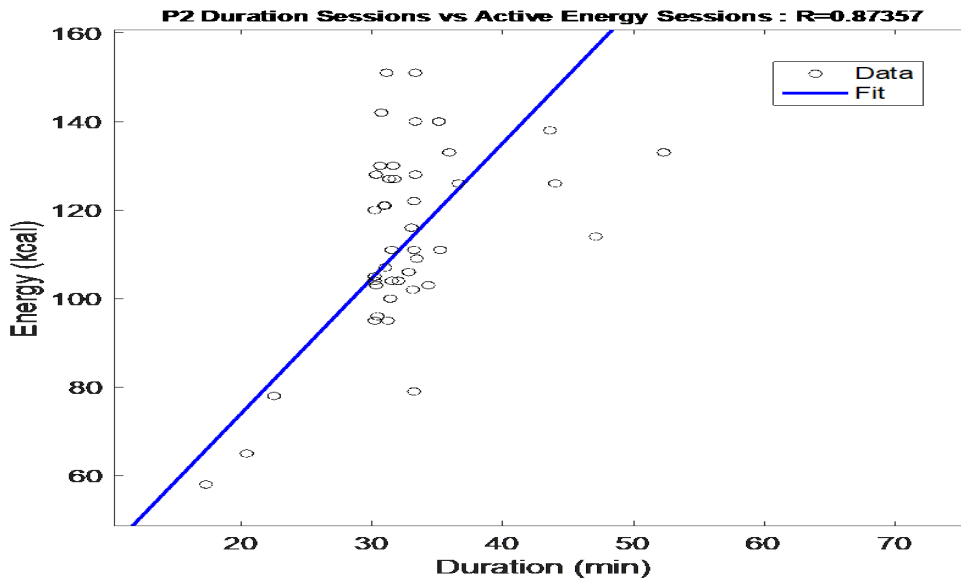


Figure A4.876: Duration Sessions vs. sessions active energy linear correlation for patient#2

**Patient 3 Active Energy:**

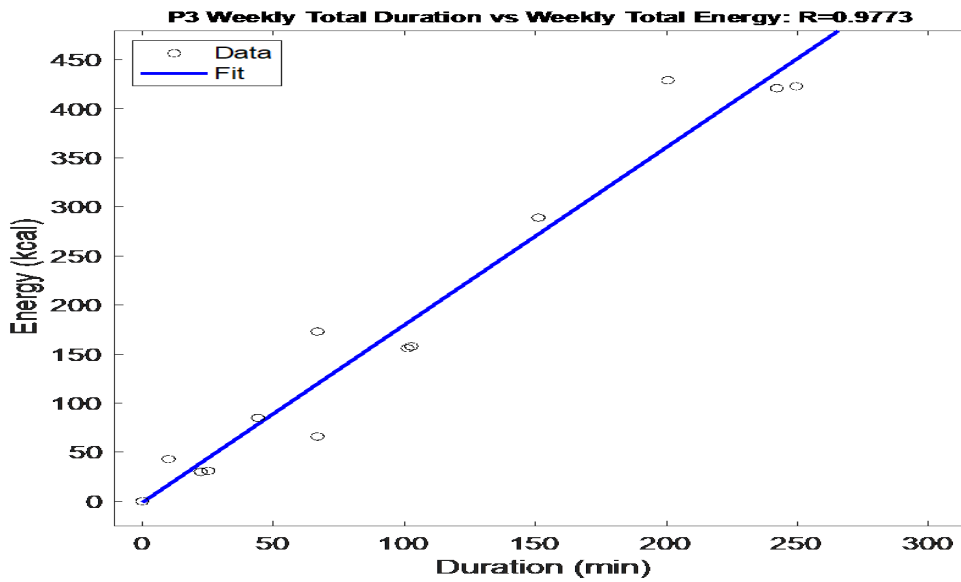


Figure A4.877: Weekly Total duration vs. weekly total active energy linear correlation for patient#3

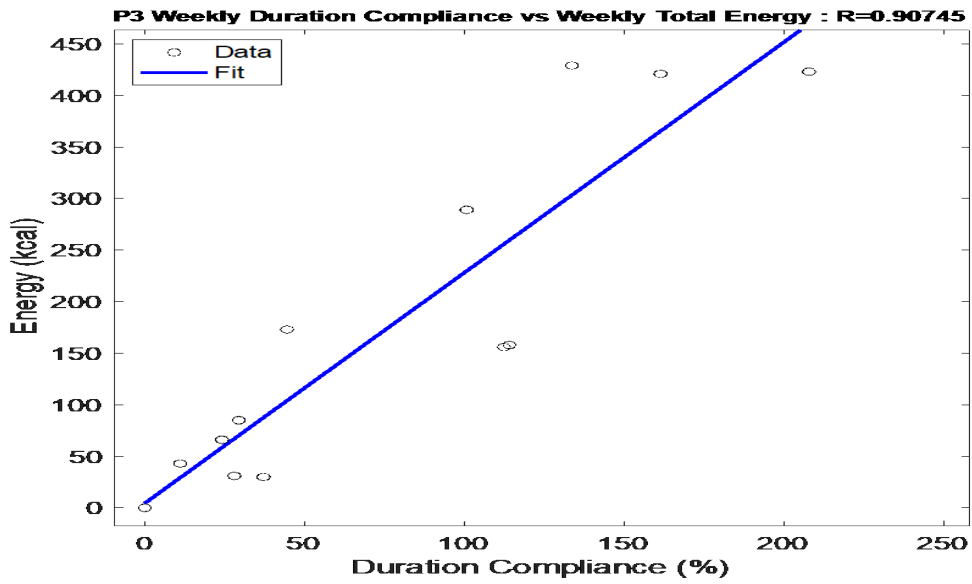


Figure A4.878: Weekly Duration Compliance vs. weekly total active energy linear correlation for patient#3

**Patient 3 Active Energy:**

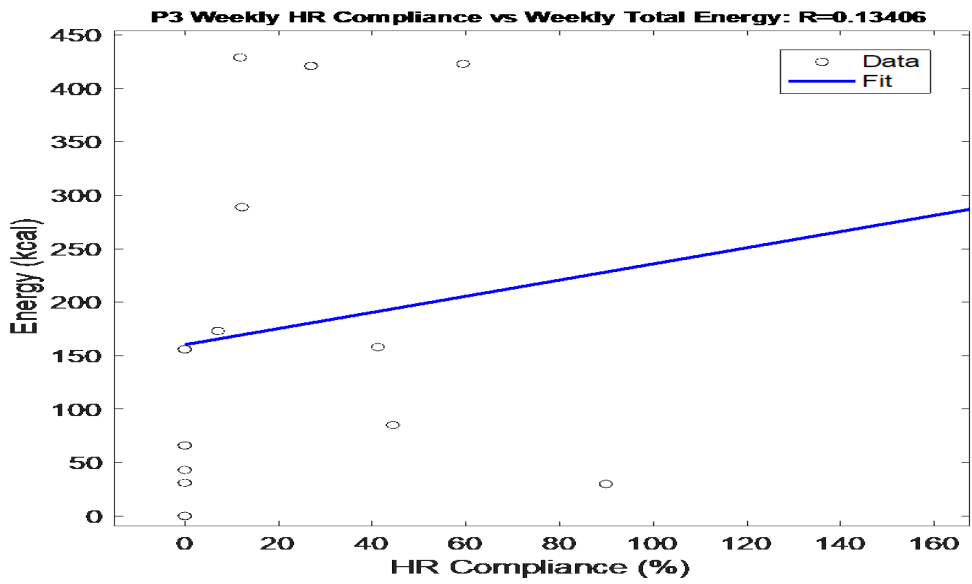


Figure A4.879: Weekly heart rate compliance vs. weekly total active energy linear correlation for patient#3

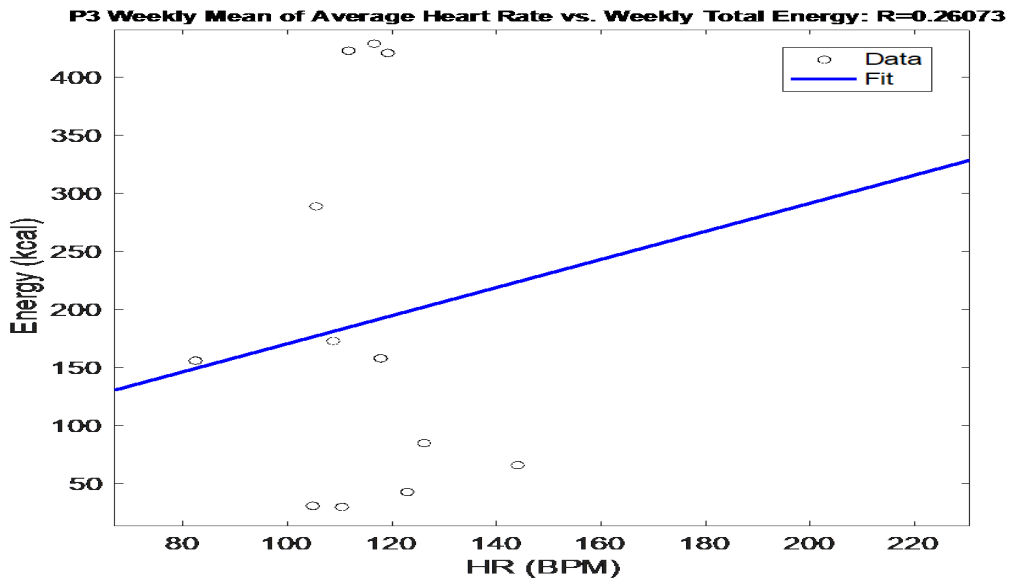


Figure A4.880: Weekly mean of average heart rate vs. weekly total active energy linear correlation for patient#3

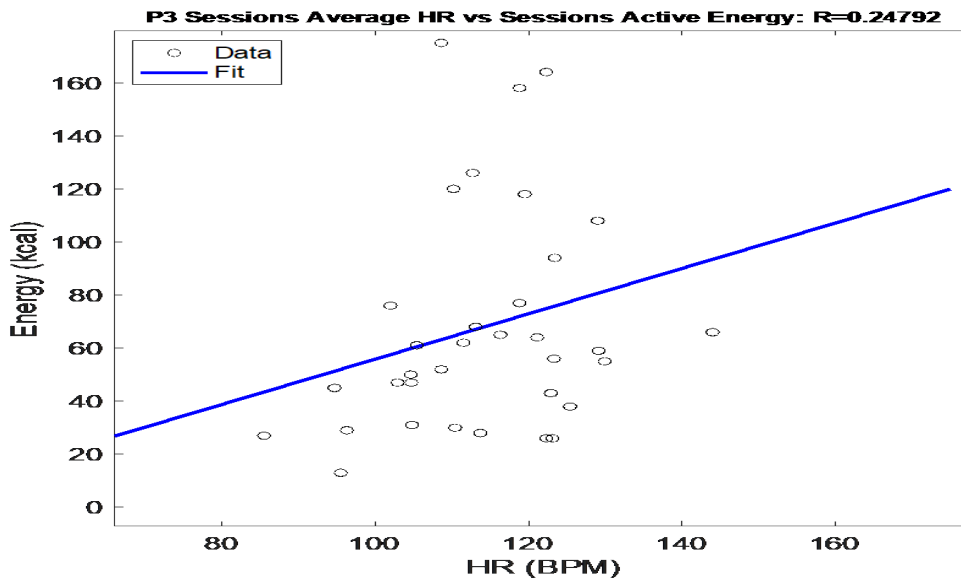


Figure A4.881: Sessions average heart rate vs. sessions active energy linear correlation for patient#3

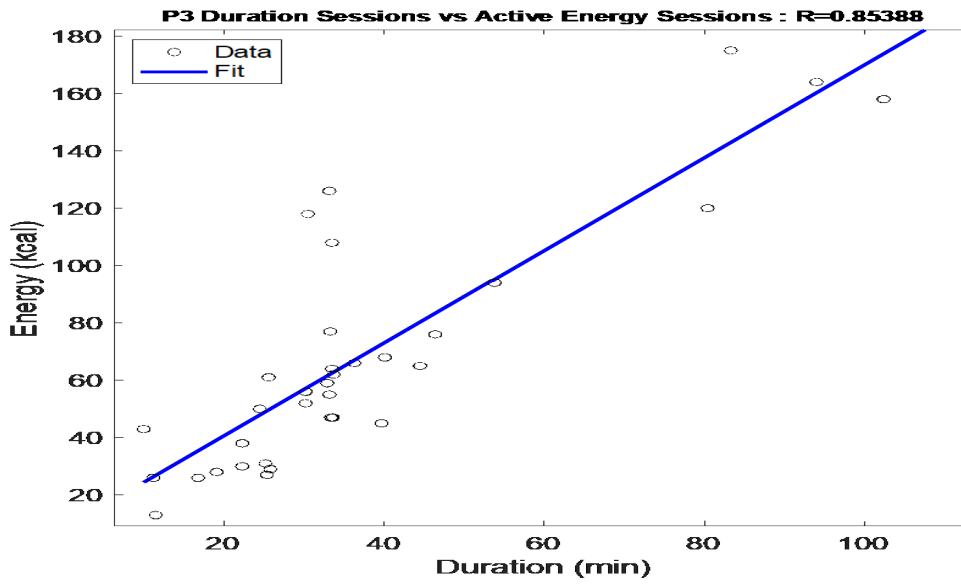


Figure A4.882: Duration Sessions vs. sessions active energy linear correlation for patient#3

**Patient 4 Active Energy:**

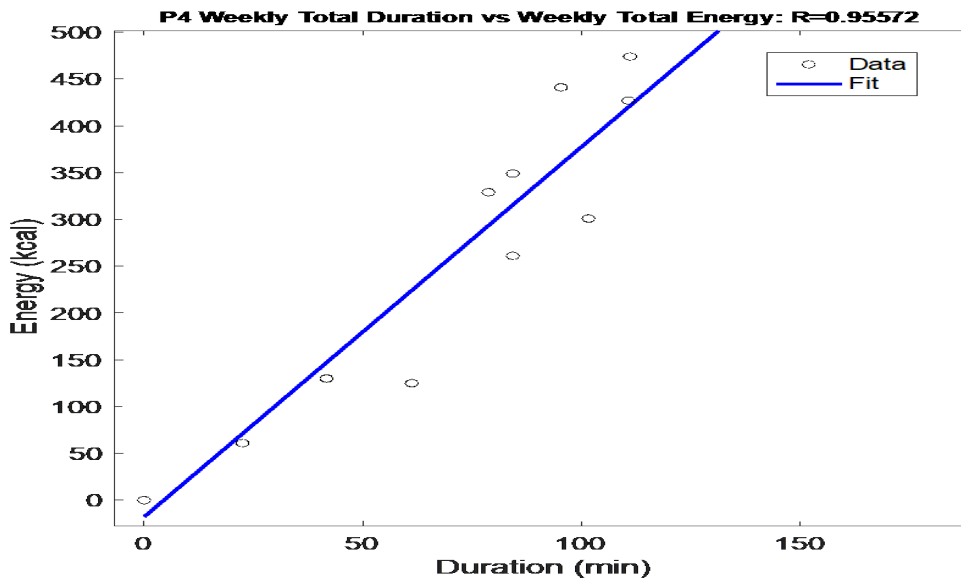


Figure A4.883: Weekly Total duration vs. weekly total active energy linear correlation for patient#4

