A distance to dose difference tool for estimating the required spatial accuracy of a displacement vector field

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Purpose: To introduce a tool, termed distance to dose difference (DTD), which estimates the required spatial accuracy of displacement vector fields (DVF) used for mapping four dimensional dose values.

Methods: Dose mapping maps dose values from an irradiated geometry to a reference geometry. DVF errors result in dose being mapped from the wrong spatial location in the irradiated geometry, with a dose error equal to the dose difference between the error-free and sampled spatial locations. The DTD, defined as the distance to observe a given dose difference in the irradiated geometry, quantifies the permitted DVF error to ensure a prespecified desired dose mapping accuracy is achieved. To demonstrate the DTD, a treatment plan is generated with a 5 mm internal target volume-to-planning target volume margin for an intensity modulated radiation therapy lung patient. The DTD is evaluated for mapping dose from the end of inhale image with a dose error tolerance of 3.30 Gy, which equals 5% of the 66 Gy prescription dose. The DTD is loaded into the treatment planning system to visualize positional dependencies of permissible DVF errors overlaid on the patient's anatomy and DTD-volume-histograms are generated.

Results: DTD values vary with location in the patient anatomy. For the test case, DTD analysis indicates that accurate DVFs (~1 mm) are required in high dose gradient regions while large DVF errors (>20 mm) are acceptable in low dose gradient regions. Within the clinical target volume (CTV), tolerated DVF uncertainties range from 1 to 12 mm, depending on location. Ninety percent of the CTV volume had DTD values less than 4 mm.

Conclusions: The DVF spatial accuracy required to meet a dose mapping accuracy tolerance depends on the spatial location within the dose distribution. For dose mapping, DVFs accuracy must be highest in dose gradient regions, while less accurate DVFs can be tolerated in uniform dose regions. The DTD tool provides a useful first estimate of DVF required spatial accuracy. © 2011 American Association of Physicists in Medicine. [DOI: 10.1118/1.3572228]

I. INTRODUCTION

When delivering radiation therapy, patient anatomy changes between one fraction and another (interfraction) and even within the same fraction (intrafraction). As a result of patient anatomic changes, patient alignment variations, and beam delivery variations, the delivered dose distribution is time dependent. If unaccounted for, the uncertainties due to setup errors,¹ random errors, tumor motion,² tissue deformations,³ and beam delivery variations will lead to a difference between planned and delivered dose distributions, which in turn can degrade patient outcomes.⁴ Margins^{5–7} are used around the tumor to compensate for uncertainties due to setup errors and tumor motion; however, tracking tissue voxels from one instance of time to another is required to include the effect of these errors, motions, and tissue deformations on the treatment outcome of the irradiated anatomy.

Deformable image registration^{8,9} utilizes a displacement vector field (DVF) to track movement of voxels from one image set to another. The DVF is used to track information between images such as image intensities, contours, or dose.

Dose mapping^{10–13} is required to sum dose components delivered to different geometric instances of a patient's geometry, such as from different phases of breathing in a four dimensional computed tomography (4DCT). Typically, for

each point of the reference geometry, the DVF is utilized to find the corresponding point in the irradiated geometry, and then the dose in the reference geometry is assigned to be equal to that in the corresponding point in the irradiated geometry.

The accuracy of dose mapping, therefore, depends on the accuracy of the DVF used in the mapping process and on the local dose gradient in the irradiated geometry. For example, if a registration DVF error occurs in a uniform dose region [Fig. 1(a)], then the resultant dose error is small. Conversely, if a registration error occurs in a high dose gradient, such as in the penumbra region, [Fig. 1(b)] then resultant dose error can be large.

One can exploit this relationship between DVF accuracy and dose mapping accuracy to determine how large a DVF can be tolerated before it introduces a given dose error. For example, if the desired dose mapping accuracy is 2% of the local dose, then DVF errors are relevant only if the dose at an incorrectly mapped point is >2% different from the dose at the “correctly” mapped dose point. This suggests that a metric which provides an upper bound of allowable DVF uncertainty can be developed based upon a distance to dose difference (DTD) analysis, where the distance to a dose difference threshold in the irradiated geometry is evaluated.

