Follow up of Differentiated Thyroid Carcinoma

Dr Sunil Malla Bujar Barua
Moderator: Prof AK Verma
Introduction: purpose of follow up

• Adequacy of LT4 suppressive therapy
  – to avoid under-replacement or overly aggressive therapy
    • Bone health - osteoporosis
    • Cardiac disease

• Early discovery and treatment of persistent or recurrent loco-regional or distant disease
Criteria for absence of persistent tumor

1) no clinical evidence of tumor,
2) no imaging evidence of tumor
   – no uptake outside thyroid bed on the initial post-treatment WBS
   – if uptake outside thyroid bed had been present, no tumor on recent diagnostic scan and neck USG
3) undetectable serum Tg levels during TSH suppression and stimulation in absence of interfering antibodies

Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer, 2009
FOLLOW-UP: 3 months after ablation

On LT4 therapy: Measurements of

• Serum Tg and anti-Tg antibodies

• T4/FT4 and TSH: to assess the appropriate dose of LT4
FOLLOW-UP: 6-12 MONTHS AFTER ABLATION

- Clinical examination
- Neck USG
- Serum Tg following TSH stimulation, ATG
- \(^{131}\text{I}-\text{total body scan}\)
Follow-up of differentiated thyroid carcinoma after surgery and radioiodine ablation

Options

1. After thyroid hormone withdrawal or after rhTSH?

2. Based on stimulated serum Tg measurement alone or in combination with 131-I WBS?
SERUM Tg DETERMINATION

• Serum Tg is a marker of disease (Van Herle, 1975), not a disease

• Measurement:
  – Functional sensitivity < 1ng/mL. Supersensitive methods (<0.1ng/mL): improved sensitivity but decreased specificity.
  – Search for interferences:
    • Measurement of anti-Tg antibodies.
DETECTABLE Tg LEVEL AFTER THYROID ABLATION.
Eustatia-Rutten, Clin Endocrinol, 61: 61, 2004

The sensitivity of serum Tg determination is improved by 15-20% following TSH stimulation.
rhTSH Testing: Metastatic Cancer Detection Rate

- rhTSH whole-body scan and Tg on thyroid hormone therapy
- rhTSH Tg

Serum Thyroglobulin (ng/mL)

<table>
<thead>
<tr>
<th>Serum Thyroglobulin (ng/mL)</th>
<th>100</th>
<th>90</th>
<th>80</th>
<th>70</th>
<th>60</th>
<th>50</th>
<th>40</th>
<th>30</th>
<th>20</th>
<th>10</th>
<th>0</th>
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</thead>
<tbody>
<tr>
<td>2</td>
<td>100</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>100</td>
<td>97</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>88</td>
<td>80</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Haugen BR, Pacini F, Reiners C, et al: J Clin Endocrinol Metab. 1999;84:3877

Follow up DTC

23/4/2013
### SIGNIFICANCE OF DETECTABLE Tg/TSH AT 1 YEAR

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>83</td>
<td>107</td>
<td>109</td>
<td>92</td>
<td>294</td>
<td>256</td>
</tr>
<tr>
<td>Tg/TSH &gt;1 ng/ml(%)</td>
<td>17</td>
<td>19</td>
<td>17</td>
<td>15</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Disease detected</td>
<td>6</td>
<td>8.4</td>
<td>8.2</td>
<td>3.3</td>
<td>7.8</td>
<td>3.5</td>
</tr>
<tr>
<td>Neck / Distant</td>
<td>4.8/1.2</td>
<td>3.7/4.7</td>
<td>4.6/3.7</td>
<td>3.3/0</td>
<td>6.1/1.7</td>
<td>1.9/1.6</td>
</tr>
</tbody>
</table>

Follow up DTC: 23/4/2013
ELEVATED SERUM Tg LEVELS

• Some months after initial treatment, detectable serum Tg (<5-10ng/mL) may be produced by:
  – irradiated cells that will disappear in 2/3 of cases (Baudin, Pacini, Torlontano, Toubeau), and serum Tg will decrease
  – neoplastic cells that will progress, and serum Tg will increase.

