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Original paper

Monte Carlo study of the influence of energy spectra, mesh size, high Z element on dose and PVDR based on 1-D and 3-D heterogeneous mouse head phantom for Microbeam Radiation Therapy

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ABSTRACT

Purpose: To evaluate the influence of energy spectra, mesh sizes, high Z element on dose and PVDR in Microbeam Radiation Therapy (MRT) based on 1-D analogy-mouse-head-model (1-D MHM) and 3-D voxel-mouse-head-phantom (3-D VMHP) by Monte Carlo simulation.
Methods: A Microbeam-Array-Source-Model was implemented into EGSnrc/DOSXYZnrc. The microbeam size is assumed to be 25 μm, 50 μm or 75 μm in thickness and fixed 1 mm in height with 200 μm c-t-c. The influence of the energy spectra of ID17@ESRF and BMIT@CLS were investigated. The mesh size was optimized. PVDR in 1-D MHM and 3-D VMHP was compared with the homogeneous water phantom. The arc influence of 3-D VMHP filled with water (3-D VMHWP) was compared with the rectangle phantom.
Results: PVDR of the lower BMIT@CLS spectrum is 2.4 times that of ID17@ESRF for lower valley dose. The optimized mesh is 5 μm for 25 μm, and 10 μm for 50 μm and 75 μm microbeams with 200 μm c-t-c. A 500 μm skull layer could make PVDR difference up to 62.5% for 1-D MHM. However this influence is limited (<5%) for the farther homogeneous media (e.g. 600 μm). The peak dose uniformity of 3-D VMHP at the same depth could be up to 8% for 1.85 mm × 1 mm irradiation field, whereas that of 3-D VMHWP is <1%. The high Z element makes the dose uniformity enhance in target. The surface arc could affect the superficial PVDR (from 44% to 21% in 0.2 mm depth), whereas this influence is limited for the more depth (<1%).
Conclusion: An accurate MRT dose calculation algorithm should include the influence of 3-D heterogeneous media.

1. Introduction

Microbeam Radiation Therapy (MRT) and Stereotactic Synchrotron Radiotherapy (SSRT) are both novel approaches to treat brain tumor and potentially other tumors using Synchrotron Radiation (SR) [1]. MRT uses highly collimated, quasi-parallel arrays of X-ray microbeams based on the very small beam divergence and an extremely high dose rate of highly brilliant SR sources [2]. Biology experiments have proved that the peak entrance doses of several hundreds of Gy are extremely well tolerated by normal tissues and at the same time provide a higher therapeutic index for various tumor models in rodents for MRT [3]. The hypothesis of a selective radio-vulnerability of the tumor vasculature versus normal blood vessels by MRT was recently more solidified [1]. MRT has been believed that has matured into a technique to be promoted soon for clinical trials after a vast amount of experience together with preclinical data accumulated over the past 25 years [1].

Dose measurements in MRT are difficult due to the high dose rates (8–16 kGy/s for SR) and the demands on the spatial resolution. Measuring the low energy photons also is a challenge for the commonly used radiation detectors [1]. Dose calculation is critical factor for the optimization and validation of Treatment Planning System (TPS). A fast convolution based algorithm was introduced by Bartzsch et al. [4] and implemented in the VIRTOUS platform based on the spatial repeatability of microbeam. But convolution algorithm only uses additional and approximate scaling rules (e.g. Equivalent Pathlength method (EPL)) to correct the influence of inhomogeneous media, which causes the dose distribution inaccuracy like in CT phantom. Although the small dimension of microbeam and center-to-center (c-t-c) distance can partly compromise the inaccuracy, the influence of small dimension

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heterogeneous media, e.g. at micron or nanometer scale, needs more evaluating quantitatively [5,6].

Monte Carlo simulation is the most accurate method of dose determination in MRT, as well as the best-suited method for MRT plan verification [7], which can be used to study the influence of various materials and sizes of heterogeneous media. Siegbahn et al. [8] has compared several MC codes, including PENELOPE, GEANT and the improved EGSnrc version, which were determined to be adequate codes for dosimetric studies in MRT due to their advanced low energy electron and photon tracking libraries. A comprehensive MC study comparing different field sizes, target sizes and geometries was performed by Anderson et al. [9]. Adequate results from research efforts including Monte Carlo simulations are prerequisite before new techniques and means being transferred to clinical trials [1].

Water phantoms were used in most of the previous MC studies [8,10]. Some studies used mathematical head phantoms to evaluate the dose distribution by MC dosimetric calculation [5,11,12]. However, Martinez-Rovira et al. [5] has pointed out that the use of realistic phantoms is essential for correct dose assessment. Gokeri et al. [6] has used a realistic (Zubal) head phantom to study the effect of its structure on the obtained dose distribution by Monte Carlo code MCNPX. Whereas the Zubal head phantom is relatively too large for low energy microbeam SR source, thus the heterogeneous media effect is limited except for the skull layer and high Z element. As to the small animal preclinical trial, as well as the SR microangiography [13], the influence of heterogeneous media actually could be notable. The validation of common used EPL in MRT TPS would also face rigorous challenge in a real 3-D heterogeneous mouse head phantom.

