A Digital X-Ray Tomosynthesis Coupled Near Infrared Spectral Tomography System for Dual-Modality Breast Imaging

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A digital x-ray tomosynthesis coupled near infrared spectral tomography system for dual-modality breast imaging

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Abstract: A Near Infrared Spectral Tomography (NIRST) system has been developed and integrated into a commercial Digital Breast Tomosynthesis (DBT) scanner to allow structural and functional imaging of breast in vivo. The NIRST instrument uses an 8-wavelength continuous wave (CW) laser-based scanning source assembly and a 75-element silicon photodiode solid-state detector panel to produce dense spectral and spatial projection data from which spectrally constrained 3D tomographic images of tissue chromophores are produced. Integration of the optical imaging system into the DBT scanner allows direct co-registration of the optical and DBT images, while also facilitating the synergistic use of x-ray contrast as anatomical priors in optical image reconstruction. Currently, the total scan time for a combined NIRST-DBT exam is ~50s with data collection from 8 wavelengths in the optical scan requiring ~42s to complete. The system was tested in breast simulating phantoms constructed using intralipid and blood in an agarose matrix with a 3 cm x 2 cm cylindrical inclusion at 1 cm depth from the surface. Diffuse image reconstruction of total hemoglobin (HbT) concentration resulted in accurate recovery of the lateral size and position of the inclusion to within 6% and 8%, respectively. Use of DBT structural priors in the NIRST reconstruction process improved the quantitative accuracy of the HbT recovery, and led to linear changes in imaged versus actual contrast, underscoring the advantages of dual-modality optical imaging approaches. The quantitative accuracy of the system can be further improved with independent measurements of scattering properties through integration of frequency or time domain data.

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1. Introduction

Digital Breast Tomosynthesis (DBT) is an emerging FDA-approved imaging modality for breast cancer screening [1–3]. The technique is similar to conventional mammography in that it images variations in breast density using x-ray attenuation and requires significant compression to enhance soft tissue contrast. Importantly, DBT extends the capabilities of conventional mammography by acquiring x-ray projection data at a limited set of angular views, which allows 3D reconstruction of tissue density over the imaged breast volume. The concept is related to conventional Computed Tomography (CT), but with limited angular sampling. DBT provides superior lateral resolution, but its depth discrimination is relatively...
poor (typically about 1 mm resolution) because of the restricted angular views, which also can cause artifacts such as ghosting. Nevertheless, DBT provides depth-resolved 3-D structural images of the breast at a dose comparable to digital mammography, but with improved diagnostic power [4].

Near Infrared Spectral Tomography (NIRST) acquires optical projection data at multiple wavelengths for reconstruction of functional parameters such as hemoglobin concentration, tissue oxygenation, fat content and water fraction, which are known to be sensitive to neoplastic changes in tissue. Since light transport in this regime is dominated by scattering, NIRST images are diffuse and lack high-resolution spatial detail, but when viewed in conjunction with a high resolution structural imaging modality, can provide complementary physiologic information to potentially improve overall diagnostic accuracy. This general approach of combining a structural imaging modality with a functional imaging technique has gained significant traction in recent years with several dual modality approaches being developed and tested clinically including optical imaging combined with MRI, Ultrasound, Mammography and DBT [5–9]. The most clinically successful implementation of dual modality imaging has been the combination of Positron Emission Tomography and Computed Tomography (PET-CT), where lower resolution PET imaging provides functional contrast to supplement higher resolution structural CT.

