Fine Needle Aspiration Improvements

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Abstract
The following document presents our final design to modify the current fine needle aspiration (FNA) procedure used to diagnose abnormal cells in breast tissue. FNA is one of four commonly performed techniques used to remove tissue or cells during a breast biopsy. Often a sample taken using FNA is declared insufficient by the cytologist doing the analysis. This can be due to either lack of cells or the cells obtained remain in a clump, which makes analysis difficult. For this reason an attempt being made to modify the needle used to perform the FNA in hope of increasing the amount of material exhumed from the site in the breast as well as to break up the cells that are removed. An increase in material would allow the cytologist to diagnose the cells or tissue with only one FNA attempt. Currently, multiple attempts need to be made before adequate material is removed. The needle design proposed is a microdrill bit insert, which has been tested on euthanized fresh mice mammary tumors and fixed tissue samples to allow for evaluation of the technique’s success. Results were promising after six series of tests. The new technique for FNA would be effective in cases where conventional FNA fails.
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Client Statement

Dr. Elizabeth Burnside, assistant professor and chief of breast imaging, performs between one and four breast biopsies each day. Two biopsy methods often used by Dr. Burnside are core biopsy and fine needle aspiration (FNA). While core biopsy almost always obtains sufficient samples, it poses many disadvantages. One disadvantage is that it is a more invasive procedure [4]. Second, a loud noise occurs during the procedure, which can scare the patient, and third if the mass is found near the ribs there may be a risk of internal injury to the ribs due to this procedure. FNA is the least invasive method for breast biopsies and is most comfortable and affordable for the patient (given that the first sample is sufficient). However, FNA is often unsuccessful due to the difficulty of retrieving a sufficient sample through a small needle (approximately 20-gauge). When an insufficient sample is obtained, either the FNA procedure is repeated or a more invasive biopsy method, such as core biopsy or vacuum-assisted biopsy is performed. The waiting involved with repetition of the FNA procedure often adds to a patient’s already heightened anxiety. As a result of the insufficient samples associated with FNA, many physicians are straying away from this minimally invasive technique.

Dr. Burnside would like us to modify the current FNA needle (Inrad Aspiration Biopsy Needle), by developing a small needle with a unique tip or insert that would maximize the tissue obtained and increase the diagnostic yield of this very valuable procedure. About 85% of conventional FNA’s give sufficient samples. The remaining 15% do not provide a sufficient sample, usually due to a fibrotic lesion, and require another means of biopsy [11]. A modified FNA design may serve as a backup for those times when conventional FNA fails.

Background Information

Techniques:
There are approximately four needle aspiration procedures performed to remove tissue or cells. Each procedure differs in how it is performed, the equipment used, and the type and amount of tissue it removes. The four procedures are fine needle aspiration, core needle biopsy, vacuum-assisted biopsy and large core biopsy.

The fine needle aspiration (Figure 1) procedure is fast, minimally painful, and involves no incision. The surgeon uses a fine hollow needle that is sometimes attached to a syringe to extract fluid from a cyst or cells from a solid lesion. Once the needle is removed the sample is delivered to a cytologist, who immediately analyzes the sample. Often the cytologist declares the sample as insufficient (lacking a large enough number of cells in question), in which case the physician either repeats the FNA procedure or uses the core biopsy procedure to obtain a larger sample [4]. In the case that the sample is sufficient, the cytologist will declare the sample as cancer or fibrinoma (non-cancerous). Often the patient will be informed of the test results before leaving.
Core needle biopsy (Figure 2) is similar to fine needle aspiration, but the needle is larger, enabling a larger sample to be obtained. It is performed under local anesthesia and ultrasound (Appendix C) or mammography (Appendix B) is used if the lump cannot be felt. Three to six needle insertions are needed to obtain an adequate sample of tissue [15]. A loud clicking sound may be heard as the samples are being taken and the patient may feel some pressure, but should not feel pain. The procedure takes a few minutes and no stitches are required. Core needle biopsy may provide a more accurate analysis and diagnosis than fine needle aspiration because tissue is removed, rather than just cells. This procedure is not accurate in patients with very small or hard lumps [3, 15].

