Transoral Laser Microsurgery for Early and Select Advanced Primary Glottic Squamous Cell Carcinoma: Oncologic Outcomes

GBMC Otolaryngology Grand Rounds
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Conflicts of Interest and Financial Disclosures

• Nothing to disclose
Questions

• Generally, which T2 glottic tumor characteristic carries a worse prognosis: 1) supraglottic and/or subglottic extension, 2) impaired vocal cord mobility?
• What structure marks the superior limit of the glottis?
• TLM is a treatment option for glottic tumors up to what T-stage? First line option up to what T-stage?
• Neck management in a patient with an T3N0 glottic tumor?
• Does every patient with T3N0 glottic cancer who is treated surgically get adjuvant therapy or are there exceptions?
• What is the standard of care for patients with stage III-IV larynx cancer, not including T4a disease?
Outline

• Introduction to glottic squamous cell carcinoma
  – History
• Transoral laser microsurgery (TLM) concepts/technique
• TLM outcomes
• Guidelines
• WashU retrospective study
Introduction: Anatomy

1. Epiglottis
   a. Surahyoid portion
   b. Infrahynoid portion
2. Aryepiglottic fold
3. Arytenoid cartilage
4. False vocal fold
5. Ventricle of Morgani
6. True vocal fold
7. Pre-epiglottic space
8. Thyroid cartilage
9. Cricoid cartilage
10. Hyoid bone

A. Supraglottis
B. Glottis
C. Subglottis

1. Epiglottis
2. Hyoepiglottic ligament
3. Hyoid bone
4. Thyrohyoid ligament
5. Ventricular ligament
6. Ventricle of Morgani
7. Petiole
8. Vocal ligament
9. Tracheal rings
10. Cricoid cartilage
11. Conus elasticus
12. Arytenoid (left)
13. Quadrangular membrane (left)
14. Aryepiglottic fold (left)
A. Pre-epiglottic space (yellow)
B. Paraglottic space lateral to Quadrangular membrane (green)
C. Paraglottic space lateral to Conus elasticus (orange)

Staging larynx anatomy

Bailey's head and neck surgery—otolaryngology, 2014
Introduction: Staging

Glottis:
TX: Primary tumor cannot be assessed
T0: No evidence of primary tumor
Tis: Carcinoma in situ
T1: Tumor limited to the vocal cord(s) (may involve anterior or posterior commissure), with normal mobility
T1a: Tumor limited to 1 vocal cord
T1b: Tumor involves both vocal cords
T2: Tumor extends to the supraglottis and/or subglottis, and/or with impaired vocal cord mobility
T3: Tumor limited to the larynx with vocal cord fixation and/or invasion of the paraglottic space and/or inner cortex of the thyroid cartilage
T4a: Moderately advanced, local disease; Tumor invades through the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of the neck, including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)
T4b: Very advanced, local disease; Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures
Introduction: Epidemiology

- Laryngeal cancer: US, 2015 estimates
  - Incidence: 13,560 patients
  - Deaths: 3,640 patients

Bailey's head and neck surgery—otorlaryngology, 2014
Introduction: Epidemiology
Incidence of Cervical Metastases in the Larynx

Bailey's head and neck surgery—otolaryngology, 2014
Introduction: History of Larynx Cancer and Transoral Laser Microsurgery

- 1873: Billroth: total laryngectomy
- 1915: Jackson: endoscopic supraglottic larynx cancer resection
- 1972: Strong, Jako: couple CO2 laser to microscope
- 1975: Strong: 11 patients T1 larynx cancer
- 1980s: Ossoff, Kaufman, Holinger: publish T1 larynx results
- 1991: VA Laryngeal Cancer Study Group results published
- 1993: Steiner: 240 larynx tumors, 23 T3-T4 tumors
- 1996: Haughey, others travel to Germany, observe Steiner
Introduction: History of Larynx Cancer and Transoral Laser Microsurgery

- 2003: RTOG 91-11 results published
- 2006: Hoffman review of NCDB 158,000 larynx cancer cases between 1985-2001
- 2007: TLM for advanced laryngeal cancer multicenter trial results published
- 2013: RTOG 91-11 long-term results published
Introduction: Trends

• In the last two decades:
  – Increased use of nonsurgical, organ-sparing methods for advanced laryngeal squamous cell carcinoma (SCCa)
  – Diminished use of open surgery
  – Increased use endoscopic laser surgery

