Stereotactic Lung Radiotherapy (SBRT) vs. Wedge Resection for Stage I NSCLC

The subject of stereotactic lung radiotherapy (SBRT) for cure of stage I disease has been extensively covered on GRACE with good cause: we may be witnessing a major change in how we treat early stage cancer. Multiple strategies for improved surveillance are being developed, and hopefully one or more will be successful, resulting in more frequent detection of early stage disease. If so, we will have what my mentor calls a “delicious dilemma” — what is the best way to cure these early-stage patients? Before turning to an important new article in JCO on the subject, I refer the curious reader to recent coverage on GRACE that leads up to the subject at hand:

**Limited Resection vs. Radiation for Marginal Patients with Early Stage NSCLC**: 11/15/2007 by Dr. Jack West
- Review of evidence that older patients may do as well with a limited, smaller resection
- Yendamuri / MD Anderson report from 2007 JTO: 160 patients with stage I NSCLC from 1988 to 2005 treated with either 3D-conformal radiation or limited resection — surgery beat radiation in overall cohort but if you matched for similar characteristics, they were equivalent.

**Dr. Le, Radiation Oncologist from Stanford, on Radiation Options for Early Stage NSCLC**: 12/19/09
- PET/CT can improve radiation planning
- We have better control now for respiratory motion
- Review of ongoing studies

**Interview with Dr. Vivek Mehta, Radiation Oncologist: Early Stage and Locally Advanced NSCLC**: 1/15/2009
- Great review of the biologic difference between small fractions every day for seven weeks (traditional radiation) vs. giving a huge dose in 1-5 fractions (stereotactic radiation)
- Simple-language review of why existing comparisons of surgery and radiation are not fair:
  - Surgery can show patients to be of a higher stage so stage I patients in a surgical group truly are stage I while in radiation studies, some patients are really more advanced
  - Since there is no randomization, radiation patients are sicker; they are often in this group because they are too sick for surgery and would die earlier no matter what you did
- Postoperative radiation vs. brachytherapy

A new article in JCO adds substantially to the conversation and moves the field forward. In current practice, patients eligible for lobectomy get a lobectomy. At most institutions, those not eligible for a lobectomy get a smaller surgery (most commonly a wedge resection). Finally, those that are too sick for a more limited resection will get some form of radiation, with SBRT gaining steam. We treat this way not because we believe that radiation is an inferior therapy, but because surgery has a much longer experience — we don’t want to deny any patient a modality that has been time-proven to cure. So, as you can see, the sickest patients with the worst prognosis tend to get the radiation, making comparisons of surgery to radiation biased in favor of surgery.
The investigators looked back at 124 patients with stage T1-2N0 NSCLC treated at their institution (William Beaumont Hospital; Royal Oak, MI) between February 2003 and August 2008 and made a comparison between the surgery patients (treated off of any study) and the stereotactic lung radiotherapy patients (treated on a phase II study). While retrospective, to the best of my knowledge their groups were far more similar than any previously reported. All patients were ineligible for lobectomy, although most of the radiation patients were judged unable to undergo any surgery—95% of them were medically inoperable with only 5% landing in this group by patient choice. I'll spare you the huge table of the patient characteristics, but will editorialize and share what I see as the key differences:

- **Charleson comorbidity index**: This is an under-used measure that I include in all of my studies. It measures how sick a person is, as judged by expected 10 year mortality. Note that you get 2 points just for having cancer. In this study, the SBRT group had a score of 4 and the wedge resection group had a score of 3. This helps explain why 95% of the SBRT patients were judged too sick for surgery (p<.01).
- **Age**: The median age of the wedge resection patients was 74 years, compared to 78 years for SBRT.
- **Clinical stage**: The difference was not statistically significant, but it is worth noting that 29% of patients in the SBRT group had T2 stage but only 19% in the wedge resection group.
- **Mediastinoscopy or node dissection**: 20% rate in the SBRT group vs. 71% in the wedge group.

Alright, we've eaten our metaphorical vegetables. We've reviewed the background, we've looked at basic methods, and we've compared the groups to see how similar the groups are. We're ready for desert, the results:

![Graph C](Click on image to enlarge)

I direct your attention first to graph C, which shows superior locoregional control for SBRT. This result generates the hypothesis that SBRT may actually be better than wedge resection. The authors (I think reasonably) speculate that high biologic dose to regional nodes may have
inadvertently treated micrometastatic disease there. Indeed, “focal” radiation is not nearly as focal as many non radiation oncologists believe. While this retrospective analysis is not sufficient to start recommending SBRT over wedge resection for patients ineligible for lobectomy, it certainly generates the hypothesis that SBRT may be better, and makes further study in a randomized trial promising and ethical.

But to see the full picture, we must look at the other graphs too. Graph D addresses a broader cancer-specific outcome: freedom from any failure. One alternative hypothesis is that radiation doesn’t really improve local results as much as we think, but creates so much scarring that you can’t tell easily on imaging. In this light, the results hold up in that curves A-D all at show the SBRT curve on top. However, curve E shows essentially similar results. Curve E is cause-specific survival; by this measure, SBRT and wedge resection do a similar job in preventing lung cancer death. Thus, a viable alternative hypothesis is that SBRT survival results are just similar to wedge resection — even this result would be worthy of additional study since more patients are eligible for SBRT, it has less hospital stay (none) and is less burdensome for the patient.

Finally, curve F must be addressed, showing superior survival for wedge resection, despite the similar cause (lung cancer) specific survival shown in figure E. The SBRT patients were sicker, had more medical problems, and were older. Regardless of lung cancer therapy, they were predisposed to die earlier, and so this graph does not hinder my conclusion that a randomized trial is merited. Only a randomized trial will treat patients with similar age and health status to truly answer this question.

As best I am aware, all of the trials going on in the US are phase II studies attempting to define the best way to do SBRT. Before going head to head against surgery, radiation oncology researchers want to put forward the best SBRT. This is important for two reasons: 1st, they want to win; 2nd, if a sub-optimal strategy is compared, and that strategy wins, it will become the standard of care and harder to improve upon. There is a randomized study going on in the Netherlands that compares SBRT to anatomic resection. Right now, most lung cancer patients present with metastatic disease. As an optimist, I hope that screening trials will present me with far more stage I patients, and that SBRT will arm me with a less-invasive, maybe even more effective way to cure them.

GRACE is supported by contributions from our membership. Be a part of the solution. Donate Today!

This content is for personal use only and is subject to the GRACE Disclaimer terms.

All Content Copyright ©GRACE - All Rights Reserved