Monte Carlo Dosimetric Study of Percutaneous Vertebroplasty and Brachytherapy for the Treatment of Spinal Metastases

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ABSTRACT

Background: Percutaneous vertebroplasty employs bone cement for injecting into the fractured vertebral body (VB) caused by spinal metastases. Radioactive bone cement and also brachytherapy seeds have been utilized to suppress the tumor growth in the VB.

Objective: This study aims to investigate the dose distributions of low-energy brachytherapy seeds, and to compare them to those of radioactive bone cement, by Monte Carlo simulation.

Material and Methods: In this simulation study, nine CT scan images were imported in Geant4. For the simulation of brachytherapy, I-125, Cs-131, or Pd-103 seeds were positioned in the VB, and for the simulation of vertebroplasty, the VB was filled by a radioactive cement loaded by P-32, Ho-166, Y-90, or Sm-153 radioisotopes. The dose-volume histograms of the VB, and the spinal cord (SC) were obtained after segmentation, considering that the reference dose is the minimum dose covered 95% of the VB.

Results: The SC sparing was improved by using beta-emitting cement because of their steep gradient dose distribution. I-125 seeds and Y-90 radioisotope showed better VB coverage for brachytherapy and vertebroplasty techniques, respectively. Pd-103 seeds and P-32 radioisotope showed better SC sparing for brachytherapy and vertebroplasty, respectively. The minimum mean doses that covered 100% of the VB were 62.0%, 56.5%, and 45.0% for I-125, Cs-131, and Pd-103 seeds, and 28.3%, 28.6%, 32.9%, and 17.7%, for P-32, Ho-166, Y-90, and Sm-153 sources, respectively.

Conclusion: I-125 and Cs-131 seeds may be useful for large tumors filling the entire VB, and also for the extended tumors invading multiple vertebrae. Beta-emitting bone cement is recommended for tumors located near the SC.

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Introduction

The most prevalent site for bone metastases is the spine. Spinal metastases, mainly arising from prostate, breast, and lung primary cancers, cause vertebral body (VB) fracture, spinal cord (SC) compression, neurological deficit, paraplegia, and death [1-3]. In addition to surgery, radiotherapy has an essential role in the treatment of spinal metastases. Stereotactic radiosurgery, intensity-modulated radiotherapy, stereotactic body radiotherapy, and brachytherapy have been

used for the treatment of spinal lesions with desirable clinical outcomes [4-8]. The allowable dose delivered to the VB is limited in external beam radiotherapy, due to the radiation tolerance of the SC. Brachytherapy has the advantage of sparing nearby tissues especially the SC by implanting tiny radioactive seeds or beta-emitting plaques near the tumor [9].

In the case of spinal fracture and deformity, percutaneous vertebroplasty is performed in which the bone cement (PMMA or polymethylmethacrylate) is injected into the collapsed VB through a needle to maintain spine stability and relieve the pain [10, 11]. The radioactive bone cement loaded by a uniformly distributed beta-emitting radioisotope (as an added component) was presented to suppress the tumor progression in the VB [12, 13]. Recently, combining vertebroplasty and brachytherapy was considered as a minimally invasive method to overcome the spine instability and the tumor growth, simultaneously [14]. Several studies investigated the feasibility and efficacy of combining vertebroplasty and brachytherapy with clinically acceptable results [15-20].