Vacuum-assisted biopsy (Figure 3) utilizes a vacuum-like device to remove breast tissue. Local anesthesia is used and no incision is made. Mammography is used to guide a breast probe to the lesion. Computers pinpoint the mass and suction draws out the breast tissue. The needle is inserted once to obtain multiple samples. In some cases, the entire lesion may be removed. Vacuum-assisted biopsy is safe, reliable, and valuable for patients who are not candidates for other minimally invasive biopsy techniques and those who wish to avoid surgical biopsy [9, 15].

Large core biopsy, also called advanced breast biopsy instrumentation (ABBI) shown in Figure 4, is an alternative for patients who prefer a less invasive procedure than surgery. Large core biopsy is able to remove a sizeable specimen or an entire lesion using a surgical device and mammography. It combines wire needle localization and the ability to remove a tissue specimen and allows the sample to be removed in one piece. After the region is numbed using a local anesthetic, the localizing needle is guided to the lesion. A very small incision is made and a cannula (i.e., a tube and a cutting device) is passed through the incision. Breast tissue is removed through the tube. The procedure takes 30 min. to 2 h., but it generally takes less than 1 h. [15]. A few stitches may be required to close the opening in the skin.
**FNA Biopsy Procedure:**

Fine needle aspiration may be performed under local anesthesia. After the skin of the breast is cleansed, ultrasound or mammography may be utilized to help the physician guide the needle into the breast and to the non-palpable lesion. Using a small gauge needle to avoid dilution with blood, the needle is inserted into the mass to be used as a cutting tool. Subsequent short 5 mm “in-and-out” motions are performed until material is seen coming up into the hub of the needle [12]. Once material is seen in the hub, negative pressure on the syringe is released and the needle is removed from the body to make slides. If no material is seen in the hub or syringe, the “in-and-out motion” is continued for approximately 15 to 20 strokes [12]. Then, the needle is removed from the body and an attempt is made to transfer the material from the needle to a slide. This procedure is repeated, using a clean needle, until enough material is removed from the site. There is no incision and a very small bandage is put over the site where the needle entered. However, the pathological evaluation can be incomplete because the tissue sample is very small. When used alone, about 10% of breast cancers may be missed [12]. The effectiveness of this procedure depends on the skill of the surgeon or radiologist who performs it.

Dr. Burnside has varied the aspiration technique in an attempt to obtain a larger number of cells. Three attempted variations include the use of: pressure induced by a syringe, a larger diameter needle, and a vacuum assistance device. However, none of the attempts have resulted in a significant increase in the number of cells obtained. The first change in technique, to augment the needle’s spearing of the lesion with a syringe, in theory would assist in packing cells into the hollow of the needle. Using the plunger of a syringe did not obtain a larger number of cells. The cells in the lesion are held tightly together so that when pressure from the syringe is applied, the clump of cells is simply held more tightly at the tip of the needle. The force from the syringe is not sufficient to overcome the forces holding the cells together.

The second attempt was to increase the diameter of the needle. Dr. Burnside used an 18-gauge needle instead of the 25 or 20-gauge needle to extract more cells. This change was not successful because the larger diameter of the 18-gauge needle collects an aggregated sample, which increases the difficulty of the cytological analysis. Also, if a 25 or 20-gauge needle does not collect a large enough sample due to aggregation of the cells in the breast, simply using a larger diameter needle is not likely to obtain a larger sample.

Another attempt to modify the procedure was to use a vacuum assistance device. This device is similar to the syringe, but uses more vacuum. The needle is attached to the device through tubing. The problem that occurred with this technique is that the tubing collapsed due to the high vacuum.

The collected sample is transferred from the physician to the cytologist. Slides are made by touching the end of the needle to the end of a glass slide and releasing one or two drops of the material that was collected. If too much material is released on the slide, the layer will be too thick for optimal interpretation. A thin monolayer of cells is desired. After the material is placed on the first slide, a second slide is set on top of the first allowing the drop to spread. The slides are then fixed with

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*Figure 5: Stained cytological slide, http://breastdoctor.com/breast/surgery/*
95% ethyl alcohol [12]. Slides are made until all the material in the needle is used. The fixed smears are stained and examined by a pathologist under a microscope. Figure 5 is an image of a stained cytological slide containing both normal and cancerous cells. The cancerous cells can be identified by their increased size and purple color.

