Hold your breath! Utilizing Deep inspiration breath hold (DIBH) and Volumetric modulated arc therapy (VMAT) for the treatment of Esophageal carcinoma

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Roswell Park Cancer Institute
outline

- SEER Statistics at a Glance
- Current Strategies
- Radiotherapy Planning, Organs at risk (OAR)
- Clinical implementation, the role of the radiation therapist
- Challenges
## SEER Stats at a glance

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Estimated New Cases in 2015</strong></td>
<td>16,980</td>
</tr>
<tr>
<td><strong>% of All New Cancer Cases</strong></td>
<td>1.0%</td>
</tr>
<tr>
<td><strong>Estimated Deaths in 2015</strong></td>
<td>15,590</td>
</tr>
<tr>
<td><strong>% of All Cancer Deaths</strong></td>
<td>2.6%</td>
</tr>
</tbody>
</table>

### New Cases vs Deaths

![Graph showing New Cases and Deaths over Years](#)

#### Percent Surviving 5 Years

**17.9%**

2005–2011

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Percent of Cases & 5-Year Relative Survival by Stage at Diagnosis: Esophageal Cancer

- Localized (21%) Confined to Primary Site
- Regional (31%) Spread to Regional Lymph Nodes
- Distant (38%) Cancer Has Metastasized
- Unknown (11%) Unstaged

Percent of Cases by Stage

5-Year Relative Survival

SEER 18 2005-2011, All Races, Both Sexes by SEER Summary Stage 2000
Most frequently diagnosed among people aged 65-74.

More prevalent in Men than women 4:1

Commonly associated with heavy alcohol use and tobacco use.

GERD

Barrett’s Esophagus
New Cases, Deaths and 5-Year Relative Survival

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</tr>
</thead>
<tbody>
<tr>
<td>5-Year Relative Survival</td>
<td>4.0%</td>
<td>5.6%</td>
<td>8.6%</td>
<td>10.0%</td>
<td>11.6%</td>
<td>17.4%</td>
<td>17.1%</td>
<td>21.6%</td>
</tr>
</tbody>
</table>

Anatomy/ Histology

- Squamous Cell Carcinoma (SCC)
  - Cervical/upper thoracic
  - Developing world

- Adenocarcinoma
  - Lower thoracic/ EGJ
  - Shift from SSC to AC in the U.S.
Epidemiology/ Histology

White Males

White Females

Esophageal Cancer by Histology
- Total
- Adenocarcinoma
- Squamous
- Cell Carcinoma
- Other and Unknown

Rate per 100,000 person-years

1980 1990 2000

1980 1990 2000
The importance of modern radiation therapy approaches
Current treatment strategies

- Surgery
- Radiation
- Chemotherapy

How to effectively utilize all three modalities to produce better overall survival?
Multidisciplinary approach

- RTOG 85-01 phase III trial
- INT 0123 (RTOG 94-05) phase III trial
- CROSS group phase III Trial

RTOG 85-01
Chemoradiotherapy of locally advanced esophageal cancer

- Squamous cell or adenocarcinoma of the esophagus
- T1-3 N0-1 M0.

<table>
<thead>
<tr>
<th>Concurrent Chemoradiation</th>
<th>RT alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>50Gy + 4 cycles of fluorouracil and cisplatin</td>
<td>64 Gy/32 Fxs over 6.4 weeks</td>
</tr>
</tbody>
</table>

5 Year overall survival

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>27%</td>
<td>0%</td>
</tr>
</tbody>
</table>

INT 0123 (RTOG 94-05)

- Follow-up trial to RTOG 85-01
- 5-FU + cisplatin + radiation (64.8 Gy or 50.4 Gy)
- 218 patients, T1-4 N0-1 M0

<table>
<thead>
<tr>
<th>Results</th>
<th>High Dose 64.8 Gy</th>
<th>Low Dose 50.4Gy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median survival</td>
<td>13.0 months</td>
<td>18.1 months</td>
</tr>
<tr>
<td>2 year survival</td>
<td>31%</td>
<td>40%</td>
</tr>
<tr>
<td>Local failure</td>
<td>56%</td>
<td>52%</td>
</tr>
</tbody>
</table>
Patients with resectable tumors randomly assigned to surgery alone or Chemoradiotherapy followed by surgery

Carboplatin and paclitaxel for 5 weeks + radiation therapy (41.4 Gy), followed by surgery

<table>
<thead>
<tr>
<th>Results</th>
<th>Chemoradiotherapy + Surgery</th>
<th>Surgery Alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>R0 Resection</td>
<td>92%</td>
<td>69%</td>
</tr>
<tr>
<td>Path CR</td>
<td>19%</td>
<td></td>
</tr>
<tr>
<td>Median Survival</td>
<td>49.4 months</td>
<td>24.0 months</td>
</tr>
<tr>
<td>5 year over survival</td>
<td>47%</td>
<td>34%</td>
</tr>
</tbody>
</table>
Multidisciplinary approach

We have established:

- Chemoradiation as the conventional nonsurgical treatment for esophageal cancer.
- Higher doses of radiation therapy do not offer a loco/regional control or survival advantage, **Controversial?!?!**
- Preoperative Chemoradiation followed by surgery has been found to be beneficial for patients with resectable esophageal cancer.

