Editorial

What is the current status of Stereotactic body radiotherapy for stage I non-small cell lung cancer?

Matthias Guckenberger

Department of Radiation Oncology, University Hospital Wuerzburg, Wuerzburg, Germany

J Thorac Dis 2011;3:147-149. DOI: 10.3978/j.issn.2072-1439.2011.06.04

Non-small cell lung cancer, if detected at early stage, is a disease with high probability for cure. However, the treatment in clinical practice is highly dependent on the co-morbidities of the patient, the performance status and age. A relevant proportion especially of the elderly patient population remains untreated despite the dismal prognosis of untreated stage I NSCLC with 5 year cancer specific survival (CSS) of only 16% (1,2). Conventionally fractionated radiotherapy has been the treatment of choice for medically inoperable patients: however, outcome is suboptimal with 5 year CSS ranging between 13% and 39% (3); most importantly, local disease recurrence is the most frequent site of failure, not systemic metastases (4). CSS is excellent after lobectomy ranging between 100% and 57.6% depending on the size of the primary tumor (5). Despite a randomized trial demonstrated inferior outcome of sublobar resection compared to lobectomy (6), sublobar resection is practiced especially in high-risk patients aiming at preservation of pulmonary function (7). Wedge resection seems to be insufficient even for small tumors whereas segmentectomy results in promising CSS if the tumor size is below 3cm (5,8).

Stereotactic body radiotherapy (SBRT) – or stereotactic ablative radiotherapy, which are different names for identical treatment methodologies – has gained much attention as a novel and promising treatment option for early stage NSCLC. The rational for the practice of SBRT is the finding that very high radiation doses are required to locally control NSCLC, higher than achievable with conventional radiation techniques (9): SBRT allows treatment with these escalated irradiation doses to the site of the primary tumor by optimal lung sparing using modern radiotherapy technologies e.g. breathing motion compensation and image-guidance. As a consequence, local tumor control after SBRT is substantially better compared to conventionally fractionated radiotherapy: in a large number of prospective phase II trials, local tumor control ranged consistently between 84 – 98% (10-14) compared to only 60% after conventional radiotherapy (3). This translates into CSS rates between 72.5% and 88% after 3 years (10,11,13).

The review in this issue of the *Journal of Thoracic Disease* summarizes the current status of SBRT (15). No randomized controlled trial tested SBRT in comparison with any other treatment modality: best-supportive care, conventionally fractionated radiotherapy, sublobar resection or lobectomy. However, there is a growing body of evidence based on prospective phase II trials and well performed retrospective analyses, which define the current status of SBRT in this wide spectrum of patients with early stage NSCLC.

A recent population based analysis demonstrated that the introduction of SBRT significantly

No potential conflict of interest.

Corresponding to: Matthias Guckenberger, MD. Department of Radiation Oncology, University Hospital Wuerzburg, Josef-Schneider Strasse 11, 97080 Wuerzburg, Germany. Tel: +49-931-201-28984; Fax: +49-931-201-28221. Email: Guckenberger_m@klinik.uni-wuerzburg.de.

Submitted Jun 14, 2011. Accepted for publication Jun 15, 2011.
Available at www.jthoracdis.com

ISSN: 2072-1439

decreased the proportion of untreated patients older than 75 years, which resulted in significantly improved overall survival (2): a non-invasive treatment practiced in an out-patient fashion with only 1 – 8 treatment fractions is a low barrier for patients and referring doctors to choose a curative treatment approach. Even very poor pulmonary function in the context of severe COPD should not be considered as contraindication for SBRT (16,17).

The difference in both local tumor control and CSS between SBRT and conventional radiotherapy is highly consistent in the literature and is considered as so large, that SBRT is widely accepted as the treatment of choice for patients who are no candidates for surgical resection. Overall survival now seems to be influenced mainly by the comorbidities of the patients (18). As stated clearly in the review, strict and comprehensive quality assurance covering indication for SBRT, staging, treatment planning, radiotherapy delivery and follow-up – the whole chain of SBRT treatment – are mandatory for the practice of this sophisticated treatment. Such quality assurance protocols are published and broadly available, which will be the basis for a broader clinical implementation of SBRT outside of highly specialist academical centres.

There is limited data comparing SBRT and surgical treatments. A retrospective study reported improved local tumor control and regional control with no difference in CSS for SBRT compared to wedge resection (19). Japanese patients, who were operable but refused surgery, experienced excellent 5 year overall survival of 72% and 62% for stage IA and IB after SBRT, respectively; these results are approaching overall survival after lobectomy, which is also indicated by a Markov-Model analysis (20). In the absence of randomized trials for both SBRT and sublobar resection, both SBRT and sublobar resection should be offered to high-risk patient as viable treatment options. For patient suitable for lobectomy, SBRT offers a curative treatment option if surgery is refused.

