DESIGN AND SIMULATION OF AN ACCURATE

BREAST BIOPSY SYSTEM

by

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ABSTRACT

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Core needle biopsy is a non-invasive technique for confirming breast and prostate cancer. Over the years, several non-real time image guided systems have been developed to guide the needle to the target lesion/tumor. Frequently used methods are those employing x-ray, ultrasound, MRI or x-ray fluoroscopy to guide the needle during biopsy. However, these methods suffer from the disadvantages that they are non-real time or the imaging technique is two dimensional or ionizing.

Our broad objective is to develop a visually guided, haptic assisted breast biopsy system (henceforth called ViHAB) using real time 3D ultrasound imaging and

haptic guidance. The system will help the radiologist in identifying target micro-calcifications and provide real time guidance for core needle biopsy.

The ViHAB simulator, the topic of this thesis, being developed at the Virtual Environment Laboratory is capable of reading and displaying three dimensional ultrasound images, keep track of micro-calcification in near real time in a sequence of images as well as provide haptic guidance to a virtual needle via a force feedback joystick.

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INTRODUCTION

1.1 Breast Cancer Facts

Breast cancer is the most common form of cancer among women, other than skin cancer. It is also the second leading cause of cancer deaths in women, after lung cancer. About 178,480 women in the United States will be found to have invasive breast cancer in 2007. About 40,460 women will die from the disease this year. Right now there are slightly over 2 million women living in the United States who have been treated for breast cancer. The chance of a woman having invasive breast cancer (cancer which breaks through normal breast tissue barriers and invades surrounding areas) some time during her life is about 1 in 8. The chance of dying from breast cancer is about 1 in 33. Breast cancer death rates are going down. This decline is probably the result of early detection and improved treatment [1].

For detection and confirmation of possible breast cancer, the steps currently followed are breast self examination, mammogram and biopsy. Breast self examination can indicate the presence of any unnatural growth in the patient's breast. It is followed up with mammography, in which x-ray images of breast are obtained for diagnosis (Figure 1.1). If the presence of micro-calcifications / calcifications is revealed in the breast, then a biopsy is advised.

Micro-calcifications or calcifications are preliminary indicators of breast cancer. They are tiny calcium deposits within the breast, present singly or in clusters. Currently, x-ray mammography is the gold standard method for the detection of micro-calcification. Mammography is very successful as a screening tool because it is sensitive to these small dense masses. The detection and localization of micro-calcifications can also serve as a useful landmark in the ultimate biopsy and diagnosis of the disease.
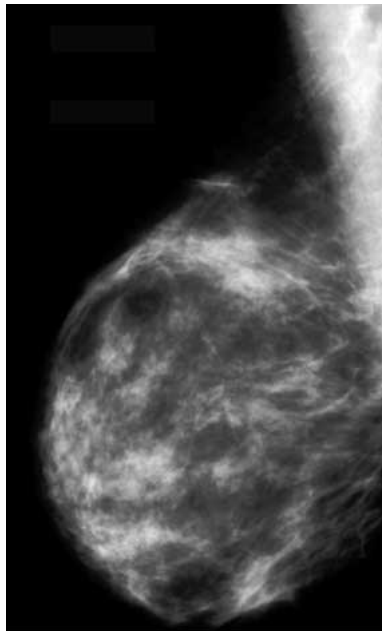

Figure 1.1 Mammogram

1.2 Existing Breast Biopsy Techniques

Every year, millions of women in USA undergo biopsy for diagnosis of breast cancer. Breast biopsy techniques can be broadly divided into 3 categories:

- Fine Needle Aspiration Biopsy (FNAB) – In this technique, a very thin (fine) needle is used to draw fluid out of the affected lump. A diagnosis is made depending on whether the fluid drawn is clear or not.

- Core Needle Biopsy – A larger needle compared to FNAB is used to remove samples of breast tissue for further analysis. Some form of image guidance is used to guide the needle to the target tissue.

- Surgical Biopsy – In this procedure, surgery under local or general anesthesia is performed to remove all or part of the suspected tissue as well as some normal tissue. The sample is then tested to see whether it is benign or malignant.

Of the breast biopsy procedures mentioned above, core needle biopsy is the most commonly employed technique. Core needle biopsy is performed with some form of image guidance. For example, Stereotactic Breast Biopsy uses x-ray images for guidance, while MRI and ultrasound guided biopsies, as their names imply, use MRI and ultrasound images for guidance.

Given below is an outline of biopsy procedures using x-rays, MRI and ultrasound images for guidance.

1.2.1 Stereotactic Breast Biopsy

Stereotactic breast biopsy using x-ray imaging and a core needle or a vacuum assisted device (VAD), is the most widely used breast biopsy technique. The principle of stereotactic biopsy is that a lesion can be located precisely in three dimensions by calculating its apparent change in position on angled x-ray images. The first x-ray

locates the abnormality in the breast, after which two stereo views are obtained; each angled 15 degrees to either side of the initial image (Figure 1.2 [2]). The physician then marks the lesion electronically on the stereo images. The computer calculates how much the lesion's position appears to have changed on each of the stereo views, and is able to determine its exact location in three-dimensional space [3]. Three to six separate core needle insertions are typically needed to obtain a sufficient sample of breast tissue in the case of core needle biopsy.

Figure 1.2 Stereotactic Breast Biopsy

Vacuum-assisted biopsy is a minimally invasive procedure that allows for the removal of multiple tissue samples. However, unlike core needle biopsy, which requires several separate needle insertions to acquire multiple samples, the special biopsy probe used during vacuum-assisted biopsy is inserted only once into the breast through a small skin nick made in the skin of the patient's breast [4]. The biopsy instrument used in this procedure is called a vacuum-assisted device (VAD), for example Mammotome, which consists of an inner needle with a trough extending from it at one end and an overlying sheath. When the sheath is retracted, a vacuum is used to pull breast tissue into the

needle trough. The outer sheath rapidly moves forward to cut the tissue and collect it in the trough. The procedure is outlined in Figures 1.3 and 1.4 below [5].
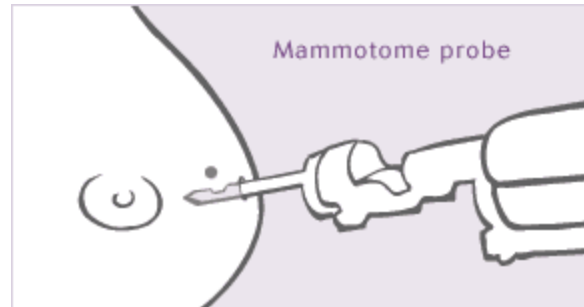
Figure 1.3 Mammotome Probe

position   vacuum   cut   remove
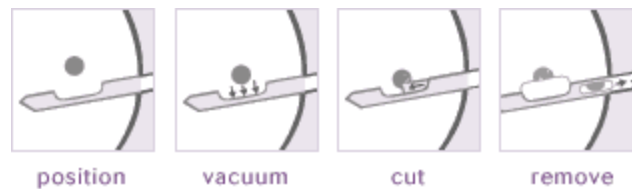
Figure 1.4 Mammotome Probe Steps

A small nick is made in the skin and the tip of the biopsy needle is advanced to the previously calculated site of the lesion. At this point, stereo images are again obtained to confirm that the needle tip is actually within the lesion. Usually six to 12 samples are collected when the VAD is used. Then a final set of images is obtained. If they show that the lesion has been mostly or completely removed, a small clip is left at the biopsy site so that it can be easily located if the lesion proves to be cancer. An advantage of the VAD is that the needle is inserted only once into the breast without having to withdraw the needle after each sampling. Biopsies are obtained in an orderly manner by rotating the probe, assuring that the entire region of interest will be sampled.

1.2.2 Ultrasound Guided Breast Biopsy

Ultrasonography uses sound waves at very high frequency to image internal structures, including those deep within the body. Either pulsed or continuous sound waves are directed at the area of interest using a hand-held device called a transducer. The transducer also receives echoes of the sound waves in a pattern that reflects the outlines of the internal structure mass. An ultrasound image showing different parts in a breast is shown in Figure 1.5 below. The transducer changes electrical signals into ultrasound waves and converts the reflected sound waves back to electrical energy. Unlike radiological procedures, the ultrasound method requires no exposure to ionizing radiation [3].

Figure 1.5 Ultrasound Image of Breast

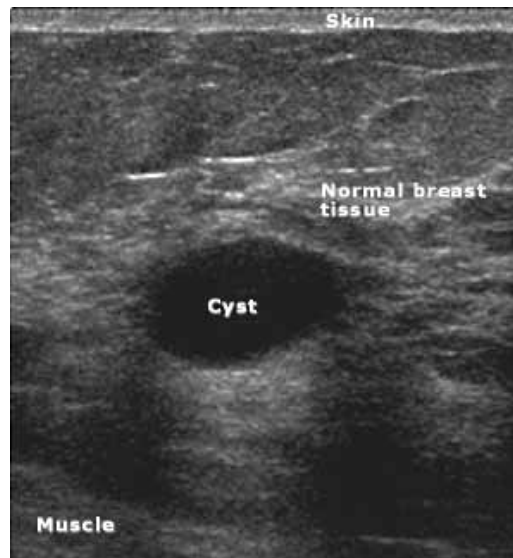When ultrasound is chosen to guide a breast biopsy, one of the biopsy instruments used is a VAD. Nodules of tissue less than about an inch in size can be totally removed using this equipment. These systems use vacuum pressure to pull tissue

into a needle and remove it without having to withdraw the probe after each sampling—as is necessary when the core needle method is used. Biopsies are obtained in an orderly manner by rotating the needle, ensuring that the entire region of interest will be sampled.

