Digital documentation of the physical examination: moving the clinical breast exam to the electronic medical record

Cary S. Kaufman, M.D. a,b,*, Leslie Jacobson, M.S. b, Barbara A. Bachman, M.D. b, Lauren B. Kaufman, M.D. b

a Department of Surgery, University of Washington, 2940 Squalicum Pkwy, Bellingham, WA 98225, USA
b Bellingham Breast Center, Bellingham, WA, USA

Manuscript received April 7, 2006; revised manuscript June 16, 2006

Presented at the 7th Annual Meeting of the American Society of Breast Surgeons, Baltimore, Maryland, April 5–9, 2006

Abstract

Background: Documentation of the clinical breast examination (CBE) has consisted of simple hand-drawings and stick figures without a common lexicon. There is a need for a device that can accurately depict the CBE in digital format while being objective, reproducible over time, and useable in the electronic medical record. This new device is called palpation imaging (PI).

Methods: We examined 110 patients with a complaint of a breast mass using PI. This laptop-sized device creates a real-time digital display of the palpable area in both video and still formats. The size, hardness, shape, homogeneity, and mass location may be extracted from the image.

Results: Of those with a true mass, PI identified the mass in 94% while physical examination identified 86%. The positive predictive value (PPV) for breast cancer using PI was 94% and 78% for physical examination. A survey of primary care physicians revealed the inclusion of the PI record in a consultation note implied competence, experience, and skill by the surgeon.

Conclusions: PI documented the CBE in a timely, efficient, and accurate manner. A reproducible record allows objective review by multiple examiners at varied times. Continued work will optimize examination methods. © 2006 Excerpta Medica Inc. All rights reserved.

Keywords: Palpation imaging; Clinical breast exam; Breast imaging; Breast lump; Electronic medical record; Mammography; Ultrasound; Breast mass

While the last 20 years have seen major improvements in breast imaging [1–8], the documentation of the clinical breast examination (CBE) has remained unchanged since the Halsted mastectomy 100 years ago [9]. Surgeons record a verbal description of their palpable findings along with a handwritten drawing. The verbal description suffers from the spectrum of descriptive words without standardized definitions. Terms such as “fibrous,” “thickened,” “dense,” and “glandular” may all describe the identical breast texture and are user dependent. Likewise, a hand drawing or stick figure of a breast mass may be interpreted differently by different observers. These subjective drawings may not communicate the same examination to a second examiner or even to the same examiner at a later date. Drawings are not standard-
method may aid in the documentation of the CBE and augment the clinical record making it more versatile, reproducible, consistent, and electronically useable. This can be used for chart documentation, communication with other physicians, education for patients, and as a medical record for insurers or medicolegal purposes.

Methods

Between October 2003 and October 2005, 110 patients referred to our breast clinic with a chief complaint of a breast mass were examined. In addition to CBE, ultrasound, and mammograms, each patient underwent PI. Some young patients did not have mammography.

After PI examination, each record was segregated into one of two groups based on the PI findings alone: those with the findings of a dominant mass (eg, cyst, benign or malignant tumor) and those without findings of a dominant mass (e.g., fibrocystic change or other normal breast tissue). Those with a dominant mass were further separated into those highly suspicious for cancer and those with palpable masses. Final histologic and/or follow-up data (minimum 6 months) was correlated with preoperative PI. Statistical analysis used the chi-square calculator from Georgetown University [12].

Description of imaging device

The cornerstone of this report is the development of an imaging device that translates palpation findings into a visual record [13]. To understand this device, it is necessary to deconstruct the CBE of a palpable mass. Upon finding a mass, the surgeon notes the location of the mass within the breast. Mass characteristics of size (in at least 2 dimensions), hardness, shape, and homogeneity are noted. PI re-creates the components of the CBE of a mass.

The palpation imager consists of a notebook computer-sized device attached to a broad-based transducer. After CBE targets a lesion, the transducer is passed over the palpable lesion. The transducer has almost 200 minute sensors able to record the pressure and location data. As the transducer scans, a real-time display of the palpable area is digitally recorded (Fig. 1). The transducer sensor data is converted to a color image in both 2- and 3-dimensional formats. Peak height of the image refers to increased firmness, while low height refers to less firm or soft tissues (Fig. 2). Images are reviewed to demonstrate the characteristics of size, hardness, shape, homogeneity, and location. The examination video and still-frame images are available for printed reports or single images may be incorporated into a consultation letter.

This palpation image can be translated into the components of the physical examination: size, hardness, shape, and homogeneity. The location within the breast is entered by the examiner (Fig. 3). The size of the lesion is demonstrated by the footprint seen on the image (Fig. 4). The hardness of a lesion is described by the absolute height of the peak.
pressure, as well as comparison of peak height to surrounding breast tissue height (surrounding breast firmness). The shape of the palpable findings may be demonstrated by a line drawn at an isobaric level surrounding the mass on a 2-dimensional image, seen as a black line in the examination result screen (Fig. 5). Homogeneity of the palpable mass is identified as the shape of the peaks within the image. Single smooth peaks are commonly seen in cysts and fibroadenomas, while images with multiple peaks within the mass suggest lobulations and nonhomogeneous masses such as cancers. PI reports describe all the building blocks of the CBE. This was not a blinded study but meant to identify any palpable abnormality and try to document its presence with PI. At no time was PI considered a substitute for biopsy, and biopsy should always be considered as the definitive test for the presence of breast cancer.

Physician survey

To assess the communication value of PI, sample breast consultations were sent out to a study set of 15 primary care referral physicians. Each of the referring physicians was provided breast surgical consultations on 3 different sample patients. All 3 had a chief complaint of a breast mass, each with a different cause; 1 had a palpable cancer, 1 had a benign palpable mass, and the third had an area of fibrocystic change.

Each sample patient was “examined” by 3 surgeons who provided different forms of consultations. Surgeon “A” wrote the consultation by longhand and included a handwritten picture of the palpable findings. Surgeon “B” typed the consultation in letter format without any drawings of the physical examination. Surgeon “C” also typed the consultation in letter format as surgeon “B,” but included a printed digital image and report of the physical examination using PI.

Each referral physician received 9 consultations in total, 3 on each of 3 patients. We asked each referral physician to rank the breast surgeons on each patient. Three questions were asked for each patient: (1) please rank these 3 breast surgeons in regards to their competence; (2) please rank these 3 breast surgeons in regards to their experience and innovation in the field of breast surgery; and (3) please rank these 3 breast surgeons in regards to their skill as a surgeon. Referring physicians were asked to avoid ties and to make choices as best as possible based on the submitted data.

Results

Table 1 of final diagnoses reveals the typical patient distribution seen in a breast clinic, including fibroadenomas, cancers, fibrocystic change, and cysts. Ninety-five of 110 patients were found to have lesions that might present as a mass as documented by pathology or other confirmatory tests. We included the patient with gynecomastia with this group. Although some of these lesions may be too small to detect, we considered these patients the potential pool of those with a dominant mass.

Each palpable finding on CBE was recorded as well as the PI results. After an initial learning curve, it was possible to recreate the digital image of the palpable findings. Because the surgeon obtained the digital image, an immediate
feedback process occurs while imaging. The surgeon can determine whether the image is a true representation of the palpable findings. During the examination, the surgeon may also examine the surrounding area with PI to confirm the absence of other palpable findings.

Identifying dominant masses

PI was used to separate patients into 2 groups: those identified with a mass and those without a mass. PI identified a dominant mass in 89/95 patients (positive predictive value [PPV] 94%). Physical examination identified 82/95 patients (PPV 86%). The sensitivity and specificity of identifying a dominant mass with PI were 88% and 88%, while the values were 81% and 81% for physical examination.

In addition, we examined clinically normal breast tissue without any mass to validate our assessment. Both methods were accurate in determining breast tissue without any mass. The negative predictive value of PI and for physical examination was 93% for both methods.

We tried to correlate the consistency of PI and CBE. For each category of PI, we noted the frequency of finding palpable masses. There was a direct correlation between the likelihood of palpating a mass on CBE and the PI firmness category, as noted in Fig. 6.

Identifying breast cancer as a mass

PI separated breast lesions into 4 categories: (1) those without a mass; (2) those with a soft mass; (3) those with a firm mass; and (4) those with a hard mass. Breast cancers were usually firm or hard with either a central single or multiple peaked image on PI. Of the 36 breast cancers examined, the PPV for PI was 94% and 78% for physical examination (Table 2). There were six cancers identified by PI that were not identified by physical examination (false negative rates of 6% and 22%, respectively).

Fibroadenoma, cyst, lipoma, seroma

PI of fibroadenomas, cysts and other benign oval nodules typically demonstrated a single smooth peak with a firm central mass. Of the 57 lesions in this group, we closely examined all fibroadenomas and cysts (n = 47) for evidence of these PI findings. All but 4 lesions (91%) demonstrated this classic PI pattern. The 4 lesions not visualized on PI included 2 cyst clusters and 2 small fibroadenomas.

PI may estimate size of the examined mass (Fig. 4). To assess the size correlation, we looked at the same group of fibroadenomas and cysts. Only 41 of 47 of these patients had an ultrasound measurement documented. We compared the length and width measurements as seen by palpation imaging with the ultrasound measurements. We classified the correlation as good when measurements on both PI and ultrasound were within 3 mm of each other. Those between 3 and 6 mm were considered fair, and those with a greater than 6-mm difference between the 2 measurements were considered poorly correlated. We found 32% of these patients had good correlation between PI and ultrasound measurements, while 46% varied by more than 6 mm between the 2 examinations. There was no difference between the ability of physical examination and PI to identify benign breast lesions (Table 3).

Primary care responses

Of the 15 clinicians surveyed, responses were received from 11. One clinician refused to respond due to concerns about commercial bias. Three others did not return their evaluation. Most clinicians favored the use of the typed consultation along with the PI report of surgeon “C.” They regarded this surgeon to have better “communication skills” and more “experience/innovation.” Of the responses received, 81% said surgeon “C” was the most experienced and 68% said he was the best communicator. Over 85% rated surgeon “A” as least experienced with the least communication skills. This was despite the fact that the written scripts were similar, essential findings were identical, and there was a neatly hand-drawn picture of the palpable find-
ings. The majority thought “surgical skill” could not be assessed via the consultation notes, although 25% said surgeon “C” was most skilled.

This may imply that a visual depiction of the palpable findings as in surgeon “A” is less important than the ease of communication. The hand-drawn consultation letter may have been harder to read than the typed consultation. Similarly, the typed consultation alone with the clear picture of PI may have been easiest to see in a hurried primary care practice.

Comments

As a documentation device, PI has several benefits over current technology. Since the device is calibrated and standardized, the PI recordings will be consistent among several examiners. Serial examinations of the identical mass over time allows for the accurate documentation of change. PI accumulates a continuous video recording of the targeted mass and then identifies a single image that best represents the physical findings. This image can be uploaded into a Word file for a consultation letter or into an electronic medical record (EMR). The electronic version of the physical examination merges with the interest in the EMR. The clinical record is in the process of change [14]. Primary care, internal medicine, cardiology, and many specialties have converted to use of the EMR. Many practices are converting to an electronic format for many reasons, including ease of creation, ease of transmission and exchange/circulation, ease of storage, and cost.

It is typical for surgeons to have their initial consultation distributed as a letter to their referring physicians. This consultation letter typically does not include any hand drawings or figures of breast masses. In our physician survey, we note that the inclusion of a hand-drawn picture of the physical examination was not valued by the referring physicians. When the PI printed report was included, the referring physicians associated surgical experience and increased communication skills with the combined report. The addition of a digital image of the palpable findings may add a new dimension to the consultation of a breast surgeon.

Since the PI device acts as an independent observer of the CBE, the PI report may be valuable if the patient’s chart is reviewed by an outside party. For insurers who wish to confirm the CBE was performed, the PI report adequately documents that examination. For medicolegal purposes, the PI report can validate a clinician’s statement as to the findings on CBE. The PI examination can provide independent confirmation of the surgeon’s examination.

The palpation image provides the opportunity for clinical review at a later time. This is useful if the referring ultrasound or mammogram are not available. When the films return, comparison to the PI physical examination can occur. Another use for PI is to communicate the physical findings to the patient. The image of the palpable findings is readily understandable by interested patients. Although the CBE has not been demonstrated to impact survival from breast cancer [9], the lack of a common documentation method and lexicon may contribute to the inability to document CBE value.

The objective documentation of PI may help some medical clinics that may have several doctors seeing the same group of patients. Using PI, a patient with a palpable finding may be followed more objectively by a series of doctors. Poor communication may occur when one surgeon’s hand drawings of a breast mass is read by another surgeon. Radiologists commonly communicate this way using serial image documentation. This may also aid doctors who are providing vacation coverage and other part-time clinicians.

PI requires training and skill to obtain accurate images. This is similar to correct positioning and exposure in mammography or proper gain and focal zone in ultrasonography. The proper examining technique and applied pressure is required for optimal PI. Ultrasound has similar requirements to obtain an optimal image. Surgeons skilled at ultrasound examination of the breast are likely to have little difficulty learning the technique of PI.

The basic examination technique is similar to the movements associated with breast ultrasound examination. Mechanical adjustments of the device are few. Calibration is required regularly but not daily. Since the device is the size of a laptop computer, it easily moves from one examination room to another. The creation of an initial image takes just minutes after the examiner identifies a lesion. Several images are obtained to confirm an accurate depiction has been obtained. Automatic storing of images occurs after the demographic information has been entered into the system. Recalling a previous examination is similar to opening a stored computer file.

The PI device is relatively inexpensive in relation to all other forms of imaging, being less costly than an entry-level portable ultrasound device. With the PI device comes the ability to document lesions, the ability to create and print a completed report of the CBE, and image storage for use later or inclusion in the EMR. Although reimbursement is not currently available for the use of this device, it adds value to the practice. This is similar to the cost of computerizing one’s office or converting to an EMR that is not reimbursed but adds value to the medical practice. Larger studies examining the impact of standardized CBE will hopefully answer the question of clinical value.

There are some disadvantages of the PI device, including no insurance reimbursement for this examination. Like other new technologies, reimbursement may follow at a
later date. Because PI is new, it will be necessary for other centers to validate and enhance the findings in this report.

We noted some instances of PI examinations were consistent with the eventual pathologic findings. Very large cancers over 4 cm in size cannot be easily examined since there is no normal tissue to compare within the 4-cm probe area. The firmness of a large cancer will be viewed as an overall elevation of the baseline, since the entire surface under the PI transducer has similar hardness.

The other end of the spectrum is also difficult to image. Very small cancers that are not palpable on CBE may or may not be demonstrated on PI. A lower threshold of PI imaging capability exists that is dependent on many factors. These include the absolute hardness of the small tumor, the size of the breast, and the depth of location of the tumor. Small firm tumors that are closer to the skin surface in smaller breasts are easier to image even when not palpable on CBE.

A third group of breast cancers that may be difficult to identify are tumors with soft consistency. Colloid carcinomas or other low grade tumors that have little growth intensity may be difficult to visualize. These tumors, which are primarily found in older patients, may have similar firmness to surrounding breast tissue.

There are several clinical components that cannot be translated into a mechanical device. The palpation imaging device must be placed over the mass in question. This is similar to limitations of breast ultrasound. When an ultrasound sensor is placed on a surgical scar, the hypoechoic shadowing area will appear suspicious for cancer, even though it is typical surgical scar. The examiner must notify the ultrasonographer that the transducer is overlying the surgical scar. Likewise, PI will report the firmness of any lesion examined without the ability to know what portion of the body is being examined.

Similarly, placing the PI device directly on an exposed rib will create an image of an elongated hard mass. Although this may be an accurate representation of a rib, the device will document the palpable findings only. The examiner is responsible to identify the location that the probe is examining.

Additionally, exophytic skin lesions such as moles or the true nipple will give a palpable image of a mass. The examiner must note the presence of skin lesions or location of the nipple as is commonly included during mammography imaging.

This imaging device is intended to be used for documentation of the CBE and improved communication. With further research and experience, it may be possible to use the PI device to aid in the clinical grouping of palpable breast disorders. Characteristics of benign and malignant masses may be teased out of the data obtained from multiple examinations and may aid the breast surgeon in the future.

Conclusions

We describe the use of a unique tabletop PI device that documents palpable breast masses with high sensitivity and specificity. Patients with truly palpable masses (cancers, benign tumors, and firm cysts) were found to have increased firmness (decreased elasticity), while those with nodular breast tissue (fibrocystic change) had less firmness. The use of PI allowed initial separation between benign and suspicious truly palpable masses. A reproducible record of the breast physical examination is created that allows objective review by multiple examiners at varied times. Further work is necessary to optimize examination methods, improve real-time software interpretation, and define the array of diagnostic capabilities.

References

Medical Tactile, Inc. Introduces First Tactile Sensing Device for Documenting Clinical Breast Exams

SureTouch(TM) System Employs Proprietary Sensing Technology to Enhance Quantify First-Line Breast Cancer Diagnostics

San Antonio Breast Cancer Symposium

LOS ANGELES, Dec. 5 /PRNewswire/ -- Medical Tactile, Inc. (MTI) -- a medical device company specializing in tactile sensing technology -- today announced the start of commercial sales of its SureTouch Visual Mapping System for electronically documenting clinical breast exam results. The system, which will be on display this week at the 28th San Antonio Breast Cancer Symposium (December 8-11), is cleared for commercial sale by the U.S. Food and Drug Administration as an adjunct device for performing and documenting clinical breast exams.

Based on the company's proprietary tactile sensing technology, the SureTouch System improves the sensitivity, specificity and objectivity of manual breast palpation exams, which are the most accessible first line of defense against breast cancer for most women.

"We are very pleased to begin commercial sales of the first-of-its-kind SureTouch System," said Steve Weiss, Medical Tactile's CEO. "We have worked hard to develop an innovative, cost-effective technology that enables healthcare practitioners to improve early breast cancer diagnostics and save lives."

The SureTouch system enhances and quantifies the operator's sense of touch during manual palpation in breast cancer screening. To use the system, the healthcare practitioner simply palpatates suspicious breast lesions with the hand-held tactile probe, which employs highly sensitive sensors clinically proven to map lesions as small as 5 mm. The portable SureTouch console creates an electronic record that provides a wealth of objective information to help recognize suspicious lesions and make informed recommendations for follow-up radiological diagnostics such as mammography and ultrasound.

The SureTouch System is the company's first commercially available tactile...
sensing device. Additional breast cancer detection products based on Medical Tactile's proprietary technology are currently in development.

"Medical Tactile is committed to improving early breast cancer detection by providing affordable, easy-to-use tactile sensing technology," Weiss added.

About MTI

Medical Tactile, Inc. (MTI) is an emerging medical device company focused on developing, manufacturing and marketing tactile sensing technology for the early detection of breast cancer. The Company's first product is the SureTouch Visual Mapping System, which is designed to improve the sensitivity, specificity and objectivity of manual palpation in breast cancer screening. The system is cleared by the FDA for commercial sale in the U.S. More information about Medical Tactile, Inc. is available at www.medicaltactile.com.

SOURCE Medical Tactile, Inc.
Background

Clinicians have long depended on their sense of touch to assess tissue abnormalities, both benign and malignant. For the evaluation of the breast, this has been formalized into the clinical breast exam (CBE), where an examiner uses his/her sense of touch to detect breast tumors. Despite the ubiquitous use of the CBE, the sense of touch is a subjective tool, leading to concerns about repeatability and interpretation.

During the last decade several objective techniques for assessing tissue hardness, or elasticity modulus, have emerged, with Ultrasound Elastography and Magnetic Resonance Elastography being the most promising. The wealth of data obtained by these techniques during the last few years has clearly demonstrated that measurements of elastic properties of tissue could be used to detect and differentiate benign and malignant breast lesions and have a potential for dramatically reducing the number of unnecessary breast biopsies. If the CBE were more quantitative and objective, it may then yield diagnostic benefits.

Electronic Palpation Imaging

An innovative technology called electronic palpation imaging (EPI) uses an array of tactile sensors mounted on a handheld probe. As opposed to ultrasound or mammography, which emit and measure ultrasonic waves and x-rays, respectively, a tactile sensor records a mechanical measurement of pressure. As the probe is pressed against the breast, the sensor array captures varying reaction pressures caused by differences in tissue hardness. Salient feature data such as lesion size, shape, and hardness are quantified using sensitive electronics and advanced algorithms.

The softer tissue in a lesion causes different reaction pressure signatures.

In addition to being more objective and repeatable, tactile array sensors can be more sensitive than the human sense of touch, capable of clearly imaging sub-palpable lesions as shown in the figure below:

EPI Device Design History

An early EPI device was developed based on a piezoresistive tactile array sensor design. However, sensor performance and other concerns required the use of a magnetic position tracking system, resulting in a large, complex, and expensive cart-based system. A new design was required with improved sensor performance and a smaller form factor.

As part of a general redesign effort, the piezoresistive array was replaced with a capacitive-based tactile array sensor to improve performance and the entire system was shrunk down to a small notebook form factor. Using the capacitive tactile sensor, the performance was significantly improved, thus eliminating the need for the 3D positioning system, and the small, portable unit was simpler and easier to use. The user interface also underwent extensive changes based on feedback from physicians and users.

Continued development is underway to improve the device performance, as well as miniaturizing the electronics to allow for an eventual prescription handheld device for use in the home.

Materials & Methods

We performed two studies using an EPI device currently FDA cleared for documentation purposes. In the first study, EPI was used to examine two sets of 3 phantoms. One set differed only in size, ranging from 11-19 mm in diameter, while the second differed only in hardness, ranging from 300-500 kPa. All six phantoms were examined five times. In the second study, 6 different users examined the same phantom in order to evaluate repeatability and precision across different users. This was repeated with a total of four different phantoms differing in both size and hardness for a total of 24 sets of measurements. Users were given only basic instruction on how to use the device and were asked to use an exam force of 1-2.1kg to remain consistent with one another.

For the single operator study, we found the standard deviation to be less than 0.6 mm in size measurements, while the relative hardness standard deviation was less than 5%. Error bars in graphs represent one standard deviation.

Discussion

The single operator study showed very consistent results when the EPI device was handled by an experienced user. As the same procedure is also used as part of the final quality acceptance testing done on each EP device, existing data was reviewed and found to be consistent with these results. When multiple users were involved, the results were very similar to the single user data. Using the single user data as a baseline, multiple users’ size data was within 7% and hardness data within 4%. Quantifying absolute accuracy is difficult, as there is no accepted standard for determining the size envelope of a lesion, and hardness measurements were to this point only qualitative in nature. However, the consistency of EP results, both within a battery of tests and across multiple users, suggests that such quantitative standards may now be possible.

An ongoing, NIH-funded, clinical study is underway to compare EP data with mammography, ultrasound, and where possible, biopsy data from over 300 patients at multiple institutions for the dual purposes of improving accuracy of salient feature metrics and for establishing a correlation between key EP metrics and pathology. A clinical trial is also being planned in China to assess the screening viability of the device. In addition, FDA-cleared devices are deployed at 8 locations in the United States, Europe, and Asia for additional clinical feedback.

Conclusion

The use of EPI allows collection of digital images that accurately and consistently correspond to known breast mass phantoms. EPI is consistent between different examiners studying the same phantom. This may allow the CBE to become an objective and more scientific tool by collecting accurate digital images that correspond to manual palpation.

References

About the BreastLogic examination procedure

• What do I need to do before my appointment?
• Do I need a referral from my General Practitioner?
• What happens during the scan?
• What should I do after the scan?
• How does it work?
• Is this technology proven?
• What about other clinical breast examination techniques?
• Can Computerised Breast Imaging be used as a diagnostic tool?
• Why choose Computerised Breast Imaging?
• Do I still need to have a mammogram?

What do I need to do before my appointment?

You do not need to do any preparation for a Computerised Breast Image scan. However it’s useful to know that the ideal time for this is between day 7 and day 21 of your menstrual cycle, counting the first day of bleeding as day 1.

Do I need a referral from my General Practitioner?

No. All you need to do is call BreastLogic for an appointment.

What happens during the scan?

You will be asked to lie on an examination table and the Breast Nurse will use a small handheld sensor to scan and record any masses or lumps in your breast tissue by gently running the sensor over the skin of your breasts. You will be able to see the scan as it is happening on a computer screen and you can ask questions as you go. The Breast Nurse will help you become familiar with any lumps or masses found too, so you can monitor them at home and be able to identify them for your doctor if discussing your report. The scan takes about 30 minutes to complete.

What should I do after the scan?

After your scan you will be more familiar with your breasts and can now feel more comfortable examining your breasts on a regular basis every month. You will receive a visual breast map that shows you the location of any masses or lumps, plus a summary of each individual lump, including size, shape, volume and relative hardness. You can use the visual breast map as a guide in your regular self examination program.

It’s important to remember that no test can find all breast changes. Regular self-examination is part of managing life-long breast health and all of us (including men!) should be aware of how our breasts normally look and feel. If you notice a lump or other change, including discharge from a nipple, you should contact your doctor as soon as possible.

About the technology

How does it work?

Computerised Breast Imaging (CBI) uses a handheld device consisting of 192 high resolution pressure transducers/sensors to mimic the sense of touch. These sensors are up to four times more sensitive than human touch and records changes in tissue elasticity brought about by developing lesions. These are converted into an electronic signal, digitized and analysed to indicate lumps or masses in the breast. The scan produces a visual image of the breast on a computer screen, and if a lesion is detected it will instantly create full-colour 2-D and 3-D images. The collated data builds a profile describing the characteristics of the lesion, including size, shape and relative hardness.

Due to the increased sensitivity of the sensors and computer algorithms CBI can detect lumps or masses as small as 5mm that cannot normally be felt by human touch.

Advantages of CBI technology

• Suitable for women of ALL AGES.
• Suitable for women with very large or very small breasts
Suitable for women with implants
Suitable for women with dense breasts
Scans the whole breast
Improved detection: 192 pressure sensitive transducers and computer algorithms combine to provide sensitivity up to 4 times greater than human touch. Small masses can be detected that might otherwise be missed when examining by hand.
Early Change identification: our record is permanently stored for future comparison and the objective description removes uncertainty of potential size or hardness changes since the last examination; small changes can now be accurately and reliably detected earlier than by hand.
Radiation and Pain free, CBI does not use X-ray (ionising radiation) or compress the breast and can be used frequently to compare potential changes in any hard mass.
It is a very comfortable examination and is well tolerated.
The report provides you with a permanent record that you can use to become more familiar with your breasts.
Is suitable for men

Is this technology proven?
Yes. CBI is a proven technique for breast examination and scanning. It was first developed in the United States and is now used in 29 countries worldwide, including the US, UK, Canada and New Zealand. The same imaging technology is well established in other medical fields, such as robotic surgery.

