DEVELOPMENTS IN ACCELERATOR BASED BORON NEUTRON CAPTURE THERAPY

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Abstract—This paper will review the current status of Boron Neutron Capture Therapy (BNCT), from basic physical mechanisms and clinical indications, to neutron beam development and dosimetry. For in-hospital facilities, particle accelerators presently provide the favoured option, and this paper concentrates on this approach to neutron beam production for BNCT. Various accelerator-based approaches will be reviewed, but discussion will concentrate on the Birmingham programme, particularly the design of a suitable neutron beam delivery system and the experimental validation of Monte Carlo simulations on a mock-up neutron beam moderation system. The use of dose modifying factors to evaluate the likely clinical utility of an epithermal neutron beam will also be discussed, with illustrations from the Birmingham programme.

INTRODUCTION
There has been a resurgence of interest in BNCT in recent years as a consequence of two separate events. Firstly, the publication of promising clinical results from BNCT treatments carried out in Japan (Hatanaka and Nakagawa, 1994) has encouraged clinicians that there might be some future in this treatment modality. Secondly, a combination of work in neutron beam design and in characterising the various available compounds which can be used to carry boronated drugs to the tumour site, has encouraged scientists that a significant dose enhancement can be achieved.

This paper provides a review of the significant developments in BNCT in recent years, and assesses the opportunities for this treatment modality to develop into mainstream radiotherapy practice. The review will concentrate on future options which use particle accelerators as the primary source of neutrons, since these give greatest potential for in-hospital facilities, and will draw specific data from the work on accelerator based BNCT in Birmingham.

OVERVIEW
Clinical indications for BNCT
BNCT may be a suitable treatment for a number of tumour types. If the tumour is located such that neutrons can be suitably delivered, and it is of a type which takes up a boronated drug, then treatment may be possible. In addition, in common with all other radical radiotherapy treatments, local control of the primary tumour should be the principal clinical problem. There are a number of tumours for which these factors apply, but the majority of interest world-wide has focused on glioblastoma multiforme and metastatic melanoma.

Glioblastoma multiforme
Two factors were mentioned above as being significant in the recent resurgence of interest in BNCT. There is also an underlying third factor which is the very poor prognosis for the majority of patients with the tumour glioblastoma multiforme. This is a grade IV astrocytoma, and is a tumour of the glial tissue which is the structural material of the brain. High grade (III or IV) astrocytomas are around 1% of cancer diagnosis in the UK, and around 2.5% of cancer deaths (James, 1996). Incidence increases with age with prognosis deteriorating with age and performance status. Patients tend to die as a result of uncontrolled local disease rather than from the effects of metastasis. However, there are a sub-group of the younger, fitter patients that do receive substantial benefit from conventional therapy, both surgery and external beam photon radiotherapy. Hence great care must be exercised in patient selection for BCNT trials which will almost certainly be sub-therapeutic in their early stages.

BNCT physical mechanisms
BNCT is a form of binary radiotherapy and therefore involves two key stages. The first is the preferential accumulation, in tumour cells, of an isotope with a suitable affinity for neutrons at a certain energy. This must then be followed by an intense irradiation of these cells with neutrons at an energy such that their probability for capture is maximised. In BNCT, this means a preferential accumulation of boron, followed by submerging the tumour and the surrounding healthy brain tissue in
a bath of thermal neutrons. These thermal neutrons may either be incident directly onto the tissue, for superficial tumours or intra-operative treatment, or may be produced locally by moderation of a higher energy neutron source which is incident on to the patient surface.

The interaction of thermal and epithermal neutrons is dominated by scattering. As a result, neutrons of these energies cannot be directed in a beam-like manner. In order to achieve the required thermal neutron fluence at the tumour, the whole head (in the case of brain tumours) is given a sub-therapeutic radiation dose, which is therapeutically effective in the tumour cells because of the increased dose from the boron capture reaction. However, for the currently available boron carrier compounds, the degree of selectivity in concentration between tumour and healthy tissues is still so low that careful treatment planning, combined with a detailed understanding of the effects of the neutron irradiation on the healthy brain, are essential prerequisites to a therapy programme.

