



Optical Intra-operative Assessment of Breast Tumor Margins



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Current Paradigm: Breast Conserving Surgery (BCS)

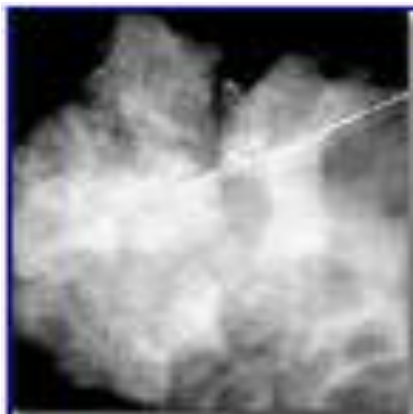
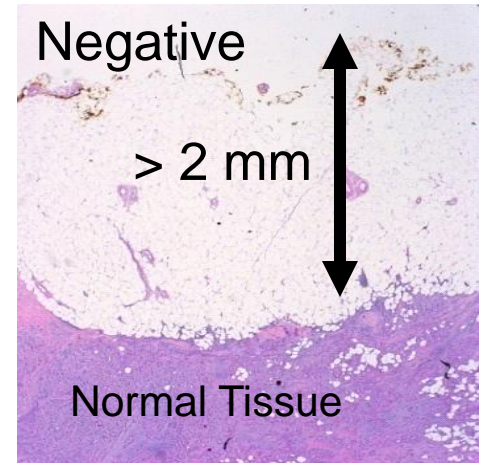
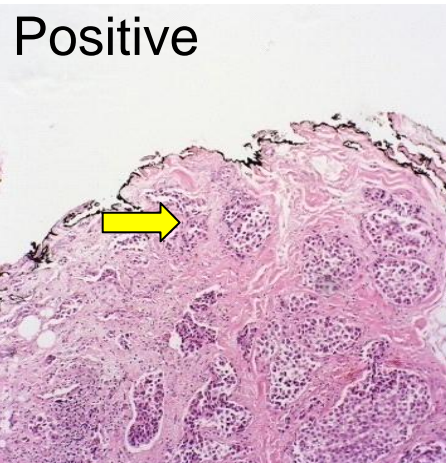
SURGERY



Lump and surrounding tissue is removed

POST SURGICAL PATHOLOGY

➔ Malignant Tissue



<http://images.google.com>

A positive margin is predictive of local recurrence ¹

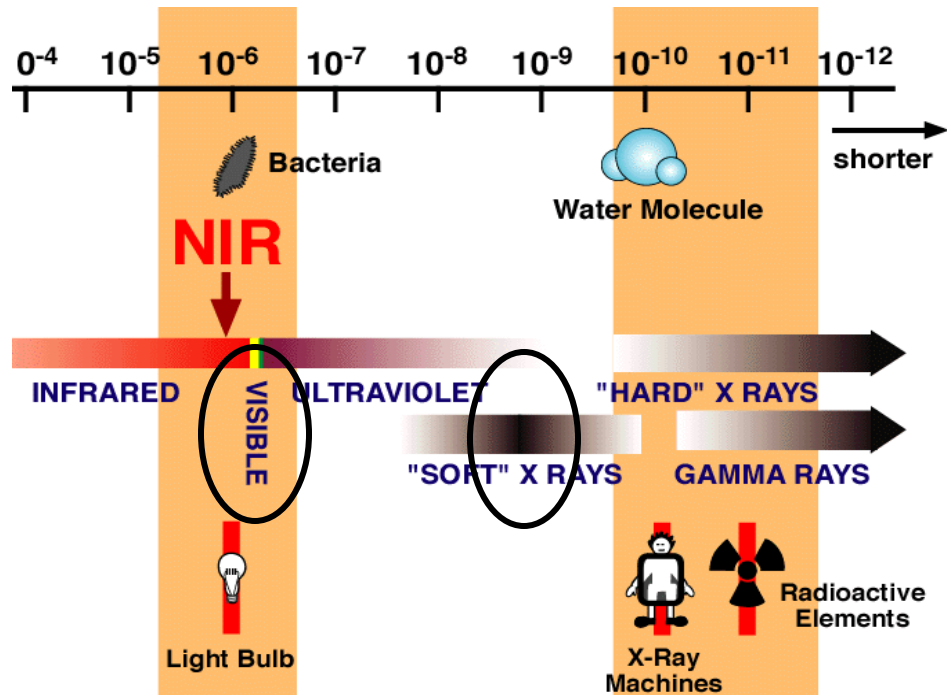
20 - 50% of women return for surgery ²

¹Breast J, 12(1): p. 28-36, 2006

²Ann Surg Onc 15:1271-1272, 2008; Am J Surg 192:509-512, 2006; Am Surg 73:337-343, 2007; Ann Surg Onc 14:1618-1628, 2007; Am J Surg, 192:538-540, 2006; Am Surg, 71:22-28, 2005

