Medical Dosimetry ▮ (2016) ▮▮▮–▮▮▮

Medical Dosimetry

journal homepage: www.meddos.org

Single-fraction flattening filter–free volumetric modulated arc therapy for lung cancer: Dosimetric results and comparison with flattened beams technique

Sara Barbiero, M.S.,[*,†] Alexandra Rink, Ph.D.,[‡,§] Fabrizio Matteucci, M.D.,[¶] David Fedele, Ph.D.,[#] Fabiola Paiar, M.D.,[¶] Francesco Pasqualetti, M.D.,[¶] and Michele Avanzo, M.S.[*]

[*]*Medical Physics Division, Centro di Riferimento Oncologico, Aviano, Italy;* [†]*Specialty School in Medical Physics, University of Pisa, Pisa, Italy;* [‡]*Radiation Physics Department, Princess Margaret Cancer Centre, University Health Network, Toronto, Canada;* [§]*Department of Radiation Oncology, University of Toronto, Toronto, Canada;* [¶]*Radiation Oncology Department, S.Chiara University Hospital, Pisa, Italy; and* [#]*Radiotherapy Department, Casa di Cura S. Rossore, Pisa, Italy*

ARTICLE INFO

Article history:
Received 21 March 2016
Received in revised form
19 August 2016
Accepted 9 September 2016

Keywords:
VMAT
Flattening filter free
Lung cancer
Dose volume
Conformity index
Homogeneity

ABSTRACT

Purpose: To report on single-fraction stereotactic body radiotherapy (RT) (SBRT) with flattening filter (FF)–free (FFF) volumetric modulated arc therapy (VMAT) for lung cancer and to compare dosimetric results with VMAT with FF.

Methods and materials: Overall, 25 patients were treated with 6-MV FFF VMAT (Varian TrueBeam STx LINAC) to a prescribed dose of 24 Gy in a single fraction. Treatment plans were recreated using FF VMAT. Dose-volume indices, monitor units (MU), and treatment times were compared between FFF and FF VMAT techniques.

Results: Dose constraints to PTV, spinal cord, and lungs were reached in FFF and FF plans. In FFF plans, average conformity index was 1.13 (95% CI: 1.07 to1.38). Maximum doses to spinal cord, heart, esophagus, and trachea were 2.9 Gy (95% CI: 0.4 to 6.7 Gy), 0.8 Gy (95% CI: 0 to 3.6 Gy), 3.3 Gy (95% CI: 0.02 to 13.9 Gy), and 1.5 Gy (95% CI: 0 to 4.9 Gy), respectively. Average V7 Gy, V7.4 Gy, and mean dose to the healthy lung were 126.5 cc (95% CI: 41.3 to 248.9 cc), 107.3 cc (95% CI: 18.7 to 232.8 cc), and 1.1 Gy (95% CI: 0.3 to 2.2 Gy), respectively. No statistically significant differences were found in dosimetric results and MU between FF and FFF treatments. Treatment time was reduced by an average factor of 2.31 (95% CI: 2.15 to 2.43) from FF treatments to FFF, and the difference was statistically significant.

Conclusions: FFF VMAT for lung SBRT provides equivalent dosimetric results to the target and organs at risk as FF VMAT while significantly reducing treatment time.

Background

Recently, there has been an increasing interest in the clinical use of linear accelerators (LINACs) with photon beams generated without the use of the flattening filter (FF).[1,2] FF–free (FFF) beams are of higher dose rate and can, therefore, reduce treatment delivery time. This results in better patient comfort and limits uncertainty of delivered dose related to intrafraction motion.[3] The removal of the FF also reduces out-of-field dose that is mainly owing to head scatter and residual electron contamination.[4]

Varian TrueBeam STx (Varian Medical System, Palo Alto, CA) is a new accelerator that produces both FF and FFF beams[5] and has volumetric modulated arc therapy (VMAT) capability. RapidArc is the commercial release of VMAT from Varian Medical Systems and is based on simultaneous optimization of multileaf collimator (MLC) shapes, dose rate, and gantry rotation speed.[6] FFF VMAT significantly reduces the time needed to deliver complex intensity-modulated plans, allowing the treatment of hypofractionated regimes within a few minutes.[1,2]

