Follow-up of the Head & Neck Cancer Patient

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Follow-up of the Head & Neck Cancer Patient

Topics for Discussion

- Current Practice and Recommendations
- Benefits of Tumor Surveillance
- Patterns of Treatment Failure
- Modalities for Tumor Surveillance
- Health Maintenance
  - Hypothyroidism/Carotid Stenosis/Dental
  - QOL Issues-Rehabilitation/Psychological
- Risk Counseling
- Future Directions
The Head and Neck Team

- Head and neck surgery
- Subspecialty consultants
  - Neurootology, neurosurgery, vascular surgery, plastic surgery, oral maxillofacial surgery, general surgery, prosthodontics, oculoplastic surgery, surgical pathology, interventional neuroradiology, and anesthesiology
- Radiation oncology
- Medical oncology
- Internal medicine
- Head and neck nursing
- Speech and swallowing rehabilitation
- Audiology
- Social work
- Physical or occupational therapy
- Psychiatry
- Religious counseling
- Nutrition
Current Guidelines

Rationale for Follow-up

- Detecting of treatment failure
  - Recurrence/2nd Primary/DM
- Evaluation of treatment results
- Detecting/Treating complications
  - Hypothyroidism/Carotid Stenosis etc.
- Health Maintenance
  - Rehab/Risk Counseling/QOL
- Emotional support
  - Psychological, Disability

Recommended Follow-up

<table>
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<tr>
<th>Posttreatment Year</th>
<th>Office Visit Examination Frequency</th>
<th>No. of Visits/Year</th>
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<tbody>
<tr>
<td>1</td>
<td>Every 1-3 mo</td>
<td>4-12</td>
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<td>3-6</td>
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* ASHNS indicates American Society for Head and Neck Surgery;
SHNS, Society of Head and Neck Surgery. Data from Clinical Practice Guidelines for the Diagnosis and Management of Cancer of the Head and Neck. Recommendations are the same for all TNM stages. Sites included oral cavity, lower lip, supraglottic larynx, glottic larynx, hypopharynx, nasopharynx, neck metastases with unknown primary, parapharyngeal, ear, and temporal bone. Tests performed annually are chest radiography, liver enzymes measurement, and thyroid function tests (if radiation therapy was given to the lower part of the neck).
Current Recommendations

- Existing Surveillance Schemes
  - 12 Generic
  - 19 Site Specific
  - Little Variance
  - LFT/TFT/CT Head/Neck/MRI
  - Cost- $1198-$7597 5 yrs.

- Site Specific
  - Lx- >CXR
  - NP- >CT/MRI/LFTs
  - HP- >Ba Swallow
    - Virgo, 1998

Table 5. Other Tests and Examinations Used by ASHNS Respondents*

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Follow-up Evaluations Used
Current Practice

- Determination of F/U Scheme
  - Evidenced Based
  - Consensus Guidelines
  - Tradition- Training/Institutional
  - Outside Issues- Payors etc.
- 30% Modify F/U by Stage
  - Johnson,1998
- No difference with age
  - Clark,1999
- Consensus by Default
  - Marchant,1993

Office Visit- First Year
Current Practice

Office Visit – Second Year

- 3 months: 31.6%
- 2 months: 56.1%
- 1 month: 3.0%
- 4 months: 9.3%

Fig 2. How often do you see the patient once treatment is complete? Second year: ■, 1 month; □, 2 months; □, 3 months; ■, 4 months.

Third to Fifth Year

- 6 months: 46.3%
- 4 months: 46.3%
- 2 months: 2.2%
- PRN: 0.40%

Fig 3. How often do you see the patient once treatment is complete? Third to fifth year: ■, 2 months; □, 4 months; □, 6 months; ■, PRN.
Current Practice

Chest X-ray

For symptoms only 14.3%

6 months 25.0%

1 year 60.7%

Fig 5. When do you perform a CXR? ■, for symptoms only; □, 6 months; ▼, 1 year.