**Other Needle Manufacturers**

If FNA is such a valuable procedure why haven’t more physicians or needle companies modified the aspiration technique to solve the widely found problem of insufficient samples? Intrad, the company producing the needle Dr. Burnside uses, has not developed modifications to the aspiration technique. Boston Scientific and Cook, two companies also producing aspiration needles have also not developed modifications to aspiration. Dialogue with Gregory Waniorek, District Manager from Cook, revealed his opinion that aspiration is an old-fashioned technique that has been updated by core biopsy. He feels that core biopsy is more accurate and quicker than aspiration. Consequently, Cook has not considered finding a modification to aspiration; in a sense, doing so would be “reinventing the wheel.” Although this sentiment may be shared among many companies, many physicians like Dr. Burnside are faithful to the benefits of aspiration.

**Diagnosis**

In preparation for our testing phase, we obtained some general information on what to look for when diagnosing FNA sample slides. Figures 6 and 7 below show slides of benign and malignant FNA samples, respectively. General distinguishing characteristics of malignant cells include the following:

- Atypical, monomorphic cell population
- Hypercellularity
- Enlarged nuclei of some or all of the cells
- Discontinuities in connections between cells

A general rule to make a benign diagnosis is to observe six clumps of 5-6 normal cells per clump. This is less for malignancy, as the suspicious cells bring distinctive characteristics than can be more easily diagnoses.

![Figure 6: Benign FNA cell sample](image1)

![Figure 7: Malignant FNA cell sample](image2)
**Design Constraints**

The client would like us to modify the needle, so FNA could gain more confidence by medical professionals as a more effective, minimally invasive means of obtaining cell samples over more invasive procedures such as core biopsy. For FNA to gain popularity among breast cancer specialists, a larger undamaged cell sample needs to be obtained on the first attempt.

The modifications made to FNA need to follow specific constraints requested by the client. These constraints include the needle gauge remaining between 20-25, but preferable 23. The cost of the needle and equipment should be kept at a minimum (currently the needle costs approximately $5.00). The cells should not be damaged or be spread too far from the needle tip (approximately 2 mm), due to any modifications made, during excision. The modifications made would penetrate varying density masses and the procedure should only be performed once. The procedure and equipment should remain approximately the same as what is currently used, causing minimal to no pain when performed. The equipment modifications should remain intact within the body (it should not break or fall apart while the procedure is being performed). A successful quantity (approximately six clumps with four to five cells in each clump) of material (material should be separated cells and not whole tissue) would be exhumed on the first attempt, instead of having to repeat the procedure over and over.

**Alternative Design Solutions**

*Prototype Designs*

Two modifications of the current aspiration needle that would meet the design constraints were chosen. These designs include the spring and drill bit inserts. These two designs involve inserting a specialized wire into the currently used needle. The purpose of the specialized wire is to break up the aggregated cells. First the whole needle (with the wire inside) would be inserted into the breast, as it is currently. Then the specialized wire would be extruded from the tip of the needle into the lesion and rotated to help break up the cells. Finally, the wire would be removed.

![Spring Insert](image)

**Figure 8: Spring Insert**

The spring insert could come from one of two methods. The first method would simply be the purchase of a pre-made spring that is of the dimensions that we need. A problem with this approach may be that at the micro-scale desired, the inner diameter of the spring may be too
small for cells to fit thereby detracting from the main benefit of using a spring design. A second form of production would be to flatten wire and then spiral it into a spring design or to buy flat, narrow strips of metal and spiral them into the spring design (Figure 6). This approach may provide a larger inner diameter thus allowing for a greater number of cells to be captured by the insert.

A second solution is the use of a pre-made microdrill bit (Figure 7). It is possible to purchase drill bits that will fit into a 22 or smaller gauge needle (see Tables 1 and 2 below). The only obstacle is that these drill bits are only manufactured about 25 mm in length, and therefore are much too short to be used effectively inside 60 mm biopsy needles. A solution involves either welding or soldering another wire onto the end of the drill bit to increase its length, but this is a very difficult task to perform accurately at such a miniature scale.

Both designs would be inserted into the lesion and twisted. As the insert is twisted, cells would travel up the fluting of the shaft and into the needle. These designs would be favorable in extracting the cells because they not only are able to break up abnormal cellular clusters but extract cells as well. After testing was completed using enlarged-scale prototypes, both spring and drill bit inserts were shown to be effective in dispersing and collecting the testing medium. Disadvantages are that the design may still damage the cells and may remove cells in chunks. Also, the process of forming the wire into a spiral may lead to an irregularly shaped wire that may no longer fit into the needle. In the case of the flattened and twisted wire, the scale may be small enough that the flattened wire will not be rigid enough to extract cells. Also it may defeat the purpose of this design because the inner lumen will be exceptionally small.

