ORIGINAL PAPER

Assessment of tumor control probability for high-dose-rate interstitial brachytherapy implants

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SUMMARY

AIM: The study was designed to propose a novel concept of biologically effective equivalent uniform dose to calculate tumor control probability for HDR implants.

MATERIALS AND METHODS: The expression of biologically effective equivalent uniform dose was derived for non-uniform dose distribution in HDR implants using quality indices and voxel-based tumor control probability.

RESULTS: The results of this study show that high dose regions of the implant have higher tumor control probability. But these regions may also have a large number of normal cells and consequently may lead to severe normal tissue complications. If tumor coverage was not proper then the overall tumor control probability would be low and might result in tumor recurrence. Higher values of external volume index, dose non-uniformity ratio and overdose volume index were related to higher normal tissue complication rates outside and inside the implants.

CONCLUSION: The present concept may provide an alternative approach to calculate tumor control probability for HDR implants.

KEY WORDS: HDR interstitial implants, quality indices, non-optimization, geometric optimization of volume, biologically effective equivalent uniform dose

BACKGROUND

In order to obtain optimal tumor cell killing with uniform clonogenic cell density and to avoid necrosis of the normal cell present within the target volume, the dose distribution within the target volume should be uniform [1, 2, 3]. However in high-dose-rate (HDR) interstitial implants it is difficult to achieve a uniform dose distribution because of the very high radiation dose in the vicinity of the radiation source. Hence, the tumor control probability (TCP) calculated on the basis of minimum or mean or median target dose would not be appropriate to predict accurate treatment outcome. To solve the problem, an imaginary ideal implant was divided into a large number of voxels to derive the biologically effective equivalent uniform dose (BEEUD) using voxel-based TCP. Then the HDR implant was divided into four different regions, based on the pattern of dose distribution, to define quality indices (QI). The BEEUD and QIs were introduced into the equation of TCP to get an expression for HDR implants.

AIM

The aim of the study was to design the TCP concept for HDR implants, by introducing a hypothetical dose, BEEUD.

MATERIALS AND METHODS

To account for non-uniform dose distribution of the HDR interstitial implant, the target volume is divided into n sub-volumes (voxels), and it is assumed that the dose distribution within each individual voxel is uniform. The TCP is calculated voxel by voxel. The TCPs of these voxels are mutually exclusive; hence the net TCP for the entire target volume can be written as

$$TCP = \Pi \exp[-\rho\, v_i \exp(-\alpha BED_i)] \qquad (1)$$

where Π, ρ, and BED_i are the clonogenic cell density, coefficient of lethal damage (radiosensitivity of lethal damage) for the target cells, and the biologically effective dose of the i^{th} voxel of volume vi of the target volume, respectively. Here i = 1, 2, 3, ...n. Equation (1) may also be written as

$$TCP = \exp[-\rho\Sigma v_i \exp(-\alpha BED_i)] \quad (2)$$

The BEEUD is a hypothetical biological dose that produces an equivalent biological effect to that of an absolutely uniform dose delivered to the entire target volume V. For such type of dose the TCP may be given by

$$TCP = \exp[-\rho V \exp(-\alpha BEEUD)] \quad (3)$$

From equations (2) and (3), it may be written as

$$BEEUD = -(1/\alpha) \ln[(1/V)\Sigma v_i \exp(-\alpha BED_i)]$$

or

$$BEEUD = \ln[(1/V)\Sigma v_i \exp(-\alpha BED_i)]^{-(1/\alpha)} \quad (4)$$

where i = 1, 2, 3, ...n. To calculate TCP for a non-uniform dose distribution within the tumor, the use of BEEUD would be an appropriate term instead of BED.

Region based TCP of tumor volume for an HDR implant

The different regions of the HDR implant are shown in Fig. 1, where the target volume is divided into four regions: (1) the region which receives a dose less than the reference dose, (2) the region which receives a dose in the range of 1.0 to 1.5 times the reference dose, (3) the region which receives a dose in the range of 1.5 to 2.0 times the reference dose, and (4) the region which receives a dose equal to or more than 2.0 times the reference dose.

With the use of BEEUD of each tumor region (Fig. 1) the expressions of TCP for each region is given as follows:

1. The TCP for the region of target volume which receives a dose less than the reference dose

$$TCP_1 = \exp[-\rho(TV-TV_{Dref})\exp(-\alpha BEEUD_1)]$$

or

$$TCP_1 = \exp[-\rho TV_{Dref}\{(1-CI)/CI\}\exp(-\alpha BEEUD_1)] \quad (5)$$

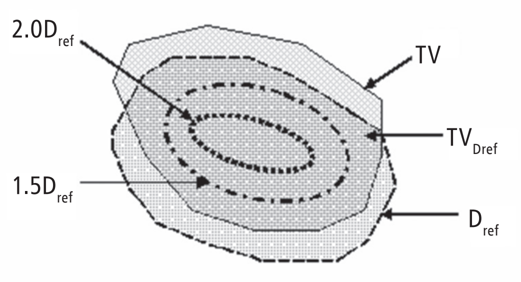

Fig. 1. Schematic diagram showing target volume (TV), portion of target volume (TVD_{ref}) that receives dose equal to or more than the reference dose D_{ref}, the isodose surface that receives 1.5 times the reference dose (1.5 D_{ref}), and that receives 2.0 times the reference dose (2.0 D_{ref}).

where CI is the coverage index [4] and is defined by TV_{Dref}/TV.

2. The TCP for the region of target volume that receives a dose in the range of 1.0 to 1.5 times the reference dose

$$TCP_2 = \exp[-\rho(TV_{Dref}-TV_{1.5Dref})\exp(-\alpha BEEUD_2)]$$

or

$$TCP_2 = \exp[-\rho TV_{Dref}.DHI \exp(-\alpha BEEUD_2)] \quad (6)$$

where DHI is the relative dose homogeneity index [4] and is defined by $(TV_{Dref}-TV_{1.5Dref})/TV_{Dref}$.

3. The TCP for the region of target volume that receives a dose in the range of 1.5 to 2.0 times the reference dose

$$TCP_3 = \exp[-\rho(TV_{1.5Dref}-TV_{2Dref})\exp(-\alpha BEEUD_3)]$$

or

$$TCP_3 = \exp[-\rho TV_{Dref}(DNR-ODI)\exp(-\alpha BEEUD_3)] \quad (7)$$

where DNR and ODI are the dose non-uniformity ratio [5] and overdose volume index [4], and are defined by $DNR = TV_{1.5Dref}/TV_{Dref}$ and $ODI = TV_{2.0Dref}/TV_{Dref}$, respectively.

4. The TCP for the region of target volume that receives a dose equal to or greater than 2 times the reference dose

$$TCP4 = \exp[-\rho TV_{2Dref} \exp(-\alpha BEEUD_4)]$$

or