TREATMENT TIME & TOBACCO: TWIN TERRORS
Of H&N Therapy

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Professor of Oncology
Director of Radiation Research
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CASE

- 53 y/o man
- T2N2cM0 Base of Tongue Cancer
- 40 pack years
- HPV positive

Can’t be changed

- Smokes 1.5 ppd
- Seen November 10
- Because of work, wants to start on a Wednesday

CAN be changed to improve outcomes
Outline

**TREATMENT TIME**

- Historical Data
- RPCI Experience pt 1
  - 3-4% per day over 50
- RPCI Experience pt 2
  - Preventing treatment prolongation works

**TOBACCO**

- It is bad for you
  - Bad during RT
- Quitting prior to RT makes a **BIG** difference
Outline

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Treatment Time is Important with RT alone

Tx Time & Hgb with ChemoRT
Rades. IJROBP. 2008.

• 153 patients
• Stage IV
• Concurrent ChemoRT
  – Definitive (70) or Post-op (83)
Prognostic Factors
Rades. IJROBP. 2008.

Fig. 1. Impact of the pretreatment hemoglobin level (<12 g/dL vs. \(\geq 12\) g/dL) on overall survival.
Prognostic Factors

Rades. IJROBP. 2008.

Fig. 2. Impact of interruptions during radiotherapy >1 week (yes vs. no) on overall survival. RT = radiation therapy.
# Prognostic Factors


<table>
<thead>
<tr>
<th>Factor</th>
<th>RR</th>
<th>95% CI</th>
<th>p</th>
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<tbody>
<tr>
<td>Age</td>
<td>1.13</td>
<td>0.61–2.12</td>
<td>.69</td>
</tr>
<tr>
<td>Sex</td>
<td>1.85</td>
<td>0.94–4.01</td>
<td>.08</td>
</tr>
<tr>
<td>Karnofsky performance score</td>
<td>2.36</td>
<td>1.20–4.93</td>
<td>.012</td>
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<tr>
<td>Tumor site</td>
<td>1.02</td>
<td>0.84–1.23</td>
<td>.85</td>
</tr>
<tr>
<td>Histologic grade</td>
<td>1.32</td>
<td>0.76–2.40</td>
<td>.33</td>
</tr>
<tr>
<td>T stage</td>
<td>1.36</td>
<td>0.86–2.27</td>
<td>.19</td>
</tr>
<tr>
<td>N stage</td>
<td>1.90</td>
<td>0.91–4.39</td>
<td>.09</td>
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<tr>
<td>Hemoglobin level pre-RT</td>
<td>1.88</td>
<td>1.01–3.53</td>
<td>.048</td>
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<tr>
<td>Surgery</td>
<td>1.40</td>
<td>0.75–2.68</td>
<td>.29</td>
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<tr>
<td>Type of chemotherapy</td>
<td>1.18</td>
<td>0.80–1.75</td>
<td>.40</td>
</tr>
<tr>
<td>RT interruptions &gt;1 week</td>
<td>2.59</td>
<td>1.15–5.78</td>
<td>.021</td>
</tr>
</tbody>
</table>

*Abbreviations:* CI = confidence interval; RT = radiation therapy.
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- *RPCI Experience pt 2*  
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Radiation Treatment Interruptions Greater Than One Week and Low Hemoglobin Levels (12 g/dL) are Predictors of Local Regional Failure After Definitive Concurrent Chemotherapy and Intensity-Modulated Radiation Therapy for Squamous Cell Carcinoma of the Head and Neck

Susan A. McCloskey, MD,* Wainwright Jaggernauth, MD,* Nestor R. Riguad, MD,† Wesley L. Hicks Jr, MD, DDS,† Saurin R. Popat, MD,† Maureen Sullivan, DDS,§ Terry L. Mashtare Jr, MS,‖ Mohamed K. Khan, MD, PhD,* Thom R. Loree, MD,† and Anurag K. Singh, MD*

RPCI Study #1

- 2004-2007
- 78 patients
- Mostly male
- Oropharynx, larynx most common
- Treatment
  - Chemotherapy AND
  - IMRT