**Fabrication Methods for Prototypes**

Currently, we have three possible modes of production for our prototypes. The first, and most feasible, is the Mechanical Engineering Shop where either the drill bit can be made from a bored out wire or the spring insert could be formed as described above. The second form is to use laser etching to form the fluting of the drill bit. The third involves the use of a geometrically set pattern of acid-catalyzed degradation of a metal wire leaving the drill bit design desired.

**Table 1:** (Left) Common FNAB needle dimensions (for regular wall thickness).
**Table 2:** (Right) Pre-fabricated micro drill bits by industry standard number.
Final Design Solution

The final design consists of a pre-manufactured microdrill bit (Figure 6) with a 6” length and a 0.015” diameter and a standard 23 gauge needle. The pre-manufactured long drill bit eliminated the task of finding a method to lengthen a more standard 25 mm length drill bit. The drill bit, manufactured by Electrodes Inc., slides smoothly inside the needle. The drill bit is housed inside the hollow of the needle. During a biopsy procedure, the needle is inserted into the tissue with the drill bit retracted. After the needle is in place, the drill bit is simultaneously twisted and inserted into the tissue. The drill bit is also twisted as it is pulled back into the needle. Finally, the needle is removed from the tissue and the sample is collected from the drill bit. The twisting motion was expected to pull cells up the fluting of the drill bit, which was theorized to collect a larger sample than the original FNA technique. One advantage of the drill bit design is that it not only extracts cells, but also breaks up abnormal cellular clusters. Disadvantages are that the design may damage the cells and may still remove chunks of cells. Also, removal of the sample from the drill bit may be more meticulous for the cytologist than from the needle alone.

Materials:
Options found for currently produced microdrill bits were stainless steel, titanium nickel (TiNi), and a cobalt alloy. Despite the many options, the use of the same material that is used in the needle itself would be ideal in order to avoid a galvanic reaction between two different metals in close contact, which would have the possibility of altering the chemical and physical properties of the needle and insert.

Testing:

Fixed Tissues
Two series of tests were carried out. The first was performed to get a general idea of the procedure, while the second was performed to determine the effectiveness of the technique.
first test was performed on November 2, 2002 in the Anatomy Lab in Noland Hall. Fixed cat lymph, fat, and mammary tissues (Figures 7) were used for testing. The test entailed performing FNA with the current and modified techniques on each of the tissue samples. Two samples were taken of each tissue using both techniques for a total of 12 samples. All samples were saved on microscope slides for comparison. For more detailed information on the procedure used see appendix D.

![Figure 11: Images of fixed cat lymph, fat and mammary tissue used during testing](image)

The current technique’s results varied from no sample to a clump of tissue. These two extremes are not desirable. The modified technique required a drop of saline to remove the sample from the drill bit, while samples from the current technique were removed without saline. Because of the saline, the drill bit technique appeared to have less material than the current technique. After microscopic analysis, it was determined that cells were present even if they were not seen by the naked eye. The main difference between the two techniques was that the current technique resulted in either a mass of cells or a minimal quantity of cells (Figure 8) depending on the tissue sample, whereas the drill bit sample contained many dispersed cells (Figure 9) which was not dependent on the tissue sample. Pictures from the first test have questionable accuracy since the slides remained exposed for approximately a week before microscopic analysis. Because the first test was performed for a better understanding of the procedure, we were able to make necessary changes due to experimental errors during the second round of tests.

The second round of testing was performed on December 6, 2002 in the Medical Sciences Center. The same procedure was performed as in the first tests, except microscopic pictures were taken immediately after the sample was obtained, and saline was used during both techniques to aid in the removal of the sample. The comparison of samples from current and modified techniques was similar that of the first test.

![Figure 12: Microscopic images of fixed cat lymph, fat and mammary tissue samples obtained using the current technique during the December 6, 2002 test date](image)
Analysis of the pictures taken after testing, leads to a hypothesis that the modified technique obtains a larger quantity of dispersed cells than the original technique. Additional testing followed by a comprehensive analysis should be performed to verify the initial assumption. Initial findings concur with Dr. Burnside’s objective.

