TITLE: Optical Computed Tomography for Imaging the Breast: First Look

Invited Paper

Optical computed tomography for imaging the breast: First look

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ABSTRACT

The purpose of the study is to compare computed tomography optical imaging with traditional breast imaging techniques. Images produced by a computed tomography laser mammography (CTLM™) scanner are compared with images obtained from mammography, and in some cases ultrasound and/or magnetic resonance imaging (MRI). During the CTLM procedure, a near infrared laser irradiates the breast and an array of photodiodes detectors records light scattered through the breast tissue. The laser and detectors rotate synchronously around the breast to acquire a series of slice data along the coronal plane. The procedure is performed without any breast compression or optical matching fluid. Cross-sectional slices of the breast are produced using a reconstruction algorithm. Reconstruction based on the diffusion theory is used to produce cross-sectional slices of the breast. Multiple slice images are combined to produce a three-dimensional volumetric array of the imaged breast. This array is used to derive axial and sagittal images of the breast corresponding to cranio-caudal and medio-lateral images used in mammography. Over 200 women and 3 men have been scanned in clinical trials. The most obvious features seen in images produced by the optical tomography scanner are vascularization and significant lesions. Breast features caused by fibrocystic changes and cysts are less obvious. Breast density does not appear to be a significant factor in the quality of the image. We see correlation of the optical image structure with that seen with traditional breast imaging techniques. Further testing is being conducted to explore the sensitivity and specificity of optical tomography of the breast.

Keywords: breast imaging, optical tomography, transillumination, laser mammography, optical imaging, image reconstruction

1. INTRODUCTION

1.1 Early optical breast-imaging experience

Optical imaging techniques for imaging the breast have been evaluated beginning with Dr. M. Cutler's article in 1929 describing a simple breast transillumination system.[1] A cooled light sourced was used to transilluminate the breast in a darkened room, and the unaided eye viewed the breast. In 1980, Ohlsson reported on his experiences with a more sophisticated form of breast transillumination called diaphanography.[2] This technique employed a 35mm camera that used near infrared sensitive film to photograph the breast transilluminated by a high-intensity strobe lamp contained within the light source. In 1984, Isard reported on his experience with this system. [3,4] The technology continued to advance with different approaches used to transilluminate the breast. Carlsen reported on a breast transilluminator that used a dual-wavelength (red, 698nm, and near infrared, 861nm) pulsed light source in a digital spectroscopy technique to evaluate the optical transmission characteristics of the breast.[5] Lafreniere reported on his experiences using a continuous wave light source and an analog infrared video transillumination system.[6]

The breast transillumination evaluations of the 1980's-era generally concluded that the dual-wavelength, digital spectroscopy technique's use was unwarranted because it provided a marginal contribution over mammography and had an undesirable number of false positives.[7,8,9]In 1991, the U.S. Food and Drug Administration (FDA) Obstetrics and Gynecology Devices Panel recommended that breast transilluminators be classified as Class III devices and that a Pre-Market Approval (PMA) would be required to allow the distribution and use of breast transilluminators in the United States.[10] In 1994, the FDA classified breast transilluminators as Class III devices, thus mandating that a PMA be submitted and approved prior to commercial distribution of this device.

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1.2 Next-generation optical breast-imaging devices

In the late 1990's, several groups explored the use of computed tomography (CT) techniques to image the breast. Jackson used a quartz halogen lamp and photomultiplier tube in a first generation CT traverse-and-rotate scanning configuration.[11] In 1989, my group exhibited a first generation CT traverse-and-rotate scanning configuration using a laser diode and photodiode detectors at the 74th annual meeting of the Radiological Society of North America (RSNA).[12] This configuration used a Intel™ 386, 33 MHz computer, acquired one slice of data in 3 ½ minutes, reconstructed one slice-plane image in 10 minutes, and could resolve a 1cm lesion. In 1989, these capabilities did not offer any competition to x-ray mammography.

In 1991, Wang reported on the use of a Nd:glass laser and optical Kerr gate to perform 2-dimensional imaging.[13] In 1994, our group designed and constructed a computed tomography laser breast imaging using a stationary collimated circular array of 600 avalanche photodiodes and a laser fan-beam produced by a rotating polygon mirror and a Argon-pumped mode-locked Ti:Sapphire (Coherent Laser, Mountain View, CA) laser. This device was exhibited at the 79th RSNA annual meeting as a work-in-progress system. Data was simultaneously acquired from groups of 150 detectors at 4,000 points in the orbit of the laser around the breast. This design did not have adequate detector collimation and the fan-beam laser did not have an adequate number of photons to allow imaging of a breast with 17+cm cross-section.

