USE OF ULTRASOUND IMAGING IN BREAST CANCER DIAGNOSIS & BIOPSY

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Diagnosing Breast Cancer

- screening mammography, or palpable mass
- about 1 million biopsies/year in N America
  - 60 to 80% will be benign
- open surgical biopsy
- trend towards percutaneous image-guided breast biopsy

Breast Cancer diagnosis: US role

- Supplement mammography
- Independent examination
- Guiding biopsy
- Treatment planning for radiation therapy

Role of US in diagnosis

- Women with dense breasts
- Women with fibrocystic disease
- When mammography alone cannot classify lesion
- Young women with masses
- Pregnant women with masses
- Women with implants
- Women who refuse mammography
Use of US in screening

**Advantages**
- Obtain tomographic images from almost any orientation
- Excellent for imaging cysts
- Determine if lesion is cyst or solid mass

**Disadvantages**
- Lacks sufficient spatial resolution
- Can’t detect microcalcifications reliably (~30%)

Limitations of US in screening

- Difficulties in imaging deep lesion
- Operator & equipment factors - variability
- Image contrast between some lesions & surrounding breast tissue
- Microcalcification detection
- Cannot document how much tissue imaged

Breast lesion classification

- Image processing - analysis of image features
- Tissue characterization - analysis is US signals

**Benign**
- Ovoid/lobulated
- Linear margins
- Homogenous texture
- Parallel to skin
- Distal enhancement
- Dilated duct/mobile

**Malignant**
- Irregular shape
- Poorly defined margin
- Central shadowing
- Distorted architecture
- Calcifications
- Skin thickening

Normal breast tissue
Multiple breast cysts (panoramic SonoCT)

Malignant breast mass

Invasive Breast Carcinoma

DCIS with micro-invasion

Moon et al. Radiographics 2002
Papillary DCIS with micro-invasion

Solid DCIS

Breast sonography adjunct to mammography

- Sensitivity: 98.4%
- Specificity: 67.8%
- Accuracy: 72.9%
- Positive predictive value: 38%
- Negative predicted value: 99.5%

Dense breasts
- Mammography alone - Sensitivity: ~50%
- Mammography/US - Sensitivity: increased by 42%

3D ULTRASOUND

Translator

Ultrasound transducer
3-D ULTRASOUND
Breast Cysts

Doppler imaging - blood flow
Small superficial vessels of the nipple

3D BREAST DUCT ECTASIA

DUCTAL BREAST CARCINOMA
3D Colour Doppler
US CONTRAST: Microbubbles

SCATTERING
Fundamental & Harmonics

RESONANCE
linear & non-linear

PRESSURE
stable & disruption

Ductal carcinoma enhancement pattern
(irregular vessels)

Benign Tumour

Malignant Tumour

Frans M.J Debruyne

Frans M.J Debruyne
Diagnosis by Biopsy

- Surgical biopsy
  - gold standard
  - all of suspicious mass is often removed
  - invasive procedure
  - very expensive
  - core needle breast biopsy is becoming accepted as an equal alternative

Needle Breast Biopsy

- Fine Needle Aspiration Cytology (FNAC)
  - 20 to 23 gauge needle
  - use a syringe to extract small samples
  - cytopathology

- Large Core Needle Biopsy (CNB)
  - 14 to 11 gauge needle
  - biopsy gun (also vacuum-assisted)
  - histopathology
  - false negative rate of 2%

Image Guided Breast Biopsy

- Stereotactic mammography guided
  - prone or upright
  - obvious continuation from screening
  - 3D information, but not real-time

- MRI-guided
  - contrast enhanced MRI is very sensitive
  - emerging application; expensive

- Free-hand US-guided
  - gaining popularity
  - 2D information, in real-time
  - requires expertise

Stereotactinic Mammography

- X-ray mammography
- Stereotactic pairs, obtained 30° apart
- Geometry gives 3D information
- Procedural images:
  - identify target
  - confirm needle trajectory
  - confirm edema in target area
Free-Hand US-Guided Biopsy

- Real-time 2D image guidance
- Requires expert radiologist
- Breast is constrained with hand-held transducer
- Needle trajectory is not constrained
  - misinterpretation possible
  - danger to patient and clinician