*Freshly Euthanized Tissues*

Two researchers on campus provided us with mice having mammary tumors, both cystic and fibrotic in nature. Eric Sandgren, PhD, provided us with three mice, all predisposed to cystic mammary tumors. Amy Moser, PhD, also provided us with three mice, these being predisposed to tumors of fibrotic character. Four trials were performed.

Testing techniques proceeded in the following format for all four trials. The conventional technique was performed first, using a standard 23 gauge needle with introducer. Following this, the needle was reinserted with introducer, the introducer was removed, and then drill bit was then inserted into the needle. The drill bit was extended approximately 0.5cm past the tip of the needle and rotated clockwise approximately ten times. Removal was done in two different ways: 1) drill bit pulled completely out through the needle and 2) drill bit retracted back into needle so tip was just inside the shaft, and the entire needle was then removed from the site.

Extracted tissue was then prepared for viewing by placing on slides. In the case of the conventional technique, the contents of the needle were tapped onto the slide pushed out using the introducer. When the drill bit was used, tissue was placed on slides in two ways. If the drill bit was pulled out completely (1 above), the drill was rolled across the slide to remove the sample. If the drill bit was kept in the needle during removal (2 above), it was pushed back out of the needle (avoiding pulling the drill bit through the entire length of the needle) and rolled across the slide to remove the sample. In the first three trials saline was used to aid in removal of the sample from the fluting of the drill bit. In the fourth trial, the above procedure was followed and no saline was used.

Slides were prepared using the air-dry method. In the first three trials, slides were allowed to air-dry for a minimum of 24 hours before being stained. In the fourth trial, slides were stained
immediately upon drying. The stain used was Diff-Quik, a set of stains typically used for FNA slides. Staining was performed by Dan Kurtycz, MD, or his staff. Cover slips were applied after the stain was dry using preparatory glue called Permount.

Results of the mice trials, while mirroring those of the fixed-tissue trials, were not as conclusive as hoped. Slides analyzed from the first three trials yielded little information. This was due to several factors. First was the use of saline, which caused crystals to form and made diagnosing and interpreting the slides difficult. Second was a lack of adequate samples obtained due to poor technique. Several of the slides contained very few or no cells. Because of this, no conclusions were made based on the slides obtained from the first three trials.

The fourth trial yielded more clear results. This was due to several factors. In this trial, Dr. Kurtycz performed the procedure himself. His expertise in the technique allowed for an adequate tissue sample, and his skill in the preparation of the slides allowed for higher quality samples for interpretation. When the slides from this fourth trial were observed under a 20-40x magnification, Dr. Kurtycz was able to draw more conclusive results from a comparison between the old and new techniques.

Based largely on the fourth trial, Dr. Kurtycz was optimistic for our new technique for various reasons. First, while he noted that although there was not a drastic increase in the number of cells gained from the new technique versus the old technique, there were noticeable volumetric and cellular differences. Namely, while the old technique seemed to extract a larger volume of fluid and cells, the new technique provided a more cellularized sample, which increases the ease of diagnosis, he said. Secondly, he mentioned that the old technique is often less effective on more dense, fibrotic tumors, but the new technique would likely be able to disperse these dense cell masses for extraction. Third, an alternate use for the new technique was discovered in that it could serve as a tool for minimally invasive removal of fibroblasts from muscle tissue. This use originated from an error in the fourth trial, where Dr. Kurtycz snagged and extracted some muscle tissue from the mouse.

Figure 14 shows results from four successful samples obtained during the fourth trial. 1a, a sample taken using the conventional technique, shows a sample with lower cellularity than the two 1b pictures, whose samples were taken using the drill bit. The increased cellularity and better dispersion in 1b pictures show the abnormal cells much more clearly, and according to Dr. Kurtycz, would be sufficient to make a malignant diagnosis. 2a was also taken using the original technique, and further shows the problem of cell clumping that makes the diagnosis difficult or impossible. Again, 1b shows dispersion of the cells from the drill bit’s ability to break up these cell clumps to allow for a diagnosis.
Figure 14: Slides from two trials. 1a and 2a show samples using old technique, and 1b shows sample using drill bit insert.

Following discussion with Dr. Kurtycz and Dr. Burnside, the future of our improved technique seems it may be useful as a backup technique to the conventional FNA procedure. Additionally, it may also serve as a useful tool in other settings requiring the use of minimally invasive biopsies (such as muscle extraction mentioned previously and biopsies of other organs such as the liver).

