Original article

Assessment of dose homogeneity in conformal interstitial breast brachytherapy with special respect to ICRU recommendations

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Abstract

Purpose: To present the results of dose homogeneity analysis for breast cancer patients treated with image-based conformal interstitial brachytherapy, and to investigate the usefulness of the ICRU recommendations.

Material and methods: Treatment plans of forty-nine patients who underwent partial breast irradiation with interstitial brachytherapy were analyzed. Quantitative parameters were used to characterize dose homogeneity. Dose non-uniformity ratio (DNR), dose homogeneity index (DHI), uniformity index (UI) and quality index (QI) were calculated. Furthermore, parameters recommended by the ICRU 58 such as minimum target dose (MTD), mean central dose (MCD), high dose volume, low dose volume and the spread between local minimum doses were determined. Correlations between the calculated homogeneity parameters and usefulness of the ICRU parameters in image-based brachytherapy were investigated.

Results: Catheters with mean number of 15 (range: 6-25) were implanted in median 4 (range: 3-6) planes. The volume of the PTV ranged from 15.5 cm^3 to 176 cm^3. The mean DNR was 0.32, the DHI 0.66, the UI 1.49 and the QI 1.94. Related to the prescribed dose, the MTD was 69% and the MCD 135%. The mean high dose volume was 8.1 cm^3 (10%), while the low dose volume was 63.8 cm^3 (96%). The spread between minimum doses in central plane ranged from –14% to +20%. Good correlation was found between the DNR and the DHI (R^2 = 0.7874), and the DNR correlated well with the UI (R^2 = 0.7615) also. No correlation was found between the ICRU parameters and any other volumetric parameters.

Conclusions: To characterize the dose uniformity in high-dose rate breast implants, DVH-related homogeneity parameters representing the full 3D dose distributions are mandatory to be used. In many respects the current recommendations of the ICRU Report 58 are already outdated, and it is well-timed to set up new recommendations, which are more feasible for image-guided conformal interstitial brachytherapy.

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Key words: breast cancer, homogeneity, dose-volume histogram, image-based brachytherapy.

Purpose

In interstitial brachytherapy (BT), the non-homogeneous dose distribution around the radioactive sources is mainly determined by inverse square law. Other factors add only little modifications to this geometrical phenomenon. In the immediate proximity of the sources there are always regions of high dose, but with appropriate source distribution regions with low dose gradient can be attained, and in proper implants, the high dose volumes are relatively small. Historically, different parameters have been defined to characterize the dose homogeneity in BT [1-4]. The International Commission on Radiation Units and Measurements (ICRU) published the ICRU Report 58 in 1997 which deals with specification of dose homogeneity in interstitial BT [5]. For a reporting purpose it is recommended to use homogeneity parameters which have been validated in classical low dose rate (LDR) BT. However, in modern image-guided, dose optimized high-dose-rate (HDR) BT in which stepping-source remote afterloading equipment is used for irradiation, the practical applicability of these parameters is questionable. Boost dose after whole breast irradiation as well as accelerated partial breast irradiation (APBI) can be delivered with image-guided BT where conformal dose distribution can be achieved with optimized dose distribution [6-9]. Among the APBI techniques, the longest experience is present in multi-catheter based inter-

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stitial BT [7-9]. Now, follow-up data of up to 12 years are already available for HDR interstitial breast BT with comparable results to the WBI in terms of safety and efficacy [8]. In 2004, a European multicentre Phase III clinical trial was initiated by the Breast Cancer Working Group of the GEC-ESTRO to investigate the efficacy of the APBI [9]. Our institution actively participated in this study.

The purpose of this paper is to present the results of a detailed analysis on dose homogeneity of dose distributions in treatment plans made for our patients enrolled into the GEC-ESTRO trial and treated with interstitial BT. Furthermore, to investigate the suitability of the ICRU recommendations for dose uniformity in image-based conformal interstitial BT.