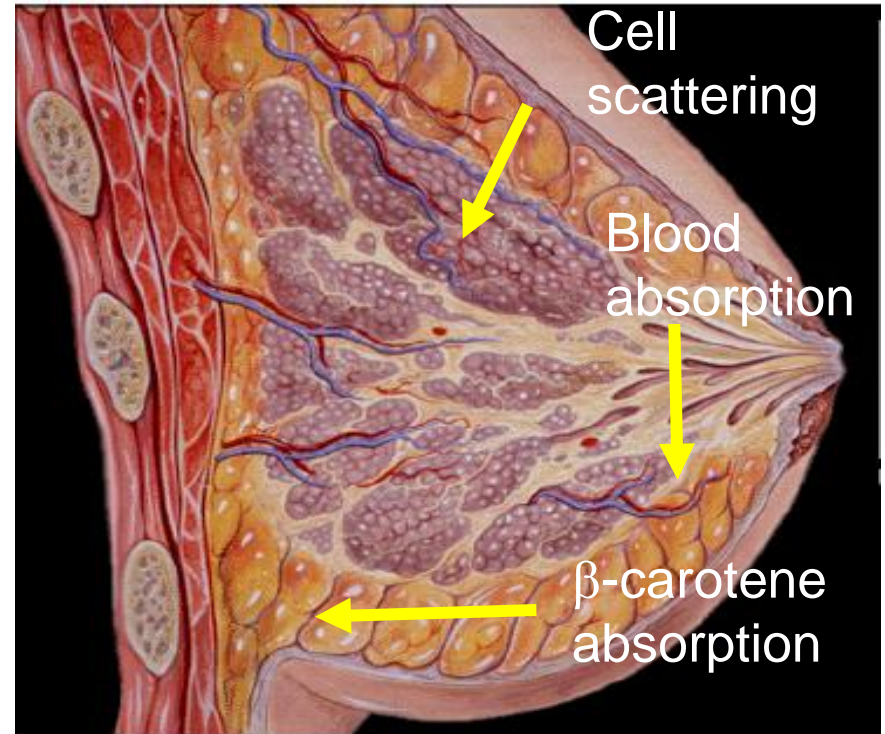
Our Solution: Diffuse Reflectance Spectroscopy

EM SPECTRUM (METERS)



Sensing depth ~ 1 - 2 mm

BREAST

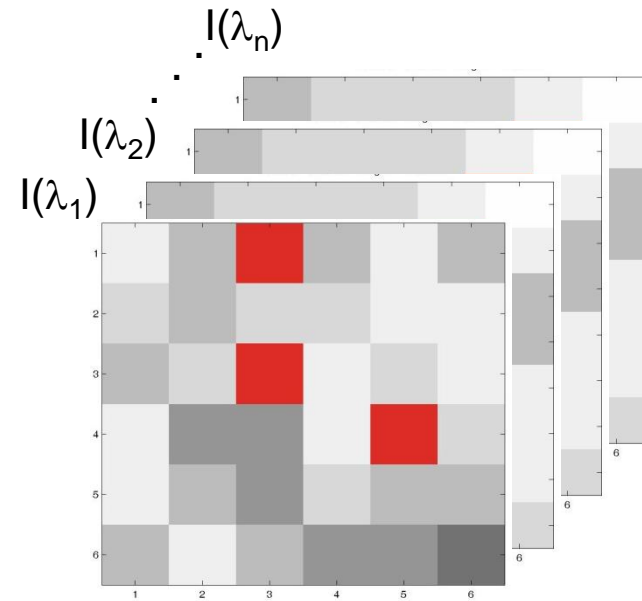
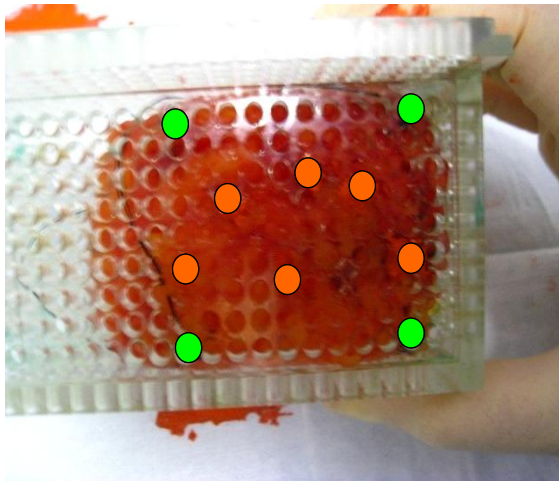
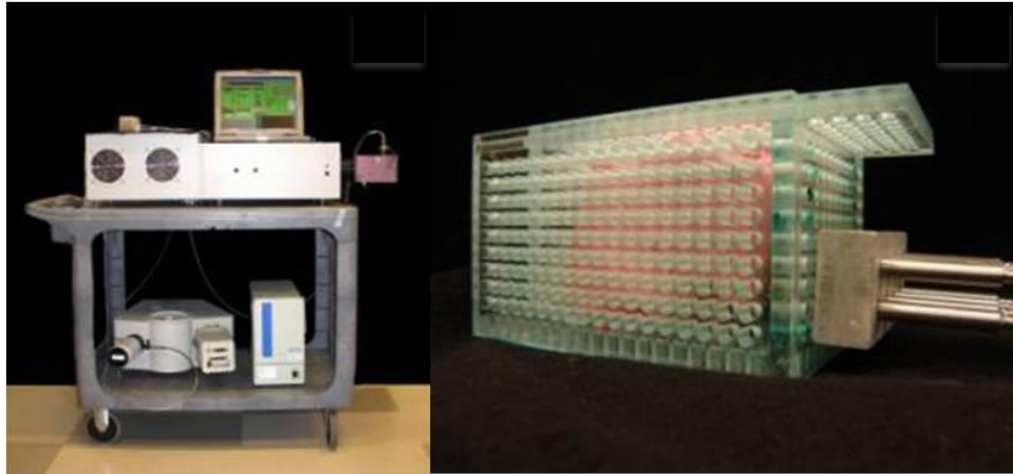


