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FULL PAPER

A simple method of evaluating margin-growing accuracy in image-guided radiation therapy

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Objective: In order to not add extra uncertainty to radiotherapy planning process, accurate margin algorithm is necessary, therefore we propose a centre-shift method to estimate its accuracy.

Methods: A series of spherical phantoms are used with different CT slice separations (SSs) and pixel sizes (PSs). They are grown by different margins, and displaced geometric centres provide a window on accuracy. Volume difference between pre- and post-expansion is also calculated to double-check the accuracy.

Results: The measured margin nearly varies as multiples of PS in the transaxial plane; in the superior-inferior direction, it is approximately equal to SS when the ideal margin is smaller than SS. A sphere's volume of $<1\text{ cm}^3$ is

underestimated by 3–70% for all PSs, and 2–100% for SS of $\leq 5\text{ mm}$ but overestimated up to 112% for $>5\text{ mm}$. For volumes of $>1\text{ cm}^3$, relative volume error decreases, and it is nearly zero for $>100\text{ cm}^3$. The dependence of margin accuracy on SS and PS is largely eliminated by volume difference method.

Conclusion: We have proposed a simple method to estimate margin-growing accuracy and suggested corrective action to minimize the variation.

Advances in knowledge: One big difference from the previous results is that SS and PS both influence the accuracy of margin growth and volume calculation in Eclipse™ treatment planning system (Varian Medical System, Palo Alto, CA).

INTRODUCTION

The treatment process of external beam radiotherapy inherently introduces several geometrical uncertainties, and the main sources are tumour delineation inaccuracies, organ motion and setup variations. A commonly used method has been to add a margin to the gross tumour volume (GTV) outline; the resulting outline being the clinical target volume (CTV) containing microscopic tumour spread or the planning target volume (PTV) to account for patient setup variations and tumour movement. In practice, generation of the PTV from the GTV is generally carried out in two steps with explicitly calculating the CTV.

The simplest method is to add a two-dimensional (2D) margin to the GTV on each slice to create a three-dimensional (3D) PTV, but this procedure ignores the margin distance in the superior–inferior direction. In 1995, Austin-Seymour et al^{1,2} proposed a cylindrical expansion method. This method firstly created the convex hull of the CTV, and then the PTV was computed by moving each point on the CTV convex hull contour away from its centre

by a distance equal to the required margin distance in transaxial plane. Finally, the PTV in the superior/inferior direction was derived by duplicating the original superior/inferior CTV contour at marginal distance above/below the tumour. However, this method altered the original CTV contour delineated by the radiotherapist/radiologist, giving rise to substantial overdosing of the critical organs.

In 1997, Belshi et al³ provided a method to automatically grow a constant 3D margin through a 2D expansion performed by transforming each vertex of GTV contours into a circle with a radius equal to the margin in the parallel slices. Also, the influence of the adjacent slice located at a distance smaller than the margin was taken into account by applying a 2D expansion using a particular formula. At the same time, Stroom and Storchi⁴ proposed an algorithm utilizing a 3D coverage matrix to describe what proportion of each CT pixel was contained within the GTV/CTV. A margin function was then convolved to generate a map of the expanded target volume consisting of values between zero and unity, and then the PTV was constructed with the 50% isovalue of the target map. Although this method

could grow 3D margins quickly, it had a limited accuracy in the superior–inferior direction due to slice spacing.

In spite of the fundamental importance of tumour margins in radiotherapy, many sophisticated 3D treatment planning systems still do not possess accurate methods for margin growing. In the past few decades, there were several reports to provide quality assurance (QA) procedures on it.^{5–7} Our goal was to propose a simple and feasible QA method to estimate the accuracy of margin growth of used treatment planning systems and suggest corrective action to minimize the variation.

METHODS AND MATERIALS

In order to represent anatomically relevant shapes (e.g. prostate, bladder, eyes), a series of spherical phantoms standing for GTV/CTV, ranging from 0.02 to 1151 cm³, were created in the Eclipse™ treatment planning system v. 8.6, 8.9, 10.0 and 11.0 (Varian Medical System, Palo Alto, CA). They were determined from CT images with 1.0, 1.5, 2.0, 2.5, 3.0, 4.0, 5.0, 7.5 and 8.0-mm slice separations (SSs), and various fields of view (FOVs) were used in conjunction with 512 × 512 matrices, giving in-plane pixel sizes (PSs) ranging from 0.3 × 0.3 to 1.3 × 1.3 mm².

