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Feasibility of Implementing Stereotactic Body Radiation Therapy Using a Non-Commercial Volumetric Modulated Arc Therapy Treatment Planning System for Early Stage Lung Cancer

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Abstract— **Nearly 25% of patients diagnosed with early-stage non-small cell lung carcinomas (NSCLC) are medically inoperable. For these patients, the radial stereotactic body radiation therapy (SBRT), planned and delivered with intensity modulated radiation therapy (IMRT) techniques, offers the only curative option. However, IMRT-SBRT has three significant deficiencies: an elevated beam-on time (MU); a reduced MU-to-cGy coefficient; and a prolonged delivery time. To address these issues, we have developed our in-house version of volumetric modulated arc therapy (VMAT). In this preliminary study, we compared VMAT-SBRT with IMRT-SBRT in terms of optimization, dosimetry, and delivery. Our goal was to investigate the feasibility of replacing the exiting IMRT-SBRT with VMAT-SBRT as a safe and viable alternative radiation modality for early-stage NSCLC.**

Keywords—**lung cancer, VMAT, VMAT-SBRT, IMRT-SBRT, RapidArc, SBRT.**

I. INTRODUCTION

According to the latest statistics, lung cancer is still the leading cause of cancer-related deaths in the United States. About 80% of all primary lung cancers are non-small cell lung carcinomas (NSCLC). At present time, the optimal curative treatment for patients with primary early-stage NSCLC without distant metastasis is complete surgical resection, with a 5-year overall survival rate of 82% and 68% for Stage T1 and T2 tumors, respectively [1]. However, because of other comorbidities, nearly a quarter of these patients are medically inoperable. For these patients, the only curative option available is the radical stereotactic body radiation therapy (SBRT), planned with beamlet-based intensity modulated radiation therapy (IMRT) and delivered with image-guided techniques. In this paper, we call this treatment approach the IMRT-SBRT. The essence of IMRT-SBRT is the intra-fractional dose escalation, delivering a significantly higher biologically effective dose per fraction to the tumor than conventional fractionation schedules. Recently published data have shown that 5-year survival rate for early stage patients treated with IMRT-SBRT was similar to that for surgical resection and local control rate was 93% at three years.

Hoverer, the beamlet-based IMRT-SBRT has three intrinsic deficiencies: an elevated number of monitor units (MU), i.e., the beam-on time, a reduced MU-to-absorbed dose (MU-to-cGy) coefficient, and a prolonged treatment time. The first deficiency significantly increases leakage and scattered radiation to uninvolved areas. In addition, the high MU also enhances the photo-neutron production through x-ray-neutron (x, n) reactions and consequently, increases neutron activation (n, γ) reactions. The photo-neutrons constitute a major hazard to patients who have an implanted pacemaker or defibrillator because of its location (Figure 1). The neutron activated elements remain radioactive and contribute to the radiation exposure to radiotherapy staff entering the treatment room immediately after an IMRT-SBRT treatment.

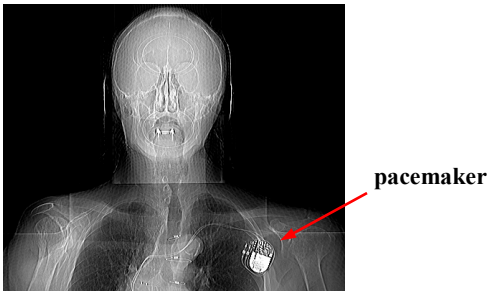

Figure 1. A CT scout anterior-posterior (AP) view shows a pacemaker implanted in the left subclavicular region for a lung cancer patient.

The second deficiency decreases the treatment delivery and energy efficiencies. This is a direct consequence of a large number of small MU and small aperture segments contained in IMRT-SBRT plans. This phenomenon is particularly pronounced in plans that use finer levels for intensity digitization and smaller beamlets for space digitization. The resulting high dose gradients lead to frequent beam hold-offs on the linear accelerator, resulting in an additionally increased delivery time. The third deficiency increases the probability of intra-fractional patient and organ motions. For a nine-beam IMRT-SBRT plan with a prescription dose of 1800 cGy x 3, the delivery time ranges from 8 to 10 minutes. If we also consider the time taken for imaging the beam apertures, the actual treatment time would be much longer.

