

Are the Reported Clinical Outcomes with Stereotactic Ablative Radiotherapy Generalizable?

Suresh Senan, MRCP, FRCR, PhD,* and Sashendra Senthil, MBChB, FRANZCR*†

Stereotactic ablative radiotherapy (SABR), or stereotactic body radiotherapy (RT), is now established as a guideline-specified curative treatment option for patients presenting with early stage non-small-cell lung cancer (NSCLC) that are unfit for surgical resection.^{1,2} Long-term follow-up in a series of 676 patients revealed local control was 90% at 5-years, with regional and distant recurrences in 13% and 20% of patients, respectively.³ As SABR is delivered on an outpatient basis, typically in as few as three treatment sessions, it is well tolerated by the elderly and those with comorbidities. In addition, prospective studies have established that SABR does not adversely impact patient-reported quality of life.⁴

SABR was pioneered in the early 1990s by clinicians in Scandinavia and Japan,⁵ and was adopted soon after by some centers in Germany. In this issue, Guckenberger et al.⁶ report patterns of care for 582 patients treated in 13 German and Austrian centers between 1998 and 2011. With one exception, these were all academic centers. Pretreatment histologic diagnosis was available in 85% of patients, and high-grade toxicity was uncommon. A rapid increase in the number of patients treated was observed in recent years, mirroring the situation in The Netherlands and United States.^{7,8} A range of dose-fractionation schemes were used, reflecting the evolving experience with SABR over time. Similarly, SABR delivery techniques evolved reflecting the availability of improving technology, and by 2011, 92% of all treatments used daily in-room image guidance immediately before treatment to ensure accuracy.

In keeping with a previous report,⁹ Guckenberger et al.³ found that delivery of biologically effective doses of at least 106 Gy were associated with local control rates in excess of 90%. Treatment outcomes were not associated with an apparent learning curve, and the authors observed that availability of improved treatment planning and image-guided SABR delivery paralleled the use of more effective doses. Their findings suggest that existing technical variations in SABR delivery could be of limited clinical significance, as long as effective planning target volume-encompassing threshold doses can be delivered in an accurate manner. The findings of the present study in 13 German and Austrian centers offers hope that reported SABR outcomes could be extrapolated to many of the 300 RT centers in these countries.¹⁰ The ability to reproduce SABR outcomes outside leading academic centers is supported by the finding of improved population-based survival in elderly Dutch patients with stage I NSCLC, in the 6-year period after the introduction of SABR.⁷

The growing availability of SABR, with its reproducible local control rates and low toxicity, make it increasingly important to address the unmet therapeutic needs on a population level. In many countries, the elderly with mainly smoking-related comorbidities, are the fastest growing population of lung cancer patients. Because of historical reasons, nationwide cancer registries have only recently become well established in Germany, when the Federal Cancer Registry Act came into force in 1995.¹¹ However, data from the Surveillance, Epidemiology and End Results-Medicare database illustrate the

*Department of Radiation Oncology, VU University Medical Center, Amsterdam, The Netherlands; and †William Buckland Radiation Oncology, Alfred Health, Melbourne, Australia.

Disclosure: The VU University Medical Center has research collaborations with Varian Medical Systems, Brainlab AG and Velocity Medical Solutions. SUS has received honoraria and travel support from Varian Medical Systems. SAS declares no conflict of interest.

Address for correspondence: Suresh Senan, MRCP, FRCR, PhD, Department of Radiation Oncology, VU University Medical Center, De Boelelaan 1118, 1081 HV Amsterdam, The Netherlands. E-mail: s.senan@vumc.nl

Copyright © 2013 by the International Association for the Study of Lung Cancer

ISSN: 1556-0864/13/0808-0995

impact of these demographic changes.¹² Between 1998 and 2007, a marked increase was seen in the number of elderly patients with lung cancer and three or more comorbidities. During the same period, access to video-assisted thoracic surgery increased threefold to 32%, despite which the proportion of patients in Surveillance, Epidemiology and End Results-Medicare database who did not undergo any local treatment increased from 14.5% in 1998, to 18.5% in 2007. As access to SABR was relatively limited in the United States in 2007,⁸ data from the Dutch cancer registry are encouraging. In The Netherlands, an absolute reduction of 7% in the untreated elderly patient population was observed in the 6 years after the introduction of SABR, which in turn resulted in a population-based improvement in median survival of 9.3 months.⁷ These findings suggest that SABR will become increasingly important to address the unmet therapeutic needs of the aging global population.

