Advances in Simultaneous Dual-Breast Optical Mammography

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INTRODUCTION

Breast cancer is an epidemic that affects more than 200,000 new patients each year. With greater than 40,000 deaths each year, breast cancer is the second leading type of cancer in women. The use of screening mammograms has been shown to reduce mortality rates from breast cancer. All over the United States mammography has been instituted to promote early detection and treatment of breast neoplasia. Currently the American Medical Association recommends yearly screening mammograms for all women over 45. However the discomfort and concern about radiation exposure deters many female patients and often leads to screening at less than the recommended yearly testing. With this in mind, **DY**namic **N**ear- Infrared **O**ptical **T**omography (DYNOT) has been developed and implemented for use in Optical Mammography. First described by Barbour et al.**[1]**, DYNOT has gained widespread use. Not only for the above mentioned Optical Mammography, but for studies involving the brain, limbs, animals and the neonatal abdomen, as well as others. Since first being reported by Barbour et al.**[2]**, several advances have been made in Optical Mammography. The most significant being the design and implementation of Simultaneous Dual-Breast Imaging. This advance, first presented at the 2004 Optical Society of America Biomedical Optics Conference **[3]**, demonstrated the newly discovered ability to image both breasts at the same time. The advance has been invaluable in the use of DYNOT for Optical Mammography for several reasons. Foremost to the patient is the reduction in imaging time. Not only does dual breast imaging allow for reduced time of actual imaging, it reduces set-up time by having the patient set in the imager only once. Prior imaging sessions would last 25 to 40 minutes per breast. With the implementation of Simultaneous Dual-Breast Imaging, the imaging session was reduced to approximately 35 minutes in total. From the viewpoint of the investigator this new innovation allows for more accurate imaging and precise comparison of results. Considering that 90 percent of tumors arise in a single breast and since vascular architecture varies from patient to patient, simultaneous imaging of the breasts allows for true comparison of the behavior and physiology of the left and right breasts. As can be seen in Figure 1, the spatial mean time series of the left and right breasts follow a similar, but not identical time course. This assures the repeatability of provocation in both breasts that is not available with separate single breast imaging.

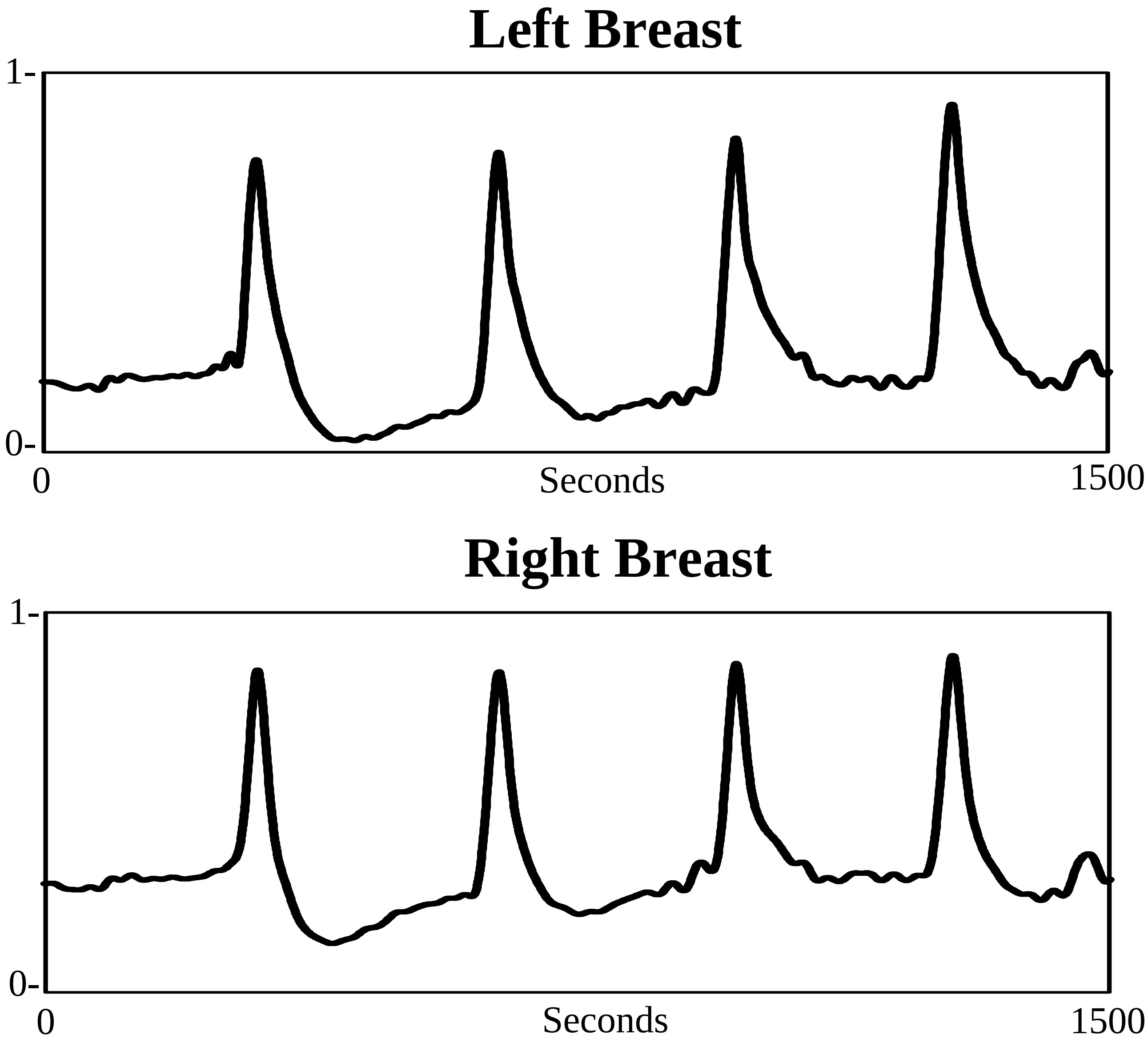


Figure 1. Spatial mean time series from the left and right breast recorded simultaneously. The similarity, without being identical shows the ability of dual-breast imaging to compare accurately one breast to the other.

METHODS and INSTRUMENTATION

All measurements were done using a multi-channel continuous wave near-infrared optical tomographic imager (DYNOT System, NIRx Medical Technologies, LLC., Glen Head, NY 11545), operating at 760 nm and 830 nm. Figure 2 shows a functional layout of the imager with expanded views of the instrument set-up and real-time data display screens. Depicted is a four-level functionality scheme comprising system hardware, system control, data analysis and image display. The basic system provides for frequency encoding having a capability of up to four laser diode sources, a fast optical switch with incoupling optics, a multichannel parallel detector module equipped with adjustable gain control, and a system controller. Dynamic measurements were performed using a dual-breast measurement head which directs near-infrared light onto the subject’s breast via multiple arrays of optical fibers mounted in a secure frame. Each optode delivers approximately 20 mW of optical power for a period of 17 ms per cycle, producing a flux of ~10 mJ·s-1·cm-2. Dual-wavelength optical energy at wavelengths 760nm and 830nm was used for imaging in a time-multiplexed fashion, such that a complete scan of the breast is accomplished in approximately 525 milliseconds. Figure 4 shows a close-up view of the dual-breast measuring head, with white silicone phantoms in place, used for system testing.

