CURRENT RESEARCH ON ACCELERATOR-BASED BORON NEUTRON CAPTURE THERAPY IN KOREA

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This paper is intended to provide key issues and current research outcomes on accelerator-based Boron Neutron Capture Therapy (BNCT). Accelerator-based neutron sources are efficient to provide epithermal neutron beams for BNCT; hence, much research, worldwide, has focused on the development of components crucial for its realization: neutron-producing targets and cooling equipment, beam-shaping assemblies, and treatment planning systems. Proton beams of 2.5 MeV incident on lithium target results in high yield of neutrons at relatively low energies. Cooling equipment based on submerged jet impingement and micro-channels provide for viable heat removal options. Insofar as beam-shaping assemblies are concerned, moderators containing fluorine or magnesium have the best performance in terms of neutron accumulation in the epithermal energy range during the slowing-down from the high energies. NCT_Plan and SERA systems, which are popular dose distribution analysis tools for BNCT, contain all the required features (i.e., image reconstruction, dose calculations, etc.). However, detailed studies of these systems remain to be done for accurate dose evaluation.

Advanced research centered on accelerator-based BNCT is active in Korea as evidenced by the latest research at Hanyang University. There, a new target system and a beam-shaping assembly have been constructed. The performance of these components has been evaluated through comparisons of experimental measurements with simulations. In addition, a new patient-specific treatment planning system, BTPS, has been developed to calculate the deposited dose and radiation flux in human tissue. It is based on MCNPX, and it facilitates BNCT efficient planning based via a user-friendly Graphical User Interface (GUI).

KEYWORDS : Accelerator-based BNCT, Epithermal Neutron, Target System, Beam-shaping Assembly, Treatment Planning System, BTPS, MCNP

1. INTRODUCTION

Boron Neutron Capture Therapy (BNCT) is a binary radiation treatment modality based on nuclear reactions between thermal neutrons and stable isotope ^{10}B concentrated primarily in cancer cells. It allows for delivery of high linear energy transfer (LET) radiation (α particles and ^{7}Li nuclei) to tumors at the cellular level whilst avoiding unnecessary dose deposition to healthy tissue. Until now, most BNCT studies and clinical treatments have been performed by using research reactors that have always produced various neutrons from a nuclear fission chain reaction [1-3]. However, these reactors are difficult to install into the hospitals and their use is burdened by licensing and spent nuclear fuel disposal issues [4]. To overcome some of the issues related to reactor-based neutron sources, research centered on accelerator-based BNCT as a useful alternative have surfaced in recent years.

BNCT treatment using accelerator-based neutron sources is not without its own requirements, however: (i) appropriate neutron-producing target and cooling equipment are required; (ii) beam-shaping assemblies consisting of moderators, reflectors, and so on, that can provide a neutron energy spectrum suitable for patient irradiation, are required; and (iii) Treatment Planning System (TPS) for determining optimal configurations are required. Research have been performed for the design, manufacturing, and testing of the above-mentioned components at the Massachusetts Institute of Technology, Idaho National Engineering and Environmental Laboratory, Lawrence Berkley National Laboratory, University of Birmingham, Hanyang University, and so on [5-11]. In particular, Japan has made the ample funds to realize accelerator-based BNCT, and extent studies including clinical demonstrations have been progressed in recent years.

Until now, most efforts for accelerator-based BNCT have been focused on the design and testing of beam-shaping assemblies to investigate the feasibility of clinical neutron beams having the desired characteristics for patient irradiation. Target and cooling equipment, on the other hand, has not seen much attention.

2. TARGET SYSTEM

In general, target systems consist of neutron-generating materials and cooling equipment. Their design balances neutron economy with mechanical and thermal stabilities. In other words, charged particles incident on the target must produce a sufficient number of neutrons, and integrity of these targets must be maintained by the cooling equipment.

2.1 Targets for Neutron Beam Generation

A variety of nuclear reactions corresponding to different combinations of incident particle and target material can serve as neutron sources in accelerator-based systems (Table 1) [12]. Based on neutron production rates and the average and maximum neutron energies, 2.5 MeV protons incident on lithium target are the most suitable reaction for accelerator-based BNCT. Neutron production rates for this reaction are very high. These neutrons have a relatively narrow energy spectrum which requires less moderation than those generated from other reactions. The optimal proton energy to obtain a high quantity of relatively low energy neutrons from the $^7Li(p,n)^7Be$ reaction has been studied in past [13]. It was found in those studies that neutron yields from incident protons below 2.5 MeV are too low for effective BNCT treatment, whereas for incident protons above 2.5 MeV, a longer moderation length is required if one wants to get same amount of epithermal neutrons due to high mean neutron energies [14-16].

Unfortunately, while the $^7Li(p,n)^7Be$ reaction is neutronically excellent, other properties of lithium metal (i.e., mechanical, chemical, and thermal properties) make it a poor candidate for a target. Its melting point is relatively low (Table 1); hence, the risk of target failure is relatively high. The thermal conductivity of lithium is also low; hence, heat accumulated in the target cannot be removed efficiently. Finally, lithium is a very reactive metal. Thus, solid lithium target must be fabricated in vacuum.

Many studies have proposed beryllium and carbon targets, as these materials do not suffer from the drawbacks associated with lithium metal in terms of manufacturing and cooling [17-19]. The melting points of these materials are about 10 times higher, and their thermal conductivities are far superior to that of lithium metal (Table 1). However, these materials are ineffective targets in accelerator-based BNCT systems; charged particles incident on these materials does not result in sufficient numbers of neutrons. In addition, the neutrons generated from these materials have average energies that are too high. Hence, beryllium and carbon targets require more extensive moderators and higher accelerator currents for efficient BNCT treatment to be realized.

2.2 Cooling Equipment in Target System

A number of methods for removing accumulated heat in the target have been proposed. In particular, many have tried to reduce the peak heat flux (power per unit area) on the target. One approach among established methods is an enlargement of incident area of proton beam on the target. Another involves heat dispersion using rotating targets. However, these simple methods cannot ensure the integrity of the target. Feasible methods for cooling the target include (i) submerged jet impingement (MIT) [20], (ii) narrow coolant passages (micro-channels) (LBL) [10,21], and (iii) complex heat removal system (the latest manufactured system) [22].

