Original Article

A quality index for equivalent uniform dose

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ABSTRACT

Equivalent uniform dose (*EUD*) is the absorbed dose that, when homogeneously given to a tumor, yields the same mean surviving clonogen number as the given non-homogeneous irradiation. *EUD* is used as an evaluation tool under the assumption that two plans with the same value of *EUD* are equivalent, and their biological effect on the tumor (clonogen survival) would be the same as the one of a homogeneous irradiation of absorbed dose *EUD.* In this work, this assumption has been studied, and a figure of merit of its applicability has been obtained. Distributions of surviving clonogen number for homogeneous and non-homogeneous irradiations are found to be different even if their mean values are the same, the figure of merit being greater when there is a wider difference, and the equivalence assumption being less valid. Therefore, *EUD* can be closer to a uniform dose for some cases than for other ones (high α values, extreme heterogeneity), and the accuracy of the radiobiological indices obtained for evaluation, could be affected. Results show that the equivalence is very sensitive to the choice of radiobiological parameters, and this conclusion has been derived from mathematical properties of *EUD*.

Key words: Equivalent uniform dose, mixed Poisson distribution, radiobiology

Introduction

Equivalent Uniform Dose (*EUD*) is defined as the absorbed dose that, if homogeneously delivered to a tumor, causes the same expected number of clonogens to survive as the actual non-homogeneous absorbed dose distribution does.[1-3] Clonogen survival is a stochastic magnitude governed by Poisson statistics, and *EUD* is obtained as an expectation value.

EUD is a simplified parameter designed to make comparisons among alternative treatment plans easy, when irradiations are non-homogeneous. The underlying assumption is that homogeneous irradiation of a tumor with absorbed dose *D*, and any non-homogeneous irradiations with *EUD* equal to *D* are equivalent in a biological sense. The biological effect is considered equal as long as the mean surviving fraction of clonogens is the same.[4]

One of the advantages pointed out in the article by Niemierko,[1] who first defined the *EUD* concept, was its robustness, i.e. its slow variation with radiobiological parameters. McGary *et al.*,[4] studied this issue further and reported non-negligible dependence of *EUD* with linear-quadratic model parameters when large-dose inhomogeneities are present.

The phenomenological *EUD* concept was introduced by Niemierko in 1999[5] in order to provide a simple formula applicable to both, tumors and normal tissue. Its basis is the power law behavior of tissue response with dose, and it has one parameter to be fitted depending on the tissue and the irradiation characteristics.

$$EUD = \left(\sum_i v_i \cdot D_i^{\,a} \right)^{\frac{1}{a}}$$

(where v_i is the partial volume with absorbed dose D_i). This formula has found widespread applications mainly due to its algebraic simplicity, despite the fact that it is not derived from cell survival models. It has sometimes been referred to as "generalized *EUD* (*gEUD*)". A brief discussion on these features was brought about by Amols and Ling[6] on the article on biological optimization by Wu *et al.*[7]

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As *gEUD* is a phenomenological concept and is not based on cell survival models, its claim of representing the absorbed dose that, if homogeneously given, would lead to the same clonogen survival (or the same response, in normal tissue) as the actual irradiation (equivalence assumption) is not as well supported as for the original mechanistic *EUD* concept.[6,7] The free parameter *a* is fitted according to published clinical data[8-14] being positive for normal tissue and negative for tumors. The benefits obtained from its simple algebraic formula and its flexibility cannot be overemphasized: its use in optimization algorithms, *TCP* and *NTCP* computation routines and the modeling of normal tissue response is now widespread.[7,15-18]

The purpose of this work is to study the equivalence assumption. A quality index describing the excess of standard deviation in surviving clonogen distribution with dose heterogeneity will be derived and its properties studied.

Materials and Methods

In the present work, the equivalence assumption on tumor *EUD* is studied from a mathematical point of view, and an index of merit for equivalence is proposed. The lower the value of the index, the greater the reliability of the equivalence assumption, as the dose inhomogeneity will not increase greatly the surviving clonogen number variance. The theory in this study is based on the different probability distribution of the number of surviving clonogens for homogeneous and non-homogeneous absorbed dose distributions, even if mean values are equal. Extensive use of mixed Poisson distributions is made to account for the effect of dose heterogeneity, instead of the voxel-oriented formula used in the original *EUD* formulation. This original approach will provide tools to obtain the variance of the distribution.