A local drug uptake of high-Z elements is used to enhance the dose deposition within the tumor, which is the typical feature of SSRT different from MRT. However, although SSRT and MRT differing by their principles, the techniques could share certain common aspects with the possibility of combining their advantages in the future [1]. The monochromatic Minibeam Radiation Therapy (MBRT) technique is being developed to improve the normal tissue sparing effect. The first experiments in MBRT (600 μm-wide beams, 1200 μm c-t-c) confirmed that this technique keeps (part of) the sparing tissue capability observed in the thinner microbeam, while significant tumor growth delay was still observed [14].

How about the effect of heterogeneous media at small scale on PVDR (Peak to Valley Dose Ratio) of microbeams for e.g. small animal mouse preclinical trial? Many interesting questions like the influence of different realistic poly-energetic spectra, air layer before skin, the arc shape of irradiated body like mouse head, and the high Z element etc. on PVDR at small scale, which have seldom been studied for MRT so far.

This work studied the effect of energy spectra, mesh sizes, high Z element on dose and PVDR in MRT using adapted Monte Carlo code EGSnrc/Dosxyznrc based on 1-D heterogeneous model and 3-D mouse head phantom. PVDR index was used to display the influence for it reflects the specific local feature, not the mean volumetric effect.

2. Materials and methods

2.1. SR irradiation source

The radiation source is assumed to be a synchrotron radiation source. Simulations were performed using the characteristics of the ID17 beamline of the European Synchrotron Radiation Facility (ESRF, Grenoble, France) (i.e. ID17@ESRF hereafter) and the BMIT 05ID-2 beamline at the Canadian Light Source (CLS) (i.e. BMIT@CLS hereafter). Their energy spectra are from the published work [8,9].

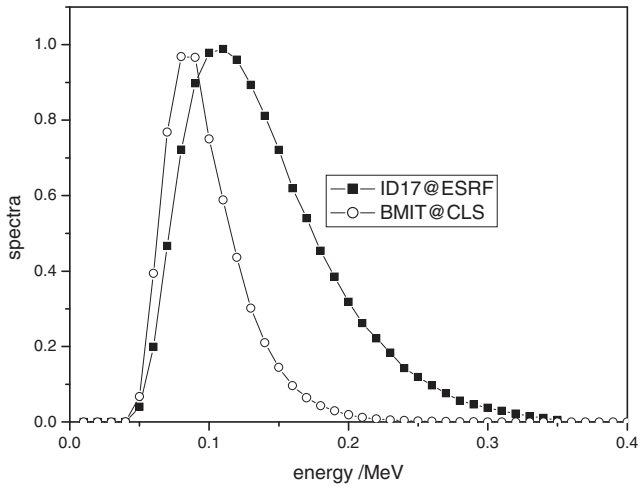

Fig. 1. The energy spectra of ID17@ESRF and BMIT@CLS for Monte Carlo simulation.

The BMIT@CLS energy spectrum with a most probable energy of 83 keV and a mean energy of 99 keV, which is slightly lower compared to the most probable energy of 109 keV and the mean energy of 107 keV [8] of ID17@ESRF (Fig. 1). The ID17@ESRF spectrum is an experimental spectrum [6,15] and widely used in published research work [6,16]. The BMIT@CLS spectrum also has been verified by comparing the Monte Carlo simulated percent depth dose (PDD) curve in water with a measurement by a thimble ionization chamber (Wellhofer IC-10) [17]. For the comparison convenience with their published research work [6,9,16], the initial energy of the unpolarized primary photon is assumed to be sampled from these energy spectra, and incidents on a phantom. The effect of different realistic SR poly-energetic spectra on PVDR was studied.

Some work indicates that the adverse effects or normal tissue complications do only correlate with the valley dose and not with the peak dose for microbeam sizes between 25 μm and 75 μm FWHM [1]. And a narrow c-t-c is more effective for tumor growth suppression than a wide one [18]. Considering the statistical uncertainty of Monte Carlo convergence, the unidirectional irradiation beam is assumed to be spatially fractionated into an array of rectangular microbeams of 25, 50 or 75 μm in thickness (i.e. width) and fixed 1 mm in height. The middle c-t-c spacing of 200 μm in X direction (i.e. width direction) was considered.

Considering the spatial repeatability of microbeams and the simulation intensity of Monte Carlo method, a relative small field like ~1.9 mm (W) × 1.1 mm (H) was investigated, which is a 10 × 1 microbeam array for 25 μm (or 50 μm, or 75 μm) in thickness and 200 μm c-t-c like Ref. [16].

2.2. High Z element

High Z elements like iodine (Z = 53) and Gd (Z = 64) contrast agents (e.g. Iopamiro and Gd-DTPA) used in medical images often have been used in SSRT research [1,19]. The irradiation is assumed to be performed in the presence of an iodinated contrast agent, which previously was introduced into the target. Due to an increased photoelectric absorption of X-rays, a localized dose enhancement will occur in the volume where the contrast agent leaks from the capillaries when compared to the healthy brain where the iodine concentration remains negligible. The high Z element concentration in the tumor is assumed to vary from 0 to 5, to 20 mgIml^{-1} with density varying from 1, to 1.005 to 1.02 g/cm^3.

The high Z materials needed by EGSnrc simulation were produced by PEGS4 (preprocessor for EGS), which is a stand-alone utility program written in Mortran language aiming at generating

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