Initial Pathology Assessment to Preoperative Therapy

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Initial Pathology Assessment Prior to Preoperative Therapy

**Needle Core Biopsy**

- Diagnosis of invasive carcinoma prior to neoadjuvant therapy is best made by Needle Core Biopsy and not Fine Needle Aspiration
  - Positive predictive value
    - 98 - 99.8 %
  - Biomarker assessment
  - Tissue procurement for research
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Needle Core Biopsy

- Concordance with Final Pathology
  - Invasive Carcinoma type - 67 - 81 %
  - Size
    - Under/Overestimate 72 – 79%
  - Grade - 59 - 75 %
    - Poorly differentiated carcinoma 84%
  - Lymphovascular Involvement 8%
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**Needle Core Biopsy**

- **Adequacy of Samples**
  - Diagnosis
  - Biomarker Analysis
  - Novel Assays
  - Research
- **Multiple Cores (4-6)**
  - More volume with wider bore needles
ACCURACY OF DIAGNOSIS

How can the accuracy of breast pathology diagnostics be improved?

• Quality Control Program
• Second Opinion
• Integration of pathologists in patient care teams

**BIOMARKER ANALYSIS**

- Concordance of biomarker status between NCB and surgical excision specimen
  - Estrogen Receptor: 79 - 95%
  - Progesterone Receptor: 69 - 95%
  - Her2/neu (IHC): 80 - 96%
  - Her2/neu (FISH): 100 %

Double-Blind Randomized Study of Neoadjuvant Tamoxifen vs Letrozole

Biopsy

ER+ and/or PgR+
Postmenopausal
Not eligible for BCS

RANDOMIZE

Tamoxifen
4 months

Letrozole
4 months

Surgery

Adjuvant therapy as appropriate

Clinical Results Summary for “On-Study Biopsy”
Confirmed ER+ and/or PgR+ Cases

12 % CASES ER-/PR- ON CENTRAL ANALYSIS

<table>
<thead>
<tr>
<th></th>
<th>Letrozole</th>
<th>Tamoxifen</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed (ER+/PgR+)</td>
<td>124 (100%)</td>
<td>126 (100%)</td>
<td></td>
</tr>
<tr>
<td>Overall tumor response</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(CR+PR)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical</td>
<td>74 (60%)</td>
<td>52 (41%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>48 (39%)</td>
<td>37 (29%)</td>
<td>0.119</td>
</tr>
<tr>
<td>Mammography</td>
<td>47 (37%)</td>
<td>25 (20%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Breast-conserving surgery</td>
<td>60 (48%)</td>
<td>45 (36%)</td>
<td>0.036</td>
</tr>
<tr>
<td>Clinical disease progression</td>
<td>10 (8%)</td>
<td>15 (12%)</td>
<td>0.303</td>
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</tbody>
</table>

¹Stratified Mantel-Haenszel chi-squared test

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BIOMARKER ANALYSIS

Estrogen And Progesterone Receptor Status Assessment By IHC Is Not a Standardized Test
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HER2 ASCO/CAO Testing Guidelines

THE PROBLEM

• False positive IHC (3- 50%)
  – Non-standardized Methods
  – No automation
  – Small Volume
• FISH laboratory variability 5-23 %

THE SOLUTION

• ASCO/CAP Guidelines
  – Specimen handling
  – Exclusion criteria
  – Assay validation
  – Laboratory testing
  – Controls
  – Reporting Criteria
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BIOMARKER ANALYSIS

• Hormone receptor negative
• Her2 negative
• Discordance with histology

• REPEAT ASSAY
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**Image Guided Core Biopsy – Tumor Yield**

- **Tumor Yield is higher**
  - Image guidance
  - First pass
  - Prior to any chemotherapy

<table>
<thead>
<tr>
<th>biopsy method</th>
<th>number of cores</th>
<th>tumor yield (% of core)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&gt;=30%</td>
</tr>
<tr>
<td>US</td>
<td>160</td>
<td>90 (56%)</td>
</tr>
<tr>
<td>MR</td>
<td>58</td>
<td>43 (74%)</td>
</tr>
<tr>
<td>palpation</td>
<td>212</td>
<td>84 (40%)</td>
</tr>
<tr>
<td>all</td>
<td>430</td>
<td>217 (50%)</td>
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</tbody>
</table>

*Rosen M et al. Factors Affecting Quality of Tumor Core Biopsy Specimens in ISPY TRIAL. SABCS 2006*
Image Guided Core Biopsy

Image Guided Core Biopsy should be the standard diagnostic procedure prior to neoadjuvant therapy
TISSUE BANKING

Guidelines from BIG/North American Cooperative Groups breast cancer specimen collection working groups

• **Goals:**
  
  • To promote and ensure proper collection of high-quality research specimen such that each patient diagnosed with breast cancer can have a reliable, interpretable molecular diagnosis.
  
  • To provide a known baseline of standardization of specimen collection and handling procedure, to the extent possible, such that more global biomarker analysis across studies is possible.
  
  • To promote specimen collection that would allow for future technologies, particularly in the molecular arena, to be applied to specimens for research.
  
  • Ultimately, to increase scientist confidence in pre-analysis variable control, to guarantee excellent quality of breast cancer specimens.

• **Concrete aim:**

  • To develop SOP templates that Group trial leadership can incorporate into clinical trial protocols.
FRESH TISSUE GUIDELINES

- Background and rationale for fresh tissue collection
- Notable “Do’s and Don’t’s”
- Recommended SOP’s:
  1. Brochure used by EORTC p53 study (Protocol 10994)
  2. SOP for TuBaFrost (European Human Frozen Tumour Tissue Bank)
  3. MIND ACT SOP’s (drafts now developed)
- Settings for specimen acquisition:
  - Diagnostic setting
  - Post-diagnostic preoperative setting
  - Surgical setting

http://ctep.cancer.gov/guidelines/spec_bc.grprials.html
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SUMMARY

- Image guided core biopsy is the standard diagnostic procedure for preoperative diagnosis
  - Multiple cores (4-6)
- Accuracy of diagnosis
- Biomarker Assays can be accurately performed on core biopsy specimens with appropriate quality control measures
- Tissue should be collected for research using published guidelines