CONCEPT OF DOSE NONUNIFORMITY IN INTERSTITIAL BRACHYTHERAPY

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Purpose: Evaluation of the 3-dimensional dose distributions of interstitial implants using the dose nonuniformity ratio.

Methods and Materials: Single source, two sources, three and four sources arranged both linearly and in the form of a triangle or a square, ribbons with different seed spacings, a single-plane and double-plane implants were evaluated. The evaluations involved the use of differential dose volume histograms and the dose nonuniformity ratio defined as the ratio of the high dose volume to the reference volume.

Results: For a single source, the dose nonuniformity is the same regardless which dose rate is selected as the treatment dose rate. For any multi-source implant, the dose nonuniformity is altered depending on the selection of the reference dose rate. In addition, the dose nonuniformity curve exhibited three characteristics zones.

Conclusion: The dose nonuniformity ratio can be a useful tool in assessing and optimizing interstitial implants.

Brachytherapy, Interstitial implants, Radiation dosimetry, Radiation therapy.

INTRODUCTION

A review of the literature indicates that the philosophical and clinical approach of performing interstitial brachytherapy among the various dosimetry systems seems to be different and sometimes contradictory (3–5, 8, 13). The spacing between the line sources is allowed to vary in the Paris system whereas the spacing remains constant at 1.0 cm in the Manchester system of interstitial implants (3, 8, 13). Sources with uniform linear density are used in the Paris system and Quimby system of interstitial implants while sources with different linear density are used in the Manchester system (3–4, 8, 13). The dose homogeneity is evaluated based on the dose distributions at the stated plane which is parallel and spaced 0.5 cm away from the implant plane in the Manchester system (8). On the other hand, in the Paris system, the dose homogeneity is evaluated based on the basal dose rates which are the minimum dose rates between the sources in the central plane, that is perpendicular and bisecting the line sources (13, 19). Today, clinical implants performed are usually customized for the patient’s target volume and their isodose distributions are promptly generated for review and prescription. Even with the computer-generated isodose distributions, there are differences in the implant techniques among the practicing institutions. The differences include the plane spacing, number of planes, ribbon spacing and source strength used. These parameters influence the dose distributions within as well as outside the target volume, and thus impact on the treatment outcome. Hence the practice of interstitial brachytherapy is rather complex. Even a seemingly simple procedure such as selecting the appropriate ribbon spacing and dose rate for the intended prescription to yield a satisfactory homogeneous dose distribution can be difficult. Since an interstitial implant is a collection of sources distributed spatially, this difficulty may be attributed in part to a failure to appreciate quantitatively the interaction of the dose distributions from individual sources in the summation process that produces the aggregate dose distributions. To improve this understanding, 3-dimensional (3-D) dose distributions arising from simple implants ranging from a single point source to clinical double-plane implants are evaluated using the dose nonuniformity ratio (16–18).

METHODS AND MATERIALS

In recent years, many volumetric parameters have been introduced to evaluate the radiation dose distributions from interstitial implants (1–2, 9–12, 14–18, 20). These parameters take into account the 3-D nature of the radiation dose distributions. An important consideration in interstitial brachytherapy has been the dose variations across the implant. Various dose homogeneity parameters

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such as the dose homogeneity index (20), the uniformity index (11–12), the ratio of two volumes (9), and the peak width of a differential volume versus dose curve (1) have been used for quantitative evaluations. Among these parameters is the dose nonuniformity ratio (DNR) proposed by Saw and Sutharalingam (16–18) to assess quantitatively the quality of radiation dose distributions from interstitial implants (16). It has simple clinical and physical interpretations. The DNR is defined as the ratio of the high dose volume relative to the reference volume. It can be written mathematically as

$$DNR = \frac{V_{hdr}}{V_{rdr}} \quad \text{(Eq. 1)}$$

where

- $V_{hdr}$ is the high dose rate,
- $V_{rdr}$ is the reference dose rate,
- $V_{hdr}$ is the volume, receiving dose rates greater than some multiplicative factor, >1.0 of the reference dose rate, and
- $V_{rdr}$ is the reference volume, the volume receiving at least the reference dose rate.

