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Original Article

A Dose Falloff Gradient Study in RapidArc Planning of Lung Stereotactic Body Radiation Therapy

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Abstract

Introduction: Radiation Therapy Oncology Group (RTOG) report #0813 and 0915 recommends using D_{2cm} and R_{50%} as plan quality metrics for evaluation of normal tissue sparing in stereotactic body radiation therapy (SBRT) of lung lesion. This study introduces dose falloff gradient (DFG) as a tool for analyzing the dose beyond the planning target volume (PTV) extending into normal tissue structures. In ascertaining the impact of PTV size and SBRT planning techniques in DFG, this study questions the independence of the RTOG recommended metrics. **Materials and Methods:** In this retrospective study, 41 RapidArc lung SBRT plans with 2 or 3 complete or partial arcs were analyzed. PTV volumes ranged between 5.3 and 113 cm³ and their geographic locations were distributed in both lungs. 6MV, 6 MV-FFF, 10 MV, or 10 MV-FFF energies were used. RTOG-0915 metrics conformity index, homogeneity index, D_{2cm}, R_{50%}, and HD_{loc} were evaluated. DFG was computed from the mean and maximum dose in seven concentric 5 mm wide rings outside the PTV. DFG was investigated against the volume of normal lung irradiated by 50% isodose volume. Treatment plans with alternate energy and couch rotations were generated. **Results:** The dose falloff beyond PTV was modeled using a double exponential fit and evaluated for relationship with intermediate lung dose. Photon energy and beam configuration had a minimal impact on the dose falloff outside. The product of normalized D_{2cm} and R_{50%} was estimated to have a slowly varying value. **Conclusions:** Dose falloff outside PTV has been studied as a function of radial distance and ascertained by intermediate dose to normal lung. DFG can serve as a complementary plan quality metric.

Keywords: Dose falloff, dose gradient, lung stereotactic body radiation therapy, stereotactic body radiation therapy dose falloff, stereotactic body radiation therapy planning

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INTRODUCTION

Stereotactic body radiation therapy (SBRT) is a leading treatment modality, especially for early-stage nonsmall cell lung cancer. SBRT involves small size radiation fields with sharp dose falloff and image-guided localization.^[1] Potential advantages of SBRT include a higher biological effective dose and greater delivery efficiency with volumetric-modulated arc therapy (VMAT).^[2,3] Similar to intensity-modulated radiation therapy (IMRT), RapidArc planning technique in Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA, USA) based on VMAT has the ability to produce conformal dose distribution around the target, reducing dose to organs at risk (OAR).^[4-8]

In plan evaluation, metrics such as volume of normal lung irradiated by 20 Gy (V_{20}) present an incomplete view of the

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dose falloff to the normal tissue. $R_{50\%}$ and D_{2cm} were used to assess the intermediate-to-low dose spillage outside the PTV. HD $_{loc}$ was recommended to evaluate the high-dose (>105%) spill outside the PTV. However, both $R_{50\%}$ and D_{2cm} could include regions outside the lung tissue or ribs that may not have known dose tolerance or clinical end-points. Conversely, D_{2cm} is estimated isotropically at 2 cm distance from PTV surface without taking water equivalent path length into account. In this study, we have identified a trend in the $R_{50\%}$ and D_{2cm} data questioning their independence that is worth

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exploring. In addition, neither of these metrics could correlate with the excessive toxicity observed when treating central lung tumors using SBRT.^[9] In this study, we propose to study the normal tissue toxicity using exponential dose falloff gradient (DFG)^[10] that can be directly related to the normal lung volume irradiated. To study the impact of planning techniques on the dose falloff, plans with alternate coplanar/noncoplanar arc configuration and alternate photon energy were also utilized.