In describing the physical basis for BNCT, it is necessary to use a number of terms which will be familiar to clinicians and physicists alike. However, in the case of BNCT, these terms may not carry their normal inferences. For example, absorbed dose is related to energy deposited by the radiation field, and in clinical radiotherapy is directly correlated with tumour control probability. In BNCT the major dose component, that from the boron capture reaction $^{10}\text{B}(n,\alpha)^7\text{Li}$, is deposited non-uniformly on the microscopic scale. The ranges of the reaction products from this reaction are 5 and 9 μm for the $^7\text{Li}$ and α respectively which are comparable with typical cellular dimensions of around 10 μm. Hence, if the boron is located far from the radiosensitive structures with in cell nucleus, dose (i.e. energy) will be deposited during the therapy with negligible impact on tumour control. This is a central problem to the whole of BNCT and has been investigated by many authors (Gabel et al., 1987; Kalend et al., 1995).

Since the tumour control is affected directly by the location of the boron atoms within a cell, it will be affected directly by the compound used to carry boron to the cell. There is therefore a need to characterise the biological effectiveness exhibited by the boron distribution associated with a particular compound. For this purpose the term Compound Biological Effectiveness (CBE) (Coderre et al., 1993) has been developed. This is an empirical term which has utility in characterising a treatment plan. It is analogous to the conventional term Radio-Biological Effectiveness (RBE) since it is a simple ratio:

$$\text{CBE} = \frac{\text{dose of photons required to give a certain surviving fraction}}{\text{dose from the neutron capture reaction which gives the same surviving fraction}}$$

It has tended to be used as a multiplier for physical dose (just as RBE is used) in order to provide an overall characterisation of the effectiveness of a particular treatment. However, by agreement of all parties at the recent Seventh Symposium on Neutron capture Therapy, Zurich, September 1996, papers and patient treatment prescriptions in BNCT will carry full information on physical and biologically equivalent dose, as well as on the conversion factors (RBE and CBE) which have been used to derive equivalent doses from absorbed dose measurements and calculations.

**Clinical BNCT programmes**

Clinical experience and results from BNCT treatments is still patchy. Following early failures at Brookhaven National Laboratory (BNL) and Massachusetts Institute of Technology (MIT) using extracted thermal neutron beams from reactors, BNCT was kept alive as a treatment modality by the work of Hatanaka in Japan. This has resulted in an extensive body of patient data from intra-operative irradiation of tumour residues post debulking. The boronated compound used was BSH. Hatanaka’s work, and his use of BSH, has been a very significant factor in the current European facility at the High Flux Reactor (HFR) in Petten, the Netherlands. However, this has yet to begin patient trials. Hatanaka’s work has attracted significant comment and criticism on a number of grounds related to patient selection, tumour classification and the handling of the BSH compound (Dorn III, 1994; Laramore and Spence, 1996). These criticisms notwithstanding, it remains a very substantial contribution to the field on BNCT and provides substantial encouragement for clinicians dealing with glioblastoma multiforme.

Experience with epithermal neutron beams is beginning to mount with the on-going programmes at BNL and MIT. The BNL group have established themselves as the focal point for western clinical interest, and are undertaking a phase I/II clinical study. This involves elements of dose escalation and normal tissue toxicity, as well as paying obvious attention to survival and quality of life. The results currently being achieved show very similar mean survival times to conventional X-ray therapy, with hopes that further dose escalation may be possible before the limit imposed by toxicity to healthy tissue is reached.

The published clinical experience has been summarised in Table 1. It should be noted that the ongoing clinical studies mean that patient numbers are now increasing rapidly in some centres.
Potential agents for neutron capture therapy

 Whilst the majority of attention world-wide has focused on $^{10}$B as the neutron capture isotope, there are also significant possibilities from other isotopes which exhibit high neutron capture cross-sections for thermal neutrons. These are summarised in Table 2, with the greatest potential being attached to $^{157}$Gd. This isotope has the highest neutron affinity of any stable isotope (248 000 barns for thermal neutrons). Gadolinium is widely used to enhance images in MRI, and is therefore widely studied for toxicity and chemical manipulation, and it also has limited potential for imaging. Imaging of the boron distribution prior to therapy is problematic, although substantial progress is now being made. It is however commonly assumed that the use of gadolinium instead of boron would provide excellent opportunities for imaging on any local MRI scanner. This is unfortunately untrue since conventional MRI images only protons, with gadolinium enhancement producing an effect on proton spin relaxation. Hence, the MRI signal is basically related to proton concentration rather than gadolinium concentration, and will be affected by the local blood supply to the tumour. Whilst conventional MRI would provide some information, this would not be of the quality required for dosimetric utility in radiotherapy.

