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A Geant4 study on dosimetric comparison between three kinds of radioactive esophageal stents to be used in treatment of advanced esophageal cancers

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HIGHLIGHTS

- Esophageal stents carrying I-125 seeds have shown advantages over iodine-eluting stents.
- The dose distribution of esophageal seed-loaded stents, significantly depends on the arrangements of the seeds.
- Appropriate dose distribution was achieved for esophageal stents carrying I-125 seeds with 15 mm inter-seed spacing.

ABSTRACT

Utilizing radioactive stents is a usual method for treatment of advanced esophageal cancer. It is necessary to investigate the dose distribution of radioactive esophageal stents before the clinical use. This study presents a dosimetric comparison between three radioactive esophageal stents: I-125 seed-loaded stent, iodine-eluting stent and double-layered iodine-eluting stent. Depth-dose and angular dose distributions were carried out using Geant4 toolkit. Moreover, the effect of interval distance between two adjacent seeds on the dose distribution was investigated. Esophageal stents loaded with I-125 seeds seems to be better than iodine-eluting stents, with the distance less than 15 mm between two adjacent seeds.

KEYWORDS

Advanced esophageal cancer
Radioactive stent
Brachytherapy
Dosimetry
Geant4

1 Introduction

Esophageal cancer is the eighth most common cancer and the sixth leading cause of cancer related deaths worldwide. Advanced esophageal cancer is referred to the stages in which the tumor invades adjacent tissues (Napier et al., 2014). Surgery is the first option to be used for treatment of the early stage esophageal cancer. Unfortunately, at the time of diagnosis, most tumors are inoperable. The most common symptom of the advanced esophageal cancer is dysphagia and palliative therapy is generally recommended for the patients. Stenting can be used to palliate dysphagia (Mariette et al., 2007).

Generally, there are uncovered, covered and partially covered stents, which are utilized in clinical studies. Uncovered stents cause the tumor to grow through the interspaces of the metal mesh. Covered stents have a polymeric membrane that prevent the tumor ingrowth, but they are more likely to migrate. Double-layered stents were introduced to overcome the tumor ingrowth and the stent migration as well (Kim et al., 2009). Radiation can be considered as the other approach to prevent the tumor recurrence in the stent.

Recently, radioactive esophageal stents loaded with I-125 brachytherapy seeds have been developed and their advantages in the palliation of dysphagia and improving the quality of patient's life have been investigated (Zhu et al., 2014; Zhongmin et al., 2012; Liu et al., 2014). Preclinical tests including the study on dose distribution and the radiation field characteristics of radioactive esophageal stents are therefore essential. Won et al. developed a radioactive esophageal stent impregnated with the beta-emitting radioisotope Ho-166 and computed the distribution of dose by EGS4 code. They also accomplished experimental studies on beagle dogs (Won et al., 2002, 2005). Chu et al. investigated the radiation field surrounding the Re-188 esophageal stent, using thermoluminescent dosimeters (TLDs) (Chu et al., 2008). Lin et al. used

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treatment planning system, TLDs, and MCNPX code to evaluate the dose distribution of biliary stents loaded with I-125 seeds (Yao et al., 2017). This work presents a dosimetric comparison between I-125 seed-loaded esophageal stents, iodine eluting stents and double-layered iodine-eluting stents, using Geant4 simulation toolkit.

2 Materials and Methods

2.1 Simulation toolkit

The Geant4 toolkit, developed based on in the C++ programming language, is the result of a collaboration of physicists and software engineers all over the world. It provides a comprehensive software package for modern simulation applications that involve the interaction and passage of particles through matter (Agostinelli et al., 2003). Livermore low-energy electromagnetic model, based on the Livermore data library, was used in these simulations. It is valid for energies down to 10 eV and can be used up to approximately 100 GeV for gamma and electron processes (Geant4, 2017). It includes the photoelectric effect, Compton scattering, Rayleigh scattering, bremsstrahlung, ionization and fluorescence emission. Auger electron from excited atoms is also included in the physics list.

