Intraoperative in vivo *reflectance spectroscopy for discrimination of normal, benign, and malignant breast tissues*

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Hypothesis

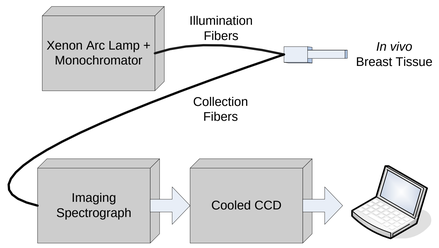
- Optical spectroscopy is a technique that provides real-time discrimination of malignant breast tissues. This methodology can be used for:
  - Assisting core-needle biopsy
  - Intraoperative tumor margin assessment
  - Monitoring tumor response to therapy
- The purpose of this study is to measure the optical signatures of normal and malignant breast *in vivo.*

Optical Signals Can Probe…

Absorption	• Hemoglobin saturation, vascularity • Water content • Lipid content
Fluorescence	• Cellular metabolism • Structural protein content • Amino acids
Scattering	• Size and density of scattering centers

Instrumentation and Analysis

- Diffuse reflectance (350-617 nm) and autofluorescence excitation-emission matrices (EEM's) are recorded from intact breast tissues *in vivo* using a custom designed fiber-optic probe interfaced with a custom optical spectrometer

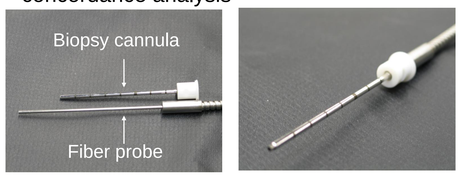


- An Inverse Monte-Carlo algorithm developed by our group is used to extract the scattering, absorption, and fluorescence properties of the tissue from the measured spectra, and can quantify the concentrations of chemical constituents and size and density of scattering centers

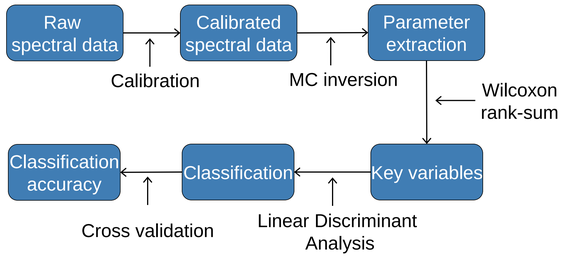
Methods

• *Intraoperative Procedure*

1. Incision made in skin of the breast
2. Ultrasound used to guide needle-biopsy cannula to site of interest
3. Needle is retracted, and probe inserted through cannula to interface with tissue
4. Optical measurement made
5. Probe retracted, and vaccum assisted biopsy of interrogated tissue made through cannula
6. On average, 3 tissue sites interrogated per patient
7. Biopsied tissues histopathologically analyzed for concordance analysis



• *Data Analysis*



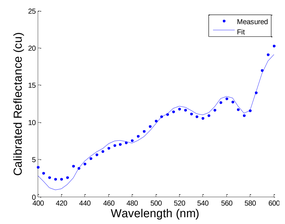
- *Parameters extracted from tissue spectra*: Scattering coefficient, concentrations of oxy- and deoxyhemoglobin, beta-carotene, lymphazurin

• *Enrollment / Sample Statistics*

Patients enrolled	32
Useable data	30 patients
Median age (range)	52 (36-74) yrs.
Mean breast density (Scale: 1-4)	2.7 ± 0.75
Chemotherapy Status	8 w/prior chemo 22 w/o chemo
Menopausal Status	13 pre- 17 post-
Tissue Breakdown (63 of 97 samples retained for analysis)	35 normal 6 benign 16 malignant (11 IDC, 3 IDC/ILC, 2 DCIS)