• A control TSH-stimulated Tg obtained some months (or years) later will differentiate these two groups of patients.

• The most relevant parameter is the trend of Tg level, rather than its level.
LOW RISK PATIENTS: UNDETECTABLE STIMULATED SERUM Tg AT 8-12 MONTHS

• False negative results are rare (excellent NPV)
• LT4 dose can be decreased to achieve a low-normal serum TSH level (0.3-2 µU/mL)
• Patients are followed up on a yearly basis on replacement LT4 treatment.
• In the absence of abnormalities, no other testing is warranted.
### ETA and ATA guidelines: LT4 therapy suppressive vs replacement

<table>
<thead>
<tr>
<th>Persistent disease</th>
<th>TSH &lt;0.1 mU/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence of remission</td>
<td></td>
</tr>
<tr>
<td>low risk</td>
<td>replacement</td>
</tr>
<tr>
<td>high risk</td>
<td>suppressive</td>
</tr>
<tr>
<td>duration</td>
<td>3-5 years</td>
</tr>
</tbody>
</table>

**ETA**

**ATA**

**RECOMMENDATION 49**

(a) In patients with persistent disease, the serum TSH should be maintained below 0.1 mU/L indefinitely in the absence of specific contraindications. Recommendation rating: B

(b) In patients who are clinically and biochemically free of disease but who presented with high risk disease, consideration should be given to maintaining TSH-suppressive therapy to achieve serum TSH levels of 0.1–0.5 mU/L for 5–10 years. Recommendation rating: C

(c) In patients free of disease, especially those at low risk for recurrence, the serum TSH may be kept within the low normal range (0.3–2 mU/L). Recommendation rating: B

(d) In patients who have not undergone remnant ablation who are clinically free of disease and have undetectable suppressed serum Tg and normal neck US, the serum TSH may be allowed to rise to the low normal range (0.3–2 mU/L). Recommendation rating: C
Diagnostic 131-Iodine Whole-Body Scan May Be Avoided in Thyroid Cancer Patients Who Have Undetectable Stimulated Serum Tg Levels After Initial Treatment

F. PACINI, M. CAPEZZONE, R. ELISEI, C. CECCARELLI, D. TADDEI, AND A. PINCHERA

J Clin Endocrinol Metab. 2002, 87:1499-501

**Fig. 1.** Results of the first control $^{131}$I WBS after surgery and thyroid ablation in 315 patients with undetectable (<3 ng/ml) serum Tg, off L-T$_4$.

**Fig. 2.** Patients status during follow-up, based on clinical data, neck ultrasound, and the results of the last serum Tg and $^{131}$I WBS during hypothyroidism.
Recombinant Human Thyrotropin-Stimulated Serum Thyroglobulin Combined with Neck Ultrasonography Has the Highest Sensitivity in Monitoring Differentiated Thyroid Carcinoma

J Clin Endocrinol Metab, August 2003, 88(8):3668–3673

F. PACINI, E. MOLINARO, M. G. CASTAGNA, L. AGATE, R. ELISEI, C. CECCARELLI, F. LIPPI, D. TADDEI, L. GRASSO, AND A. PINCHERA

### Accuracy of Tg after rhTSH and neck ultrasound

Positive test = Tg > 1 ng/ml and/or lymph node metastases at ultrasound

<table>
<thead>
<tr>
<th>Tumor Pos</th>
<th>Tumor Neg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Pos</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>TP=96.2%</td>
</tr>
<tr>
<td>Test Neg</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>FN=3.7%</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Total 250</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>rhTSH-Tg (%)</th>
<th>Diagnostic WBS (%)</th>
<th>rhTSH-Tg + US (%)</th>
<th>rhTSH-Tg + WBS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>85.7</td>
<td>4.7</td>
<td>100</td>
<td>85.7</td>
</tr>
<tr>
<td>High risk</td>
<td>84.6</td>
<td>33.3</td>
<td>92.3</td>
<td>100</td>
</tr>
</tbody>
</table>
Meta-analysis of the rate of false negative stimulated Tg and WBS