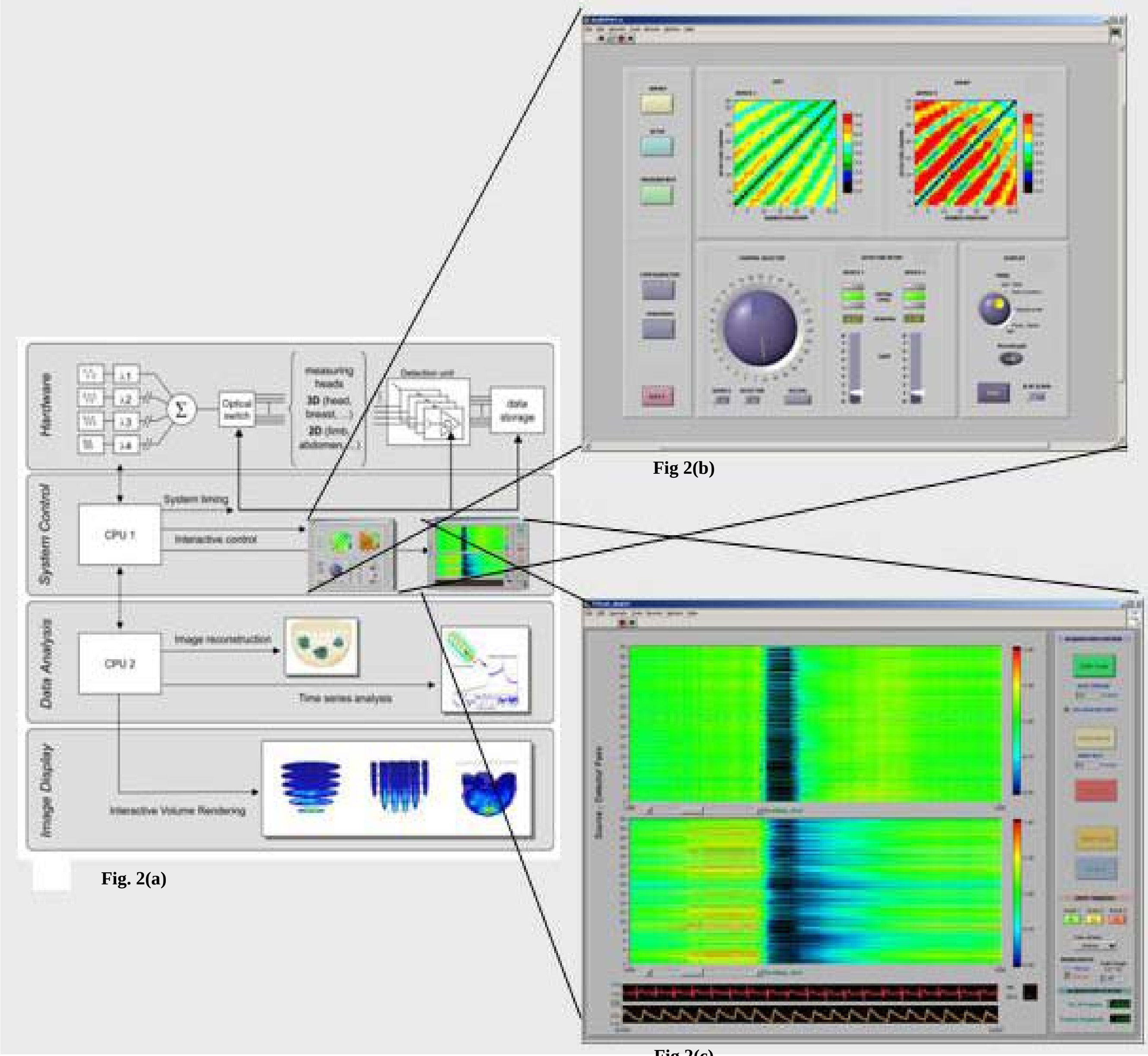
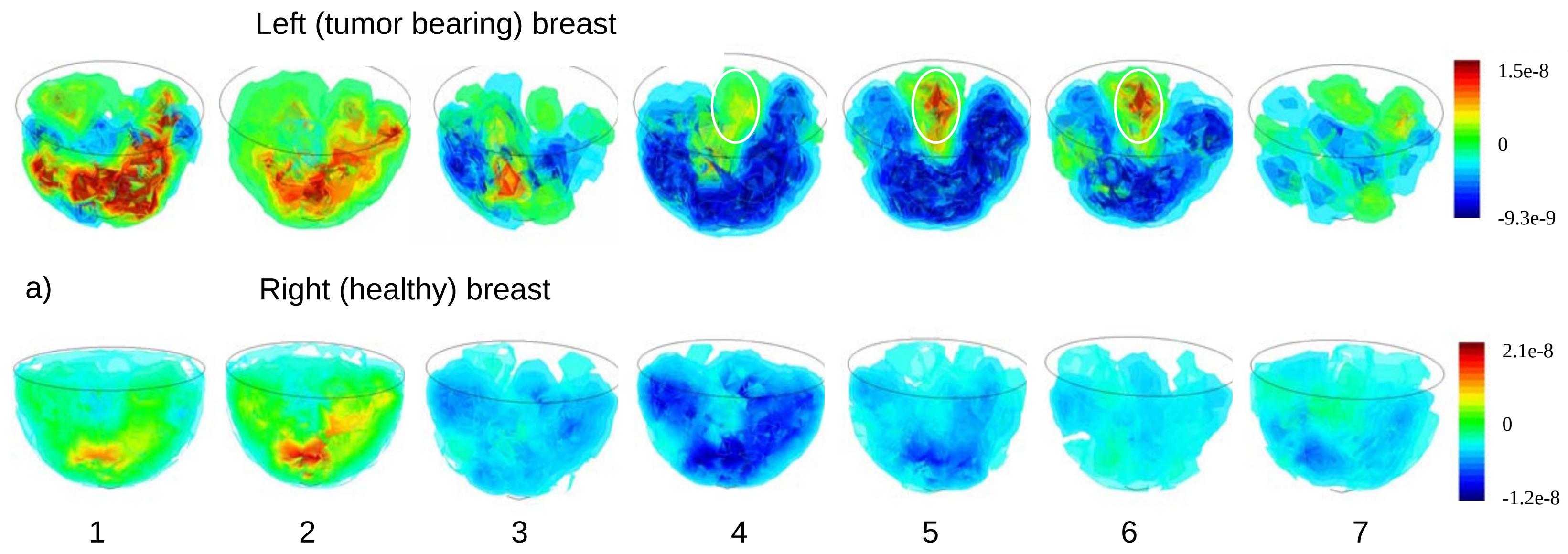


Fig 2(b)

Fig. 2(a)

Fig 2(c)

Figure 2. Functional layout of our imager (Fig. 2(a)) with expanded views of the instrument set-up (Fig. 2(b)) and real-time dual-breast data display (Fig. 2(c)) screens. Depicted is a four-level functionality scheme comprising system hardware, system control, data analysis and image display. The data display in Fig. 2c represents a patient with a left breast tumor and a healthy right breast.



