SERA — an advanced treatment planning system for neutron therapy

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Abstract. The technology for computational dosimetry and treatment planning for Boron Neutron Capture Therapy (BNCT) has advanced significantly over the past few years. Because of the more complex nature of the problem, the computational methods that work well for treatment planning in photon radiotherapy are not applicable to BNCT. The necessary methods have, however, been developed and have been successfully employed both for research applications as well as human trials. Computational geometry for BNCT applications can be constructed directly from tomographic medical imagery and computed radiation dose distributions can be readily displayed in formats that are familiar to the radiotherapy community. The SERA system represents a significant advance in several areas for treatment planning. However further improvements in speed and results presentation are still needed for routine clinical applications, particularly when optimization of dose pattern is required.

1. INTRODUCTION

The Simulation Environment for Radiotherapy Applications (SERA) system, developed independently by INEEL in collaboration with Montana State University, is entering the applications phase. SERA consists of several modules for 1) image manipulation, 2) model reconstruction based on medical images, 3) dose computations by Monte Carlo simulation, 4) three dimensional model and dose display, 5) two dimensional dose contour display over image slices, 6) planning tools for field and fraction selection, and 7) tools for creation and display of line plots and dose-volume relationships. SERA is currently in initial clinical testing in connection with BNCT trials at Brookhaven[1] and will replace the present BNCT_Rtpe system upon general release in 1999.

The SERA system incorporates a new method for reconstructing patient geometry from medical images and for subsequently tracking particles through this geometry during a Monte Carlo radiation transport simulation[2]. The method, in contrast to the Non-Uniform Rational Bspline (NURBS) method used in BNCT_Rtpe, is based on a pixel by pixel uniform-volume element ("univel") reconstruction of the patient geometry. Fast line rasterization methods, implemented largely with integer arithmetic, are used to allow rapid particle tracking through the univel geometry. Univels along the particle track are investigated, and precise region intersection points can be rapidly calculated as the particle moves from one region to the next. By scaling the univels to match the resolution of the original image data, the geometric fidelity of the NURBS reconstruction method is retained, and the computed doses have similar statistical accuracy. The execution time is reduced by a factor of five to ten. This speedup factor holds even though the new univel model may consist of several million elements. Execution times for the method, with current moderate-priced desktop computing hardware, are in the range of 15–20 CPU minutes per field. Parallelization of the algorithm to, for example, four CPUs would yield computation times in the range of five minutes per field, since the execution speed would scale nearly linearly with the number of CPUs.

A number of other new features are available for the SERA system. For example, a capability to input patient-specific boron localization data derived from PET, as described by Kabalka[3], is under development. The boronated pharmaceutical of interest (in this case boronated phenaylalanine, or BPA) is labeled with ^{18}F, permitting the localization properties of the drug to be observed by PET. This information can be registered with the anatomical images used for the patient geometry construction and thereby incorporated into the treatment planning calculations. Currently, BNCT treatment planning is typically based on the rather simple assumption of a uniform boron concentration within each anatomical region of interest in the model. The new capability thus will offer the potential for increased fidelity in the boron dose computations. In addition, a technique for further increasing the speed of the radiation transport computations that is based on the application of weight windows is under investigation by INEEL collaborators at the University of Michigan[4]. The basic physics modules of SERA will allow incident neutron energies up to 100 MeV, with an explicit treatment of recoil proton transport. This expands the utility of the SERA system into the field of fast-neutron radiotherapy, with or without BNCT augmentation[5].

2. SERA DESCRIPTION

The main menu for SERA is shown in Figure 1. This window may be used to launch the modules of SERA or they may be launched independently. It accommodates an expert mode, and allows global preferences to be set. The main menu provides the ability to launch or close individual SERA components on different displays and to provide command line parameters to a software module when it is launched. At this time, SERA will run on either Linux-based Intel systems or Solaris 2.6 (or newer) systems with high-end video support. Other computer systems will be supported only under special arrangements.

