Introduction

- Palpation is an important diagnostic tool
- Practiced by Egyptian physicians in 2600 BCE
- "It is the business of the physician to know, in the first place, things similar and dissimilar; ... which are to be perceived in the sight, and the touch, and the hearing ...."
  Hippocrates, On the Surgery, 400 BC
- "Such swellings as are soft, free from pain, and yield to finger ...... and are less dangerous than the others. ......then, as are palpated hard, and large, indicate danger of speedy death; but such as are soft, and yield when pressed with the finger, are more chronic than these"
  Hippocrates, The Book of Prognostics, 400 BC

Discussion of problem

- Prevalence – 3 to 8%, 50% after 65 years
- Incidence on US – 60%
- Bmode US and Doppler – low accuracy
- FNA – standard procedure
  - Invasive procedure
  - Inadequate samples – 10-20%
- Palpation

Principle of palpation

- To be palpable, the object must be harder than the tissue surrounding it.
- Fingers displace tissue downward, and the pressure receptors on the skin of the fingers are used to sense the local stress values
- Stress is
  - higher on fingers overlying a superficial "hard" lesion
  - lower on receptors of fingers overlying softer surrounding tissues

B-mode ultrasound

- Echopalpation or sonopalpation
  - Object of interest is imaged with US and resulting deformation of tissue from compression is watched for.
  - Harder lesions - move as a unit,
  - Softer lesions - deform more under the localized pressure
- Another method –
  - compress a lesion using the US transducer and
  - measure the relative flattening of the lesion compared with the thinning of an adjacent tissue layer
Ultrasound elasticity imaging

- Tissue motion studies in late 1970s and early 1980s
- Sonoelasticity in approx 1988
  - Used Doppler ultrasound to detect tissue motion in response to external vibration.
  - Ultrasound Elastography 1991
    - Small external compression used and tissue response tracked using crosscorrelation methods
    - Capable of high quality images of tissue stiffness

Principles of Elastography

- In 1991, Ophir et al used external compression to induce strain and tracked tissue motion and called this method elastography.  
- Method of imaging tissue hardness is based on Young elastic modulus
  - Mathematical description of a substance’s tendency to be deformed when an external force is applied
  - Unit is Pascal (Pa)
- Pre and post-compression ultrasound images of the same tissue are taken
  - Tissue movement during compression is analyzed to estimate strain.  

Ultrasound Elastography

- Certain pathologic processes cause changes in tissue stiffness
- Ultrasound elastography (UE) allows tissue stiffness to be imaged and measured
  - Specialized software calculates the difference in tissue movement and estimates deformation

Imaging tissue strain

- Tissue is interrogated before (a) and after (b) a small uniform compression.  Stiffer tissues will be less distorted than the surrounding tissues.
- Echoes returned to the transducer are analyzed before converting to B mode.  Then US transducer compresses the tissue (b) and another set of RF signals is collected.  Rate of change, or strain values are mapped onto an elastogram.

Elastography

- Elasticity Modulus measurement of excised thyroid tissues
- Lyshchik et al. 2005
  - Tissue samples from papillary carcinoma (~80% thyroid cancer), were stiffer than those from benign tumors and normal thyroid tissues (p<0.01).
Quasistatic – with transducer

- Radiofrequency echo signals acquired before and after a small (about 1%) of applied deformation – correlated to estimate tissue displacements
- Pre- and post-deformation signals compared for local tissue displacement and corresponding strain distribution computed.
  - Stepper motor control (with the transducer held in a fixture) or
  - Freehand compression using the transducer

Elastography – External compression

- Thyroid Elastography using external compression
  - Lyshchik et al. 2005
  - Potential for differential diagnosis of thyroid nodules
  - Noise caused by external freehand compression and pulsation of the carotid artery.

Quasistatic – with normal physiologic motion

- Deformation applied through physiologic function
  - Respiratory, cardiac muscle deformations and natural pulsations of cardiovascular sources
  - Pulsation induced strain of thyroid nodules can be analyzed

Table 1. Elasticity Scores in Thyroid Nodules (n=145)

<table>
<thead>
<tr>
<th>Score</th>
<th>Number (n)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5-0</td>
<td>3</td>
<td>&lt;0.01</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>2</td>
<td>5-5</td>
<td>2</td>
<td>&lt;0.01</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>3</td>
<td>0-5</td>
<td>3</td>
<td>&lt;0.01</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>4</td>
<td>0-5</td>
<td>3</td>
<td>&lt;0.01</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>5</td>
<td>0-5</td>
<td>3</td>
<td>&lt;0.01</td>
<td>00</td>
<td>00</td>
</tr>
</tbody>
</table>