Materials and Methods

Patient data

This study was approved by the institutional review board. Forty-one lung tumor patients previously treated with VMAT-based SBRT were included in this study. Four-dimensional computed tomography (4D-CT) scanning was performed in GE-Discovery CT scanner (GE Medical Systems, Waukesha, WI, USA) and CT images were reconstructed at 2 mm slice spacing. The 4D-CT image data were sorted into 10 phase bins ranging from 0% to 90% with 0% phase being end-inspiration and 90% phase end-expiration. The maximum intensity projection images were used in generating an internal target volume (ITV). ITV is grown into PTV anisotropically using 10, 5, and 5 mm margins along longitudinal, lateral, and anterior-posterior axes, respectively. Table 1 shows the patient statistics.

VMAT-based SBRT plan was calculated on the respiration-averaged CT of the ten phases of 4D-CT using Acuros XB dose calculation algorithm on Eclipse treatment planning software version 11.0 (Varian Medical System, Palo Alto, CA, USA). RapidArc technique was used for delivery on either a Novalis Tx or a TrueBeam™ STx equipped with high-definition multileaf collimators. SBRT plans were created using either 2 or 3 complete or partial arcs based on 6MV, 6 MV-FFF, 10 MV, or 10 MV-FFF energies. Coplanar

Table 1: The maximum, minimum, average and standard deviation of Rx dose (Gy), number of MUs, normalization (%), planning target volume (cm³), equivalent diameter (cm), number of arcs, total gantry span, and total couch span of the 41 lung tumor stereotactic body radiation therapy patient plans

	Maximum	Minimum	Average	SD
Rx dose (Gy)	55	48	49.3	1.75
Total MU	27712	10194	16065.0	3383.4
Normalization (%)	94	62	76.5	14.1
Volume of PTV (cm ³)	112.7	5.3	30.9	26.4
PTV equivalent diameter (cm)	6	2.2	3.63	1.0
# arcs	3	2	2.2	0.4
Total gantry rotation span (°)	716	388	509.1	119.0
Total couch rotation span (°)	30	0	16.1	9.8

PTV: Planning target volume, SD: Standard deviation

or noncoplanar field configuration with up to \pm 15° couch rotation was generated.

Plans were normalized such that 95% of PTV received the prescription dose (Rx) of 48–55 Gy. Among the 41 clinical plans, 35 plans involved couch rotations ranging between 0° and 30° with a mean \pm standard deviation (SD) of $16.1^{\circ} \pm 9.8^{\circ}$. Dose constraints to the OARs include maximum point dose of 18 Gy to spinal cord, 30 Gy to heart, 24 Gy to brachial plexus, 30 Gy to trachea, and a mean dose of 27 Gy to esophagus as well as maximum percent V_{20} of 15%. Dose calculation grid size was set at 2 mm for SBRT at our institution.

Thorax phantom study

A phantom study was contrived to (a) study the asymmetrical spread in spatial dose distribution around the lung tumor number and (b) identify the optimum width of rings outside the PTV for dose falloff calculations. While the former is intended to address the predominantly coplanar dose distribution due to large fraction of coplanar beams in our clinical plans. the latter facilitates dose evaluation outside PTV in a lung SBRT plan. The steep dose falloff along the longitudinal axis was known to skew the spatial dose distribution and a "ring terminator" region can be considered similar to setting a low-dose threshold. The longitudinal and lateral extents of the "ring terminator" region are identified using linear dose profile measurement. While thin rings may explore dose falloff accurately, they could be impaired by noise fluctuations. On the other hand, wider rings may suffer from low spatial resolution. The slope of mean and maximum dose falloffs and the rate of change of slope that corresponds to curvature were computed. These measurements were compared for the four ring sizes considered here, 2.5 mm, 5 mm, 7.5 mm, and 10 mm width.

A thorax phantom (Model 002 LFC; CIRS Inc., Norfolk, VA, USA) with spherical lung lesions varying between 5, 10, 20, 40, and 80 cm³ was used in this study. A VMAT SBRT plan was created for each target meeting the clinical dose coverage. The target coverage, dose conformity, and mean and maximum dose in the rings were evaluated in addition to the proposed metric, DFG.

