Iranian Journal of Medical Physics
Vol. 12, No. 4, Autumn 2015, 278-283
Received: June 16, 2015; Accepted: October 06, 2015

Original Article

Calculation of the Dose of Samarium-153-Ethylene Diamine Tetramethylene Phosphonate (^{153}Sm-EDTMP) as a Radiopharmaceutical for Pain Relief of bone Metastasis

Fatemeh Razghandi[1], Reza Izadi[1], Ali Mowlavi[2, 3*]

Abstract

Introduction
One of the important applications of nuclear physics in medicine is the use of radioactive elements as radiopharmaceuticals. Metastatic bone disease is the most common form of malignant bone tumors. Samarium-153-ethylene diamine tetramethylene phosphonate (^{153}Sm-EDTMP) as a radiopharmaceutical is used for pain palliation. This radiopharmaceutical usually emits beta particles, which have a high uptake in bone tissues. The purpose of this study was to calculate the radiation dose distribution of ^{153}Sm-EDTMP in bone and other tissues, using MCNPX Monte Carlo code in the particle transport model.
Materials and Methods
Dose delivery to the bone was simulated by seeking radiopharmaceuticals on the bone surface. The phantom model had a simple cylindrical geometry and included bone, bone marrow, and soft tissue.
Results
The simulation results showed that a significant amount of radiation dose was delivered to the bone by the use of this radiopharmaceutical.
Conclusion
The bone acted as a fine protective shield against rays for the bone marrow. Therefore, the trivial absorbed dose by the bone marrow caused less damage to bone-making cells. Also, the high absorbed dose of the bone could destroy cancer cells and relieve the pain in the bone.

Keywords: Dose Distribution, MCNPX Code, ^{153}Sm-EDTMP

1- *Department of Physics, School of Sciences, Ferdowsi University of Mashhad, Mashhad, Iran*
2- *Department of Physics, Hakim Sabzevari University, Sabzevar, Iran*
3- *International Centre for Theoretical Physics, Associate and Federation Schemes, Medical Physics Field, Trieste, Italy*

*Corresponding author: Tel: +98-51-44013159: Fax: +98-51-44013170; E-mail: amolavi@ictp.it, amwolavi@hsu.ac.ir

1. Introduction

Bone metastasis is one of the major complications of cancer, normally associated with severe pain and fragile bones. In fact, when an individual is afflicted with cancer (e.g., lung, breast, or prostate cancer), the affected cells separate from the primary tumor, reach the bones through the bloodstream, and start to grow [1].

Pain in the bones is one of the major symptoms of bone metastasis. Bone metastasis occurs as a result of a complex destructive interaction between the host and tumor cells, leading to cell invasion, spread of abnormal cells, and stimulation of the activities of osteoblasts (responsible for the formation of new bones) and osteoclasts (responsible for bone breakdown) [1, 2].

Systemic administration of beta-emitting radiopharmaceuticals for pain alleviation in advanced metastatic bone disease is an effective and established therapeutic option. Today, various radiopharmaceuticals are applied for palliation of bone pain, each with its own advantages and disadvantages [3].

There are various strategies to treat and alleviate the pain caused by bone metastasis. Among these strategies, radiopharmaceuticals are the most commonly used materials for the treatment and alleviation of bone damages, particularly palliation of pain in the bones [4, 5]. Beta-emitting radiopharmaceuticals are normally used for pain alleviation. Besides, some of these radiopharmaceuticals emit gamma rays, which can be used for imaging and gathering information on the dose distribution of radiopharmaceuticals in the tissue [4].

Bone-seeking radiopharmaceuticals, including samarium-153 (^{153}Sm), strontium-89 (^{89}Sr), and phosphorus-32 (^{32}P), are generally used for the palliation of pain in the bones. Other radionuclides are used for the same purpose, with higher or lower rates of success, include rhenium-186/188-dimercaptosuccinic acid, rhenium-186/188-hydroxyethylidine diphosphonate (HEDP), yttrium-90-DOTA, thorium-227-ethylene diamine tetramethylene phosphonate (EDTMP), thorium-227-ethylenediamine tetra(methylene phosphonic acid) (DOTMP), and lead/bismuth-12-DOTMP [4-8].