Hong et al. 2012, Core compression applied to the thyroid nodules and surrounding tissues.
Elastography – Internal compression

- Using internal compression
  - Pulsation of carotid artery as the compression source
- Compared to using external freehand compression
  - No conflict between external and internal compression sources
  - Direct contact with the compression source
  - Repeatable and operator-independent outcome

Elastography

- Subjective method
  - No parameter to compare the different lesions

New metric for thyroid nodule characterization

Thyroid stiffness index (TSI)

\[
TSI = \frac{\text{Strain near carotid artery (high strain area)}}{\text{Strain in the thyroid nodule (low strain area)}}
\]

- Strain near the carotid artery can indicate the amount of compression applied by carotid artery pulsation
- Higher TSI indicates a stiffer lesion

Dynamic – Vibratory systems

- Vibration elastography displaces tissue by using an external vibration source
  - Displacement is measured via Doppler imaging which depicts differential motion
Dynamic – Transient Elastography

- Acoustic radiation force impulse (ARFI)
- Transient shear wave imaging (SWI)
- Supersonic shear wave imaging (SSWI)
  - Uses acoustic radiation force of the ultrasound wave to push the tissue.
  - Repeated focused pulses are generated with a conventional transducer.
  - Implemented in the Aixplorer system, introduced by SuperSonic Imagine.
  - No manual compression is applied, thus removing user-dependence of strain elastography.


Elastography – Shearwave technique

- Based on the automatic generation and analysis of transient shear waves.
- Quantitative, user-independent, and can be performed in real time.
- Dr. Frederic Sebag, Department of General and Endocrine Surgery at Hôpital de la Timone in Marseille, France.
- Mean normal thyroid elasticity index (EI):
  - 59 controls - 15.9 kPa.
  - 25 malignant nodules - 137.2 kPa (range, 35–355 kPa).
  - 115 benign nodules - 36.4 kPa (range, 0–200 kPa).


Elastography – Shearwave technique

- Conventional ultrasound parameters
  - Sensitivity - 44% and
  - Specificity of 99%
- Elasticity index
  - Sensitivity – 74%
  - Specificity - 98%.
- Cutoff elasticity index - 69 kPa to yield a positive predictive value of 90%

Author Sensitivity Specificity PPV NPV
Asteria et al, Thyroid 2008 94.1 81.1 55.2 98.2
Rubaltelli et al. Ultraschall in Med 2009 81.8 87.5 64 94.5
Rago et al. JCEM 2007 97 100 100 98
Hong et al. JUM 2009 88 90 81 93
Dighie et al. Radiology 2008 87.8 77.5 47.4 97.1
Lyschikh et al. Radiology 2005 82 96 95 88
Friedrich-Rust et al. Exp Clin Endocrinol Diabetes 2009 86 87 50 98
Tranquart et al. J Radiol 2008 100 93.1 46.2 100

Overall

<table>
<thead>
<tr>
<th>US pattern</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Micronodules ≤ 10 mm</td>
<td>41.1–69.1</td>
<td>85.8–95.0</td>
<td>24.3–56.7</td>
<td>6.8–94.2</td>
</tr>
<tr>
<td>Hypoechogenicity</td>
<td>76.5–87.1</td>
<td>63.6–96.3</td>
<td>71.5–100</td>
<td>77.8–92</td>
</tr>
<tr>
<td>Irregular margins or no margins</td>
<td>76.5–87.1</td>
<td>63.6–96.3</td>
<td>71.5–100</td>
<td>77.8–92</td>
</tr>
<tr>
<td>Sclerosing cysts or complex cysts</td>
<td>76.5–87.1</td>
<td>63.6–96.3</td>
<td>71.5–100</td>
<td>77.8–92</td>
</tr>
<tr>
<td>Irregular shape (3 or more of the above)</td>
<td>76.5–87.1</td>
<td>63.6–96.3</td>
<td>71.5–100</td>
<td>77.8–92</td>
</tr>
<tr>
<td>Taller than wide (T/W)</td>
<td>76.5–87.1</td>
<td>63.6–96.3</td>
<td>71.5–100</td>
<td>77.8–92</td>
</tr>
</tbody>
</table>

PPV: positive predictive value; NPV: negative predictive value.

Table 1. Ultrasound signs suggestive of malignancy.

Elastography

98.6 89.1 87.3 96

Conclusion

- Thyroid elastography has the potential to noninvasively diagnose malignancy.
- Can help reduce the number of fine needle aspirations.
- Improve health care utilization.