2.2.1 Submerged Jet Impingement

Submerged jet impingement involves the injection of coolant, via one or more nozzles, through a region of the same fluid onto the target backing plate (the cooled surface supporting the target). Submerged jet impingement can efficiently transport heat. It has thus been studied for use in applications related to electronic devices and target cooling mechanisms. A target system using this approach for accelerator beam applications has been designed and tested at MIT laboratory [20,23]. In that work, beryllium targets were cooled at a heat fluence of 6×10^7 W/m^2 using high-velocity submerged water jets. This implies that beryllium target can be sufficiently cooled to allow the delivery of 13 cGy/mA-min to tumors 4 cm deep. At the

Table 1. Characteristics of Four Charged-particle Reactions Considered for Accelerator-based BNCT

	$^7Li(p,n)^7Be$	$^9Be(p,n)^9B$	$^9Be(d,n)^{10}C$	$^{13}C(d,n)^{14}O$
Bombarding Energy [MeV]	2.5	4.0	1.5	1.5
Neutron Production Rate [# / min-mA]	5.34×10^{13}	6.0×10^{13}	1.3×10^{13}	1.09×10^{13}
Calculated Average Neutron Energy at 0° [MeV]	0.55	1.06	2.01	1.08
Calculated Maximum Neutron Energy [MeV]	0.79	2.12	5.81	6.77
Target Melting Point [°C]	181	1287	1287	3550
Target Thermal Conductivity [W / m-K]	85	201	201	230

University of Birmingham, a submerged jet heavy water cooling system was developed to cool copper backing plate of thick lithium target [24]. This heat removal system was demonstrated as adequate up to 1 mA operation. Submerged jet impingement could, therefore, allow efficient BNCT treatment in a short time without the risk of target failure.

2.2.2 Narrow Coolant Passages (Micro-channels)

At LBL, cooling using narrow coolant passages was developed primarily for accelerator-based BNCT [10]. Their heat removal system uses a small, micro-channeled finned structure, which enhances the area for heat transfer (Figure 1). The form of coolant passage is a rectangular shape in cross section, with 0.5 mm width and 6 mm height. These coolant passages (micro-channels) run across the width of the target backing [10]. In addition, the LBL target was tilted 30° with respect to the incident beam in order to reduce heat-load per surface area in half. Finite element code ANSYS [25] was used to simulate heat flow and at the same time, perform temperature and stress analysis. Their results show that the surface temperature of lithium metal can be kept below 150 °C. Further analyses indicated that beam currents up to 50 mA can be handled by optimizing the beam profile and increasing the target area (up to 15 cm × 15 cm). Consequently, this micro-channel cooling technology works well for solid lithium targets.

2.2.3 Complex Heat Removal System (the Latest Manufactured System)

A complex heat removal system has been designed at Hanyang University in Korea (Figure 2) [26-28] and some physical considerations were supplemented to reduce the peak heat flux of proton beam on lithium target and to increase the heat transfer rate. First, the concentration of induced heat from the incident proton beam was reduced by extending the incident area of proton beam on solid

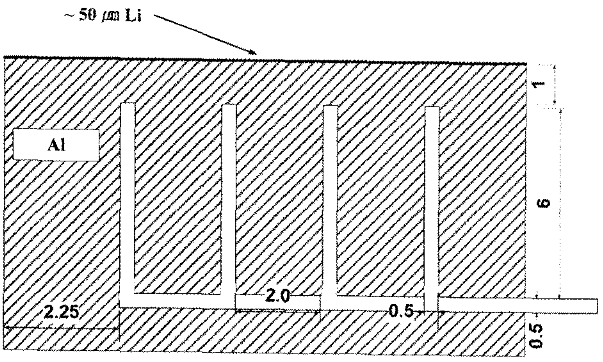


Fig. 1. Design of Prototype of Neutron Production Target (units in mm)

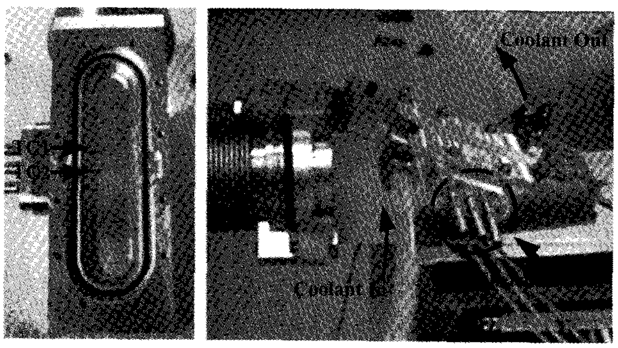
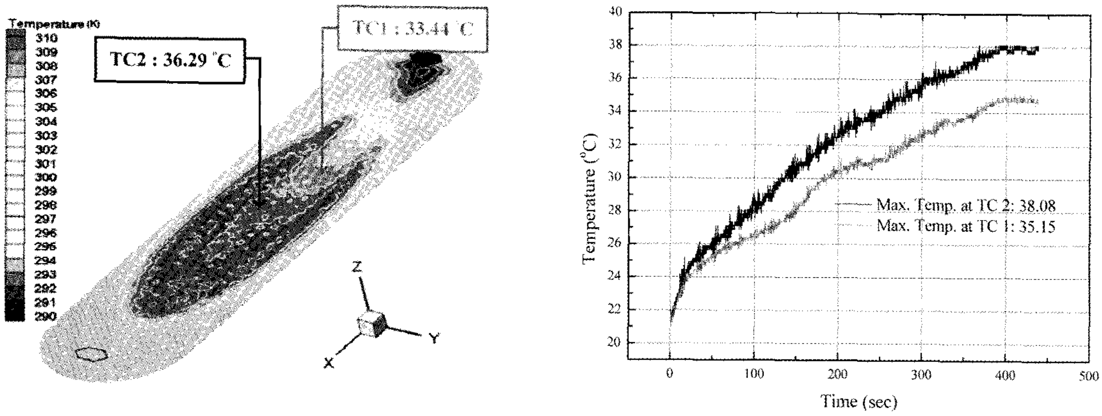


Fig. 2. The Experiment Configuration for Performance Evaluate of Manufactured Target System



(a) Calculated Result (b) Experimental Result

Fig. 3. A Comparison of Experimental and Calculated Results for the Lithium Target Temperature

lithium target. Second, solid target to produce the primary neutrons was tilted to 70° with respect to the direction of incident protons in order to increase the effective thickness of the target for the incident ones. Finally, a copper plate of high thermal conductivity and low corrosiveness for the coolant (i.e., ordinary water) was attached to the back of lithium target to increase the heat transfer rate. In addition, the coolant inlet and outlet were positioned on the side of the target system; this allowed for an increase in the number of the neutrons that could travel in the forward direction.