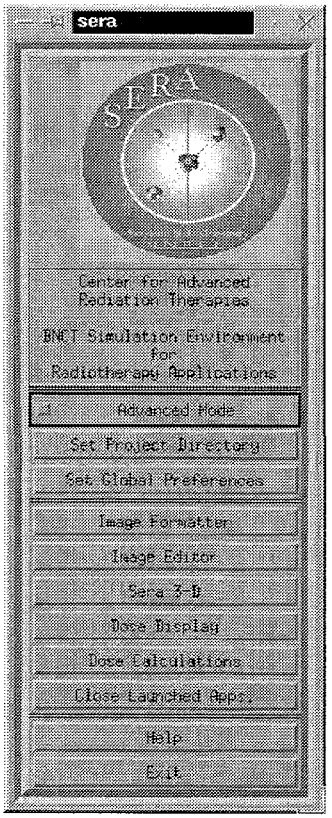

FIG. 1. SERA main menu.

2.1. Image Formatter (seraImage)

Most treatment plans developed with SERA will begin with the **seraImage** formatting module. Its basic function is to convert the original medical image format into the QSH format, which is the internal format used within the SERA modules. QSH is an image file format based on the American Association of Physicists in Medicine (AAPM) standard and described further in the SERA manual located at the Universal Locator Address (URL) http://www.cs.montana.edu/~bnct. The image formatting function will accept unformatted (raw) and QSH formatted images. Images may be deleted, re-arranged, translated, scaled, or rotated. The image header file can also be modified.

2.2. Image Modeling (seraModel)

The purpose of the **seraModel** module is to easily and rapidly divide an image set into regions of interest. The user interface for **seraModel** is shown in Figure 2.

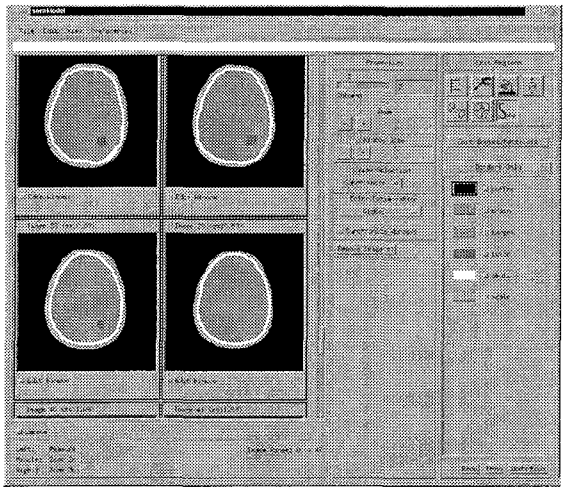

FIG. 2. seraModel user interface.

The image matrix used for display in this program has been generalized to work on systems with different color depths. Images may be viewed at an arbitrary zoom level, in an arbitrary window, and with an arbitrary number of columns.

The **seraModel** module provides many useful image operations, including manual and automatic definition and generation of univel-based regions of interest that form the geometry used by the Monte Carlo radiation transport simulation (**seraMC**). Various tools are provided to aid in the manual/automatic definition of regions including region copying, scaling, overwriting, and painting by fill or borders. Thresholding-based segmenting, 3D region growing, and margin definition operations are also provided. The regions are painted in colors chosen by the user, with an option of viewing just the borders of the regions to see the underlying image. The user can edit regions as small as an individual pixel. These tools are being extended to make region creation by treatment planners as intuitive and efficient as possible. Other features include the ability to:

(1) set and save the preferences for the program,
(2) maintain a list of the recently used files for quick access,

(3) undo one or more operations as may be necessary,
(4) save disk space by transparently reading compressed files,
(5) look at axial, sagittal, and corneal slices, and
(6) use control panels to give the user easy access to important functions.

Another feature of the program saves the regions in a uniform volume element format that lends itself to fast geometry interrogation. A resultant univel (uv/uvh) file format has been developed to describe the voxelized regions.