Dosimetric analysis of radioactive bone cement is essential as a pre-clinical investigation. Hirsch et al. performed a Monte Carlo dosimetric study of radioactive bone cement mixed with ^{32}P, ^{166}Ho, ^{90}Y, ^{125}I, ^{18}F, and ^{99m}Tc radioisotopes in a cortical bone phantom [13], using MCNP v.5 code [21]. Montaño et al. represented a new bone cement material loaded with ^{153}Sm, ^{166}Ho, and ^{188}Re radioisotopes and used MCNP v.5 code for a dosimetric comparison [22]. Kaneko et al. evaluated a radiation transport modeling method for dose calculation in a vertebra containing radioactive bone cement, using MCNP extended code (MCNPX v. 2.5) and EBT radiochromic film [12]. The same group also simulated some clinical scenarios such as bone cement leakage with MCNP v.5 [23]. However, there are insufficient data for the dose distributions of brachytherapy seeds and beta-emitting bone cement in the spinal canal. In this study, a dosimetric

analysis of ^{125}I, ^{103}Pd, and ^{131}Cs brachytherapy seeds as well as radioactive bone cement loaded by uniformly distributed ^{32}P, ^{90}Y, ^{166}Ho, and ^{153}Sm radioisotopes, was conducted using Geant4 Monte Carlo toolkit. The corresponding dose distributions in the VB and the SC were obtained and compared with each other.

Material and Methods

Geant4.10.6 Monte Carlo toolkit [24] with the standard electromagnetic physics model of "G4EmStandardPhysics_option3" was used in this simulation study. The G4EmStandardPhysics_option3 physics model includes photoelectric effect, pair production, Compton scattering, and Rayleigh scattering data for the interactions of photons and bremsstrahlung, ionization, fluorescence emission, multiple scattering, and positron annihilation data for the interactions of electrons and positrons [25]. For more accuracy, particle-induced X-ray emission and Auger electron from excited atoms were manually implemented in the physics list. The production range cut was set to 0.1 mm for secondary particles, i.e. the secondary particles with a range of 0.1 mm or lower will be killed in the simulation. With 300 million primary particles, all statistical uncertainties were below 1% in the regions of interest (i.e., SC and VB).

Nine computed tomographie (CT) image slices, with 6 mm thickness, of a normal spinal case (obtained from Imam Hossein Hospital, Tehran) were imported in Geant4. One thoracic VB was determined as a tumor location. The whole VB was considered as the gross tumor volume (GTV), which is the palpable region of tumor seen on the image according to the ICRU Report 50 [26]. In the case of vertebroplasty, a cylindrical volume with a radius of 14 mm, and a height of 6 mm, composed of PMMA ($C_5O_2H_8$, density=1.19 g/cm^3) was simulated in the VB as the bone cement. This cylinder was cut with a smaller cylindrical section with a radius of 7 mm to make an offset region for the spinal canal as shown in

Figure 1a. The bone cement surface was approximately 3 mm away from the SC. Four separate simulations were performed with ^{32}P, ^{90}Y, ^{166}Ho, and ^{153}Sm uniformly distributed in the cement.

For the simulation of brachytherapy, the structure of the Amersham model 6711 seed was simulated with a full length of 4.6 mm. It has a cylindrical silver core with a radius of 0.25 mm, and a length of 3 mm, located inside a 0.05 mm thickness titanium shield [27]. The outer surface of the core was uniformly coated by low-energy ^{125}I, ^{103}Pd, or ^{131}Cs radioisotopes in this simulation. Thirty seeds were placed in the VB in three CT slices with the 8-9

Figure 1: The visualization of imported phantom (the central slice) in Geant4 with (a) radioactive bone cement and (b) brachytherapy seeds.

mm inter-seed spaces on each plane as shown in Figure 1b. The distance from the center of the closest seed to the spinal canal was nearly 8 mm. Note that the position of seeds in this simulation is based on a typical treatment planning system that is not optimal for all patients. The actual seeds position should be calculated based on a treatment plan specialized for each patient [28]. Since brachytherapy seeds are inserted percutaneously through the pedicles, they are tilted inward on either side of the VB [29]. Therefore, our simulation of seed positions seems desirable since the entire VB is assumed to be the GTV. Related Nuclear data are shown in Table 1. Beta particles, electrons, gamma, and X-rays are shown by β⁻, e⁻, γ, and x symbols, respectively.