Material and methods

Dose plans of forty-nine patients were evaluated with respect to dose homogeneity. All patients were treated with microSelectron V2 HDR afterloader (Nucletron BV, Weenendaal, The Netherlands), and the used planning system was the Nucletron's Plato Brachytherapy v.14.6. The details of our planning and implant techniques have been published elsewhere [10]. We used pre- and post-implant CT imaging for catheter placements and treatment planning. Following geometrical and graphical optimization, the dose was normalized to basal dose points and an isodose line was individually selected for dose prescription in order to obtain at least 90% of target volume coverage. The prescribed dose (PD) was 30.1 Gy delivered by 7 × 4.3 Gy, 2 fractions daily. Quantitative evaluation of dose plans was performed with dose volume histograms (DVHs). To characterize the homogeneity of dose distributions, the most common DVH based quality indices and parameters recommended by the ICRU were calculated. Descriptive statistics was calculated and correlation analysis between the indices and parameters was performed. Volumetric homogeneity parameters used for calculations were as follows:

Dose non-uniformity ratio (DNR)

The DNR is a simple and easy to interpret parameter for quantitative analysis of dose homogeneity in interstitial implants. The DNR is the ratio of the high dose volume to the reference dose volume [3]. The reference dose volume is the volume that receives dose equal or greater than PD, and the high dose volume is the volume that receives 1.5 times PD or more. The optimal dose distribution in terms of dose uniformity can be achieved at the minimum DNR value.

Dose homogeneity index (DHI)

The concept of DHI is similar to DNR, though different definitions exist in the literature [11-13]. Sometimes it is used as a complementary parameter to the DNR (DHI = 1 – DNR). It can be calculated only for the implant geometry and can also be related to the volume of the PTV. In the latter case it is called relative homogeneity index (HI). In this paper we used the definition as follows: DHI = (V100 – V150)/V100. Where, V100 and V150 is the relative volume of the PTV in percent irradiated at least by the 100% and 150% of the PD, respectively.

Uniformity index (UI)

The UI is calculated from the "natural" volume dose histogram (NVDH) [1]. In the NVDH the "u" parameter is defined as –3/2 power of dose ($D^{-3/2}$), and the volume (V) per unit "u" (dV/du) is plotted versus the "u" parameter. With this transformation the inverse square law is suppressed, and from this follows that for a point source the NVDH is a horizontal line. For a real implant, there is a peak on the graph which is graphical representation of the dose uniformity. The narrower the peak, the more uniform the dose distribution is. Evaluation of other peak parameters such as width, position and contained volume, in relation to treatment dose permits to define other quantitative volume-dose parameters such as UI and QI.

Per definition,

$$UI = \frac{V(TD) - V(HD)}{V(TD)} \Big/ \frac{u(TD) - u(HD)}{u(TD)},$$

where *TD* is the treatment dose (or PD) and *HD* (high dose) is dose value at *dV/du* that is half way between the $(dV/du)_{max}$ (peak dose, PkD) and the asymptotic value of dV/du as u → infinity (see HD definition in Fig. 1). The UI depends on the prescribed dose, thus it can be used to compare implants with the same dose prescription only.

Quality index (QI)

The formula of QI is similar to UI, but instead of the treatment dose (TD) the low dose (LD) is used, where LD is dose value at dV/du that is half way between the $(dV/du)_{max}$ (peak dose, PkD) and the asymptotic value of dV/du as u → 0 (see LD definition in Fig. 1). Since treatment dose is excluded from the formula, QI is independent on the prescribed dose.

ICRU Report 58 recommendations

The ICRU recommends using the following parameters in interstitial BT: Minimum Target Dose (MTD) – minimum dose at the periphery of the clinical target volume, which in most cases practically coincides with the PTV, Mean Central Dose (MCD) – arithmetic mean of the local minimum doses between sources in the central plane (same as basal dose in the Paris system), High dose volume – volume encompassed by the isodose corresponding to 150% of the MCD, Low dose volume – volume within the clinical target volume encompassed by the isodose corresponding to 90% of the PD (corresponds to V90).

