Quantitative Physiology of the Breast: Impacting Patient Care on Multiple Levels

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Current Strategies in the Breast Clinic

QUANT PHYSIOLOGY TOOLBOX | *IN VIVO* OPTICAL BIOPSY | *EX VIVO* MARGIN ASSESSMENT

Screening

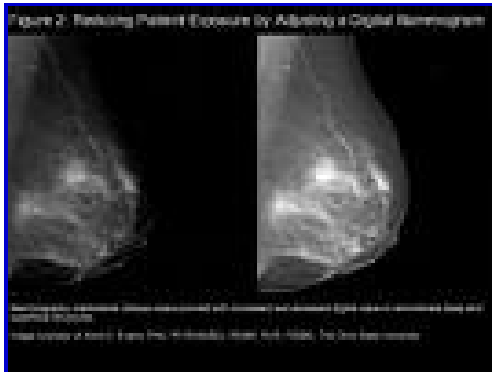
www.madisonradiologists.com

Diagnosis

www.britannica.com

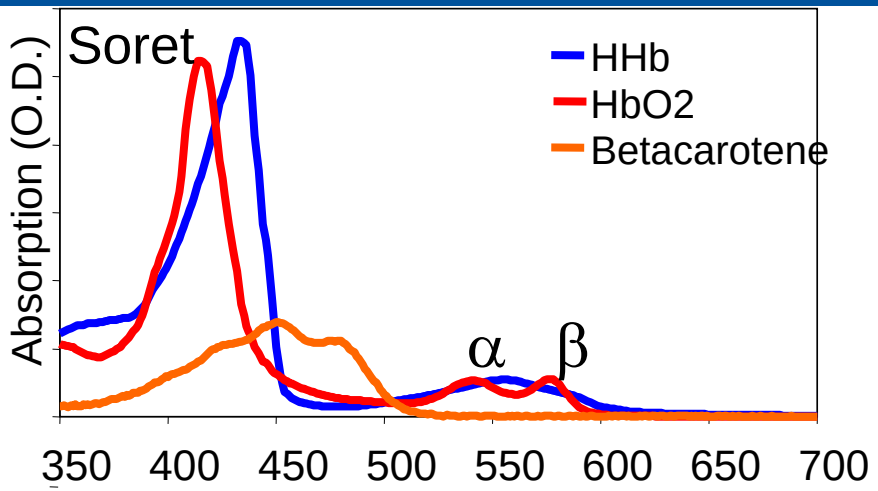
Treatment

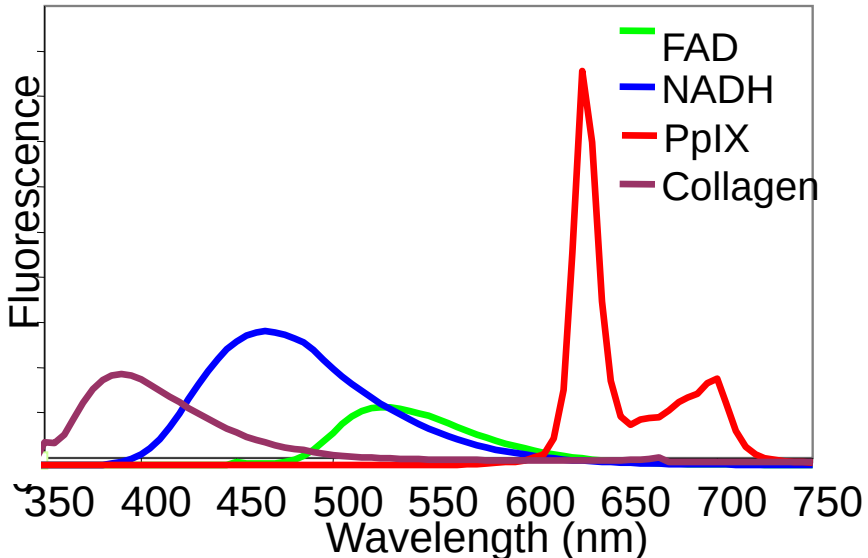
www.cooperhealth.org

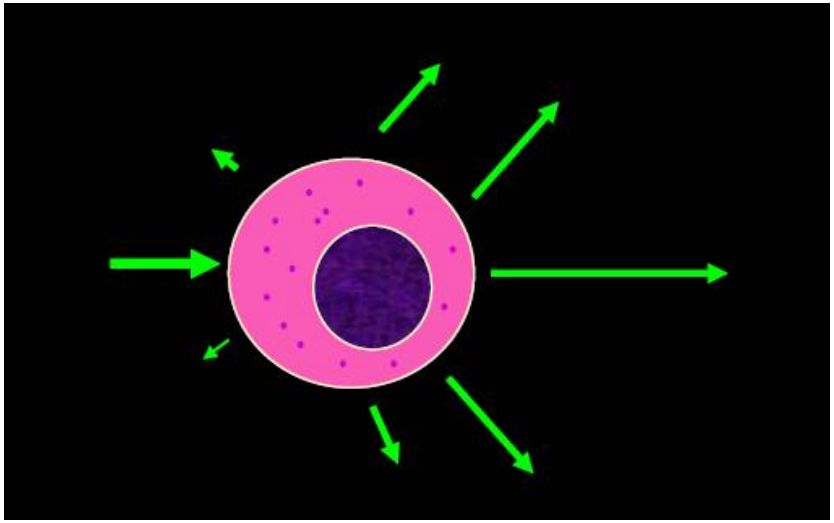


http://images.google.com/

Tissue Absorbers, Scatterers and Fluorophores







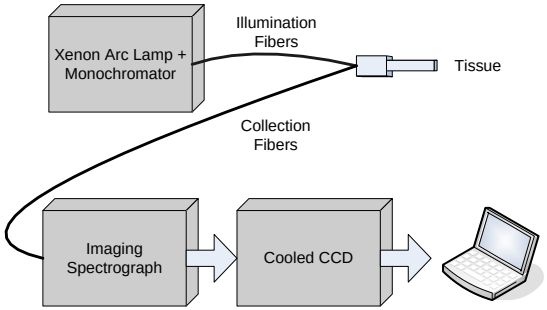
Scatterers

- Cells
- Nuclei
- Chromatin / DNA
- Mitochondria / organelles
- Melanin granules