Neutron sources

The neutron beam characteristics which are required for a useful BNCT facility are quite difficult to achieve. If we consider only BNCT based on externally applied beams of epithermal neutrons, then we can consider the design criteria put forward by the Petten group as a useful guide (Moss et al., 1992). These criteria, along with the characteristics of neutron beams in use at BNL, Petten, and that projected for Birmingham are shown in Table 3. Essentially one is looking to produce a beam with good penetration, to ensure sufficient dose to the distal edge of a target volume, with low fast neutron and photon contamination, and of sufficient intensity to allow a therapeutic dose to be delivered in an acceptable time (less than 1 hour for example).

The only external source of neutrons of sufficient intensity for a practical BNCT treatment that is currently available is that from a nuclear reactor. While both boron enhanced fast neutron therapy, and capture-based brachytherapy are possible, neither currently available particle accelerators, or radioisotope neutron sources can provide an external beam suitable for BNCT. Nevertheless, the potential utility of accelerators in a real hospital environment provides such an attractive proposition, that a number of groups around the world are investing their research effort into this topic. This effort gains impetus from the fairly certain knowledge that new nuclear reactors are very unlikely to be located at hospital sites, and that the potential income which could be generated from a clinical BNCT programme is unlikely to be sufficient to support the running costs of a nuclear reactor.

The use of radioisotope neutron sources for external ‘beam’ BNCT has also been investigated (Yunch et al., 1993). These investigations suggest that a beam of sufficient intensity for a practical treatment facility is unlikely to be realised by this route. However, a number of centres are already working clinically with neutron therapy based on interstitial placement of neutron sources. The moderation of these, usually fission, neutrons within the body, might produce a sufficiently high local thermal fluence to mean that the introduction of a boronated capture agent is clinically useful in certain circumstances (Allen and Ralston, 1996).

The potential for a dose enhancement in fast neutron therapy has been considered at a number of centres (Maughan et al., 1996). It is significant here to recall that tumour control probability is a very strong function of applied dose, so the small potential for dose enhancement by using tumour specific

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**Table 1. Published BNCT clinical experience world-wide**

<table>
<thead>
<tr>
<th>Country/Lab</th>
<th>Compound</th>
<th>Condition</th>
<th>Neutron beam</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan/Kagawa (Nakagawa et al., 1997)</td>
<td>BSH</td>
<td>Gliomas (all grades)</td>
<td>Thermal</td>
<td>152</td>
</tr>
<tr>
<td>Japan/JAERI (Matsumura et al., 1997)</td>
<td>BSH</td>
<td>Gliomas (III and IV)</td>
<td>Thermal</td>
<td>4</td>
</tr>
<tr>
<td>Japan/Kyoto (Oto et al., 1997)</td>
<td>BSH/BPA</td>
<td>Gliomas (III and IV)</td>
<td>Thermal</td>
<td>44</td>
</tr>
<tr>
<td>USA/BNL (Elowitz et al., 1997)</td>
<td>BPA</td>
<td>Glioblastoma</td>
<td>Epithermal</td>
<td>10</td>
</tr>
<tr>
<td>USA/BNL (Elowitz et al., 1996)</td>
<td>BPA</td>
<td>Glioblastoma</td>
<td>Thermal</td>
<td>44</td>
</tr>
<tr>
<td>USA/BNL (Elowitz et al., 1997)</td>
<td>BPA</td>
<td>Melanoma</td>
<td>Epithermal</td>
<td>5</td>
</tr>
</tbody>
</table>