In this study, NIRST is integrated into a commercial DBT system to allow tomographic recovery of hemoglobin parameters in local regions of the breast. The combined NIRST-DBT platform can provide co-registered functional information that could be synergistically interpreted with the DBT images to improve diagnostic accuracy. In particular, NIRST images could improve specificity in delineating malignant from benign masses, which is relatively difficult in women with dense breasts, and leads to the high false positive rates currently observed in mammography and DBT. The combination of NIRST and DBT was first developed at the Massachusetts General Hospital (MGH) [8]. In a recently published study, the MGH system examined 125 women and the results showed statistically significant differences in hemoglobin concentration in malignant versus benign masses relative to the fibroglandular region in the same breast [7]. The system consisted of an array of optical fibers, which deliver and collect light from discrete locations on the top and bottom surfaces of the compressed breast. Both continuous wave (CW, 3 wavelengths) and frequency domain (FD, 2 wavelengths) projection measurements were made to allow tomographic reconstruction of functional optical images. While the MGH design is effective, it is complex, expensive and not readily scalable. The NIRST-DBT system described here takes a different design approach, which is cost-effective, offers better integration with DBT and is simpler to implement. The focus is primarily on CW imaging based on tomographic projection measurements acquired at multiple wavelengths with provisions for adding limited FD recordings optimized to the design. Other breast-imaging approaches with a similar emphasis on CW imaging with solid-state detectors have been developed in the recent years [10,11].

2. Materials and methods

2.1 NIRST system instrumentation

The NIRST system was fabricated to attach to a commercial Digital Breast Tomosynthesis scanner (Genesis Dimensions, Hologic Inc., CT). A schematic of the NIRST system components is shown in Fig. 1(a). The source module is comprised of eight fiber-coupled, temperature controlled laser diode units (Power Technology, NY) with individual emission wavelengths at 660, 785, 808, 830, 852, 905, 915 and 940 nm. These specific wavelengths were selected for spectral un-mixing of oxy-hemoglobin, de-oxy hemoglobin, water and fat absorption spectra from combined measurements [12,13]. Each microprocessor-controlled, temperature-stabilized laser unit is individually addressable through a standard RS-232 communication protocol.
Fig. 1. (a) Schematic of the NIRST/DBT imaging system. (b) Photograph of the fully assembled NIRST/DBT system installed at the Dartmouth-Hitchcock Medical Center (DHMC). (c) Photograph showing the silicon photodiode detector panel inserted into the custom designed cassette assembly to allow easy insertion and removal of the panel during sequential DBT/NIRST scans. (d) Photograph of the 2-axis galvanometric scanning mirror assembly mounted adjacent to the x-ray emission port on the DBT scanner. The source unit allows arbitrary positioning and scanning of laser light beams onto the compressed breast surface without obstructing the x-ray field-of-view.

A USB to 8-port RS-232 adapter (CPS) allowed a single USB port on the instrument computer to control the operating parameters of the eight lasers. Two-hundred micron core diameter multimode optical fibers were used to couple light from individual lasers into a 9x1 piezoelectric fiber optic switch (FSM 9x1-200, OptoJena, MA), which allowed fast sequential switching of the lasers into a single 200 micron core diameter output optical fiber. The output optical fiber is coupled into a computer controlled fiber optic attenuator (DD-100 series, OzOptics, Canada), which adaptively attenuates the light output appropriately to differences in attenuation properties between individual breasts. The output from the attenuator is coupled to a fiber optic collimator (FC) to produce a collimated beam of light of approximately 5mm in diameter, which diverges slightly due to the finite size of the source optical fiber. A pair of orthogonally mounted galvanometric scanners (GS) with 5mm scan mirrors (Cambridge Systems, MA) is used to direct and scan this beam over the surface of the breast through the transparent polycarbonate compression paddle (TCP) of the DBT system as shown in Fig. 1(a), resulting in a source-light spot diameter at the imaging plane of approximately 8 mm. The source assembly containing the FC and GS is permanently mounted beside the x-ray port on the DBT such that it does not interfere with DBT exposures. The independently controlled scanners allow arbitrary positioning of the source beam over the top surface of the compressed breast, but a standard raster scanning pattern was used in all experiments described in this work.