The temperature distribution at two positions (TC1 and TC2) in the lithium target was measured as a function of time. The FLUENT [29] computational fluid dynamics (CFD) flow modeling code was used to analyze the temperature distribution of the entire lithium target (Figure 3). Measured temperatures increased significantly from the beginning of each experiment to 400 sec, whereas after 400 sec these temperatures were maintained as constant by the use of cooling equipment (Figure 3b). A comparison between calculated and experimental results also shows that the maximum temperatures calculated at TC2 and TC1 positions were 36.29°C and 33.44°C, respectively, almost the same as the experimental results (38.08°C and 35.15°C). In the case of the use of 1 mA proton beam, it is calculated that temperature of the lithium target does not exceed its melting point if a diameter of incident proton one is extended to more than 2 cm [26,28].

3. BEAM-SHAPING ASSEMBLY

The primary neutrons produced from a nuclear reactor or accelerator cannot be used directly for BNCT treatment. Suitable beam-shaping assemblies are required to moderate the primary neutrons into the epithermal energy range. While the main purpose of this assembly is to moderate neutrons to epithermal energy range, other considerations are needed to achieve the successful BNCT treatment. In the following sections, important issues related to the beam-shaping assembly and current researches on production of clinical neutron beams are discussed.

3.1 Design Limitations of Beam-shaping Assemblies

The radiobiology of BNCT is more complicated than other radiation modalities because the radiation field in BNCT consists of several radiation dose components (fast and thermal neutron doses, boron dose, and gamma dose), in which these radiations have different physical properties and biological effectiveness [30-32]. Hence, the clinical neutron beams produced from the beam-shaping assembly is allowed to include only minimal contaminants from the above-mentioned dose components such that the background dose to healthy tissue is kept within the tolerance limits. Some recommended values by IAEA are described as follows [4]:

(i) Fast Neutron Dose (D_n/Φ_{epi}) $< 2.0 \times 10^{-13}$ $Gy{\cdot}cm^2/n_{epi}$

(ii) Gamma Dose (D_γ/Φ_{epi}) $< 2.0 \times 10^{-13}$ $Gy{\cdot}cm^2/n_{epi}$

(iii) Thermal Neutron Flux Ratio (Φ_{th}/Φ_{epi}) < 0.05

(iv) Forward Directional Property (J_{total}/Φ_{total}) > 0.7

The last parameter (J_{total}/Φ_{total}) has been added to reflect the forward directionality of the neutrons, which would range from 0.5 for a completely isotropic beam to 1.0 for a purely parallel beam [4]. A high value is required for two reasons: (i) to limit divergence of the neutron beam, thereby reducing undesired irradiation to other tissues, and (ii) to permit flexibility in patient positioning along the beam central axis. The above requirements enable a full-dose treatment to be completed in a reasonable time (~1 hour), with in the case of using fractionation individual exposure times of 15-30 minutes each.

3.2 Characteristics of Moderator Materials

Effective shaping materials should reduce fast neutron flux while enhancing epithermal flux. In other words, they allow for efficient slowing–down from the fast to

Table 2. Macroscopic Cross Section of Some Candidate Moderators

Material	Al/AlF$_3$*	AlF$_3$	^{7}LiF	Al	D$_2$O	Pb
$\sum_{s,fast}$	0.247	0.340	0.325	0.112	0.259	0.2720
$\sum_{s,epi}$	0.186	0.268	0.278	0.080	0.322	0.3720
$\sum_{s,fast\rightarrow epi}$	0.012	0.012	0.021	0.002	0.038	0.0007
$\sum_{s,epi\rightarrow th}$	0.003	0.005	0.006	0.001	0.032	0.0007
$\sum_{r,fast}$	0.012	0.013	0.013	0.002	0.039	0.0008
$\sum_{r,epi}$	0.004	0.005	0.006	0.001	0.032	0.0007
$\sum_{s,fast\rightarrow epi}/\sum_{r,epi}$	3.227	2.296	1.940	1.560	1.183	1.0500

*A 30% Al plus 70% AlF$_3$ mixture

the epithermal energies without removing these epithermal neutrons. The net result would be an accumulation of epithermal neutrons. Many studies have searched for optimal materials for accelerator-based BNCT. "Good" shaping materials are described as follows:

3.2.1 Fluental™

Fluental™ is a composite material (i.e., metal and ceramic) for neutron moderation [33]. It consists of a mixture of AlF_3 (69%), Al (30%), and LiF (1%) and this material is an excellent moderator for accelerator-based neutron sources for BNCT.

Table 2 summarizes the values of important ratios together with some other parameters for several moderator materials [34]. Energy groups are divided into three ranges: fast (E > 40 keV), epithermal (4 eV ≤ E ≤ 40 keV), and thermal (E < 4 eV). It was reported that the ratio $\sum_{s,fast\rightarrow epi} / \sum_{r,epi}$ is the most important parameter identifying good moderators. Compounds containing fluorine are better able to concentrate neutrons in the epithermal energy (during slowing-down from higher energies). In particular, the 30% Al and 70% AlF_3 mixture has the best performance in terms of $\sum_{s,fast\rightarrow epi} / \sum_{r,epi}$ because the scattering cross-sections of fluorine and aluminum have a series of resonances at high energies (Figure 4). Fluental™ contains a small amount of LiF (1%). It acts as a thermal neutron absorber, and reduces porosity in compound materials thus giving them a high overall density. The high thermal absorption cross-section of the ^6Li isotope helps to remove thermal neutrons from clinical neutron beams. The result is lower thermal contamination and lower gamma contamination due to thermal neutron absorption.

3.2.2 Al and F Compounds

Al and AlF_3 are the most common moderator materials in beam-shaping assemblies for accelerator-based BNCT. However, their low density compared to Fluental™ is one of their main drawbacks-relatively thick Al and AlF_3 are required for the same neutron attenuation. On the other hand, these materials are often used because of their low cost compared to Fluental™.