A set of library routines (libuv) has been written to handle reading and writing the uv/uvh files, and to interrogate the geometry of the bodies represented in these files. The stepping algorithms used for the intersections have increased the Monte Carlo performance by more than a factor of five over the NURBS based algorithm. By maintaining a high resolution set of univels, the accuracy of the simulation is maintained. Additionally, lost particle occurrences are greatly reduced compared to the NURBS geometry interrogation.

2.3. Three Dimensional Viewer (sera3d)

The three dimensional viewer, **sera3d**[6], provides flexible three dimensional displays of the univel-based solid models (see Figure 3) and isodose contour data after all of the bodies are created with **seraModel**. Points, solid regions, hollow regions, or polygonal surfaces can be used to view the geometry. The beam line and selected particle paths may also be displayed in the viewing window. A surface colouring feature for viewing two and three dimensional isodose contours is also provided.

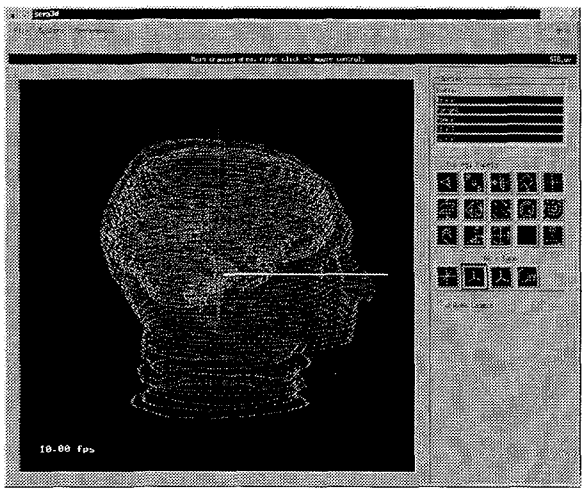

FIG. 3. Three dimensional viewer user interface.

The Open GL graphics standard is used for the **sera3d** three dimensional display. The main purpose of the viewer is to provide the user with a fuller understanding of the proposed treatment plan.

The program will take a segmented uv/uvh file and reconstruct the segmented regions for 3D viewing. Various rendering options provide varying levels of reconstruction performance and detail. Features are provided to further explore the model geometry. User-defined region transparency allows a view through the outer regions to inner regions of interest. Similarly, six orthogonal clipping planes provide a defined "cut" out of the regions to see the regions inside. Full rotational capabilities, various camera positions including a beam-line view, and multiple rendering windows provide additional control.

An additional advancement in the program is the ability to inlay the original medical image into its corresponding location within the reconstructed geometry and to optionally display dose contours on selected planes. The method allows a slice plane to be drawn in an arbitrary direction through the "medical slice volume", resulting in an oblique slice.

This ability has been extended to the loaded beam line, and slices perpendicular to the beamline are now available. It also allows a detailed volume rendering of the original slices.

2.4. Dose Contouring (seraDose)

The **seraDose** (see Figure 4) dose contouring module employs a new locally developed contour library that replaces the contouring libraries used by xcontours, which were supplied by the National Center for Atmospheric Research (NCAR). The addition of the new contouring library allows for more customization of the contour displayed levels. This includes the selection of specific percentage levels at which contour lines are to be placed, the ability to color individual isodoses, and the option of viewing various sizes of contour line labels The user also may save their specific settings in a preferences file for later use.