As defined, the DNR is based on volumetric data. This formulation allows the DNR to vary as a function of the reference dose rate and the multiplicative factor. The multiplicative factor of 1.5 as suggested by Saw et al. (14) was used in this study. The schematic representation of the DNR in the plane through a single source is depicted in Figure 1a. Since $V_{hdr}$ is a subset of $V_{rdr}$, the DNR represents the fraction of the reference volume that receives high doses. In other words, the DNR corresponds to the degree of dose nonuniformity within the reference volume. The range of DNR, therefore, varies from zero to unity or expressed as a percentage, from 0 to 100%. A lower DNR value implies a smaller high dose volume, that is, a better dose homogeneity for the implant.

The DNR was determined for a single source, for two sources, for three and four sources (both arranged linearly and to form a triangle or a square), for ribbons of the same length with different seed spacing, and for both single-plane and double-plane implants. In these configurations, uniform source strengths of Ir-192 were used. For the multi-source configurations, the source strengths were adjusted such that the minimum DNR ($DNR_{min}$) occurred at about 50 cGy/hr. Three-dimensional dose distributions were generated by computing the dose rates for volume elements of 0.5 mm $\times$ 0.5 mm $\times$ 0.5 mm. In our algorithm, the dose rates were computed 4.0 cm beyond the radioactive sources in all directions. The small effects of radiation attenuation and scatter in tissue for Ir-192 photons were not taken into account in the computation (7). An exposure rate constant of 4.6 R-cm$^2$/mCi-hr and an f-factor of 0.957 R/cGy were used. Volume versus dose rate curves were generated by summing these volume elements. For a given reference dose rate, both $V_{hdr}$ and $V_{rdr}$ were computed by counting the number of volume elements receiving dose rates equal to or greater than the high dose rate and the reference dose rate respectively. The ratio was computed to obtain the DNR as defined in equation (1). The procedure was repeated for reference dose rates from 12 cGy/hr to 200 cGy/hr in steps of 4 cGy/hr.

**RESULTS**

The DNR versus the reference dose rate for a single point source is shown in Figure 1b. The fact that the data fall on a horizontal straight line indicates that the DNR is independent of the reference dose rate, suggesting that the high dose volume and the reference dose volume are described by the same relationship.

The DNR versus the reference dose rate curve for the two point source configuration is shown in Figure 2a. The sources were spaced 2.0 cm apart. As seen in the figure,

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**Fig. 1.** (a) Schematic representation of the DNR for a point source. The cross section of the high dose volume is shaded. (b) The DNR vs. the reference dose rate for a point source.
the DNR decreases rapidly to a minimum and thereafter increases slowly approaching the value of a single source as the reference dose rate increases. At very low and high reference dose rates the DNR approaches the value of a single source configuration. The minimum DNR at a particular reference dose rate ($RDR_{\text{min}}$) represents the condition where the high dose volume relative to the reference volume is the smallest. At this $RDR_{\text{min}}$, the dose homogeneity as defined here is considered optimal for the implant. If the intent is to obtain an optimal dose homogeneity, $RDR_{\text{min}}$ should be used for prescription. Figure 2b depicts the isodose rate distributions in a plane passing through the sources. The $RDR_{\text{min}}$ isodose rate line of 50 cGy/hr encloses both sources, while the HDR isodose surface of 75 cGy/hr encloses each source individually. The volume receiving a homogeneous dose, that is 100–150% of the prescribed dose is the volume between these two isodose surfaces.

The DNR versus the reference dose rate curves for the linearly arranged source configurations are shown in Figure 3a. The configurations of up to four point sources spaced 2.0 cm apart were examined. The DNR curves show the presence of $DNR_{\text{min}}$ for all source configurations. The magnitude of $DNR_{\text{min}}$ decreases as the number of sources increases. However, the decrement rate is minimal if a source is added to a ribbon with many sources. Isodose
rate distributions in the plane passing through the sources are depicted in Figure 3b. Again, the \( RDR_{\text{min}} \) surface encloses all the sources while the HDR isodose surface encloses each source individually.

