Physica Medica ■■ (2015) ■■–■■

Contents lists available at ScienceDirect

Physica Medica

journal homepage: http://www.physicamedica.com

Original Paper

Monte Carlo evaluation of the effect of inhomogeneities on dose calculation for low energy photons intra-operative radiation therapy in pelvic area

Sophie Chiavassa [a,*], François Buge [b], Chloé Hervé [a], Gregory Delpon [a], Jérome Rigaud [b], Albert Lisbona [a], Stéphane Supiot [c]

[a] Medical Physics Department, Institut de Cancérologie de l'Ouest, Bld Jacques Monod, 44805 St Herblain Cedex, France
[b] Nantes University Hospital, 1 place Alexis Ricordeau, 44000 Nantes, France
[c] Department of Radiation Oncology, Institut de Cancérologie de l'Ouest, Bld Jacques Monod, 44805 St Herblain Cedex, France

ARTICLE INFO

Article history:
Received 16 February 2015
Received in revised form 10 June 2015
Accepted 3 July 2015
Available online

Keyword:
Monte Carlo
Intra-operative radiation therapy
Inhomogeneities
Pelvis

ABSTRACT

The aim of this study was to evaluate the effect of inhomogeneities on dose calculation for low energy photons intra-operative radiation therapy (IORT) in pelvic area. A GATE Monte Carlo model of the INTRABEAM® was adapted for the study. Simulations were performed in the CT scan of a cadaver considering a homogeneous segmentation (water) and an inhomogeneous segmentation (5 tissues from ICRU44). Measurements were performed in the cadaver using EBT3 Gafchromic® films. Impact of inhomogeneities on dose calculation in cadaver was 6% for soft tissues and greater than 300% for bone tissues. EBT3 measurements showed a better agreement with calculation for inhomogeneous media. However, dose discrepancy in soft tissues led to a sub-millimeter (0.65 mm) shift in the effective point dose in depth. Except for bone tissues, the effect of inhomogeneities on dose calculation for low energy photons intra-operative radiation therapy in pelvic area was not significant for the studied anatomy.

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Introduction

Intra-operative radiation therapy (IORT) consists of irradiating the tumor bed during surgery. This technique offers several potential advantages, including better targeting of tumor cells and a drastic reduction in total treatment time [1,2]. Its low energy photons or electrons allow a steep dose falloff, sparing normal tissues. Small mobile X-ray generators are increasingly used in IORT [3–7]. The INTRABEAM® system, a 50 kV X-ray generator (Carl Zeiss Surgical, Oberkochen, Germany), has been in clinical use for over ten years, predominantly for breast irradiation [8]. The 50 kV X-ray source is placed at a fixed position in a spherical applicator designed to obtain an isotropic photon beam at the applicator's surface. The applicator's diameter is chosen to obtain perfect tissue adhesion at the applicator's surface and to control the irradiation geometry. Dose calculation delivered with the INTRABEAM® system is usually performed in a large volume of water, neglecting the tissues inhomogeneities and the potential lack of backscatter due to air interfaces behind the target tissue. However, the impact of tissue composition and density is highly significant when low energy photons are employed because of the atomic number dependence of the photoelectric effect ($Z^{\approx 3}$). In a previous study, Ebert and Carruthers evaluated the impact of such assumption for breast irradiation [6]. According to Ebert and Carruthers, the maximal variations in dose deposition in breast tissues relative to water ranged from 10% to 2% depending on the applicator's diameter. Moreover, they showed that the dose delivered to bone adjacent to the treatment site was significantly higher than dose to water at all depths. This behavior increased dramatically when the distance between bone and applicator's surface decreased leading to a higher risk of rib fracture in case of deep-seated tumors or small-breasted, low-weight women. Finally, Ebert and Carruthers [6] evaluated the dose reduction due to the absence of backscatter in the presence of a tissue/air interface of the order of 20–40%.

Combined surgery and adjuvant radiotherapy with external beam radiation therapy (EBRT) is a standard of care for prostate cancer. Postoperative irradiation is usually carried out between 3 and 6 months after surgery in order to allow for a better sphincter recovery. However, this long time period exposes the patients to the risk of residual tumor growth and metastatic spread, especially for poorly differentiated tumors. In this context, IORT could replace EBRT advantageously. Thoms et al. showed that locally advanced high-risk prostate cancer is a suitable location for IORT [9]. To our knowledge, all current techniques of IORT for prostate bed are based

* Corresponding author. Medical Physics Department, Institut de Cancérologie de l'Ouest, Bld Jacques Monod, 44805 St Herblain Cedex, France. Tel.: +33 0 2 40 67 99 53; fax: +33 0 2 40 67 97 52.
E-mail address: sophie.chiavassa@ico.unicancer.fr (S. Chiavassa).

http://dx.doi.org/10.1016/j.ejmp.2015.07.144
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on electron beams (IOERT). Results of clinical studies show that IOERT is safe and feasible for the treatment of high-risk prostate cancer, with a low complication rate after short-intermediate follow-up [10–14]. Krengli et al. showed the potential strength of IOERT in locally advanced prostate cancer but highlighted some limitations such as the relatively small number of patients in clinical studies and the lack of availability of the appropriate radiotherapy equipment in operating theatres worldwide [15]. The use of a dedicated system with low energy photons could facilitate the development of this technique. Nevertheless, pelvic area is complex with the presence of bone tissue (symphysis and ischiopubic rami) and air (rectal gas or surgical cavities). Despite the clinical use for breast cancer, the impact of dose calculation approximation (infinite water volume) has to be evaluated in this treatment site.

The aim of this study was to evaluate the dosimetric impact of inhomogeneities in the pelvic area for low energy photons IORT in the prostate bed. Monte Carlo dose calculations were computed in the CT scan of a cadaver with and without tissue considerations for the INTRABEAM® system. Both calculations were compared to EBT3 measurements in the cadaver.