The pixel values of CT images represent CT numbers or Hounsfield Units. In this scale, water is assigned as a value of 0 and other CT numbers are computed by equation 1:

$$HU=1000\times(\mu_t-\mu_w)/\mu_w \tag{1}$$

In which μ_t and μ_w are tissue and water linear attenuation coefficients, respectively. The materials defined in the simulation are tabulated in Table 2. Data were obtained from the ICRU report 46 [31]. A linear interpolation was implemented in Geant4 for the conversion of CT numbers to densities.

A cubic mesh with the same resolution of the CT images (512×512 pixel^2) was defined to calculate the deposited dose in the voxels. The prescribed dose is usually defined as the minimum dose covering 90% [7] or 95% [8] of the GTV. In this simulation, the minimum dose delivered to 95% of the VB (D95%) was determined as the referenced dose for each radioisotope's radiation field. The tumor and the SC were segmented using MATLAB 2015a code and dose-volume histograms (DVHs) were obtained.
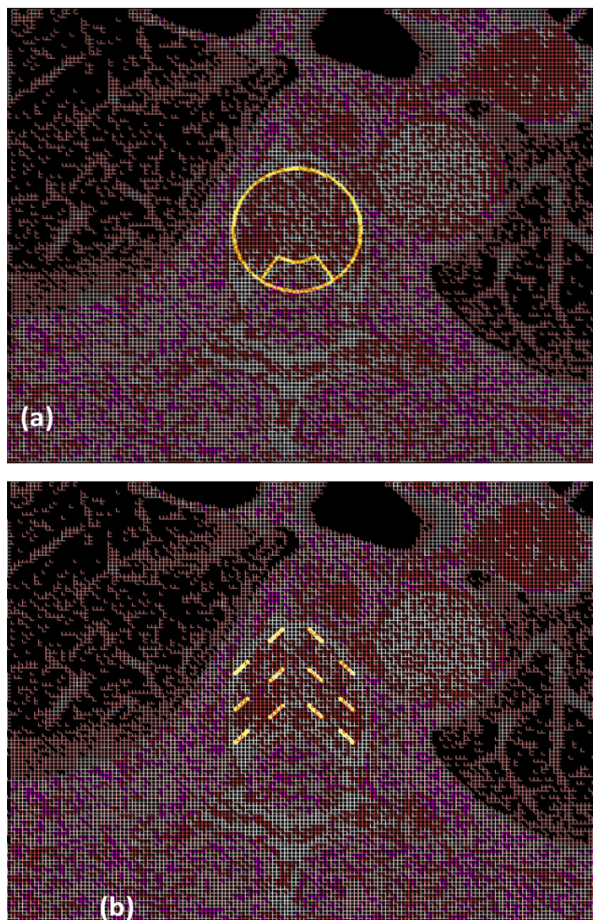
Results

The normalized isodose contours in the central CT slice are shown in Figure 2 for low-energy brachytherapy seeds as well as

Table 1: Nuclear data for seven radioisotopes mentioned above [30].

Name	Half-life	Radiation: Energy (MeV) (intensity %)
^{32}P	14.28 h	*β⁻: 1.71 (100%)
^{90}Y	64.06 h	β⁻: 2.28 (100%)
^{166}Ho	26.8 h	β⁻: 1.85 (48.8%), 1.77 (49.9%), 0.394 (1%), 0.394 (1%)
		γ: 1.38 (1%), 0.080 (6.6%)
		e⁻: 0.029 (72%)
		x: 0.056 (9%), 0.049 (8%), 0.007 (8%)
^{153}Sm	46.8 h	β⁻: 0.810 (20%), 0.710 (49%), 0.640 (30%)
		γ: 0.103 (28%), 0.070 (5%)
		e⁻: 0.045 (135%), 0.043 (63%), 0.006 (10%)
^{125}I	60.25 d	γ: 0.035 (7%)
		e⁻: 0.018 (246%)
		x: 0.030 (138%)
^{103}Pd	16.96 d	γ: 0.498 (0.011%), 0.362 (0.02%), 0.297 (0.011%)
		e⁻: 0.043 (258%)
		x: 0.021 (77%)
^{131}Cs	9.69 d	e⁻: 0.006 (76%)
		x: 0.032 (74%), 0.004 (7%)

*The β⁻ energies refer to the maximum energy in the beta-emission spectrum

Table 2: Materials defined in Geant4 to construct the phantom.