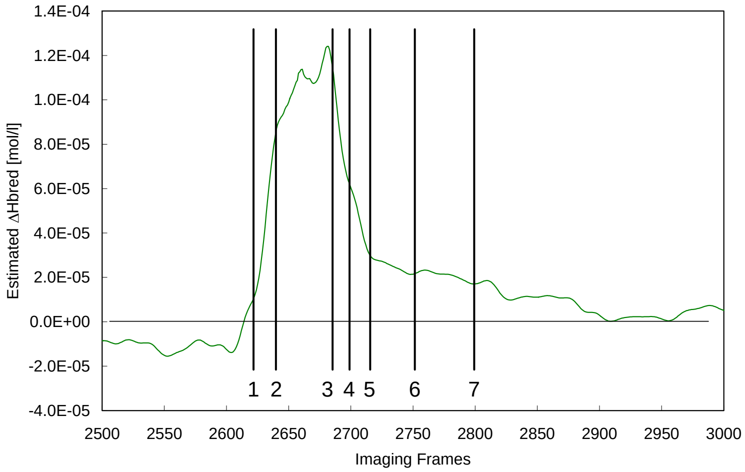


Figure 3. 3D spatial map of data display from Figure 2. Panel a: Reconstructed volumetric image time series of the change in deoxyhemoglobin during a Valsalva maneuver. Top row: Left breast with tumor. Bottom row: Healthy right breast. Indicated is the approximate location and size of a ductal carcinoma as known from radiologic findings. Panel b: Spatial mean of reconstructed changes in Hb_{red} for the healthy breast. Numbers indicate approximate location of time points for the reconstruction results.

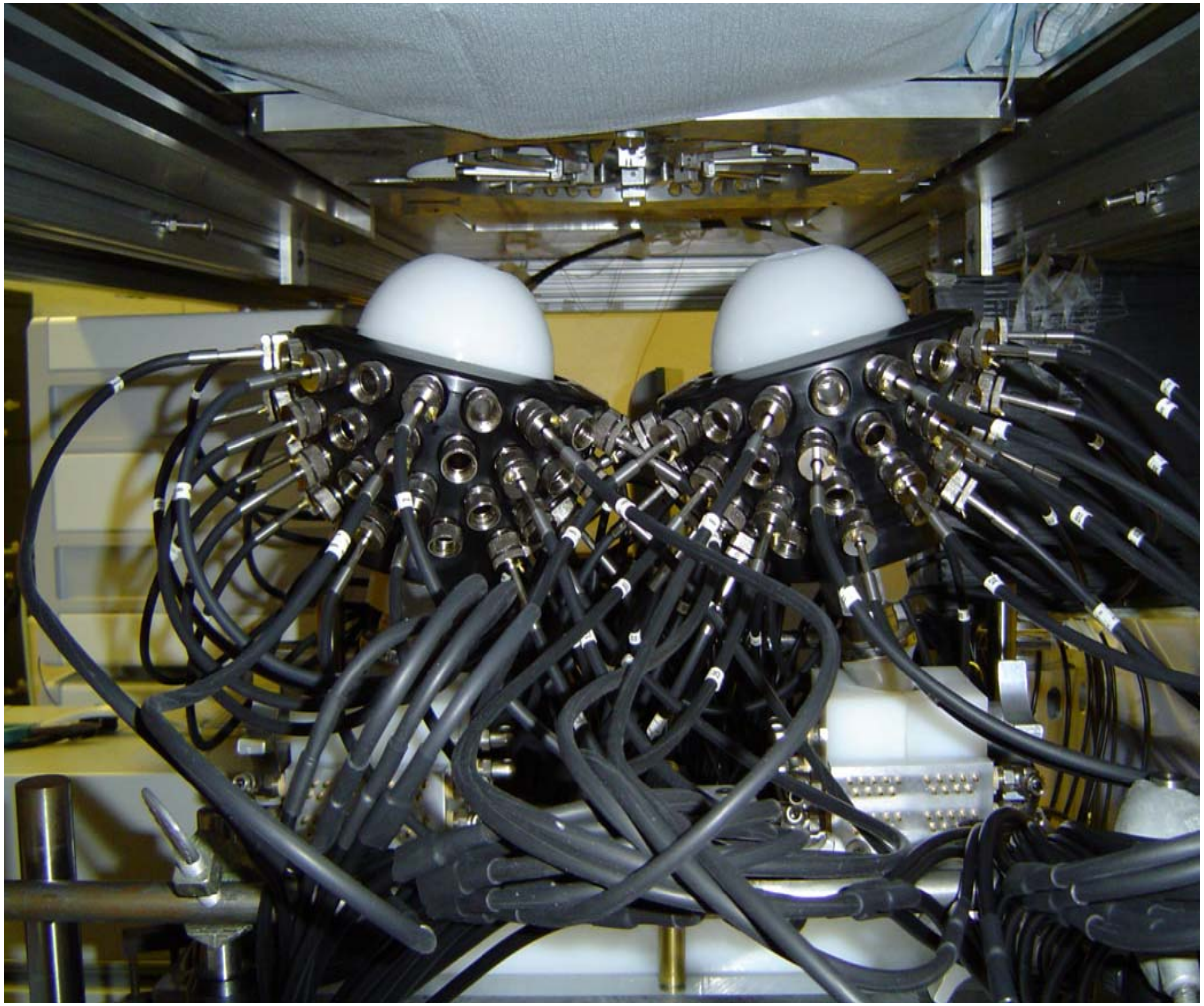


Figure 4. Photograph of measuring head used for simultaneous dual-breast measurements. Thirty-one source-detector fibers are distributed over the surface of each breast.