For high dose volume and low dose volume the maximum dimension of the volumes in the calculated planes should be reported. Dose uniformity parameters are the mean spread between the local minimum doses in the central plane (maximal ± percentage deviations of the individual minimum doses from the MCD) and the MTD/MCD (ratio of MTD and MCD).

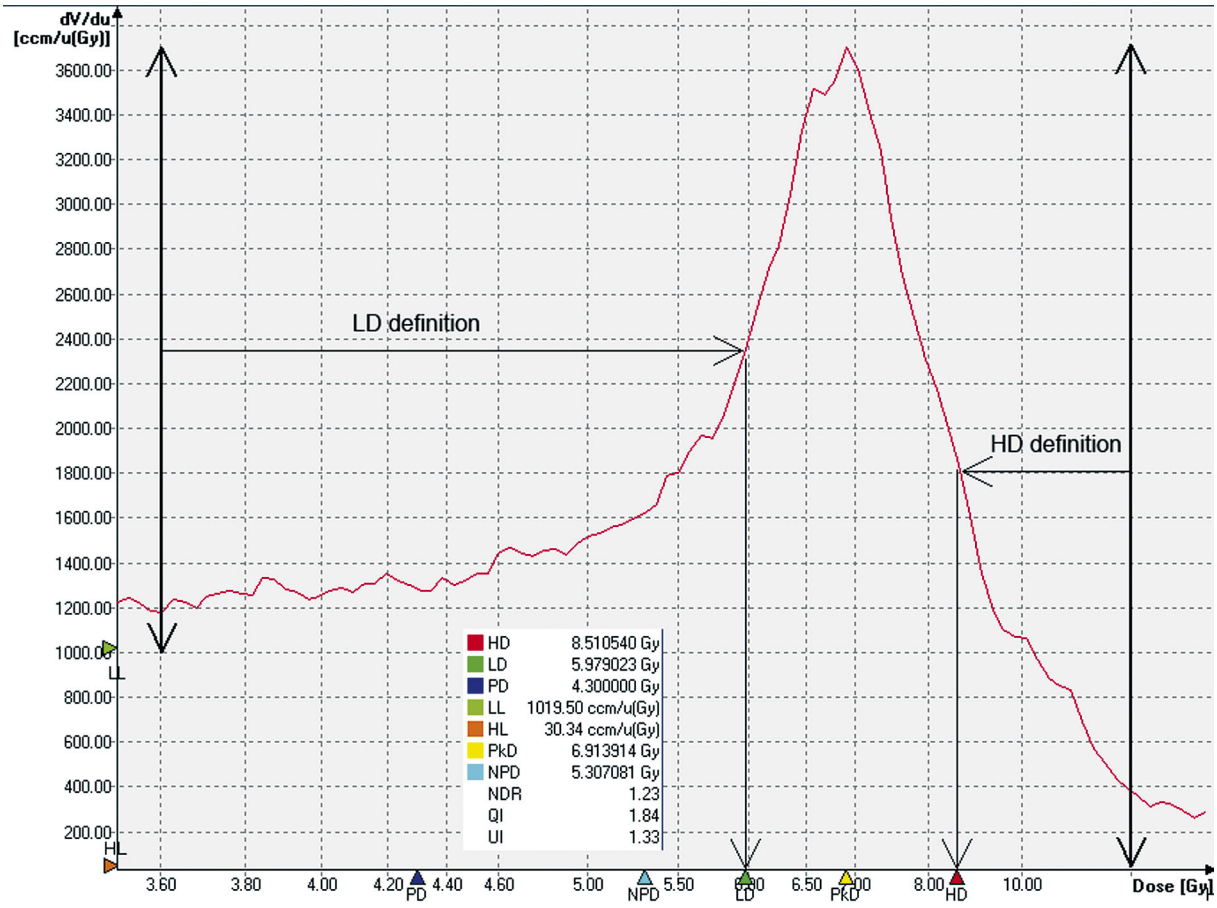

Fig. 1. Natural volume-dose histogram for a breast implant. The arrows shows how the LD and HD are defined. The LD and HD is used to define the QI and UI, respectively