Recently, Correa-González et al. reported the use of ^{153}Sm-EDTMP for pain relief in bone metastasis, induced by prostate and breast cancers or other malignancies [8]. ^{153}Sm with the physical half-life of 46.27 h emits three types of beta particles with different intensities of 30%, 49%, and 20% and corresponding maximum energies of 0.64MeV, 0.71MeV, and 0.81 MeV, respectively. Also, this complex emits several gamma rays, with 103-keV gamma ray being the major one [1, 10].

In the present study, we considered all photon spectra in our simulation. Generally, ^{153}Sm is stored on the bone surface [9]. Therefore, we calculated the absorbed dose in the bone phantom. The goal of this study was to identify the dose distribution in the bone phantom model and evaluate the doses received by the bone and bone marrow as a vital organ.

2. Materials and Methods

^{153}Sm combines with EDTMP in order to form ^{153}Sm-EDTMP. This combination of phosphonate deposits in the skeleton, proportional to bone regeneration activities. After intravenous injection, nearly 65% of the radiopharmaceutical remains in the skeleton, and after almost six hours, it is fully excreted through the urine. ^{153}Sm-EDTMP normally has fewer side-effects, compared to other radiopharmaceuticals. However, its application is associated with multiple problems such as the high cost of enriched samarium and its short half-life [1, 3, 9].

2-1. *Monte Carlo simulation*

To determine the radiation dose for various tissues in the bone phantom, Mont Carlo simulation model was applied, using the MCNPX code. With the simulation of bone phantom model and its gridding by mesh tally type 3, the energy deposited per unit volume was obtained. Considering the density composition of each part, we calculated the dose stored in each part volume of the phantom.

The data related to gamma and beta energies and the emission probabilities of ^{153}Sm decay are listed in Table 1. The data were retrieved from the online Medical Internal Radiation Dose (MIRD) website [10]. Also, the beta spectrum of ^{153}Sm, used in this simulation, is presented in Figure 1 [11, 12].

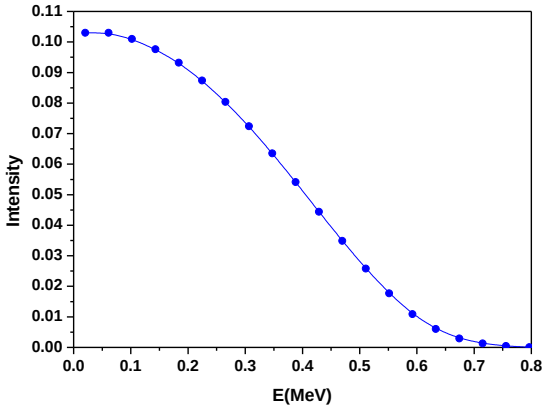

Figure 1. The beta spectrum of ^{153}Sm

2-2. *Phantom input data*

A cylindrical geometry with a constant material density was used as the bone phantom. In the bone cortex, the minimum and maximum radii were 1.5 and 2.5 cm for the bone marrow and bone, respectively. Also, the length of bone tissue along the *z* axis was 46 cm. A soft tissue surrounded the phantom with the radius of 8 cm and length of 50 cm. A grid size of 1 mm is used along the r and x axes. The data related to the composition elements of bone marrow were obtained from the International Commission on Radiation Units and Measurements (ICRU), while the data on bone and soft tissue were retrieved from the International Commission on Radiological Protection (ICRP) reports, as listed in Table 2 [13, 14].