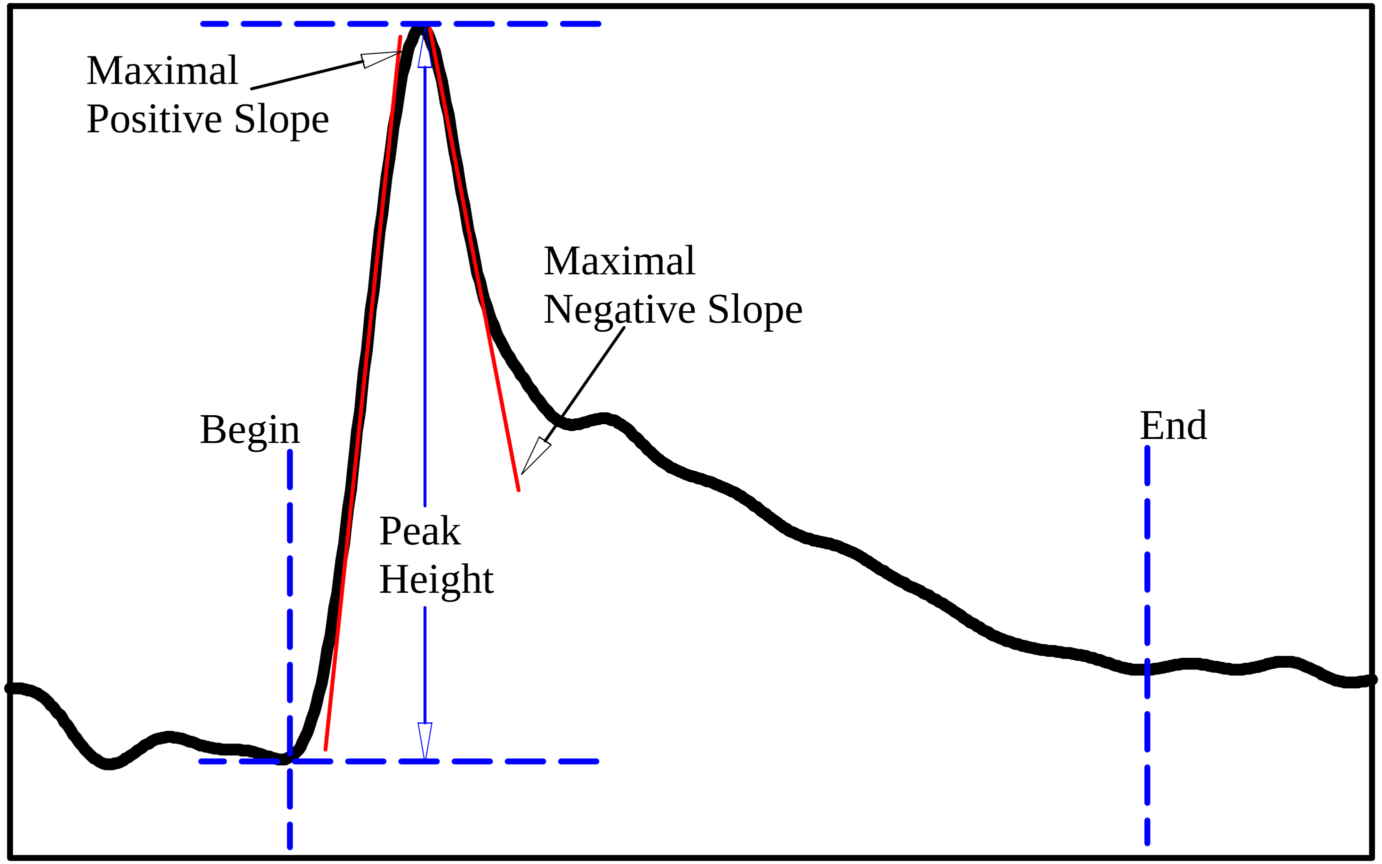
Forty breasts from twenty female subjects were imaged in this study; six subjects had a history of current or past breast cancer, eight subjects had non-neoplastic breast disease (fibrocycstic disease, fibroadenoma or galactorrhea) and six subjects were healthy volunteers.

Data collection was performed using a simultaneous dual-breast DYNOT breast measuring head supporting 31 source fibers and 31 detector fibers. Each subject was placed prone in the breast imager with the breast held pendant within the measuring heads. The subject placed their head to one side while in the imager. Baseline measurements were then obtained for approximately 13 minutes (1500 time points). The subject then performed the Valsalva maneuver, maintaining a pressure of 40 mmHg against a fixed resistance. The subject was allowed to recover to baseline for at approximately 4 minutes (500 time points). This was performed two times. The subject then turned their head to the other side and after normalization of blood volume performed two additional Valsalva maneuvers, each followed by at least 4 minutes (500 time points) of rest for recovery to baseline.

DATA ANALYSIS and RESULTS

Figure 1 shows the normalized spatial mean oxy-hemoglobin time series for the left and right breasts, performed on a healthy volunteer. As can be seen, they are markedly similar without being identical. This goes to the aforementioned advantage of being able to compare the same provocation in one breast to the other without dealing with variation in force or duration of the Valsalva. The following data analysis was done to diagnose and locate breast disease: After raw data from each breast were collected, they were low pass filtered with a cutoff frequency of 0.05 Hz and normalized. Any source detector channel with a baseline coefficient of variation greater than 20 was rejected . The resulting data was then spatially deconvolved using the Normalized Difference Method **[4]** which produced voxel data classified by hemoglobin state. The resulting voxel data was then analyzed to isolate the maximum and minimum slope of the time series for each provocation in each voxel. The maximum slope is affected by the force of the Valsalva with a more forceful Valsalva causing a greater maximum slope. The minimum slope is affected by the maximum slope with a greater maximum slope giving rise to a greater minimum slope. Since each person’s performance of the Valsalva maneuver varies to some degree from others as well as one’s own performance from one to the next, the maximum and minimum derived slopes must be normalized to be able to compare breasts in a subject. This was accomplished via normalizing each maximum and minimum slope value to the corresponding Valsalva peak height (See Figure 5). The results of the normalization were then displayed on scatterplots (See Figures 6 through 10) with the normalized maximal positive slope as the x-coordinate and the normalized maximal negative slope as the y-coordinate.

Figure 5. Representation of a single epoch of the Valsalva maneuver. The maximal slope, minimal slope and peak height of provocation are illustrated here. Each slope was derived and then divided by the peak height of its respective provocation for normalization.