Theoretical background

A tumor is modeled as a set of *N* clonogens, with identical properties and independent evolution. If the tumor is irradiated with a uniform dose *D*, the probability distribution of surviving clonogens is a Poisson one, and its parameter, according to the linear-quadratic model, is:

$$\lambda = N \cdot e^{-\alpha D - \beta D^2} \qquad \text{.....(1)}$$

with α and β parameters. For conventional fractionated external irradiations, the linear term in the exponent is greater than the other one[19] and:

$$\lambda = N \cdot e^{-\alpha D} \qquad \text{.....(2)}$$

This is an assumption already made by Niemierko when *EUD* was first defined[1] and it is applicable to a wide range of tumors. Modern techniques like biologically guided radiation therapy would require the full model[20] but the *EUD* concept would be of little use in that case. McGary *et al.*,[4] presented a formulation of *EUD* with both parameters present.

The fact is that absorbed doses are not uniform throughout the tumor even though they are intended to be homogeneous. A common approach to compute radiobiological indices is to divide the tumor volume into voxels small enough to have constant dose, and then assume that they behave as independent pieces of tumor put together.[1,21,22]

A different approach is possible without building up artificial structures inside the tumor, if a mixture model is substituted for the Poisson probability model used so far.

Mixture models are often introduced on empirical problems; a variable is described by a probability distribution, but one of its parameters is allowed to be a random variable itself.[23] The distribution of the parameter is said to be "mixing" the model.

When uniform absorbed dose is not possible, survival fractions will vary across the tumor volume, and their values can be described according to a probability distribution determined by the absorbed dose distribution.

A discrete mixture distribution is defined in terms of its probability function with the following equation:[23]

$$p(x) = \int_{\Theta} p(x \mid \lambda) \cdot g_{\lambda}(\lambda) \cdot d\lambda \qquad \text{.....(3)}$$

$p(x|\lambda)$ is the conditional probability function, for a particular value of λ in Θ; $g_{\lambda}(\lambda)$ is the mixing density function. $p(x|\lambda)$ is a probability function with a free parameter, and $g_{\lambda}(\lambda)$ is the density function describing the distribution of this parameter as a random variable.

In the radiobiological case, the conditional probability function $p(x|\lambda)$ is the Poisson survival model for a particular value of λ. $g_{\lambda}(\lambda)$ is the mixing density function: it is the density function of λ because of its dependence on the absorbed dose, which in turn is distributed according to the differential dose volume histogram (DVH_d, relative volume). As a matter of fact, the density distribution of λ depends on the dose volume histogram, and its expression is simpler when written as a function of *D*:

$$\begin{aligned} &p(x \mid D) = \frac{\left(N \cdot e^{-\alpha D}\right)^x \cdot e^{-N \cdot e^{-\alpha D}}}{x!} \\ &g_D(D) = DVH_d(D) \\ &\Theta = [0, \infty) \end{aligned} \qquad \text{.....(4)}$$

The probability function for the number of clonogens is:

$$p(x) = \int_0^{\infty} \frac{\left(N \cdot e^{-\alpha D}\right)^x \cdot e^{-N \cdot e^{-\alpha D}}}{x!} \cdot DVH_d(D) \cdot dD \qquad \text{.....(5)}$$

A simple property of mixture models can be used to find expectation values[23] (the symbol $E_{x|\lambda}$ means conditional expectation value):

$$E[X]=\int_{\Theta} E_{x|\lambda}[X]\cdot g_{\lambda}(\lambda)\cdot d\lambda = E\left[E_{x|\lambda}(X)\right] \quad .....(6)$$

but $p(x|\lambda)$ is a Poisson distribution, with parameter $\lambda = N.e^{-\alpha D}$; therefore its mean is:

$$E_{x|\lambda}(X)= N\cdot e^{-\alpha D} \quad .....(7)$$

Thus, the mean number of surviving clonogens is:

$$E[X]=\int_{0}^{\infty} N\cdot e^{-\alpha D}\cdot DVH_d(D)\cdot dD \quad .....(8)$$

On the other hand, there is a similar formula for variance in mixture models:[23]

$$V[X]=V\left[E_{x|\lambda}(X)\right]+E\left[V_{x|\lambda}(X)\right] \quad .....(9)$$

The conditional distribution is a Poisson one, thus (from Eq.7):

$$V_{x|\lambda}(X)=E_{x|\lambda}(X)=N\cdot e^{-\alpha D}$$

$$E\left[V_{x|\lambda}(X)\right]=E\left[E_{x|\lambda}(X)\right]=\int_{0}^{\infty} N\cdot e^{-\alpha D}\cdot DVH_d(D)\cdot dD$$

$$V\left[E_{x|\lambda}(X)\right]=E\left[E_{x|\lambda}(X)^2\right]-\left\{E\left[E_{x|\lambda}(X)\right]\right\}^2 =$$

$$=\int_{0}^{\infty} N^2\cdot e^{-2\alpha D}\cdot DVH_d(D)\cdot dD-\left\{\int_{0}^{\infty} N\cdot e^{-\alpha D}\cdot DVH_d(D)\cdot dD\right\}^2$$