Table 1. Particle emission, energy, and intensity from the decay of ^{153}Sm

Radiations	Intensity (Bq^{-1})	Energy (MeV)
Beta-14	3.22×10^{-01}	2.003×10^{-01}
Beta-16	4.96×10^{-01}	2.261×10^{-01}
Beta-17	4.10×10^{-03}	2.282×10^{-01}
Beta-18	1.75×10^{-01}	2.652×10^{-01}
Gamma 5	4.85×10^{-02}	6.967×10^{-02}
Ce-K, gamma 5	2.17×10^{-01}	2.115×10^{-02}
Ce-L, gamma 5	3.54×10^{-02}	6.162×10^{-02}
Ce-M, gamma 5	7.70×10^{-03}	6.787×10^{-02}
Gamma 6	3.49×10^{-03}	7.542×10^{-02}
Gamma 7	1.85×10^{-03}	8.337×10^{-02}
Gamma 8	1.67×10^{-03}	8.949×10^{-02}
Gamma 10	8.46×10^{-03}	9.743×10^{-02}
Gamma 11	2.98×10^{-01}	1.032×10^{-01}
Ce-K, gamma 11	4.32×10^{-01}	5.466×10^{-02}
Ce-L, gamma 11	6.44×10^{-02}	9.513×10^{-02}
Ce-M, gamma 11	1.39×10^{-02}	1.014×10^{-01}
Ce-N+, gamma 11	4.02×10^{-03}	1.028×10^{-01}
Gamma 17	8.05×10^{-04}	1.729×10^{-01}
Gamma 24	1.46×10^{-04}	4.636×10^{-01}
Gamma 30	6.26×10^{-04}	5.314×10^{-01}
Gamma 31	3.19×10^{-04}	5.332×10^{-01}
Gamma 32	2.18×10^{-04}	5.391×10^{-01}
Gamma 41	1.16×10^{-04}	5.967×10^{-01}
K-alpha1 X-ray	3.12×10^{-01}	4.154×10^{-02}
K-alpha2 X-ray	1.73×10^{-01}	4.090×10^{-02}
K-beta X-ray	1.24×10^{-01}	4.700×10^{-02}
L X-ray	1.11×10^{-01}	5.850×10^{-03}
Auger-K	4.63×10^{-02}	3.370×10^{-02}
Auger-L	5.49×10^{-01}	4.690×10^{-03}

Table 2. Data related to the composition elements of bone marrow, bone, and soft tissue [13, 14]

Element	Symbol	Bone marrow (atomic%) (ICRU)	Bone (mass%) (ICRP)	Soft tissue (mass%) (ICRP)
Hydrogen	H	61.840	7.337	10.454
Carbon	C	20.310	25.475	22.663
Nitrogen	N	1.440	3.057	2.490
Oxygen	O	16.200	47.893	63.525
Fluorine	F	0.000	0.025	0.000
Sodium	Na	0.000	0.326	0.112
Magnesium	Mg	0.000	0.112	0.013
Silicon	Si	0.000	0.002	0.030
Chlorine	Cl	0.034	0.143	0.133
Phosphorus	P	0.000	0.095	0.134
Sulfur	S	0.037	0.173	0.204
Potassium	K	0.0309	0.153	0.208
Calcium	Ca	0.000	10.190	0.024
Iron	Fe	0.0106	0.008	0.005
Zinc	Zn	0.000	0.005	0.003
Rubidium	Rb	0.000	0.002	0.001
Strontium	Sr	0.000	0.003	0.000
Zirconium	Zr	0.000	0.000	0.001
Lead	Pb	0.000	0.001	0.000
Density (g/cm^3)		1.03	1.40	1.04

Figure 2 shows the cylindrical phantom of an adult man's femur bone, which is one of the most common sites of bone metastasis [9].
Bone metastatic cells and tumors are usually located on the skeletal bone surface. In the study of the dose received by the cylindrical phantom, we made the following assumptions:

- ^{153}Sm-EDTMP as a radiopharmaceutical is uniformly deposited on the endosteal surface of the bone.
- Charge particles deposit all their energy into the phantom.

2-3. *Dose-volume histogram (DVH)*

DVH is a useful tool for the assessment of treatment quality. The purpose of DVH is to summarize a three-dimensional dose distribution in a graphical two-dimensional format. In the cumulative DVH, a bar or column height represents the volume of the structure receiving a dose higher than or equal to the corresponding DVH height. By using this factor, we could determine the coverage amount of different doses in a specified volume [15].

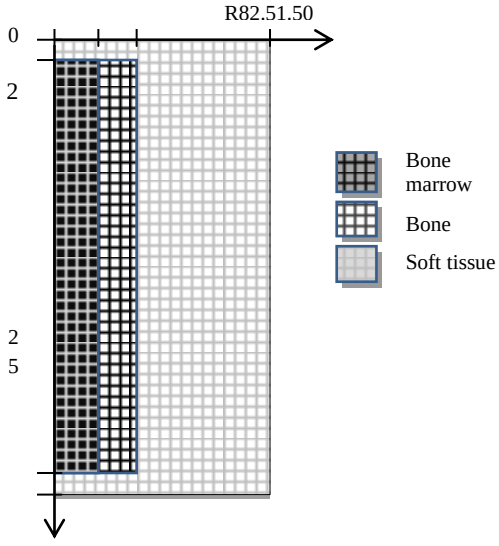

Figure 2. A view of the femur bone phantom with a cylindrical geometry

3. Results

We calculated the absorbed dose of uniformly-distributed beta and gamma rays from ^{153}Sm in different radii of the phantom. The results related to beta and gamma rays are plotted in Figure 3. In the diagram of beta absorbed dose, the energy deposits of Auger electrons were also considered, whereas in the diagram of the

absorbed dose of gamma rays, the energy deposits of gamma and X-rays were taken into account. For total dose evaluation of ^{153}Sm decay, all photon radiations including gamma rays and X-rays needed to be considered for more accuracy. The X-rays are a secondary process coming from energy levels that were occupied before by Auger electrons.

