Biophysical Assessments for Lymphedema Detection in Patients with Breast Cancer before and One Year after Breast Cancer Surgery

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Goal: Earlier Detection and Intervention Women Diagnosed with Breast Cancer

A Rationale and Sensible Approach

Pre-Surgical Baseline

Periodic Follow-ups

Change Detection

Measures and Criteria
• Limb Volumes and Metrics
• Limb Bioimpedance
• Local Tissue Water

Therapy Initiation

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Goal: Earlier Detection and Intervention

Not Often Done

Pre-Surgical Baseline

Can We Characterize?

Periodic Follow-ups

Change Detection?

N=76

Measures and Criteria
- Limb Volumes and Metrics
- Limb Bioimpedance
- Local Tissue Water

Therapy Initiation

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Unilateral Breast Cancer Patients

Age range: 28 – 82 (59.6 ± 13.3 years)
BMI range: 17.8 – 48.1 (28.3 ± 6.4 Kg/m²)
Cancer: Dominant Arm Side 36/76 (47.4%)

Data as of 8/25/2011
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Measurement Methods
### Girth and Limb Volume Measurements

#### Girth at 4 cm intervals

#### Arm Volumes

<table>
<thead>
<tr>
<th>Segment Length (cm)</th>
<th>Total # Segments</th>
<th>Right Proximal</th>
<th>Right Distal</th>
<th>Left Proximal</th>
<th>Left Distal</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>12</td>
<td>1390</td>
<td>722</td>
<td>1390</td>
<td>731</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Limb Volumes</th>
<th>Right</th>
<th>Left</th>
<th>Edema</th>
<th>%Edema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Volume (ml)</td>
<td>2112</td>
<td>2122</td>
<td>-0.10</td>
<td>-0.5</td>
</tr>
<tr>
<td>Limb only (ml)</td>
<td>2112</td>
<td>2122</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand only (ml)</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Visit 3**

<table>
<thead>
<tr>
<th>Affected Limb</th>
<th>Limb Length</th>
<th>Segment Length (cm)</th>
<th>Total # Segments</th>
<th>Right Proximal</th>
<th>Right Distal</th>
<th>Left Proximal</th>
<th>Left Distal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right Limb</td>
<td>12</td>
<td>4</td>
<td>12</td>
<td>1390</td>
<td>722</td>
<td>1390</td>
<td>731</td>
</tr>
</tbody>
</table>

From data there are 12 full segments plus one partial segment of length 4 cm. Note that the first circumference pair to be entered is for "0" cm corresponds to either the wrist or ankle.

<table>
<thead>
<tr>
<th>Circumferences (cm)</th>
<th>Segment</th>
<th>Right</th>
<th>Left</th>
<th>Number</th>
<th>Volume (ml)</th>
<th>Right</th>
<th>Left</th>
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<tbody>
<tr>
<td>0</td>
<td>15.2</td>
<td>15.5</td>
<td>1</td>
<td>60</td>
<td>74</td>
<td>77</td>
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<tr>
<td>4</td>
<td>15.3</td>
<td>15.4</td>
<td>1</td>
<td>61</td>
<td>81</td>
<td>82</td>
<td></td>
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<tr>
<td>8</td>
<td>16.5</td>
<td>16.6</td>
<td>2</td>
<td>82</td>
<td>103</td>
<td>104</td>
<td></td>
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<tr>
<td>12</td>
<td>19.4</td>
<td>19.5</td>
<td>3</td>
<td>103</td>
<td>139</td>
<td>139</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>21.7</td>
<td>21.9</td>
<td>4</td>
<td>135</td>
<td>158</td>
<td>161</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>22.9</td>
<td>23</td>
<td>5</td>
<td>158</td>
<td>171</td>
<td>172</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>23.5</td>
<td>23.5</td>
<td>6</td>
<td>171</td>
<td>183</td>
<td>183</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>24.7</td>
<td>24.5</td>
<td>7</td>
<td>183</td>
<td>214</td>
<td>213</td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>25.5</td>
<td>25.5</td>
<td>8</td>
<td>214</td>
<td>241</td>
<td>240</td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>26.4</td>
<td>26.2</td>
<td>9</td>
<td>241</td>
<td>271</td>
<td>271</td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>28.4</td>
<td>28.1</td>
<td>10</td>
<td>271</td>
<td>293</td>
<td>293</td>
<td></td>
</tr>
<tr>
<td>44</td>
<td>29.2</td>
<td>30</td>
<td>11</td>
<td>293</td>
<td>324</td>
<td>324</td>
<td></td>
</tr>
<tr>
<td>48</td>
<td>31.8</td>
<td>31.5</td>
<td>12</td>
<td>324</td>
<td>357</td>
<td>357</td>
<td></td>
</tr>
</tbody>
</table>

**www.limbvolumes.org**

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MoistureMeter-D

- Low power 300 MHz incident wave
- Reflected wave depends on the tissue’s dielectric constant
- Dielectric constant depends on total tissue water (free + bound)
- Pure water has a dielectric constant of about 78
- Can measure at almost any anatomic site

Penetration Depth (0.5 – 5 mm)

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TDC: Tissue Sampling Principle