Radiation Dose Guidelines
National Comprehensive Cancer Network (NCCN)

Preoperative

- 41.4 – **50.4** Gy (1.8 – 2.0 Gy/day)

Postoperative

- 45 - **50.4** Gy (1.8 – 2.0 Gy/day)

Definitive

- 50 – **50.4** Gy (1.8 – 2.0/day)

** Higher dose (60-66 Gy) may be appropriate for cervical esophagus where surgery is not planned, but no randomized evidence to support this over 50-50.4 Gy

## Radiotherapy for Palliative Care

### Table: Radiation vs. Chemoradiotherapy

<table>
<thead>
<tr>
<th></th>
<th>Radiation</th>
<th>Chemoradiotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Survival</td>
<td>203 days</td>
<td>210 days</td>
</tr>
<tr>
<td>Dysphagia response</td>
<td>67%</td>
<td>74%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increased GI toxicity</td>
</tr>
</tbody>
</table>

- Improved dysphagia!
- RT or CRT over Stent placement

**Best Practice in Advanced Esophageal Cancer: A Report on Trans-Tasman Radiation Oncology Group TROG 03.01 and NCIC CTG ES.2 Multinational Phase 3 Study in Advanced Esophageal Cancer (OC) Comparing Quality of Life (QOL) and Palliation of Dysphagia in Pat**
Review

Resectable Cancer

- pre-operative concurrent chemo-radiotherapy
- Postoperative radiotherapy – in positive cut margins, nodal positivity and presence of residual disease (Not talked about but a possibility)

Un-resectable cancer

- Concurrent chemo-radiotherapy

Advanced & metastatic cancer

- Palliative radiotherapy
RT plays an important role in the treatment of Esophageal cancer!
Esophageal Cancer

Percent Surviving 5 Years

17.9%

2005-2011

Percent of Cases by Stage

- Localized (21%) Confined to Primary Site
- Regional (31%) Spread to Regional Lymph Nodes
- Distant (38%) Cancer Has Metastasized
- Unknown (11%) Unstaged
The Goal of modern Radiation Therapy

Gross Tumor Volume definition (PET-CT)
Inter-fraction motion (IGRT)
Intra-fraction motion (Respiratory-Gating)
Precise Dose Delivery to the PTV (IMRT/VMAT)

Minimize post-treatment complications
Reduce radiotherapy-related toxicity
Improve overall clinical results!!!
RT planning process
Defining the Tumor Volume?

- Pre-treatment diagnostic studies
  - CT scans
  - Barium swallow
  - **Endoscopic ultrasound (EUS)**
  - Endoscopy reports
  - PET or PET/CT scans
PET/CT based planning?

- Retrospective study by Gondi et. al.
- PET/CT based targets volumes compared to CT only-based target volumes in 16 patients
- 10 cases found the addition of the PET to the planning process led to a reduction of the GTV!
Improved GTV definition and involved regional lymph nodes

https://www.med-ed.virginia.edu/courses/rad/PETCT/Eosophageal.html
Target Volume guidelines form the NCCN

- Gross Tumor Volume (GTV) = primary tumor and involved regional lymph nodes*

- Clinical Tumor Volume (CTV) = GTV + 3-4cm superior and inferior and 1cm radial expansion along the esophagus.

Nodal CTV = GTV + 0.5 to 1.5cm expansion of the nodal GTV

- Planning Tumor Volume (PTV) = GTV + 0.5 to 1cm expansion

CTV coverage of elective nodal regions

- **Cervical** Esophagus: supraclavicular and possible cervical nodes
- **Proximal** third: supraclavicular and para-esophageal nodal chains
- **Middle** third: para-esophageal nodes
- **Distal** third and **GE Junction**: para-esophageal, lesser curvature, and celiac axis nodal regions

The Goal of modern Radiation Therapy

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<td>\textit{Inter-fraction motion}</td>
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Minimize post-treatment complications

- Reduce radiotherapy-related toxicity
- Improve overall clinical results!!!
Inter-fraction motion

- Daily setup errors
- Image-guided radiotherapy (IGRT)
- Daily KV/KV match
- Cone-beam CT?
Inter-fraction motion

advanced adenocarcinoma of the lower esophagus

heart

left lung

cancer

right lung

aorta
The Goal of modern Radiation Therapy

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Minimize post-treatment complications
- Reduce radiotherapy-related toxicity
- Improve overall clinical results!!!
Intra-fraction motion

- Deep Inspiration Breath Hold (DIBH)
- Lung & breast cancer
- Account for Respiratory and cardiac cycles
- Reduce tumor movement

- Improve Internal Target volumes
- Reduce Surrounding tissue irradiation (Lungs and Heart)
Deep Inspiration breath Hold (DIBH)

