RADIOSTEOPLASTY STUDY IN ANIMAL BONE AND
RADIodosimetric EVALUATION USING MONTE CARLO CODE

Márcia Flávia Silveira and Tarcísio Passos Ribeiro de Campos

Departamento de Engenharia Nuclear – Escola de Engenharia
Universidade Federal de Minas Gerais
Av. Presidente Antônio Carlos 6627
31270010 Belo Horizonte, MG
marciaflaviafisio@gmail.com
campos@nuclear.ufmg.br

ABSTRACT

The radiosteoplasty is a procedure that consists of the injection of a radioactive biomaterial incorporated to the bone cement into the osseous structure affected by cancer. This technique has been developed with the major objective to control the tumor or the regional bone metastasis (in situ) besides pain reduction and structural resistance increasing. In the present study the radiosteoplasty is applied to the bovine and swine bones in vitro using non-radioactive cement. The objective is to know the spatial distribution of the cold compound (non radioactive) in pig and ox bones after implant. A 2mm needle was introduced into the cortical bone previously perforated. The distribution of this biomaterial was observed trough radiological images obtained just after the compound application. Recent dosimetric studies using Monte Carlo N-Particle method (MCNP-5) concluded that the spacial dose distribution is suitable for the protocol namely radiosteoplasty applied to treat bone tumors on superior and inferior members. The Monte Carlo method simulates the present process and it is particularly interesting tool to solve the complex photon and electron particle transport problems that can not be modeled by codes based on deterministic methods. These related radiosimetric studies are presented and discussed.

1. INTRODUCTION

The most frequent bone tumors are: osteossarcoma, Ewing’s sarcoma and condrossarcoma. The amputations and disarticulations were standards procedures for treating this diseases until the 70’s. Approximately 85% of the osteossarcoma and the Ewing’s sarcoma goes to the obit up to the first and second year of life after diagnosis due to lung metastasis consequences [1].

The osteossarcoma or osteogenic sarcoma is the most frequent primary malignant bone tumor; predominates in teenager and young nigger man. It’s placed mainly in large bone which has higher metabolic activity, like around knees (distant femur and nearby close segment. Pain and tumor developments are the most predominant complains [2].

The benign lesions have no symptom and are detected occasionally. Many tumors, however, can cause pain or can be detected as a slow mass growing up. In some circumstances, the first sign of the disease’s presence is a suddenly fracture. The principal treatments that can be used in bone tumors are: surgery, chemotherapy and radiotherapy [3].

The present paper introduces a new protocol named radiosteoplasty for members to treat bone tumors. The insight is the possibility of a treatment for bone tumor lesions in situ, propitiating a bone brachytherapy. The technique challenge is to guarantee that the damaged
bone structure will receive appropriated absorbed dose for its tumor control, mainly to avoid local recurrence. To do so, two essential goals can be reached: controlling local tumor and preserving the motor function of the damaged structure, avoiding member’s amputation. For the present development step of the radiosteoplasty, the radiososimetric evaluation is necessary, once the control tumor dose must be reached.

For this evaluation, the MCNP-5 (Monte Carlo N-Particle Transport Code, version 5) can be used to simulate theoretically a statistic process (such the nuclear particles interaction with materials) and it’s an interesting method to solve nuclear transport problems that can not be modeled by codes based on deterministic methods. In particle transport problems, the Monte Carlo method consists in follow each particle during the entire trajectory until its absorption or escape. The three-dimensional simulation of the nuclear particles transport is an important tool for improvement of the radiotherapy’s procedures in oncology [4].

The SISCODES - Sistema de Códigos para Cálculos de Dose Absorvida por Método Estocástico (system of codes for calculation of the absorbed dose through stocastic methods) is a tool recently developed for the three-dimensional computational planning that works as in interface for MCNP5 code.

This system helps to simulate the radiotherapic treatment in a three-dimensional fashion, considering human heterogeneity with his antanomical and morphologic features. For the radiotherapical treatment simulation, a computational voxel phantom, which means a simulator object, is prepared and incorporated on the data bank. This model is generated from a set of digitalized image from computerized tomography (CT) of a patient region. In the SISCODES the voxels distribution or digitalized image morphology is presented by various grey tons, corresponding to the tissue. The user identifies these tons, informing the tissue type corresponding to each area, creating a colored three-dimensional model. The available tissues have chemical compositions and mass density previously inserted in a data bank, coupled to the nuclear information according to ICRU-46 [5].

2. RADIODOSIMETRIC STUDIES

The construction of a computational model for a specific bone structure of a child with osteossarcoma was prepared. A set of computerized tomography images converted into a voxel model by the SISCODES system. The child was a 15 years old boy, with a bone tumor placed in third proximal left fibula. The images obtained by CT in axial cuts were digitalized and transferred to SISCODES generating the three-dimensional voxel model.