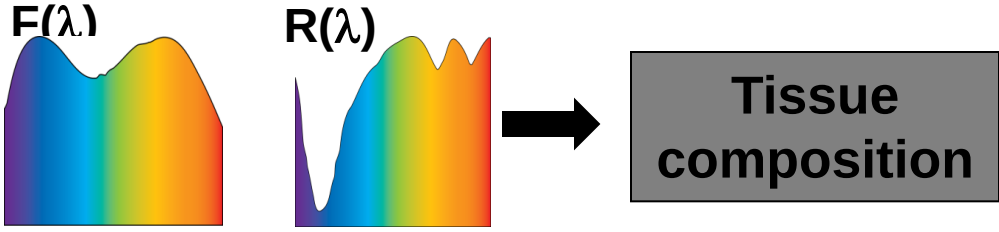
Quantitative Optical Physiology "Toolbox"

QUANT PHYSIOLOGY TOOLBOX | *IN VIVO* OPTICAL BIOPSY | *EX VIVO* MARGIN ASSESSMENT

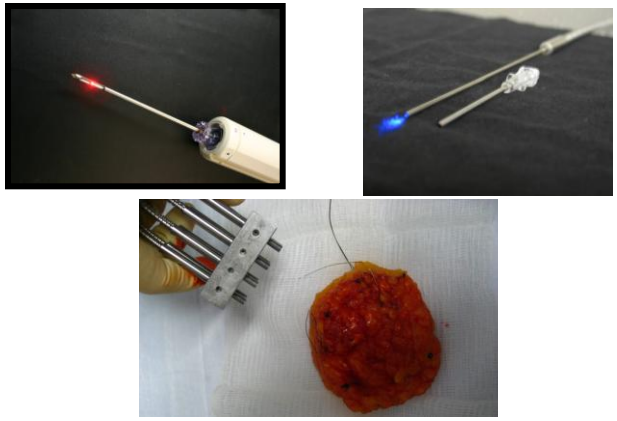
Optical spectrometer



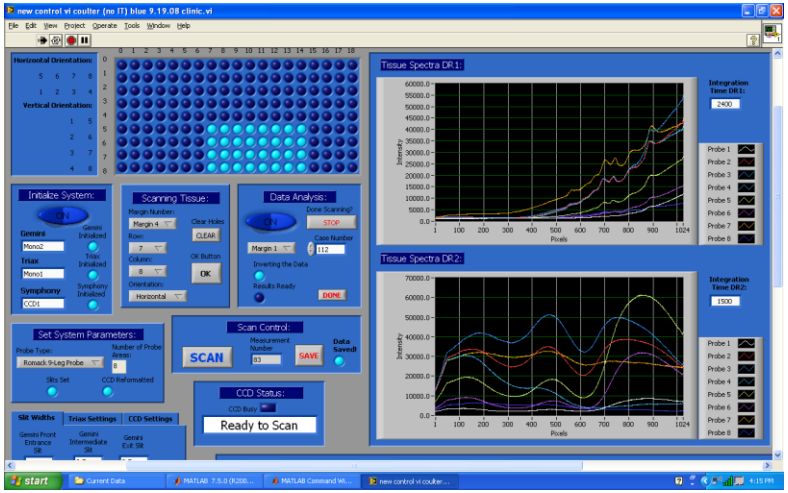
Inverse Monte Carlo Models



Fiber-optic probes

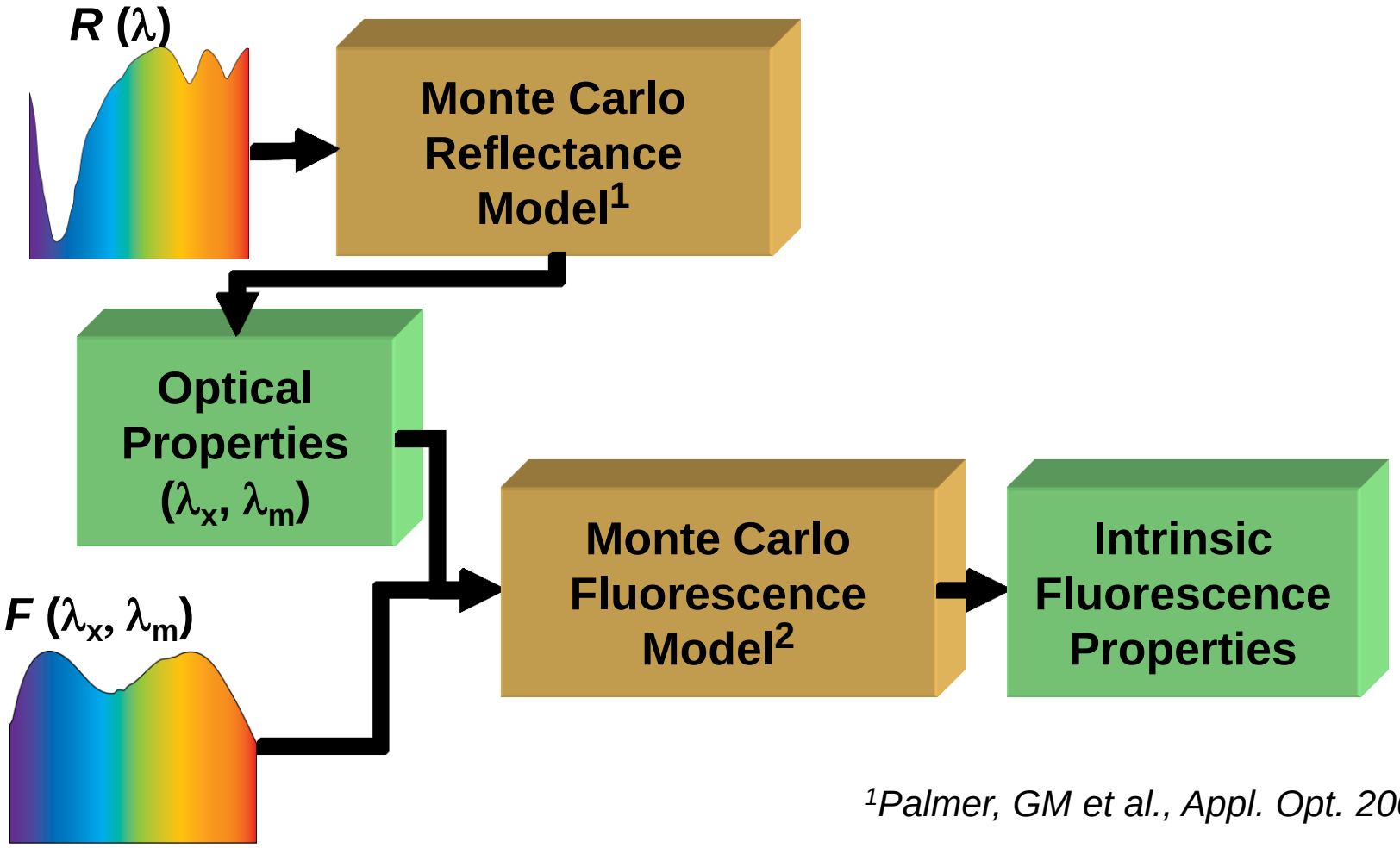


Real-time Control / Analysis Software



Inverse MC: An Enabling Technology for Quantitative Physiology

QUANT PHYSIOLOGY TOOLBOX | *IN VIVO* OPTICAL BIOPSY | *EX VIVO* MARGIN ASSESSMENT

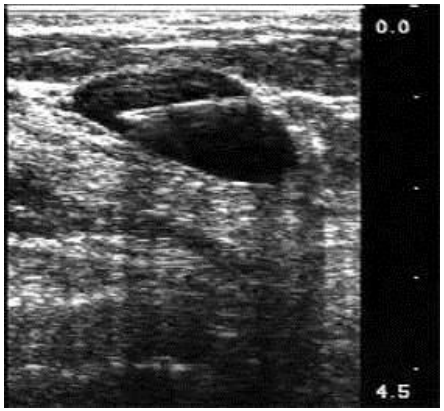


[1]*Palmer, GM et al., Appl. Opt. 2006*

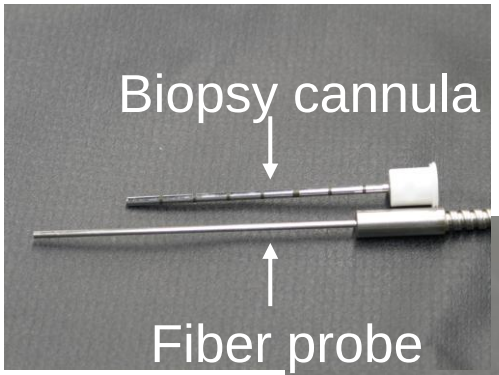
[2]*Palmer, GM et al., JBO, 2008*

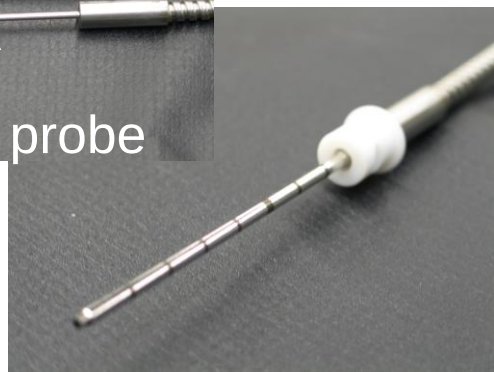
Clinical Studies – 1) *In vivo* Optical Biopsy (40 Patients)