A range of clinical studies has been undertaken on the use of Computerised Breast Imaging around the world. These studies have shown that CBI is capable of identifying tiny lesions and masses that are too small to be detected by a standard clinical breast examination in which an examiner relies on human touch. The system used by BreastLogic, known as SureTouch, has been found to be up to four times more sensitive than human touch and capable of detecting lesions as small as 5mm (Kaufman CS, Jacobsen L, Bachman BA, Kaufman LB. “Digital Documentation of the Physical Examination: Moving the Clinical Breast Exam to the Electronic Medical Record,” American Journal of Surgery, 2006; 192:444-449).

What about other clinical breast examination techniques?
There is a range of techniques available for examining the breast. It is very important to distinguish between ‘screening’ the breast for an abnormality when there are no symptoms and examining a particular abnormality within the breast.

The most common currently used techniques are:

- Self Breast examination. No particular technique is now recommended to self examine your breasts. All recognised health authorities recommend Breast Awareness ie being familiar with the normal look and feel of your breasts. This will help you recognise any changes as early as possible.

- Clinical Breast Exam – a clinical, hands-on exam performed by your doctor. There is not clear evidence to support yearly clinical (screening) examinations by your doctor when there are no symptoms present. It is of course essential to have a clinical breast examination by your doctor as part of the investigation of any changes in your breast which may be abnormal.

- Mammography – a process using x-ray (ionising radiation) to examine the breast. Mammography is used for screening and for the diagnostic workup of an abnormality within the breast.

- Ultrasound – a process using very high frequency sound waves which ‘bounce off’ the tissue in the breast to create an image called a sonogram. It is important to note ultrasound is used for the diagnostic investigation of a known mass, and is not used as a screening tool to find masses.

- Biopsy –The removal of cells or tissues using an extremely fine needle. Not used for screening. The cells are then examined microscopically. (This is the gold standard for diagnosis of breast lesions.)

If lumps or masses are detected in a breast examination, and your doctor decides these require further investigation, it is common for more than one of these tests to be used to develop a diagnosis and, if necessary, a plan for treatment.

Can Computerised Breast Imaging be used as a diagnostic tool?
Computerised Breast Imaging is not a diagnostic tool. Its purpose is to generate an objective, accurate and consistent digital record of any hard breast masses. The record can then be used to improve your Breast Awareness. It can also be used to review any hard masses and as a guide for the further investigation of masses that change. It is also useful for localising an area of concern for ultrasound.

Why choose Computerised Breast Imaging?
CBI is unique and offers some significant advantages;
It is suitable for all age groups and breasts types.

- Suitable for women of ALL AGES.
- Suitable for women with very large or very small breasts
- Suitable for women with implants
- Suitable for women with dense breasts
- Scans the whole breast
- Improved detection: 192 pressure sensitive transducers and computer algorithms combine to provide sensitivity up to 4 times greater than human touch. Small masses can be detected that might otherwise be missed when examining by hand.
- Early Change identification: our record is permanently stored for future comparison and the objective description removes uncertainty of potential size or hardness changes since the last examination; small changes can now be accurately and reliably detected earlier than by hand.
- Radiation and Pain free, CBI does not use X-ray (ionising radiation) or compress the breast and can be used frequently to compare potential changes in any hard mass.
- It is a very comfortable examination and is well tolerated.
- The report provides you with a permanent record that you can use to become more familiar with your breasts.
- Is suitable for men

This technique also offers a breast scanning option for:

- women for whom other techniques may not be suitable, such as women with implants
- women with dense breast tissue (usually younger women)
- women who wish to avoid the discomfort of compression of the breast
- women who wish to avoid exposure to radiation

Computerised Breast Imaging should be considered as one of a range of activities in your breast health plan.

Each person has different requirements and different health issues and your doctor can help you decide on your ongoing breast health plan.

Do I still need to have a mammogram?

1. We recommend you find out about the recommendations, risks, benefits and how they relate to you personally. Discuss these issues with your doctor. BreastLogic support the current screening guidelines.

2. As an option or additional to mammography we advise:

**Increase your chances of finding breast changes early by:**
- Monthly self breast examinations to become Breast Aware
- Annual Computerised Breast Imaging scans with BreastLogic
- Regular assessment of your Breast Health by your Doctor or health professional
- Report any symptoms early

**Reduce your risk by:**
- Consuming a diet low in fat and high in fresh fruit and vegetables
- Healthy weight control
- Moderate alcohol intake and regular exercise (can reduce your risk by 30%)
Computerised Breast Imaging: Clinical studies and literature review

Clinical studies

Most studies of tactile imaging/computerised breast imaging (SureTouch) address both the patient benefit and the implied system benefit. Although SureTouch technology has regulatory approval in the USA and Australia as a means to document the clinical breast examination, in other countries such as China and India, SureTouch is used for breast screening in the general population. In addition, ongoing research is exploring the role of tactile imaging in differentiating breast lesions. This research uses both the SureTouch device and virtually identical devices incorporating supplementary algorithms.

The limitations of CBE include lack of training and clinical skills in manual breast palpation resulting in missed lesions as well as over diagnosed lesions resulting in unnecessary referrals, problems with subjectivity by the examiner, lack of uniformity in reporting results, and absence of digital documents and pictures illustrating exam results.

Patient and system benefits of SureTouch Computerised Breast Imaging technology:

- SureTouch can produce more objective and reliable data than CBE in the important areas of breast mass size, hardness, consistency and location.
- SureTouch is less likely to miss breast masses than CBE, especially when CBE is practiced by less experienced clinicians, those in training and those who perform CBE infrequently. Fewer missed lesions could mean earlier detection for some women.
- In some women with dense breasts (especially those under age 40), SureTouch technology can better detect lesions than mammography or CBE.
- SureTouch is suitable for women who are not in the recommended groups for mammography (eg less than 50yrs of age) or are in an interval between regularly scheduled mammography. It is also an option for women who have elected voluntarily to opt out of mammography screening and are currently not otherwise being encouraged to be breast aware.
- The digital record that SureTouch provides each patient standardizes the CBE, provides pictures, and allows for easy and rapid communication of results among clinicians.
- The SureTouch digital record provides an opportunity for enhanced communication with patients about their examination and can raise breast health awareness.
- Current research has demonstrated the role of SureTouch in differentiating lesions. If confirmed by additional studies, SureTouch has the potential to be used as a cost-effective device for differentiation of breast lesions. This may be especially true in countries where expensive mammography equipment is not available or supportable.
- In developed countries, screening mammography is the recommended tool for detection. The mammography results are used as the basis in making the decision about whether or not to perform a biopsy at suspicious breast sites. In the United States alone, more than one million breast biopsies are performed annually and approximately 80% of these findings are benign. The use of SureTouch after standard screening procedures (mammography alone or combination of mammography and conventional ultrasound) has the potential to reduce the benign biopsy rate. Modelling studies suggest that by adding SureTouch to mammography, a 23% reduction of the benign biopsy rate is possible without any missed cases and a 50% reduction of the benign biopsy with 4.6% missed cases.

Eight clinical studies have been conducted using the SureTouch technology:

Ergorov (2009) - Published study of 179 patients with breast masses identified by mammography, ultrasound and/or CBE. All patients had a SureTouch examination plus a biopsy. SureTouch was able to differentiate the lesions with a sensitivity and specificity of 91.4% and 86.8% respectively. Authors conclude that SureTouch has the potential to be used as a cost-effective device for diagnostics. This could
reduce the benign biopsy rate, serve as an adjunct to mammography and be utilized as a screening device.

Griffith (2009) - Presented abstract describing study of 137 patients at a UK NHS breast clinic, 66 of whom had palpable breast masses. Seventy-seven of these were chosen at random to have a SureTouch examination in addition to CBE. Use of SureTouch reduced the percentage of missed lesions by senior and junior surgical trainees. The reproducible reports allowed efficient review by examiners with various levels of experience. Authors state that SureTouch imaging improved patients’ safety in breast clinic and likely had a role in the training and assessment of surgical trainees.

Kaufman (2009) ASBD Abstract Palpation imaging (SureTouch) for breast screening in developing countries 74 barely palpable breast masses were examined with CBE, mammography, ultrasound and SureTouch, and then excised. Average size variation was compared to final pathologic size. SureTouch provided breast tumor size measurements in 93% of patients. All modalities of breast tumor size estimates were within 0.5-0.7cm of true pathologic size. While mammography was most accurate estimate of size (0.48+0.14cm), SureTouch was very close to mammography (0.71+0.14cm) and was most reliable provider (93% versus 51%).

Kaufman (2006) - Published study of 110 patients presenting with a complaint of breast mass. Of those with a true mass, SureTouch identified the mass in 94% of cases versus 86% by CBE. Positive predictive value was 94% by SureTouch and 78% by CBE. Results were confirmed by biopsy or follow up. The sensitivity and specificity of identifying a mass were 88% and 88% compared to 81% and 81% for CBE. As part of the study, a survey of primary care physicians revealed that the inclusion of a SureTouch record in the consultation note implied competence, experience and skill by the breast surgeon.

Ables (2007) - Presented abstract describing study of 7 operators examining six breast phantoms. SureTouch use demonstrated consistent measurements of lesion size and hardness as well as reproducibility on repeated measurements.

Kearney (2004) - Published abstract describing study of six breast specialists and seven unskilled lay persons to determine their ability to detect masses in breast phantoms by manual palpation and SureTouch scan. SureTouch imaging by lay persons had higher sensitivity than manual breast palpation in identifying masses. In addition, lay persons then received four training sessions in the use of SureTouch. This training increased the detection of masses to the level achieved by the specialists.

Helvie (2003) - Published abstract of 31 women with breast masses. SureTouch sensitivity and specificity for detection of masses were 80% and 75% and for tumour detection, 92% and 72% respectively. A majority of patients reported that SureTouch screening was at least as comfortable as CBE.

Wellman (2001) - Published study of 23 women undergoing surgical excision of breast masses following pre-operative CBE, ultrasound and SureTouch examination. SureTouch measurements were repeatable and estimates of lesion size showed good correlation with the post-resected lesion measurements.

**Planned studies**

UK - supported by the NHS

South Africa - supported by CANSA and private specialists,

USA - various studies supported by the NIH and privately funded research grants with participation by public and private institutions

India - supported by the Andhra Pradesh government and private clinics

China - on-going government backed studies

South Korea – Government supported studies

Italy – NCI of Naples and government health care agencies,

West Africa – supported by Breast Care International and others.

A number of these studies involve significant participation rates. A full list of current and pending trial data is available on request.

**Literature review**
Journal publications


Conference Proceedings and Abstracts


05.03.2011


Additional publications related to the technology of tactile/mechanical imaging

- Egorov and Sarvazyan Page 14 / IEEE Trans Med Imaging. Author manuscript; available in PMC 2009 September 1.
- Egorov and Sarvazyan Page 15 / IEEE Trans Med Imaging. Author manuscript; available in PMC 2009 September 1.
- Barr, RG. Clinical applications of a real time elastography technique in breast imaging. Proc 5th Int Conf Ultrasonic Measure Imag Tissue Elasticity; Snowbird, UT. Oct. 8–11, 2006; p. 112


Welcome to Natural Therapies Clinic where we are dedicated to improving the Early Detection of Breast Cancer with new technology such as the highly acclaimed SureTouch™ Visual Mapping System.

The introduction of SureTouch now provides women of all ages with the option of having a regular Sensitive, Accurate, Pain Free and Radiation Free Computerised Breast Imaging with their own GP or primary health care professional. The procedure is totally non-invasive, requires no compression of the breast tissue and will not cause any harm to the patient as it uses no radiation to create an image.

* FACT: You could be 18 or 80, have dense breast tissue or have undergone augmentation (implants) a SureTouch Computerised Breast Imaging is suitable for you.

* FACT: Breast Cancer does not discriminate as it can occur at any age.

* FACT: Women under 40 years do get breast cancer.

* FACT: A SureTouch CBI is a totally pain free breast exam.

* FACT: SureTouch is TGA Approved (Therapeutics Goods Administration)

**FREQUENTLY ASKED QUESTIONS**

**What is SureTouch?**

SureTouch Visual Mapping System is a unique digital sensing device that assists a physician or other trained healthcare professional in screening for breast cancer during routine exams, greatly increasing the chances of early diagnosis of breast cancer in women.

**How does the technology work?**

The SureTouch hand-held sensor is made up of a high resolution array of many small, proprietary, pressure-sensitive elements. These elements are the integral part of the technology that converts the measure of tissue elasticity into an electronic signal, which is then digitized and computer...
Why should women get Computerised Breast Imaging?

Currently, women typically rely on the self-examination or a similar hand exam by their primary care physician or gynecologist to identify breast lesions. Computerised Breast Imaging that's simple to obtain and accurately displayed is beneficial to all women but especially to those between the ages of 25-40, who, unless they detect a concern, would not likely seek a mammogram. With breast cancer, early detection can make the difference between life and death.

Is the SureTouch exam accurate?

A two-year study of SureTouch funded by the National Institute of Health (NIH), and its extraordinary results for identifying and mapping breast lesions have been documented by the American Journal of Surgery and by the researchers involved in the project. Eight clinical studies carried out in various countries show that Suretouch is more accurate than conventional breast exams. In countries like India and China, Suretouch is used for breast screening in the general population.

Can SureTouch be used as a diagnostic tool?

It is not a diagnostic product. Its responsibility is to visualize the sense of touch and generate an objective, accurate and consistent printed report for review by the patient, a second formatted report for review by the attending medical practitioner and a digital report file that can be appended to the patient’s electronic medical record viewable by mammographers and attending breast surgeons.

For more information on the clinical studies carried out, and their results, you may click on this link.
Tumor size and breast cancer detection: what might be the effect of a less sensitive screening tool than mammography?

Duffy SW, Tabar L, Vitak B, Warwick J.

Cancer Research UK Center for Epidemiology, Mathematics, and Statistics, Wolfson Institute of Preventive Medicine, London, United Kingdom. stephen.duffy@cancer.org.uk

Abstract
In some limited-resource areas, a state-of-the-art mammography program is not affordable. In such circumstances, one might consider a less resource-intensive, but also less sensitive screening tool such as clinical breast examination (CBE). We used data from the Swedish Two-County Trial to estimate the shift in tumor size resulting from invitation to mammographic screening. By postulating a lesser benefit of a less sensitive screening tool (CBE), particularly in terms of detecting very small tumors, we predicted its likely effect on tumor size distribution. In addition, using the observed association between tumor size and nodal status, and between tumor size and fatality, we predicted the likely benefit in terms of reductions in node-positive disease and in breast cancer mortality. An invitation to mammographic screening was associated with a 27% reduction in the number of node-positive tumors and a 31% reduction in the number of breast cancer deaths. We estimate that in the trial population, screening with CBE alone would have led to an 11% reduction in node-positive tumors and an 11% reduction in breast cancer deaths (approximately 42 deaths prevented per 1,000 cases). Assuming instead a tumor size distribution typical of a limited-resource setting (70% of tumors are 30 mm at presentation), we estimate that screening with CBE alone would lead to a 13% reduction in node-positive tumors and a 12% reduction in breast cancer deaths (approximately 72 deaths prevented per 1,000 cases). Thus, although the relative benefit of CBE is only slightly greater in the limited-resource setting, the absolute reduction in deaths per case is about 70% higher. Our findings suggest that a less sensitive tool might be expected to confer a breast cancer mortality reduction about half of that observed with mammography.

PMID:16430402[PubMed - indexed for MEDLINE]

MeSH Terms

LinkOut - more resources

Abstract Mechanical imaging yields tissue elasticity map and provides quantitative characterization of a detected pathology. The changes in the surface stress patterns as a function of applied load provide information about the elastic composition and geometry of the underlying tissue structures. The objective of this study is the clinical evaluation of breast mechanical imager for breast lesion characterization and differentiation between benign and malignant lesions. The breast mechanical imager includes a probe with pressure sensor array, an electronic unit providing data acquisition from the pressure sensors and communication with a touch-screen laptop computer. We have developed an examination procedure and algorithms to provide assessment of breast lesion features such as hardness related parameters, mobility, and shape. A statistical Bayesian classifier was constructed to distinguish between benign and malignant lesions by utilizing all the listed features as the input. Clinical results for 179 cases, collected at four different clinical sites, have demonstrated that the breast mechanical imager provides a reliable image formation of breast tissue abnormalities and calculation of lesion features. Malignant breast lesions (histologically confirmed) demonstrated increased hardness and strain hardening as well as decreased mobility and longer boundary length in comparison with benign lesions. Statistical analysis of differentiation capability for 147 benign and 32 malignant lesions revealed an average sensitivity of 91.4% and specificity of 86.8% with a standard deviation of ±6.1%. The area under the receiver operating characteristic curve characterizing benign and malignant lesion discrimination is 86.1% with the confidence interval ranging from 80.3 to 90.9%, with a significance level of \( P = 0.0001 \) (area = 50%). The multisite clinical study demonstrated the capability of mechanical imaging for characterization and differentiation of benign and malignant breast lesions. We hypothesize that the breast mechanical imager has the potential to be used as a cost effective device for cancer diagnostics that could reduce the benign biopsy rate, serve as an adjunct to mammography and to be utilized as a screening device for breast cancer detection.

Keywords Breast cancer · Diagnostic elastography · Tissue differentiation · Malignancy detection

Introduction

The current methods of breast pathology assessment include Clinical Breast Examination (CBE), Mammography, Ultrasound, Magnetic Resonance Imaging (MRI), and biopsy. Positron emission mammography and sestamibi
scans are also used occasionally. A recent large-scale clinical study (42,760 patients in USA and Canada) on the diagnostic performance of mammography for breast-cancer screening revealed that the diagnostic accuracy of digital and film mammography is 78 and 74\%, respectively [1]. A European randomized mammography screening trail (23,929 patients in Norway) demonstrated a sensitivity of 77.4\% and specificity of 96.5\% for full-field digital mammography while a screen-film mammography yielded a 61.5\% sensitivity and 97.9\% specificity. Notably, the median size of detected invasive cancers was about 13.5 mm [2]. Despite the recommendation for an annual mammogram, only 58.3\% of women 40 years or older in the United States had a mammogram in 2004 [3].

Ultrasound is being increasingly used as a complementary method for the assessment of mammographically or clinically detected breast masses for supplemental information on dense tissue [4]. However, there is limited data supporting the use of ultrasound in breast cancer screening as an adjunct to mammography [5]. The conventional ultrasound is more often used to determine whether an area of concern on the mammogram or clinical exam is cystic or solid. The majority of cystic masses are benign while solid masses need further evaluation [6]. Many indications for clinical breast MRI are recognized. These include resolving mammography findings, staging of breast cancer when multiple or bilateral disease is suspected, and detecting the occult primary breast cancer presenting with malignant axillary lymphadenopathy [7, 8].

The CBE is applied to detect abnormalities or to evaluate a patient’s report of symptoms or findings of palpable breast cancers at an earlier stage of progression [9]. The American Cancer Society guidelines suggest an annual CBE for age 40 and older for early detection of breast cancer in asymptomatic women [3]. The CBE identifies some cancers missed by mammography [10, 11] and provides an important screening tool among women for whom mammography is not advised or for those that do not receive high-quality screening mammography. Nevertheless, CBE performance and reporting approaches are known to be inconsistent. Health care providers report a lack of confidence in their CBE skills and would welcome training and practical recommendations for optimizing performance and reporting [12]. Data for the six studies examined by Barton and colleagues resulted in an overall estimate of 54.1\% for CBE sensitivity and 94.0\% for CBE specificity [13]. These findings are comparable to the published values of CBE sensitivity (58.8\%) and specificity (93.4\%) observed in the US national screening program of 752,081 CBE reports [14].

Therefore, a method that mimics CBE but with enhanced sensitivity and specificity might consequently lead to a greater screening yield. Such method for detection and visualizing breast abnormalities and assessing their mechanical properties with sensitivity exceeding that of manual palpation was developed. The method, called Mechanical Imaging, is based on reconstructing the internal structure of soft tissues using the data obtained by a pressure sensor array pressed against the examined site [15]. The changes in the surface stress patterns as a function of displacement, applied load, and time provide information about elastic composition and geometry of the underlying tissue structures.

We have demonstrated earlier that the Breast Mechanical Imager (BMI), a compact device comprised of a handheld probe equipped with a pressure sensor array, allows calculation of size, shape, consistency/hardness, and mobility of detected lesions [16]. The BMI prototype has also been validated in laboratory experiments on tissue models and tested in a clinical environment [17]. The objective of this study is the clinical evaluation of the BMI for breast pathology characterization and differentiation between benign and malignant breast lesions.

Materials and methods

Study design and protocol

The primary objective of the clinical study was to assess the BMI’s capability in lesion characterization. The examination was performed specifically for the concerned breast areas with the suspected lesions. Lesion features were calculated from the recorded BMI examination data and were used for lesion characterization. Additional diagnostic information provided by other diagnostic modalities was collected and used for the analysis of the potential of differentiation of benign and malignant lesion by BMI. Thus, the primary objective of lesion characterization has been extended to a more practical question of benign and malignant lesion discrimination. Evaluation of the classification accuracy of the BMI has been done in a non-blinded data analysis.

The clinical protocol was approved by the Institutional Review Boards at each of the clinical sites. The study was done in compliance with the Health Insurance Portability and Accountability Act. The clinical study has been conducted through a non-randomized multi-center trial in the four investigational sites: New Jersey (The Cancer Institute of New Jersey, New Brunswick), New York (Mercy Medical Center, Rockville Centre), Pennsylvania (The Breast Care Center & General Surgery Practice, Easton), and Florida (Breast Health Institute, Maitland). The exams were performed by BMI trained breast surgeons enrolled as co-investigators in the study.
Study inclusion criteria were:

(a) women (over the age of 21) with a breast mass identified by mammography, ultrasound, and/or CBE,
(b) women (over the age of 21) referred to a breast surgeon for evaluation of a particular area of concern identified either by the woman herself or her primary physician,
(c) patients with a clinical record containing CBE, US, and mammography reports with clear localization of lesion of interest.
(d) patients with a clinical record containing a pathology report with the results from a fine needle biopsy, core needle biopsy, or excisional biopsy for the identified lesion with an exception in cases where the ultrasound and mammography reports both clearly stated that the lesion is benign, predominantly a cyst, and biopsy is not required.

Study exclusion criteria were:

(a) patients with skin infection or inflammation in the breast,
(b) patients with prior breast cancer surgery or radiation,
(c) patients with scleroderma or other connective tissue disorders,
(d) patients with epidermal cysts,
(e) patients that had a biopsy recommendation, but for various reasons a pathology report was unavailable,
(f) immoderate deviation from the recommended BMI examination procedure such as losing the lesion image or keeping lesion image at the edge of pressure array during the scan, poor pressure patterns due to insufficient level of applied force (well below the recommended level).
(g) the BMI examination was performed after biopsy.

A hard copy of lesion related clinical data with the results of clinical diagnostics for all enrolled patients was submitted for data review and analysis. Classification of each scanned lesion as benign or malignant was determined by the result of the pathology report or, as in the case of a cyst or other benign findings that did not recommend biopsy testing, from the results of the mammogram and ultrasound.

BMI system

The BMI is comprised of a probe, an electronic unit, and a touch screen laptop [17]. A pressure sensor array positioned on the probe head is designed to acquire pressure patterns between the probe surface and the exterior skin layer of the breast during contact. The sensory array size is 40 mm by 30 mm and is comprised of 192 pressure sensors. Special software was developed for processing of the data collected from the probe sensors and the calculation of certain lesion features as described below in this paper.

BMI examination procedure

Prior to the biopsy, a BMI examination was conducted on the area of clinical concern. At first, the breast surgeon (oncologist) would perform a standard CBE to determine the location of the concern. Some of the patients had non-palpable lesions and the lesion was observed by ultrasound prior to biopsy. With the knowledge of this location, the patient was placed in a similar position to that of a standard CBE with her breast in the supine position on an examination table. The examiner placed a disposable sheath over the sensor head of the BMI and then applied a water soluble lubricating lotion to the sensor head or applied directly to the area of concern. Once ready, the local scan of the lesion by the BMI was done in either one of two different variations: by applying up and down probe compressions over the lesion or circular probe motions around the lesion. During the examination, the acquired pressure response patterns from the probe sensors, being processed in real time, provided visualization of the current pressure pattern and a composition of the accumulated lesion image as described earlier [17]. The examination was recorded and stored by the BMI system in a digital format file, which was analyzed later in a research laboratory environment to calculate lesion features and verify the constructed multiparameter classifier. The duration of a typical lesion scan was approximately 1–2 min. In addition to the real time lesion image, the examiner was able to observe signals indicating excessive probe tilt, the total number of collected pressure frames and their distribution versus applied force and the level of the force applied to the probe. The acquired level of applied force was used as a guide in maintaining the recommended operational range from 7 to 18N.

Study population

The BMI clinical data set presented in this paper was collected and recorded during the period of July 2005 to November 2007. Initially, after giving written informed consent, 219 women were enrolled in the study at four different clinical sites. However, due to various clinical and procedural factors, a total of 40 patients were found to be ineligible and were excluded from the data analysis. Among them, 13 patients that were recommended for biopsy did not have the biopsy for various reasons (such as: they did not return for the appointment, their insurance
changed, they moved or switched to another physician); 9 patients had the biopsy done before the BMI examination; we were unable to determine from the record the location of the lesion for 3 patients; and 2 patients had an epidermal cyst. An additional 13 patients were excluded due to the specific limitations implied by the examination procedure requirements, such as poor distribution of recorded pressure patterns versus applied force (7 patients), lesion image was imaged on the perimeter of the pressure sensor array (3 patients), pressure sensors were zeroed on an incorrect level (2 patients), and applied force level to the BMI probe was beyond the operational range (1 patient). We observed some excessive tilt of the probe head during the lesion examinations, however, we did not exclude these cases from further consideration and analysis. Summary of the patient enrollment and exclusion for all four sites is shown in Table 1.

Table 2 displays the lesion diagnosed pathology distribution among the analyzed patients. Collectively there are 179 patients included in the data analysis of the clinical study as stated in Table 1. There are 19 patients from the first clinical site, 19 patients from the second site, 37 patients from the third site, and finally 104 patients from the fourth site. The median patient age was 43 years, from 21 to 92 years, with 36 and 52 years as the low and upper quartiles, respectively.

Overall, 147 and 32 cases were classified as benign and malignant, respectively. In 150 cases we had the pathology reports (fine needle biopsy, core biopsy or excisional biopsy) and in 29 cases we had ultrasound and mammography examination results that clearly stated that the lesion is benign, mostly diagnosed as cysts (19 cases), with no biopsy recommended. This diagnostic clinical information was used as the ‘gold standard’ for BMI data analysis. The benign classified lesions were divided into 11 subclasses [18] and malignant classified lesions were divided into 5 subclasses [19] as shown in Table 2.

