Published in final edited form as:

Opt Lett. 2010 December 1; 35(23): 3964–3966.

Rapid magnetic resonance-guided near-infrared mapping to image pulsatile hemoglobin in the breast

Zhiqiu Li^{1,2}, Venkataramanan Krishnaswamy¹, Shudong Jiang¹, Scott C. Davis¹, Subhadra Srinivasan¹, Keith D. Paulsen¹, and Brian W. Pogue^{1,*}

¹Thayer School of Engineering, Dartmouth College, Hanover, New Hampshire 03755, USA

²zhiqiu.li@dartmouth.edu

Abstract

A near-IR (NIR) tomography system with spectral-encoded sources was built to quantify the temporal contrast in human breast tissue using guidance from magnetic resonance imaging. The systems were integrated with a custom breast coil interface to provide simultaneous acquisition. The NIR signal was synchronized to simultaneous finger pulse oximeter plethysmogram, which offered a frequency reference. A 0:1 s temporal delay of the absorption pulse within adipose tissue relative to fibroglandular tissue was found, in an initial human study, showing the potential for novel contrast imaging of fast flow signals in deep tissue.

A near-IR (NIR) tomography system with spectral-encoded sources near 785 nm waveband was built, and its capacity to reveal the small-scale pulsatile variations of hemoglobin within the human breast was analyzed [1,2]. In this Letter, the system was incorporated into a magnetic resonance (MR) scanner with online finger pulse oximeter (PO) plethysmogram, and the temporal signatures of the human breast were recorded and analyzed with frequency synchronized to the PO signal. The value of NIR spectroscopy to breast tumor imaging has been demonstrated in several single-investigator trials [3–6] and is just about to enter multicenter trials to study the prognostic value for neoadjuvant chemotherapy [7]. This design potentially adds a different dimension of data to this type of imaging, providing temporal pulsatile feature information of specific regions.

The NIR fibers were integrated into a customized MR breast coil interface, thereby providing MR tissue structural information for improved local parameter estimation. The MR-compatible pulse oximeter (PO) (Veris Vital Signs Monitor, MEDRAD, Inc.) was used in the scanner room to provide continuous monitoring of the subject finger pulse waveform during the imaging session. The plethysmogram output was a continuous analog signal proportional to the intensity of the detected optical signal through the finger, allowing analog sampling at the same rate as the breast imaging system. The data signals were processed with the plethysmogram as a phase reference, since the heart pulse frequency drives both signals. The individual hardware components are shown in Fig. 1.

Two healthy female subjects have been imaged, twice each, in this hybrid system. The breast to be imaged was pressed into a slab shape between the two fiber plates. In the example shown in Fig. 2, the breast was compressed to be 54 mm thick. The subject was imaged by both the NIR system and the MR system at the same time, and the PO was attached to the subject's finger. The MR required 15 min to complete all scout scans and T1-

and T2-weighted coronal scans of the breast. The NIR sources were seven 785 nm single-mode laser diodes (Hitachi HL-7851G). The source locations were spectrally encoded into the signal, by having a different center wavelength at each laser diode, by about 1:5 nm interval [1,2]. These were set and maintained by current and temperature control. Thus, each source fiber illuminated the tissue with a slightly different wavelength simultaneously, but all within the 783 to 791 nm wavelength range. In this paradigm, the wavelength-shifting technique was used only to encode the source positions, and the optical properties were assumed to be the same for all wavelengths in this relatively narrow band. The NIR system sampled all wavelengths simultaneously at 10 Hz, and a dataset of 275 s length was acquired.

A coronal T1 MR image of the breast is shown in Fig. 2(a). The darker region inside the tissue is fibro-glandular tissue with higher hemoglobin, while the lighter regions are mostly adipose or fatty tissues, which generally have lower hemoglobin content [8]. Based on the MR image, a two-dimensional mesh with 8000 pixels was created and segmented into two regions [Fig. 2(b)] to perform region-based reconstruction. A 15 s section of the output analog signal from the PO is shown in Fig. 2(c). The fast Fourier transform (FFT) of the entire signal sequence, shown in Fig. 2(d), shows that the heart rate of the subject was between 1.1 and 1:4 Hz during imaging. Detected signals of three typical source-detector pairs and their FFTs are shown in Figs. 2(e)–2(j). In addition to the low-frequency noise, there is a strong peak at around 0:25 Hz in each signal, which was attributed to the breathing rate of the subject. The signal of blood flow in the breast tissue can be seen as a smaller peak, sharing the same 1.1 to 1:4 Hz frequency band as the PO output. Because the blood flow in the breast was directly oscillating from the heartbeat signal, a bandpass filter with 1.1 to 1:4 Hz range was used. The data used for image recovery consisted of the bandpass-filtered data and their time-averaged dc component.