Future Plans

Thus far, animal testing with the drill bit has revealed that the new device often extracts sufficient samples. More trials should be conducted in order to obtain statistical significance. This semester Dr. Kurtycz’s cytological expertise has allowed for significant progress with qualitative cytological evaluation. A future goal would be to quantify a “good” or “sufficient” sample and then conduct tests with numerical results. Doing so would involve an even more standardized method for slide preparation, a method to quantify cells in the microscope’s large field of view, and threshold values for determining sample sufficiency.

Recalling that the drill bit design has great potential as a backup for cases in which conventional FNA fails, focusing testing on such conditions would be helpful. Since the 15% insufficiency rate of FNA’s is usually attributed to fibrotic tissue [11], Dr. Sandgren suggested testing on a model with more fibrosis, such as an animal with extreme pancreatic fibrosis [14].
Future testing will eventually need to move beyond non-human, non-living tissue into clinical trials. This will require Board approval at the given hospital as well as approval for testing by the Federal Drug Administration.

Although the design of our prototype may not have ethical implications, the testing phase does. In early the stages, testing on foods and fixed tissue was acceptable, but more advanced trials required animal testing. All animal trials were conducted immediately after euthanasia, skirting the need to receive RARC approval (for our specific test); however, all testing was conducted under principal investigators with RARC approved protocols. RARC protocol approval assures compliance to all laws, regulations, and rules governing the care and use of laboratory animals. RARC regulates experimental conditions such as animal housing, maximum allowable tumor size, and method of euthanasia. If future plans were to involve live animal testing, RARC approval must be obtained. Dr. Sandgren, principal investigator, reminded students (independently of RARC) of the importance of at least acknowledging that animals were once living creatures, and should not be thought of simply as objects on which one can conduct tests [14]. Human testing would entail finding individuals on which to test, gaining their consent, and considering necessary precautions for handling of human tissue. In both animal and human testing that involves cancerous cells, there may be a possibility that seeding of the tumor to other sites may occur.

Since the device would only have a single use, there is less concern with how the material will react with the body but there is still need to test how long the product’s shelf life may be or probability that a portion of the drill bit would break off inside the patient. These issues have not been addressed as of yet since we were primarily concerned with prototype testing. Human trials will require Board approval at the given hospital and if successful, later approval for testing by the Food and Drug Administration.

Conclusion

Fine needle aspiration (FNA) is a minimally invasive technique that extracts cells from a lesion in the breast to determine if the lesion is cancerous. The client Dr. Elizabeth Burnside prefers using FNA to other biopsy methods, but finds that it often leads to samples lacking in a sufficient number of questionable cells. Dr. Burnside seeks a modification to the current FNA needle that will extract a sufficient sample on the first attempt. To obtain a sufficient sample, the design must loosen the cells before packing them into the needle. The proposed design is a drill bit insert design, which consists of pre-manufactured drill bit that is housed in a standard FNA needle. Testing of this design was performed on fixed cat tissues and freshly euthanized mice with cystic and fibrotic mammary tumors. Through testing, it was determined that the new technique provides more cellularized samples. In addition the proposed technique is more effective than the conventional FNA for more dense, fibrotic tumors because of its ability to disperse these dense cell masses for extraction. Therefore another application for the new technique may be as a tool for minimally invasive removal of fibroblasts from muscle tissue. The proposed technique may also serve as a useful tool in other settings requiring the use of minimally invasive biopsies. Overall this new technique for FNA would be effective in cases where conventional FNA fails.
Title: Improvement for fine needle aspiration (FNA) used during breast cell biopsies.

Function:
A 20-25-gauge aspiration needle is inserted into the breast to extract questionable cells found during ultrasound mammography. Using ultrasound, the needle is positioned at the site where it is used to break up and disperse the cells. Once the cells are loosened, there is a small chance that the hollow of the needle will collect the cells. The client, in the hopes that more cells would be removed for analysis, suggested modifications to the needle.

Client requirements:
The client would like us to modify the needle, so FNA could gain more confidence by medical professionals as a more effect, minimally invasive means of obtaining cells samples over more invasive procedures such as core biopsy. For FNA to gain popularity among breast cancer specialists, a larger undamaged cell sample needs to be obtained on the first attempt.

