Intraoperative assessment of breast physiology via in vivo *optical biopsy: Potential for cancer diagnostics*

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Motivation

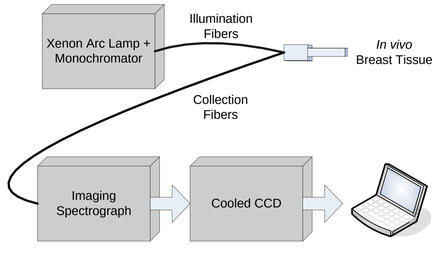
- Optical spectroscopy is a method that could provide real-time discrimination of malignant tissues for application in:
  - Adjunct to core-needle biopsy
  - Intraoperative tumor margin assessment
  - Monitoring tumor response to therapy
- The purpose of this study is to measure the optical signatures of normal and malignant breast *in vivo* to serve as a foundation for future studies and applications

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

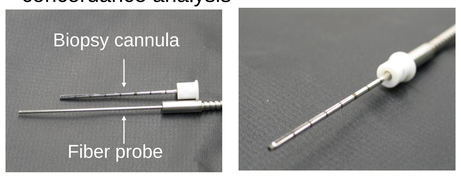


- An Inverse Monte-Carlo algorithm developed by our group is used to extract the scattering, absorption, and fluorescence properties of the tissue from the measured spectra, and can quantify the concentrations of chemical constituents and size and density of scattering centers

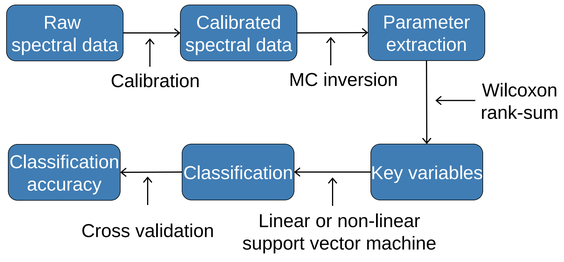
Methods

• *Intraoperative Procedure*

1. Incision made in skin
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 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*



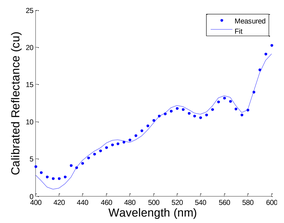
- Parameters extracted from tissue spectra: Scattering coefficient, concentrations of oxy- and deoxyhemoglobin, beta-carotene, relative contributions of NADH, FAD, collagen, vitamin A

• *Enrollment / Sample Statistics*

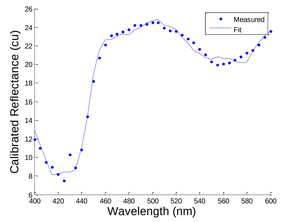
Patients enrolled	25
Useable data	23 patients
Median age (range)	51.5 (36-74) yrs.
Mean breast density (Scale: 1-4)	2.67 ± 0.66
Menopausal Status	10 pre- 12 post- 1 not recorded
Tissue Breakdown (76 total)	46 normal 20 benign 10 malignant

Results

• *Representative Spectra*

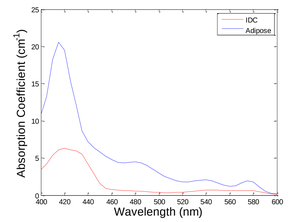


Adipose

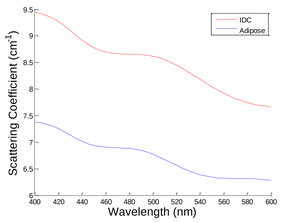


Invasive Ductal Carcinoma

• *Extracted Optical Properties*

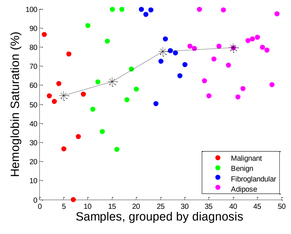


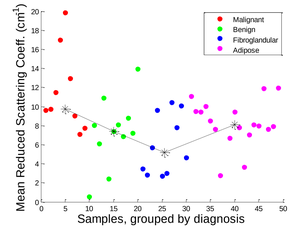
Adipose
Hemoglobin saturation: 95.6%
Mean Scattering Coefficient: 6.32 cm^{-1}



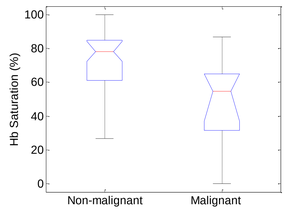
Invasive Ductal Carcinoma
Hemoglobin saturation: 42.2%
Mean Scattering Coefficient: 7.9 cm^{-1}

• *Tissue Parameter Extraction, All Samples*

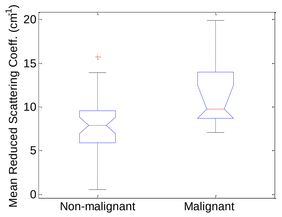




• *Tissue Parameter Extraction: Malignant vs. Nonmalignant*



Wilcoxon rank-sum: $p < 0.01$



Wilcoxon rank-sum: $p < 0.02$

• *Variables Display Differences*

● = Significant at $p < 0.05$

	Hemoglobin saturation	Mean reduced scattering coefficient
Normal (fibroglandular) v. malignant	●	●
Normal (adipose) v. malignant	●	
Benign v. malignant		●
Nonmalignant v. malignant	●	●

• *SVM Classification*

Tissue Classification Performance*	
	Balanced training set: 10 malignant, 10 random non-malignant (Validation set: 46 non-malignant, 10 malignant)
Sensitivity	100%
Specificity	85.7%
Accuracy	93.8%

***Nonlinear Support Vector Machine, leave-one-out cross validation**

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)
- Analysis of fluorescence spectra from *in vivo* study in progress, as well as a study on the effect of lymphazurin contamination on extraction accuracy
- Future work will include determining the contribution of methemoglobin in optically assessed tissues

Acknowledgments

- Study patients
- NIH
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