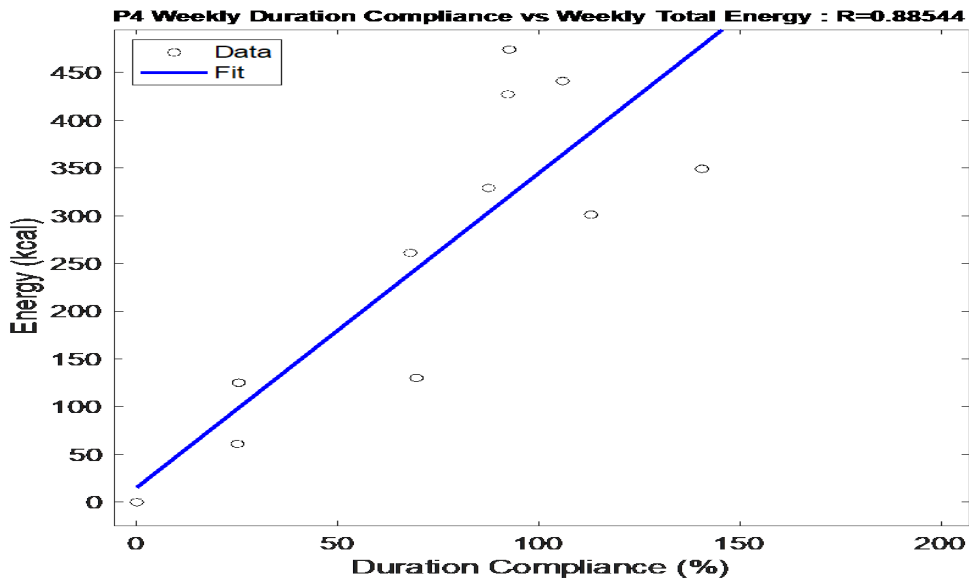


Figure A4.884: Weekly Duration Compliance vs. weekly total active energy linear correlation for patient#4

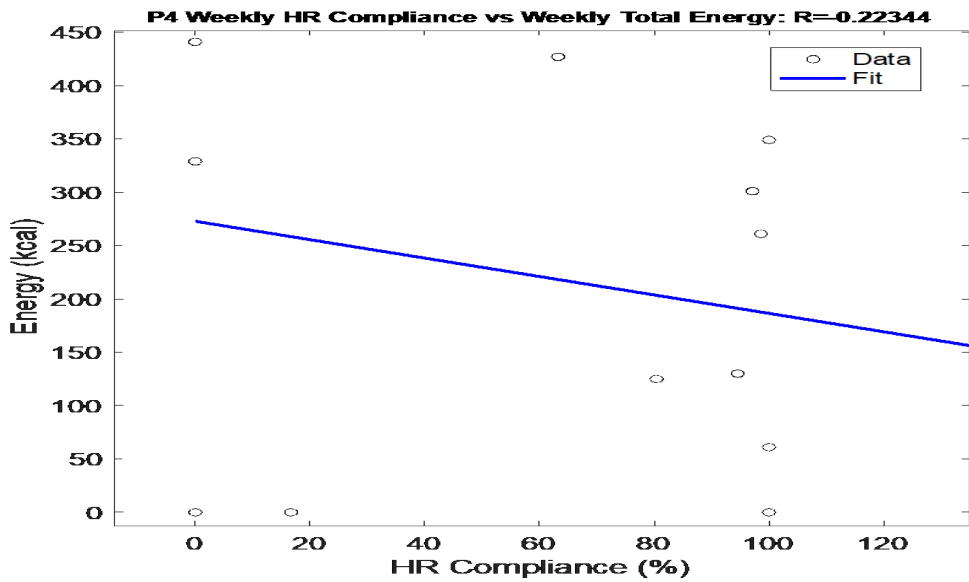


Figure A4.885: Weekly heart rate compliance vs. weekly total active energy linear correlation for patient#4

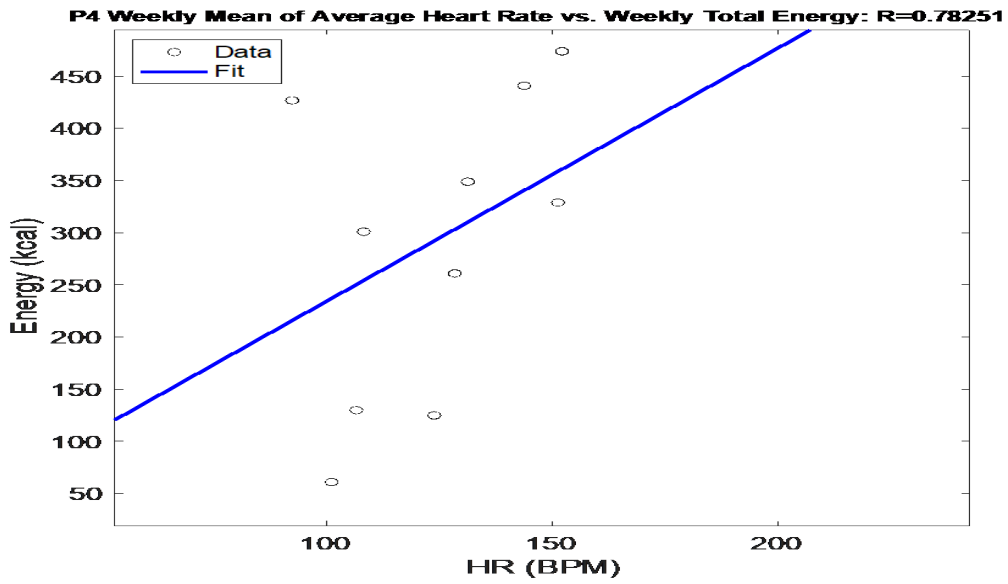


Figure A4.886: Weekly mean of average heart rate vs. weekly total active energy linear correlation for patient#4

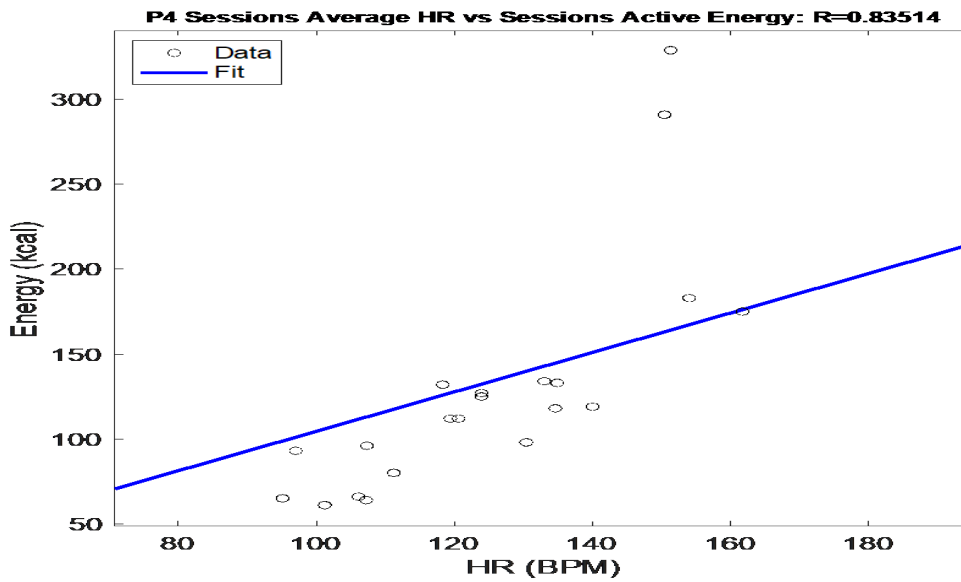


Figure A4.887: Sessions average heart rate vs. sessions active energy linear correlation for patient#4



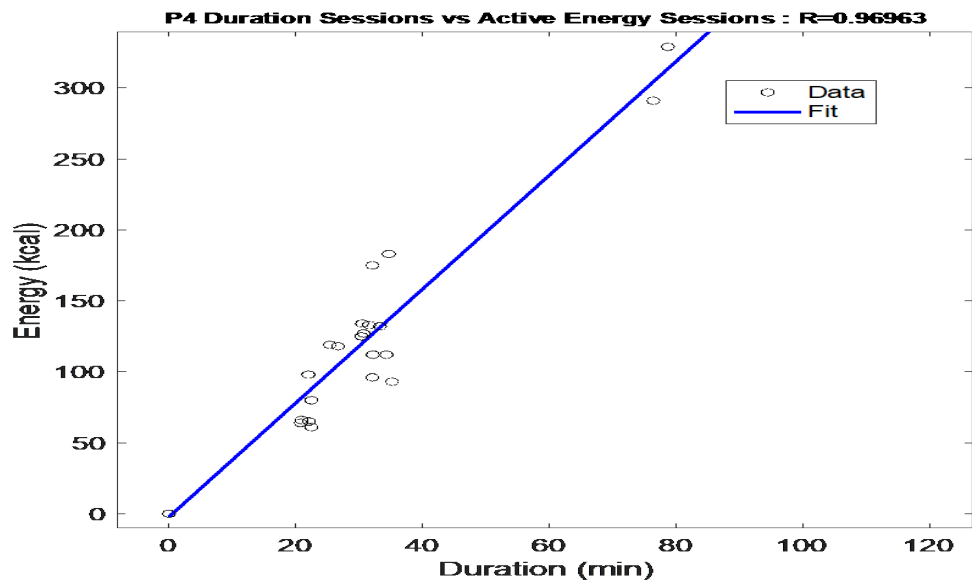


Figure A4.888: Duration Sessions vs. sessions active energy linear correlation for patient#4

### Patient 5 Active Energy:

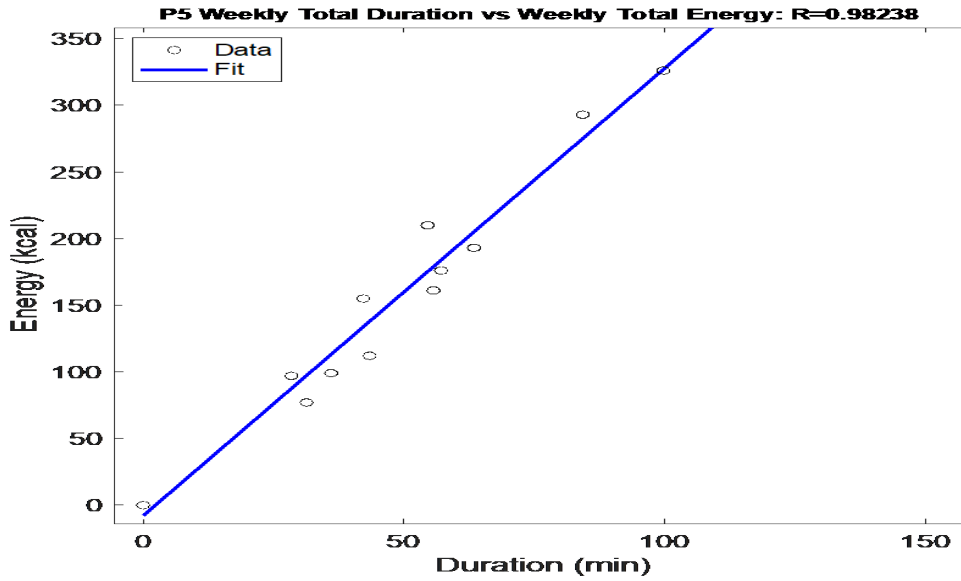


Figure A4.889: Weekly Total duration vs. weekly total active energy linear correlation for patient#5

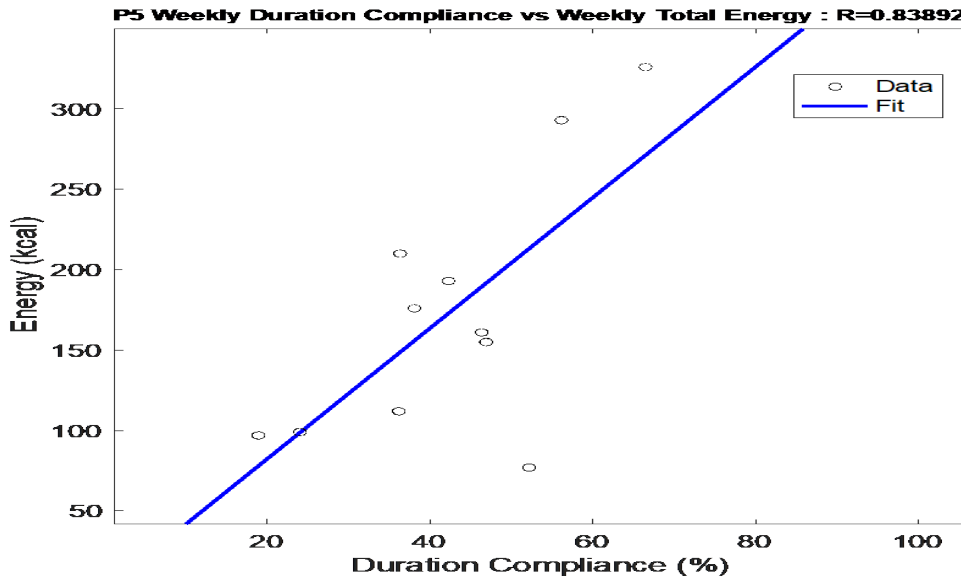


Figure A4.890: Weekly Duration Compliance vs. weekly total active energy linear correlation for patient#5

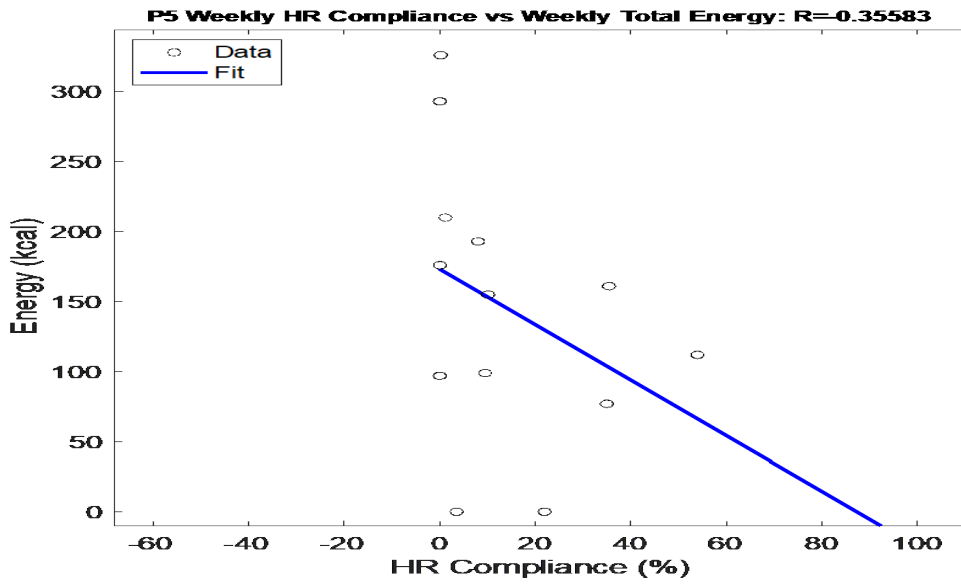


Figure A4.891: Weekly heart rate compliance vs. weekly total active energy linear correlation for patient#5