Lesion features calculation

A detailed description of the lesion feature calculations has been given in an earlier publication [17]. Here, we will briefly outline the algorithms used for evaluation of features proposed for differentiating benign and malignant cases. Three features are related to tissue hardness and two other features are parameters characterizing lesion mobility and shape. Patient age was used as an additional input parameter for the classifier since the breast cancer risk is increased with age [20].

The input data to compose a 3D image of the breast lesion is comprised of a continuous sequence of 2D filtered images. The 3D image reconstruction starts with the formation of an initial 3D structure by stacking the series of 2D structure images along the vertical Z-coordinate (transverse plane) during the first tissue compression. Further, every 2D imprint is integrated by a parallel translation inside the 3D structure image, where x,y coordinates (coronal plane) are determined by a matching algorithm [17]. The Z-coordinate (layer number) is calculated according to:

\[
Z = A \times \sum_{i=k}^{i=l} \sum_{j=0}^{j=L} S_{ij} - B
\]

where \(A = 1.04 \times 10^{-5}\) and \(B = -5\) are empirical constants, \(k\) and \(l\) are quantities of horizontal and vertical pixels inside the pressure response frame with the analyzed lesion pattern, and \(S_{ij}\) is the current pressure signal of \(i,j\)-pixels expressed in \(P_{ax}\). Consequently, the final 3D image is composed of 2D images \(P(x,y,Z)\), which are the layers inside the 3D image, and we can calculate the maximum pressure value \(M(Z)\) for each Z-layer:

\[
M(Z) = \max\{P(x,y,Z)\}
\]

where \(x,y\) are coordinates in the plane parallel to a breast surface. Further, we approximate the experimental value of \(M(Z)\) by the second order polynomial:

Table 1 Patient enrollment and exclusion

<table>
<thead>
<tr>
<th>Relevant data</th>
<th>Clinical location</th>
<th>Total for all sites (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Site 1</td>
<td>Site 2</td>
</tr>
<tr>
<td>Enrolled patients</td>
<td>25</td>
<td>21</td>
</tr>
<tr>
<td>Excluded patients from data analysis</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Patients included into data analysis</td>
<td>19</td>
<td>19</td>
</tr>
</tbody>
</table>

Reasons of exclusion patients from data analysis

- Critical deviations in examination procedure (see text): 1
- Biopsy was recommended but not done: 4
- BMI examination was done after biopsy: 0
- No clear relation what lesion what examined: 1
- Lesion was diagnosed as epidermal cyst: 0
Lesion hardness related features are $F_1$, $F_2$, and $P_a(Z_m)$. The $F_1$-parameter characterizes nonlinearity of loading curve and is defined as strain hardening of the lesion. The parameter $F_2$ characterizes the average slope of a stress-strain loading curve and the parameter $P_a(Z_m)$ is the maximum pressure value for the $Z_m$-layer, where the total force applied to the probe is 12N.

The mobility of the lesion $M_{b\text{aver}}$ is evaluated as an averaged value of $M_b(t)$ through the examination time $t$ for all pressure patterns containing the lesion image:

$$M_b(t) = \left( 1 - \frac{\sum_{x=0}^{x=k} \sum_{y=0}^{y=k} Ph(x,y,Z,\text{Th}) \times Sh(x,y,t)}{\sum_{x=0}^{x=k} \sum_{y=0}^{y=k} Ph(x,y,Z,\text{Th})} \right) \times 100\%$$

(4)

$$Sh(x,y,t) = \begin{cases} 1, & S(x,y,t) \geq \text{Th} \\ 0, & S(x,y,t) < \text{Th} \end{cases}$$

(5)

where $Ph$ is the accumulated 3-D binary lesion image, $\text{Th}$ is the threshold of binarization, $Sh(x,y,t)$ is a binary image of a momentary lesion image to be placed in comparison with the $Z$-layer, $S(x,y,t)$ is the momentary pressure response of sensor with $x,y$-coordinates at time $t$. Prior to Eqs. 4 and 5, the image $Sh(x,y,t)$ is matched with the accumulated image $P_z(x,y)$ as detailed in a prior publication [17]. The $M_{b\text{aver}}$ value, expressed in percentage, characterizes the capability of the lesion to change its form and position under applied mechanical indentation by the probe’s curved surface. The shape of the lesion is characterized by the ratio of the lesion boundary length to the perimeter of a circle with the same area as that of the lesion visible projection. The age of enrolled patients was the sixth parameter used in data analysis.

<table>
<thead>
<tr>
<th>Gold standard for lesion diagnosis</th>
<th>Biopsy pathology report</th>
<th>US + mammography reports</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total for all sites</td>
<td>150</td>
<td>29</td>
</tr>
</tbody>
</table>

| Total malignant                  | 32                      |
| Total benign and malignant       | 179                     |

Table 2: Pathology distribution according to clinical data for analyzed lesion

<table>
<thead>
<tr>
<th>Clinical pathology diagnosis (see text)</th>
<th>Clinical location</th>
<th>Total for all sites</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Site 1</td>
<td>Site 2</td>
</tr>
<tr>
<td>Benign</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Cyst</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Fibrocystic changes</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Stromal fibrosis</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Fibroadipose or adipose tissue/fragments/cells</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fibrotic changes</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Sclerosing adenosis, nodular adenosis</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Fat necrosis, fat lobules</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Sclerotic tissue</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Intraductal papillomas</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Others</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Total benign</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>Malignant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Invasive ductal carcinoma</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Ductal carcinoma in situ</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Invasive lobular carcinoma</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Medullary carcinoma</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total malignant</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Total benign and malignant</td>
<td>19</td>
<td>19</td>
</tr>
</tbody>
</table>

Statistical analysis

A statistical assessment of the diagnostic significance of each feature was completed with the aid of the statistical toolbox in MATLAB 6.1 (MathWorks, Natick, MA) and MedCalc 9.2 (MedCalc Software, Mariakerke, Belgium). For visual evaluation of the analyzed clinical data distributions within the benign and malignant patient samples, we used boxplots for data representation of each analyzed
Bayesian classification for our situation is to calculate the strong independence (naive) assumptions. The goal of the dependencies [28]. A naive Bayesian classifier is a probabilistic classifier based on applying Bayes’ theorem with strong independence (naïve) assumptions. The goal of the Bayesian classification for our situation is to calculate the probability \( P \) of lesion being benign \( C_b \) or malignant \( C_m \) for a given set of lesion features \( F \). Formal presentation of the probability will look as \( P(C_i|F_j) \), where \( i \) is the lesion number and \( j \) is the lesion feature number. If one the values of \( P(C_b|F_j) \) or \( P(C_m|F_j) \) was greater than the other, then the classification of the lesion would be that of the greater value. The Bayes’ theorem facilitates the computation of the \( P(C_i|F_j) \) probability:
\[
P(C_i|F_j) = \frac{P(F_j|C_i) \times P(C_i)}{P(F_j)}
\]
where \( P(C_i) \) is the prior probability of \( C_i \) and \( P(F_j) \) is the prior probability of \( F_j \), which acts as a normalized constant often referred to as evidence. To calculate the conditional probability \( P(F_j|C_i) \) requires that we estimate the joint probability distribution, in all 6-dimensions for the six features, for the point for each of the classes. Under the independence (naïve) assumption, the covariance matrix has only diagonal members. Hence, the conditional probability \( P(F_j|C_i) \) might be calculated as:
\[
P(F_j|C_i) = \prod_{a=1}^{6} P(F_{ja}|C_i)
\]
where \( F_{ja} \) is the value of \( F_j \) in the \( a \)-th dimension. For numeric data we assume that each dimension is normally distributed. Thus, we have to estimate the variance \( \sigma_{ja}^2 \) and mean \( \mu_{ja} \) for each class \( C_i \), separately, directly from data. Once these values are computed for benign and malignant patient samples, we calculate:
\[
P(F_{ja}|C_i) = N(F_{ja}|\mu_{ja},\sigma_{ja}^2) = \exp \frac{-(F_{ja}-\mu_{ja})^2}{2(\sigma_{ja}^2)}
\]

The value of the prior probability \( P(C_i) \) is defined by the ratio of the sample size to the total number of patients. The evidence value was calculated according to:
\[
P(F_j) = \sum_{a=1}^{6} \left( P(F_{ja}|C_b) \times P(C_b) + P(F_{ja}|C_m) \times P(C_m) \right)
\]

The difference between \( P(C_b|F_j) \) and \( P(C_m|F_j) \) was used as a threshold parameter for the construction of the ROC curve for a set of specified features.

Statistical classifier

To differentiate benign from a malignant breast lesions, we employed a naïve Bayesian classifier [26, 27]. Large-scale comparison of this Bayesian classifier with state-of-the-art algorithms for decision tree induction and instance-based learning on standard benchmark datasets found that the simple Bayesian classifier was superior to each of the other learning schemes, even on datasets with substantial feature dependencies [28]. A naïve Bayesian classifier is a probabilistic classifier based on applying Bayes’ theorem with strong independence (naïve) assumptions. The goal of the Bayesian classification for our situation is to calculate the probability \( P \) of lesion being benign \( C_b \) or malignant \( C_m \) for a given set of lesion features \( F \). Formal presentation of the probability will look as \( P(C_i|F_j) \), where \( i \) is the lesion number and \( j \) is the lesion feature number. If one the values of \( P(C_b|F_j) \) or \( P(C_m|F_j) \) was greater than the other, then the classification of the lesion would be that of the greater value. The Bayes’ theorem facilitates the computation of the \( P(C_i|F_j) \) probability:
\[
P(C_i|F_j) = \frac{P(F_j|C_i) \times P(C_i)}{P(F_j)}
\]
where \( P(C_i) \) is the prior probability of \( C_i \) and \( P(F_j) \) is the prior probability of \( F_j \), which acts as a normalized constant often referred to as evidence. To calculate the conditional probability \( P(F_j|C_i) \) requires that we estimate the joint probability distribution, in all 6-dimensions for the six features, for the point for each of the classes. Under the independence (naïve) assumption, the covariance matrix has only diagonal members. Hence, the conditional probability \( P(F_j|C_i) \) might be calculated as:
\[
P(F_j|C_i) = \prod_{a=1}^{6} P(F_{ja}|C_i)
\]
where \( F_{ja} \) is the value of \( F_j \) in the \( a \)-th dimension. For numeric data we assume that each dimension is normally distributed. Thus, we have to estimate the variance \( \sigma_{ja}^2 \) and mean \( \mu_{ja} \) for each class \( C_i \), separately, directly from data. Once these values are computed for benign and malignant patient samples, we calculate:
\[
P(F_{ja}|C_i) = N(F_{ja}|\mu_{ja},\sigma_{ja}^2) = \exp \frac{-(F_{ja}-\mu_{ja})^2}{2(\sigma_{ja}^2)}
\]

The value of the prior probability \( P(C_i) \) is defined by the ratio of the sample size to the total number of patients. The evidence value was calculated according to:
\[
P(F_j) = \sum_{a=1}^{6} \left( P(F_{ja}|C_b) \times P(C_b) + P(F_{ja}|C_m) \times P(C_m) \right)
\]

The difference between \( P(C_b|F_j) \) and \( P(C_m|F_j) \) was used as a threshold parameter for the construction of the ROC curve for a set of specified features.

Results

The comparative benign-malignant paired boxplots for the lesion strain hardening (\( F1 \)), loading curve average slope (\( F2 \)), maximum pressure peak for the fixed total force applied to the probe (\( F3 \)), lesion shape (\( F4 \)), lesion mobility (\( F5 \)), and patient age (\( F6 \)) are shown in Fig. 1. The central horizontal line inside each boxplot corresponds to the median value of the sample distribution, as the confidence interval for the median is depicted by a notched beam range on each boxplot. Lower and upper horizontal lines of the box correspond to the first (25%) quartile and the third (75%) quartile, respectively. Small circles beyond
the horizontal bars illustrate the outlier data, which begins at the value of the interquartile range multiplied by 1.5 and extends beyond. Nine breast lesions (7 benign and 2 malignant) out of 179 were not palpated in the area of concern during the corresponding CBE, yet were discovered by the mammography examination.

The area under the ROC curve (AUC) characterizing the discrimination of benign and malignant lesions was calculated separately for each clinical site for each feature of the set $F_1$–$F_6$ as displayed in Fig. 2. This plot demonstrates the variability of diagnostic effectiveness of the analyzed features from site to site. We found that the average AUC value and standard deviation for feature $F_1 = 68.5.1 \pm 12.6\%$, $F_2 = 76.6 \pm 8.1\%$, $F_3 = 79.3 \pm 4.1\%$, $F_4 = 63.8 \pm 8.3\%$, $F_5 = 80.2 \pm 11.2\%$, and $F_6 = 77.4 \pm 6.9\%$.

Fig. 1 Benign-malignant paired boxplots for features $F_1$ through $F_6$. $F_1$, strain hardening; $F_2$, loading curve slope; $F_3$, max pressure signal; $F_4$, lesion shape; $F_5$, lesion mobility; and $F_6$, patient age

Fig. 2 Performance of discrimination between benign and malignant lesions separately for the four clinical sites in consideration of features $F_1$ through $F_6$. $F_1$—strain hardening, $F_2$—loading curve slope, $F_3$—max pressure signal, $F_4$—lesion shape, $F_5$—lesion mobility, and $F_6$—patient age
Pair correlation coefficients for features $F1$–$F6$ used in benign and malignant lesion differentiation are shown in Table 3. The correlation indicates 1 in the case of perfect linear relationship, −1 for a decreasing linear relationship, and another value in between 1 and −1 signifying the degree of linear dependence between the variables. The closer the coefficient is to either −1 or 1, the stronger the correlation between the features. If the features are independent then the correlation is 0, though the converse is not true since the correlation coefficient detects only linear dependencies between two variables. This table has diagonal symmetry, which is expressed by 1, given that each data set perfectly correlates to itself.

ROC curves constructed for each of the BMI parameters $F1$–$F5$ are shown in Fig. 3. Features $F3$ and $F5$ appeared to have the highest diagnostic information value with AUC of 79.4% with the 95% confidence interval (CI) from 72.7 to 85.1%. The least efficient single feature $F4$ has AUC of 60.9% with the 95% CI from 53.4 to 68.1%. The right bottom panel in Fig. 3 presents ROC curve for performance of discrimination between benign and malignant lesions for the Bayesian classifier output when the complete set of parameters $F1$–$F6$ for all 179 patients was used as input data of the classifier. The AUC is equal in this case to 86.1% with the 95% CI from 80.3 to 90.9% while a significance level $P = 0.0001$ for the area of 50%; sensitivity is equal to 87.5% with the 95% CI from 71.0 to 96.4 ± 12% (95% CI) and specificity 84.4% with the 95% CI from 77.5 to 89.8%. It is important to emphasize that clinical data from all four sites have been combined together. In addition, distributions for the lesion features calculated according to Eq. 8 are different from that for the data shown in Fig. 4 where all distributions have been calculated separately for each clinical site. Figure 3 includes the calculated 95% CI lines above and below the ROC curve.

Figure 4 presents the calculated sensitivity, specificity, and AUC for the output of the Bayesian classifier applied for differentiation of benign from malignant lesions for each clinical site. All $F1$–$F6$ features have been used as input parameters in this analysis as described in the method section. We found the sensitivity to range from 85.7 to 100%, specificity from 78.7 to 100%, and AUC from 83.4 to 100%.

Figure 5 demonstrates the sensitivity, specificity, and AUC values calculated as average values and as combined for the 179 patients. The left bar (averaged results) represents the clinical data from all four sites analyzed separately by the Bayesian classifier as shown in Fig. 3, thus the resulting data for sensitivity, specificity and AUC have been averaged. The right bar (combined data) presents clinical data from all sites used as an input data set for the Bayesian differentiation of benign from malignant lesions. All $F1$–$F6$ features have been used as input parameters in this analysis as described in the method section. The average sensitivity is $91.4 \pm 6.1%$ (±standard deviation), average specificity is $86.8 \pm 9.2%$, and AUC is $90.7 \pm 7.6%$.

### Discussion

As shown in Table 1, 219 patients were enrolled in the study at four clinical sites. A total of 40 patients were found not eligible and their data were excluded from the analysis. That constituted 18.3% exclusion with the largest exclusion due to the procedure deviations (13 patients or 5.9% of the total enrollment) and patients not returning for scheduled biopsy (13 patients or 5.9% of the total enrollment). The remaining 14 patients or 6.4% were excluded due to not meeting the protocol requirements. Sites 1 and 2 were only able of enroll a limited number of patients for the given period, 25 and 21 respectively, which cannot be considered reliable statistical samples. Nevertheless, the data combination from all four clinical sites (179 patients) represents a meaningful statistical population. The exclusion of 18.3% of enrolled patients cannot provide any bias because these 40 patients represent a statistically independent sub-population and related data were not analyzed due to the absence of pathology diagnosis.

It is important to emphasize that the BMI provided detection and image composition for all 179 subjects, including 9 with non palpable lesions. This observation supports an earlier conclusion that computerized palpation is more sensitive than a human finger [29–31].

Table 2 presents the breast pathology distribution among 179 cases. The benign group is subdivided into 11 categories, which were not uniform among all clinical sites. In total, the largest benign categories were fibroadenoma (37 patients or 25.2%), cyst (26 patients or 17.7%), and fibrocystic changes (17 patients or 11.6%). More uniformity was found in the malignancy cases from each site with invasive ductal carcinoma diagnosed in 80% of site 1, 57.1% of site 2, 80% of site 3, and 70% of site 4. Invasive

### Table 3 Correlation coefficients for features $F1$–$F6$ used in the benign and malignant lesion differentiation

<table>
<thead>
<tr>
<th>Lesion features</th>
<th>$F1$</th>
<th>$F2$</th>
<th>$F3$</th>
<th>$F4$</th>
<th>$F5$</th>
<th>$F6$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$F1$</td>
<td>1</td>
<td>0.10</td>
<td>0.04</td>
<td>0.00</td>
<td>−0.12</td>
<td>0.14</td>
</tr>
<tr>
<td>$F2$</td>
<td>0.10</td>
<td>1</td>
<td>0.68</td>
<td>−0.31</td>
<td>−0.32</td>
<td>0.06</td>
</tr>
<tr>
<td>$F3$</td>
<td>0.04</td>
<td>0.68</td>
<td>1</td>
<td>−0.33</td>
<td>−0.33</td>
<td>0.13</td>
</tr>
<tr>
<td>$F4$</td>
<td>0.00</td>
<td>−0.31</td>
<td>−0.33</td>
<td>1</td>
<td>0.17</td>
<td>0.06</td>
</tr>
<tr>
<td>$F5$</td>
<td>−0.12</td>
<td>−0.32</td>
<td>−0.33</td>
<td>0.21</td>
<td>1</td>
<td>−0.16</td>
</tr>
<tr>
<td>$F6$</td>
<td>0.14</td>
<td>0.06</td>
<td>0.13</td>
<td>0.06</td>
<td>−0.16</td>
<td>1</td>
</tr>
</tbody>
</table>

© Springer
Ductal carcinoma was diagnosed in 23 out of 32 malignant cases or 71.9%, which bears close to the screening results received for 1 million women—58.9% of invasive ductal carcinoma or 3215 cases from 5458 total detected malignant cases [32]. The breast pathology distribution observed in this study is in agreement with the data received from large scale screening and research trials [1, 2, 4, 18, 19].

Features $F_1$ through $F_3$ are related to the lesion hardness characterization. The increased hardness of a tissue correlates with the presence of cancer in the tissue as confirmed by various elasticity imaging techniques [33]. Measurements of excised breast specimens exhibited that normal breast tissue has a modulus that was noticeably lower than the modulus of the breast cancer tissue. Tumors or a tissue
blocked from receiving blood nutrients are stiffer than normal tissue. Benign and cancerous tumors were also shown to have distinguishing elastic properties [34–36].

Both Fig. 1 and 2 demonstrate the limited discrimination capability of the selected features being analyzed individually due to possible influence by numerous factors, such as breast lesion location, its depth, breast size, and deviation in the examination technique. The averaged values of AUC for features F1–F5 calculated for four clinical sites vary from 64.3 to 80.0%. We can conclude that the confidence intervals of benign and malignant patient samples for features F2 (loading curve slope), F3 (maximum lesion signal for the fixed force applied to the probe), and F5 (lesion mobility) are not overlapped and in agreement with the relatively increased value AUC of 76.6, 79.3, and 80.2%, respectively. However, a relatively decreased AUC of 68.5 and 63.8% is seen for features F1 (strain hardening) and F4 (lesion shape) and their confidence intervals for benign and malignant boxplots have certain intersections.

Two features, strain hardening and lesion mobility, revealed standard deviations of 12.6 and 11.2% and ranged from 60.7 to 87.1% and from 73.8 to 91.9%, respectively. The relatively high variance of strain hardening F1 might be explained by sensitivity to deviations in the examination procedure and the significant range of tissue deformation (up to 30%) under the probe manipulation. The lesion mobility variance might also be explained by operator specific deviations in examination procedure. We believe that more detailed instructions and extended training of the operators, as well as real time feedback signaling on deviations in the examination technique, will increase the accuracy and robustness of the procedure.

The correlation coefficients calculated for features F1–F5 demonstrate a low linear correlation (<0.35), except for the F2–F3 pair of 0.68 (see Table 2). We anticipated that these two features would correlate at a more notable level due to the larger value of F2, which would definitely cause an increase in the value of F3. The decrease in the F2–F3 correlation is observed in the beginning of the loading curve, which is plotted as the pressure maximum signal from the lesion versus the total applied force to the probe. We set the range for the initial part of the loading curve as 0–5N of the total force. Initially, the loading curve exhibits substantial nonlinearity that is not taken into account in the F2 calculation, but is incorporated into the F3 feature. Furthermore, with the addition of feature F3 into input parametric set of the Bayesian classifier, the lesion diagnostic accuracy and the confidence interval of AUC appeared to be better.

The F4 value characterizing the lesion shape for malignant lesions decreases relative to the benign lesions as it follows from Fig. 1. This reflects the fact that the shape of a harder core of a malignant lesion is closer to spherical than a benign lesion. The lesion mobility F5 for malignant lesions is decreased relative to the benign lesions (Fig. 1). As we mentioned in the method section, this parameter integrates not only lesion mobility, but also its deformability during the probe pressing against the lesion. Intuitively, this result might be anticipated since the
malignant lesion must be more conservative and stable in these terms. It seems reasonable that $F5$ has mild correlation coefficients of $-0.32$ and $-0.33$ with $F2$ and $F3$.

Aside from the gender, age is the most important factor affecting breast cancer risk [20]. The patient age $F6$ demonstrated a clear divergence between the benign and malignant patients (see Fig. 1). The correlation coefficients of the patient age with features $F1$–$F5$ ranged from 0.16 to 0.14. This result confirms the weak correlation of patient age with other features, a fact which enhances its significance and usefulness as an additional independent coordinate in a multidimensional space for classification. Therefore, we have decided to incorporate this feature into the benign-malignant classifier.

A combined multi-parameter assessment composed of relatively low correlated parameters increases the discriminating power of BMI binary lesion classification. It might be seen in Fig. 3 where we represented ROC curves for BMI parameters $F1$ through $F5$ and ROC curve for the Bayesian classifier output (right bottom). Averaged value of AUC for parameters $F1$ through $F5$ is 73.5%. Combining these five BMI parameters by means of the Bayesian classifier the diagnostic accuracy is increased in averaged by 11.3%, from 72.3 to 83.6%. Additional increase by 2.5% was provided by taking into account patient age $F6$ as the input parameter for the classifier. The feature combination decreases the confidence interval for diagnostic accuracy relative parameter $F1$ through $F5$ alone as it might be concluded from Fig. 3. On average, the confidence interval is narrowing from 13.3% for single feature to 10.6% which is also beneficial effect of features combination.

Figure 4 demonstrates the differentiation capability for benign and malignant lesions with the use of the Bayesian classifier in the case when the data have been analyzed separately for each clinical site. The variability of diagnostic accuracy from clinical site to site might be explained by deviations in the nature of patient groups enrolled at the sites, especially among the patients with benign findings. The diagnostic accuracy calculated as average values for the four clinical sites exceeds the diagnostic accuracy calculated for the combined 179 patients, as it clearly seen in Fig. 5. This difference is 3.9% for sensitivity, 2.4% for specificity, and 4.5% for AUC. That means that the Bayesian classifier can discriminate more accurately among data sets in which the data is separated into groups (clinical sites) than those in which all patient data are combined together.

It is well recognized in the literature that the tissue elastic properties provide means for not only characterizing tissue but differentiating normal and diseased conditions. This conclusion is based on a wealth of data obtained in the studies on excised breast specimens [34, 35] and clinical studies conducted by numerous researchers worldwide [37–47]. We summarized in Table 4 recently published clinical results directly related to the breast benign–malignant

<table>
<thead>
<tr>
<th>No.</th>
<th>Method</th>
<th>Number of analyzed lesions</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Citation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>USE*</td>
<td>52 malignant</td>
<td>86.5</td>
<td>89.8</td>
<td>Itoh et al. [37]</td>
</tr>
<tr>
<td>2</td>
<td>USE</td>
<td>135 total</td>
<td>100.0</td>
<td>95.0</td>
<td>Zhang et al. [38]</td>
</tr>
<tr>
<td>3</td>
<td>USE</td>
<td>49 malignant</td>
<td>82.0</td>
<td>87.0</td>
<td>Thomas et al. [39]</td>
</tr>
<tr>
<td>4</td>
<td>MRE*</td>
<td>38 malignant</td>
<td>95.0</td>
<td>80.0</td>
<td>Sinkus et al. [40]</td>
</tr>
<tr>
<td>5</td>
<td>USE</td>
<td>88 total</td>
<td>96.0</td>
<td>61.0</td>
<td>Renger et al. [41]</td>
</tr>
<tr>
<td>6</td>
<td>USE</td>
<td>43 malignant</td>
<td>100.0</td>
<td>96.0</td>
<td>Barr [42]</td>
</tr>
<tr>
<td>7</td>
<td>USE</td>
<td>115 total</td>
<td>90.0</td>
<td>–</td>
<td>Garra et al. [43]</td>
</tr>
<tr>
<td>8</td>
<td>USE</td>
<td>50 malignant</td>
<td>99.3</td>
<td>25.7</td>
<td>Burnside et al. [44]</td>
</tr>
<tr>
<td>9</td>
<td>USE</td>
<td>237 malignant</td>
<td>97.5</td>
<td>48.0</td>
<td>Svensson et al. [45]</td>
</tr>
<tr>
<td>10</td>
<td>PI*</td>
<td>34 malignant</td>
<td>94.4</td>
<td>–</td>
<td>Kaufman et al. [46]</td>
</tr>
<tr>
<td>11</td>
<td>SSI*</td>
<td>4 malignant</td>
<td>100</td>
<td>100</td>
<td>Tanter et al. [47]</td>
</tr>
</tbody>
</table>

USE* ultrasound elastography, MRE* magnetic resonance elastography, PI* palpation imaging, SSI* supersonic shear imaging

---

Breast Cancer Res Treat
lesion differentiation by elasticity imaging. These data clearly demonstrate the significant diagnostic potential of elasticity imaging. The BMI data with a sensitivity of 91.4% and specificity of 86.8% is close to the results shown in Table 4. Notably, this accuracy level (AUC 91.4%) was reached using the more cost effective approach of Mechanical Imaging, rather than other elastography techniques [48]. Based on these findings, we hypothesize that the BMI has a potential to be used as a cost effective device for cancer detection as a diagnostic modality. We further hypothesize that the BMI can be used not only for binary classification but for calculating the probability distribution for multiple possible outcomes subdividing various benign and malignant classes, to distinguish between fibroadenoma, cyst, fibrosis, ductal, lobular carcinoma and other conditions.