2.2 Radioactive seeds

I-125 model IR-Seed brachytherapy source manufactured in the Nuclear Science and Technology Research Institute of Atomic Energy Organization of Iran, was simulated. It consists of a silver cylindrical core with diameter of 0.5 mm and length of 3.2 mm. I-125 radioactive material is uniformly distributed on the surface of the core. The core is surrounded with a Titanium shield. Dosimetric parameters of this seed was calculated before (Lohrabian et al., 2013). A schematic diagram of the source is shown in Fig. 1.

The nuclear data for I-125 for dosimetry, recommended by the American Association of Physicists in Medicine (AAPM-TG43) are tabulated in Table 1 (Rivard et al., 2004).

Table 1: Recommended nuclear data for I-125 source (half-life=59.4 days) for dosimetry.

Photon energy (keV)	Abundance (%)
27.202	40.6
27.472	75.7
30.98	20.2
31.71	4.39
35.492	6.68

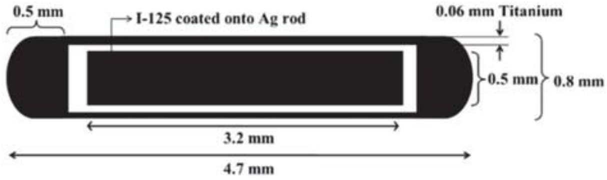

Figure 1: A schematic diagram of I-125 model IR-Seed brachytherapy source (Lohrabian et al., 2013).

2.3 Esophageal stents

Nitinol (an alloy of Nickel and Titanium) esophageal stents with 18 mm in diameter and 50 mm in length were simulated. Esophageal stent loaded with I-125 seeds includes three parts: esophageal Nitinol stent, covering membrane and Nitinol sheaths fixed outside the membrane which contains I-125 seeds. The sheaths were symmetrically deployed along the axis of the stent. Each layer contained four I-125 seeds, placed in the same plane at 90° angles. The I-125 seeds between two adjacent layers were intersected to form a diamond shape (Zhongmin et al., 2012). As listed in Table 2, three interval distances between adjacent seeds (Δ), were simulated and the corresponding dose distribution were investigated.

Iodine-eluting stent is composed of two parts: esophageal Nitinol stent and radioactive membrane. I-125 was uniformly distributed on the surface of the membrane (Won et al., 2002; Chu et al., 2008; Dai et al., 2013). Double-layered iodine eluting stent is similar, with an additional Nitinol layer which covers the stent. The mentioned stents and the simulated ones are shown in Figs. 2 and 3, respectively.

2.4 Phantom configuration

The radioactive stents were simulated in the center of a spherical water phantom with radius of 20 cm. The cylindrical scoring mesh was used to calculate the dose deposited in the mentioned phantom. Actually, the phantom was divided into concentric rings with thickness of 0.5 mm along the stent axis. These the rings were divided into 90 voxels in the angular direction for different radial distances of 1, 1.5, 2, 3, 5, 7, 10, 15 and 20 mm from the stent surface. The dose deposited in the mentioned voxels were calculated, and the dose distribution of different radial distances were figured.

3 Results

Dose distribution of iodine eluting stent and that of the double-layered one are shown in Figs. 4 and 5, respectively. Dose distribution of I-125 seed-loaded stent with Δ =5, 10 and 15 mm are illustrated in Figs. 6-8, respectively. All diagrams and dose distributions were plotted using the Origin software(Origin Lab, Northampton, MA).

The Peak to valley dose (PVD) ratio was considered as a criterion of dose uniformity for esophageal stents carrying I-125 seeds. PVD ratio can be used to compare the dose intensity between the location of the seed and the adjacent vacant place. PVD ratios for different I-125

Table 2: The data taken into account for simulations.

Stent material	Nitinol (55.8% Ni , 44.2% Ti), ρ= 6.45 g/cm^3
Polymeric membrane material	Polyurethane ($C_3H_8N_2O$), ρ= 1.005 g/cm^3
Length and thickness of Membrane	35 mm and 8 μm (Zhen et al., 2014)
Sheath dimensions	4.71×0.81×0.81 mm^3
The distance between two adjacent	5, 10, 15 mm
Energy cutoff for photons	5 keV (Rivard et al., 2004)
Second layer diameter (at the center) for double-layered stent	11 mm

Figure 2: I-125 seed-loaded stent (a) (Zhongmin et al., 2012), simple Nitinol stent (b), double-layered stent (c) (Kim et al., 2009).