**Table 2. Characteristics of different isotopes for neutron capture therapy**

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Cross-section (barns)$^a$</th>
<th>Natural abundance (%)</th>
<th>Reaction Q (MeV)</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{10}$B</td>
<td>38000</td>
<td>19.6</td>
<td>2.79</td>
<td>$\gamma$, $^7$Li, $^7$Be</td>
</tr>
<tr>
<td>$^{157}$Gd</td>
<td>248 000</td>
<td>15.7</td>
<td>7.9</td>
<td>$\gamma$, $^7$Li</td>
</tr>
<tr>
<td>$^7$Li</td>
<td>917</td>
<td>7.4</td>
<td>4.78</td>
<td>$\gamma$, $^7$Li</td>
</tr>
<tr>
<td>$^{252}$U</td>
<td>566</td>
<td>0.72</td>
<td>200</td>
<td>$\alpha$, $^8$Be, $^8$B, $\gamma$, n</td>
</tr>
</tbody>
</table>

$^a$Values taken from the JEF data library at 0.025 eV (JEF-2.2).
capture agents in fast neutron therapy, could have a significant impact on overall cure-rates. Clinical enthusiasm for such an approach is constrained by the fact that the presently available capture agents, combined with the low capture cross-sections of isotopes such as $^{10}$B at high energy ($^{10}$B(n,α) cross-section at 10 MeV is approximately 0.06 barns), means that the potential for dose enhancement is thought to be around 5%. Hence this modality sees unlikely to have a substantial clinical impact at present. Calculations suggest (Maughan et al., 1996) that modifications to conventional fast neutron beams could improve this figure to in excess of 10%, and the development of capture agents with improved specificity would certainly have a dramatic impact here.

### Accelerator neutron sources

A particle accelerator suitable for BNCT is estimated to be of a similar cost to systems for high energy neutron and proton therapy. That is approximately three to four times the cost of a conventional high energy linear accelerator used routinely in hospitals around the world. It is therefore substantially cheaper than reactor technology, and would be acceptable for an in-hospital location.

From the physics and neutronics point of view there are also a number of advantages to accelerator systems. It is possible, by manipulating such parameters as incident beam, energy, and moderator thickness, to produce neutron beams of different characteristics. There is also the option of using different target materials and different incident particle types but generally attention has focused on low energy proton accelerators with the choice of either lithium or beryllium as the target material. Nevertheless, there are a number of alternative accelerator configurations which also deserve some attention, including moderation of beams from high energy proton accelerators, and designs for neutron production at threshold for direct incidence onto the patient without a moderator. These two alternative approaches will be described first, before concentrating on the application of moderated low energy proton accelerators as the principal route to accelerator based BNCT.

### High energy accelerators.

The role of cyclotrons in the treatment of cancer is now well established. Their contribution to both fast neutron and proton therapy is substantial, and they are now an established part of the armoury against cancer around the world. It is also possible that high energy accelerators such as the one at PSI, Switzerland, will be useful in producing a beam suitable for BNCT. Moderator design studies (Teichmann and Crawford, 1996) have been undertaken which indicate that a suitable epithermal beam can be produced from this facility.

### Unmoderated low energy accelerator systems.

It may also be possible to use a low energy accelerator without a moderator system (Kononov, 1996). In this case, the target material, usually lithium, is bombarded with protons with an energy of around 1890 keV, i.e. only slightly above the threshold for this reaction at 1881 keV. From kinematic considerations, there will be neutron emission in a narrow forward directed cone, with neutron energies in the desired epithermal (around 10 keV) region. Since the neutron production cross-section of the target material will be changing very rapidly near threshold, small fluctuations in incident particle energy may lead to dramatic changes in all properties of the emergent neutron beam, i.e. in its energy, angular distribution, and intensity. Hence, this approach, while still requiring the production of high proton beam currents and targets with high power dissipation capabilities, also requires very good voltage stability in the accelerator system.

One very interesting variant of the accelerator option for BNCT, is that described by Song et al. (1996) using a miniature accelerator tube, stereotactically inserted into the centre of the tumour through a bore-hole in the skull. This approach could, in principle, provide a very substantial increase in dose-rate around the tumour, but with some cost in terms of the radiobiological characteristics of the beam. Further technical work is necessary to determine the heat removal capabilities of such a miniature accelerator and target system.

