

## ABSTRACT

An optical tomography system was developed that allows the simultaneous bilateral imaging of the breast's vascular dynamics with a high spatial probing density (2096 measuring channels per wavelength per breast). The system features novel arrays of fiber-optic probes, which afford high-fidelity optical contact in a well-defined geometry, and which conform to a wide range of breast shapes and sizes without undue compression or the use of coupling fluids. The sensing arrays use strain gauges to monitor the compression of the breasts and to measure the tissue's reaction to pressure-modulating patient maneuvers.

The system is described, and preliminary experimental results from combined optical/strain measurements on the healthy breast are shown.

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## MOTIVATION

Our strategy for increasing diagnostic power of optical imaging:

- Imaging of hemodynamic activity of breast vasculature during rest or in response to provocation allows identification of tissues with deranged autoregulation (e.g., cancerous and pre-cancerous states), with high contrast [1].
- Simultaneous dual-breast imaging allows for paired comparison between diseased and healthy tissue. This increasing statistical robustness [2].
- Multitude of hemodynamic metrics may be considered for use as uni- and multivariate disease predictors [3].

Previously described instrumentation was used for method evaluation, and demonstrated:

- Instrumental feasibility of dual-breast imaging
- Potentially high diagnostic power for many uni-variate and multivariate diagnostic metrics based on bilateral dynamic contrasts

Some practical shortcomings also became clear, which were addressed in the new imager design:

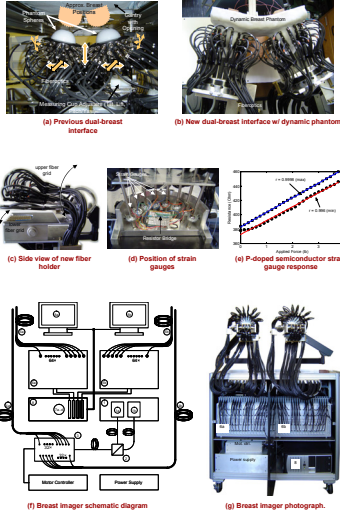
- Patients were required to lie prone, which for many was uncomfortable, and which interfered with the proper performance of provocation protocols, such as the quantitative Valsalva maneuver.
- Fixed-size plastic cups as fiber-optic interface
- limited anatomical adaptability: good optical contact could be achieved only for a subset of breast sizes and shapes;
- circular cross-section maximizes measuring distances in the coronal plane, thus decreasing the achievable signal-to-noise ratio.
- Fairly sparse optode arrangement of 31 sources (S) x 31 detectors (D) per breast. Rigid dual-cup probe holder accommodated only limited breast sizes, or only a portion of the breast
- To alleviate these shortcomings, the new instrument was designed with the following features:
  - Flat-based design and probe holders on two articulated arms, for independent positioning of the fibers on each breast, to allow imaging the subject in a comfortable sitting position.
  - Increased no. of channels: 325 x 64D per breast (total of 2 x 2048 Ch. x 2 Wavelengths @ 1.8Hz)
  - Measuring head design: clamshell mechanism
    - allows mild compression for better transmission
    - accommodates large range of breast sizes
    - allows pressure modulation
    - high spatial sensing density
  - Integrated strain gauges measure pressure/displacement of tissue

## INSTRUMENTATION

The instrument design (see Fig. 1) expands on proven technology described before [4]:

- Detection:** 2x 64-channel detector modules with Si photodiodes, adaptive gain switching, and analog lock-in amplification for demodulation of two frequency-encoded wavelengths. Signal sampling by 64-analog-channel data acquisition boards (National Instruments PCI 6033).
- Illumination:** 2x fiber-coupled laser diodes (400 mW<sub>avg</sub>, 760 nm, 830 nm, from High Power Devices, Inc., NJ), combined by dichroic mirrors (OZ Optics, Canada) and focused into a home-built optical switch (OS) [2,4]. OS uses rotating 2-mirror stack for parallel multiplexed illumination of both breasts through two source-fiber arrays. Physical separation of breasts sufficiently separates optical cross-talk between measuring sites.
- Probe holders:** A clamshell design comprising mechanical fingers to arrange optodes in linear arrays of four (Fig. 1c) on the superior breast surface. The inferior half consists of 4 metal fingers, each carrying 8 fibers, forming the lower breast support. Horizontal distance between top and bottom fingers is variable, via a single adjustment screw, to accommodate different breast sizes. The upper half of the clamshell is formed by 8 cantilevered metal rods (Fig. 1b,c) which can be adjusted to accommodate different breast sizes and to apply a controlled pressure to the tissue.
- Strain gauges:** 8 semiconductor strain gauges (SS-090-060-500P by Micro Instruments, Inc., CA) are incorporated into each measuring head to monitor pressure exerted onto the breast tissue by sensing minute bending in the support rods, causing changes in resistance (Fig. 1d). Gauge resistance changes linearly with the force applied to the rod (57.7 kN), linearly better than 1% over a range of 15N, see Fig. 1e). Nominal resting resistance of the devices: 540 Ω @ 25.5°C, load-free mounted resistance (offset) = 410 Ω. Individual gauge response differences (stable, within 10%) are calibrated. Gauges are read with a voltage divider and sampled by a data acquisition board (USB 6218 by National Instruments Corp., TX). Achievable measurement sensitivity is 16 mN.