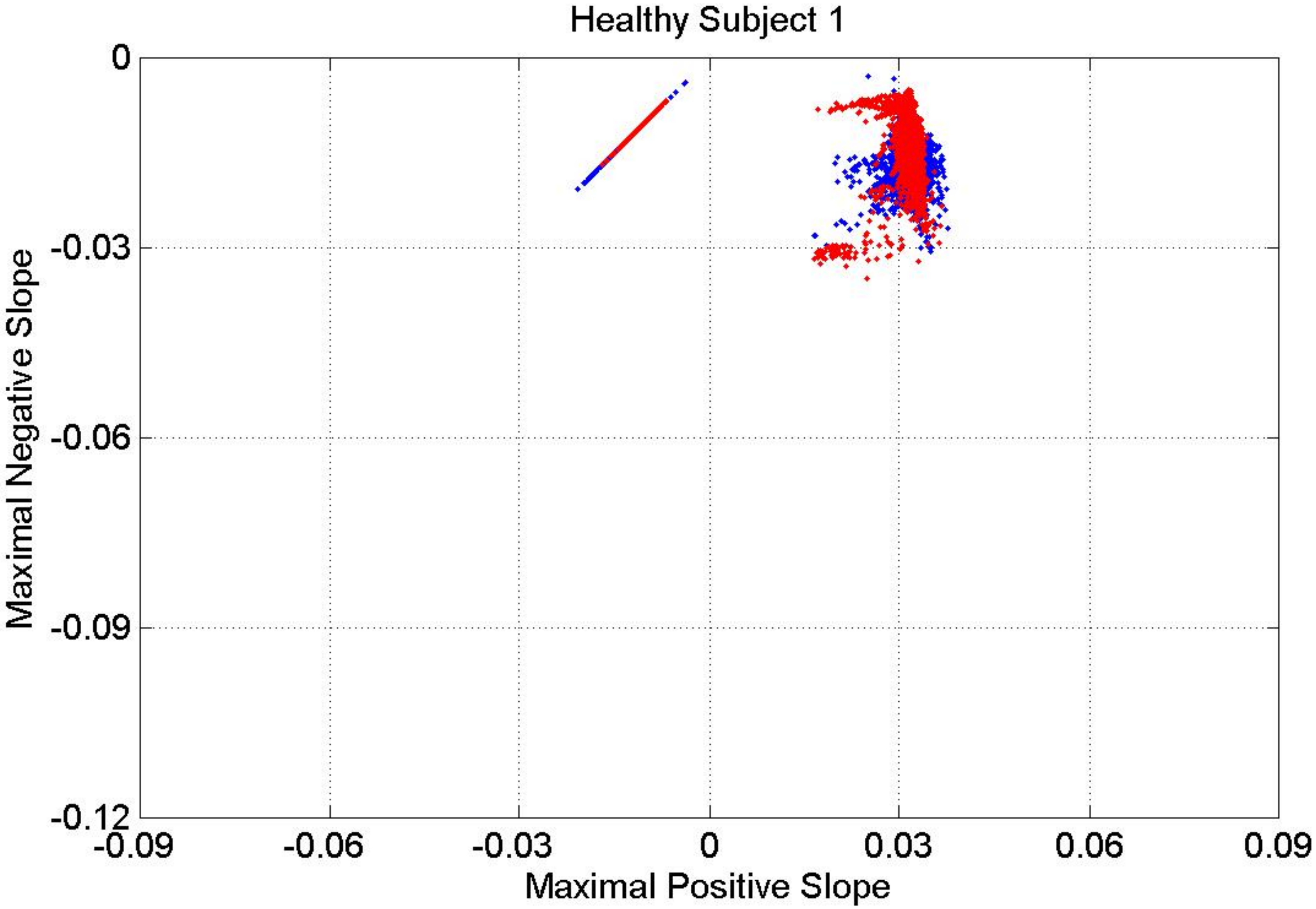


Figure 6. Scatterplots of the left and right breast of healthy subject. As can be seen the two plots overlay, hence showing little variation between left and right breast.

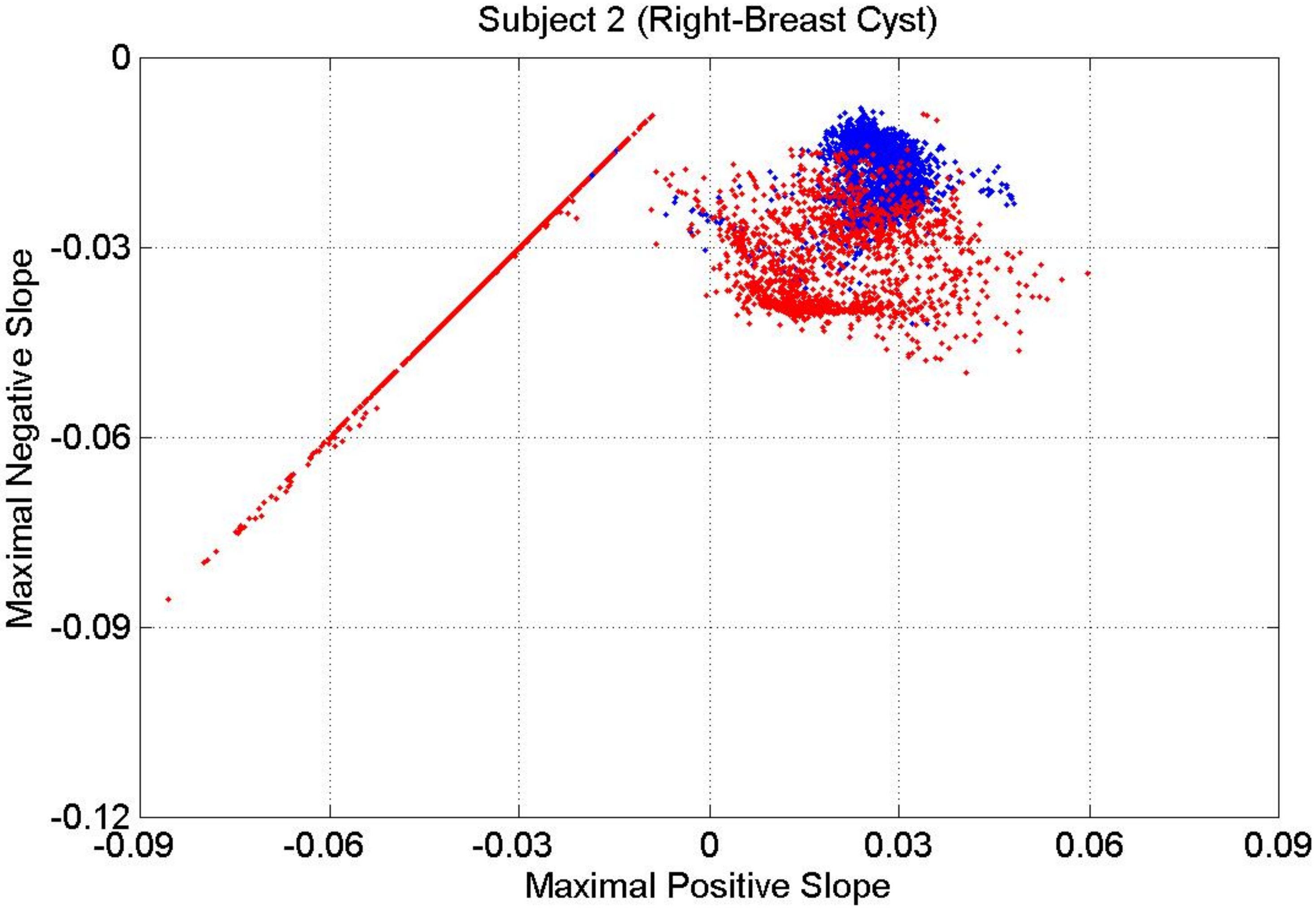


Figure 7. Scatterplots of the left and right breast of a subject with a right breast cyst. The right breast shows a much higher variation in normalized slopes than the left breast.

