Dynamic Risk Stratification in DTC: IMAGING BEYOND ULTRASOUND

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Objectives

- To reacquaint participants with the basic concepts of dynamic risk stratification in the follow-up of differentiated thyroid cancer
- To evaluate the roles of contrasted CT scanning, $^{131}$I total body scanning and FDG PET CT as supplements to neck imaging with high resolution US
- To use clinical cases to demonstrate the efficacy of each of these imaging modalities and how they complement high resolution neck US
Response To Therapy Definitions

Excellent Response
No clinical, biochemical, or structural evidence of disease

Biochemical Incomplete Response
Persistent abnormal thyroglobulin values in the absence of localizable disease

Structural Incomplete Response
Persistent or newly identified loco-regional or distant metastases

Indeterminate Response
Non-specific biochemical or structural findings which cannot be confidently classified as either benign or malignant

## Response To Therapy Definitions

**TG cut points based on initial therapy**

<table>
<thead>
<tr>
<th></th>
<th>Total Thyroidectomy &amp; RAI ablation</th>
<th>Total Thyroidectomy</th>
<th>Lobectomy</th>
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</thead>
<tbody>
<tr>
<td><strong>Excellent</strong></td>
<td>Tg &lt;0.2</td>
<td>Tg &lt;0.2</td>
<td>Tg &lt;30</td>
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<tr>
<td><strong>Indeterminate</strong></td>
<td>Tg 0.2-1.0</td>
<td>Tg 0.2-5.0</td>
<td>-</td>
</tr>
<tr>
<td><strong>Biochemical Incomplete</strong></td>
<td>Tg &gt;1.0</td>
<td>Tg &gt;5.0</td>
<td>Tg &gt;30</td>
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*Momesso, Tuttle. Endo Metab Clin North American, 2014*

*Momesso, Tuttle JCEM 2016*
## Using Response to Therapy to Guide Clinical Management

<table>
<thead>
<tr>
<th>Response</th>
<th>Expected Outcomes</th>
<th>Clinical Implications</th>
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<tbody>
<tr>
<td>Excellent</td>
<td>1-4% recurrence</td>
<td>Decrease intensity and frequency of follow up and degree of TSH suppression.</td>
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<tr>
<td></td>
<td>&lt;1% death</td>
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<tr>
<td>Biochemical Incomplete</td>
<td>&gt;30% spontaneously resolve</td>
<td>Observation with stable/decreasing Tg and TgAb.</td>
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<tr>
<td></td>
<td>20% develop structural disease</td>
<td>Rising Tg or TgAb should prompt additional investigations.</td>
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<tr>
<td></td>
<td>&lt;1% death</td>
<td></td>
</tr>
<tr>
<td>Structural Incomplete</td>
<td>50-85% will have persistent disease despite additional treatments</td>
<td>Some require additional treatments.</td>
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<tr>
<td></td>
<td>Nearly all deaths arise from this group</td>
<td>Some can be followed with observation depending on the specifics of the individual case.</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>20% develop structural disease</td>
<td>Continued observation with mild TSH suppression.</td>
</tr>
<tr>
<td></td>
<td>&lt;1% death</td>
<td></td>
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Results That Modify Risk

Clinical utility beyond simple disease detection

- Change in serum thyroglobulin over time
- Change in serum Tg antibodies over time
- Results of stimulated thyroglobulin determinations
- Results of follow up Neck US
- Results of RAI scanning
- Other cross sectional imaging
- Results of FDG PET imaging
- Physical examination

Tuttle. Endocrine Practice 2008.
Imaging that Alters Staging

(Other than US)

- **CT with contrast of neck, chest, abdo and head**
  - Structure only
  - Good for deep, mediastinum, retro-tracheal disease
  - Not as good as US for lateral neck

- **Total body iodine imaging**
  - Structure and iodine incorporation functionality

- **FDG PET CT**
  - Structure and metabolic function/aggressiveness
  - Resolution not as good as conventional CT
When Initial Imaging Requires More Than Good Neck US

- Copious central neck metastatic nodes-looking for nodes in deep and US invisible locations
- Potential involvement of vascular structures, nerves, esophagus and trachea
- High grade malignancy- looking for distant mets
- When US is limited by patient issues
Case 1: 85 Year Old Female with Back Pain and Thyroid Nodules

- Thyroid nodules noted 10 months ago by ENT
- Outside US showing R and L large (>3 cm) thyroid nodules
- Back, R hip and R leg pain recently with “partial R hip replacement” 11 years ago
- R thyroid nodule 3 cm, firm and fixed
My Neck Ultrasound

R transverse

R longitudinal
Power Doppler Views

High Transverse

Low Transverse

No malignant lateral or central LN’s seen
Other Important Details

- Anaphylaxis with IV Contrast
- Worsening R hip and back pain
- Cough and “sinus issues”
- R FNA- Pap Ca with high grade features, BRAF +
- TG 0.7 with TG abs >3000

