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Treatment planning

Comparison between the ideal reference dose level and the actual reference dose level from clinical 3D radiotherapy treatment plans

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ABSTRACT

Purpose: Retrospective study of 3D clinical treatment plans based on radiobiological considerations in the choice of the reference dose level from tumor dose–volume histograms.
Methods and materials: When a radiation oncologist evaluates the 3D dose distribution calculated by a treatment planning system, a decision must be made on the percentage dose level at which the prescribed dose should be delivered. Much effort is dedicated to deliver a dose as uniform as possible to the tumor volume. However due to the presence of critical organs, the result may be a rather inhomogeneous dose distribution throughout the tumor volume. In this study we use a formulation of tumor control probability (TCP) based on the linear quadratic model and on a parameter, the *F* factor. The *F* factor allows one to write TCP, from the heterogeneous dose distribution (TCP$\{(\varepsilon_j,D_j)\}$), as a function of TCP under condition of homogeneous irradiation of tumor volume (V) with dose D (TCP(V,D)). We used the expression of the *F* factor to calculate the "ideal" percentage dose level (iDL_r) to be used as reference level for the prescribed dose D delivery, so as to render TCP$\{(\varepsilon_j,D_j)\}$ equal to TCP(V,D).*Methods and materials:* The 3D dose distributions of 53 clinical treatment plans were re-evaluated to derive the iDL_r and to compare it with the one ($D_{tp}L$) to which the dose was actually administered.
Results: For the majority of prostate treatments, we observed a low overdosing following the choice of a $D_{tp}L$ lower than the iDL_r. While for the breast and head-and-neck treatments, the method showed that in many cases we underdosed choosing a $D_{tp}L$ greater than the iDL_r. The maximum difference between the iDL_r and the $D_{tp}L$ was −3.24% for one of the head-and-neck treatments.
Conclusions: Using the TCP model, the probability of tumor control is compromised following an incorrect choice of $D_{tp}L$; so we conclude that the application of the *F* factor is an effective tool and clinical aid to derive the optimal reference dose level from the dose–volume histogram (DVH) of each treatment plan.
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Traditional methods of evaluating and ranking radiotherapy treatment plans are based on visual inspection of the isodose distributions and on the evaluation of dose–volume histograms (DVHs). Using normal tissue complication probability (NTCP) and tumor control probability (TCP) is another approach to condense the dose distribution data, taking into account radiobiological parameters and to rank treatments plans.

Much effort is dedicated to deliver a dose as uniform as possible to the tumor volume. However due to the presence of some critical organs, the result is a rather inhomogeneous dose distribution throughout the tumor volume. The literature has partially clarified the biological implications of nonuniform dose distributions on the eradication of a tumor [1–4]. For small dose nonuniformity, tumor control is best determined by the mean target dose; for large dose inhomogeneities the tumor response is best related to the minimum target dose, since cold spots cannot be compensated by any dose delivered to the rest of the tumor [5–7]. Additionally in the literature there are studies dealing with dose–response indices derived from radiobiological considerations.

Niemierko et al. [8,9] introduced the concept of equivalent uniform dose (EUD) in an attempt to establish a reliable scalar for reporting nonuniform dose results. The EUD is the dose that when applied uniformly to tumor volume has the same biological effect (i.e. tumor cell kill) as the inhomogeneous tumor DVH from which it is has been derived. The EUD concept uses the surviving fraction of clonogenic tumor cells in the definition of the uniform dose and so it does not provide a definitive indication of radiobiological response, as does the TCP; the clinicians are generally more interested to know the probability that a patient will respond if he receives a certain dose distribution than what the precise cell survival level will be.

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Brahme [10] used the concept of effective total dose. However this factor accounts for dose nonuniformity via the mean and the standard deviation of the dose distribution, whereas the EUD and TCP incorporate the detailed structure of the dose distribution (in the form of dose–volume histograms). This difference may become significant if highly nonuniform dose distributions are delivered where the minimum doses dominate tumor response [11].

Sanchez-Nieto et al. [12] illustrated the potential gain in TCP of prostate cancer patients by individualizing the prescription dose according to both normal-tissue dose–volume and radiosensitivity data. In reality, the lack of reliable normal tissue complication probability (NTCP) models and parameters for most tissues implies that this method is currently very empirical.

Mavroidis et al. [13] introduced the concept of biologically effective uniform dose. It assumed that two dose distributions are equivalent if they cause the same probability for tumor control or normal tissue complication. In addition the concept makes use of the fact that probabilities averaged over both dose distribution and organ radiosensitivity are more important to the clinical outcome than the expected number of surviving clonogenic tumor cells.