Name	Density (g/cm³)	Components: Element (abundance %)
Air	1.29 e⁻³	N (70.0%), O (30.0%)
Lung Inhale	0.210	O (74.9%), C (10.5%), H (10.3%), N (3.10%), S (0.30%), K (0.30%), Na (0.20%), P (0.20%), Cl (0.20%)
Lung exhale	0.508	O (74.9%), C (10.5%), H (10.3%), N (3.10%), K (0.30%), S (0.30%), Na (0.20%), P (0.20%), Cl (0.20%)
Adipose	0.967	C (59.8%), O (27.8%), H (11.4%), N (0.70%), Cl (0.10%), Na (0.10%), S (0.10%)
Breast	0.990	C (50.6%), O (35.8%), H (10.9%), N (2.30%), Na (0.10%), P (0.10%), S (0.10%), Cl (0.10%)
Soft tissue	1.00	O (76.2%), N (2.60%), C (11.10%), H (10.10%)
Muscle	1.061	O (71.0%), C (14.3%), H (10.20%), N (3.40%), S (0.30%), K (0.30%), P (0.20%), Cl (0.20%), Na (0.10%)
Liver	1.071	O (71.6%), C (13.9%), H (10.2%), N (3.00%), K (0.40%), P (0.30%), S (0.30%), Na (0.20%), Cl (0.10%)
Spinal Disc	1.10	O (74.4%), C (9.90%), H (9.60%), N (2.20%), P (2.20%), S (0.90%), Na (0.50%), Cl (0.30%)
Trabecular bone	1.159	C (40.4%), O (36.7%), H (8.50%), N (5.80%), Ca (4.40%), P (3.40%), Cl (0.20%), S (0.20%), Na (0.10%), K (0.10%), Fe (0.10%), Mg (0.01%)
Dense Bone	1.575	O (43.4%), C (23.5%), Ca (14.6%), P (7.20%), H (5.60%), N (5.00%), S (0.30%), Na (0.10%), Cl (0.10%), K (0.10%), Mg (0.01%)

radioactive bone cement. Figures 3 and 4 show the VB and the SC DVHs for brachytherapy and vertebroplasty, respectively.

According to the DVHs shown in Figures 3 and 4, ^{125}I seeds and ^{90}Y-loaded cement show better VB coverage for brachytherapy and vertebroplasty techniques, respectively. On the other hand, ^{103}Pd seeds and ^{32}P-loaded cement have the advantage of more SC sparing for brachytherapy and vertebroplasty techniques, respectively.

