Diffuse Optical Imaging of the Female Breast: High Spatial Sampling for Enhanced Resolution, and Broadband Spectroscopy for Quantitative Oximetry

Yang Yu, Ning Liu, Angelo Sassaroli, and Sergio Fantini

Tufts University, Department of Biomedical Engineering, 4 Colby Street, Medford, MA 02155, USA

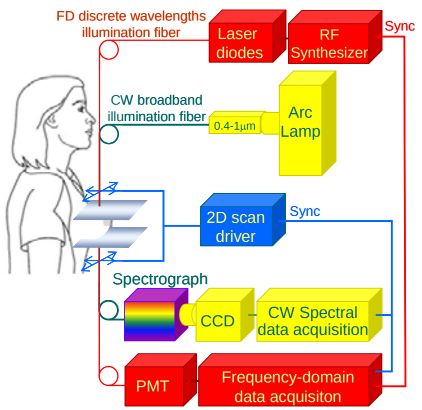
Introduction

Traditional X-ray mammography, though providing high spatial-resolution images, bears no functional information about tissue compositions. X-ray does not have significant benefits for women under 40 and 18% of women with no breast cancer have to go through a biopsy after 10 mammograms [1]. Optical imaging, on the other hand, has the potential to be generally applicable and can offer unique functional information about the breast tissue to improve the diagnostic accuracy. Near infrared (NIR) optical imaging [2-4] relies mainly on the absorption of hemoglobin for the source of image contrast, and is highly sensitive to the oxygen saturation of hemoglobin (SO_2). NIR imaging reveals both angiogenesis and hypermetabolism, both of which are considered hallmarks of cancer [5,6]. NIR has the great potential to be an adjunct modality to the current clinical diagnostic methods by providing another layer of information and can also serve as a continuous monitoring method for post-treatment breast health conditions [7]. Here, we present the NIR imaging system and results developed in our lab.

Methods

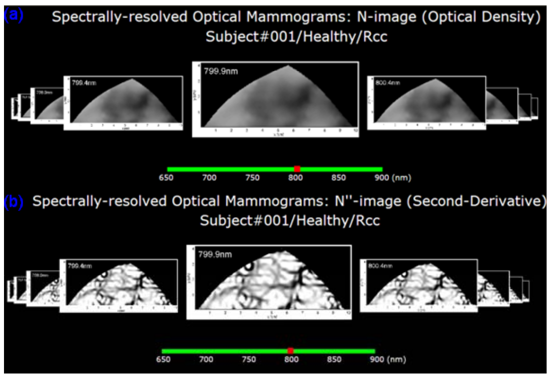
We present a hybrid continuous-wave (CW)/frequency-domain (FD) instrument for NIR spectral imaging of the female breast based on a tandem, planar scanning of one illumination optical fiber and one collection optical fiber configured in a transmission geometry [8]. The breast is placed between two glass plates under mild compression. The spatial sampling rate of 25 points/cm² is increased to 400 points/cm² by post-processing the data with a 2-D cubic spline interpolation. In order to compensate the higher photon transmission due to smaller breast thickness in the edge portion of the breast, namely edge effects, we use the phase information from the FD data to estimate the breast thickness for each pixel [9] and then co-register it with the CW image to counteract the edge effects. We then apply a previously developed spatial second-derivative high-pass algorithm to the edge-corrected intensity image (*N*-image) to enhance the visibility and resolution of optical inhomogeneities in breast tissue such as blood vessels and tumors (*N*′′-image) [10]. The spectral data at each image pixel consists of 515-point spectra over the wavelength range 650-900 nm, thus featuring a spectral density of two data points per nanometer. *N*′′-image is used to determine the pixels of interest which represents a local absorption peak. For those pixels of interest, we process the measured spectra with a paired-wavelength spectral analysis method to quantify the oxygen saturation of detected optical inhomogeneities [11], under the assumption that they feature a locally higher hemoglobin concentration.