Development of optical breast imaging devices continued throughout the 1990's. By the end of this period several groups had developed different scanning configurations. van de Mark reported on use of continuous wave (CW) laser diodes at multi-wavelengths (679nm, 779nm, and 867nm) in an optical computed tomography 3-dimension breast imaging device developed by Philips Research Laboratories of the Netherlands.[14] Over 300 woman have been scanned with this device in European clinical trials. The woman is prone on the scanning table, with one breast at a time immersed in a 13cm diameter container filled with optical matching fluid. 255 source-detector pairs are used to reconstruct the images. The CW optical tomography device yields the oxygen saturation level and bloodvolume data and suggests that characterization of tumors is possible. Data acquisition is completed in about 9 minutes, and image reconstruction requires several hours.

Heffer reported on the results obtained from studying 130 women with a 70 MHz frequency-domain multi-wavelength scanner.[15] The breast is compressed between two clear plastic plates and immersed in an optical matching fluid. Cranio-caudal and medio-lateral oblique views of each breast are acquired. A planar-tandem scan is performed and amplitude and phase information is obtained and is used to create a two-dimensional projection image of each breast. The differences in the spectral properties of malignancies and benign tumors are being studied and results are reported to be encouraging. Culver reported on a similar CW, compression plate, CCD imaging system that used Intralipid® (Pharmacia AB) as an optical coupling matching fluid.[17] A total of 32 source positions were used and 10,000 measurements are made in about 30 seconds. The field of view is approximately 2.6cm by 2.6cm, with a typical breast compressed thickness of 6cm-7cm. An Algebraic Reconstruction Technique (ART) is used for image reconstruction. Three-dimensional reconstruction of a tissue phantom demonstrates resolution of about 5mm.

Paulsen reported on the results obtained from a pilot study of 15 women using a frequency domain scanner using 16 sources and 16 detectors.[16] The patient is prone on a scanning table with one breast pendant through an opening. The imaging system sensors can be radially translated to form a variable diameter opening ranging from 7-10cm. Illumination at several wavelengths is used in order to convert the multispectral absorption coefficient images into functional parameters such as hemoglobin concentration. Preliminary clinical experience has been positive. In vivo quantative estimates of the hemoglobin concentration can be made.

In all of these scanner configurations, the breast is either immersed in an optical matching fluid or is contacted by the source and detector optics. Only the system reported by van de Mark is capable of performing a computed tomography reconstruction. The other systems employ a sophisticated form of breast transillumination, i.e., the breast is positioned between the source(s) and detector(s) and single projection images are obtained.

2. Optical Computed Tomography Design

2.1 Scanner Configuration

The optical computed tomography scanners that we have tested, with one exception, did not contact the breast. The one exception used a source fiber that was placed in light contact with the breast through use of a pivoted arm. Safety and sanitary considerations arising from having the scanner's source in physical contact with the breast convinced us to abandon this approach.

The design of the scanner places the patient prone on a scanning table, with one breast at a time extending through the tabletop into the scanning area. Interchangeable rings are provided to accommodate the range of breast sizes, up to 20cm, normally encountered, and to generally center the breast in the scanning chamber. There is no breast contact, i.e., the breast is not compressed, and no optical matching fluid is used.

The current design uses two rows of 84 silicon photo-diodes arranged in a circular arc around the breast. One row of detectors is fitted with optical filters to remove the laser excitation wavelength when fluorescence imaging is used. Each detector is fitted with an optical collimator to define its field of view. The laser source and the detector array are rotated 360^0 around the breast. Measurements are made at about 200 points in the orbit to provide over 16,000 measurements. A single slice of data is acquired in about 30 seconds.

In order to obtain multiple slices, the laser source and the detector array are moved vertically between acquisitions, usually downward, in increments of a few millimeters (typically 4mm). The direction of the orbit is reversed from clock-wise to counter-clock-wise for each data acquisition to prevent excessive twisting of the electronic cables. Depending on the breast size as many as 50 slice-planes of data are acquired to cover a maximum vertical distance of 20cm. A bilateral breast examination requires about 15 minutes.