With the patient lying on her back or turned slightly to the side, the ultrasound probe is used to locate the lesion. Enough local anesthesia is injected to be sure that she will feel no discomfort during the procedure. Ultrasound also is used to guide the injection of anesthetic along the route to the lesion and about the mass. A very small nick is made in the skin at the site where the biopsy needle is to be inserted. The radiologist, constantly monitoring the lesion site with the ultrasound probe, guides a hollow core biopsy needle or the vacuum-assisted needle directly into the mass and obtains specimens. Usually at least four samples are taken. <u>In some cases it may be difficult to visualize the needle in the breast tissue and considerable skill is needed to coordinate movements of the ultrasound transducer with needle insertion</u>. If the lesion is nearly or completely removed during the biopsy procedure, a clip is placed where the lesion was located to ensure that the site can be easily located for additional surgery if the lesion proves to be malignant.

Recently, an ultrasound guided commercial breast biopsy system has been developed by Robarts Imaging, Canada [6]. The prototype 3D ultrasound guided biopsy apparatus has been designed with features from both stereotactic-guided and ultrasound guided biopsy procedures. With the breast compressed in a similar manner as for stereotactic procedures, a three dimensional ultrasound image is acquired and a target is

identified within the volume. The US probe is translated so that the target is seen on the monitor in 2D. A needle guide is also moved into position and a needle inserted through the guide and into the breast. The guide provides a trajectory to the target, which keeps the needle in the plane of the 2D ultrasound image. Needle guidance is in real-time, as in ultrasound guidance. At any point throughout the procedure, 3D ultrasound images may be acquired and the relative needle and target positions checked. This is particularly useful after biopsy, to confirm that the needle penetrated the target.

1.2.3 Magnetic Resonance Imaging Guided Breast Biopsy

X-ray-guided (or stereotactic) and ultrasound-guided breast biopsy procedures are ruled out if an abnormality is not clear with mammography or ultrasound scanning. When an abnormality is only visible with MRI, the physician may choose to perform an MR-guided breast biopsy [3].

The patient is positioned face down on her stomach on a moveable table. The affected breast or breasts are positioned into a cushioned opening containing a wire coil that sends and receives radio waves to help create the MR images. The breast is gently compressed between two compression plates (similar to those used in a diagnostic MRI exam), one of which is marked with a grid structure. Using computer software, the radiologist measures the position of the lesion with respect to the grid and calculates the position and depth of the needle placement. <u>After placing the needle, MR imaging is performed to verify its position.</u> Depending on the type of MRI unit being used, the patient may remain in place or be moved out of the center or bore of the MRI scanner so that the tissue samples can then be obtained.

When the tissue sampling is complete, a marker clip may be placed where the lesion was located to ensure that the site can be easily located for additional surgery if the lesion proves to be malignant.

Figure 1.6 below [3] shows the MR image of breast.
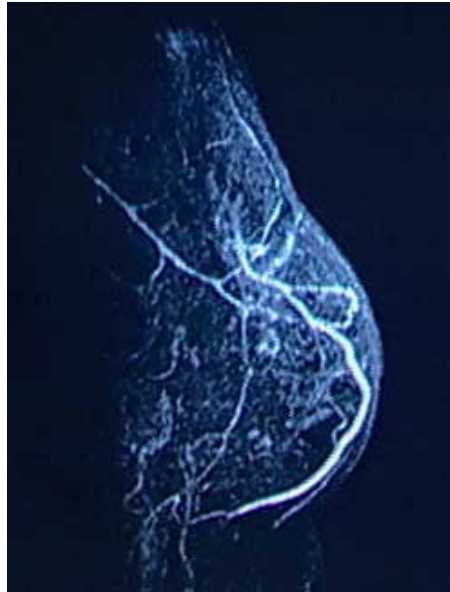
Figure 1.6 MRI Image of Breast

Apart from the imaging modalities discussed above, CT Scans or x-ray fluoroscopy may also be used to guide the needle. X-ray fluoroscopy can provide high resolution real time images while CT Scans provide 3D images.

1.3 Prototype Systems

Over the years several prototype systems have been developed in order to improve breast biopsy procedure. Effort has been directed along different lines.

Some groups have aimed to develop better imaging systems. For example those using cylindrical array of piezoelectric transducers to obtain 3D images of breast (US Patent # 7025725, 6878115). Others have tried to develop breast stabilization devices

(US Patent # 6304770, 6146377) which could be used for imaging and interventional procedures. Some other systems have used non-real time 3D images to guide needle insertion (US Patent # 5660185).

The systems developed have used ultrasound images and tried to address the issue of breast compression and real time guidance. However, none of these systems have integrated the ideas of a biopsy with breast stabilization, real time 3D ultrasound images and use of these images to provide visual as well as haptic guidance during biopsy.

1.4 Problem Statement

Let us examine the shortcomings of the existing approaches [6,7,8,9]

- Procedures guided by stereotactic mammography are lengthy, with compression of the breast mandatory throughout and use ionizing radiations

- Needle position within a lesion is usually not confirmed for all passes to minimize the dose of ionizing radiation received by the breast and to shorten the procedure

- Motion of the breast or patient may occur during procedures. If motion occurs, the whole biopsy procedure must be restarted

- CT scans and x-ray fluoroscopy involve harmful ionizing radiations

- All imaging modalities used today, except x-ray fluoroscopy and handheld ultrasound , are non-real time

- Due to poor resolution, current clinical ultrasound systems cannot detect micro-calcifications which were originally visible in the mammograms. Furthermore, they provide only 2D images and do not have a fixed reference co-ordinate system. These result in reduced spatial accuracy in locating the biopsy target.

Summarizing the problem, there is a need for a breast biopsy system which uses high-resolution, non-ionizing, real time, 3D images and uses the information provided by the images to guide a biopsy needle with pin point accuracy to the targeted suspicious tissue.

This thesis concentrates on the design and simulation of such a system which we call ViHAB.

The following chapters describe in detail the evolution of the system and its simulation.

CHAPTER 2

EVOLUTION AND DESIGN OF ViHAB

The team consisting of Dr Venkat Devarjan and Mr Sumit Tandon of The University of Texas at Arlington and Dr Edmond Richer and Dr Peter Antich of UT Southwestern Medical School at Dallas aimed at the development of a breast biopsy system which would overcome the shortcomings of the existing systems listed in the previous chapter.

Current breast cancer diagnosis has the following steps, a) mammography indicating the presence of suspicious tissue, followed by b) biopsy using image guidance. Mammography is a fairly well established gold standard for initial diagnosis. However, biopsy using image guidance clearly requires further research and development.

Mammograms reveal the presence of suspicious tissue. However, they can present only approximate location information because the breast of the patient has to be compressed during imaging. Thus, during minimally invasive biopsy procedure, with the surgeon going in blind, some form of image guidance is needed to maneuver the biopsy needle to the target tissue. Open surgical biopsy obviously does not require any image guidance.

The sections that follow describe our take on the various aspects of image guided biopsy followed by description of the evolution of ViHAB.

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2.1 Choice of Imaging Technology

The imaging technique chosen could be x-ray, ultrasound or MRI. The choice of imaging technology is driven by whether the target is visible in a particular imaging modality or not. Let us discuss the pros and cons of each of them separately.

MRI undoubtedly is by far the best imaging technique available in terms of image resolution. X-ray comes a close second. However, the primary concern with X-Ray is the fact that it is ionizing in nature – in fact over exposure to any form of ionizing radiation causes cancer! Besides, x-ray images are 2D. X-ray CT scans provide 3D information, but they are time consuming and obviously non-real time. Real time X-ray fluoroscopy does exist, which uses low doses of radiation. However, the problem of exposure to radiation remains – both for the patient and the surgeon.

Let us next consider Magnetic Resonance Imaging. MRI is high resolution, 3D and non-ionizing in nature, but it is again not true-real time. Some of the biopsy systems using MRI guidance claim to be real time. As in stereotactic breast biopsy, images are taken *before* needle insertion to give the surgeon an idea of the location of the target and *after* the needle has been inserted to confirm if the needle has reached the target. Note, however, the system does not provide guidance *while* the surgeon is inserting the needle. Moreover, MRI is expensive and cannot be used in the presence of any ferromagnetic objects like pacemakers.

The third popular form of imaging technique is Ultrasound Imaging. Unlike mammography, ultrasound does not use ionizing radiation that limits how often screening can be performed. Ultrasound is also effective in the dense breast of younger

women, for whom mammography is not effective, and can often be used without painful breast compression.