Screening mammography is generally the recommended tool for breast cancer detection and is recognized throughout the world. The mammography results are used as the basis in making a decision about performing a biopsy at suspicious breast sites. In the United States alone, more than 1 million breast biopsies are performed annually and approximately 80% of these findings are benign [49, 50].

We simulated how the use of the BMI after standard screening procedures (mammography alone or combination of mammography and conventional ultrasound) could reduce the benign biopsy rate. Figure 6 shows the results of this simulation. Applying the BMI cancer sensitivity and specificity calculated for the combined data including 179 patients (147 benign, 32 malignant) to the patient sample referred for the biopsy (20% of which will be malignant and 80% benign), we built the dependence of the benign biopsy reduction (%) versus the percentage of missed cancers as shown in Fig. 6. These results indicate that a 23% reduction of the benign biopsy is possible without any missed cancer cases and a 50% reduction of the benign biopsy with 4.6% missed cancer cases. Category 3 BIRADS results in a 6 months follow up rather then a biopsy. About 1% of those are cancers. Anything over 1% is probably too high. Clearly, the decrease of the benign biopsy rate is accompanied by an increased proportion of missed cancers. This could be further mitigated by the recommended 3 or 6 months clinical follow up for all patients that were originally recommended for a biopsy but then diagnosed by the BMI as benign.

Conclusions

The multisite clinical study proved the capability of mechanical imaging for real time characterization and differentiation of benign and malignant breast lesions. The BMI has the potential to be used as a cost effective device for cancer diagnostics, and it could effectively reduce the benign biopsy rate. The BMI has the potential to be positioned as an adjunct to mammography and utilized as a screening device for breast cancer detection.

Acknowledgments

The authors would like to thank Ralph Tullo, MD, Breast Health Institute of Maitland, Florida, for his assistance in the clinical study. They also appreciate the engineering support of Milind Patel for the Breast Mechanical Imager. This work was supported by National Institute of Health under research grant CA091392 “Imaging Network for Breast Cancer Mass Screening”.

References

Digital documentation of the physical examination: moving the clinical breast exam to the electronic medical record

Cary S. Kaufman, M.D.\textsuperscript{a,b,\ast}, Leslie Jacobson, M.S.\textsuperscript{b}, Barbara A. Bachman, M.D.\textsuperscript{b}, Lauren B. Kaufman, M.D.\textsuperscript{b}

\textsuperscript{a}Department of Surgery, University of Washington, 2940 Squalicum Pkwy, Bellingham, WA 98225, USA
\textsuperscript{b}Bellingham Breast Center, Bellingham, WA, USA

Manuscript received April 7, 2006; revised manuscript June 16, 2006

Presented at the 7th Annual Meeting of the American Society of Breast Surgeons, Baltimore, Maryland, April 5–9, 2006

Abstract

\textbf{Background:} Documentation of the clinical breast examination (CBE) has consisted of simple hand-drawings and stick figures without a common lexicon. There is a need for a device that can accurately depict the CBE in digital format while being objective, reproducible over time, and usable in the electronic medical record. This new device is called palpation imaging (PI).

\textbf{Methods:} We examined 110 patients with a complaint of a breast mass using PI. This laptop-sized device creates a real-time digital display of the palpable area in both video and still formats. The size, hardness, shape, homogeneity, and mass location may be extracted from the image.

\textbf{Results:} Of those with a true mass, PI identified the mass in 94\% while physical examination identified 86\%. The positive predictive value (PPV) for breast cancer using PI was 94\% and 78\% for physical examination. A survey of primary care physicians revealed the inclusion of the PI record in a consultation note implied competence, experience, and skill by the surgeon.

\textbf{Conclusions:} PI documented the CBE in a timely, efficient, and accurate manner. A reproducible record allows objective review by multiple examiners at varied times. Continued work will optimize examination methods. © 2006 Excerpta Medica Inc. All rights reserved.

\textbf{Keywords:} Palpation imaging; Clinical breast exam; Breast imaging; Breast lump; Electronic medical record; Mammography; Ultrasound; Breast mass

While the last 20 years have seen major improvements in breast imaging [1–8], the documentation of the clinical breast examination (CBE) has remained unchanged since the Halsted mastectomy 100 years ago [9]. Surgeons record a verbal description of their palpable findings along with a handwritten drawing. The verbal description suffers from the spectrum of descriptive words without standardized definitions. Terms such as “fibrous,” “thickened,” “dense,” and “glandular” may all describe the identical breast texture and are user dependent. Likewise, a hand drawing or stick figure of a breast mass may be interpreted differently by different observers. These subjective drawings may not communicate the same examination to a second examiner or even to the same examiner at a later date. Drawings are not standardized or consistent, and the descriptions have no common lexicon. Estimated sizes of drawn masses are not consistently given in either text or drawings.

A need exists for a device that accurately and objectively depicts the CBE in digital format which is reproducible over time, and able to be uploaded into various electronic medical records. There exists now a new device that can be utilized by breast surgeons to accurately record the CBE of palpable lesions [10,11]. Using this device results in an imaging method called palpation imaging (PI). The target of the current study was the creation of a consistent repeatable digital image of the CBE that may accompany the clinician’s verbal description.

PI obtains a digital image of the CBE and stores it in one of several digital versions. PI captures the characteristics of the palpable findings, including the estimated size and shape, the degree of firmness relative to the surrounding breast tissue, and the homogeneity of the mass. Use of this
method may aid in the documentation of the CBE and augment the clinical record making it more versatile, reproducible, consistent, and electronically useable. This can be used for chart documentation, communication with other physicians, education for patients, and as a medical record for insurers or medicolegal purposes.

**Methods**

Between October 2003 and October 2005, 110 patients referred to our breast clinic with a chief complaint of a breast mass were examined. In addition to CBE, ultrasound, and mammograms, each patient underwent PI. Some young patients did not have mammography.

After PI examination, each record was segregated into one of two groups based on the PI findings alone: those with the findings of a dominant mass (e.g., cyst, benign or malignant tumor) and those without findings of a dominant mass (e.g., fibrocystic change or other normal breast tissue). Those with a dominant mass were further separated into those highly suspicious for cancer and those with palpable masses. Final histologic and/or follow-up data (minimum 6 months) was correlated with preoperative PI. Statistical analysis used the chi-square calculator from Georgetown University [12].

**Description of imaging device**

The cornerstone of this report is the development of an imaging device that translates palpation findings into a visual record [13]. To understand this device, it is necessary to deconstruct the CBE of a palpable mass. Upon finding a mass, the surgeon notes the location of the mass within the breast. Mass characteristics of size (in at least 2 dimensions), hardness, shape, and homogeneity are noted. PI re-creates the components of the CBE of a mass.

The palpation imager consists of a notebook computer-sized device attached to a broad-based transducer. After CBE targets a lesion, the transducer is passed over the palpable lesion. The transducer has almost 200 minute sensors able to record the pressure and location data. As the transducer scans, a real-time display of the palpable area is digitally recorded (Fig. 1). The transducer sensor data is converted to a color image in both 2- and 3-dimensional formats. Peak height of the image refers to increased firmness, while low height refers to less firm or soft tissues (Fig. 2). Images are reviewed to demonstrate the characteristics of size, hardness, shape, homogeneity, and location. The examination video and still-frame images are available for printed reports or single images may be incorporated into a consultation letter.

This palpation image can be translated into the components of the physical examination: size, hardness, shape, and homogeneity. The location within the breast is entered by the examiner (Fig. 3). The size of the lesion is demonstrated by the footprint seen on the image (Fig. 4). The hardness of a lesion is described by the absolute height of the peak.
pressure, as well as comparison of peak height to surrounding breast tissue height (surrounding breast firmness). The shape of the palpable findings may be demonstrated by a line drawn at an isobaric level surrounding the mass on a 2-dimensional image, seen as a black line in the examination result screen (Fig. 5). Homogeneity of the palpable mass is identified as the shape of the peaks within the image. Single smooth peaks are commonly seen in cysts and fibroadenomas, while images with multiple peaks within the mass suggest lobulations and nonhomogeneous masses such as cancers. PI reports describe all the building blocks of the CBE. This was not a blinded study but meant to identify any palpable abnormality and try to document its presence with PI. At no time was PI considered a substitute for biopsy, and biopsy should always be considered as the definitive test for the presence of breast cancer.

Physician survey

To assess the communication value of PI, sample breast consultations were sent out to a study set of 15 primary care referral physicians. Each of the referring physicians was provided breast surgical consultations on 3 different sample patients. All 3 had a chief complaint of a breast mass, each with a different cause; 1 had a palpable cancer, 1 had a benign palpable mass, and the third had an area of fibrocystic change.

Each sample patient was “examined” by 3 surgeons who provided different forms of consultations. Surgeon “A” wrote the consultation by longhand and included a hand-drawn picture of the palpable findings. Surgeon “B” typed the consultation in letter format without any drawings of the physical examination. Surgeon “C” also typed the consultation in letter format as surgeon “B,” but included a printed digital image and report of the physical examination using PI.

Each referral physician received 9 consultations in total, 3 on each of 3 patients. We asked each referral physician to rank the breast surgeons on each patient. Three questions were asked for each patient: (1) please rank these 3 breast surgeons in regards to their competence; (2) please rank these 3 breast surgeons in regards to their experience and innovation in the field of breast surgery; and (3) please rank these 3 breast surgeons in regards to their skill as a surgeon. Referring physicians were asked to avoid ties and to make choices as best as possible based on the submitted data.

Results

Table 1 of final diagnoses reveals the typical patient distribution seen in a breast clinic, including fibroadenomas, cancers, fibrocystic change, and cysts. Ninety-five of 110 patients were found to have lesions that might present as a mass as documented by pathology or other confirmatory tests. We included the patient with gynecomastia with this group. Although some of these lesions may be too small to detect, we considered these patients the potential pool of those with a dominant mass.

Each palpable finding on CBE was recorded as well as the PI results. After an initial learning curve, it was possible to recreate the digital image of the palpable findings. Because the surgeon obtained the digital image, an immediate
feedback process occurs while imaging. The surgeon can determine whether the image is a true representation of the palpable findings. During the examination, the surgeon may also examine the surrounding area with PI to confirm the absence of other palpable findings.

**Identifying dominant masses**

PI was used to separate patients into 2 groups: those identified with a mass and those without a mass. PI identified a dominant mass in 89/95 patients (positive predictive value [PPV] 94%). Physical examination identified 82/95 patients (PPV 86%). The sensitivity and specificity of identifying a dominant mass with PI were 88% and 88%, while the values were 81% and 81% for physical examination.

In addition, we examined clinically normal breast tissue without any mass to validate our assessment. Both methods were accurate in determining breast tissue without any mass. The negative predictive value of PI and for physical examination was 93% for both methods.

We tried to correlate the consistency of PI and CBE. For each category of PI, we noted the frequency of finding palpable masses. There was a direct correlation between the likelihood of palpating a mass on CBE and the PI firmness category, as noted in Fig. 6.

**Identifying breast cancer as a mass**

PI separated breast lesions into 4 categories: (1) those without a mass; (2) those with a soft mass; (3) those with a firm mass; and (4) those with a hard mass. Breast cancers were usually firm or hard with either a central single or multiple peaked image on PI. Of the 36 breast cancers examined, the PPV for PI was 94% and 78% for physical examination (Table 2). There were six cancers identified by PI that were not identified by physical examination (false negative rates of 6% and 22%, respectively).

**Fibroadenoma, cyst, lipoma, seroma**

PI of fibroadenomas, cysts and other benign oval nodules typically demonstrated a single smooth peak with a firm central mass. Of the 57 lesions in this group, we closely examined all fibroadenomas and cysts (n = 47) for evidence of these PI findings. All but 4 lesions (91%) demonstrated this classic PI pattern. The 4 lesions not visualized on PI included 2 cyst clusters and 2 small fibroadenomas.

PI may estimate size of the examined mass (Fig. 4). To assess the size correlation, we looked at the same group of fibroadenomas and cysts. Only 41 of 47 of these patients had an ultrasound measurement documented. We compared the length and width measurements as seen by palpation imaging with the ultrasound measurements. We classified the correlation as good when measurements on both PI and ultrasound were within 3 mm of each other. Those between 3 and 6 mm were considered fair, and those with a greater than 6-mm difference between the 2 measurements were considered poorly correlated. We found 32% of these patients had good correlation between PI and ultrasound measurements, while 46% varied by more than 6 mm between the 2 examinations. There was no difference between the ability of physical examination and PI to identify benign breast lesions (Table 3).

**Primary care responses**

Of the 15 clinicians surveyed, responses were received from 11. One clinician refused to respond due to concerns about commercial bias. Three others did not return their evaluation. Most clinicians favored the use of the typed consultation along with the PI report of surgeon “C.” They regarded this surgeon to have better “communication skills” and more “experience/innovation.” Of the responses received, 81% said surgeon “C” was the most experienced and 68% said he was the best communicator. Over 85% rated surgeon “A” as least experienced with the least communication skills. This was despite the fact that the written scripts were similar, essential findings were identical, and there was a neatly hand-drawn picture of the palpable find-
ings. The majority thought “surgical skill” could not be assessed via the consultation notes, although 25% said surgeon “C” was most skilled.

This may imply that a visual depiction of the palpable findings as in surgeon “A” is less important than the ease of communication. The hand-drawn consultation letter may have been harder to read than the typed consultation. Similarly, the typed consultation along with the clear picture of PI may have been easiest to see in a hurried primary care practice.

Comments

As a documentation device, PI has several benefits over current technology. Since the device is calibrated and standardized, the PI recordings will be consistent among several examiners. Serial examinations of the identical mass over time allows for the accurate documentation of change. PI accumulates a continuous video recording of the targeted mass and then identifies a single image that best represents the physical findings. This image can be uploaded into a Word file for a consultation letter or into an electronic medical record (EMR). The electronic version of the physical examination merges with the interest in the EMR. The clinical record is in the process of change [14]. Primary care, internal medicine, cardiology, and many specialties have converted to use of the EMR. Many practices are converting to an electronic format for many reasons, including ease of creation, ease of transmission and exchange/circulation, ease of storage, and cost.

It is typical for surgeons to have their initial consultation distributed as a letter to their referring physicians. This consultation letter typically does not include any hand drawings or figures of breast masses. In our physician survey, we note that the inclusion of a hand-drawn picture of the physical examination was not valued by the referring physicians. When the PI printed report was included, the referring physicians associated surgical experience and increased communication skills with the combined report. The addition of a digital image of the palpable findings may add a new dimension to the consultation of a breast surgeon.

Since the PI device acts as an independent observer of the CBE, the PI report may be valuable if the patient’s chart is reviewed by an outside party. For insurers who wish to confirm the CBE was performed, the PI report adequately documents that examination. For medicolegal purposes, the PI report can validate a clinician’s statement as to the findings on CBE. The PI examination can provide independent confirmation of the surgeon’s examination.

The palpation image provides the opportunity for clinical review at a later time. This is useful if the referring ultrasound or mammogram are not available. When the films return, comparison to the PI physical examination can occur. Another use for PI is to communicate the physical findings to the patient. The image of the palpable findings is readily understandable by interested patients. Although the CBE has not been demonstrated to impact survival from breast cancer [9], the lack of a common documentation method and lexicon may contribute to the inability to document CBE value.

The objective documentation of PI may help some medical clinics that may have several doctors seeing the same group of patients. Using PI, a patient with a palpable finding may be followed more objectively by a series of doctors. Poor communication may occur when one surgeon’s hand drawings of a breast mass is read by another surgeon. Radiologists commonly communicate this way using serial image documentation. This may also aid doctors who are providing vacation coverage and other part-time clinicians.

PI requires training and skill to obtain accurate images. This is similar to correct positioning and exposure in mammography or proper gain and focal zone in ultrasonography. The proper examining technique and applied pressure is required for optimal PI. Ultrasound has similar requirements to obtain an optimal image. Surgeons skilled at ultrasound examination of the breast are likely to have little difficulty learning the technique of PI.

The basic examination technique is similar to the movements associated with breast ultrasound examination. Mechanical adjustments of the device are few. Calibration is required regularly but not daily. Since the device is the size of a laptop computer, it easily moves from one examination room to another. The creation of an initial image takes just minutes after the examiner identifies a lesion. Several images are obtained to confirm an accurate depiction has been obtained. Automatic storing of images occurs after the demographic information has been entered into the system. Recalling a previous examination is similar to opening a stored computer file.

The PI device is relatively inexpensive in relation to all other forms of imaging, being less costly than an entry-level portable ultrasound device. With the PI device comes the ability to document lesions, the ability to create and print a completed report of the CBE, and image storage for use later or inclusion in the EMR. Although reimbursement is not currently available for the use of this device, it adds value to the practice. This is similar to the cost of computerizing one’s office or converting to an EMR that is not reimbursed but adds value to the medical practice. Larger studies examining the impact of standardized CBE will hopefully answer the question of clinical value.

There are some disadvantages of the PI device, including no insurance reimbursement for this examination. Like other new technologies, reimbursement may follow at a
later date. Because PI is new, it will be necessary for other centers to validate and enhance the findings in this report.

We noted some instances of PI examinations were consistent with the eventual pathologic findings. Very large cancers over 4 cm in size cannot be easily examined since there is no normal tissue to compare within the 4-cm probe area. The firmness of a large cancer will be viewed as an overall elevation of the baseline, since the entire surface under the PI transducer has similar hardness.

The other end of the spectrum is also difficult to image. Very small cancers that are not palpable on CBE may or may not be demonstrated on PI. A lower threshold of PI imaging capability exists that is dependent on many factors. These include the absolute hardness of the small tumor, the size of the breast, and the depth of location of the tumor. Small firm tumors that are closer to the skin surface in smaller breasts are easier to image even when not palpable on CBE.

A third group of breast cancers that may be difficult to identify are tumors with soft consistency. Colloid carcinomas or other low grade tumors that have little growth intensity may be difficult to visualize. These tumors, which are primarily found in older patients, may have similar firmness to surrounding breast tissue.

There are several clinical components that cannot be translated into a mechanical device. The palpation imaging device must be placed over the mass in question. This is similar to limitations of breast ultrasound. When an ultrasound sensor is placed on a surgical scar, the hypoechoic shadowing area will appear suspicious for cancer, even though it is typical surgical scar. The examiner must notify the ultrasonographer that the transducer is overlying the surgical scar. Likewise, PI will report the firmness of any lesion examined without the ability to know what portion of the body is being examined.

Similarly, placing the PI device directly on an exposed rib will create an image of an elongated hard mass. Although this may be an accurate representation of a rib, the device will document the palpable findings only. The examiner is responsible to identify the location that the probe is examining.

Additionally, exophytic skin lesions such as moles or the true nipple will give a palpable image of a mass. The examiner must note the presence of skin lesions or location of the nipple as is commonly included during mammography imaging.

This imaging device is intended to be used for documentation of the CBE and improved communication. With further research and experience, it may be possible to use the PI device to aid in the clinical grouping of palpable breast disorders. Characteristics of benign and malignant masses may be teased out of the data obtained from multiple examinations and may aid the breast surgeon in the future.

Conclusions

We describe the use of a unique tabletop PI device that documents palpable breast masses with high sensitivity and specificity. Patients with truly palpable masses (cancers, benign tumors, and firm cysts) were found to have increased firmness (decreased elasticity), while those with nodular breast tissue (fibrocystic change) had less firmness. The use of PI allowed initial separation between benign and suspicious truly palpable masses. A reproducible record of the breast physical examination is created that allows objective review by multiple examiners at varied times. Further work is necessary to optimize examination methods, improve real-time software interpretation, and define the array of diagnostic capabilities.

References

Cost-Effective Screening for Breast Cancer Worldwide: Current State and Future Directions

A. Sarvazyan¹, V. Egorov¹, J.S. Son² and C.S. Kaufman³

¹Artann Laboratories, 1459 Lower Ferry Rd., Trenton, NJ 08618, U.S.A. ²Medical Tactile, Inc., 5757 Century Blvd., Suite 600, Los Angeles, CA 90045, U.S.A. ³Department of Surgery, University of Washington, 2940 Squalicum Pkwy, Bellingham, WA 98225, U.S.A.

Abstract: Affordability of healthcare is highly limited by its skyrocketing cost. Access to screening and diagnostic medical equipment and medicine in developing countries is inadequate for the majority of the population. There is a tremendous worldwide need to detect breast cancer at its earliest stage. These needs must be balanced by the ability of countries to provide breast cancer screening technology to their populations. We reviewed the diagnostic accuracy, procedure cost and cost-effectiveness of currently available technique for breast screening and diagnosis including clinical breast examination, mammography, ultrasound, magnetic resonance imaging, biopsy and a new modality for cancer diagnostics termed elasticity imaging that has emerged in the last decade. Clinical results demonstrate that elasticity imaging even in its simplest and least sophisticated versions, like tactile imaging, has significant diagnostic potential comparable and exceeding that of conventional imaging techniques. In view of many countries with limited resources, effective yet less expensive modes of screening must be considered worldwide. The tactile imaging is one method that has the potential to provide cost-effective breast cancer screening and diagnostics.

Keywords: breast cancer, screening, cost-effectiveness, elastography

Introduction

Affordability of healthcare is highly limited by its skyrocketing cost. Access to screening and diagnostic medical equipment and medicine in developing countries is inadequate for the majority of the population. More than 70% of all cancer deaths occur in low and middle income countries, where resources available for diagnosis, prevention, and treatment of cancer are limited or nonexistent[1, 2]. One of reasons for rapid escalation of the healthcare costs is an application of new advanced techniques for diagnostics, treatment and prevention which often is not cost-effective. For example, Medicare’s reimbursement system is establishing the minimum reimbursement for mammography services as 81.86 USD for film and 131.50 USD for digital bilateral screening mammography[3] which corresponds to 60.6% increase in the procedure cost. Despite such an increase of costs, the improvement of diagnostic accuracy of digital relative to film mammography is not significant. The overall diagnostic accuracy in a large-scaled clinical study was found of 0.78 ± 0.02 for digital mammography and of 0.74 ± 0.02 for film mammography (difference 0.03; 95% confidence interval, −0.02 to 0.08; P = 0.18)[4]. Digital mammography, compared with film, would cost more than 300,000 USD per quality-adjusted life-year gained, which is not cost effective[5]. These and other similar data indicate that there is an urgent need in cost effective screening and diagnostic methods for breast cancer, making it affordable all around the world[6].

Current Screening and Diagnostic Methods

Current methods of breast screening and diagnosis include Breast Self-Examination (BSE), Clinical Breast Examination (CBE), Mammography, Ultrasound, Magnetic Resonance Imaging (MRI), and biopsy. Other breast screening methods which are currently in an exploratory stage include: tomosynthesis, supersonic shear wave imaging, electrical impedance tomography, optical tomography, and several second line breast pathology diagnostic techniques such as positron emission tomography and scintimammography.
BSE
The studies of the effectiveness of BSE as a detection modality has shown mixed results, but recent data reviews have focused on the lack of direct benefit in randomized clinical trials[7–9]. The studies found no reduction in the breast cancer mortality but higher rate of benign biopsy, in women who regularly perform BSE compared to women who do not regularly perform BSE [8]. Although the American Cancer Society no longer recommends that all women perform monthly BSE, women are recommended to be informed about the potential benefits (self-awareness) and limitations (false-positive rate) associated with BSE. Women who detect their own breast cancer usually find it outside of a structured breast self-exam while bathing or getting dressed. A woman who wishes to perform periodic BSE should receive instruction from her health care provider and/or have her technique reviewed periodically[10].

CBE
The premise underlying CBE is utilizing a trained clinician to visually inspect and palpate the breast in order to detect abnormalities to find palpable breast cancers at an earlier stage[11]. American Cancer Society guidelines recommend an annual CBE for age 40 and older for early detection of breast cancer in asymptomatic women[10]. The CBE may identify some cancers missed by mammography[12, 13] and provide an important screening tool among women for whom mammography is not recommended or who do not receive recommended high-quality screening mammography. At the same time, CBE performance, reports and documentation are inconsistent and not standardized. Health care providers report a lack of confidence in their CBE skills and would welcome training and practical recommendations for optimizing performance and reporting[14].

Data from six studies examined by Barton et al. resulted in an overall estimate of 54.1% for CBE sensitivity and 94.0% for CBE specificity[15]. Over 20 years ago, Haagensen [16] estimated that 65% of 2,198 breast cancer cases, identified before the use of screening mammography, presented as a breast masses detected by BSE or CBE. These findings are comparable to the published values for CBE sensitivity (58.8%) and specificity (93.4%) observed in the U.S. national screening program for 752,081 CBE reports[17]. The CBE cost effectiveness in cancer screening is 3.5 fold better than that of mammography[18]. The CBE detects only 34% fewer breast cancers than mammography, as it was demonstrated for population of 1 million women and the cost-effectiveness of biennial CBE is evaluated as 522 USD per life-year saved in India [18]. From this point, CBE may be a suitable option for countries in economic transition, where incidence rates are on the increase but limited resources do not permit screening by mammography.

In Japan, for women aged 40–49 years, having the highest incidence rate of breast cancer, the cost-effectiveness of annual CBE per life-year was evaluated as 31,900 USD[69].

Mammography
Mammography provides X-ray images of the breasts with at least two sets of images, the mediolateral oblique and cranial-caudal views. A recent large-scale clinical study (42,760 patients in U.S.A. and Canada) on the diagnostic performance of mammography for breast-cancer screening demonstrated a sensitivity of 70.0%, specificity of 92.0%, and diagnostic accuracy interpreted as AUC of 78.0%[4]. The European randomized mammography screening trial (23,929 patients in Norway) revealed a sensitivity of 77.4% and specificity of 96.5% at full-field digital mammography. The median size of screening-detected invasive cancers was about 13.5 mm[19]. In the United States, despite the recommendation for an annual mammogram, in 2005 only 47.8% of women aged 40–49 years had a mammogram within the past year. Among the women without health insurance coverage this value decreases to 24.1% [10]. The cost-effectiveness screening film mammography are estimated as 902–1,946 USD per year of life saved in India, 2,450–14,790 USD per year of life saved in Europe, and 28,600–47,900 USD per year of life saved in U.S.A.[6]. Among the limitations of mammography are increased breast density, technical factors, e.g. areas adjacent to the chest wall may not be imaged[20], lack of insurance coverage, disagreements among primary care physicians on frequency of mammographic screening, variation in interpretation skills of radiologists.