Radiation Therapy Oncology Group plan quality metrics

Radiation Therapy Oncology Group (RTOG) report #0915 treatment plan quality metrics include the conformity index (CI) of the target coverage which is defined as the ratio of prescription isodose volume to the volume of PTV.

$$CI = \frac{PIV}{PTV} \tag{1}$$

Dose homogeneity index (HI) within the target can be estimated using the ratio of differences between the doses delivered to 2% and 98% of volume with the median dose to the PTV, which was originally proposed in ICRU-83.^[11]

$$HI = \frac{\left(D_{2\%} - D_{98\%}\right)}{D_{50\%}} \tag{2}$$

For estimation of dose falloff outside the target, RTOG recommended metrics evaluated include $R_{50\%}$, D_{2cm} and HD_{loc} .

Narayanasamy, et al.: Dose falloff in lung SBRT plans

$$R_{50\%} = \frac{50\% \ Rx \ isodose \ volume}{PTV \ Volume} \tag{3}$$

 D_{2cm} is defined as the maximum dose (in % of prescribed dose) at a point 2 cm away from the surface of PTV along any direction. For estimation of high-dose spillage (HD $_{loc}$), volume of 105% isodose volume outside the PTV is estimated as a ratio of the volume of PTV.

$$HD_{loc} = \frac{105\% \ Rx \ isodose \ volume \ outside \ PTV}{PTV \ Volume} \eqno(4)$$

Published tables provide desirable range of values for these metrics. [12] Dose falloff product (DFP) defined as the product of D_{2cm} and $R_{50\%}$ was introduced to study the dependence of the two metrics (D_{2cm} and $R_{50\%}$) on one another by investigating the relationship between DFP and PTV. An SBRT plan of high quality would have low values for $R_{50\%}$, D_{2cm} , HD_{loc} as well as DFP.

Dose falloff

In evaluating IMRT and VMAT plans, the peripheral dose to the OARs may need the spatial dose distribution in addition to dose–volume histogram (DVH) statistics. The proposed dose falloff was modeled as a double exponential fit of the radial distance (*r*) from the PTV surface in the form:

$$%DD(r) = A1e^{-a1r} + A2e^{-a2r}$$
 (5)

where A1, a1, A2, and a2 refer to fitting coefficients and %DD (r) denotes the dose as a percent of the Rx at a radial distance r (mm) from PTV. Value of the coefficients was obtained using the statistics toolbox in Matlab ver R2016a (The Mathworks, Inc., Natick, MA, USA). The first and second terms in Equation 5 represents steep and shallow exponential dose falloff. Notice that as r approaches 0, the first term dominates and as r approaches large clinical distances, the second term dominates. By definition, steep DFG is numerically equal to al and the shallow DFG is a2. A large DFG implies fast dose falloff outside PTV and less volume of normal lung tissue irradiation which holds significance in our study. The relationship between DFG and the 50% isodose volume irradiating the normal lung (outside PTV and not including the chest wall or ribs) is studied on the patient plans.

Alternate planning strategy

The aim of the alternate planning strategies was to study any reduction in dose to normal tissue in addition to improved RTOG metrics. Alternate research plans utilize two strategies. In the first method, all noncoplanar beams were changed to coplanar beams, and dose was computed after plan optimization for coplanar beam arrangement. This would test the hypothesis that the altered footprint of radiation passing through the patient's body would change the low and intermediate dose levels. Papiez *et al.* had postulated steep dose falloff from multiple noncoplanar, nondivergent beams in extracranial stereotactic radioablation. [13] While the authors attempted to

"imitate" Gamma Knife treatments using linear accelerator for extracranial sites, there was limited clinical feasibility.

The use of FFF beams with cone-shaped profile could alter the dose statistics including RTOG metrics, dose to OARs in a lung SBRT plan besides reduced treatment time. In the second alternate planning strategy, photon energy of 6MV was replaced by 6 MV-FFF and vice versa. Likewise, 10 MV photon beam was replaced by 10 MV-FFF and vice versa.