After calibration with a slab-shaped homogeneous phantom measurement, the data were reconstructed using a region-based reconstruction algorithm [1,9,10]. This algorithm minimizes the difference of the measured data, Φ^M , and the calculated data, Φ^C , from the forward model

$$\chi^2 = \sum_{i=1}^{NM} \left(\Phi_i^C - \Phi_i^M \right)^2, \quad (1)$$

where i is the index for each source-detector pair and NM is the total number of measurements.

In the inversion, the Jacobian derivative matrix, $\mathbf{J}$, with elements $j_{i,n} = \partial(\ln I_i)/\partial\mu_{a,n}$, was remapped such that nodes in each tissue were grouped into just two tissue regions (adipose or fibroglandular), where the vector of values μ_a were reduced to a smaller subset $\tilde{\mu}_a$ vector. Similarly, $\mathbf{J}$ was mapped to a smaller matrix $\tilde{\mathbf{J}}$, such that the update equation was

$$\delta\tilde{\mu}_a = \left(\tilde{\mathbf{J}}^T \tilde{\mathbf{J}} + \lambda \mathbf{I} \right)^{-1} \tilde{\mathbf{J}}^T \times \left(\Phi^C - \Phi^M \right)^T, \quad (2)$$

where $\sim$ indicates the parameters for the region-mapped areas [10]. This regionized update was used to estimate μ_a at 785 nm for the two regions within the breast. The assumption of uniform absorption in each region allows examination of the phase relationship between the two regions.

Calibrated datasets at each time point were reconstructed separately, which gave a homogeneous μ_a in each region. Scattering coefficients were assumed 0:6 mm⁻¹ in the

adipose region and 1 mm^{-1} in the fibroglandular region [8]. Values of μ_a over the first 15 s of acquisition and their FFT spectra are shown in Figs. 3(a)–3(d). Both the mean value and the variation of μ_a are larger in the fibroglandular region than in the adipose region, which agrees with common physiological knowledge and previous data [8]. The frequency range of μ_a in both regions agreed with the output of the PO.

The temporal change of μ_a in the two regions was analyzed using an algorithm developed to estimate the phase shift in each frequency band of the signal using 0.02 Hz narrow steps. This frequency filter was used, because the signal was spread over a wide band of frequencies with a stable phase shift. In each frequency band, the filtered μ_a values were Fourier transformed, and then the phase delay in the two tissue types was calculated. The time delay in pulsatile flow was then estimated from the phase delay.

The phase relation and the corresponding time relation of μ_a in two regions are shown in Figs. 3(e) and 3(f), where positive values indicate that the variation of μ_a in the fibroglandular region is ahead of that in the adipose region, and vice versa. Within the 1.2 to 1.4 Hz range, there was a stable phase difference of near 50 deg offset. If translated into time, this phase difference means that the variation of μ_a in the fibro-glandular region is about 0.1 s ahead of that in the adipose region, indicating physiologically that the fibroglandular vascular response to the heartbeat is ahead of that in the adipose region by about 0.1 s. This observation reveals that the hemoglobin variation in the two regions is not in phase. To our knowledge, this is the first temporal phase comparison of μ_a or hemoglobin content between different types of breast tissue. Previous results from NIR brain imaging have repeatedly shown phase shifts between oxyhemoglobin and deoxyhemoglobin [11,12]. To further explore this phenomenon and find the cause of the phase shift of μ_a in the two regions, the system has been expanded to include two central wavelengths, 785 nm and 830 nm, to image both species of hemoglobin.

In summary, this high-frame rate MR-guided NIR tomography system can detect small-scale temporal variations of the optical signal, caused by the blood pulsation at the heartbeat rate. The pulsation of the absorption properties in the breast can be reconstructed with the structural information from MR imaging (MRI) and the frequency reference from a PO. A phase comparison algorithm was developed and applied. It was found that the response to the heartbeat in the fibro-glandular region is about 0.1 s ahead of that in the adipose region. This observation is likely an indication of the fact that the vasculature feeding the fibroglandular tissue is largely more directly from the heart, as compared to that vasculature feeding the adipose tissue. The response of the tissue to the arterial pulsation from the heart is an indirect measure of the tissue vascular resistance and mechanical properties. It is possible that being able to image this or to quantify changes may provide a novel contrast for human tissue imaging and disease diagnosis. Human subject experiments are ongoing to investigate physiology and pathology applications of this imaging paradigm. Additionally, the system is being improved to provide two-wavelength video-rate tomography to facilitate video-rate quantification of hemoglobin content and oxygen saturation, providing a platform for pulse oximetry imaging of the breast tissue.

