Abstract. Background/Aim: In the present article we review on the use of Volumetric Modulated Arc Therapy (VMAT) for a small lung nodule that was centrally located in close proximity to the mediastinal structures. Case Report: An inoperable patient with central, clinical stage IA adenocarcinoma of the right lung was treated with external-beam radiation therapy of 52.5 Gy in 15 fractions. A single 360° coplanar arc VMAT plan (360-VMAT) was used for treatment and compared to step-and-shoot Intensity Modulation Radiotherapy (IMRT) and a single 180° ipsilateral partial arc VMAT plan (180-VMAT). Results: Planning Target Volume (PTV) coverage was not different, and 360-VMAT had the highest dose homogeneity. Both 360-VMAT and 180-VMAT reduced esophageal dose compared to IMRT. While IMRT had the lowest lung dose, all 3 plans achieved acceptable sparing of the lung. 180-VMAT had the highest dose conformity. Both 360-VMAT and 180-VMAT improved esophageal sparing compared to IMRT. Conclusion: Use of VMAT in early-stage, centrally located NSCLC is a promising treatment approach and merits additional investigation.

Volumetric Modulated Arc Therapy (VMAT) is a novel technique of rotational radiotherapy that achieves dose modulation by simultaneous variation of arc speed, position of multi-leaf collimator (MLC) leaves and dose rate (1). Planning studies of VMAT for various disease sites have demonstrated favorable dose distribution and short treatment delivery time (2).

Definitive external-beam radiation therapy is the primary treatment modality used for patients with non-small cell lung cancer (NSCLC) who are not candidates for surgical resection with curative intent (3, 4). For early-stage, peripherally located NSCLC, stereotactic body radiation therapy has emerged as a safe and effective treatment, most often consisting of 1-5 fractions of high-dose radiotherapy (5). Patients with locally advanced (stage IIIA and IIIB), unresectable NSCLC are most commonly approached with conventionally fractionated radiotherapy, combined with systemic chemotherapy for fit patients (6). For early-stage NSCLC, the VMAT technique was found to be advantageous, improving dose conformity, reducing dose to adjacent organs at risk (OAR) and shortening time of treatment delivery (2, 7-11). Location of lung cancers in the chest varies, but patients with stage I and II NSCLC commonly present with peripheral lung nodules. Consequently, the existing studies of VMAT for early-stage NSCLC are mostly comprised of patients whose radiotherapy targets were situated at the periphery of the lung parenchyma (7-11).

In locally advanced NSCLC the opposite is true, and the bulk of malignant disease is usually centrally located in the chest. Therefore, a large radiotherapy target is surrounded by substantial amount of pulmonary parenchyma. Several planning studies of VMAT for stage III NSCLC have reported increased lung volume receiving low doses of radiation, compared to three-dimensional conformal radiotherapy or IMRT using static fields, which may be of clinical concern (12-14). In many patients with stage I and II NSCLC, malignant masses are also centrally-situated and therefore are bordered by large volumes of uninvolved lung tissue. A commonly used clinical criterion defines early NSCLC as central if the lesion is located within 2 cm from the proximal bronchial tree or is touching the mediastinal/pericardial pleura (15). In such situation, use of VMAT has the potential to increase unwanted irradiation of pulmonary parenchyma. Existing studies have not yet specifically addressed VMAT in early-stage, central NSCLC. Therefore, we reviewed the use of VMAT for a patient with stage IA NSCLC, located in close proximity to the esophagus, the trachea and the right mainstem bronchus.
Case Report

Clinical information. A 50-year-old female was diagnosed with adenocarcinoma of the upper lobe of the right lung, 14 mm × 14 mm × 20 mm in size (maximal anterior/posterior, medial/lateral, superior/inferior dimensions, respectively). The patient was deemed medically inoperable due to poor pulmonary function secondary to chronic obstructive pulmonary disease, and she was referred for definitive radiotherapy. Review of diagnostic computed tomography (CT) images revealed that the lesion was centrally located. The minimal distance from the esophagus, the trachea and the right mainstem bronchus was 10 mm, 6 mm and 15 mm, respectively (Figure 1). Absence of clinically detectable nodal or distant metastases was established by positron emission tomography, and clinical stage IA (T1a, N0, M0) was assigned. Hypofractionated external-beam radiation therapy to a total dose of 52.5 Gy in 15 factions once daily, 5 times per week, was prescribed (16).

