Chapter 8

Summary and Conclusions

A Time-Domain Optical Breast Imaging System has been presented that combines the unique strengths of both optical and X-ray imaging tomography in a multi-modality probe designed for the clinical environment. The resulting co-registered imagery promises to provide the clinician with both structural and functional information that will be necessary for more accurate and sensitive identification and localization of benign and cancerous breast lesions, thereby offering an opportunity to save thousands of lives each year. It is generally agreed that the contrast to function, unique to optical imaging, should play a vital role in the early identification and diagnosis of the progression of breast cancer in women. It is an assertion of this dissertation that in order to gain wide clinical acceptance, optical imaging must be directly associated with the gold standard of mammography, X-ray imaging. On its own, DOT is not likely to gain acceptance as the standard of care in breast cancer screening, given its relatively poor spatial resolution. It is critical to the future of DOT that the optical community adopts this perspective.

A comprehensive noise theory for the Time-Domain Optical Breast Imaging System was developed and used to provide insight, along with the lessons learned from system characterization, into ways to optimize the system's performance for clinical measurements. The recommendations developed throughout this dissertation are summarized in Section 8.1, along with recommendations for future work outlined in Section 8.2.

8.1 Conclusions and Recommendations

The negative effects of ambient light on the system performance were noted. The incorporation of bandpass or longpass optical interference filters would minimize the ambient light effects. Additionally, reducing the near infrared spectral content of ambient lighting may be desirable to decrease the concern of ambient light to the point of insignificance. Care must be exercised, however, in using light-shielding cloths, as the boundary conditions for the sides of the phantom or tissue are affected.

To the extent that background ambient light is not reduced to insignificance, a fast shutter should be added to the laser to allow the background to be properly measured and subtracted from the data. Additionally, a shutter should be added to the camera to allow the system to maintain a high voltage on the MCP at all times to reduce the associated transients and MCP warm up that were demonstrated when the high voltage was turned on only during measurement periods. This occurred even after the camera had been turned on (warmed up) for hours.

The negative effect of subtracting background frames from the data could be minimized by averaging a statistically relevant number of background frames (10 to 30) prior to subtraction. This practice would have a minimal effect on the total measurement time, but would reduce the noise associated with a single background frame.

Two approaches could be used to minimize instrument warm up effects. The instrument could be allowed to stabilize for a minimum period of 30 to 60 minutes. Alternatively, reference detectors and sources could be incorporated in the design to essentially eliminate warm up requirements beyond the time of system start up. The measurement of any system drift, however, would have an associated finite noise, thereby

reducing the system-level noise performance slightly. Monitoring the laser output may have the advantage of reducing overall measurement time, by reducing the time required to stabilize the laser upon the wavelength changes that are necessary for optical spectroscopy.

The cooling of the ICCD should be improved, either by isolating the camera from other heat producing equipment and adding forced air cooling, or by changing to the water-cooling option for the camera. This would also allow operation at higher MCP gains and prevent thermal shut down.

Photocathode and MCP saturation effects were observed to be dependant on instrument parameters and measurement configuration, which will likely vary for different applications and even from breast to breast. Thus, it is important to take proper account of these effects. For example, the photocathode saturation is affected by the width of the TPSF, which is determined by the background optical properties and thickness of the breast tissue. Therefore, it may be necessary to take a quick read of these parameters, either to adjust the measurement timing sequence or to apply the appropriate correction to the data, if necessary. A set of neutral density filters could be incorporated within the camera objective to allow the ICCD linearity to be assessed for any given measurement conditions. MPE calculations indicated that the average laser power could be increased substantially, however, the effect of increased intensity on the photocathode saturation must be considered.

The polarizing beamsplitter in the source Multiplexer could be motorized to allow the laser output to be increased with increasing wavelength to counteract the loss in

camera response with increasing wavelength. Ultimately, longer wavelength response photocathodes should be used in the ICCD.

The CCD camera of the ICCD was found to have nonlinear response below 25 msec, establishing a lower bound for the integration time. This minimum applies to 8 x 8 binning, which should always be used for breast imaging applications. In fact, the SNR could be further improved for a camera capable of greater than 8 x 8 binning. Additionally, a new ICCD system should have a CCD camera with TTL synchronization to allow for faster data collection.

The optimal operating voltage of the MCP was found to be 600 Volts in agreement with recommendations from the ICCD camera manufacturer. Below 600 Volts, the saturation effects were dominated by photocathode saturation. Above 600 Volts saturation was primarily due to the MCP. At voltages above 600 volts and without further cooling of the MCP, the amplified thermionic emission could cause large random noise pulses that could introduce significant fluctuations in some of the data, further obviating the need for improved cooling of the intensifier. On average, the thermionic noise is not a problem, but for an individual detection fiber for an individual time gate, it could be problematic.

Due to their relative switch times, the order of measurements should be; (1) scan fibers (300 μsec switch time), (2) scan delays (500 msec switch time), and (3) scan wavelengths (15 seconds minimum switch and stabilization time).

The secondary peak in the impulse response appears to be due to reflections from the photocathode to the fiber array and back. The simplest fix may be to attach an index-

matched, antireflection-coated window to the detection fiber array within the ICCD objective lens assembly.

It appears that, on the order of 6 to 8 time gate delays may represent the optimal trade off between the # of sources and the # of time gate delays. The total number of measurements is limited by the clinical measurement window of between 2 and 3 minutes. The optimal operating point would be dependent on whether more emphasis was placed on the localization or the probability of detecting a given lesion optically. The requirement for localizing the lesion, in turn, would depend on whether or not the lesion had X-ray contrast. Thus, ultimately it would be preferable to take an X-ray image before the optical image, given real-time feedback of X-ray contrast to the optical system, sometime in the future.

Finally, it would be advantageous to incorporate a beamsplitter into the source fiber Multiplexer between the laser and the galvanometer mirrors to aid in localization of the tissue boundaries. The tissue boundaries must be identified prior to the optical data acquisition to prevent saturation of the image data and possible permanent damage to the ICCD. Again, ultimately, it would be preferred to have the boundary information as feedback from the X-ray prior to optical imaging. This would reduce the total time required for the co-registered image.

8.2 Recommendations for future work

The body of work completed as part of this dissertation has shown the tremendous promise of the Time-Domain Optical Breast Imaging System. Much has been learned about means for improving image performance, but there is much more to learn. Future

efforts should focus on implementing as many of the recommendations outlined in Section 8.1 as possible. Additionally, it will be critical to get the system into the clinical environment as soon as possible, as much can be learned in that setting beyond what is possible in the laboratory with breast tissue phantoms. Improvements must be made in the forward models to incorporate boundary problems, but the nature and extent of these problems must first be assessed by clinical measurements.

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