New promising Modalities

Breast Cancer Staging

- Mammography is still the number one breast modality to find breast cancer at the earliest stage possible.
- All other breast modalities are diagnostic tools to help find breast cancer along with screening mammography.
- So let's take a journey and look at these breast imaging tools.

Mammography

- Gold standard in United States to find breast cancer.
- Misses about 1-35 percent of breast cancers in breast
- Started table top, xeromammography, film/screen, digital, tomosynthesis.
- Different density categories can hinder finding breast cancer.
Different type of compression device

- Sigma screening device to help achieve the perfect compression year after year of breast exams.
Prevent under- and over-compression of the breast by standardization on pressure.

We personalize breast compression

Breasts have different sizes. A small breast obviously needs less force to compress than a bigger breast. Why do current guidelines still advise to standardize compression based on force and not on pressure?

We developed a patented new technology which takes breast sizes and stiffness into account. It optimizes compression for every single breast, thus preventing unnecessary discomfort or pain: a highly reproducible procedure with a same physical experience, year after year.

Sensitive Sigma Paddle

Integrated force sensor

X-ray transparent foil

Compression Paddle (small)

Sensitive Sigma Paddle controller

LED pressure indicator
The Sensitive Sigma Paddle redefines the traditional approach. It has been designed to optimize breast compression to 75mmHg pressure. Every technological element, from the X-ray transparent foil to multiple sensors and the controller, has been designed to measure each breast individually. This data is processed instantly and the integrated LED lights serve as real time indicators when the Sensitive Sigma Paddle is lowered onto the breast. It provides the lab assistants a clear guidance when sufficient pressure has been applied. It avoids extreme pressures and prevents unnecessary pain, thus making the procedure more predictable. The Sensitive Sigma Paddle is not just better, simpler, and more convenient for the women. It sets a whole new standard.

How does the Sensitive Sigma Paddle work?

• The mammography technologists positions the breast and starts the compression;
• During compression, the real time pressure value is calculated and visualized using the integrated LED lights;
• At the start of the procedure, without breast compression, only the first LED will light up;
• As pressure increases, additional LED’s will light up;
• When reaching the target pressure (75 mmHg) the sixth LED (counted from the left) will light up;
• The target pressure is an indication of the optimal compression for this breast in this position;
Breast Ultrasound

- Best demonstrates masses
- Hard to see calcifications
- Ultrasound helps distinguish between cysts (fluid-filled sacs) and solid masses. In someone with a breast mass, it can be used to look for enlarged lymph nodes. Breast ultrasound is often used to guide a needle to biopsy breast lesions and enlarged lymph nodes. It can also be used to guide a needle to draw fluid from cysts.
- Can measure masses with three dimensions.
- Shows breast anatomy so let's learn some
Radial 7 o'clock  
Radial 9 o'clock

Antiradial 7 o'clock

ABUS (Automatic Breast Ultrasound)
ABUS (automatic Breast Ultrasound)

There are three ABUS systems currently in use, the first of which is SonoCiné’s Adjunctive Breast Ultrasound System. According to the SonoCiné website, the system received U.S. Food and Drug Administration (FDA) 510(k) clearance in the United States in 2008. It is indicated for use as an adjunct to mammography for B-mode ultrasonic imaging of the patient’s breast when used with an automatic scanning linear array transducer.[4] A robotic device holds the hand-held ultrasound transducer, which produces between 2,000 and 5,000 axial images of the screened area. Use of a robotic device to hold the transducer in place further limits operator dependency and guarantees that breast ultrasound screening can take place without the presence of an accredited technologist.

ABUS’s increased sensitivity — about 97 percent — when used in conjunction with mammography demonstrates this technology can be a beneficial screening tool for those women within the dense breast population. However, because it is a relatively new technology there are certain areas that will need to be addressed as more companies decide to develop systems, and as use and technology continues to increase.
One such area relates directly to radiologists. Although the technology reduces the need for an accredited operator, radiologists will now need formal training. Because radiologists are not as familiar with ultrasound as with other imaging, and because the scans are volumetric 3-D images, there will need to be standardized training for all radiologists so that they can correctly interpret these images.

Skin:
- Average skin thickness is from .5 - 2mm

Chest Wall:
- The pectoralis major and minor and the sternalis
Nipple:

- Lactiferus Duct:
  - Carry milk from lobules to the lactiferous sinus.