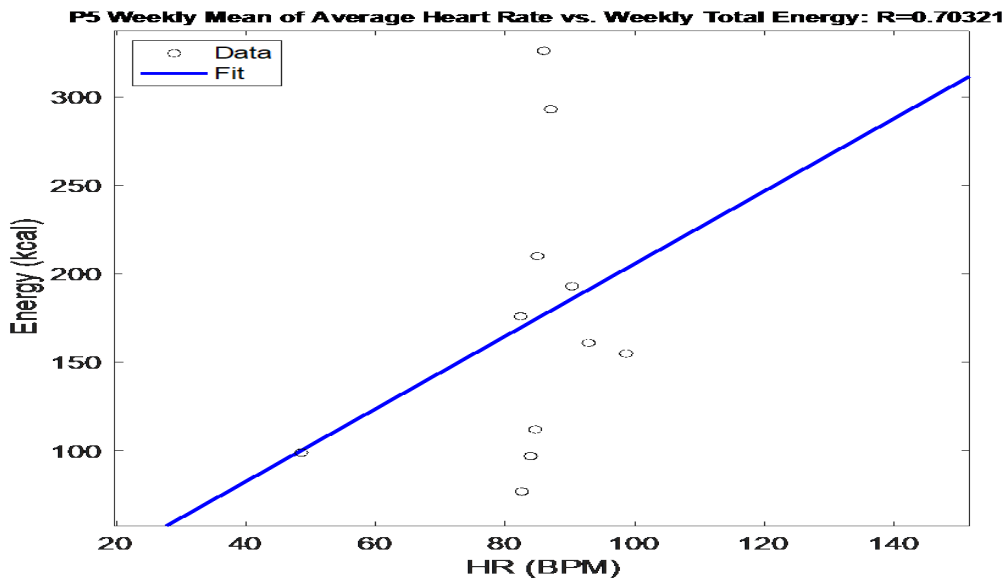


Figure A4.892: Weekly mean of average heart rate vs. weekly total active energy linear correlation for patient#5

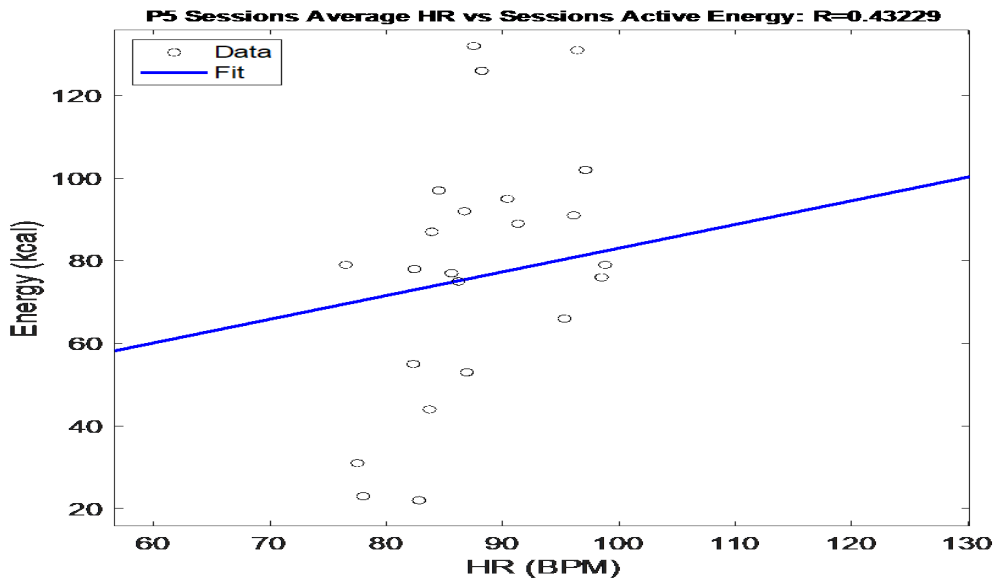


Figure 893: Sessions average heart rate vs. sessions active energy linear correlation for patient#5

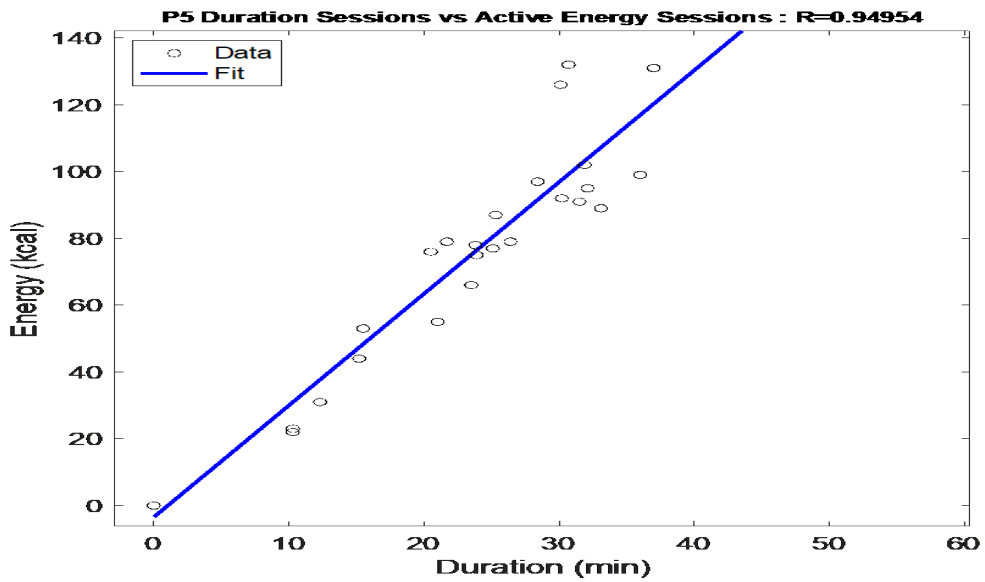


Figure A4.894: Duration Sessions vs. sessions active energy linear correlation for patient#5

### Patient 6 Active Energy:

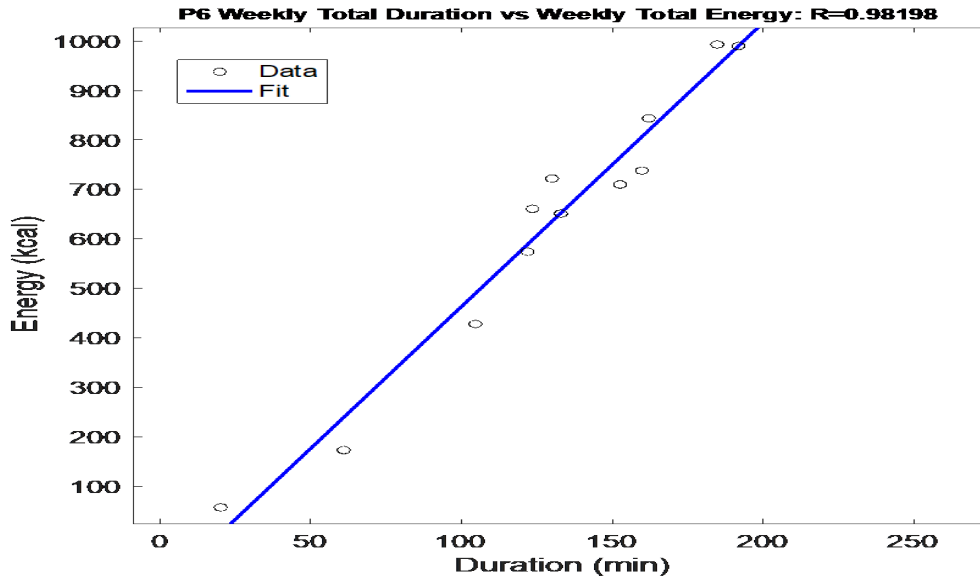


Figure A4.895: Weekly Total duration vs. weekly total active energy linear correlation for patient#6

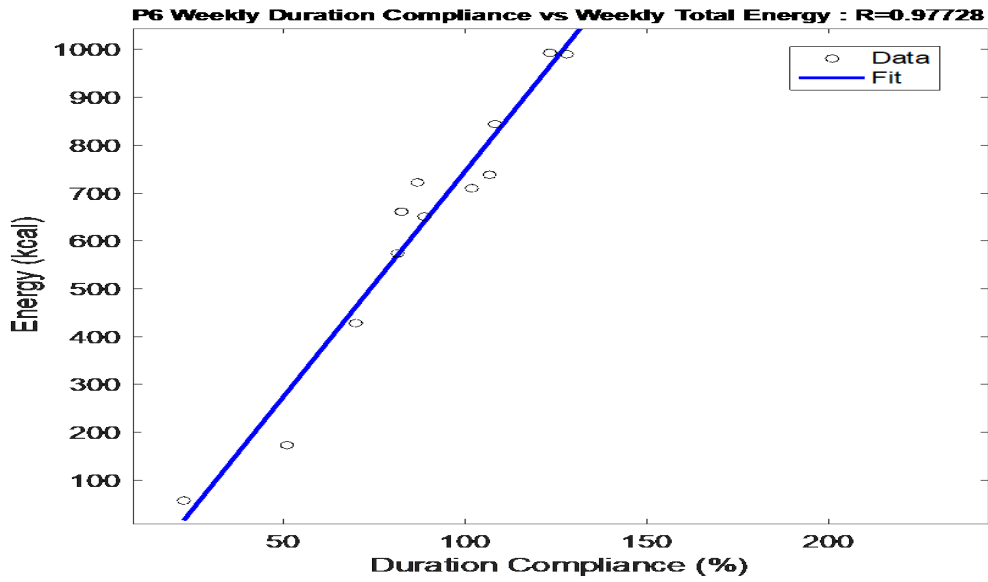


Figure A4.896: Weekly Duration Compliance vs. weekly total active energy linear correlation for patient#6

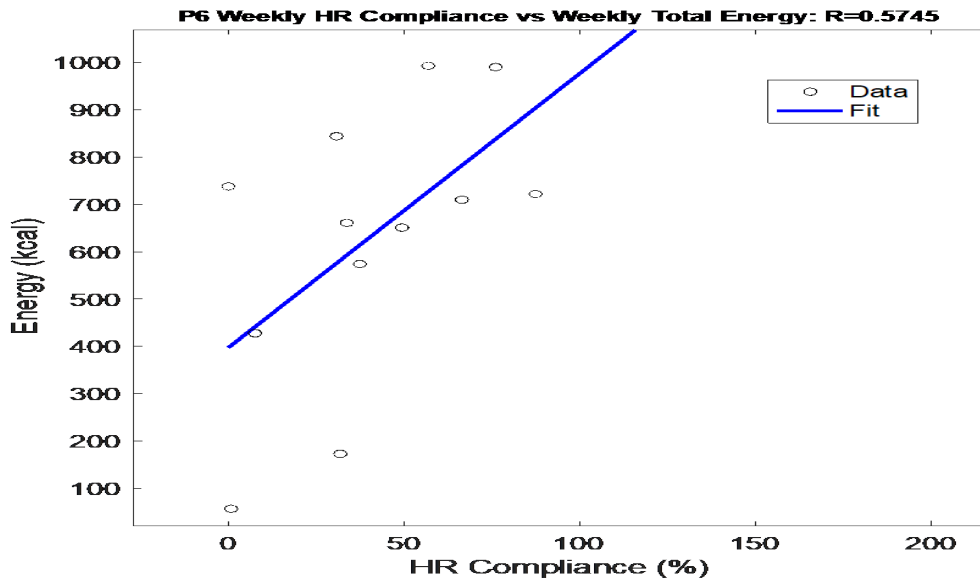


Figure A4.897: Weekly heart rate compliance vs. weekly total active energy linear correlation for patient#6

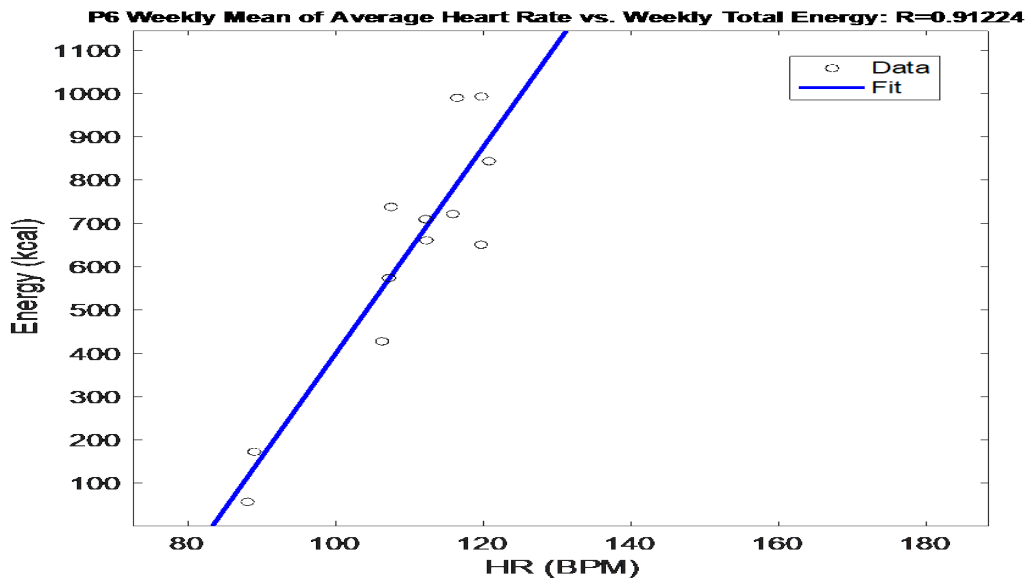


Figure A4.898: Weekly mean of average heart rate vs. weekly total active energy linear correlation for patient#6

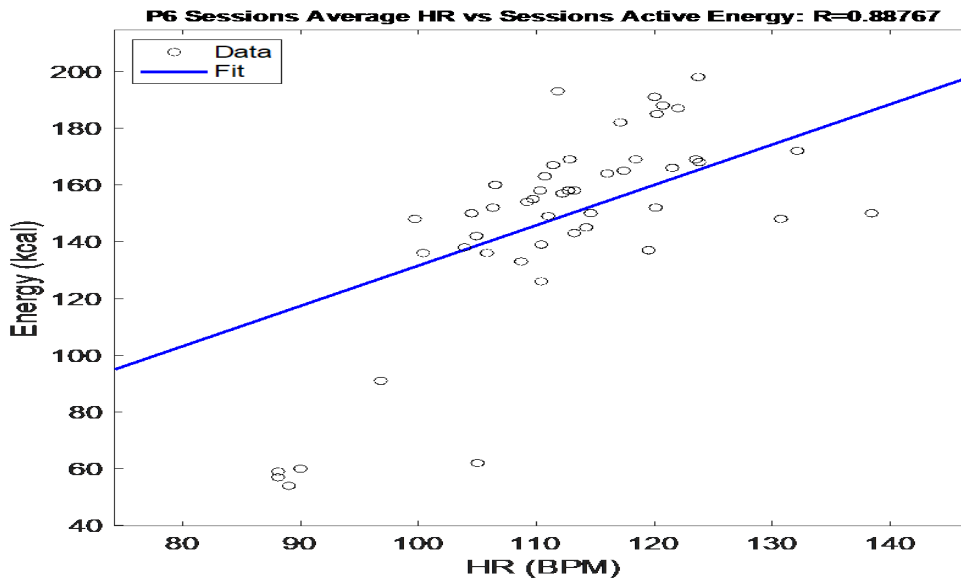


Figure A4.899: Sessions average heart rate vs. sessions active energy linear correlation for patient#6