Radiation therapy. Computed tomography (CT) for virtual simulation was performed with the patient positioned supine on inclined board due to orthopnea. Free breathing axial images with 2.5-mm slice thickness were obtained to include the entire lungs. Those images were used to contour the gross tumor volume (GTV) and to assign the location of the isocenter. With the patient remaining in the same position, a four-dimensional CT (4D-CT) scan of the tumor region was performed. Internal target volume (ITV) was then created using images obtained by 4D-CT study. The isotropic 8-mm margin was added to ITV to create the planning target volume (PTV).

Single 360˚ coplanar arc VMAT plan (360-VMAT), utilizing 6-MV photons was created and used to deliver radiotherapy to the patient. Treatment planning was performed using the Pinnacle software, version 9.0 (Philips Medical System Inc., Cleveland, OH, USA). Inhomogeneity correction was used, while the aim of optimization was to deliver the prescribed dose to the periphery of the PTV.

Spinal cord, esophagus and bilateral lung parenchyma excluding PTV were chosen as the principal avoidance structures. Radiation therapy was delivered using Elekta Synergy S® (Elekta, Stockholm, Sweden) linear accelerator with 4-mm-thick MLC. Daily cone-beam CT was used for image guidance.

Study design. For a retrospective comparison with the 360-VMAT, two treatment plans were created and reviewed by the attending radiation oncologist: a step-and-shoot intensity modulated radiotherapy (IMRT) plan using 6 coplanar fields and a single 180˚ ipsilateral partial arc VMAT plan (180-VMAT). The same treatment planning objectives and the use of 6-MV photons were maintained for all 3 plans. Representative planning images from 180-VMAT plan are illustrated by Figure 1. Dose-volume histogram data from 3 plans were retrieved and compared. The study was approved by the Institutional Review Board and informed consent was waived since no individually-identifiable health information was collected.

Results

Target coverage. The volume of GTV, ITV and PTV was 3.17, 5.32 and 36.62 cm³, respectively. Volume of PTV receiving at least 95% of prescribed dose (V95) was the same for all 3 plans (Table I). The 360-VMAT plan was the most homogenous, achieving the lowest maximum point dose within the PTV.

OAR sparing. Both 360-VMAT and 180-VMAT decreased the maximum dose to the esophagus as well as the volume of the esophagus encompassed by high iso-doses compared to IMRT (Table I). IMRT had the lowest mean total lung dose (MLD) and the lowest volume of the lung receiving at least 5 Gy (V5) and V20. 180-VMAT resulted in the lowest V30. The absolute difference in lung dose was small and all 3 plans achieved excellent sparing of the uninvolved lung (Table I).
Dose conformity and efficiency of delivery. The ratio of 50% iso-dose volume to PTV (R50) for 360-VMAT, 180-VMAT and IMRT was 8.6, 7.3 and 7.8, respectively. The maximum dose to any point 2 cm away from the PTV (D2cm) was 41.7, 36.0 and 39%, respectively. Therefore, 180-VMAT achieved the best dose conformity. The total number of monitor units per fraction for 360-VMAT, 180-VMAT and IMRT was 654, 696 and 773, respectively.

Discussion

For NSCLC treated with either conventional radiotherapy or SBRT, pulmonary toxicity is one of the most clinically important secondary reactions (17). In particular, radiation pneumonitis is a relatively common post-treatment syndrome and its incidence correlates with radiation dose to uninvolved lung tissue (18). Among dose-volume histogram (DVH) metrics used to model the risk of pulmonary toxicity, MLD and V20 are the ones most extensively studied and utilized in clinical practice (18-22). As IMRT is being evaluated in lung cancer, concerns arose about potentially adverse impact of large volumes of lung receiving low doses of radiation. Emerging data appear to link incidence of pulmonary toxicity with “low-dose” DVH metrics, such as V10 and V5 (23, 24). Relative importance of low-dose thresholds to clinical practice remains under investigation.

