Inverse planning for IMRT with nonuniform beam profiles using total-variation regularization (TVR)

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Purpose: Radiation therapy with high dose rate and flattening filter-free (FFF) beams has the potential advantage of greatly reduced treatment time and out-of-field dose. Current inverse planning algorithms are, however, not customized for beams with nonuniform incident profiles and the resultant IMRT plans are often inefficient in delivery. The authors propose a total-variation regularization (TVR)-based formalism by taking the inherent shapes of incident beam profiles into account.

Methods: A novel TVR-based inverse planning formalism is established for IMRT with nonuniform beam profiles. The authors introduce a TVR term into the objective function, which encourages piecewise constant fluence in the nonuniform FFF fluence domain. The proposed algorithm is applied to lung and prostate and head and neck cases and its performance is evaluated by comparing the resulting plans to those obtained using a conventional beamlet-based optimization (BBO).

Results: For the prostate case, the authors' algorithm produces acceptable dose distributions with only 21 segments, while the conventional BBO requires 114 segments. For the lung case and the head and neck case, the proposed method generates similar coverage of target volume and sparing of the organs-at-risk as compared to BBO, but with a markedly reduced segment number.

Conclusions: TVR-based optimization in nonflat beam domain provides an effective way to maximally leverage the technical capacity of radiation therapy with FFF fields. The technique can generate effective IMRT plans with improved dose delivery efficiency without significant deterioration of the dose distribution. © 2011 American Association of Physicists in Medicine.

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I. INTRODUCTION

High dose rate flattening filter-free (FFF) photon beam treatment has recently become available for clinical use with TrueBeam™ linear accelerator (linac) (Varian Medical Systems, Palo Alto, CA).¹ In addition to a dramatically increased dose rate, the use of FFF beams has several potential advantages over conventional delivery with flattened beam fluencies, including decreased collimator scatter, head leakage, and out-of-field dose to the patient.² Beamlet-based inverse planning for nonuniform beams is available in Tomotherapy and Varian Eclipse treatment planning system.^{3,4} However, the conventional beamlet-based optimization (BBO) treats each beamlet as an independent variable and does not con-

sider the nonflat beam profile during optimization, which may lead to a solution requiring a large number of segments for dose delivery.⁵⁻⁷ This limitation can partially outweigh the time benefit of increased dose rate. Indeed, a recent study by Wang *et al.*⁸ indicated that the monitor unit increase can be as high as 63% for FFF-based head and neck IMRT as compared to that with flat beams. Fluence smoothing was suggested to reduce the modulation complexity,⁹ but the improvement is limited because of the local and interpolative nature of traditional smoothing methods and the target dose conformity may suffer from the operation.¹⁰

Several algorithms exist for IMRT planning with flattened beams.¹¹⁻¹⁴ Notably, Zhu and Xing recently proposed a total-

FIG. 1. These images depict profiles of flat and nonflat beams. One-dimensional nonuniform beam profile cross sections with three different base radii ($R=43$ cm/60 cm/80 cm) and the flat beam cross section. The profile with $R=43$ cm fits to the 6 MV FFF beam from the TrueBeam linac well.

variation based compressed sensing (CS) technique to better balance the tradeoff between fluence modulation complexity and plan deliverability.^{10,15} This CS-based planning technique naturally accounts for the interplay between planning and delivery and balances the dose optimality and delivery efficiency in a controlled way.^{10,15,16} The central idea of the approach is to introduce an L-1 norm to encourage piecewise constant fluence maps, such that the number of beam segments is minimized, while using a quadratic term to ensure the goodness of dose distribution. The method produces highly conformal IMRT plans with sparse fluence maps. This theoretical framework is applicable to FFF-based IMRT treatment planning. By properly introducing a total-variation regularization (TVR), the method can greatly facilitate the search for fluencies that are piecewise constant in a domain defined by the basis function of the nonuniform incident beams. The goal of this work is to establish a TVR-based inverse planning technique for IMRT with FFF beams. For this purpose, an L-1 objective function specific to the known nonflat beam profile characteristics is constructed. We demonstrate that optimization of the system provides nonflat beam IMRT solutions that are piecewise constant in the selected FFF-domain and thus efficiently deliverable.