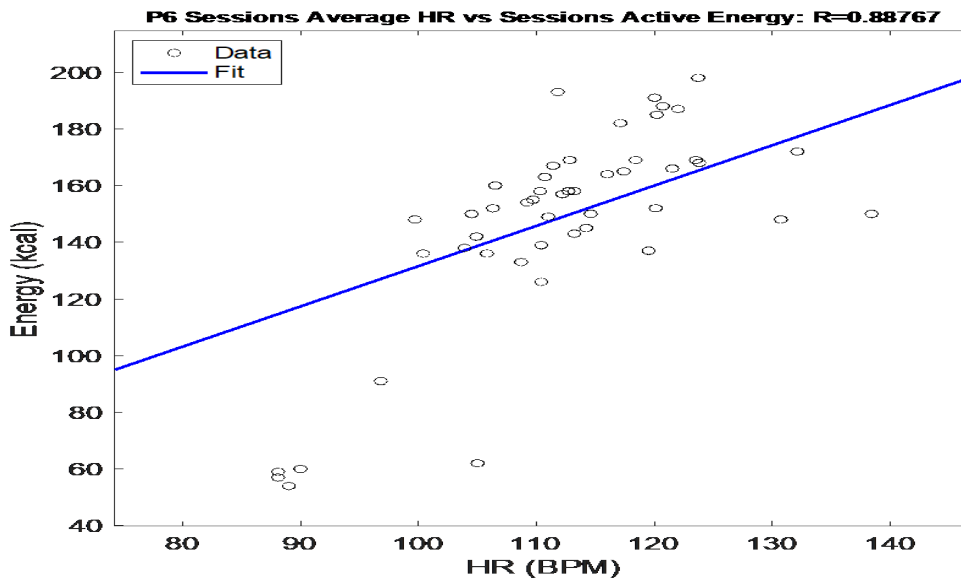


Figure A4.900: Duration Sessions vs. sessions active energy linear correlation for patient#6

### Patient 7 Active Energy:

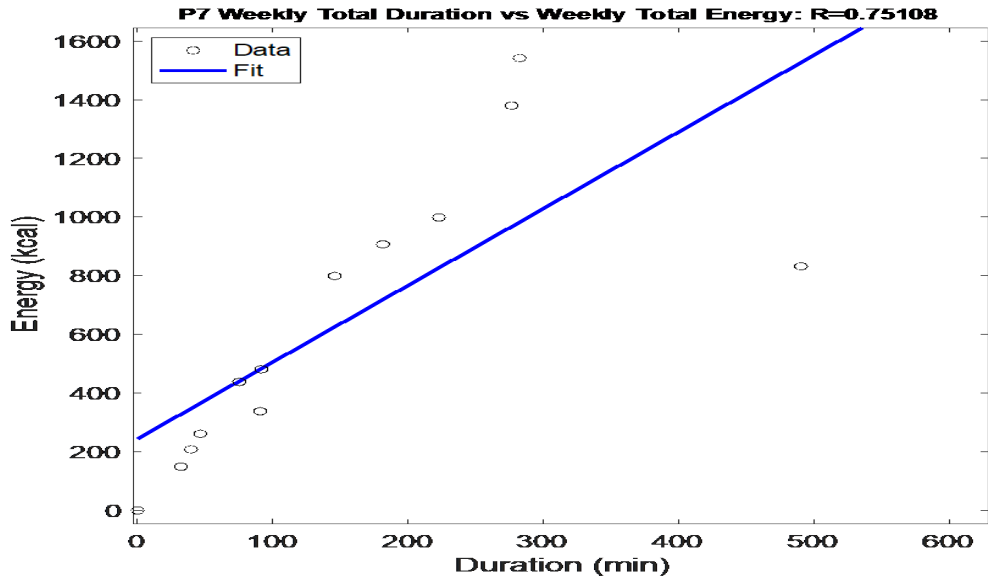


Figure A4.901: Weekly Total duration vs. weekly total active energy linear correlation for patient#7

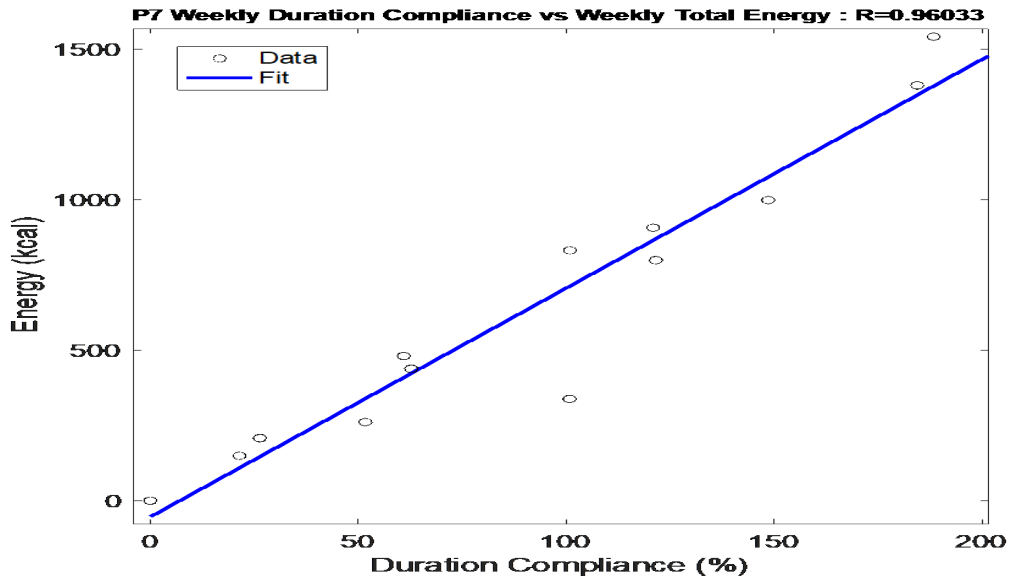


Figure A4.902: Weekly Duration Compliance vs. weekly total active energy linear correlation for patient#7



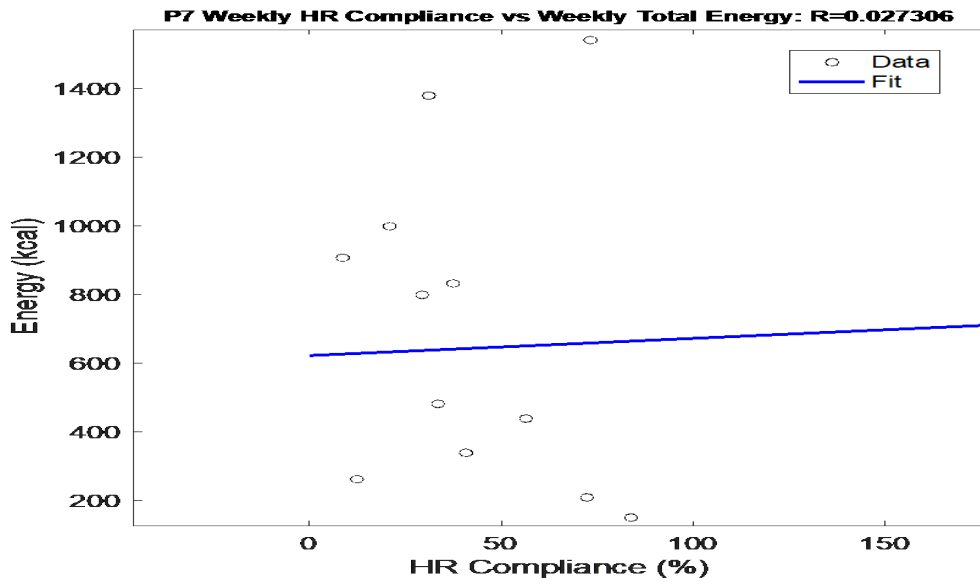


Figure 903: Weekly heart rate compliance vs. weekly total active energy linear correlation for patient#7

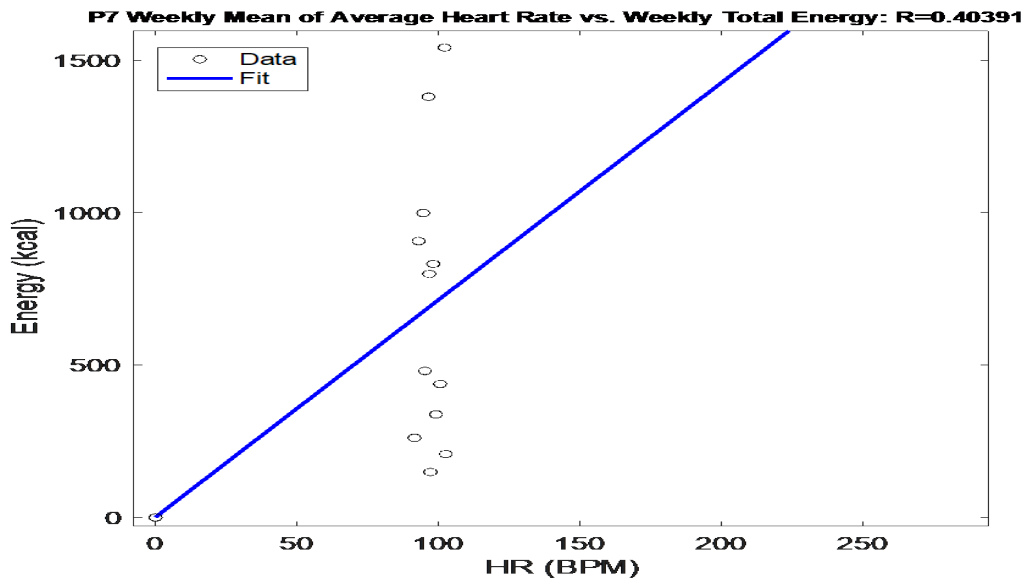


Figure A4.904: Weekly mean of average heart rate vs. weekly total active energy linear correlation for patient#7

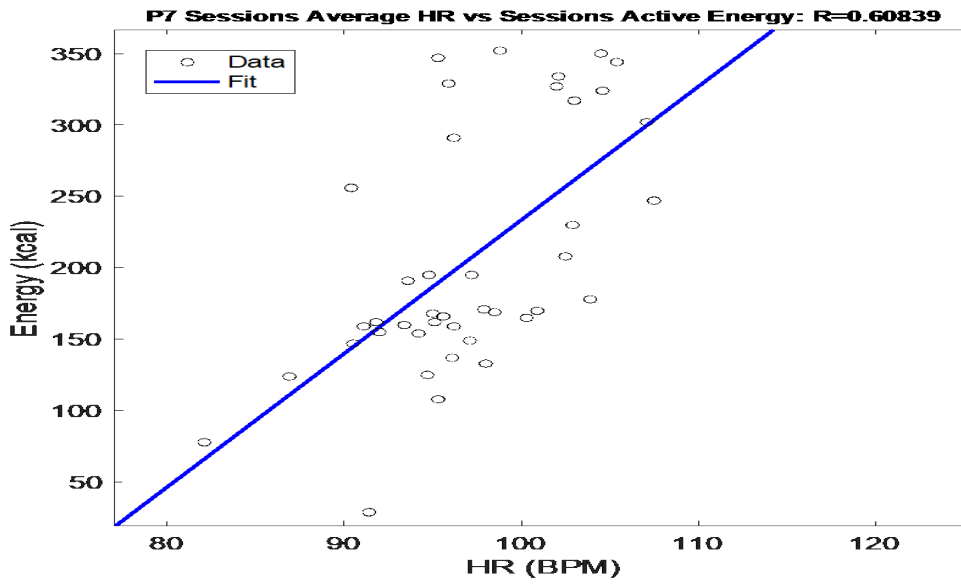


Figure A4.905: Sessions average heart rate vs. sessions active energy linear correlation for patient#7

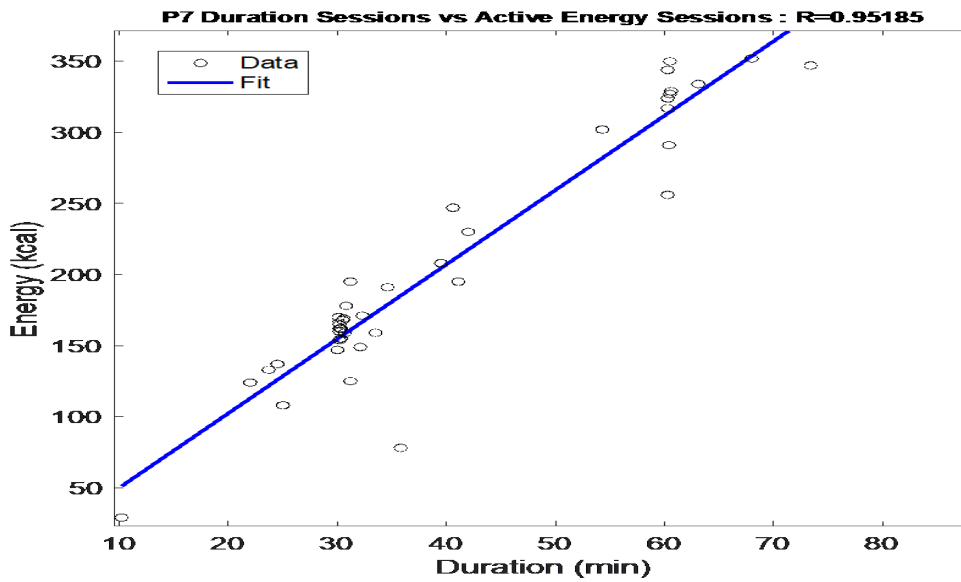


Figure A4.906: Duration Sessions vs. sessions active energy linear correlation for patient#7

Patient 8 Active Energy:

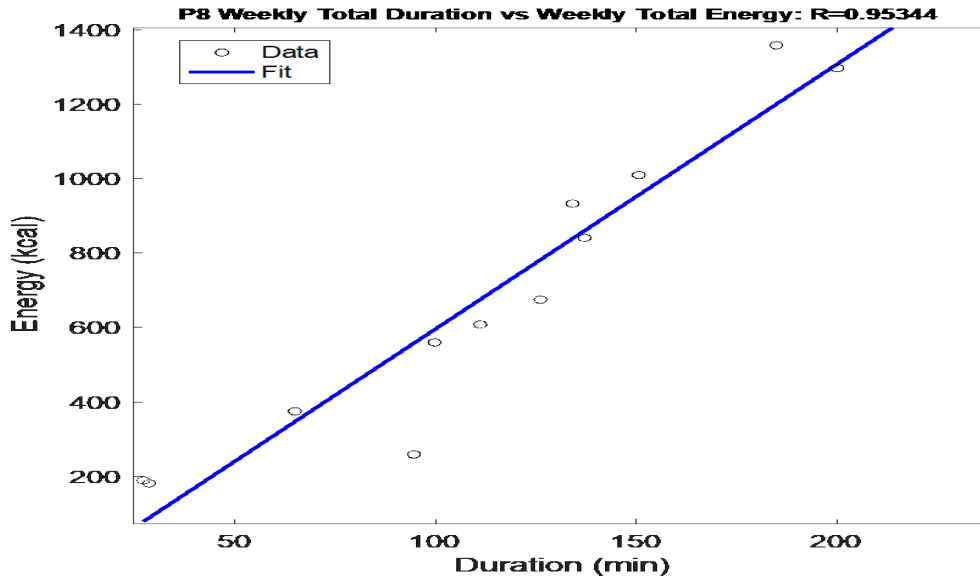


Figure A4.907: Weekly Total duration vs. weekly total active energy linear correlation for patient#8

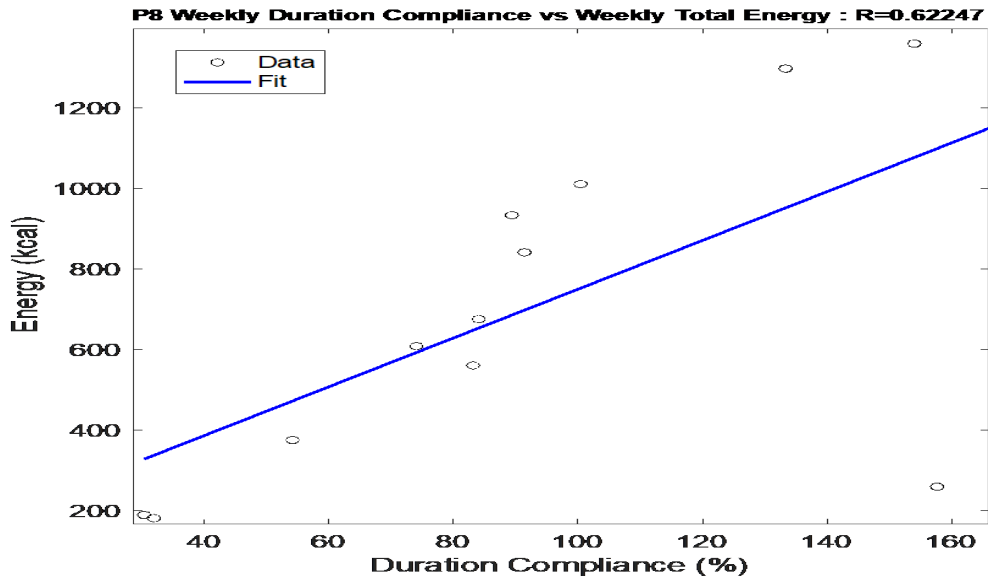


Figure A4.908: Weekly Duration Compliance vs. weekly total active energy linear correlation for patient#8