Fiber probe inserted into normal and diseased tissues under ultrasound guidance



Diffuse reflectance and Fluorescence EEM's in UV-Visible

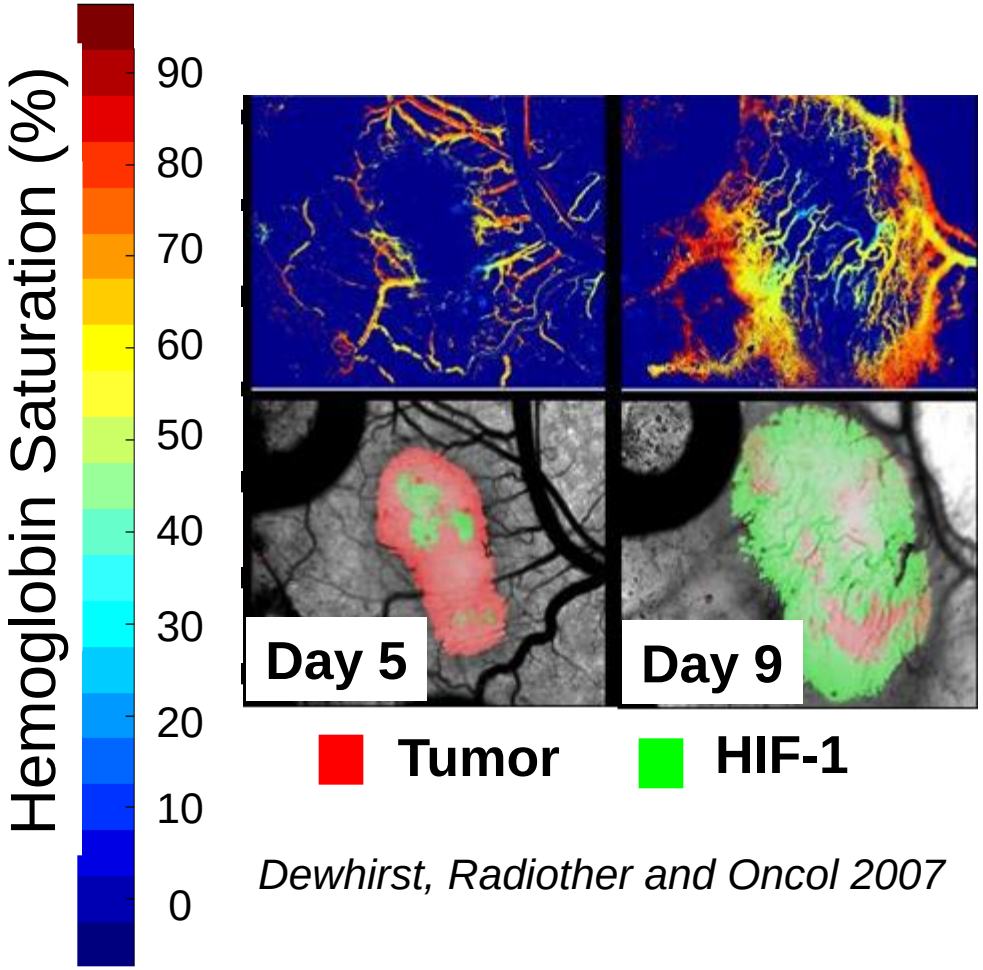




Robust tool for use at time of biopsy

- diagnostics
- prognostics / prescription
- therapeutics

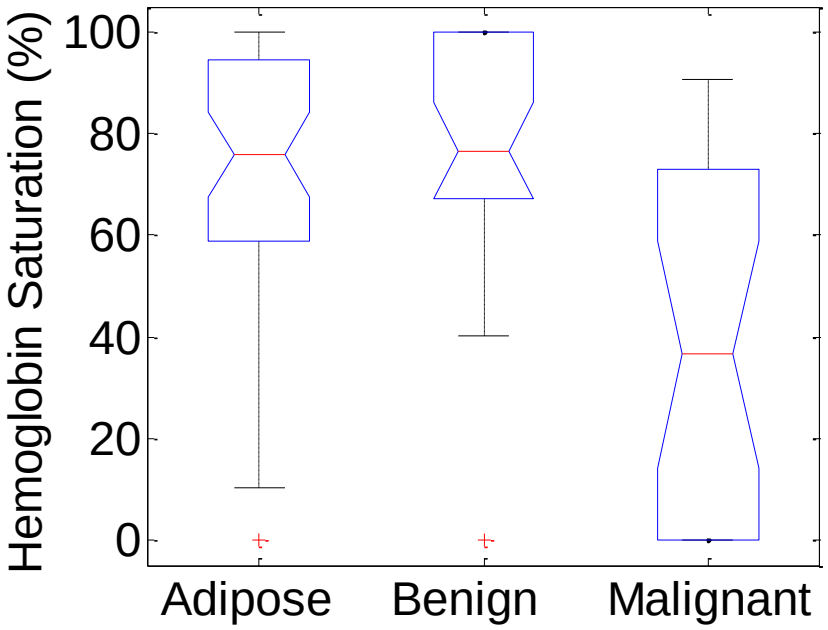
Hypoxia = Aggressive tumors



Dewhirst, Radiother and Oncol 2007

- Under hypoxic conditions, HIF-1 is upregulated
- HIF-1 upregulates >100 genes that promote angiogenesis, anaerobic metabolism, therapy resistance, metastasis
- ***Applications***
  - Drug discovery (pre-clinical)
