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CLINICAL INVESTIGATION **Lung**

RADIOLOGICAL AND CLINICAL PNEUMONITIS AFTER STEREOTACTIC LUNG RADIOTHERAPY: A MATCHED ANALYSIS OF THREE-DIMENSIONAL CONFORMAL AND VOLUMETRIC-MODULATED ARC THERAPY TECHNIQUES

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Purpose: **Lung fibrosis is common after stereotactic body radiotherapy (SBRT) for lung tumors, but the influence of treatment technique on rates of clinical and radiological pneumonitis is not well described. After implementing volumetric modulated arc therapy (RapidArc [RA]; Varian Medical Systems, Palo Alto, CA) for SBRT, we scored the early pulmonary changes seen with arc and conventional three-dimensional SBRT (3D-CRT).**
Methods and Materials: **Twenty-five SBRT patients treated with RA were matched 1:2 with 50 SBRT patients treated with 3D-CRT. Dose fractionations were based on a risk-adapted strategy. Clinical pneumonitis was scored using Common Terminology Criteria for Adverse Events version 3.0. Acute radiological changes 3 months post-treatment were scored by three blinded observers. Relationships among treatment type, baseline factors, and outcomes were assessed using Spearman's correlation, Cochran-Mantel-Haenszel tests, and logistic regression.**
Results: **The RA and 3D-CRT groups were well matched. Forty-three patients (57%) had radiological pneumonitis 3 months after treatment. Twenty-eight patients (37%) had computed tomography (CT) findings of patchy or diffuse consolidation, and 15 patients (20%) had ground-glass opacities only. Clinical pneumonitis was uncommon, and no differences were seen between 3D-CRT vs. RA patients in rates of grade 2/3 clinical pneumonitis (6% vs. 4%, respectively; $p = 0.99$), moderate/severe radiological changes (24% vs. 36%, respectively, $p = 0.28$), or patterns of CT changes ($p = 0.47$). Radiological severity scores were associated with larger planning target volumes ($p = 0.09$) and extended fractionation ($p = 0.03$).**
Conclusions: **Radiological changes after lung SBRT are common with both approaches, but no differences in early clinical or radiological findings were observed after RA. Longer follow-up will be required to exclude late changes.** **© 2011 Elsevier Inc.**

Lung cancer, Radiotherapy, Volumetric modulated arc therapy, Pneumonitis, Stereotactic body radiation therapy.

INTRODUCTION

Radiographic pneumonitis has been reported to occur in more than 60% of patients following lung stereotactic body radiotherapy (SBRT) (1, 2). However, clinical pneumonitis is uncommon, with an incidence of less than 10% in many series (1–4). Acute computed tomography (CT) changes occurring within 6 months of treatment include development of consolidation and ground-glass opacities (GGO) in the region of the tumor (2, 5, 6). Classification systems with five categories of acute CT changes after lung SBRT have been proposed (5), but no standard system of classification exists.

Differentiating between treatment effects and residual/recurrent tumor is challenging, but the distinction is crucial because benign CT changes are much more common than recurrence. Proper identification of residual or recurrent disease allows for surgical salvage; however, misinterpreting treatment effects as malignancy could expose patients to unnecessary interventions (7). Currently, a range of SBRT techniques are in clinical use, including three-dimensional conformal radiotherapy (3D-CRT), intensity-modulated radiation therapy (IMRT), helical tomotherapy, and volumetric modulated arc therapy, all of which could result in different patterns of radiological pneumonitis due to differences in dose distributions.

The VU Medical Centre implemented lung SBRT in 2003, using 3D-CRT (3) until September 2008, when RapidArc

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Conflict of interest: VU Medical Center has a research collaboration with Varian Medical Systems.

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(RA) (Varian Medical Systems, Palo Alto, CA) was introduced (8). Key advantages of RA include shorter treatment time and improved sparing of the chest wall (8), but as a tradeoff, the low-dose regions are larger and more commonly involve the contralateral lung. Figure 1 shows RA and 3D-CRT plans for a single patient, depicting all areas receiving more than 3 Gy. During post-SBRT follow-up, isolated anecdotal observations were made of radiological pneumonitis that appeared to be more extensive than findings expected after conventional 3D-CRT SBRT (Fig. 2). This prompted us to perform the present study in order to compare patterns of radiological changes after SBRT with RA and 3D-CRT and to evaluate the severity of acute clinical and radiological pneumonitis.

METHODS AND MATERIALS

Patient selection

Patients were identified from a prospective database of SBRT patients. Our routine practice requires outpatient assessments at 3 and 6 months post-SBRT, with a diagnostic scan performed at each visit. Patients were selected for this study if they had been treated for a stage I non-small-cell lung cancer with SBRT and had a follow-up scan completed within 4 months. Patients were excluded if the planning target volume (PTV) was >100 cc or if they had previously received radiotherapy for a lung cancer. Twenty-five RA patients met the inclusion criteria, 2 of whom had two PTVs in close proximity. Conventional SBRT patients were selected by matching with RA patients in a 2:1 ratio, with a preference for choosing the patients most recently treated with conventional SBRT. Matches were chosen based on the following criteria, in order of importance: dose/fractionation, PTV size, tumor location (peripheral vs. central [defined as within 2 cm of mediastinal structures]; upper vs. lower [relative to the carina], and left vs. right), age, and gender. Matching was done without knowledge of outcomes, using a semiautomated method with Microsoft Access (Microsoft Corp., Redmond, WA). For RA patients with two PTVs, matches were sought with two similarly sized PTVs in the same location; otherwise a match with a larger PTV in a similar location was chosen.