The minimum dose covered 95% of the VB (VB D95%), the minimum dose of the VB (VB Dmin), the minimum dose delivered to 90% of the SC (SC D90%), and the maximum dose of the SC (SC Dmax), in terms of pico-gray per particle are tabulated in Table 3. A representative comparison of V150% (the VB vol-
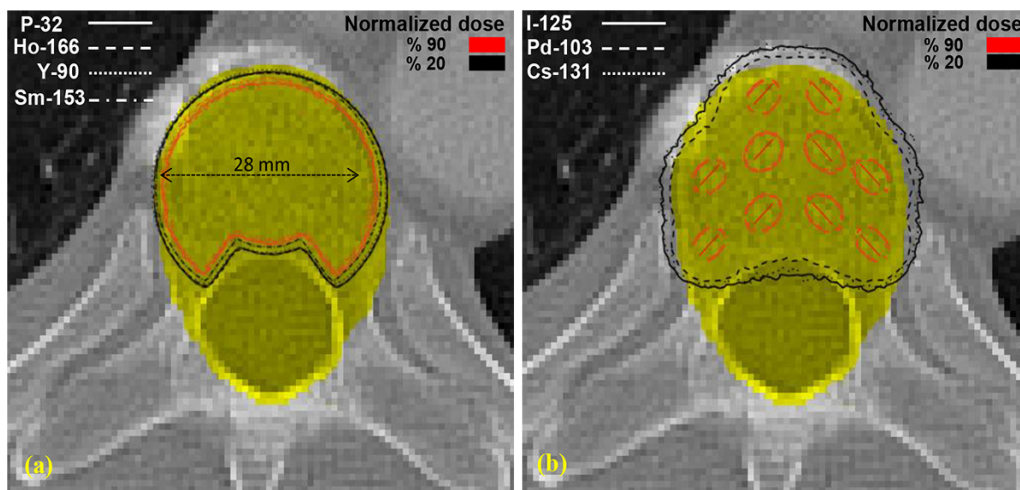

Figure 2: Normalized isodose contours in the central computed tomography slice for (a) radioactive bone cement (in the case of vertebroplasty) and (b) radioactive seeds (in the case of brachytherapy). The segmented parts are shown in yellow.
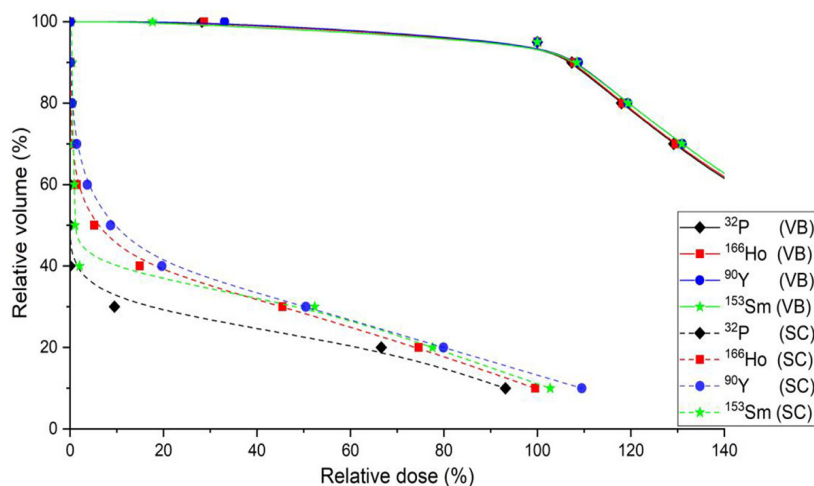

Figure 3: The vertebral body (VB) and the spinal cord (SC) dose-volume histograms obtained by simulating radioactive bone cement loaded with several radioisotopes to be used in the vertebroplasty approach.
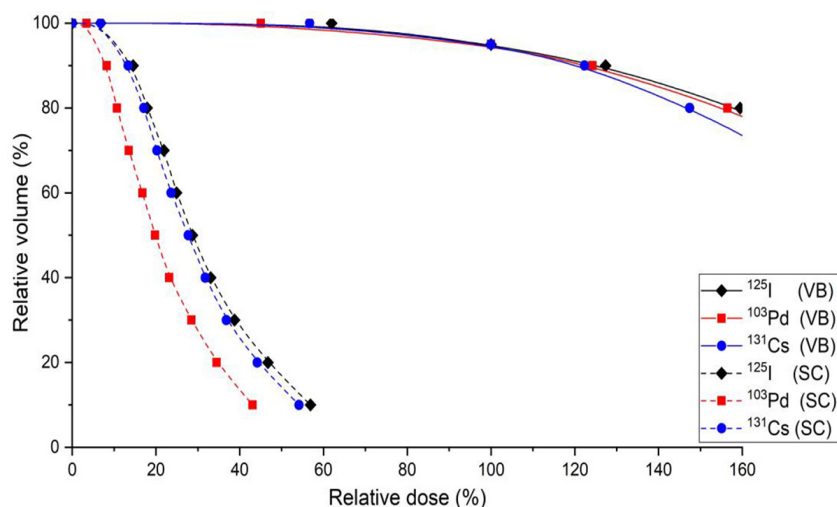
Figure 4: The vertebral body (VB) and the spinal cord (SC) dose-volume histograms obtained by simulating thirty brachytherapy seeds in the vertebral body to be used in the brachytherapy approach.