The detector panel (DP) consisting of a matrix of 75 large-area silicon photodiodes was custom fabricated. The individual photodiode units (S9270, Hamamatsu Corp., Japan) have 1cm x 1cm active areas with high gain transimpedance amplifiers built into each diode package. The diode is configured to produce 0-10 V signal range, which is digitized directly using a standard off-the-shelf 80-channel Analog-to-Digital Converter (ADC, USB-6255, National Instruments, TX), without the need for additional signal conditioning. A custom printed circuit board (PCB) was designed to interface the photodiode outputs to the analog input channels of the ADC through a pair of 68-pin standard Small Computer System Interface (SCSI) connectors.
Interface (SCSI) connectors. A six-layer PCB design was used to isolate the power, signal, and ground planes to minimize noise coupling. A single −10V-0-10V dual mode linear power supply (Acopian, US) was used to power the detectors. Since the photodiodes were driven from a single power supply, 0.1µF ceramic decoupling capacitors were included to isolate individual photodiodes from transient loading effects and power-line fluctuations. Noise floor measurements indicated that the detector panel offers a full-scale dynamic range of approximately 51 dB.

Since the detector panel is not transparent to x-rays, simultaneous NIRST/DBT imaging is not possible at this time. Hence, imaging is performed sequentially, where the detector panel is inserted into the field-of-view during the optical scan and removed during the DBT scan. To facilitate panel insertion/removal, a custom-designed detector cassette assembly (DC) was fabricated into the DBT base plate to allow the detector panel to slide in and out of the field without altering the breast position. The cassette was also designed to allow the detector panel to be inserted from either side of the scanner to accommodate left or right breast imaging. A photograph of the detector panel inserted into the cassette assembly is shown in Fig. 1(c).

2.2 Data pre-processing and calibration

The response of individual silicon sensors in the detection panel to a uniform field of light was measured to characterize differences in sensitivity. Since the detectors were mounted on a panel, a special calibration puck was designed to expose each of the detector units to a uniform field of light and record the corresponding voltage signal. The calibration puck consisted of an optical fiber light source coupled to a homogeneous diffuse resin phantom with a raised square notch machined on the top surface that allowed precise, repeatable alignment of this surface with the active area of the exposed detector.

A schematic of the measurement configuration and the calibration puck are shown in Figs. 2(a) and 2(b), respectively. Three individual measurements were made on each detector by removing and re-inserting the calibration puck and the average response was used for calibration. Detector number 5 was arbitrarily chosen as the reference and the signal strengths from the other sensors were referenced to its value to obtain a correction factor for the individual detectors. Figure 2(c) shows a plot of the correction factor for each of the 80 detectors characterized. No correction factors were needed on the source side as the differences in source strengths across the entire imaging field were measured and found to be negligible.

In a typical data collection sequence, measurements from all detectors were recorded for each source position. The data acquisition system used a front-end 80x1 analog multiplexer to digitize all the 75 measurement channels sequentially (5 ADC channels are left unused). While this analog multiplexing scheme leads to simple and cost-effective data acquisition, it is prone to isolation artifacts, where a high voltage signal on a particular channel could corrupt measurements in an adjacent channel carrying a low voltage signal. These inaccuracies were detected and eliminated automatically by analyzing relative signal strengths in all adjacent channel pairs and applying an empirical threshold determined from a series of homogeneous phantom measurements. An overall path-length threshold was also used to exclude noisy data from detectors that were far from the illumination source position. Currently, for a homogeneous 260 x 180 x 60 mm test phantom (BioMimic, Institut national d'optique, Canada) with μa = 0.01 mm−1 and μs' = 1 mm−1 at 830 nm, a path-length limit of 100 mm is used, which corresponds to lateral distances of up to 80 mm from directly beneath the source position. Figure 2(d) shows the raw data measured from the test phantom at 660 nm and 785 nm wavelengths and the processed data used for image reconstruction is shown in Fig. 2(e).
2.3 Measurement geometry and co-registration

Co-registration of the optical scan with the DBT field is achieved by using the DBT compression paddle (CP) as a common frame of reference. The optical beam is incrementally scanned in the X and Y directions in 2 cm intervals. Since the height of the compression paddle changes for every patient, the scan angles are adjusted automatically, using simple trigonometry calculations, to preserve the scan geometry at any given height of the compression paddle. The optical scan position accuracy was verified manually with a rectangular grid pattern of 2 cm x 2cm spacing overlaid on the top compression paddle. The phantoms were placed at a known fixed position relative to the detector panel, which allowed calculation of the individual detectors positions.