Results

The median number of implanted catheters was 15 (range: 6-25) in a median of 4 (range: 3-6) planes. The mean volume irradiated by the PD was 78.8 cm^3 (range: 23.2-209.5 cm^3). The volume of the PTV ranged from 15.5 cm^3 to 176 cm^3 with a mean of 66.4 cm^3. The volumetric dose homogeneity parameters are shown in Table 1. In 6 out of 49 cases (12%) the DNR value was higher than 0.35 which was the upper limit in the study. But, this was always accepted in order to obtain proper dose coverage. The dose homogeneity inside the PTV is characterized by 0.66 (range: 0.50-0.76) as a mean of the DHI.

Table 2 shows calculated parameters recommended by the ICRU. The wide range of the MTD (53-92%) indicates weakness of the use of this parameter in conformal BT. The average of the MCDs is 135%, which means that the mean isodose selected for dose prescription was 74% (range: 69-85%). The mean volume irradiated by 1.5 times

Table 1. Volumetric homogeneity parameters for 49 HDR breast implants

Characteristics	Mean	Range
V_{PTV}	66.4 cm^3	15.5-176.0 cm^3
V_{ref}	78.8 cm^3	23.2-209.5 cm^3
DNR	0.32	0.25-0.41
DHI	0.66	0.50-0.76
UI	1.49	1.18-1.62
QI	1.94	1.22-3.07

Table 2. Homogeneity parameters recommended by the ICRU Report 58 for 49 breast implants

Characteristics	Mean	Range
Minimum target dose (MTD)	69%	53-92%
Mean central dose (MCD)	135%	118-145%
High dose volume	10%	6-36%
Low dose volume	96%	93-100%
Spread in mimimum doses	–14-+20%	–25-+61%
MTD/MCD	0.51	0.37-0.69
High dose volume	8.1 cm^3	3.4-21.4 cm^3
Low dose volume	63.8 cm^3	14.9-165.4 cm^3

MCD was 10% (range: 6-36%) which corresponds to absolute volume of 8.1 cm^3 (range: 3.4-21.4 cm^3). The mean low dose volume (96%) was close to 100% corresponding to 63.8 cm^3. The mean deviation in local mean minimum doses from the MCD was 14% in negative and 20% in positive direction. The largest deviation was –25% and +61%. The minimum dose in the target related to the MCD (MTD/MCD) was quite low with 0.51 (range: 0.37-0.69) value.

Figure 2 shows the correlation between DNR and DHI. Although, the former relates to the implant geometry and the latter to the PTV, the correlation is quite good ($R^2 = 0.7874$). The UI also correlates with the DNR, which is presented in Fig. 3. No correlation ($R^2 < 0.5$) was found between the ICRU parameters (spread in individual minimum doses, MTD/MCD, low dose volume, high dose volume) and any other volumetric parameters (DNR, DHI, UI).

