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Microdosimetry study of THOR BNCT beam using tissue equivalent proportional counter

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ABSTRACT

Boron neutron capture therapy (BNCT) is a cancer treatment modality using a nuclear reactor and a boron compound drug. In Taiwan, Tsing Hua open-pool reactor (THOR) has been modulated for the basic research of BNCT for years. A new BNCT beam port was built in 2004 and used to prepare the first clinical trial in the near future. This work reports the microdosimetry study of the THOR BNCT beam by means of the tissue equivalent proportional counter (TEPC). Two self-fabricated TEPCs (the boron-doped versus the boron-free counter wall) were introduced. These dual TEPCs were applied to measure the lineal energy distributions in air and water phantom irradiated by the THOR BNCT mixed radiation field. Dose contributions from component radiations of different linear energy transfers (LETs) were analyzed. Applying a lineal energy dependent biological weighting function, $r(y)$, to the total and individual lineal energy distributions, the effective relative biological effectiveness (RBE), neutron RBE, photon RBE, and boron capture RBE (BNC RBE) were all determined at various depths of the water phantom. Minimum and maximum values of the effective RBE were 1.68 and 2.93, respectively. The maximum effective RBE occurred at 2 cm depth in the phantom. The average neutron RBE, photon RBE, and BNC RBE values were 3.160 ± 0.020, 1.018 ± 0.001, and 1.570 ± 0.270, respectively, for the THOR BNCT beam.

1. Introduction

Tsing Hua open-pool reactor (THOR), a 2 MW research reactor at the National Tsing Hua University in Taiwan, has been used in a feasibility study for boron neutron capture therapy (BNCT) for years. A new BNCT beam port was built in 2004 and used to prepare the first clinical trial in the near future. BNCT is a binary therapy involving two components: a boron-labeled compound that is administered to the patient and that accumulates in tumour cells; and irradiation by an epithermal neutron beam. The neutron beam induces the $^{10}B(n,\alpha)^{7}Li$ capture reaction that emits very short-ranged and high linear energy transfer (LET) particles. These particles have a high probability of selectively killing the boron-loaded tumour cells. The relative biological effectiveness (RBE) and the consequent therapeutic efficacy of BNCT are due to the range-energy properties of the secondary particles, the boron micro-distribution and the morphological properties of cells. Because of the scale of events, microdosimetric analysis is the method of choice in modeling radiation effects. The spectrum of lineal energy, a microdosimetric parameter defined as the deposited energy per event divided by the mean chord length, is an important factor in determining the RBE. This work reports the microdosimetry study of the THOR BNCT beam using the tissue equivalent proportional counter (TEPC). Spectra of the lineal energy were obtained using such paired TEPCs in free air and at various depths in a PMMA phantom. These spectra were determined for various concentrations of boron and different site diameters. The measured lineal energy spectra revealed peaks associated with alpha particles and lithium ions from boron captures, protons from ^{14}N captures and elastic interactions, and contaminating gamma rays. The RBE values were estimated using measured spectra and a biological weighting function that depended on the lineal energy.

2. Materials and methods

Two 2.5 cm diameter TEPCs (boron-doped versus boron-free counter wall) were self-fabricated. These dual TEPCs were applied to measure the lineal energy distributions in air and water phantom irradiated by the THOR BNCT mixed radiation field. The counter walls were made of A-150 tissue equivalent (TE) conducting plastic of 2.5 mm thickness. The filled gas was a standard TE mixture containing 55.4% propane, 39.9% carbon

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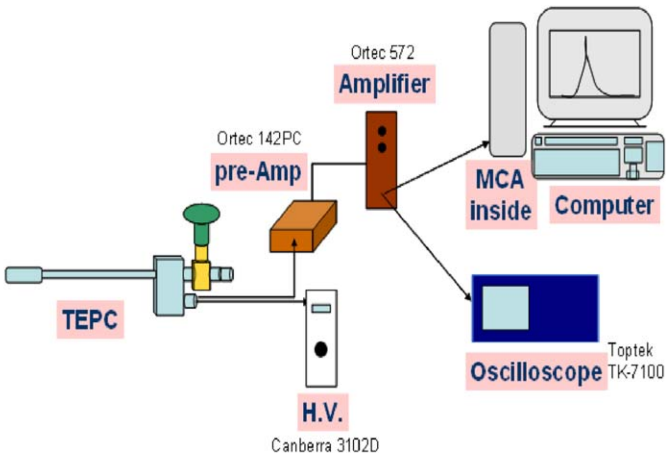

Fig. 1. The schematic diagram of the experimental setup used in microdosimetric measurements.

dioxide, and 4.7% nitrogen by molar weight. When making the measurements, the chambers of TEPCs were filled with TE gas at the pressure of 17 Torr corresponding to simulated cell nuclei with diameters of 1 μm.

Measurements were made using standard microdosimetry equipment including a low-pressure gas flow system, low noise sensitive preamplifier, linear amplifier, oscilloscope, and multi-channel analyzer (MCA) (Hsu et al., 2003). Fig. 1 presents the schematic diagram of the experimental setup for microdosimetric measurements. Due to the wide range of lineal energy distribution for the THOR BNCT mixed radiation field, an americium-241 alpha source and a cesium-137 gamma source were used to calibrate the TEPCs for the radiations with different (high and low) lineal energies.