*Breast Cancer Changes*³

- β -carotene absorption
- blood absorption
- scattering

³ J Biomed Opt: 13(3):4-15, 2008;
Appl. Opt.. 45(5):1072-8, 2006.

Clinical Procedure

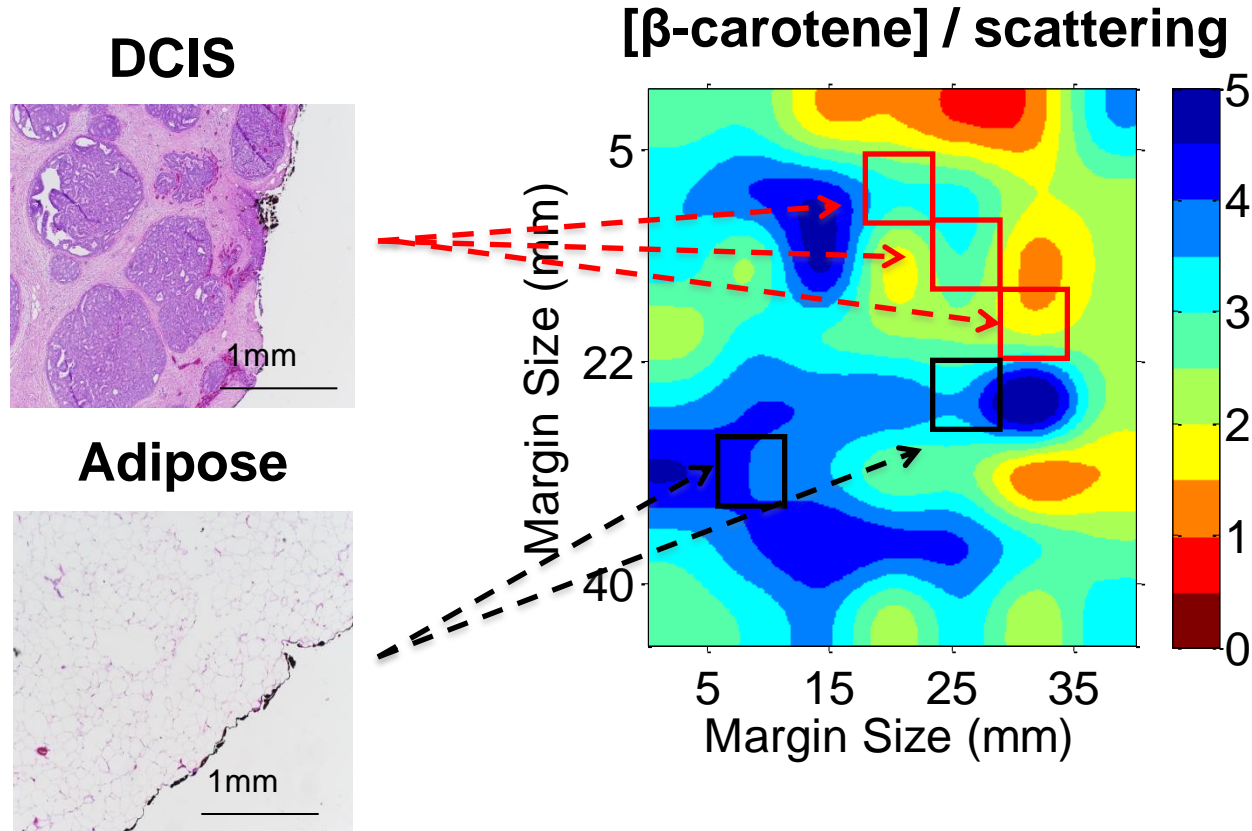


Patient Demographics

Patients	48
Positive Margins	34
Negative Margins	21

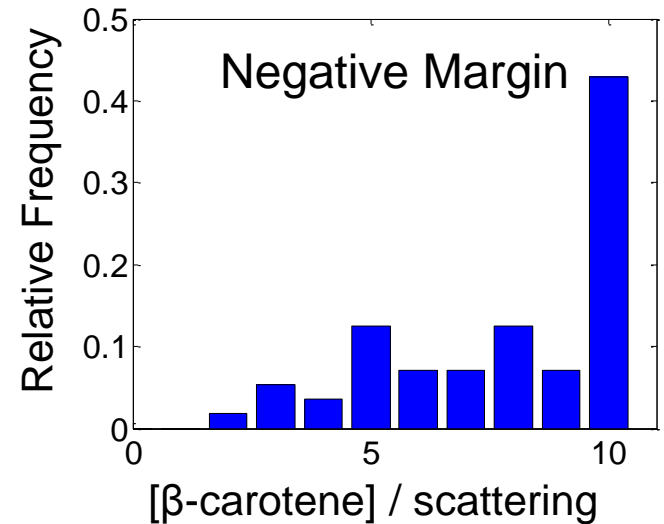
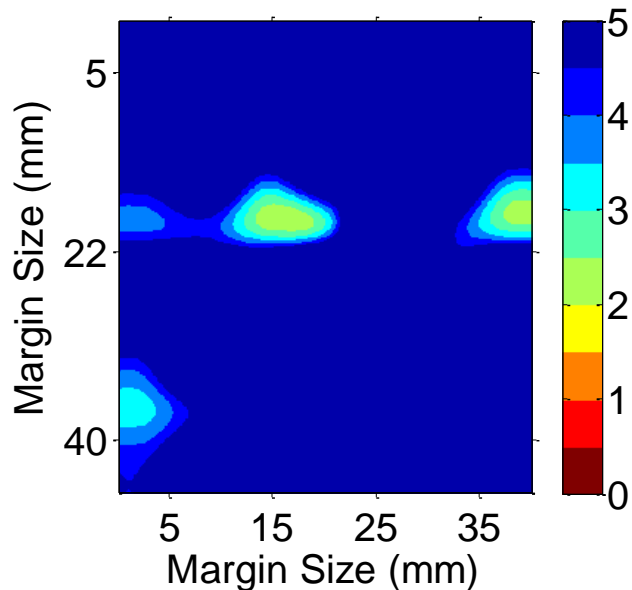
