Random Generator of Computational Phantoms “Trabecula” for Bone Marrow Dosimetry

Abstract—This study was motivated by the efforts on evaluation of radiation risk for leukemia incidence in the Techa River Cohort, where the main bone marrow dose contributors were \(^{89,90}\text{Sr}\) (bone-seeking beta emitters). Energy deposition in bone marrow targets was evaluated by simulating radiation particle transport using computational phantoms. The present paper describes the computer program “Trabecula” implementing an algorithm for parametric generation of computational phantoms, which serve as the basis for calculating bone marrow doses. “Trabecula” is a user-friendly tool that automatically converts analytical models into voxelized representations that are directly compatible as input to MCNP.

Key words: phantom, mathematical; bone marrow; radiation dose; \(^{90}\text{Sr}\)

INTRODUCTION

Results of bone marrow dosimetry feed the assessment of leukemia risk (stochastic effects) (Krestinina et al. 2013) or marrow toxicity (deterministic effects) (Lewington 2005). One of the tasks related to bone marrow dosimetry is to estimate the dose factors that apply to bone-seeking radionuclides deposited more or less uniformly throughout the trabecular and/or cortical bone (Spiers et al. 1978). A method for evaluation of energy deposition in bone marrow targets per an emitted particle is through radiation transport simulation using computational phantoms (Nie and Richardson 2009; Bolch et al. 2010; Kramer et al. 2012). Different phantoms can be constructed assuming different degrees of shape and structural realism. The accuracy and details of phantom geometry depend on the needs of the specific dosimetry task. For example, dose calculations for bone-seeking gamma-emitters (such as organic phosphate and phosphonate complexes of \(^{99m}\text{Tc}\) employed for skeletal imaging purposes (Ogawa et al. 2006) do not require a detailed description of spongiosa microarchitecture (Lee et al. 2006). In contrast, bone marrow dosimetry for alpha- and lower-energy beta-emitters such as \(^3\text{H}\), \(^{14}\text{C}\), \(^{169}\text{Er}\) or \(^{177}\text{Lu}\) (Nie and Richardson 2009; Fischer and Kampen 2012) require a higher resolution description of trabecula surfaces and adjacent intertrabecular space. However, due to the short path length of the charged particles, description of the bone shape is not required; the dimensions of the computational phantom do not typically exceed 2 mm (Dant et al. 2013).

Doses in active marrow exposed to bone-seeking beta-emitters, such as \(^{89}\text{Sr}\) or \(^{90}\text{Sr}/^{90}\text{Y}\) (energies of electron emission are 0–1.5 MeV and 0–2.4 MeV, respectively), should be calculated considering both macro and micro structures. Assuming the continuous-slowing-down approximation, the mean free path of electrons in spongiosa can reach 1 cm. This range is comparable to the linear dimensions of small skeletal bones. Therefore, both bone size and shape should be considered in computational phantoms. The description of spongy bone microarchitecture is also important due to the high probability of low-energy electron emission.

Computational phantoms for bone marrow dosimetry, in particular for \(^{89}\text{Sr}\) and \(^{90}\text{Sr}/^{90}\text{Y}\), have evolved from simple chord-based infinite models of spongiosa (Whitwell and Spiers 1976) to paired-image based voxel representations based on combinations of ex-vivo CT images and \(\mu\)CT or nuclear magnetic resonance microimages (Shah et al. 2005; Zankl et al. 2018). The progress in phantom development has resulted in highly-realistic image-based geometric models. However, because the image-based models are not parameteric and are based on a single cadaver, they can be non-representative of a population and do not allow for the estimation of uncertainties associated with individual variability of human anatomy.

This study was motivated by the efforts on evaluation of radiation risk for leukemia incidence in the Techa River Cohort (Krestinina et al. 2013), where the main dose contributors were \(^{89,90}\text{Sr}\) (bone-seeking beta emitters). The epidemiological study utilizes the stochastic implementation of the Techa River Dosimetry System (TRDS) that calculates dose estimates and associated uncertainty information, in contrast to traditional deterministic dosimetry systems that calculate only point estimates (Zhang et al. 2017). Therefore, dose factors that convert the activity concentration of a strontium isotope
(incorporated in cortical or trabecular bone tissue) into a bone marrow dose rate are estimated in terms of both an unbiased central estimate and a standard uncertainty.