The DNR versus the reference dose rate curves for the two source and those sources arranged in a triangle and a square are shown in Figure 4a. The spacing between the adjacent sources was 2.0 cm. Again, the DNR curves exhibit the presence of \( DNR_{\text{min}} \) for each source configuration. The \( DNR_{\text{min}} \) value decreases as the number of sources increases. The \( DNR_{\text{min}} \) value is lower for the square configuration than for the linear source configuration. As for the linear configuration, the rate of dose homogeneity improvement decreases as the number of sources increases. Figures 3a and 4a show that the \( DNR_{\text{min}} \) value depends on the implant configuration and the rate of dose homogeneity improvement decreases as the number of sources increases for either type of source configuration. Isodose rate distributions in the plane passing through the sources are depicted in Fig. 4b. Again, the \( RDR_{\text{min}} \) surface encloses all the sources while the HDR isodose surface encloses each source individually.

The DNR vs. the reference dose rate curves for the 6.0 cm long ribbons with different seed spacing are shown in Figure 5. The seed spacings were 0.5 cm, 1.0 cm, 1.5 cm, and 2.0 cm. All the DNR curves show the presence of \( DNR_{\text{min}} \) for each seed spacing. The source strengths were adjusted such that all \( DNR_{\text{min}} \) occurred at about 42 cGy/hr. The \( DNR_{\text{min}} \) improves as the number of seeds increases. As the number of sources increases, the width of \( RDR_{\text{min}} \) decreases as depicted in Figure 5b. This inverse relationship results from requiring the ribbon to have a fixed length. The decrease in the \( RDR_{\text{min}} \) width produces a smaller reference volume. Since the reference volume depends on the target volume size, the number of sources needed is determined by the thickness of the target volume. To maintain the same dose homogeneity indicated by \( DNR_{\text{min}} \) value, it is also feasible to use more sources and select a lower reference dose rate to adequately cover the same target volume. For example, the DNR value is the same for the ribbon using 2.0 cm spacing with 42 cGy/hr reference dose rate and the ribbon using 1.5 cm spacing with 35 cGy/hr reference dose rate. Hence a defined dose homogeneity can be obtained by either using the appropriate number of sources with \( RDR_{\text{min}} \) or more sources with a lower reference dose rate.

The DNR vs. the reference dose rate curves and isodose rate distributions for a single-plane and a double-plane clinical implants are shown in Figures 6 and 7, respectively. These implants were performed following lumpectomy to irradiate surgical beds. The single-plane implant consisted of an implant area of 8.0 cm \( \times \) 8.0 cm. The ribbons were spaced approximately 1.0 cm apart. Each ribbon consisted of two seeds per centimeter with each seed having an activity of 0.45 mCi. The configuration of the double-plane implant was based on the pre-implant plan shown in Figure 8. In the pre-implant plan, the implant consisted of two planes with implant areas of 6.0 cm \( \times \) 6.0 cm and 7.5 cm \( \times \) 7.5 cm. The ribbon and plane separation were spaced 1.5 cm apart. The difference in the \( DNR_{\text{min}} \) value between the pre-implant and post-implant is within 1%. The DNR curves shown in Figures 6a and 7a were computed using both multiplicative factors of 1.50 and 2.00. The use of the latter multiplicative factor on clinical implants has been reported (9). It is instructive to examine the differences and similarities between the two curves. These curves show the presence of \( DNR_{\text{min}} \) in both implants. The \( DNR_{\text{min}} \) is narrower when calculated.