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Concept/Technique: TLM and Advantages

**Technique**
Microscopy, CO2 laser: tumor transected, tumor-host interface identified, multi-bloc resection performed, serial frozen sections

**Advantages**
Shorter hospital stay, decreased morbidity
Decreased treatment length, decreased cost
Organ-sparing approach
Early swallowing postoperatively
Avoidance of extensive reconstruction
General avoidance of tracheostomy
Preserves all treatment options in setting of recurrence, including radiotherapy

Concept/Technique: Transoral Laser Microsurgery (TLM) Glottic Larynx

Bailey's head and neck surgery—otolaryngology, 2014
Concept/Technique: TLM Supraglottic Larynx

Bailey's head and neck surgery—otolaryngology, 2014

• Subepithelial cordectomy (type I)
• Subligamental cordectomy (type II)
• Transmuscular cordectomy (type III)
• Total cordectomy (type IV)
• Extended cordectomy, contralateral vocal fold and anterior commissure (type Va)
• Extended cordectomy, arytenoid (type Vb)
• Extended cordectomy, which encompasses the subglottis (type Vc)
• Extended cordectomy, ventricle (type Vd).
• Anterior commissurectomy with bilateral anterior cordectomy (type VI)

Concept/Technique: Diagnostic Work-up

8 T’s of Access
- teeth (prominent)
- trismus
- transverse dimensions (narrow mandibular arch)
- tori (mandibular)
- tongue (bulk)
- tilt (atlanto-occipital extension)
- treatment (prior radio- or chemoradiotherapy)
- tumor (site and size)

**TABLE 123.1 DIAGNOSTIC APPROACH TO EARLY GLOTTIC CANCERS**

<table>
<thead>
<tr>
<th>Glottis</th>
</tr>
</thead>
<tbody>
<tr>
<td>History and physical examination, office-based fiberoptic laryngoscopy and videostroscopy</td>
</tr>
<tr>
<td>Imaging: Limited role, evaluation of invasion in bulky lesions</td>
</tr>
<tr>
<td>Pulmonary function test</td>
</tr>
<tr>
<td>Direct laryngoscopy under anesthesia for biopsy and assessment of</td>
</tr>
<tr>
<td>- Site, size, surface, and extent of primary tumor</td>
</tr>
<tr>
<td>- Tumor extension to subglottis, arytenoid, supraglottis, anterior commissure, petiole of epiglottis</td>
</tr>
<tr>
<td>- Cord mobility</td>
</tr>
<tr>
<td>- Adequacy of transoral exposure, especially anterior commissure</td>
</tr>
<tr>
<td>- UADT examination for second primaries</td>
</tr>
</tbody>
</table>

UADT, upper aerodigestive tract.
Concept/Technique: OR, Postop Care

- 5.0 laser endotracheal tube
- Aquaplast mouthguard
- Standard laser precautions
- Steiner, Kleinsasser preferred laryngoscopes
- Zeiss microscope coupled to CO2 laser, usually via micromanipulator; consider handheld
- CO2 laser: superpulse continuous mode, 1-3W+ (up to 15W)
- Margins carefully oriented; deep margins of specimen inked and evaluated by frozen section; consider deeper 1-5 mm margins
- Postoperative nasogastric tube for larger resections
- PPI, humidity, hydration, light voice rest
- Speech/swallow therapy
Outline

• Introduction to glottic squamous cell carcinoma
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• Transoral laser microsurgery (TLM) concepts/technique
• **TLM outcomes**
• Guidelines
• WashU retrospective study
Local Control and Survival Outcomes of Primary Glottic SCCa: Selected Studies