The mean glandular radiation dose from 2-view mammography is approximately 4 to 5 mGy and the dosage varies among facilities and increases with breast density. The average cumulative exposure from screening during the decade will be
around 60 mGy[70]. There is a strong linear trend of increasing risk of radiation-induced breast cancer with increasing radiation dose (P = 0.0001) [71]. A statistically significant increase in the incidence of breast cancer following radiation treatment of various benign breast diseases was observed[72]. Several recent studies suggesting that carriers of pathogenic alleles in DNA repair and damage recognition genes may have an increased risk of breast cancer following exposure to ionizing radiation, even at low doses[73]. Based on review of 117 studies related to screening mammography the authors concluded that “the risk for death due to breast cancer from the radiation exposure involved in mammography screening is small and is outweighed by a reduction in breast cancer mortality rates from early detection.”[74].

**Ultrasound**

Ultrasoundography as an imaging tool uses sound waves that pass through breast tissue and are reflected back characterizing tissue structure. Ultrasoundography is typically used as a complementary method for the assessment of mammographically or clinically detected breast masses and for supplemental information on dense tissue[11]. However, there is limited data supporting the use of ultrasound in breast cancer screening as an adjunct to mammography[21]. The conventional ultrasound is more often used to evaluate an area of concern on mammogram. The majority of cystic masses are benign while solid masses need further evaluation[22]. Ultrasound is often confused as a screening tool by both patients and healthcare providers. However, ultrasonic screening the entire breast is not only labor-intensive, but operator-dependent; therefore, ultrasound is a difficult tool to use if there is not an identifiable area of concern. Ongoing studies are trying to determine whether there is a population of women who would benefit from an ultrasonic screening; however, at this time, it is not the standard of care and whole-breast ultrasonography for screening has not been established as useful[23]. The cost associated with unilateral or bilateral ultrasound diagnostic procedure is 70.11 USD according to 2005 U.S. average Medicare reimbursements[5].

**MRI**

MRI utilizes magnetic fields to produce detailed cross-sectional images of the breast tissue. Image contrast between tissues in the breast (fat, glandular tissue, lesions, etc.) depends on the mobility and magnetic environment of the hydrogen atoms in water and fat that contribute to the measured signal that determines the brightness of tissues in the image. Many indications for clinical breast MRI are recognized, including resolving findings on mammography and staging of breast cancer[22]. Overall, the results of 6 nonrandomized prospective studies in the Netherlands[24], the United Kingdom[25], Canada[26], Germany[27], the United States[28], and Italy[29] of MRI efficacy in breast cancer screening for high risk women populations demonstrate an averaged sensitivity of 87.5% and specificity of 92.8%. Only limited data are available on the cost effectiveness of breast MRI screening being combined with mammography. The cost per quality-adjusted life year saved for annual MRI plus film mammography, compared with annual film mammography alone, varied by age and other factors to be found in the range of 27,544–130,420 USD. The reimbursement for bilateral MRI diagnostic procedures was 1,037 USD according to 2005 U.S. average Medicare reimbursements, which is about eight times higher than the screening mammography[5] and out of pocket charges by private clinics are as much as 5 times higher.

**Ultrasound and MR elasticity imaging**

In the last decade a new modality for cancer diagnostics termed Elasticity Imaging (EI) has emerged. EI allows visualization and semi quantitative assessment of mechanical properties of soft tissue. Mechanical properties of tissues, i.e. is elastic modulus and viscosity, are highly sensitive to tissue structural changes accompanying various physiological and pathological processes. A change in Young’s modulus of tissue during the development of a tumor could reach thousands of percent [30–32]. EI is based on generating a stress in the tissue using various static or dynamic means and measuring resulting strain by ultrasound or MRI [33–39]. The current increasing flow of publications from many countries all over the world on Elastography covers practically all key human organs[40–46].

**Tactile imaging**

Tactile Imaging (TI), an alternative version of Elasticity Imaging, yields a tissue elasticity map, similarly to other elastographic techniques. At the
same time, TI, which is also called “stress imaging” or “mechanical imaging” [56–61], most closely mimics manual palpation, since the TI probe with a pressure sensor array mounted on its face acts similar to human fingers during clinical examination, slightly compressing soft tissue by the probe.

There are limited clinical data on diagnostic/screening potential of breast TI. In one clinical study that included 110 patients with a complaint of a breast mass, TI demonstrated detection of 94% of the breast mass, while physical examination identified only 86%[57]. The positive predictive value for breast cancer using TI was 94% and 78% for physical examination. Clinical results of another study for 187 cases, collected at 4 different clinical sites, have demonstrated that TI produces a reliable image formation of breast tissue abnormalities with increased hardness and calculation of lesion features[60]. Malignant breast lesions (histologically confirmed) demonstrated increased hardness and strain hardening as well as decreased mobility and relative boundary length in comparison with benign lesions. Statistical analysis of the TI differentiation capability for 154 benign and 33 malignant lesions revealed an average sensitivity of 89.4% and specificity of 88.9% with a standard deviation of ±7.8%. The area under the receiver operating characteristic curve characterizing benign and malignant lesion discrimination was 87.8% with the confidence interval range from 82.1% to 92.1%, with a significance level P = 0.0001.

In Table 1 we summarized recent clinical results on benign/malignant breast lesion differentiation by various elasticity imaging modalities: USE—Ultrasound Elastography, MRE—Magnetic Resonance Elastography and TI. These data show that elasticity imaging even in its simplest and least sophisticated versions, like TI, has significant

<table>
<thead>
<tr>
<th>No.</th>
<th>Method</th>
<th>Number of analyzed lesions</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Citation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>USE*</td>
<td>52 malignant</td>
<td>86.5%</td>
<td>89.8%</td>
<td>Itoh A, et al. 2006 [47]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>59 benign</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>USE</td>
<td>135 total</td>
<td>100.0%</td>
<td>95.0%</td>
<td>Zhang XF, et al. 2006 [48]</td>
</tr>
<tr>
<td>3</td>
<td>USE</td>
<td>49 malignant</td>
<td>91.8%</td>
<td>91.5%</td>
<td>Thomas A, et al. 2006 [49]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>59 benign</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>MRE*</td>
<td>38 malignant</td>
<td>95.0%</td>
<td>80.0%</td>
<td>Sinkus R, et al. 2006 [50]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30 benign</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>USE</td>
<td>88 total</td>
<td>96.0%</td>
<td>61.0%</td>
<td>Renger DM, et al. 2006 [51]</td>
</tr>
<tr>
<td>6</td>
<td>USE</td>
<td>43 malignant</td>
<td>100.0%</td>
<td>96.0%</td>
<td>Barr RG, 2007 [52]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>150 benign</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>USE</td>
<td>115 total</td>
<td>90.0%</td>
<td>–</td>
<td>Garra BS, et al. 2006 [53]</td>
</tr>
<tr>
<td>8</td>
<td>USE</td>
<td>50 malignant</td>
<td>99.3%</td>
<td>25.7%</td>
<td>Burnside ES, et al. 2007 [54]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>48 benign</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>USE</td>
<td>237 malignant</td>
<td>97.5%</td>
<td>48.0%</td>
<td>Svensson WE, et al. 2007 [55]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>584 benign</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>TI*</td>
<td>34 malignant</td>
<td>94.4%</td>
<td>–</td>
<td>Kaufman CS, et al. 2006 [57]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>76 benign</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>TI</td>
<td>33 malignant</td>
<td>89.4%</td>
<td>88.9%</td>
<td>Egorov V, et al. 2008 [60]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>154 benign</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>SSI*</td>
<td>4 malignant</td>
<td>100.0%</td>
<td>100.0%</td>
<td>Tanter M, et al. 2008 [75]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11 benign</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

USE*—Ultrasound Elastography, MRE*—Magnetic Resonance Elastography, TI*—Tactile Imaging, SSI*—Supersonic Shear Imaging.
diagnostic potential comparable and exceeding that of conventional imaging techniques such as mammography, MRI and ultrasound.

Biopsy

Although the most of women who undergo screening each year do not have breast cancer, about 5%–10% of women have their mammogram interpreted as abnormal or inconclusive until further tests are done. In most instances, additional tests (imaging studies and/or biopsy) lead to a final interpretation of normal breast tissue or benign [10]. In the United States alone, more than 1 million breast biopsies are performed annually and approximately 80% of these findings are benign[62, 63]. In general, the biopsy diagnostic cancer sensitivity varies from 91% to 100% (in average 96.6%) for 8 clinical trials, and depends on biopsy type (needle, core, or surgical) and used image–guided technique (X-rays, ultrasound, MRI)[64]. The evaluations of cost effectiveness of biopsy are extremely diverse depending on biopsy type, used technique, and accepted model; it is varying from 2,250 USD to 77,500 USD per life year saved [65, 66]. The cost associated with biopsy diagnostic procedure is in average about 1,000 USD, changing from 456 USD for fine needle aspiration biopsy to 2,061 USD for open biopsy, according to 2005 US average Medicare reimbursements[5].

Cost-Effectiveness of Breast Cancer Screening and Diagnostic Methods

About 80% of the 1.6B women live in developing countries and 70% of breast cancer related deaths occur in these regions [2]. However, less than 10% of mammograms are conducted in these developing regions (Fig. 1) [67].

Diagnostic efficacy is certainly an important measure, but affordability is another critical factor which needs to be considered. Based on data from [62] we see that the adoption of mammography is strongly correlated with physician income and consequently much more utilized in developing counties. As Figure 2 shows, the number of mammography equipment in comparison to number of physicians that perform CBE is close to 20% in U.S.A. but less than 0.25% in India.

Table 2 presents a summary of breast cancer screening/diagnostic efficiency for various techniques, procedure cost and cost-effectiveness numbers. The cost-effectiveness data listed in the table are mostly taken from published sources. We included the range for cost-effectiveness for
analyzed modalities in the Table 2 because the specific data depend on accepted population-based model simulating histories of women, which, as a rule, include breast cancer natural history, breast cancer detection capability of the modality, breast cancer treatment, and competing-cause mortality. Different authors often use different models for the cost-effectiveness evaluation.

The 'gold standard' in cancer diagnostics, biopsy, demonstrates the highest diagnostic accuracy close to 100%. It costs in average over 2,000 USD for one analyzed breast lesion/location. The biopsy cost-effectiveness varies from 2,250 USD for developing countries to 77,500 USD for developed countries. The cost-effectiveness of biennial film mammography screening is evaluated as

<table>
<thead>
<tr>
<th>Screening/Diagnostic technique</th>
<th>Sensitivity/Specificity, %</th>
<th>Procedure cost of lateral exam, USD</th>
<th>Cost-effectiveness, USD per life year gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBE</td>
<td>56.5/93.7</td>
<td>–</td>
<td>522, India [7]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>31,900, Japan [69]</td>
</tr>
<tr>
<td>Mammography</td>
<td>73.7/94.3</td>
<td>112*</td>
<td>1,846, India [7]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>26,500–331,000 [5]</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>Limited, see text</td>
<td>70*</td>
<td>–</td>
</tr>
<tr>
<td>MRI</td>
<td>87.7/92.8</td>
<td>1,037*</td>
<td>55,420–130,695 [68]</td>
</tr>
<tr>
<td>Biopsy</td>
<td>96.6/100.0</td>
<td>2,061**</td>
<td>2,250–77,500 [65, 66]</td>
</tr>
<tr>
<td>Elasticity Imaging</td>
<td>95.1#/73.4</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Tactile Imaging</td>
<td>91.9###/88.9</td>
<td>5–50###</td>
<td>162###</td>
</tr>
</tbody>
</table>

*a the U.S. average Medicare reimbursements in 2005;  
**in average for one biopsy;  
***projections based on a physician’s assistant performing the exam;  
#averaged for 9 clinical studies;  
##averaged for 2 clinical studies.  

Figure 2. Relative cost of mammography equipment vs. physician adoption.
1,846 USD per life-year saved in India[18]. In the United States, the selective use of digital mammography screening for women aged 40 years or older had costs per quality adjusted life-year (QALY) ranging from 26,500 USD for age-targeted digital mammography to 84,500 USD for age- and density-targeted digital mammography. All-digital mammography screening was also more costly and no more effective than age-targeted digital mammography. The cost per QALY gained for all-digital mammography relative to all-film mammography screening was 331,000 USD (Confidence interval, 268,000 USD to 403,000 USD)[4].

Using cost-effectiveness of biennial CBE, 522 USD per life-year saved in India[18], one can estimate the impact of TI using CBE data. Taking 92% TI cancer sensitivity, which is 62% higher than CBE, may result in proportional improvement in TI cost-effectiveness. Further, the TI examination may be performed by a nurse or qualified technician, rather than a physician, which may additionally improve the cost effectiveness by a factor of two. As a result, we may expect TI cost effectiveness for developing countries to be equaled to 162 USD (in prices of 2001), which is over ten times more cost-effective than film mammography. A rough estimate shows that the TI procedure could cost about 5 USD in developing countries and 50 USD in the United States. In addition, clinical results indicate that TI screening may substantially decrease the benign biopsy rate[60].

**Conclusions**

There is a tremendous worldwide need to detect breast cancer at its earliest stage. These needs must be balanced by the ability of countries to provide breast cancer screening technology to their populations. We reviewed the current available screening and diagnostic techniques with their relative cost-effectiveness ratios. In view of many countries with limited resources, effective yet less expensive modes of screening must be considered worldwide. Tactile imaging is one method that has the potential to provide cost-effective breast cancer screening and diagnostics.

**Acknowledgment**

This work was supported in part by National Institute of Health under grants CA094444 “Use of a tactile breast imager for mass prescreening” and CA091392 “Imaging network for breast cancer mass screening”.

**References**


# SureTouch: Clinical Papers

## TABLE OF CONTENTS

- Development of a Device for Documenting the Clinical Breast Exam .................................................p3
- Cost Effective Screening for Breast Cancer Worldwide: Current State and Future Directions ...............................................................p4
- Digital Documentation of the Physical Examination: Moving the Clinical Breast Exam to the Electronic Medical Record ........p12
- Differentiation of Benign and Malignant Breast Lesions by Mechanical Imaging ..............................p18
Developing a Device for Documenting the Clinical Breast Exam Using a Capacitive Tactile Array Sensor

David C. Ablès1, Jae S. Son1, Vladimir Egorov2, Armen P. Sarvazyan3
1Medical Tactile, Inc., Los Angeles, CA; 2Artann Laboratories, West Trenton, NJ

Background
Clinicians have long depended on their sense of touch to assess tissue abnormalities, both benign and malignant. For the evaluation of the breast, this has been formalized into the clinical breast exam (CBE), where an examiner uses his/her sense of touch to detect breast masses. Despite the ubiquitous use of the CBE, the sense of touch is a subjective tool, leading to concerns about repeatability and reproducibility. During the last decade several objective techniques for assessing tissue hardness, or elasticity modulus, have emerged, with Ultrasonic Elastography and Magnetic Resonance Elastography being the most promising. The wealth of data obtained by these techniques during the last few years has clearly demonstrated that measurements of elastic properties of tissue could be used to detect and differentiate benign and malignant breast lesions and have a potential for dramatically reducing the number of unnecessary breast biopsies.1 If the CBE were more quantitative and objective, it may then yield diagnostic benefits.

Electronic Palpation Imaging
An innovative technology called electronic palpation imaging (EPI) uses an array of tactile sensors mounted on a handheld probe. As the probe is pressed against the breast, the tactile array captures varying reaction pressures caused by differences in tissue hardness. Salient feature data such as lesion size, shape, and hardness are quantified using sensitive electronics and advanced algorithms.

EPI Device Design History
An early EPI device was developed based on a piezoresistive tactile array sensor design. However, sensor performance and other concerns required the use of a magnetic position tracking system, resulting in a large, complex, and expensive cart-based system. A new design was required with improved sensor performance and a smaller form factor.

EPI Device Current Design
As part of a general redesign effort, the piezoresistive array was replaced with a capacitive-based tactile array sensor to improve performance and the entire system was shrunk down to a small notebook form factor. Using the capacitive tactile sensor, the performance was significantly improved, thus eliminating the need for the 3D positioning system, and the small, portable unit was simpler and easier to use. The user interface also underwent extensive changes based on feedback from physicians and users. Continued development is underway to improve the device performance, as well as minimizing the electronics to allow for an eventual prescription handheld device for use in the home.

Materials & Methods
We performed two studies using an EPI device currently FDA cleared for documentation purposes. In the first study, EP was used to examine two sets of 3 phantoms. One set differed only in size, ranging from 11-19 mm in diameter, while the second did not only in hardness, ranging from 30-500 kPa. All six phantoms were examined five times. In the second study, 6 different users examined the same phantom in order to evaluate repeatability and precision across different users. This was repeated with a total of four different phantoms differing in both size and hardness for a total of 24 sets of measurements. Users were given only basic instruction on how to use the device and were asked to use an exam force of 1.2-1.3 kg to remain consistent with one another.

Multi-User Study
When compared across multiple users, the EP data was found to be statistically similar both to itself and to the single-user data. The standard deviation for size measurements was better than 0.6 mm, and for hardness was better than 6%.

Discussion
The single operator study showed very consistent results when the EP device was handled by an experienced user. As the same procedure is also used as part of the final quality acceptance testing done on each EP device, existing data was reviewed and found to be consistent with these results. When multiple users were involved, the results were very similar to the single user data. Using the single user data as a baseline, multiple users’ size data was within 7% and hardness data within 4%. Quantifying absolute accuracy is difficult, as there is no accepted standard for determining the size envelope of a lesion, and hardness measurements were up to this point only qualitative in nature. However, the consistency of EP results, both within a battery of tests and across multiple users, suggests that such quantitative standards may now be possible.

Conclusion
The use of EPI allows collection of digital images that accurately and consistently correspond to known breast mass phantoms. EPI is consistent between different examiners studying the same phantom. This may allow the CBE to become an objective and more scientific tool by collecting accurate digital images that correspond to manual palpation.

References

An ongoing, NIH-funded, clinical study is underway to compare EPI data with mammography, ultrasound, and where possible, biopsy data from over 300 patients at multiple institutions for the dual purposes of improving accuracy of salient feature metrics and for establishing a correlation between key EP metrics and pathology. A clinical trial is also being planned in China to assess the screening viability of the device. In addition, FDA-cleared devices are deployed at 8 locations in the United States, Europe, and Asia for additional clinical feedback.

Table: Size Measurement Repeatability

<table>
<thead>
<tr>
<th>Lesion S1</th>
<th>Lesion S2</th>
<th>Lesion S3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>11.2</td>
<td>11.6</td>
</tr>
<tr>
<td>Sigma</td>
<td>0.52</td>
<td>0.59</td>
</tr>
</tbody>
</table>

Table: Hardness Measurement Repeatability

<table>
<thead>
<tr>
<th>Lesion S1</th>
<th>Lesion S2</th>
<th>Lesion S3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>4.5</td>
<td>4.6</td>
</tr>
<tr>
<td>Sigma</td>
<td>4.7</td>
<td>2.5</td>
</tr>
</tbody>
</table>

An ongoing, NIH-funded, clinical study is underway to compare EPI data with mammography, ultrasound, and where possible, biopsy data from over 300 patients at multiple institutions for the dual purposes of improving accuracy of salient feature metrics and for establishing a correlation between key EP metrics and pathology. A clinical trial is also being planned in China to assess the screening viability of the device. In addition, FDA-cleared devices are deployed at 8 locations in the United States, Europe, and Asia for additional clinical feedback.

The single operator study showed very consistent results when the EP device was handled by an experienced user. As the same procedure is also used as part of the final quality acceptance testing done on each EP device, existing data was reviewed and found to be consistent with these results. When multiple users were involved, the results were very similar to the single user data. Using the single user data as a baseline, multiple users’ size data was within 7% and hardness data within 4%. Quantifying absolute accuracy is difficult, as there is no accepted standard for determining the size envelope of a lesion, and hardness measurements were up to this point only qualitative in nature. However, the consistency of EP results, both within a battery of tests and across multiple users, suggests that such quantitative standards may now be possible.

Table: Size Measurement Repeatability

<table>
<thead>
<tr>
<th>Lesion S1</th>
<th>Lesion S2</th>
<th>Lesion S3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>11.2</td>
<td>11.6</td>
</tr>
<tr>
<td>Sigma</td>
<td>0.52</td>
<td>0.59</td>
</tr>
</tbody>
</table>

Table: Hardness Measurement Repeatability

<table>
<thead>
<tr>
<th>Lesion S1</th>
<th>Lesion S2</th>
<th>Lesion S3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>4.5</td>
<td>4.6</td>
</tr>
<tr>
<td>Sigma</td>
<td>4.7</td>
<td>2.5</td>
</tr>
</tbody>
</table>
Cost-Effective Screening for Breast Cancer Worldwide: Current State and Future Directions

A. Sarvazyan¹, V. Egorov¹, J.S. Son² and C.S. Kaufman³

¹Artann Laboratories, 1459 Lower Ferry Rd., Trenton, NJ 08618, U.S.A. ²Medical Tactile, Inc., 5757 Century Blvd., Suite 600, Los Angeles, CA 90045, U.S.A. ³Department of Surgery, University of Washington, 2940 Squalicum Pkwy, Bellingham, WA 98225, U.S.A.

Abstract: Affordability of healthcare is highly limited by its skyrocketing cost. Access to screening and diagnostic medical equipment and medicine in developing countries is inadequate for the majority of the population. There is a tremendous worldwide need to detect breast cancer at its earliest stage. These needs must be balanced by the ability of countries to provide breast cancer screening technology to their populations. We reviewed the diagnostic accuracy, procedure cost and cost-effectiveness of currently available technique for breast screening and diagnosis including clinical breast examination, mammography, ultrasound, magnetic resonance imaging, biopsy and a new modality for cancer diagnostics termed elasticity imaging that has emerged in the last decade. Clinical results demonstrate that elasticity imaging even in its simplest and least sophisticated versions, like tactile imaging, has significant diagnostic potential comparable and exceeding that of conventional imaging techniques. In view of many countries with limited resources, effective yet less expensive modes of screening must be considered worldwide. The tactile imaging is one method that has the potential to provide cost-effective breast cancer screening and diagnostics.

Keywords: breast cancer, screening, cost-effectiveness, elastography

Introduction
Affordability of healthcare is highly limited by its skyrocketing cost. Access to screening and diagnostic medical equipment and medicine in developing countries is inadequate for the majority of the population. More than 70% of all cancer deaths occur in low and middle income countries, where resources available for diagnosis, prevention, and treatment of cancer are limited or nonexistent[1, 2]. One of reasons for rapid escalation of the healthcare costs is an application of new advanced techniques for diagnostics, treatment and prevention which often is not cost-effective. For example, Medicare’s reimbursement system is establishing the minimum reimbursement for mammography services as 81.86 USD for film and 131.50 USD for digital bilateral screening mammography[3] which corresponds to 60.6% increase in the procedure cost. Despite such an increase of costs, the improvement of diagnostic accuracy of digital relative to film mammography is not significant. The overall diagnostic accuracy in a large-scaled clinical study was found of 0.78 ± 0.02 for digital mammography and of 0.74 ± 0.02 for film mammography (difference 0.03; 95% confidence interval, −0.02 to 0.08; P = 0.18)[4]. Digital mammography, compared with film, would cost more than 300,000 USD per quality-adjusted life-year gained, which is not cost effective[5].

These and other similar data indicate that there is an urgent need in cost effective screening and diagnostic methods for breast cancer, making it affordable all around the world[6].

Current Screening and Diagnostic Methods
Current methods of breast screening and diagnosis include Breast Self-Examination (BSE), Clinical Breast Examination (CBE), Mammography, Ultrasound, Magnetic Resonance Imaging (MRI), and biopsy. Other breast screening methods which are currently in an exploratory stage include: tomosynthesis, supersonic shear wave imaging, electrical impedance tomography, optical tomography, and several second line breast pathology diagnostic techniques such as positron emission tomography and scintimammography.
**BSE**

The studies of the effectiveness of BSE as a detection modality has shown mixed results, but recent data reviews have focused on the lack of direct benefit in randomized clinical trials[7–9]. The studies found no reduction in the breast cancer mortality but higher rate of benign biopsy, in women who regularly perform BSE compared to women who do not regularly perform BSE [8]. Although the American Cancer Society no longer recommends that all women perform monthly BSE, women are recommended to be informed about the potential benefits (self-awareness) and limitations (false-positive rate) associated with BSE. Women who detect their own breast cancer usually find it outside of a structured breast self-exam while bathing or getting dressed. A woman who wishes to perform periodic BSE should receive instruction from her health care provider and/or have her technique reviewed periodically[10].

**CBE**

The premise underlying CBE is utilizing a trained clinician to visually inspect and palpate the breast in order to detect abnormalities to find palpable breast cancers at an earlier stage[11]. American Cancer Society guidelines recommend an annual CBE for age 40 and older for early detection of breast cancer in asymptomatic women[10]. The CBE may identify some cancers missed by mammography[12, 13] and provide an important screening tool among women for whom mammography is not recommended or who do not receive recommended high-quality screening mammography. At the same time, CBE performance, reports and documentation are inconsistent and not standardized. Health care providers report a lack of confidence in their CBE skills and would welcome training and practical recommendations for optimizing performance and reporting[14].

Data from six studies examined by Barton et al. resulted in an overall estimate of 54.1% for CBE sensitivity and 94.0% for CBE specificity[15]. Over 20 years ago, Haagensen [16] estimated that 65% of 2,198 breast cancer cases, identified before the use of screening mammography, presented as a breast masses detected by BSE or CBE. These findings are comparable to the published values for CBE sensitivity (58.8%) and specificity (93.4%) observed in the U.S. national screening program for 752,081 CBE reports[17]. The CBE cost effectiveness in cancer screening is 3.5 fold better than that of mammography[18]. The CBE detects only 34% fewer breast cancers than mammography, as it was demonstrated for population of 1 million women and the cost-effectiveness of biennial CBE is evaluated as 522 USD per life-year saved in India [18]. From this point, CBE may be a suitable option for countries in economic transition, where incidence rates are on the increase but limited resources do not permit screening by mammography.

In Japan, for women aged 40–49 years, having the highest incidence rate of breast cancer, the cost-effectiveness of annual CBE per life-year was evaluated as 31,900 USD[69].