![Fig. 4](image)

(a) The DNR vs. the reference dose rate for the two sources configuration, and for the three and four sources forming a triangle and a square, respectively. (b) Isodose distributions in the plane passing through the sources. The isodose rate lines, expressed in cGy/hr are 0.5, 1.0, and 1.5 times the \( RDR_{\text{min}} \). The shaded areas represent the cross sections of the high dose volume.
using the 1.50 multiplicative factor. The \( DNR_{\text{min}} \) is shifted to lower reference dose rate for both implants when a multiplicative factor of 2.00 was used. This shift is due to the \( RDR_{\text{min}} \) being the lower limit of a large window gated on the peak in the differential volume dose curves. The peak represents a large volume receiving a narrow range of dose rates. It should be mentioned that at low reference dose rate the DNR may be lower or higher than the single source DNR value. This phenomenon is caused by the volume element size effect and cut-off effect since calculations were only extended up to 4.0 cm away from the sources. The volume element size effect is due to the summation of elemental volumes that have different dose rates within a specified range into a single volume identified with a particular dose rate. On the other hand, at high reference dose rate, the DNR may be seen as not reaching the single source DNR value as shown in the figures. This feature suggests that each source is only isolated from the rest of the sources in the implant at a much higher reference dose rate. Figures 6b and 7b depict the isodose rate distributions in the central plane for both implants. Again, the \( RDR_{\text{min}} \) surface encloses all the sources while the HDR isodose surface encloses each source individually.

**DISCUSSION**

The \( DNR \) has been useful in identifying several characteristics about interstitial implants. It is worthwhile to understand how these characteristics are presented in the
Fig. 7. The DNR and isodose rate distributions for a double-plane Ir-192 clinical implant are shown in Figures a and b, respectively. (a) DNR was calculated using the multiplicative factors of 1.50 and 2.00. In both Figures 6 and 7, the multiplicative factor of 2.0 shows a larger range of reference dose rates having DNR values within 1% of $DNR_{\text{max}}$. (b) The isodose rate lines expressed in cGy/hr are labeled. The cross sections of the high dose volumes are shaded.

The basic equation that describes the dose distributions from radioactive sources. Neglecting the effects of attenuation and scatter, the dose rate delivered to a volume element located at any point $P$ from a point source can be described as

$$
\frac{dD}{dt} = \frac{k_1 S}{|r|^2} \quad \text{(Eq. 2)}
$$

where

$S$ is the source strength, $k_1 = f \Gamma'$,

$\Gamma'$ is the exposure rate constant,

$f$ is the conversion factor from exposure to absorbed dose, and

$|r|$ is the magnitude of the vector from the source to the point of interest.

Eq. 2 states that the dose rates are higher for all points located closer to the source than point $P$. The total volume receiving dose rates equal to and greater than the dose rate at point $P$ can be expressed in the standard volume formula as

$$V = k_2 |r|^3 \quad \text{(Eq. 3)}$$

Fig. 8. The DNR versus the reference dose rate and isodose rate distributions for a double-plane Ir-192 implant. The $DNR_{\text{max}}$ occurred at approximately 54 cGy/hr. The isodose rate lines expressed in cGy/hr are 0.5, 1.0 and 1.5 times the RDR$_{\text{max}}$. The shaded areas represent the cross sections of the high dose volume. Compared to Figure 7, the difference in DNR$_{\text{max}}$ between the pre-implant and post-implant arrangements is less than 1%.
where $k_2 = 4\pi/3$ which is a constant. By solving for $|r|$ in equation (2) and substituting into equation (3), the volume is related to the dose rate as

$$V = k_3 \left(\frac{dD}{dt}\right)^{-3/2} \quad (\text{Eq. 4})$$

where $k_3 = k_3(k_1S)^{3/2}$ which is a constant. Choosing any reference dose rate, $RDR$, the $DNR$ in Eq. 1 becomes:

$$DNR = \frac{k_3(1.5RDR)^{-3/2}}{k_3(RDR)^{-3/2}} = \left(\frac{1.5RDR}{RDR}\right)^{-3/2} = 0.544 \quad (\text{Eq. 5})$$

which is a constant. By having a constant value, the $DNR$ suppresses the volumetric dependence on $|r|^3$ and dose rate dependence on $|r|^{-3}$ as well as showing that the dose homogeneity is independent of the strength of the source. By not having a zero value, the $DNR$ indicates that any interstitial implant consisting of discrete sources will give rise to a non-uniform dose distributions seen as local hot spots around the individual sources. This single point source allows for the analytic calculations of the $DNR$ and is the limiting value of the $DNR$ for multi-source implants at very low and high dose rates as discussed below.

