Optical imaging of breast tissue: influence of clinical factors on measured data

Torre M. Dybdon1, J. Quincy Brown1, William T. Barry2, Joseph Geradts3, Lee G. Wilke4, Stephanie A. Kennedy4, Lisa M. Richards5, Marlee S. Junker, Nimmu Ramanujam4

1 Dept. of Biomedical Engineering, Duke University, 2 Dept. of Biostatistics and Bioinformatics, Duke University, 3 Dept. of Pathology, Duke University School of Medicine, 4 Dept. of Surgery, Duke University School of Medicine

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 due to the high-excision rate in this patient population (20.7%)1. A multivariate model to differentiate positive/close margins from negative margins was developed on data from 48 patients and had a sensitivity of 79.4% and a specificity of 66.7%2.

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

RESULTS
Table 2. Breakdown of the number of imaged margins. A close margin is defined as disease < 2mm from the margin. A predictive model based on the data from Set #1 has been published5. Set #2 includes 4 additional margins.

Comparison to pathology: The area imaged by the probe was delineated with green for pathologic correlation of margins surfaces. Pathologic margin status of the inked areas was collected from standard pathological pathology reports.

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

METHODS

Objectives
• Demonstrate the feasibility of a handheld optical spectral imaging probe for intra-operative assessment of breast tumor margins
• Determine the effect of menopausal status and breast density on the accuracy of the margin prediction model
• Determine the effect of menopausal status and breast density on the underlying sources of optical contrast used in the margin prediction model

Instrumentation
Sensing Depth of Probe
- Multicat: 0.1-10mm
- Adipoc: 30-70mm
- Optically: 50-150mm

Portable spectrometer and computer interface

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

The fiber optic probe covers an area of ~1cmx3cm 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.

Figure 1. This figure represents the data analysis steps. Images are of β-carotene (βC), one of the two distinctive parameters. The βC image is taken from a margin with DCIS while the bottom image is from a negative margin. The box and whisker plots are for the two descriptive variables in the multivariate model and their relationship to breast density.

Table 2. Classification results from the model.

What descriptive variables provide the best contrast between negative and positive margins?

Figure 2. Box and whisker plots of negative and positive/close margins from Set #1 and Set #2 for the descriptive variables used in the predictive model. Plots are separated by low (1-2) and high (3-4) density breast tissue.

The fiber optic probe was interfaced with the margin surface via the holes of the pinfix glass box. A predictive model based on the data from Set #1 has been published5. Set #2 includes 4 additional margins.

Figure 3. Box and whisker plots of negative and positive/close margins from Set #2. These variables provide the best contrast between negative and positive margins. There are additional descriptive variables which also show good contrast for the specific patient characteristics shown here.

DISCUSSION
• This preliminary predictive model is best at distinguishing negative from positive margins in patients with high density breast tissue and/or in women with pre-menopause.
• These results show that breast density and menopausal status will be important parameters in building future predictive models. Patient characteristics clearly have an impact on the optical properties of tissues. Better results are obtained by patient characteristics or including patient characteristics as predictors in a model may yield better results.

In post-menopausal women or women with low breast density, contrast in β-carotene is diminished due to more adipose tissue in the margin. The median value of β-carotene (post-menopausal) in negative margins is 21.4µM and in positive margins is 8.8µM. In pre-menopausal women or women with high breast density, this contrast is not confounded by the adipose tissue. The median value of β-carotene (pre-menopausal) in negative margins is 33.1µM and in positive margins is 11.9µM. Median values show much greater contrast in pre-menopausal breast.

REFERENCES

Figure 3. Box and whisker plots of negative and positive/close margins from Set #2. These variables provide the best contrast between negative and positive margins. There are additional descriptive variables which also show good contrast for the specific patient characteristics shown here.

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