2.4 Blood-intralipid phantom preparation and imaging

Breast tissue simulating intralipid and blood phantoms were created in an agarose matrix. Type 1 agarose powder was mixed in phosphate buffered saline (PBS) at a ratio of 0.02 g/ml and heated in a microwave oven to bring the solution to a rolling boil. An appropriate quantity of 20% intralipid solution pre-mixed to achieve 1% volume fraction of lipids overall was added to the PBS-agarose stock solution and the mixture was transferred to a stir plate, where it was continuously stirred until it cooled to ~38°C. Porcine blood was then added to this mixture at an appropriate dilution to achieve ~15 uM hemoglobin concentration overall. This mixture was stirred for a minute and then transferred into a mold for casting. The mixture was refrigerated for approximately 30 minutes in the mold and then removed for measurements. The concentration of intralipid and hemoglobin used here results in optical properties comparable to that of a typical breast. For fabricating inclusions, a cylindrical tube with a flat covered base was suspended to a predetermined depth at the position of interest, before the mixture began solidifying. The tube was removed after the phantom solidified to leave a cylindrical hole, which was filled with liquid contrast inclusions.

A homogeneous 24 cm x 16 cm x 5.2 cm block of solid phantom and an inclusion phantom with the same overall dimensions were cast with the same background optical properties using the procedure described above. The cylindrical inclusion measured approximately 3 cm in diameter and 2 cm in depth and its center was located 7 cm from the
bottom edge and 8.4 cm from the left edge of the phantom block as shown in the schematic in Fig. 3(a). An additional 24 cm x 16 cm x 1 cm block was cast to act as a stacking layer, which when placed on the inclusion phantom positioned the heterogeneity 1 cm below the top surface. This stacked phantom design also allowed the top layer to be easily removed, which facilitated the creation of liquid inclusions with different hemoglobin and lipid contrast values relative to the homogeneous background. Photographs of the homogeneous top layer and inclusion phantom casts are shown in Fig. 3(b). The overall thickness of the phantom was 6.2 cm, which is representative of typical maximum breast thicknesses achieved through compression during mammography exams [14].

Liquid inclusions with hemoglobin contrasts of 2:1, 3:1 and 4:1 were imaged relative to the background hemoglobin concentration of 15 µM. A 1% intralipid stock solution was used in all cases, fixing the scatter contrast to 1:1. A homogeneous phantom measurement was obtained by filling the inclusion with 1% intralipid stock solution containing 15 µM of hemoglobin matching the absorption and scatter properties of the background. The homogeneous phantom measurements served as a calibration for the contrast phantom data and account for variations in source strengths across the measured wavelengths [15–17]. The eight-wavelength scan time for each phantom was approximately 42s.

2.5 NIRST image reconstruction

The NIRFAST software package version 7 was used to reconstruct the chromophore images directly with a spectrally constrained inversion algorithm [18]. Its finite element method (FEM) image reconstruction process is described in detail elsewhere [19]. FEM meshes representing the homogeneous and contrast phantoms were created with a 3-D meshing algorithm developed in-house. Three-dimensional (3D) diffuse reconstruction of total hemoglobin concentration was performed from data on 2:1, 3:1 and 4:1 contrast phantoms. Images of total hemoglobin concentration (HbT), oxygenation, water fraction and fat content were recovered from the experimental data calibrated with the reference phantom measurements.