Treatment details

The risk-adapted fractionation schemes and treatment planning techniques have been described in detail previously (3, 8).

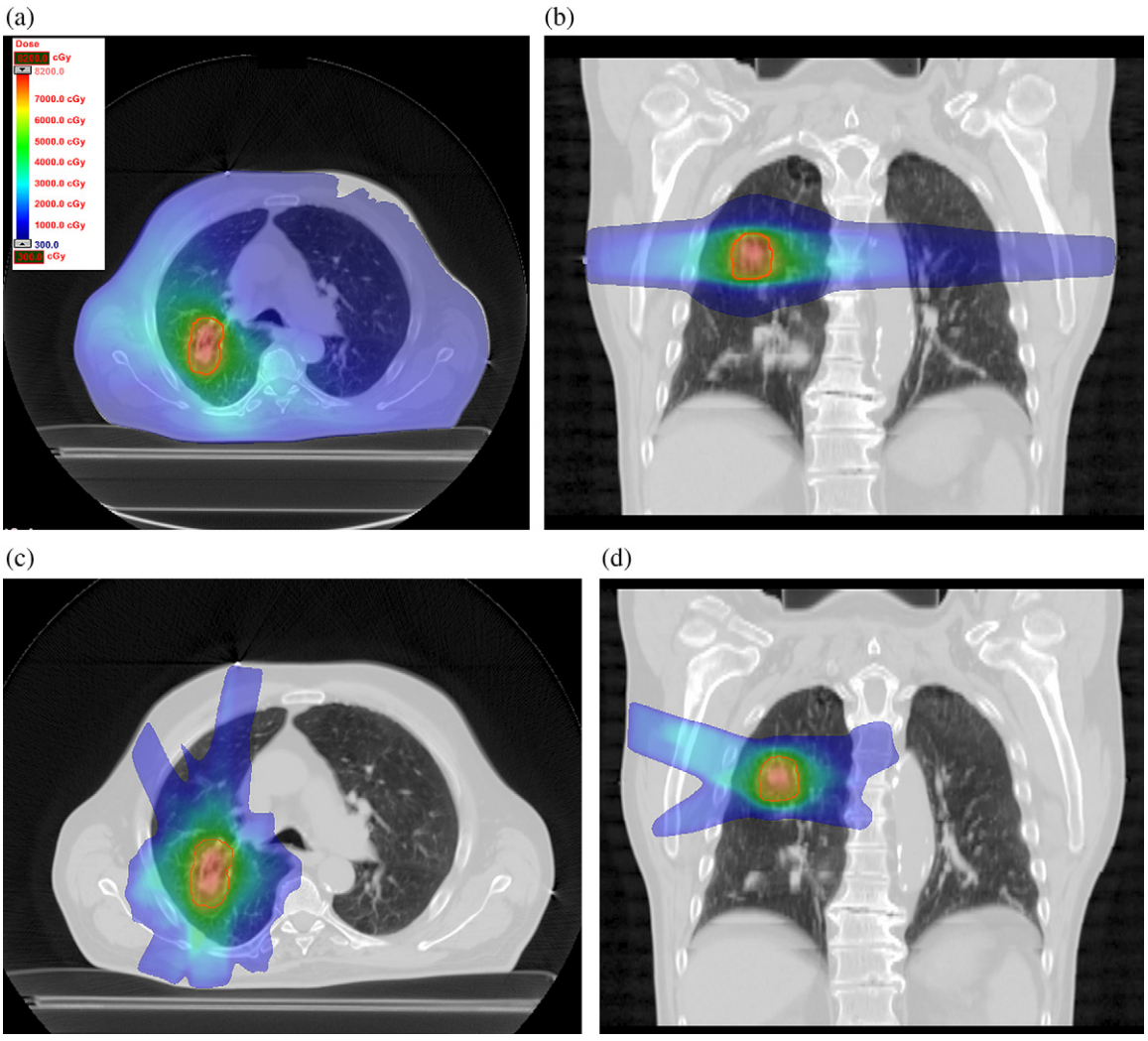

Fig. 1. (a and b) Volumetric modulated arc therapy (RA) and (c and d) 3D conformal plans for stereotactic hypofractionated lung radiotherapy, with the planning target volume outlined in red. Regions receiving 3 Gy or more are shown, with dose color scale at left. Although the RA plans are more conformal and improve chest wall sparing, the low-dose regions are larger and involve more contralateral lung.