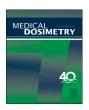
## ARTICLE IN PRESS

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A planning comparison of 3-dimensional conformal multiple static field, conformal arc, and volumetric modulated arc therapy for the delivery of stereotactic body radiotherapy for early stage lung cancer

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#### ABSTRACT

The primary objective of this study was to compare dosimetric variables as well as treatment times of multiple static fields (MSFs), conformal arcs (CAs), and volumetric modulated arc therapy (VMAT) techniques for the treatment of early stage lung cancer using stereotactic body radiotherapy (SBRT). Treatments of 23 patients previously treated with MSF of 48 Gy to 95% of the planning target volume (PTV) in 4 fractions were replanned using CA and VMAT techniques. Dosimetric parameters of the Radiation Therapy Oncology Group (RTOG) 0915 trial were evaluated, along with the van't Riet conformation number (CN), monitor units (MUs), and actual and calculated treatment times. Paired ttests for noninferiority were used to compare the 3 techniques. CA had significant dosimetric improvements over MSF for the ratio of the prescription isodose volume to PTV ( $R_{100\%}$ , p < 0.0001), the maximum dose 2 cm away from the PTV (D $_{2 \text{ cm}}$ , p=0.005), and van't Riet CN (p<0.0001). CA was not statistically inferior to MSF for the 50% prescription isodose volume to PTV ( $R_{50\%}$ , p=0.05). VMAT was significantly better than CA for  $R_{100\%}$  (p < 0.0001),  $R_{50\%}$  (p < 0.0001),  $D_{2 \text{ cm}}$  (p = 0.006), and CN (p < 0.0001) 0.0001). CA plans had significantly shorter treatment times than those of VMAT (p < 0.0001). Both CA and VMAT planning showed significant dosimetric improvements and shorter treatment times over those of MSF. VMAT showed the most favorable dosimetry of all 3 techniques; however, the dosimetric effect of tumor motion was not evaluated. CA plans were significantly faster to treat, and minimize the interplay of tumor motion and dynamic multileaf collimator (MLC) motion effects. Given these results, CA has become the treatment technique of choice at our facility.

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#### Introduction

Non–small cell lung cancers (NSCLC) comprise 85% to 90% of all lung cancer pathologies. Historically, only 15% of patients present with early stage disease; however, this number will likely increase with uptake of lung cancer screening. Early screening for atrisk populations may become more routine subsequent to recent results from the National Lung Screening trial and on-going European screening trials, as well as approval from the American Cancer Society. Therefore, the use of stereotactic body radiotherapy

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(SBRT) for patients with early stage NSCLC who are completely or marginally inoperable, or refuse surgery, will become more common as early screening proceeds and studies continue to show its effectiveness. Grills *et al.*<sup>6</sup> recently retrospectively compared SBRT *vs* wedge resection for patients with Stage I NSCLC, illustrating that although overall survival was better with wedge resection, cause-specific survival was identical. In another study, results have shown that high-surgical-risk, Stage I A/B patients given SBRT have performed similarly for local recurrence and disease-specific survival to a high-risk cohort that had surgery. Other studies have confirmed that SBRT is an effective and definitive treatment. 8.9

With a shift in standard of care approach in the treatment of lung cancer, lung SBRT utility will continue to increase. Beyond its demonstrated achievements in survival outcomes and local

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control, a hypofractionated course of treatment allows additional patient timeslots within radiation departments, translating into reduced wait times. The cost advantage in resource use reduction has also been compared favorably *vs* surgery.<sup>10</sup> As a result, numerous centers are initiating and expanding upon existing lung SBRT programs, as has been predicted from reviews in both Canada and the United States.<sup>11,12</sup> Simplicity in implementation and treatment delivery is desirable for any program, to maximize the use of health care resources.

Volumetric modulated arc therapy (VMAT) for lung SBRT has been compared with other conventional techniques, multiple static fields (MSFs) or arcs, and is being used by many centers owing to its favorable dosimetry and treatment times. 13-15 However, employing VMAT for a target in motion without actively accounting for breathing phases (e.g., 4-dimensional [4D] VMAT/4D cone-beam computed tomography, tumor tracking) or limiting tumor motion (e.g., abdominal compression, active breathing control, and gating) has gone against general recommendations from the American Association of Physicists in Medicine Radiation Therapy Committee Task Group 76. Since then, recent reports regarding the use of VMAT during respiratory motion are conflicting regarding the interplay effects on dose delivery, especially during hypofractionation. 17-21

Patients in this study were selected to have T1-2 N0 M0, mostly peripheral lesions. All patient underwent a free-breathing 4Dcomputed tomography scan, from which an internal target volume (ITV) was defined from the maximum intensity projection followed by an expansion to a planning target volume (PTV). Patients were all treated using 9 to 11 static coplanar or noncoplanar beams and with a prescribed dose of 48 Gy covering 95% of the PTV, delivered in 4 fractions on alternate days. There are some drawbacks when using a MSF treatment technique. The planning time is significant, involving choosing appropriate field arrangements, modifying multileaf collimator (MLC) positions per field, and frequent reevaluation of conformity indices. Beam delivery times (after setup imaging) are in the order of 8 to 9 minutes when using 600 MU/ minute, and longer if noncoplanar fields are involved. Although the position of the ITV is confirmed before and after treatment, intrafraction movement is a concern and has been shown to increase with prolonged treatment times.<sup>22</sup> Using a conformal arc (CA) technique with an arc or more arcs should reduce planning time, improve dosimetry, and decrease treatment times.