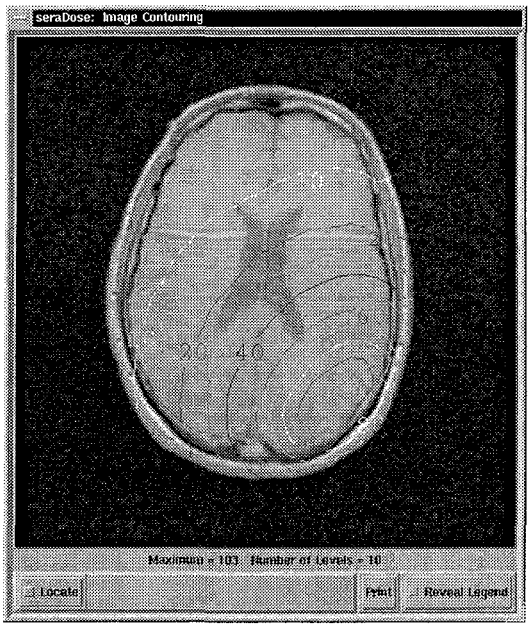

FIG. 4. seraDose display for single image.

The **seraDose** module can display contour color washes in 16, 24, or 32 bit color-depth displays. An image/results directory scheme has been developed for improved file organization and easier manipulation of multiple slices. Finally, **seraDose** can read either raw image files or QSH formatted files.

2.5. Dose Plots (seraPlot)

The **seraPlot** module provides the integrated control of dose-depth and dose-volume plotting utilities that post-process the results of the treatment simulation. The dose-depth and dose-volume utilities read the outputs from the Monte Carlo calculations (**seraMC**) and invoke the xmgr generalized plotting module for each encounter of a line edit and for specified dose-volume edits.

Dose-depth plots can be shown for any or all of the following dose-components:

total dose	Group 1 fluence
boron-10 dose	Group 2 fluence
gamma dose	Thermal fluence
nitrogen-14 dose	Gamma production
hydrogen dose	Ultrafast gamma dose
other dose	

2.6. Field and Fraction Combinations (seraPlan)

The **seraPlan** module allows the user to statistically combine fields and fractions for final treatment planning so that single effective dose can be presented. The user may select between 1 and 6 fractions and between 1 and 4 fields per fraction.

3. DOSE CALCULATIONS

The output from **seraMC** (and other methods) is usually considered to be dose when in fact it is Kinetic Energy Released in Matter (KERMA). In only one instance, the simulation of ultra-fast recoil proton transport (where the incident neutron has energy > 16.9 MeV), is absorbed dose calculated. The KERMA from other charged particles is calculated assuming a uniform macroscopic concentration of the precursor nuclides. The microscopic distribution and charged-particle non-equilibrium is accounted for in the weighted dose by use of an empirical Relative Biological Effect (RBE) or in the case of the boron dose, a Compound Factor (CF). The RBE and CF also includes biological effects which are due to radiation quality. There is no correction from gamma KERMA to gamma dose, which leads to an underprediction or overprediction of gamma dose near boundaries. It is felt that this approximation of dose is adequate for present applications of BNCT.

3.1. Calculation of Pointwise Dose

Patient treatment planning requires the ability to determine pointwise dose. Monte Carlo, in general, computes volume-integrated values since the variance at a single point is infinite. There are methods to determine pointwise dose in Monte Carlo but it is not practical to use these since so much detail is required. In the **seraMC** module, flux and dose is computed as a volume integral for each region. In addition, to provide detail, a virtual edit mesh is imposed over all anatomical regions. This edit mesh consists of an orderly array of cubes, usually with width 10 mm. For every particle path, the contribution to flux and all dose

components for each edit cube intersected by the ray is tallied. After the Monte Carlo simulation, pointwise dose is then determined as a function of the volume-integrated values determined for the edit cubes. The value at a point is determined as a function of the nearest 7 edit cubes in orthogonal directions. The following constraints are assumed to compute each point value.

(1) The flux shape in each orthogonal direction is assumed to be a second order polynomial.
(2) The coefficients of the polynomial are determined using the integral values of the three edit cubes in each orthogonal direction.
(3) The volume integral of all point values within each edit cube is equal to the volume integral value determined in the Monte Carlo process.
(4) At the boundaries of the edit mesh, where there are only two edit cubes, it is assumed that the slope of the function at the boundary is that determined by the two integral values of the cubes.