Acknowledgments

We gratefully acknowledge National Institutes of Health (NIH) research grants R33CA100984, RO1CA069544, and P01CA080139.

References

1. Li Z, Krishnaswamy V, Davis SC, Srinivasan S, Paulsen KD, Pogue BW. Opt. Express. 2009; 17:12043. [PubMed: 19582120]

2. Piao D, Dehghani H, Jiang S, Srinivasan S, Pogue B. *Rev. Sci. Instrum.* 2005; 76:124301.
3. Choe R, Corlu A, Lee K, Durduran T, Konecky SD, Grosicka-Koptyra M, Arridge SR, Czerniecki BJ, Fraker DL, DeMichele A, Chance B, Rosen MA, Yodh AG. *Med. Phys.* 2005; 32:1128. [PubMed: 15895597]
4. Jiang S, Pogue BW, Carpenter CM, Poplack SP, Wells WA, Kogel CA, Forero JA, Muffly LS, Schwartz GN, Paulsen KD, Kaufman PA. *Radiology.* 2009; 252:551. [PubMed: 19508985]
5. Cerussi AE, Tanamai VW, Mehta RS, Hsiang D, Butler J, Tromberg BJ. *Acad. Radiol.* 2010; 17:1031. [PubMed: 20542448]
6. Soliman H, Gunasekara A, Rycroft M, Zubovits J, Dent R, Spayne J, Yaffe MJ, Czarnota GJ. *Clin. Cancer Res.* 2010; 16:2605. [PubMed: 20406836]
7. Tromberg BJ, Cerussi AE. *Clin. Cancer Res.* 2010; 16:2486. [PubMed: 20406838]
8. Brooksby B, Pogue BW, Jiang S, Dehghani H, Srinivasan S, Kogel C, Tosteson TD, Weaver J, Poplack SP, Paulsen KD. *Proc. Natl. Acad. Sci. USA.* 2006; 103:8828. [PubMed: 16731633]
9. Dehghani H, Eames M, Yalavarthy P, Davis S, Srinivasan S, Carpenter C, Pogue B, Paulsen K. *Commun. Numer. Methods Eng.* 2009; 25:711. [PubMed: 20182646]
10. Brooksby B, Dehghani H, Pogue B, Paulsen K. *IEEE J. Sel. Top. Quantum Electron.* 2003; 9:199.
11. Reinhard M, Wehrle-Wieland E, Grabiak D, Roth M, Guschlbauer B, Timmer J, Weiller C, Hetzel A. *J. Neurol. Sci.* 2006; 250:103. [PubMed: 17011584]
12. Obrig H, Neufang M, Wenzel R, Kohl M, Steinbrink J, Einhaupl K, Villringer A. *NeuroImage.* 2000; 12:623. [PubMed: 11112395]

Fig. 1.

(Color online) The system includes (a) a source cart with seven spectrally-encoded laser diodes and (b) a detection cart with eight spectrometer/CCD systems. (c) A 3 Tesla MRI system is used with (d) the finger pulse oximeter to measure heartbeat of the subject. (e) The customized MR breast coil is shown with (f) the patient breast interface, which couples into the MR breast coil. A complete schematic is shown in [1].

Fig. 2.

(Color online) (a) MR image of the breast with (b) a finite-element mesh segmented into fibroglandular (white) and adipose (black). (c) The first 15 s of the PO output with (d) its FFT. The first 15 s of the detected signals from the NIR system for source 1 to detector 1, source 4 to detector 4, source 7 to detector 7 are plotted in (e), (g), and (i), respectively, with their FFT spectra shown in (f), (h), and (j).

Fig. 3.

(Color online) Reconstructed values of μ_a in (a) the fibroglandular region and (b) the adipose region. (c) The Fourier power spectrum of μ_a for the fibroglandular region and (d) for the adipose region. (e) The phase difference of μ_a between the fibroglandular and adipose regions versus frequency. (f) The temporal relation of μ_a between the two tissues versus frequency.