Another approach is employed in this study; it uses a formulation of TCP based on the linear quadratic model and on a parameter, the *F* factor. The *F* factor allows one to write the TCP from a heterogeneous dose distribution (TCP$\{(\varepsilon_j,D_j)\}$), as a function of the TCP under condition of homogeneous irradiation of tumor volume (V) with dose D (TCP(V,D)). By means of the expression of *F* factor, we derived the "ideal" percentage dose level at which the prescribed dose must be referred. This dose level prescription is ideal because it renders the TCP from a given inhomogeneous DVH equal to that corresponding to the desired uniform tumor irradiation with the prescribed dose. This method, which has been already applied to 2D treatment planning [14], is used to re-evaluate the 3D dose distributions of 53 treatment plans at three different tumor sites and to compare the ideal percentage dose level with the one to which the dose was actually administered. This allowed us to compare the modeled biological effect of dose distribution of the clinical treatment of each patient to the one corresponding to a homogeneous tumor irradiation using physical dosimetric measures (e.g. mean, minimum, ideal and treatment plan dose levels) in conjunction with radiobiological measures (TCP, NTCP).

Clearly the application of radiobiological modeling to radiotherapy incorporates the available clinical data regarding the dose–volume characteristics of different tissues. Presently there are insufficient clinical data on the dose–response characteristics of human tissues and tumors on which to base reliable estimates of radiobiological parameters. This precludes the use of an exclusive radiobiological evaluation. However it is a valuable complement to clinical experience.

Methods and materials

The F factor

Using the LQ model, the TCP calculated for the entire V volume irradiated uniformly with dose D can be expressed as follows:

$$\mathrm{TCP}(V,D) = \exp\{-K\exp[-(\alpha+\beta d)D]\} \quad (1)$$

where K is the number of clonogenic cells, α and β are tissue specific parameters related to cell radiosensitivity (they are expressed in units Gy^{-1} and Gy^{-2}, respectively), d is dose per fraction.

To generate the TCP representative of a population average, α is assumed to be distributed normally amongst the patient population with mean $\overline{\alpha}$ and standard deviation $\sigma_{\overline{\alpha}}$.

When the dose in the V volume is nonuniform, its distribution must be taken into account. A standard way to condense the dose distribution data in the V volume is to use the differential dose–volume histogram (dDVH), where the dose range is divided into M bin values and for each bin value D_j, the sum volume v_j of all voxels receiving the dose D_j is calculated. Indicating the fraction of volume v_j/V with ε_j, the dDVH is expressed by the set of M couples $\{(\epsilon_j, D_j)\}$ with $j = 1, \ldots, M$ and the TCP can be calculated as [14]:

$$\mathrm{TCP}\{(\epsilon_j, D_j)\} = [\mathrm{TCP}(V,D)]^F \quad (2)$$

The *F* factor summarizes the effect of an inhomogeneous dose distribution on the TCP for the desired uniform dose distribution. As TCP(V,D) values range between 0 and 1, from Eq. (2) it is clear that:

- if *F* is less than 1 the inhomogeneous dose distribution gives a higher tumor control than the uniform one;
- if *F* is greater than 1, the inhomogeneous dose distribution gives a lower tumor control than the uniform one.
- and finally, if *F* is equal to 1, the tumor control of the inhomogeneous dose distribution is exactly equal to the tumor control of the desired uniform distribution;

The *F* factor is expressed as [14]:

$$F = \sum\nolimits_j \epsilon_j \exp\{\alpha D\Delta j + (\beta/N)D^2[\Delta j(2-\Delta j]\}$$

$$\text{and } \Delta j = (DL_\mathrm{r} - DL_j)/DL_\mathrm{r}$$

DL_j is the percentage dose level of the dose distribution normalized to the maximum, corresponding to the dose D_j in the volume fraction ε_j and DL_r, is the percentage dose level chosen as reference level to which the prescribed dose D is administered in N fractions, so $D_j = D(DL_j/DL_\mathrm{r})$.

The percentage dose level which makes *F* equal to 1 is calculated by a gradual increase of the DL_r and later on it is referred to as the ideal dose level (iDL_r).

Patient population, treatment planning and delivery technique

3D treatment plans of 53 patients were available and reviewed for this study; the dose distributions were normalized to the maximum dose. 19/53 were treated for prostate cancer with a five-coplanar fields 3DCRT technique (0°, 45°, 90°, 270°, 315°), 24/53 were irradiated for breast cancer with two tangential fields, finally 10/53 were treated with intensity-modulated radiotherapy for head-and-neck cancer using seven-coplanar fields arrangement [15]. The target volumes were defined in accordance with the 1993 International Commission on Radiation Units and Measurements Report 50 (ICRU Report 50). The gross tumor volumes (GTVs) included all known gross diseases as determined by imaging and clinical findings. GTVs were expanded to yield corresponding clinical target volumes (CTVs) according to clinical assessment in each case. For prostate cancer the CTV was considered to be the prostate plus seminal vesicles; the planning treatment volume (PTV) was obtained by expanding in 3D the CTV by 1.0 cm and 0.7 cm on the prostate–rectum interface to avoid excessive rectal wall involvement. For head-and-neck cancer, the margins were adjusted to 1.0 cm beyond the GTV to obtain the CTV; the CTV was expanded symmetrically by 0.3 cm in all directions to account for patient setup and motion within the thermoplastic mask. Finally for breast cancer the CTV was glandular breast tissue and the PTV was generated by expanding the CTV by 0.7 cm isotropically, except in the direction of the skin surface. All patients were treated with one fraction per day, 5 days a week, with the fraction dose equal to 2 Gy in the ICRU reference point [16]. For prostate and