For two point sources with source strength $S_1$ and $S_2$, the dose rate delivered to a volume element located at point $P$ is simply the summation of dose rate contributions from each source as,

$$\frac{dD}{dt} = \frac{k_1S_1}{|r|^2} + \frac{k_1S_2}{|r_0 - r|^2} \quad (\text{Eq. 6})$$

In the case where the source strength is identical, that is $S_1 = S_2$, equation (6) reduces to:

$$\frac{dD}{dt} = k_1S_1 \left(\frac{1}{|r|^2} + \frac{1}{|r_0 - r|^2}\right) \quad (\text{Eq. 7})$$

where $r_0$ is the vector from one source to the other source. Equation (7) can be easily analyzed by examining the position of point $P$ relative to the spacing between the sources. At large distance from the source, that is $|r| \gg |r_0|$, corresponding to low reference dose rate, the second term reduces to a term identical to the first term in equation (7). Hence the resulting radiation dose patterns behave as if it is derived from an effective point source that has twice the strength of the individual source. At close distance, that is $|r| \ll |r_0|$, corresponding to high reference dose rate, the value of the second term is much smaller and hence negligible compared to the first term.

As such, the resulting radiation dose patterns can be perceived as derived principally from the nearest source. In summary, the 3-D dose distributions can be characterized into three characteristics zones. At the very low and high reference dose rates, the dose distributions behave as if it is from an effective point source. At the intermediate reference dose rate where $|r| \approx |r_0|$, the dose rate contributions are summed from the two sources causing the $DNR$ to decrease resulting in the existence of the $DNR_{\text{min}}$ as demonstrated in Figure 2. Note that the source strength $S_1$, and the distance between the sources, $|r_0|$ are two variables in equation (7). Since $S_1$ is only a multiplicative factor in the equation, any value assigned to $S_1$ merely change the magnitude of the dose rate but not the relative dose distributions. Consequently, the source strength does not affect the $DNR_{\text{min}}$ value. Likewise for any value assigned to $|r_0|$, the three characteristics zones remains the same. Therefore, for any two sources spaced either 1.0 cm or 3.0 cm the dose homogeneity is the identical. The above presentations are merely arguments supporting the independence of $DNR_{\text{min}}$ value from the source spacing or the source strength. However, further work is needed to validate these claims.

In the formulation of the $DNR$, the high dose volume was defined as the volume receiving dose rates greater than a multiplicative factor of the reference dose rate. As the multiplicative factor increases, the $DNR$ approaches zero. This can be interpreted as accepting a wider range of dose rates. The acceptability of the dose rates depend on the type of malignancies being irradiated and the tolerance of the surrounding normal tissues. In addition to the multiplicative factor of 1.5, other factors of 1.25, 2.00, 2.50, and 3.00 have also been examined. The minimum in the $DNR$ curve broadens as the multiplicative factor increases. This broadening effect can be seen in the $DNR$ curves shown in Figures 6a and 7a for the two clinical implants. There have been clinical observations that tissue necrosis occurred in the vicinity of the sources. To quantify this effect, overdose "sleeve" has been defined as the volume of tissue immediately surrounding a line source that receives doses equal to or greater than twice the reference dose (3). The frequent occurrence of radiation necrosis relates to the diameter of this sleeve exceeding 8 mm to 10 mm as indicated by Dutreix et al. (3). This indication may be used to suggest the maximum spacing of ribbons allowed in planar implants. A multiplicative factor of 2.0 compared to 1.5 offers a wider range of reference dose rates for almost identical $DNR$ value as shown in Figures 6a and 7a.