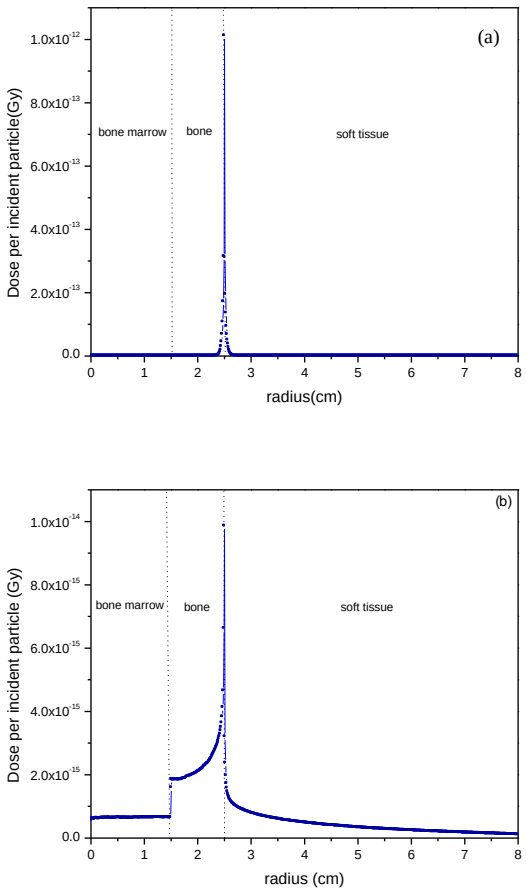

Figure 3. The dose distribution diagram of ^{153}Sm-EDTMP as a radiopharmaceutical based on different radii of the phantom for (a) beta rays and (b) gamma rays

As presented in Figure 3, all beta rays and a major fraction of gamma rays were absorbed by a very thin layer of the bone. Also, Figure 4 indicates the cumulative DVH for the summation of beta and gamma ray doses from ^{153}Sm-EDTMP in the bone phantom. Clearly, a small fraction of the total volume (0.75%), i.e., a thin layer of bone surface, had the largest dose absorption (90%). Here, the relative volume is a ratio of the volume with an absorption dose higher than a specific level, relative to the total volume of the phantom.

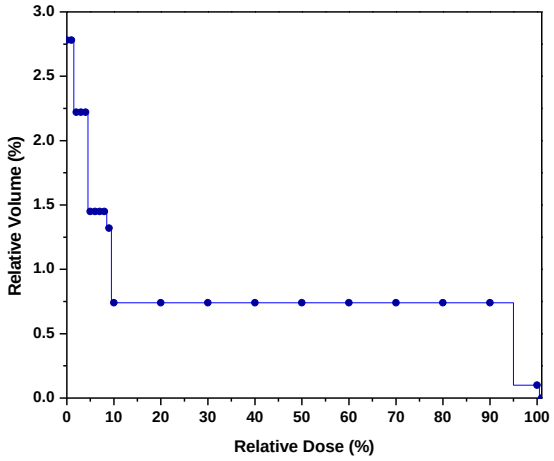

Figure 4. The dose-volume histogram (DVH) for all beta and gamma rays of ^{153}Sm-EDTMP

4. Discussion

In nuclear medicine, dosimetry is an important component of radiation therapy, which provides information about the amount of dose delivered to each part of the body. We used MCNP code to simulate the effect of ^{153}Sm-EDTMP as a radiopharmaceutical on a portion of the bone, with a prior knowledge of radiopharmaceutical deposition on the endosteal surface of the bone. The dose distribution diagrams in Figure 3 show the significant distribution of this radiopharmaceutical in the bone tissue as the target, whereas in other parts of the phantom, the distribution was significantly low and negligible.