  - Prognosis
  - Therapy planning
  - Therapy monitoring

Quantitation of Tumor Oxygenation

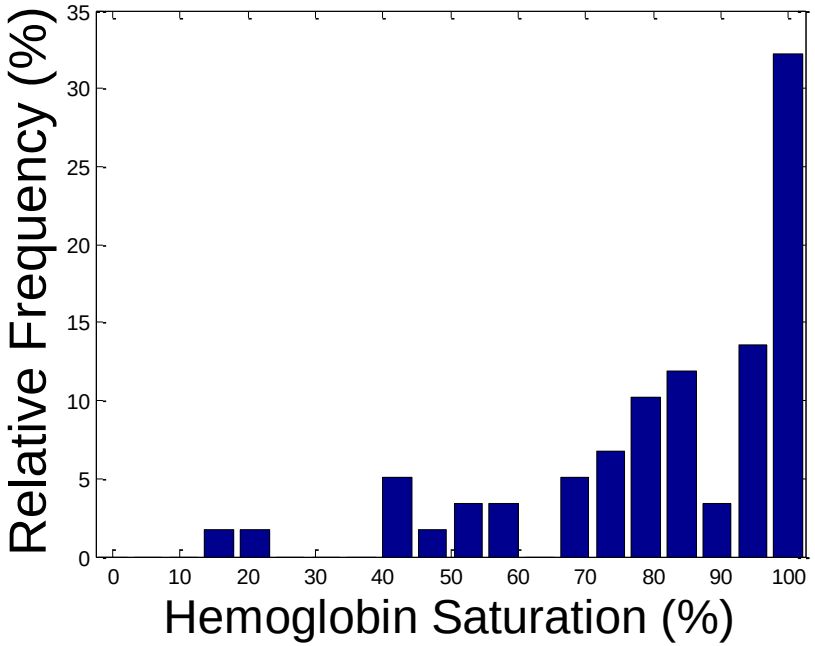


Mean pO_2	***Malignant***		***Non-malignant***	
Reference	***N***	**pO_2**	***N***	**pO_2**
Badib et al. 1969	6	**21**	6	**41**
Runkel et al. 1994	18	**31.5**	18	**58**
Hohenberger et al. 1998	32	**42**	6	**56**
Brown et al. 2008	20	**24**	59	**39**

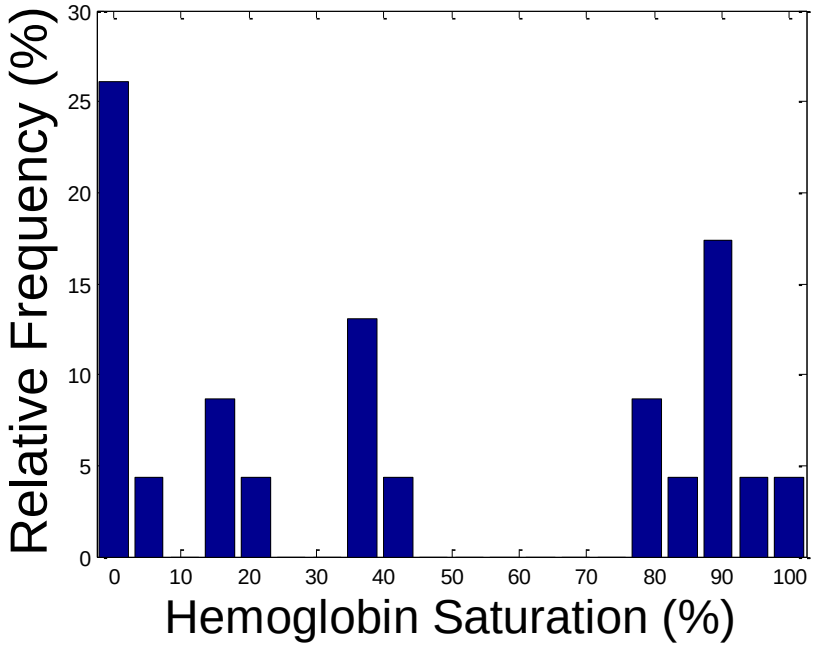
**Hemoglobin saturation converted to pO_2 using a model of hemoglobin dissociation. Assumptions: T = 37°C, pH = 7.4, pCO_2 = 40 mmHg, (P_{50} = 26.6 mmHg)*