T1 Primary Glottic Cancer

<table>
<thead>
<tr>
<th>STUDY</th>
<th>TX MODALITY</th>
<th>STAGE</th>
<th># PTS</th>
<th>LC 5 YR</th>
<th>OS 5 YR</th>
<th>DSS 5 YR</th>
<th>ULC 5 YR</th>
<th>LP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motta 2005</td>
<td>TLM</td>
<td>T1</td>
<td>432</td>
<td>85</td>
<td>NR</td>
<td>NR</td>
<td>93</td>
<td>97.3</td>
</tr>
<tr>
<td>Peretti 2010</td>
<td>TLM</td>
<td>pT1</td>
<td>404</td>
<td>NR</td>
<td>NR</td>
<td>99</td>
<td>NR</td>
<td>98.1</td>
</tr>
<tr>
<td>Canis 2014</td>
<td>TLM</td>
<td>pT1a</td>
<td>404</td>
<td>86.6</td>
<td>87.8</td>
<td>98</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Brumund 2005</td>
<td>OVPL</td>
<td>T1</td>
<td>232</td>
<td>91</td>
<td>83.1</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Mendenhall 2000</td>
<td>RT</td>
<td>T1a</td>
<td>253</td>
<td>94</td>
<td>82</td>
<td>97</td>
<td>98</td>
<td>95</td>
</tr>
<tr>
<td>Mendenhall 2000</td>
<td>RT</td>
<td>T1b</td>
<td>72</td>
<td>93</td>
<td>83</td>
<td>99</td>
<td>97</td>
<td>94</td>
</tr>
<tr>
<td>NCDB 1998-1999</td>
<td>All Modalities</td>
<td>Stage I</td>
<td>NR</td>
<td>NR</td>
<td>70.6</td>
<td>89.8</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

Legend: NR: not recorded; OVPL: open vertical partial laryngectomy; TLM: transoral laser microsurgery
### Local Control and Survival Outcomes of Primary Glottic SCCa: Selected Studies
#### T2 Primary Glottic Cancer

<table>
<thead>
<tr>
<th>STUDY</th>
<th>TX MODALITY</th>
<th>STAGE</th>
<th># PTS</th>
<th>LC 5 YR</th>
<th>OS 5 YR</th>
<th>DSS 5 YR</th>
<th>ULC 5 YR</th>
<th>LP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motta 2005</td>
<td>TLM</td>
<td>T2</td>
<td>236</td>
<td>66</td>
<td>NR</td>
<td>NR</td>
<td>79</td>
<td>82.5</td>
</tr>
<tr>
<td>Canis 2013</td>
<td>TLM</td>
<td>pT2a</td>
<td>142</td>
<td>NR</td>
<td>72</td>
<td>93</td>
<td>NR</td>
<td>93</td>
</tr>
<tr>
<td>Canis 2013</td>
<td>TLM</td>
<td>pT2b</td>
<td>127</td>
<td>NR</td>
<td>65</td>
<td>84</td>
<td>NR</td>
<td>83</td>
</tr>
<tr>
<td>Laccourreye 2000*</td>
<td>OVPL</td>
<td>T2</td>
<td>85</td>
<td>69.3</td>
<td>46.2</td>
<td>NR</td>
<td>94.1</td>
<td>78.1</td>
</tr>
<tr>
<td>Laccourreye 2000**</td>
<td>SCL</td>
<td>T2</td>
<td>118</td>
<td>94.6</td>
<td>66.4</td>
<td>NR</td>
<td>99.2</td>
<td>93.7</td>
</tr>
<tr>
<td>Chevalier 1997</td>
<td>SCL</td>
<td>T2b</td>
<td>90</td>
<td>94.4</td>
<td>81.3</td>
<td>96</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Mendenhall 2010</td>
<td>RT</td>
<td>T2a</td>
<td>165</td>
<td>80</td>
<td>76</td>
<td>94</td>
<td>96</td>
<td>81</td>
</tr>
<tr>
<td>Mendenhall 2010</td>
<td>RT</td>
<td>T2b</td>
<td>95</td>
<td>70</td>
<td>78</td>
<td>90</td>
<td>93</td>
<td>74</td>
</tr>
<tr>
<td>NCDB 1998-1999</td>
<td>All Modalities</td>
<td>Stage II</td>
<td>NR</td>
<td>NR</td>
<td>59.1</td>
<td>74</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

*: 18.8% received induction chemotherapy; 10-yr estimates
**: 85.1% received induction chemotherapy; 10-yr estimates

Legend: NR: not recorded; OVPL: open vertical partial laryngectomy; SCL: supracricoid laryngectomy; TLM: transoral laser microsurgery
Local Control and Survival Outcomes of Primary Glottic SCCa: Selected Studies
T3-T4 Primary Glottic Cancer