Therefore, the variance of the number of clonogens is:

$$V[X]=\int_{0}^{\infty} N\cdot e^{-\alpha D}\cdot DVH_d(D)\cdot dD+\int_{0}^{\infty} N^2\cdot e^{-2\alpha D}\cdot DVH_d(D)\cdot dD-\left\{\int_{0}^{\infty} N\cdot e^{-\alpha D}\cdot DVH_d(D)\cdot dD\right\}^2$$

.....(10)

Equivalent uniform dose

If an irradiation is perfectly homogeneous, $g_D(D)$ would be a Dirac delta, and its integration would simply turn every D symbol into the homogeneous absorbed dose value D_h. Applying this mixing density to equation (8):

$$E[X]=\int_{0}^{\infty} N\cdot e^{-\alpha D}\cdot DVH_d(D)\cdot dD = N\cdot e^{-\alpha D_h} = X_{D_h} \quad .....(11)$$

The problem of computing *EUD* consists in finding the homogeneous dose D_h corresponding to a given mean clonogen number (the mean number derived from a non-homogeneous irradiation).

$$D_h = -\frac{1}{\alpha}\cdot\ln\left(\frac{X}{N}\right) \quad .....(12)$$

Therefore, if X is the mean survival number of clonogens, then:

$$EUD = -\frac{1}{\alpha}\cdot\ln\left(\int_{0}^{\infty} e^{-\alpha D}\cdot DVH_d(D)\cdot dD\right) \quad .....(13)$$

This is the same equation found by Niemierko,[1] although the derivation and change of notation will be shown in the Appendix.

If the same procedure is applied to equation (10):

$$V[X]=\int_{0}^{\infty} N\cdot e^{-\alpha D}\cdot DVH_d(D)\cdot dD+\int_{0}^{\infty} N^2\cdot e^{-2\alpha D}\cdot DVH_d(D)\cdot dD-\left\{\int_{0}^{\infty} N\cdot e^{-\alpha D}\cdot DVH_d(D)\cdot dD\right\}^2 =$$

$$= N\cdot e^{-\alpha D_h}+N^2\cdot e^{-2\alpha D_h}-\left\{N\cdot e^{-\alpha D_h}\right\}^2 = N\cdot e^{-\alpha D_h} = E[X]$$

.....(14)

Therefore, the Poisson property is obtained (mean and variance are equal). When the dose is homogeneous, the mixture model becomes a standard Poisson model.

Equations (8), (10) and (13) are computed in practice as summations:

$$E[X]=\sum_i N\cdot e^{-\alpha D_i}\cdot DVH_d(D_i)\cdot\Delta D \quad .....(15)$$

$$V[X]=\sum_i N\cdot e^{-\alpha D_i}\cdot DVH_d(D_i)\cdot\Delta D+\sum_i N^2\cdot e^{-2\alpha D_i}\cdot DVH_d(D_i)\cdot\Delta D-\left\{\sum_i N\cdot e^{-\alpha D_i}\cdot DVH_d(D_i)\cdot\Delta D\right\}^2$$

.....(16)

$$EUD = -\frac{1}{\alpha}\cdot\ln\left(\sum_i e^{-\alpha D_i}\cdot DVH_d(D_i)\cdot\Delta D\right) \quad .....(17)$$

Generalized equivalent uniform dose

As the phenomenological formulation of *EUD* for tumors is to be fitted to clinical outcome data, equality of means is not a hypothesis to be derived from the linear quadratic model. *EUD* would equal the mean dose because of goodness of fit and from a practical point of view, this fit could provide evidence about α values. Therefore:

$$gEUD=\left[\sum D^{a^*}\cdot v_i\right]^{\frac{1}{a^*}} \cong -\frac{1}{\alpha^*}\cdot\ln\left(\int_{0}^{\infty} e^{-\alpha^* D}\cdot DVH_d(D)\cdot dD\right) = EUD^* \quad .....(18)$$

As long as the generalized *EUD* for a tumor is a uniform dose causing the same biological effect as a heterogeneous irradiation, it will fit a mechanistic EUD^* model, and the variance problem can be treated with the same tools for both formulations of the index.

Quality index for EUD equivalence

If an additional random variable is defined, Y, as the number of surviving clonogens after a uniform irradiation with dose $D_Y = EUD$, its mean will be

$$E[Y]=E[X]=N\cdot e^{-\alpha\cdot EUD}$$

and its variance will be:

$$V[Y]=E[Y]=N\cdot e^{-\alpha\cdot EUD}$$

$$\sigma[Y]=N^{\frac{1}{2}}\cdot e^{-\frac{\alpha\cdot EUD}{2}} \quad .....(19)$$

If a non-homogeneous distribution is considered equivalent to a uniform distribution with absorbed dose $D_Y = EUD$, it is implicitly assumed that the resulting surviving

probability distribution is that of a uniform distribution of dose $D_Y = EUD$, i.e., that the surviving clonogens' distribution is Y, not X.

