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PHYSICS CONTRIBUTION

A NOVEL METHOD FOR THE EVALUATION OF UNCERTAINTY IN DOSE–VOLUME HISTOGRAM COMPUTATION

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Purpose: Dose–volume histograms (DVHs) are a useful tool in state-of-the-art radiotherapy treatment planning, and it is essential to recognize their limitations. Even after a specific dose-calculation model is optimized, dose distributions computed by using treatment-planning systems are affected by several sources of uncertainty, such as algorithm limitations, measurement uncertainty in the data used to model the beam, and residual differences between measured and computed dose. This report presents a novel method to take them into account.
Methods and Materials: To take into account the effect of associated uncertainties, a probabilistic approach using a new kind of histogram, a dose–expected volume histogram, is introduced. The expected value of the volume in the region of interest receiving an absorbed dose equal to or greater than a certain value is found by using the probability distribution of the dose at each point. A rectangular probability distribution is assumed for this point dose, and a formulation that accounts for uncertainties associated with point dose is presented for practical computations.
Results: This method is applied to a set of DVHs for different regions of interest, including 6 brain patients, 8 lung patients, 8 pelvis patients, and 6 prostate patients planned for intensity-modulated radiation therapy.
Conclusions: Results show a greater effect on planning target volume coverage than in organs at risk. In cases of steep DVH gradients, such as planning target volumes, this new method shows the largest differences with the corresponding DVH; thus, the effect of the uncertainty is larger. © 2008 Elsevier Inc.

Dose uncertainty, Dose distribution, Dose–volume histogram, Treatment planning system, Probability distribution.

INTRODUCTION

Dose–volume histograms (DVHs) were introduced as a tool for plan evaluation in the late 1980s, at a time when three-dimensional dose computations were becoming state of the art (1). Soon after that, DVHs started being used routinely for plan evaluation. They also provided a criterion in dose prescription. At present, the constraints on DVHs are used as input data for optimization of intensity-modulated radiation therapy (IMRT) treatment planning. Because of the limitations and difficulties involved in practical use of recommendations (2, 3), prescriptions based on DVHs replaced the traditional dose to a point approach when prescribing and reporting IMRT treatments. Thus, careful evaluation of the accuracy of DVH computation is now as essential as point dose calculations. The most recent reports on quality assurance of treatment planning make recommendations regarding assessments of the accuracy of DVHs (4–11).

Despite these efforts, evaluation of the uncertainty associated with a particular DVH is not as simple and straightforward as it is for a dose at a specific point. The DVH is a composite entity that involves dose bins and corresponding fractional organ or target tissue volumes. Its evaluation at any particular dose level involves computation of doses at many points. Uncertainties involved in the computation of point doses are not mutually correlated.

Niemierko and Goitein (12) and Lu and Chin (13) published work on the accuracy of DVH computation. They compared two methods of volume computation: random (or quasi random) sampling and grid placement. Advantages and disadvantages of both methods were the subject of further comments (14, 15). Kooy *et al.* (16) published a new method for volume assessment in small nearly spherical volumes of interest and adapted its use in radiosurgery plans, which improved the accuracy of volume computation. The uncertainty associated with dose computation and its effect on DVH was not addressed in these articles.

Uncertainties for point dose computations arise from several different sources, as follows: (*1*) inherent random type A measurement uncertainty in data used for modeling the

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beams; (*2*) type B uncertainty caused by algorithm limitations that depends on patient geometry, characteristics of organs of interest (geometry and tissue density), and beam characteristics; this type B uncertainty can vary for each particular point, being dose gradient, tissue heterogeneity, and blocking some of the parameters affecting this uncertainty; and (*3*) type B uncertainty caused by imperfect matching between measured and computed data when modeling the beam.

When specifying dose to a point, a composition of uncertainties from all sources must be used. The problem of combining these uncertainties to obtain the uncertainty of a DVH value is complex. Different voxels with the same computed absorbed dose can have very different irradiation conditions (*e.g.,* they can be in penumbra regions, close to a low- or high-density organ, or under a beam modifier), and they depend on the beam arrangement and patient anatomy.

A probabilistic approach is presented in this report to account for dose uncertainty in DVH computation. A modified version of the DVH was developed that takes into account the probability of each voxel receiving a dose greater than the dose level considered. Some applications to clinical plans are presented to illustrate the effects of dose uncertainty on DVHs; a summary of statistical parameters also is provided. Although volume computation uncertainty is not dealt with in this report, previous published studies (12–15) are applicable to this modified histogram.