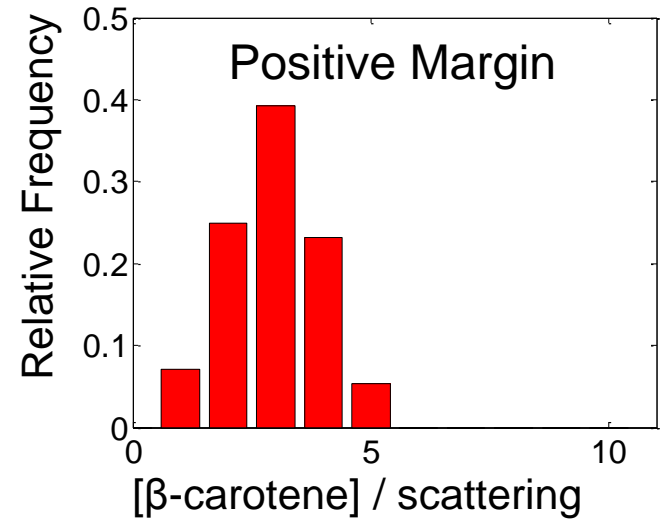
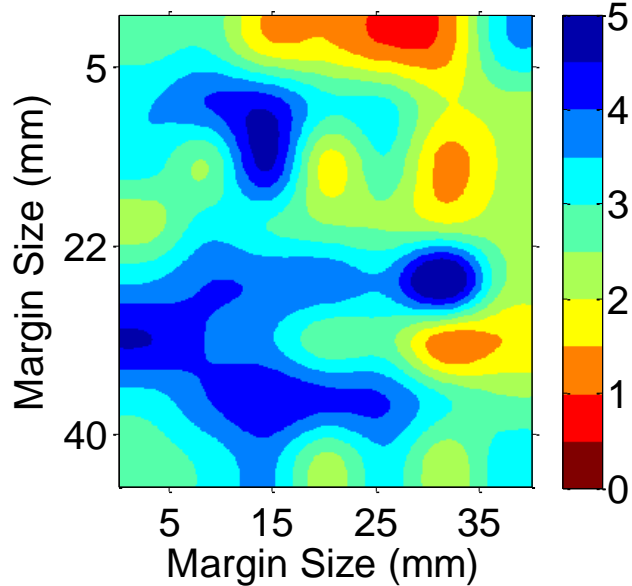
Characteristics of the Study Population	
Age (average)	57 (Range 30-78)
Primary Tumor Histology	
Invasive Ductal	8 (17%)
Ductal Carcinoma in Situ	3 (6%)
Combined Invasive Ductal/DCIS	24 (50%)
Other	10 (21%)
No Tumor Present/Negative	3 (6%) (post chemotherapy)
Surgical Re-excision Rate	12 (25%)