DVH-based statistics from the two alternate plans were compared against DVH of the clinical plan. Plans were evaluated according to the following parameters: CI, $R_{50\%}$, D_{2cm} , HD_{loc} , DFG, and dose to OARs.

Statistical analysis

The dose statistics from the alternate plans were compared to the clinical plan. Test for normal distribution was performed using Shapiro-Wilk test in R statistical software ver 3.2.0 (R Development Core Team). Statistical significance was tested using a paired Student's *t*-test for normally distributed data and a Wilcoxon signed-rank test, otherwise with a threshold P = 0.05.

RESULTS

Radiation therapy oncology group patient plan quality metrics

Clinical plan metrics met the RTOG reports 0813, [15] 0915[16] guidelines tabulated in Table 2. The CI values have an average of 1.1 (range: 0.99–1.24) which is close to the value of 1.2 for acceptable plan. Based on PTV, the plans should have $R_{50\%}$ values <3.2-5.3 for an acceptable plan and <4.2-6.3 for a plan with minor deviation. The observed values of D_{2cm} ranged within 43.0%–74.1% and are well within the range of an acceptable plan or a plan with minor deviation. An ideal plan should have values of $HD_{loc} < 0.15$ which was observed in all the patient plans. The mean \pm SD of DFP was 253 \pm 36 for the patient plans. Figure 1 shows the relationship of DFP and PTV with a slope of -0.016 and R² of 10⁻⁴. Such a small value of slope implies a negligible change in DFP with PTVs observed in lung tumor patients treated with SBRT at our institution. This indicates that DFP is independent of PTV which implies that D_{2cm} and R_{50%} may not be independent of each other.

Dosimetry – thorax phantom plan

A thorax phantom plan with multiple rings outside the PTV and the ring terminator region is displayed in Figure 2. Linear dose profiles outlined in Figure 3 confirms a steeper dose falloff along the longitudinal axis than along a lateral side of the phantom. Figure 3 also confirms that dose drops off to <10% of Rx dose at distances of 1 cm along the longitudinal and 4 cm along the lateral direction from the PTV surface. These were considered as extents of the "ring terminator" region, and dose outside this region could be neglected without an impact on the dose statistics.

Figure 4 displays the rate of change of slope of the maximum dose (measured in cGy/mm²) for the 4 ring widths considered.

Table 2: Statistics of the quality metrics from patient plans along with the acceptable range and the number of plans outside the scope of a minor deviation, as per Radiation Therapy Oncology Group-0915 specifications

	Minimum	Maximum	Average	SD	RTOG-0915 acceptable range	RTOG-0915 minor deviation	Number of plans with major deviation
CI	0.99	1.24	1.1	0.1	<1.2	<1.5	0
HI	0.1	0.3	0.2	0.1	NA	NA	NA
R _{50%}	3.3	6.7	4.6	0.7	<3.2-5.3	<4.2-6.3	1
D_{2cm}	43.0	74.1	55.0	6.8	<50.0-71.7	<57.4-90.1	0
$\mathrm{HD}_{\mathrm{loc}}$	0.0	0.1	0.01	0.02	< 0.15	NA	0
DFP	189	333.5	253	35.9	NA	NA	NA

HI: Homogeneity index, CI: Conformity index, DFP: Dose falloff product, HD_{loc}: High-dose spillage, NA: Not available, SD: Standard deviation, RTOG: Radiation Therapy Oncology Group

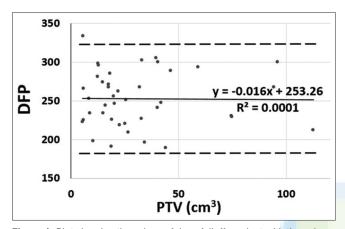


Figure 1: Plot showing the values of dose falloff product with the volume of PTV. The solid line represents trend line represented by the equation while dashed lines shows twice standard deviation

The huge fluctuations in rate of change in slope observed in 2.5 mm ring data hinder their usage. With low spatial resolution, the 7.5 mm and 10 mm rings fail to capture the trend or curvature of dose falloff outside the PTV. In addition, the number of rings has to be sufficient to study the dose falloff down to <10% of Rx dose. An optimum choice was determined to be 7 rings of 5 mm width. Figure 5 shows the maximum and mean dose falloff as well as DFG for 100% target coverage.