The primary objective of this study was to evaluate treatment time and monitor units (MUs) and standard dosimetric variables when comparing 3D conformal MSF plans to CA and VMAT plans in a retrospective planning study.

#### Methods and Materials

This retrospective study identified 23 patients with NSCLC previously treated using SBRT with a prescribed dose of 48 Gy to cover 95% of the PTV in 4 fractions. The PTVs varied in size from 16.0 to 67.0 cc. These MSF plans consisted of 9 to 11 static fields distributed in a wide arc of approximately  $200^\circ$ . Each patient treatment was replanned using CA and VMAT techniques.

#### Treatment Planning

All 3 techniques used 6 MV photons with a dose rate of 600 MU/min. The Eclipse treatment planning system was used for all plans (Varian Medical Systems, Palo Alto, CA), with the Anisotropic Analytical Algorithm (AAA version 10.0.25) used for volume dose calculations and the Progressive Resolution Optimizer (PRO version 10.0.28) used for VMAT optimization. To reduce comparison bias all 23 patient treatments were planned and data were recorded in separate spreadsheets first for CA planning, then for VMAT planning.

#### **End Points**

All planning followed the dosimetric parameters from the Radiation Therapy Oncology Group (RTOG) 0915 trial, including at least 95% of the PTV receiving the

prescription dose, 99% of the PTV receiving at least 90% of the prescription, and the maximum dose lying within the PTV. All plans were normalized such that 100% of the prescribed dose covered 95% of the PTV.

Metrics evaluated included the ratio of the prescription isodose volume to PTV volume ( $R_{100\%}$ ), 50% prescription isodose volume to PTV volume ( $R_{50\%}$ ), the maximum dose 2-cm away from the PTV ( $D_{2~cm}$ ), van't Riet conformation number (CN),<sup>23</sup> total MUs, and treatment time. The van't Riet CN combines isodose and target conformity, and has an ideal value of 1.<sup>23</sup>

Normal tissue constraints for all structures, along with the V20 lung constraint, were achieved for all planning techniques, following the limits outline in Radiation Therapy Oncology Group (RTOG) 0915 trial. As most of the tumors were peripherally located, the planning technique had no clinically significant effect on normal tissue dosimetry.

#### CA Planning

These plans used a treatment arc of  $320^\circ$ , leaving an untreated sector in the contralateral lung. To allow weighting between arcs for improved conformality, the CA plans required at least 2 arcs; however, only 3 of the 23 patients called for more than 2. The isocenter was positioned asymmetrically toward the center of the patient to minimize collisions, while the collimator was set at  $10^\circ$  to reduce the tongue and groove effect. Using the Varian Eclipse treatment planning system, MLC margins were automatically generated and maintained dynamically around the target during rotation. Margins around the PTV were 1 mm in the lateral, anterior, and posterior directions, and 4 mm in the craniocaudal directions. This provided both appropriate coverage and tight conformity indices. A 1-cm thick spherical structure with an inner surface 2 cm away from the PTV was used as a guide to ensure high conformity and minimal dose spillage.

#### VMAT Planning

Each VMAT plan shared the same isocenter and  $320^\circ$  treatment arc as those of the CA plans. A  $360^\circ$  clockwise rotation with a 0 dose rate avoidance sector was created. In this way, only 1 arc was required. Along with routine OARs, a normal tissue objective was used to encourage rapid falloff to undefined tissue outside the PTV. Occasionally, it was necessary to reenter the optimization algorithm in attempts to improve the distribution.

#### Treatment Time

This study has evaluated actual and estimated treatment times. For all 3 techniques, imaging before and after treatment remains the same; consequently we have recorded the treatment-only time stamps from the original MSF plans. For the CA and VMAT plans, estimated treatment times were calculated by dividing the total MUs by the dose rate of 600 MU/minute. CA plans had 15 seconds added to the calculation for each additional arc to account for setting new parameters before beam on. VMAT plans also had 15 seconds added to account for no dose delivered during the  $40^\circ$  avoidance sector. These calculations were validated by performing dry run treatments on 3 plans from both techniques. Treatment of the arcs using automation on a Varian Truebeam machine would reduce time between sub-arcs.

#### **Statistical Considerations**

Using 1-sided, 2-sample t-tests to detect noninferiority in a total of 24 subjects, a power of 82% was achieved. The margin of noninferiority is -0.40 in the difference between the planning methods. The true ratio of the mean at which the power was evaluated was 1. A total of 23 patients provide a power of 80% with a significance level of 5%. Descriptive statistics was used to describe the study variables. Mean and standard deviations were reported for normally distributed data, median and range for nonnormally distributed data, and frequency and proportions for categorical data. Paired t-tests were used to compare the mean difference between the three treatment techniques, with 2 pairs compared at a time. As we had 3 hypotheses to be tested, we used a *p*-value of 0.017 (0.05/3) to account for the multiple hypotheses. Statistical Package for the Social Sciences (SPSS) version 15 was used to conduct the analysis.

#### Results

Fig. 1 shows an axial dose distribution for each treatment technique for a typical patient. All 3 techniques show excellent

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