### Moderated low energy accelerator systems.

Low energy accelerators, generating neutrons up to around 1.5 MeV, require quite small, compact, and inexpensive beam modification systems such as the one shown in Fig. 1. This kind of accelerator system for BNCT is favoured by many laboratories around the world (Allen and Beynon, 1995; Yanch et al., 1992; Chu et al., 1996) and appears to offer the best possibility for clinical use. The design of these systems can be tuned to produce neutron beams with different characteristics, as illustrated in

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**Table 3. Neutron beam characteristics of a number of BNCT centres**

<table>
<thead>
<tr>
<th>Centre</th>
<th>Useful neutron fluence-rate (cm$^{-2}$ s$^{-1}$)</th>
<th>Mean neutron kerma per unit neutron fluence (g$_{eq}$/Gy cm$^2$)</th>
<th>Mean photon kerma per unit neutron fluence (g$_{eq}$/Gy cm$^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petten Design (Moss et al., 1992)</td>
<td>$2.3 \times 10^9$</td>
<td>$&lt;8.1 \times 10^{-13}$</td>
<td>$&lt;2.8 \times 10^{-13}$</td>
</tr>
<tr>
<td>BNL I (Liu, 1996)</td>
<td>$1.4 \times 10^9$</td>
<td>$4.5 \times 10^{-13}$</td>
<td>$1.5 \times 10^{-13}$</td>
</tr>
<tr>
<td>BNL II (Liu et al., 1997)</td>
<td>$0.84 \times 10^9$</td>
<td>$4.8 \times 10^{-13}$</td>
<td>$2.0 \times 10^{-13}$</td>
</tr>
<tr>
<td>Birmingham (Allen and Beynon, 1995)*</td>
<td>$0.82 \times 10^9$</td>
<td>$7.4 \times 10^{-13}$</td>
<td>$0.8 \times 10^{-13}$</td>
</tr>
</tbody>
</table>

*For a moderator depth of 20 cm and a proton beam of 5 mA at 2.8 MeV.*
Fig. 2. Increased thermal components in the beam (lower \( G_n \) in Fig. 2) would be useful for delivering an enhanced boron-capture dose to more superficial region, while beam apertures, decreased moderation and the use of thermal neutron absorbers such as lithium in the moderation system, can be used to enhance the beam penetration. In this way it is possible, in principle, to tune the delivered neutron beam to suit a range of clinical situations. However, this process must be accompanied by detailed radiobiological studies to assess the impact of each beam adjustment on the response of normal tissues placed in the beam.

**Target cooling**

The removal of heat from an accelerator target is one of the principal technological challenges to be overcome by all low energy accelerator systems. The melting point of lithium metal is around 180\(^\circ\)C, which means that heat removal must be highly efficient if the target is to remain solid. The minimum beam power requirements for a moderated low energy accelerator system approximates to a proton beam current of 5 mA at an energy of 2.5 MeV. This is a beam power of 12.5 kW, deposited over a few square centimetres in a target layer which is only around 150 \( \mu \)m thick. The power density is therefore approximately 1 kW/cm\(^2\) for a uniform 4 cm diameter beam and is near the limit that can be removed by water-based cooling mechanisms (see Table 4).
Table 4. Heat transfer coefficients from a range of cooling mechanisms (Blackburn et al., 1996)

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Coefficient (W/m² K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free Liquid Convection</td>
<td>50–1000</td>
</tr>
<tr>
<td>Forced Liquid Convection</td>
<td>50–20000</td>
</tr>
<tr>
<td>Convection with a phase change</td>
<td>2500–10³</td>
</tr>
<tr>
<td>Submerged jet with a phase change</td>
<td>&gt;6 × 10⁷</td>
</tr>
</tbody>
</table>

Of the available options it appears that submerged jet cooling is the only option worth pursuing. This involves placing the back surface of the target in contact with a fluid bath which contains a jet of the same fluid, injected via a nozzle onto the centre of the target. In this way the jet is maintained at a lower temperature than in forced convection cooling and in addition, localised boiling is allowed on the target rear surface. Any vapour bubbles are blown away by the impact of the jet which spreads out radially from the centre. Experimental evidence from Blackburn et al. (1996) suggests that submerged jet cooling is capable of accommodating power densities up to 6 kW/cm², which gives a factor of 6 safety margin over that required for a uniform beam power, and should deal adequately with the non-uniform proton beams which are likely to be encountered in practice.

