WCTC – ACS/Advanced Thyroid Ultrasound Course
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Daniel S Duick, MD
Clinical Professor of Medicine, University of Arizona College of Medicine, Phoenix-Tucson Campuses
Endocrinology Associates, PA, Scottsdale, Arizona
Historical Perspective of Ethanol Ablation – Percutaneous Ethanol Injection (PEI):

1) PEI (Ethanol Injection) for \textit{non-functioning} thyroid adenoma;
2) PEI for \textit{hyperfunctioning} thyroid adenoma;
3) PEI for mass reduction in \textit{MNG/nodules}
Current Utility of PEI ablation therapy

1. Thyroid PEI procedures:
   - Thyroid cyst
   - Thyroid cystic adenoma (greater efficacy if more than 75% cystic and preferably uni- or bi-cameral)
   - DTC or MTC cervical residual lymph node disease - palliative (with or without complete obliteration) in patients who are not candidates or refuse further surgery for enlarging node

2. Parathyroid PEI procedures:
   - Parathyroid adenoma/Primary HPT - palliative for rare patient who is not able to tolerate primary surgery or refuses surgery; recurrent/multiple recurrences/parathyreosis; multigland or Primary Hyperplasia/failed multiple surgeries
   - Parathyroid cyst & Parathyroid cystic adenoma (non-functioning and hyperfunctioning)

3. Parathyroid hyperplasia diseases and PEI procedures:
   - Palliative for primary hyperparathyroidism due to multigland and/or hyperplasia - post one or multiple surgical procedures with disease persistence/recurrence/parathyreosis
   - Palliative for secondary hyperparathyroidism (SHPT) in poorly controlled CKD/CRF/Dialysis
   - Palliative for tertiary hyperparathyroidism (THPT) in patients intolerant or not controlled by cinacalcet and non- surgical candidates
   - Palliative for hyperparathyroidism due to implantation parathyroid tissue in SCM or forearm
<table>
<thead>
<tr>
<th>Study</th>
<th>Patients (Gender)</th>
<th>Mean Follow-up (months)</th>
<th>Mean volume at baseline (ml)</th>
<th>Number of sessions</th>
<th>Amount of EtOH injected (% of the extracted fluid)</th>
<th>Mean Volume reduction (%)</th>
<th>Success rate (%)</th>
<th>Major side effects</th>
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<tbody>
<tr>
<td>Yasuda et al., 1994</td>
<td>61</td>
<td>6</td>
<td>n.r.</td>
<td>1-3</td>
<td>10</td>
<td>n.r.</td>
<td>72.1</td>
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<td>Monzani et al., 1994</td>
<td>20</td>
<td>12</td>
<td>~12.0</td>
<td>1-2</td>
<td>~30</td>
<td>n.r.</td>
<td>95</td>
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<td>Verde et al., 1994</td>
<td>32</td>
<td>12</td>
<td>14.5 (1.5-65.8)</td>
<td>n.r.</td>
<td>n.r. (1-10 ml)</td>
<td>71</td>
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<td>Antonelli et al., 1994</td>
<td>26</td>
<td>12</td>
<td>16.8 ± 9.9</td>
<td>1-5 (mean 2.5)</td>
<td>10-33</td>
<td>n.r.</td>
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<td>Zingrillo et al., 1999</td>
<td>43</td>
<td>37.0± 14.0</td>
<td>38.4 (4.8-166)</td>
<td>1-4 (mean 1.5)</td>
<td>10-15</td>
<td>91.9</td>
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<td>Cho et al., 2000</td>
<td>22 (13/9)</td>
<td>3.5 (1-10)</td>
<td>13.0(3.5-42.0)</td>
<td>1-6</td>
<td>40-100</td>
<td>64.0</td>
<td>68.1</td>
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<td>Del Prete et al., 2002</td>
<td>98</td>
<td>120 ± 14</td>
<td>35.2 ± 20</td>
<td>1-4 (mean 1.8)</td>
<td>70-150</td>
<td>59.9</td>
<td>93.8</td>
<td>Dysphonia (1)</td>
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<td>Kim et al., 2003</td>
<td>20</td>
<td>4.4 (1-6)</td>
<td>15.7 (12.0-48.6)</td>
<td>1-3 (mean 1.8)</td>
<td>40-68</td>
<td>64.0</td>
<td>65.0</td>
<td>0</td>
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<td>Bennedbaek et al., 2003</td>
<td>33 (26/7)</td>
<td>6</td>
<td>8.0 (5.0-14.0)</td>
<td>1-3</td>
<td>25-50</td>
<td>100^</td>
<td>82.0</td>
<td>Dysphonia (1)</td>
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<td>Valcavi et al., 2004</td>
<td>135</td>
<td>12</td>
<td>19.0 ± 19.0</td>
<td>1-3</td>
<td>50-70</td>
<td>85.6^</td>
<td>n.r.</td>
<td>Dysphonia (1)</td>
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<td>Guglielmi et al., 2004</td>
<td>58</td>
<td>82</td>
<td>13.7± 14.0</td>
<td>2.2± 1.3</td>
<td>25</td>
<td>86.6</td>
<td>86.2</td>
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<td>Lee et al., 2005</td>
<td>432</td>
<td>36.5 ± 12.9</td>
<td>15.6± 12.6</td>
<td>1-7 (mean 2.3)</td>
<td>40-100</td>
<td>66.1</td>
<td>79.4</td>
<td>Dysphonia (3)§</td>
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<td>Kanotra et al., 2008</td>
<td>40 (24/16)</td>
<td>13.8 ± 5</td>
<td>12.2 (5.8-18.5)</td>
<td>1-3 (mean 1.5)</td>
<td>50</td>
<td>70.0</td>
<td>85.0</td>
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<td>Sung et al., 2011</td>
<td>36</td>
<td>17.0± 7.46</td>
<td>13.8± 11.9</td>
<td>1-2 (mean 1.2)</td>
<td>50</td>
<td>93.0</td>
<td>94.4</td>
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Ultrasound-guided percutaneous ethanol injection therapy in thyroid cystic nodules