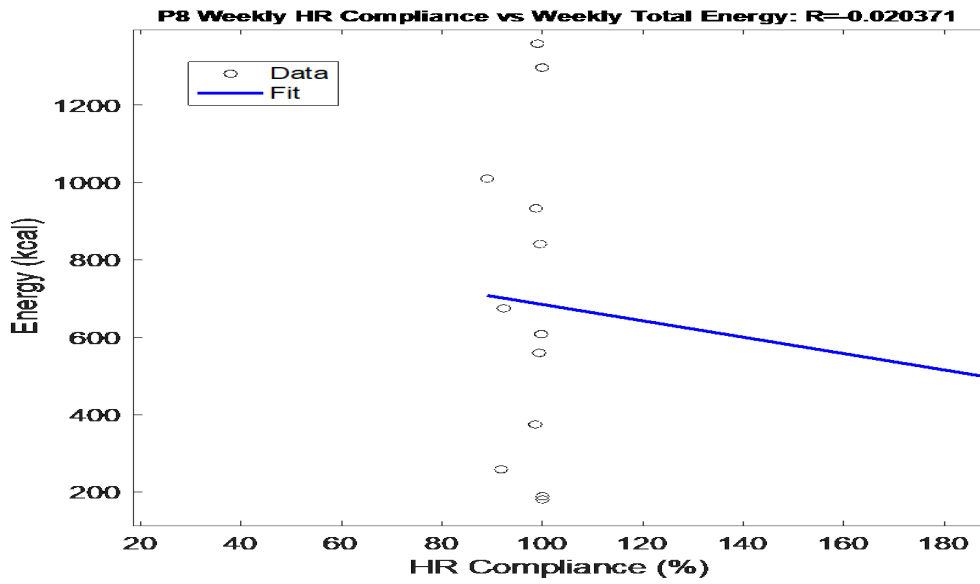


Figure A4.909: Weekly heart rate compliance vs. weekly total active energy linear correlation for patient#8

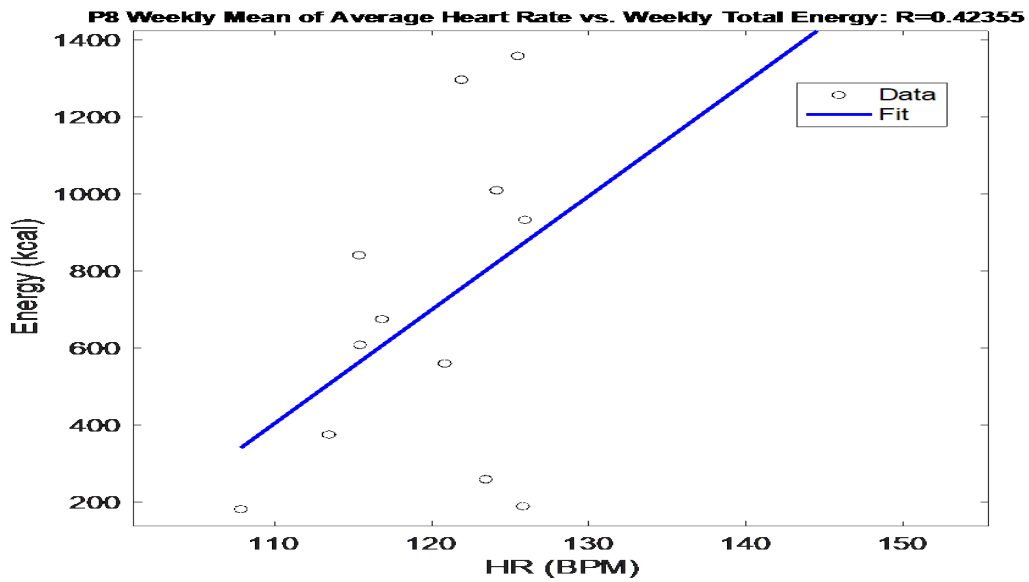


Figure A4.910: Weekly mean of average heart rate vs. weekly total active energy linear correlation for patient#8

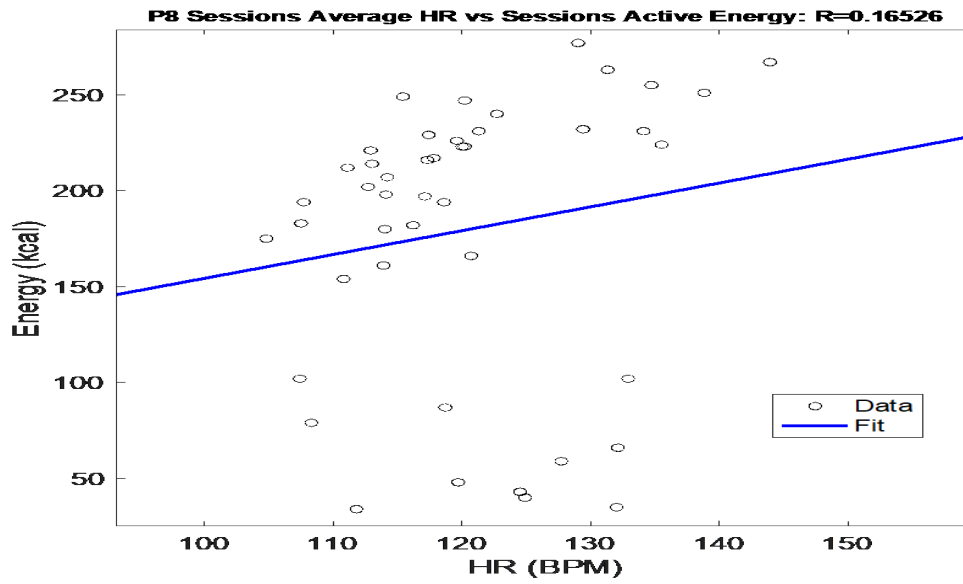


Figure A4.911: Sessions average heart rate vs. sessions active energy linear correlation for patient#8

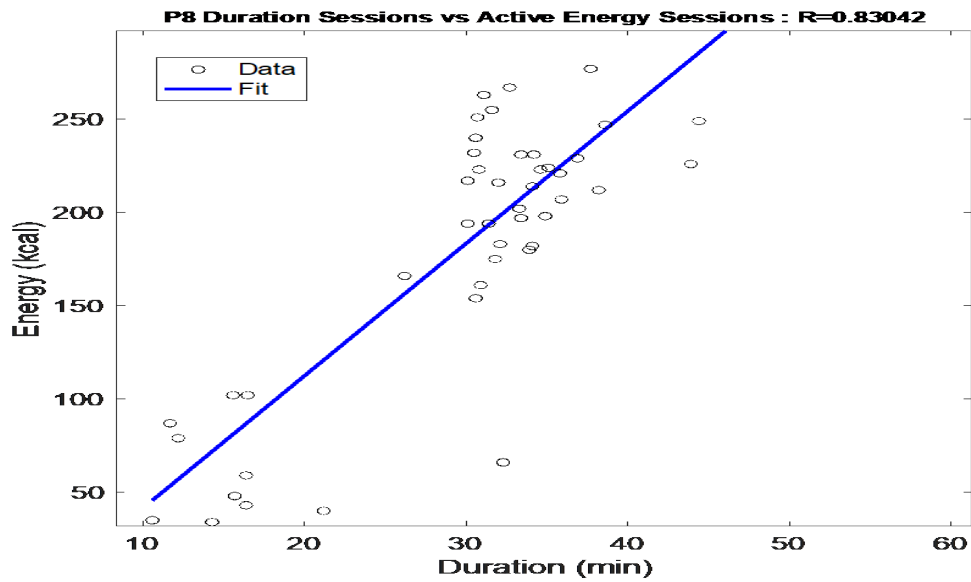


Figure A4.912: Duration Sessions vs. sessions active energy linear correlation for patient#8

Patient 9 Active Energy:

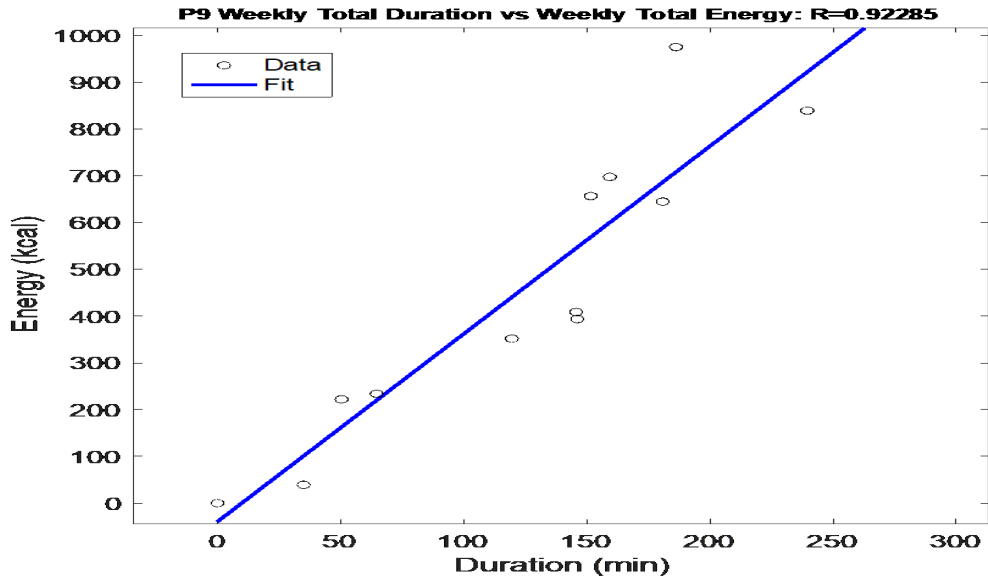


Figure A4.913: Weekly Total duration vs. weekly total active energy linear correlation for patient#9

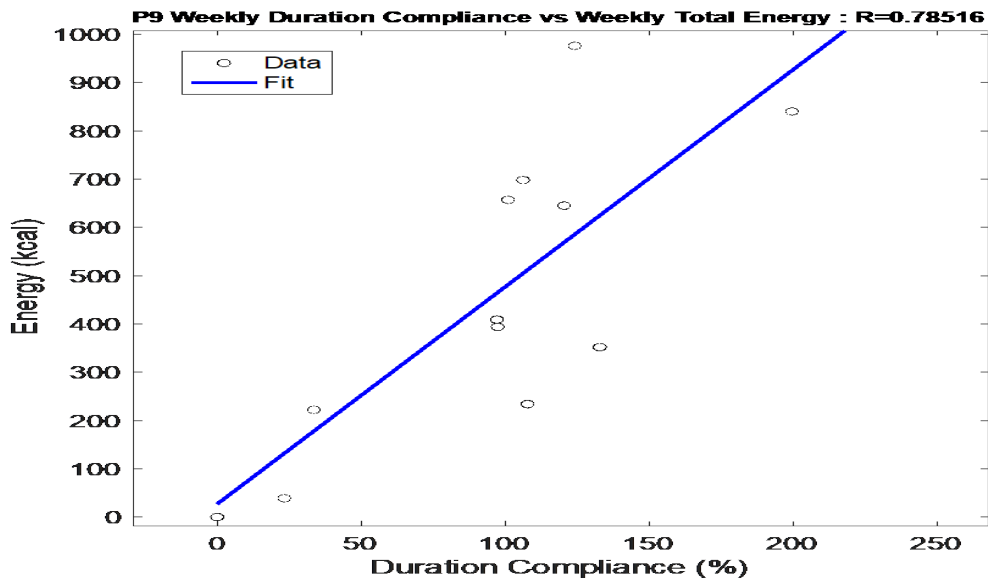


Figure A4.914: Weekly Duration Compliance vs. weekly total active energy linear correlation for patient#9

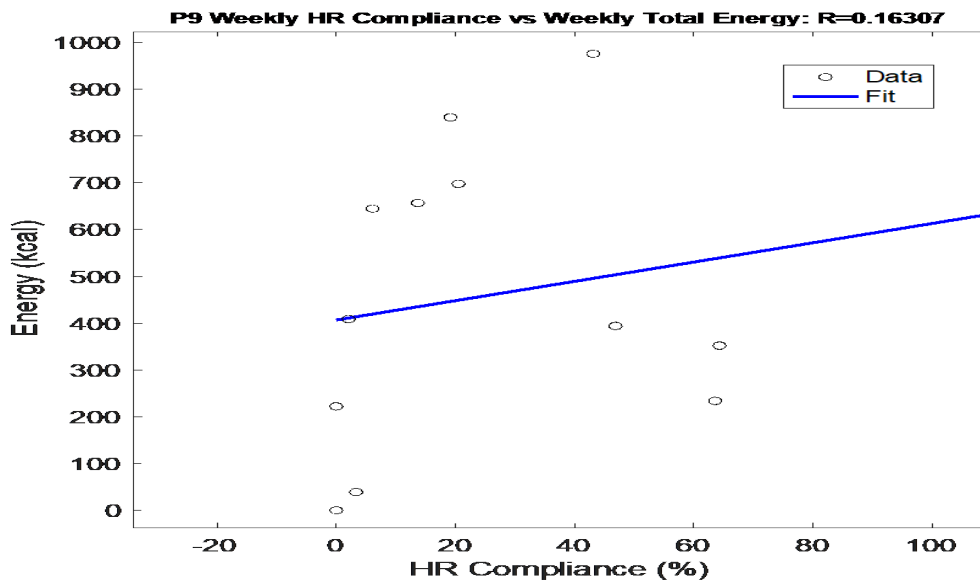


Figure A4.915: Weekly heart rate compliance vs. weekly total active energy linear correlation for patient#9



Figure A4.916: Weekly mean of average heart rate vs. weekly total active energy linear correlation for patient#9

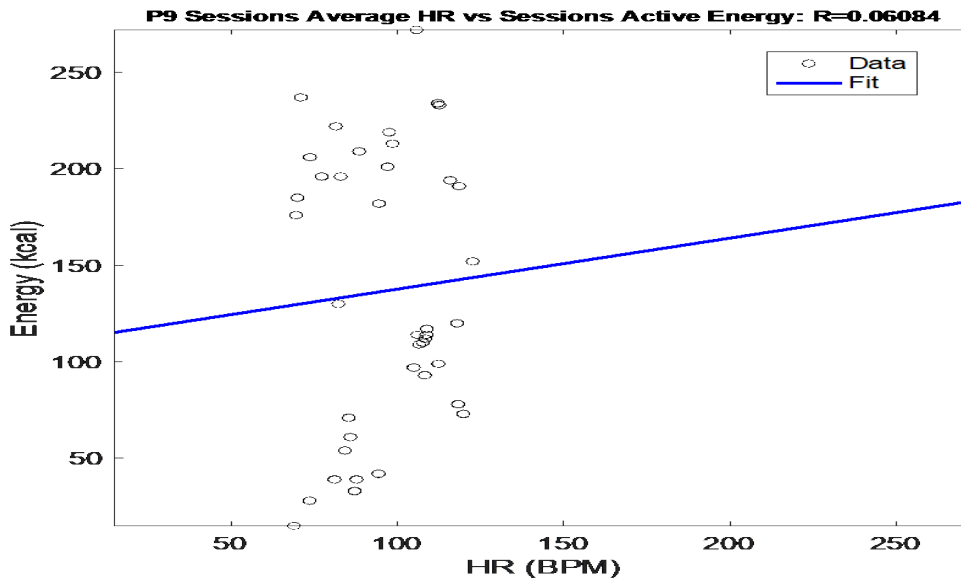


Figure A4.917: Sessions average heart rate vs. sessions active energy linear correlation for patient#9

