MEDICAL APPLICATION OF DOORS

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INTRODUCTION

DOORS[1] is a collection of codes anchored by the one- two- and three-dimensional discrete ordinates transport codes, ANISN[2], DORT[3], and TORT[4], respectively. Pre- and post-processing codes are included in the collection to prepare cross-section data, pass data from one code to another, and help interpret calculated results. Two- and three-dimensional semi-analytic uncollided flux and first collision source codes and a two-dimensional last flight estimation code are available to help reduce some of the problems that arise in large low scattering regions. Coupling codes that allow extremely large problems to be run using bootstrapping techniques are also included in DOORS. These coupling codes allow complex three-dimensional structures embedded in large two- or three-dimensional geometrically simple zones to be efficiently treated using more than one transport code. In addition, graphics codes together with a graphics library are included in DOORS to generate contour plots of particle flux or specified responses.

In Section I, a number of investigations directed at optimizing Boron Neutron Capture Therapy (BNCT) facility designs are described. Doses calculated with DOORS in a section of a human leg are compared against those obtained from Monte Carlo calculations in Section II. In Section III, fluxes calculated with DOORS in a dog head phantom are compared against measure fluxes and Monte Carlo calculated fluxes. Finally, a brief summary is given in Section IV.

I. BNCT Facility Design Optimization

ANISN and DORT have been used at a number of institutions to optimize material selections for Boron Neutron Capture Therapy beam filter designs. Both "brute force" optimizations and optimizations using gradient information have been performed.

BNCT is a bimodal therapy first proposed over 50 years ago as a means of treating malignant brain tumors, in particular, glioblastoma multiforme (GBM). In BNCT, the patient is first given a suitable boronated pharmaceutical that preferentially seeks the malignant tissue. The tumor region is then irradiated with an epithermal or near epithermal neutron beam to generate a thermal fluence in the diseased tissue. Due to the high ^{10}B thermal neutron capture cross section, the ^{10}B readily absorbs a neutron. It then up into two charged ions (^{4}He & ^{7}Li) that range out over cellular dimensions thereby enhancing the destruction of tumor tissue with minimal dose to the surrounding healthy tissue.

In what follows, BNCT optimizations performed employing one-dimensional methods are first discussed. A multidimensional optimization method is then discussed.

A. One-Dimensional Calculations

Ingersoll, Slater, and Williams[5] performed several one- and two-dimensional analyses using ANISN and DORT to determine if the Tower Shielding Reactor (TSR-II) at Oak Ridge National Laboratory (ORNL) could provide a suitable beam for BNCT. In their analyses, they investigated the use of a number of materials commonly considered in BNCT filter designs, e.g., aluminum, heavy water, sulfur, bismuth, lead, cadmium, boral and lithiated polyethylene, and found the best balance between beam intensity and energy spectrum could be obtained using an aluminum/aluminum fluoride material.

Their preliminary one-dimensional calculations led to a beam filter design consisting of 0.8 m of Al/AlF_3 (in a 1:1 mixture) followed by 92 mm of sulfur, 0.2 mm of cadmium, and 0.1 m of bismuth. Two-dimensional calculations then indicated that a 0.1-m-thick lithiated polyethylene collimator provided acceptable beam definition with minimal beam loss. The calculated patient incident epithermal flux and beam purity (ratio of epithermal current divided by four times the fast neutron kerma plus photon free-in-air tissue kerma) for this design indicated that a beam having a magnitude and spectral purity comparable to other proposed BNCT facilities could be obtained at the TSR-II.

In addition to the above work, a large number (too large to be referenced here) of other investigators have also employed ANISN to design possible BNCT facilities since this code is extremely fast and thus well suited for preliminary or conceptual design calculations.

The TSR-II beam filter design was achieved using “brute force” methods, i.e., by manually varying the different materials until an acceptable filter was obtained. Other investigators, in particular, Karni, Greenspan, Vujic, and Ludewigt,[6,7] have utilized gradient information to help select optimal materials for use in BNCT facilities.
Karni and Greenspan[6] investigated the feasibility of using the SWAN[8] optimization code to identify suitable neutron source assemblies for BNCT applications. SWAN uses gradient information to calculate material replacement effectiveness functions. The material replacement effectiveness function of material j relative to a reference material k predicts the change in a performance parameter due to the replacement of material j by an equal amount of material k at a given location. SWAN is based on a perturbation theory approach and as such requires the calculation of both forward and adjoint fluxes. In their investigation, these fluxes were obtained employing the one-dimensional discrete ordinates transport code ANISN.