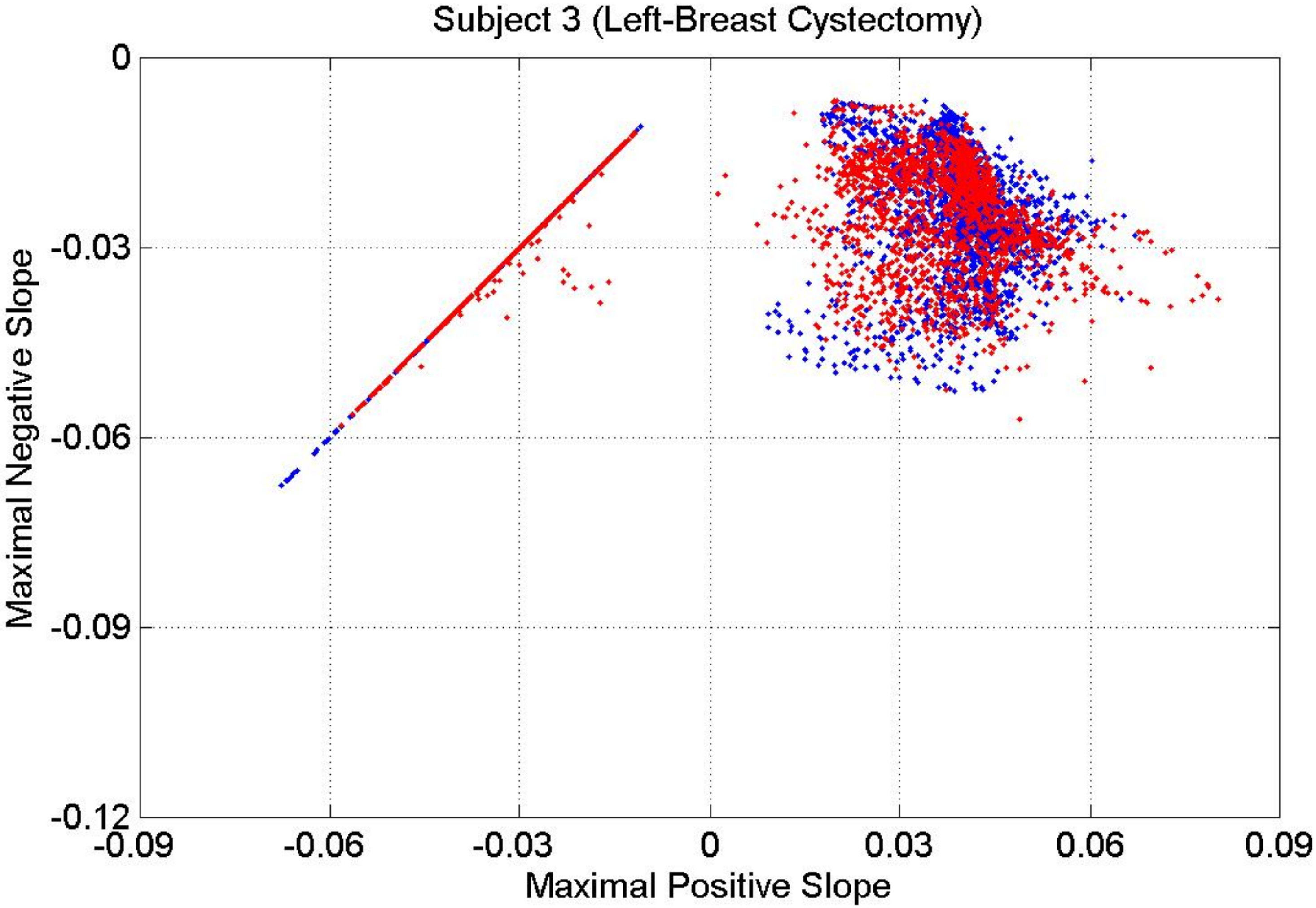


Figure 8. Scatterplots of the left and right breast of a subject after having a cyst removed from the left breast. The two scatterplots correlate well. Hence, there is no residual variation between the left and right breast after removal of the cyst.

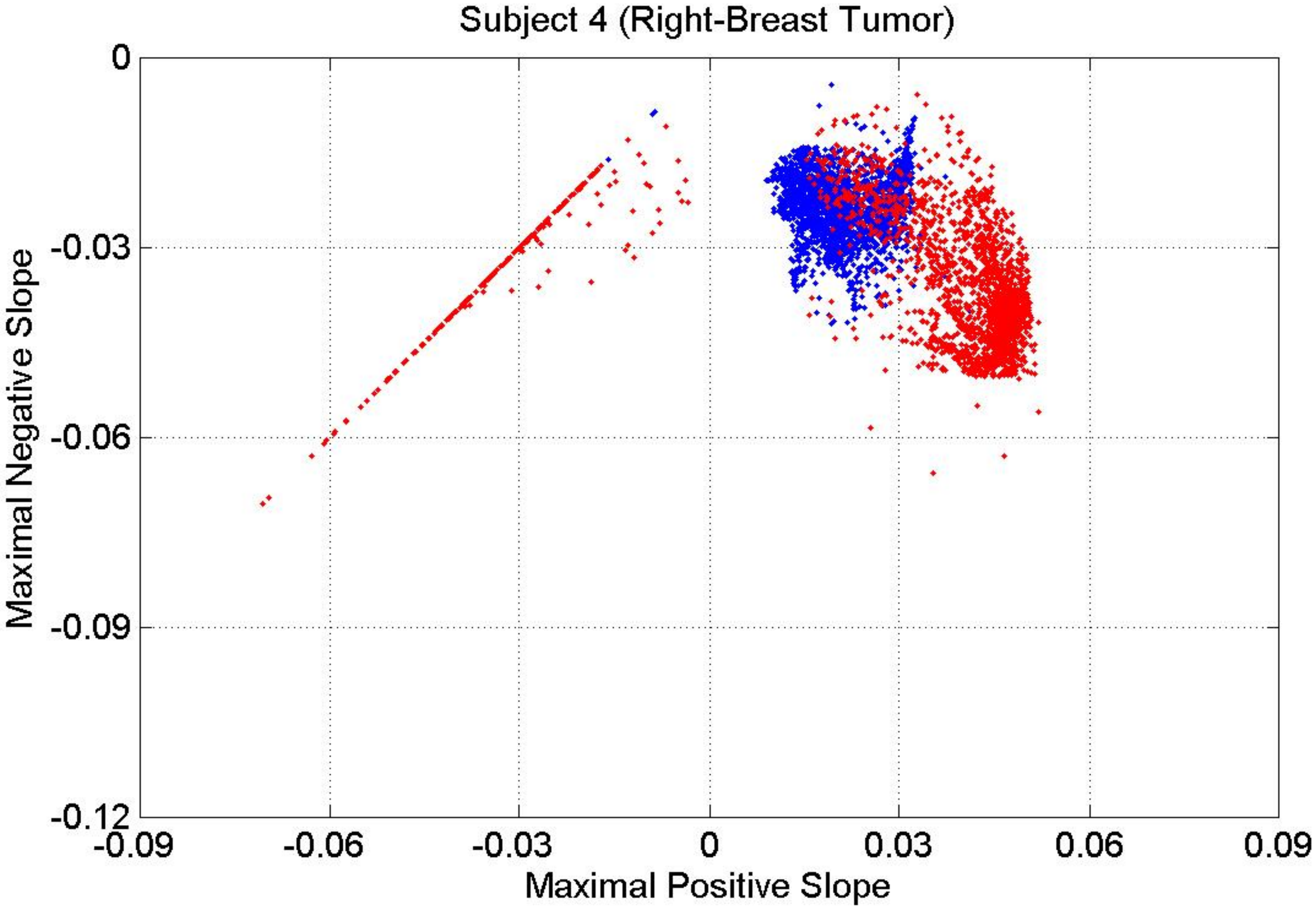


Figure 9. Scatterplots of the left and right breast of a subject with a right breast tumor. Variation between the breasts is seen with the affected breast showing greater maximal positive and negative slopes.