- Normal Tissue Sparing (Heart & Lung)
- Improved Internal Target Volume
Organs at risk (OARs)

- **Heart** - 1/3 of heart < 40 Gy
- **Lung**
- **Spinal cord** - Max 45 Gy
- **Liver** - 60% of the liver < 30 Gy
- **Kidneys** - 2/3 of one kidney < 20 Gy
- **Stomach**

Distal Esophagus and GE Junction
Lung

- Percent of lung volume receiving 20 Gy (V20) < 25%
- Total Lung mean dose
Strong correlation between parameter V20 and the incidence of grade 2 pneumonitis

Clinical dose–volume histogram analysis for pneumonitis after 3D treatment for non-small cell lung cancer (NSCLC)

Graham et al
The Goal of modern Radiation Therapy

- Minimize post-treatment complications
- Reduce radiotherapy-related toxicity
- Improve overall clinical results!!!

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Precise Dose Delivery to the PTV

- 3-D Conformal Radiation Therapy
- Intensity-Modulated Radiation therapy (IMRT)
- Volumetric Modulated Arc Therapy (VMAT)

All three modalities get the job done but at what cost?
Comparative study by Wu. et al.
VMAT combined with DIBH

- Effectively reduce Lung Dose (V20)
- Shorter Treatment time
- Improved target accuracy
The Goal of modern Radiation Therapy

Gross Tumor Volume definition (PET-CT & Margins)
Inter-fraction motion (IGRT)
Intra-fraction motion (Respiratory-Gating)
Precise Dose Delivery to the PTV (VMAT)

Minimize post-treatment complications
Reduce radiotherapy-related toxicity
Improve overall clinical results!!!
Deep Inspiration Breath-hold (DIBH) and Volumetric Modulated Arc Therapy (VMAT) In Action!
Clinical implementation

- Patient Selection
- Simulation
- Treatment planning
- On treatment
Patient selection

- patient’s performance status
- stage and extent of the disease
- histology
- and location of the primary tumor.
Simulation

- GE Lightspeed CT simulator scan is obtained.

Patient positioning

- Supine
- Arms above head
- Oral contrast administered (when possible)**
Simulation

- RPM gating system is utilized to capture a breath-hold scan
- Free breath scan is also capture (Setup purposes)
- Staff present during SIM
  - SIM Therapist
  - Radiation Oncologist
  - Physicist
RT planning process

- Images are imported into the treatment planning computer
RT planning process

- VMAT with DIBH
- 2 Arcs
- Dose constraints entered for inverse planning
- Arcs consist of 130 control points
  - Arc 1 - 181 to 178
  - Arc 2 – 179 to 180
Radiation Technique

Real-time Position Management™ (RPM) system

Gated RapidArc radiotherapy
The role of the radiation therapist - SIM

- Initial coaching of the patient for the deep inspiration breath hold technique
- Easing anxiety
The role of the radiation therapist – On Treatment

- 10 – 14 days from SIM to start of Treatment
- Week 1 = Learning Curve
- Week 2-3 = patient comfortable with process
- Week 4-5 = side effects/ patient health
Treatment delivery Time

- Patient setup (3-4 minutes)
- KV/KV match (3-4 minutes)
- 2 Arcs (patient specific)
# Treatment delivery Time

## 2 Arcs

<table>
<thead>
<tr>
<th>Patient</th>
<th>Arc duration</th>
<th>Number of breaks</th>
<th>Breath hold time</th>
<th>Rest time</th>
<th>2 arcs overall time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>2 min 6 secs</td>
<td>2</td>
<td>26 secs</td>
<td>24 secs</td>
<td>7 min</td>
</tr>
<tr>
<td>Below average</td>
<td>4 min 18 secs</td>
<td>6</td>
<td>10-17 secs</td>
<td>30 secs</td>
<td>12 min</td>
</tr>
<tr>
<td>Outlier</td>
<td>1min 14 secs</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>4 min</td>
</tr>
</tbody>
</table>
Challenges

- Lung complication (COPD)
- Anxiety, nervous
- Degrading health of the patient during treatment course
- Language barrier
- Hearing
Supportive Services during RT

• Assess tolerability of RT before SIM
• Avoid treatment interruptions or dose reductions
• Manage acute toxicities
• Catch it before it becomes an issue!
• It takes a Team!

Supportive care during RT

- On treatment visit once a week (patient specific)
  - Vitals, weight, blood counts

- Prophylactic Antiemetic

- Antacid and antidiarrheal as needed

- Adequate Enteral and/or IV hydration

- Caloric intake of at least 2000 kcal/day

- Feeding tube (based on weight loss from onset of symptoms to diagnosis)
  - Grade 3-4 dysphagia/ <1500kcal/day

- Nutritional services (as needed)

Future Studies

- Dose escalation for un-resectable disease due to high infield (GTV) failure rate
- Protons
- Systemic therapies
  - HER-2 targeting therapy
Question