The GTV/CTV outlines were displayed slice by slice, and margins ranging from 0.1 to 3.0 cm in steps of 0.1 cm were then added using the 3D margin-growing algorithm provided by the commercial treatment planning systems in the *x*, *y* and *z* directions to derive the PTV (Figure 1). In this work, the *x* dimension was the right–left (lateral), *y* dimension was anterior–posterior (vertical) and *z* dimension was superior–inferior (longitudinal).

The geometric centre shift method

Expansion of the GTV/CTV in the *x*, *y* or *z* direction was calculated for each contour independently. First, the geometric centre of the original sphere standing for GTV/CTV (orange or white line) was marked as “O” in Figure 1a. Next, the margin was added to generate PTV in the *x* (pink), *y* (green) or *z* (blue dashed line) direction separately. The PTV centre was marked as “O_x”, “O_y” or “O_z”. In theory, the distance of “O” from “O_x”,

“O_y” or “O_z” should be half of the corresponding measured margin, so the difference between double of the distance and the ideal margin would provide an estimation of the accuracy of margin-growth algorithms.

The volume difference method

In this method, the first step was to test the accuracy of volume calculation of the treatment planning system because the accuracy of tumour volume depended on CT slice thickness.⁸ CT images with different SSs (1.0, 1.5, 2.0, 2.5, 3.0, 4.0, 5.0, 7.5, 8.0 and 10.0 mm) and PSs (0.1, 0.3, 0.5, 0.7, 0.9, 1.1 and 1.3 mm) were imported into the treatment planning system to reconstruct 3D images. A series of spheres, which had diameters ranging from 0.1 to 13.0 cm, were generated in the above images, and the theoretic volume was calculated by Equation (1).

$$V = \frac{4}{3}\pi r^3 \quad (1)$$

where *r* was the radius of a sphere and *V* was the volume. The difference between the theoretic volume and the measured one was the error of volume calculation.

The ideal volume of a spherical phantom (*V_{idl}*) was calculated by plugging the required radius into Equation (1), and the measured volume (*V_{msd}*) was obtained from the treatment planning system. The relative volume error (ΔV) between them was calculated

$$\Delta V = \frac{V_{idl} - V_{msd}}{V_{idl}} \times 100\% \quad (2)$$

In order to minimize the influence of SS on volume calculation, the SS of 1.0 mm was used to calculate the dependence of volume on PS. Also, the PS of 0.1 × 0.1 mm² was used for a similar purpose.

Under the condition of minimizing the effect of SS and PS on volume calculation, a symmetric 3D margin was added on to GTV/CTV (orange), which had a specific radius of *r_{GTV/CTV}* to

Figure 1. The schematic of three-dimensional margin growing. (a) The geometric centre shift method; (b) the volume difference method.

Figure 2. The influence of pixel size and slice separation on the margin-growing accuracy. (a) Pixel sizes ranging from 0.3 to 1.0 mm in steps of 0.02 mm; (b) pixel sizes ranging from 0.31 to 1.05 mm in steps of 0.02 mm; (c) pixel sizes of ≥ 1.1 mm and various slice separations.

derive PTV (green) (Figure 1b). The PTV volume was measured using the algorithm of treatment planning systems, and its radius (r_{PTV}) was calculated by plugging the volume into Equation (1). The difference between the ideal margin and $r_{PTV} - r_{GTV/CTV}$ was regarded as the error of margin growing.

Data analysis

A two-sided Wilcoxon signed-rank test was used to compare the results between the centre shift method and the volume difference method. Statistical analyses were performed using Statistical Package of Social Sciences (SPSS® statistics v. 22; IBM Corporation, Armonk, NY), and the threshold for statistical significance was $p < 0.05$.

RESULTS

Margin-growing accuracy based on centre shift method

In Figure 2, the numbers outside each panel on the left were ideal margins; and those below each panel were PSs or SSs. The numbers in each panel were the measured margins determined by the corresponding ideal margins and PSs or SSs. The statistical uncertainties included the shape and geometric centre errors of the spherical phantom and FOV uncertainties. They were expressed by different colours combined with symbols.