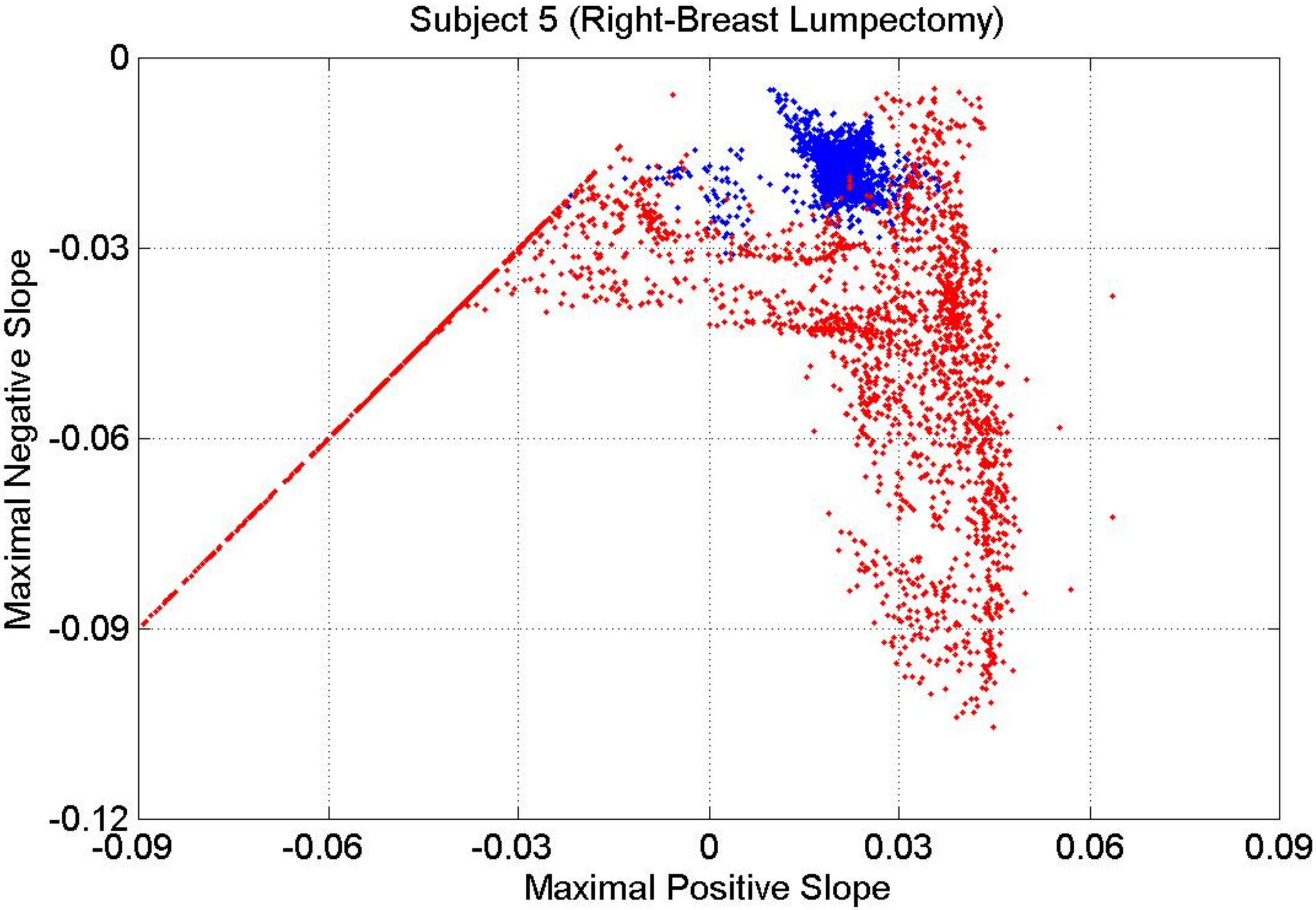


Figure 10. Scatterplots of the left and right breasts of a subject after a right breast lumpectomy for cancer. Even after removal of the tumor, the effect on the vasculature remains.

One factor that was found to affect the provocation was head positioning while in the imager. Figure 11 shows the normalized spatial mean oxy-hemoglobin time series for left and right breasts noting the head positioning during the imaging session.

- The amplitude and rate of both increase and decrease in blood volume is dependent on head positioning and is reciprocal.

- The blood volume increases to a greater magnitude and has a longer return to baseline when the patient's head is to the ipsilateral side. The opposite is seen when the patient has her head to the contralateral side.

- The reason for this is due to vascular compression when the subject turns their head to the side. The main blood supply to the breast is from the branches of the internal mammary artery and the lateral thoracic artery as well as other branches off the subclavian artery. (See Fig. 12)

•The subclavian artery, along with the carotid, comes from the bifurcation of the brachiocephalic on the right, and branches off the aorta close to the origin of the carotid on the left. When the subject turns their head to the ipsilateral side, the carotid artery is compressed.

•This diverts more of the increased blood volume from the Valsalva to the subclavian artery and its branches causing the increased oxy-hemoglobin blood volume in the ipsilateral breast versus the contralateral side.

•On the contralateral side the carotid artery is dilated allowing for increased and compensatory blood flow to the head. This diverts blood volume away from the subclavian and its braches and causes the observed blunted response. The augmented rate and amplitude of the blood volume increase in the ipsilateral breast leads to engorgement and hence decreased blood volume return in comparison to the contralateral breast.