Because of the reduced treatment times, the FFF technique is particularly appealing for delivering stereotactic body radiation-therapy (RT) (SBRT).[6–8] SBRT is the standard of practice for early-stage lung cancers, because it has been shown to achieve control rates greater than 90% for patients who have nonresectable disease or are unable to tolerate surgery.[3]

Reprint requests to Michele Avanzo, Medical Physics Unit, CRO Aviano National Cancer Institute, 33081 Aviano, Italy.
E-mail: mavanzo@cro.it

http://dx.doi.org/10.1016/j.meddos.2016.09.002

FFF beams have different characteristics compared with the flattened beams, including beam profile and mean energy. Because of lack of beam hardening with FF, FFF beams have a lower mean energy than FF beams with the same nominal energy. Owing to shorter secondary particle ranges,[5] a larger penumbra was measured at shallow depths and for small fields for 6-MV FFF beams compared with 6-MV FF beams.

Given these physical characteristics of unflattened beams, previous investigators have compared dosimetric results of FF and FFF VMAT for SBRT. In one of the first FFF studies,[1] VMAT plans were generated with and without FF using the same nominal beam energy and were evaluated using dose to organs at risk (OARs) and the heterogeneity index, defined as the ratio of doses to 5% and 95% of planning target volume (PTV). No significant differences were found in dose to the PTV; however, mean doses to spinal cord, heart, and contralateral lung showed a small (tens of cGy), yet statistically significant, increase with FFF beams.

In the study by Ong *et al.*,[7] 20 patients with peripheral lung tumors and vertebral metastases were treated with 6-MV RapidArc. Dosimetric results of these plans were compared against VMAT plans generated with 10-MV FFF. They found no significant differences in any dosimetric indices to the target region in lung treatments, which included conformity index (CI) calculated at 80% and 60% dose and maximum dose to PTV. In treatments of the spine, mean and maximum doses to the PTV were significantly higher in FFF treatments, and no statistically significant difference was found between doses to the organs at risk. In the study by Hrbacek *et al.*,[9] 6-MV FF VMAT plans were compared against 6-MV FFF VMAT and 10-MV FFF VMAT plans for SBRT of stage I non–small-cell lung cancer. The radiation schedule used was 50 Gy in 5 fractions. They found an improvement in dose distribution with 6-MV FFF plan compared with 6-MV FF plan, with better sparing of lung tissue and better conformity to the target. No significant differences were found between 6-MV FF and 10-MV FFF plans.

FFF is expected to give the highest reduction of treatment time in single-fraction RT because of the highest number of monitor units in a single treatment session.[5,7] Single-dose radiotherapy is the most extreme form of hypofractionation and results in a large biological effectiveness because of the delivery of large dose in a single fraction.[10] Moreover, by reducing the overall treatment time to only one session, single-dose radiotherapy enhances convenience to the patient and reduces the treatment burden of RT in busy treatment centers. Very good results for side effect profile and local control rate have been reported for single-fraction SBRT of lung cancer.[11]

By shortening the treatment time, FFF beam delivery can reduce the chance of patient intrafraction motion in single-fraction VMAT. On the contrary, the interplay effect between the motion of MLC leaves, gantry, jaws, and tumor motion can cause more blurring of delivered dose when treatment time is shorter.[12] To the best of our knowledge, studies on lung RT with FFF are about fractionated SBRT, usually delivered in 3 to 8 fractions, with fraction doses ranging from 7.5 to 18 Gy,[1,7,9] and no dosimetrical report exists on single-fraction SBRT with FFF RapidArc. The primary aim of this work was to determine the feasibility of FFF treatment plans for SBRT in a single fraction by comparing dosimetric results with plans obtained using the FF technique. The secondary aim was to determine the reduction of delivery time owing to removal of FF in single-fraction SBRT.

Methods and Materials

Patients

Overall, 25 patients with small, isolated lung lesions were randomly selected from the pool of patients of the Azienda Ospedaliero-Universitaria Pisana treated between January and November 2013 at San Rossore Clinic in Pisa, Italy. Table 1 summarizes the main characteristics of the patients.