Head Neck CT

For symptoms only 81.4%

3 months 1.5%

As base line* 8.0%

6 months 4.2%

1 year 4.9%

Fig 7. How often do you perform a CT scan of the head and neck? □, 3 months; ■, 6 months; ▼, 1 year; □, for symptoms only; ▼, as baseline. *Responders performing baseline CT increases to 15.2% when the neck is radiated.
Current Practice

For symptoms only
95.5%

Barium Swallow

Liver Function Tests

Figure 4. Use of liver function tests by American Society for Head and Neck Surgery respondents (group 4), given as percentage practicing within or varying from Task Force guidelines. Data shown are for stage III/IV only (stages I and II were similar). Overuse decreases and underuse increases with advancing postoperative year.
Benefits Of Tumor Surveillance: Salvage

Neck Recurrence

Carotid Reconstruction/ Brachytherapy
Benefits Of Tumor Surveillance

- Routine Vs. PRN Follow-up
  - Increased Survival for Salvage
    - 58 mos. Vs. 32 mos.
  - Increased Tx for Cure
    - 64% Vs. 40%
- Complaints/Symptoms
  - 1/3 Symptomatic pts – CA
  - Explore all complaints
    (deVisscher, 1994)

“Frog in the Throat”
Benefits Of Tumor Surveillance: Patient and Surgeon Perspectives

- **Surgeon-**
  - Perceived survival benefit
    - 70% - Stage I
    - 40% - Stage III-IV
    - (Virgo, 1998)

- **Patient-**
  - Not Anxious - 69%
  - 85% will self-refer
  - 10% - c/o not reassured
    - (deVisscher, 1994)

Neck Mass
Benefits Of Tumor Surveillance: Salvage

• Ideal Salvage Candidates-
  – Stage I-II Primary
  – Recur >6 mos. From Primary Treatment
    – Swartz,1999
  – Surgically Resectable Recurrence
    • Lx-48% > OC-43% > OP-21%
      – Glottic - 61%
      – Supraglottic - 34%
        • deVisscher,1994
Benefits Of Tumor Surveillance: Salvage

Survival after Salvage Surgery by Site

Fig. 2. Cancer-specific mortality by recurrent site.
**Benefits Of Tumor Surveillance: Salvage**

**Survival by Stage/ Site  Goodwin, 2000**

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**TABLE IV.**

Two-Year Disease-Free Survival After Salvage Surgery.

<table>
<thead>
<tr>
<th>Stage (P = .0005)</th>
<th>Site (P = .0645)</th>
<th>Meta-Analysis Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>73%</td>
<td>Pharynx</td>
<td>28%*</td>
</tr>
<tr>
<td>67%*</td>
<td>Oral cavity</td>
<td>47%*</td>
</tr>
<tr>
<td>33%*</td>
<td>Larynx</td>
<td>58%</td>
</tr>
<tr>
<td>22%</td>
<td>Neck</td>
<td>25%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>44%</td>
</tr>
</tbody>
</table>

*Maximum percent, since follow-up does not cover 2 full years for some patients.
Benefits Of Tumor Surveillance: Salvage

Salvage by Specific Sites

**Larynx**

**After XRT**
- HemiLx-75% (Endoscopic)
- SGL- less salvageable
- 65% T1-2 – Total Laryngectomy

**After Conservation Surgery**
- HemiLx- 2/3
- SGL- Much less salvageable

**OC- 25-50%**
- Tonsil- depends on site-Composite
- BOT- Need for laryngectomy?

**OP**
- Neck-RND
- Primary- Re-XRT, Nasopharyngectomy

**NP**
- Skull Base- dismal
Benefits Of Tumor Surveillance: Salvage

Recurrent Tumor

Resection and Reconstruction
Treatment Failure

Mode of Failure
- Primary Recurrence
- Second Primary
- Distant Metastasis

Patterns of Failure
- Occurrence Rates
- Time Course
- Risk Factors

FIGURE 2. Treatment failure occurred in 68 of 137 determinate patients (50%). This excludes 5 “lost,” 2 who died of other causes within 3 years, and 6 dead of disease without information about treatment failure. Local recurrence was documented in a total of 33 patients.
Treatment Failure: Recurrence

**Recurrence Rate**
- 50% relapse in 1\textsuperscript{st} year
- 85% relapse by 2\textsuperscript{nd} year
- <5% after 3 yrs.
- Most Ca Deaths by 3 years

**Timing Vs. Prognosis**
- (Stell, 1991)
- 5 yr Survival vs. Recurrence
  - 0-1yr- 19%
  - 1-2yr- 22%
  - 2-4yr- 26%
  - >4- 48%