<table>
<thead>
<tr>
<th></th>
<th># patients</th>
<th>%</th>
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<tbody>
<tr>
<td>Total</td>
<td>78</td>
<td></td>
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<tr>
<td>Median age (range)</td>
<td>62 (37-81)</td>
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<tr>
<td>Sex</td>
<td></td>
<td></td>
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<tr>
<td>Male</td>
<td>56</td>
<td>72%</td>
</tr>
<tr>
<td>Female</td>
<td>22</td>
<td>28%</td>
</tr>
<tr>
<td>Tumor Site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oropharynx</td>
<td>42</td>
<td>54%</td>
</tr>
<tr>
<td>Larynx</td>
<td>28</td>
<td>36%</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>4</td>
<td>5%</td>
</tr>
<tr>
<td>Oral Cavity</td>
<td>4</td>
<td>5%</td>
</tr>
</tbody>
</table>
RPCI Study #1

- H&N Cancers
  - Mostly advanced
    - 51% T3 or T4
    - 55% N2 or N3

<table>
<thead>
<tr>
<th>T Stage</th>
<th>#</th>
<th>%</th>
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<tr>
<td>1</td>
<td>11</td>
<td>14%</td>
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<tr>
<td>2</td>
<td>27</td>
<td>35%</td>
</tr>
<tr>
<td>3</td>
<td>32</td>
<td>41%</td>
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<td>4</td>
<td>8</td>
<td>10%</td>
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<table>
<thead>
<tr>
<th>N Stage</th>
<th>#</th>
<th>%</th>
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<tr>
<td>0</td>
<td>25</td>
<td>32%</td>
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<tr>
<td>1</td>
<td>10</td>
<td>13%</td>
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<tr>
<td>2a</td>
<td>5</td>
<td>6%</td>
</tr>
<tr>
<td>2b</td>
<td>21</td>
<td>27%</td>
</tr>
<tr>
<td>2c</td>
<td>13</td>
<td>17%</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>5%</td>
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</table>
RPCI Study #1

• Median follow-up was 12 months.

• Fifteen of 78 (19%) patients experienced loco-regional failure.
  – 6 primary site failures,
  – 5 nodal/ regional failures, and
  – 4 failures in both the primary site and regional lymph nodes.
RPCI Study #1

• Loco-regional failure variables
  – Age
  – Sex
  – Disease site
  – Stage
  – Baseline hemoglobin
  – Treatment interruption > 1 week

* Statistically significant – meaning high level of correlation with loco-regional failures
RPCI Study #1

- Low hemoglobin
  - 7/19 (37%) failures

- Normal hemoglobin
  - 8/59 (14%) failures

P = 0.042
RPCI Study #1

- Interruption > 1 week
  - 6/13 (46%) failures

- Interruption < 1 week
  - 9/65 (14%) failures

P = 0.015
RPCI Study #1 : Summary

More loco-regional failures in H&N with

- Low hemoglobin
  - Not easily / realistically correctable
- Treatment interruptions
  - Easily Correctable!... but will it matter?
Outline

**TREATMENT TIME**
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- **RPCI Experience pt 2**
  - Preventing treatment prolongation works

**TOBACCO**
- It is bad for you
  - Bad during RT
- Quitting prior to RT makes a **BIG** difference
Quantification of the effect of treatment duration on local-regional failure after definitive concurrent chemotherapy and intensity-modulated radiation therapy for squamous cell carcinoma of the head and neck

Mary E. Platek, PhD,1* Susan A. McCloskey, MD,2 Myra Cruz, MD,3 Mark S. Burke, MD,4 Mary E. Reid, PhD,5 Gregory E. Wilding, PhD,6 Nestor R. Riguăl, MD,7 Saurin R. Popat, MD, MBA, FRCSC,8 Thom R. Loree, MD,4 Vishal Gupta, MD,7 Graham W. Warren, MD, PhD,3 Maureen Sullivan, DDS,9 Wesley L. Hicks, Jr, MD,7 Anurag K. Singh, MD3

Head and Neck. 2012.
RPCI Study #2

- 2007-2010
- 62 patients
- Mostly male
- Oropharynx, larynx most common
- Treatment
  - Chemotherapy AND
  - IMRT
- Avoid treatment interruptions

<table>
<thead>
<tr>
<th></th>
<th># patients</th>
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<tbody>
<tr>
<td>Total</td>
<td>62</td>
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<tr>
<td><strong>Median age</strong></td>
<td>59</td>
<td>82%</td>
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<tr>
<td>(range)</td>
<td>(38-82)</td>
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<tr>
<td><strong>Sex</strong></td>
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<tr>
<td>Male</td>
<td>51</td>
<td>82%</td>
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<tr>
<td>Female</td>
<td>11</td>
<td>18%</td>
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<tr>
<td><strong>Tumor Site</strong></td>
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<td>Hypopharynx</td>
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<td>9%</td>
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<tr>
<td>Oral Cavity</td>
<td>0</td>
<td>0%</td>
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## Treatment Time at RPCI