FIG. 1. Illustration of the effect of DVf errors on dose mapping errors. On each panel, the green arrows are possible displacement vectors for mapping information from the irradiated image to the reference image. The red arrow represents the DVf error. In (a), the error occurs in a uniform dose region; hence the dose mapping error is minimal. In (b), the error occurs in a dose gradient region, resulting in a large dose mapping error.

The DTD concept is unique in that it does not require knowledge of the DVf. Instead, DTD indicates how large a DVf error can be before the DVf error could introduce a predetermined maximum tolerable dose mapping error. The DTD threshold is adaptable based on the desired evaluation; DTD can be for a given percentage of the local dose, given percentage of maximum dose, for any arbitrary absolute dose difference, or even to an absolute dose level.

This note introduces the DTD concept, demonstrates its use for mapping dose between two phases of a 4D lung plan, and compares the DTD with a method based on the gradient of the dose distribution.

II. METHOD AND MATERIALS

II.A. DTD algorithm

The DTD algorithm (Fig. 2) used in this work is developed using a technique similar to those used for distance to agreement (DTA) analysis. DTA utilizes two dose distribu-

FIG. 2. Basic flow diagram of the DTD algorithm for the case with ΔD being an absolute (# Gy) dose value. See text for full description of the method.

tions, A and B, on a common coordinate system which are to be compared. For each dose value at a point in distribution A, the DTA is the shortest distance that must be traversed in B to have an equivalent dose value.^{14,15} This concept can be extended to a DTD concept. DTD utilizes a single dose distribution as input since the desire is to determine the minimum distance one must traverse in this dose distribution to observe a dose difference greater than the tolerance. For example, if the desired dose accuracy is $n = 2\%$ of the local dose, then beginning with dose distribution A, a dose distribution B^+ is created by multiplying the dose values in A by $(1 + n/100) = 1.02$. The DTA at each point between A and B^+ is then determined, producing DTA^+ . Similarly, a dose distribution B^- is created by multiplying the dose values in A by $(1 - n/100) = 0.98$ with the DTA at each point between A and B^- determining DTA^- . At each point, the DTD to ensure a maximum of an $n\%$ local dose error will be the minimum of (DTA^+, DTA^-) . If one would like to know the DTD in terms of an absolute (# Gy) dose value, e.g., $\Delta D = 0.02 \text{ DRx}$, then $B^+ = A + \Delta D$ and $B^- = A - \Delta D$, respectively, in the computation of DTA^+ and DTA^- . Of course, one could directly write a DTD algorithm without directly utilizing DTA code; however, the simple method stated above enables use of established quality-assured algorithms for this study.

In this study, the DTD is based upon an in-house developed C++ DTA algorithm. The DTA algorithm progressively searches in shells of increasing radius (number of voxels) for

the dose agreement point in matrix $B^{(\pm)}$ which surrounds the point of interest from matrix A . Internally, the DTA algorithm trilinearly interpolates the dose to a $1 \times 1 \times 1 \text{ mm}^3$ resolution in the search matrix to reduce errors inherent to the discrete voxel-based DTA algorithm used. Future implementations could be based on a more accurate or more efficient DTA algorithm, e.g., those described in Refs. 16–18.

II.B. DTD example

To demonstrate the utility of the DTD, intensity modulated radiation therapy (IMRT) lung treatment plan is generated using Pinnacle³ (Philips Medical Systems, Fitchburg, WI). The plan uses an internal target volume (ITV), generated from the union of the clinical target volume (CTV) on all breathing phases of a ten phase 4DCT (phase 0%–90%) plus a 0.5 cm ITV-planning target volume (PTV) margin. The treatment plan is generated on phase 0% (end of inhale). The minimum prescribed dose to the target is 66 Gy using direct machine parameters optimization, IMRT optimization with a $4 \times 4 \times 4 \text{ mm}^3$ dose grid resolution. The DTD is computed for both $4 \times 4 \times 4 \text{ mm}^3$ and $2 \times 2 \times 2 \text{ mm}^3$ dose grid resolutions based on the collapsed-cone dose algorithm dose values. The figures show the $4 \times 4 \times 4 \text{ mm}^3$ results unless otherwise noted.