<table>
<thead>
<tr>
<th>Series</th>
<th>Patients (n)</th>
<th>Stimulus</th>
<th>False neg. Tg (WBS+/Tg-)</th>
<th>False neg. WBS (WBS-/Tg+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robbins</td>
<td>366</td>
<td>rhTSH</td>
<td>54/175 (31%)</td>
<td>75/191 (39%)</td>
</tr>
<tr>
<td>Pacini</td>
<td>315</td>
<td>hypo</td>
<td>0/315 (0%)</td>
<td>Not included</td>
</tr>
<tr>
<td>Cailleux</td>
<td>256</td>
<td>hypo</td>
<td>0/210 (0%)</td>
<td>46/46 (100%)</td>
</tr>
<tr>
<td>Mazzaferrri</td>
<td>107</td>
<td>rhTSH</td>
<td>0/68 (0%)</td>
<td>39/39 (100%)</td>
</tr>
<tr>
<td>Torlontano</td>
<td>99</td>
<td>rhTSH</td>
<td>0/78 (0%)</td>
<td>21/21 (100%)</td>
</tr>
<tr>
<td>Pacini</td>
<td>72</td>
<td>rhTSH</td>
<td>0/41 (0%)</td>
<td>20/31 (64.5%)</td>
</tr>
<tr>
<td>All</td>
<td>1215</td>
<td></td>
<td>54/887 (6.1%)</td>
<td>201/328 (61.2%)</td>
</tr>
</tbody>
</table>

23/4/2013 Follow up DTC
Functional evaluation

• Functional scanning with $I^{131}$ or $I^{123}$ is a widespread form of post operative surveillance

• With oral use of 2-5 mCi of $I^{131}$, neck can be visualized in 24 hrs.

• For WBS- for clearance of the physiologically accumulated dye in the GIT and renal system one should wait for 48-72 hrs.
Functional evaluation

• Stunning effect- over doses of 3 mCi

• Results in reduced uptake in the tissue during subsequent RAI ablation.

• Mechanism doubtful.

• Speculated to induce Follicular cell injury due to
  – Reduced Activity of NIS
  – Increased iodide leak from the cell
  – Both

• $^{123}$I may avoid the stunning effect
  – Expensive
Functional evaluation

- Follicular cell iodide concentration (normal and malignant) is TSH dependent

- Recommended TSH levels for scanning / therapy
  - >30 mIU/L *(ATA & European guidelines)*
  - >25 mIU/L *(AACE/AAES guidelines)*
    - Hormone withdrawal 4-6 weeks
    - Switch to T3(Cytomel) for 2 weeks (25 ugm TDS) and withdraw for 2 weeks
    - rhTSH
rhTSH Protocol

Patient continues levothyroxine therapy without interruption

• Day 1 & 2: rhTSH, 0.9 mg, is administered I/M
• Day 3: 4 mCi of I\textsubscript{131} is administered
• Day 5: WBS is performed
  • Serum TSH and Tg levels are measured before injection and on the day of scanning.

This protocol involves 5 days and is best begun on Monday and concluded on Friday
Summary of Appropriate Patient Preparation for $^{131}$I DWBS

Appropriate patient preparation

- Withdrawal of T₄ for 4–6 wk or of T₃ for 2 wk.
- A strict low-iodine diet ($\leq 50 \mu g$ iodine per day) followed for 7–14 d before $^{131}$I DWBS and continuing throughout period of imaging.
- Avoidance of iodine-containing medications (e.g., iodinated contrast medium, amiodarone, betadine), iodine-rich foods (e.g., kelp), and possible additives of iodine in vitamin and electrolyte supplements.
- $TSH \geq 30$ mIU/L.
- A mild laxative sometimes administered on the evening before $^{131}$I DWBS to simplify image interpretation.
- Information relating to patient’s compliance with low-iodine diet, TSH level, history of thyroid hormone withdrawal, measurement of Tg, history of prior administration of contrast medium or iodine-containing drugs (e.g., amiodarone), menstrual history/pregnancy test, nursing/lactation history, etc.
- Measurement of urinary iodine in doubtful cases to rule out iodine contamination; repeated WBS 4–6 wk after iodine-depletion regimen such as diuretic program.
- Rule out women with pregnancy and breast feeding.

