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Original research article

Radiotherapy dose enhancement using BNCT in conventional LINACs high-energy treatment: Simulation and experiment

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ABSTRACT

Aim: To employ the thermal neutron background that affects the patient during a traditional high-energy radiotherapy treatment for BNCT (Boron Neutron Capture Therapy) in order to enhance radiotherapy effectiveness.

Background: Conventional high-energy (15–25 MV) linear accelerators (LINACs) for radiotherapy produce fast secondary neutrons in the gantry with a mean energy of about 1 MeV due to (γ, n) reaction. This neutron flux, isotropically distributed, is considered as an unavoidable undesired dose during the treatment. Considering the moderating effect of human body, a thermal neutron fluence is localized in the tumour area: this neutron background could be employed for BNCT by previously administering ^{10}B-Phenyl-Alanine (^{10}BPA) to the patient.

Materials and methods: Monte Carlo simulations (MCNP4B-GN code) were performed to estimate the total amount of neutrons outside and inside human body during a traditional X-ray radiotherapy treatment.

Moreover, a simplified tissue equivalent anthropomorphic phantom was used together with bubble detectors for thermal and fast neutron to evaluate the moderation effect of human body.

Results: Simulation and experimental results confirm the thermal neutron background during radiotherapy of 1.55E07 cm^{-2} Gy^{-1}.

The BNCT equivalent dose delivered at 4 cm depth in phantom is 1.5 mGy-eq/Gy, that is about 3 Gy-eq (4% of X-rays dose) for a 70 Gy IMRT treatment.

Conclusions: The thermal neutron component during a traditional high-energy radiotherapy treatment could produce a localized BNCT effect, with a localized therapeutic dose enhancement, corresponding to 4% or more of photon dose, following tumour characteristics. This BNCT additional dose could thus improve radiotherapy, acting as a localized radio-sensitizer.

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1. Background

Present-day cancer treatments still require further improvements in order to obtain a better dose control to target volume, reducing the incidence of secondary radio-induced tumours. One of the main drawbacks when dealing with radiotherapy is the necessity to precisely select the cells to be treated, reducing the damage to the healthy ones.

Today the efficiency of newer radio-sensitizers, acting on tumour cells, is investigated in many tumour diseases to improve the radiotherapy efficacy, intended to enhance tumour cell killing while having much less effect on normal tissues.[1] Considering that BNCT[2] (Boron Neutron Capture Therapy) is a selective therapy, because the carrier transporting ^{10}B is preferentially accumulated in tumour cells, in this paper the combined effect of high-energy X-rays radiotherapy coupled with BNCT is studied.

BNCT consists of a two-step procedure: firstly a ^{10}B carrier (usually ^{10}B-Phenyl-Alanine – ^{10}BPA) is administered to the patient; this substance is mainly localized in tumour cells, due to their faster metabolism.[3] Secondly the patient is irradiated with an intense thermal neutron fluence rate; because of the high cross section of ^{10}B for thermal neutrons (3840 barns at 0.025 eV), a nuclear reaction takes place producing heavy fragments from ^{10}B (^{7}Li and ^{4}He) that release their energy inside the cells.[4]

1.1. *Photoneutron production in medical LINACs*

During conventional radiotherapy using high-energy e-LINACs (energy higher than 15 MV) neutron production results from the interaction of high-energy photons with various nuclides present in LINACs gantry. The production is governed by Giant Dipole Resonance reaction (GDR), and neutrons are generated when the incident photon energy exceeds the GDR reaction threshold (6–20 MeV).[6] The nuclear photon absorption cross section, as a function of photon energy E, is described by the Levinger and Bethe formula,[7] in which cross section is proportional to the atomic number Z of the nuclide considered.

Depending on the atomic number Z of the target nucleus, it is thus possible to distinguish two main cases: GDR threshold energy[8] ($E_{GDR,\ Th}$) of about 7–8 MeV for high-Z materials ($Z > 20$, such as Pb, W, Cu, Fe) that compose LINACs head and collimators, and $E_{GDR,\ Th}$ of about 16–18 MeV for low-Z ones ($Z < 20$ such as P, Ca, O, C) that constitute human body. Moreover, resonance peaks are several times higher for high-Z elements respect to low-Z ones (e.g. ^{186}W resonance peak is ≈400 mbarns, at 13.5 MeV; ^{12}C resonance peak is ≈20 mbarns at 24 MeV), so photo-neutron production is more important for high-Z elements. As a matter of fact, in conventional medical LINACs, neutrons production is mainly localized in the accelerator's gantry: target, filters, primary and secondary collimators, as multileaf collimator (MLC) or lead blocks, used for the final shaping of the treatment field, are made by high-Z materials (W, Pb, Au). Only 10% of undesired neutrons are directly produced inside human body in the treatment zone.[9,10]

2. Aim

In this work the possibility to employ the unavoidable thermal neutron background that affects the patient during a standard high-energy radiotherapy[5] treatment for BNCT application is investigated. If ^{10}BPA is previously administered, ^{10}B, especially localized in neoplastic cells, undergoes fission after thermal neutron capture, thus inducing heavy damages to the DNA of the cancer cells themselves, with a specific selectivity. So, the additional BNCT equivalent dose, due to ^{10}BPA administration to the patient, could enhance radiotherapy treatment effectiveness, acting as a localized radio-sensitizer.

3. Materials and methods

3.1. *Simulation method: Monte Carlo MCNP4B-GN code*

Linear accelerators (LINACs) are the most commonly used devices for external beam radiation treatments. Apart from delivering X-rays to the region of interest for tumour treatment, high-energy ($E > 15$ MV) LINACs are the source of photoneutrons due to their inner structure, as explained in the section above, emitting neutrons isotropically from the LINAC head.

In this work Monte Carlo simulations[11] were performed to estimate the total amount of neutrons outside and inside human body during a traditional X-ray radiotherapy treatment. A routine implemented in the MCNP4B code, the MCNP4B-GN code (NEA 1733), especially developed by INFN (National Institute of Nuclear Physics) of Turin, for (γ, n) reaction was used. Its principal aim is to simulate the sophisticated LINACs geometry and to treat the electromagnetic cascade, the photon and electron transport and the photoneutron production by GDR reaction inside e-LINACs gantry and their transport in matter. The technique used is based on the division of space into cells bounded by surfaces of the first and second order as plane, sphere or cylinder. To compile an input

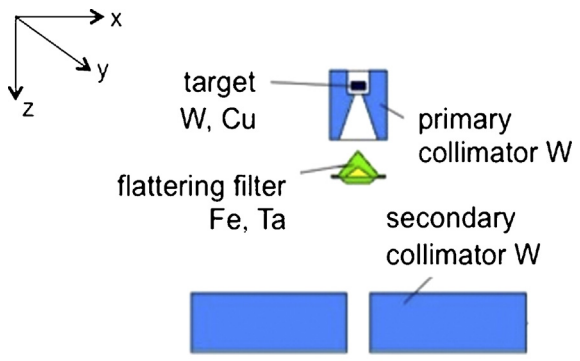

Fig. 1 – LINAC head simulated by MCNP4B-GN code. LINAC VARIAN 2300 CD 18 MV. Target (made up by tungsten and copper), flattering filter (iron and tantalum), primary and secondary collimators (tungsten), are represented. Section on plane y = 0. The origin of the reference system is placed in the centre of target and the z axis is directed downward, along the isocenter line.