Following planning, the DTD is determined for $n = 2\%$ of the local dose computed on phase 0% ($\text{DTD}_{2\%}$), and for $\Delta D = 1.32$ ($\text{DTD}_{1.32\text{Gy}}$) and 3.30 Gy ($\text{DTD}_{3.30\text{Gy}}$), corresponding with 2% and 5% of the prescription dose. These values are chosen in accordance with suggested dose accuracy values listed in ICRU report #62.⁵

To visualize and analyze DTD, the externally computed DTD values are loaded into Pinnacle as a beam in a separate trial and the monitor units are adjusted so that dose values can be interpreted as distance values (in mm). This enables viewing of isoDTD lines on the patient's anatomy and creation of DTD-volume-histograms (DTDvh) using pre-existing Pinnacle tools.

II.C. Comparison with dose gradient

An approach similar to the DTD is to evaluate the gradient of the 3D dose distribution, then divide the desired dose tolerance value by the dose gradient. This method is called TDG, for tolerance divided by gradient. The 3D dose gradient is computed using the central difference method, yielding gradients in the x , y , and z directions. TDG values are computed in two ways, one using the magnitude of the 3D dose gradient (TDG^{3D}) and the other using the maximum of the dose gradient $[\partial D/\partial x, \partial D/\partial y, \partial D/\partial z]$ in a given direction (TDG^{max}). The TDG method is compared with the DTD method by comparing color wash distributions, DTDvhs with TDGvhs, and plotting point-by-point DTD values with respect to TDG values.

III. RESULTS

Figure 3 shows the isodose lines on phase 0% for the IMRT plan overlaid on a transverse slice of the patient's

FIG. 3. Isodose lines on phase 0% on a single transverse slice of the IMRT plan used in this study. The minimum prescribed dose (66 Gy) is indicated in blue. Structures in color wash are CTV (purple), esophagus PRV (blue), and cord PRV (orange).

anatomy. This same transverse slice is used to show the DTD values in the later figures. Figure 4(a) shows the $\text{DTD}_{2\%}$ overlaid on this transverse slice. The maximum $\text{DTD}_{2\%}$ value observed inside the CTV is 6 mm, with values of 1–4 mm surrounding the CTV. Within the entire image, $\text{DTD}_{2\%}$ values as low as 0.1 mm are observed.

Figure 4(b) shows color wash isoDTDs for the $\text{DTD}_{1.32\text{Gy}}$. Outside the irradiated region, the plan can tolerate up to 10 mm DVF errors. Inside the irradiated region, but outside the CTV in large dose gradient regions, DVF errors between 0.5 and 1 mm can be tolerated. Inside the CTV, the plan can tolerate up to 4 mm DVF error. Similarly, Fig. 4(c) shows color wash isoDTDs for the $\text{DTD}_{3.30\text{Gy}}$. The $\text{DTD}_{3.30\text{Gy}}$ differs from the $\text{DTD}_{1.32\text{Gy}}$ demonstrating the variation of DTD with the required dose accuracy. Outside the irradiated region, the plan can tolerate up to 10 mm DVF errors. Inside the irradiated region, but outside the CTV in large dose gradient regions, DVF errors between 1 and 8 mm can be tolerated. Inside the CTV, the plan can tolerate up to 10 mm DVF errors.

These preliminary results suggest that accurate DVFs are not needed for the whole image for dose mapping purposes. For the two DTD distributions calculated, both results show that in high dose gradient regions, spatial dose or DVF accuracy requirements are tight, whereas inside the CTV or outside the treatment region both requirements can be relaxed and the plan can absorb more errors. While isoDTDs overlaid on the patient's anatomy allow visual identification of areas which are tolerant or intolerant to DVF errors, to statistically interpret the spatial dose or DVF accuracy requirements, the DTD can be plotted as function of the volume of any structure. Figure 5 shows an example DTDvhs for the CTV structure for the 3.30 and 1.32 Gy dose difference DTD criteria. From these graphs, one can read out the DVF accuracy required as a function of the percentage volume of the structure. While not as useful as 3D visualization of the DTD, these DTDvhs enable simple statistical analysis of DTD properties.

