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IORT in breast cancer

On-line optimization of intraoperative electron beam radiotherapy of the breast

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ABSTRACT

Purpose: To optimize the dose delivery to the breast lumpectomy target treated with intraoperative electron beam radiotherapy (IOERT).
Materials and methods: Two tools have been developed in our MU calculation software NEMO X to improve the dose homogeneity and the in-vivo dosimetry effectiveness for IOERT treatments. Given the target (tumor bed) thickness measured by the surgeon, NEMO X can provide auto dose normalization to cover 95% of the target volume with 95% of the prescription dose (PD) and a "best guess" of the expected dosimeter dose (EDD) for a deep seated in-vivo dosimeter. The tools have been validated with the data of 91 patients treated with IOERT on a LIAC mobile accelerator. In-vivo dosimetry has been performed with microMOSFETs positioned on the shielding disk inserted between the tumor bed and the chest wall.
Results: On average the auto normalization showed to provide better results if compared to conventional normalization rules in terms of mean target dose ($|MTD-PD|/PD \leqslant 5\%$ in 95% vs. 53% of pts) and V107 percentage ($\langle V107 \rangle = 19\%$ vs. 32%). In-vivo dosimetry MOSFET dose (MD) showed a better correlation with the EDD guessed by our tool than just by assuming that EDD = PD ($|MD-EDD|/EDD \leqslant 5\%$ in 57 vs. 26% of pts).
Conclusions: NEMO X provides two useful tools for the on-line optimization of the dose delivery in IOERT. This optimization can help to reduce unnecessary large over-dosage regions and allows introducing reliable action levels for in-vivo dosimetry.
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Intraoperative electron beam radiotherapy (IOERT) is an emerging technique for accelerated partial breast irradiation (APBI) [1–5]. If compared with other APBI techniques, IOERT has some definite advantage including an excellent sparing of normal tissues due to the electrons steep absorbed dose fall-off and to the opportunity to insert a shielding disk above the chest wall. However some critical aspects have still to be considered: (i) the technique is one-shot and high-dose so in-vivo dosimetry is highly recommended, (ii) the planning of the beam-on time (or Monitor Units, MU) has to be made on-line because the actual size and the thickness of the target is known only after the lumpectomy and the prescription dose can depend on histological findings, (iii) in order to cover adequately the target with the prescribed dose, large regions of over-dosage are often unavoidable. For these reasons we have developed a calculation system which can help the medical physicist to optimize the treatment parameters in terms of dose homogeneity and in-vivo control of the delivered dose.

Materials and methods

In our hospital IOERT is delivered by a dedicated mobile LIAC (Sordina) accelerator operating in the surgery room. Our accelerator (S/N 0012) generates electron beams with nominal energy 4, 6, 8 and 10 MeV collimated by means of circular polymethylmethacrylate applicators. For these beams the 90% central-axis percent dose depth (R90 or therapeutic range) for the 5 cm applicator is 12, 15, 20 and 26 mm, respectively, with entrance dose $\geqslant$85% of peak dose. Given that the stability of a mobile accelerator may be a concern due to its portable nature and cooling system, the morning (on average about 4 h) before the treatments, we perform a check of the output with a Roos (PTW Freiburg) plane-parallel ion chamber, positioned on central axis at the point of maximum dose (D_{max}) in a RW3 slab phantom. For each beam we can then calculate the daily output correction F defined as:

$$F = M^{10}/M^{10}_{ref} \quad (1)$$

where M^{10} is the Roos reading (corrected for temperature and pressure) of the day for the 10 cm applicator and M^{10}_{ref} is its reference value measured during beam calibration.

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For breast treatments a two-layer (3 mm PTFE + 3 mm INOX steel) shielding disk supplied by Sordina is put on the chest wall just below the target volume (lumpectomy site) providing nearly total beam attenuation. In-vivo dosimetry is performed for each treatment with the mobileMOSFET system (Best Medical) using a microMOSFET 502-RDM inserted into a closed-end 6Fr brachytherapy catheter. The treatment setup is similar to what is described by Ciocca et al. [6] but in our case the MOSFET is taped on the shielding disk, thus directly measuring tissue dose. The thickness of the target is measured by the surgeon using a graded needle in at least three different points in the tumor bed area. The target thickness is used by the medical physicist for selection of the beam energy and dose normalization. Usually the beam energy is chosen so to have the R90 to fully cover the distal part of the target. Dose normalization is made between 90% and 100% of peak dose [7–12]. Based on beam energy, applicator size, prescription dose (PD) and dose normalization, the medical physicist computes the MUs taking also into account the daily output correction. The irradiation is split into two consecutive fractions: in the first one the expected dosimeter dose (EDD) is compared against the measured MOSFET dose (MD) and the result can be used to correct the MUs in the second fraction to achieve a better agreement with the prescription.