Ultrasound images (20 MHz) modified from Mellor et al. 2004 (The Breast Journal, 2004;10:496-503)
TDC: Tissue Sampling Principle

Ultrasound images (20 MHz) modified from Mellor et al. 2004 (The Breast Journal, 2004;10:496-503)

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TDC Measurement Sites

Each site measured to an effective depth of 2.5 mm
Forearm site measured to effective depths of 0.5, 1.5, 2.5 and 5.0 mm
Pre-Surgery Measurement Results
Pre-Surgery by Site – TDC values

No significant differences between sides

- TDC (2.5 mm)

N = 76
8/26/11

Data as of 06/05/2011

- Cancer Side
  - 21.8 ± 3.3
    - Biceps
  - 34.8 ± 7.0
    - Axilla
  - 24.8 ± 3.5
    - Forearm

- Healthy Side
  - 26.7 ± 5.1
    - Thorax
  - 34.7 ± 8.0
    - Axilla
  - 21.8 ± 3.7
    - Biceps
  - 24.8 ± 3.7
    - Forearm

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Pre-Surgery by Site – All Parameters

No significant differences between sides

- TDC (2.5 mm)
- BIOZ
- VOLUME

N = 76
8/26/11

Arm Volumes (ml)

<table>
<thead>
<tr>
<th>Site</th>
<th>Cancer Side</th>
<th>Healthy Side</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forearm</td>
<td>2273 ± 657</td>
<td>2292 ± 652</td>
</tr>
<tr>
<td>Biceps</td>
<td>26.4 ± 4.6</td>
<td>26.7 ± 5.1</td>
</tr>
<tr>
<td>Thorax</td>
<td>34.8 ± 7.0</td>
<td>34.7 ± 8.0</td>
</tr>
</tbody>
</table>

Z = 293 ± 43
Z = 292 ± 43

No significant differences between sides

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Significant differences among all depths

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Forearm TDC by Depth: Pre-Surgery

Significant differences among all depths

BUT: No difference between sides at any depth

Effective Measurement Depth (mm)

N=76

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Sequential: Pre-Surgery → One Year Post

At-Risk/Control Ratio

N=35

Error bars excluded for clarity

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Changes in Risk/Control → 1.0 yr

Thorax TDC is the only significant increase compared to pre-surgery

Ratio (Risk/Control)

N=35

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Possible Thresholds via Risk/Control Ratio

What change over time might constitute evidence for ‘pre-clinical’ lymphedema?

Pre-Surgery Ratio (Risk/Control)

- 3.0 SD: 99.87%
- 2.5 SD: 99.38%
- 2.0 SD: 97.71%
- 1.0 SD: 99.87%

N=76
- Forearm -TDC
- Biceps-TDC
- Thorax-TDC
- Axilla-TDC
- Volume
- Bioz

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# TDC Thresholds (Risk/Control)

## 2.5 mm Effective Measurement Depth (N=76)

<table>
<thead>
<tr>
<th>Threshold Level</th>
<th>Forearm</th>
<th>Thorax</th>
<th>Biceps</th>
<th>Axilla</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2 SD (97.7%)</strong></td>
<td>1.20</td>
<td>1.21</td>
<td>1.29</td>
<td>1.43</td>
</tr>
<tr>
<td><strong>2.5 SD (99.38%)</strong></td>
<td>1.24</td>
<td>1.26</td>
<td>1.36</td>
<td>1.53</td>
</tr>
<tr>
<td><strong>3.0 SD (99.87%)</strong></td>
<td>1.29</td>
<td>1.32</td>
<td>1.43</td>
<td>1.63</td>
</tr>
</tbody>
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## Threshold Comparison (Risk/Control)

<table>
<thead>
<tr>
<th>Threshold Level</th>
<th>Forearm TDC</th>
<th>Thorax TDC</th>
<th>Volume</th>
<th>Bioz</th>
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<td>2 SD (97.7%)</td>
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<td>1.32</td>
<td>1.14</td>
<td>1.16</td>
</tr>
</tbody>
</table>

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Exceeding Threshold 1-Year Post-surgery

% of patients

- **Volume**: 8/35 (22.9%)
- **Forearm**: 4/35 (11.4%)
- **Biceps**: 2/35 (5.7%)

N = 35

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Main Points Summary

• In 76 newly diagnosed breast cancer patients, biophysical measures showed no difference between cancer and control sides prior to surgery.

• In 35 pts followed for one year a significant increase was found only in TDC of at-risk thorax suggesting early increased thorax tissue water.

• Exploratory lymphedema thresholds based on pre-surgery variances indicate thorax thresholds are exceeded in 5.7% -22.9% of patients by 1 year depending on the threshold criteria employed.
Main Point Conclusions

• Pre-surgery side-to-side similarities suggest that if pre-surgery data are unavailable, differentials measured later can still be diagnostically useful.

• Tracking of thorax tissue water changes via TDC measurements emerges as a potentially new and useful parameter to detect incipient lymphedema.

• The validity of the exploratory lymphedema thresholds is not yet established but depends on method, TDC site and its measurement depth.
This presentation is available at www.lymphedema-research.org in Flash and PDF formats.

My sincere thanks to Dr. Tapani Lahtinen for his heroic efforts on my behalf!