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To address these issues, we have developed a novel volumetric modulated radiation therapy (VMAT)-based SBRT for the treatment of early stage NSCLC, abbreviated as VMAT-SBRT in this paper. In VMAT-SBRT, the MU reduction is realized by using aperture-based inverse optimization, and the desired radiation dose distribution is achieved through simultaneous modulations of multi-leaf collimator (MLC) linear speed, temporal dose rate, and linear accelerator (LINAC) gantry angular speed. The significance is that this was the first non-commercial VMAT system successfully developed by a single academic institution, fully tested and commissioned, and clinically implemented in the United States. The goal of our current research is to investigate the feasibility of replacing IMRT-SBRT with our in-house version of VMAT-SBRT as a safe and viable radiation modality for early stage NSCLC. In this paper, we report our preliminary results and findings.

II. MATERIALS and METHODS

1. 4DCT simulation

Three patients, who have been preciously treated with IMRT-SBRT, were re-planned retrospectively with VMAT-SBRT and analyzed. For each patient, a 4DCT scan was performed using a Brilliance Big Bore CT scanner (Philips Medical Systems, Cleveland, OH, USA). The scanner has an 85-cm bore, providing a maximum of 60-cm field of view (FOV). The patient was in a supine position in a customized thermoplastic mold to minimize movement during the data acquisition. A pulmonary 4D retrospective spiral protocol was used for the scan. Once a steady pulmonary waveform had been observed, the scan was triggered. The scan was acquired from the thoracic inlet to the costophrenic angles. During the scan, the patient was instructed to breathe in a normal shallow pattern to reduce artifacts in the reconstructed multiphase images. The scan time was about 90 ~ 110 seconds for a typical 4DCT lung simulation.

2. VMAT-SBRT treatment planning

Once the 4DCT reconstruction was completed and maximum intensity projection (MIP) images were created, the internal target volume (ITV) was drawn slice by slice on the MIP images by the radiation oncologist using a volume drawing utility on the CT console. The ITV delineated on the MIP images was essentially the union of the individual gross tumor volumes (GTV) defined at selected phases of a breathing cycle. The planning target volume (PTV) was created by adding an appropriate setup uncertainty margin to the ITV. To minimize the electron build-up and build-down effects at the lung-tissue interfaces, an expanded PTV, named as PTVE, was created by adding a uniform 3-mm margin to the PTV. The organs at risk (OAR) were the cord, esophagus, heart, and lungs. To better spare the cord and esophagus, a 3-mm uniform margin was added to the cord and esophagus. In addition, a series of tuning structures concentric to the PTV were also created for dose tuning purpose. The tuning structures had 1-cm increment in radius. By assigning proper dose constraints, these tuning structures were able to drive the higher isodose curves closer to the PTV, thus eliminating the undesirable hot spots in normal tissue and reducing integral dose as well.

One of the novel features of our VMAT planning system is the inclusion of a normal tissue objective (NTO) function into the total dose-volume based quadratic objective function. The NTO is a function of the distance from the PTV surface and is designed to limit the undesirable dose in the normal tissue outside the PTV in a physical manner. The NTO is defined as follows:

$$D(x) = \begin{cases} D_0 e^{-k(x-x_0)} + D_\infty (1 - e^{-k(x-x_0)}), & x > x_0 \\ D_0, & x < x_0 \end{cases} \quad (1)$$

where D_0 is the dose at the PTV surface, D_∞ is the dose at infinity, and k is the dose fall-off constant. In order for the NTO to work properly, a structure called the Normal Tissue has to be created prior to optimization. In our initial investigation, the Normal Tissue was a concentric structure 5 cm from the PTV surface, as shown in Figure 2.