Hemoglobin Saturation Histography

Non-malignant

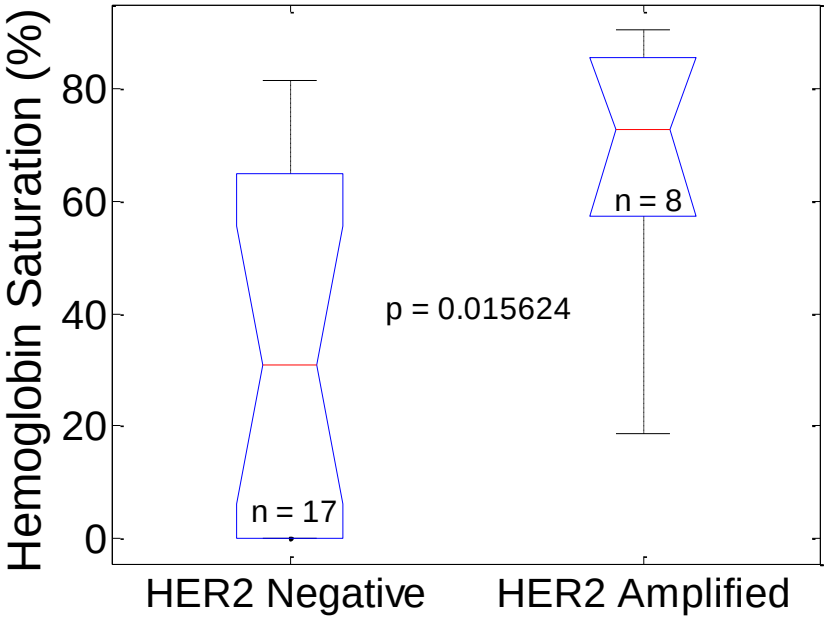


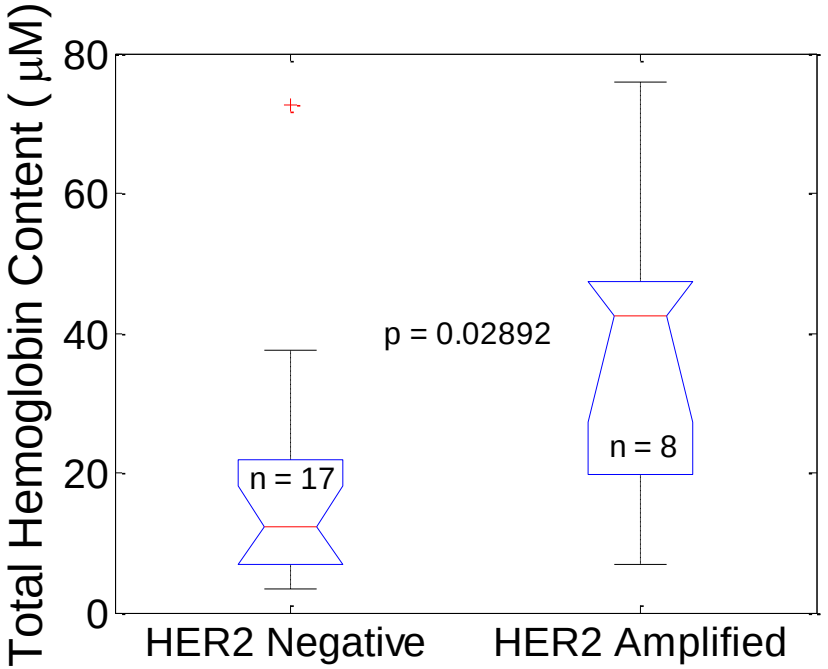
Malignant



Why is there such a diverse range in tumor oxygenation?

Tumor oxygenation and HER2/neu Status

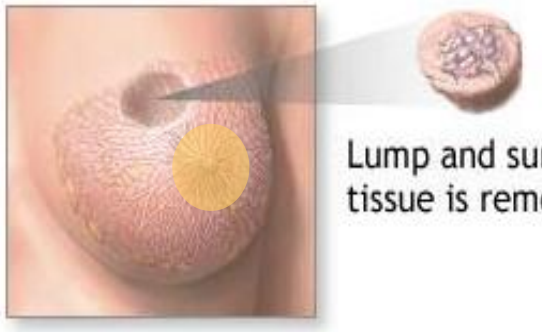


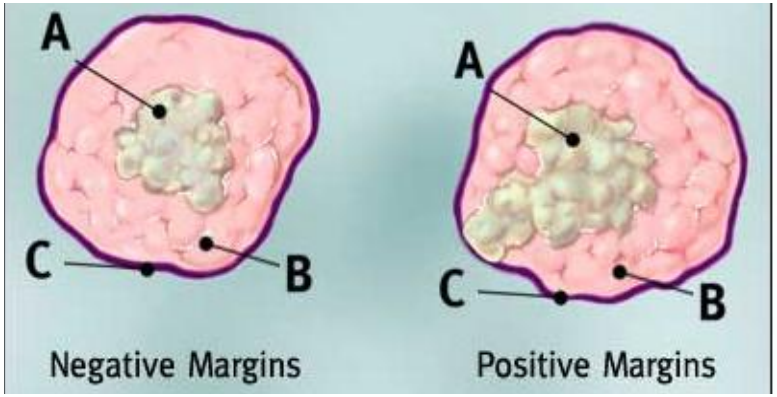


A tumor's oxygenation state at the time of diagnostic biopsy can have important prognostic and therapeutic implications!

Clinical Studies – 2) Breast tumor margin assessment *ex vivo* (80 Patients)

Surgery (lumpectomy)



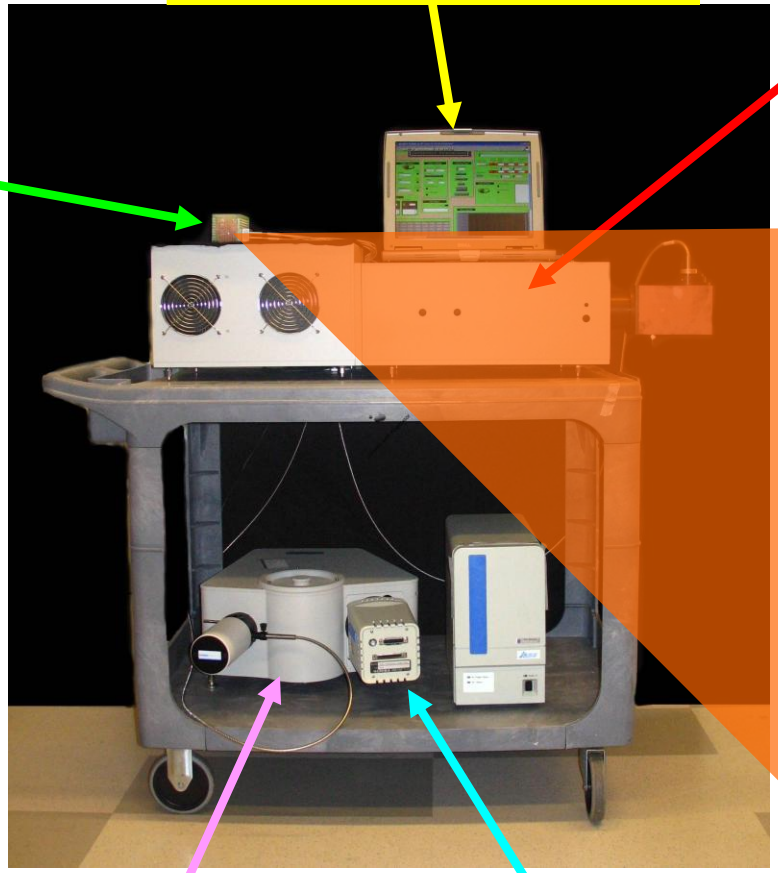


http://www.breastcancer.org/pictures/

- Women with stage 0,I,II undergo breast conservation surgery
- The pathologic margin status is an important predictor of local recurrence after BCS.
- 20-70% of women undergo re-excision surgery because of positive tumor margins*