In fact, *EUD* is derived because absorbed dose is inhomogeneous, and its variance is the one computed before (equations 10 and 16). Its square root is the actual standard deviation:

$$\sigma[X]=\left\{\int_0^\infty N\cdot e^{-\alpha D}\cdot DVH_d(D)\cdot dD+\int_0^\infty N^2\cdot e^{-2\alpha D}\cdot DVH_d(D)\cdot dD-\left\{\int_0^\infty N\cdot e^{-\alpha D}\cdot DVH_d(D)\cdot dD\right\}^2\right\}^{\frac{1}{2}} \quad .....(20)$$

This variance is different from the one that a truly uniform distribution would show. Therefore, dose heterogeneity has an effect on clonogen survival that is absent in uniform irradiations. This fact makes equivalence between a uniform irradiation and a heterogeneous one, approximate but never exact.

A useful quality index of *EUD* should measure how much standard deviation is increased due to the fact that it is not a uniform dose, but an actual heterogeneous distribution. It should measure how different the true standard deviations of X and Y are.

$$qEUD(\%)=\frac{\sigma[X]}{\sigma[Y]} \quad .....(21)$$

The greater this index is, the more inconsistent is the variance value with a uniform distribution and, therefore, the less informative *EUD* could be.

Practical application on clinical treatment plans

A set of dose-volume histograms was prepared. Their shape is Gaussian, their mean is 2 Gy and their standard deviations range from 0.02 Gy to 0.20 Gy [Figure 1]. *EUD* and *qEUD* were computed in every case using equations 12 and 20, implemented in a spreadsheet application. No special software was needed apart from mathematical and logical commands already implemented in the spreadsheet application. Two more *DVHs* were obtained by adding a cold spot to the *DVHs* with standard deviations 0.02 Gy and 0.10 Gy: the minimum dose inside the cold spot was reduced in 0.005 Gy. To explain the effect of dose inhomogeneity, examples of treatment plans of 1) head and neck (H and N) treatment, 2) bladder treatment and 3) prostate treatments by linear accelerator have been used as well. The central slice dose distribution for the head and neck treatment is shown in Figure 2 and a conventional and an IMRT prostate plan are shown in Figure 3. Their dose volume histograms are outlined in Figures 4 (head and neck), 5 (bladder) and 6 (prostate). Figure 4 shows that the head and neck treatment plan is more heterogeneous with minimum dose 88% and maximum dose 110%. Figures 5 and 6 show better dose homogeneity values (minimum 97% and maximum 102% for bladder, minimum 98% and maxima 104% and 107% for prostate).

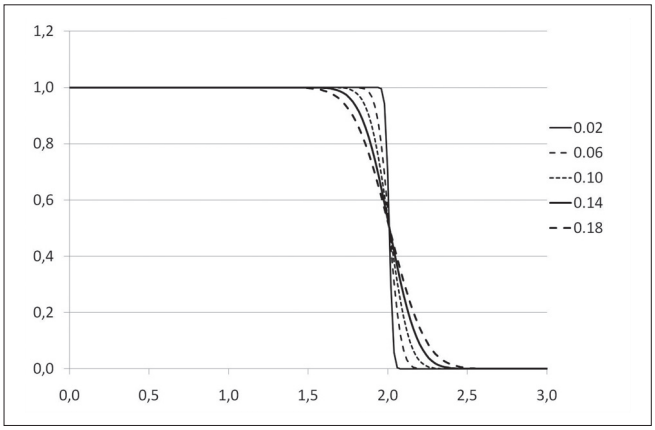

Figure 1: Dose volume histograms for Gaussian dose distributions with standard deviations 0.02, 0.06, 0.10, 0.14, 0.18

Results

Results for the quality index *q* are shown in Table 1. The effect of several values of the parameter α and a set of standard deviations for the dose distribution on *q* is seen. It is apparent that the wider the dose distribution, the greater the quality index value is: the more different from a