As shown in Figure 2, the margin growth showed different variations among various PSs and SSs, and a correlation between them was found. The measured margin nearly varied as multiples of PS in the left–right or anterior–posterior direction. For example, when the PS was 0.6 mm and the ideal margins were 1.0–5.0 mm, the corresponding measured margins were 1.2 ± 0.1 (2×0.6), 2.4 ± 0.1 (4×0.6), 2.6 ± 0.1 (4×0.6), 3.6 ± 0.1 (6×0.6) and 4.7 ± 0.1 (8×0.6) (Figure 2a). The majority of errors in margin growing in the transaxial plane were within 1.0 mm, and the observed maximum variation was 1.6 ± 0.1 mm. In the superior–inferior direction, a large variation was observed and the measured margin was approximately equal to SS when the ideal margin was smaller than the SS (Figure 2c); otherwise, it nearly varied as multiples of the slice spacing.

Volume calculation accuracy

As shown in Figure 3, the sphere's volume of $<1 \text{ cm}^3$ was underestimated by 3–70% for all of PSs and by 2–100% for SS of $\leq 5 \text{ mm}$, but it was overestimated up to 112% when SS was $>5 \text{ mm}$. For the volume of $>1 \text{ cm}^3$, the relative error of volume decreased, and it was nearly zero for the volume of $>100 \text{ cm}^3$. In order to not add extra error to the margin calculating process, the sphere of $>100 \text{ cm}^3$ was adopted in the following analysis.

Figure 3. The relative volume error as a function of different sphere volumes. Top panel: the maximum slice separation of 1.0 mm and seven kinds of pixel sizes; bottom panel: the maximum pixel size of $0.1 \times 0.1 \text{ mm}^2$ and ten kinds of slice separations.

Margin-growing accuracy based on volume difference method

Table 1 showed the ideal and measured margins derived from the centre shift and volume difference methods with maximum PS of 1.3 mm and common SS of 3.0 and 5.0 mm. There was no significant difference in the margin-growing accuracy between the two methods in the transaxial plane ($p = 0.878$), but the discrepancies were obvious in the superior–inferior direction (3 mm: $p = 0.007$; 5 mm: $p = 0.011$), therefore the dependence of margin accuracy on SS was largely eliminated by the volume difference method.

DISCUSSION

In conformal radiotherapy, the treatment volume is shaped to the PTV. If the PTV is incorrectly delineated, there is a risk of increasing the normal tissue complication probability or marginal tumour recurrence, therefore a 3D definition of PTV is necessary. The important factors contributing to PTV delineation include the CT pixel value, PS, SS and margin. The different CT parameters lead to different image quality, and different margins cover different treatment volume. It is, however, not known if varying the CT parameters influences derived margin growth. Also, it is useful to choose the optimum parameters for PTV delineation.

In clinical practice, PTV is mostly composed of soft tissue, bone or cavity. However, the CT Hounsfield numbers of them are different. If margin growth depends on pixel value, target delineation would become very difficult. In this work, margin growth of up to 3.0 cm was shown to be consistent among different pixel values, so the pixel value did not appear to influence the margin-growing accuracy. We do not need to take into account the difference of tissues when the structures are expanded.

In general, the matrix size is 512×512 in CT, so the PS is within 1.37 mm because of extended display FOV of 700 mm using the big bore CT. The common PSs in many clinical trials were 0.7–1.0 mm,

and the errors in margin growing were within 1.0 mm (Figure 2). Compared with the current mechanical precision of linear accelerator (millimeters), margin growth is considered to be perfect.

The physicist always generates a PTV in one or two steps; the one step: $PTV = (GTV + \text{Margin}_{GTV \rightarrow PTV})$; the two steps: $PTV = GTV + \text{Margin}_{GTV \rightarrow CTV} + \text{Margin}_{CTV \rightarrow PTV}$. If margin growth variation does not exist, there should not be discrepancy between the two processes. In fact, every margin growth showed substantial variation (Figure 2). The discrepancy would be accentuated by double margining.

When retrospectively analyzing clinical data from different cohorts, slice thicknesses of acquired CT images used for treatment planning may vary between cohorts. Olsson et al⁹ investigated this for rectal bleeding using dose–volume histograms of the rectum and rectal wall with varying CT slice thicknesses from two prostate cancer cohorts treated with 3D conformal radiotherapy and found that the investigated SS variations had minimal impact on rectal dose–response estimations.⁹ New delivery techniques, such as intensity-modulated radiotherapy and volumetric-modulated arc therapy, enable complex dose distributions with sharp dose gradients to be delivered and achieve superior target conformity than conventional 3D conformal radiotherapy. It is not known if similar results can be found for these advanced techniques due to the influence of SS on target volume (Figure 3).