US Images pre Breast Biopsy

Target Definition & Location

Confirm needle position

Post Biopsy images

3D Ultrasound Imaging

Research Objectives:

3D US Guided Breast Biopsy (USB)
- Attributes combined from:
  - stereotactic mammography
    - breast fixation
    - controlled needle trajectory
  - 2D ultrasound
    - real-time imaging for guidance
  - 3D ultrasound
    - near real-time 3D imaging for targeting, guidance and verification
3D USB System

Transducer
Sweep Direction
Needle Guide & Guide Movers
Insertion Direction

3D US-Guided Biopsy Protocol

- Identify target in 3D US image
- Transducer moved over target
- Needle guide moved to in-line with target
- Needle is inserted under real-time 2D US
- Biopsy is performed
- 3D scan acquired to confirm hit
- Needle removed
- Another target point identified

Evaluation

1. Needle placement in tissue mimic
   - establish positioning accuracy
2. Biopsy of ‘lesions’ in tissue mimic
   - relate target size to biopsy success rates
3. Biopsy of ‘lesions’ in animal tissue
   - compare with performance of expert free-hand US guidance

1. Needle Placement Accuracy

- Beads in agar
- Needle tip at target
- 3D US record
- Tip to target distance
- 3D analysis of accuracy

⇒ 0.85 mm targeting accuracy, with 95% confidence

2. Biopsy Accuracy

- White PVA-C 'tissue'
- Green PVA-C 'lesions'
  - 1.6 to 16 mm diameter
- Scored as hit or miss
- Biopsy of 'lesions' in tissue mimic
  - relate target size to biopsy success rates


2. Biopsy Accuracy

- Post-fire 3D US showed positioning accuracy

Biopsy Specimens

2. Biopsy Accuracy

0.53 mm bias in placement
- sampling notch direction bias

2. Biopsy Accuracy

<table>
<thead>
<tr>
<th>Lesion Size (mm)</th>
<th>95%</th>
<th>99%</th>
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<tr>
<td>0.5</td>
<td>180</td>
<td>309</td>
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<td>1.0</td>
<td>45</td>
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<td>2.0</td>
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<td>3.0</td>
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<td>2</td>
<td>4</td>
</tr>
<tr>
<td>10.0</td>
<td>1</td>
<td>1</td>
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</table>
3. Comparison to Clinical Standard

Designed to show equivalence between the new method and a clinical standard

- 55 biopsies by each of:
  - 3 radiologists, free-hand
  - 1 team of scientists, 3D US apparatus

KJM Surry et al. Med Im Analysis, 8(2):201-212, 2002

3. Results

- Radiologists
  - 94.5% success

- 3D US system
  - 96% success

Equivalence has been proven, within 5%, with 95% confidence
Summary of Results

1. Needle placement at a target
   – fundamental to placement accuracy
2. Biopsy of a target
   – add needle firing and sample collection
3. Comparison with a standard
   – relate performance to current practice

We can sample a 3.2 mm lesion at a 96% success rate.

Advantages of Dual Modality

• Information fusion for diagnosis confirmation
  – most relevant at the screening stage
• Pre-procedural target identification
  – x-ray mammography
• Real time 2D imaging and near real time 3D imaging for targeting and guidance
  – ultrasound

Visibility and Detection

• screening mammography (XM)
• often followed with ultrasound (US)

<table>
<thead>
<tr>
<th>Modality</th>
<th>Sensitivity</th>
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<tr>
<td></td>
<td>all</td>
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<tr>
<td>XM</td>
<td>78%</td>
</tr>
<tr>
<td>US</td>
<td>75%</td>
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<tr>
<td>both together</td>
<td>97%</td>
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</table>

n(all) = 11,130; n(cancers) = 145
compiled from Kolb et al, Radiology, 225:165-175, 2002.
Dual Modality Biopsy Protocol

1. Acquire SM image pair of target region
2. Identify target in both views
3. Calculate 3D position of target
4. Transform target to 3D US image space
5. 3D US image of target region
6. Place SM target into 3D US image
7. Align transducer and needle guide with target
8. Insert needle & acquire biopsy sample
9. Acquire 3D US image & confirm biopsy in 3D US
10. Remove needle