*Ann 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

The Clinical Device (alpha version)



Informative Parameter Maps From Diffuse Reflectance

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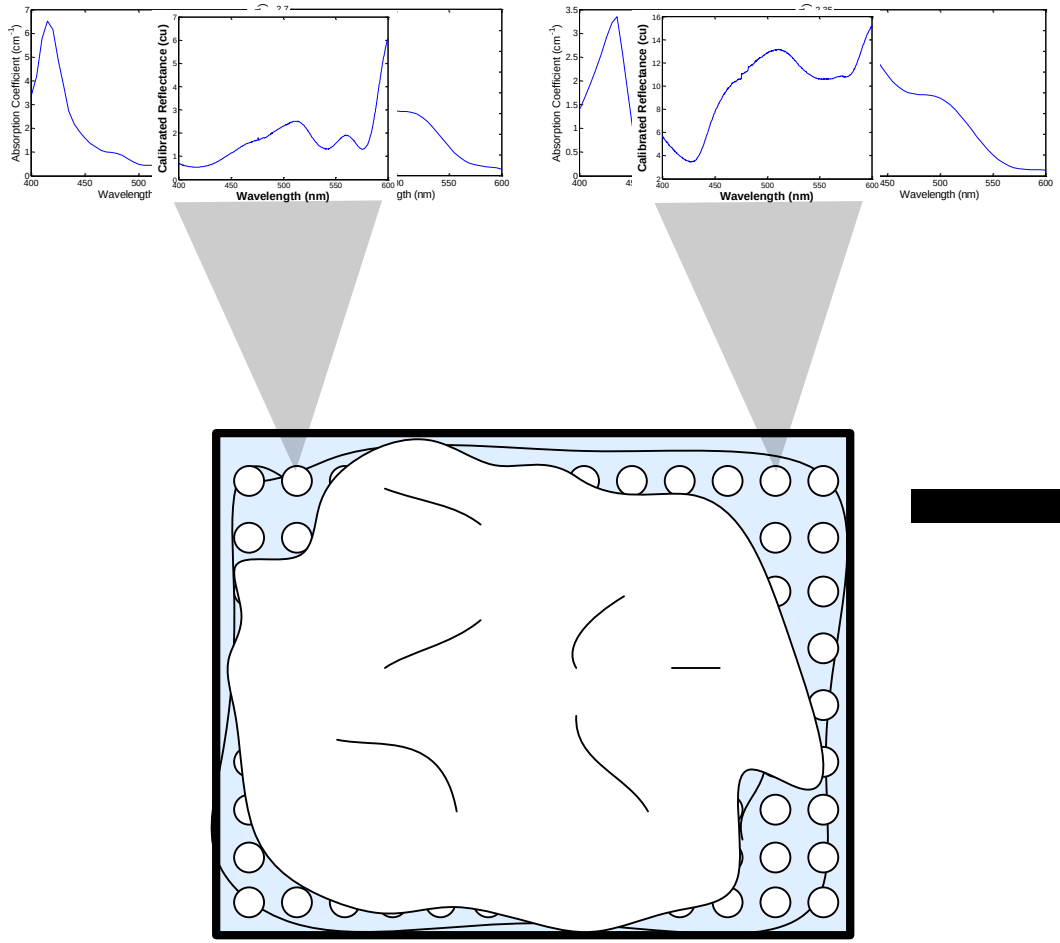
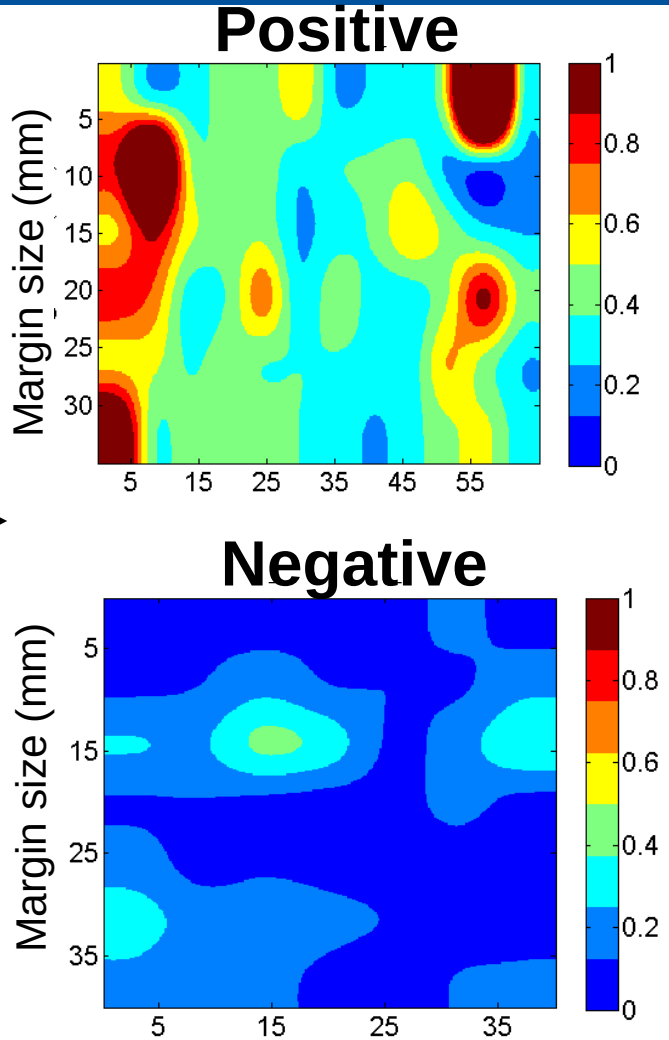
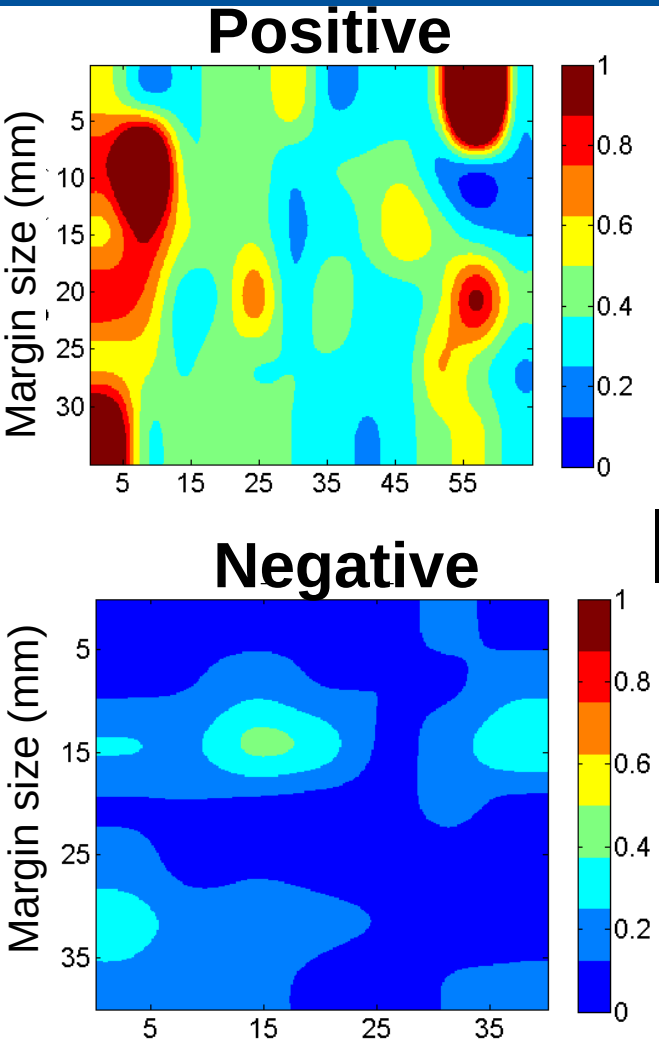
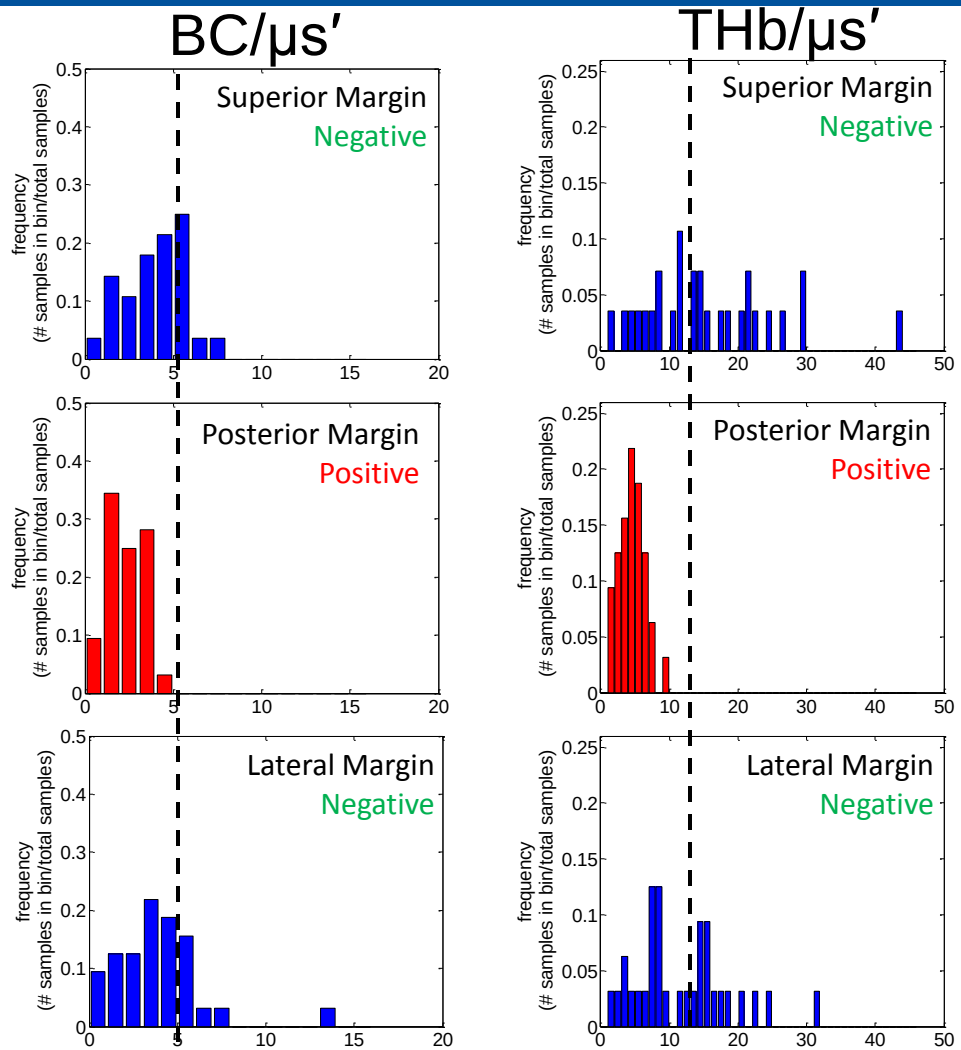