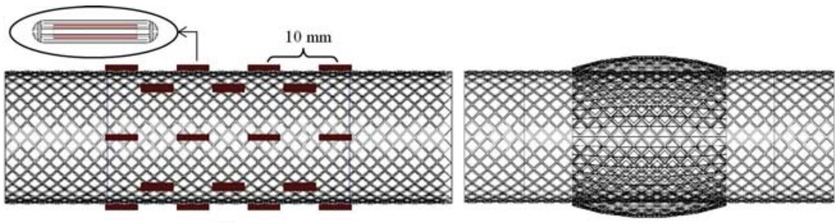

Figure 3: The simulated stents: I-125 seed-loaded stent (a), double-layered iodine-eluting stent (b).

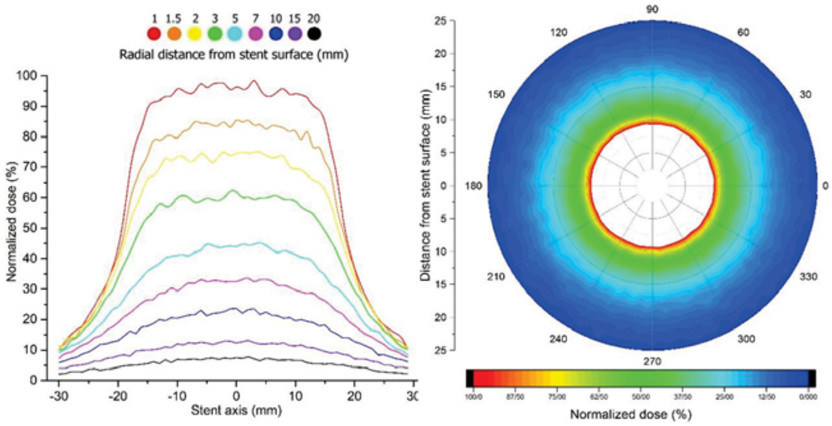

Figure 4: Depth-dose and angular dose distributions of iodine eluting stent.

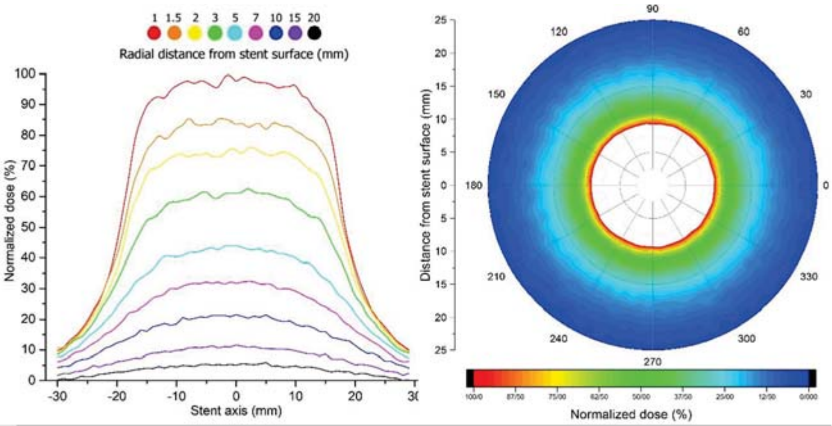

Figure 5: Depth-dose and angular dose distributions of double-layered iodine eluting stent.