2.2 Image Reconstruction

After the raw data has been processed to compensate for hardware-induced variations, a data reconstruction algorithm is applied to create the slice-plane image. We are currently working with two reconstruction schemes. One is a variation on the classic filtered back projection technique in which the effects of optical absorption and scattering are taken into account. The other is an iterative scheme that takes advantage of finite-element modeling as well as standard algebraic reconstruction methods. The modified back projection reconstruction technique reconstructs a single slice of data in typically 75 seconds using a 700 MHz CPU. Due to its computational intensity, the iterative reconstruction scheme may take from several minutes to several hours to reconstruct a slice, depending upon which reconstruction options are selected. Both techniques may be extended to include three-dimensional data and effects at the expense of increased reconstruction times.

2.3 Image Display

The individual slice-plane images can be directly displayed as individual coronal views of the breast. A volumetric reconstruction technique is applied to the array of slice-plane images to allow simultaneous display of axial and sagittal optical images, i.e., equivalent to cranio-caudal (CC) and medio-lateral (ML) projections routinely seen with mammography. However, instead of a single axial and sagittal projections, a series of sequential axial and sagittal projections are provided. These projections are used to examine the features seen in the mammography films by positioning the axial and sagittal views to better visualize the suspect area.

A bilateral axial and sagittal display is also provided. This features emulates the common practice of placing left and right CC and ML mammography films on a film display box.

The displayed optical coronal, axial, and sagittal views are available for printing on an external printer.

3.0 Clinical Images

Over 200 women and 3 men have been scanned with the computed tomography laser mammography (CTLM™) scanner. In the clinical trial series, CTLM images are compared with x-ray mammography and, where appropriate, ultrasound and magnetic resonance imaging (MRI).

Figure 1 is a cranio-caudal and Figure 2 is a medio-lateral mammogram that reveals grouped or clustered, heterogeneous or pleomorphic calcifications (granular) in the 7 o'clock position, posterior third of the breast. This is a new finding when compared to the previous examination and is suspicious for abnormality. The radiologist classified the lesion as a BIRADS (BIRADS = Breast Imaging Reporting And Data System) category 4. The lesion is suspected solely on the basis of the calcifications. No mass is associated with the lesion.

Figure 3 illustrates Computed Tomography Laser Mammography™ coronal, axial and sagittal views for the same breast. The optical signature of the lesion is clearly seen.

Pathological results demonstrated infiltrated ductal carcinoma of grade III out of III. There was also ductal carcinoma in situ of solid type and high grade. It was difficult pathologically to determine how much of the lesion represented invasive carcinoma versus ductal carcinoma in situ, although at least minimal invasion was thought present.

Figure 1, Cranio-Caudal View

Figure 2, Medio-lateral Oblique View

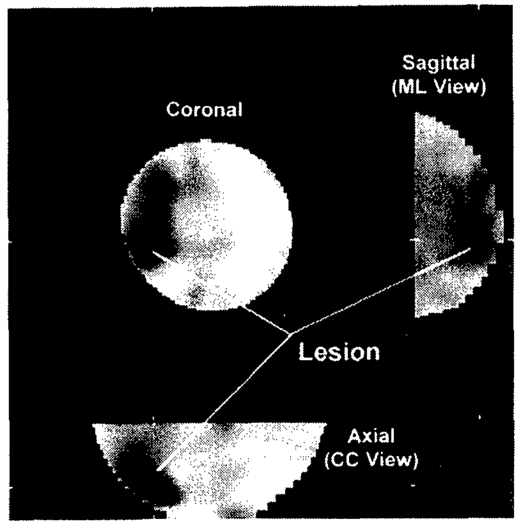

Figure 3, Computed Tomography Coronal, Axial, & Sagittal Views

Figure 4 is a cranio-caudal and Figure 5 is a medio-lateral mammogram that reveals two irregular, speculated masses measuring 3.5cm and 2.5cm in the upper inner portion of the left breast at the nine-thirty position. Spicules link the two masses suspicious for satellite, bridging, and multifocal carcinoma. The radiologist classified the lesion as a BIRADS category 5. A multifocal malignancy was diagnosed following biopsy.

Figure 6 illustrates Computed Tomography Laser Mammography™ coronal, axial and sagittal views for the same breast. The optical signature of the lesion is clearly seen.