II. METHOD AND MATERIALS

II.A. Dose calculation

Each incident beam is divided into a collection of 0.5×0.5 cm² beamlets. We utilize the linear relationship

$$d = Ax \quad (1)$$

between the dose distribution d and beam fluence maps x to calculate the dose delivered to a patient. The beamlet kernel matrix A , which corresponds to pencil beam contributions from each voxel, is precalculated using the VMC++ Monte Carlo method¹⁷ through the CERR interface (<http://radium.wustl.edu/CERR>).

II.B. Dose optimization in nonuniform beam domain

The profile of a FFF beam can be generally expressed as

$$U = 1 - (1/R)^* \sqrt{u^2 + v^2}, \quad (2)$$

where U is the beam intensity, (u, v) are the beamlet indices, and R is the base radius that describes the level of nonflatness of the beam.^{2,9,18,19} The general nonuniform beam has a cone-shaped profile and the dose decreases with increased distance from the central axis. When $R=\infty$, Eq. (2) describes a conventional uniform beam. Figure 1 depicts the flat and nonuniform beam profiles with varying base radii, including the 6 MV FFF beam from the TrueBeam linear accelerator. The profile with $R=43$ cm fits the 6 MV FFF beam profile from the TrueBeam linear accelerator well. We use the measured nonuniform beam profile to transform a nonuniform beam into a flat beam (i.e., one may view the transformation as a voxel specific scaling).

Similar to that in Ref. 10, we introduce a TVR term in the objective function to accommodate the inherent profile of the nonuniform fluence to encourage piecewise constant fluence in the nonuniform fluence domain. The optimization problem including the TVR term is expressed as minimize

FIG. 2. Examples of intensity-modulated beams: (a) A single cycle of a sine wave along the v direction and (b) a single cycle of a sine wave along both u and v directions.

TABLE I. The MI for 2D intensity-modulated beams shown in Fig. 2. Results for a flat beam and a beam with random intensity are also included.

2D modulation (12×13)	MI
Flat plane	0
Random values	42.62
One cycle of a sine wave (v direction)	18.89
Two cycles of a sine wave (v direction)	21.95
One cycle of a sine wave (u/v direction)	30.48
Two cycles of a sine wave (u/v direction)	38.06

$$\sum_{i=1}^N r_i (A_i x - d_i)^T (A_i x - d_i) + \beta \sum_{f=1}^{N_f} \sum_{u=2}^{N_u} \sum_{v=2}^{N_v} (|X_{u,v,f} - X_{u-1,v,f}| + |X_{u,v,f} - X_{u,v-1,f}|)$$

subject to

(a)

(b)

FIG. 3. (a) The prostate and OAR DVHs for the proposed TVR optimization plans with various nonuniform beams profile radii of 43, 60, and 80 cm and the 6 MV FFF beam from the TrueBeam linear accelerator. (b) The PTV and OAR DVHs of a head and neck case for the proposed TVR optimization plans with various nonuniform beams profile radii of 43, 60, and 80 cm and the 6 MV FFF beam profile from the TrueBeam linear accelerator.

TABLE II. The MI for 2D intensity-modulated beams of the prostate case with various beam profiles ($R=43, 60$, and 80 cm) and the FFF beam profile of the TrueBeam using BBO and TVR.

R (base radius)	Algorithm	MI
43 cm	BBO	21.38
	TVR	6.01
60 cm	BBO	21.43
	TVR	5.60
80 cm	BBO	21.46
	TVR	5.38
FFF beam of TrueBeam	BBO	21.44
	TVR	5.55

(a)

(b)

FIG. 4. (a) Normal and critical structure DVHs of the prostate case obtained using BBO (circles) and TVR (solid line) optimization with 114 and 21 segments, respectively. The BBO plans with fewer than 35 segments result in significant dose deviation and are not included in the evaluation. The inset depicts the PTV DVHs of the BBO with 114 segments and TVR-based optimization with 21 and 50 segments. (b) The PTV DVHs of the BBO and TVR-based optimization with various regularization parameters (β). Decreasing the TVR generally leads to improvement in dose conformity, but it leads to increase the fluence complexity such as $MI=5.55$ ($\beta=0.1$), 10.39 ($\beta=0.01$), 14.37 ($\beta=0.001$), and 21.44 (BBO), indicating an increase in the total segment number.