Fat:
- Cooper's Ligament:
- Dense supportive strands of fascia that connect to the skin.

- Ribs

- Lymph Node:
- Part of the immune system. Helps to identify foreign objects and filter out disease.
MRI for Advanced Breast Cancer's and Mets

IBC

Metastatic Disease

Lymph Nodes
- axillary
- suprclavicular
Transillumination Breast Spectroscopy

Transillumination breast spectroscopy (TiBS) uses nonionizing optical radiation to gain information about tissue properties directly from the breast. Normal white light is shone into the tissue and the light that leaves the breast on the other side from the source is detected and analyzed. Since the same physiological conditions that contribute to dense breast tissue, as seen in mammography, also will have unique optical signatures.

Optical transillumination has been shown to give information about tissue composition and tissue density. Unlike x-ray mammography which uses ionizing radiation, optical transillumination uses normal white light and is deemed safe to be used frequently for women of all ages and therefore can be used for those situations where mammography is not an option.

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To help women spot suspicious breast lumps in the privacy of the home. By shining light of specific frequencies that best penetrates breast tissue, it should be possible to locate darker, and therefore denser spots for further review by a physician.
Breast Specific Gamma Imaging (BSGI)

The differentiation of malignant and benign tissue. Nuclear medicine procedure that images the metabolic activity of breast lesions through radiotracer uptake.

Imaging is done using a high-resolution anatomic-specific gamma camera. Used as a “next step measure” when post-mammogram evaluation is indicated. Scintimammography has long shown promise as a diagnostic tool for breast cancer detection however it was limited because it used a standard gamma camera and did not allow for the reliable detection of sub-centimeter lesions or direct correlation to mammograms.
- Improves lesion contrast for detection of earlier stage cancers as small as 3 mm
- Located in breast centers for same-day diagnosis
- Mobile system-no installation costs

- Mammography remains the critical first screening measure
- BSGI images metabolic activity which aids in the differentiation of benign and malignant masses
- Metabolic imaging of nuclear medicine is less affected by variations in tissue density
- Offers a vital adjunct to mammography and ultrasound

Crainocaudal view
Breast Cancer Diagnostics - A Historical Perspective

- In 1980, average size of breast cancer lesion = 2.6 cm, the treatment was radical mastectomy
- In the 1990s, treatment progressed to modified mastectomy for smaller tumors
- Today, median size of breast cancer = 1.5 cm, lumpectomy with irradiation is the approach of choice, if there is an absence of additional disease
- However, one in three women have index lesions less than 1 cm in size making it even more difficult to localize satellite lesions and DCIS using current imaging modalities

Simple conclusion?
Need improved detection for cancers < 1.0 cm
40 y/o female who was told following her first mammogram that she had an area of density in the left inferior part of the breast. She had additional imaging (US bx & MRI) which confirmed invasive ductal carcinoma.

PEM found bilateral cancer.
PEM Flex™ Solo II

- High (1.5 - 2.0 mm) spatial resolution
- Short 4-10 minute scan time
- Compact, portable, easy to use
- High Value 3-D tomographic PET images
- Gentle Immobilization vs. Compression

Diagnostic Value - The Power of PEM

- Sensitivity and specificity are key to early detection of breast cancer lesions
- PEM Flex demonstrated >90% "sensitivity and specificity" (TBJ, Vol. 12 #4)
- MRI false positive rate is an issue in diagnosis and accurate image reads

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mammo SPECT</th>
<th>HD PET</th>
<th>Breast MRI</th>
<th>PEM Flex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>66-88%</td>
<td>89% (&gt;1cm)</td>
<td>50 - 85%</td>
<td>91%</td>
</tr>
<tr>
<td>Specificity</td>
<td>&lt;50%</td>
<td>68%</td>
<td>70%</td>
<td>93% - 98%</td>
</tr>
</tbody>
</table>

How does PEM differ from PET?

- Both provide "functional" imaging and use FDG (fludeoxyglucose or fluorodeoxyglucose)
- PEM:
  - Optimized for small body parts
  - Gentle immobilization
  - Designed for patient comfort
  - $850K
  - 1-2 mm spatial resolution
- PET:
  - Whole Body Imaging
  - $2-3 Million
  - 5-6mm resolution
  - Siemens Biograph 16 High Res PET/CT
PET and PEM

Images Courtesy Dr. Kathy Schilling, MD
Boca Raton Community Hospital

History:
45 y/o female with breast implants. PEM done as an adjunct to conventional imaging.