Design requirements:
Physical and Operational Characteristics:
Performance requirements:
Device will be used 1 time.
Obtain a sample of approximately 6 clumps of cells, 4 or 5 cells each.
Constrained to standard 20-25-gauge needle, client prefers 23-gauge.
Any added material to the needle should not extend 1 cm past the tip of the needle.
Needle should remain steady during the procedure.
Large clumps of cells should be avoided due to problems with analysis.
Minimal noise during procedure as to not startle the patient.
Remain minimally invasive.
Should not cause additional pain.
Cells cannot be damaged during the procedure.

Safety:
No part of the device should remain in the body after the procedure.
When dislodging cells, device shouldn’t spread cells a large distance from the needle.
**Accuracy and Reliability:**
The device should obtain cells from varying density masses.

**Life in Service:**
One use.

**Shelf Life:**
Should be the same as current needle shelf life.

**Operating Environment:**
Biological components (blood, fat, tissue).
Body temperature.
Operator should be a medical professional able to judge distance using an ultrasound machine.
If electric component added to the device, shock could be a hazard.

**Ergonomics:**
Similar to normal needle.
If device requires manual rotation, operator movement should be minimal.

**Size:**
Needle gauge should be 20 to 25.
Any material added to the device needs to fit within the hollow of the needle.

**Weight:**
Needle should not increase more than three times its original weight.

**Materials:**
Hypoallergenic
Noncorrosive
Not brittle
Semi-hard

**Aesthetics, Appearance, and Finish:**
Outside of needle should remain smooth

**Production Characteristics**

**Quantity:**
Client currently only wants one device for testing. If device were successful, a medical company would need to mass-produce the product.

**Target Product Cost:**
Less than $5.00 per needle.
Miscellaneous

Standards and Specifications:
Must be FDA approved for human use

Customer:
Affordable
User-friendly
Effective – short time required performing aspiration or cell sample (i.e. – less than 20 minutes)

Patient-related concerns:
Does not cause procedure to be more painful or more difficult

Competition:
No known variations to the standard 20+ gauge needle for FNA use with breasts
May be variation in technique that is more efficient
Appendix B - Mammography

Mammography (Figure 13) is a special type of x-ray imaging used to create detailed images of the breast. Mammography uses low dose x-ray; high contrast, high-resolution film; and an x-ray system designed specifically for imaging the breasts. Successful treatment of breast cancer depends on early diagnosis. Mammography plays a major role in early detection of breast cancers. The US Food and Drug Administration reports that mammography can find 85 to 90 percent of breast cancers in women over 50 and can discover a lump up to two years before it can be felt [10]. The benefits of mammography far outweigh the risks and inconvenience.

Mammography can show changes in the breast well before a woman or her physician can feel them. Once a lump is discovered, mammography can be invaluable in evaluating the lump to determine if it is cancerous. If a breast abnormality is found or confirmed with mammography, additional breast imaging tests such as ultrasound (sonography) or a breast biopsy may be performed. Many times, mammography or ultrasound is used to help the radiologist or surgeon guide the needle to the correct area in the breast during biopsy.

There are two types of mammography exams, screening and diagnostic. Screening mammography is an x-ray examination of the breasts in a woman who is asymptomatic (has no complaints or symptoms of breast cancer). The goal of screening mammography is to detect cancer when it is still too small to be felt by a woman or her physician. Early detection of small breast cancers by screening mammography greatly improves a woman's chances for successful treatment. Screening mammography is recommended each year for women once they reach 40 years of age. In some instances, physicians may recommend beginning screening mammography before age 40 (i.e. if the woman has a strong family history of breast cancer).

Diagnostic mammography is an x-ray examination of the breast in a woman who either has a breast complaint (for example, a breast lump or nipple discharge is found during self-exam) or has had an abnormality found during screening mammography. Diagnostic mammography is more involved and time-consuming than screening mammography and is used to determine exact size and location of breast abnormalities and to image the surrounding tissue and lymph nodes. Typically, several additional views of the breast are imaged and interpreted during diagnostic mammography. Thus, diagnostic mammography is more expensive than screening mammography. Women with breast implants or a personal history of breast cancer will usually require the additional views used in diagnostic mammography [10].
Appendix C - Ultrasound