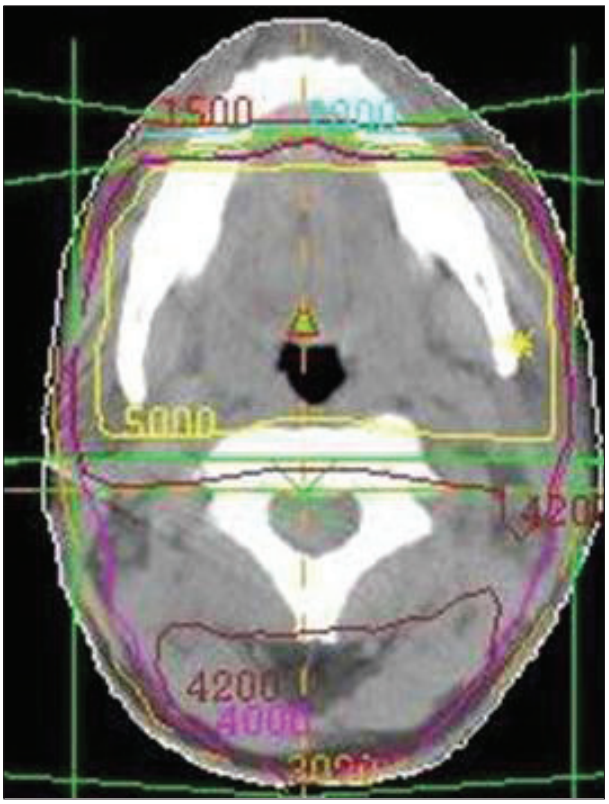

Figure 2: Central slice isodose map for a head and neck treatment used as practical application. Major causes of heterogeneity are the proximity of the skin and organs at risk

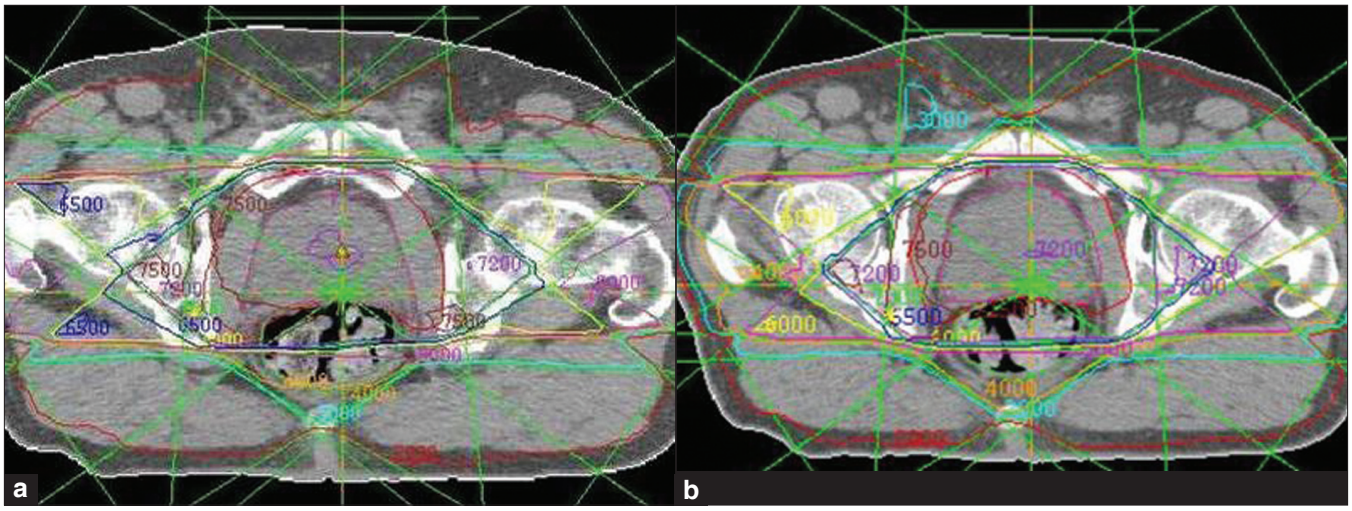

Figure 3: Central isodose map for a prostate treatment practical example: (a) conventional treatment; (b) intensity-modulated treatment