Representative Margin Image



Margin Level Histograms

[β -carotene] / scattering



Results of Prediction Algorithm

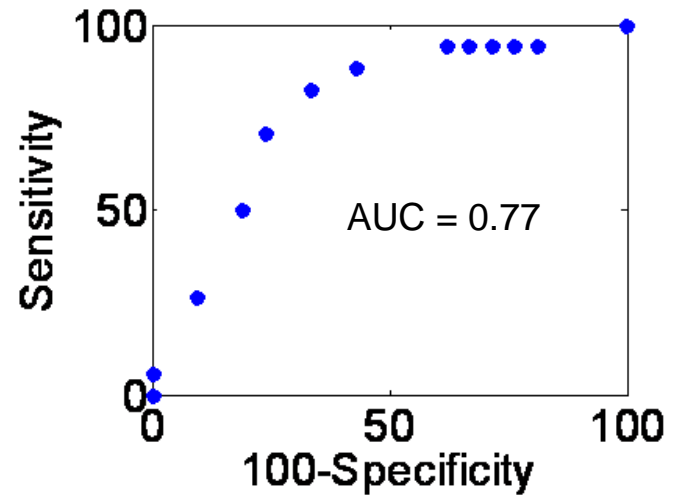
Predictors

% of pixels < 6

[β -carotene] / scattering

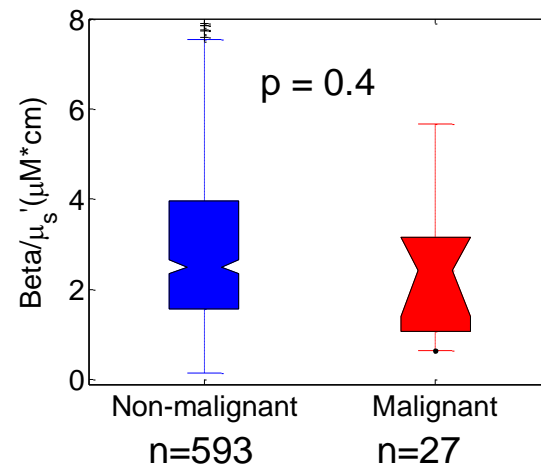
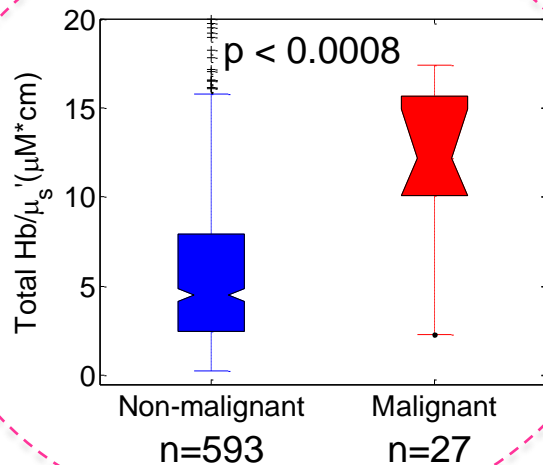
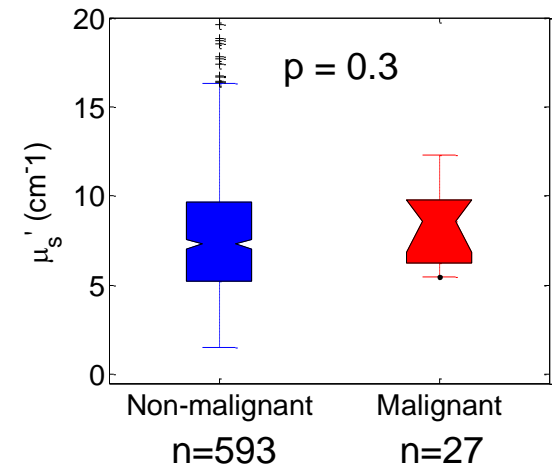
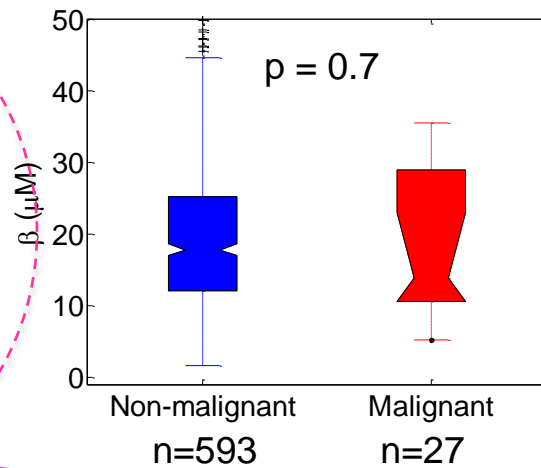
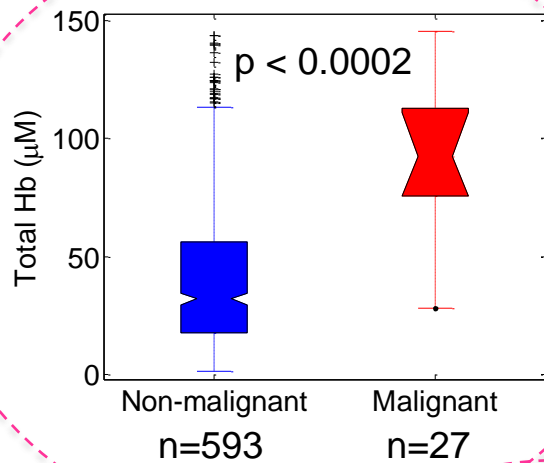
% of pixels < 8