Do we need any more imaging?
What would you order?
FDG-PET CT

- Reserved for imaging non-iodine avid recurrent or persistent disease, but may be useful in unusual initial circumstances with pre-op planning
- PET positive tumors are generally viewed as being more hyper-metabolic and aggressive
- Sometimes FDG-PET helps to guide surgical intervention in patients with nodal recurrences that are small or with potentially threatening location
- Finally, an important means of checking for unsuspected disease in patients in whom you are considering repeat surgery for US or CT demonstrated local or nodal recurrence
- Getting FDG-PET CT pre-approved remains a prior authorization nightmare and may require dedicated staff and physician peer-to-peer consultation on the phone
PET CT- Whole Body
CT Scanning With Contrast

- Use for patients whose initial US evaluations show possible larynx, tracheal or esophageal invasion, carotid sheath invasion, posterior invasion or copious central or lateral nodal disease to identify disease that will be difficult for your surgeon to locate or remove without thoracic surgical or vascular surgical help.

- Use CT to find structural disease in patients with biochemically incomplete, indeterminate or structurally incomplete responses to initial or follow-up therapies.

- Remember that contrast use allows better delineation of proximate vascular structures and improves the resolution of tumor tissue.

- Also remember that recent studies suggest that a 3 month waiting period between contrasted CT and RAI imaging and therapy is often unnecessary.
Case 2: 83 Year Old with Enlarging Goiter

- Presented with several weeks of R neck mass enlargement
- Voice OK
- No Hx thyroid disease
- US performed in office with FNA
- FNA - poorly diff malignant neoplasm with TTF-1 and PAX8 staining
- RET/PTC1 rearrangement
CT with Contrast
MRI Seals the Deal
Surgical Approach vs Palliative XRT

- CT and MRI do not demonstrate clearcut invasion of trachea, carotid or prevertebral fascia
- We opted for an initial combined surgical approach-ENT and Endo Surg team
Case 3: Toxic Goiter with SOB

- 48 yo C4-5 quadriplegic female with thyroid enlargement, hyperthyroidism and SOB
- Huge goiter into chest
- FT4-2.8 TSH<0.01
- Unable to be moved from her wheelchair
- US sub-optimal
Standing US

R Trans

L Trans
CT Scan with Contrast

Transverse Apices

More inferior in Chest
Aberrant Origin of R Carotid Artery from the Aortic Arch With Non-Recurrent Laryngeal Nerve

- On R side surgeon will expect the laryngeal nerve to have a primary origin laterally from the vagus
- May need thoracic surgical help to get this toxic MNG out of the chest
- Note the R carotid passing behind the esophagus from L to R
Radioiodine Imaging

- 2-4 mCi $^{131}$I after 1-2 weeks iodine withdrawal and recombinant TSH alpha (or 3-4 weeks LT4 withdrawal)
- Not necessary with low risk disease
- A useful way to pick up unsuspected lung metastases in intermediate and high risk patients
- Not always necessary with intermediate risk disease but a reasonable way to document that RAI bed ablation or treatment has eliminated iodine sensitive disease
- Important to document post treatment RAI uptake or lack thereof with high risk disease, but be aware that rarely a 2-4 mCi dose can be falsely negative
- In general, when the $^{131}$I total body scan after an RAI treatment shows no uptake, you are done with RAI efficacy (resensitization with various TKI’s is still the holy grail of thyroid nuclear medicine research)
Italian Data Suggests One Month is Enough:

Padovani et al. Thyroid 2012 Sept;22(9):926-930

- Evaluated 25 DTC patients who received iodinated contrast to localize metastases with head and neck CT
- 24 hour urine and spot urine urinary iodine specimens collected baseline, 1 week and 1, 2 and 3 month specimens before and after contrast
- Baseline 24 hour urine iodine 21.8 micrograms/dl (spot urine 26)
- One week post contrast 800 mcg/dl
- One month after contrast 24 hour urine iodine returned to baseline in all pts averaging 19 micrograms/dl (spot urine 20)
- Spot urine iodine determinations correlated with 24 hour urine values
- Bottom line: One month wait is generally enough and spot urine iodine can be checked at one month for ultimate proof if you wish
32 subjects with longitudinal cognitive, mood and functional testing before, during and after thyroid hormone withdrawal

With severe hypothyroidism (median TSH 83) reaction times in braking tests and hand fine motor performance were impaired

Hypothyroidism-related depression was present, typified by vegetative and mood alterations, but lacking reported guilt and lowered self-esteem seen in other types of depression

Braking times increased in hypothyroidism by 8.5%, equivalent to reported effects from a blood alcohol level of 0.082 g/100 mL (above the U.S. legal driving limit)