DOSIMETRY FOR BNCT BEAMS

The dosimetry of the neutron beams used in BNCT is extremely complex. Neutron interactions in boron-loaded and normal tissues give rise to a range of secondary particles which deposit the radiation dose. The very wide spread in LET of these reaction products, and by implication the wide range of RBEs involved, means that these dose components must be separately quantified if an accurate overall assessment of the radiation dose is to be made.

Practical beam dosimetry in photon radiotherapy is exclusively based on ion-chambers, with reference to Primary standards which may either be based on ionisation yield or on more direct measures of energy deposited such as calorimetry. Centres in North America that already have active clinical BNCT programmes have also chosen to use ion-chambers as their routine dosimetric tool (Rogus et al., 1994) with reference to a Primary standard through a photon calibration of the dosimeters. In Europe, efforts are in hand to develop an agreed dosimetry protocol amongst the centres that are pursuing clinical BNCT facilities (Stechet-Rasmussen et al., 1996).

A number of authors have reported on the use of the microdosimetric technique for BNCT dosimetry (Wu et al., 1992; Maughan et al., 1992). In Birmingham, we are also attempting to further understand the radiation absorbed dose deposition by making use of the microdosimetric technique using specially designed proportional counters. The feasibility of this approach has been demonstrated at low fluence rates, but needs to be confirmed in the full therapy beam (Green et al., 1996).

These techniques notwithstanding, macroscopic dosimetry (i.e. determination of absorbed dose in cm sized voxels) is not truly possible without some information on the macroscopic distribution of boron in the tissues of the patient. It has become routine practice in active BNCT centres, to rely on a pre-therapy bio-distribution study to measure the boron partitioning between tumour, blood and normal brain tissue, for a particular infusion protocol. These relative partitions are assumed to be reproduced at the time of therapy, even when this follows a de-bulking procedure (Chanana, 1996).

Whilst these approximations are certainly appropriate for early trials, greater understanding of clinical outcomes may be possible if the boron distribution can be measured at the time of the therapy irradiation. Promising techniques in this area are based on spectroscopic magnetic resonance imaging (Flego et al., 1996) where the spin relaxation of ¹¹B is measured, and also on direct measurement and possible imaging of the capture gammas from the ¹⁰B capture reaction (Allen et al., 1996).

EXPERIENCE IN BIRMINGHAM

The dynamitron accelerator

The Birmingham BNCT programme is based around the 3 MV Dynamitron accelerator in the School of Physics and Space Research at The University of Birmingham. In such an accelerator, the terminal voltage is maintained through a series of Cockroft–Walton type voltage doubling stages, but unlike a conventional Cockroft Walton cascade accelerator where power is delivered in series through the chain of doubling stages, in the Dynamitron, radio-frequency power is delivered in parallel from large cylindrical plates placed outside the doubling chain, and coupled to it via circular metal strips. This coupling of the power delivery in parallel means that much higher charging rates are possible, giving the Dynamitron a potential for stable production of high beam powers.

In addition, the Dynamitron is built with an internal electrode geometry which is designed to reduce the path for scattered and divergent particles, preventing them from reaching significant energies within the accelerator column. Hence the production of background X-rays and neutrons within the accelerator column is minimised. In its present configuration, the accelerator has produced...
reliable beams of around 2 kW power (1 mA protons at 2 MV).

The Birmingham programme is nearing the end of a second design stage. Work on the initial beam moderation system has now been completed. This includes design (Allen and Beynon, 1995), measurement validation (Tattam et al., 1996) and dosimetric characterisation (Green et al., 1996). Work is shortly to begin on two key areas, namely the upgrade of the accelerator ion source to give the potential for beams up to 10 mA, and construction of a beam moderation system which will produce a horizontal epithermal neutron beam from an incident vertical proton beam.