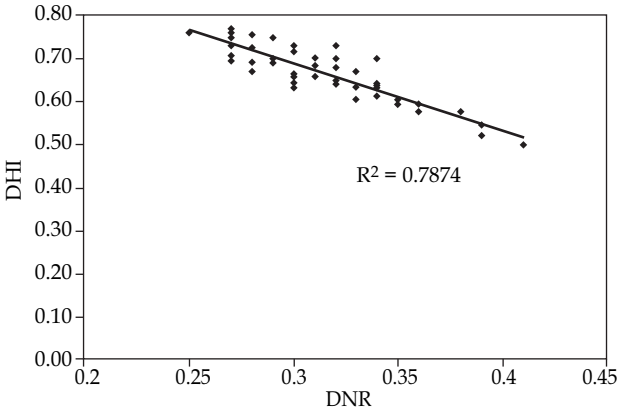

Fig. 2. Correlation between the DHI and DNR

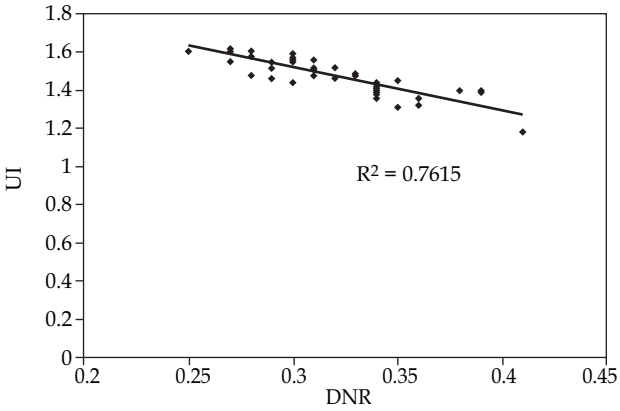

Fig. 3. Correlation between the UI and DNR

Discussion

In interstitial BT, the classical Paris system has been successfully used clinically for different treatment sites for decades [14]. One of the advantages of the Paris system is that following its rules the resulting dose distribution will be always homogeneous. Although, it was originally based on LDR wire sources, its application is also possible with a HDR stepping source, when uniform dwell times are used [15]. In a previous study, comparing different dosimetry systems we found that the most homogeneous dose distributions occurred in the Paris dosimetry system and in the geometrical optimization [16]. For both systems the mean DNR was 0.25. The clinical availability of dose optimization algorithms and recent evolution of image-based brachytherapy have highlighted the limitations of the Paris system [17]. With 3D imaging, the exact definition of the PTV is possible, and this calls for tailoring the reference isodose surface to the PTV. However, good dose coverage sometimes can be achieved only with deterioration of dose homogeneity [16, 18].

At the time of publication of the ICRU Report 58, conformal interstitial BT was not widely available. This is well reflected by the recommended parameters which can be effectively used in projection-based classical implants. Use of an implant related parameters and point doses is recommended, and DVH is mentioned only as an additional representation of dose distributions. This is understandable, since at that time individual computerized treatment planning was not common. Without 3D volume calculation, the dimensions of the high dose volume in different planes have to be determined as per the recommendations. In current planning systems, however, calculation of the high dose volume can be easily performed from the DVH. In LDR BT or in HDR stepping source BT with uniform dwell times, the volume irradiated by 1.5 times MCD (high dose volume according to the ICRU) can be approximated by the dimensions measured in three planes, since the high dose region closely follows the catheters. But, in conformal BT the source dwell times can be very different due to optimization algorithms. From this follows, that the high dose volume will be irregular (bumpy) and its size can not be estimated with dimensions measured only in three planes. This is demonstrated in Fig. 4, where 3D representation of the high dose volume is shown in uniform and various dwell times in a two-plane breast implant. In the latter case, the dwell times were determined by optimization algorithm. It is evident from the images that knowing the dimensions in 2D planes only, can not be equivalent to calculation of the full 3D volume if the source dwell times are not uniform.

In BT the dose inhomogeneity is unavoidable and it is particularly important in cases of breast implants, where all the breast tissue can be considered equally at risk for developing late side effects (e.g. fibrosis or fat necrosis). Wazer *et al.* [12] found a significant relationship between dose homogeneity and cosmetic outcome in interstitial LDR boost breast implants. With higher value of DHI they observed less late fibrosis. In another study from the same department, no clear statistical correlation between dose homogeneity and complication risk was found at sole HDR brachytherapy treatment for early-stage breast cancer [19]. In a study with LDR implants the probability of excellent cosmetic outcome linearly increased with DHI [20]. Vicini *et al.* [11] reported the DHI of 0.89–0.90 calculated for the implants of five patients. In the study of Das *et al.* [13] the DHI ranged from 0.46 to 0.85 with a mean of 0.73. Converting these values into DNR, the range will be from

