Nuclear Engineering and Technology xxx (2016) 1–7

Available online at ScienceDirect

Nuclear Engineering and Technology

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

Original Article

# Investigation of Dose Distribution in Mixed Neutron-Gamma Field of Boron Neutron Capture Therapy using N-Isopropylacrylamide Gel

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ARTICLE INFO

*Article history:*
Received 27 March 2016
Received in revised form
18 July 2016
Accepted 30 July 2016
Available online xxx

*Keywords:*
BNCT
Gel Dosimetry
Mixed Field Dosimetry
NIPAM Polymer Gel
TRR BNCT Beam Line

ABSTRACT

Gel dosimeters have unique advantages in comparison with other dosimeters. Until now, these gels have been used in different radiotherapy techniques as a reliable dosimetric tool. Because dose distribution measurement is an important factor for appropriate treatment planning in different radiotherapy techniques, in this study, we evaluated the ability of the N-isopropylacrylamide (NIPAM) polymer gel to record the dose distribution resulting from the mixed neutron-gamma field of boron neutron capture therapy (BNCT). In this regard, a head phantom containing NIPAM gel was irradiated using the Tehran Research Reactor BNCT beam line, and then by a magnetic resonance scanner. Eventually, the $R_2$ maps were obtained in different slices of the phantom by analyzing T2-weighted images. The results show that NIPAM gel has a suitable potential for recording three-dimensional dose distribution in mixed neutron-gamma field dosimetry.


## 1. Introduction

Boron neutron capture therapy (BNCT) is a chemically targeted radiotherapy that uses the high neutron capture cross section of $^{10}B$ at thermal neutron energies to achieve a preferential dose increase within the tumor volume. In this radiotherapy technique, boron is first selectively accumulated in the tumor cells by a tumor-specific boron carrier, and then the patient is exposed with a neutron beam from a nuclear reactor or an accelerator. A variety of boron delivery agents have been investigated to date, including amino acids, porphyrins, nanoparticles, polyamines, biochemical precursors, DNA-binding agents, sugars, antisense agents, peptides, proteins, monoclonal antibodies, and liposomes. However, there are only two boron delivery agents available for clinical BNCT trials for malignant glioma: $^{10}B$-enriched boronophenylalanine and biodistribution of sodium borocaptate. These drugs are distributed through passive

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http://dx.doi.org/10.1016/j.net.2016.07.012


Please cite this article in press as: E. Bavarnegin et al., Investigation of Dose Distribution in Mixed Neutron-Gamma Field of Boron Neutron Capture Therapy using N-Isopropylacrylamide Gel, Nuclear Engineering and Technology (2016), http://dx.doi.org/10.1016/j.net.2016.07.012

diffusion from the blood to tumor tissues via the disrupted blood–brain barrier. The boron concentration in a normal brain with an intact blood–brain barrier remains minimal, whereas the tumor $^{10}B$ concentration is related to both the tumor vessel density and the blood $^{10}B$ level [1].

In BNCT, the energy of the neutron beam is chosen with respect to the depth of the tumor. Thus, for treating superficial tumors such as melanoma and meningioma, a thermal neutron ($E < 0.5$ eV) or a mixed thermal–epithermal neutron beam is used, whereas epithermal neutron beams (0.5 eV < $E$ < 10 keV) are used for the treatment of deep-seated tumors such as glioblastoma multiforme. Epithermal neutrons are thermalized in tissue, and when they reach the boron-labeled tumor cells, their capture reaction probability by $^{10}B$ isotopes is thus increased. This reaction produces alpha and lithium particles that have high linear energy transfer and release their energy at the cellular level. In addition to the dose resulting from the boron neutron capture reaction, there are three other dose components in BNCT [2]:

1. The gamma dose from neutron beam and $^{1}H(n_{th}, \gamma)^{2}H$ reaction
2. The dose resulting from thermal neutron capture in nitrogen [$^{14}N(n_{th}, p)^{14}C$]
3. Fast and epithermal neutrons dose from the $^{1}H(n,n')^{2}H$ reaction