Treatment planning

Patients were initially set up and immobilized in an evacuated cushion (VacLok, Civco Medical Soultions, Kalona, IA) in a supine and overhead arm position. Subsequently, 4-dimensional computed tomography (CT) scans (GE Lightspeed RT, GE Medical Systems, Waukesha, WI) were acquired for treatment planning using 140 kVp and 100 to 110 mAs. During the planning CT scan, patients were allowed to breathe freely. The target was contoured by a radiation oncologist. The clinical target volume (CTV) included macroscopic and microscopic disease, accounting for all tumor positions in the 4-dimensional CT data set as well as on positron emission tomography imaging. The CTV to PTV margin was isotropic 3 mm. The spinal cord and combined lungs were contoured as OARs. Healthy lungs were defined as combined lungs minus the PTV, and healthy tissue was defined as the outer contour of the patient excluding the CTV. The total dose prescribed was 24.0 Gy delivered in a single fraction to the PTV.

A RapidArc technique with FFF photon beams of nominal 6-MV energy and the maximum dose rate of 1400 Mu/min was used for all 25 treatments. All plans had 1 isocenter, placed in the center of the volume of the PTV, and 2 partial arcs (179° to 340° and 30° to 181°), chosen to obtain the best dose distribution for each patient. These 2 arcs were delivered in opposite rotations (clockwise and counterclockwise). The collimator was rotated to a value other than zero to avoid the tongue and groove effect. All dose distributions were computed with the analytical anisotropic algorithm (AAA, version 10) [13] implemented in the Eclipse planning system version 10 (Varian Associates, Palo Alto, CA) with a calculation grid resolution of 2.5 mm and heterogeneity correction turned on.

During optimization of FFF VMAT plans, complete coverage of the PTV by the prescription dose was requested, with maximum dose (D_{max}) of 24.5 Gy. The priority of dose constraints to the PTV was 999. The treatment plans were considered clinically acceptable when 95% of the prescribed dose was covering at least 95% of the PTV, and D_{max} was less than 110%.

For the organs at risk, the tolerance doses previously recommended for single-fraction SBRT[10] were adopted as constraints during inverse planning and criteria for plan acceptance: D_{max} for spinal cord, esophagus, heart, and trachea was 14 Gy, 15.4 Gy, 22 Gy, and 20.2 Gy, respectively; 1000 cc and 1500 cc of the lungs to receive maximum dose of 7.4 and 7 Gy, respectively. To reduce dose to the healthy tissue and OARs and reach the aforementioned objectives, during inverse planning optimization, we also used the normal tissue objective (NTO), a set of input parameters that defines how dose decreases outside the PTV.[14] The NTO parameters were set as follows: distance from target border of 0.5 cm, start dose of 100%, end dose of 40%, and decrease of 0.3, with a priority of 350. The use of NTO consistently ensured that the plans for isolated lesions met the desired objective for lung and spared the spinal cord. Dose constraints were readjusted if necessary to further reduce dose to OARs. In particular, in cases with spinal cord close to the PTV, a D_{max} of 10 Gy to the spinal cord was applied with priority of 350. All dose constraints were applied on the first multiresolution level of RapidArc optimization and readjusted during the following phases.

Treatment delivery and follow-up

All the VMAT treatments were delivered using a Varian TrueBeam STx linear accelerator. On the treatment day, the patients were positioned within their cushion and aligned to the room lasers using skin tattoos. For image guidance of the treatment, a kilo-voltage cone beam CT was acquired and registered to the planning 4DCT (exhale phase). The registration process was performed automatically based on bony structures, followed by manual refining performed by a therapist to ensure that the tumor was registered to the CTV contoured on the planning CT. The patient position was then corrected by manually translating the couch according to the results of image registration, and the treatment was delivered.[15]

All cases were replanned using RapidArc with 6-MV FF photon beams with maximum dose rate of 600 MU/min. The same prescribed dose, dose objectives during optimization, and criteria for plan acceptance were used as for FFF treatments. The response of the patients to the treatment was prospectively assessed during follow-up. Diagnostic CT scans were acquired during follow-up at 3 months, 6 months, 1 year, and once per year after the end of RT. The follow-up studies were reviewed by a radiation oncologist.

Plan analysis

Differences between FF and FFF VMAT treatment plans were evaluated using dosimetric indices calculated from dose-volume histograms. For the PTV, the

Table 1
Main characteristics of the patients included in the study

Sex (male/female)	16 (64%)/9 (36%)
Age (median/range)	71/56-85
Prescribed dose	24.0 Gy
PTV volume (median ± ST/range)	13.5 ± 9.3 cc/1.2-31.3 cc
Laterality (left/right)	12/13
Healthy lung volume	3487.4 ± 1117.0 cc