Dose falloff – patient plans

The maximum and mean dose falloffs with distance from PTV were plotted in Figure 6 for patient plans. Using Equation 5 to fit the dose falloff, values of the fitting coefficients for the maximum dose falloff in the patient plans were:

$$A1 = 65.7 \pm 8.1$$
 (%); $a1 = 0.094 \pm 0.016$ (1/mm)

$$A2 = 50.8 \pm 9.7$$
 (%); $a2 = 0.006 \pm 0.005$ (1/mm)

It can be noticed that the values of steep DFG (a1) are larger than the slow DFG (a2) by one order of magnitude and the slow dose falloff term can be replaced by a constant for distances of clinical interest. Notice that although DFG of maximum doses decrease with increasing PTV, there is no such trend in the DFG of mean doses with PTV.

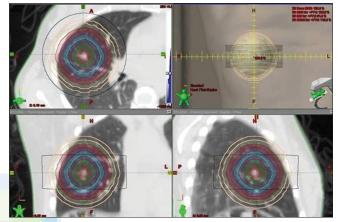


Figure 2: Cross-sectional views of a representative patient's volumetric-modulated arc therapy-based stereotactic body radiation therapy plan showing seven 5 mm wide rings generated concentric with the PTV surface. Also seen is the ring terminator with 1 cm gap from the superior and inferior extremes of the PTV surface

DFG of the maximum dose was hypothesized to have a trend with the intermediate-to-low isodose volumes. The 50% Rx isodose volume has been observed to decrease with PTV and expected to be lower in a plan with higher DFG. By normalizing with the PTV, the volume of normal lung irradiated by 50% isodose volume (VNL50%) has been evaluated against DFG. Figure 7 displays exponentially decreasing relation of VNL50% normalized to PTV with DFG of maximum dose. Note that VNL50% is calculated from the intersection of bilateral lungs with 50% isodose volume and could be extended to estimate V_{20} or mean lung dose. However, $R_{50\%}$ calculation could include chest wall, ribs, and other organs outside the lungs.

PLAN QUALITY METRICS - ALTERNATE PLANS

The alternate plans were reoptimized to meet the target coverage and OAR dose constraints. Barring $R_{50\%}$ of one clinical plan, the values of both D_{2cm} and $R_{50\%}$ of all the clinical plans can be considered acceptable or with minor deviation, as shown in Figures 8 and 9, respectively. Among the coplanar plans, 4 and 5 patients had major deviations in D_{2cm} and $R_{50\%}$, respectively. Corresponding numbers for alternate energy plans were 4 and 7 patients.

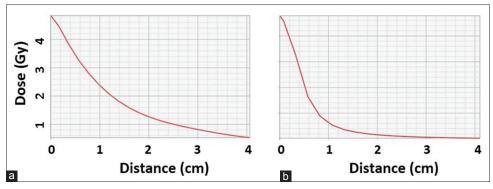


Figure 3: Point dose falloff along the (a) right and (b) superior direction as a function of distance from the PTV surface in a patient plan shows moderate and steep gradient, respectively

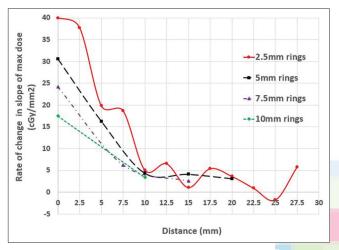


Figure 4: Rate of change of slope of the maximum dose (cGy/mm²) for the 4 ring widths in thorax phantom

Statistical significance – alternate plans

None of these metrics (CI, HI, $\mathrm{HD_{loc}}$, $\mathrm{D_{2cm}}$, and $\mathrm{R_{50\%}}$) of the alternate plans displayed significant differences with the clinical plans at 5% threshold.