As with other radiotherapy techniques, the goal of BNCT is to deliver the maximum dose to the tumor and the least dose to the normal healthy tissue for obtaining a high cure rate and limiting radiation toxicity. This goal necessitates the measurement of radiation dose and exact knowledge of radiation effects. Therefore, understanding the radiation field characteristics through measurement of the radiation dose at the desired location of the body is very important. Radiation dosimetry is a process to quantitatively measure the energy deposited in various organs using dosimetric systems with the highest level of accuracy. Dosimetry for BNCT is much more complicated than other radiotherapies because of the various dose components with different relative biological effectiveness. Commonly in the clinical dosimetry of BNCT, the dose from thermal neutron reactions with $^{14}N$ and $^{10}B$ is calculated using the kerma approach, after measuring the thermal neutron flux using the neutron activation technique [2]. Moreover, the dose resulting from fast and epithermal neutrons and photons are determined using the dual ionization chamber technique as described in ICRU Report 45 [2]. These techniques have several drawbacks [3]:

1. These methods are very time consuming.
2. Thermal neutron and boron doses are not measured directly, and the measured thermal neutron flux should be multiplied by the appropriate kerma coefficient for dose evaluation.
3. At least two dosimetry methods are required for calculation of total absorbed dose.
4. Ionization chambers require several correction factors.

To date, numerous studies have been conducted to overcome these drawbacks and improve the absorbed radiation dose measurement in BNCT. In this context, several dosimeters have been evaluated for acceptable application in BNCT dosimetry, considering all advantages and disadvantages, including GafChromic films, TLDs, alanine detectors, and gel dosimeters [3–6]. The radiation-sensitive gels have unique advantages in comparison with other dosimeters. In general, they are tissue equivalent phantom dosimeters capable of measuring three-dimensional (3D) dose distributions with high spatial resolution [7]. To date, several attempts have been made to use gel dosimeters in BNCT dosimetry [8–13]. The results of such studies indicate that dosimeters have significant potential for dose measurement in BNCT.

The main objective of this study is to evaluate the potential of *N*-isopropylacrylamid (NIPAM) gel for recording the 3D dose distribution in Tehran Research Reactor (TRR) BNCT beam line. In this regard, NIPAM gel was irradiated with the neutron beam in an acrylic ellipsoidal head phantom and then imaged by a magnetic resonance (MR) scanner. Subsequently, the T2-weighted images were obtained from different slices of the phantom containing the gel. These images were analyzed using the Matlab software in order to extract the relaxation rate ($R_2$) values. Finally, it was shown that NIPAM gel as a 3D dosimeter has suitable potential for applying in the mixed neutron-gamma field of BNCT.

## 2. Materials and methods

### 2.1. *Gel preparation*

A NIPAM gel dosimeter was prepared using the method proposed by Senden et al [14], inside of a fume hood, and under normal atmospheric conditions. According to this method, gelatin (300 Bloom Type A; Sigma-Aldrich) was added to 80% of deionized water. While the gelatin was dissolving, the temperature was increased to 50°C, and then *N*-*N*′-methylene-bis acrylamide (BIS) (Sigma-Aldrich) was added to the solution as a crosslinker agent for the radiation-induced polymerization process. Following BIS, *N*-isopropylacrylamide (NIPAM; Sigma-Aldrich) was added to the gelatin–BIS mixture after cooling the temperature down to 37°C. When the monomers were completely dissolved, a solution of the antioxidant tetrakis(hydroxymethyl)phosphonium chloride (THPC) with the remaining water was prepared, and added to the solution at 35°C. All chemicals were sourced from Sigma-Aldrich, and their weight percentages in the NIPAM gel formulation are presented in Table 1.

**Table 1 – Elemental composition of NIPAM gel and Kerma factor for each element.**

| Elements | Weight percent |
|---|---|
| H | 10.81 |
| C | 6.51 |
| N | 1.65 |
| O | 80.42 |
| P | 0.29 |
| Cl | 0.33 |

NIPAM, *N*-isopropylacrylamide.

Please cite this article in press as: E. Bavarnegin et al., Investigation of Dose Distribution in Mixed Neutron-Gamma Field of Boron Neutron Capture Therapy using *N*-Isopropylacrylamide Gel, Nuclear Engineering and Technology (2016), http://dx.doi.org/10.1016/j.net.2016.07.012