DTDs calculated based on the $2 \times 2 \times 2 \text{ mm}^3$ dose grid resolution (not shown) look similar to the $4 \times 4 \times 4 \text{ mm}^3$ results shown in Fig. 4. DTD values should not vary

FIG. 4. Color wash of DTD values overlaid on a transverse slice of the patient anatomy. Each color wash value represents the lower bound of the value, e.g., 1 mm corresponds to DTDs ranging from 1.0 to 2.0 mm. (a) $DTD_{2\%}$, tolerance is 2% of the local dose value; (b) $DTD_{1.32 \text{ Gy}}$, tolerance is 1.32 Gy (2% of the prescription dose); and (c) $DTD_{3.30 \text{ Gy}}$, tolerance is 3.30 Gy (5% of the prescription dose). On this slice, in (a), outside the treatment region DTD values range from 0.1 to 1 mm, around the CTV values range from 1 to 4 mm, and inside the CTV DTDs up to 6 mm are observed. In (b), inside the CTV volume, the plan absorbs DVF 4 mm errors. In dose gradients around the CTV, 0.5–1 mm DVF errors are permitted, and outside the treatment region, DVF errors up to 10 mm are tolerated. In (c), inside the CTV, 10 mm DVF error is permitted. In dose gradients around the CTV, 1–8 mm DVF errors are permitted, and outside the treatment region, DVF errors up to 10 mm are tolerated.

significantly with dose grid resolution when the dose resolution is sufficient such that intermediate points can be trilinear interpolated with errors small compared with the size of the DTD criteria. For points within the patient contour, the average DTD values computed at the $4 \times 4 \times 4 \text{ mm}^3$ and $2 \times 2 \times 2 \text{ mm}^3$ resolutions differ by less than 0.05 mm, with a root-mean-square difference of 0.7 mm. Figure 5 shows that differences in the 3.3 Gy CTV DTDvh values are less than 0.5 mm for the different dose matrix resolutions. The deviations are due to differences in dose values computed

FIG. 5. CTV distance to difference volume histogram (DTDvh) for the $DTD_{3.30 \text{ Gy}}$ and $DTD_{1.32 \text{ Gy}}$ values. The DTD data indicates that 90% of the CTV can tolerate DVF errors up to 1.01 mm for $\Delta D = 1.32 \text{ Gy}$ and 2.8 mm for $\Delta D = 3.30 \text{ Gy}$. 30% of the CTV can tolerate DVF errors up to 2.1 mm for $\Delta D = 1.32 \text{ Gy}$ and 6.6 mm for $\Delta D = 3.30 \text{ Gy}$. Also plotted is the histogram of the dose tolerance divided by gradient values for a 3.30 Gy dose tolerance, which indicates that 90% of the CTV tolerated DVF errors up to 5 mm, and 30% of the volume can tolerate up to 12 mm errors. DTD and TDG values shown are computed using a dose matrix resolution of $4 \times 4 \times 4 \text{ mm}^3$, except for one 3.30 Gy DTD curve (noted as $DTD_{3.30 \text{ Gy}}$ 2 mm dose resolution) computed with a $2 \times 2 \times 2 \text{ mm}^3$ dose matrix to show deviations caused by computing at a different dose resolution.

within the CTV for the different resolutions and due to limitations of the underlying DTA algorithm used.

The $TDG_{3.30 \text{ Gy}}^{3D}$ image for 3.30 Gy dose difference tolerance ($TDG_{3.30 \text{ Gy}}^{3D}$) is shown in Fig. 6. Qualitatively, this image is similar to the $DTD_{3.3 \text{ Gy}}$ [Fig. 4(c)] in dose gradient regions but differs in regions inside the CTV and outside the radiation beams where $TDG_{3.30 \text{ Gy}}^{3D}$ indicates larger tolerances of DVF or spatial dose errors from the DTD method. Figure 7 compares the point-by-point $DTD_{3.30 \text{ Gy}}$ values with the $TDG_{3.30 \text{ Gy}}^{3D}$ values for dose points within the patient contour. The banding in the DTD values is due to the $1 \times 1 \times 1 \text{ mm}^3$ resolution used within the DTA algorithm. Generally, TDG values are larger than DTD values for this case. Poor correlation between $DTD_{3.30 \text{ Gy}}$ and $TDG_{3.30 \text{ Gy}}^{3D}$ values is observed, especially for large values. Points with large $TDG_{3.30 \text{ Gy}}^{3D}$ values yet small $DTD_{3.30 \text{ Gy}}$ values are detected. The TDG is inversely proportional to the dose gradient. Because $TDG_{3.30 \text{ Gy}}^{3D}$

FIG. 6. Color wash of the $TDG_{3.30 \text{ Gy}}^{3D}$. Small TDG values (1–4 mm) are observed inside the treated region excluding the CTV.