TABLE III. The computation time for the optimization with the FFF beams using BBO and TVR methods.

Case	Algorithm	Calculation time (s)
Prostate	BBO	1.3
	TVR	6.5
Lung	BBO	6.8
	TVR	51.7
Head and neck	BBO	21.0
	TVR	172.0

$$x \geq 0$$

$$X = U^{-1}x, \quad (3)$$

where x is the beamlet intensity, X is the beamlet intensity in the flat fluence domain (which is related to the beamlet intensity by a transformation matrix U^{-1} that normalizes a non-flat beam to a flat beam according to the beam profile), r_i is the importance factor,^{14,20} β is an empirical regularization parameter,¹⁰ d_i is the desired dose, Nu and Nv are the total numbers of discretization perpendicular and along the MLC leaf motion direction, and Nf is the number of fields. The

FIG. 5. The fluence maps of the TRV plan for the prostate case.

FIG. 6. Isodose lines of (a) the BBO plan and (b) the TVR plan using 21 segments for the prostate case. The 74.1, 50.7, and 23.4 Gy isodose lines correspond to 95%, 65%, and 30%, of the prescribed dose of 78 Gy, respectively.

proposed algorithm is implemented in Matlab and uses the MOSEK software package (<http://www.mosek.com>) for optimization.

II.C. Case studies

We demonstrate the performance of our proposed framework on prostate, lung, and head and neck cases. For the prostate patient, five fields with gantry angles of 0°, 70°, 145°, 215°, 290° are used. A dose of 78 Gy is prescribed to the planning target volume (PTV). Six field angles (30°, 60°, 90°, 120°, 180°, and 210°) are used to generate the lung IMRT plan and the prescribed dose to the PTV is 74 Gy. Seven field angles (0°, 45°, 125°, 160°, 200°, 235°, and 315°) are used to generate the head and neck IMRT plan and the prescribed dose to the PTV is 66 Gy. All plans are normalized so that 95% of the PTV volume receives the prescribed dose. For efficient computation, the pixel size of the CT images is downsampled to $3.92 \times 3.92 \times 2.5 \text{ mm}^3$ for the beamlet kernel and dose calculations. The performance of the proposed method is evaluated by comparing against IMRT plans obtained using conventional beamlet-based optimization without TVR.

II.D. Modulation index

The level of beam modulation complexity of an IMRT plan, which is a general measure of the deliverability, can be evaluated using the modulation index (MI) suggested by Webb.²¹ In Webb's work, a series of 1D fluence profiles were introduced in 2D planning. In this study, the MI is modified to measure the modulation complexity of 2D fluence maps as described below

FIG. 7. DVHs of the lung plan using the proposed TVR algorithm using 11 segments. The inset depicts the PTV DVHs of the BBO and TVR-based optimization with 11 and 60 segments. All plans are normalized to 95% of the target volume receiving the prescribed dose of 74 Gy.

$$\Delta_u = \text{abs}(x_{u,v,f} - x_{u-1,v,f}),$$

$$\Delta_v = \text{abs}(x_{u,v,f} - x_{u,v-1,f}),$$

$$N(f; \Delta_u \text{ and } \Delta_v > f\sigma),$$

$$f = 0.01, 0.02, \dots, 2,$$

$$z(f) = \left(\frac{1}{(Nu - 1)Nv + Nu(Nv - 1)} \right)^* N(f),$$

$$\text{MI} = \int_0^{0.5\sigma} z(f) df. \quad (4)$$

Here, σ is the standard deviation of the beamlet intensities and Δ is the intensity change between adjacent beamlets. N is the number of adjacent beamlet intensity changes satisfying the test condition, Δ_u and $\Delta_v > f\sigma$, where $f = 0.01, 0.02, \dots, 2$. For illustration purposes, 2D intensity-modulated beam examples of 12×13 beamlets are depicted in Fig. 2. Table I provides the MI values of beams plotted in Fig. 2, as well as a flat beam and a beam with random intensity values. Note that the MI value is zero for the flat plane and increases as the complexity of intensity maps increases.