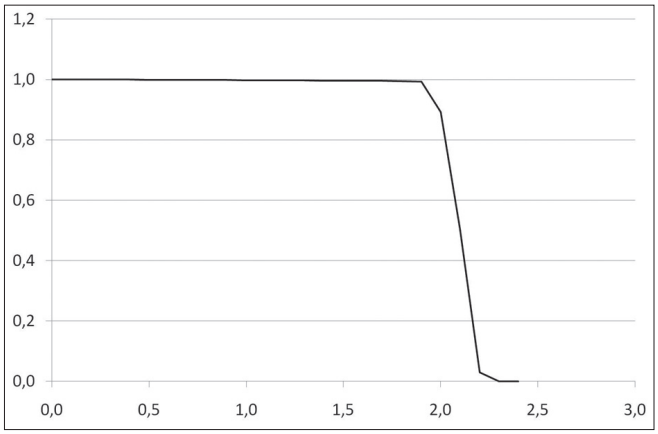

Figure 4: Dose volume histogram for a bladder treatment

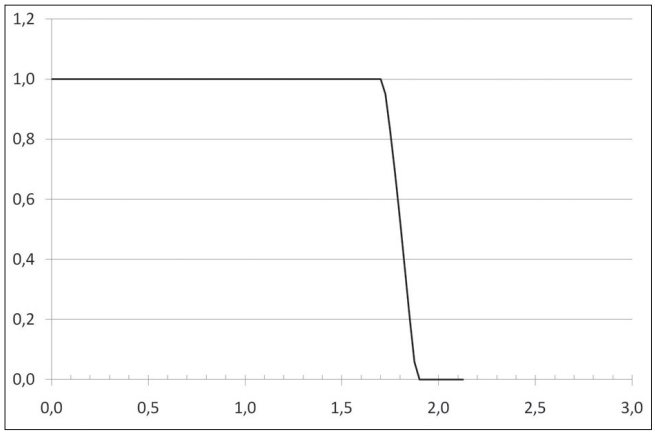

Figure 5: Dose volume histogram for a head and neck treatment

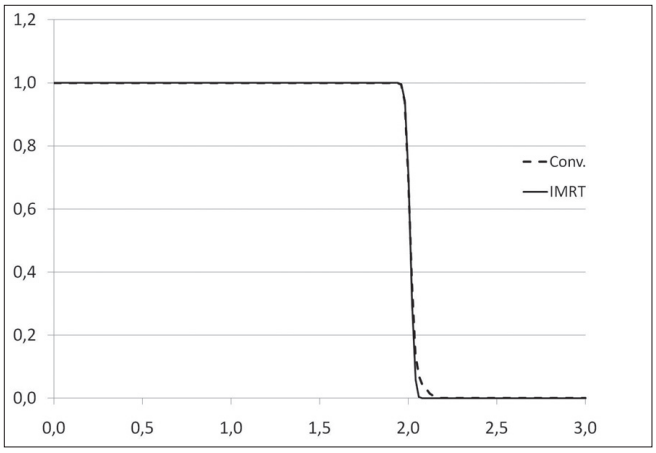

Figure 6: Dose volume histograms for prostate treatment plans

homogeneous dose, the less representative a *EUD* value is. When a cold spot is present, values grow with regards to the previous ones for any value of α.

Finally, the bladder treatment resulted in values *qEUD=0.98-1.00* for *α=0.3 to α=0.4* due to the homogeneity of the dose. Both prostate plans resulted in values close to 1 (0.99-1.00) for the same range of α values; the head and neck treatment scored *qEUD=3.26*. These clinical results confirm the dependency on dose heterogeneity shown in Table 1.

The effect of the radiobiological parameter α is remarkable; taking into account that radiobiological parameters show large uncertainties, a critical outlook should be taken when large values of α are to be used. It is clearly seen that equivalence of radiobiological effects suffers when heterogeneity causes such increase in dispersion though *EUD* in each case is the same.

Discussion

The present work develops a method to estimate the survival distribution of a non-homogeneous distribution described by Niemierko's *EUD* concept. A mixture Poisson model was found to be applicable, and variance could be separated into a contribution from the variability of the

Table 1: Quality index for *EUD* for several values of dose dispersion (Gaussian distribution with mean dose 2 Gy), and α

Standard deviation (Gy)	*α = 0.15*	*α = 0.20*	*α = 0.25*	*α = 0.30*	*α = 0.35*	*α = 0.40*	*α = 0.45*
0.02	1.29	1.44	1.59	1.72	1.85	1.97	2.07
0.04	1.91	2.30	2.66	2.98	3.28	3.54	3.77
0.06	2.65	3.26	3.83	4.33	4.79	5.19	5.54
0.08	3.42	4.26	5.03	5.71	6.32	6.86	7.33
0.10	4.20	5.27	6.24	7.10	7.87	8.54	9.14
0.12	5.00	6.30	7.46	8.50	9.42	10.24	10.95
0.14	5.80	7.32	8.68	9.90	10.98	11.93	12.77
0.16	6.61	8.35	9.91	11.30	12.54	13.63	14.59
0.18	7.42	9.38	11.14	12.71	14.10	15.33	16.42
0.20	8.23	10.41	12.37	14.12	15.67	17.04	18.25
0.02+cold spot	1.77	2.10	2.41	2.70	2.96	3.19	3.39
0.10+cold spot	4.68	5.89	6.98	7.96	8.82	9.59	10.26

random process of cell killing and a second component due to the variability of absorbed dose, and therefore survival probability, across the tumor.