*Ma et al J Nucl Med. 2005 46(9)*
Radio-iodine WBS

• Diseases not visualized on DxWBS may occasionally be visualized on Tx WBS images done after larger, therapeutic amounts of I$^{131}$

  Mazzaferri et al 2001 J Clin Endocrinol Metab 86: 1447-1463
  Paccini et al. European consensus; European J Endocrinology (2006) 154;787-803

• After RAI ablation, subsequent DxWBS have a lower sensitivity and are usually not necessary in the low risk patents who are free from the disease.

  Calileux AF et al 2000 J Clin Endocrinol Metab 85: 175-178
Diagnostic WBS

• After the first RxWBS performed after remnant ablation, low risk patients with negative TSH stimulated Tg and cervical USG do not require routine DxWBS during follow up.

• Dx WBS 6-12 months after remnant ablation is of value in high or intermediate risk of persistent disease but should be done with low dose I\textsuperscript{131} or I\textsuperscript{123}
I$^{131}$ Whole Body Scan
SGPGI protocol

• Thyroid hormone withdrawal 4 weeks
• rhTSH stimulation in selected patients
  • Who cannot tolerate hypothyroidism
  • Affordable

• Saturday
  – Blood samples TSH, Tg levels
• Oral Capsules 3 mCi and 5 mCi.
• DxWBS on Monday
Summary of Reasons for $^{131}$I DWBS$^-$ Tg$^+$

Reasons for $^{131}$I DWBS$^-$ Tg$^+$

- False-positive Tg and true-negative $^{131}$I DWBS
  - Interference of circulating Tg Ab.
  - Benign lesions (possibly containing thyroiditis) of persistent residual thyroid tissue or nonthyroidal tissue producing Tg.

- True-positive Tg and false-negative $^{131}$I DWBS
  - Defective iodine-trapping mechanism such as acquired inactivation mutation of NIS, TPO gene, and pendrin.
  - Dedifferentiation of tumor such that it can still produce Tg but has lost its iodine-trapping ability.
  - Dispersed microscopic metastases too small to be visualized.
  - Improper patient preparation before $^{131}$I DWBS such as stable iodine contamination and inadequate TSH elevation.

Ma et al J Nucl Med. 2005 46(9)
PET scan in follow up

• Fluorine $^{18}$ FDG, $^{18}$F (DOPA) and $^{124}$ I PET are the three radiopharmaceuticals used.

• Indication:
  – Tg +ve , WBS –ve patient
  – Tg –ve with suspicious metastasis

  *N Khan, Oriuchi et al The British Journal of Radiology. 76(2003) 690-695*

• Sensitivity of 75% and specificity of 90%.

  *Fecine E. Eur J Endocrinol 1998; 138: 492-496*

• Flip-flop phenomena
  – Inverse relation between FDG-PET & Radio Iodine
FDG PET in DTC

• TSH can modulate glucose transport in thyroid carcinoma cells by enhancing the GLUT 1 expression.  
  
  Sisson JC, Ackerman RJ et al. JCEM 1993:77:1090-94

• Higher FDG uptake has been reported after TSH stimulation.  
  

Hall et al Arq Bras Enocrinol Metab 2007 51(5); 793-806
Table 2. Results of FDG PET during thyroid stimulating hormone (TSH) stimulation and TSH suppression