**Mammography**

Mammography provides X-ray images of the breasts with at least two sets of images, the mediolateral oblique and cranial-caudal views. A recent large-scale clinical study (42,760 patients in U.S.A. and Canada) on the diagnostic performance of mammography for breast-cancer screening demonstrated a sensitivity of 70.0%, specificity of 92.0%, and diagnostic accuracy interpreted as AUC of 78.0%[4]. The European randomized mammography screening trial (23,929 patients in Norway) revealed a sensitivity of 77.4% and specificity of 96.5% at full-field digital mammography. The median size of screening-detected invasive cancers was about 13.5 mm[19]. In the United States, despite the recommendation for an annual mammogram, in 2005 only 47.8% of women aged 40–49 years had a mammogram within the past year. Among the women without health insurance coverage this value decreases to 24.1% [10]. The cost-effectiveness screening film mammography are estimated as 902–1,946 USD per year of life saved in India, 2,450–14,790 USD per year of life saved in Europe, and 28,600–47,900 USD per year of life saved in U.S.A.[6]. Among the limitations of mammography are increased breast density, technical factors, e.g. areas adjacent to the chest wall may not be imaged[20], lack of insurance coverage, disagreements among primary care physicians on frequency of mammographic screening, variation in interpretation skills of radiologists.

The mean glandular radiation dose from 2-view mammography is approximately 4 to 5 mGy and the dosage varies among facilities and increases with breast density. The average cumulative exposure from screening during the decade will be
there is a strong linear trend of increasing risk of radiation-induced breast cancer with increasing radiation dose (P = 0.0001) [71]. A statistically significant increase in the incidence of breast cancer following radiation treatment of various benign breast diseases was observed[72]. Several recent studies suggesting that carriers of pathogenic alleles in DNA repair and damage recognition genes may have an increased risk of breast cancer following exposure to ionizing radiation, even at low doses[73]. Based on review of 117 studies related to screening mammography the authors concluded that “the risk for death due to breast cancer from the radiation exposure involved in mammography screening is small and is outweighed by a reduction in breast cancer mortality rates from early detection.”[74].

Ultrasound
Ultrasonography as an imaging tool uses sound waves that pass through breast tissue and are reflected back characterizing tissue structure. Ultrasonography is typically used as a complementary method for the assessment of mammographically or clinically detected breast masses and for supplemental information on dense tissue[11]. However, there is limited data supporting the use of ultrasound in breast cancer screening as an adjunct to mammography[21]. The conventional ultrasound is more often used to evaluate an area of concern on mammogram. The majority of cystic masses are benign while solid masses need further evaluation[22]. Ultrasound is often confused as a screening tool by both patients and healthcare providers. However, ultrasonic screening the entire breast is not only labor-intensive, but operator-dependent; therefore, ultrasound is a difficult tool to use if there is not an identifiable area of concern. Ongoing studies are trying to determine whether there is a population of women who would benefit from an ultrasonic screening; however, at this time, it is not the standard of care and whole-breast ultrasonography for screening has not been established as useful[23]. The cost associated with unilateral or bilateral ultrasound diagnostic procedure is 70.11 USD according to 2005 U.S. average Medicare reimbursements[5].

MRI
MRI utilizes magnetic fields to produce detailed cross-sectional images of the breast tissue. Image contrast between tissues in the breast (fat, glandular
tissue, lesions, etc.) depends on the mobility and magnetic environment of the hydrogen atoms in water and fat that contribute to the measured signal that determines the brightness of tissues in the image. Many indications for clinical breast MRI are recognized, including resolving findings on mammography and staging of breast cancer[22]. Overall, the results of 6 nonrandomized prospective studies in the Netherlands[24], the United Kingdom[25], Canada[26], Germany[27], the United States[28], and Italy[29] of MRI efficacy in breast cancer screening for high risk women populations demonstrate an averaged sensitivity of 87.5% and specificity of 92.8%. Only limited data are available on the cost effectiveness of breast MRI screening being combined with mammography. The cost per quality-adjusted life year saved for annual MRI plus film mammography, compared with annual film mammography alone, varied by age and other factors to be found in the range of 27,544–130,420 USD. The reimbursement for bilateral MRI diagnostic procedures was 1,037 USD according to 2005 U.S. average Medicare reimbursements, which is about eight times higher than the screening mammography[5] and out of pocket charges by private clinics are as much as 5 times higher.

Ultrasound and MR elasticity imaging
In the last decade a new modality for cancer diagnostics termed Elasticity Imaging (EI) has emerged. EI allows visualization and semi quantitative assessment of mechanical properties of soft tissue. Mechanical properties of tissues, i.e. is elastic modulus and viscosity, are highly sensitive to tissue structural changes accompanying various physiological and pathological processes. A change in Young’s modulus of tissue during the development of a tumor could reach thousands of percent [30–32]. EI is based on generating a stress in the tissue using various static or dynamic means and measuring resulting strain by ultrasound or MRI[33–39]. The current increasing flow of publications from many countries all over the world on Elastography covers practically all key human organs[40–46].

Tactile imaging
Tactile Imaging (TI), an alternative version of Elasticity Imaging, yields a tissue elasticity map, similarly to other elastographic techniques. At the
same time, TI, which is also called “stress imaging” or “mechanical imaging” [56–61], most closely mimics manual palpation, since the TI probe with a pressure sensor array mounted on its face acts similar to human fingers during clinical examination, slightly compressing soft tissue by the probe.

There are limited clinical data on diagnostic/screening potential of breast TI. In one clinical study that included 110 patients with a complaint of a breast mass, TI demonstrated detection of 94% of the breast mass, while physical examination identified only 86%[57]. The positive predictive value for breast cancer using TI was 94% and 78% for physical examination. Clinical results of another study for 187 cases, collected at 4 different clinical sites, have demonstrated that TI produces a reliable image formation of breast tissue abnormalities with increased hardness and calculation of lesion features[60]. Malignant breast lesions (histologically confirmed) demonstrated increased hardness and strain hardening as well as decreased mobility and relative boundary length in comparison with benign lesions. Statistical analysis of the TI differentiation capability for 154 benign and 33 malignant lesions revealed an average sensitivity of 89.4% and specificity of 88.9% with a standard deviation of ±7.8%. The area under the receiver operating characteristic curve characterizing benign and malignant lesion discrimination was 87.8% with the confidence interval range from 82.1% to 92.1%, with a significance level $P = 0.0001$.

In Table 1 we summarized recent clinical results on benign/malignant breast lesion differentiation by various elasticity imaging modalities: USE—Ultrasound Elastography, MRE—Magnetic Resonance Elastography and TI. These data show that elasticity imaging even in its simplest and least sophisticated versions, like TI, has significant

<table>
<thead>
<tr>
<th>No.</th>
<th>Method</th>
<th>Number of analyzed lesions</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Citation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>USE*</td>
<td>52 malignant 59 benign</td>
<td>86.5%</td>
<td>89.8%</td>
<td>Itoh A, et al. 2006 [47]</td>
</tr>
<tr>
<td>2</td>
<td>USE</td>
<td>135 total</td>
<td>100.0%</td>
<td>95.0%</td>
<td>Zhang XF, et al. 2006 [48]</td>
</tr>
<tr>
<td>3</td>
<td>USE</td>
<td>49 malignant 59 benign</td>
<td>91.8%</td>
<td>91.5%</td>
<td>Thomas A, et al. 2006 [49]</td>
</tr>
<tr>
<td>4</td>
<td>MRE*</td>
<td>38 malignant 30 benign</td>
<td>95.0%</td>
<td>80.0%</td>
<td>Sinkus R, et al. 2006 [50]</td>
</tr>
<tr>
<td>5</td>
<td>USE</td>
<td>88 total</td>
<td>96.0%</td>
<td>61.0%</td>
<td>Renger DM, et al. 2006 [51]</td>
</tr>
<tr>
<td>6</td>
<td>USE</td>
<td>43 malignant 150 benign</td>
<td>100.0%</td>
<td>96.0%</td>
<td>Barr RG, 2007 [52]</td>
</tr>
<tr>
<td>7</td>
<td>USE</td>
<td>115 total</td>
<td>90.0%</td>
<td>–</td>
<td>Garra BS, et al. 2006 [53]</td>
</tr>
<tr>
<td>8</td>
<td>USE</td>
<td>50 malignant 48 benign</td>
<td>99.3%</td>
<td>25.7%</td>
<td>Burnside ES, et al. 2007 [54]</td>
</tr>
<tr>
<td>9</td>
<td>USE</td>
<td>237 malignant 584 benign</td>
<td>97.5%</td>
<td>48.0%</td>
<td>Svensson WE, et al. 2007 [55]</td>
</tr>
<tr>
<td>10</td>
<td>TI*</td>
<td>34 malignant 76 benign</td>
<td>94.4%</td>
<td>–</td>
<td>Kaufman CS, et al. 2006 [57]</td>
</tr>
<tr>
<td>11</td>
<td>TI</td>
<td>33 malignant 154 benign</td>
<td>89.4%</td>
<td>88.9%</td>
<td>Egorov V, et al. 2008 [60]</td>
</tr>
<tr>
<td>12</td>
<td>SSI*</td>
<td>4 malignant 11 benign</td>
<td>100.0%</td>
<td>100.0%</td>
<td>Tanter M, et al. 2008 [75]</td>
</tr>
</tbody>
</table>

USE*—Ultrasound Elastography, MRE*—Magnetic Resonance Elastography, TI*—Tactile Imaging, SSI*—Supersonic Shear Imaging.
Cost-effective screening for breast cancer worldwide

Biopsy
Although the most of women who undergo screening each year do not have breast cancer, about 5%–10% of women have their mammogram interpreted as abnormal or inconclusive until further tests are done. In most instances, additional tests (imaging studies and/or biopsy) lead to a final interpretation of normal breast tissue or benign [10]. In the United States alone, more than 1 million breast biopsies are performed annually and approximately 80% of these findings are benign [62, 63]. In general, the biopsy diagnostic cancer sensitivity varies from 91% to 100% (in average 96.6%) for 8 clinical trials, and depends on biopsy type (needle, core, or surgical) and used image-guided technique (X-rays, ultrasound, MRI) [64]. The evaluations of cost effectiveness of biopsy are extremely diverse depending on biopsy type, used technique, and accepted model; it is varying from 2,250 USD to 77,500 USD per life year saved [65, 66]. The cost associated with biopsy diagnostic procedure is in average about 1,000 USD, changing from 456 USD for fine needle aspiration biopsy to 2,061 USD for open biopsy, according to 2005 US average Medicare reimbursements [5].

Cost-Effectiveness of Breast Cancer Screening and Diagnostic Methods
About 80% of the 1.6B women live in developing countries and 70% of breast cancer related deaths occur in these regions [2]. However, less than 10% of mammograms are conducted in these developing regions (Fig. 1) [67].

Diagnostic efficacy is certainly an important measure, but affordability is another critical factor which needs to be considered. Based on data from [62] we see that the adoption of mammography is strongly correlated with physician income and consequently much more utilized in developing counties. As Figure 2 shows, the number of mammography equipment in comparison to number of physicians that perform CBE is close to 20% in U.S.A. but less than 0.25% in India.

Table 2 presents a summary of breast cancer screening/diagnostic efficiency for various techniques, procedure cost and cost-effectiveness numbers. The cost-effectiveness data listed in the table are mostly taken from published sources. We included the range for cost-effectiveness for

![Figure 1](image)

**Figure 1.** Population of women (first column), breast cancer deaths (second column) and mammography processes (third column) in developing countries (red boxes) in comparison with developed countries (grey boxes). The data are for 2005 [62].

**Abbreviations:** NA: North America; WE: Western Europe; JPN: Japan; LA: Latin America; EEMEA: Eastern Europe, Middle East, Africa; APAC: Asian Pacific, Australia, China.
analyzed modalities in the Table 2 because the specific data depend on accepted population-based model simulating histories of women, which, as a rule, include breast cancer natural history, breast cancer detection capability of the modality, breast cancer treatment, and competing-cause mortality. Different authors often use different models for the cost-effectiveness evaluation.

The ‘gold standard’ in cancer diagnostics, biopsy, demonstrates the highest diagnostic accuracy close to 100%. It costs in average over 2,000 USD for one analyzed breast lesion/location. The biopsy cost-effectiveness varies from 2,250 USD for developing countries to 77,500 USD for developed countries. The cost-effectiveness of biennial film mammography screening is evaluated as

Table 2. Comparative data for breast cancer detection effectiveness and cost effectiveness.

<table>
<thead>
<tr>
<th>Screening/Diagnostic Technique</th>
<th>Sensitivity/Specificity, %</th>
<th>Procedure cost of bilateral exam, USD</th>
<th>Cost-effectiveness, USD per life year gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBE</td>
<td>56.5/93.7</td>
<td>–</td>
<td>522, India [7]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>31,900, Japan [69]</td>
</tr>
<tr>
<td>Mammography</td>
<td>73.7/94.3</td>
<td>112*</td>
<td>1,846, India [7]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>26,500–331,000 [5]</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>Limited, see text</td>
<td>70*</td>
<td>–</td>
</tr>
<tr>
<td>MRI</td>
<td>87.7/92.8</td>
<td>1,037*</td>
<td>55,420–130,695 [68]</td>
</tr>
<tr>
<td>Biopsy</td>
<td>96.6/100.0</td>
<td>2,061**</td>
<td>2,250–77,500 [65, 66]</td>
</tr>
<tr>
<td>Elasticity Imaging</td>
<td>95.1*/73.4</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Tactile Imaging</td>
<td>91.9*/88.9</td>
<td>5–50***</td>
<td>162***</td>
</tr>
</tbody>
</table>

*the U.S. average Medicare reimbursements in 2005;
**in average for one biopsy;
***projections based on a physician’s assistant performing the exam;
*averaged for 9 clinical studies;
**averaged for 2 clinical studies.
1,846 USD per life-year saved in India[18]. In the United States, the selective use of digital mammography screening for women aged 40 years or older had costs per quality adjusted life-year (QALY) gained ranging from 26,500 USD for age-targeted digital mammography to 84,500 USD for age- and density-targeted digital mammography. All-digital mammography screening was also more costly and no more effective than age-targeted digital mammography. The cost per QALY gained for all-digital mammography relative to all-film mammography screening was 331,000 USD (Confidence interval, 268,000 USD to 403,000 USD)[4].

Using cost-effectiveness of biennial CBE, 522 USD per life-year saved in India[18], one can estimate the impact of TI using CBE data. Taking 92% TI cancer sensitivity, which is 62% higher than CBE, may result in proportional improvement in TI cost-effectiveness. Further, the TI examination may be performed by a nurse or qualified technician, rather than a physician, which may additionally improve the cost effectiveness by a factor of two. As a result, we may expect TI cost effectiveness for developing countries to be equaled to 162 USD (in prices of 2001), which is over ten times more cost-effective than film mammography. A rough estimate shows that the TI procedure could cost about 5 USD in developing countries and 50 USD in the United States. In addition, clinical results indicate that TI screening may substantially decrease the benign biopsy rate[60].

Conclusions
There is a tremendous worldwide need to detect breast cancer at its earliest stage. These needs must be balanced by the ability of countries to provide breast cancer screening technology to their populations. We reviewed the current available screening and diagnostic techniques with their relative cost-effectiveness ratios. In view of many countries with limited resources, effective yet less expensive modes of screening must be considered worldwide. Tactile imaging is one method that has the potential to provide cost-effective breast cancer screening and diagnostics.

Acknowledgment
This work was supported in part by National Institute of Health under grants CA094444 “Use of a tactile breast imager for mass prescreening” and CA091392 “Imaging network for breast cancer mass screening”.

References
Cost-effective screening for breast cancer worldwide


Digital documentation of the physical examination: moving the clinical breast exam to the electronic medical record

Cary S. Kaufman, M.D.\textsuperscript{a,b,*}, Leslie Jacobson, M.S.\textsuperscript{b}, Barbara A. Bachman, M.D.\textsuperscript{b}, Lauren B. Kaufman, M.D.\textsuperscript{b}

\textsuperscript{a}Department of Surgery, University of Washington, 2940 Squalicum Pkwy, Bellingham, WA 98225, USA
\textsuperscript{b}Bellingham Breast Center, Bellingham, WA, USA

Manuscript received April 7, 2006; revised manuscript June 16, 2006

Presented at the 7th Annual Meeting of the American Society of Breast Surgeons, Baltimore, Maryland, April 5–9, 2006

Abstract

\textbf{Background:} Documentation of the clinical breast examination (CBE) has consisted of simple hand-drawings and stick figures without a common lexicon. There is a need for a device that can accurately depict the CBE in digital format while being objective, reproducible over time, and useable in the electronic medical record. This new device is called palpation imaging (PI).

\textbf{Methods:} We examined 110 patients with a complaint of a breast mass using PI. This laptop-sized device creates a real-time digital display of the palpable area in both video and still formats. The size, hardness, shape, homogeneity, and mass location may be extracted from the image.

\textbf{Results:} Of those with a true mass, PI identified the mass in 94\% while physical examination identified 86\%. The positive predictive value (PPV) for breast cancer using PI was 94\% and 78\% for physical examination. A survey of primary care physicians revealed the inclusion of the PI record in a consultation note implied competence, experience, and skill by the surgeon.

\textbf{Conclusions:} PI documented the CBE in a timely, efficient, and accurate manner. A reproducible record allows objective review by multiple examiners at varied times. Continued work will optimize examination methods. © 2006 Excerpta Medica Inc. All rights reserved.

\textbf{Keywords:} Palpation imaging; Clinical breast exam; Breast imaging; Breast lump; Electronic medical record; Mammography; Ultrasound; Breast mass

While the last 20 years have seen major improvements in breast imaging [1–8], the documentation of the clinical breast examination (CBE) has remained unchanged since the Halsted mastectomy 100 years ago [9]. Surgeons record a verbal description of their palpable findings along with a handwritten drawing. The verbal description suffers from the spectrum of descriptive words without standardized definitions. Terms such as “fibrous,” “thickened,” “dense,” and “glandular” may all describe the identical breast texture and are user dependent. Likewise, a hand drawing or stick figure of a breast mass may be interpreted differently by different observers. These subjective drawings may not communicate the same examination to a second examiner or even to the same examiner at a later date. Drawings are not standardized or consistent, and the descriptions have no common lexicon. Estimated sizes of drawn masses are not consistently given in either text or drawings.

A need exists for a device that accurately and objectively depicts the CBE in digital format which is reproducible over time, and able to be uploaded into various electronic medical records. There exists now a new device that can be utilized by breast surgeons to accurately record the CBE of palpable lesions [10,11]. Using this device results in an imaging method called palpation imaging (PI). The target of the current study was the creation of a consistent repeatable digital image of the CBE that may accompany the clinician’s verbal description.

PI obtains a digital image of the CBE and stores it in one of several digital versions. PI captures the characteristics of the palpable findings, including the estimated size and shape, the degree of firmness relative to the surrounding breast tissue, and the homogeneity of the mass. Use of this...
Method may aid in the documentation of the CBE and augment the clinical record making it more versatile, reproducible, consistent, and electronically useable. This can be used for chart documentation, communication with other physicians, education for patients, and as a medical record for insurers or medicolegal purposes.

Methods
Between October 2003 and October 2005, 110 patients referred to our breast clinic with a chief complaint of a breast mass were examined. In addition to CBE, ultrasound, and mammograms, each patient underwent PI. Some young patients did not have mammography.

After PI examination, each record was segregated into one of two groups based on the PI findings alone: those with the findings of a dominant mass (eg, cyst, benign or malignant tumor) and those without findings of a dominant mass (e.g., fibrocystic change or other normal breast tissue). Those with a dominant mass were further separated into those highly suspicious for cancer and those with palpable masses. Final histologic and/or follow-up data (minimum 6 months) was correlated with preoperative PI. Statistical analysis used the chi-square calculator from Georgetown University [12].

Description of imaging device
The cornerstone of this report is the development of an imaging device that translates palpation findings into a visual record [13]. To understand this device, it is necessary to deconstruct the CBE of a palpable mass. Upon finding a mass, the surgeon notes the location of the mass within the breast. Mass characteristics of size (in at least 2 dimensions), hardness, shape, and homogeneity are noted. PI re-creates the components of the CBE of a mass.

The palpation imager consists of a notebook computer-sized device attached to a broad-based transducer. After CBE targets a lesion, the transducer is passed over the palpable lesion. The transducer has almost 200 minute sensors able to record the pressure and location data. As the transducer scans, a real-time display of the palpable area is digitally recorded (Fig. 1). The transducer sensor data is converted to a color image in both 2- and 3-dimensional formats. Peak height of the image refers to increased firmness, while low height refers to less firm or soft tissues (Fig. 2). Images are reviewed to demonstrate the characteristics of size, hardness, shape, homogeneity, and location. The examination video and still-frame images are available for printed reports or single images may be incorporated into a consultation letter.

This palpation image can be translated into the components of the physical examination: size, hardness, shape, and homogeneity. The location within the breast is entered by the examiner (Fig. 3). The size of the lesion is demonstrated by the footprint seen on the image (Fig. 4). The hardness of a lesion is described by the absolute height of the peak.
pressure, as well as comparison of peak height to surrounding breast tissue height (surrounding breast firmness). The shape of the palpable findings may be demonstrated by a line drawn at an isobaric level surrounding the mass on a 2-dimensional image, seen as a black line in the examination result screen (Fig. 5). Homogeneity of the palpable mass is identified as the shape of the peaks within the image. Single smooth peaks are commonly seen in cysts and fibroadenomas, while images with multiple peaks within the mass suggest lobulations and nonhomogeneous masses such as cancers. PI reports describe all the building blocks of the CBE. This was not a blinded study but meant to identify any palpable abnormality and try to document its presence with PI. At no time was PI considered a substitute for biopsy, and biopsy should always be considered as the definitive test for the presence of breast cancer.

Physician survey

To assess the communication value of PI, sample breast consultations were sent out to a study set of 15 primary care referral physicians. Each of the referring physicians was provided breast surgical consultations on 3 different sample patients. All 3 had a chief complaint of a breast mass, each with a different cause; 1 had a palpable cancer, 1 had a benign palpable mass, and the third had an area of fibrocystic change.

Each sample patient was “examined” by 3 surgeons who provided different forms of consultations. Surgeon “A” wrote the consultation by longhand and included a hand-drawn picture of the palpable findings. Surgeon “B” typed the consultation in letter format without any drawings of the physical examination. Surgeon “C” also typed the consultation in letter format as surgeon “B,” but included a printed digital image and report of the physical examination using PI.

Each referral physician received 9 consultations in total, 3 on each of 3 patients. We asked each referral physician to rank the breast surgeons on each patient. Three questions were asked for each patient: (1) please rank these 3 breast surgeons in regards to their competence; (2) please rank these 3 breast surgeons in regards to their experience and innovation in the field of breast surgery; and (3) please rank these 3 breast surgeons in regards to their skill as a surgeon. Referring physicians were asked to avoid ties and to make choices as best as possible based on the submitted data.

Results

Table 1 of final diagnoses reveals the typical patient distribution seen in a breast clinic, including fibroadenomas, cancers, fibrocystic change, and cysts. Ninety-five of 110 patients were found to have lesions that might present as a mass as documented by pathology or other confirmatory tests. We included the patient with gynecomastia with this group. Although some of these lesions may be too small to detect, we considered these patients the potential pool of those with a dominant mass.

Each palpable finding on CBE was recorded as well as the PI results. After an initial learning curve, it was possible to recreate the digital image of the palpable findings. Because the surgeon obtained the digital image, an immediate
feedback process occurs while imaging. The surgeon can determine whether the image is a true representation of the palpable findings. During the examination, the surgeon may also examine the surrounding area with PI to confirm the absence of other palpable findings.

**Identifying dominant masses**

PI was used to separate patients into 2 groups: those identified with a mass and those without a mass. PI identified a dominant mass in 89/95 patients (positive predictive value [PPV] 94%). Physical examination identified 82/95 patients (PPV 86%). The sensitivity and specificity of identifying a dominant mass with PI were 88% and 88%, while the values were 81% and 81% for physical examination.

In addition, we examined clinically normal breast tissue without any mass to validate our assessment. Both methods were accurate in determining breast tissue without any mass. The negative predictive value of PI and for physical examination was 93% for both methods.

We tried to correlate the consistency of PI and CBE. For each category of PI, we noted the frequency of finding palpable masses. There was a direct correlation between the likelihood of palpating a mass on CBE and the PI firmness category, as noted in Fig. 6.

**Identifying breast cancer as a mass**

PI separated breast lesions into 4 categories: (1) those without a mass; (2) those with a soft mass; (3) those with a firm mass; and (4) those with a hard mass. Breast cancers were usually firm or hard with either a central single or multiple peaked image on PI. Of the 36 breast cancers examined, the PPV for PI was 94% and 78% for physical examination (Table 2). There were six cancers identified by PI that were not identified by physical examination (false negative rates of 6% and 22%, respectively).

**Fibroadenoma, cyst, lipoma, seroma**

PI of fibroadenomas, cysts and other benign oval nodules typically demonstrated a single smooth peak with a firm central mass. Of the 57 lesions in this group, we closely examined all fibroadenomas and cysts (n = 47) for evidence of these PI findings. All but 4 lesions (91%) demonstrated this classic PI pattern. The 4 lesions not visualized on PI included 2 cyst clusters and 2 small fibroadenomas.

PI may estimate size of the examined mass (Fig. 4). To assess the size correlation, we looked at the same group of fibroadenomas and cysts. Only 41 of 47 of these patients had an ultrasound measurement documented. We compared the length and width measurements as seen by palpation imaging with the ultrasound measurements. We classified the correlation as good when measurements on both PI and ultrasound were within 3 mm of each other. Those between 3 and 6 mm were considered fair, and those with a greater than 6-mm difference between the 2 measurements were considered poorly correlated. We found 32% of these patients had good correlation between PI and ultrasound measurements, while 46% varied by more than 6 mm between the 2 examinations. There was no difference between the ability of physical examination and PI to identify benign breast lesions (Table 3).

**Primary care responses**

Of the 15 clinicians surveyed, responses were received from 11. One clinician refused to respond due to concerns about commercial bias. Three others did not return their evaluation. Most clinicians favored the use of the typed consultation along with the PI report of surgeon “C.” They regarded this surgeon to have better “communication skills” and more “experience/innovation.” Of the responses received, 81% said surgeon “C” was the most experienced and 68% said he was the best communicator. Over 85% rated surgeon “A” as least experienced with the least communication skills. This was despite the fact that the written scripts were similar, essential findings were identical, and there was a neatly hand-drawn picture of the palpable find-

---

**Table 1**

<table>
<thead>
<tr>
<th>Lesions that might present as a mass</th>
<th>Carcinoma</th>
<th>36</th>
<th>Fibroadenoma</th>
<th>31</th>
<th>Cyst</th>
<th>16</th>
<th>Lipoma</th>
<th>6</th>
<th>Hematoma/seroma</th>
<th>4</th>
<th>Radiation fibrosis</th>
<th>1</th>
<th>Gynecomastia</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variants of glandular tissue</td>
<td>Fibrocystic</td>
<td>7</td>
<td>Normal breast</td>
<td>8</td>
<td>Total</td>
<td>110</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th></th>
<th>Breast cancer</th>
<th>Not breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI reveals mass lesion</td>
<td>34</td>
<td>2</td>
</tr>
<tr>
<td>Physical examination reveals mass lesion</td>
<td>28</td>
<td>8</td>
</tr>
</tbody>
</table>

*P < .05; chi-square = 4.1806.*
The palpation image provides the opportunity for clinical review at a later time. This is useful if the referring ultrasound or mammogram are not available. When the films return, comparison to the PI physical examination can occur. Another use for PI is to communicate the physical findings to the patient. The image of the palpable findings is readily understandable by interested patients. Although the CBE has not been demonstrated to impact survival from breast cancer [9], the lack of a common documentation method and lexicon may contribute to the inability to document CBE value.