For this purpose, a parametric approach for computational phantom generation was implemented using a stochastic algorithm (Zalyapin et al. 2018). The premise of the approach was that a vast amount of biomedical information on bone-specific micro- and macro-dimensions (and corresponding variability) is available in the literature and could be used for parameterization of bone segment models. Accurate treatment of the literature-derived morphometric data should yield unbiased parameter estimates. The algorithm implements the random generation of rod-like spongiosa structure inscribed into a stylized bone shape coated by a uniform layer of cortical bone. The use of the parametric approach allows for the generation of models corresponding to population-average sex- and age-specific data as well as sets of random models reflecting the individual variability of bone micro- and macro-dimensions.

The present paper describes the computer program “Trabecula” implementing an algorithm for parametric generation of computational phantoms (Zalyapin et al. 2018), which serve as the basis for calculating doses of irradiation of the bone marrow. “Trabecula” is a user-friendly tool that converts analytical models into voxelized representations. The output is directly compatible as input to MCNP (Sood 2017). [Note to Health Physics reviewers: The developers are seeking permission to distribute at no cost the computer program “Trabecula” and an answer is expected by April 2019. Prior to publication, it is proposed to add here information for the reader on where to obtain a copy of the program.]

TERMS AND DEFINITIONS

Basic parameters of the bone microstructure model were fixed according to histomorphometry nomenclature (Dempster et al. 2013) as follows:

- **Tb.Th** – trabecular thickness (mm);
- **Tb.Sp** – trabecular separation (mm);
- **BV/TV** – bone volume fraction of spongiosa (%);
- **Ct.Th** – cortical thickness (mm).

Stochastic modeling of a bone segment is based on population-average values of the above parameters and the intra-specimen variability of Tb.Sp and Tb.Th – (σTb.Sp and σTb.Th) describing how much the bone micro dimensions vary inside a bone segment of an individual.

Stochastic imitation of individual variability of bone geometry considers the variations in both micro- and macro-dimensions within a population under study.

MODEL APPROACHES

Bones are subdivided into segments that can be described by simple-shape geometry (stylized phantoms) (Sharagin et al. 2018). The cortical layer is a homogeneous and isotropic bone substance located between two surfaces, one of which is the outer boundary of the phantom, and the other is separated from it inside the phantom by a distance equal to the Ct.Th. Cortical layer covers spongiosa.

Spongiosa is assumed to be a binary (bone and bone marrow) three-dimensional media, where rod-like bone trabeculae penetrate the bone marrow. The spongiosa model results from deformation of a three-dimensional grid by stochastic node perturbation and random variation of the node thickness. The node perturbation was done based on the data on intra-specimen variability of Tb.Sp assuming a normal distribution (\(\text{Norm}[0;\sigma_{Tb.Sp}]\)). The rod-like trabeculae along the edges of a deformed grid are the space bounded by truncated cones, which are based on the cross sections of the spheres at the nodes of the lattice. The diameters of the spheres are randomly drawn according to the assumption of a lognormal distribution of **Tb.Th** (\(\text{LogNorm}[\mu(Tb.Th, \sigma_{Tb.Th});\sigma(Tb.Th, \sigma_{Tb.Th})]\)). Fig. 1 shows an example of deformation of a single cell in a spongiosa grid.
**Fig. 1.** Example of deformation of a single cell in a spongiosa grid.

*Tb.Sp* is a highly uncertain parameter, which is very sensitive to the measurement method. As a result, the BV/TV ratio of a generated model can differ from the corresponding literature-derived value. Therefore, a special multi-step procedure for calibrating *Tb.Sp* has been implemented (Zalyapin et al. 2018) that fits the BV/TV of the generated model to a corresponding user-defined parameter.

Unlike the analytically modeled trabecular structures and bone segment shape, the homogeneous cortical layer is generated in the process of voxelization (at a given resolution). The voxel belonging to a particular structure (cortical bone, trabecular bone, bone marrow or void) was defined according to the central point of the voxel.