<table>
<thead>
<tr>
<th>STUDY</th>
<th>TX MODALITY</th>
<th>STAGE</th>
<th># PTS</th>
<th>LC 5 YR</th>
<th>OS 5 YR</th>
<th>DSS 5 YR</th>
<th>LP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motta 2005</td>
<td>TLM</td>
<td>T3*</td>
<td>51</td>
<td>63</td>
<td>NR</td>
<td>NR</td>
<td>81</td>
</tr>
<tr>
<td>Vilaseca 2010</td>
<td>TLM</td>
<td>T3</td>
<td>51</td>
<td>47.1</td>
<td>73.1</td>
<td>86.3</td>
<td>NR</td>
</tr>
<tr>
<td>Canis 2013</td>
<td>TLM</td>
<td>pT3</td>
<td>122</td>
<td>NR</td>
<td>59</td>
<td>84</td>
<td>83</td>
</tr>
<tr>
<td>Canis 2013</td>
<td>TLM</td>
<td>pT4a</td>
<td>31</td>
<td>67</td>
<td>65</td>
<td>75</td>
<td>NR</td>
</tr>
<tr>
<td>Chevalier 1997</td>
<td>SCL</td>
<td>T3</td>
<td>22</td>
<td>95.4</td>
<td>85.5</td>
<td>94.1</td>
<td>NR</td>
</tr>
<tr>
<td>Mendenhall 1997</td>
<td>RT</td>
<td>T3</td>
<td>73</td>
<td>63</td>
<td>54</td>
<td>78</td>
<td>68</td>
</tr>
<tr>
<td>Groome 2001</td>
<td>All Modalities**</td>
<td>T3</td>
<td>NR</td>
<td>NR</td>
<td>44</td>
<td>51</td>
<td>NR</td>
</tr>
<tr>
<td>Hoffman 2006***</td>
<td>Surgery</td>
<td>T3N0</td>
<td>398</td>
<td>NR</td>
<td>56.2</td>
<td>69</td>
<td>NR</td>
</tr>
<tr>
<td>Hoffman 2006</td>
<td>Surgery + RT</td>
<td>T3N0</td>
<td>290</td>
<td>NR</td>
<td>54.7</td>
<td>65.6</td>
<td>NR</td>
</tr>
<tr>
<td>Groome 2001</td>
<td>All Modalities****</td>
<td>T4</td>
<td>NR</td>
<td>NR</td>
<td>48</td>
<td>57</td>
<td>NR</td>
</tr>
<tr>
<td>Hoffman 2006</td>
<td>All Modalities</td>
<td>T4N0</td>
<td>638</td>
<td>NR</td>
<td>NR</td>
<td>52.6</td>
<td>NR</td>
</tr>
<tr>
<td>Hoffman 2006</td>
<td>All Modalities</td>
<td>T4N+</td>
<td>344</td>
<td>NR</td>
<td>NR</td>
<td>28.1</td>
<td>NR</td>
</tr>
</tbody>
</table>

* T3 by fixed cord only
** SEER 1988-1994 (TL +/- RT: 44.3%, RT: 38.9%; other conservation: 10.5%; NTI: 6.3%)
*** 94-96 group
**** SEER 1988-1994 (TL +/- RT: 77.9%, RT: 9.0%; other conservation: 8.0%; NTI: 5.1%)
Legend: NR: not recorded; NTI: no treatment; OVPL: open vertical partial laryngectomy; RT: radiotherapy; SCL: supracricoid laryngectomy; TL: total laryngectomy; TLM: transoral laser microsurgery
Outline

• Introduction to glottic squamous cell carcinoma
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Introduction: ASCO Clinical Practice Guideline, 2006

Table 1. Summary of Recommended Strategies for Treatment of the Primary Site for Larynx Preservation

<table>
<thead>
<tr>
<th>Type of Cancer</th>
<th>Organ-Preservation Strategy</th>
<th>Other Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 glottis</td>
<td>Endoscopic resection (ER) (selected patients) OR radiation therapy (RT)</td>
<td>Open organ-preservation surgery (OPS)</td>
</tr>
<tr>
<td>T2 glottis, favorable</td>
<td>Open OPS OR radiation therapy</td>
<td>ER (selected patients)</td>
</tr>
<tr>
<td>T2 glottis, unfavorable*</td>
<td>Open OPS OR concurrent chemoradiation therapy (CRT) (selected patients with node-positive disease)</td>
<td>RT; ER (selected patients)</td>
</tr>
<tr>
<td>T3-T4 glottis or supraglottis</td>
<td>Concurrent CRT OR open OPS (in highly selected patients)</td>
<td>RT</td>
</tr>
</tbody>
</table>