The objective documentation of PI may help some medical clinics that may have several doctors seeing the same group of patients. Using PI, a patient with a palpable finding may be followed more objectively by a series of doctors. Poor communication may occur when one surgeon’s hand drawings of a breast mass is read by another surgeon. Radiologists commonly communicate this way using serial image documentation. This may also aid doctors who are providing vacation coverage and other part-time clinicians.

PI requires training and skill to obtain accurate images. This is similar to correct positioning and exposure in mammography or proper gain and focal zone in ultrasonography. The proper examining technique and applied pressure is required for optimal PI. Ultrasound has similar requirements to obtain an optimal image. Surgeons skilled at ultrasound examination of the breast are likely to have little difficulty learning the technique of PI.

The basic examination technique is similar to the movements associated with breast ultrasound examination. Mechanical adjustments of the device are few. Calibration is required regularly but not daily. Since the device is the size of a laptop computer, it easily moves from one examination room to another. The creation of an initial image takes just minutes after the examiner identifies a lesion. Several images are obtained to confirm an accurate depiction has been obtained. Automatic storing of images occurs after the demographic information has been entered into the system. Recalling a previous examination is similar to opening a stored computer file.

The PI device is relatively inexpensive in relation to other forms of imaging, being less costly than an entry-level portable ultrasound device. With the PI device comes the ability to document lesions, the ability to create and print a completed report of the CBE, and image storage for use later or inclusion in the EMR. Although reimbursement is not currently available for the use of this device, it adds value to the practice. This is similar to the cost of computerizing one’s office or converting to an EMR that is not reimbursed but adds value to the medical practice. Larger studies examining the impact of standardized CBE will hopefully answer the question of clinical value.

There are some disadvantages of the PI device, including no insurance reimbursement for this examination. Like other new technologies, reimbursement may follow at a

Table 3

<table>
<thead>
<tr>
<th>Type of breast tissue identified as “mass” during physical examination and palpation imaging</th>
<th>PI</th>
<th>Physical examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign mass lesion* no mass identified</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Benign mass lesion* identified as mass</td>
<td>55</td>
<td>53</td>
</tr>
<tr>
<td>Breast cancer no mass identified</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Breast cancer identified as mass</td>
<td>34</td>
<td>28</td>
</tr>
<tr>
<td>Benign breast tissue† identified as mass</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Benign breast tissue† no mass identified</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>110</td>
<td>110</td>
</tr>
</tbody>
</table>

* For example, fibroadenoma, cyst, lipoma, seroma, hematoma.
† For example, benign breast tissue, fibrocystic change without dominant cyst.

Comments

As a documentation device, PI has several benefits over current technology. Since the device is calibrated and standardized, the PI recordings will be consistent among several examiners. Serial examinations of the identical mass over time allows for the accurate documentation of change. PI accumulates a continuous video recording of the targeted mass and then identifies a single image that best represents the physical findings. This image can be uploaded into a Word file for a consultation letter or into an electronic medical record (EMR). The electronic version of the physical examination merges with the interest in the EMR. The clinical record is in the process of change [14]. Primary care, internal medicine, cardiology, and many specialties have converted to use of the EMR. Many practices are converting to an electronic format for many reasons, including ease of creation, ease of transmission and exchange/circulation, ease of storage, and cost.

It is typical for surgeons to have their initial consultation distributed as a letter to their referring physicians. This consultation letter typically does not include any hand drawings or figures of breast masses. In our physician survey, we note that the inclusion of a hand-drawn picture of the physical examination was not valued by the referring physicians. When the PI printed report was included, the referring physicians associated surgical experience and increased communication skills with the combined report. The addition of a digital image of the palpable findings may add a new dimension to the consultation of a breast surgeon.

Since the PI device acts as an independent observer of the CBE, the PI report may be valuable if the patient’s chart is reviewed by an outside party. For insurers who wish to confirm the CBE was performed, the PI report adequately documents that examination. For medicolegal purposes, the PI report can validate a clinician’s statement as to the findings on CBE. The PI examination can provide independent confirmation of the surgeon’s examination.
later date. Because PI is new, it will be necessary for other centers to validate and enhance the findings in this report.

We noted some instances of PI examinations were consistent with the eventual pathologic findings. Very large cancers over 4 cm in size cannot be easily examined since there is no normal tissue to compare within the 4-cm probe area. The firmness of a large cancer will be viewed as an overall elevation of the baseline, since the entire surface under the PI transducer has similar hardness.

The other end of the spectrum is also difficult to image. Very small cancers that are not palpable on CBE may or may not be demonstrated on PI. A lower threshold of PI imaging capability exists that is dependent on many factors. These include the absolute hardness of the small tumor, the size of the breast, and the depth of location of the tumor. Small firm tumors that are closer to the skin surface in smaller breasts are easier to image even when not palpable on CBE.

A third group of breast cancers that may be difficult to identify are tumors with soft consistency. Colloid carcinomas or other low grade tumors that have little growth intensity may be difficult to visualize. These tumors, which are primarily found in older patients, may have similar firmness to surrounding breast tissue.

There are several clinical components that cannot be translated into a mechanical device. The palpation imaging device must be placed over the mass in question. This is similar to limitations of breast ultrasound. When an ultrasound sensor is placed on a surgical scar, the hypoechoic shadowing area will appear suspicious for cancer, even though it is typical surgical scar. The examiner must notify the ultrasonographer that the transducer is overlying the surgical scar. Likewise, PI will report the firmness of any lesion examined without the ability to know what portion of the body is being examined.

Similarly, placing the PI device directly on an exposed rib will create an image of an elongated hard mass. Although this may be an accurate representation of a rib, the device will document the palpable findings only. The examiner is responsible to identify the location that the probe is examining.

Additionally, exophytic skin lesions such as moles or the true nipple will give a palpable image of a mass. The examiner must note the presence of skin lesions or location of the nipple as is commonly included during mammography imaging.

This imaging device is intended to be used for documentation of the CBE and improved communication. With further research and experience, it may be possible to use the PI device to aid in the clinical grouping of palpable breast disorders. Characteristics of benign and malignant masses may be teased out of the data obtained from multiple examinations and may aid the breast surgeon in the future.

Conclusions

We describe the use of a unique tabletop PI device that documents palpable breast masses with high sensitivity and specificity. Patients with truly palpable masses (cancers, benign tumors, and firm cysts) were found to have increased firmness (decreased elasticity), while those with nodular breast tissue (fibrocystic change) had less firmness. The use of PI allowed initial separation between benign and suspicious truly palpable masses. A reproducible record of the breast physical examination is created that allows objective review by multiple examiners at varied times. Further work is necessary to optimize examination methods, improve real-time software interpretation, and define the array of diagnostic capabilities.

References

Abstract Mechanical imaging yields tissue elasticity map and provides quantitative characterization of a detected pathology. The changes in the surface stress patterns as a function of applied load provide information about the elastic composition and geometry of the underlying tissue structures. The objective of this study is the clinical evaluation of breast mechanical imager for breast lesion characterization and differentiation between benign and malignant lesions. The breast mechanical imager includes a probe with pressure sensor array, an electronic unit providing data acquisition from the pressure sensors and communication with a touch-screen laptop computer. We have developed an examination procedure and algorithms to provide assessment of breast lesion features such as hardness related parameters, mobility, and shape. A statistical Bayesian classifier was constructed to distinguish between benign and malignant lesions by utilizing all the listed features as the input. Clinical results for 179 cases, collected at four different clinical sites, have demonstrated that the breast mechanical imager provides a reliable image formation of breast tissue abnormalities and calculation of lesion features. Malignant breast lesions (histologically confirmed) demonstrated increased hardness and strain hardening as well as decreased mobility and longer boundary length in comparison with benign lesions. Statistical analysis of differentiation capability for 147 benign and 32 malignant lesions revealed an average sensitivity of 91.4% and specificity of 86.8% with a standard deviation of ±6.1%. The area under the receiver operating characteristic curve characterizing benign and malignant lesion discrimination is 86.1% with the confidence interval ranging from 80.3 to 90.9%, with a significance level of \( P = 0.0001 \) (area = 50%). The multisite clinical study demonstrated the capability of mechanical imaging for characterization and differentiation of benign and malignant breast lesions. We hypothesize that the breast mechanical imager has the potential to be used as a cost effective device for cancer diagnostics that could reduce the benign biopsy rate, serve as an adjunct to mammography and to be utilized as a screening device for breast cancer detection.

Keywords Breast cancer · Diagnostic elastography · Tissue differentiation · Malignancy detection

Introduction

The current methods of breast pathology assessment include Clinical Breast Examination (CBE), Mammography, Ultrasound, Magnetic Resonance Imaging (MRI), and biopsy. Positron emission mammography and sestamibi
scans are also used occasionally. A recent large-scale clinical study (42,760 patients in USA and Canada) on the diagnostic performance of mammography for breast-cancer screening revealed that the diagnostic accuracy of digital and film mammography is 78 and 74%, respectively [1]. A European randomized mammography screening trail (23,929 patients in Norway) demonstrated a sensitivity of 77.4% and specificity of 96.5% for full-field digital mammography while a screen-film mammography yielded a 61.5% sensitivity and 97.9% specificity. Notably, the median size of detected invasive cancers was about 13.5 mm [2]. Despite the recommendation for an annual mammogram, only 58.3% of women 40 years or older in the United States had a mammogram in 2004 [3].

Ultrasound is being increasingly used as a complementary method for the assessment of mammographically or clinically detected breast masses for supplemental information on dense tissue [4]. However, there is limited data supporting the use of ultrasound in breast cancer screening as an adjunct to mammography [5]. The conventional ultrasound is more often used to determine whether an area of concern on the mammogram or clinical exam is cystic or solid. The majority of cystic masses are benign while solid masses need further evaluation [6]. Many indications for clinical breast MRI are recognized. These include resolving mammography findings, staging of breast cancer when multiple or bilateral disease is suspected, and detecting the occult primary breast cancer presenting with malignant axillary lymphadenopathy [7, 8].

The CBE is applied to detect abnormalities or to evaluate a patient’s report of symptoms or findings of palpable breast cancers at an earlier stage of progression [9]. The American Cancer Society guidelines suggest an annual CBE for age 40 and older for early detection of breast cancer in asymptomatic women [3]. The CBE identifies some cancers missed by mammography [10, 11] and provides an important screening tool among women for whom mammography is not advised or for those that do not receive high-quality screening mammography. Nevertheless, CBE performance and reporting approaches are known to be inconsistent. Health care providers report a lack of confidence in their CBE skills and would welcome training and practical recommendations for optimizing performance and reporting [12]. Data for the six studies examined by Barton and colleagues resulted in an overall estimate of 54.1% for CBE sensitivity and 94.0% for CBE specificity [13]. These findings are comparable to the published values of CBE sensitivity (58.8%) and specificity (93.4%) observed in the US national screening program of 752,081 CBE reports [14].

Therefore, a method that mimics CBE but with enhanced sensitivity and specificity might consequently lead to a greater screening yield. Such method for detection and visualizing breast abnormalities and assessing their mechanical properties with sensitivity exceeding that of manual palpation was developed. The method, called Mechanical Imaging, is based on reconstructing the internal structure of soft tissues using the data obtained by a pressure sensor array pressed against the examined site [15]. The changes in the surface stress patterns as a function of displacement, applied load, and time provide information about elastic composition and geometry of the underlying tissue structures.

We have demonstrated earlier that the Breast Mechanical Imager (BMI), a compact device comprised of a handheld probe equipped with a pressure sensor array, allows calculation of size, shape, consistency/hardness, and mobility of detected lesions [16]. The BMI prototype has also been validated in laboratory experiments on tissue models and tested in a clinical environment [17]. The objective of this study is the clinical evaluation of the BMI for breast pathology characterization and differentiation between benign and malignant breast lesions.

Materials and methods

Study design and protocol

The primary objective of the clinical study was to assess the BMI’s capability in lesion characterization. The examination was performed specifically for the concerned breast areas with the suspected lesions. Lesion features were calculated from the recorded BMI examination data and were used for lesion characterization. Additional diagnostic information provided by other diagnostic modalities was collected and used for the analysis of the potential of differentiation of benign and malignant lesion by BMI. Thus, the primary objective of lesion characterization has been extended to a more practical question of benign and malignant lesion discrimination. Evaluation of the classification accuracy of the BMI has been done in a non-blinded data analysis.

The clinical protocol was approved by the Institutional Review Boards at each of the clinical sites. The study was done in compliance with the Health Insurance Portability and Accountability Act. The clinical study has been conducted through a non-randomized multi-center trial in the four investigational sites: New Jersey (The Cancer Institute of New Jersey, New Brunswick), New York (Mercy Medical Center, Rockville Centre), Pennsylvania (The Breast Care Center & General Surgery Practice, Easton), and Florida (Breast Health Institute, Maitland). The exams were performed by BMI trained breast surgeons enrolled as co-investigators in the study.
Study inclusion criteria were:

(a) women (over the age of 21) with a breast mass identified by mammography, ultrasound, and/or CBE,
(b) women (over the age of 21) referred to a breast surgeon for evaluation of a particular area of concern identified either by the woman herself or her primary physician,
(c) patients with a clinical record containing CBE, US, and mammography reports with clear localization of lesion of interest.
(d) patients with a clinical record containing a pathology report with the results from a fine needle biopsy, core needle biopsy, or excisional biopsy for the identified lesion with an exception in cases where the ultrasound and mammography reports both clearly stated that the lesion is benign, predominantly a cyst, and biopsy is not required.

Study exclusion criteria were:

(a) patients with skin infection or inflammation in the breast,
(b) patients with prior breast cancer surgery or radiation,
(c) patients with scleroderma or other connective tissue disorders,
(d) patients with epidermal cysts,
(e) patients that had a biopsy recommendation, but for various reasons a pathology report was unavailable,
(f) immoderate deviation from the recommended BMI examination procedure such as losing the lesion image or keeping lesion image at the edge of pressure array during the scan, poor pressure patterns due to insufficient level of applied force (well below the recommended level).
(g) the BMI examination was performed after biopsy.

A hard copy of lesion related clinical data with the results of clinical diagnostics for all enrolled patients was submitted for data review and analysis. Classification of each scanned lesion as benign or malignant was determined by the result of the pathology report or, as in the case of a cyst or other benign findings that did not recommend biopsy testing, from the results of the mammogram and ultrasound.

BMI system

The BMI is comprised of a probe, an electronic unit, and a touch screen laptop [17]. A pressure sensor array positioned on the probe head is designed to acquire pressure patterns between the probe surface and the exterior skin layer of the breast during contact. The sensory array size is 40 mm by 30 mm and is comprised of 192 pressure sensors. Special software was developed for processing of the data collected from the probe sensors and the calculation of certain lesion features as described below in this paper.

BMI examination procedure

Prior to the biopsy, a BMI examination was conducted on the area of clinical concern. At first, the breast surgeon (oncologist) would perform a standard CBE to determine the location of the concern. Some of the patients had non palpable lesions and the lesion was observed by ultrasound prior to biopsy. With the knowledge of this location, the patient was placed in a similar position to that of a standard CBE with her breast in the supine position on an examination table. The examiner placed a disposable sheath over the sensor head of the BMI and then applied a water soluble lubricating lotion to the sensor head or applied directly to the area of concern. Once ready, the local scan of the lesion by the BMI was done in either one of two different variations: by applying up and down probe compressions over the lesion or circular probe motions around the lesion. During the examination, the acquired pressure response patterns from the probe sensors, being processed in real time, provided visualization of the current pressure pattern and a composition of the accumulated lesion image as described earlier [17]. The examination was recorded and stored by the BMI system in a digital format file, which was analyzed later in a research laboratory environment to calculate lesion features and verify the constructed multi-parameter classifier. The duration of a typical lesion scan was approximately 1–2 min. In addition to the real time lesion image, the examiner was able to observe signals indicating excessive probe tilt, the total number of collected pressure frames and their distribution versus applied force and the level of the force applied to the probe. The acquired level of applied force was used as a guide in maintaining the recommended operational range from 7 to 18N.

Study population

The BMI clinical data set presented in this paper was collected and recorded during the period of July 2005 to November 2007. Initially, after giving written informed consent, 219 women were enrolled in the study at four different clinical sites. However, due to various clinical and procedural factors, a total of 40 patients were found to be ineligible and were excluded from the data analysis. Among them, 13 patients that were recommended for biopsy did not have the biopsy for various reasons (such as: they did not return for the appointment, their insurance
Lesion was diagnosed as epidermal cyst. No clear relation what lesion what examined. BMI examination was done after biopsy. Biopsy was recommended but not done. Critical deviations in examination procedure (see text). Reasons of exclusion patients from data analysis as stated in Table 1. There are 19 patients from the first clinical site, 19 patients from the second site, 37 patients from the third site, and finally 104 patients from the fourth site. The median patient age was 43 years, from 21 to 92 years, with 36 and 52 years as the low and upper quartiles, respectively.

Overall, 147 and 32 cases were classified as benign and malignant, respectively. In 150 cases we had the pathology reports (fine needle biopsy, core biopsy or excisional biopsy) and in 29 cases we had ultrasound and mammography examination results that clearly stated that the lesion is benign, mostly diagnosed as cysts (19 cases), with no biopsy recommended. This diagnostic clinical information was used as the ‘gold standard’ for BMI data analysis. The benign classified lesions were divided into 11 subclasses and malignant classified lesions were divided into 5 subclasses as shown in Table 2.

Lesion features calculation

A detailed description of the lesion feature calculations has been given in an earlier publication [17]. Here, we will briefly outline the algorithms used for evaluation of features proposed for differentiating benign and malignant cases. Three features are related to tissue hardness and two other features are parameters characterizing lesion mobility and shape. Patient age was used as an additional input parameter for the classifier since the breast cancer risk is increased with age [20].

The input data to compose a 3D image of the breast lesion is comprised of a continuous sequence of 2D filtered images. The 3D image reconstruction starts with the formation of an initial 3D structure by stacking the series of 2D structure images along the vertical Z-coordinate (transverse plane) during the first tissue compression. Further, every 2D imprint is integrated by a parallel translation inside the 3D structure image, where x,y coordinates (coronal plane) are determined by a matching algorithm [17]. The Z-coordinate (layer number) is calculated according to:

$$Z = A \times \sum_{j=0}^{k} \sum_{i=0}^{l} S_{ij} - B$$  \hspace{1cm} (1)

where \( A = 1.04 \times 10^{-5} \) and \( B = -5 \) are empirical constants, \( k \) and \( l \) are quantities of horizontal and vertical pixels inside the pressure response frame with the analyzed lesion pattern, and \( S_{ij} \) is the current pressure signal of \( i,j \) pixels expressed in \( P_{x,y} \). Consequently, the final 3D image is composed of 2D images \( P(x,y,Z) \), which are the layers inside the 3D image, and we can calculate the maximum pressure value \( M(Z) \) for each Z-layer:

$$M(Z) = \max \{ P(x,y,Z) \}$$  \hspace{1cm} (2)

where \( x,y \) are coordinates in the plane parallel to a breast surface. Further, we approximate the experimental value of \( M(Z) \) by the second order polynomial:

<table>
<thead>
<tr>
<th>Table 1 Patient enrollment and exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Relevant data</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Enrolled patients</td>
</tr>
<tr>
<td>Excluded patients from data analysis</td>
</tr>
<tr>
<td>Patients included into data analysis</td>
</tr>
</tbody>
</table>

Reasons of exclusion patients from data analysis

- Critical deviations in examination procedure (see text): 1 | 2 | 1 | 9 | 13 | 5.9
- Biopsy was recommended but not done: 4 | 0 | 2 | 7 | 13 | 5.9
- BMI examination was done after biopsy: 0 | 0 | 0 | 9 | 9 | 4.1
- No clear relation what lesion what examined: 1 | 0 | 0 | 2 | 3 | 1.4
- Lesion was diagnosed as epidermal cyst: 0 | 0 | 0 | 2 | 2 | 0.9
\[ P_a(Z) = F_1 \times Z^2 + F_2 \times Z + C \]  

Lesion hardness related features are \( F_1, F_2 \) and \( P_a(Z_m) \). The \( F_1 \)-parameter characterizes nonlinearity of loading curve and is defined as strain hardening of the lesion. The \( F_2 \)-parameter characterizes the average slope of a stress-strain loading curve and the parameter \( P_a(Z_m) \) is the maximum pressure value for the \( Z_m \)-layer, where the total force applied to the probe is 12N.

The mobility of the lesion \( M_{b\text{aver}} \) is evaluated as an averaged value of \( M_b(t) \) through the examination time \( t \) for all pressure patterns containing the lesion image:

\[
M_b(t) = \left( 1 - \frac{\sum_{x=0}^{x=l} \sum_{y=0}^{y=l} \text{Ph}(x,y,Z,\text{Th}) \times \text{Sh}(x,y,t)}{\sum_{x=0}^{x=l} \sum_{y=0}^{y=l} \text{Ph}(x,y,Z,\text{Th})} \right) \times 100\%
\]  

\[ \text{Sh}(x,y,t) = \begin{cases} 
1, & S(x,y,t) \geq \text{Th} \\
0, & S(x,y,t) < \text{Th} 
\end{cases} \]  

where \( \text{Ph} \) is the accumulated 3-D binary lesion image, \( \text{Th} \) is the threshold of binarization, \( \text{Sh}(x,y,t) \) is a binary image of a momentary lesion image to be placed in comparison with the \( Z \)-layer, \( S(x,y,t) \) is the momentary pressure response of sensor with \( x,y \)-coordinates at time \( t \). Prior to Eqs. 4 and 5, the image \( \text{Sh}(x,y,t) \) is matched with the accumulated image \( \text{P}_z(x,y) \) as detailed in a prior publication [17]. The \( M_{b\text{aver}} \) value, expressed in percentage, characterizes the capability of the lesion to change its form and position under applied mechanical indentation by the probe’s curved surface. The shape of the lesion is characterized by the ratio of the lesion boundary length to the perimeter of a circle with the same area as that of the lesion visible projection. The age of enrolled patients was the sixth parameter used in data analysis.

**Statistical analysis**

A statistical assessment of the diagnostic significance of each feature was completed with the aid of the statistical toolbox in MATLAB 6.1 (MathWorks, Natick, MA) and MedCalc 9.2 (MedCalc Software, Mariakerke, Belgium). For visual evaluation of the analyzed clinical data distributions within the benign and malignant patient samples, we used boxplots for data representation of each analyzed

---

**Table 2** Pathology distribution according to clinical data for analyzed lesion

<table>
<thead>
<tr>
<th>Clinical pathology diagnosis (see text)</th>
<th>Clinical location</th>
<th>Total for all sites</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Site 1</td>
<td>Site 2</td>
</tr>
<tr>
<td>Benign</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Cyst</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Fibrocystic changes</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Stromal fibrosis</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Fibroadipose or adipose tissue/fragments/cells</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fibroptic changes</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Sclerosing adenosis, nodular adenosis</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Fat necrosis, fat lobules</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Sclerotic tissue</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Intraductal papillomas</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Others</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Total benign</td>
<td>14</td>
<td>12</td>
</tr>
</tbody>
</table>

Malignant

<table>
<thead>
<tr>
<th>Clinical pathology diagnosis (see text)</th>
<th>Clinical location</th>
<th>Total for all sites</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Site 1</td>
<td>Site 2</td>
</tr>
<tr>
<td>Invasive ductal carcinoma</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Ductal carcinoma in situ</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Invasive lobular carcinoma</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Medullary carcinoma</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total malignant</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Total benign and malignant</td>
<td>19</td>
<td>19</td>
</tr>
</tbody>
</table>

Gold standard for lesion diagnosis

<table>
<thead>
<tr>
<th>Clinical pathology diagnosis (see text)</th>
<th>Clinical location</th>
<th>Total for all sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy pathology report</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>US + mammography reports</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>
feature and their combination. In descriptive statistics, the boxplot is a convenient and widely accepted way of graphically depicting groups of numerical data or data samples [21]. Boxplots are able to visually show distinctions of data samples without making any assumptions about the underlying statistical distribution. The spacings between the different parts of the box help to compare variance. The boxplot also identifies skewness (asymmetry) and outliers. We have used a notched boxplot [22] showing a confidence interval for the median value. The intersection or divergence of confidence intervals for two patient samples is a visual analog of the paired t-test.

A correlation coefficient calculated by the standard procedure implemented in MATLAB software [23] was applied to analyze the strength and direction of the linear relationship between each of the six calculated features. We calculated Pearson product-moment correlation coefficients, which are obtained by dividing the covariance of the two variables by the product of their standard deviations.

To compare diagnostic performance of a test for the features characterizing the lesion and to evaluate feature combined effectiveness, we used the receiver operating characteristic (ROC) curve analysis [24]. The area under the curve (AUC) is determined from plotting sensitivity versus 1-specificity of a test as the threshold varies over its entire range. Conceptually, AUC is interpreted as the probability that the test will produce a value for a randomly chosen diseased subject that is greater than the value for a randomly chosen healthy subject [25]. Each data point on the plot represents a particular setting of the threshold. An area of 1 indicates a perfect prediction; an area of 0.5 is a chance result.