Studying the anatomy of the inferior members, each structure was identified. The pixel sets from the images were related to a predefined color. This color represents a tissue in a biomedical and nuclear data bank from the SISCODES. Figure 1 shows an image of the SISCODES interface depicted the anatomic section that was digitalized. All tissues were identified in the tissue bank. It can be observed that blue was the color choose for bone cement and purple for bone tumor, among other color representing surrounding tissue.
The Sm\textsuperscript{153} (samarium) radionuclide was used in the simulation. It was distributed in a defined region representative of the implanted composite. The source is distributed in a small set of voxels arbitrarily defined into tumor region. This radiopharmaceutical provides 810keV beta particle and 103keV gamma ray, among others. It allows ideal conditions to cintilography imaging even if it is applied systemically [6]. The Sm\textsuperscript{153} has half-life of 46.3h and biological half-life of 50.6 days [7].

Only the Sm\textsuperscript{153} gamma rays will be considered for the spatial dose distribution. The beta emissions are limited in 2 to 3mm range, far from the voxels occupied by the radioactive composite. Then the spatial dose distribution studies due to beta rays will have low spatial resolution in such discrete millimeter mesh. However, it is obvious that all beta rays that will be emitted from the source will be absorbed in the tumor.

### 3. RADIOSTEOPLASTY

The radiosteoplasty can be defined as an interventionist procedure, less invasive, that consists in the injection of a biomaterial, named radioactive bone composite, into the damaged bone structure. Its objective is to control tumor \textit{in situ} with a local radiation delivery, as well, the decreasing of pain and increasing of the structure mechanical resistance. This composite is produced by mixing bone cement and macroaggregates with incorporated radionuclide. The radioactive element used on the simulation was Sm\textsuperscript{153} and it permits the bone cement fixation close to the local tumor.

The polymethylmethacrylate (PMMA) is an acrylic polymer already used in medicine. As an injectable product, for example, it is used in bioplasty (plastic surgery). It is a vehicular gel that can be absorbed and eliminated. In this case, the collagen helps in biomaterial fixation in the local implantation, forbidding it to migrate [8]. On the other side, the hydroxyapatita (HA) has been used in synthetic grafts as a substitute of the natural bone in case of traumatic, infectious, degenerated, and congenital or tumor lesions [9]. The combination of these material, like bone cement, make the composite be available for the radiosteoplasty application.
In the tumor treatments, the hydroxyapatite has been used as a mechanical support with a prolonged action. The anticarcinogenic drugs inserted into hydroxyapatite porous permits that the disease be treated with the gradual liberation of drug into the organism [10]. Upon this aspect, this technique is attractive, because it combines tumor treatment with sick bone replacement [11].

In the present work, the radiosteoplasty technique is experimented non-radioactive (cold), using ox and swine bones. The ox bones were used keeping its organic structure and had suffered no physical preparation. The swine bones were prepared by moving organic material by acid action. In this case, the entire organic structure was dried.

4. RESULTS

A computational voxel phantom was obtained with the radiodosimetric simulation. The dose rate evaluation was processed in all voxel model; however, only a unique representative section it printed. Figure 2 illustrates a section of the computational phantom. It can be observed that the blue region corresponds to the region that received the radioactive cement; the purple is the tumor region; the pink region has no tumor, among other tissues. It can also be observed the standard color assumed by the SISCODES. Those colors are different from those adopted by in the graphic interface running on MCNP-5. A 130x117x10 voxels matrix was considered in the present study, with a 13cm, 12cm and 5cm volume size. The MCNP-5 code evaluate the absorbed dose rate for each smash voxel in function of an injected source, activity, in unities of de Gy.h⁻¹.MBq⁻¹.

Figure 2. Voxel computational phantom. A. Section of the voxel model, showing the anatomic equivalence. B. Longitudinal cut of the analytic phantom with emphasis to the voxel phantom region.

Figure 3 illustrates an arbitrary transversal section of the tumor region among the 15 axial tomography sections involved on the study. The color illustrates the dose rate distribution: 1-5% (blue), 5-10% (green), 10-50% (yellow), 50-80% (orange) e 80-100% (red) from maximal absorbed dose. This figure is obtained in the graphic interface of SISCODES. In this interface, the tomography model is designed in dark blue, in a transparent fashion so it would not interfere with the color assumed to the spatial dose rate distribution.
Figure 3. Spatial dose distribution image in the average transversal section of the tumor region.

The maximal dose rate reached in the studied was $9.02 \times 10^{-5}$ Gy$h^{-1}MBq^{-1}$ and the minimum dose was $1.0 \times 10^{-7}$ Gy$h^{-1}MBq^{-1}$ on the voxel matrix. Taking these values, it’s possible to estimate the total absorbed dose in GyMBq$^{-1}$. It is obtained by applying the following expression, $1.44T_{1/2}$ (hr) times the dose rate (Gy.h$^{-1}$MBq$^{-1}$), in which $T_{1/2}$ represents the half life in hours of the radionuclide. Then, the accumulated dose in the implant will be $6.23 \times 10^{-3}$ Gy.MBq$^{-1}$.