**Study Design:**
- 281 pts, controlled and randomized
- 138 pts simple cyst evacuation controls (C) vs 143 pts cyst evacuation plus PEI treated (T)
- Exclusion criteria: inadequate, suspicious, or positive FNA cytology; high serum calcitonin; contralateral laryngeal cord palsy
- Ethanol injected = 50 to 70% of aspirated cystic fluid volume

**Results:**
- Pre-treatment, (m+/-SD) nodule volume in (C) = 20.0 +/- 13.4 mL vs (T) = 19.0 +/- 19.0 mL (NS)
- After 1 year, (C) volume = 16.4 +/- 13.7 mL vs (T) = 5.5 +/- 11.7 mL (P<0.001)
- Respective median reduction of initial volume was (C) 7.3% vs (T) 85.6% (P<0.001)
- Compressive/cosmetic symptoms disappeared in 24.4%/37.4% of (C) pts vs 74.8%/80.0% of (T) pts (P<0.001).
- No serious AEs and side effects were minor

**Conclusion:**
These data provide definitive evidence that PEI is a safe and effective treatment for thyroid cystic nodules. Unicameral thyroid cysts are the most suitable candidate nodules for PEI.

Thyroid Cyst and Cystic Adenoma

Management approach:

- Small or asymptomatic - observe only
- Large or symptomatic (e.g., compression, dysphagia, hoarseness, unsightly neck distortion): drain and perform FNA of any residual nodular tissue
- If cytology reveals benign tissue and cystic component returns or is increasing in volume, consider PEI if cystic component > 50% and preferably > 75% of total nodule volume
PEI FOR THYROID AND PARATHYROID DISEASE

Thyroid Cyst and Cystic Adenoma

PEI Technique:
- requires experienced physician operator;
- experienced sonographer to handle transducer and imaging (needle bevel must be constantly imaged and tracked throughout the drainage and reinstillation of absolute ethanol);
- any perforation of the cyst can cause pain/sclerosis; transient or permanent injury to RLN, trachea, esophagus, sterile abscess, transient Horner’s syndrome
- medical assistant for monitoring procedure tray, aspirate, ethanol, etc.
66 Y/O, M, with neck enlarging neck mass over 2-3 months; US = cystic mass; primary physician referred to endocrinologist who FNA’d....serous fluid/normal thyroid tissue.... mass recurred over 1 week +...... then referred to surgeon who recommended removal.

Pt sought another opinion ...... Initial evaluation revealed recurrent mass – US appeared primarily cystic (volume 63 cc) and based on Hx, a good candidate for PEI
PERCUTANEOUS ETHANOL INJECTION (PEI)
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CASE 2

78 Y/O F with neck mass x 6 months and intermittent, progressive, compressive and swallowing awareness/fullness in L neck. Evaluated by previous endocrinologist and two surgeons; 2 prior negative FNAs; surgery recommended; patient repeatedly refused. Initial evaluation and US revealed a multiloculated (complex) cystic nodule (volume = 43 cc).
PEI FOR THYROID AND PARATHYROID DISEASE