3.2. seraMC Outputs

Treatment planning requires the use of zero, one, two, and three dimensional outputs. A zero dimensional output is the dose at a single point. This point value may be the minimum dose in the target (treatment volume) which may represent a goal of treatment planning or the point value could represent a constraint in treatment planning.

A one dimensional edit may be a dose-depth relationship, such as shown in the example presented in Figure 5.

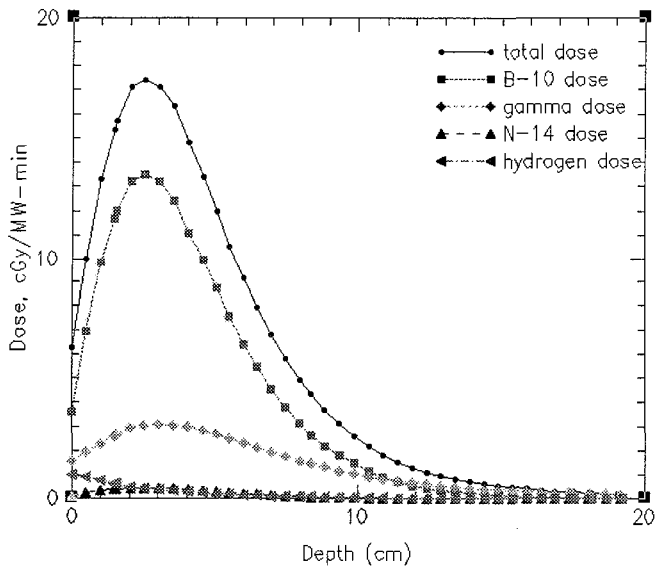

FIG. 5. Dose profile for standard model; 50 ppm boron, 120-mm aperture.

For Figure 5, the boron concentration was set to 50 ppm in the edit even though it was 14.3 in the transport simulation. It is usually assumed that the boron concentration is low enough that the thermal neutron flux is not perturbed by the boron and edits can be obtained for any reasonable boron concentration. If this is not the case and the boron distribution is

known then it can be set to that value for the transport simulation and the flux perturbation would be properly accounted for.

An example of a two dimensional edit is the important isodose display, such as previously presented in Figure 4. To obtain this edit, **seraMC** writes a file consisting of values for a uniform grid, set by the user. This grid is often a 40 by 40 grid over the field of view and the pointwise dose components are written to the file at each grid line intersection. The **seraDose** module then determines the contour lines as interpolated values from the grid points.

An example of a three dimensional edit is the dose-volume integral. The results from this integration provide perhaps the most important information for treatment planning. The dose space is divided into N + 1 percentile bins where N defaults to 10 to give bins of width 10 percent but N can also be set by the user. The additional bin is for dose values exceeding 100% of the reference dose. For each bin and each component, the associated volume is computed. The user specifies a grid width (delta) and the integration is performed over the grid for a specified region or set of regions. The integration is performed at least twice where the grid spacing is halved for successive integrations until the total volume of integration determined by the process differs from the previous integral value by less than a specified epsilon. An example of a cumulative dose-volume plot is provided in Figure 6.