Each treatment planning system has its calculation algorithm handling structural modelling. For example, structures are modelled as 3D-point clouds in Eclipse. The point cloud generation algorithm places more points close to the structure's external surface to ensure proper representation of complex shapes. Two models could be chosen, high- and low-resolution. The volume calculated by high-resolution algorithm is nearly the ideal volume, but the default volume calculation was in low resolution. There was significant

Table 1. Comparison of margin growing accuracy between geometrical centre shift method (Method #1) and volume difference method (Method #2)

Ideal margin (mm)	Measured margin (mm)					
	Pixel size = 1.3 mm		Slice separation = 3.0 mm		Slice separation = 5.0 mm	
	Method #1	Method #2	Method #1	Method #2	Method #1	Method #2
1.0	2.6 ± 0.1	1.8 ± 0.1	3.0 ± 0.1	1.9 ± 0.2	5.0 ± 0.1	2.7 ± 0.1
2.0	2.6 ± 0.1	2.3 ± 0.1	3.0 ± 0.1	2.3 ± 0.2	5.0 ± 0.1	3.0 ± 0.2
3.0	2.6 ± 0.1	3.2 ± 0.2	3.0 ± 0.1	3.1 ± 0.1	5.0 ± 0.1	3.8 ± 0.2
4.0	5.0 ± 0.1	3.9 ± 0.2	4.9 ± 2.8	4.0 ± 0.2	5.0 ± 0.1	4.7 ± 0.1
5.0	5.2 ± 0.1	5.3 ± 0.2	6.0 ± 0.1	5.2 ± 0.1	5.0 ± 0.1	5.4 ± 0.2
6.0	5.2 ± 0.1	6.1 ± 0.2	6.4 ± 0.3	6.2 ± 0.2	7.8 ± 5.0	6.1 ± 0.1
7.0	7.8 ± 0.1	7.2 ± 0.1	8.0 ± 2.3	6.9 ± 0.1	9.1 ± 1.8	7.4 ± 0.2
8.0	7.8 ± 0.1	8.2 ± 0.2	8.9 ± 0.1	8.3 ± 0.1	10.0 ± 0.1	8.5 ± 0.1
9.0	8.6 ± 0.6	9.2 ± 0.1	10.1 ± 2.8	9.1 ± 0.2	9.9 ± 0.1	9.5 ± 0.2
10.0	10.4 ± 0.1	10.2 ± 0.2	11.2 ± 1.3	10.3 ± 0.1	11.8 ± 4.5	10.3 ± 0.1
<i>p</i> -value	0.878		0.007		0.011	

difference between two resolutions (Figure 3), especially for small-volume structures such as the optic nerves and chiasm. Also, it is not known if the radiation dose–volume effect of the optic nerves and chiasm would change due to different SS.¹⁰

Deforming a planning CT to match a daily cone beam CT provides the tools needed for calculation of the “dose of the day” to inform adaptive radiotherapy without the need to acquire a new CT. Veiga et al¹¹ presented the first step into a full implementation of a “dose-driven” online ART. As a potential source of error, the electron density calibration was widely discussed,¹² but the difference of CT parameters between planning CT and cone beam CT, and the effect of them on dose–volume distribution still need to be investigated.

Individual physicians and institutions differ significantly in their creation of PTV,¹³ and different planning systems measure target volumes in different ways;¹⁴ hence, the use of digital imaging and communications in medicine RT to transfer structure sets, or the comparison of structure sets among different cohorts could potentially lead to a loss or misjudgement of information. As the potential influence factors, the consistencies of CT parameters should be taken into account during entire radiotherapy.

A simple empirical correction can be applied to correct their inconsistencies. If the margins applied are smaller than slice

spacing, the extent of the expanded contours in the superior and inferior directions should be checked; on the other hand, the margin growth will approximately vary as multiples of slice spacing. The results from the geometric centre shift method do not depend on the target shapes, just regular-shaped objects such as a sphere or cube. Moreover, we only focus on the Eclipse treatment planning system in this study, and our goal is not to determine the difference of margin growing among the various treatment planning systems but just to recommend a simple method to rapidly implement QA in margin growing.

CONCLUSION

In summary, a method based on geometric centre shift is proposed to quickly complete margin-growing QA. One big difference from the previous results is that SS and PS both influence the accuracy of margin growth and volume calculation in Eclipse.¹⁵ The geometric centre shift method can provide the accuracy of arbitrary margin, but the previous volume-difference method would eliminate the above influence. The corresponding QA is recommended.

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