However, detection of the smallest micro-calci?cations (less than 300 μm) has proven to be a frustrating problem for clinical ultrasound. The development of a micro-calcification sensitive ultrasound that rivals the capabilities of mammography would obviously be of great clinical importance for millions of women. This was the first consideration in the design of ViHAB. This aspect of the problem is being tackled by our collaborators, Dr Edmond Richer and Dr Matthew Lewis, at UT Southwestern Medical Center at Dallas.

Table 2.1 below shows a comparison of different imaging techniques including the one we propose to use in ViHAB.

Table 2.1 Popular Imaging Techniques

	Real Time	Ionizing	3 Dimensional	Resolution
X-Ray Fluoroscopy	Yes	Yes	No	Good
CT Scans	No	Yes	Yes	Good
Mammography	No	Yes	No	Good
Magnetic Resonance Imaging	No	No	Yes	Good
Clinical Ultrasound	Yes	No	Yes	Poor
Our Proposed Ultrasound Imaging System	Yes	No	Yes	Good enough to detect micro-calcifications

2.2 Design of ViHAB

With the imaging modality decided we set out designing a system which would address the issues with the current biopsy systems as far as possible.

The imaging system will be designed to provide us with real time (5-10 frames per second) true 3D ultrasound images of the breast. We would then use the images to extract information which would assist the surgeon in maneuvering the biopsy needle towards the target micro-calcification. Since the image would be true 3D in nature, the problems associated with the needle being out of the image plane can be avoided.

It is clear that this would be a complicated system and we would have to solve the design problem by breaking it up into smaller parts. As it turned out, the operation of the system could in fact be divided into two broad parts – a) offline processing or the initial non-real time setup and b) the continuous real time operation.

The first thing that the surgeon would need to do would be to *view and identify* the calcification. Thus the system should be capable of displaying 3D images. Thus, we decided that three orthogonal slices of the 3D image should be displayed on the screen. Additionally, the surgeon should be given the freedom of choosing which slice is displayed. Once the surgeon identified the target, the system needs to be intelligent enough to calculate the target's co-ordinates in 3D space. Further, localizing the calcification in 3D space would require accurate calibration of the biopsy setup and the imaging system. This would constitute the non-real time preparation for biopsy.

With the system setup and ready for biopsy, it would have to start operating in real time mode. In this mode, it would receive images at 5-10 frames per second and keep track of the target identified by the surgeon. It would also provide guidance to the surgeon inserting the needle by displaying some form of 3D model of the breast and targeted tissue.

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Visual assistance in 3D while inserting the needle would go a long way in assisting the surgeon. We decided to go a step further. What if we could provide haptic guidance? Breast tissue being very soft, it is nearly impossible to use the actual resistance provided by it for guidance. Hence, we chose to use an amplified synthetic force feedback. As the surgeon maneuvered a joystick controlled robotic needle, real time information of the location of the target and the needle would be used to check if the surgeon was moving in the correct direction. In case the surgeon veered from the correct path, an artificial force would be applied to the joystick to set him/her in correct direction. In other words, the system would provide an "invisible haptic tunnel" to guide the surgeon. The synergy between the visual guidance and the haptic guidance, will allow the surgeon to perform a biopsy with increased accuracy, in a single attempt, without compressing the breast.

Based on the above arguments we developed the following sub-systems (Figure 2.1) [10]:

- A newly designed and constructed experimental 3D real time ultrasound imaging system (UTSW)

- Software to track micro-calcifications in the real-time 3D US images of breast (that will run on the "Computer" in the block diagram) (UTA)

- System that assists the physician in the insertion of the biopsy needle using invisible haptic guidance (UTA)

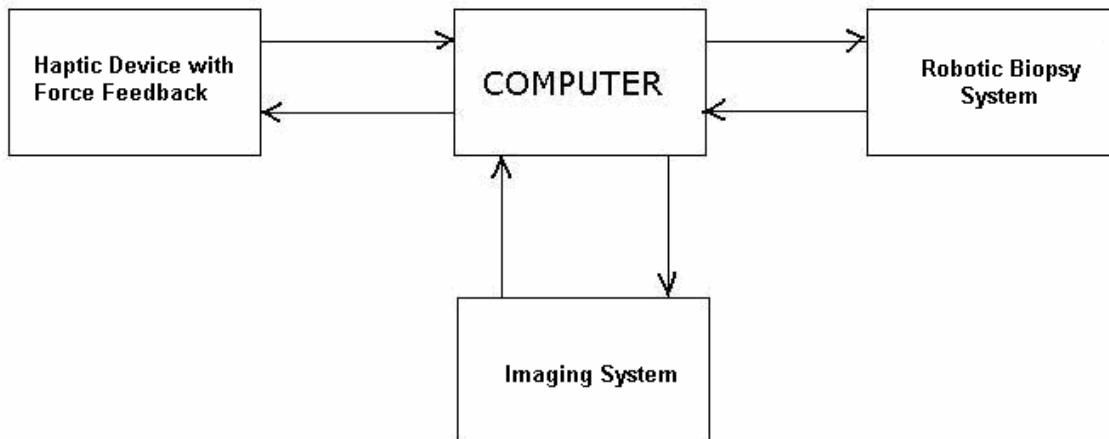- Joystick control with force feedback (UTA)

Figure 2.1 ViHAB Block Diagram

The workflow for the system is given below and the flowchart in Figure 2.2 follows. We start from the flow chart on the left.

Once the radiologist confirms the presence of suspicious tissue (micro-calcifications) in the mammogram , the patient will be referred to the proposed system to undergo US guided biopsy.

The system flow chart starts with the initial imaging of the breast. In an offline process, new calibration algorithms and software will be developed to calibrate a new US scanner. Initial 3D US images obtained will be used to calibrate the system with the help of fiducial markers. This will help create a digital map of the breast which can be used to accurately calculate the 3D coordinates of any visible point inside the breast such as the micro-calcifications.

Slices of US images of breast are displayed on the screen from which the surgeon identifies the target area and its boundaries.

As the target area is identified by the surgeon on the screen, the software calculates the initial coordinates of the micro-calcification and an optimal needle trajectory from an external entry point to the targeted micro-calcification.

All of the above steps constitute the *non-real time* part of the procedure and essentially help in the *planning of the biopsy*. This is followed by the real-time steps of the actual biopsy described below and shown on the flow chart on the right side.

At first, the initial trajectory calculated earlier is loaded in to the real time program to track the micro-calcification. The initial position of the micro-calcification is obtained with the surgeon locating the micro-calcification in 3 orthogonal views of the initial image. After this, the target is tracked in the subsequent images and its position accurately obtained.

The position of the needle is tracked in real time. Since the needle is attached to the haptic system, its motion can be restricted in predetermined directions, thus creating an *invisible haptic guidance system*. The trajectory of the needle is continuously updated from the information about the location of the target area and the needle tip. The surgeon inserts the needle (attached to a robotic arm) and receives continuous corrective feedback regarding the path of the needle. In addition, the needle can be stopped at the location of the micro-calcification so that it does not overshoot the target. Location of the tip of the needle can be verified from the real time images.
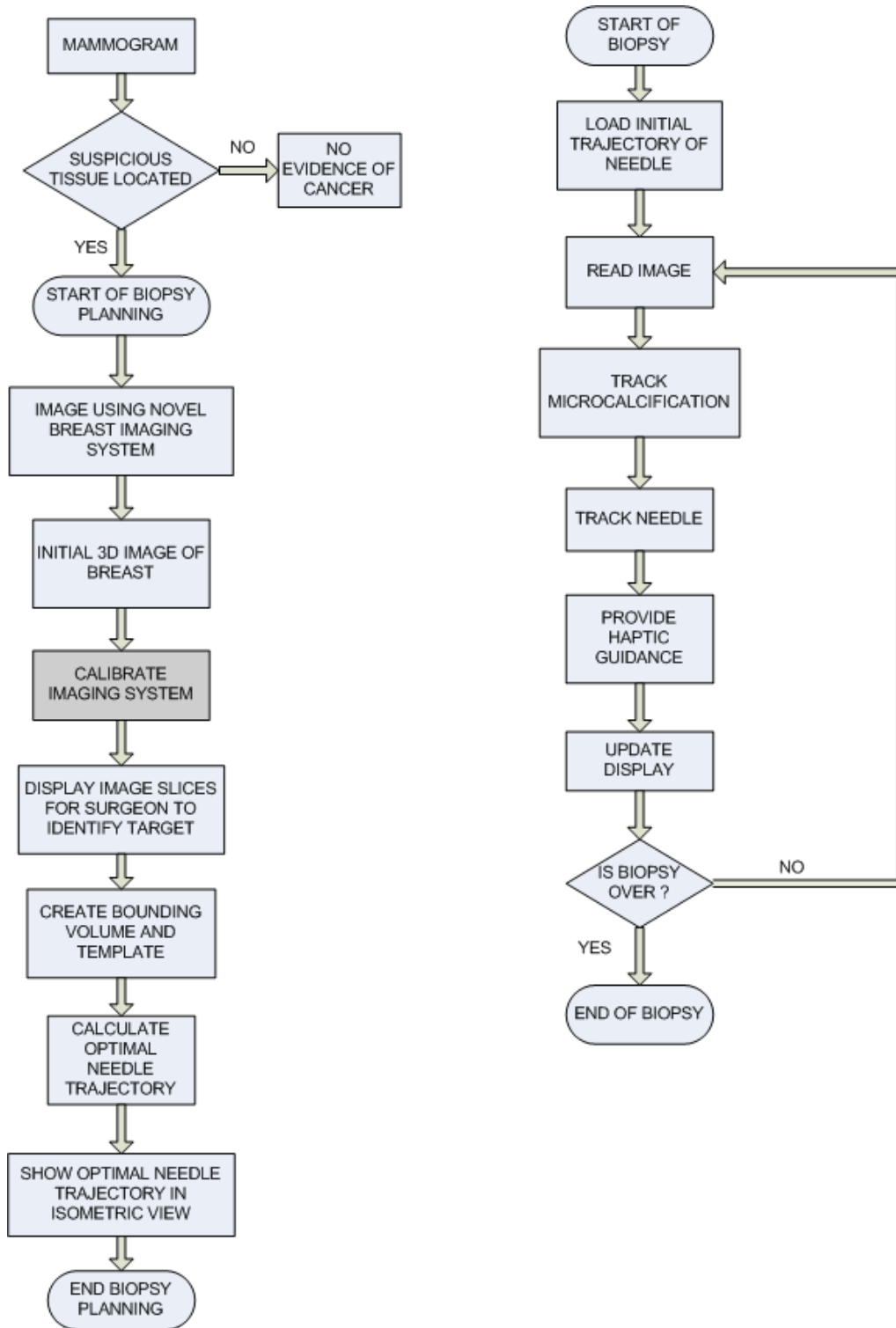
Figure 2.2 ViHAB Operation