- Unfavorable T2: impaired cord mobility, subglottic extension

Introduction: ABEA, 2009 Position Statement

“Endoscopic laser resections are oncologically safe when applied judiciously and by a skilled oncological surgeon”

Relative contraindications

- Instances in which the whole tumor cannot be visualized
- Large tumors that require removing too much of the functional laryngeal unit, severely decreasing airway protection and leading to aspiration
- Cartilage invasion
Introduction: ENT-UK Head & Neck Group: 2009 Consensus Statement

• The standard of care for all patients with glottic SCCa, staged T\textsubscript{1}a, T\textsubscript{1}b or T\textsubscript{2}a is that they are offered TLM as part of informed choice treatment options.

• The option of TLM should be discussed by the multidisciplinary team for all patients with glottic SCCa of stages T\textsubscript{1}a, b or T\textsubscript{2}, as a treatment option, with documentation of reasons why the particular treatment was selected.

• The patient should be clearly informed of the range of feasible treatment choices (TLM, radiation, open surgery); clinicians should ensure informed choice, using standardised information to avoid risk of bias.

Introduction: NCCN: 2015
Introduction: Guidelines Summary

- ASCO: first line for select T1 tumors; second line for select T2a-T2b tumors
- ABEA: T1-select T3 tumors
- ENT-UK Head & Neck Group: first line option for T1-T2a tumors, offer to patients with T2b tumors
- NCCN: T1-select T3 tumors
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Washington University in St Louis Retrospective Cohort Study

- 90 previously untreated patients
- Biopsy-proven primary glottic SCCa
- Treated from 1996-2011
- TLM +/- neck dissection +/- adjuvant therapy
- At least 12 months follow-up
Study Objectives

• Assessment of:
  – Local control, laryngeal preservation, and survival
  – Management of recurrences
  – Prognostic factors impacting local control and disease free survival
Study Outcomes

Primary
- Local Control (LC)
- Disease Free Survival (DFS)

Secondary
- Ultimate Local Control (ULC)
- Laryngeal Preservation (LP)
- Overall survival (OS)
- Disease Specific Survival (DSS)
Analytical Approach

- Standard descriptive statistics
- Bivariate analysis
- Kaplan Meier survival analysis
- Multivariate Cox PH regression
Results: Follow-up and Survival

• Median follow-up: 44.6 months
• Range follow-up: 9-179 months

<table>
<thead>
<tr>
<th>STATUS AT LAST FOLLOW-UP</th>
<th>N=90</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive and well</td>
<td>57</td>
<td>63%</td>
</tr>
<tr>
<td>Died of disease</td>
<td>8</td>
<td>9%</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>2</td>
<td>2%</td>
</tr>
<tr>
<td>Died of second primary tumor</td>
<td>10</td>
<td>11%</td>
</tr>
<tr>
<td>Died of other causes</td>
<td>13</td>
<td>15%</td>
</tr>
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# Demographic Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (std. dev)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &gt; 70</td>
<td></td>
<td>24</td>
<td>27%</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>80</td>
<td>89%</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>10</td>
<td>11%</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>Never</td>
<td>7</td>
<td>8%</td>
</tr>
<tr>
<td></td>
<td>Ever</td>
<td>77</td>
<td>86%</td>
</tr>
<tr>
<td></td>
<td>Not documented</td>
<td>6</td>
<td>6%</td>
</tr>
<tr>
<td>Comorbidity (ACE-27)</td>
<td>0 to 1: none-mild</td>
<td>68</td>
<td>76%</td>
</tr>
<tr>
<td></td>
<td>2 to 3: moderate-severe</td>
<td>22</td>
<td>24%</td>
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# Tumor Stage and Local Control

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>N</th>
<th>%</th>
<th>Local Control</th>
<th>LC %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor stage</td>
<td>Tis</td>
<td>5</td>
<td>6%</td>
<td>5</td>
<td>100%</td>
</tr>
<tr>
<td>Tumor stage</td>
<td>T1</td>
<td>52</td>
<td>58%</td>
<td>44</td>
<td>85%</td>
</tr>
<tr>
<td>Tumor stage</td>
<td>T2A</td>
<td>8</td>
<td>9%</td>
<td>8</td>
<td>100%</td>
</tr>
<tr>
<td>Tumor stage</td>
<td>T2B</td>
<td>9</td>
<td>10%</td>
<td>7</td>
<td>78%</td>
</tr>
<tr>
<td>Tumor stage</td>
<td>T3</td>
<td>12</td>
<td>13%</td>
<td>8</td>
<td>66%</td>
</tr>
<tr>
<td>Tumor stage</td>
<td>T4</td>
<td>4</td>
<td>4%</td>
<td>3</td>
<td>75%</td>
</tr>
</tbody>
</table>
## Tumor Extension, Margins and Local Control