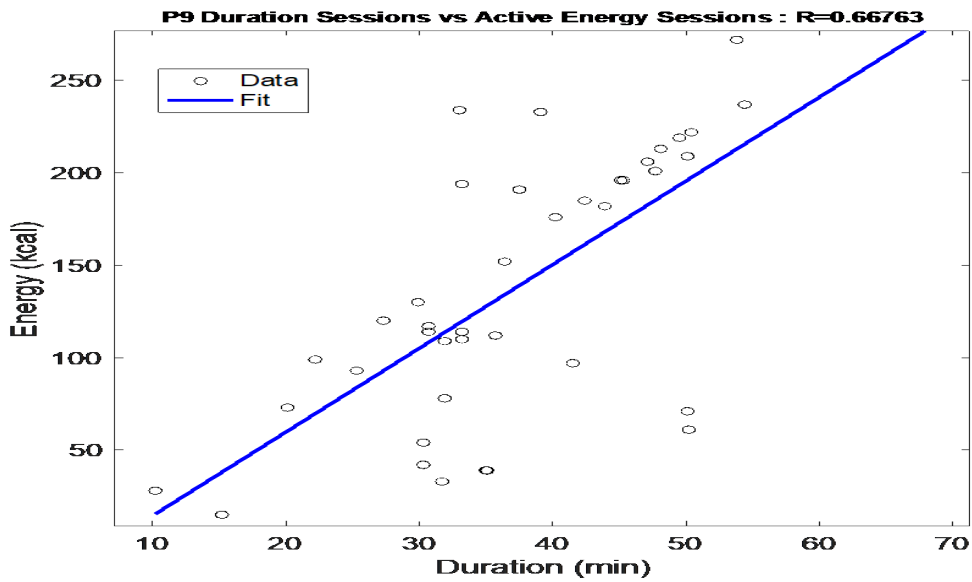


Figure A4.918: Duration Sessions vs. sessions active energy linear correlation for patient#9



## References

- [1] P. Eggenberger, S. Annaheim, K. A. Kündig, R. M. Rossi, T. Münzer and E. D. de Bruin, "Heart Rate Variability Mainly Relates to Cognitive Executive Functions and Improves Through Exergam Training in Older Adults: A Secondary Analysis of a 6-Month Randomized Controlled Trial," *Frontiers in aging neuroscience*, vol. 12, 07/2020.
- [2] M. Galgano, G. Toshkezi, X. Qiu, T. Russell, L. Chin and L.-R. Zhao, "Traumatic Brain Injury: Current Treatment Strategies and Future Endeavors," *Cell transplantation*, vol. 26 , no. 7, 2017.
- [3] H. J. Thompson, W. C. McCormick and S. H. Kagan, "Traumatic Brain Injury in Older Adults: Epidemiology, Outcomes, and Future Implications," *Journal of the American Geriatrics Society*, vol. 54, no. 10, 2006.
- [4] L. R. Lucchesi, S. Agrawal and A. Ahmadi, "Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016," *Lancet neurology*, vol. 18, no. 1, 2019.
- [5] A. A. Hyder, C. A. Wunderlich, P. Puvanachandra, G. Gururaj and O. C. Kobusingye, "The impact of traumatic brain injuries: a global perspective. NeuroRehabilitation.," *NeuroRehabilitation* , vol. 22, no. 5, 2007.
- [6] A. Ziemer, "Epidemiology of Traumatic Brain Injury," Physiopedia, [Online]. Available: [physio-pedia.com/Epidemiology\\_of\\_Traumatic\\_Brain\\_Injury](https://www.physio-pedia.com/Epidemiology_of_Traumatic_Brain_Injury). [Accessed 08 05 2021].
- [7] N. Agarwal, R. Thakkar and K. Than, "Traumatic Brain Injury," American Association of Neurological Surgeons., 03 02 2020. [Online]. Available: <https://www.aans.org/Patients/Neurosurgical-Conditions-and-Treatments/Traumatic-Brain-Injury>. [Accessed 08 05 2021].
- [8] S. T. Dawodu, "Traumatic Brain Injury (TBI) - Definition, Epidemiology, Pathophysiology," Medscape, 19 Mar 2021. [Online]. Available: <https://emedicine.medscape.com/article/326510-overview>. [Accessed 8 May 2021].

- [9] A. Feinstein and M. Rapoport, "Traumatic brain injury: the silent epidemic," *Canadian journal of public health*, vol. 91, no. 5, 09/2000.
- [10] D. K. Quinn, A. R. Mayer, C. L. Master and J. R. Fann, "Prolonged Postconcussive Symptoms," *The American journal of psychiatry*, vol. 175, no. 2, 2018.
- [11] D. Laskowitz and G. Grant, in *Translational Research in Traumatic Brain Injury*, Boca Raton (FL), CRC Press/Taylor and Francis Group, 2016.
- [12] J. H. Cole, R. Leech and D. J. Sharp, "Prediction of brain age suggests accelerated atrophy after traumatic brain injury," *Annals of neurology*, vol. 77, no. 4, 2015.
- [13] A. Ziemer, "Classification of Traumatic Brain Injury," Physiopedia, 2021. [Online]. Available: [https://www.physio-pedia.com/Classification\\_of\\_Traumatic\\_Brain\\_Injury](https://www.physio-pedia.com/Classification_of_Traumatic_Brain_Injury). [Accessed 25 05 2021 ]
- [14] D. B. Arciniegas, C. A. Anderson, J. Topkoff and T. W. McAllister, "Mild traumatic brain injury a neuropsychiatric approach to diagnosis, evaluation, and treatment," *Neuropsychiatric disease and treatment*, vol. 1, no. 4, 2005.
- [15] J. P. Kelly, "Loss of Consciousness: Pathophysiology and Implications in Grading and Safe Return to Play," *Journal of athletic training*, vol. 36, no. 1, 2001.
- [16] "Traumatic Brain Injury Information Page," NIH, [Online]. Available: <https://www.ninds.nih.gov/Disorders/All-Disorders/Traumatic-Brain-Injury-Information-Page>. [Accessed 08 05 2021].
- [17] S. Y. Ng and A. Y. W. Lee, "Traumatic Brain Injuries: Pathophysiology and Potential Therapeutic Targets," *Frontiers in cellular neuroscience*, vol. 13, 2019.
- [18] Y. Zhou and N. C. Danbolt, "Glutamate as a neurotransmitter in the healthy brain," *Journal of Neural Transmission*, vol. 121, no. 8, 2014.
- [19] A. J. Sorby-Adams, A. M. Marconi, E. R. Dempsey, J. A. Woenig and R. J. Turner, "The Role of Neurogenic Inflammation in Blood-Brain Barrier Disruption and Development of Cerebral Oedema Following Acute Central Nervous System (CNS) Injury," *International journal of molecular sciences*, vol. 18, no. 8, 2017.

- [20] V. E. Johnson, W. Stewart and D. H. Smith, "Axonal Pathology in Traumatic Brain Injury," *Experimental neurology*, vol. 246, 2013.
- [21] A. N. Hale, D. J. Ledbetter, T. R. Gawriluk and I. E. B. Rucker, "Autophagy Regulation and role in development," *Autophagy*, vol. 9, no. 7, 2013.
- [22] F. Sivandzade, F. Alqahtani and L. Cucullo, "Traumatic Brain Injury and Blood–Brain Barrier (BBB): Underlying Pathophysiological Mechanisms and the Influence of Cigarette Smoking as a Premorbid Condition," *International journal of molecular sciences*, vol. 21, no. 8, 2020.
- [23] M. P. Charles Patrick Davis, "Types of Traumatic Brain Injury (TBI) Medications," *MedicineNet* 2 07 2021. [Online]. Available: [https://www.medicinenet.com/types\\_of\\_traumatic\\_brain\\_injury\\_tbi\\_medications/article.htm](https://www.medicinenet.com/types_of_traumatic_brain_injury_tbi_medications/article.htm). [Accessed 3 08 2021].
- [24] "What are the treatments for traumatic brain injury (TBI)?," NIH, 24 11 2020. [Online]. Available: <https://www.nichd.nih.gov/health/topics/tbi/conditioninfo/treatment>. [Accessed 08 05 2021].
- [25] "Aerobic Fitness Reduces Brain Tissue Loss in Aging Humans," *The Journals of Gerontology*., vol. 58, no. 2, p. M176–M180, 2003.
- [26] K. Ding, T. Tarumi, T. Tomoto, K. R. Bell, C. Madden, M. Dieppa, C. M. Cullum, S. Zhang and R. Zhang, "A proof-of-concept trial of a community-based aerobic exercise program for individuals with traumatic brain injury," *Brain Injury*, vol. 35, no. 2, pp. 233-240, 2021.
- [27] L. M. Vecchio, Y. Meng, K. Xhima, N. Lipsman, C. Hamani and I. Aubert, "The Neuroprotective Effects of Exercise: Maintaining a Healthy Brain Throughout Aging," *Brian Plasticity* , pp. 17-52, 2018.
- [28] K. Ustinova, J. Perkins, W. Leonard and C. Hausbeck, "Virtual reality game-based therapy for treatment of postural and co-ordination abnormalities secondary to TBI: A pilot study," *Brain Injur* , 2014.

- [29] S. R. Steinhubl, E. D. Muse and E. J. Topol, "The emerging field of mobile health," *Science translational medicine*, vol. 7, no. 283, 2015.
- [30] N. Stocchetti and E. R. Zanier, "Chronic impact of traumatic brain injury on outcome and quality of life: a narrative review," *BioMed Central*, pp. 20-148, 2016.
- [31] T. Takashi and Z. Rong, "The Role of Exercise-Induced Cardiovascular Adaption in Brain Health Review," *Exercise and sport sciences*, 2015.
- [32] K. Dams-O'Connor, G. Guetta, A. E. Hahn-Ketter and A. Fedor, "Traumatic brain injury as a risk factor for Alzheimer's disease: current knowledge and future directions," *NEURODEGENERATIVE DISEASE MANAGEMENT*, vol. 6, no. 5, 2016.
- [33] D. Plantier and J. Luauté, "Drugs for behavior disorders after traumatic brain injury: Systematic review and expert consensus leading to French recommendations for good practice," *Annals of Physical and Rehabilitation Medicine*, vol. 59, no. 1, pp. 42-57, 2016.
- [34] I. Pastor, H. Hayes and S. Bamberg, "A feasibility study of an upper limb rehabilitation system using kinect and computer games.," *Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society*, 2012.
- [35] B. Li, B. Harvey and T. Gallagher, "Using barometers to determine the height for indoor positioning," in *International Conference on Indoor Positioning and Indoor Navigation*, 10/2013.
- [36] W. Jun, H. Jian, W. Yongji and X. Kexin, "A Wearable Rehabilitation Robotic Hand Driven by PM-TS Actuators," *Intelligent Robotics and Applications*, pp. 440-450, 2010.
- [37] K. Shuval, E. T. Hébert, Z. Siddiqi, T. Leonard, S. C. Lee, J. A. Tiro, K. McCallister and C. S. Skinner, "Impediments and facilitators to physical activity and perceptions of sedentary behavior among urban community residents: the Fair Park Study," *Preventing chronic disease*, vol. 10, 2013.
- [38] S. M. Pinto, M. A. Newman and M. A. Hirsch, "Perceived Barriers to Exercise in Adults with Traumatic Brain Injury Vary by Age," *Journal of functional morphology and kinesiology*, vol. 3, no. 3, 2018.

- [39] H. F. Mulligan, L. A. Hale, L. Whitehead and G. D. Baxter, "Barriers to Physical Activity for People With Long-Term Neurological Conditions: A Review Study," *Adapted physical activity quarterly*, vol. 29, no. 3, 2012.
- [40] C. L. Ventola, "Mobile Devices and Apps for Health Care Professionals: Uses and Benefits," *P&T (Lawrenceville, N.J.)*, vol. 39, no. 4, 2014.
- [41] R. Argent, A. Daly and B. Caulfield, "Patient Involvement With Home-Based Exercise Program: Can Connected Health Interventions Influence Adherence?," *JMIR mHealth and uHealth*, vol. 6, no. 3, 2018.
- [42] L. M. P. Chin, R. E. P. Keyser, J. P. Dsurney and L. M. M. Chan, "Improved Cognitive Performance Following Aerobic Exercise Training in People with Traumatic Brain Injury," *Archives of Physical Medicine and Rehabilitation*, vol. 96, no. 4, 2015.
- [43] John Hopkins Hospital, "Re-Engineering Heart Attack Discharge and Recovery," Corrie, [Online]. Available: <https://corriehealth.com/>. [Accessed 16 11 2019].
- [44] "Starting an antidepressant," IODINE, August 2015. [Online]. Available: <https://www.iodine.com/starting-an-antidepressant>. [Accessed 16 11 2019].
- [45] M. PG and P. L., "Monitoring in traumatic brain injury," *Clin Neurosurg*, vol. 44, pp. 267-94, 1997.
- [46] J. M. Bland and D. G. Altman, "Statistical methods for assessing agreement between two methods of clinical measurement," *International journal of nursing studies*, vol. 47, no. 8, 2010.
- [47] G. A. Walker and J. Shostak, *Common Statistical Methods for Clinical Research*, Cary, NC, USA: SAS Institute Inc., 2010.
- [48] J. M. Hoffman, K. R. Bell, J. M. Powell, D. Behr, E. C. James, S. Dikmen and C. H. Bombardier, "A Randomized Controlled Trial of Exercise to Improve Mood After Traumatic Brain Injury," *PM&R*, vol. 2, no. 10, pp. 911-919, 2010.

- [49] A. F. Turki, M. B. Jani, K. Ding, R. Zhang and K. Behbehani, "An Investigation of Heart Rate Sensing Accuracy by Wrist-worn Fitness Tracking Devices," in *IEEE Engineering in Medicine and Biology Conference*, Berlin, Germany, 2019, pp. 3337-3340.
- [50] L. Chin, R. Keyser, J. Dsurney and L. Chan, "Improved cognitive performance following aerobic exercise training in people with traumatic brain injury," *Arch Phys Med Rehabil*, pp. 754-759, 2015
- [51] C. Chien-Yen, L. Belinda, Z. Mi, K. Sebastian, R. Phil, S. Noom, A. S. Alexander and A. R. Albert, "Towards pervasive physical rehabilitation using Microsoft Kinect," *IEEE Xplore*, 2012 .
- [52] D. Bassett, L. Toth, S. LaMunion and S. Crouter, "Step Counting: A Review of Measurement Considerations and Health-Related Applications," *SPORTS MEDICINE*, vol. 47, no. 7, 2017.
- [53] Apple, "Your heart rate. What it means, and where on Apple Watch you'll find it.," Apple, 19 9 2019. [Online]. Available: <https://support.apple.com/en-us/HT204666>. [Accessed 21 11 2019].
- [54] Apple, "ResearchKit and CareKit," Apple, [Online]. Available: <https://www.apple.com/researchkit/>. [Accessed 9 11 2019].
- [55] A. Soltan Zadi, R. Alex, R. Zhang, D. E. Watenpaugh and K. Behbehani, "Mathematical Modeling of Arterial Blood Pressure Using Photo- Plethysmography Signal in Breath-hold Maneuver," *40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, 2018.
- [56] L. Narasimhan G, "Database Migration on Premises to AWS RDS," *EAI Endorsed Transactions on Cloud Systems*, vol. 3, no. 11, 2018.
- [57] "AWS," Amazon Web services, [Online]. Available: <https://aws.amazon.com/>. [Accessed 27 06 2021].
- [58] "Swift," [Online]. Available: <https://developer.apple.com/swift/>. [Accessed 27 06 2021].
- [59] J. E. Manson, F. B. Hu, J. W. Rich-Edwards, G. A. Colditz, M. J. Stampfer, W. C. Willett, F. E. Speizer and C. H. Hennekens, "A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women," *The New England journal of medicine*, vol. 341, no. 9, 1999.