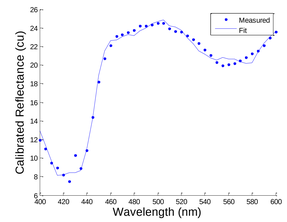
Results

• *Representative Spectra*



Adipose

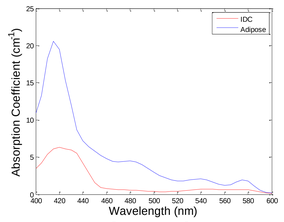
Hemoglobin saturation: 95.6%
Mean Scattering Coefficient: 6.32 cm^{-1}



Invasive Ductal Carcinoma

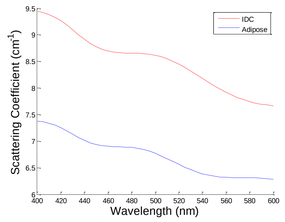
Hemoglobin saturation: 42.2%
Mean Scattering Coefficient: 7.9 cm^{-1}

• *Representative Extracted Optical Properties*



Absorption

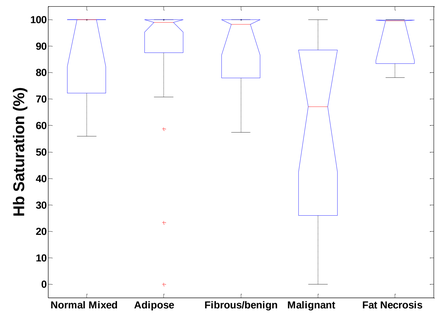
(Oxy- and deoxy-hemoglobin, β-carotene)

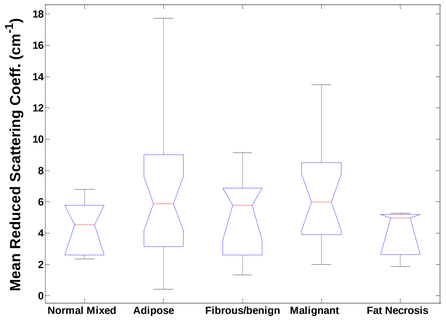


Scattering

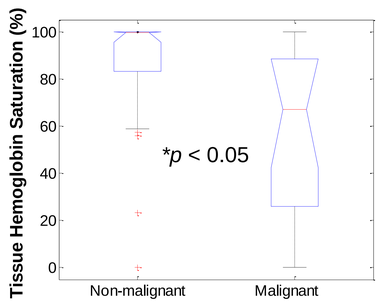
(Nuclear-to-cytoplasmic ratio, DNA and organelle content)

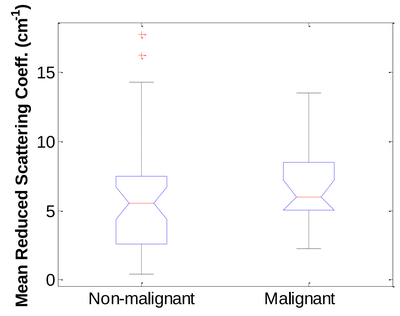
• *Extracted Tissue Parameters by Histology*

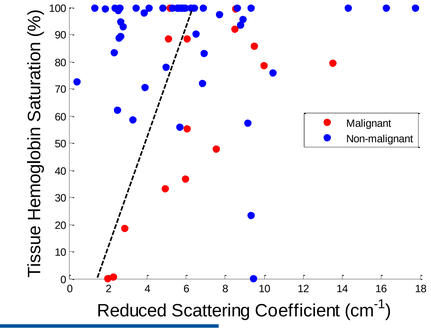




• *Discriminatory variables, Cancer (n=16) vs Non-cancer (n=41)*







Conclusions and Future Work

- Diffuse reflectance spectroscopy can discriminate between malignant and non-malignant tissues on the basis of extracted physiological parameters
- More robust classification algorithm expected with more malignant samples (larger balanced training set)
- Future work will include assessing utility of optical spectroscopy in early monitoring of neo-adjuvant chemotherapy

Acknowledgments

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