<table>
<thead>
<tr>
<th>Authors (reference)</th>
<th>Year</th>
<th>No. of patients</th>
<th>FDG PET</th>
<th>TSH stimulation</th>
<th>TSH suppression</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feine et al [28]</td>
<td>1996</td>
<td>4</td>
<td>4/4</td>
<td>4/4</td>
<td></td>
<td>No significant difference between TSH stimulation and TSH suppression</td>
</tr>
<tr>
<td>Wang et al [40]</td>
<td>1999</td>
<td>4</td>
<td>4/4</td>
<td>4/4</td>
<td></td>
<td>No significant difference between TSH stimulation and TSH suppression</td>
</tr>
<tr>
<td>Moog et al [54]</td>
<td>2000</td>
<td>10</td>
<td>15/17(^a) (88%)</td>
<td>12/17(^a) (70%)</td>
<td></td>
<td>New lesions detected in 3 of 10 patients under TSH stimulation</td>
</tr>
<tr>
<td>Vant Tol et al [55]</td>
<td>2002</td>
<td>8</td>
<td>5/8 (62.5%)</td>
<td>4/8 (50%)</td>
<td></td>
<td>In 1 of 5 patients, lesions detected only on TSH stimulation and in 2 other patients more lesions detected during stimulation</td>
</tr>
<tr>
<td>Petrich et al [56](^b)</td>
<td>2002</td>
<td>7</td>
<td>13/15(^a) (87%)</td>
<td>8/15(^a) (53%)</td>
<td></td>
<td>Histologically verified lesions in 7 patients</td>
</tr>
</tbody>
</table>

Data are expressed as number of patients (sensitivity).
\(^a\)Number of lesions.
\(^b\)In this study, authors used recombinant human thyroid stimulating hormone (rhTSH) and not endogenous TSH as in other studies.

*Khan et al Br J Radiol. 2003; 76: 690-695*
**FDG PET/CT in recurrent DTC**

- **Tg-off value < 10 ng/ml**
  - FDG-PET should not be performed
    - Low sensitivity
    - High risk of false positive results

- **Tg-on values > 100 ng/ml**
  - Resemble bulky disease
  - TSH stimulation in not absolutely necessary

- **Tg values 10-100 ng/ml**
  - FDG-PET should be performed after adequate TSH stimulation (TSH > 20 U/L) for optimal response.
  - TSH stimulation in this subpopulation increases the sensitivity on patient basis and also on lesion basis.

*Stokkel et al Value of FDG-PET in follow-up of differentiated thyroid cancer: review of literature. Quat J of Nucl Med & Mol Imag 2006: 50(1); 78-87*
Protocol for FDG-PET

Halil et al Arq Bras Endocrinol Metab 2007 51(5); 793-806
Other scans

- **Thallium ($^{210}$Tl) scan**
  - Does not require Thyroxin withdrawal
  - Imaging regional nodal disease
  - Less reliable for bony an pulmonary metastases

- **$^{99m}$Tc-Sestamibi scan & $^{99m}$Tc-Tetrfosmin scan**
  - Does not require Thyroxin withdrawal
  - Imaging regional nodal disease
  - Less reliable for bony an pulmonary metastases

  *Nishiyama et al Nucl Med Commun 2000;21: 917-923*

- **$^{111}$In-octreotide scan**
  - Rare expression of somatostatin receptor in DTC
  - Sensitivity of around 82% for distant mets.

  *Haslinguis et al J Endocrinol Invest 2001; 24: 415-422*
  *Stokkel et al J Nucl Med Molc Imag 2004; 31: 950-7*
Role of USG

- Most sensitive for anatomical evaluation of regional LN and the thyroid bed.
- High resolution 7.5-10 MHz transducer
- Tumour deposits of 2 mm in bed and LN can be detected.
- Advantage of guided FNAC
- Disadvantage- Operator dependent
Role of USG

• Highly characteristic USG features of recurrent PTC
  – Intra-lesion calcifications result in multiple tiny bright echoes within the deposits

• Lymph Node
  – Enlarged, rounded,
  – Loss of normally visible hyper-echoic hilar structures