Findings:
PEM showed hypermetabolic retroareolar lesion and 2nd focus of uptake right upper outer quadrant.

Pathology:
Retroareolar lesion - IDC, DCIS
Upper outer quadrant lesion - IDC

Images Courtesy Diagnostic Specialty Imaging, Bensalem, Pennsylvania

PEM and Implants

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Images Courtesy Diagnostic Specialty Imaging, Bensalem, Pennsylvania

Can see through the implant to the posterior side

Images Courtesy Dr. Kathy Schilling, MD
Boca Raton Community Hospital
Advantages
- Shows glucose uptake in cancer cells
- FDG - no significant allergic reactions
- Not affected by hormonal modulated dense breast
- Less expensive device
- No claustrophobia
- Good diagnostic capability for DCIS

Disadvantages
- Uses radiation

The LumaGem molecular breast imaging (MBI) camera is a dedicated breast imaging system with cadmium zinc telluride (CZT) digital detectors.
MBI

MBI is the latest arrival in a new generation of functional breast imaging technology designed to overcome the limitations of anatomic breast imaging.

Though mortality rates have declined, breast cancer remains a nefarious disease. In the U.S. alone, it killed more than four women every hour of every day in 2006, the last year for which complete data are available.

MBI shares family ties with other functional approaches to breast imaging, including breast-specific gamma imaging (BSGI) and positron emission mammography (PEM). All three capitalize on diagnostic nuclear imaging methods...
MBI and BSGI employ gamma cameras specifically designed for breast examination using technetium-99m (Tc-99m) sestamibi, the preferred radiopharmaceutical probe for tumor localization and imaging. Tc-99m is the workhorse radioisotope for such single-photon imaging. Sestamibi concentrates in cells with increased mitochondrial density, a common condition for metastatic breast disease.

MBI proponents believe that it could first have a role in breast cancer screening for at-risk populations, and possibly later aid older women in the general population. The realization of that vision could lead MBI into the mainstream of breast imaging, a goal that neither BSGI nor PEM have yet realized. But MBI developers acknowledge they will have to reduce the radiation dose from MBI before it will be acceptable for screening use.

Case Study # 1

- Area was seen on right breast in the CC view only
- Spot view was inconclusive and U.S. was negative
- MBI was ordered
Case Study #2

- 64 year old female
- Outside facility diagnosed a right IDC at 9:00
- Had US which confirmed the cancer - otherwise no new findings
- Decided on MBI exam which showed two areas of uptake in the right breast 9:00 and 4:00
- Had a repeat US which did show another cancer at 4:00 -- Invasive Mucinous
CTLM-Computed Tomography Laser Mammography

Unlike x-ray mammography, CTLM images blood hemoglobin and the process of neoangiogenesis or new vessel formation which is often associated with breast cancer.
CT Laser breast imaging is part of the field of optical imaging.
CTLM images blood flow to the breast to identify tumors.
CTLM doesn’t use ionizing radiation.
CTLM images through implants and dense tissue easily.
There is NO breast compression – the breasts hang in the
machine in its natural position.
The average scan time is about 10-15 minutes per breast.

The current CTLM will initially be used in conjunction with x-ray and ultrasound to assist in differentiating malignant from benign lesions and help reduce the great number of invasive biopsies performed which later prove to be negative.

Extensive microcalcification unchanged from prior mammograms but patient now feels lump.
This standard CTLM maximum intensity (MIP) projection, shows a large central vessel (normal) but a mass of irregularly shaped neovascularity behind this.
1970's - Thermography

Right Fibroadenoma

Right Medial 3.4 cm

Leß-ca

Now there is Breast Thermography DITI
Why would I want to use Thermography for breast screening?

- Angiogenesis, or new blood vessel formation, is necessary to sustain the growth of a tumor. Breast thermography may be the first signal that such a possibility is developing.

- Breast thermography offers women information that no other procedure can provide. However, breast thermography is not a replacement for or alternative to mammography or any other form of breast imaging. Breast thermography is meant to be used in addition to mammography and other tests or procedures.