Magnesium fluorine (MgF_2) is also useful for producing neutrons in the epithermal energy range [35]. This is mainly due to strong, elastic-scattering cross section for fast neutrons and also these two elements have relatively small mass number. A recent publication highlights that moderators containing MgF_2 produce neutron spectra appropriate for BNCT while at the same time minimizing fast neutrons. The result is relatively low radiation damage of surface tissue compared with others.

3.3 Current Research on the Production of Clinical Neutron Beams

3.3.1 Argentina

Several studies have been performed by Argentinean scientists in collaboration with MIT for accelerator beam applications [36-37]. High current accelerators capable of producing ~mA proton and deuteron beams up to 4.1 MeV in energy have been realized. In addition, 2.3 MeV proton beams incident on lithium metal targets were used to produce neutrons. The assembly proposed in their work consists of successive stacks of aluminum, polytetrafluoroethylene (Teflon), and LiF as the moderator and thermal neutron absorber. In that design, lead acts as a reflector material-it was shown to outperform graphite in their previous work. This assembly can be manufactured easily with relatively low costs compared designs employing Fluental™ moderators. Three moderator thicknesses were considered (18, 26, and 34 cm). The 34 cm thick moderator performed best.

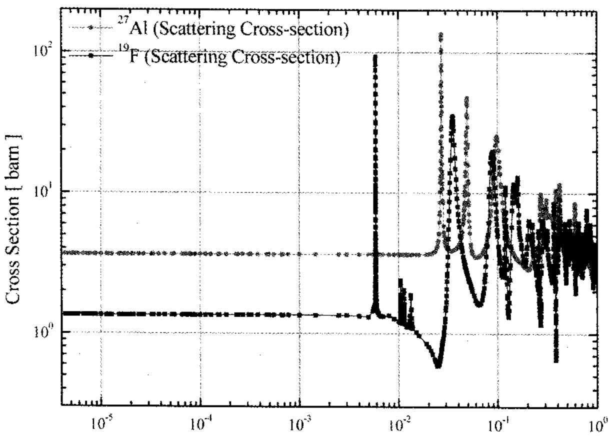


Fig. 4. Elastic Scattering Cross-section of AlF_3 Moderator

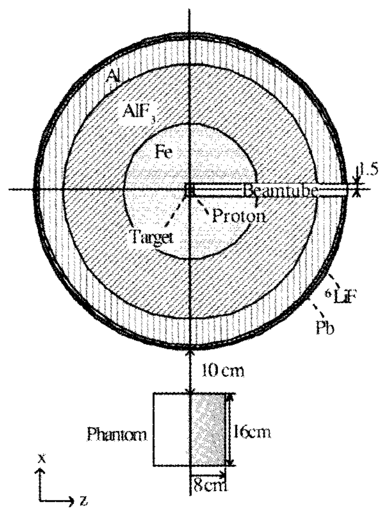


Fig. 5. A Cross-sectional View of the Geometry Used in the MCNPX Calculations

3.3.2 Japan

Japan has contributed substantially to scientific contributions studying BNCT. Some research has investigated the feasibility of neutron capture therapy using accelerator-based neutron sources [38-39]. A recent study at the Cyclotron and Radioisotope Center of Tohoku University focuses on optimizing the epithermal neutron field with an energy spectrum and intensity suitable for BNCT, based on various combinations of neutron-producing reactions and moderator materials [40-41]. Neutrons emitted from thick Ta target bombarded by 50 MeV protons of 300 mA beam current served as the neutron source. This choice resulted from analyses of angular distributions and neutron energy spectra. The beam-shaping assembly composed of iron, $AlF_3/Al/^6LiF$ was also designed as shown in Figure 5 and lead was chosen as a moderator based on the simulation trials using the MCNPX code [42]. The depth dose distributions in a cylindrical phantom indicated that the beam-shaping assembly, which was composed of 30 cm thick iron, 39 cm thick $AlF_3/Al/^6LiF$, and 1 cm thick lead, provided an epithermal neutron fluence rate of 0.7×10^9 n/cm^2·s. Within 1 hour, the epithermal neutron beam could allow a tumor dose of 20.9 RBE·Gy at a depth of 8 cm in the phantom.

3.3.3 United Kingdom

Several studies have been performed to design the epithermal neutron beam for successful BNCT treatment, and these investigations are constructed at the University of Birmingham [24,43]. As shown in Figure 6, the final moderator and facility design included a region of Fluental™ to provide a neutron spectrum appropriate for therapy. A graphite reflector and Li-polyethylene sheet was used to delimited the neutron beam port. A dual ionization chamber technique was used together with foil activation to measure the fast neutron, photon, and thermal neutron dose to a large rectangular phantom exposed to the beam. The measured doses agreed well with MCNP4C calculations: within 10% for the photon dose, 10% for thermal neutron dose, and 25% for the proton recoil dose along the main beam axis.

3.3.4 Korea

In Hanyang University, a new beam-shaping assembly was designed both to shape the primary neutrons generated from the target into the epithermal energy range (4 eV $\leq$ E $\leq$ 40 keV) and to reduce the undesired radiations as much as possible. This assembly was composed of two moderators and a surrounding reflector (Figure 7) [44-46]: the moderators were filled with aluminum fluoride (2.78 g/cm^3) and aluminum (2.78 g/cm^3), and the reflector was made of graphite (1.85 g/cm^3). The external form of designed assembly is a cylindrical shape, while internal moderators are made into a conical shape to improve forward directional property of epithermal neutrons.

The beam qualities of the designed beam-shaping

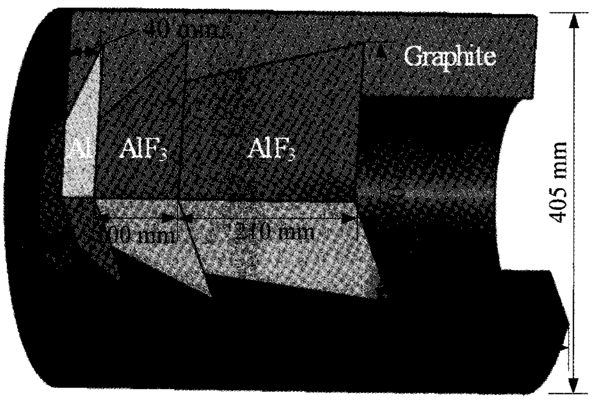


Fig. 7. A Figure of Designed Beam-shaping Assembly

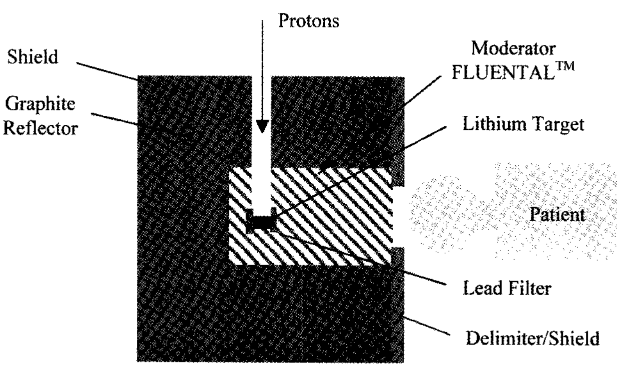


Fig. 6. Layout of Orthogonal Fluental™ Neutron Moderating Structure

Table 3. A Comparison of Calculation Results and IAEA Recommendations for Epithermal Neutron Beam