DISCUSSION

The analysis of SBRT plans of lung tumor showed that $R_{50\%}$ and D_{2cm} were, respectively, decreasing and increasing with PTV. Similar values of $R_{50\%}$ and D_{2cm} were reported by a phase III multicenter randomized trial (ROSEL) on Stage 1A lung cancer. To the best of our knowledge, this is the first study which revealed that the product of these two metrics, DFP has slowly varying value which questions the complete independence of $R_{50\%}$ and D_{2cm} . This study questions the need to have two metrics when either one could perform this job equally well. It is evident from Figures 8 and 9 that RTOG constraints on D_{2cm} can be easier to meet than those of $R_{50\%}$, thereby suggesting that $R_{50\%}$ is possibly a superior metric.

In this study, the dose falloff outside PTV in lung SBRT plans that take the spatial dose distribution was taken into account. Our analysis shows that asymmetric dose distribution, possibly due to beam arrangement or avoidance structures, can be

quantified by DFG derived from Equation 5. The contrasting dose falloff along axial and longitudinal axes illustrated in Figure 3 agrees with similar results from an extracranial SBRT study.^[13] The authors studied the isotropicity of dose distribution and gradient of dose falloff in regions adjacent and away from the tumor boundary. For a target with significant longitudinal movement seen in lung tumors, this dose distribution presents a potential risk of marginal miss, especially when small PTV margins are used.

Equation 5 is a fitting function for the dose distribution in the region outside PTV. For the 41 plans studied here, V50% of normal lung normalized by the PTV was found to decrease exponentially with DFG of maximum dose. From a known DFG, one can estimate VNL50% or any intermediate dose including, V₂₀. Thus, DFG can be used as a surrogate of normal lung irradiation with high DFG symbolizing low percent of normal lung irradiated by intermediate dose, as shown in Figure 7. Although not considered during plan optimization, the radial dose dependence dropoff measured by DFG can be used as a complementary measure.

Alternate treatment plans were created to study the effect of beam arrangement and beam energy on dose reduction to normal tissue. In a 37 lung cancer patient SBRT study, Lim et al. found that multiple noncoplanar static fields produce significantly lower R_{50%} than multiple coplanar static fields or VMAT.[18] In a retrospective study on 15 lung cancer patients, VMAT plans scored substantially better RTOG metrics than 3D plans, and noncoplanar VMAT plans were slightly better than coplanar VMAT plans.^[19] In our study, 4 and 5 coplanar plans had a major deviations in $D_{\mbox{\tiny 2cm}}$ and $R_{\mbox{\tiny 50\%}}$ respectively, while the corresponding numbers were 1 and 0 in noncoplanar plans. However, a significant gain in dose to OARs or RTOG metrics was not observed in our study using noncoplanar arcs (P > 0.1 in Wilcoxon signed-rank test). Possible explanations could be the amount of noncoplanarity from about $\pm 15^{\circ}$ couch angle limitation due to collision issues and lack of statistical power. It is feasible to achieve better results on lateral tumors and smaller sized patients where the couch angle could be larger. The main advantage of noncoplanar arc and FFF beams is the ability to spare critical organs with additional degrees

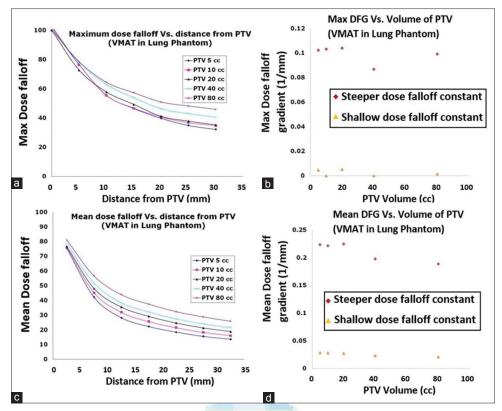


Figure 5: (a) Maximum dose falloff (%) from the PTV surface and (b) maximum dose falloff gradient (1/mm) as a function of PTV volumes in the thorax phantom. (c) Mean dose falloff (%) from the PTV surface and (d) mean dose falloff gradient (1/mm) as a function of PTV volumes in the thorax phantom