CHARACTERISATION OF THE BIRMINGHAM EPITHERMAL BEAM

Initial design studies for an accelerator based neutron source for BNCT applications have been performed using the radiation transport code MCNP (Briesmeister, 1993). These have been followed by experimental validation based on the system similar to that shown in Fig. 1, but without the outer D2O and Li shield. This is basically the Li target and moderator system described by Tattam et al. (1996).

Outline of the experimental programme

The experimental programme comprised the following elements.

1. Construction of a rectangular Perspex enclosed water phantom. Following the computational work of Gupta et al. (1993) we have chosen a phantom of dimensions 17 cm × 14 cm × 15 cm, which is the intermediate of the three phantoms which they investigated.

2. Measurements at four positions along the central axis of this phantom of:

- fast neutron dose from a Tissue Equivalent (TE) microdosimetric detector
- photon dose from a TE microdosimetric detector
- boron dose indirectly using thermal fluence figures derived from gold foil activation

3. Comparison of absolute experimental results (in terms of dose rate/mA of proton beam) with an absolute MCNP simulation of the exact experimental configuration.

4. Assessment of the clinical utility of this beam using the CBE factors derived for BPA and the fast neutron RBE from the Brookhaven group (Chanana, 1996). These are:

<table>
<thead>
<tr>
<th>Component</th>
<th>Physical dose (Gy)</th>
<th>(RBE or CBE) x dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumour</td>
<td>Normal brain</td>
<td>Tumour Normal brain</td>
</tr>
<tr>
<td>10B</td>
<td>64.5</td>
<td>21.5</td>
</tr>
<tr>
<td>Neutron</td>
<td>6.5</td>
<td>6.5</td>
</tr>
<tr>
<td>Photon</td>
<td>29.0</td>
<td>29.0</td>
</tr>
<tr>
<td>Total</td>
<td>100.0</td>
<td>57.0</td>
</tr>
</tbody>
</table>

Validation of the MCNP simulations

The comparisons between experimental and MCNP simulation results are represented in Table 4 as ratios between the experimental and simulation results at each depth. Hence good agreement between experiment and calculation would result in a value of 1.0. It is clear from Table 5 that the validation is successful for fast neutron, photon, and boron dose derived from gold foils.

Dosimetric data

In order to derive estimates of the likely biologically equivalent dose which will be delivered by the Birmingham beam, and to further understand its clinical utility, the factors listed above for concentration, CBE and RBE have been combined with the physical dose measurements to give information on the variation with depth of each dose component to both tumour and normal tissue. These data are represented in Table 6 which shows both physical (Gy) and Gy-equivalent dose data at 5 cm deep in phantom.

Hence, from Table 6, the total dose to normal brain (in Gy-Eq) at 5 cm deep is only approximately 26% of the total dose to tumour at this depth, whereas the corresponding figure in terms of physical dose is 57%. It is therefore clear that by using our understanding of the different degrees of cell damage that result from the different dose components in BNCT, a significantly increased relative dose to the tumour is predicted, being greater than that derived from considerations of physical dose alone.

SUMMARY AND CONCLUSIONS

The field of accelerator based BNCT is rapidly expanding, reflecting an increased clinical interest.
following positive results from work in Japan and North America. Data presented here indicate that the enhanced toxicity of the boron capture reaction leads to a dose enhancement which appears favourable for therapy. The ways in which particle accelerators may be used in BNCT are diverse, and cover a possible range of incident particle (almost exclusively proton) energies from around 2 to 600 MeV, with accelerators ranging in size from those which might be sufficiently small to allow direct insertion into the tumour site, to spallation sources which use synchrotron rings of many metres in diameter.

This area has become very a very productive one for radiation physicists throughout the world, who function as part of multi-disciplinary teams brought together to struggle with the many scientific and technical challenges that BNCT involves. However, this is not simply a subject for abstract research. Despite the best efforts of modern medicine, patients diagnosed with the tumour glioblastoma multiforme will be dead within 5 years of the initial diagnosis, the vast majority dying within the first 2 years. BNCT offers some hope for these patients.

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