Moreover, the delivered dose of beta and gamma rays in the bone marrow was low. The bone tissue played an effective role as a radiation shield for the bone marrow, resulting in less damage to the soft tissue and bone marrow. DVH of all beta and gamma rays of ^{153}Sm showed that the delivered dose had only accumulated in a small fraction of the total volume (i.e., bone marrow, bone, and soft tissue), since the radiopharmaceutical was deposited on the bone tissue and the soft tissue constituted the largest volume of the phantom.

5. Conclusion

In conclusion, ^{153}Sm-EDTMP as a radiopharmaceutical is an effective material for palliation of pain caused by bone metastasis. This radiopharmaceutical showed a high uptake in the bone tissue, whereas absorption by the bone marrow and soft tissue was insignificant and the received dose was excreted through the kidneys. The results showed that a significant amount of the dose delivered to the bone was due to the use of radiopharmaceutical. Also, given the high density and high atomic number of bone, a more deposited dose was observed in the bone in comparison with other tissues. Moreover, bone acted as a fine protective shield against rays for the bone marrow. Therefore, the trivial absorbed dose by the bone marrow caused less damage to bone-making cells. Also, the high absorbed dose of the bone could destroy cancer cells and relieve the pain in the bone.

Acknowledgments

The authors would like to thank Ferdowsi University of Mashhad and Hakim Sabzevari University for their support.

References

1. Meftahi M, Bahrami Samani A, Babaei MH, Shamsaei Zafarghandi M, Ghannadi Maragheh M. Biodistribution Study of ^{153}Sm-EDTMP Produced by Irrational of Natural and Enriched Samarium, in Rats. J Nucl Sci Tech. 2010;50,9-13.
2. Serafini AN. Therapy of metastatic bone pain. J Nucl Med. 2001;42(6): 895-906.
3. Pandit-Taskar N, Batraki M, Divgi CR. Radiopharmaceutical therapy for palliation of bone pain from osseous metastases. J Nucl Med. 2004;45(8):1358-65.
4. Sartor O, Hoskin P, Bruland OS. Targeted radio-nuclide therapy of skeletal metastases. Cancer Treat Rev 2013;39(1):18-26.
5. Fischer M, Kampen WU. Radionuclide therapy of bone metastases. Breast Care (Basel). 2012;7(2):100-7.
6. Maini CL, Sciuto R, Romano L, et al. Radionuclide therapy with bone seeking radionuclides in palliation of painful bone metastases. J Exp Clin Cancer Res. 2003 Dec; 22(4 Suppl):71-4.
7. Ogawa K, Wasiyama K. Bone target radiotracers for palliative therapy of bone metastases. Curr Med Chem. 2012;19(20):3290-300.
8. Correa-González L, Arteaga de Murphy C, Pichardo-Romero P, Pedraza-López M, Moreno-García C, Correa-Hernández L. ^{153}Sm-EDTMP for pain relief of bone metastases from prostate and breast cancer and other malignancies. Arch Med Res. 2014; 45(4):301-8.
9. Strigari L, Sciuto R, D'Andrea M, Pasqualoni R, Benassi M, Maini CL .Radiopharmaceutical therapy of bone metastases with $^{89}SrCl_2$, ^{189}Re-HEDP and ^{153}Sm-EDTMP: a dosimetric study using Monte Carlo simulation. Eur J Nucl Med Mol Imaging. 2007;34(7):1031-8.
10. ENSDF Decay Data in the MIRD (Medical Internal Radiation Dose) Format for ^{153}Sm. Available at: http://www.orau.org/ptp/PTP%20Library/library/DOE/bnl/nuclidedata/MIRSm153.htm. Accessed April 7, 2016.
11. Eckerman KF, Westfall RJ, Ryman JC, Cristy M. Availability of Nuclear Decay Data in Electronic Form, Including Beta Spectra not Previously Published. Health Phys. 1994; 67(4):338-45.
12. RADAR - The decay data. Available at: http://www.doseinfo-radar.com/RADARDecay.html. Accessed Jan 21, 2016.
13. ICRU 46. Photon, Electron, Proton and Neutron Interaction Data for Body Tissues. ICRU Report 46, ICRU, Washington D.C., 1992.
14. Basic Anatomical and Physiological Data for Use in Radiological Protection Reference Values, ICRP Publication 89. Ann ICRP. 2002;32(3-4):5-265.
15. Drzymala RE, Mohan R, Brewster L, Chu J, Goitein M, Harms W, Urie M. Dose-Volume Histograms. Int J Radiat Oncol Biol Phys. 1991;21(1):71-8.