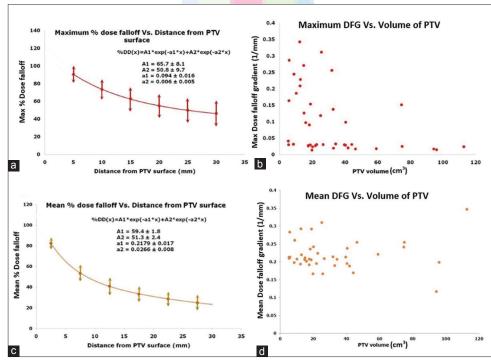


Figure 6: (a) Maximum dose falloff (%) from the PTV surface and (b) maximum dose falloff gradient (1/mm) as a function of PTV volumes in the patient plans. (c) Mean dose falloff (%) from the PTV surface and (d) mean dose falloff gradient (1/mm) as a function of PTV volumes in the patient plans

of freedom.^[20,21] Zhang *et al.* had demonstrated slightly better RTOG metrics for noncoplanar VMAT plans with FFF beams than their flattened counterpart beams, with the exception of

number of monitor units.^[19] Higher MUs in FFF beams does not necessarily imply large peripheral doses due to lower head leakage with the absence of flattening filter. In fact,

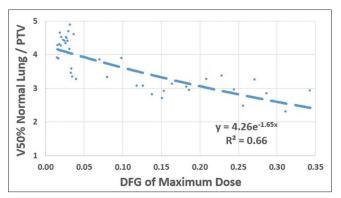


Figure 7: Normalized 50% Rx isodose volume irradiating the normal lung as a function of dose falloff gradient of maximum dose

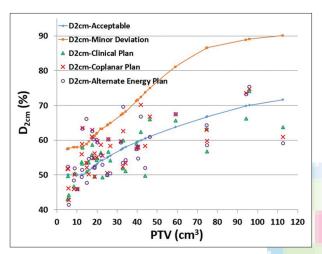


Figure 8: Values of D_{2cm} of the clinical plan, coplanar plan, and the alternate energy plan. Notice the maximum D_{2cm} values of an acceptable plan and a plan with minor deviation were obtained from interpolations of data in Table 1 of the radiation therapy oncology group-0915 report

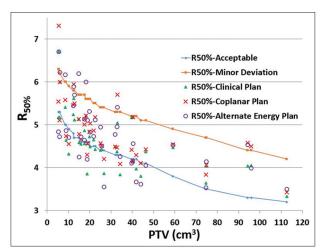


Figure 9: Values of $R_{50\%}$ of the clinical plan, coplanar plan, and the alternate energy plan. Notice the maximum $R_{50\%}$ values of an acceptable plan and a plan with minor deviation were obtained from interpolations of data in Table 1 of the Radiation Therapy Oncology Group-0915 report

when treating with FFF-VMAT plan, the percent of normal lung exceeding 5 Gy and 20 Gy (V_5 and V_{20} , respectively)

were lower, [22] both of which were correlated to pneumonitis. The dose rate of FFF beams is substantially higher than conventional beams leading to lower treatment time and less chances of patient motion. In a 132 lung cancer patient study, Navarria *et al.* had concluded that SBRT with FFF beams permitted safe delivery of high dose per fraction in a short treatment time resulting in an earlier radiological response compared with FF beams. [23]

Conclusions

An exponential fit function was attempted to study the dose distribution outside the PTV from which dose falloff coefficients, namely, DFG were extracted. This new variable was used to evaluate dose to the normal tissue outside the PTV and could act as an SBRT DFG in addition to other metrics. In addition, DFG could be used to predict the percent of normal lung receiving medium-to-intermediate dose. The independence of RTOG recommended metrics, $R_{50\%}$, and D_{2cm} was found to be questionable, although further research is required for conclusive evidence.

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Conflicts of interest

There are no conflicts of interest.

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