	IAEA Recommendations	Work Performed in Korea
D_n/Φ_{epi} [Gy-cm^2/n$_{epi}$]	$< 2.0 \times 10^{-13}$	7.12×10^{-14}
D_γ/Φ_{epi} [Gy-cm^2/n$_{epi}$]	$< 2.0 \times 10^{-13}$	2.48×10^{-14}
Φ_{th}/Φ_{epi}	< 0.05	0.04
J_{total}/Φ_{total}	> 0.7	0.62
Φ_{th} [%]	3.5	
Φ_{epi} [%]	87.4	
Φ_{fast} [%]	9.1	

- D_n: Fast Neutron Dose, D_γ: Gamma Dose, J_{total}: Neutron Current
- Φ_{th}, Φ_{epi}, Φ_{total}: Thermal, Epithermal, and Total Neutron Flux

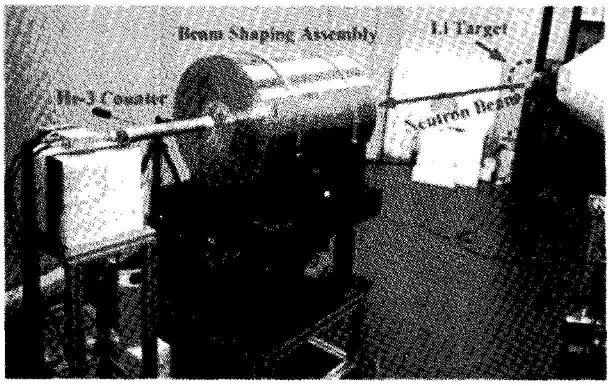


Fig. 8. An Experiment Condition for Measuring Moderated Neutrons from the Beam-shaping Assembly

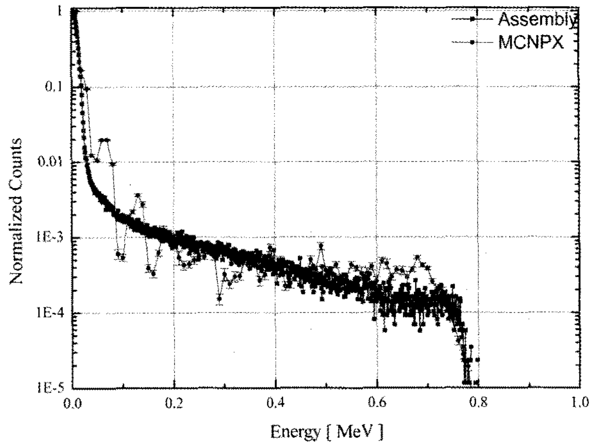


Fig. 10. A Comparison of the Neutron Spectrum Measured from the Experiment with the Calculated One Using MCNPX at the Port of Beam-shaping Assembly

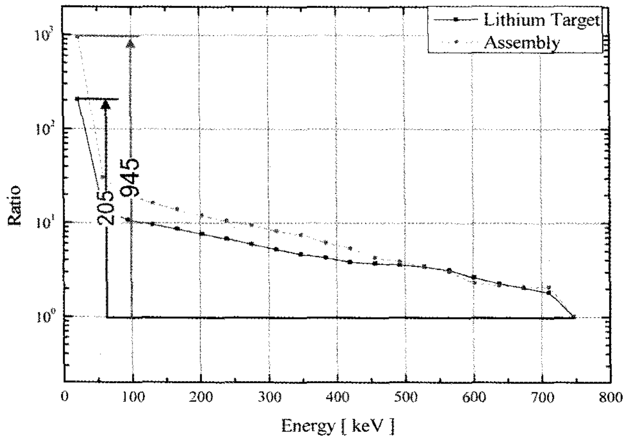


Fig. 9. A Comparison of the Count Ratios with Reference to Those in the Highest Energy Bin (748.89 - 785.13 keV), between the Neutron Source and Moderated Neutrons from the Assembly

assembly were evaluated by using MCNPX simulation with reference to the parameters recommended by IAEA. The results were compared as presented in Table 3. Beam qualities of this assembly satisfied all IAEA recommendations except for the ratio between the total neutron current and the total neutron flux. In particular, unnecessary radiations (fast neutron and gamma-ray) were significantly reduced by the beam-shaping assembly, and 87.4% of the neutrons moderated by this assembly were concentrated in the epithermal energy range (4 eV $\leq$ E $\leq$ 40 keV). Even though one IAEA recommendation was not satisfied (i.e., the ratio between the total neutron current and the total neutron flux), this assembly was comparable to those of other ones.

To evaluate the performance of the above beam-shaping assembly, two experiments were carried out at the Korea Institute of Geoscience and Mineral Resource (KIGAMS). Primary neutrons emitted from the lithium target were first measured; neutrons moderated by the assembly were re-measured using a He-3 counter (Figure 8). The main purpose of these experiments was to evaluate the beam-shaping assembly, hence a solid lithium target of 100 μm thickness instead of a manufactured target system was employed. It was cooled with a separate system. In addition, the diameter of the proton beam and average beam current of the accelerator were 1 cm and 0.53 μA, respectively. The He-3 counter was arranged to be paralleled with the assembly.

The measured neutron energies were divided into 21 ranges, including the epithermal range (Figure 9). The measured counts in each energy range were compared with those in the highest neutron energy range (748.89-785.13 keV) for each experiment. It was found that the epithermal neutrons generated from the assembly were more than ≈950 times as many neutrons, whereas this ratio in the source spectrum was about 210 times.