Breast ultrasound (Figure 14), also known as sonography or ultrasonography, is frequently used to evaluate breast abnormalities that are found with screening or diagnostic mammography or during a physician performed clinical breast exam [4]. Ultrasound allows significant freedom in obtaining images of the breast from almost any orientation. Ultrasound is excellent at imaging cysts (round, fluid-filled, pockets inside the breast). Additionally, ultrasound can often quickly determine if a suspicious area is in fact a cyst (always non-cancerous) or an increased density of solid tissue (dense mass), which may require a biopsy to determine if it is malignant (cancerous). [10]

If a patient’s ultrasound and mammogram results are both negative (no evidence of cancer is seen), but the physician is still concerned about the thickening or mass, then he/she may proceed further with a fine needle aspiration biopsy (FNA) of the area.

Ultrasound vs. Mammography:

Ultrasound has excellent contrast resolution. This means, for example, that an area of fluid (cyst) and an area of normal breast tissue are easy to differentiate on an ultrasound image. However, ultrasound does not have good spatial resolution like mammography, and therefore cannot provide as much detail as a mammogram image. Ultrasound is also unable to image microcalcifications, tiny calcium deposits that are often the first indication of breast cancer. Mammography, on the other hand, is excellent at imaging calcifications. Ultrasound may be able to detect macrocalcifications (larger calcium deposits) in some cases.

Though most true breast lumps will be found by mammography or ultrasound, some abnormalities escape detection on both imaging tests. For example, a lump may be able to be felt but does not appear on mammography or ultrasound images. If this is the case, then fine needle aspiration biopsy (FNA) is often performed. Less than 30% of all breast biopsies are cancerous [10]. In cases where the abnormality is not apparent on mammogram or ultrasound, the chances of cancer are significantly less.
Appendix D – Testing Procedure

Fixed Tissue
November 2, 2002

General Procedure
1) Prepare samples (lymph, fat, mammary)
2) Gather supplies (needles, drill bits, gloves, saline, slides)
3) Label slides

Current Technique Procedure
1) Insert needle into sample
2) Perform subsequent short .5cm “in-and-out” motions
3) Remove the needle from the sample
4) Tap needle on slide (approximately 5 times) to remove cells

Modified Technique Procedure
1) Place 1 drop of saline on slides
2) Place drill bit down hollow of the needle
3) Align the drill bit flush with the tip of the needle
4) One person steadies the sample, while second person performs insertion
5) Insert needle and drill bit into sample approximately 1cm
6) Turn drill bit (approximately .5cm) as it is extended out the tip of the needle
7) Twist drill bit, at full .5cm extension, for approximately 5 twists
8) Continue to twist drill bit as you retract it back into the needle
9) Remove the needle and drill bit combination from the sample
10) Extend the drill bit out of the tip of the needle into the saline on the slide
11) Twist drill bit (approximately 5 times) in saline to release cells
12) Dispose of needle and drill bit

December 6, 2002
Changes that were made to the above procedure during the December 6, 2002 tests include:
1) Adding saline to all slides prior to cell collection
2) Examining all results with a microscope and taking pictures of the results
**Euthanized Fresh Tissue**

Testing Subjects: Three mice, all predisposed to cystic mammary tumors and three mice predisposed to fibrotic tumors of character.

**General Procedure**
1) Gather supplies (needles, drill bits, gloves, saline, slides)
2) Label slides
3) Alternate current technique trial with new technique trial as far as which is used first with each tumor.

**Current Technique Procedure**
Same as with fixed tissue

**Modified Technique Procedure**
1) Insert standard 23 gauge needle with introducer into tumor
2) Reinsert needle with introducer
3) Remove introducer
4) Insert drill bit into needle
5) Extend drill bit approximately 0.5cm past the tip of the needle
6) Rotate drill bit clockwise approximately ten times
7) Remove device and prepare slide by either:
   a) pulling drill bit completely out through the needle
      i) roll drill bit across slide to remove sample*
   b) retract drill bit back into needle so tip was just inside the shaft and remove entire needle
      i) push drill bit back out end of needle
      ii) roll drill bit across slide to remove sample*

*In the first three trials saline was used to aid in the removal of sample from the drill

**Slide Preparation Procedure**
1) Air dry for at least 24 hours (this was skipped for the fourth trial)
2) Stain with Diff-Quik
3) Apply coverslip after stain is dry using Permount
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