[THb] / scattering



	All Margins		Positive, IDC	Positive, DCIS	Positive, Other	All Positive	All Close
	Path Positive	Path Negative	Path Positive	Path Positive	Path Positive	Path Positive	Path Close
Probe Positive	27	7	11	8	8	14	13
Probe Negative	7	14	3	1	3	3	4
Sensitivity	79.4%		78.6%	88.9%	72.7%	82.4%	76.5%
Specificity	66.7%						

Site Level Sources of Contrast



Summary and Conclusions

Method / Technology	Optical Imaging Probe
Pathologist required in OR?	Pathologist not required
Percentage of Margin Examined	Entire margin
Time Required	< 20 min
Interferes with pathology?	Non-destructive
Problematic with fatty tissues	Able to use on all tissues
Sensing Depth	Up to 2mm
Sensitivity	79.4%
Specificity	66.7%

Our optical imaging device has the potential to significantly impact breast cancer treatment during BCS

Our Team and Sponsors



Lee Wilke
Surgery



Nimmi Ramanujam
Biomedical
Engineering



Joseph Geradts
Pathology



Bill Barry
Bioinformatics
and Statistics



Quincy Brown



Jennifer Gallagher



Lisa Richards

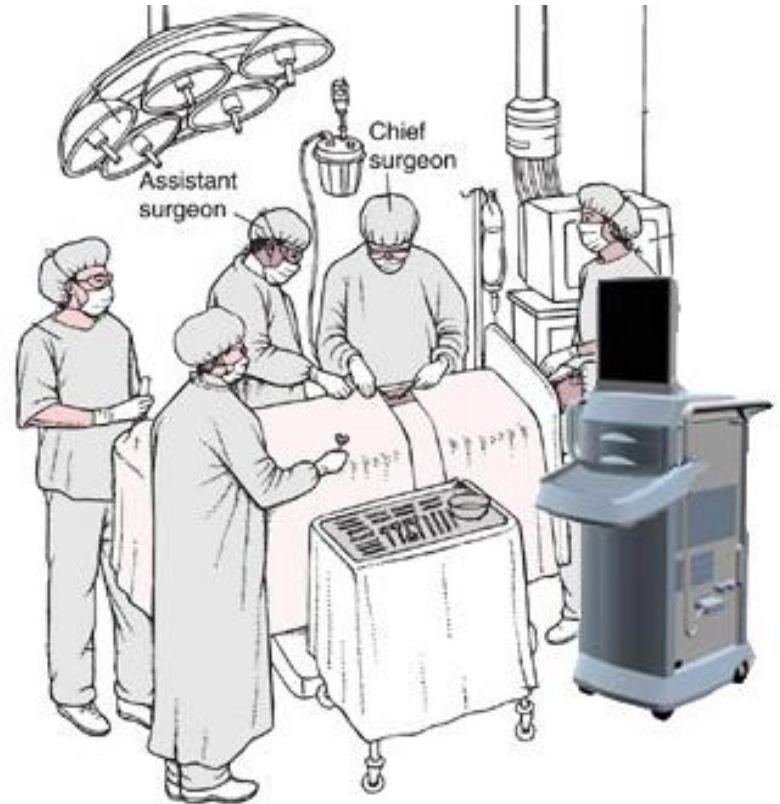
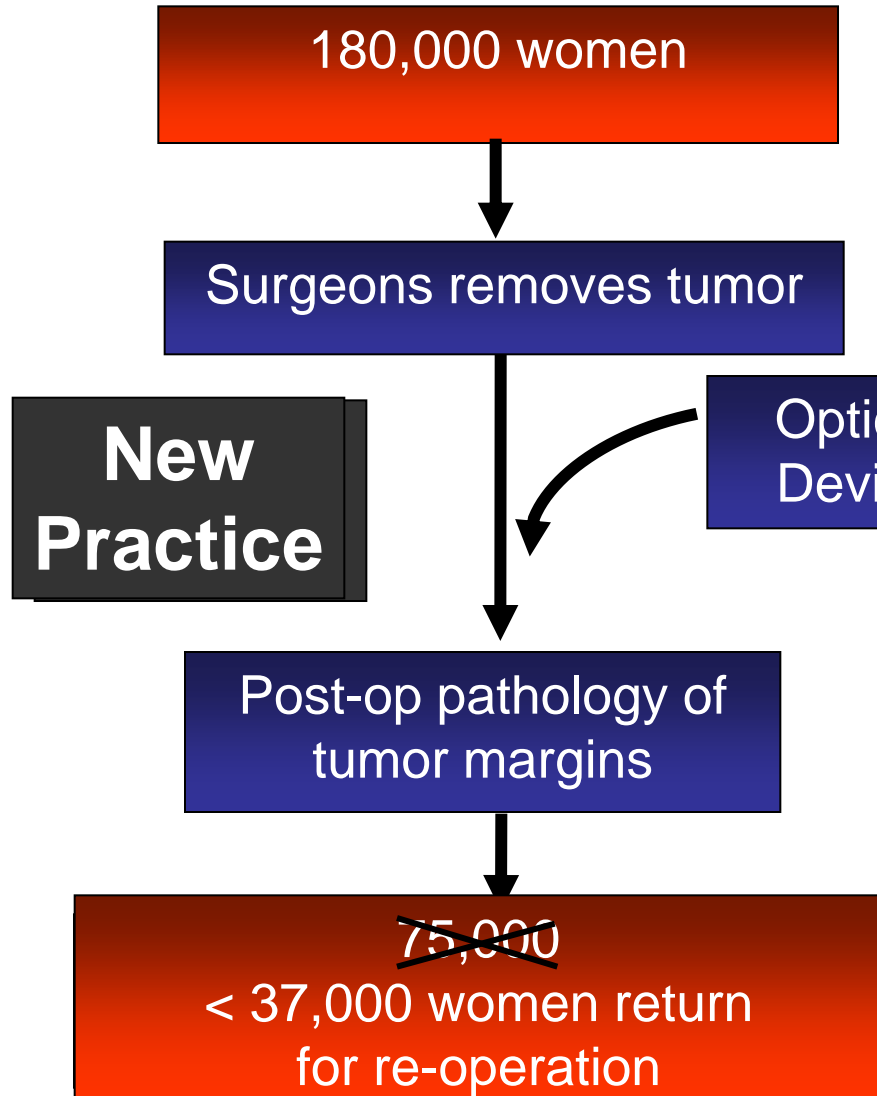