III. RESULTS

III.A. Prostate case study

In Fig. 3, we present the DVHs for the prostate case and the head and neck case using the proposed optimization with nonuniform beam profiles of 43, 60, and 80 cm radii and the FFF beam profile from TrueBeam ($40 \times 40 \text{ cm}^2$). The total segment numbers in the two cases are 21 and 80, respectively. Note that for typical cases as tested in this work, the DVHs of the PTV and the sensitive structures depend only slightly on the beam profile radius, indicating the optimal solutions using the proposed algorithm are insensitive to the variation of the beam profile radius. Table II lists the MIs of

FIG. 8. Panels (a)–(f) depict fluence maps from the TVR plan for the lung case. Fluence maps (a)–(f) require one, two, two, two, two, and two segments for delivery, respectively.

the prostate case for 43, 60, and 80 cm and the FFF beam profile with and without TVR. In Table III, the computation time of each plan is presented. The TVR plan for the prostate case took 6.5 s on a 2.6 GHz PC and the BBO plan took 1.3 s.

Figure 4 shows the DVHs of the involved structures in TVR and BBO plans obtained with the FFF beam profile of TrueBeam. The MI of the BBO plan is 21.44, which is simi-

lar to that of the two cycles of sine wave modulation and indicates a significant intensity complexity. The complex fluence maps produced by the BBO requires a large number of segments ($N_t=114$). In contrast, the MI of the TVR plan, which maintains a similar PTV dose coverage and organs-at-risk (OAR) sparing as compared to the BBO plan, is only 5.55 and can be delivered with a small number of segments ($N_t=21$). The results here are consistent with the previous

FIG. 9. Isodose lines for the lung patient TVR plan. The 70.3, 48.1, and 22.2 Gy isodose lines correspond to 95%, 65%, and 30% of the prescribed dose of 74 Gy, respectively.

reports.^{10,22} It is important to emphasize that the dose conformity for TVR-based plans can be improved by increasing the total segment number [the inset of Fig. 4(a)]. In Fig. 4(b), the PTV DVHs of the BBO and TVR-based optimization with various regularization parameters (β) are included to show the effect of varying the TVR. Decreasing the TVR generally leads to an improvement in dose conformity, but it leads to increase the fluence complexity such as MI=5.55 ($\beta=0.1$), 10.39 ($\beta=0.01$), 14.37 ($\beta=0.001$), and 21.44 (BBO), indicating an increase in the total segment number.

Fluence maps obtained using the proposed TVR algorithm are presented in Fig. 5. The cone-shaped fluence maps are indicative of piecewise constant fluence maps in the nonuniform beam domain. The reduced fluence map complexity as compared to the conventional BBO plans can be delivered with a small number of segments. The field specific number of segments for the five fields is five, four, two, four, and six, respectively. Additionally, the cone-shaped fluence map of field 3 can be achieved with two nonuniform beam segments, whereas the fluence map of field 1 requires five segments. Unlike the TVR optimization in the flat beam domain,^{10,15} the distinctive cone-shaped feature appears in all fluence maps. Figure 6 shows the dose distribution of the BBO and TVR plans for the prostate case. The 74.1, 50.7, and 23.4 Gy isodose lines corresponding to 95%, 65%, and 30%, of the prescribed dose of 78 Gy, respectively. Consistent with the DVH results, the isodose lines show that the proposed TVR algorithm results in conformal dose distributions.

