Effects of Radiographic Breast Density on the Optical Properties of Treatment Naïve Breast Tissue Margins

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Background and Objectives

Optical spectroscopy can quantify the tissue composition of normal and malignant breast tissues. Our group is seeking to utilize optical technology for the intra-operative assessment of tumor margins during breast-conserving surgery (BCS) due to high re-excision rates (20-70%) [1]. We also attempt to devise strategies to exploit optical contrast for the detection of close-positive tumor margins in a variety of patient populations. It is well known that breast tissue undergoes a variety of changes throughout a woman’s lifetime; the relative contributions of fat, fibrous, and glandular tissue are ever changing. Radiographic breast density, derived from x-ray mammograms, is a measure of these relative tissue contributions and has been shown to be a major risk factor for breast cancer [2-4]. In an image, the fibroglandular (FG) tissue appears white while fat appears dark gray [2]. Density is measured as the percent of light gray/white areas relative to the amount of dark gray/black areas and is defined, in our study, on a 4-point scale (1=predominately fatty, 2=fat with some FG tissue, 3-heterogeneously dense, 4-extremely dense). Density can be quantified subjectively by a radiologist or with computer segmentation techniques [2]. Some issues with measuring breast density are 1) that the relative amounts of tissues in a 3D volume cannot be derived from a 2D image, 2) reader variability, and 3) positioning of the breast in the machine greatly affects the measured density [2]. Regardless of these issues, tissue density typically decreases with age as the FG component of the breast atrophies and fat becomes the predominant tissue type. Therefore, it is expected that optical parameters related to tissue morphology will differ in patients with different breast densities.

Methods

The increased β-carotene is NOT due to differences in BMI or age

Figure 5. Boxplots of adipose sites from neoadjuvant naïve, negative margins; separated by radiographic breast density and BMI or age. Arrow indicates a p<0.05 from a Wilcoxon rank-sum test. Outliers are not shown past the longest whisker.

The increased β-carotene is due to adiopocyte density

Figure 6. Boxplots of adipose sites separated by breast density and A) the stage of cancer at the margin (N = negative margin, IDC = invasive ductal carcinoma, DCIS = ductal carcinoma in situ) or B) the margin status (N = negative, C = close, P = positive). Arrow indicates p<0.05 from a Wilcoxon rank-sum test. Outliers are not shown past the longest whisker.

Impact of breast density on optical properties of tissue margins

Figure 7. Boxplots of malignant sites separated by breast density and A) the stage of cancer (IDC = invasive ductal carcinoma, DCIS = ductal carcinoma in situ) or B) distance from the margin (C = close, P = positive). No significant differences were found. Outliers are not shown past the longest whisker.

8-carotene decreases with distance from DCIS sites

Figure 8. Scatterplots showing the distance between histologically confirmed adipose sites to the closest histologically confirmed cancer (IDC or DCIS) site on a close/positive margin. Correlation coefficients and p-values were calculated using Pearson’s correlations.

Discussion

Our technology allows for the measurement of parameters that are directly related to tissue morphology. In the benign tissue of breast cancer patients, tissue morphology is affected by radiographic breast density, proximity to the tumor, and tumor type. This data suggests that THb and β-carotene are most affected by density. β-carotene is also greatly impacted by proximity to tumor which is seen with the increase in β-carotene in margins with DCIS and the decrease in positive margins.

Although we show that β-carotene is higher in high density patients who still need to understand why this is happening. Using high resolution imaging combined with spectroscopic measurements of carotene would allow for a direct comparison of the β-carotene concentrations to the morphology of the adipose sites.