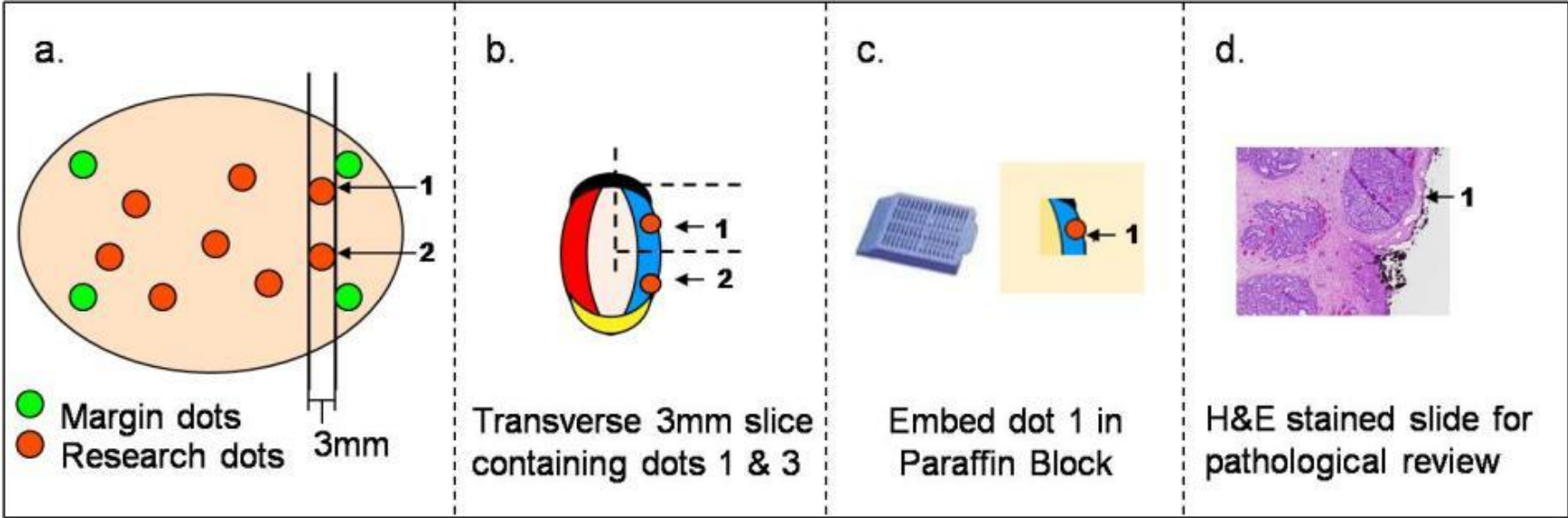
Marlee Junker



Extra Slides

Solution: Light can Detect Positive Breast Tumor Margins in the O.R.