At the time of their investigation SWAN could only be used to optimize linear functionals. However, BNCT material optimization generally requires the optimization of a ratio of functionals, i.e., the ratio of the damage rate or dose in a tumor to that in some selected healthy tissue near the tumor. To overcome this problem they developed a strategy that consisted of calculating the forward flux and two adjoint fluxes, i.e., one for the numerator and one for the denominator. This allowed them to easily obtain from SWAN a material replacement effectiveness function versus position for the ratio of responses by subtracting the effectiveness function for the denominator from that for the numerator.

The one-dimensional model employed in their study consisted of an inner 40 cm thick alumina reflector, a 1 cm thick isotropic neutron source region, and a 40 cm thick beryllia moderator. Immediately outside the moderator, a layer of ^{6}LiF separated 18 cm of healthy tissue that was assumed to contain a tumor loaded with ^{10}B. In the optimization, Al_2O_3, BeO, Be, D_2O, H_2O, C, MgO, SiC, $CaCO_3$, ^{7}LiF, ^{6}LiF, and Pb were allowed to replace the initial reflector and moderator materials and the concentration of the ^{6}LiF was allowed to vary.

The optimization strategy chosen by the authors to illustrate the use of SWAN consisted of first selecting promising constituents based on the calculated material replacement effectiveness functions. Once promising constituents were identified and substituted for the original reflector and moderator materials, they searched for optimal constituent distributions by analyzing calculated material replacement effectiveness functions for the new reference configuration.
Although the results from their investigation may not be directly applicable to actual BNCT treatment facilities since only one-dimensional models were employed, their study did demonstrate the feasibility of using SWAN. In addition, (and probably more important), some if not many of the material changes predicted by SWAN would most likely not have been predicted by even an experienced BNCT facility designer.

In a separate study[7], Karni and Greenspan together with Vujic and Ludewigt illustrated the use of SWAN in identifying optimal beam shaping assemblies for two accelerator energies. Their results indicated that SWAN could be used to reliably compare different BNCT facility designs.

B. Multi-Dimensional Calculations
Shortly after the one-dimensional optimization efforts described above, a multi-dimensional optimization strategy for BNCT filter design including a local (versus global) optimizer was developed by Lillie[8] at Oak Ridge National Laboratory. The optimizer employed a fairly simple quasi one-dimensional line search based on gradient information obtained using forward and adjoint fluxes calculated with the two-dimensional transport code DORT.

The overall optimization strategy consisted of first calculating two adjoint leakages from a patient’s head using the three-dimensional transport code

TORT. The adjoint sources for these calculations consisted of dose response functions distributed over the tumor volume and over the healthy brain tissue between the tumor and the beam entrance to the head. After processing these leakages into source terms, the optimization code executed, through system calls, the DORT code to obtain one forward and two adjoint flux distributions throughout a two-dimensional beam tube-filter (BTF) geometry. These flux distributions were then used to obtain the gradient of the dose ratio (dose in tumor divided by dose in healthy tissue) with respect to the materials comprising the BTF geometry.

The optimizer was initially tested using two fairly simple one-dimensional models. The leakage spectrum from the TSR-II was chosen as the radiation source for both test cases. In the first test, epithermal to non-epithermal (including photon) flux ratios were maximized. The initial filter compositions consisted of one of six candidate materials, i.e., either LiF, D_2O, Pb, Be, Al_2O_3, or Cd. After optimization, improvements in the flux ratios ranged from 1.5 to over 200. This wide range readily illustrates that the optimizer could only search for local maximums. In the second test, the final "brute force" filter design given above for the TSR-II was chosen for the initial filter composition. After optimization, increases of between 26 and 43 percent in beam purity were obtained using three different criteria to select changes in composition during each step of the optimization search.

In the final test of the optimization strategy, a patient's head was simulated using a simple three-dimensional parallelepiped model and a small tumor was placed in center of the model. The initial BTF geometry consisted of a 1 m thick filter having a 0.2 m radius which was in turn surrounded by 0.05 m thick beam tube comprised of a 50-50 mixture of Be and lithiated paraffin containing 7.5 weight percent Li. The filter consisted of 0.6 m of a 25-75 mixture of Al and AlF_3, 0.2 m of Al at 75 percent theoretical density, 0.1 m of AlF and Bi at 10 and 35 percent theoretical density, respectively, and 0.1 m of Bi at full density. This filter design was based on the final filter compositions from the second test case. As in the simple tests, the TSR-II spectrum was employed as the radiation source.