The differences and similarities between the $DNR$ and other volumetric parameters are examined. The dose homogeneity index defined by Wu et al. (20) is essentially the difference between the treatment volume and the volume enclosed by the dose rate that is 50% higher than the prescribed treatment dose rate. As illustrated by the authors, this index was determined after the treatment dose rate has been selected. This index equals the difference
between the DNR and unity. As such, it merely represents a data point on the DNR versus reference dose rate curve. The double dose volume ratio introduced by Metcalf et al. (9) is the ratio of the volume of tissue receiving twice the prescribed dose divided by the volume of tissue receiving the prescribed dose. This ratio is identical to the DNR curve determined using a multiplicative factor of 2.0. Anderson (1) expressed uniformity of an implant as the extent to which the treatment volume is concentrated between the treatment dose rate and the high dose rate located on the upper side of a peak seen in a "natural" volume-dose histogram. The narrowness of the peak described the dose rate uniformity of the implant. Though the high dose rate is not explicitly defined, it is taken as the half-peak dose rate.

The DNR has the potential to be useful in assessing the dose nonuniformity of any interstitial implant. Because the DNR represents the dose nonuniformity as a function of reference dose rate, it serves as a method of assessing different choices of reference dose rate in a given implant. In addition, it allows the comparison of maximum dose homogeneity achievable by alternate implant geometries. Thus, the DNR serves as a tool that incorporates dose homogeneity into the decision making process of selecting the appropriate dose rate for prescription and the resulting treatment volume. For any reference dose rate selected, the DNR plot allows a direct extraction of the dose non-uniformity for that implant configuration. The DNR can also be used to compare pre- and post-implant configurations as shown in Figures 7 and 8. Since the DNR versus the reference dose rate yields DNR_{min}, the DNR can be used to obtain RDR_{min} resulting in optimizing dose homogeneity. It should be mentioned that the DNR only determines the quality of the dose distributions and not the extent to which the implant adequately delivers the prescribed dose to the target volume. The latter task is best evaluated using volumetric irradiation indices (14-16). In addition to dose homogeneity, these indices take into account the adequacy of the coverage of the target volume and the amount of surrounding normal tissues outside the target volume being irradiated equal to and greater than the prescribed dose.

Although only a limited range of simplified implants have been presented in this paper, the features of DNR thereby illustrated have important generalizations for clinical use. Two examples of the conceptual applications to clinical implants are discussed below. As shown in Figures 2b, 3b, 4b, 5b, and 8b, the DNR_{min} encloses most if not all the sources for any multi-source implant. On the other hand, the high dose volume encloses each source individually. This enclosure property can also be extended to single source configuration as shown in Figure 1a. Even clinical implants shown in Figures 6b and 7b exhibit such enclosure property. The above features suggest that sources should be implanted within the target volume to yield a dose rate that may enclose the target volume and also optimize dose nonuniformity for the implant. As shown in Figures 7 and 8, the implant performed clinically is not identical to the pre-implant plan. Yet, the DNR curves shown in Figures 7a and 8a are similar for these implants, implying that even though there are some deviations of source placement, these small displacements do not affect the dose nonuniformity significantly.

**CONCLUSION**

The dose nonuniformity of any implant depends on the design of the implant and the choice of the reference dose rate. For a single point source, the dose nonuniformity is the same regardless of which reference dose rate is selected as the treatment dose rate. Compared to the single source, the DNR is drastically different for any multi-source implant. In any multi-source implant, there exists a DNR_{min} at a particular reference dose rate. At this dose rate, the dose homogeneity is maximized for the implant. The dose nonuniformity ratio presents a method of optimizing the dose homogeneity for any implant. As a technique for calculating the degree of dose nonuniformity for any fixed reference dose rate, the DNR is no different that the volume ratio method.

**REFERENCES**