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<th>2004-2007 (n = 78)</th>
<th>2007-2009 (n = 62)</th>
<th>Local Control</th>
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<tr>
<td><strong>Median RT duration (days)</strong></td>
<td>51 (39-83)</td>
<td>46 (38-67)</td>
<td>81 vs 95%, P=0.01</td>
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<tr>
<td><strong>Duration &lt; 56 days</strong></td>
<td>64</td>
<td>58</td>
<td>90%</td>
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<tr>
<td><strong>Duration &gt; 56 days</strong></td>
<td>14</td>
<td>4</td>
<td>61%</td>
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Optimal Treatment Time

Start on a Monday!

<table>
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<tr>
<th>Sun</th>
<th>Mo</th>
<th>Tu</th>
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<th>Th</th>
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<th>Sat</th>
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Treatment time = 47 days

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<td>35</td>
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</tbody>
</table>

Treatment time = 49 days

Up to 6 fx/week if needed
RPCI Study #2

• IMRT Prescription
  – Total dose 70 Gy
  – 2 Gy per fraction
  – 35 treatments.

• Treatment time
  – 35 fractions (35 days)
  – 6 weekends (12 days)
  – Total time 47 days
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TOBACCO

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  – Bad during RT
• Quitting prior to RT makes a **BIG** difference
RTOG 0129 – Post Hoc Analysis

• Retrospective Analysis
• Randomized Trial
  – Stage III and IV Oropharyngeal cancer
  – Accelerated fractionation vs Standard fractionation
• 2002-2005
• 721 patients
  – 323 patients had HPV status known.

RTOG 0129 – Post Hoc Analysis

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Effect of Smoking on H&N Ca

- Retrospective Study 1989 -2006
- 1871 patients
- All H&N disease sites
- All stages
- Follow up time approximately 3 years.

Effect of Smoking on H&N Ca

Effect of Smoking on H&N Ca

Smoking During RT → Bad Outcome

- Retrospective Study, case matched (1999-2008)
- 202 patients
- “Former smoker”
  - anyone who quit anytime prior to RT

- Squamous cell cancer of
  - Oral cavity
  - Pharynx (Naso -, Oro -, Hypo -)
  - Larynx
- Median follow up
  - 49 months
Smoking During RT → Bad Outcome

Smoking During RT $\rightarrow$ Bad Outcome

Smoking + RT = bad idea.

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<thead>
<tr>
<th></th>
<th>5 yr LRC</th>
<th>5 yr OS</th>
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<tbody>
<tr>
<td></td>
<td>Former</td>
<td>Active</td>
</tr>
<tr>
<td>Fortin (2009)</td>
<td>80%</td>
<td>67%</td>
</tr>
<tr>
<td>Chen (2011)</td>
<td>69%</td>
<td>58%</td>
</tr>
</tbody>
</table>

*Int Jn of Rad Onc Biol Phys*
### Outline

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  makes a *BIG* difference
Smoking Cessation Is Associated With Improved Survival in Oropharynx Cancer Treated by Chemoradiation

Alexis J. Platek, BSc; Vijayvel Jayaprakash, MBBS, PhD; Mihai Merzianu, MD; Mary E. Platek, PhD; David M. Cohan, MD; Wesley L. Hicks, Jr., MD; Sathiya P. Marimuthu, MBBS; Timothy B. Winslow, MS; Vishal Gupta, MD; Hassan Arshad, MD; Moni A. Kuriakose, MD; Shiva Dibaj, MS; James R. Marshall, PhD; Mary E. Reid, PhD; Graham W. Warren, MD, PhD; Anurag K. Singh, MD
90% OS in those who quit 30 days prior to starting RT.
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• 40 pack years
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Can’t be changed

Smokes 1.5 ppd
• Seen November 10
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CAN be changed to improve outcomes
CASE

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- Seen November 10
- Because of work, wants to start on a Wednesday

Smoking Cessation

TX 6 fx/wk wknd/bid to complete in 47d

Start on a Monday

WILL Improve Outcomes