Jin *et al.* (17) presented a comprehensive summary of sources of deviations between measurement and computation, identifying non–spatial-oriented and spatial-oriented differences. Considering the whole radiotherapy process, including setup uncertainties, spatial-oriented uncertainties become an important source of uncertainty.

The overall uncertainty in delivered dose to the patient includes geometric and anatomic uncertainties. Several methods were proposed to take setup uncertainty and organ motion into account in a dose distribution. It could be possible to apply the new method described in this report to some published methods to account for systematic and random errors, such as the one described by Cho *et al.* (18).

This work focuses on the effect of point dose calculation uncertainty in DVH computation, a component of the overall uncertainty in DVHs that was not dealt with to date. A careful study of the effect of point dose computation uncertainty is important to evaluate which goals can be achieved when planning a treatment and to assess plans.

METHODS AND MATERIALS

Theory

The standard definition of cumulative DVH, $DVH_c(x)$, of a region of interest (ROI) at dose level x is the volume contained in the ROI receiving a dose of x or greater (1). It is common practice to use relative volumes and/or doses with respect to total ROI volume and doses to an arbitrary chosen level (prescription dose). Another variant of this concept is the differential DVH, $DVH_d(x)$, defined as the volume contained in the ROI receiving dose level x. Relationships between both functions can be obtained easily.

$$DVH_c(x) = \int_x^{\infty} DVH_d(y)dy,$$

$$DVH_d(x) = -\frac{d}{dx}DVH_c(x).$$

The DVHs are usually computed for a discreet set of dose intervals of uniform length. Random sampling or regular grids are possible methods to sample dose points inside the ROI. In practice, DVHs are computed on a discreet set of N voxels with volume v_i, where the computed dose is assumed to be approximately constant and equal to the dose at a representative point z_i (its center).

Accounting for its variation caused by associated uncertainties, absorbed dose at sample point z_i can be represented mathematically as a random variable Δ_i, with density function $f_i(\delta_i)$, for which mean is $D(z_i)$ (computed dose in z_i) and variance is σ_i^2. The dose distribution is effectively presented in terms of its variance or SD. Regardless of its source, probability distributions from different sources can be combined according to the specific rules (19–21) using SD. Thus, SDs are the most recommended parameters to evaluate and present uncertainties associated with parameters.

We are interested in evaluating probabilities for this random variable Δ_i. Depending on the source of dose uncertainty and whether it is a type A or type B uncertainty, different probability density functions could be assumed. If there is a dominant type A component caused by experimental uncertainty or a composition of many small uncertainty sources independent and identically distributed with finite variance, the central limit theorem may be applicable and Gaussian distribution can be used.

$$f_i(\delta_i) = \frac{1}{\sqrt{2\pi}\sigma_i} e^{-\frac{(\delta_i - D(z_i))^2}{2\sigma_i^2}}$$

In other situations, when there is no definitive information regarding probability distributions of the random variables, a rectangular probability density function is assumed, giving equal probability to any result within an upper and a lower bound (International Standards Organization Guide[19]). The choice of bounds depends on the particular features of each problem and has to be based in physical considerations.

Regardless of the choice, it is assumed that the SD is a constant percentage of the computed dose, *i.e.,* relative uncertainty is constant within the ROI R, so $\sigma_y = u \cdot D(y)$ (discussed next). We can then define a density function $f(w)$ verifying

$$f_i(\delta_i) = f\left(\frac{\delta_i - D(z_i)}{\sigma_i}\right) = f\left(\frac{\delta_i - D(z_i)}{u \bullet D(z_i)}\right)$$

and $f(w)$ has mean *0* and SD *1*.

Cumulative dose–expected volume histogram, $DeVH_c(x)$, for the ROI R and dose level x is defined as the expected value of the volume contained in R receiving a dose of x or greater.

If T_i^x is defined as a random variable with value *1* when $\delta_i \geq x$ and *0* otherwise, then the sum $\sum_{i=1}^{N} T_i^x \bullet v_i$ is a random variable corresponding to the volume receiving a dose greater than x. Each voxel adds the value v_i to this summation according to T_i^x. The dose–expected volume histogram (DeVH) is obtained as the expectation value of this sum:

$$DeVH_c(x) = E\left[\sum_{i=1}^{N} T_i^x \bullet v_i\right] = \sum_{i=1}^{N} E\left[T_i^x\right] \bullet v_i$$