Active Cancer Cells Can Double in Number Every 90 Days

<table>
<thead>
<tr>
<th>Time</th>
<th>Cells</th>
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<tbody>
<tr>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>1 year</td>
<td>16</td>
</tr>
<tr>
<td>2 years</td>
<td>266 cells</td>
</tr>
<tr>
<td>3 years</td>
<td>4,896 cells</td>
</tr>
<tr>
<td>4 years</td>
<td>65,536 cells (still undetectable with mammogram)</td>
</tr>
<tr>
<td>5 years</td>
<td>1,048,576 cells</td>
</tr>
<tr>
<td>6 years</td>
<td>16,777,216 cells</td>
</tr>
<tr>
<td>7 years</td>
<td>268,432,406 cells (doubled 27 times)</td>
</tr>
<tr>
<td>8 years</td>
<td>4,304,867,396 cells</td>
</tr>
</tbody>
</table>

*Usually undetectable by mammogram at this stage. 40 (doublings) (approx 10 years), considered lethal. Thermal Imaging can detect growth patterns in the 2nd year. Why wait until it’s too late? Schedule Thermal Imaging NOW!"
Breast thermography and mammography are complementary procedures, one test does not replace the other. All thermography reports are meant to identify thermal emissions that suggest potential risk markers only and do not in any way suggest diagnosis and/or treatment.

The use of Digital Infrared Imaging is based on the principle that metabolic activity and vascular circulation in both pre-cancerous tissue and the area surrounding a developing breast cancer is almost always higher than in normal breast tissue.

In an ever-increasing need for nutrients, cancerous tumors increase circulation to their cells by holding open existing blood vessels, opening dormant vessels, and creating new ones (neoangiogenesis). This process frequently results in an increase in regional surface temperatures of the breast.

Breast Thermography uses ultra-sensitive medical infrared cameras and sophisticated computers to detect, analyze, and produce high-resolution diagnostic images of these temperature variations.
The Procedure

- The patient is left for 15 minutes in order for your body to reach a steady temperature state in equilibrium with the special temperature conditions of the room (19°C-23°C). About 66-73°F
- The patient is positioned in front of the imaging system so that all of the surfaces of the breasts, upper chest, and under arms are imaged.

- The images are captured in real-time from an ultra-sensitive medical infrared imaging camera and sent to a sophisticated computer for storage and analysis (the images are kept on archival media for precision comparison of future images so that the breasts can be monitored over time). Sophisticated computer programs allow the doctor to isolate temperature differentials, perform vascular analyses, dynamic thermal subtraction studies, and more.

- After the images have been analyzed, they are graded using a strict standardized reading protocol. Each breast’s image is placed into one of five thermobiological (TH) categories:
  - TH 1 - Normal uniform non-vascular
  - TH 2 - Normal uniform vascular
  - TH 3 - Equivocal (questionable)
  - TH 4 - Abnormal
  - TH 5 - Severely abnormal
TH 1 Uniform Non-Vascular

TH 2 ESTROGEN DOMINANCE
- Note the symmetrical streaks of orange and red in both breasts (blood vessels). This increase in metabolism is caused by a relative progesterone deficiency (estrogen dominance). Finding this and correcting the problem may play a significant role in breast cancer prevention.

Right Breast TH 3 – Equivocal (Questionable) Image
Note the single hot blood vessel in the right breast. This finding will need to be watched over time for change. If it remains stable, or improves, the finding is normal for the physiology of this patient.
Right Breast TH 4 - Abnormal Image
- Note the increased temperature (metabolism) of the right breast. There are three suspicious areas of higher temperatures. Especially significant is the highly vascular area closest to the right nipple.

Left Breast TH 5 - Severely Abnormal Image
- Note the intensely increased temperature (metabolism) and vascularity of the entire left breast. In this case, a recent mammogram was negative. This is a patient with inflammatory carcinoma in the left breast. This image served to direct the patient for immediate care.

Case 1
- Lump right breast
- Had negative mammogram
Significant heat and Vascularity in right breast especially over the area of the palpable lump in the upper outer quadrant.

Left breast shows to be cool with normal limited vascular pattern.

Right breast with area of lump directly facing the infrared detector. Increased heat and Vascularity are very evident.
Diagnosis

- Invasive ductal

Case 2

- Recent mammogram was normal.
- Ultrasound was also done and recommended repeat imaging in 6 months.
- Patient’s doctor was concerned over a thickening of the left breast during CBE.