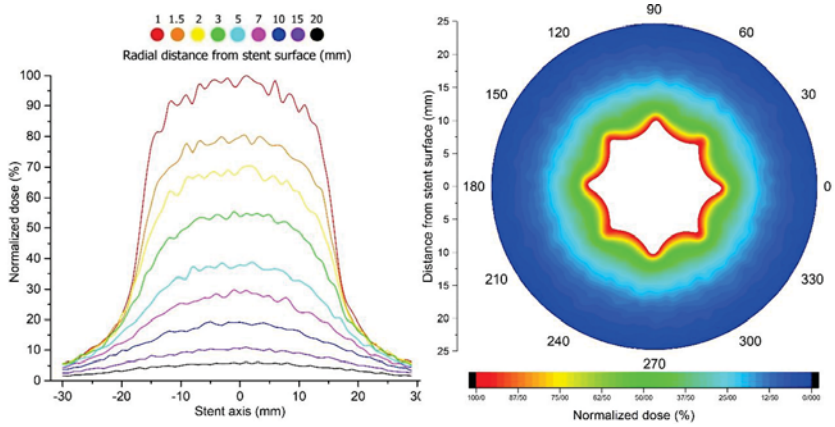

Figure 6: Dose distributions of the esophageal stent loaded with I-125 seeds for Δ =5 mm.

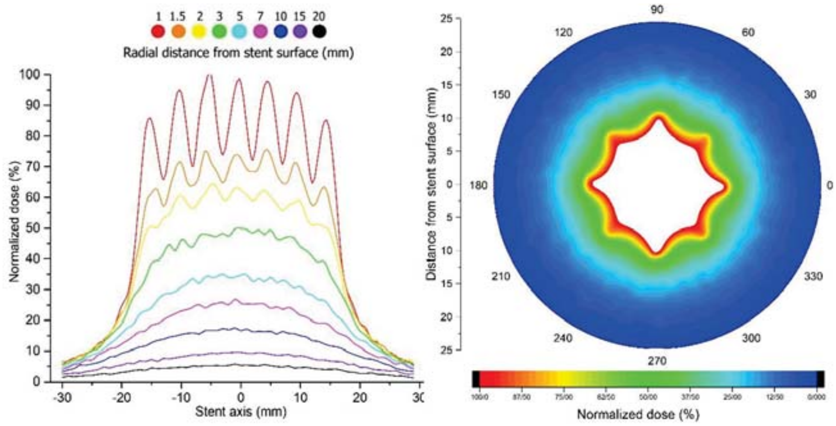

Figure 7: Dose distributions of the esophageal stent loaded with I-125 seeds for Δ =10 mm.

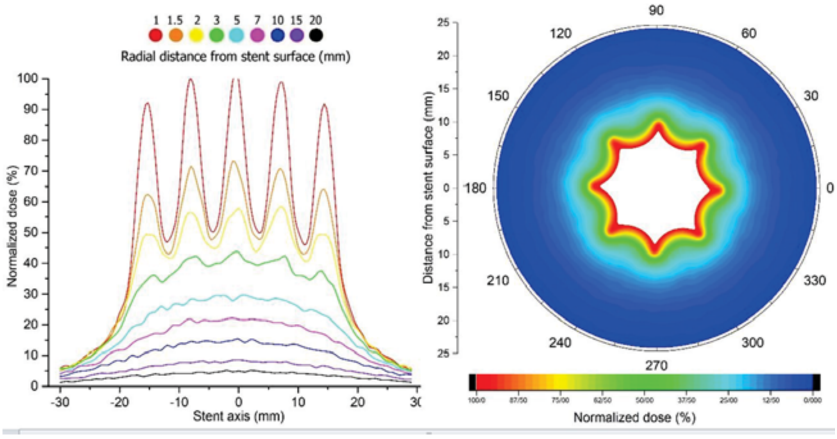

Figure 8: Dose distributions of the esophageal stent loaded with I-125 seeds for Δ =15 mm.

Table 3: PVD ratios of the esophageal stents loaded with I-125 seeds for different radial distances.

Interval distances between two adjacent seeds (Δ)	Radial distance from the stent surface			
	1 mm	2 mm	3 mm	5 mm
5 mm	1.04	1.01	1	1
10 mm	1.32	1.11	1.06	1
15 mm	1.9	1.46	1.24	1

seed arrangements are tabulated in Table 3. Dose reference point in clinical applications is usually considered at 5 mm from the stent surface (Zhu et al., 2014; Gaspar et al., 1997).