The epithermal neutron beam generated from the manufactured beam-shaping assembly was simulated to verify the accuracy of the experiments (Figure 10). The many peaks in the calculated energy spectrum resulted from the cross-section of moderator materials (Al and F), aside from that, the calculations agreed with the measurements over the energy range 0-800 keV. It was therefore recognized that the manufactured beam-shaping assembly for accelerator-based BNCT can efficiently concentrate primary neutrons into the epithermal energy range.

4. TREATMENT PLANNING SYSTEM FOR BNCT

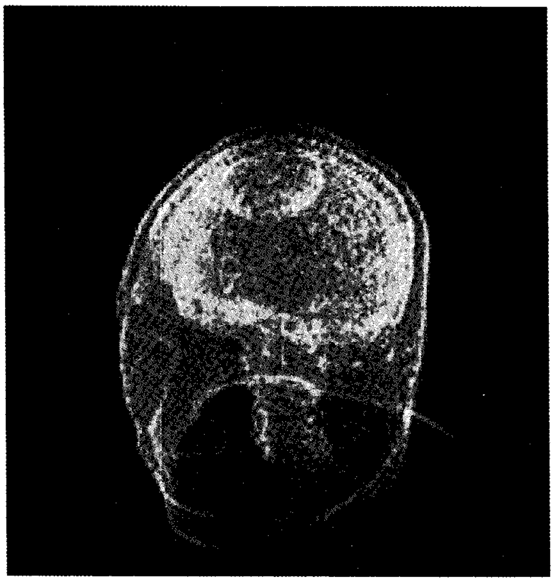
Treatment Planning (TP) is the process of defining the best irradiation modality for cancer treatment in terms of delivering the optimal dose to the tumor whilst minimizing damage to healthy tissue. Since this decision process is performed prior to irradiation, it establishes an important point in respect to the success of the BNCT and is generally determined through Treatment Planning System (TPS). Particularly, the main goal of these systems is the simulation of the irradiation, in order to obtain the optimal configuration in terms of neutron spectrum, patient positioning and dose distributions in the tumor and healthy tissue. The most frequently used TPSs in this field, NCT_Plan [47] and Simulation Environment for Radiotherapy Applications (SERA [48]), are described in brief below. The main functions and capabilities of the latest BNCT Treatment Planning System (BTPS) [49-50] are also introduced.

4.1 NCT_Plan

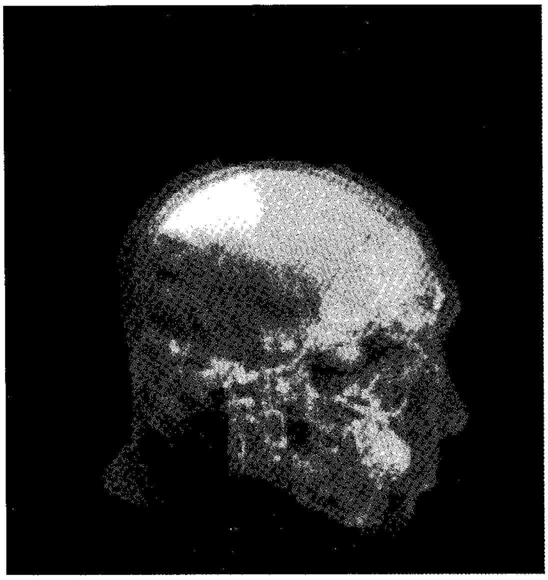
NCT_Plan was designed to optimize beam configurations (dimensions, orientations, and energy). It has been upgraded and improved several times since its conception. The latest version (NCT_Plan 1.0) was developed jointly by National Atomic Energy Commission (CNEA), Harvard Medical School, and MIT. It was written using Microsoft Visual Basic™ 6.0 and runs under Windows 95/98/NT and 2000. A 3D mathematical model of the patient's head is created from a set of 2D images by making use of voxel reconstruction technique. Here, 2D planes of (medical) images are partitioned into regularly sized squares. They are then mathematically stacked to construct a large 3D array of 11,025 cells (1 cm^3 volume). In order to assign the materials to each voxel, image qualities are selected by the user from medical images. A volume-weighted contribution of the four primary materials (air, normal tissue, bone, and tumor tissue) is calculated for each voxel. NCT_Plan provides a graphical environment for deriving dose patterns. It uses the results of MCNP radiation transport calculations and can display the results in 1D, 2D, and 3D formats. Cumulative Dose Volume Histograms (DVHs) for tumor or normal tissue volumes can also be generated.

4.2 SERA

SERA was developed at the Idaho National Engineering and Environmental Laboratory (INEEL) in collaboration with the University of Montana (MSU). The SERA package can be divided into three main parts according to the general scheme: reconstruction of patient geometry, radiation transport, and contouring and display of the computed dose. In contrast to NCT_Plan, SERA uses a reconstruction technique based on a pixel-by-pixel uniform volume element (univel). The resolution of the model is therefore only limited by that of the original medical image. This allows for very accurate representation of patient geometry (Figure 11). A list of predefined bodies (brain, skull, tumors, ventricles, etc.,), which refer to files containing all the information required for dose computation, are available. Radiation transport simulations are based on a modified version of MCNP (SERAMC) specifically designed for BNCT. In contrast to MCNP, radiation transport in SERAMC is based on multi-group neutron and photon cross sections. The neutron cross sections were processed at INEEL from ENDF- B/V and ENDF-



(a) Wireframe Rendered 3D Model



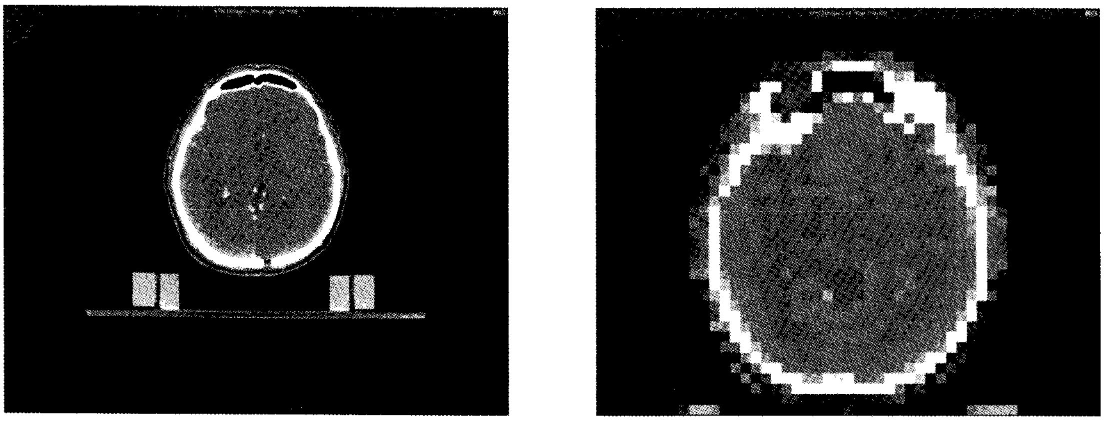
(b) Transparent Regions in 3D Model

Fig. 11. Reconstructed Images by Using the SERA System

B/VI libraries below 20 MeV. Finally, SERA offers a dose contouring utility that displays 2D isodose curves, depth-dose curves, and DVHs.