Survival vs. Time for Stage III & IV
Treatment Failure: Recurrence

- **Pertinent Risk Factors for Recurrence**
  - Increased Stage
  - Grade -> poor diff
  - Delay in XRT > 6 weeks
  - Perineural Invasion
    - >LR recurrence not DM
    - >Mortality
    - >Nodal Metastasis
    - Vasc/Lymph Invasion +/-
      - Fagan, 2000

- **Tumor Markers**
  - oncogene CyclinD1
  - P53 mutations/over expression/antibodies
Treatment Failure: Recurrence

- Margin Status
- >1.0 cm. – improved survival
  - Bradford, 1996
- Local Recurrence-
  - 2X if + margin (36% vs. 18%)
- Post-op XRT-
  - Trend to lower recurrence
  - Not = negative margins
    - Loree & Strong, 1990
Treatment Failure: Second Primary

- **Occurrence Rate**-
  - 3-7 %/year
  - 14.2% during follow up (Haughey, 1992)
  - Up to 21% / 8 yrs. (Roberts, 1990)
    - Most metachronous
    - Constant Risk for life
    - >3 yrs. = most common cause of failure

- **Time Course**-
  - Mean to occurrence = 4 yrs.
  - Depends on Follow-up duration
    - ½ occurred > 5 yrs. – with 30 yr. follow-up
      - (Haughey, 1992)
# Treatment Failure: Second Primary

## Table 1. Distribution of second neoplasms in relation to the location of the index tumor.

<table>
<thead>
<tr>
<th></th>
<th>Lungs</th>
<th>Esophagus</th>
<th>Head and neck</th>
<th>Others</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral cavity (n = 215)</td>
<td>4</td>
<td>2</td>
<td>24</td>
<td>7</td>
<td>37 (17%)</td>
</tr>
<tr>
<td>Oropharynx (n = 369)</td>
<td>12</td>
<td>9</td>
<td>36</td>
<td>9</td>
<td>66 (18%)</td>
</tr>
<tr>
<td>Hypopharynx (n = 187)</td>
<td>13</td>
<td>3</td>
<td>12</td>
<td>2</td>
<td>30 (16%)</td>
</tr>
<tr>
<td>Larynx (n = 1074)</td>
<td>66</td>
<td>13</td>
<td>48</td>
<td>42</td>
<td>169 (16%)</td>
</tr>
<tr>
<td>Supraglottis (n = 439)</td>
<td>35</td>
<td>5</td>
<td>18</td>
<td>19</td>
<td>77 (18%)</td>
</tr>
<tr>
<td>Glottis* (n = 635)</td>
<td>31</td>
<td>8</td>
<td>30</td>
<td>23</td>
<td>92 (14%)</td>
</tr>
<tr>
<td>Rhinopharynx (n = 106)</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>8 (8%)</td>
</tr>
<tr>
<td>Others† (n = 58)</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>5 (7%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>100 (32%)</td>
<td>27 (9%)</td>
<td>122 (39%)</td>
<td>66 (20%)</td>
<td>315</td>
</tr>
</tbody>
</table>

*Grouping glottis, transglottis and subglottis
†Including ear, nose, paranasal sinuses and salivary glands

## Distribution of 2nd Primaries by Index Site
Treatment Failure: Second Primary

Other Risk Factors
Stage- Early stage at > risk?
XRT unclear / difficult to determine
Continued Smoking
    Marchant, 1993
Older > Younger Increased Risk
    Vershuur, 1999
Lung Ca: 7-10X risk of General Population
Family risk of 2nd Primary patients
Treatment Failure:
Second Primary

- **Prognosis for 2\textsuperscript{nd} Primary**
  - 5 yr. Survival
    - H&N(49%)
    - Lung(15%)
    - Esophagus(0%)
    (Leon, et al., 1999)

- **Reasons for Poor Outcome**
  - Poor Prognosis of Esoph & Lung
  - Late Diagnosis
    - Inadequate surveillance?
      - Not usually
  - Previous Treatment
    - Precludes further Tx

Lung Cancer
Treatment Failure: Distant Metastasis

70% Relapse above the Clavicle
Same Timeframe as LRR
  50%-9mos.; 80%-2yrs.
    (Merino, 1977)
  15 mos after Primary Tx
    (Aijaz, 1997)
Autopsy Studies- 50-60%
    (Zbaren et al., 1987)
Survival- dismal

Multiple Lung Metastasis
Treatment Failure: Distant Metastasis

- Risk Factors for DM
  - Nodal Status
    - >3 nodes/ Bilateral/ >6cm.
  - Low Jugular/ 2\textsuperscript{nd} Primary
  - ECS -up to 1/3
    - (deBree,2000)