• Ahuja et al Clin Radiol 1995:50;229-231
<table>
<thead>
<tr>
<th>Long axis</th>
<th>All LNs detected on US, n = 103 (%)</th>
<th>Se% (95% CI)</th>
<th>Sp% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 1 cm</td>
<td>66 (74)</td>
<td>68</td>
<td>75</td>
</tr>
<tr>
<td>1 cm or greater</td>
<td>37 (36)</td>
<td>(48–84)</td>
<td>(55–89)</td>
</tr>
</tbody>
</table>

| Short axis | | | |
| ≤ 5 mm | 73 (71) | 61 | 96 |
| > 5 mm | 30 (29) | (41–78) | (82–100) |

| L/S | | | |
| Two or more | 52 (50) | 46 | 64 |
| Less than 2 | 51 (50) | (28–66) | (44–81) |

| Hyperechogenic hylum | | | |
| Present | 11 (11) | 100 | 29 |
| Absent | 92 (89) | (88–100) | (13–49) |

| Hypoechochogenicity | | | |
| No | 39 (48) | 39 | 18 |
| Yes | 64 (62) | (22–59) | (6–37%) |

| Cystic appearance | | | |
| No | 100 (97) | 11 | 100 |
| Yes | 3 (3) | (2–28) | (88–100) |

| Hyperechogenic punctuations | | | |
| Absent | 84 (82) | 46 | 100 |
| Present | 19 (18) | (28–66) | (88–100) |

| Presence of a peripheral vascularization | | | |
| No | 66 (64) | 86 | 82 |
| Yes | 37 (36) | (67–96) | (63–94) |

Lobolleux et al. J Clin Endocrinol Metab 2007; 92(9) 3590-3594
Loboulleux et al. J Clin Endocrinol Metab 2007; 92(9) 3590-3594
Role of CT scan

• Usually done without contrast as iodine loading from the contrast precludes the subsequent use of RAI therapy
  • Hopkins et al. Seminars in USG, CT and MR. 1995: 16;279-295

• Resolution not as good as USG
  • Radiographic density of recurrence same as other soft tissue

• Minimum size detectable is about 0.5-1.0 cm

• More expensive

• Radiation exposure
DETECTION OF NECK RECURRENCES

**STUDY INFORMATION:**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Pacini</th>
<th>Frasoldati</th>
<th>Torlontano</th>
</tr>
</thead>
<tbody>
<tr>
<td>N₁/Pts</td>
<td>27/340</td>
<td>51/494</td>
<td>38/456</td>
</tr>
</tbody>
</table>

**METHOD:**

<table>
<thead>
<tr>
<th></th>
<th>Pacini</th>
<th>Frasoldati</th>
<th>Torlontano</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tg/TSH</td>
<td>85% (rhTSH)</td>
<td>57% (WD)</td>
<td>82% (WD)</td>
</tr>
<tr>
<td>¹³¹I TBS</td>
<td>21%</td>
<td>45%</td>
<td>34%</td>
</tr>
<tr>
<td>Neck US</td>
<td>70%</td>
<td>94%</td>
<td>100%</td>
</tr>
<tr>
<td>Neck US+Tg/TSH</td>
<td>96%</td>
<td>99.5%</td>
<td>100%</td>
</tr>
</tbody>
</table>

*Combination of neck US and Tg/TSH determination.*
Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer

The American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer

David S. Cooper, M.D.¹ (Chair)*, Gerard M. Doherty, M.D.,² Bryan R. Haugen, M.D.,³ Richard T. Kloos, M.D.,⁴ Stephanie L. Lee, M.D., Ph.D.,⁵ Susan J. Mandel, M.D., M.P.H.,⁶ Ernest L. Mazzaferrri, M.D.,⁷ Bryan McIver, M.D., Ph.D.,⁸ Furio Pacini, M.D.,⁹ Martin Schlumberger, M.D.,¹⁰ Steven I. Sherman, M.D.,¹¹ David L. Steward, M.D.,¹² and R. Michael Tuttle, M.D.¹³
ALGORITHM FOR REMNANT ABLATION:
Initial Follow-Up in Patients with Differentiated Thyroid Carcinoma in Whom Remnant Ablation is Indicated
One to Three Months after Surgery

Final Surgery is a Total or Near-Total Thyroidectomy

No

Completion Thyroidectomy Prior to Ablation (R29, R30)

Yes

Known Residual Macroscopic Tumor?