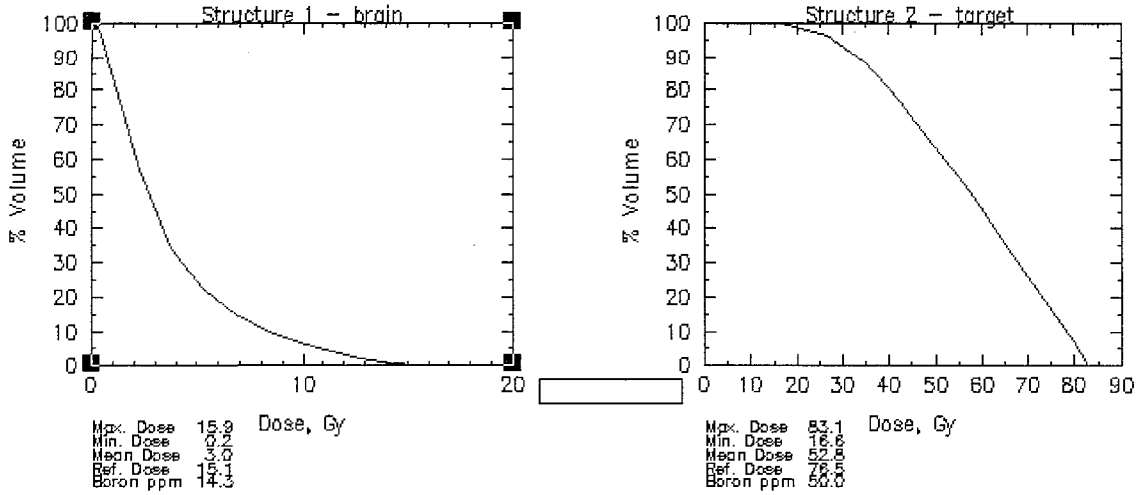

FIG. 6. Dose-volume relationships for standard model.

In addition to volumes for each bin, this edit provides the minimum, maximum, and mean value for each component of dose. These values are mandatory for proper treatment planning. The output for up to 6 plans can be displayed simultaneously for selection by the radiotherapist.

Another important output is the reference dose. The **seraMC** code has several options for determining reference dose. The reference dose can be a specified point, a point at a specified depth along the beam line, or it can correspond to an edit voxel or cluster of edit voxels. If an edit voxel, the reference dose can be the voxel of peak thermal flux or peak weighted dose. One can specify an acceptance region list, for example allowing the reference dose to be in healthy brain but not in the tumor. If the reference dose is an edit voxel it is computed as the mean value of the voxel and a point lying within that voxel could have a

value larger than the voxel value. If the reference volume is more than one voxel then the reference dose is the mean value of the minimum-dose voxel within the reference volume. Typically, the reference volume is some volume in healthy brain and the corresponding reference dose is used to determine the irradiation time such that a certain dose value is not exceeded. The computed reference dose is the concentration and RBE weighted value of dose and is set to be the 100% dose value for contouring and calculation of dose-volume relationships.

Various positioning parameters can be calculated and may be useful in determining the position of the patient relative to the beam. Using the "fiducial" edit one can get the distances (in patient coordinates) from a fiducial marker to the entry point at the center of the beam and to a laser positioning system. One also gets a trace from the marker to the beam exit plane in a direction perpendicular to the plane.

3.3. Optimization

Some work has been done in optimization, or in determining fields etc. such that the tumor control probability is at a maximum and all constraints are met. Manual optimization is a very time consuming process requiring great resource and in the future we plan to automate the optimization process as much as is practical. Optimization is very important because a small increase in minimum target dose can result in a very significant gain in tumor control. For single field applications, positioning the beam such that the distance along the beamline to the center of the target is a minimum is often a good approximation of the optimum single field. As more fields are added, the process becomes much less intuitive and resource intensive, in fact manual optimization becomes an impossible process under time and resource constraints always existing at a particular facility.

A simple example of optimization would be a grid search which can be done manually for single field applications. In this method, the beam orientation is modified in step increments in a range of effectiveness and the orientation yielding the maximum tumor control or other desired goal is selected. As the number of fields increase and the necessary constraints are imposed, this method becomes impractical and more sophisticated approaches are required. One such approach is the differential approach where each beam variable is varied and the differential response is determined. If the response is positive, the search continues in that direction until an optimum or zero differential is determined for each variable. This search is modified by constraints such that situations where the constraint is violated are omitted. This approach has been tried with the doses calculated by a lookup table and it appears to work well. In the future, computer speeds may be such that it would be possible to do this search using Monte Carlo transport. Multiple CPU units would result in linear reductions in the required clock time and it may be possible to find the approximate optimums overnight or even sooner.

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