TEPCs of boron-doped (50 ppm) and boron-free counter walls were used to make comparative measurements. The lineal energy spectra of the BNCT beam were determined from measurement data of such paired TEPCs in free air and at various depths in a PMMA phantom. Counters were positioned at multiple locations in a 16 cm diameter by 22 cm height cylindrical acrylic phantom to simulate the tumors at various depths in a human head. Fig. 2 shows the photos of lineal energy measurements in free air (left) and in a PMMA phantom (right). The phantom was positioned at the location of 6 cm from the exit of the THOR BNCT beam. Microdosimetric data at different depths (0, 2, 4, 6, 8, and 12 cm) were determined.

To determine the relationship between lineal energy and RBE, Pihet et al. (1990) presented a biological weighting function, $r(y)$, from observations of the early radiation damage (such as regenerations of crypt cells) in rats irradiated with neutrons. $r(y)$ is approximately equal to 1 for low lineal energy, but has fluctuation for higher lineal energies. According to the measured spectra of lineal energy, the effective RBE could be calculated from (Coutrakon et al., 1997)

$$\text{effective RBE} = \frac{\int yD(y)r(y)\,\mathrm{d}[\log(y)]}{\int yD(y)\,\mathrm{d}[\log(y)]}. \tag{1}$$

If the spectrum is normalized to a unit dose $d(y)$, i.e.

$$\int yd(y)\,\mathrm{d}[\log(y)] = 1, \tag{2}$$

Eq. (1) becomes

$$\text{effective RBE} = \int yd(y)r(y)\,\mathrm{d}[\log(y)]. \tag{3}$$

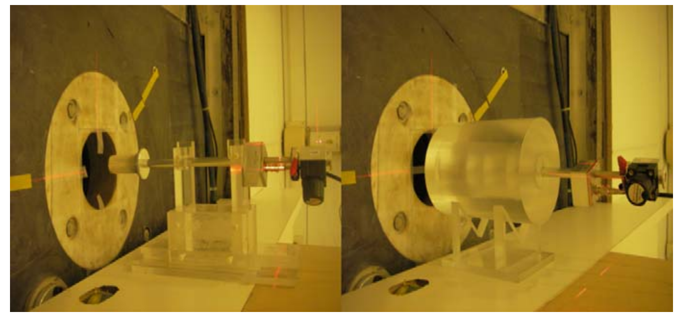

Fig. 2. Photos showing lineal energy measurements in free air (left) and in a PMMA phantom (right).

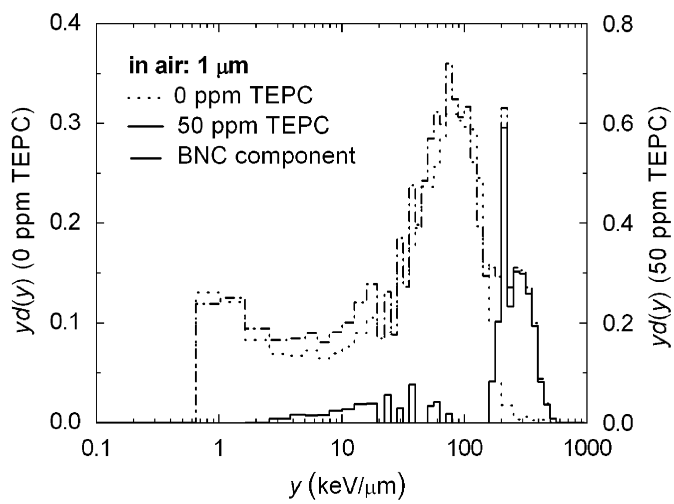

Fig. 3. The lineal energy spectra of the dual TEPCs (0 and 50 ppm boron-doped) measured in air.

In this work, the effective RBE was calculated from Eq. (3) using $d(y)$ of the boron-free TEPC and $r(y)$ of Pihet et al. (1990). The effective RBE is one of the indices characterizing the THOR beam quality.

BNCT dose contributions from component radiations of different LETs were analyzed. Applying the lineal energy dependent biological weighting function, $r(y)$, to the total and individual lineal energy distributions, the effective RBE, neutron RBE, photon RBE, and boron capture RBE (BNC RBE) were determined. Also, the physical dose components, D(BNC), D(neutron), and D(photon), were determined from integrations of the $d(y)$ spectra for the total and individual lineal energy distributions. The RBE dose of the BNCT beam was then calculated from

$$\text{RBE dose} = \text{RBE(BNC)} \times D(\text{BNC}) + \text{RBE(neutron)} \times D(\text{neutron}) + \text{RBE(photon)} \times D(\text{photon}). \tag{4}$$

Alternatively, the RBE dose may be expressed as

$$\begin{aligned}\text{RBE dose} &= \text{effective RBE} \times \sum(\text{physical dose}) \\ &= \text{effective RBE} \times [D(\text{BNC}) + D(\text{neutron}) + D(\text{photon})].\end{aligned} \tag{5}$$

3. Results

Fig. 3 depicts the lineal energy spectra of the dual TEPCs (0 and 50 ppm boron-doped) simulating 1 μm cell nuclei at 6 cm from the