In order to improve the treatment delivery in terms of target dose homogeneity and in-vivo dosimetry, we implemented IORT electron beams in our MU calculation software NEMO X [13] available at www.agolabs.com. The MUs are calculated according to the following formula:

$$\mathrm{MU} = \mathrm{PD}/[O(c) \times F \times N] \quad (2)$$

where N is the dose normalization, $O(c)$ is the output factor (i.e. Gy/MU) measured at the $D_{\max}$ for the beam collimated by applicator of size c.

In addition to MU calculation we developed into NEMO X two tools which can improve the optimization of the treatment: auto normalization and in-vivo dosimetry dose prediction. Both tools rely on simple 1D modeling of the target, neglecting tissue inhomogeneities and multiple Coulomb scattering. Considering the beam to be perfectly uniform on transverse planes, the dose D at depth z is simply given by:

$$D(z) = \mathrm{MU} \times O(c) \times F \times \mathrm{PDD}(c; z) \quad (3)$$

where $\mathrm{PDD}(c; z)$ is the central-axis percent depth dose at depth z for the beam collimated by applicator of size c. The target is modeled as a cylinder extending from the body surface to the greatest measured tumor bed thickness. Eq. (3) is used to calculate the entrance dose, the dose at the distal part of the target and the target DVH including minimum and maximum dose, mean target dose (MTD) and the V95 and V107 percentages. These data may help the medical physicist to make a proper choice of dose normalization both in terms of target coverage and reduction of unnecessary over-dosage. To this end NEMO X provides an auto normalization option (auto-norm) that computes the value of N which makes the V95 = 95% (i.e. 95% of PD to cover 95% of the target).

The in-vivo dosimetry tool has been designed to provide a "best guess" of the EDD as measured by a MOSFET dosimeter sitting on the shielding disk. The guess is computed assuming that the dose at different points of the target surface lying on the disk is given by Eq. (3) where z is the physical depth of the considered point. This assumption neglects possible over or under-scatter effects due to multiple Coulomb scattering of the electrons hitting an irregular target surface [14] and the backscatter from the high-Z layer of the shielding disk [15]. In our setup the latter has been found [16] to be <5% thanks to the PTFE layer which stops low-energy backscattered electrons; this is similar to what was found by others [17,18] for two-layer disks. In our model we can then calculate the modal value of the distal dose by sampling Eq. (3) in the thickness range measured by the surgeon. The modal value can be used as a "best guess" of the EDD for comparison with the dose read by the MOSFET in order to achieve a robust in-vivo dosimetry system in which proper action levels can be determined.

To examine the impact on the treatment delivery of the optimization tools provided by NEMO X we made *a posteriori* analysis of 91 patients treated with IOERT after breast lumpectomy. The main characteristics of analyzed treatments are summarized in Table 1.

For each patient the MUs were calculated by hand calculation with beam energy and dose normalization chosen on-line by the medical physicist. Correction for daily output was always considered if exceeding 3%. MOSFETs, operated in Standard Bias Mode (nominal sensitivity = 1 mV/cGy), were previously inter-calibrated for each energy with the Roos chamber directly on the LIAC accelerator.

The *a posteriori* analysis of the treatment data investigated two end-points: dose homogeneity within the target and in-vivo dose prediction. For dose homogeneity we compared the MTD, the V95 and V107 percentages calculated with real treatment data (i.e. dose normalization chosen at treatment time) vs. the values calculated with auto-norm. For in-vivo dose prediction we investigated the agreement between the in-vivo dose measured with MOSFETs and NEMO X's best guess. Statistical analysis of the results included significance tests (Wilcoxon signed-rank test or χ^2 variance test) rated as p-values. Tests with p-values >0.05 were scored as not significant (NS).

Results

Dose homogeneity

Dose homogeneity was found to be good in almost all the examined treatments with a general tendency to over-dose the target. Fig. 1 compares the MTD calculated using real treatment data compared to NEMO X's auto-norm. We see that auto-norm does a better job in keeping the MTD close to the prescription value in a consistent manner: using auto normalization |MTD–PD|/PD is within 5% in 95% of the patients, while this result drops to 53% using conventional normalization rules.

Table 1
Main characteristics of analyzed treatments.

	$n = 91$	%
Energy (MeV)		
4	1	1
6	14	15
8	36	40
10	40	44
Applicator (cm)		
4	16	18
5	47	52
6	28	30
PD (Gy)		
10	11	12
18	27	30
21	53	58
N (%)		
Other	5	5
90	50	55
95	31	34
100	5	6
Target thickness	Range (mm)	Mean (mm)
Min.	2–20	9
Max.	5–25	17

Abbreviations: PD, prescription dose; N, normalization.