# Effect of Patient Characteristics on the Optical Properties of Breast Tumor Margins

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## BACKGROUND

Optical spectroscopy can quantify the tissue composition of normal and malignant breast tissues. Our multi-disciplinary group is seeking to utilize optical technology for the intra-operative assessment of tumor margins during breast-conserving surgery (BCS) due to the high re-excision rate in this patient population (20-70%)[1]. A multivariate model to differentiate positive/close margins from negative margins was previously developed on data from 48 patients and had a sensitivity of 79.4% and a specificity of 66.7%[2].

## OBJECTIVES

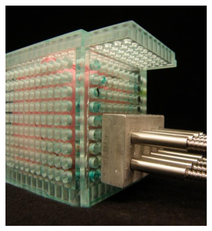
✓ Demonstrate the feasibility of a handheld optical spectral imaging probe for intra-operative assessment of breast tumor margins.

✓ Determine the effect of patient characteristics on the optical tissue parameters of negative margins

✓ Determine the effect of patient characteristics on the optical contrast observed between negative and close/positive margins

## INSTRUMENTATION

Portable spectrometer and computer interface



Adjustable plexi-glass box and 8-channel fiber optic imaging probe

*Sensing Depth of Probe[3]*

| | |
|---|---|
| Malignant | 0.50-1.50 mm |
| Adipose | 0.70-2.20 mm |
| Fibro-glandular | 0.60-1.50 mm |

Table 1. Sensing depth was determined with Monte Carlo simulations based on the optical properties of sites with pathological confirmation.

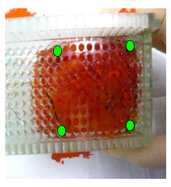
The fiber optic probe has a footprint of ~2cmx4cm and takes ~25 seconds for data acquisition and processing. The sensing depth for clear margins at Duke University Medical Center is 2mm; the probe design was optimized to sense close and positive margins.

## METHODS

**Clinical Study:** Patients undergoing BCS were consented under an IRB approved protocol. 10-15 minutes after excision, the lumpectomy specimen was oriented in a plexi-glass box for optical imaging. The fiber optic probe was interfaced with the margin surface via the holes of the plexi-glass box.

**Comparison to pathology:** The area imaged by multiple placements of the probe on a single margin was delineated with green ink for pathologic correlation of margin surfaces. Pathologic margin status of the inked areas was collected from standard surgical pathology reports. Close and positive margins were grouped together since both require a re-excision. Neo-adjuvantly treated patients were excluded from this data analysis.

| | |
|---|---|
| # of Imaged Patients | 72 |
| # of Imaged Margins | 92 |
| # of Positive/Close Margins | 46 |
| # of Negative Margins | 46 |



**Data Analysis:** Total hemoglobin (THb) and β-carotene concentrations, along with the wavelength-averaged reduced scattering coefficient from 450-600 nm (<$\mu_s$'>) which reflects cell and collagen density were extracted from each site using an inverse Monte Carlo model[4]. These parameters were used to create images of the entire measured tumor margin. The mean of each margin image was then calculated.

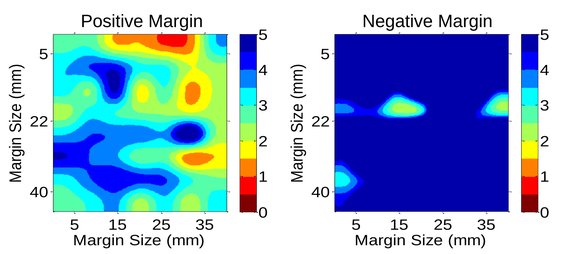



Figure 1. Example Images are of β-carotene/<$\mu_s$'>. The positive margin contains DCIS

## RESULTS

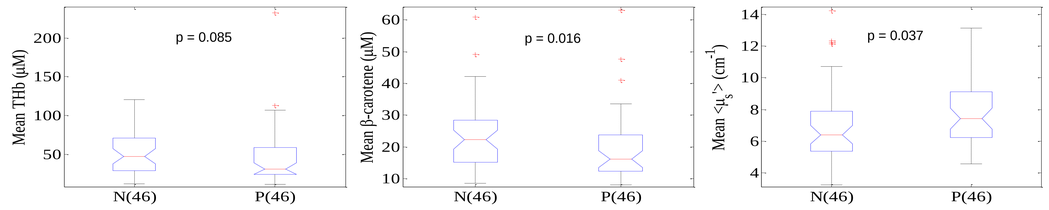



Figure 2. Box and whisker plots for the total subset of negative and positive margins