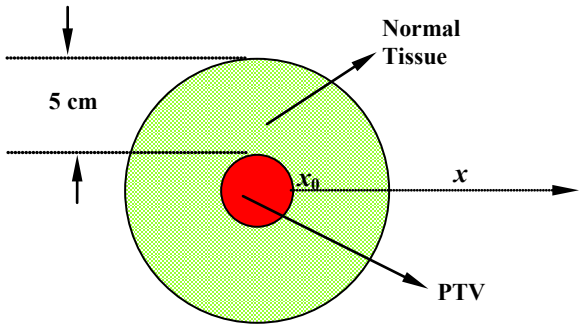

Figure 2. A schematic diagram of the PTV and Normal Tissue.

All VMAT-SBRT plans consisted of a single full arc, covering 360° from 180° to E180° in IEC scale in counter clockwise rotation. A full arc contained 180 equally-spaced beams, i.e., control points (CP). The collimator was rotated to 90° for better PTV conformity. The plans were computed on a Quad-core Intel® Xeon® 5400 sequence processor with 4 GB RAM and 3 GHz clock signal. Unlike the direct aperture optimization (DAO), where the only optimization parameters are the MU weights of some pre-defined MLC apertures, our VMAT was designed to simultaneously optimize both MLC aperture shapes and their MU weights using a multi-level source sampling optimization scheme (MSSO) [2]. The advantages of this approach are its flexibility and efficiency. They allow more iterations at lower source sampling frequencies and less iterations at higher source sampling frequencies, reaching a balance

between speed and quality. The optimization was performed on a quadratic objective function, constructed by dose-volume constraints of targets and OARs.

$$Obj = \frac{1}{N_T}\sum_{i=1}^{N_T}\Big[r^T(D_i - D_p)^2 + r_L^T H(D_L - D_i) + r_H^T H(D_i - D_H)\Big] + \sum_{k=1}^{N_c}\frac{1}{N_{OARK}}\sum_{j=1}^{N_{OARk}} r^{OARk} H(D_{jk} - D_{HOARk}) \quad (2)$$

where N_T and N_{OARk} are the number of points in the target and the k^{th} organ at risk, N_c is the number of organs at risk, D_i and D_{jk} represent the dose at the point i in the target and the point j in the k^{th} organ at risk, D_p is the target prescription dose, r^T is the weighting factor for the prescription dose, r_L^T and r_H^T are the weighting factors for the target dose lower limit D_L and upper limit D_H, r^{OARk} and D_{HOARk} are the weighting factor and upper dose limit for the k^{th} organ at risk, and $H(x)$ is the Heaviside step function defined as $H(x) = 0$ when $x < 0$ and $H(x) = 1$ when $x \geq 0$.

III. RESULTS

1. VMAT-SBRT optimization performance

Table I shows the comparison between IMRT-SBRT and VMAT-SBRT in terms of anatomical volumes and the number of dose calculation points used in optimization. The number of dose calculation points used in VMAT-SBRT optimization was only 20~35% of that used in IMRT-SBRT in order to speed up computation. The mean total number of dose calculation points used in VMAT-SBRT planning was 26403. This gave an optimization time of 45.27±4.93 min and a dose calculation time of 3.48±0.13 min, respectively, while the corresponding times for IMRT-SBRT were 20~40 seconds and 10~30 seconds, respectively. To obtain a dosimetrically acceptable VMAT-SBRT plan, the number of optimizations needed ranged from 2 to 8, as compared to 5~15 for IMRT-SBRT planning.