- [60] R. S. Paffenbarger, R. Hyde, A. L. Wing and C.-c. Hsieh, "Physical activity, all-cause mortality, and longevity of college alumni," *The New England journal of medicine*, vol. 314, no. 10, 1986.
- [61] J. R. S. Paffenbarger, J. B. Kampert, I. M. Lee, R. T. Hyde, R. W. Leung and A. L. Wing, "Changes in physical activity and other lifeway patterns influencing longevity," *Medicine and science in sports and exercise*, vol. 26, no. 7, 1994.
- [62] L. Anderson, N. Oldridge, D. R. Thompson, A.-D. Zwisler, K. Rees, N. Martin and R. S. Taylor, "Exercise-based cardiac rehabilitation for coronary heart disease: Cochrane systematic review and meta-analysis," *Journal of the American College of Cardiology*, vol. 67, no. 1, 2016.
- [63] S. N. Blair, 3. H. W. Kohl, C. E. Barlow, J. R. S. Paffenbarger, L. W. Gibbons and C. A. Macera, "Changes in physical fitness and all-cause mortality A prospective study of healthy and unhealthy men," *JAMA : the journal of the American Medical Association*, vol. 273, no. 14, 1995.
- [64] D.-c. Lee, X. Sui, E. G. Artero, I.-M. Lee, T. S. Church, P. A. McAuley, F. C. Stanford, 3. H. W. Kohl and S. N. Blair, "Long-term effects of changes in cardiorespiratory fitness and body mass index on all-cause and cardiovascular disease mortality in men: the Aerobics Center Longitudinal Study," *Circulation (New York, N.Y.)*, vol. 124, no. 23, 2011.
- [65] P. T. Williams and P. D. Thompson, "Walking versus running for hypertension, cholesterol, and diabetes mellitus risk reduction," *Arteriosclerosis, thrombosis, and vascular biology*, vol. 33, no. 5, 2013.
- [66] S. C. Moore, A. V. Patel, C. E. Matthews, A. Berrington de Gonzalez, Y. Park, H. A. Katki, M. S. Linet, E. Weiderpass, K. Visvanathan, K. J. Helzlsouer, M. Thun, S. M. Gapstur, P. Hartge and I.-M. Lee, "Leisure time physical activity of moderate to vigorous intensity and mortality: a large pooled cohort analysis," *PLoS medicine*, vol. 9, no. 11, 2012.
- [67] P. D. THOMPSON, D. BUCHNER, G. F. FLETCHER, N. F. GORDON, R. R. PATE, B. L. RODRIGUEZ, A. K. YANCEY, N. K. WENGER, I. L. PINA, G. J. BALADY, M. A. WILLIAMS B. H. MARCUS, K. BERRA, S. N. BLAIR and COSTA, "Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: a statement from the Council on

Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention) and the Council on Nutrition, Physical," *Circulation (New York, N.Y.)*, vol. 107, no. 24, 2003.

- [68] D. J. Green, G. O'Driscoll, M. J. Joyner and N. T. Cable, "Exercise and cardiovascular risk reduction: time to update the rationale for exercise?," *Journal of applied physiology*, vol. 105, no. 2, 1985.
- [69] M. J. Joyner and D. J. Green, "Exercise protects the cardiovascular system: effects beyond traditional risk factors," *The Journal of physiology*, vol. 578, no. 23, 2009.
- [70] M. H. Laughlin, S. C. Newcomer and S. B. Bender, "Importance of hemodynamic forces as signals for exercise-induced changes in endothelial cell phenotype," *Journal of Applied Physiology*, vol. 104, no. 3, 2008.
- [71] D. Green, M. Hopman, J. Padilla, M. Laughlin and D. Thijssen, "Vascular Adaptation to Exercise in Humans: Role of Hemodynamic Stimuli," *Physiological reviews*, vol. 97, no. 2, 2017.
- [72] H. van Praag, M. Fleshner, M. W. Schwartz and M. P. Mattson, "Exercise, Energy Intake, Glucose Homeostasis, and the Brain," *The Journal of neuroscience : the official journal of the Society for Neuroscience*, vol. 34, no. 46, 2014.
- [73] S. Buppajarntham, "What is the difference between insulin sensitivity and insulin resistance?," Medscape, 16 June 2021. [Online]. Available: <https://www.medscape.com/answers/2089224-170952/what-is-the-difference-between-insulin-sensitivity-and-insulin-resistance>. [Accessed 16 June 2021].
- [74] A. P. Hills, N. Mokhtar and N. M. Byrne, "Assessment of Physical Activity and Energy Expenditure: An Overview of Objective Measures," *Frontiers in nutrition*, vol. 1, 2014.
- [75] W. L. Haskell, I.-M. Lee, R. R. Pate, K. E. Powell, S. N. Blair, B. A. Franklin, C. A. Macera, G. W. Heath, P. D. Thompson and A. Bauman, "Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association.," *Medicine and science in sports and exercise*, vol. 39, no. 8, 2007.



- [76] M. Jetté, K. Sidney and G. Blümchen, "Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation of functional capacity," *Clinical Cardiology*, vol. 13, no. 8, 1990.
- [77] C. d. F. Coelho-Ravagnani, F. C. L. Melo, F. C. P. Ravagnani, F. H. P. Burini and R. C. Burini, ' Estimation of metabolic equivalent (MET) of an exercise protocol based on indirect calorimetry," *Revista Brasileira de Medicina do Esporte*, vol. 19, no. 2, 2013.
- [78] C. A. Conn, "The Remarkable Calorie," The University of New Mexico, [Online]. Available: <http://www.unm.edu/~lkravitz/Article%20folder/remarkablecalorie.html>. [Accessed 27 June 2020].
- [79] A. J. Visek, S. M. Achrati, H. Mannix, K. McDonnell, B. S. Harris and L. DiPietro, "The Fun Integration Theory: Toward Sustaining Children and Adolescents Sport Participation," *Journal of physical activity & health*, vol. 12, no. 3, 2015.
- [80] S. Fox and W. Haskell, "The exercise stress test: needs for standardization," in *Cardiology: Current Topics and Progress*, New York, Academic Press, 1970, pp. 149-54.
- [81] G. Sporis, V. Vucetic, I. Jukic, D. Omrcen, D. Bok and Z. Custonja, "How Reliable Are the Equations for Predicting Maximal Heart Rate Values in Military Personnel?," *Military medicine*, vol. 176, no. 3, 2011.
- [82] D. Micklewright, A. St Clair Gibson, V. Gladwell and A. Al Salman, "Development and Validity of the Rating-of-Fatigue Scale," *Sports Medicine*, vol. 47, no. 11, 2017.
- [83] J. Holz, "The Rating of Perceived Exertion (RPE) Scale," Maximize Potential, 19 08 2019. [Online]. Available: <https://maximizepotentialtx.com/blogs/sports-performance-training/the-rating-of-perceived-exertion-rpe-scale>. [Accessed 10 05 2021].
- [84] G. Borg, "Perceived exertion as an indicator of somatic stress," *Scandinavian journal of rehabilitation medicine*, vol. 2, no. 2, 1970.
- [85] B. A. STAMFORD, "Validity and reliability of subjective ratings of perceived exertion during work. Ergonomics," *Ergonomics*, vol. Volume 19, no. Issue 1, 01/1976.

- [86] A. Lang, *Measuring Psychological Responses To Media Messages*, Hillsdale, N.J.: L. Erlbaum Associates, 1994.
- [87] J. P. Neary, "How concussion stresses the heart, to protect the brain," *National Post*, 20 August 2018. [Online]. Available: <https://nationalpost.com/pmn/news-pmn/how-concussion-stresses-the-heart-to-protect-the-brain>. [Accessed 10 11 2019].
- [88] U. S. D. o. H. Staff, *Physical Activity and Health: A Report of the Surgeon General*, 1998.
- [89] C. Schneider, F. Hanakam, T. Wiewelhoeve, A. Döweling, M. Kellmann, T. Meyer, M. Pfeiffer and A. Ferrauti, "Heart Rate Monitoring in Team Sports—A Conceptual Framework for Contextualizing Heart Rate Measures for Training and Recovery Prescription," *Frontiers in physiology*, vol. 9, 2018.
- [90] W. Stockton, "Fitness; Target Heart Rate: Is It Important, Or Overrated?," *The New York Times* 4 4 1988. [Online]. Available: <https://www.nytimes.com/1988/04/04/sports/fitness-target-heart-rate-is-it-important-or-overrated.html>. [Accessed 10 11 2019].
- [91] A. L. Millar, D. Village, T. King, G. McKenzie, J. Lee and C. Lopez, "Heart Rate and Blood Pressure Assessment by Physical Therapists in the Outpatient Setting—An Observational Study," *Cardiopulmonary physical therapy journal*, vol. 27, no. 3, 2016.
- [92] F. S. P. R. Routledge, T. S. P. Campbell, J. A. P. R. McFetridge-Durdle and S. L. P. Bacon, "Improvements in heart rate variability with exercise therapy," *Canadian journal of cardiology*, vol. 26, no. 6, 2010.
- [93] C. J. Lavie, C. Ozemek, S. Carbone, P. T. Katzmarzyk and S. N. Blair, "Sedentary Behavior, Exercise, and Cardiovascular Health," *Circulation research*, vol. 124, no. 5, 2019.
- [94] F. Shaffer and J. P. Ginsberg, "An Overview of Heart Rate Variability Metrics and Norms," *Frontiers in public health*, vol. 5, 2017.
- [95] H.-G. Kim, E.-J. Cheon, D.-S. Bai, Y. H. Lee and B.-H. Koo, "Stress and Heart Rate Variability: A Meta-Analysis and Review of the Literature," *Psychiatry investigation*, vol. 15, no. 3, 2018.

- [96] M. Campos, "Heart rate variability: A new way to track well-being," Harvard Health Publishing, Harvard Medical School of Harvard University, 22 November 2017. [Online]. Available: <https://www.health.harvard.edu/blog/heart-rate-variability-new-way-track-well-2017112212789>. [Accessed 10 11 2019].
- [97] J. A. Chalmers, D. S. Quintana, M. J.-A. Abbott and A. H. Kemp, "Anxiety Disorders are Associated with Reduced Heart Rate Variability: A Meta-Analysis," *Frontiers in psychiatry*, vol. 5, 2015.
- [98] S. W. Porges, "Cardiac vagal tone: a physiological index of stress," *Neuroscience and Biobehavioral Reviews*, vol. 19, no. 2, 1995.
- [99] A. L. Hansen, B. H. Johnsen and J. F. Thayer, "Vagal influence on working memory and attention. Int. J. Psychophysiol," *International Journal of Psychophysiology*, vol. 48, no. 3, 2003.
- [100] S. Duschek, M. Muckenthaler, N. Werner and G. A. Reyes del Paso, "Relationships between features of autonomic cardiovascular control and cognitive performance," *Biological Psychology*, vol. 81, no. 2, 2009.
- [101] J. F. Thayer and R. D. Lane, "A model of neurovisceral integration in emotion regulation and dysregulation," *Journal of Affective Disorders*, vol. 61, no. 3, 2000.
- [102] J. F. Thayer and R. D. Lane, "Claude Bernard and the heart–brain connection: further elaboration of a model of neurovisceral integration," *Neuroscience and Biobehavioral Reviews*, vol. 33, no. 2, 2009.
- [103] G. A. Reyes Del Paso, M. I. González, J. A. Hernández, S. Duschek and N. Gutiérrez, "Tonic blood pressure modulates the relationship between baroreceptor cardiac reflex sensitivity and cognitive performance," *Psychophysiology*, vol. 46, no. 5, 2009.
- [104] G. Forte, F. Favieri and M. Casagrande, "Heart Rate Variability and Cognitive Function: A Systematic Review," *Frontiers in neuroscience*, vol. 13, 2019.
- [105] F. Shaffer and J. P. Ginsberg, "An Overview of Heart Rate Variability Metrics and Norms," *Frontiers in public health*, vol. 5, 2017.

- [106] T. Theorell, Y. Liljeholm-Johansson, H. Björk and M. Ericson, "Saliva testosterone and heart rate variability in the professional symphony orchestra after "public faintings" of an orchestra member," *Psychoneuroendocrinology*, vol. 32, no. 6, 2007.
- [107] L. Bernardi, F. Valle, M. Coco, A. Calciati and P. Sleight, "Physical activity influences heart rate variability and very-low-frequency components in Holter electrocardiograms," *Cardiovascular research*, vol. 32, no. 2, 1996.
- [108] V. E. Claydon and A. V. Krassioukov, "Clinical correlates of frequency analyses of cardiovascular control after spinal cord injury," *American Journal of Physiology - Heart and Circulatory Physiology*, vol. 294, no. 2, 2008.
- [109] J. A. TAYLOR, D. L. CARR, C. W. MYERS and D. L. ECKBERG, "Mechanisms underlying very-low-frequency RR-interval oscillations in humans.," *Circulation (New York, N.Y.)*, vol. 98, no. 6, 1998.
- [110] T. F. o. t. E. S. Electrophysiology, "Heart rate variability: standards of measurement, physiological interpretation, and clinical use," *Circulation (New York, N.Y.)*, vol. 93, no. 5, 1996.
- [111] G. G. BERNTSON, J. THOMAS BIGGER JR, D. L. ECKBERG, P. GROSSMAN, P. G. KAUFMANN, M. MALIK, H. N. NAGARAJA, S. W. PORGES, J. P. SAUL, P. H. STONE and M. W. VAN DER MOLEN, "Heart rate variability: origins, methods, and interpretive caveats," *Psychophysiology*, 1997.
- [112] J. Armour, *Neurocardiology: Anatomical and Functional Principles*, Boulder Creek, CA: Institut of HeartMath, 2003.
- [113] G. C. Kember, G. A. Fenton, K. Collier and J. A. Armour, "Aperiodic stochastic resonance in a hysteretic population of cardiac neurons.," *Physical review. E, Statistical physics, plasmas, fluids, and related interdisciplinary topics*, vol. 61, no. 2, 2000.
- [114] G. C. Kember, G. A. Fenton, J. A. Armour and N. Kalyaniwalla, "Competition model for aperiodic stochastic resonance in a Fitzhugh-Nagumo model of cardiac sensory neurons," *Physical review. E, Statistical, nonlinear, and soft matter physics*, vol. 63, no. 4, 2001.