Fig. 7. Scatter plot between the calculated $DTD_{3,30\text{Gy}}$ and the $TDG_{3,30\text{Gy}}^{3D}$. Poor correlation between these quantities is observed, particularly at large values.

uses the magnitude of the gradient vector, which can have small components in one direction but large components in others, it can overestimate permissible spatial dose errors in low dose gradient region. In high dose gradient region, the TDG can overestimate or underestimate spatial dose errors depending on the curvature of the dose distribution.

$TDG^{\max}$, which uses the maximum dose gradient, has similar poor correlation with the DTD (not shown). Overall, the TDG method is limited in its ability to evaluate acceptable DVF errors.

IV. DISCUSSION

The uncertainty in a deformable image registration algorithm will lead to uncertainty in the DVF generated. Several groups have been working on estimating the uncertainty in deformable image registration algorithms; however, little work has been done on finding the required spatial accuracy of a DVF. In this work, a simple algorithm is introduced to compute a distance to a dose difference tolerance that can be related to how accurate the DVF used in dose mapping has to be before violating the specified dose accuracy tolerance. Current deformable image registration algorithms focus on creating an as-accurate-as-possible registration for an entire image or restrict over a given region of interest. The results of this work indicate that for dose mapping purposes, accurate registration is needed in high dose gradient regions, with less accuracy in uniform dose areas.

For simplicity, the example presented in this work evaluated the DTD between phases of a 4D lung treatment plan. Specifically, the DTD estimates the required DVF spatial accuracy needed to map dose delivered on the end of inhale breathing phase (phase 0%) to any of the other breathing phases. The tolerance values are selected as if the full treat-

ment delivery occurred on the phase 0% image set. If dose delivery on multiple 4D breathing phases is considered, the sum of the DVF induced dose mapping errors (from the different mappings) would need to be less than the tolerance value. If the DTD dose error tolerance is equidistributed among the breathing phases, the dose delivered and DTD threshold values change by the same fraction, resulting in the same DTD for the phase 0% to phase $N\%$ mappings as given above. Alternatively, the DTD dose error tolerance could be unequally distributed among the different image sets, while still requiring that the total dose error induced is less than the threshold. This complex analysis is left for further study.

The example presented in this paper utilized DTD tolerance values with respect to target dose values. However, the DTD concept is general and DTDs can be computed to arbitrary, even region of interest specific tolerances. For example, for critical structures, an appropriate tolerance could be the maximum tolerated dose.

The DTD tool provides qualitative utilities when interfaced with a treatment planning system; DTD can be visualized as isoDTD lines/color washes that provide the planner with the ability to see geographical maps of tolerated and intolerated DVF errors before using a specified DVF with a given uncertainty for dose mapping. DTD-volume-histograms can provide volume-based statistical error analysis for targets, organs at risk, or arbitrary regions of interest in an image.

The DTD tool is not limited to estimating the spatial accuracy of a DVF. For a given dose difference tolerance (absolute or %), one can determine the distance error that can be tolerated before violating the specified dose accuracy. For a CTV, the DTD can be used as a first estimate of how large a setup error can be before introducing a clinically significant dose error. Similarly, knowledge of the maximum tolerated setup error can be used in plan evaluation, possibly affecting CTV-to-PTV or organ at risk-to-planning risk volume (PRV) planning margins.

V. CONCLUSIONS

This work introduces a new method which estimates how large a DVF error can be tolerated before introducing a potentially clinically significant error in the dose mapping processes. The required DVF spatial accuracy will depend on the particular dose distribution. For dose mapping, DVFs accuracy must be highest in dose gradient regions, while less accurate DVFs can be tolerated in uniform dose regions. The DTD tool can be used as a first estimate of DVF required spatial accuracy and can be applied to other areas when the distance to a dose difference tolerance is required to be known.

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