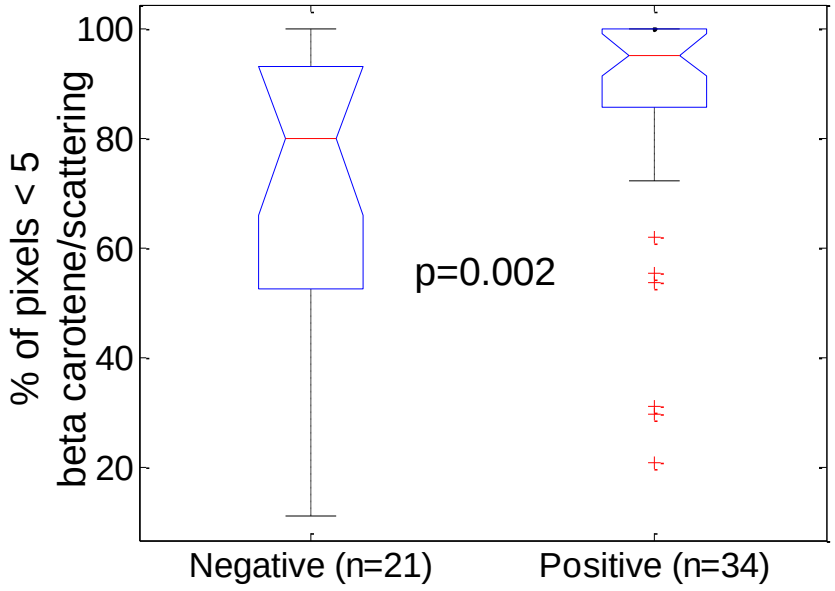
Margin image analysis

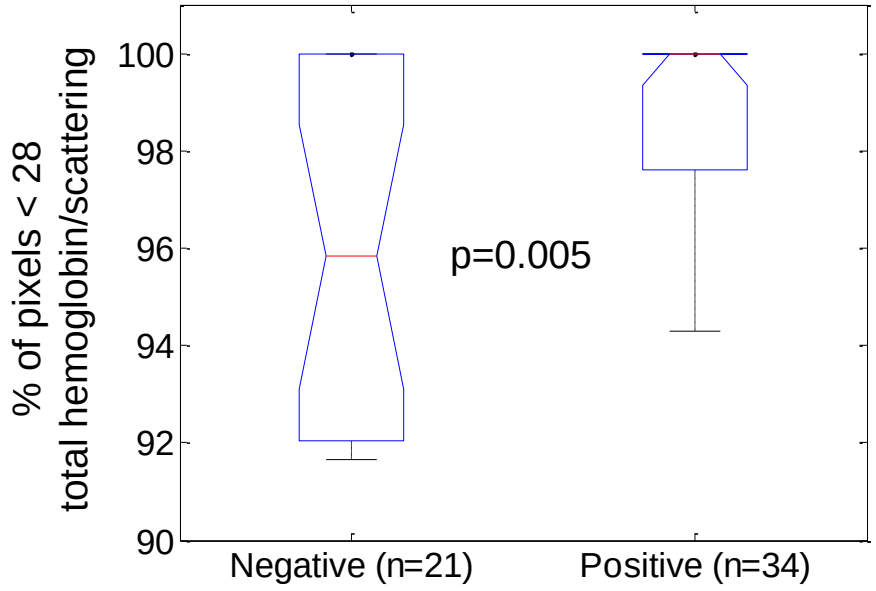
QUANT PHYSIOLOGY TOOLBOX | *IN VIVO* OPTICAL BIOPSY | ***EX VIVO*** MARGIN ASSESSMENT





Diagnostic Parameters

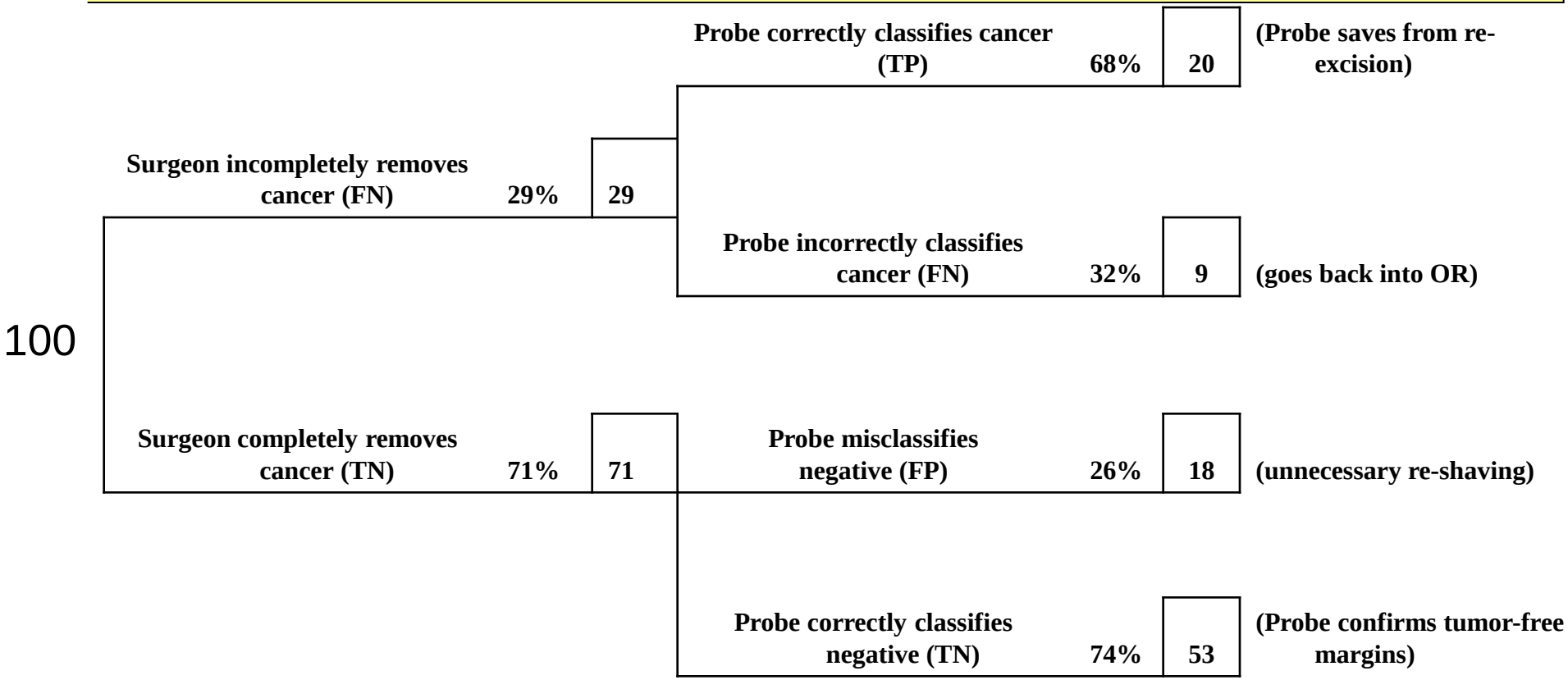




The parameter ratios shown above indicate there are significant differences between normal and cancerous margins

What is the Potential Clinical Impact?

Without probe: 29% re-excision rate, 65% unnecessary tissue removal rate



With probe: 9% re-excision rate, 18% unnecessary tissue removal rate

Summary and Future Directions

- Quantitative optical spectroscopy of the breast may be a useful tool for clinical breast cancer management
  - Results from over 150 patients in 2 parallel clinical studies are promising
  - Applications: Diagnostic biopsy, prognosis and prediction, therapeutic monitoring, surgical margin assessment

- Future directions:
  - *Optical biopsy*: Investigate optical biomarkers which predict response, or are modulated by response to neo-adjuvant chemotherapy (pilot study underway)

  - *Margin assessment*: Complete 150-patient clinical study; Complete development of faster beta device

Acknowledgements

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