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With the overall blocks of ViHAB in place, it was required to design and implement the details of the individual blocks. Calibration of the system, tracking of the target and haptic guidance were identified as the key components of ViHAB. Calibration of ViHAB is not possible unless the imaging hardware is constructed. Hence, target tracking and guidance were picked to be the main issues to be addressed by this thesis. The sections that follow give a description of the development of the algorithms for micro-calcification tracking and needle guidance.

2.3 Target Tracking

We are assuming here that we will have real time 3D ultrasound images available to us, in which we will be required to keep track of a target micro-calcification.

The target micro-calcification moves during biopsy procedure. This motion is mainly due to breathing. There may be other reasons for motion too, for example, displacement of tissue by the needle.

Current biopsy techniques, like those employing MRI or x-rays for guidance, take images of the breast before biopsy and after needle placement to confirm proper placement of needle. For 100% accuracy of the system, however, it is imperative that the position of the target is tracked continuously, and the location information used to guide the needle. Real time target location information can be used to provide continuous guidance to the surgeon. This goes a long way in minimizing, if not eliminating the human error.

Accurate tracking of calcification is one of the most important objectives of ViHAB. Since we will be targeting micro-calcifications, it is very important that the needle is guided to the target accurately. Otherwise, owing to the small size of the target, it may be missed completely.

A large body of research exists in tracking objects through different media. Target tracking in the military, for instance, is a well developed field. What makes the problem in medicine harder is the lack of real time, non-ionizing imagery to help with such tracking. Ultrasound imaging is just now coming in to experimental arena so that small groups have started working on tracking medical objects (tissues and instruments) inside human body. In this context, the guidance of surgical robotic systems by ultrasound images has been studied by a few researchers. Abolmaesumi et al [11] have reported the study, development and comparison of several algorithms for tracking of soft tissue in ultrasound images. These algorithms however work on 2D ultrasound images. Merdes et al [12] have worked with the tracking of instruments in 3D ultrasound fields and use active tracking devices. Von Ramm et al [13] have proposed a method called Feature Location and Shape Correlation for real-time tracking of tissue in volumetric ultrasound data. This proposal remains to be tested in a real time system. More recently, Novotny et al [14] have reported developing a method based on a modified version of Radon Transform which tracks the instrument in real time.

There are several issues to be considered however, when tracking of micro-calcifications in 3D Ultrasound images. Firstly, as we can see in Figure 2.3 [15], the micro-calcification is very small ($\sim 300 \mu$m), and would occupy a very small area in the

image. Secondly, ultrasound images are noisy. These two factors eliminate several techniques like segmentation, velocity flow, Kalman Filtering etc. for tracking the targeted micro-calcification.
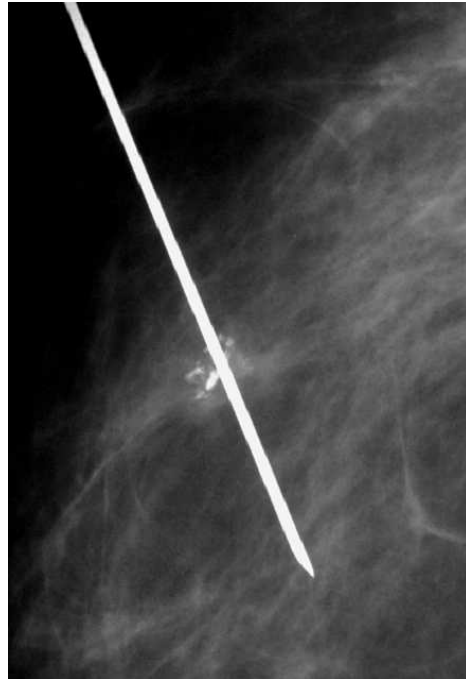

Figure 2.3 Needle Through Micro-calcification Cluster

This led to our developing the idea of a dynamic template matching based tracking algorithm which does not require segmentation for tracking of the target. However, an initial position and an estimate of the size of the micro-calcification is required which can be obtained from the preliminary 3D image. Subsequently, a virtual bounding-box can be constructed around the calcification which will completely enclose it. This virtual bounding-box is also the starting template for the tracking process. In the next image, this template is scanned over a search volume to find the best match. Once the best matching image block is found, it is now considered the

template for the next image and the center of this image block/template will be the location of the target calcification.

Correlation coefficient is used as the measure of best match because among the various measures of similarity like Normalized Cross Correlation, Mean Absolute Difference, Sum of Squared Differences, correlation coefficient is perhaps the most stable in the presence of noise [16].

$$CorrelationCoefficient(X,Y) = \frac{E(XY) - E(X)E(Y)}{s_X s_Y} \tag{2.2}$$

2.4 Invisible Channel Guidance

To improve the accuracy of the system, and to fully utilize the capabilities of continuous tracking of the target micro-calcification, we decided to include some form of haptic guidance system which would provide another degree of assistance to the surgeon.

Breast tissue by itself is very soft and does not offer a large resistance. Moreover, the measured force has little correlation with the following error. As such, it would be difficult to capture and amplify the force offered by the tissue and provide it to the surgeon as feedback. Hence a synthetic force is applied to the joystick to indicate that the needle is going off the prescribed path.

We initially started out with the idea of a pipe-like virtual guidance channel. It would guide the movement of needle and take it to the target. Figure 2.5 below shows the idea.
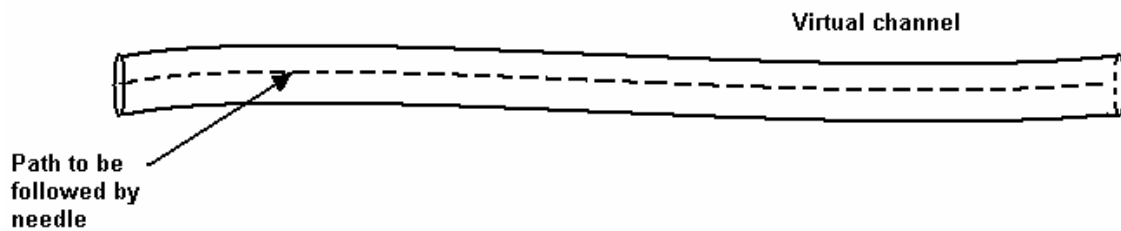
Figure 2.4 Pipe Channel

The pipe model of guidance channel had a few shortcomings. First of all, it was very rigid and would not allow any room to the surgeon to make any errors. The surgeon would be allowed the same distance from the ideal needle path during the entire procedure. Thus, reaching the target accurately would again be dependant on the surgeon's expertise, as the needle may overshoot the target.

Reducing the diameter of the pipe would result in force feedback being applied more frequently. This would make the biopsy procedure more difficult for the surgeon.

To take care of these disadvantages, the shape of the guidance volume was chosen to be conical. The tip of the guidance cone is always at the target. As the target moves, so does the guidance cone. The needle tip is not allowed to go outside the guidance cone at any given point of time. If the needle goes outside the cone, it is pushed back to the surface of the cone.

The concept of a guidance cone (Figure 2.5) is unique and effective in several ways. Initially it allows some leeway to the surgeon as to the position of the needle. However, as the needle approaches the target, the conical shape of the guidance volume automatically decreases the tolerance to deviation of the needle tip from the axis of the

cone. The axis of the cone is also the straight line path that the needle needs to follow in order to accurately reach the target.