Also, Fig. 9 compares the dose fall-off curves for the three esophageal stents.

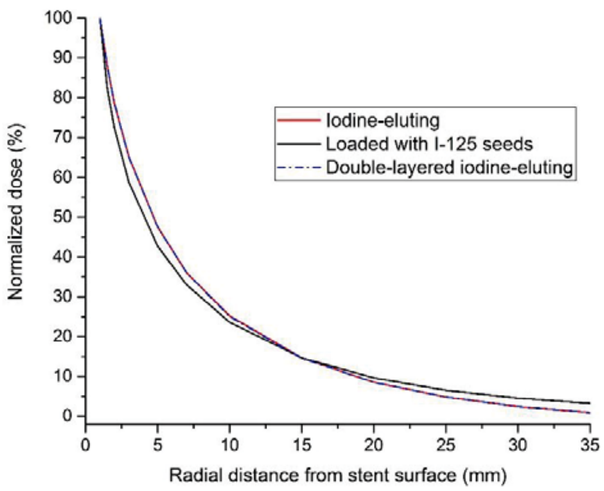

Figure 9: Dose calculated in radial distances from the surfaces of three mentioned stent.

4 Discussion and conclusion

As recommended by AAPM-TG 60 and 149, understanding the dose distribution around any radioactive stent is necessary before any clinical use (Nath et al., 1999; Chiu-Tsao et al., 2007). In the present work, three kinds of radioactive esophageal stents, I-125 seed-loaded stent, iodine eluting stent and double-layered iodine eluting stent, were simulated using Geant4 toolkit and the corresponding dose distributions were investigated. It was shown that I-125 with the penetration depth of up to 20 mm can deliver acceptable dose to the tumor located in the esophagus wall especially at the reference point. The fact that deeper penetration of photons increases the probability of radiation injuries on the adjacent healthy tissues should be considered in clinical studies.

The dose distribution of esophageal stents loaded with I-125 brachytherapy seeds presents an obvious variation near the stent surface. This non-uniformity will escalate by increasing Δ. Figures 7 and 8 show a peak at the location of a brachytherapy seed which is expected to become sharper by increasing Δ. The values calculated for PVD (see Table 3) suggest that delivering a uniform dose distribution at dose reference point is of high importance in assessment the quality of radioactive esophageal stent. It is due to the presence of cold spots in the valleys which are the locations of the tumor recurrence (Lin et al., 2015).

According to Table 3, PVD ratios for a stent carrying I-125 seeds with $\Delta > 15$ is not acceptable, especially at the reference point. The results show that the dose distribution of esophageal stent carrying I-125 with $\Delta = 5$ approximately behaves similar to that of iodine-eluting stent. As can be seen in Fig. 6, dose uniformity is attainable with decreasing Δ. It should be noted that to cover the entire lesion of the tumor with the I-125 seeds, it is required to exceed at least 2 cm from the tumor margins (Guo et al., 2008), which causes a limitation on changing Δ. By decreasing Δ and subsequently increasing the number of seeds, their activities should be reduced compared with the previous state. It should be noted that using a large number of seeds is not economically reasonable. The number, the arrangement and the activity of seeds should be determined by the treatment planning system (TPS) considering the size and the location of the tumor as well.

One advantage of I-125 seed-loaded stent compared with iodine-eluting stent is that the distribution of I-125 seeds can be arranged according to the asymmetrical growth of tumor (Zhongmin et al., 2012). The results of comparison between the angular dose distributions and the dose fall-off curves, show that the dose intensity of radioactive esophageal stents loaded with I-125 seeds decreases more rapidly than that of iodine-eluting stents. Furthermore, the dose intensity near the surface of esophageal stents carrying I-125 seeds is higher than that of iodine-eluting stents. It is of high importance for satisfying the aim of an appropriate treatment, *i.e.* delivering a high dose to the tumor and sparing the surrounding healthy tissue as much as possible. As a result, esophageal stents loaded with I-125 seeds provide more acceptable treatment compared with that of iodine-eluting stents; although keeping the distance between two adjacent seeds less than 15 mm should be taken into account.

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