- Recurrence- (Papac,1984)
  - 80-90% with LRR

- Distribution: Lung\textgreater\textgreater Liver\textgreater\textgreater Bone
  - Few liver and bone without lung
  - Other mediastinum, adrenal, brain less common

- Primary Site in DM Patients
  - OC/OP>HP>Lx>NP/Sinus (deBree,2000)
## Treatment Failure: Distant Metastasis

### TABLE I.
Cumulative Distant Metastases.

<table>
<thead>
<tr>
<th>Stage</th>
<th>T Stage</th>
<th>N Stage</th>
<th>Pathologic Grade</th>
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<tr>
<td>I</td>
<td>2.5%</td>
<td>11.4%</td>
<td>N0 20.3% Well</td>
</tr>
<tr>
<td>II</td>
<td>3.8%</td>
<td>17.7%</td>
<td>N1 12.7% Mod</td>
</tr>
<tr>
<td>III</td>
<td>12.7%</td>
<td>26.6%</td>
<td>N2 31.6% Poor</td>
</tr>
<tr>
<td>IV</td>
<td>74.7%</td>
<td>38.0%</td>
<td>N3 27.8% Un</td>
</tr>
<tr>
<td>Un</td>
<td>6.3%</td>
<td>6.3%</td>
<td>NX 7.6%</td>
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Well = well differentiated; Mod = moderately differentiated; Poor = poorly differentiated; Un = unknown.
Treatment Failure: Distant Metastasis

Skin Metastasis
6 mos. from Initial Tx
90% DOD @3 mos.
Increased Risk
>2 nodes and ECS
Neck and Face- 70%
31% with no other mets
Excision may increase survival
2 vs. 20 months

Skin Metastasis
Modalities for Tumor Surveillance

Laboratory Studies
- Liver Function Tests
- Alkaline Phosphatase
- Tumor Markers

Imaging Studies
- CXR/CT/MRI/PET

Procedures
- FNA Biopsy
- Operative Endoscopy

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Modalities for Tumor Surveillance: Lab Tests

- **Bone Metastasis Detection**
  - AP: Sensitivity- 20%/ Specificity-98%
  - Calcium: Non Specific
    - Hypercalcemia in HNCA- 25% Bone Mets
- **Liver Metastasis Detection**
  - LFTs: Sensitivity-81%/ Specificity-50%
  - Etoh abuse renders LFTs unhelpful
- **Chest CT**
  - Detects Bone and Liver mets
  - Very Sensitive- bone mets spine/ribs common
Modalities for Tumor Surveillance: CXR

- **Yearly CXR-** fails to detect 65% Lung Ca
  - Present in between CXRs with tumor
    - Shah, 2000
  - Poor Screening Tool? - few Ca detected early

- **Sensitivity-** 50%  Specificity- 94%
  - Troell, 1995

- **Slight increase in survival frequent CXR**
  - 4-6 mos. (lead time bias?)
    - Egelen, 1991

- **75% of 2nd Lung Ca found in 3 years**

- **Spiral CT-** very sensitive but less specific
Modalities for Tumor Surveillance: CT/MRI

- CT/MRI – Gold Standard
- CT:
  - Sensitivity-70%  Specificity-59%
- MRI:
  - Sensitivity-75%  Specificity-80
    - Lapala,2000
- MRI superior to CT:
  - Cartilage Invasion
  - Perineural Invasion
  - Soft Tissue Differentiation
  - Defines tumor margins

- Baseline CT/MRI
  - High Recurrence Risk
  - Post Tx Pain
  - Flap reconstruction
  - Difficult anatomy

- Obtain > 3mos. Post-Tx
Modalities for Tumor Surveillance: CT

CT Post Surgery/XRT

Occult Tumor
Modalities for Tumor Surveillance: PET

- High Cost /Limited Availability
- Utility still being Assessed
- Sensitivity- 86%  Specificity- 93%
  - Farber, 1999
- Must be >4 mos post XRT
  - McGuirt, 1997
- PET Advantages
  - Radionecrosis vs. Tumor
  - CT- suspicious/ PET- negative
  - CT- negative/ PET- positive
Modalities for Tumor Surveillance: PET