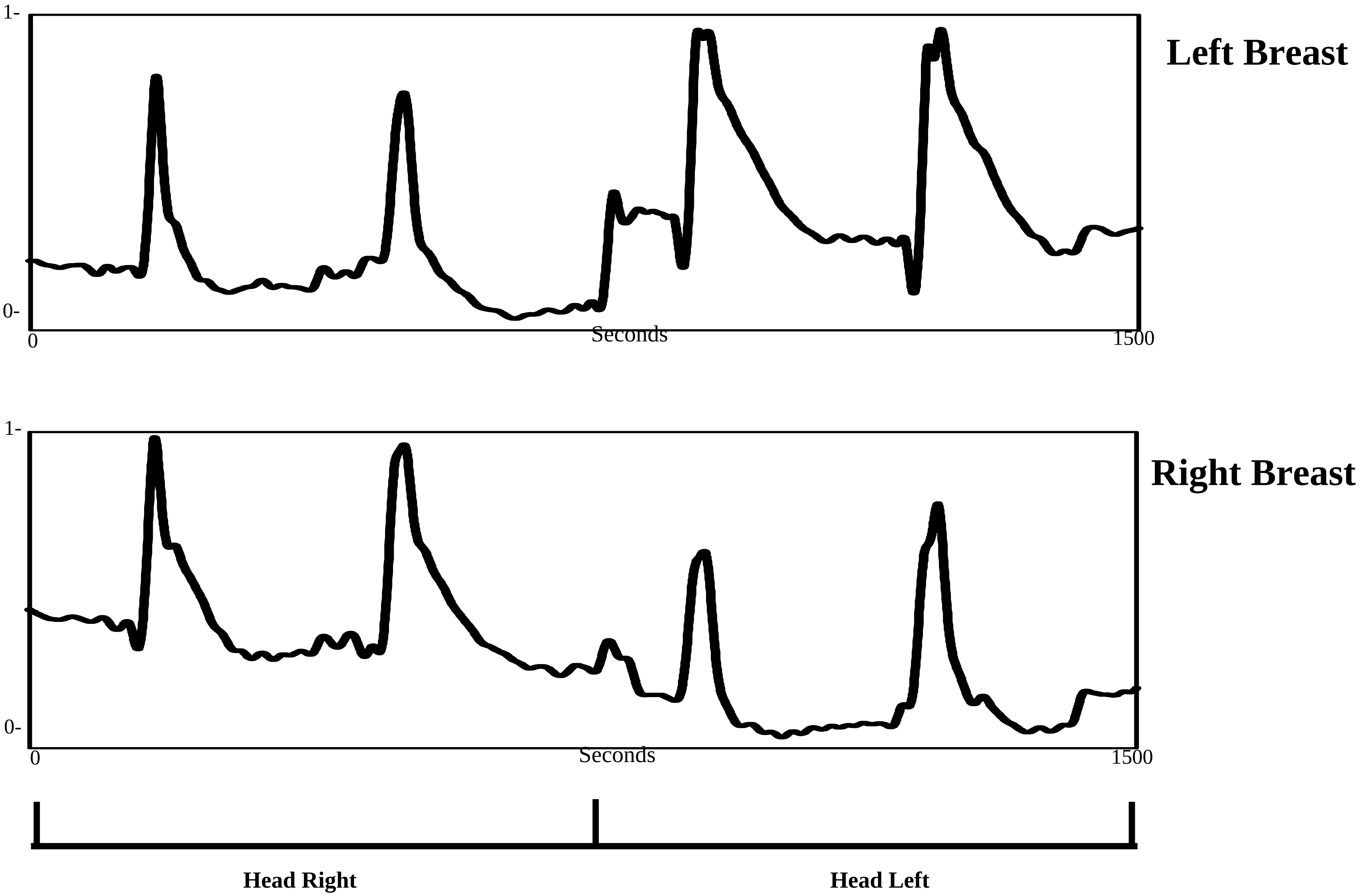


Figure 11. Normalized spatial mean time series of the left and right breast with respect to head positioning. The amplitude of blood volume is increased and the rate of return to baseline is decreased due to compression of the neck vasculature that takes place when the head is turned to the ipsilateral side.

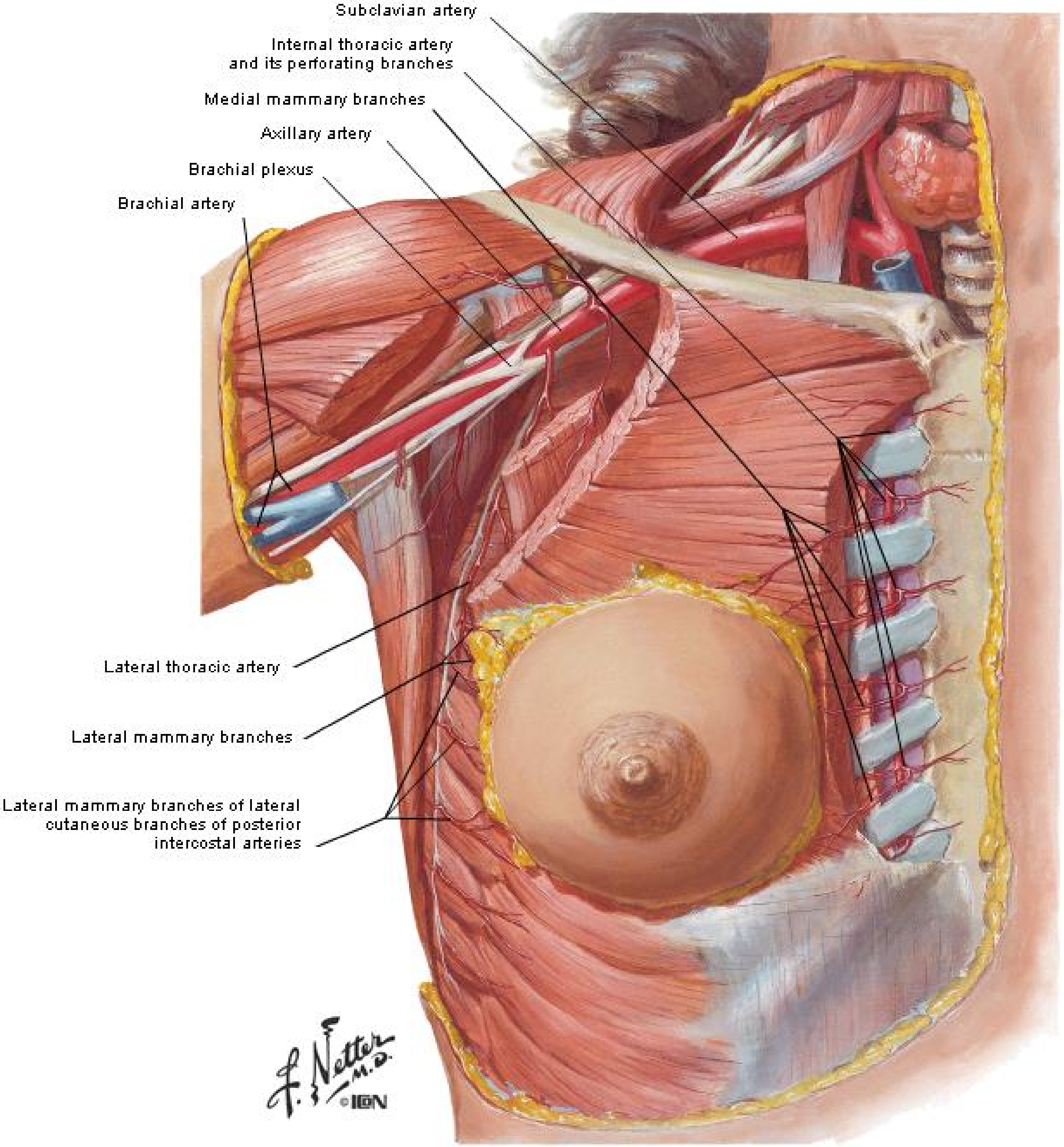


Figure 12. Arterial blood supply of the right breast. The bifurcation of the brachiocephalic at the base of the neck gives rise to the subclavian with it branches feeding the breast. ©2003, ICON Learning Systems, LLC.

CONCLUSION

- Simultaneous Dual-Breast Optical Mammography has proven to be a major advance over the previous separate single breast imaging.
- A truer assessment of physiological functioning is done, and the vasculature of both breasts in healthy subjects correlates well.
- Breast disease causes variation in the vasculature of one breast versus the other. With cystic disease the subjects vascular physiology returns to normal after removal of the cyst.
- Breast cancer causes variation in vascular physiology that remains even after the removal of the pathological tissue.
- Head positioning can influence variation in the time series by diverting blood to the ipsilateral breast. While this variation can be normalized, head positioning must be noted and accounted for during any imaging session.

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