Table 3: A comparison of dosimetric parameters obtained for brachytherapy seeds and radioactive bone cement.

Dosemetric Parameters (pico-Gy/particle)	Brachytherapy seeds			Radioisotope-loaded bone cement			
	^{125}I	^{103}Pd	^{131}Cs	^{32}P	^{166}Ho	^{90}Y	^{153}Sm
VB D90%	8.49e^{-2}	6.32e^{-2}	4.22e^{-2}	3.11	3.12	5.02	1.23
VB D95%	6.66e^{-2}	5.08e^{-2}	3.45e^{-2}	2.89	2.90	4.61	1.13
VB Dmin	4.13e^{-2}	2.29e^{-2}	1.95e^{-2}	0.818	0.83	1.52	0.20
SC D90%	9.70e^{-3}	4.20e^{-3}	4.97e^{-3}	1.58e^{-4}	2.23e^{-3}	2.51e^{-3}	5.59e^{-3}
SC Dmax	8.05e^{-2}	5.01e^{-2}	3.87e^{-2}	6.48	6.45	10.187	2.53

VB: Vertebral Body, SC: Spinal Cord

ume received at least 150% of the reference dose), and V200% parameters are shown in Figure 5. Note that the V100% is 95% for all radioisotopes due to the definition of the reference dose (D95%) in this simulation. One should be careful about the occurrence of cold spots in dose distribution. As inferred from Table 3, the ratio of D95% to D100% of the VB reaches up to 161%, 221%, 176%, 353%, 349%, 303%, and 565% for ^{125}I, ^{103}Pd, ^{131}Cs, ^{32}P, ^{166}Ho, ^{90}Y, and ^{153}Sm, respectively. From another perspective, the minimum "mean" dose covered 100% of the VB was 62.0%, 45.0%, 56.5%, 28.3%, 28.6%, 32.9% and

17.7% of the reference dose for ^{125}I, ^{103}Pd, ^{131}Cs, ^{32}P, ^{166}Ho, ^{90}Y, and ^{153}Sm, respectively. The term mean is referred to the average of two separate simulations performed for each radioisotope. Therefore, the occurrence of cold spots in the dose distributions of the cement mixed with ^{153}Sm is more probable. However, the presence of cold spots is not significant for ^{125}I and ^{131}Cs seeds, provided that a maximum inter-seed space of 10 mm is maintained on each plane.