PEI for DTC/MTC LYMPHADENOPATHY
## SUMMARY OF PEI THERAPY OF PTC LN AND NECK TUMOR RECURRENCES

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<thead>
<tr>
<th>Study</th>
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<th>Mean Follow-up (months)</th>
<th>Location (central vs. lateral neck)</th>
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<th>Mean Volume Decrease (%)</th>
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<th>RLN injury</th>
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<td>29 (14)</td>
<td>18 (2-77)</td>
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<td>492 mm³</td>
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<td>24 (16)</td>
<td>24 (13-43)</td>
<td>11 vs.13</td>
<td>9.9 (5.5-29.0) mm</td>
<td>37.5-43.5</td>
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<td>Kim et al., 2008</td>
<td>47 (27)</td>
<td>26 (10-38)</td>
<td>7 vs.40</td>
<td>678.8 ± 87.4 mm³</td>
<td>93.6 ± 12.6</td>
<td>44.7%</td>
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<td>109 (63)</td>
<td>32 (3-72)</td>
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<td>Duick, et al</td>
<td>43 (29)</td>
<td>34 (7-88)</td>
<td>11 vs. 32</td>
<td>&gt;470 mm</td>
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<td>35/43</td>
<td>35/43</td>
<td>35/43</td>
<td>35/43</td>
<td>43</td>
</tr>
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</table>
PEI FOR THYROID AND PARATHYROID DISEASE

PEI of Lymph Node Metastases - Technique
- requires experienced physician operator;
- prior FNA for verification for cytology and Tg (NOTE: in Level VI need to have cytology (+) and if < 5-6 mm, be sure not a remaining parathyroid gland); in lateral Levels II, III, IV and V, Tg from aspirate is sufficient if cytology (-).
- experienced sonographer to handle transducer and imaging

Avoidance of Nerve Injury during PEI – Technique
- RLN (Level VI) and VN (Levels II, III, IV located in postero-medial carotid sheath) – common locations for persistent, recurrent PTC
- Best avoidance technique: DON’T PENETRATE LYMPH NODE DURING PROCEDURE

Lewis BD: AJR2002;178:699-704
Kim BM: Eur Radiol 2008; 17:835-842
Schematic of Vagus N and Recurrent Laryngeal N in lower neck
Avoidance of Nerve Injury during PEI- Technique (cont’d)

PEI (95-99%) performed with 1 cc tuberculin syringe and 25 gauge needle with slow instillation in 0.05-0.1cc increments

NOTE: any extravasation or perforation of node during PEI can cause injury to central structures RLN, trachea, esophagus, and lateral neck structures: vagus n, spinal accessory n, vascular, thoracic duct, etc.

Lewis BD: AJR2002;178:699-704
Kim BM: Eur Radiol 2008; 17:835-842
76 Y/O M recurrent PTC Level IV – 3 separate Rxs
CASE 4

72 Y/O M with FVPTC widely metastatic to lungs, bones, brain – 14 years duration. New LN mass in Level III with rapid growth
PEI of Parathyroid cyst

Parathyroid cysts are uncommon.
In a minority of cases they represent functioning tumors.
FNA of a parathyroid cyst reveals clear, water-like fluid.
May submit for PTH assay for either documentation or if aspirated from an atypical location.
Frequently recur after aspiration.
In a series of 13 PT cysts:
  75% mean volume reduction
  84.6% cure rate
  5 pts had or developed evidence of elevated calcium

Valcavi, R – personal communication
PEI TECHNIQUE OF PARATHYROID CYST

Essentially same technique utilized as for PEI of thyroid cyst
PEI OF PARATHYROID CYSTS (PARATHYROID ADENOMA)

ADVERSE EFFECTS:
Neck pain
Recurrent nerve palsy
Transient Horner’s syndrome
Dysphonia
N.27 patients (age 67 ± 13 years)
Survey 22 ± 10 months
Biochemical recovery 58%
Failure 7%
Recurrence 4 of 15 cured patients

18 consecutive patients; follow-up median 45 mos
  - 8 patients later underwent surgery
  - Successful in 10 of 18 patients (56%)
14 patients (high risk/refusal of surgery); follow-up median 39 mos
  - Successful in 11 of 14 patients (79%)
  - 2 patients required surgery
  - Fibrosis of the PTAs was found in all patients (both groups) who later had surgery
  - 1 patient in each group had vocal cord paralysis following PEI
Conclusion: PEI should be reserved for patients not fit for surgery

Karstrup S et al. Clin Endocrinol, 1993
**SUMMARY OF PEI OF PARATHYROID TUMOR/CYST**

- **PEI** of parathyroid cyst utilized if recurs post aspiration
- **PEI** of adenoma or hyperplastic disorders is a palliative procedure for occasional PHPT; used in SHPT and THPT on a selective basis

- NOTE: An **FNA** for PTA should be performed only in select cases (e.g., non-localization by US or MIBI is discordant or lesion cannot be determined in posterior thyroidal, intra-thyroidal or inferior neck/Level VII)