The reached dose into implant will be 46.6Gy for a 7400MBq activity (200mCi), corresponding to the Sm$^{153}$ gamma emission. The maximum dose will be 446Gy for a 2Ci activity (370GBq). The region corresponding to 10-5% of this dose (green region) will receive 46.6Gy, and the one corresponding to 5-1% (blue region) will receive 23.3Gy. These values are appropriate to obtain tumor control, obeying a security margin of 2cm. The Sm$^{153}$ beta emission will be totally absorbed in the implant and it was not evaluated in the moment. However, it’s expected that the beta dose in the tumor will be at least ten times greater than the gamma dose.

The aim of this work is also, to investigate, the spatial distribution of the cold composite (non-radioactive) in the animal bones. To do so, the composite was prepared with a PMMA mixture formed by 2mL of monomer added to 1g of polymer, together with 3g of Sm$^{153}$ mixed to Si and Ca (Si-Ca-Sm$^{152}$ bioglass), 1g of barium sulfate, a small amount of a green contrast agent for the bone composite identification in vitro. Thus, approximately 4mL of the composite was injected in each bone, on its extremities and body. Figure 4 shows the application of 4mL of the cold composite in a swine bone (Figure 4.A) and in an ox bone (Figure 4.B).

Figure 4. The bone composite injection during the radiosteoplasty technique execution. A. Injection in swine humerus. B. Composite being injected in ox femur.
The physical distribution of this material was observed through radiological images obtained promptly after the composite implantation. It shows the possibility of incorporating suitable quantities of the cold bone cement in the tubercular bone structure. Figure 5 shows the radiological image of the swine humerus after the bone composite implantation. It can be observed that the composite distribution into the swine humerus fills great part of the trabeculate (spongy) space of the treated bone.

![Swine humerus after bone composite implantation.](image)

**Figure 5.** Swine humerus after bone composite implantation.

The ox bone can be visualized before (Figure 6.A) and after (Figure 6.B) the application of the bone composite in the extremity of the ox femur (Figure 6).

![An ox bone femur radiography. A. Bone radiography before. B. After the bone composite application.](image)

**Figure 6.** An ox bone femur radiography. A. Bone radiography before. B. After the bone composite application.

The bone composite distribution stayed restricted to the orifice prepared in the bone body, plus few millimeters far. It is important highlights that this bone kept its organic integrity, since it was used 2h after the animal death.

The spatial distribution of the composite injected in swine humerus (Figure 7.A) and in ox femur (Figure 7.B) can be identified by the green color distribution on the bone cross section.

INAC 2007, Santos, SP, Brazil.
It can be seen that the composite injected in ox bone remained restricted to the orifice. Into the swine bone, with non organic structure the canals were better filled. The composite got well distributed into the empty trabecular bone (ox bone).

5. CONCLUSIONS

In this present study, the estimated activity of 7,4GBq is appropriated to reach the patient bone tumor control. A 74GBq activity will reach 23,3Gy absorbed doses in a large volume including 2.0cm of security margin, taking the bone cement as point reference. The bone pain reduction using a systemic radiopharmaceutical named EDTMP-153 uses 111MBq/kg prescribed activity per mass which represents 9,25GBq for a 70kg patient. This activity represents 1/4 of the previously defined activity. However the radionuclide is held locally on the implant, while in the EDTMP-153, its application is systemic. So, the damage effects in healthy tissues will be different, possible less for the radiosteoplasty.

The present experimental procedures involving the bone composite implantation in animal subject confirms the possibility of introducing 3-4mL of the bone composite in a ressectable and intact bone with organic material inside.

The bone composite solidified after the injection in according to what was expected. It could be shown after the cutting of the anatomic bone and observing its cross-sections.

The cement flowed few millimeters far from the bone perforation, filling the hole fully turning it fully closed after the implant. Therefore, there was no possibility that the radioactive material to flow out the locus, keeping the radioisotopes in situ. A spatial dose distribution of the bone composite was suitable, keeping radiation in situ.
Future experiments will address hot composite, including macroaggregates of hydroxyapatite and bioglass made of sol-gel processing. The viability of this technique is encouraging and the authors expected that this procedure can be included on the arsenal to faint against primary bone tumors or in situ metastasis.

ACKNOWLEDGMENTS

The authors give special thanks to CAPES – Coordenação de Aperfeiçoamento de Pessoal de Nível Superior for the scholarship to Márcia Flávia Silveira for the master degree studies collaborating with the preparation of this work.

REFERENCES