III.B. Lung case study

The DVHs of the involved structures for the lung case are plotted in Fig. 7. Nonuniform beams of TrueBeam are used to generate the plan with Nt=11 and 60, respectively. The inset of Fig. 7 shows the plans with and without TVR. Only a minor difference is noted in PTV coverage, while the OAR sparing is clinically acceptable for the TVR and BBO plans. The BBO shows high dose conformity but exhibits complex fluence maps (MI=12.02 and Nt=146). In contrast, the proposed TVR algorithm leads to a reduced fluence map complexity (MI=7.50 and Nt=11) without significantly deteriorating the final dose distribution. Once again, we note that improved dose conformity can be obtained by increasing the

FIG. 10. DVHs of the head and neck plan using the proposed TVR algorithm using 80 segments. The inset depicts the PTV DVHs of the BBO and TVR-based optimization with 80 and 100 segments. All plans are normalized to 95% of the target volume receiving the prescribed dose of 66 Gy.

total number of segments in TVR. The proposed TVR plans provide target dose uniformity and OAR sparing comparable to previous studies with flat beams.²³

Figure 8 shows the fluence maps for the TVR-based plan with Nt=11. The fluence maps require one, two, two, two, two, and two delivery segments, respectively. All fluence maps include a cone-shaped feature. The cone-shaped fluence map of the fifth field is achieved with a single nonuniform beam segment. Figure 9 displays the dose distribution for the lung patient case with Nt=11. The 70.3, 48.1, and 22.2 Gy isodose lines correspond to 95%, 65%, and 30% of the prescribed dose of 74 Gy, respectively. As evidenced in the figure, the proposed TVR algorithm produces a highly conformal isodose distribution.

III.C. Head and neck case study

The DVHs of the involved structures for the head and neck case are plotted in Fig. 10. The FFF beam profile of TrueBeam are used to generate the plan with Nt=80. The inset of Fig. 10 shows the plans with and without TVR. Only a minor difference is noted in PTV coverage while the OAR sparing is clinically acceptable for the TVR and BBO plans. The BBO shows high dose conformity but exhibits complex fluence maps (MI=17.15 and Nt=171). In contrast, the proposed TVR algorithm leads to a reduced fluence map complexity (MI=7.69) without significantly deteriorating the final dose distribution. The inset of Fig. 10 shows that improved dose conformity can be obtained by relaxing the TVR (or increasing the total number of segments in TVR). The proposed TVR plans provide target dose uniformity and OAR sparing comparable to previous studies with flat beams.²³

Figure 11 shows the fluence maps for the TVR-based plan with Nt=80. The fluence maps require 23, 2, 6, 1, 12, 16, and 20 delivery segments, respectively. In Fig. 12, the 62.7, 42.9, and 19.8 Gy isodose lines correspond to 95%, 65%, and 30% of the prescribed dose of 66 Gy, respectively. The blue line

FIG. 11. Panels (a)–(g) depict fluence maps from the TVR plan for the head and neck case.

represents the PTV. The result shows that the proposed TVR algorithm is capable of producing a conformal isodose distribution in the complicated head and neck case.

IV. DISCUSSION AND CONCLUSION

Two commonly used approaches for IMRT inverse planning are BBO^{5,6,24} and direct aperture optimization

(DAO).^{25–27} In BBO, the intensity of each beamlet is an independent variable and the optimized intensity map is highly complex and entails a large number of segments for delivery. This complexity reduces not only delivery efficiency but also treatment accuracy due to increased patient motion during the increased treatment time. Some algorithms use smoothing techniques, which have limited success in simplifying

FIG. 12. Isodose lines for the head and neck patient TVR plan. The 62.7, 42.9, and 19.8 Gy isodose lines correspond to 95%, 65%, and 30% of the prescribed dose of 66 Gy, respectively.

delivery due to their interpolative nature. On the other hand, DAO overemphasizes the delivery constraints and obtains a directly deliverable solution at the cost of dose conformity and compromised optimization convergence. Indeed, the DAO method enforces a prechosen (often unjustified) number of segments for each incident beam and then optimizes the shapes and weights of the apertures. However, searching for an optimal solution by using DAO is inherently complicated because of the nonconvex dependence of the objective function on the MLC coordinates. As a result, the optimality of the final solution is not guaranteed. Moreover, the use of FFF beams for IMRT aggravates the problem, especially for large and irregularly shaped target.⁸ In this work, we propose a generalized TVR method for IMRT treatment planning with beams of arbitrary profile shapes. The objective function's quadratic form conserves the convexity of the optimization problem and allows utilization of existing optimization software packages.