Block Diagram of Hybrid CW/FD Instrument for Optical Mammography



Instrument Capabilities

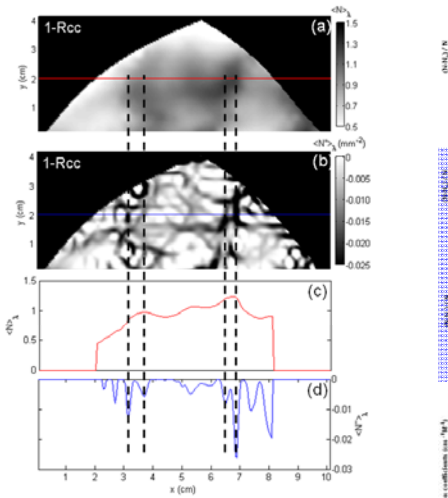
1) Measure bulk breast tissue optical properties (with separate FD handheld probe)
2) Perform independent scan for CW and FD domains
3) Feature high information content: both structural and functional
4) Automatic detection of the border of the breast
5) Real-time breast spectrum and raw image display
6) Non-invasive, non-ionizing, painless



Spectrally-resolved *N*-images (panel (a)) and second-derivative *N*′′-image (panel (b)) for a healthy 40-year-old subject, right breast, cranio-caudal projection (Rcc).

We are able to form an individual image at wavelengths in the range 650-900 nm, at approximately 0.5 nm intervals for the corresponding *N*-image or *N*′′-image, respectively. The spectral data is used to extract the functional information and the structural information is employed to determine the pixels which feature a significant local absorption contrast.

Female breast structural images enhanced with second-derivative algorithms



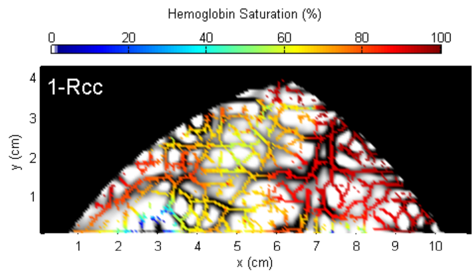
Contrast enhancement due to second-derivative high-pass filter approach

(a) *N*-image showing blurred optical inhomogeneities;

(b) *N*′′-image showing fine structures, assigned to blood vessels, that are not resolvable in the *N*-image;

(c) line data of spectrally averaged *N* (<*N*>) for *y* = 2 cm in *N*-image;

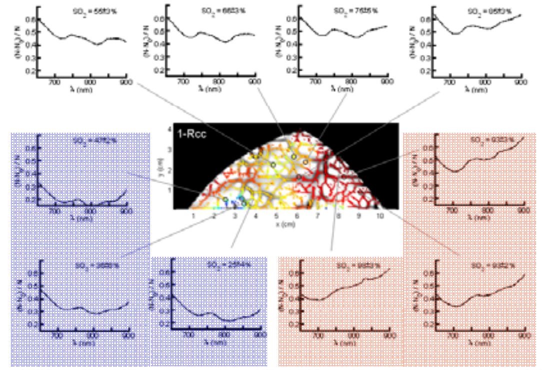
(d) line data of spectrally averaged second derivative (<*N*′′>) for *y* = 2 cm.

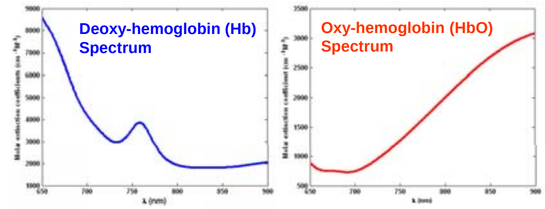


Hemoglobin saturation maps measured on the same subject with paired-wavelength spectral analysis

The color representation of oxygenation values is superimposed to the gray-level display of *N*′′-image. Only pixels which feature a local absorption peak are analyzed for their oxygen content. The oxygenation values range from 25%~98%, with 86% of the oxygenation values between 60% and 95%, which agrees with reasonable physiological expectations because typical venous oxygenation is 60%~80% and typical arterial saturation is around 98%.

Representative spectra acquired for ten different oxygenation values





Spectral shapes corresponding to different oxygenation values

Spectra corresponding to lower oxygenation values (marked in blue color) carry the signature absorption peak for Hb around 758 nm and spectra for higher oxygenation values (marked in red color) demonstrate a similar ascending trend to the HbO absorption spectra.

Conclusions

The most notable features of the optical mammograms reported here are a high spatial density of pixels (400 points/cm² or 0.5 mm X 0.5 mm pixel size), and 515-point spectra data over the wavelength range 650-900 nm at every image pixel (or one image every 0.5 nm). These features have the potential to better exploit the high intrinsic contrast provided by hemoglobin in breast tissue, and to perform more accurate functional measurements to detect, diagnose, and monitor breast pathologies. So far we have been able to obtain the oxygenation and 2D structural information from healthy breast tissues. The absolute value of hemoglobin saturation is an important parameter to determine tissue abnormality and hypoxic fractions in breast lesion sites. We plan to study patients with various types of breast cancer to further assess the clinical potential of our imaging modality.

Acknowledgments

This research is supported by the National Institutes of Health (Grant CA95885).

References:

[1] R. Choe, S. D. Konecky, A. Corlu, K. Lee, T. Durduran , D. R. Busch, S. Pathak, Ñ and A. G. Yodh, "Differentiation of benign and malignant breast tumors by in-vivo three-dimensional parallel-plate diffuse optical tomography," J. Biomed. Opt. **14**, (2009).
[2] S. Srinivasan, B. W. Pogue Ñ and K. D. Paulsen, "In vivo hemoglobin and water concentrations, oxygen saturation, and scattering estimates from near-infrared breast tomography using spectral reconstruction," Acad. Radiol. **13**, (2006).
[3] D. Grosenick, H. Wabnitz, H. Rinneberg, K. T. Moesta and P. M. Schlag, "Development of a time-domain optical mammograph and first in-vivo applications," App. Opt. **38**, (1999).
[4] M. A. Franceschini, K. T. Moesta, S. Fantini, G. Gaida, E. Gratton, H. Jess, W. W. Mantulin, M. Seeber, P. M. Schlag and M. Kaschke, "Frequency-domain techniques enhance optical mammography: initial clinical results," Proc. Natl. Acad. Sci. **94**, (1997).
[5] L. Spinelli, A. Torricelli, A. Pifferi, P. Taroni, G. Danesini and R. Cubeddu , "Characterization of female breast lesions from multi-wavelength time-resolved optical mammography," Phys. Med. Biol. **50**, (2005).
[6] B. Wassermann Ñ and H. Rinneberg, "In-vivo tissue optical properties derived by linear perturbation theory for edge-corrected time-domain mammograms," Opt. Express **13**, (2005).
[7] B. J. Tromberg, B. W. Pogue, K. D. Paulsen, A. G. Yodh, D. A. Boas and A. E. Cerussi, "Assessing the future of diffuse optical imaging technologies for breast cancer management," Med. Phys. **35**, (2008).
[8] Y. Yu, N. Liu, A. Sassaroli, and S. Fantini, "Near-infrared spectral imaging of the female breast for quantitative oximetry in optical mammography," App. Opt. **48**, (2009).
[9] S. Fantini, M. A. Franceschini, G. Gaida, E. Gratton, H. Jess, W. W. Mantulin, K. T. Moesta, P. M. Schlag, and M. Kaschke, "Frequency-Domain Optical Mammography: Edge Effect Corrections," Med. Phys. **23**, (1996).
[10] V. E. Pera, E. L. Heffer, H. Siebold, O. Schütz, S. Heywang-Köbrunner, L. Götz, A. Heinig, and S. Fantini, "Spatial second-derivative image processing: An application to optical mammography to enhance the detection of breast tumors," J. Biomed. Opt. **8**, (2003).
[11] E. L. Heffer and S. Fantini, "Quantitative oximetry of breast tumors: A novel near-infrared method that identifies two optimal wavelengths for each tumor," Appl. Opt. **41**, (2002).