When VMAT is used to treat centrally located lung tumors, various number and spatial arrangements of arcs can be employed in planning. Regardless, incidental irradiation of uninvolved pulmonary parenchyma is unavoidable. Jiang et al. compared full 360° arc VMAT, partial 180-200° arc VMAT and 5-7-field coplanar IMRT plans in a study of 12 patients with stage III NSCLC (12). Median PTV was 221 cm³ and 68 GY/34 fractions was prescribed. Both full and partial arc VMAT produced lower V20, V30 and MLD while increasing V5 and V10, compared to IMRT plans. Total lung V5 was 59.7%, 59.3% and 50.6% for full-arc VMAT, partial-arc VMAT and IMRT, respectively (12). Rousseau et al. compared VMAT utilizing ≥2 partial arcs to conformal radiotherapy (CR) employing 4-5 beams in 10 patients with stage III
NSCLC (13). Median PTV volume was 723 cm³ and the prescribed dose was 66 Gy/33 fractions. Compared to CR, VMAT resulted in lower MLD, V30, V20, equal V13 but higher V5 (52% vs. 45%, p=0.008). Chan et al. studied VMAT utilizing 2 partial arcs, CR employing 5-7 beams and hybrid static fields/VMAT plans in 24 patients with locally advanced NSCLC (14). Average volume of the PTV was 508 cm³ and 60 Gy/30 fractions was prescribed. VMAT produced the same total lung MLD and V20 as CR, while V10 and V5 were worse for VMAT (V5 of 64% vs. 57.2%, p=0.001). Hybrid static fields/two partial VMAT arcs plans were deemed superior to both CR and VMAT plans (14).

In our study, the PTV volume was much smaller at 37 cm³. However, we still observed that a full 360° arc VMAT plan resulted in 12% relative increase in total lung MLD and 15% relative increase in V5 compared to IMRT. This is predictable, because use of the 360° arc results in irradiation of the entire circumference of the chest. 180-VMAT also produced MLD and V5 of 6% higher than the IMRT plan. Furthermore, IMRT resulted in the lowest V20, which was 7% lower than in 180-VMAT and 6% lower than for 360-VMAT. However, we concluded that all 3 plans achieved acceptable lung dose, and resulting probability of developing clinically relevant pulmonary toxicity was low, even if accounting for moderate dose hypofractionation used for this patient (16). While the importance of minimizing volume of the lung receiving 5-10 Gy has been recognized, the clinical relevance of thresholds such as V5, V10 or V13 is yet to be conclusively established. We noted that 180-VMAT had the best total lung V30 and the highest dose conformity, with $R_{50}$ being 17% and 7% lower than in 360-VMAT and IMRT, respectively.

Compared to IMRT, VMAT for early-stage, peripheral NSCLC may decrease dose to adjacent OAR such as chest wall (7, 10), skin (8) and rib (10). For the patient described in this study, tumor was central and adjacent to the esophagus, which was selected as an avoidance structure for plan optimization. Compared to IMRT, both 180-VMAT and 360-VMAT decreased esophageal $D_{\text{max}}$ by 11% and 10%, respectively. Esophageal V35 Gy (67% of the prescribed dose) was 64% and 85% lower, respectively. This may or may not be of clinical significance given the low absolute volume of esophagus within high-to-moderate dose region in this patient. In the report by Jiang et al., where tumors were locally advanced and the median PTV volume was almost 20 times greater than the one in our study, the mean esophageal dose as well as V55 Gy (81% of prescribed) were not different between IMRT and VMAT plans (12). It is likely that sparing of adjacent OAR in VMAT and IMRT planning is highly dependent on the anatomy of each patient, the aims of optimization, planning system type as well as the individual operator.

In addition to superior conformity and OAR sparing, fast treatment delivery is an important advantage of VMAT over conformal techniques employing static fields (2, 7-9, 11). This was especially pronounced when coplanar VMAT was compared to non-coplanar IMRT, which requires couch rotation. Prolongation of radiotherapy delivery time may potentially impact on treatment tolerance and introduce intrafraction errors. In our study, we compared efficiency of treatment delivery. 360-VMAT required the fewest number of monitor units (MU), achieving 6% relative improvement over 180-VMAT and 18% relative decrease over IMRT.

In conclusion, for a small central lung nodule, both full- and partial-arc VMAT plans improved esophageal sparing compared to coplanar IMRT. Lung dose, while being acceptably low in all 3 plans, was modestly higher in partial-arc VMAT compared to IMRT and it was the highest in full 360° arc VMAT. The partial ipsilateral arc VMAT plan resulted in the best dose conformity and appeared to be superior in this study, when all parameters were taken into consideration. An important limitation of this study is use of data from a single patient. Therefore, use of VMAT in a specific scenario of early-stage, centrally located NSCLC needs additional investigation.

**Conflicts of Interest**

Conflicts of interests do not exist for any of the Authors of this study.

**References**