The diffuse reconstruction process is ill posed often leading to poor quantitative accuracy of the recovered contrast. Another approach to reconstructing the chromophore contrast applies prior knowledge of the size and location of the heterogeneity in the reconstruction problem to recover chromophore concentrations from these pre-defined “regions-of-interest” [20]. The region-guided approach provides better quantitative accuracy through reduced dimensionality of the inverse problem, but also assumes optical property homogeneity within the defined regions. The method is known to improve diagnostic performance in multi-modality imaging frameworks, such as the NIRST-DBT system described here, where accurate anatomic information is available [20].
3. Results

3.1 NIRST-DBT system performance

Table 1 summarizes key performance metrics of the NIRST-DBT system. The dynamic range of the detection panel was calculated from the measurements of the maximum and minimum signal levels that could be detected. The maximum dynamic range offered by the detection panel was ~59.6 dB. However in the presence of other noise sources the effective dynamic range is reduced to about ~50.1 dB. Table 1 also shows signal to noise ratio (SNR) values for a typical source-detector projection measurement producing a nominal signal range of ~1-2V. This metric was computed from the mean and standard deviation of 5 independent, calibrated projection measurements made on a homogeneous phantom, to provide an assessment of the overall fidelity of the raw measured signals.

Table 1. Key Performance Parameters of the NIRST-DBT System

| Parameter                          | Value          |
|------------------------------------|----------------|
| Detector dynamic range (dB)        | 59.6           |
| Effective detector dynamic range (dB) | 50.1           |
| Typical SNR at nominal signal level of ~1-2V (N = 5) (dB) |               |
| 660 nm | 785 nm | 808 nm | 830 nm | 852 nm | 905 nm | 915 nm | 940 nm |
| 15.8   | 30     | 30.9   | 37.6   | 34.4   | 29.1   | 30.9   | 24.2   |
| NIRST scan time                    | 42 s (~5s per wavelength) |
| DBT scan time                      | 6 s            |

3.2 Diffuse image reconstruction of blood contrast phantoms

A 3D FEM mesh was created in NIRFAST based on the phantom dimensions and the relative positions of the sources and detectors. A diffuse, spectrally constrained, chromophore image reconstruction was performed on the data from phantoms with 2:1, 3:1 and 4:1 HbT contrast in the inclusion relative to the background hemoglobin concentration of 15 µM. A fixed regularization value of 0.1 was applied in a modified Newton-type inversion implemented in NIRFAST. The scatter properties were defined and fixed in the CW reconstruction process and the \( \mu_s' \) values for 1% intralipid solutions were obtained from empirical relations described in [21].

Since blood is the primary contrast in these phantoms only HbT images are presented here. Figure 4 shows the X-Z (Figs. 4(a)-4(d)), X-Y (Figs. 4(e)-4(h)) and Y-Z (Figs. 4(i)-4(l)) cross-sectional views of the actual location of the contrast and the reconstructed total hemoglobin images in the same views for the 2:1, 3:1 & 4:1 contrast phantoms. Figure 4(m) contains a line plot in the X direction across the center of the contrast region in the X-Y images shown in Figs. 4(f)-4(h). Figure 4(n) presents a line plot in the Y direction in a region beyond the inclusion (see dotted line in Fig. 4e), where some change in recovered hemoglobin is observed across the phantom background.
3.3 Region-guided reconstruction of intralipid/blood contrast phantoms

The presence of an HbT gradient in the background region did not allow for region-based recovery of HbT from the first set of phantom experiments; hence, another set of contrast phantoms with 1:1, 2:1 and 3:1 HbT contrasts were cast and were measured on the NIRST-DBT system. The inclusion-to-background scatter contrast was set to 2:1, and the equivalent scattering properties for these regions were assigned based on literature values [21], and were constrained to remain fixed during the reconstruction process to minimize potential crosstalk between scatter and absorption signal recovery. Care was taken during the setting process to
ensure that the phantom molds were placed on a level surface to minimize variations in phantom thickness and to maintain mixture homogeneity.

