Evaluation and Surgical Management of Recurrent/Persistent DTC and MTC; and Advancing, Structurally Invasive Thyroid

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Recurrent Thyroid Cancer:

- Most of the time - initial advance disease
- Unsatisfactory Resection
- Aggressive histology
- Needs multidisciplinary approach
- Surgery - High risk of recurrence and poor salvage
- Increased surgical complications
- Increased mortality
Paradigm Shift in Detection of Recurrent Thyroid Cancer

- RAI Scan
- CT, MRI
- Thyroglobulin
- Ultrasound & Ultrasound-guided FNA
- FDG – PET
Recurrent Thyroid Cancer

- Local Recurrence (Thyroid Bed)
- Nodal Recurrence
- Distant Mets (Lungs, bone, brain)
Recurrent Thyroid Cancer

Central Compartment
- Thyroid Bed
- Central Compartment Nodes

Lateral Neck
- Lateral Neck
- Retropharyngeal, and parapharyngeal nodes

Distant

Recurrence of Thyroid, local recurrence. Likely to include visceral structures
- Level VI, VII
Recurrent Thyroid Cancer

Don’t Miss the Boat!
Thyroid Cancer

Good: 20 yr survival 99%
Low: 20 yr survival 85%
Bad: 20 yr survival 57%
Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer

Estimating Risk of Recurrence
2009 Update

Low Risk
Classic PTC
No local or distant mets
Complete resection
No tumor invasion
No vascular invasion
If given, no RAI uptake outside TB

Intermediate Risk
Microscopic ETE
Cervical LN mets
Aggressive Histology
Vascular invasion

High Risk
Macroscopic gross ETE
Incomplete tumor resection
Distant Mets
Inappropriate Tg elevation
Recurrent Thyroid Cancer

Good, Bad, Ugly

Biochemical  Imaging  Clinical
Recurrent Thyroid Cancer

Good, Bad, Ugly

Lateral Neck

Central Neck

Visceral Involvement
Risk Factors Associated with Recurrent Disease

- Extrathyroidal extension
- Lymph node Metastasis
- Macroscopic Local invasion
- Aggressive histologic subtypes
- Older age
- BRAF mutation
- Thyroglobulin doubling time (Miyauchi)
How to Avoid or Predict?

- Fixed mass to the central compartment
- Rapidly growing tumor
- Preop vocal cords evaluation
- Older patient
- FNA – Poorly differentiated cancer
- CT scan (Imaging)
- Preop endoscopy
Differentiated Thyroid Cancer 1930-1985

**SURVIVAL: Extrathyroidal Extension**

- **No extension**\(n=952\)
- **Extension**\(n=86\)

\[\text{TIME (years)}\]

- **T1-3**: 95% survival
- **T4**: 59% survival
- **Extension**: 34% survival

\[p < 0.001\]

**MSKCC-1038 pts. (DOD)**
Intraop Decisions

Principles of Management of Recurrent Thyroid Cancer

All gross tumor should be removed
Preserve functioning structures
Preserve vital structures
Balance between tumor control and best functional results
Use adjuvant treatments - RAI, Ext RT
Principles of Management of Recurrent Thyroid Cancer

1) Understand the biology of recurrent cancer
2) Time of recurrence
3) Review the pathology
4) Evaluate exact extent of tumor
   - Imaging
5) Evaluate vocal cord function
6) Be prepared to handle intra-op nerve, trachea, etc.
7) First do no harm, ‘Primum non Nocere’
8) Observation is also a good approach on select patients
9) Let the punishment fit the crime
Recurrent Thyroid Cancer

- Send to tertiary care center
- Multidisciplinary approach
Intraop Decisions

Trachea

Preop evaluation
Endoscopy
All gross tumor to be removed
Shave off
Tracheal window & reconstruction
Segmental resection & primary anastomosis
Resection of cricoid & subglottic region
The staging system for papillary carcinoma of the thyroid invading the trachea, based on the histologic extent of invasion.
External-Beam Radiotherapy

**Memorial Sloan-Kettering 2009**

<table>
<thead>
<tr>
<th>N</th>
<th>Histologic Types</th>
<th>2-yr and 4-yr Locoregional control</th>
<th>Overall Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>76</td>
<td>64 DTC, 12 MTC</td>
<td>86% 72%</td>
<td>74/55%</td>
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<tr>
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<td>84% T4</td>
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**MD Anderson Cancer Center 2009**

<table>
<thead>
<tr>
<th>N</th>
<th>Histologic Types</th>
<th>4-yr Locoregional control</th>
<th>Local Failure</th>
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</thead>
<tbody>
<tr>
<td>131</td>
<td>DTC</td>
<td>79%</td>
<td>16 (25%)</td>
</tr>
<tr>
<td></td>
<td>96% extrathyroidal extension</td>
<td></td>
<td>4/12 Tall-cell (33%)</td>
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</tbody>
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External-Beam Radiotherapy