Materials and methods

INTRABEAM® system

The INTRABEAM® X-Ray Source (XRS) device (Carl Zeiss Surgical, Oberkochen, Germany), which has been described elsewhere extensively [3–5] produces up to 50 kVp X-rays from a near-isotropic effective point source. Spherical polyetherimide (PEI, (C37H24O6N2)) applicators were developed for breast irradiation with diameters of 15–50 mm in 5 mm increments. Spherical applicators are placed in the tumor bed. The position of XRS inside the applicator is fixed. This position and the applicator design allow to obtain an isotropic photon beam at the applicator's surface. Using a water phantom and soft X-ray ionization chambers (type 23342 for relative measurements and 34013 for absolute measurements, PTW, Freiburg, Germany), the manufacturer has already determined the theoretical absolute depth dose rate (DDR, Gy/min) curve in water for each XRS, and the transfer coefficient (TC) curve representative of the influence of each applicator. These manufacturer's data are supplied with each source or applicator and entered by the user in the software that controls the system. The absolute dose rate at a given depth for a specific XRS/applicator pair is obtained from equation 1:

$$\dot{D}(z)_{XRS/A} = \dot{D}(z)_{XRS} \times Transfer\ Coefficient\,(z)_A \quad (1)$$

Where $\dot{D}(z)_{XRS/A}$ is the absolute dose rate at a given depth z for the given XRS/applicator A pair, $\dot{D}(z)_{XRS}$ is the absolute dose rate at the given depth z for XRS source and $Transfer\ Coefficient\,(z)_A$ the transfer coefficient factor at the given depth z for the applicator A.

DDR and TC curves are measured along the probe axis, and the isotropy of the XRS/applicator pair is assumed to be theoretically perfect when calculating treatment delivery. However, although neglected, the beam anisotropy is not zero. According to the manufacturer, maximal anisotropy is −7% and −8% for the XRS and the 50 mm applicator respectively, leading to a maximal anisotropy of −15% for the complete system.

Monte Carlo simulations

GATE (Geant4 Application for Tomography Emission) is a Monte Carlo code originally developed for positron emission tomography and single-photon emission computed tomography [16]. A recent release (v6.0) enables simulation of external beam radiation therapy, brachytherapy and IORT through the use of dose actors [17]. A dose actor stores the dose deposited in a given volume into a 3D image according to the spatial position of the hits and takes into account the weight of the particles. GATE v6.2 based on the Geant4 v9.3 libraries was used in this study.

The initial model of INTRABEAM® was taken from Bouzid et al. [18]. It consists of a mathematical description of the XRS. Photons are emitted isotropically from a hemispherical surface (radius 1.6 mm) centered on the effective source position. Spherical PEI applicators from 35 to 50 mm of diameter were modeled. The initial model was adapted for our study with the modification of physical processes, energy cuts and the XRS position.

In the initial model, for electron tracking, the Geant4 standard energy model, including electron ionization and multiple scattering, was selected. For photon tracking, Geant4 standard energy model including Compton scattering and photoelectric effect was selected. Both models are effective above 1 keV. In this study, as we used a reduced voxel size for the anatomical study (from $1 \times 1 \times 1\ mm^3$ to $0.43 \times 0.43 \times 1\ mm^3$) and we focused on inhomogeneities interfaces, we replaced the standard model by the Livermore model [19,20] for photon tracking. Indeed, this model includes Rayleigh scattering above 250 eV. A production threshold below which no secondary particle will be generated was set to 0.02 mm for photons and electrons. In GATE v6.2, a production threshold defined as a distance is internally converted to an energy for individual materials. These physical processes and cuts were applied both in applicators, water tank and cadaver.

Preliminary simulations were performed to adjust the XRS position inside the applicator. The ideal position was determined by MC simulations to obtain an isotropic distribution in 3 dimensions around the applicator (Fig. 1a). All simulations were performed on the GateLab system which makes infrastructure for computationally intensive studies available online [21]. The simulation jobs were split into 25 sub-simulations requiring 6 to 7 hours of system time.

Simulation in a water tank

Using the modified Monte Carlo model, the absorbed dose was calculated in a $20 \times 20 \times 16\ cm^3$ water tank with a resolution grid of $1 \times 1 \times 1\ mm^3$. The applicator composition was considered to be PEI. DDR curve was extracted from this 3D dose distribution and compared with manufacturer's values in order to validate the dose calculation in water for reference conditions. Three billion photons were generated to reach 5% maximal statistical uncertainty.

In parallel, in the same reference conditions, a phase-space file (PSF) was created at the 50 mm applicator's surface. The PSF scored energy, position and direction of each photon crossing the applicator's surface. As the applicator has fixed geometry, the use of a PSF reduces effectively the computation time avoiding tracking particles from the source. It is composed of 1.234 billion photons. Due to beam hardening, the average energy spectrum increased from 20 keV for the XRS to 29 keV for the phase-space at the 50 mm applicator's surface. Photons are emitted isotropically at the surface of the phase-space except in the area of the shank (Fig. 1b). Finally, a conversion factor was determined to calculate the dose rate distribution in Gy/min from the MC simulation for the 50 mm applicator (equation 2):

$$C_{MC,50mm} = \left(\frac{\dot{D}_{ZEISS}}{\dot{D}_{MC}} \right)_{50mm} \quad (2)$$

Where $C_{MC,50mm}$ is the conversion factor in incident particle/min, $\dot{D}_{ZEISS}$ is the manufacturer's dose rate in Gy/min at the applicator's surface and $\dot{D}_{MC}$ is the Monte Carlo dose in Gy/incident particle at the applicator's surface.

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