Discussion

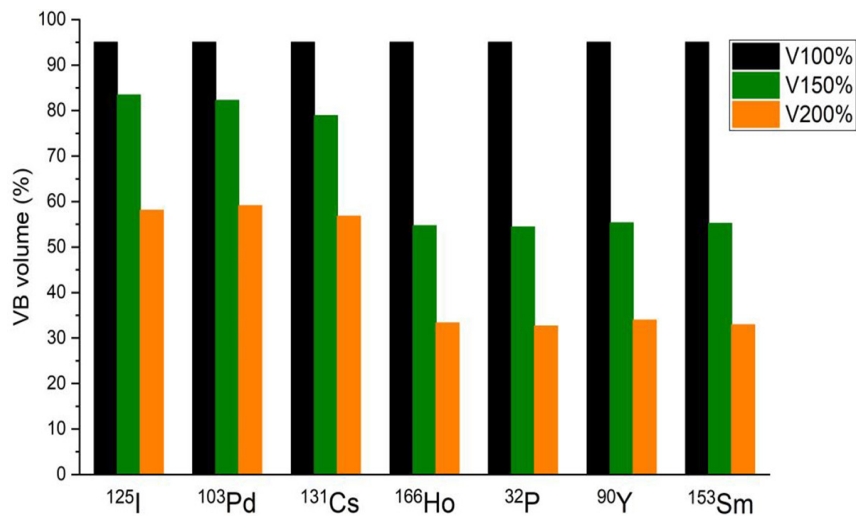The main goal was to compare the dose

Figure 5: V150% and V200% comparison for brachytherapy seeds and beta-emitting bone cements in the case of brachytherapy and vertebroplasty, respectively.

distributions of various radioactive bone cement with those of low-energy brachytherapy seeds. Although the DVHs of ^{125}I and ^{131}Cs seeds are nearly the same, ^{125}I seeds show an improvement of 9.7% in the tumor coverage. The isodose curves shown in Figure 2 demonstrate the high potential of brachytherapy seeds for the treatment of large lesions in the VB, particularly for tumors that invade more than one vertebra. Nevertheless, due to the deep penetration of the photons emitted from the seeds, sparing of the radiosensitive nearby tissues, i.e., SC and nerve roots need more attention. It is not serious for beta-emitting bone cement since the dose rapidly drops off up to 3 mm from the cement surface [12, 22]. Therefore, the employment of beta-emitting bone cement is more interesting for situations in which the tumor is near the spinal canal due to its steep dose gradient. However, the SC sparing is not concerned with beta-emitting cement, high-energy beta particles of ^{90}Y should be considered according to the SC DVH in Figure 3. Although ^{166}Ho and ^{153}Sm are not pure beta-emitting radioisotopes with relatively high-energy photons in their decay schemes, their utilization may not be limited,

due to the similarity of their isodose curves to those of ^{32}P. The behavior of the ^{32}P isodose curve is similar to those obtained by Kaneko et al. [22] since the dose decreases by 50% for each ~0.5 mm incremental distance from the cement surface. The brachytherapy technique provides more flexibility in modifying dose distributions by changing the arrangement and the activity of the seeds that are difficult for radioactive bone cement, particularly for large and extended tumors. Note that the tumor is an incompressible volume limiting the volume of bone cement for injection into the VB, and increasing the cement volume results in increasing the risk of cement leakage [32]. Therefore, tumor ablation techniques should be performed before the cement injection. The seeds cannot be implanted in the cement, therefore we assumed a VB that is completely occupied by the tumor in the case of brachytherapy. Partial tumor volumes in the VB result in different seed arrangements that need more investigation in a separate simulation. Only tumors located in the VB were considered in this simulation, not the epidural tumors, and for epidural lesions, brachytherapy seeds cannot be used due to their vicinity to the spine

and its dose tolerance concern.

Conclusion

Using brachytherapy seeds as the more penetrating sources can be used for large tumors filling the whole VB, and also for the extended tumors in multiple vertebrae. When the tumor is located in the posterior part of the VB near the SC, beta-emitting bone cement (preferably ^{32}P) should be employed at least 4 mm from the SC. Otherwise, the aim of SC sparing may be achieved by using ^{103}Pd seeds with more than 5 mm distance from the SC. From a simulation viewpoint, it is recommended that ^{125}I (or ^{131}Cs) seeds be implanted in the tumor with at least 10 mm distance from the SC. However, more clinical studies should be conducted to assess the feasibility of such radioactive sources in various clinical scenarios.

Authors' Contribution

P. Rafiepour wrote the Monte Carlo simulation code. S. Sina wrote and designed the manuscript. P. Azimi proposed the idea of the study, and provided the CT images. R. Faghihi performed the final editing and revision. All the authors read and approved the final version of the manuscript.

Ethical Approval

This is a pure simulation study that no ethical approval is required.

Conflict of Interest

None

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