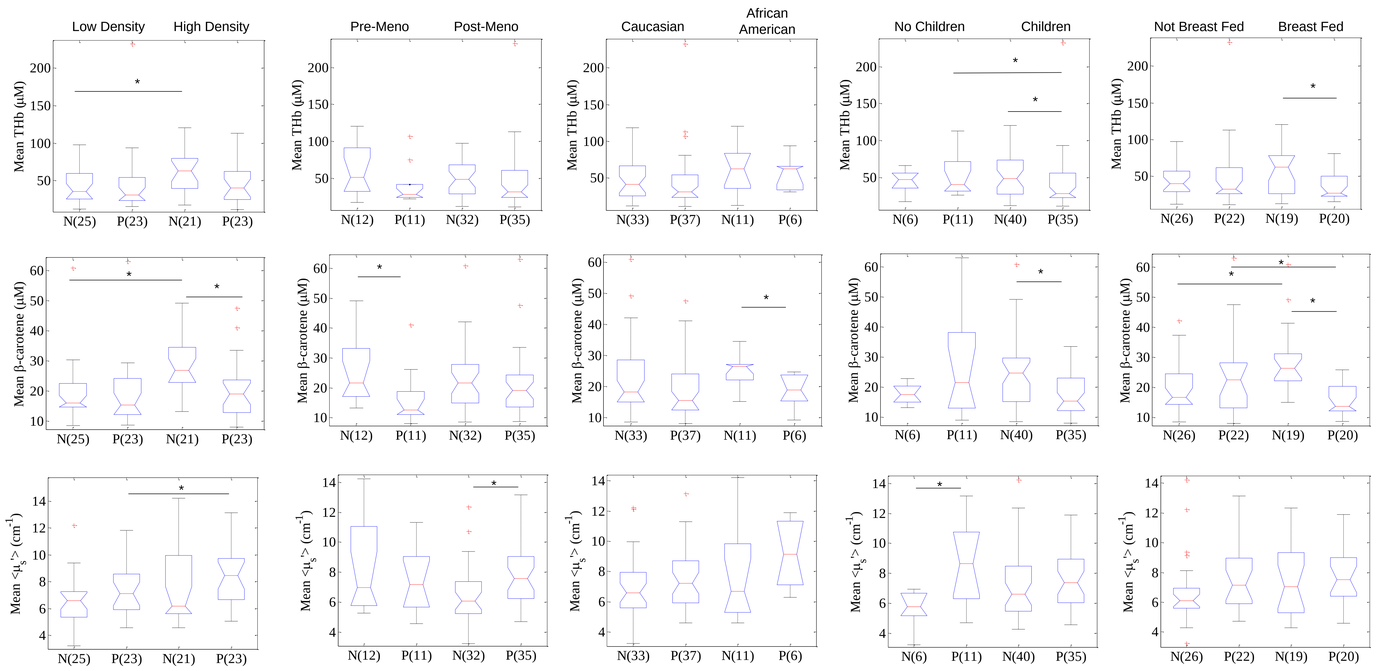



Figure 3. Box and whisker plots of mean THb, β-carotene, and <$\mu_s$'> separating negative and close/positive margins for various patient characteristics. Only significant p-values are shown. * $p < 0.05$.

## DISCUSSION

Understanding the relationship between the heterogeneity and "age-related" changes of the normal breast and the subsequent development of breast cancer remains a paramount challenge towards diagnosing and treating women with breast malignancies. In this study we have evaluated the optical characteristics of "normal" breast tissue in women who have breast cancer undergoing BCT. The optical parameters were sub-analyzed based on pre-selected patient characteristics and then compared to the margin tissue with evident malignancy. The following conclusions are offered:

1. Mean total hemoglobin is higher in the normal margins of high density patients but does not change with the other patient stratifications. Increased contrast is observed in parous women.

2. Mean <$\mu_s$'> is influenced by the existent tissue density and is best utilized in post-menopausal and nulliparous women with likely greater breast involution.

3. Optical measurement of β-carotene (surrogate for fat) had a paradoxical effect. Higher β-carotene was seen in the normal tissue of patients with higher breast density and pre-menopausal women. Because of this paradoxical increase this optical parameter offers better contrast between normal and malignant margins.

Future studies will incorporate the normal tissue factors into the selection of optical parameters for benign and malignant differentiation in breast margins.

References:

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