- [115] F. Shaffer, R. McCraty and C. L. Zerr, "A healthy heart is not a metronome: an integrative review of the heart's anatomy and heart rate variability.," *Frontiers in psychology*, , vol. 5, 2014.
- [116] R. Mccraty and F. Shaffer, "Heart rate variability: new perspectives on physiological mechanisms, assessment of self-regulatory capacity, and health risk," *Global Advances in Health and Medicine*, 2015.
- [117] T. F. o. t. E. S. Electrophysiology, "Heart rate variability: standards of measurement, physiological interpretation, and clinical use," *Circulation (New York, N.Y.)*, vol. 93, no. 5, 1996.
- [118] S. Akselrod, D. Gordon, F. A. Ubel, D. C. Shannon, A. C. Berger and R. J. Cohen, "Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control.," *Science (American Association for the Advancement of Science)*, vol. 213, no. 4504, 1981.
- [119] G. G. Berntson, J. T. Cacioppo and P. Grossman, "Wither vagal tone.," *Biol Psychol* ., vol. 74, no. 2, 2007.
- [120] P. Lehrer, R. Woolfolk and W. Sime, *Biofeedback training to increase heart rate variability.*, New York, NY: Guilford Press, 2007.
- [121] G. A. Reyes del Paso, W. Langewitz, L. J. M. Mulder, A. van Roon and S. Duschek, "The utility of low frequency heart rate variability as an index of sympathetic cardiac tone: a review with emphasis on a reanalysis of previous studies," *Psychophysiology*, vol. 50, no. 5, 2013.
- [122] D. S. Goldstein, O. Benth, M. Park and Y. Sharabi, "Low-frequency power of heart rate variability is not a measure of cardiac sympathetic tone but may be a measure of modulation of cardiac autonomic outflows by baroreflexes," *Experimental physiology*, vol. 96, no. 12, 2011.
- [123] F. Shaffer, R. McCraty and C. L. Zerr, "A healthy heart is not a metronome: an integrative review of the heart's anatomy and heart rate variability," *Frontiers in psychology*, vol. 5, 2014.
- [124] A. K. Ahmed, J. B. Harness and A. J. Mearns, "Respiratory control of heart rate," *European Journal of Applied Physiology and Occupational Physiology*, vol. 50, no. 1, 1982.
- [125] W. A. Tiller, R. McCraty and M. Atkinson, "Cardiac coherence: a new, noninvasive measure of autonomic nervous system order.," *Alternative therapies in health and medicine*, vol. 2, no. 1, 1996

- [126] T. E. Brown, L. A. Beightol, J. Koh and D. L. Eckberg, "Important influence of respiration on human R-R interval power spectra is largely ignored," *Journal of applied physiology*, vol. 75, no. 5, 1983.
- [127] P. Grossman and E. W. Taylor, "Toward understanding respiratory sinus arrhythmia: relations to cardiac vagal tone, evolution and biobehavioral functions," *Biological psychology*, vol. 74, no. 2, 2007.
- [128] D. L. Eckberg and M. J. Eckberg, "Human sinus node responses to repetitive, ramped carotid baroreceptor stimuli," *American journal of physiology. Heart and circulatory physiology*, vol. 424, no. 4, 1982.
- [129] J. F. Thayer, S. S. Yamamoto and J. F. Brosschot, "The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors.," *International journal of cardiology*, vol. 141, no. 2, 2009.
- [130] L. DA and H. SW, "The effectiveness of exercise as an intervention in the management of depression: systematic review and meta-regression analysis of randomised controlled trials," *BMJ*, pp. 322-763, 2001.
- [131] H. Svendsen, T. W. Teasdale and M. Pinner, "Subjective experience in patients with brain injury and their close relatives before and after a rehabilitation programme," *Neuropsychological Rehabilitation*, vol. 14, no. 5, pp. 495-515, 2004.
- [132] E. L. Mailey, J. Huberty, D. Dinkel and E. McAuley, "Physical activity barriers and facilitators among working mothers and fathers," *BMC public health*, vol. 14, no. 1, 2014.
- [133] A. Barman, A. Chatterjee and R. Bhide, "Cognitive Impairment and Rehabilitation Strategies After Traumatic Brain Injury," *Indian journal of psychological medicine*, vol. 38, no. 3, 2016.
- [134] D. Meichenbaum and D. C. Turk, *Facilitating treatment adherence: a practitioner's guidebook*, New York: Plenum Press, 1987.
- [135] J. Shafirin, K. Bognar, K. Everson, M. Brauer, D. N. Lakdawalla and F. M. Forma, "Does knowledge of patient non-compliance change prescribing behavior in the real world? A claims-

based analysis of patients with serious mental illness," *ClinicoEconomics and outcomes research*, vol. 10, 2018.

- [136] L. R. Martin, S. L. Williams, K. B. Haskard and M. R. Dimatteo, "The challenge of patient adherence," *Therapeutics and clinical risk management*, vol. 1, no. 3, 2005 .
- [137] S. Mühlig, K. C. Bergmann, O. Twesten and F. Petermann, "Therapy participation in ambulatory asthma patients: empirical comparison of compliance rates using different operationalization methods for drug compliance," *Pneumologie*, vol. 55, no. 4, 2001.
- [138] J. Strong and J. Fleming, "Self-Awareness of Deficits following Acquired Brain Injury: Considerations for Rehabilitation," *British Journal of Occupational Therapy*, vol. 58, no. 2, pp. 55-60, 1995.
- [139] S. K. Kime, D. G. Lamb and B. A. Wilson, "Use of a comprehensive programme of external cueing to enhance procedural memory in a patient with dense amnesia," *American Psychological Association*, vol. 10, no. 1, p. 17, 1996.
- [140] O. Ezrachi, Y. Ben-Yishay, T. Kay, L. Diller and J. Rattok, "Predicting employment in traumatic brain injury following neuropsychological rehabilitation," *Journal of Head Trauma Rehabilitation*, vol. 6, no. 3, 1991.
- [141] M. Schönberger, F. Humle, P. Zeeman and T. W. Teasdale, "Working alliance and patient compliance in brain injury rehabilitation and their relation to psychosocial outcome.," *Neuropsychological Rehabilitation*, vol. 16, no. 3, 2006.
- [142] M. Schönberger, F. Humle and T. W. Teasdale, "The development of the therapeutic working alliance, patients' awareness and their compliance during the process of brain injury rehabilitation," *Brain Injury*, vol. 20, no. 4, p. 445, 2006.
- [143] P. contributors, "Rehabilitation in Sport," *Physiopedia* , 2 October 2018. [Online]. Available: [https://www.physio-pedia.com/index.php?title=Rehabilitation\\_in\\_Sport&oldid=198967](https://www.physio-pedia.com/index.php?title=Rehabilitation_in_Sport&oldid=198967). [Accessed 16 11 2019].

- [144] WHO, ADHERENCE TO LONG-TERM THERAPIES, Geneva: World Health Organization, 2003.
- [145] B. Gholipour, "What Is a Normal Heart Rate?," Live Science, 12 1 2018. [Online]. Available: <https://www.livescience.com/42081-normal-heart-rate.html>. [Accessed 10 11 2019].
- [146] A. Malliani, "Heart rate variability:A challenge for a new way of thinking," *Journal of cardiac failure*, vol. 2, no. 3, 1996.
- [147] R. Hartmann, F. M. Schmidt, C. Sander and U. Hegerl, "Heart Rate Variability as Indicator of Clinical State in Depression," *Frontiers in psychiatry*, vol. 9, 2018.
- [148] S. Hillebrand, K. B. Gast, R. de Mutsert, C. A. Swenne, J. W. Jukema, S. Middeldorp, F. R. Rosendaal and O. M. Dekkers, "Heart rate variability and first cardiovascular event," *Europace : European cardiac electrophysiology*, 2013.
- [149] A. Inoue, T. Hifumi, Y. Kuroda, N. Nishimoto, K. Kawakita, S. Yamashita, Y. Oda, K. Dohi, H. Kobata, E. Suehiro and T. Maekawa, "Mild decrease in heart rate during early phase of targeted temperature," *Critical care* , 2018.
- [150] R. L. Conder and A. A. Conder, "Heart rate variability interventions for concussion and rehabilitation," *Frontiers in Psychology* , vol. 5, 2014.
- [151] G. A. Reyes Del Paso, M. I. González, J. A. Hernández, S. Duschek and N. Gutiérrez, "Tonic blood pressure," *Psychophysiology*, vol. 46, no. 5, 2009.
- [152] M. Malik, J. T. Bigger, A. J. Camm, R. E. Kleiger, A. Malliani, A. J. Moss and P. J. Schwartz, "Heart rate variability : Standards of measurement, physiological interpretation, and clinical use," *European heart journal*,, vol. 17, no. 3, 1996.
- [153] E. Lam, S. Aratia, J. Wang and J. Tung, "Measuring Hear Rate Variability in Free-Living Conditions Using Consumer-Grade Photoplethysmography," *JMIR*, 2020.
- [154] M. Sakaki, H. J. Yoo, L. Nga, T.-H. Lee, J. F. Thayer and M. Mather, "Heart rate variability is associated with amygdala functional connectivity with MPFC across younger and older adults," *NeuroImage*, vol. 139, 2016.



- [155] J. F. Thayer, F. Åhs, M. Fredrikson, J. J. Sollers and T. D. Wager, "A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health," *Neuroscience and Biobehavioral Reviews*, vol. 36, no. 2, 2012.
- [156] J. F. Thayer and E. Sternberg, "Beyond heart rate variability: vagal regulation of allostatic systems," *Annals of the New York Academy of Sciences*, vol. 1088, no. 1, 2006.
- [157] G. Park and J. F. Thayer, "From the heart to the mind: cardiac vagal tone modulates top-down and bottom-up visual perception and attention to emotional stimuli.," *Frontiers in Psychology*, vol. 5, 2014.
- [158] J. F. Thayer and B. H. Friedman, *A neurovisceral integration model of health disparities in aging*, Washington, DC: National Academies Press, 2004.
- [159] C. Deziel, "sciencing.com," sciencing, 13 March 2018. [Online]. Available: <https://sciencing.com/effects-small-sample-size-limitation-8545371.html>. [Accessed 01 07 2021].
- [160] T. A. Novack, A. L. Alderson, B. A. Bush, J. M. Meythaler and K. Canupp, "Cognitive and functional recovery at 6 and 12 months post-TBI," *Brain injury*, vol. 14, no. 11, 2000.
- [161] "overload principle. Medical Dictionary for the Health Professions and Nursing," 2012. [Online] Available: <https://medical-dictionary.thefreedictionary.com/overload+principle>. [Accessed 07 July 2020].
- [162] W. J. Kraemer and S. J. Fleck, *Strength training for young athletes*, Champaign, IL: Human Kinetics, 2005 2nd edition.
- [163] C. Foster, C. V. Farland, F. Guidotti, M. Harbin, B. Roberts, J. Schuette, A. Tuuri, S. T. Doberstein and J. P. Porcari, "The Effects of High Intensity Interval Training vs Steady State Training on Aerobic and Anaerobic Capacity," *Journal of sports science & medicine*, vol. 14, no. 4 2015.
- [164] C. W. Cotman, N. C. Berchtold and L.-A. Christie, "Exercise builds brain health: key roles of growth factor cascades and inflammation.," *Trends in Neurosciences*, vol. 30, no. 9, 2007.

- [165] N. Sallam and I. Laher, "Exercise Modulates Oxidative Stress and Inflammation in Aging and Cardiovascular Diseases.," *Oxidative medicine and cellular longevity*, 2016.
- [166] N. J. Stimpson, G. Davison and A.-H. Javadi, "Joggin' the Noggin: Towards a Physiological Understanding of Exercise-Induced Cognitive Benefits," *Neuroscience and Biobehavioral Reviews*, vol. 88, 2018.
- [167] E. Garcia, "The Self-Weighting Model," *Communications in statistics. Theory and methods*, vol. 41, no. 8, 2012.
- [168] "Workout Type on Apple Watch," Apple , [Online]. Available: <https://support.apple.com/en-asia/HT207934>. [Accessed 01 07 2021].
- [169] B. Klug, "An Overview of the System Usability Scale in Library Website and System Usability Testing," *Weave: Journal of Library User Experience*, vol. 1, no. 6, 2017.
- [170] F. Stephanie, "System Usability Scale: A Quick Usability Scoring Solution," Satori Interactive, 1 Septemper 2015. [Online]. Available: <https://satoriinteractive.com/system-usability-scale-a-quick-usability-scoring-solution-2/>. [Accessed 10 11 2019].
- [171] "HIPAA Compliance Checklist," *HIPPAA Journal* .
- [172] CDC, "Facts about Concussion and Brain Injury," [Online]. Available: [https://www.cdc.gov/headsup/pdfs/providers/facts\\_about\\_concussion\\_tbi-a.pdf](https://www.cdc.gov/headsup/pdfs/providers/facts_about_concussion_tbi-a.pdf). [Accessed 08 05 2021].
- [173] "Subdural hematoma," MedlinePlus., 22 March 2020. [Online]. Available: <https://medlineplus.gov/ency/article/000713.htm>. [Accessed 08 05 2021].
- [174] N. H. Rogers, J. W. Perfield, K. J. Strissel, M. S. Obin and A. S. Greenberg, "Reduced Energy Expenditure and Increased Inflammation Are Early Events in the Development of Ovariectomy-Induced Obesity," *Endocrinology*, vol. 150, no. 5, 2009.
- [175] U. J. Jung and M.-S. Choi, "Obesity and Its Metabolic Complications: The Role of Adipokines and the Relationship between Obesity, Inflammation, Insulin Resistance, Dyslipidemia and

- Nonalcoholic Fatty Liver Disease," *International journal of molecular sciences*, vol. 15, no. 4, 2014.
- [176] J. Jensen, P. I. Rustad, A. J. Kolnes and Y.-C. Lai, "The Role of Skeletal Muscle Glycogen Breakdown for Regulation of Insulin Sensitivity by Exercise," *Frontiers in physiology*, vol. 2, 2011
- [177] S. Mann, C. Beedie and A. Jimenez, "Differential Effects of Aerobic Exercise, Resistance Training and Combined Exercise Modalities on Cholesterol and the Lipid Profile: Review, Synthesis and Recommendations," *Sports Medicine*, vol. 44, no. 2, 2014.
- [178] S. Bathina and U. N. Das, "Brain-derived neurotrophic factor and its clinical implications," *Archives of medical science*, vol. 11, no. 6, 2015.
- [179] D. Cabral, J. Rice, T. Morris, T. Rundek, A. Pascual-Leone and J. Gomes-Osman, "Exercise for Brain Health: An Investigation into the Underlying Mechanisms Guided by Dose," *Neurotherapeutics*, vol. 16, no. 3, pp. 580-599, 2019.
- [180] E. Boots, S. Schultz, J. Oh, J. Larson, D. Edwards, D. Cook, R. Kosciak, M. Dowling, C. Gallagher, C. Carlsson, H. Rowley, Bendlin, B. L. A. S. Asthana, B. Hermann, M. Sager, S. Johnson and O. Okonkwo, "Cardiorespiratory fitness (CRF), the health-related component of physical fitness reflecting these parameters, has shown to be related to better cognitive function in healthy adults.," *Brain Imaging Behav.*, vol. 9, no. 3, 2015.
- [181] L. F. DeFina, W. L. Haskell, B. L. Willis, C. E. Barlow, C. E. Finley, B. D. Levine and K. H. Cooper, "Physical activity versus cardiorespiratory fitness: two (partly) distinct components of cardiovascular health?," *Progress in cardiovascular diseases*, vol. 57, no. 4, 2014.
- [182] J. A. Hawley, M. Hargreaves, M. J. Joyner and J. R. Zierath, "Integrative biology of exercise," *Cell*, vol. 159, no. 4, 2014.
- [183] L. B. Rowell, G. L. Brengelmann, J. R. Blackmon, R. A. Bruce and J. A. Murray, "Disparities between aortic and peripheral pulse pressures induced by upright exercise and vasomotor changes in man," *Circulation (New York, N.Y.)*, vol. 37, no. 6, 1968.