Two dose distributions are radiobiologically equivalent if the clonogen survival they lead to are equal. Because of the variance introduced by the variation in absorbed dose, uniform distributions are not equivalent to non-uniform ones, and a quality index *q(%)* was introduced in order to measure the magnitude of this effect. It was found to be dependent on the radiobiological parameter α, causing the radiobiological equivalence for dose distributions with the same *EUD* to be critical for large α. The study by McGary *et al.*,[4] arrived at the conclusion that when large inhomogeneities were present, *EUD* was not independent of linear-quadratic model parameters, as initially assumed by Niemierko.[1] In this work, it becomes clear that there is a further reason, based on clonogen population, as to how and why the equivalence hypothesis can be deteriorated when tumor dose is less uniform, and this conclusion has been reached through theoretical considerations. When evaluating the results from this study, it can be concluded that tumor control probability (TCP) is more reliable as an evaluation parameter for the bladder and prostate treatments (conventional or intensity-modulated) than for the head and neck plan studied here. It is also remarkable that equivalence does not seem to be reliable for extremely non-uniform distributions and, in that case, the effects cannot be expected from the assumption of a hypothetical uniform dose that corresponds to *EUD*.

It is worth mentioning that TCP are often computed on the assumption that *EUD* does represent an equivalent dose for tumors:[24] when applying the equation,

$$TCP = \frac{1}{1+\left(\frac{TCP_{50}}{EUD}\right)^{4\gamma_{50}}} \qquad \text{.....(22)}$$

the equivalence assumption is being made. The increase in variance can be thought of as the adding of uncertainty to *EUD*, what eventually can lead to unreliable results. Computation of a quality index for *EUD* can provide a warning for cases when values of *EUD* lack accuracy, or when a computer optimization tool chooses inadequate parameters.

Incidentally, the theory of mixed Poisson models has made possible a rigorous derivation of the original Niemierko's *EUD* formula for heterogeneous irradiations with no artificial setting-up of an array of voxels inside the tumor. This derivation is shown in the appendix, and has been the starting point of the theoretical derivations in this work.

Appendix

Derivation of Niemierko's *EUD* formula for non-homogeneous irradiations:

Equation 2 shows the mean value of the clonogen number for a non-homogeneous irradiation. On the other hand, it has been proved that for a homogeneous irradiation with Dose D_h the following equation is true,

$$D_h = -\frac{1}{\alpha}\cdot\ln\left(\frac{X}{N}\right) \qquad \text{.....(12)}$$

EUD has to be obtained applying the condition that it results in the same mean clonogen number, if homogeneously applied, as the non-homogeneous irradiation,

$$E[X] = \int_0^\infty N\cdot e^{-\alpha D}\cdot DVH_d(D)\cdot dD \qquad \text{.....(8)}$$

Therefore, *E[X]* has to be substituted for *X* in the formula for D_h to obtain *EUD*:

$$EUD = -\frac{1}{\alpha}\cdot\ln\left(\frac{E[X]}{N}\right) = -\frac{1}{\alpha}\cdot\ln\left(\int_0^\infty e^{-\alpha D}\cdot DVH_d(D)\cdot dD\right) \qquad \text{.....(23)}$$

This is the general equation to obtain *EUD* from an arbitrary dose distribution. In Niemierko's original article[1] a different notation is used, based on the survival fraction associated to a dose of 2 Gy according to the survival curve and the following notation:

$$SF(D) = e^{-\frac{D}{D_0}} \qquad \text{.....(24)}$$

For the reference dose D_r:

$$SF(D_r) = e^{-\frac{D_r}{D_0}} \Rightarrow D_0 = -\frac{D_r}{\ln(SF_r)}$$

This means that the radiobiological parameter α is equivalent, in Niemierko's notation, to $\frac{1}{D_0} = -\frac{\ln(SF_r)}{D_r}$. Substituting in the equation for *EUD*:

$$EUD = \frac{D_r}{\ln(SF_r)} \cdot \ln\left(\int_0^\infty \exp\left(\ln(SF_r)\cdot\frac{D}{D_r}\right)\cdot DVH_d(D)\cdot dD\right) = \frac{D_r}{\ln(SF_r)} \cdot \ln\left(\int_0^\infty SF_r^{\frac{D}{D_r}} \cdot DVH_d(D)\cdot dD\right) \qquad \text{.....(25)}$$

This is the final formula for EUD; its relationship with the equation in Niemierko's paper[1] can only be shown if dose is supposed to be a discrete random variable $D \in \{D_i\}_{i=1..N}$. Integrals become summations when the variable is a discrete one, and, calling the differential *DVH* "partial volume" v_i, Niemierko's formula is obtained:

$$EUD = D_r \cdot \frac{\ln\left(\sum_{i=1}^{N} SF_r^{\frac{D_i}{D_r}} \cdot v_i\right)}{\ln(SF_r)} \qquad \text{.....(26)}$$