In Figure 2.5, Target Location 1 and Target Location 2 indicate the locations of the target micro-calcification at two different time instants. The red and the black cones are the corresponding guidance cones. In both cases, the dotted axis of the cone is the ideal path that the needle should follow in order to reach the target.
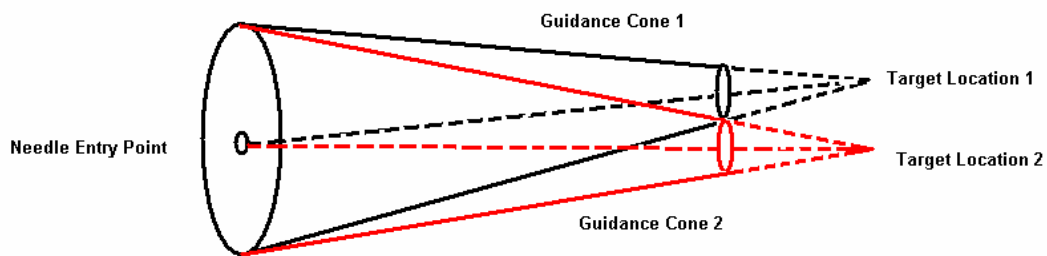

Figure 2.5 Needle Guidance Cone

It is planned that as the surgeon gets a force feedback from the joystick, he will make the required change in position of the joystick, which in turn would adjust the position of a robotic biopsy needle.

CHAPTER 3

SIMULATION APPROACH

This chapter describes the simulation approach in detail. The first section describes simulated image of cylinder phantom and in the second section we describe the simulation of motion of micro-calcification in an image sequence due to breathing. The final section gives a description of the needle guidance cone concept.

3.1 Simulation of Images of Cylinder Phantom

The synthetic image of phantom (Figure 3.1), provided by Dr Edmond Richer and Dr Matthew Lewis of UT Southwestern Medical School at Dallas, shows a 90mm diameter cylinder that simulates the normal tissue of the breast. It contains a 6 mm spherical region that simulates the properties of a higher reflectivity tumor tissue. Random noise has been added in order to approximate the signal to noise ratio expected in the actual reconstructed 3D image.

The size of the a simulated image used for testing purposes is 128X128X128 voxels, with the targeted area containing micro-calcifications occupying an approximately spherical volume of size 5X5X5 voxels with the center at (51, 71, 61).

Figure 3.2 shows the Axial, Frontal and Sagittal slices of the volumetric image which contain the micro-calcification
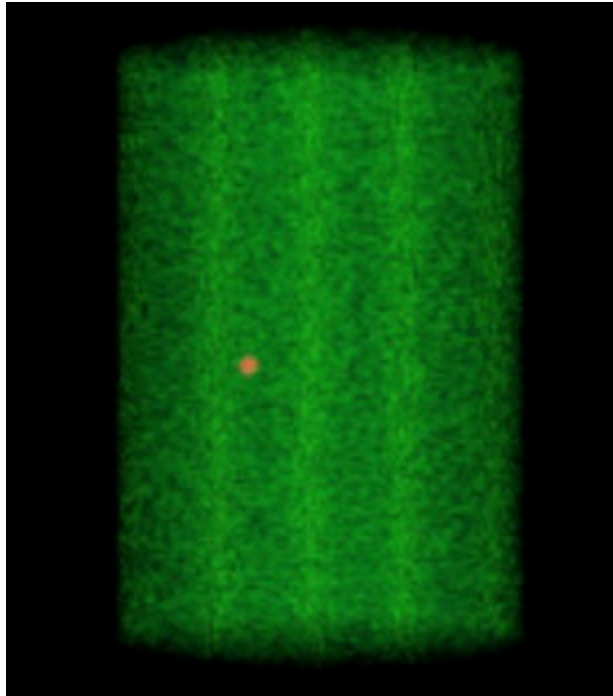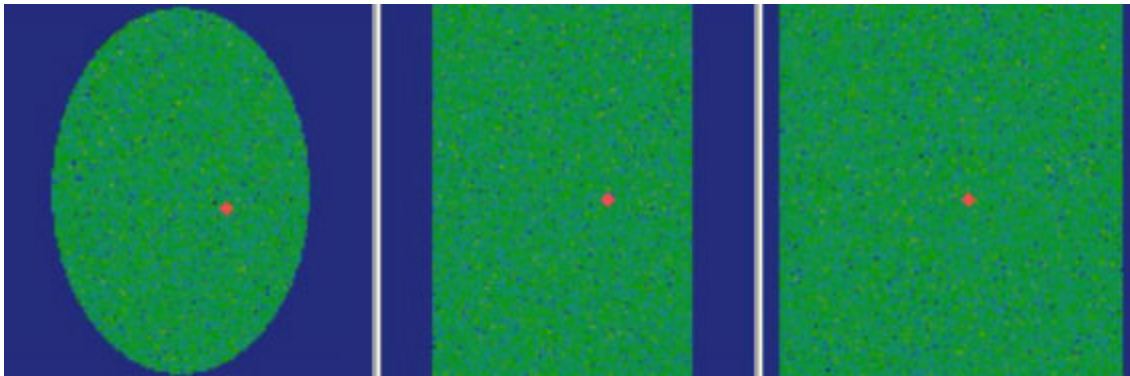
Figure 3.1 Volumetric View of Cylinder Phantom

Figure 3.2 Axial, Frontal and Sagittal Slices Showing the Simulated Target Area

3.2 Generation of Image Sequence

The tracking algorithm developed here is planned to be used on real-time 3D ultrasound images acquired as a sequence.

For simulation purposes, a sequence of 200 images was created by moving the calcification successively in each image. To generate this sequence of images it was

assumed that the maximum contribution to the motion of the calcification will come from patient breathing. This will correspond to motion along Z direction and minimal motion along X/Y directions. There will also be some randomness in the motion of the calcification owing to uneven breathing or due to displacement of tissue by the biopsy needle. Furthermore, the motion of the tumor along the Z direction, if plotted against time, can be considered to be nearly a cosine wave [17].

The diameter of typical micro-calcifications that we are targeting will be about 4 voxels and the maximum motion of the calcification will be about 3-4 times its diameter. Accordingly, perturbations along Z axis were generated according to the following equation:

$$Z = K\left(A + B\cos 2t + C\cos 4t + D\cos 6t + E\cos 8t + F\cos 10t\right) \tag{3.1}$$

For a particular image sequence, the values chosen for the constants above were:

Table 3.1 Variables Used for Motion of Target Area

Variable	Value
K	12
A	2/P
B	$-4/(3\pi)$
C	$-4/(15\pi)$
D	$-4/(35\pi)$
E	$-4/(55\pi)$
F	$-4/(65\pi)$

Apart from this, a random number generated between -2 and 3 was added to the sequence generated above. This accounted for randomness in displacement of the tumor.

Plot of the motion along Z direction is shown in Figure 3.3. As we can see, the generated motion satisfies all the simulation requirements outlined above. The motion is nearly a rectified cosine wave, has randomness and the variation in location is about 16 voxels, which is about 4 times the diameter of the target area.
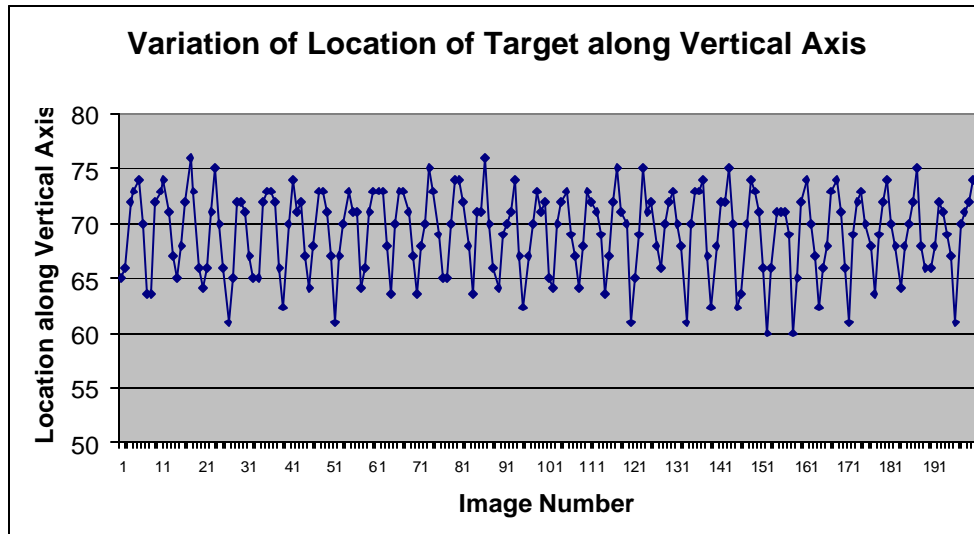
Figure 3.3 Plot Showing Generated Motion of Target Area in Images

3.3 Haptic Guidance

As discussed in the previous chapters, a conical guidance volume is used to restrict the motion of biopsy needle. The needle is pushed back to the surface of the cone in case it goes out of it. Figure 3.4 shows a 2D view of the concept. The dotted line represents the surface of the cone, which is also the boundary within which the needle should lie, and the solid line represents the ideal path that the needle should follow.
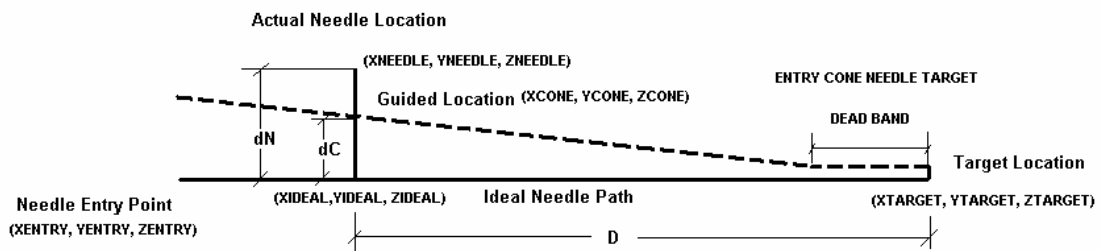

Figure 3.4 Different Points in Space Used for Needle Guidance

To push the needle back to the surface of the cone, we need to calculate the coordinates of a point on the surface of the cone which would be closest to the actual needle position at a particular instant of time.

