Physica Medica 45 (2018) 156–161

Contents lists available at ScienceDirect

Physica Medica

journal homepage: www.elsevier.com/locate/ejmp

Original paper

Experimental optimisation of the X-ray energy in microbeam radiation therapy

Jayde Livingstone[a,*], Andrew W. Stevenson[a], Daniel Häusermann[a], Jean-François Adam[b,c]

[a] Australian Synchrotron, Australian Nuclear Science and Technology Organisation, 800 Blackburn Road, Clayton, Victoria, Australia
[b] Equipe d'accueil Rayonnement Synchrotron et Recherche Médicale, Université Grenoble-Alpes, Grenoble, France
[c] Centre Hospitalier Universitaire de Grenoble, Grenoble, France

ARTICLE INFO

Keywords:
Diamond detectors
Microbeam radiation therapy
Synchrotron

ABSTRACT

Microbeam radiation therapy has demonstrated superior normal tissue sparing properties compared to broad-beam radiation fields. The ratio of the microbeam peak dose to the valley dose (PVDR), which is dependent on the X-ray energy/spectrum and geometry, should be maximised for an optimal therapeutic ratio. Simulation studies in the literature report the optimal energy for MRT based on the PVDR. However, most of these studies have considered different microbeam geometries to that at the Imaging and Medical Beamline (50 µm beam width with a spacing of 400 µm). We present the first fully experimental investigation of the energy dependence of PVDR and microbeam penumbra. Using monochromatic X-ray energies in the range 40–120 keV the PVDR was shown to increase with increasing energy up to 100 keV before plateauing. PVDRs measured for pink beams were consistently higher than those for monochromatic energies similar or equivalent to the average energy of the spectrum. The highest PVDR was found for a pink beam average energy of 124 keV. Conversely, the microbeam penumbra decreased with increasing energy before plateauing for energies above 90 keV. The effect of bone on the PVDR was investigated at energies 60, 95 and 120 keV. At depths greater than 20 mm beyond the bone/water interface there was almost no effect on the PVDR. In conclusion, the optimal energy range for MRT at IMBL is 90–120 keV, however when considering the IMBL flux at different energies, a spectrum with 95 keV weighted average energy was found to be the best compromise.

1. Introduction

Spatial fractionation in the context of radiotherapy is the practice of collimating a beam into an array of smaller beams to deliver a non–-homogeneous distribution of radiation dose to the target. It is a concept that was first introduced to radiotherapy more than half a century ago via grid therapy [1]. Grid therapy was at first performed using orthovoltage X-ray tubes but later transferred to megavoltage (MV) linacs [2,3]. In grid therapy, the beam is collimated into smaller beams (1 cm wide) to allow delivery of high doses to deep-seated tumours whilst minimising damage to skin [4], thus enhancing the therapeutic ratio. The tissue sparing effects of microbeams were first shown in the 1960s using 25 µm wide deuteron beams to simulate heavy cosmic ray particles [5,6]. When compared with 1 mm wide deuteron beams, it was found that tissues and cells irradiated with the microbeam could withstand much higher doses before cell death was observed. This illustrates that the tissue sparing effect increases with decreasing irradiation volume. Since the 1990s synchrotron microbeam radiation therapy has been under development and continued to demonstrate a sparing effect in many normal tissues [7–15]. Radiation resistant brain tumours, particularly in infants, have been identified as a suitable target patient group for MRT due to the ability to deliver extremely high doses without causing significant damage to the surrounding healthy brain [16–18].

Various irradiation geometries, based on different ratios of irradiated and "unirradiated" tissue, have been theoretically and experimentally investigated in an attempt to optimise the therapeutic ratio [19–22]. Based on the findings of these investigations, the Imaging and Medical Beamline (IMBL) at the Australian Synchrotron has settled on a fixed geometry of 50 µm wide microbeams separated (centre-to-centre) by 400 µm.

Kilovoltage synchrotron wiggler generated x-rays are ideal for creating such arrays of microbeams as the small lateral range of secondary electrons results in a very steep dose gradient between the peaks and the regions of lower dose, "valleys" between the peaks. The low beam divergence also allows the microbeams to be preserved as the beam penetrates absorbing material. Since the valley dose is believed to be linked to the normal tissue tolerance [10,23], it is important to

* Corresponding author.
E-mail address: Jayde.Livingstone@synchrotron.org.au (J. Livingstone).

https://doi.org/10.1016/j.ejmp.2017.12.017
Received 28 September 2017; Received in revised form 18 December 2017; Accepted 23 December 2017

maintain a low valley dose and high peak-to-valley-dose ration, or PVDR. The most important disadvantage of kV photons is the reduced penetration in matter. For deep-seated tumours, it may thus be necessary to make a compromise between PVDR and beam penetration. A number of Monte Carlo based investigations have been performed to characterise the energy dependence of the PVDR [20,24–28]. Shinohara et al. [28] made a recommendation on the optimal energy range, 100–300 keV, for MRT treatment of deep-seated tumours and Prezado et al. [27] found the optimal energy to be 175 keV. However, of the studies mentioned, only one [27] is based on the same microbeam geometry used at IMBL. Furthermore, to the knowledge of the authors, no experimental investigation of the energy dependence of the PVDR has been performed. Experimental data is required to verify the simulation results.

This study aims to present the optimal energy range for synchrotron MRT based on measurements of PVDR and microbeam penumbra as a function of beam energy. Given the interest in brain tumours as a clinical case for MRT, the effect of bone on the PVDR at depth has been investigated using a simple phantom to approximate a human head.

2. Materials and methods

2.1. X-ray source

This study was performed using the preclinical radiotherapy instrumentation in Hutch 2B of the Imaging and Medical Beamline (IMBL) at the Australian Synchrotron [29].