![Fig. 5. X-Y cross-sectional views of the reconstructed HbT images for the 1:1 (a), 2:1 (b), and 3:1 (c) contrast phantoms. (d) Cut-away view of the FEM mesh showing the background and inclusion regions. (e) Plot of recovered HbT contrast in the background (solid triangles) and inclusion region (solid circles) vs actual HbT concentration in the background and inclusion. Linear fits show that the HbT concentration is nearly constant in the background and varies linearly in the inclusion as expected.]

Figure 5 shows results from region-guided recovery of total hemoglobin contrast in 1:1, 2:1 and 3:1 contrast phantoms. Figure 5(d) provides a cut-away view of the FEM mesh and the inclusion region inside. Figures 5(a)-5(c) contain X-Y cross-sections of the recovered total hemoglobin image through the inclusion region for each contrast phantom. Figure 5(e) plots the recovered HbT as a function of the actual values in the phantom inclusion and background.

**4. Discussion**

This paper describes the design, development and integration of NIRST into a commercial DBT scanner. Agarose-based intralipid and blood contrast phantoms were fabricated to demonstrate the imaging capabilities of the NIRST component of this multi-modality platform. When no spatial priors were used in the reconstruction process, the recovered HbT concentration in the background region was approximately 73% of the actual concentration for three contrast cases. The recovered peak HbT concentration in the inclusion region was approximately 41%, 29% and 26% of the actual HbT concentrations, respectively. The recovered centroid location of the contrast was approximately 6.3, 6.6 and 6.8 cm from the edge of the phantom, which is close to the actual location of the inclusion (7 cm from the edge). A full-width at half maximum (FWHM) criterion was used to analyze the size of the contrast from the Z-plane (depth) images and the recovered sizes were approximately 3.4, 3.2 and 3.1 cm (which is close to the actual inclusion diameter of 3 cm). The size of the recovered contrast appears to be larger than that of the actual contrast in the Z-direction, where it extends to the surface, likely due to the more modest imaging resolution in the depth direction, which is common in the transmission imaging mode used here.

An overall gradient in HbT in the Y direction was also observed in the background, which is visible in the X-Y cross-sectional images in Fig. 4. Figure 4(n) shows a line plot of HbT concentration.
concentration along this gradient, which indicates that the magnitude of the effect is similar in all three imaged phantoms despite their inclusion contrast differences. The X-Y cross sectional images also show that the direction of this gradient is similar and consistent in each of the three phantoms. A similar gradient was observed in the raw projection data (not shown here) suggesting either a gradient distribution in hemoglobin concentration existed in the actual phantom or variation occurred in the phantom thickness in this direction. While the occurrence of a gradient distribution in HbT concentration is unlikely with the fabrication methods applied, a linear change in phantom thickness could easily be induced if the phantom molds were not level during the setting process. Forward data simulations performed in slab meshes with varying Z thickness and constant optical properties matching that of the measured phantoms indicate that a 2-3 mm change in thickness could cause the magnitude of forward data change observed in the experimental phantoms. The large slab phantoms used here are soft when cured and are compressible, which likely made it hard to notice this small but significant height change.

In the case of region-guided image reconstructions, the background concentration of HbT was consistent and equal to approximately 67% of the actual concentration. The recovered HbT concentration in the inclusion region was slightly over-estimated (around 110% of the actual concentration) in the 1:1 HbT contrast case, and was approximately 74% of the actual concentration in the 2:1 and 3:1 contrast cases. Figure 5(e) also shows that the recovered peak HbT concentration in the inclusion region increases linearly with actual HbT concentration, while the recovered background HbT concentration remains nearly constant throughout, as expected. For the no-HbT contrast case (1:1), the recovered HbT value was overestimated and created an artificial contrast. The recovered contrast values are approximately 1:1.6, 1:2.2 and 1:3.1 respectively, compared to the actual values of 1:1, 1:2 and 1:3. Even though the recovered contrast matches the true contrast values for the 1:2 and 1:3 cases closely, it should be noted that the absolute HbT concentrations for the background and inclusion regions were equally underestimated by ~25-30% in both these cases. These deviations in reconstructed HbT concentration values are likely caused due to a combination of several effects including, mismatch in the refractive index between the gelatin background and the liquid inclusions and mismatch in the specification of scatter properties obtained from literature recipes [21], which could result in a cross-talk between scatter and absorption parameters, and numerical artifacts caused by fixing the scatter properties during the CW reconstruction process. However, the region-guided approach provided a consistent recovery of hemoglobin parameters in the background and inclusion regions overall.