- Patients with high-risk disease EB-XRT provides durable locoregional disease control
- IMRT associated with less frequent toxicity
<table>
<thead>
<tr>
<th>Lower Risk (&lt;5% risk of recurrence):</th>
<th>Higher Risk (&gt;20% risk of recurrence):</th>
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</thead>
<tbody>
<tr>
<td>Micro Metastases (&lt;2mm)</td>
<td>LM metastases identified by US or palpation</td>
</tr>
<tr>
<td>3 or fewer small metastatic LN’s</td>
<td>More than 5 metastatic LN’s</td>
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<tr>
<td></td>
<td>Extra nodal extension</td>
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<tr>
<td></td>
<td>Metastatic LN larger than 3cm</td>
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</table>
Elective ND
Radical ND

U/S & U/S FNA
No clinical finding
Rising TGB

Thyroglobulin follow-up

Clinical follow-up

Central compartment ND

No prognostic implication

Only therapeutic ND
Recurrent Central Compartment Disease

A Scientific Reality

OR

Iatrogenic Problem

Victim of Technology

A Balance Between Risk of the Disease & Risk of the Treatment
Patients with multiple positive neck nodes from papillary ca may have additional paratracheal, sup mediastinal, or lateral neck nodes, and may remain with persistent mild hyperthyroglobulinemia. We may not achieve biochemical cure.
How to Treat?

• Treatment – Local Recurrence
  – **Surgery**
  – $^{131}$I therapy
  – TSH suppression
  – External beam radiotherapy
  – Ethanol ablation
  – Cyber Knife
  – Stereotactic Body radiotherapy
  – Radiofrequency Ablation
  – Chemo-Embolization
  – Targeted Therapy- Antiangiogenic therapy
Complications

• RLN Injury- Role of nerve monitor
• Parathyroid Issues- Parathyroid autotransplantation
• Accessory nerve injury
• Horner’s Syndrome
• Chyle Leak- Seroma
• Tracheal and Esophageal Injury
• Inability to remove all gross tumor
Continuum of Papillary Thyroid Cancer

- Classic PTC
- Tall Cell Variant
- Moderately Differentiated
- Poorly Differentiated
- Anaplastic

FDG PET Positivity

RAI Avidity
Treatment Options for Metastatic Disease

- Radioactive Iodine
- External Beam Irradiation
- Surgical Metastasectomy
- Arterial Embolization
- Traditional Chemotherapy
- Novel Therapies
Surgery and External Beam Irradiation

58 year old male with wide spread metastatic Hürthle Cell Carcinoma
Arterial Embolization without Surgery

74 year old female with metastatic papillary thyroid cancer

Left superior gluteal artery embolization

Prior to Embolization  Mid-Embolization  After Embolization

100 – 900 micron embospheres
500 micron polyvinyl alcohol particles
Molecular Abnormalities in the Primary Tumor

MAP Kinase Pathway

70% of all PTC have mutations in either the RET/PTC, RAS or BRAF

Proliferation Growth

RET/PTC

GTP

RAS

GDP

BRAF

MEK

ERK

PI3K

AKT

MTOR

c-jun
c-fos
Phase 2 Clinical Trials

Adapted from Tuttle RM. Clinical Thyroidology 2009

Paclitaxel (ATC): 5 Progression, 47 Stable, 47 Complete
Celecoxib (DTC): 5% Stable, 47 Complete
Thalidomide (DTC/ATC): 38% Stable, 3 Partial, 6 Complete
Vorinostat (DTC/MTC): 32% Stable, 6 Complete
Adria/IF alpha (DTC/ATC): 56% Stable, 6 Complete
Gefitinib (DTC/ATC/MTC): 81% Stable, 14 Complete
Motesanib (DTC): 63% Stable, 14 Complete
Axitinib (DTC/MTC/ATC): 67% Stable, 40% Complete
Sorafenib (DTC/ATC/MTC): 51% Stable, 40% Complete
Sorafenib (DTC/ATC): 64% Stable, 28% Complete
Pazopanib (DTC): 46% Stable, 49% Complete

The Goals & Principles of Management of Recurrent Thyroid Cancer

- Achieve Best Cure Rate
- Adhere to the Oncologic Principles
- Minimized the Morbidity
- Adjuvant Therapy
- Follow-Up Strategy
- RAI
- Ext. RT
- Chemotherapy
- Targeted Therapy
Recurrent Thyroid Cancer

Don’t Miss the Boat!