At any given instant, $(X_{NEEDLE}, Y_{NEEDLE}, Z_{NEEDLE})$, $(X_{ENTRY}, Y_{ENTRY}, Z_{ENTRY})$ and $(X_{TARGET}, Y_{TARGET}, Z_{TARGET})$ are the position of the tip of the needle, entry point of the needle and the current tracked target location.

Using these three points, we can calculate $(X_{IDEAL}, Y_{IDEAL}, Z_{IDEAL})$, which is a point on the ideal path that the needle should follow.

Now we calculate dN and D which are current needle distance from ideal path and distance of ideal point from target respectively.

From this information and knowing the vertical angle of the cone we can calculate dC, the distance of closest point on surface from $(X_{IDEAL}, Y_{IDEAL}, Z_{IDEAL})$.

Now, dividing the line segment connecting the actual and ideal needle positions in the ratio $dC/(dN - dC)$, we can find out the point $(X_{CONE}, Y_{CONE}, Z_{CONE})$ on the surface of the cone.

Once the point on the surface of the cone is found, a force is applied to the joystick as feedback. The force applied is proportional to the distance of the needle tip from the surface of the cone $(dN - dC)$. The force applied is such that the *direction* of motion of the needle is changed. In real tissue this will result in slight compression of tissue. The needle will now be guided to follow the surface of the cone. As the needle approaches the target, the cone converges and the needle hits the target As one end of

the needle will always be fixed at the needle entry point, the force applied will only

change the direction of motion of the needle (Figure 3.5). Obviously in an actual system

the force will be applied to the robotic arm holding the needle and would move the arm

up-down or sideways to change the direction of needle advancement.
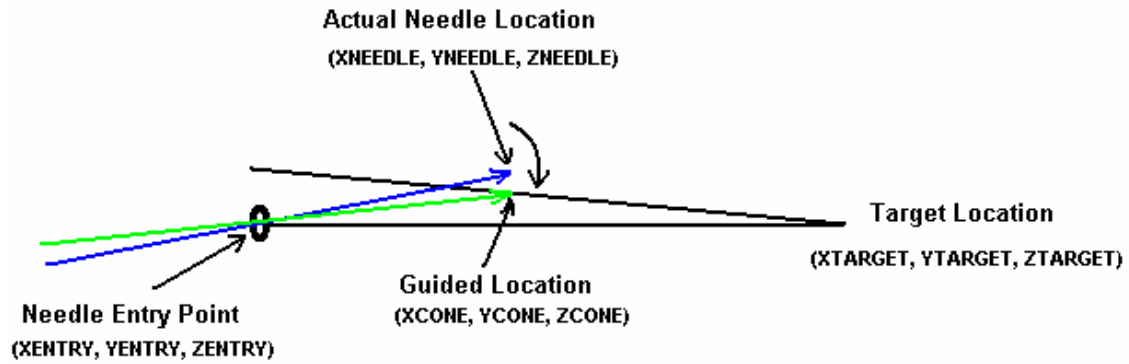

Figure 3.5 Change in Needle Direction

CHAPTER 4

IMPLEMENTATION AND RESULTS

This chapter describes in detail the algorithms for implementing the different components of ViHAB and, the observations and results.

4.1 Display of 3D Images

The images received from the imaging system will be true 3D in nature. The images will contain 3D voxel information which needs to be displayed on the screen.

The image received will tentatively be 128X128X128 voxels in size. For display purposes, slices along the 3 axes are displayed on the screen. The target area appears as bright spots on a dark background in the image. For ease of identification, different slices of the image are pseudo-colored. The calcifications or any areas of higher intensity appear bright red on a blue and green background.

Figure 4.1 illustrates a grayscale image showing a slice of the 3D image containing the target and a pseudo-colored version of the same slice. It is clear that the target is visible better in the pseudo-colored image.

Once a 3D image is read into a 3D matrix, a particular slice from the image can be selected for display. This slice is actually a grayscale image stored in the form of a 2D matrix. To create a pseudo-colored image, a 3D matrix is created which has 3 slices of size 128X128 each. These are the R, G and B slices. Typically, voxels with intensity greater than 50 are rendered red while those with intensity between 10 and 50 are

rendered green and the rest are colored blue. The flowchart in Figure 4.2 outlines the steps followed in pseudo-coloring the grayscale images. For fast rendering, OpenGL was used to display the images.
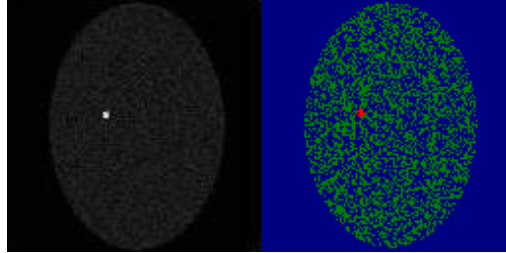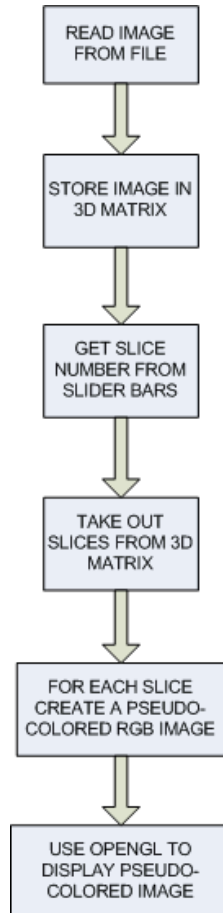

Figure 4.1 Grayscale and Pseudo-colored Image Slice

Figure 4.2 Flowchart Showing Steps in Pseudo-coloring of Image Slices

During biopsy, the relative position of target micro-calcification is required and should be shown with respect to the image as a whole. The large image is represented by a wire-frame cube while the target micro-calcification is shown as a smaller cube within the larger cube.

Figure 4.3 shows a snapshot of the system with 3 slices of the image along with 3 different views of the image being displayed during tracking procedure.
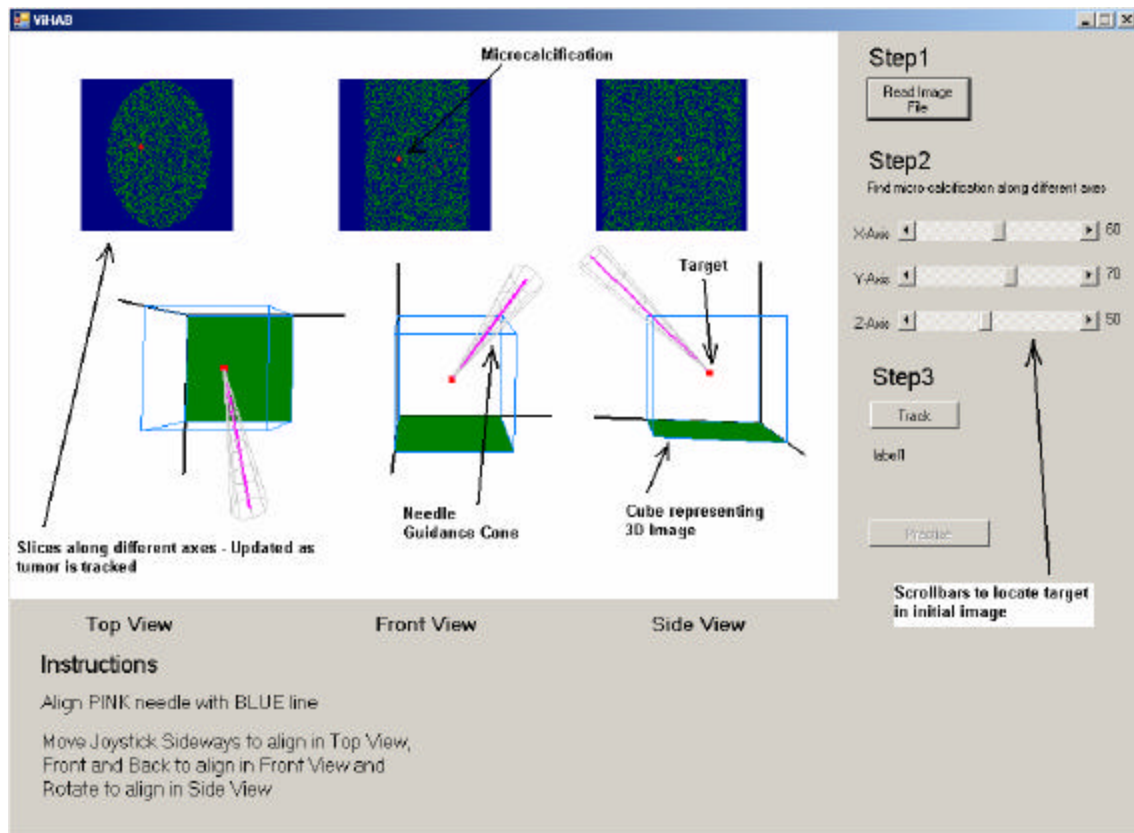

Figure 4.3 Screenshot of ViHAB

4.2 Tracking of Micro-calcification

To track the micro-calcification, an initial template is generated from the first image. The coordinates of the center of the micro-calcification can be found manually by viewing different slices of the image along different axes. A bounding box of size

35

7X7X7 is then constructed around that point. The initial size of the bounding box is decided initially by estimating the size of the target area.

