This activity has not been approved for category 1 CME credit because the conflict indicated by the speaker could not be resolved according to guidelines from the Accreditation Council for Continuing Medical Education.
Use of PTH at Point of Surgery for Non-Localized Cases of Hyperparathyroidism
Keck Hospital of USC

- Private, non-profit 400 bed hospital
- Teaching and research, USC Keck School of Medicine
- Approx. 40 parathyroid surgeries per year
Hyperparathyroidism: Facts

- Hyperparathyroidism (HPT) is a disease of “stones, bones and abdominal groans”
- 100,000 new cases of HPT each year in U.S.¹
- Annual parathyroidectomy cost of $282 million²
- More common in women than men, increase with age in both sexes

¹Melton LJ 3rd, J Bone Miner Res. 2002 Nov; 17 Suppl2: N12-7
²Right Diagnosis. Com
• 85-88% of cases present single benign parathyroid adenoma
• ~11% result from diffuse hyperplasia of all parathyroid glands
• 1-5% of cases caused by multiple adenomas¹
• Other challenges: ectopic gland location & supernumerary glands
• Hyperplastic or adenomatous tissue? Hard to tell even with frozen sections!

¹American Academy of Otolaryngology-Head and Neck Surgery Foundation 2011
HPT Diagnosis

- Diagnosis starts w/ elevated serum + 24-hour urine calcium
- Elevated intact chain PTH Levels
- Imaging studies: ultrasonography, sestamibi scintigraphy, MRI and gamma probe
- Is minimally invasive parathyroidectomy an option?
- Bilateral neck dissection: an option or a requirement?
- Of 320 labs surveyed in 2002, 92 performed introperative PTH’s¹

¹Arch Pathol Lab Med. 2002 Sep; 126(9):1045-9.
Pre-Op Imaging Studies

Ultrasound Localization
Pre-Op Imaging Studies

Sestamibi Scans

• 80-90 % positive adenoma localization
Sestamibi Scan: Predictive Value

427 Patients with Hyperparathyroidism

<table>
<thead>
<tr>
<th>Type of Scan</th>
<th>Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Scan (240)</td>
<td>56%</td>
</tr>
<tr>
<td>Equivocal Scan (105)</td>
<td>25%</td>
</tr>
<tr>
<td>Negative Scan (82)</td>
<td>19%</td>
</tr>
</tbody>
</table>

Bumpos JM, et. al Laryngoscope 119 2009
Operative Technique, Parathyroid Gland Surgery

• Experience counts
• Minimally invasive surgery
  – The proper candidate
  – Positive sestamibi scan/ and Ultrasound
  – Can be done under local if necessary
• Need for a 4 gland exploration
Intraoperative PTH Monitoring at Point of Surgery

- PTH ½ life about 5 minutes
- Can obtain an immunoassay in 10 minutes
- Future Diagnostics, STAT IO-IPTH, Netherlands
- Immunochemiluminescence Methodology
- http://www.future-diagnostics.nl/
PTH Concentrations Post Gland Removal

PTH in pg/ml

Time in minutes after gland removal
Positive Pre-op Localization

- Peripheral serum PTH
- Open neck
- Remove adenoma
- Confirm cure 10-15 minutes after tumor removed
- Good candidate for minimally invasive, video-assisted approach
Negative Pre-op Localization

• All imaging studies negative
• What options available?
  – Elective 4 gland exploration
  – Use Intraoperative PTH central vein (or intra-jugular vein) sampling
Algorithm for Non-localization

- Use baseline intra-operative PTH split samples from the internal jugular (IJ) veins
- Split IJ samples can direct surgical exploration based upon the IOPTH gradient between the 2 sides (>20pg/ml)
- Blood must be obtained from the internal jugular veins low in the neck, before manipulation of the glands
Internal Jugular Vein Samples

Samples Taken Low in the Neck
• 66 patients with split IJ samples (2005-2010)
• 10 cases were secondary hyperparathyroidism

33 had positive localization
23 had negative localization

• There were 2 negative explorations in each group
• 52 cases were ultimately analyzed
### Site of Pathology

<table>
<thead>
<tr>
<th>Site of Adenoma</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left</td>
<td>23</td>
</tr>
<tr>
<td>Right</td>
<td>23</td>
</tr>
<tr>
<td>Hyperplasia</td>
<td>6</td>
</tr>
</tbody>
</table>
## PTH Gradient Results

<table>
<thead>
<tr>
<th>Site of Adenoma</th>
<th>RIJ Mean</th>
<th>LIJ Mean</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left 23</td>
<td>156</td>
<td>561</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Right 23</td>
<td>609</td>
<td>154</td>
<td>&lt;0.004</td>
</tr>
<tr>
<td>Hyperplasia 6</td>
<td>158</td>
<td>133</td>
<td>0.43</td>
</tr>
<tr>
<td>$P$-value Left v. Right</td>
<td>&lt;0.005</td>
<td>&lt;0.003</td>
<td></td>
</tr>
</tbody>
</table>
Results

- The greater the absolute value of the gradient between the right and left IJ samples, the more likely the gradient was to predict the side of the tumor.
- A gradient of $>200$ was associated with a 100% accuracy of adenoma localization.
- A gradient of 20-200 was associated with an 88% accuracy (15/17).
Surgery for Hyperparathyroidism: Suggested Algorithm

- Imaging Studies
  - Positive Localization
    - Minimally Invasive Operation
      - Confirm with IOPTH Drop >50%
  - No Pre-op Localization
    - Neck exploration
      - IJ Split samples to direct exploration
Intra-Operative PTH Testing

• Done in lab or at POS? A matter of time.
• Operating room turnover, billed @ $94 per minute!
• If test done POS, save 15-30 minutes
• Cost/test difference: $37.50 POS vs. $3.61 in central lab
• Technologist has improved job satisfaction w/ POS/POCT
IO-PTH: Summary

- Enhance patient outcomes by decreasing morbidity, mortality & hospital LOS¹
- Short half life of PTH (~5 minutes) & suppressed secretion of PTH in normal glands after excision make IO-PTH useful
- Exclusion of hyperplasia is challenging in minimally invasive video-assisted procedures
- Increased success rate of surgery promotes culture of quality & consistency in patient care @ bedside

¹Vikram Reddy, MD, Adil I. Khan, PhD, Alan T. Remaley, MD, PhD, Frank H. Wians, Jr, PhD, LabMedicine, Volume 37, Number 12, December 2006
Is IO-IPTH Considered Lean¹?

- Paperless ✓
- Quicker results ✓
- Pre-analytical, processing time eliminated ✓
- Less biohazard waste ✓
- Lower specimen volume, blood conservation ✓
- Lower medical errors ✓
- Enable integration of testing into clinical flow & clinical judgment ✓
- Improve clinical outcomes ✓

¹Dr. Jay B. Jones, PhD, DABCC, Geisinger Health Systems: Process Improvement for Critical & Point of Care Testing, a Lean Perspective, 13 October, 2011.