- Significant increase in temperature of the entire left breast with noticeable vascularity.
Right breast normal and cool without evidence of suspicious blood vessel activity.

Left breast has significant amount of thermovascular activity
Patient referred back to her doctor for biopsy
Inflammatory CA

Case 3

19 year old with lump in right breast
Had CBE and doctor felt it was a cyst
Patient insisted on further testing
Mammogram and ultrasound were done and both were negative.
- Aggressive increase in temperature and vascularity in right breast

- Left breast is cool and without suspicious vascular pattern

- Right breast shows a single large hot blood vessel leading to the area of the lump
  - Referred back to doctor for biopsy
  - Invasive ductal with DCIS
Case 4

- 42 YO with pain in left breast
- Negative CBE

- Significant increase in temperature and vascularity in left breast

- Right breast shows some heating but no suspicious patterns
Left breast large hot and engorged blood vessels throughout most of the breast
Referred back to her doctor for mammogram and ultrasound
Mammogram and ultrasound showed a suspicious area in left breast
Invasive ductal

Fee: $150 for baseline, 3 months later $130 for comparison
Thereafter, yearly appointments are $160

Dedicated Breast CT Scanner
Breast CT Scanners

- John Boone, PhD. has developed a dedicated breast CT scanner at the University of California in 2001.
- It produces 3-D images of the breast to help radiologists detect those hard-to-find tumors.
- A breast CT scanner has better contrast resolution than mammography.
- The scanner has an x-ray tube and detector - positioned on opposite sides of a patient.
- It rotates 360 degrees while sending x-rays through the body at many different angles.

Dedicated Breast CT Scanner

- Created by John Boone, PhD and his research team at the University of California in 2001
- His colleagues originally thought CT would do more harm than good
- Boone believed that the dose would be greatly reduced if only the breasts were imaged
- Since 2004 used on 600 women in clinical trials
- Clinical trials now being done in Georgia and New York
- 300 images in 16 seconds
- Higher contrast 3-D images
- No compression

Dedicated Breast CT Scanner

- Breast can be imaged in three dimensions and could help to detect hard-to-find tumors
- The scanner uses a radiation dose comparable to standard x-ray mammography and doesn’t require compression of the breast. An image takes 16.6 seconds
- Optimized the scanners by integrating imaging modalities such as positron emission tomography (PET) and contrast-enhanced CT.
- After 45 minutes for uptake of a radioactive sugar molecule, patient is scanned to see whether a tumor is present
Boone’s Breast CT Scanners

- Each rotation produces a series of cross-sectional images or “slices” and multiple slices are acquired along the length of the subject while moving through the scanner.
- The slices are then reconstructed by a computer to generate a composite 3D image that radiologists can view as an entire volume or as component slices.
- Radiation dose is comparable to standard x-ray mammography and doesn’t require compression of the breast.

Dedicated Breast CT Scanner

CC view shows 4 mm IDC

Coronal view CT shows 12.09/4mm IDC

Right CC spot magnification view shows 7 mm cluster of calcifications – arrow shows DCIS mass

Transverse CT shows calcifications in an ill-defined lesion (DCIS)
LCC view shows 1:00 spiculated mass

Transverse CT shows 1:00 spiculated lesion - IDC

Coronal CT shows 1:00 spiculated mass IDC

Pros and Cons for Breast CT

- Many women found it difficult to arch forward into the scanner, their necks were uncomfortable and the table too firm. (6.7)
- Holding breath for 16.6 seconds (7.7)
- Overall comfort (7.9)
- Breast CT verses getting a mammogram (10)

Score from 1 (poor) to 10 (excellent)

<table>
<thead>
<tr>
<th>Section</th>
<th>Rate - 10</th>
<th>Metric</th>
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<tbody>
<tr>
<td>Postar</td>
<td>6.7 - 2.4</td>
<td>7.6 - 1.7</td>
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<tr>
<td>Breast left</td>
<td>7.2 - 2.3</td>
<td>8.2 - 0.7</td>
</tr>
<tr>
<td>Optic</td>
<td>2.9 - 0.5</td>
<td>0.2 - 1.8</td>
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<tr>
<td>Breast CT vs mammography</td>
<td>6.9 - 1.8</td>
<td>10.75 - 1.8</td>
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