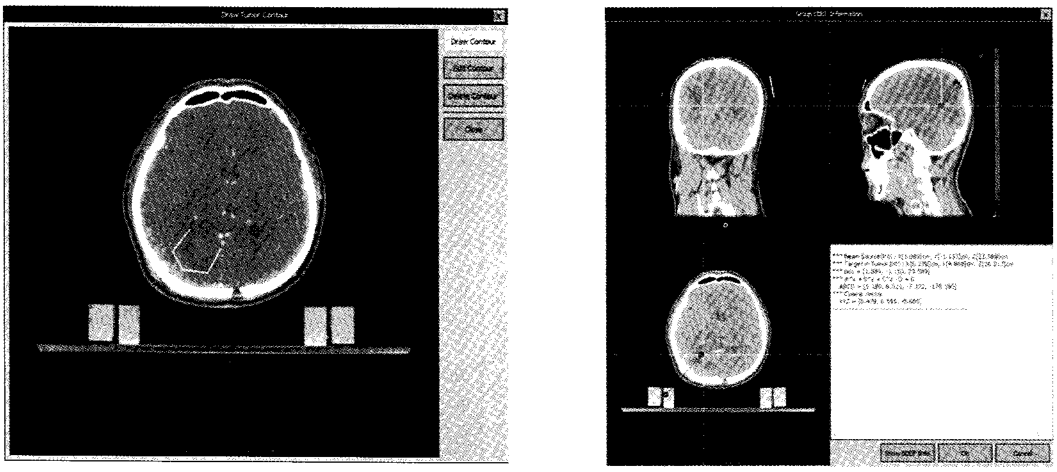
4.3 BNCT Treatment Planning System (BTPS)

The BNCT Treatment Planning System (BTPS) was developed at Hanyang University in order to calculate doses and radiation flux in human, and to facilitate planning BNCT using a user-friendly Graphical User Interface (GUI). Special tally techniques used in MCNPX (i.e., mesh tally) and parallel computing system were employed to enhance the capabilities of this system. BTPS was written in C++ (C++ Builder), and it can be run on Windows® platforms. The overall procedures of this system were designed to be followed with the treatment step of BNCT, which was divided into planning and posterior estimation for the treatment. First, the planning step determines optimized treatment environments: image reconstruction from the patient image to the Voxel phantom, determinations of treatment regions, incident beam conditions, and so on. The next step derives the optimized irradiation time from repeated calculations of absorbed dose with measured boron concentrations in normal/tumor tissues. BTPS consists of image, plan, and analysis modules and a dose calculation engine based on MCNPX. Specific functions of each module are described as follows:



(a) Diagnosis Image of the Patient (b) Reconstructed Voxel Phantom

Fig. 12. The Conversion from Patient's Diagnostic Image to the Voxel Phantom by Using Image Module



(a) Delineating the Target Volume (b) Positioning the Irradiation Field

Fig. 13. The Determination of Some Treatment Plan by Using Plan Module

4.3.1 Image Module

The main function of this module is image reconstruction from patient image (i.e., DICOM) to Voxel phantom for MCNPX calculations. This module can reconstruct any diagnostic image to Voxel phantoms suitable for calculations: CT, MRI, PET, and others. The structure materials (i.e., air, normal tissue, and bone) of each Voxel are automatically defined from averaged CT numbers which are classified according to the density ranges. In addition, the target volume is easily delineated and the region-of-interest (ROI) and Voxel size are efficiently defined using a computer mouse. A comparison of an original diagnostic image and reconstructed head phantom of $5 \times 5 \times 5$ cm^3 Voxel size using this image module is presented in Figure 12.

4.3.2 Plan Module

The main function of this module is to define all treatment environments and dose calculation types. Hence, this module can define the specific condition of the incident neutron beam including source position and direction, energy spectrum, and other indicators. The calculation type for dose components and various radiation fluxes can be selected by simple manipulation of a computer mouse. Boron, total neutron, and gamma doses are very important in evaluating BNCT treatment modalities. As such, these calculations are essentially derived from this module, whereas other ones are optional. In short, boron concentration is assumed to be homogeneous in tumor and normal tissue. Figure 13 shows a sample image that is conducted with some arbitrary plans.

4.3.3 Dose Calculation Engine Based on MCNPX Code

The main function of this engine is advanced preparation for dose calculations and arrangement of calculated results. The dose calculation engine unites a