Unknown

US to Assess Remnant

No

Suspected or Known Residual Disease

Yes

Consider Pretherapy Diagnostic WBS Using rhTSH or THW if Expected to Change Management (R35)

No

Technetium Tc 99m or THW 30-100 mCi
(R32, R36)

Follow-Up 6-12 Months with TSH-Stimulated DxWBS, Tg and Neck US

RxWBS 5-8 Days Post 131I

No

Yes

Uptake Only in Thyroid Bed

Uptake Outside Thyroid Bed

Further Testing and/or Treatment as Indicated

Follow-up
FIG. 5. Considerations for empiric treatment with radioiodine.
Follow up of papillary micro-carcinoma

• Patients undergoing hemi-thyroidectomy for carcinomas < 1cm who have a well- differentiated histology.
• Radio-iodine therapy can be withheld for these patients
• These patients should be followed up annually with clinical examination and neck USG.
• Fine needle aspiration should be performed if new lesions are detected.
• Because the potential of microscopic DTC foci to be present in the contra-lateral lobe, long term thyroxin therapy is recommended to maintain TSH levels at the lower limit of normal.

Current concepts in the follow-up of patients with DTC. Banbassat CA IMAJ July 2007 (9) 2007
Redifferentiation therapy

- Dedifferentiation makes thyroid cancer difficult to treat with conventional agents
- Retinoids, Aromatic fatty acids, PPAR gamma agonists, histone deacetylase inhibitors, HMG CoA reductase inhibitors
- Increases expression of thyroid specific differentiated genes.
- Response rates of 38-50% have been described
  - J.W.Park et al SCNA 84; 2004 921-943
Gene Therapy

• Transfer of nucleic acid into genes to replace defective genes.

• Differentiation related genes are TTF-1, p53, PAX 8, NIS genes

• TTF s regulate Tg, TPO, TSH-R, & NIS gene expression

• Multigene transfection and combination of gene therapy with redifferentiation agents are needed for development of effective gene therapy.

J.W. Park et al SCNA 84; 2004 921-943
Leslie J. DeGroot; Rusheng Zhang
Current Drug Targets - Immune, Endocrine & Metabolic Disorders,
September 2004, vol. 4, no. 3, pp. 235-244(10)
Chemotherapy

• Response rates to alkylating agents 10-15%. (5FU, Methotrexate)
• Response rate to Bleomycin and Adriamycin 20-33%.
• Indicated in
  – Symptomatic & advancing tumors, not responding to Radio-iodine
  – Not amenable to external RT

Radiotherapy

- Painful osseous metastasis can be palliated
- Bone mets not amenable to surgery
  - Base of skull, Vertebral column.
- No significant role apart from external RT for gross residual disease in neck

Radiotherapy

- External RT can complement I 131 therapy in inoperable metastases.
- Rapid pain relief
- 30 Gy over 15 days

Schlumberger, F Pacini. Thyroid Tumors: Chapter 9, 167-180: 1999
## Distant Metastasis: Results

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Remission %</th>
<th>10yr survival</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lung Mets</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal X ray</td>
<td>73</td>
<td>83</td>
<td>91</td>
</tr>
<tr>
<td>Micronodules</td>
<td>64</td>
<td>53</td>
<td>63</td>
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<tr>
<td>Macronodules</td>
<td>77</td>
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<tr>
<td><strong>Bone Mets</strong></td>
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<tr>
<td>Single</td>
<td>37</td>
<td>22</td>
<td>21</td>
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<tr>
<td>Multiple</td>
<td>71</td>
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<tr>
<td><strong>Lung and Bone Mets</strong></td>
<td>72</td>
<td>07</td>
<td>13</td>
</tr>
</tbody>
</table>

Schlumberger, F Pacini. Thyroid Tumors: Chapter 9, 167-180: 1999. Institute Gustave-Roussy Data
Factors influencing survival

• Age
• Histology
• I 131 uptake
• Extent of Disease
  • Poor in macronodular lung metastasis
  • Multiple bone Metastasis

Survival – Our experience

Overall survival =

Non metastatic – 5yr SR (98%); 10 yr SR (89%)
Metastatic – 5yr SR (65%); 10 yr SR (38%)
Department Publications:


