In vivo near-infrared spectral detection of pressure-induced changes in breast tissue

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A diffuse near-infrared tomography system was used to measure dynamic changes in the absolute optical properties of the human breast that were induced through pressure applied to the tissue surface. Results from five subjects show that absorption and scattering coefficients changed measurably when pressure was increased and that these relative changes correlated with the subjects' body-mass index, indicating that the effect depends on tissue composition. Fitting the absolute absorption and scattering coefficients at six wavelengths to the molar absorption spectra of the three predominant chromophores revealed that both the average total hemoglobin and oxygen saturation increased by 10%, while water concentration decreased by more than 12%. These changes indicate that the pressure-induced variation is likely due to water displacement and vascular volume increase in the region being imaged, for mild application of pressure to the breast. These results suggest that the pressure applied during optical measurements of tissue may alter the tissue physiology, and care should be taken to factor this effect into the design of optical medical instrumentation. In addition, the technique provides a unique approach to measuring tissue elastic changes *in vivo* in the female breast and may offer a new method for dynamic contrast imaging based on elasto-optical measurements.

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Near-infrared (NIR) diffuse imaging is a clinical diagnostic system that can provide physiological information such as total hemoglobin, oxygen saturation, and water concentration within breast tissue. Quantitative tomographic methods were recently demonstrated that provide an absolute measure of tissue absorption and reduced scattering coefficients at multiwavelengths, allowing true quantitative multispectral tomography of the breast.[1,2] In this study we present what is believed to be the first quantitative estimates of changes in breast tissue composition as measured by NIR tomography, with the goal of understanding the magnitude of these changes and determining what their mechanism of contrast is in this setting.

In NIR tomography systems the human breast is either compressed by flat glass plates[3,4] or encircled by an array of fiber bundles[5,6]; pressure is applied to the exterior of the tissue, causing significant deformation in many cases. It is thought that blood and water concentrations in glandular and adipose tissue are variable when pressure is applied and that the response to pressure is nonlinear, with a brief elastic response followed by a longer-term plastic response. Thus the measured optical properties will likely change as a function of time after the tissue is in the array and will be affected by the overall magnitude of the pressure applied. In addition, some authors have proposed using dynamic changes in the signal as the basis for discriminating different tissue types within an image.[6]

In this Letter the dynamic response of the optical properties of breast tissue to externally applied pressure has been studied in a tomographic array geometry in which pressure can be applied equally to the breast in a circular manner. Results of measurements from five normal subjects were included in this study. The dynamic responses of absorption (μ_a) and reduced scattering (μ_s') coefficients at the wavelength of 785 nm were observed as pressure was increased and decreased. Differences at the highest (P_h) and lowest (P_0) applied pressures were proportional to the body-mass index (BMI) of each patient with μ_a and μ_s' slopes of 2.4 and −8.1, respectively. Fitting μ_a and μ_s' on six wavelengths revealed that the average of both of the total hemoglobin (Hb_T) and oxygen saturation (S_tO_2) increased by ~10% and the water concentration decreased by ~12% when the pressure was increased.

The detection system and the optical property fitting algorithm are similar to those reported previously.[5,7,8] In the current version of the system, three circular planes, each composed of 16 fiber bundles (6-mm diameter), are used, allowing pressure to be applied and permitting imaging along 4 cm of breast length. The distal ends of these 48 fiber bundles are rigidly coupled to a circular plate that rotates such that one of the 16 fiber bundles in the measured plane is aligned with the light source while the other 15 fiber bundles in the same plane are each connected to a photomultiplier tube detector, each of which samples in parallel. The diameter of the circular interface of fiber optics can be changed from 40 to 200 mm by control of stepper-motor-controlled linear stages. NIR light from six laser diodes is used serially to illuminate the region of interest at wavelengths of 661, 761, 785,

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808, 826, and 849 nm. One complete measurement at all 16-source positions occurs in approximately 20 s.

The pressure applied to the breast was directly measured with two force transducers located at opposite positions within the ring of fibers (Omega Engineering, LCFD-1KG) using a sensing area of 0.35 cm^2. The sensitivity and response of these sensors were determined by prior calibration to be less than 3 Pa.

A group of five normal subjects aged 41–71 years, with a BMI of 19–30 kg/m^2 (i.e., mass divided by height squared), were tested. Typical patient μ_a and $\mu_s{}'$ changes with applied pressure are shown in Fig. 1 for a woman with heterogeneously dense breasts. Light at the 785-nm wavelength was used as the source, and the acquisition time between each data point was approximately 30 s. We increased the pressure step by step to the limit that patient could manage by decreasing the diameter of the circular array uniformly, followed by increasing the diameter until the pressure sensors indicated low pressure. In Fig. 1, the filled circles show data during the compression phase, and the filled triangles show data during the release phase. As a control comparison, the changes in absorption and reduced scattering coefficients are also plotted for a silicon resin phantom,[9] and the results indicate that very little change occurred when an inanimate object with tissuelike optical properties was squeezed. The data indicate that μ_a decreased gradually, first from 0.0056 to 0.0045 mm^{-1}, when the pressure increased from 0 to 1100 Pa and then increased gradually to 0.0063 mm^{-1} as the pressure decreased back to 0 Pa. This is a significant change in μ_a, indicating a change in the optical character of the breast as a result of the internal stress that was induced, which initially decreased under pressure and then increased above the prestudy tissue baseline value after completion of the pressure experiment. The changes in $\mu_s{}'$ shown in Fig. 1(b) indicate that the reduced scattering coefficient increased gradually from 1.0 to 1.7 mm^{-1} as the pressure increased and decreased gradually back to 1.0 mm^{-1} when pressure decreased to baseline. Compared with the dynamic changes in the absorption coefficient, the reduced scattering coefficient has much less of a hysteresis effect.

Similar trends occurred in the dynamic changes of μ_a and $\mu_s{}'$ in all five subjects when the pressures that could be applied for the same displacement were varied and the absolute values of μ_a and $\mu_s{}'$ were significantly different. A clear trend is illustrated in Fig. 2, showing the percent change in μ_a and $\mu_s{}'$ between the values in P_h, relative to P_0, plotted as a function of the BMI of the subject. The circles are the values of each patient, and the lines are linear fits to the data. Both μ_a and $\mu_s{}'$ differences are correlated with BMI. The slopes of the difference in absorption and reduced scattering coefficients versus BMI are 2.4 and −8.1, with R^2 values of 0.9 and 1.0, respectively. This strong correlation with BMI would indicate that the pressure-induced changes are a strong function of the tissue composition. This correlation is likely due to the fact that lower values of BMI would have higher glandular tissue composition in the breast with higher water and blood content. It is likely that the blood and water components of the breast would change the most under applied pressure. The subjects with lowest BMI values also exhibited the largest magnitude of pressure-induced changes in μ_a and $\mu_s{}'$.

To interpret these changes in terms of composition, we estimated six wavelength fits to total hemoglobin (Hb_T), tissue oxygen saturation (S_tO_2), and water concentration, as plotted in Fig. 3, using averaged relative values from three patients with complete spectral measurements. These data indicate that both Hb_T and S_tO_2 increased by 10%, whereas water decreased more than 12% on average.

The goal of this work has been to understand how the pressure that is applied to the surface affects to the composition of the breast tissue. The data in Figs. 1 and 2 illustrate that the pressure-induced changes are significant and that they are likely dependent on the tissue composition; they are strongest in more glandular and less fatty tissues (i.e., low BMI), which is the type of breast tissue that has the most water and blood in it. There is a measurable hysteresis effect that causes an overall increase in μ_a following a pressure increase–decrease cycle; however, no hysteresis effect occurs in $\mu_s{}'$, as might be expected. The cause of the longer hysteresis effect is likely increased blood flow and local swelling in the area of compression after release. The acute changes in μ_a and $\mu_s{}'$ appear

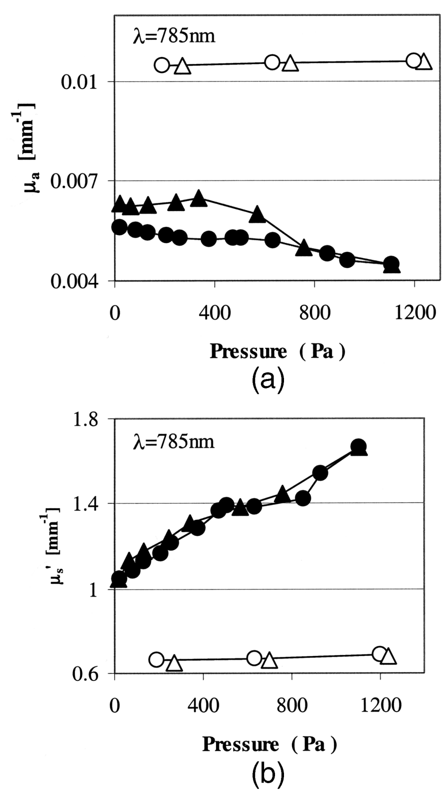

Fig. 1. (a) Typical absorption coefficient and (b) reduced scattering coefficient changes with applied pressure from a human subject and elastic phantom. In both (a) and (b) the open symbols are phantom data and the filled symbols are human data. The circles represent measurements during closing of the array (increasing pressure), and the triangles represent measurements acquired during reopening (decreasing pressure) of the array.

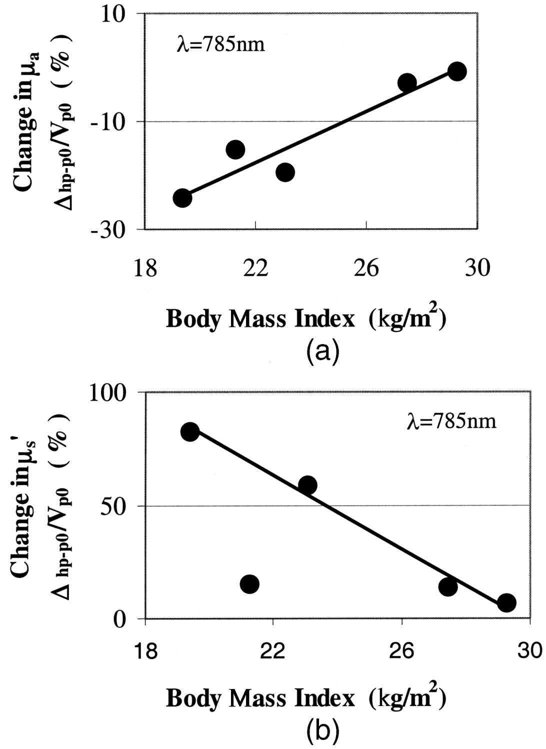

Fig. 2. Plot (for each of the five subjects) of the difference in (a) absorption and (b) reduced scattering coefficients (at 785 nm) between the values at maximum pressure, hp, and minimum pressure, $p0$ (difference denoted as $\Delta_{hp\text{-}p0}$), normalized by the value at $p0$ as a function of the subject's BMI.

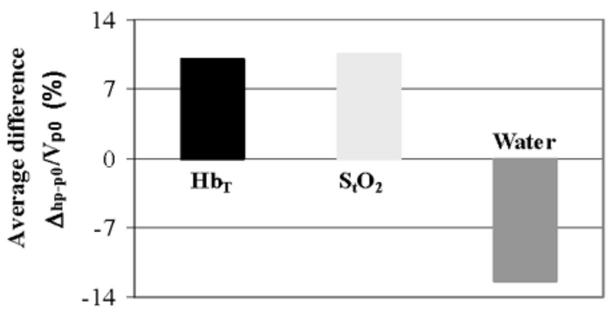

Fig. 3. Plot of percent average (all five subjects) changes in total hemoglobin (Hb_T), oxygen saturation (S_tO_2), and water concentration between the values at maximum pressure, hp, and minimum pressure, $p0$, normalized by the value at $p0$.

to result from decreases in water concentration, likely because of interstitial water transport. The increases of Hb_T and S_tO_2 indicate that the prolonged pressures applied here may cause vasodilation and (or) blood flow, thereby increasing overall total blood concentration in the tissue as well as oxygen saturation.

An important aspect of this work is that pressure-induced changes must be considered when optical properties are estimated in human tissues. It is very difficult to record optical measurements on human tissue without applying some pressure; yet, NIR spectroscopy and tomography systems are used for this purpose regularly, and the data are subject to misinterpretation because of the effect. A second and perhaps more important observation is that pressure-induced changes provide functional information about tissue composition and elastic response that may be exploited as sensitive measures of physiology or pathophysiology. Further study of these changes over different temporal periods and force-displacement combinations is needed to determine the potential medical utility in the setting of breast disease characterization and (or) detection.

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