Current treatment practices for limited-stage small cell lung cancer: A survey of US radiation oncologists on the timing of thoracic radiotherapy with chemotherapy

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CONFLICTS OF INTEREST

• No conflicts
BACKGROUND:
Limited-Stage Small Cell Lung Cancer (LS-SCLC)

• Small cell lung cancer accounts for 10-15% of lung cancer cases\(^1\)

• Limited stage: confined to ipsilateral hemithorax
  • More favorable outcomes than extensive stage: five-year survival rates over 25% and median survival around 25-30 months when treated aggressively\(^2,3\)

• Standard treatment = chemotherapy + concurrent thoracic radiotherapy + prophylactic cranial irradiation

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BACKGROUND: Timing of Thoracic Radiotherapy (TRT) with Chemotherapy

National Comprehensive Cancer Network (NCCN) recommendations:\(^1\):

- Administer TRT *concurrently* with chemotherapy, rather than sequentially
- Start TRT *early*, in cycle 1 or 2 of chemo
- If starting TRT after cycle 1 of chemo, target volume can be reduced to account for tumor shrinkage

Evidence:

- Phase III trial of 231 patients showed that concurrent therapy improved overall survival compared to sequential, but statistical significance was not achieved (*P*=0.097)\(^2\)
- Several systematic reviews and meta-analyses show a survival benefit to early start of TRT,\(^3,4\) but the benefit seems to disappear in trials with once-daily RT and/or nonplatinum-based chemo regimens
METHODS

• OHSU IRB-approved online questionnaire of US radiation oncologists designed using REDCap
• 39 questions
• Invitations sent in October, 2016
• Purpose: Assess practice patterns of US radiation oncologists for patients with LS-SCLC
• Hypothesis: Most respondents are expected to follow national guidelines and recommend early concurrent chemoradiotherapy
RESULTS: Survey Respondents

- Survey invitations sent to 6954 email addresses, with 732 undeliverable automatic replies and 11 ineligible responses
- 309 complete responses from radiation oncologists

<table>
<thead>
<tr>
<th>Practice Setting</th>
<th>Number of Respondents (%)</th>
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<tbody>
<tr>
<td>Private</td>
<td>182 (58.9%)</td>
</tr>
<tr>
<td>Academic</td>
<td>127 (41.1%)</td>
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<tr>
<th>Practice Region</th>
<th>Number of Respondents (%)</th>
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<tbody>
<tr>
<td>Central</td>
<td>79 (25.6%)</td>
</tr>
<tr>
<td>Northern</td>
<td>72 (23.3%)</td>
</tr>
<tr>
<td>Pacific</td>
<td>58 (18.8%)</td>
</tr>
<tr>
<td>Southern</td>
<td>66 (21.4%)</td>
</tr>
<tr>
<td>Western</td>
<td>31 (10.0%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (1.0%)</td>
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<tr>
<th>Number of years since completing residency training</th>
<th>Number of Respondents (%)</th>
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<tbody>
<tr>
<td>Currently in residency training</td>
<td>11 (3.6%)</td>
</tr>
<tr>
<td>0-2</td>
<td>20 (6.5%)</td>
</tr>
<tr>
<td>3-5</td>
<td>49 (15.9%)</td>
</tr>
<tr>
<td>6-10</td>
<td>61 (19.7%)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>168 (54.4%)</td>
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<tr>
<th>Number of lung cancer patients treated with definitive intent in the past year</th>
<th>Number of Respondents (%)</th>
</tr>
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<tbody>
<tr>
<td>None</td>
<td>6 (1.9%)</td>
</tr>
<tr>
<td>1-2</td>
<td>7 (2.3%)</td>
</tr>
<tr>
<td>3-4</td>
<td>13 (4.2%)</td>
</tr>
<tr>
<td>5-10</td>
<td>41 (13.3%)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>242 (78.3%)</td>
</tr>
</tbody>
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<th>Number of limited-stage small cell lung cancer patients treated in the past year</th>
<th>Number of Respondents (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>137 (44.3%)</td>
</tr>
<tr>
<td>5 or more</td>
<td>172 (55.7%)</td>
</tr>
</tbody>
</table>
RESULTS: Concurrent Radiotherapy is Universally Preferred

What is your general recommendation about the timing of TRT with chemotherapy?

- **Concurrent therapy:**
  Thoracic RT delivered at the same time as systemic chemotherapy

- **Sequential therapy:**
  Thoracic RT delivered alone after all cycles of chemotherapy are finished
RESULTS: Preferred and Actual Timing of TRT with Chemo

In general, when do you prefer to start TRT in relation to chemotherapy?

- Cycle 1: 71%
- Cycle 2: 25%
- Cycle 3 or Later: 4%

In reality, when do most of your patients start TRT in relation to chemotherapy?

- Cycle 1: 44%
- Cycle 2: 48%
- Cycle 3 or Later: 8%
Phase III trial of concurrent thoracic radiotherapy with either first- or third-cycle chemotherapy for limited-disease small-cell lung cancer†


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• 2013 South Korean trial1 of 222 patients with LS-SCLC, randomly assigned to receive TRT early (with cycle 1 of chemotherapy) or late (with cycle 3).

• No survival difference seen between the two arms.

• Neutropenic fever occurred more frequently with early TRT than late (P=0.02).

• In our survey, over half (51%) of respondents said they were not familiar with this trial.

RESULTS: Thoughts on the Evidence

- Strong association between preferring early timing of TRT in cycle 1 and believing this practice improved survival ($P=0.0002$).

- Knowledge of the South Korean trial was not associated with preference for any TRT timing, but it was associated with respondents being more flexible in terms of delaying TRT in actual practice ($P=0.02$).

Is survival improved by starting thoracic RT with cycle 1 of chemotherapy rather than cycle 3?

- Yes: 54%
- No: 18%
- Evidence is unclear: 28%
RESULTS: Target Volume for Primary Disease

When starting TRT after cycle 1 of chemo, do you treat based on pre-chemo or post-chemo volume?

- In the South Korean trial, target volume in the late TRT arm was based on post-chemotherapy volume.
- Significant tumor shrinkage occurred in 76% of patients in the late TRT arm, so patients were more likely to receive reduced TRT volume.
- Thus, starting TRT in cycle 3 based on post-chemo volume was noninferior to starting TRT in cycle 1, and it had a more favorable side effect profile.
Conclusions

• Respondents strongly aligned with NCCN guidelines, which recommend early concurrent chemoradiotherapy.
• Nearly three quarters of respondents preferred to start TRT with cycle 1 of chemotherapy, but starting in cycle 2 was more common in actual practice.

Limitations

• Low response rate
• Selection bias
• Recall bias

Future Directions

• There is significant disagreement over whether starting TRT early improves survival.
• Given implications for survival, toxicity, logistics, and quality of life, further research is needed to determine how best to care for patients with LS-SCLC.
Thank You!

OTHER RESULTS FROM THIS SURVEY:

Prophylactic Cranial Irradiation (PCI)
- 98% recommended PCI
- 96% obtained pre-PCI brain MRI
- 33% routinely obtained post-PCI serial brain MRI
- 35% recommended memantine for PCI patients

Elective Nodal Irradiation (ENI)
- 64% did not recommend ENI for N0, N1, or N2 disease

Radiation Dose and Fractionation
- 60% preferred to administer thoracic RT once daily
- 76% administered thoracic RT once daily most commonly in practice
- Most common doses: 60 Gy for once-daily RT, 45 Gy for twice-daily RT