References

1. Raz DJ, Zell JA, Ou SH, Gandara DR, Anton-Culver H, Jablons DM. Natural history of stage I non-small cell lung cancer: implications for early detection. Chest 2007;132:193-9.
2. Palma D, Visser O, Lagerwaard FJ, Belderbos J, Slotman BJ, Senan S. Impact of introducing stereotactic lung radiotherapy for elderly patients with stage I non-small-cell lung cancer: A population-based time-trend analysis. J Clin Oncol 2010;28:5153-9.
3. Rowell NP, Williams CJ. Radical radiotherapy for stage I/II non-small cell lung cancer in patients not sufficiently fit for or declining surgery (medically inoperable). Cochrane Database Syst Rev 2001:CD002935.
4. Sibley GS, Jamieson TA, Marks LB, Anscher MS, Prosnitz LR. Radiotherapy alone for medically inoperable stage I non-small-cell lung cancer: the Duke experience. Int J Radiat Oncol Biol Phys 1998;40:149-54.
5. Okada M, Nishio W, Sakamoto T, Uchino K, Yuki T, Nakagawa A, et al. Effect of tumor size on prognosis in patients with non-small cell lung cancer: the role of segmentectomy as a type of lesser resection. J Thorac Cardiovasc Surg 2005;129:87-93.
6. Ginsberg RJ, Rubinstein LV. Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Lung Cancer Study Group. Ann Thorac Surg 1995;60:615-22; discussion 622-3.
7. Blasberg JD, Pass HI, Donington JS. Sublobar resection: a movement from the Lung Cancer Study Group. Journal of thoracic oncology: official publication of the International Association for the Study of Lung Cancer 2010;5:1583-93.
8. Kates M, Swanson S, Wisnivesky JP. Survival following lobectomy and limited resection for the treatment of stage I non-small cell lung cancer<=1 cm in size: a review of SEER data. Chest 2011;139:491-6.
9. Partridge M, Ramos M, Sardaro A, Brada M. Dose escalation for non-small cell lung cancer: Analysis and modelling of published literature. Radiother Oncol 2011;99:6-11.
10. Baumann P, Nyman J, Hoyer M, Wennberg B, Gagliardi G, Lax I, et al. Outcome in a prospective phase II trial of medically inoperable stage I non-small-cell lung cancer patients treated with stereotactic body radiotherapy. J Clin Oncol 2009;27:3290-6.
11. Fakiris AJ, McGarry RC, Yiannoutsos CT, Papiez L, Williams M, Henderson MA, et al. Stereotactic body radiation therapy for early-stage non-small-cell lung carcinoma: four-year results of a prospective phase II study. Int J Radiat Oncol Biol Phys 2009;75:677-82.
12. Bral S, Gevaert T, Linthout N, Versmessen H, Collen C, Engels B, et al. Prospective, risk-adapted strategy of stereotactic body radiotherapy for early-stage non-small-cell lung cancer: Results of a phase II trial. Int J Radiat Oncol Biol Phys 2010 Aug 12. [Epub ahead of print]
13. Ricardi U, Filippi AR, Guarneri A, Giglioli FR, Ciammella P, Franco P, et al. Stereotactic body radiation therapy for early stage non-small cell lung cancer: results of a prospective trial. Lung Cancer 2010;68:72-7.
14. Timmerman R, Paulus R, Galvin J, Michalski J, Straube W, Bradley J, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. JAMA 2010;303:1070-6.
15. Senan S, Palma DA, Lagerwaard FJ. Stereotactic ablative radiotherapy for stage I NSCLC: Recentadvances and controversies. J Thorac Dis 2011;3:189-96.
16. Stephans KL, Djemil T, Reddy CA, Gajdos SM, Kolar M, Machuzak M, et al. Comprehensive analysis of pulmonary function test (PFT) changes after stereotactic body radiotherapy (SBRT) for stage I lung cancer in medically inoperable patients. J Thorac Oncol 2009;4:838-44.
17. Palma D, Lagerwaard F, Rodrigues G, Haasbeek C, Senan S. Curative treatment of stage I non-small-cell lung cancer in patients with severe COPD: Stereotactic radiotherapy outcomes and systematic review. Int J Radiat Oncol Biol Phys. 2011 Jun 1. [Epub ahead of print]
18. Kopek N, Paludan M, Petersen J, Hansen AT, Grau C, Høyer M. Co-morbidity index predicts for mortality after stereotactic body radiotherapy for medically inoperable early-stage non-small cell lung cancer. Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology 2009;93:402-7.

19. Grills IS, Mangona VS, Welsh R, Chmielewski G, McInerney E, Martin S, et al. Outcomes after stereotactic lung radiotherapy or wedge resection for stage I non-small-cell lung cancer. J Clin Oncol 2010;28:928-35.
20. Louie AV, Rodrigues G, Hannouf M, Zaric GS, Palma DA, Cao JQ, et al. Stereotactic body radiotherapy versus surgery for medically operable stage I non-small-cell lung cancer: A markov model-based decision analysis. Int J Radiat Oncol Biol Phys. 2010 Oct 5. [Epub ahead of print]

Cite this article as: Guckenberger M. What is the current status of Stereotactic body radiotherapy for stage I non-small cell lung cancer? J Thorac Dis 2011;3:147-149. DOI: 10.3978/j.issn.2072-1439.2011.06.04