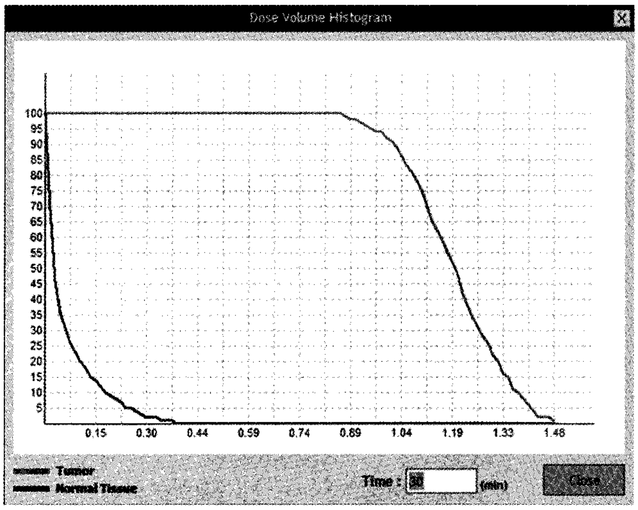


Fig. 15. Dose Volume Histogram and Irradiation Time

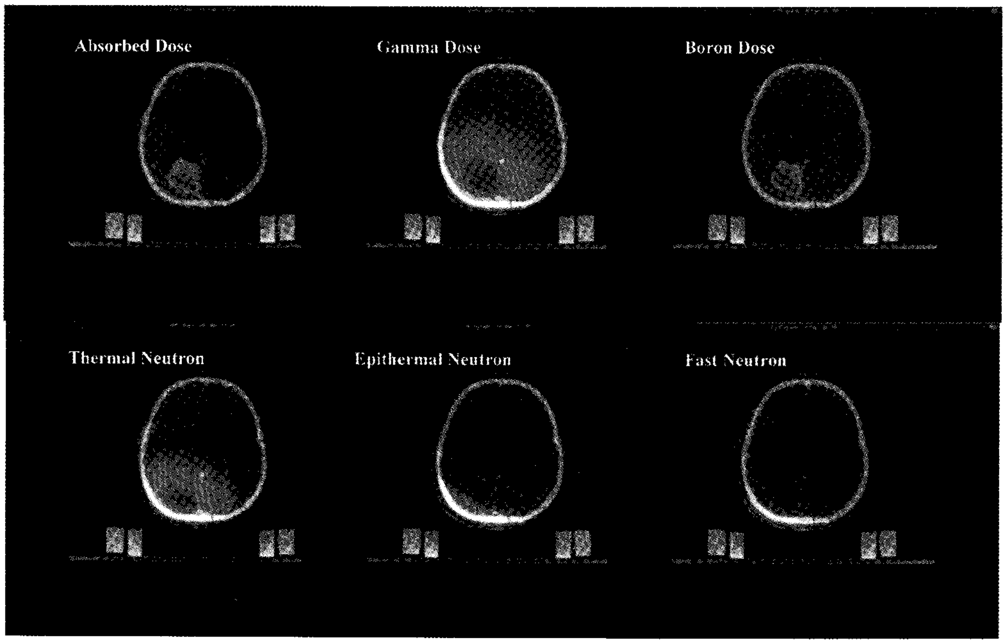


Fig. 14. The Isodose Contours for Each Dose Component

Table 4. A Characteristic Comparison of Each Treatment Planning System (BTPS, SERA, and NCT_Plan)

	BTPS	SERA	NCT_Plan
OS	Windows	Linux/Unix	Windows
Patient's Diagnostic Image	Dicom (Standard Data Type)	QSH, Raw, TIFF, etc.	CT Image
Determination of ROI	Direct Delineation	Direct Delineation	Direct Delineation
3D Phantom	Voxel	Univel	Voxel
Voxel Size	Adjustable	1 cm^3	1 cm^3
Material Determination in Each Voxel	Automatic Classification by Using CT Number or Adjustable	Direct Classification by the User	Automatic Classification by Using CT Number
Neutron Beam	Position and Direction Defined with Easy Manipulation	Direct Input (Distance and Direction)	Position and Direction Defined with Easy Manipulation
Boron Contamination	Separate Definition in Tumor or Normal Tissue	Difference According to Each Organ	Separate Definition in Tumor or Normal Tissue
Dose Calculation Engine	MCNPX	seraMC or PEREGINE	Modified MCNP
Clustering Consideration	O	X	X
Calculation Time (1 cm^3 Voxel Phantom)	~ 5 min/10^7 history (Pentium IV, 48 Nodes)	a Few min per field (Pentium IV, 1 GHz)	-
Considered Dose Components	Four Dose Components or Adjustable		
Plot Type for Dose Evaluation	Isodose Contour Dose Volume Histogram Fluence/Dose Profile	Isodose Contour Dose Volume Histogram Fluence/Dose Profile	Isodose Contour Dose Volume Histogram

3D Voxel phantom, converted from the image module, with the treatment environment defined from the plan module and prepares them for MCNPX input. Selected dose components in the plan module are also calculated based on Kerma value matched with each one-self. Finally, this engine imports and arranges the calculated results through the MCNPX code.

4.3.4 Analysis Module

The main function of this module is data conversion from raw data to analyzable profile images for efficient treatment planning. First, this module imports all of the dose calculation results, such as absorbed dose rate and flux related with neutron, gamma-ray, and nuclear reactions. Next, these results are displayed as isodose contours (Figure 14) and DVHs (Figure 15) in order to evaluate dose distributions and therapeutic effects resulting from BNCT. These profiles are very useful in evaluating dosimetric characteristics of neutrons generated from the target and beam-shaping assembly.

The main characteristics and roles of importance of several treatment planning systems used in BNCT have been described in this paper. TPSs are also invaluable for conventional radiotherapy; however, this role in BNCT is particularly weighted by the presence of neutrons, which increase the complexity in radiation simulation. The TPSs (NCT_Plan, SERA, and BTPS) previously mentioned are able to accurately simulate complicated radiation fields associated with BNCT. Simulation run-times are now on the order of a few minutes per field in many cases. These TPSs are usually designed following the general scheme previously described, and their main characteristics are summarized in Table 4.

5. CONCLUSIONS

Considerable progress has been made towards the development of various components for accelerator-based BNCT. For target systems, some studies have examined

2.5 MeV proton beam with lithium target. Others studies have investigated alternatives beam-target configurations including proton and deuteron beams on beryllium and proton beams of various energies on lithium. In addition, much research has focused on development of effective target cooling methods, such as submerged jet impingement, narrow coolant passages, and complex heat removal system. Research associated with beam-shaping assemblies has investigated optimal materials that can efficiently moderate primary neutrons emitted from the target into the epithermal energy range. Finally, several research teams have developed fast and accurate treatment planning systems for BNCT using accelerator-based neutron sources.

Advanced research in Korea has addressed a wide scope of issues associated with accelerator-based BNCT. The latest results indicate that the integrity of target system can be maintained for proton beams up to 1 mA, and manufactured beam-shaping assembly can shape the primary neutrons into clinical neutron beams (whose composition consists of 87.4% epithermal neutrons) for BNCT treatment. The BNCT Treatment Planning System (BTPS) has also been developed to calculate deposited doses and radiation fluxes in humans and to facilitate BNCT planning that uses a user-friendly GUI. It is expected that the current research efforts underway in Korea will contribute substantially to accelerator-based BNCT studies worldwide.

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