The bounding box so created becomes the template for the next image. In the next image, a search volume is defined. Figure 4.4 shows the concept of 3D image, search volume and template.
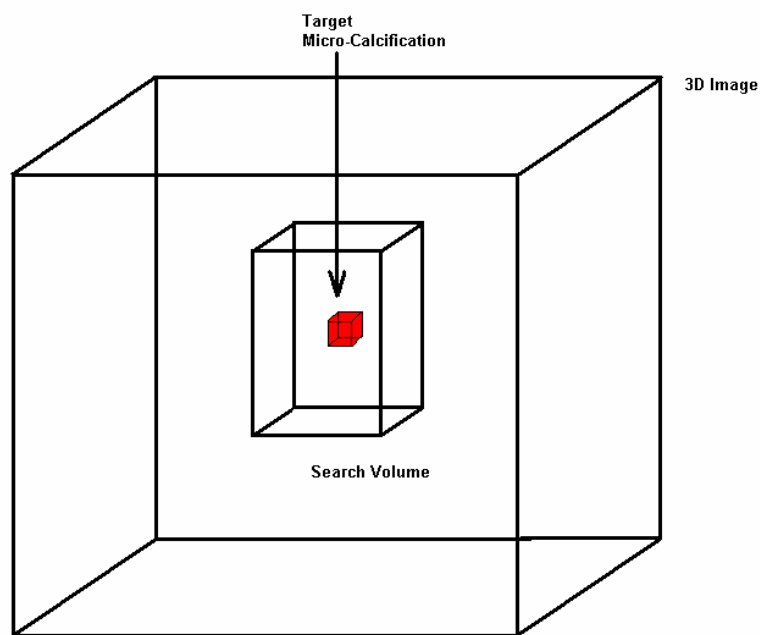

Figure 4.4 Image, Search Volume and Target Area

Correlation coefficient, defined in equation 2.2 is used as the measure of match between the template and image because it is one of the most stable measures in the presence of noise.

Correlation coefficient (RHO) between a template and a block of the image within the search volume is calculated as below:

$$RHO(Template, Block) = \frac{Mean(Template * Block) - Mean(Template) * Mean(Block)}{SD(Template) * SD(Block)}$$

Where,

$$Mean(Template * Block) = \frac{1}{n} \sum_i \sum_j \sum_k Template * Block$$

$$Mean(Template) * Mean(Block) = \frac{1}{n^2} \sum_i \sum_j \sum_k Template * \sum_i \sum_j \sum_k Block$$

$$SD(Template) = \sqrt{\frac{1}{n} \sum_i \sum_j \sum_k Template^2 - \left(\frac{1}{n} \sum_i \sum_j \sum_k Template\right)^2}$$

$$SD(Block) = \sqrt{\frac{1}{n} \sum_i \sum_j \sum_k Block^2 - \left(\frac{1}{n} \sum_i \sum_j \sum_k Block\right)^2}$$

Once a match is found, which is the image block corresponding to maximum correlation coefficient; the center of the box is calculated. This center is considered to be the location of micro-calcification for that image in the sequence. The box itself is the template for the next image. Dynamic template matching is used to track the micro-calcification in a sequence of images. See flowchart in Figure 4.5.
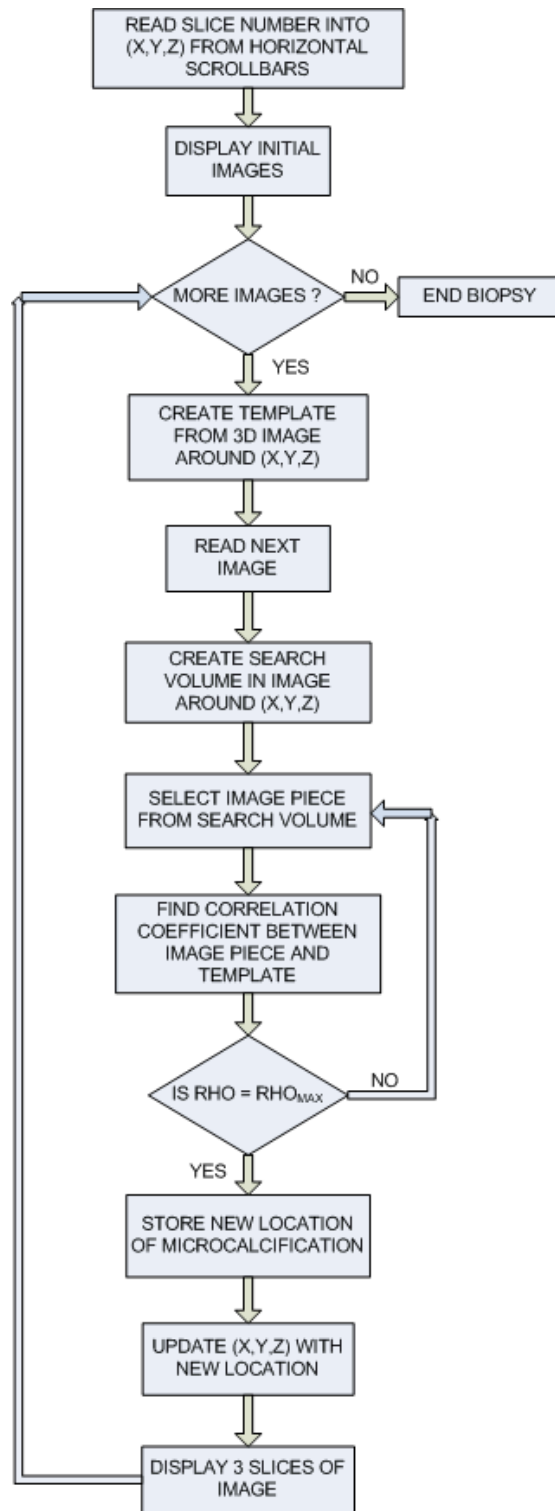
Figure 4.5 Tracking Algorithm

It was found that the tracking procedure is very accurate and was able to detect the exact location of the micro-calcification in 192 out of 200 images i.e. 96% of the time. In the remaining 4% cases, the localization error was 1 voxel, which is quite insignificant. Figure 4.6 shows the localization error in a sequence of 200 images.
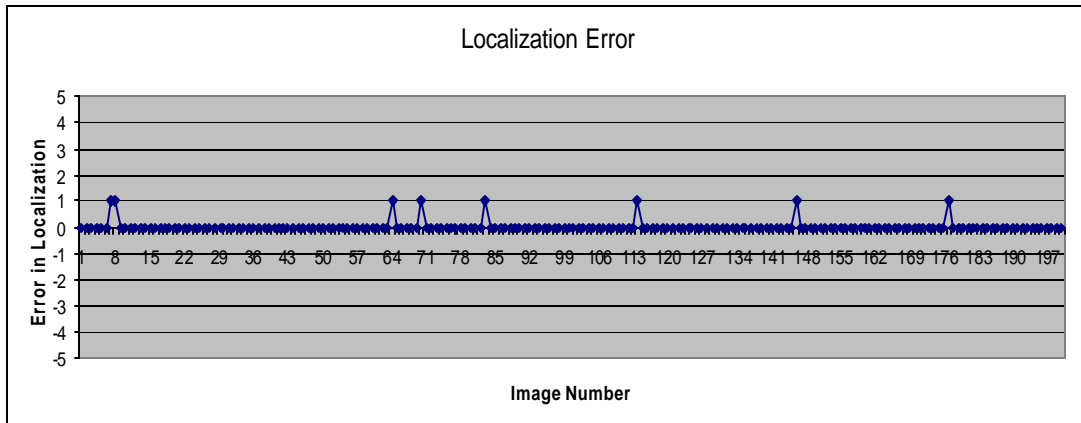

Figure 4.6 Chart Showing Localization Error

The dynamic template matching algorithm is both accurate and fast. Table 4.1 shows the mean image processing time (time to read image + time to localize target + time to create new template) for 5 runs of the program on a sequence of 200 images each.

Table 4.1 Average Time to Process Each Image

Run Number	Average Time to Process Image (seconds)
1	0.1363
2	0.1359
3	0.1345
4	0.136
5	0.1352

From the table above we can conclude that ViHAB is capable of processing images at the rate of around 8 frames per second, which is in the original system design.