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>N</th>
<th>%</th>
<th>Local Control</th>
<th>LC %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disease Extension within the Larynx</strong></td>
<td>Glottis</td>
<td>56</td>
<td>62%</td>
<td>49</td>
<td>88%</td>
</tr>
<tr>
<td></td>
<td>Supraglottis</td>
<td>20</td>
<td>22%</td>
<td>17</td>
<td>85%</td>
</tr>
<tr>
<td></td>
<td>Subglottis</td>
<td>5</td>
<td>6%</td>
<td>4</td>
<td>80%</td>
</tr>
<tr>
<td></td>
<td>Combined supra/subglottis</td>
<td>9</td>
<td>10%</td>
<td>5</td>
<td>56%</td>
</tr>
<tr>
<td><strong>Margins</strong></td>
<td>Negative</td>
<td>77</td>
<td>86%</td>
<td>68</td>
<td>88%</td>
</tr>
<tr>
<td></td>
<td>Indeterminate+ positive</td>
<td>13</td>
<td>14%</td>
<td>6</td>
<td>54%</td>
</tr>
</tbody>
</table>
Sites of Initial Recurrence

Number of Patients

Local: 14
Locoregional: 2
Regional: 2
Distant: 0
Salvage Method of Patients with Local and Locoregional Recurrences

<table>
<thead>
<tr>
<th>Local/Locoregional Recurrence Salvage Method</th>
<th># of Patients/Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>SURGICAL +/- ADJUVANT TX</td>
<td>13/15</td>
</tr>
<tr>
<td>TLM</td>
<td>3</td>
</tr>
<tr>
<td>TLM +/- ND/RT/CRT</td>
<td>5</td>
</tr>
<tr>
<td>Open Conservation Surgery</td>
<td>1</td>
</tr>
<tr>
<td>Total Laryngectomy +/- ND/RT/CRT</td>
<td>4</td>
</tr>
<tr>
<td>NONSURGICAL</td>
<td>2/15</td>
</tr>
</tbody>
</table>

- Post-salvage surgery: 6/13 patients died of disease
  - Distant: 5 patients
  - Local: 1 patient
Study: Complications/Morbidity

• Clinically-significant recurrent aspiration: 3 patients
• Severe laryngeal edema requiring urgent tracheostomy: 1 patient
• Postoperative bleeds that resolved without surgical intervention: 2 patients
• Laryngeal stenosis: 5 patients
  – Three underwent at least one balloon dilatation, one required a laryngeal stent, and one required debridement
• Keel placement: 5 patients
• Injection/medialization thyroplasty: 1 patient
• Anterior glottic webs requiring laser excision: 2 patients
• Severely loosened central incisor: 1 patient
• Mild unilateral cranial nerve palsies: 1 patient
• Tracheotomy: 8 patients
  – 3 remained tracheostomy-dependent
• Gastrostomy tube: 9 patients
  – 7 remained gastrostomy-dependent
    • 6 became gastrostomy-tube dependent after treatment for recurrence
    • 5 patients received radiation therapy
## 5-Year Local Control and Survival Estimates by T-Classification and T-Classification Grouping

