Monitoring and Predicting Breast Cancer Neoadjuvant Chemotherapy Response Using Diffuse Optical Spectroscopic Imaging (DOSI)

A phase I/II experimental imaging technology study

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Technical: Albert Cerussi, Amanda Durkin, Brian Hill, Anaïs Leproux, Tom O’Sullivan, Hideki Takeuchi
Coordinates: Erin Sullivan, Montana Compton
Goal: Bedside *Functional* Oncologic Imaging

**Barriers to New Technology**

- Sensitivity to Breast Cancer and Cancer Therapy (~15 yrs)
- Technology Standardization and Validation (~5 yrs)
- Accessibility, Ease of Use (~5 yrs)
ACRIN 6691 NAC Trial

http://acrin.bli.uci.edu/ 2 yrs, 60 patients

ACRIN: David Mankoff, Zheng Zhang, Donna Hartfeill, Sharon Mallett

Dartmouth
Brian Pogue, Keith Paulsen, Shudong Jiang, Peter Kaufman

MGH
David Boas, Stefan Carp, Steven Isakoff

UCSF
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UPenn
Arjun Yodh, Mitch Schnall, Sophie Chung
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**UCSF**

**Boston University**
Darren Roblyer

**M.D. Anderson**
Wei Yang, Fraser Symmans

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**New!**

**Arjun Yodh**
Mitch Schnall, Sophie Chung

**NATIONAL CANCER INSTITUTE**

**LASER MICROBEAM AND MEDICAL PROGRAM**

**BECKMAN LASER INSTITUTE • UC IRVINE**

**NIBIB**
What is DOSI?

Diffuse Optical Spectroscopic Imaging
NIR Light (850 nm)
What is DOSI?

Technology for Quantifying Optical Path Length

Molecular Absorption Loss

\[ A = \varepsilon b C; \ b = 1\text{cm} \]

*Fixed pathlength*

Absorption + Scattering Loss

\[ A = \varepsilon b C; \ b = ?? \]

*Unknown pathlength*
What is DOSI?

Making The Body a “Cuvette”
DOSI Functional Contrast

**TUMOR**

- **Elevated blood**
  - Increased tumor perfusion, and metabolism detected by elevated Total Hb, Oxy Hb, and Deoxy Hb

- **Elevated water**
  - Tumor edema and tumor cell proliferation lead to increased water content

- **Decreased lipid**
  - Tumors displace bulk lipid when growing leading to decreased lipid content
Tumors Create Optical Contrast

Breast Cancer

- 33 year old female with 2.8cm DCIS mass / 1.2cm invasion in right breast

\[ TOI = \frac{ctHHb \times Water}{Lipid} \]

Tumor Optical Index
Vision

Tissue Optical Index (TOI) = (HbR x H2O)/lipid

Vision

Tissue Optical Index (TOI) = (HbR x H2O)/lipid


Predict Response: optimize outcome
Goals

1st Standardized ACRIN Trial Using Optical Imaging
(New expertise to ACRIN; leverage MRI, PET experience)

1) Standardize DOSI measurements, analysis.
   http://acrin.bli.uci.edu/trainingvideos
   • Determine inter-site agreement
     – Phantoms, protocols, test subjects
     – Long-term recording stability

2) Conduct Multi-Center Clinical Study
Correlate DOSI TOI measurements with pathological complete response (pCR)

Baseline ➔ Mid-therapy

Underlying hypothesis: functional optical biomarkers of tumor metabolism can predict chemotherapy response by mid-therapy

30/60 patients to date
Functional changes are observed in a pCR during NAC.

Baseline

Early-therapy

Mid-therapy

Post-therapy

Human subject 6691-08

TOI Tumor contrast

2.1

1.5

0.2

0.1
Investigative Aims

- Frequent Monitoring
- Early Timepoints
- Pre-Therapy Prediction
Frequent Imaging

Cerussi et al., Acad Radiol. (2010)

A/C

DAY:

-8
HHb(LEFT)

3
HHb(LEFT)

4
HHb(LEFT)

5
HHb(LEFT)

7
HHb(LEFT)

20 30 40
x (mm)

70 60 50 40 30 20 10 0
y (mm)

12

11

10

9

8

7

6

5

4

3

2

LASER MICROBEAM AND MEDICAL PROGRAM
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ACRIN
American College of Radiology Imaging Network

NIBIB
Frequent Imaging

20 Measurements

TOI = \[(\text{water} \times \text{deoxy})/\text{lipid}\]

- Vascular normalization?
- Inflammation?
- Switch Therapy?
- Perform Surgery?

When is best time for clinical decision?

Day 1 Flare Response

NR

PR

pCR

N = 24 tumors
5 NR, 11 PR, 8 pCR

HbO₂ Flare

D. Roblyer et al. PNAS, 2011

6cm x 6cm maps
Predicting Response Prior to Chemotherapy

Breast Tumor Oxygenation (%stO$_2$)

<table>
<thead>
<tr>
<th></th>
<th>pCR (n = 12)</th>
<th>non-pCR (n = 30)</th>
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<tbody>
<tr>
<td></td>
<td>75 ± 2.4</td>
<td>73.3 ± 6.4</td>
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- **p** < 0.01

<table>
<thead>
<tr>
<th>Variable</th>
<th>Receiver operative characteristics (ROC)</th>
<th>Binary classification</th>
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<tbody>
<tr>
<td></td>
<td>AUC  SE</td>
<td>Optimal cut-off  Sensitivity (%)  Specificity (%)</td>
</tr>
<tr>
<td>stO$_2$</td>
<td>0.76  0.06</td>
<td>76.7%  75.0  67.7</td>
</tr>
<tr>
<td>stO$_2$ + ER</td>
<td>0.91  0.09</td>
<td>-  100  85.7</td>
</tr>
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Technological Advances

Desktop miniature DOSI: Handheld Scanning

- Board-based, 400 MHz BW, 4 lasers, 2 APD Detectors
DOSI Clinical Role

Oncology

- Portable, individualized therapy
- Understanding therapeutic mechanisms
- New drugs, dosing, side effects

Detection and Diagnosis

- Frequent screening in younger, high-risk subjects
- Find, diagnose tumors in dense breast
- Inform use of DCE-MRI

Reduce Barriers to Access
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NCI  *Chao Family Comprehensive Cancer Center*

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American College of Radiology Imaging Networks (ACRIN)

DOD Breast Cancer Research Program

CA Breast Cancer Research Program

UCOP POC Program

http://www.bli.uci.edu