The role of total variation is fundamentally different from the conventional smoothing based on quadratic function. The difference between quadratic smoothing and total-variation regularization (L-1 norm) can be found in classic textbooks²⁸ and they have different advantages in different applications. L-1 norm is known to be able to generate piecewise constant solutions (e.g., piecewise constant signals in the case of signal processing) and L-2 norm (quadratic smoothing) tends to yield solutions that are “smooth” in nature. Our algorithm based on total variation obtains a reduced number of segments by encouraging the field intensity to be piecewise constant in the nonuniform fluence domain (a simple example of piecewise constant fluence is that from conventional DAO method). The algorithm is distinct from the existing methods, which use smoothing techniques^{29–31} to obtain continuous, but not necessarily simple-shaped fluence maps. Instead of smoothing regionally, the total-variation regularization focuses on shaping the intensity maps to be piecewise constant such that they can be delivered using a small number of apertures. The optimized intensity maps contain sharp transitions, which would otherwise be smoothed if quadratic

smoothing is used. The advantage of using total-variation regularization over using quadratic smoothing has also been demonstrated in a comparative study previously for the case of flattened beams.¹⁰

A focus of TVR-based inverse planning is to find a domain in which the fluence is sparse and most efficiently deliverable. As opposed to IMRT with flat beams, the fluence sparseness occurs in a domain characterized by a nonuniform beam profile. Equation (2) essentially provides a basis function by which to decompose IMRT fluence maps. The TVR defined in this domain as given in Eq. (3) encourages a solution that minimizes the number of segments. When the beam profile is flat, Eq. (2) becomes identical to the TVR previously introduced by Zhu and Xing. The proposed algorithm regularizes the fluencies in the nonuniform beam domain and produces plans that can be delivered with a small number of segments without significantly degrading the conformity of the dose distribution. In general, the quality of the resultant treatment plan depends on the level of intensity modulation. This dependence may saturate as the complexity of the beam intensity modulation increases to a certain level. The purpose of introducing total variation is to get rid of “dispensable” segment or remove the “unnecessary” modulations in the solution. The final solution is a tradeoff between the conformity of the dose distribution and the deliverability of the plan. The effect of varying the TVR is well elaborated in Fig. 4(b). As shown in the inset of the Figs. 4(a), 7, and 10, relaxing the TVR generally leads to improvement in dose conformity. The value of the proposed formalism is that it provides an effective way for us to “tune” the complexity of the resultant fluence maps and thus “control” the deliverability of the plan with minimal deterioration of the resultant plan.

The proposed TVR method uses a regularization weighting factor β to control the degree of regularization. In this work, the value of β is determined empirically by examining the DVHs and MI values of resultant fluence maps.¹⁰ Alternatively, L-curve analysis, which has been applied successfully to many inverse problems,^{32–34} can be used to find an adequate value of β . Indeed, Chvetsov introduced the L-curve analysis to radiotherapy optimization problems to obtain efficient IMRT plans regularization by searching for the regularization parameter that minimizes the fidelity residual norm against the constraint norm.³³ The analysis is similar to the determination of structure specific importance factors²⁰ and is computationally intensive.

In summary, a novel IMRT inverse planning formalism is proposed for IMRT with nonuniform beams. By taking the inherent shapes of incident beams into consideration through a TVR, the formalism allows to change the tradeoff between the deliverability and the dose distribution in a controlled way. The method takes advantage of the desirable features of BBO and DAO while avoiding their drawbacks. Field-specific and sparse number of segments is a direct result of the TVR-based optimization.¹⁰ The proposed method provides clinically acceptable IMRT plans with a minimal number of segments. Comparison of treatment plans obtained

using the proposed method and a conventional BBO for the prostate and lung patients show the significant potential of the TVR-based inverse planning.

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