Table 1. Number of Dose Calculation Points Used in IMRT-SBRT and VMAT-SBRT Optimization

Anatomical Structures	Volume (cm3)	Dose Points IMRT-SBRT	Dose Points VMAT-SBRT
PTV	50.3±28.4	3667±2309	1950±638
CORD	32.3±16.2	3122±1820	1017±318
HEART	557.8±100.6	12467±8958	2667±289
ESOPH	25.3±6.3	1705±262	769±677
LEFT LUNG	2184.9±796.2	20000±0	5000±0
RIGHT LUNG	2516.4±706.8	20000±0	5000±0
TOTAL LUNG	4701.3±1405.9	34000±1732	10000±0

2. Morphological characteristics of VMAT-SBRT plans

Figure 2 shows the isodose distribution on a transverse CT slice for a representative VMAT-SBRT plan. Figure 3 shows the isodose distribution on the same CT slice for the corresponding IMRT-SBRT plan. The latter was optimized with nine equally-spaced co-planar beams. Both plans were computed with 6 MV photons. As seen in the figures, VMAT-SBRT plans, in general, exhibited smoother, more homogenous, and more conformal isodose distribution than IMRT-SBRT plans for all isodose curves, while IMRT-SBRT plans showed isodose smoothness and conformity only to a certain level, normally up to 70% isodose line. The isodose lines lower than 70% demonstrated various degrees of roughness and inconformity, which could result in unexpected high dose and even hot spots in normal tissue.

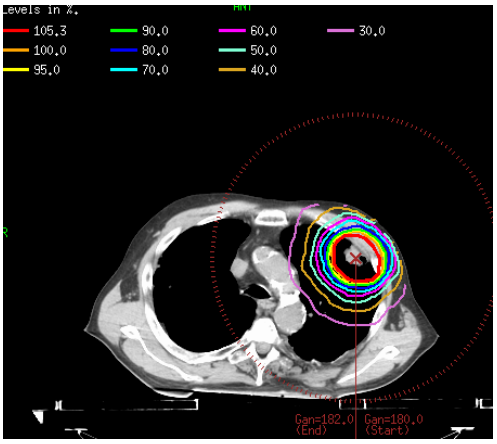

Figure 2. A typical VMAT-SBRT isodose distribution for a CT transverse slice. The red solid line represents the PTV and the dotted circle surrounding the PTV represents 180 beams.

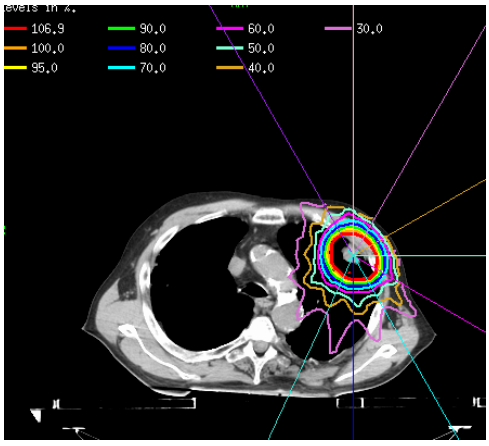

Figure 3. The corresponding IMRT-SBRT isodose distribution for the same transverse slice as in Fig. 2

To quantitatively assess the target dose conformity, we computed the conformity index PITV, defined as the volume covered by the prescription isodose surface (PI) divided by the planning target volume (TV): PITV = PI/TV. Theoretically, for a perfect target conformity, PITV should be equal to 1.0. Clinically, a PITV value ranging

from 1.0 to 2.0 is acceptable. In this study, we found that PITV for VMAT-SBRT and IMRT-SBRT were 1,421±0.031 and 1.466±0.003, respectively.