### SOFTWARE DESCRIPTION

**General description**

The “Trabecula” computer program is written in the Java programming language to be run on all platforms that support Java (Version 8 and higher) without the need for recompiling. It is a simple, user-friendly program that does not require computer programming knowledge to use. Monte Carlo simulation algorithms are applied for random model generation. Uniform random variable generation was performed using the `java.lang.Math.random()` function, which is part of the Java Development Kit (JDK). Normal and lognormal distribution of independent parameters were simulated using the Box-Muller transform. For simulating individual variability, macro-parameter values were assumed to be correlated; the inverse transform method was used for simulation of correlated normal distributions.

The generation of computational phantoms uses a medium-scale optimization algorithm. Therefore, generation of large models with high-voxel resolution could take up a significant amount of computer memory and time to execute.

“Trabeluca” underwent extensive verification and validation testing.

A beneficial feature of the “Trabecula” computer program is its ability to generate output files that are formatted as MCNP input (for further simulation of electron-photon transport) as three lattices.
of voxels, viz., a whole computational phantom and two separate source-tissues (cortical and trabecular bones).

User interface

The user interface is designed to support parameter input through an interactive dialogue on the computer monitor-screen. The overall structure of the program is quite simple. Three tabs are displayed in a single browser window (Fig. 2), with the exception of pop-up windows that indicate progress in model generation in the process of program execution (Fig. 2a). The main window contains a wizard, which guides the user through all the tabs for setting the simulation parameters (menu File -> New model).

Fig. 2a shows the tab “General”, which contains user-input fields for administrative information. The field “Results folder” indicates the path where program output will be stored; the default path is the user’s home folder. The field “Name” is the name of the folder to be created to store program output. The field “Number of models” is used to select the size of the model set to be generated; the default size is 1. Additionally, the option to subdivide a segment into pieces according to voxel number indicated is available as check-box “Split results by number of voxels (M)”. The field “Comment” is optional; the content of the field will be included in the output report.

Fig. 2b illustrates the tab “Micro”, which includes the user-specified fields for parameters of spongiosa microstructure modeling, viz., Tb.Th and Tb.Sp (mm) and corresponding intra-specimen variabilities (“st.dev”) as well as individual variabilities (“variability”). The fields “variability” become active when the number of models (indicated in tab “General”) is greater than 1. Two fields indicated as “BV/TV interval” corresponds to the minimum and maximum of the range of possible values. The option “Calibration point” is a desirable option used to fit the model to the user-defined population-mean BV/TV value (Shishkina et al. 2018b, Zalyapin et al. 2018). One more calibration option, viz., check-box “Precise calibration” is also available. Selecting this option calibrates the model following voxelization, taking into account the introduced density (BV/TV) distortions at the border of the spongiosa grid and cortical bone layer. Note that the density distortion effect is significant for small-sized models only (linear dimensions of spongiosa grid are comparable with the Tb.Sp value). The procedure of precise calibration could take up a significant amount of computer memory and time to execute. Therefore, it should be used only if necessary. To assess the need for this option, a preliminary quick generation of a model with calibration point only should be done to compare the obtained and required values of BV/TV. If the values are not equal, then precise calibration is necessary. The field “Voxel size (mm)” indicates the user-defined voxel resolution for the model (ideally, it should be ≤1/2Tb.Th).

Fig. 2c illustrates the tab “Macro”, which includes optional choices for segment stylization, user-specified fields for corresponded linear dimensions as well as for the thickness of cortical layers at different walls of the stylized phantom. The fields “variability” to the right of the parameters become active when the number of models (indicated in tab “General”) is greater than 1. The two fields “Walls interval” are intended to imitate individual variability of Ct.Th as a normal distribution, but truncated by the range of literature-derived values; these fields are activated by the choice of the number of models (indicated in tab “General”) >1.

Two buttons for execution (“Test” and “Start”) are in the upper right corner of the main window. The “Test” button is for preliminary calculations (based on the analytical modeling before voxelization) of volumetric parameters. The test calculates the expected time to generate the model, as well as the expected voxel size and voxel dimensions for a phantom with population-average parameters. The results of the test are shown in the window “Results”. As shown by Fig. 2c, the approximate time to generate a model generation with given parameters and voxel resolution is 12 min (the result window).