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>LC 5 YR (%)</th>
<th>DFS 5 YR (%)</th>
<th>OS 5 YR (%)</th>
<th>DSS 5 YR (%)</th>
<th>ULC 5 YR (%)</th>
<th>LP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>52</td>
<td>83 (72-94)</td>
<td>66 (51-80)</td>
<td>73 (58-88)</td>
<td>100</td>
<td>100</td>
<td>96</td>
</tr>
<tr>
<td>T2</td>
<td>17</td>
<td>86 (68-100)</td>
<td>52 (25-79)</td>
<td>46 (17-76)</td>
<td>60 (28-93)</td>
<td>90 (71-100)</td>
<td>88</td>
</tr>
<tr>
<td>T3</td>
<td>12</td>
<td>58 (27-90)</td>
<td>38 (9-67)</td>
<td>46 (16-75)</td>
<td>60 (30-90)</td>
<td>80 (55-100)</td>
<td>83</td>
</tr>
<tr>
<td>Tis - T2a</td>
<td>65</td>
<td>86 (77-95)</td>
<td>65 (52-78)</td>
<td>70 (56-84)</td>
<td>96 (89-100)</td>
<td>100</td>
<td>97</td>
</tr>
<tr>
<td>T2b - T4a</td>
<td>25</td>
<td>67 (46-87)</td>
<td>45 (24-66)</td>
<td>46 (25-67)</td>
<td>59 (37-81)</td>
<td>84 (66-100)</td>
<td>80</td>
</tr>
</tbody>
</table>

Legend: Data for Tis, T1b, T2a, T2b, and T4a disease are not separately shown given the numbers in each of these groups were too low.
Local Control Kaplan Meier Estimates for Tis-T2a versus T2b-T4a

Log Rank Chi Square=3.784, df=1; p-value=0.052
Disease Free Survival Kaplan Meier Estimates for Tis-T2a versus T2b-T4a

Log Rank Chi Square=4.489 (df=1); p-value=0.034
Variables Associated with Local Control and Survival after TLM

- Ventricle roof and/or false cord extension
- Subglottic extension
- Vocalis muscle involvement
- Arytenoid involvement
- Anterior commissure involvement
- Vocal cord fixation
- Cartilage infiltration
# Multivariate Cox PH Analysis for Local Control

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>CATEGORY</th>
<th>aHR</th>
<th>95% CI</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td>1.07</td>
<td>1.00 to 1.14</td>
<td>0.06</td>
</tr>
<tr>
<td>Disease Extension within the Larynx</td>
<td>Glottic</td>
<td>1.0</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>Supraglottic</td>
<td>0.86</td>
<td>0.17 to 4.42</td>
<td>0.86</td>
</tr>
<tr>
<td></td>
<td>Subglottic</td>
<td>1.89</td>
<td>0.15 to 24.70</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td><strong>Simultaneous supra/subglottic</strong></td>
<td>5.98</td>
<td><strong>1.13 to 31.55</strong></td>
<td>0.04</td>
</tr>
<tr>
<td>Margins</td>
<td>Negative</td>
<td>1.0</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td><strong>Indeterminate + positive</strong></td>
<td>5.14</td>
<td><strong>1.30 to 20.37</strong></td>
<td>0.02</td>
</tr>
</tbody>
</table>
## Multivariate Cox PH Analysis for Disease Free Survival

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>CATEGORY</th>
<th>aHR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td>1.07</td>
<td>1.03 to 1.12</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Disease Extension within the Larynx</td>
<td>Glottic</td>
<td>1.0</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>Supraglottic</td>
<td>2.19</td>
<td>0.76 to 6.34</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
<td>Subglottic</td>
<td>1.41</td>
<td>0.29 to 6.81</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td><strong>Simultaneous supra/subglottic</strong></td>
<td><strong>6.54</strong></td>
<td><strong>1.59 to 26.89</strong></td>
<td><strong>&lt; 0.01</strong></td>
</tr>
<tr>
<td>Comorbidity (ACE-27)</td>
<td>None-Mild</td>
<td>1.0</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>Moderate-Severe</td>
<td>1.54</td>
<td>0.70 to 3.42</td>
<td>0.28</td>
</tr>
<tr>
<td>T-Stage Grouping</td>
<td>TIS-T2A</td>
<td>1.0</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>T2B-T4</td>
<td>0.86</td>
<td>0.29-2.61</td>
<td>0.79</td>
</tr>
</tbody>
</table>
Limitations

- Observational study
- Small sample size
- Limited number of advanced stage tumors
Conclusion

• Largest NA study documenting TLM management Tis-T4a disease
• Support TLM as first line treatment option for T1 glottic tumors
• Satisfactory LC, ULC, LP rates across all T-stages
• Satisfactory salvage rate of stage I-II recurrences
• Additional studies needed to assess survival of TLM-managed T2-T4 glottic tumors
Conclusions/Next Steps

• Additional studies needed to assess prognostic significance of simultaneous supraglottic/subglottic extension, indeterminate/positive margins
• Management of the N0 neck in advanced disease
• Role of adjuvant therapy in TLM
Questions