The rapid improvements in technology for SABR have led to greater clinician confidence in delivering curative doses. With SABR now poised to have a major impact on the treatment of early-stage NSCLC, programs to ensure compliance with current guidelines^{13,14} and to monitor outcomes in populations are important. The need for continued audit is supported by analysis of quality-assurance data from prospective trials, which revealed that a failure to adhere to protocol-specified RT requirements was associated with decreased survival, poorer local control, and potentially increased toxicity.¹⁵

REFERENCES

1. NCCN: NCCN Clinical practice guidelines in oncology: non-small cell lung cancer. Version 1.2013, Available at: <http://www.nccn.com> Accessed January 3, 2013
2. Howington JA, Blum MG, Chang AC, Balekian AA, Murthy SC. Treatment of stage I and II non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2013;143(5 Suppl):e278S–e313S.
3. Senthil S, Lagerwaard FJ, Haasbeek CJ, Slotman BJ, Senan S. Patterns of disease recurrence after stereotactic ablative radiotherapy for early stage non-small-cell lung cancer: a retrospective analysis. *Lancet Oncol* 2012;13:802–809.
4. Palma DA, Senan S. Improving outcomes for high-risk patients with early-stage non-small-cell lung cancer: insights from population-based data and the role of stereotactic ablative radiotherapy. *Clin Lung Cancer* 2013;14:1–5.
5. Solberg TD, Siddon, RL, Kavanagh, B.; *Historical Development of Stereotactic Ablative Radiotherapy*. Heidelberg, Springer-Verlag 2012
6. Guckenberger M, Allgäuer, M, Appold, S, et al. Safety and efficacy of stereotactic body radiotherapy for stage I non-small-cell lung cancer in routine clinical practice: a patterns-of-care and outcome analysis. *J Thorac Oncol* 2013;8:1050–1058.
7. Haasbeek CJ, Palma D, Visser O, Lagerwaard FJ, Slotman B, Senan S. Early-stage lung cancer in elderly patients: a population-based study of changes in treatment patterns and survival in the Netherlands. *Ann Oncol* 2012;23:2743–2747.
8. Pan H, Simpson DR, Mell LK, Mundt AJ, Lawson JD. A survey of stereotactic body radiotherapy use in the United States. *Cancer* 2011;117:4566–4572.
9. Grills IS, Hope AJ, Guckenberger M, et al. A collaborative analysis of stereotactic lung radiotherapy outcomes for early-stage non-small-cell lung cancer using daily online cone-beam computed tomography image-guided radiotherapy. *J Thorac Oncol* 2012;7:1382–1393.
10. Rosenblatt E, Izewska J, Anacak Y, et al. Radiotherapy capacity in European countries: an analysis of the Directory of Radiotherapy Centres (DIRAC) database. *Lancet Oncol* 2013;14:e79–86
11. Haberland J, Bertz J, Wolf U, et al. German cancer statistics 2004. *BMC Cancer* 2010;10:52
12. Vest MT, Herrin J, Soulos PR, et al. Use of new treatment modalities for non-small cell lung cancer care in the medicare population. *Chest* 2013;143:429–35
13. Potters L, Kavanagh B, Galvin JM, et al.; American Society for Therapeutic Radiology and Oncology; American College of Radiology. American Society for Therapeutic Radiology and Oncology (ASTRO) and American College of Radiology (ACR) practice guideline for the performance of stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys* 2010;76:326–332.
14. De Ruysscher D, Faivre-Finn C, Nestle U, et al. European Organisation for Research and Treatment of Cancer recommendations for planning and delivery of high-dose, high-precision radiotherapy for lung cancer. *J Clin Oncol* 2010;28:5301–5310.
15. Weber DC, Tomsej M, Melidis C, Hurkmans CW. QA makes a clinical trial stronger: evidence-based medicine in radiation therapy. *Radiother Oncol* 2012;105:4–8.