Fig. 1: Instrument Setup



Imager components: 1. Laser controller; 1a,b. Laser diode 760 nm and 830 nm, resp.; 2. Wavelength combiner; 3. Optical switch; 4a,b. Illumination fibers for left and right breast; 5a,b. Detector fibers for left and right breast; 6 a,b. Optical detectors for left and right breast; 7a,d. Data acquisition cards; 8. Personal computer; 8a. Display of left, right breast data.

Fig. 2: FEM Model

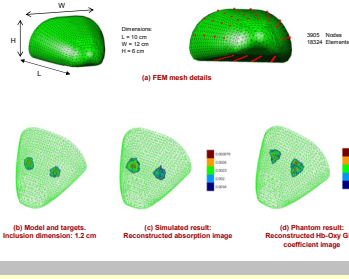


Fig. 3: New Instrument Phantom Results

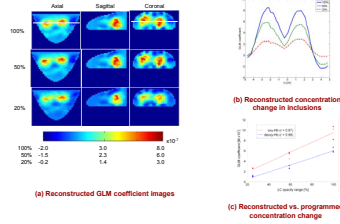
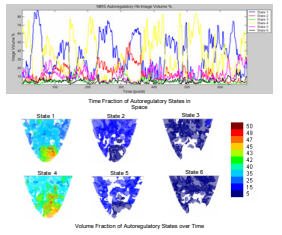


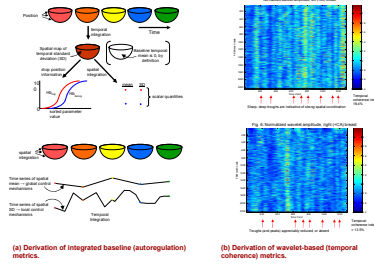
Fig. 4: New Instrument Volunteer Results



## ACKNOWLEDGMENTS

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Fig. 5: Patient Study



Tab. 1: Mean values and significance levels of the explored functional metrics.

Metric	Units	Healthy		Malignant		Pre-malignant	
		Mean	SD	Mean	SD	Mean	SD
CA <sub>integrated</sub>	1/s	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>temporal</sub>	1/s	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub>	1/s	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.05)	1/s	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.01)	1/s	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.001)	1/s	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.0001)	1/s	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.00001)	1/s	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.000001)	1/s	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.0000001)	1/s	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.00000001)	1/s	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.000000001)	1/s	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.0000000001)	1/s	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.00000000001)	1/s	0.000	0.000	0.000	0.000	0.000	0.000

Tab. 2: Multivariate metrics explored in

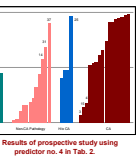
Activity	Healthy	Malignant	Pre-malignant	CA <sub>integrated</sub>	CA <sub>temporal</sub>	CA <sub>total</sub>	CA <sub>total</sub> (p < 0.05)	CA <sub>total</sub> (p < 0.01)	CA <sub>total</sub> (p < 0.001)	CA <sub>total</sub> (p < 0.0001)	CA <sub>total</sub> (p < 0.00001)	CA <sub>total</sub> (p < 0.000001)	CA <sub>total</sub> (p < 0.0000001)	CA <sub>total</sub> (p < 0.00000001)	CA <sub>total</sub> (p < 0.000000001)	CA <sub>total</sub> (p < 0.0000000001)	CA <sub>total</sub> (p < 0.00000000001)
CA <sub>integrated</sub>	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>temporal</sub>	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub>	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.05)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.01)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.0001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.00001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.000001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.0000001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.00000001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.000000001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.0000000001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Tab. 3: Diagnostic accuracy parameters for all metrics.

Metric	Healthy	Malignant	Pre-malignant	CA <sub>integrated</sub>	CA <sub>temporal</sub>	CA <sub>total</sub>	CA <sub>total</sub> (p < 0.05)	CA <sub>total</sub> (p < 0.01)	CA <sub>total</sub> (p < 0.001)	CA <sub>total</sub> (p < 0.0001)	CA <sub>total</sub> (p < 0.00001)	CA <sub>total</sub> (p < 0.000001)	CA <sub>total</sub> (p < 0.0000001)	CA <sub>total</sub> (p < 0.00000001)	CA <sub>total</sub> (p < 0.000000001)	CA <sub>total</sub> (p < 0.0000000001)
CA <sub>integrated</sub>	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>temporal</sub>	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub>	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.05)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.01)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.0001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.00001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.000001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.0000001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.00000001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.000000001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CA <sub>total</sub> (p < 0.0000000001)	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Tab. 4: Study group demographics.

Training Set	Age (years)	Healthy		Malignant		Pre-malignant	
		Mean	SD	Mean	SD	Mean	SD
CA	50	45	10	55	65	10	55
CA	50	45	10	55	65	10	55
CA	50	45	10	55	65	10	55
CA	50	45	10	55	65	10	55
CA	50	45	10	55	65	10	55
CA	50	45	10	55	65	10	55
CA	50	45	10	55	65	10	55
CA	50	45	10	55	65	10	55
CA	50	45	10	55	65	10	55



Tab. 5: Lesion details for FP and FN patients.