Dual Modality Biopsy: 2D SM / 3D US

The Challenge

- stereotactic mammography guided biopsy inserts the needle vertically
- the needle has a 19 mm sampling notch
- our system: horizontal insertion
Registration of US and 3D SM

- dual modality phantom
- pin tips were used for fiducials and targets
  - 15 points were used to define the registration
  - 15 points were used to evaluate the registration
- linear least squares (translation + rotation)
  - vtkLandmarkTransform

Registration: Results

- Fiducial Registration Error, FRE = 0.86 mm
- Target Registration Error, TRE = 0.98 mm

<table>
<thead>
<tr>
<th></th>
<th>x</th>
<th>y</th>
<th>z</th>
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<tbody>
<tr>
<td>FRE</td>
<td>0.31</td>
<td>0.25</td>
<td>0.76</td>
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<tr>
<td>TRE</td>
<td>0.35</td>
<td>0.35</td>
<td>0.84</td>
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TRE, may be limited by the geometry

Beads in Agar Phantom

3D Ultrasound
Stereo-mammography

Pin Phantom Registered
Agar and Bead Phantom

- TRE = 0.94 mm
- TREx = 0.24 mm
- TREy = 0.30 mm
- TREz = 0.86 mm

Animal Tissue Phantom

3D USB Evaluation: Conclusions

- Methods were developed for evaluating and assessing the accuracy of a biopsy apparatus
- 3.2 mm lesions were sampled with a 96% success rate
- We have demonstrated that the 3D US guided biopsy procedure is equivalent to current clinical practice
Conclusions

- Attributes of Combined 3D US and Stereotactic Mammography System:
  - breast compression for stability and safety
  - dual modality imaging for target localisation
  - real-time US for needle guidance
  - 3D US for targeting and guidance
  - 3D US image record for biopsy verification

Measurement Errors

A 2 mm measurement error on the films, leads to large errors in the z-direction

<table>
<thead>
<tr>
<th></th>
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<th>y</th>
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<tbody>
<tr>
<td>either SM image</td>
<td>10 mm in z</td>
<td>20 mm in z</td>
</tr>
<tr>
<td>both SM images</td>
<td>20 mm in z</td>
<td>35 mm in z</td>
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The Back Plate and Top Plate

Acknowledgements

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- Dr. Chris Ellis

2. Biopsy Accuracy

Ductal Carcinoma in situ

- Non-palpable, early stage cancer
- Under-diagnosis rate is 11 to 36%
- Hypothesis:
  - Dual modality will clarify biopsy target areas
  - Real-time imaging will ensure accurate guidance
- Proposal:
  - µ-calcs in SM can identify where to look in 3D US
  - architectural distortions and duct geometry in 3D US
Defining the Geometry

What’s known:
- phantom geometry
- distances between points on the phantom in the right and left images

What’s not known:
- position of the source
  - height
  - horizontal position
  - angle from vertical
- position of the film
  - height
  - horizontal position
  - rotation in the cassette
- position of the phantom
  - orientation

From 2D SM to 3D US

3DSM to 3DUS transform
vertical offset in 3DUS

Defining the Geometry

requires four points to define the geometry
- reference point plus three others

used 10 points to evaluate the relationship
- accuracy of localising a point in 3D SM space
- fiducial localisation error (FLE)
- target localisation error (TLE)
Defining the Geometry: Errors

- Target Localisation Error
  \[
  TLE = \sqrt{\frac{1}{n} \sum_{i=1}^{n} (x_i - x_{sa})^2 + (y_i - y_{sa})^2 + (z_i - z_{sa})^2}
  \]

- TLE = 1.36 mm
  - TLE_x = 0.48 mm
  - TLE_y = 0.36 mm
  - TLE_z = 1.23 mm
Future Work

- Test the SM-US guided biopsy procedure
  - needle targeting with SM guidance only
  - biopsy task when identification is an issue
    (cysts, solid and calcified masses, calcifications)
- Integrate the 3D US guidance system with digital stereotactic mammography
  - immediate identification of a target seen in SM by placing a marker in the 3D US image

Towards Clinical Application

- Re-design for comfort
- Integration with digital SM imaging
- Real-time needle tracking (3D)
- Oblique insertion (away from chest)
- Automatic target identification and segmentation
- Biopsy planning

3D US with SM Imaging