Dose Broadening Due to Target Position Variability During Fractionated Breath-held Radiation Therapy

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I. Introduction

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Recent advances in Stereotactic Radiosurgery/Conformal Radiotherapy have made it possible to deliver surgically precise radiation therapy to small lesions while preserving the surrounding tissue. However, because of physiologic motion, the application of conformal radiotherapy to extra-cranial tumors is, at present, geared toward slowing the progression of disease rather than obtaining a cure. At the University of Rochester, we are investigating the use of patient breath-holding to reduce respiratory-derived motion in fractionated radiotherapy. The primary targeting problem then becomes the small variation in tumor location over repeated breath-holds. This presentation describes the effects of residual target position uncertainty on the dose distribution observed by small extra-cranial tumors and their neighboring tissues during fractionated radiation treatment using breath holding.

II. Methods

The effect of the magnitude of the position variability on the changes in the observed dose was studied using standard deviations in tumor position that ranged from 1 to 4 mm. For a human subject, tumor position variability data was gathered from pretreatment MRI datasets (results presented previously [1]) and also applied in the analysis. Using representative tumor position variability values and corresponding margin definitions, a comparison was made between the volumes of lung tissue that would be expected to receive harmful doses of radiation using end-expiration breath-holding during treatment planning and radiation delivery.

Target Position Variability Model

For fractionated radiotherapy with breath holding, the variability in position of the target over all the repeated breath-holds was modeled as a Gaussian distribution. The standard deviation in position about the mean position was allowed to vary independently with coordinate direction, where the coordinates were defined with respect to the patient: Superior-Inferior (SI); Anterior-Posterior (AP); and Right-Left (RL). The resulting 3D Gaussian ellipsoid was sampled at 1 mm intervals in each direction to create a digitized position probability matrix.

Dose Perturbation via Convolution

As the number of treatment fractions approaches infinity, the cumulative dose seen by the target can be modeled as the convolution of the 3D dose distribution with the 3D Gaussian probability distribution for target position, as described previously by several authors [2]. The convolution operation is described by:

$$\mathbf{f}[l,m,n] = \mathbf{g}[l,m,n] \otimes \mathbf{h}[i,j,k] = \sum_{i} \sum_{j} \sum_{k} \mathbf{h}[i,j,k] \cdot \mathbf{g}[l-i,m-j,n-k]$$

where **g** is the original (planned) dose field represented as a 3D matrix (of size LxMxN) of dose values, **h** is the 3D Gaussian distribution model represented by a 3D matrix of size IxJxK, and **f** is the resulting, altered dose distribution.

Dose Perturbation via Monte-Carlo Simulation

The dose field perturbation for a finite number of treatment fractions can be assessed using Monte-Carlo simulation, as demonstrated by Leong [3] and others, and validated against the convolution method by Lujan [4], and others. A random-number generator was modified to produce both negative and positive output displacements that fall within a prescribed Gaussian distribution. The generator's output was used to shift the prescribed dose field in each of the SI, AP, and RL directions randomly for 10, 20, 100, or 1000 treatment fractions.



Lung Lesion Treatment Plan

A realistic treatment 3D dose field was obtained from a conventional conformal beam treatment plan for a representative 12mm-diameter lung lesion located posteriorly-inferiorly in the patient's left lung. The treatment plan for this lesion consisted of 6-MV X-rays applied in two, 110-degree arc pathways separated by 20 degrees. The clinical target volume (CTV) was defined by the observable tumor as manually segmented using the commercial planning system software. The planning target volume was defined as the CTV with a margin specification of 7x7x10 mm in the AP, RL and SI directions, respectively.

III. Results

Target Position Variability and Dose Broadening

The result of the convolution of the dose matrix by the position variability matrix is an eroded version of the original dose distribution, as described by previous authors [1, 19]. The relationship between the leftward shift of the tumor DVH curve and the magnitude of the position variability is monotonic but non-linear. The volume of surrounding tissue receiving 50% dose and that receiving 80% dose dropped as the position standard deviation increased.



Broadening Versus Number of Fractions

There is a statistical relationship between the expected results from any given 10-fraction simulation and the infinitefraction results (the convolution method), as described by sampling theory. From 50 trials, the mean, 25^{th} quartile, and 75^{th} quartile DVH curves, were compiled for each of 10 and 20 fractions and compared with the convolution results.



IV. Conclusions

Preliminary Clinical Results:

These results demonstrate that the entire tumor volume was irradiated to >47 Gy – well above the tumoricidal threshold. This finding was substantiated by the clinical results: there was evidence of tumor shrinkage during treatment and all but one of the lesions had disappeared completely by the end of the ten-day therapy. At the 6 and 12-month follow-ups, all 5 lesions had been eradicated with no indication of disease recurrence at the treatment sites.

End-Expiration Breath-Holds Better than Deep-Inspiration BH

Using end-expiration breath holds (EEBH) to compensate for respiratory-derived lung tumor motion results in a more favorable lung mass exposure in the high dose region compared with using a deep end-inspiration breath-holding (DIBH) approach for these targets, even after considering the decrease in lung tissue density due to the increased volume of air in the lungs for DIBHs, based on the results of [3-4] and our analysis. This is primarily a result of the larger variability in diaphragm position over repeated breath holds at end-inspiration compared with end-expiration, even when lung volume feedback via a spirometer is used in the end-inspiration method and not in the EEBH method.

Take Home Message

This information suggests that curative treatment of lung and liver lesions is possible when simple end-expiration breath holding is used to compensate for respiratory-derived motion.

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