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References

1. Niemierko A. Reporting and analyzing dose distributions: A concept of equivalent uniform dose. Med Phys 1997;24:103-10.
2. McGary JE, Grant W 3rd, Woo SY, Butler EB. Comment on 'Reporting and analyzing dose distributions: A concept of equivalent uniform dose'. Med Phys 1997;24:1323-4.
3. Niemierko A. Response on "Comment on 'Reporting and analyzing dose distributions: A Concept of equivalent uniform dose'". Med Phys 1997;24:1325-7.
4. McGary JE, Grant W 3rd, Woo SY. Applying the equivalent uniform dose formulation based on the linear-quadratic model to inhomogeneous tumor dose distributions: Caution for analyzing and reporting. J Appl Clin Med Phys 2000;1:126-37.
5. Niemierko A. A generalized concept of equivalent uniform dose (*EUD*). Med Phys 1999;26:1100.
6. Amols HI, Ling CC. *EUD* but not QED. Int J Radiat Oncol Biol Phys 2002;52:1-2.
7. Wu Q, Mohan R, Niemierko A, Schmidt-Ullrich R. Optimization of intensity-modulated radiotherapy plans based on the equivalent uniform dose. Int J Radiat Oncol Biol Phys 2002;52:224-35.
8. Emami B, Lyman J, Brown A, Coia L, Goitein M, Munzenrider JE, *et al*. Tolerance of normal tissue to therapeutic irradiation. Int J Radiat Oncol Biol Phys 1991;21:109-22.
9. Bentzen SM, Constine LS, Deasy JO, Eisbruch A, Jackson A, Marks LB, *et al*. Quantitative analyses of normal tissue effects in the clinic (QUANTEC): An introduction to the scientific issues. Int J Radiat Oncol Biol Phys 2010;76:S3-9.
10. Kwa SL, Lebesque JV, Theuws JC, Marks LB, Munley MT, Bentel G, *et al*. Radiation pneumonitis as a function of mean lung dose: An analysis of pooled data of 540 patients. Int J Radiat Oncol Biol Phys 1998;42:1-9.
11. Eisbruch A, Ten Haken RK, Kim HM, Marsh LH, Ship JA. Dose, volume, and function relationships in parotid salivary glands following conformal and intensity-modulated irradiation of head and neck cancer. Int J Radiat Oncol Biol Phys 1999;45:577-87.
12. Chao KS, Deasy JO, Markman J, Haynie J, Perez CA, Purdy JA, *et al*. A prospective study of salivary function sparing in patients with head-and-neck cancers receiving intensity-modulated or three-dimensional radiation therapy: Initial results. Int J Radiat Oncol Biol Phys 2001;49:907-16.
13. Powers BE, Thames HD, Gillette SM, Smith C, Beck ER, Gillette EL. Volume effects in the irradiated canine spinal cord: Do they exist when the probability of injury is low? Radiother Oncol 1998;46:297-306.
14. Brenner DJ. Dose, volume, and tumor-control predictions in radiotherapy. Int J Radiat Oncol Biol Phys 1993;26:171-9.
15. Warkentin B, Stavrev P, Stavreva N, Field C, Fallone BG. A TCP-NTCP estimation module using DVHs and known radiobiological models and parameter sets. J Appl Clin Med Phys 2004;5:50-63.
16. Thieke C, Bortfeld T, Niemierko A, Nill S. From physical dose constraints to equivalent uniform dose constraints in inverse radiotherapy planning. Med Phys 2003;30:2332-9.
17. Park CS, Kim Y, Lee N, Bucci KM, Quivey JM, Verhey LJ, *et al*. Method to account for dose fractionation in analysis of IMRT plans: Modified equivalent uniform dose. Int J Radiat Oncol Biol Phys 2005;62:925-32.
18. Kuperman VY. General properties of different models used to predict normal tissue complications due to radiation. Med Phys 2008;35:4831-6.
19. Deacon J, Peckham MJ, Steel GG. The radioresponsiveness of human tumours and the initial slope of the cell survival curve. Radiother Oncol 1984;2:317-23.
20. South CP, Evans PM, Partridge M. Dose prescription complexity versus tumor control probability in biologically conformal radiotherapy. Med Phys 2009;36:4379-88.
21. Webb S, Nahum AE. A model for calculating tumour control probability in radiotherapy including the effects of inhomogeneous distributions of dose and clonogenic cell density. Phys Med Biol 1993;38:653-66.
22. Källman P, Agren A, Brahme A. Tumour and normal tissue responses to fractionated non-uniform dose delivery. Int J Radiat Biol 1992;62:249-62.
23. Karlis D, Xekalaki E. Mixed poisson distributions. Int Stat Rev 2005;73:35-58.
24. Niemierko A. A unified model of tissue response to radiation. In: Proceedings of the 41th AAPM annual meeting; 1999. Nashville, Tennessee: Med Phys 1999. p. 1100.

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