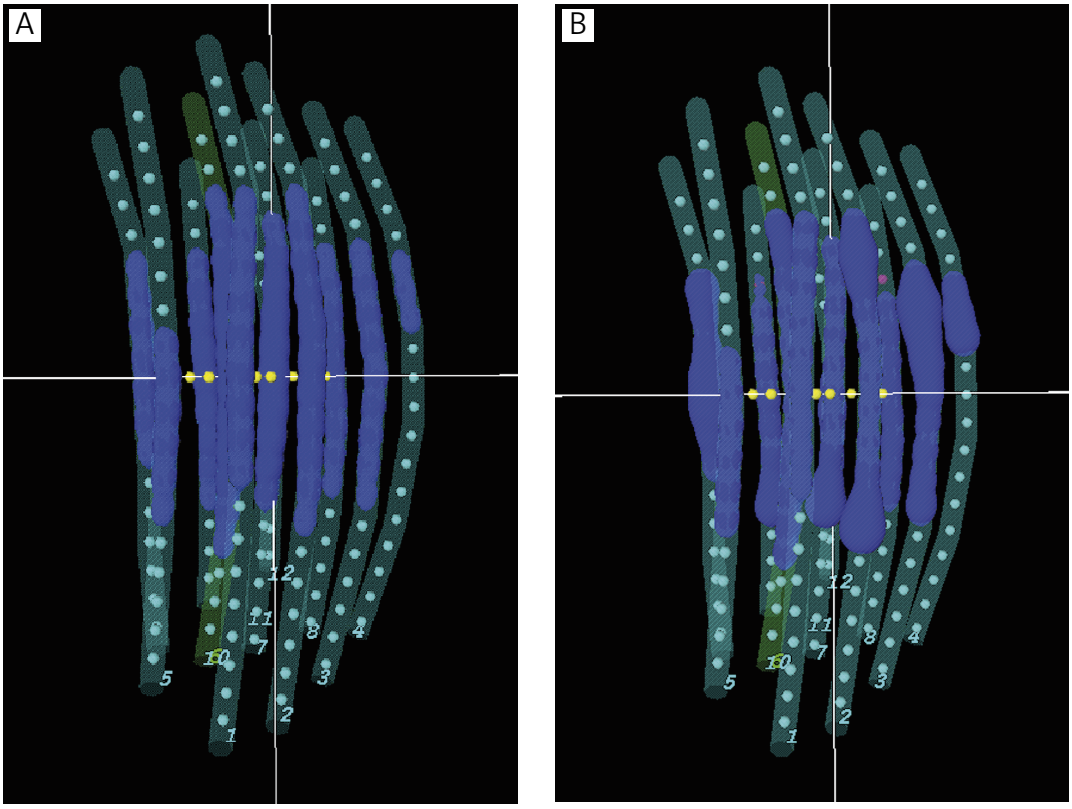

Fig. 4. 3D representation of high dose volume according to the ICRU Report 58 in a breast implant planned A) without optimization, B) with geometrical and graphical optimization

0.15 to 0.54 with a mean of 0.27. Recently, a new dose volume uniformity index has been proposed where all volume elements irradiated by higher than the prescribed dose is taken into account [21].

The parameters for dose uniformity recommended by the ICRU relates to 2D dose distributions and point doses. Our results demonstrated that this simple representation of dose homogeneity did not correlate with volumetric parameters in HDR implants. The spread in individual minimum doses in the central plane may describe dose homogeneity in that plane, but the degree of homogeneity in the whole volume can be very different. In our study, there was no correlation between the deviations in the midpoint doses between the catheters in the central plane and volumetric parameters (DNR, DHI). The explanation for this is that in optimized dose plans the dose distributions in planes parallel to central plane can be unrelated to each other, not like in classic LDR implants or HDR implants with uniform source dwell times. Therefore, the central plane is no longer representative of the implant, as it was before. Nowadays, 3D assessments of dose distribution is mandatory with volumetric parameters to characterize the dose homogeneity.

Conclusions

In the era of image-guided conformal interstitial BT, the recommendations of the ICRU Report 58 seem to be outdated in many respects. The progress in imaging and dose optimization algorithms has recently made conformal BT as a routine procedure in many institutions. Considering this, it is mandatory to use DVH-related homogeneity parameters representing fully the 3D dose distributions. To decide which parameters have clinical significance requires more studies with clinical validation of their correlation with treatment outcome and side effects. In order to report the treatments in consistent way, new recommendations from international bodies and/or professional societies are highly awaited.

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