The optical scan time for single wavelength imaging is currently ~5 s, which is comparable to the DBT scan time. However for spectral imaging using 8 wavelengths the overall scan time increases to approximately 42 s, as the wavelengths are sequentially scanned. Reduction in overall scan time is possible through wavelength multiplexing approaches, but the large area silicon photodiodes used here are not fast enough to allow implementation of commonly used time or frequency based multiplexing strategies. As an alternate, avalanche photodiodes (APD) offer much higher photon sensitivity and have better dynamic response, but integration of APDs into this form factor would lead to significantly increased instrumentation complexity and cost. APDs are also inherently noisier compared to silicon photodiodes, which could impact signal-to-noise ratio (SNR) and dynamic range, so it is not readily clear whether an APD based detector panel would offer significant improvements in scan time at a comparable SNR to justify increased cost and instrumentation complexity. Small scale testing of other types of silicon photodiodes and post-processing circuitry are currently underway to optimize the detection panel for the subsequent design iteration of the NIRST system.
5. Conclusion

Integration and co-registration of DBT and NIRST imaging allow synergistic structural and functional imaging of breast abnormalities, which could improve diagnostic accuracy overall. Success with this approach depends on how well the NIRST technology can be integrated into existing workflow for clinical DBT imaging. The major focus of this first generation NIRST-DBT imaging system design was to balance integration and imaging performance with instrumentation complexity and cost. Creation of a high sensitivity, multi-element, solid-state detector panel, along with a simple, permanently mounted non-contact source scanning assembly offers high-speed scanning, compact DBT integration and reduced instrumentation complexity. Results from contrast phantom studies demonstrate the ability of the system to detect and localize hemoglobin contrast. While the diffuse image reconstructions recovered the approximate position and size of the HbT contrast, the quantitative performance in terms of actual property values was not optimal. The use of prior information on the size and location of the contrast in the reconstruction algorithm improved the quantitative optical property performance significantly, which underscores the benefits of dual modality optical imaging platforms, such as the one described here. Knowledge of optical scattering properties is important to accurate recovery of hemoglobin values. The CW system implemented here is not capable of measuring scatter signals directly, but could be augmented with some frequency domain (FD) measurements if necessary. Several design approaches are being considered, and an important tradeoff is the number of FD measurement channels and wavelengths needed for robust sampling of scattering properties across the breast. A separate study [22] of scattering properties effects on the quantitative recovery of hemoglobin contrast suggests that limited, region-averaged sampling of scatter properties is sufficient for accurate reconstruction of hemoglobin contrast. Another interesting approach is to map optical scatter properties to tissue density images acquired with DBT. Tissue density is known to affect its optical scattering response, but a complete mapping between optical and DBT images is not trivial, mainly because DBT images are typically not quantitative. Significant efforts have been underway to make DBT imaging quantitative [23, 24], and advances could impact the design and integration of DBT coupled optical imaging in the future.

The phantom imaging experiments described here involved a fixed-size for the inclusions and the lateral and depth positions were also fixed. Though these experiments provided an initial quantitative assessment of the performance of the imaging instrumentation, a more extensive evaluation would generate contrast-detail analyses, where both the size and the location of the contrast are changed. The phantom design outlined here is not suitable for this type of characterization, which is required for a comprehensive analysis of diagnostic performance using standard receiver operating characteristic (ROC) metrics. Currently, a multilayer, stackable, spectral resin phantom is being designed in collaboration with the Institut National d'Optique (INO, Quebec, Canada) to facilitate the imaging of different contrast sizes at multiple depth locations in order to complete this analysis in the future.

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