Problem:

Re-excision Rate of BCS

20 - 40% of women return for surgery ²

- Not all cancers are solitary “masses”
- Intra-operative specimen mammograms do not show the “extent” of microscopic disease
- “In-situ” or Stage 0 cancers cannot be felt or seen by the surgeon

Intra-operative Frozen Section/Touch Prep Cytology reduce re-excision rate to 20% ³ but are not widely adopted

- A minority of hospitals have an on-site surgical pathologist with expertise in evaluating fatty breast tissue
- Greater than 20 minutes is required to evaluate all 6 sides of a breast specimen

All patients still undergo post-operative pathology

²Ann Surg Onc 15:1271-1272, 2008; Am J Surg 192:509-512, 2006; Am Surg 73:337-343, 2007; Ann Surg Onc 14:1618-1628, 2007; Am J Surg, 192:538-540, 2006; Am Surg, 71:22-28, 2005

³ Ann Surg Oncol, 15(5): 1271-2, 2008

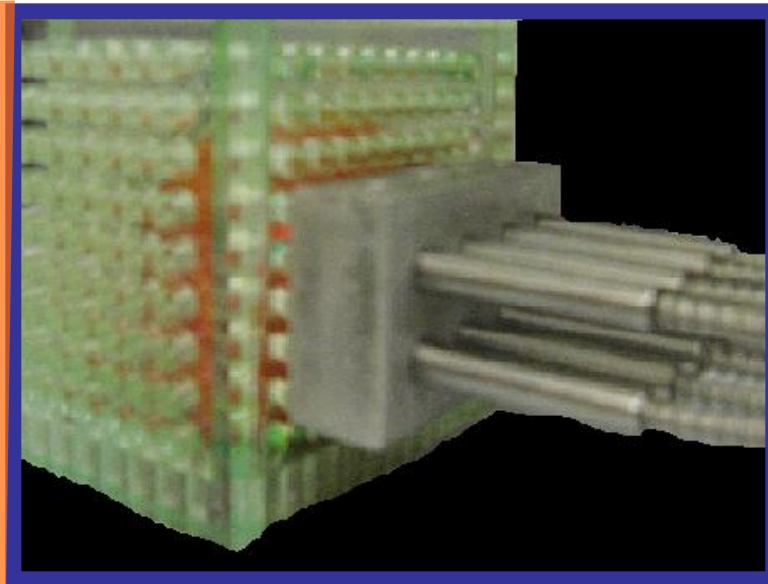
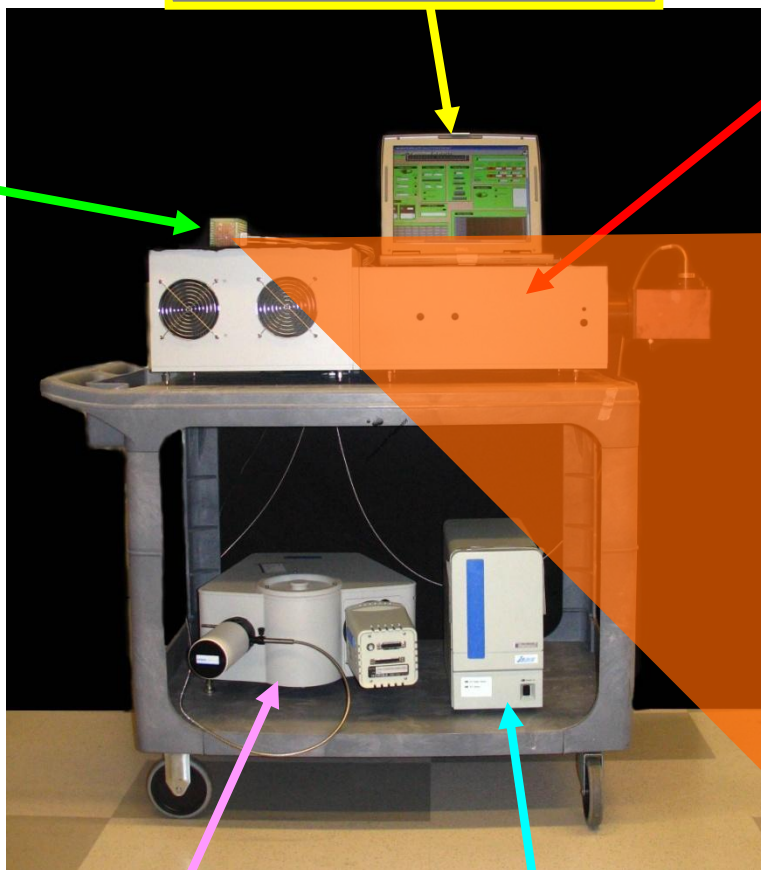
The Clinical Device

Computer+ software

Xenon lamp +
monochromator

Tissue
interface

Probe interfaced with tissue



Spectrograph

CCD

Characteristics of the Study Population

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Tumor Histology	
Invasive Ductal	8 (17%)
Ductal Carcinoma in Situ	3 (6%)
Combined Invasive Ductal/DCIS	24 (50%)
Other	10 (21%)
No Tumor Present/Negative	3 (6%) (post chemotherapy)
Estrogen Positive	38 (79%)
HER-2/neu Positive	6 (13 %)
Node Positive	13 N1 (27%)
Surgical Re-excision Rate	12 (25%)
Neoadjuvant Therapy	Chemotherapy 6 (13%); Endocrine 2 (4%)
Lumpectomy Volume (average)	513 cm ³ (Range 93-2237 cm ³)
Margins Assessed	Anterior 14 (25%); Posterior 15 (27%); Superior 12 (22%); Inferior 3 (5%) Medial 7 (13%); Lateral 4 (7 %)