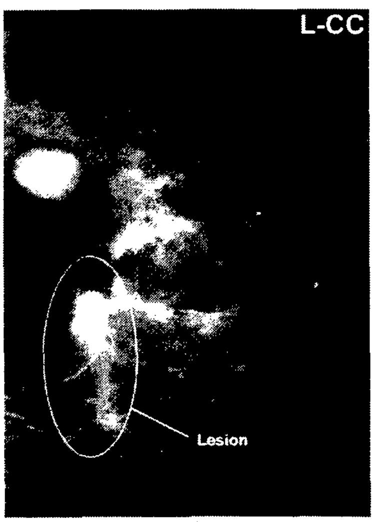

Figure 4, Cranio-Caudal View

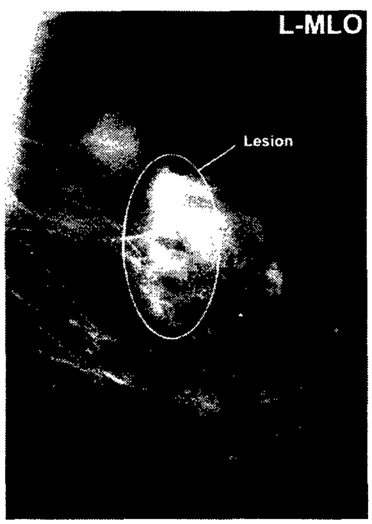

Figure 5, Medio-lateral Oblique View

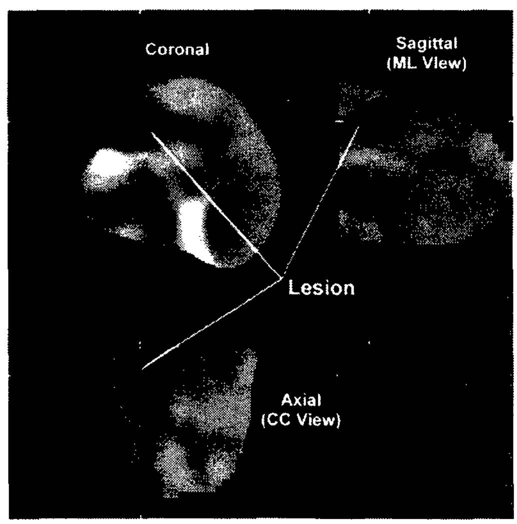

Figure 6, Computed Tomography Coronal, Axial, & Sagittal Views

Figure 7 is a cranio-caudal and Figure 8 is a medio-lateral mammogram that reveals a 27mm, round, high-density mass with speculated margins in the two-o'clock position, posterior third of the left breast. The mass is associated with grouped or clustered fine, linear (casting) calcifications. Pathology reported invasive ductal carcinoma, grade II or III. Ductal carcinoma in situ (DCIS), high grade, with comedonecrosis.

Figure 9 illustrates Computed Tomography Laser Mammography™ coronal, axial and sagittal views for the same breast. The optical signature of the lesion is clearly seen.