4.3 Guidance with Force Feedback Joystick

With the information about the location of the target available from the tracking module of ViHAB, the haptic module can guide the surgeon during biopsy procedure.

For simulation purposes, a Logitech Force 3D Pro joystick was interfaced with ViHAB. This joystick allows linear motion along two perpendicular axes and has rotation of handle as the third degree of freedom. It can also give force feedback along two linear axes.

The connection of the ViHAB with the force feedback joystick is accomplished using DirectInput API available in Microsoft DirectX, which is a set of low-level APIs for creating games and other high-performance multi-media applications.

The joystick is used in bidirectional mode – i.e. for both input and output. The joystick is periodically polled to read its position data and during simulation, this position is used to move the virtual needle on the screen. This simulation is a good

approximation of a real system, where the needle will be moved with the help of a high precision real 3D joystick or a medical robot and whose position information can be obtained from the hardware itself. This information combined with needle geometry information can provide accurate location information for the tip of the needle. Figure 4.7 shows the schematic of a typical joystick [18].
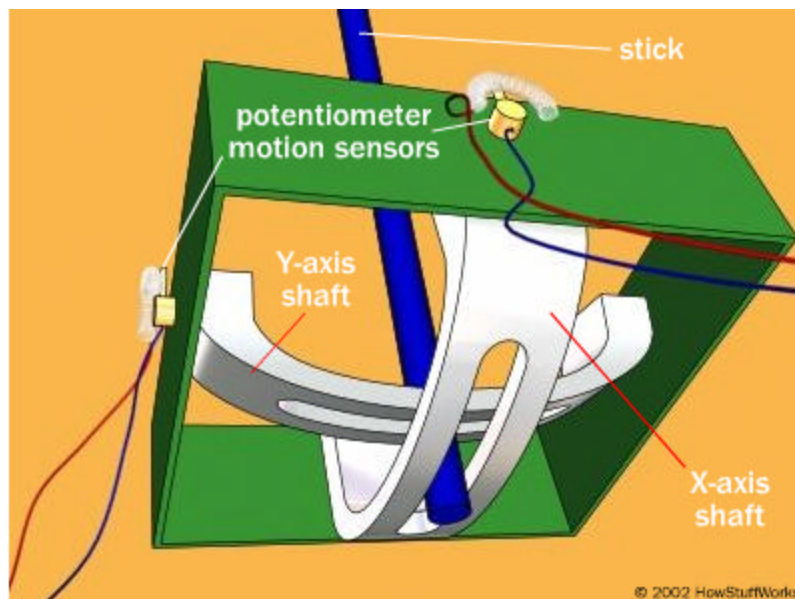

Figure 4.7 Joystick Hardware

Forward motion of the needle in the simulation has been assigned to rotation of joystick handle, while vertical and sideways motion has been assigned to the two linear axes.

As the joystick is moved to maneuver the virtual biopsy needle on screen, a force-feedback signal is sent to the joystick if the needle goes outside the cone. The direction and magnitude of the force felt by the user depends on how far the needle is

off sideways and vertically on the screen. For example, in Figure 4.8, horizontal offset Δx and vertical offset Δy are both positive, hence the force will be along F1.
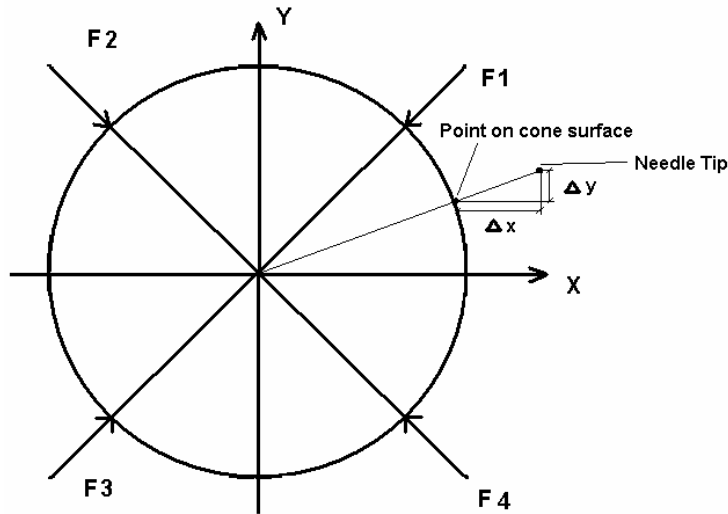

Figure 4.8 Direction of Applied Force

4.4 System Operation and Features

The whole simulation is designed in the way an actual biopsy procedure will be performed in ViHAB. The steps to be followed are given in detail below. Each step is accompanied by a description of what goes on in the background.

4.4.1 Identification of Target Micro-calcification

The first step is identification of the target. For this, an initial image 3D is read from a file and 3 pseudo-colored orthographic slices, along axial, frontal and sagittal sections are displayed on the screen. The surgeon can view different slices (Figure 4.8) by moving the horizontal scroll-bars provided for the purpose. As he/she scrolls through the slices, the slice numbers are also displayed.

Figure 4.9 Scrollbars for Selecting Image Slices

In this step, the surgeon is required to identify the target in all 3 slices. The target will appear as a bright red spot in each image slice. The surgeon would select the slices in which the spot appears largest.

In the background, the slice numbers are recorded as the initial co-ordinates of the center of the target micro-calcification.

4.4.2 Tracking of Target Micro-calcification

In the next step, the surgeon would press the "TRACK" button and the system takes over (Figure 4.9). In the background, a box / template is created around the co-ordinates identified in step above. With this initial template, tracking of target is performed in the manner described in section 4.2.
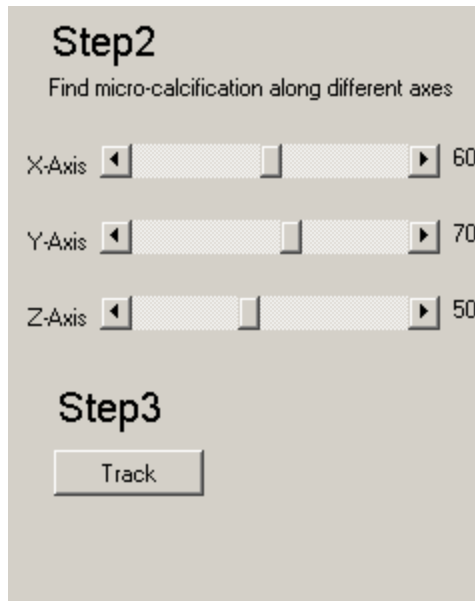
Figure 4.10 Track Button

As the calcification is automatically tracked, the user can use the joystick to maneuver the virtual needle in the scene. The co-ordinates of the tip of the needle are read directly from the hardware and sent to the guidance algorithm.

The guidance algorithm checks if the needle is following the correct path. If the needle goes outside the virtual guidance cone, it is pushed to the surface of the cone and the user can feel the push as a force being applied in the direction he should move the needle in order to be on track.

4.4.3 Practicing with the system

Apart from normal operation, a user can practice his skills with the joystick. A "PRACTICE" button is also provided. Once the button is pressed, the joystick is activated and the user can practice his needle maneuvering skills by moving a virtual needle in the scene towards a fictitious target.

4.5 Conclusion

We have presented here a proof of concept of a novel breast biopsy system called ViHAB. It is capable of keeping track of micro-calcifications in near real time and provide guidance, both visual and haptic, to a surgeon performing the biopsy procedure.

ViHAB diminishes the importance of the human factors like experience, steadiness of hands, etc which still go a long way in determining the accuracy of current breast biopsy system.

In addition to this, ViHAB has been designed to operate with a completely new non-ionizing ultrasound imaging technique being developed at UT Southwestern Medical Center at Dallas.

Given the advantages that ViHAB has over conventional biopsy procedures, we believe that it has the potential to revolutionize breast biopsy and biopsies of other accessible soft tissues.

CHAPTER 5

FUTURE WORK

The ViHAB simulator described in the chapters above has been designed to be eventually a part of an actual ViHAB system. However, some modifications will be required to for it to work with the hardware.

Currently, it reads images from files and keeps track of the target micro-calcification in those images. To make it work with a real system, the images have to be received in the form of a real-time video sequence.

The tracking algorithm is quite fast. However its speed and performance can be improved by changing the template scanning process (currently raster scan is used). Besides this, the search volume can also be minimized by the use of a predictive algorithm based on velocity and / or acceleration of the target.

Target area identification can be made more accurate by making the pseudo-coloring process to be dynamic. After the surgeon identifies the target area in one image slice, the system could display it in the other two views when the surgeon clicks on the target area in the first view. This will minimize the chances of identifying different target areas in different views.

This system is currently built on a Windows Forms application using VC++ 2005 and uses OpenGL for graphics display and DirectInput (DirectX) for interfacing

the joystick. It is suggested that for better handling, the code be changed to VC# using DirectInput for hardware interfacing and Direct3D for graphics.

When UT Southwestern researchers build the real time ultrasound scanning system, its photogrammetric calibration and interface to the tracking software developed will involve significant challenges.

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BIOGRAPHICAL INFORMATION

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