Both polychromatic and monochromatic X-ray beams were used in this investigation of microbeam peak to valley dose ratio as a function of X-ray energy. The IMBL X-ray source is a superconducting multipole wiggler with a maximum operating magnetic field of 4.2 T and typical operating field of 3.0 T. The latter was used for this study. The wiggler produces a high flux of x-rays in the kV energy range, peaking around 20 keV. Filtering the X-ray beam using metallic foils such as copper, aluminium and molybdenum changes the shape of the spectrum. Different combinations of filters can be inserted in the beam to give the desired mean energy or X-ray flux. Filtered beams are referred to as "pink" beams. The program *spec.exe* described by Stevenson et al.[30] was used to calculate parameters such as the peak energy, weighted mean energy and half-value layer for given combinations of filters or pink beams. A summary of the filtrations used and the corresponding parameters is given in Table 1 and a graphical representation of the spectra is given in Fig. 1. Monochromatic beams in the range 40–120 keV were selected from the Al-Al filtered spectrum using the silicon crystal monochromator. The energy resolution ($\Delta E/E$) of the IMBL monochromator is of the order of 10^{-3}. Pink beams with weighted average energies of 82.9, 95.1 and 124 keV were used in the study.

Microbeams are produced by a multislit collimator (Usinage et Nouvelles Technologies, Morbier, France), which collimates the beam into 125 vertical microbeams of 50 mm width with a 400 mm centre-to-centre (c-t-c) spacing [29]. Tungsten carbide layers of 350 mm are sandwiched together to create a 50 mm spacing between them. The tungsten carbide layers are 8 mm thick in the beam direction. The multislit collimator is housed in an aluminium box (fabricated at the Australian Synchrotron) which is flushed with helium gas and water-cooled. Kapton entrance and exit windows minimise beam perturbance. For alignment with the beam, the collimator was rotated about the z (vertical) axis. The current recorded from a free-air ionisation chamber immediately downstream of the collimator was simultaneously recorded, and the angle of the collimator (with respect to the vertical axis) was set to the angle at which the maximum current was recorded.

Table 1
Peak energy, weighted average energy and aluminium half-value layers for the spectra produced by each filtration combination.

Filter name	Peak energy (keV)	Weighted ave. energy (keV)	HVL Al (mm)
Al-Al	47.8	55.0	6.27
Al-Cu	76.2	82.9	11.9
Cu-Cu	87.5	95.1	13.6
AlMo-AlMo	117	124	16.5

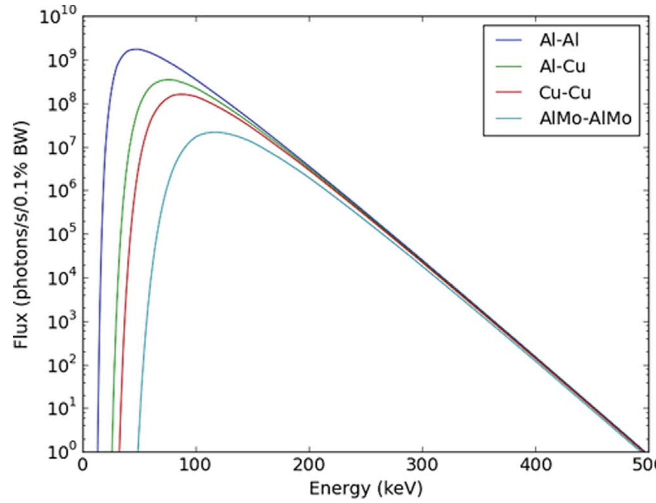

Fig. 1. The spectra produced by the different filtration combinations given in Table 1.

2.2. Measurements

Dosimetric measurements were performed using a PTW (Freiburg, Germany) microDiamond 60019 detector read-out using a PTW Unidos Webline electrometer. Lateral profiles were acquired over the central 1.2 mm (corresponding to three microbeam peaks and two valleys) of the beam at various depths in a water phantom using the method described in [31]. The PVDR was calculated using the mean of the three peak doses and the mean of the doses in the central 100 µm of the two valleys. For a graphical representation of the points used to calculate the PVDR in an example profile exhibiting four peaks and three valleys, see §2.3 of [29]. The PVDR was measured for monochromatic energies between 40 and 120 keV at depths of 5, 10, 20 and 50 mm in a water tank. As MRT studies are typically performed using a pink beam, the relationship between PVDR and pink beam energy (82.9, 95.1 and 124 keV) was also measured at the same measurement depths. Percentage depth dose curves (PDD) were also acquired in the water tank for beams of different energies.

In addition to comparing PVDRs at different energies, the penumbra, defined as the lateral distance between the 80% and 20% of maximum dose points on one side of a beam profile [32], was also measured as a function of energy. The penumbra was measured on each side of the central microbeam from the lateral profile acquired at each monochromatic energy. This measurement was repeated on profiles acquired at different depths in water (between 5 mm and 50 mm). As it was observed that the penumbra does not change with depth in this range, a mean and standard deviation was calculated using the measurements at different depths.

Radioresistant brain tumours have been identified as a clinical case for MRT. As a result of this, most of the preclinical MRT survival data exists for small animal brain tumour models. To simulate a clinically relevant scenario, Gammex (Middleton, USA) inner bone (456) equivalent material was positioned at the entrance of the water tank to approximate an adult male head. The thickness of bone material used was 8 mm, which closely approximates the average thickness of the frontal and occipital regions of the adult male skull [33]. Lateral profiles and PVDRs were obtained using the same method described above and PVDRs were compared to those obtained in the absence of bone