3. Dosimetric characteristics of VMAT plans

For an objective comparison, the minimum PTV dose was normalized to 100% of the prescription dose for both IMRT-SBRT and VMAT-SBRT plans. It was found that the mean maximum PTV dose was 105.98±0.58% and 111.15±4.02% for VMAT-SBRT and IMRT-SBRT, respectively. The VMAT-SBRT showed a better target dose homogeneity than IMRT-SBRT. The dose delivered to 95% of the PTV, i.e., D_{95}, was 102.08±0.92% and 105.07±2.6% for VMAT-SBRT and IMRT-SBRT, respectively. To further assess the target dose homogeneity, we calculated the widely adopted homogeneity index HI, defined as the maximum dose delivered to 2% of the PTV (D_2) minus the dose delivered to 98% of the PTV (D_{98}) divided by the median PTV dose (D_{median}): $HI = (D_2 - D_{98})/D_{median}$. For a perfect target dose homogeneity, HI should be equal to 0.0. A smaller HI indicates a more homogenous, thus a better target dose distribution. In this study, we found that HI for VMAT-SBRT and IMRT-SBRT were 0.0366±0.0028 and 0.0535 ±0.0001, respectively. In addition, we also found that the doses to the OARs for VMAT-SBRT were, in general, comparable or close to those for IMRT-SBRT. As to beam-on time, VMAT-SBRT demonstrated a huge advantage over IMRT-SBRT in delivery efficiency. The mean Monitor Units (MU) for VMAT-SBRT and IMRT-SBRT were 2292.33±137.07 and 3744.33±121.71, respectively. On average, VMAT-SBRT showed a 38.78% reduction in beam-on time. The mean MU-to-cGy coefficient was 1.229±0.059 for VMAT-SBRT and 2.010±0.117 for IMRT-SBRT, respectively. For the most time and energy efficient treatment plans, MU-to-cGy ratio should be close to 1.0.

4. Dose rate and gantry angular speed modulations

Due to high prescription dose per fraction, VMAT-SBRT requires a much higher MU than conventional fractionation schedules. As the current models of RapidArc-enabled Trilogy machines can only deliver temporal dose rates between 30 MU/min and 600 MU/min, this would require a combination of a fast and frequent temporal dose rate modulation and a nearly continuous gantry angular speed modulation in order to deliver VMAT-SBRT plans most efficiently. Figure 4 shows the gantry angular speed modulation as a function of control point (beam number) for a left lung cancer VMAT-SBRT plan. Control points 0 to 90 correspond to ipsi-lateral side (patient left) and 91 to 180 correspond to contra-lateral side (patient right).

IV. DISCUSSIONS AND CONCLUSIONS

Due to high MU, IMRT-SBRT has a long treatment time. This not only increases the possibility of target miss caused by intra-fractional patient and organ motions, but also leads to increased leakage and scattered doses to uninvolved healthy tissue. As increasing number of patients treated with IMRT-SBRT have shown long-term survival, there has been a concern over the risk of developing secondary malignancies and other long-term morbidities. Our VMAT-SBRT, through inverse aperture-based optimization and multi-modes of modulation, significantly reduced the beam-on time, while achieving a better target dose coverage and similar OAR sparing. Thus, it is a promising alternative treatment option for patients with early stage lung cancer. Nevertheless, VMAT-SBRT is an extremely computationally intensive planning procedure due to several compounding factors, including 180 beams and huge planning volumes. Thus, improving converging speed of optimization is the key to its routine clinical application. Currently, we are developing faster and more efficient algorithms and parallel computing techniques specific for VMAT-SBRT planning. We believe that the deficiency in optimization time will be either eliminated or alleviated in the near future.

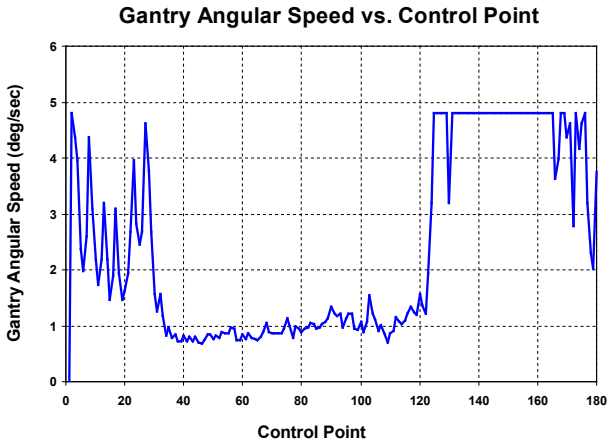

Figure 4. Gantry angular speed as a function of control point (beam number) for a left lung cancer VMAT-SBRT plan.

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