Fig. 3. Example of image fusion in a patient with recurrent squamous cell carcinoma of the soft palate. A. FDG-PET images demonstrating the recurrent tumor (black arrow): the activity posterior and cephalad to the lesion corresponds to normal cerebellar metabolic activity. B. Gadolinium-enhanced, T1-weighted magnetic resonance imaging (MRI) of corresponding transaxial slice; the MRI result was considered suspect but inconclusive because of extensive prior surgery, flap reconstruction, and irradiation. The arrow identifies the area of suspicion. C. Fused MRI-PET images. This technique, difficult to implement in routine practice, allows precise anatomic localization of the abnormal PET findings.
Modalities for Tumor Surveillance: FNA

- **FNA in Post Tx Patients**
  - Very good test- minimally invasive
  - 92% or better Accuracy
  - False Positives uncommon
    - Experienced Cytopathologists
    - Adequate Communication
      - Abrams, 1993

- **CT/US Guided FNA**
  - Very Reliable
  - Experience Dependant
Modalities for Tumor Surveillance: Follow-up Endoscopy

Use of Panendoscopy

Difficult Exam
Health Maintenance: Hypothyroidism

- 10-40% Hypothyroidism
- 12% Non-Lx Surgery
- 14% XRT only
- 61% TL/Hemithyroid/XRT
- 83% Present in 12 mos
  - Mean time 8.2 mos
- Recommend TSH
  - Preop- 6%
  - 3 mos after Tx
  - Q6 mos X 2 yrs
    - (Sinard, 2000)
Health Maintenance: Hypothyroidism

Detection of posttreatment hypothyroidism. TSH indicates thyrotropin. Asterisks indicate that either option 1 or option 2 is acceptable.
Health Maintenance: Carotid Stenosis

Accelerated Arteriosclerosis
  Atypical Locations
  Increased Severity
  Post XRT
  Surgery +/-
Smoking >> Increases Risk
¼ - NPC @5 yrs.
  Cheng, 2000
Carotid Endarterectomy - possible
  2X wound complications

Carotid Stenosis
Health Maintenance: Quality of Life

- Depression
  - 40% -6 mos. to 3 yrs. Post treatment
    • Campbell, 2000
  - Pain Control- Most important
- Suicide
  - 2-10X Suicide Risk
  - 50% Male CA pt. Suicides- Lung/Lx/Tongue
    • Henderson, 1997
- Disability
  - 31.1% Disabled after Tx
  - Combined Tx- Disability 6X
    • Terrell, 2000
- Other- Speech/Swallowing/PT Support
Health Maintenance: Dental

Xerostomia vs. Time

Prosthetics
Health Maintenance: Dental

**Osteoradionecrosis**
- OC/OP Radiation
- 3% Spontaneous
- 3% Post Extraction
- 10% Tumor
- Brachytherapy – 3X rate
- Tx- HBO/Long Term Care

**Dentures**
- New Dentures
- Limit Use
- Wait 6 mos. After XRT

Mandibular ORN
Risk Counseling: Smoking

- 82% Smoke at Presentation
- 40-71% H&N Ca Patients Quit
  - vs. Cardiac or Healthy Smokers- 8-10%
  - 95% TL / 84% ChemoXRT
  - Brief Physician Counseling Best Approach
    - Gritz, 1993
- Most Likely to Continue Smoking
  - Single Tx, OC Tumor, Younger Patient
- 4X risk of 2nd Primary if Smoking
- Risk <<< after 5 years of abstinence
  - Day, 1994
Risk Counseling: ETOH

- 44% of HNCA pts. - Alcoholism
- Risk of 2nd Primary- 3.8X >15 beers/week
  - Beer worse than wine/liquor
- Etoh Cessation Rate- 20-45%
- Comorbidities begin at >6 drinks/day
  - Risk of death >>if Etoh complication ensues
Future Directions

- Tumor Biology
  - Margin Assessment
  - Early Recurrence Detection
    - Exfoliative Analysis
    - Serum Markers
- Improved Conventional Detection
  - Spiral CT/ PET
- Chemoprevention
- Improved salvage
  - Advanced Surgical Treatment
  - Immunotherapy/Gene Therapy
  - Advanced Reconstruction
Cancer Follow-up: Be Vigilant

- IS IT CANCER? No.
- IS IT CANCER? NO!
- IS IT CANCER? I SAID NO!!
- IS IT CANCER? You are absolutely right!! No, I can't operate. It's too BIG!!