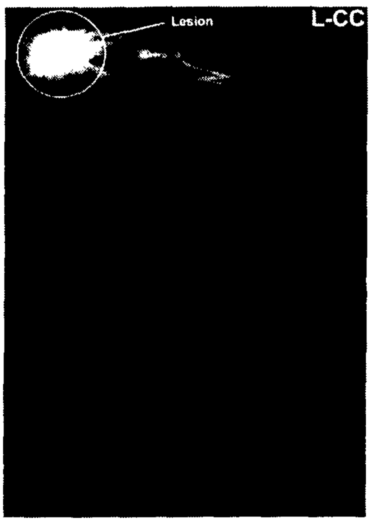

Figure 7, Cranio-Caudal View

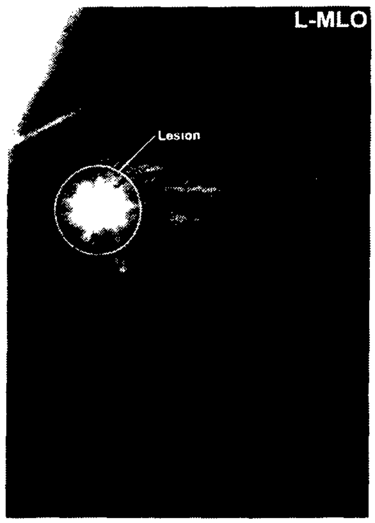

Figure 8, Medio-lateral Oblique View

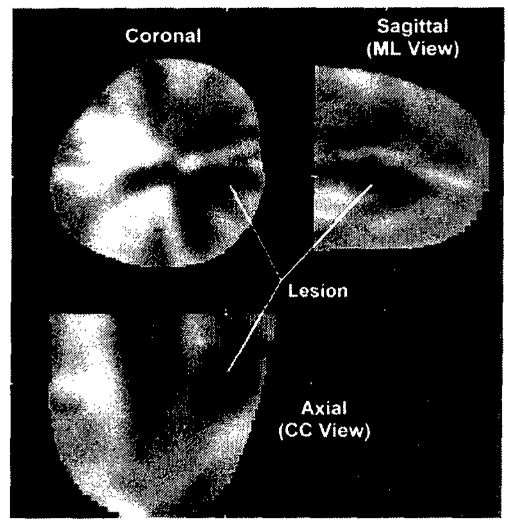

Figure 9, Computed Tomography Coronal, Axial, & Sagittal Views

4.0 Summary

Clinical testing has confirmed the ability of the CTLM to detect and display breast cancer that has been confirmed by biopsy and that was seen in the respective mammograms. Preliminary results with this scanner configuration are encouraging, and clinical testing is ongoing to properly assess the capabilities of this device.

REFERENCES

1. Cutler M., "Transillumination as an aid in the diagnosis of breast lesions", Surg Gynecol Obstet; 48:721-9, 1929
2. Olhsson B, Gunderson J, Nilsson DM. Diaphanography: A method for evaluation of the female breast. World J Surg 1980; 4:701-7
3. Isard HJ. Diaphanography: Transillumination of the breast revisited. Schwartz GF, Marchant DJ, ed. Breast Disease: Diagnosis and Treatment, New York: Elsevier North Holland, 1981; 67-71
4. Isard HJ. Other imaging techniques. Cancer; 53:658-664, 1984
5. Carlsen EN, Transillumination light scanning. Diag Imag; 3:28-33, 1982
6. Lafreniere R, Ashkar FS, Ketcham AS, Infrared light scanning of the breast, Amer Surg; 52(3):123-8
7. Monsees B, Destouet JM, Totty WG. Light scanning verses mammography in breast cancer detection. Radiology; 163:463-5, 1987
8. Monsees B, Destouet JM, Gresell D. Light Scan evaluation of non palpable breast lesions. Radiology; 163:467-70, 1987
9. Alveryd A, Andersson I, Aspegren K, et al. Lightscanning verses mammography for the detection of breast cancer in screening and clinical practice. Cancer; 4:1671-7, 1990
10. Summary Minutes of the 45th Meeting of the Obstetrics and Gynecology Devices Panel, Food and Drug Administration, U.S. Public Health Service, January 11, 1991
11. Jackson PC, Stevens PH, Smith JH, Kear D, Key H, Wells PNT. The development of a system for transillumination computed tomography. Br. J. Radiol.;60:375-80, 1987
12. Personal papers

13. Wang L, Ho PP, Liu C, Zhang G, Alfano RR, Ballistic 2-D imaging through scattering walls using an ultrafast optical Kerr gate. Science; 253: 769-771, 1991
14. van der Mark MB, Hooft GW, Wachters AJH, de Vries UH, Janssen JP, Masser MNJM. Clinical study of the female breast using spectroscopic diffuse optical tomography, Paper presented at Optical Society of America Biomedical Topical Meeting, April 2000
15. Heffer E, Franceschini MA, Schutz O, Siebold H, Heywang-Kobrunner S, Gotz G, Heinig A, Fantini S. Analysis of frequency domain optical mammograms using spectral information. , Paper presented at Optical Society of America Biomedical Topical Meeting, April 2000
16. Paulsen KD, Osterman KS, Kerner TF, Hartov A, Pogue BW, McBride TO, Osteberg UL, Poplack SP. Model-based image reconstruction: A general framework for multi-modality imaging of the breast. Paper presented at Optical Society of America Biomedical Topical Meeting, April 2000
17. Culver JP, Ntziachristos V, Zubkov L, Durduran T, Pattanayak DN, Yodh AG, Data size set and image quality in diffuse optical mammography: Evolution of a clinical prototype. . Paper presented at Optical Society of America Biomedical Topical Meeting, April 2000