Statistical classifier

To differentiate benign from a malignant breast lesions, we employed a naïve Bayesian classifier [26, 27]. Large-scale comparison of this Bayesian classifier with state-of-the-art algorithms for decision tree induction and instance-based learning on standard benchmark datasets found that the simple Bayesian classifier was superior to each of the other learning schemes, even on datasets with substantial feature dependencies [28]. A naïve Bayesian classifier is a probabilistic classifier based on applying Bayes’ theorem with strong independence (naïve) assumptions. The goal of the Bayesian classification for our situation is to calculate the probability \( P \) of lesion being benign \( C_b \) or malignant \( C_m \) for a given set of lesion features \( F \). Formal presentation of the probability will look as \( P(C_i|F) \), where \( i \) is the lesion number and \( j \) is the lesion feature number. If one the values of \( P(C_b|F) \) or \( P(C_m|F) \) was greater than the other, then the classification of the lesion would be that of the greater value. The Bayes’ theorem facilitates the computation of the \( P(C_i|F_j) \) probability:

\[
P(C_i|F_j) = \frac{P(F_j|C_i) \times P(C_i)}{P(F_j)}
\]

(6)

where \( P(C_i) \) is the prior probability of \( C_i \) and \( P(F_j) \) is the prior probability of \( F_j \). We have used a notched boxplot [22] showing a confidence interval for the median value. The intersection or divergence of confidence intervals for two patient samples is a visual analog of the paired t-test.

\[
P(F_j|C_i) = \prod_{a=1}^{6} P(F_j^a|C_i)
\]

(7)

where \( F_j^a \) is the value of \( F_j \) in the \( a \)-th dimension. For numeric data we assume that each dimension is normally distributed. Thus, we have to estimate the variance \( \sigma_i^2 \) and mean \( \mu_i^a \) for each class \( C_i \) separately, directly from data. Once these values are computed for benign and malignant patient samples, we calculate:

\[
P(F_j^a|C_i) = \mathcal{N}(F_j^a | \sigma_i^2, \mu_i^a) = \exp \left( -\frac{\left( F_j^a - \mu_i^a \right)^2}{2\left(\sigma_i^2\right)} \right)
\]

(8)

The value of the prior probability \( P(C_i) \) is defined by the ratio of the sample size to the total number of patients. The evidence value was calculated according to:

\[
P(F_j) = \sum_{a=1}^{6} \left( P(F_j^a|C_b) \times P(C_b) + P(F_j^a|C_m) \times P(C_m) \right)
\]

(9)

The difference between \( P(C_b|F_j) \) and \( P(C_m|F_j) \) was used as a threshold parameter for the construction of the ROC curve for a set of specified features.

Results

The comparative benign-malignant paired boxplots for the lesion strain hardening (F1), loading curve average slope (F2), maximum pressure peak for the fixed total force applied to the probe (F3), lesion shape (F4), lesion mobility (F5), and patient age (F6) are shown in Fig. 1. The central horizontal line inside each boxplot corresponds to the median value of the sample distribution, as the confidence interval for the median is depicted by a notched beam range on each boxplot. Lower and upper horizontal lines of the box correspond to the first (25%) quartile and the third (75%) quartile, respectively. Small circles beyond
The horizontal bars illustrate the outlier data, which begins at the value of the interquartile range multiplied by 1.5 and extends beyond. Nine breast lesions (7 benign and 2 malignant) out of 179 were not palpated in the area of concern during the corresponding CBE, yet were discovered by the mammography examination.

The area under the ROC curve (AUC) characterizing the discrimination of benign and malignant lesions was calculated separately for each clinical site for each feature of the set $F_1$–$F_6$ as displayed in Fig. 2. This plot demonstrates the variability of diagnostic effectiveness of the analyzed features from site to site. We found that the average AUC value and standard deviation for feature $F_1 = 68.5.1 \pm 12.6\%$, $F_2 = 76.6 \pm 8.1\%$, $F_3 = 79.3 \pm 4.1\%$, $F_4 = 63.8 \pm 8.3\%$, $F_5 = 80.2 \pm 11.2\%$, and $F_6 = 77.4 \pm 6.9\%$.

**Fig. 1** Benign-malignant paired boxplots for features $F_1$ through $F_6$. $F_1$, strain hardening; $F_2$, loading curve slope; $F_3$, max pressure signal; $F_4$, lesion shape; $F_5$, lesion mobility; and $F_6$, patient age.

**Fig. 2** Performance of discrimination between benign and malignant lesions separately for the four clinical sites in consideration of features $F_1$ through $F_6$. $F_1$—strain hardening, $F_2$—loading curve slope, $F_3$—max pressure signal, $F_4$—lesion shape, $F_5$—lesion mobility, and $F_6$—patient age.
Pair correlation coefficients for features $F_1$–$F_6$ used in benign and malignant lesion differentiation are shown in Table 3. The correlation indicates 1 in the case of perfect linear relationship, −1 for a decreasing linear relationship, and another value in between 1 and −1 signifying the degree of linear dependence between the variables. The closer the coefficient is to either −1 or 1, the stronger the correlation between the features. If the features are independent then the correlation is 0, though the converse is not true since the correlation coefficient detects only linear dependencies between two variables. This table has diagonal symmetry, which is expressed by 1, given that each data set perfectly correlates to itself.

ROC curves constructed for each of the BMI parameters $F_1$–$F_5$ are shown in Fig. 3. Features $F_3$ and $F_5$ appeared to have the highest diagnostic information value with AUC of 79.4% with the 95% confidence interval (CI) from 72.7 to 85.1%. The least efficient single feature $F_4$ has AUC of 60.9% with the 95% CI from 53.4 to 68.1%. The right bottom panel in Fig. 3 presents ROC curve for performance of discrimination between benign and malignant lesions for the Bayesian classifier output when the complete set of parameters $F_1$–$F_6$ for all 179 patients was used as input data of the classifier. The AUC is equal in this case to 86.1% with the 95% CI from 80.3 to 90.9% while a significance level $P = 0.0001$ for the area of 50%; sensitivity is equal to 87.5% with the 95% CI from 71.0 to 96.4 ± 12% (95% CI) and specificity 84.4% with the 95% CI from 77.5 to 89.8%. It is important to emphasize that clinical data from all four sites have been combined together. In addition, distributions for the lesion features calculated according to Eq. 8 are different from that for the data shown in Fig. 4 where all distributions have been calculated separately for each clinical site. Figure 3 includes the calculated 95% CI lines above and below the ROC curve.

Figure 4 presents the calculated sensitivity, specificity, and AUC for the output of the Bayesian classifier applied for differentiation of benign from malignant lesions for each clinical site. All $F_1$–$F_6$ features have been used as input parameters in this analysis as described in the method section. We found the sensitivity to range from 85.7 to 100%, specificity from 78.7 to 100%, and AUC from 83.4 to 100%.

Figure 5 demonstrates the sensitivity, specificity, and AUC values calculated as average values and as combined for the 179 patients. The left bar (averaged results) represents the clinical data from all four sites analyzed separately by the Bayesian classifier as shown in Fig. 3, thus the resulting data for sensitivity, specificity and AUC have been averaged. The right bar (combined data) presents clinical data from all sites used as an input data set for the Bayesian differentiation of benign from malignant lesions.

All $F_1$–$F_6$ features have been used as input parameters in this analysis as described in the method section. The average sensitivity is 91.4 ± 6.1% ($\pm$ standard deviation), average specificity is 86.8 ± 9.2%, and AUC is 90.7 ± 7.6%.

### Discussion

As shown in Table 1, 219 patients were enrolled in the study at four clinical sites. A total of 40 patients were found not eligible and their data were excluded from the analysis. That constituted 18.3% exclusion with the largest exclusion due to the procedure deviations (13 patients or 5.9% of the total enrollment) and patients not returning for scheduled biopsy (13 patients or 5.9% of the total enrollment). The remaining 14 patients or 6.4% were excluded due to not meeting the protocol requirements. Sites 1 and 2 were only able of enroll a limited number of patients for the given period, 25 and 21 respectively, which cannot be considered reliable statistical samples. Nevertheless, the data combination from all four clinical sites (179 patients) represents a meaningful statistical population. The exclusion of 18.3% of enrolled patients cannot provide any bias because these 40 patients represent a statistically independent sub-population and related data were not analyzed due to the absence of pathology diagnosis.

It is important to emphasize that the BMI provided detection and image composition for all 179 subjects, including 9 with non palpable lesions. This observation supports an earlier conclusion that computerized palpation is more sensitive than a human finger [29–31].

Table 2 presents the breast pathology distribution among 179 cases. The benign group is subdivided into 11 categories, which were not uniform among the all clinical sites. In total, the largest benign categories were fibroadenoma (37 patients or 25.2%), cyst (26 patients or 17.7%), and fibrocystic changes (17 patients or 11.6%). More uniformity was found in the malignancy cases from each site with invasive ductal carcinoma diagnosed in 80% of site 1, 57.1% of site 2, 80% of site 3, and 70% of site 4. Invasive

<table>
<thead>
<tr>
<th>Table 3 Correlation coefficients for features $F_1$–$F_6$ used in the benign and malignant lesion differentiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion features</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>$F_1$</td>
</tr>
<tr>
<td>$F_2$</td>
</tr>
<tr>
<td>$F_3$</td>
</tr>
<tr>
<td>$F_4$</td>
</tr>
<tr>
<td>$F_5$</td>
</tr>
<tr>
<td>$F_6$</td>
</tr>
</tbody>
</table>

© Springer
 ductal carcinoma was diagnosed in 23 out of 32 malignant cases or 71.9%, which bears close to the screening results received for 1 million women—58.9% of invasive ductal carcinoma or 3215 cases from 5458 total detected malignant cases [32]. The breast pathology distribution observed in this study is in agreement with the data received from large scale screening and research trials [1, 2, 4, 18, 19].

Features $F_1$ through $F_3$ are related to the lesion hardness characterization. The increased hardness of a tissue correlates with the presence of cancer in the tissue as confirmed by various elasticity imaging techniques [33]. Measurements of excised breast specimens exhibited that normal breast tissue has a modulus that was noticeably lower than the modulus of the breast cancer tissue. Tumors or a tissue

**Fig. 3** ROC curves for performance of discrimination between benign and malignant lesions for BMI parameters $F_1$ through $F_5$ calculated for 179 patients and for the Bayesian classifier output (right bottom). Calculated parameters $F_1$–$F_6$ for all 179 patients were used as input data of the classifier

<table>
<thead>
<tr>
<th>Feature</th>
<th>ROC Curve Area</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>$F_1$</td>
<td>64.8%</td>
<td>59.4%</td>
<td>73.5%</td>
</tr>
<tr>
<td>$F_2$</td>
<td>78.7%</td>
<td>78.1%</td>
<td>72.1%</td>
</tr>
<tr>
<td>$F_3$</td>
<td>79.4%</td>
<td>78.1%</td>
<td>72.8%</td>
</tr>
<tr>
<td>$F_4$</td>
<td>60.9%</td>
<td>68.7%</td>
<td>51.0%</td>
</tr>
<tr>
<td>$F_5$</td>
<td>77.9%</td>
<td>81.2%</td>
<td>63.3%</td>
</tr>
<tr>
<td>$F_6$</td>
<td>86.1%</td>
<td>87.5%</td>
<td>84.4%</td>
</tr>
</tbody>
</table>

*Breast Cancer Res Treat*
blocked from receiving blood nutrients are stiffer than normal tissue. Benign and cancerous tumors were also shown to have distinguishing elastic properties [34–36].

Both Fig. 1 and 2 demonstrate the limited discrimination capability of the selected features being analyzed individually due to possible influence by numerous factors, such as breast lesion location, its depth, breast size, and deviation in the examination technique. The averaged values of AUC for features F1–F5 calculated for four clinical sites vary from 64.3 to 80.0%. We can conclude that the confidence intervals of benign and malignant patient samples for features F2 (loading curve slope), F3 (maximum lesion signal for the fixed force applied to the probe), and F5 (lesion mobility) are not overlapped and in agreement with the relatively increased value AUC of 76.6, 79.3, and 80.2%, respectively. However, a relatively decreased AUC of 68.5 and 63.8% is seen for features F1 (strain hardening) and F4 (lesion shape) and their confidence intervals for benign and malignant boxplots have certain intersections.

Two features, strain hardening and lesion mobility, revealed standard deviations of 12.6 and 11.2% and ranged from 60.7 to 87.1% and from 73.8.1 to 91.9%, respectively. The relatively high variance of strain hardening F1 might be explained by sensitivity to deviations in the examination procedure and the significant range of tissue deformation (up to 30%) under the probe manipulation. The lesion mobility variance might also be explained by operator specific deviations in examination procedure. We believe that more detailed instructions and extended training of the operators, as well as real time feedback signaling on deviations in the examination technique, will increase the accuracy and robustness of the procedure.

The correlation coefficients calculated for features F1–F5 demonstrate a low linear correlation (<0.35), except for the F2–F3 pair of 0.68 (see Table 2). We anticipated that these two features would correlate at a more notable level due to the larger value of F2, which would definitely cause an increase in the value of F3. The decrease in the F2–F3 correlation is observed in the beginning of the loading curve, which is plotted as the pressure maximum signal from the lesion versus the total applied force to the probe. We set the range for the initial part of the loading curve as 0–5N of the total force. Initially, the loading curve exhibits substantial nonlinearity that is not taken into account in the F2 calculation, but is incorporated into the F3 feature. Furthermore, with the addition of feature F3 into input parametric set of the Bayesian classifier, the lesion diagnostic accuracy and the confidence interval of AUC appeared to be better.

The F4 value characterizing the lesion shape for malignant lesions decreases relative to the benign lesions as it follows from Fig. 1. This reflects the fact that the shape of a harder core of a malignant lesion is closer to spherical than a benign lesion. The lesion mobility F5 for malignant lesions is decreased relative to the benign lesions (Fig. 1). As we mentioned in the method section, this parameter integrates not only lesion mobility, but also its deformability during the probe pressing against the lesion. Intuitively, this result might be anticipated since the
malignant lesion must be more conservative and stable in these terms. It seems reasonable that $F5$ has mild correlation coefficients of $-0.32$ and $-0.33$ with $F2$ and $F3$.

Aside from the gender, age is the most important factor affecting breast cancer risk [20]. The patient age $F6$ demonstrated a clear divergence between the benign and malignant patients (see Fig. 1). The correlation coefficients of the patient age with features $F1$–$F5$ ranged from 0.16 to 0.14. This result confirms the weak correlation of patient age with other features, a fact which enhances its significance and usefulness as an additional independent coordinate in a multidimensional space for classification. Therefore, we have decided to incorporate this feature into the benign-malignant classifier.

A combined multi-parameter assessment composed of relatively low correlated parameters increases the discriminating power of BMI binary lesion classification. It might be seen in Fig. 3 where we represented ROC curves for BMI parameters $F1$ through $F5$ and ROC curve for the Bayesian classifier output (right bottom). Averaged value of AUC for parameters $F1$ through $F5$ is 73.5%. Combining these five BMI parameters by means of the Bayesian classifier the diagnostic accuracy is increased in averaged by 11.3%, from 72.3 to 83.6%. Additional increase by 2.5% was provided by taking into account patient age $F6$ as the input parameter for the classifier. The feature combination decreases the confidence interval for diagnostic accuracy relative parameter $F1$ through $F5$ alone as it might be concluded from Fig. 3. On average, the confidence interval is narrowing from 13.3% for single feature to 10.6% which is also beneficial effect of features combination.

Figure 4 demonstrates the differentiation capability for benign and malignant lesions with the use of the Bayesian classifier in the case when the data have been analyzed separately for each clinical site. The variability of diagnostic accuracy from clinical site to site might be explained by deviations in the nature of patient groups enrolled at the sites, especially among the patients with benign findings.

The diagnostic accuracy calculated as average values for the four clinical sites exceeds the diagnostic accuracy calculated for the combined 179 patients, as it clearly seen in Fig. 5. This difference is 3.9% for sensitivity, 2.4% for specificity, and 4.5% for AUC. That means that the Bayesian classifier can discriminate more accurately among data sets in which the data is separated into groups (clinical sites) than those in which all patient data are combined together.

It is well recognized in the literature that the tissue elastic properties provide means for not only characterizing tissue but differentiating normal and diseased conditions. This conclusion is based on a wealth of data obtained in the studies on excised breast specimens [34, 35] and clinical studies conducted by numerous researchers worldwide [37–47]. We summarized in Table 4 recently published clinical results directly related to the breast benign–malignant differentiation by elasticity imaging.

<table>
<thead>
<tr>
<th>No.</th>
<th>Method</th>
<th>Number of analyzed lesions</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Citation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>USE*</td>
<td>52 malignant, 59 benign</td>
<td>86.5</td>
<td>89.8</td>
<td>Itoh et al. [37]</td>
</tr>
<tr>
<td>2</td>
<td>USE</td>
<td>135 total</td>
<td>100.0</td>
<td>95.0</td>
<td>Zhang et al. [38]</td>
</tr>
<tr>
<td>3</td>
<td>USE</td>
<td>49 malignant, 59 benign</td>
<td>82.0</td>
<td>87.0</td>
<td>Thomas et al. [39]</td>
</tr>
<tr>
<td>4</td>
<td>MRE*</td>
<td>38 malignant, 30 benign</td>
<td>95.0</td>
<td>80.0</td>
<td>Sinkus et al. [40]</td>
</tr>
<tr>
<td>5</td>
<td>USE</td>
<td>88 total</td>
<td>96.0</td>
<td>61.0</td>
<td>Renger et al. [41]</td>
</tr>
<tr>
<td>6</td>
<td>USE</td>
<td>43 malignant, 150 benign</td>
<td>100.0</td>
<td>96.0</td>
<td>Barr [42]</td>
</tr>
<tr>
<td>7</td>
<td>USE</td>
<td>115 total</td>
<td>90.0</td>
<td>–</td>
<td>Garra et al. [43]</td>
</tr>
<tr>
<td>8</td>
<td>USE</td>
<td>50 malignant, 48 benign</td>
<td>99.3</td>
<td>25.7</td>
<td>Burnside et al. [44]</td>
</tr>
<tr>
<td>9</td>
<td>USE</td>
<td>237 malignant, 584 benign</td>
<td>97.5</td>
<td>48.0</td>
<td>Svensson et al. [45]</td>
</tr>
<tr>
<td>10</td>
<td>PI*</td>
<td>34 malignant, 76 benign</td>
<td>94.4</td>
<td>–</td>
<td>Kaufman et al. [46]</td>
</tr>
<tr>
<td>11</td>
<td>SSI*</td>
<td>4 malignant, 11 benign</td>
<td>100</td>
<td>100</td>
<td>Tanter et al. [47]</td>
</tr>
</tbody>
</table>

USE* ultrasound elastography, MRE* magnetic resonance elastography, PI* palpation imaging, SSI* supersonic shear imaging
lesion differentiation by elasticity imaging. These data clearly demonstrate the significant diagnostic potential of elasticity imaging. The BMI data with a sensitivity of 91.4% and specificity of 86.8% is close to the results shown in Table 4. Notably, this accuracy level (AUC 91.4%) was reached using the more cost effective approach of Mechanical Imaging, rather than other elastography techniques [48]. Based on these findings, we hypothesize that the BMI has a potential to be used as a cost effective device for cancer detection as a diagnostic modality. We further hypothesize that the BMI can be used not only for binary classification but for calculating the probability distribution for multiple possible outcomes subdividing various benign and malignant classes, to distinguish between fibroadenoma, cyst, fibrosis, ductal, lobular carcinoma and other conditions.

Screening mammography is generally the recommended tool for breast cancer detection and is recognized throughout the world. The mammography results are used as the basis in making a decision about performing a biopsy at suspicious breast sites. In the United States alone, more than 1 million breast biopsies are performed annually and approximately 80% of these findings are benign [49, 50].

We simulated how the use of the BMI after standard screening procedures (mammography alone or combination of mammography and conventional ultrasound) could reduce the benign biopsy rate. Figure 6 shows the results of this simulation. Applying the BMI cancer sensitivity and specificity calculated for the combined data including 179 patients (147 benign, 32 malignant) to the patient sample referred for the biopsy (20% of which will be malignant and 80% benign), we built the dependence of the benign biopsy reduction (%) versus the percentage of missed cancers as shown in Fig. 6. These results indicate that a 23% reduction of the benign biopsy is possible without any missed cancer cases and a 50% reduction of the benign biopsy with 4.6% missed cancer cases. Category 3 BIRADS results in a 6 months follow up rather then a biopsy. About 1% of those are cancers. Anything over 1% is probably too high. Clearly, the decrease of the benign biopsy rate is accompanied by an increased proportion of missed cancers. This could be further mitigated by the recommended 3 or 6 months clinical follow up for all patients that were originally recommended for a biopsy but then diagnosed by the BMI as benign.

Conclusions

The multisite clinical study proved the capability of mechanical imaging for real time characterization and differentiation of benign and malignant breast lesions. The BMI has the potential to be used as a cost effective device for cancer diagnostics, and it could effectively reduce the benign biopsy rate. The BMI has the potential to be positioned as an adjunct to mammography and utilized as a screening device for breast cancer detection.

Acknowledgments

The authors would like to thank Ralph Tullo, MD, Breast Health Institute of Maitland, Florida, for his assistance in the clinical study. They also appreciate the engineering support of Milind Patel for the Breast Mechanical Imager. This work was supported by National Institute of Health under research grant CA091392 “Imaging Network for Breast Cancer Mass Screening”.

References

1275–1287. doi:10.1109/TMI.2008.922192
SUMMARY OF CLINICAL STUDIES:

WHAT IS ELASTICITY IMAGING

The Suretouch Visual Mapping System is based on measuring the elastic properties of the underlying breast tissue. This method has also been called various equivalent names in the attached clinical papers. These names includes elasticity imaging, tactile imaging, and palpation imaging.

Elasticity Imaging has been gaining attention in the field of Breast Cancer beyond the research community due to positive clinical results. The reason behind the success of elasticity imaging is due to the fact that the elasticities of cancerous lesions are hundreds of times greater than other breast tissue. This phenomenon has been used by clinicians for thousands of years with their sense of touch to diagnose breast cancer.


Here is a simplified technical definition of elasticity. When you take any object and apply enough force to it, it will compress as shown by the diagrams below.
Stress is defined as the amount of force applied over a given area and Strain is defined as the amount of change in length divided by the original length.

Modulus of elasticity or Young’s modulus, $E$, can be calculated by dividing the stress by the strain:

$$E \equiv \frac{\text{tensile stress}}{\text{tensile strain}} = \frac{\sigma}{\varepsilon} = \frac{F/A_0}{\Delta L/L_0} = \frac{FL_0}{A_0\Delta L}$$

where

- $E$ is the Young’s modulus (modulus of elasticity)
- $F$ is the force applied to the object;
- $A_0$ is the original cross-sectional area through which the force is applied;
- $\Delta L$ is the amount by which the length of the object changes;
- $L_0$ is the original length of the object.

SureTouch measures the reactive pressures generated by the lesion just like clinicians have done for thousands of year with their sense of touch. By using hundreds of individual sensors, a stress image of the lesion can be generated as shown in the figure below.

When asked about the effectiveness difference between strain and stress imaging, expert scientist in this field, Armen Sarvazyan, PhD stated, “There is no dramatic difference.”

SUMMARY OF CLINICAL STUDIES:

Seven clinical studies have been conducted using the SureTouch (ST) or equivalent medical device:

**Wellman** (2001) - Published study of 23 women undergoing surgical excision of breast masses following pre-operative CBE, ultrasound and ST examination. ST measurements were repeatable and estimates of lesion size showed good correlation with the post-resected lesion measurements.

**Helvie** (2003) - Published abstract of 31 women with breast masses. ST sensitivity and specificity for detection of masses were 80% and 75% and for cancer detection, 92% and 72% respectively. A majority of patients reported that ST screening was at least as comfortable as CBE.

**Kearney** (2004) - Published abstract describing study of six breast specialists and seven unskilled lay persons to determine their ability to detect masses in breast phantoms by manual palpation and ST scan. ST imaging by lay persons had higher sensitivity than manual breast palpation in identifying masses. In addition, lay persons then received four training sessions in the use of ST. This training increased the detection of masses to the level achieved by the specialists.

**Ables** (2007) - Presented abstract describing study of 7 operators examining six breast phantoms. ST use demonstrated consistent measurements of lesion size and hardness as well as reproducibility on repeated measurements.
Kaufman (2006) - Published study of 110 patients presenting with a complaint of breast mass. Of those with a true mass, ST identified the mass in 94% of cases versus 86% by CBE. Positive predictive value for breast cancer was 94% by ST and 78% by CBE. As part of the study, a survey of primary care physicians revealed that the inclusion of an ST record in the consultation note implied competence, experience and skill by the breast surgeon.

Griffith (2009) - Presented abstract describing study of 137 patients at a UK NHS breast clinic, 66 of whom had palpable breast masses. Seventy-seven of these were chosen at random to have an ST examination in addition to CBE. Use of ST reduced the percentage of missed lesions by senior and junior surgical trainees. The reproducible reports allowed efficient review by examiners with various levels of experience. Authors state that ST imaging improved patients’ safety in breast clinic and likely had a role in the training and assessment of surgical trainees.

Ergorov (2009) Published study of 179 patients with breast masses identified by mammography, ultrasound and/or CBE. All patients had an ST examination plus a biopsy. ST was able to differentiate 174 benign and 32 malignant lesions with a sensitivity and specificity of 91% and 80% respectively. Authors conclude that ST has the potential to be used as a cost-effective device for cancer diagnostics. This could reduce the benign biopsy rate, serve as an adjunct to mammography and be utilized as a screening device for breast cancer detection.

SUMMARY OF CONCLUSIONS:

These studies, along with accumulated clinical experience to date, suggests the following patient and system benefits associated with ST use:

1. ST can produce more objective and reliable data than CBE in the important areas of breast mass size, hardness, consistency and location
2. ST is less likely to miss breast masses than CBE, especially when CBE is practiced by less experienced clinicians, those in training and those who perform CBE infrequently. Fewer missed lesions could mean earlier detection of breast cancer for some women
3. In some women with dense breasts (especially those under age 40), ST technology could better detect lesions than mammography or CBE
4. Because ST does not use radiation, has far lower equipment costs than mammography and can be performed in the medical office by non-physician staff, ST has fewer risks and is much less expensive to perform than mammography. It is suitable for women who are not in the recommended groups for mammography (e.g., women less than 50 years of age) or are in an interval between regularly scheduled mammography
5. As a result of A through D, ST has the potential to improve the overall referral process between primary care providers and breast surgery consultants
6. The digital record that ST provides each patient standardizes the CBE, provides pictures, and allows for easy and rapid communication of results among clinicians
7. The ST digital record provides an opportunity for enhanced communication with patients about their examination and has the potential to raise breast health awareness.
8. Current research has demonstrated the role of ST in differentiating benign and malignant lesions. If confirmed by additional studies, ST has the potential to be used as a cost-effective device for breast cancer detection. This may be especially true in countries where expensive mammography equipment is not available nor supportable.

9. In developed countries, screening mammography is the recommended tool for breast cancer detection. The mammography results are used as the basis in making the decision about whether or not to perform a biopsy at suspicious breast sites. In the United States alone, more than one million breast biopsies are performed annually and approximately 80% of these findings are benign. The use of ST after standard screening procedures (mammography alone or combination of mammography and conventional ultrasound) has the potential to reduce the benign biopsy rate. Modelling studies suggest that by adding ST to mammography, a 23% reduction of the benign biopsy rate is possible without any missed cancer cases and a 50% reduction of the benign biopsy with 4.6% missed cancer cases.

**COMPLETE LIST OF CLINICAL PAPERS**

**Scientific Background – Elasticity Imaging**


**Scientific Background – Breast Cancer Screening**


**Patient and System Benefits of Tactile Imaging**


**Cost Considerations in Tactile Imaging**