The “Start” button is a command to begin modeling. The actual time needed to generate s given model (after the selecting “Start”) was 9 min. Increases in voxel size reduces the time for model generation.
Fig. 2. User interface of the software “Trabecula”: (a) tab “General”; (b) tab “Micro”; (c) tab “Macro”.
The window “Sample Trabecula Model” shows a typical single cell of the simulated spongiosa grid (Fig. 1) in the process of modeling.

The user interface supports two languages: Russian and English.

**Selection of simulation mode**

The computer program supports dual functionality: generation of a model with fixed parameters and generation a set of models based on the individual variability of the model parameters. Users of the computer program are able to select one of the options by choosing the size of a model set. If the “Number of models” is equal to 1, then the population-average model is generated. If the “Number of models” is greater than 1, then a random simulation of individual variability is performed (the input of individual variability parameters are required), but no population-average model will generated.

**Output file description**

The computer program generates the files internally and assigns them names. The simulation results are stored in the user-specified directory in the field “Result folder” of the tab “General”. The hierarchy of outputs is as follows:

1. User-defined folder (for example, C:\Trabecula Model\Male, as it is shown in Fig. 2a);
   
   1.1. Folder with the date and time of numerical simulation (for example, C:\Trabecula Model\Male\2018-07-18_14_30_35);
      
      1.1.1. File “settings.txt” includes the data on input parameters as well as the results of the preliminary model description as performed with the “Test” button.
      
      1.1.2. Folder “Model n”, were n is a sequential number of a model from the set of generated phantoms.
         
         1.1.2.1. File “results.txt” includes the data on generated parameters as well as volumetric and voxel-metric data.
         
         1.1.2.2. File “model.txt” includes the voxel description of the phantom.
         
         1.1.2.3. Archive “sources.zip” comprises four files representing separate voxel descriptions of each generated media (trabecular bone - “trab_source.txt”, cortical bone - “cort_source.txt”, bone marrow - “marr_source.txt” and the void - “void_source.txt”)
         
         1.1.2.4. Folder “images” contains the images of phantom cross-sections in X, Y and Z directions.

The data structure in the file “model.txt” as well as files from “sources.zip” are created according to the requirements for MCNP input, where a box (macro body) that holds the entire three-dimensional array of voxels defined by the number B in the MCNP input cell card. The space lattice filling the box is indicated by the number L in the MCNP input cell card.

The data structure in the files from “sources.rar” is represented by a list of cells in the form of $B:L(i j k):T$. Indexes $(i j k)$ define the coordinates of a cell in the lattice structure. $T$ is a cell-specific media.

The data structure in the file “model.txt” represents the consequent voxel-to-voxel description of fillings of the lattice structure $(T)$ of the entire three-dimensional array $B$. If a set of successively repeated digits is encountered, then the record is shortened with an additional symbol R. For example, an entry of “1 1 1 1 1 1” is reduced to “1 5R”.

**APPLICATION OF THE SOFTWARE**
The generator of bone segment geometry “Trabecula” was designed for construction of computational phantoms of human hematopoetic sites with consequent dosimetric application, viz., for evaluation of energy deposition in bone marrow targets per emitted particle. In the present time, the phantoms are generated in the frame of bone marrow dosimetry for bone-seeking $^{89}$Sr and $^{90}$Sr/$^{90}$Y (Shishkina et al. 2018a; Sharagin et al. 2018) to be used in the TRDS (Degteva et al. 2006). Segment-specific energy deposition per emitted particle is recalculated to a skeletal-average dose factor, converting the radionuclide activity concentration in the cortical or trabecular bone to the value of dose rate in bone marrow. Obtained results will be incorporated into dose conversion factors (annual dose rates in active marrow following unit intake of a radionuclide) used in the TRDS.

Generated models with “Trabecula” can be applied to dosimetric calculations for other bone-seeking beta emitters, such as $^{32}$P; $^{153}$Sm; $^{186,188}$Rh and for some other radionuclides used in medical treatments.

The proposed stochastic modeling approach allows, for the first time, estimation of dosimetric uncertainties due to individual variability of bone geometry. The results obtained with the representative morphometric parameters will be useful for verification and calibration of the single-cadaver-based models constructed using the pair-image method (Pafundi et al. 2010; Hough et al. 2010; O'Reilly et al. 2016).

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