In this final test, adoint leakages from the patient's head were first calculated using TORT. Adjoint sources equal to tumor and healthy brain tissue kerma, assuming 30 ppm natural B in the tumor and 3 ppm in the healthy tissue, were employed in these calculations. Inspection of the adjoint leakages indicated that only neutrons with energies between 100 eV and 100 keV can produce tumor-to-healthy-tissue dose ratios greater than 1.0. In addition, only neutrons with energies between 10 and 40 keV can produce a maximum possible dose ratio of 1.33. The low maximum possible dose is due to the use of natural B (not enriched) and due to the tumor being located more than a few cm from the surface of the head where BNCT is most effective. After optimization, the neutron flux between 100 eV and 100 keV at the filter exit increased by almost a factor of 200, whereas over the remainder of the spectrum the maximum increase was less than a factor of 40. This spectral shift after optimization increased the tumor to healthy tissue dose ratio from 0.78 to 1.17. Thus the optimization strategy was successful in increasing the dose ratio from approximately 59 to 88 percent of the maximum possible dose ratio.

II. LOWER LEG DOSE COMPARISON

Ingersoll, Slater, Williams, Redmond, and Zamenhof[9] have compared dose distributions obtained with TORT with those obtained from the Monte Carlo code MCNP.[10] The primary purpose of their study was to assess the relative computational merit of a deterministic transport code against a stochastic transport code.

Their comparison was performed using a voxel model of a lower leg built from computed tomography (CT) images with the MCNP model containing 11,025 voxels and the TORT model containing 15,782 voxels. The increased number of voxels in the TORT model was required since TORT requires its parallelepiped mesh to extend over the entire geometric model. They varied a number of input parameters to both codes and used cross-section data based on Versions V and VI of the Evaluated Nuclear Data File (ENDF). They observed very little difference with the choice of cross sections. However, they found that the use of $S(\alpha,\beta)$ scattering kernels in MCNP greatly improved the comparison between the two codes. They also found that most of the parameter changes in TORT produced relatively minor differences in calculated doses whereas a fairly significant differences appeared in the MCNP calculated doses when the number of histories was increased from 3 to 10 million.

Running times for those cases in which better than 5 percent agreement was found to exist in more than 95 percent of comparable voxels (not all of the TORT voxels were in the MCNP model) indicated that TORT was nearly a factor of 15 times faster than MCNP. It was clear from their study that TORT provided an excellent alternative to Monte Carlo methods for BNCT treatment planning when voxel-based anatomical models were employed.

III. PHANTOM DOG HEAD COMPARISON

Wheeler and Nigg[11] have performed numerous studies in which they compared calculated dose distributions in a lucite dog head phantom using both stochastic and deterministic methods against measured data. The measured data was obtained using the existing Brookhaven Medical Research Reactor (BMRR) beam at Brookhaven National Laboratory. In addition to comparisons to measured data, they also performed calculations to evaluate important dose parameters for the proposed Power Burst Facility beam at Idaho National Engineering Laboratory (INEL). In their comparisons, the stochastic calculations were carried out using the Monte Carlo module rtt_MC under development at INEL and the deterministic calculations were carried out using TORT.

To obtain their measured data, they activated copper-gold alloy wires in catheters that had been inserted into vertical pre-drilled holes in the dog head phantom. This alloy was chosen so that the thermal flux could be measured separately from the total flux.

The dog head phantom was irradiated with the beam incident on the top center of the phantom and all normalizations were performed based on a nominal BMRR power of 2.9 MW. The vertical thermal flux profiles obtained from both calculational methods through the phantom at the center of the beam agreed with the measured profile within 15 percent or better. The peak thermal flux obtained from the Monte Carlo calculation was approximately 12 percent greater than the measured value whereas the TORT calculated peak thermal flux was only approximately 6 percent greater. The TORT calculation did however require more than three times as much computation time. In spite of the increased run time, Wheeler and Nigg conclude that deterministic codes such as TORT are very well suited for BNCT applications.

IV. SUMMARY

ANISN and DORT have been used at a number of institutions to optimize material selections for Boron Neutron Capture Therapy (BNCT) filter designs. Both “brute force” optimizations and optimizations using gradient information have been performed. TORT has been used to calculate dose distributions throughout a phantom dog head and throughout a human lower leg. The TORT calculated dose in the dog’s head agreed very well with measured doses. Excellent agreement with Monte Carlo calculated results in the lower leg indicated that deterministic transport codes can produce satisfactory dose mappings for voxel-based anatomical models with significantly less computation cost than Monte Carlo methods.

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