Dosimetric study of radioactive esophageal stents for the treatment of advanced esophageal cancer

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Abstract:
A dosimetric investigation of photon- and beta-emitting esophageal stents has been performed for the treatment of advanced esophageal cancer. Using Geant4 toolkit, esophageal stents carrying 125I, Pd-103 and Ce-131 brachytherapy sources were studied as well as esophageal stents coated with Ho-166 and Re-188 radioisotopes were simulated and their dose distributions were investigated. The absorbed dose to the stent were measured and the arrangement of the seeds on dose distributions were investigated. For validation, radioluminescent EBTR film dosimetry was performed for 125I seed-loaded and Ho-166 impregnated esophageal stents. Furthermore, the accumulated dose of each radioactive stent (at the dose reference points), was calculated for different activities. Peak to valley dose (PVD) ratio is defined as a measure of dose uniformity for esophageal stents loaded with brachytherapy seeds in order to show the difference of dose intensity between the location of the presence of a radioactive seed and the adjacent vacant place. Due to the short penetration depth of beta particles in tissue, only palliative treatment is expected for beta-emitting esophageal stents. Pd-103 and Ce-131 seed-loaded stents cannot deliver the sufficient dose at the referance point, due to their short half-lifes. It is shown that the edge hotspots in beta-emitting esophageal stents are more prominent with due to their long half-life compared to the stent endges. The presence of a magnetic field (1.5 Tesla) along the stent axis, has a significant effect on dose distributions of beta-emitting stents. The interval of 5 mm between two adjacent seeds (center to center) produces a 65% decrease in dose at 15 mm, due to the presence of cold spots in the space between seeds that are the locations of the tumor recurrence and it's more critical for Pd-103 seeds. Since the radioactive esophageal stents are permanent implants, 125I seeded with 28.4 keV mean energy and 59.4 days half-life is the best choice along the low energy brachytherapy seeds.

Keywords:
advanced esophageal cancer, radioactive stent, brachytherapy, dosimetry, Geant4, Monte Carlo

Introduction:
Over 455000 new esophageal cancer cases and 400000 deaths were reported in 2012 worldwide [1]. The use of self-expanding metal stents is the safest solution to relief dysphagia, which is the most common symptom of advanced esophageal cancer. Recently, using 125I-brachytherapy seeds placed in the esophageal stents helps to palliate dysphagia as well as to prevent the growth of tumor in the stent [2]. Both beta- and photon-emitting esophageal stents have been studied [3-6]. However, there is still a shortage in the study of dose distribution of radioactive esophageal stents carrying radioactive seeds based on the arrangement and activity of the seeds. This work is intended to investigate dose distributions of beta-emitting Ho-166 and Re-188 and photon-emitting 125I, Pd-103, Cs-131 esophageal stents, using Geant4 toolkit. The effects of seed arrangements, stent material and presence of a magnetic field on dose distribution were investigated.

Methods:
A bare stent with 120 mm length and 18 mm diameter, a covering membrane and plastic sheaths containing radiactive seeds, were simulated in the center of a cylindrical water phantom (figure 1). For beta-emitting esophageal stents, the membrane is uniformly coated with a radionuclide. Brachytherapy seeds were simulated based on Amersham model 6711 source, which has a silver cylindrical core with 0.5 mm in diameter and 3 mm in length. The full length and diameter of the source is 4.6 and 0.8 mm, respectively. It is shown in figure 1, four seeds, as a group, were arranged in a plane perpendicular to the stent axis with an angular distance of 90 degrees. Each group has an angular distance of 45 degree respect to the nearby groups. Three interval distances between adjacent seeds (10, 15, and 20 mm) were chosen for both seeds and the distances were simulated. The cylindrical scoring mesh was performed to obtain the relative dose distribution around the stent. The dose rate is calculated by:

\[ D_{r}(x,y,z) = \frac{\sum_{i=1}^{N} D_{i}(x,y,z) N_{i}}{F_{a}} \cdot A_{a} = 100 \cdot 3600 \]  

(1)

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The number of primaries (4-10^3) and D_{i}(x,y,z) is the dose deposited per emitted particle. F is the correction factor and equals to number of bare stent seeds per disintegrations that emit the decay products decay schemes [8]. The dose reference point is considered at the depth of 5 mm for radioactive esophageal stents and the prescription dose is reported to be 40 to 50 GY [9-10].

Results:
The axial dose distributions of 125I seed-loaded esophageal stents with arrangement 1, are shown in figure 2. The normalized dose distribution of Cs-131 and Pd-103 are nearly the same.

Discussion and Conclusion:
As it is shown in the dose distributions in figure 2, the high gradient of dose decreases with the radial distance from the stent surface. Dose Intensity at the reference point is 30-40% of that at a depth of 1 mm for photons. It is less than 1% for Ho-166 and Re-188 ones. In the case of photon-emitting stents for more than 20 mm, dose distribution at the reference point shows more fluctuation than that of the arrangements of seeds [7]. The difference of dose intensity at the location of a seed and the adjacent vacant place reaches to 15% (table 1). However, for less than 20 mm, the distribution of dose at the reference point has almost reached a perfect uniformity. The lack of uniformity especially at the reference depth is not clinically desirable, because of the appearance of cold spots in the valleys, which increases the probability of the tumor recurrence. According to table 1, it is more critical for Pd-103, due to its lower average energy of emitted photons [7].

One can obtain dose uniformity by reducing the activity. Note that to cover the entire lesion of the tumor with brachytherapy seeds, at least 2 cm exceeding the tumor margins is required [21]. By decreasing the activity that the number of seeds, their activities should be reduced compared to the previous state. Otherwise, a large dose will be delivered to the esophageal wall. The number, the arrangement and the activity of seeds should be determined by the treatment planning system based on the size and the location of tumor.

Figure 5-c indicates the good potential of photon-emitting stents to deliver a therapeutic dose to the deep tumors. However, the higher range of photons may lead to radiation damage to nearby tissues and should be considered in treatment planning procedure. According to figure 5-b, 125I with 28.4 keV mean energy [7] and 59.4 days half-life is the best choice among the low energy brachytherapy seeds.

For a specific activity, Ho-166-beta-emitting stents have the highest dose delivery near the stent surface (figure 4-c). Due to the short penetration depth of beta particles in tissue, the deposited dose will decrease drastically by increasing depth and it is much smaller than that of gamma-emitters at the reference point. Therefore, only palliative treatment is expected for beta-emitting stents.

According to figure 5-a a uniform magnetic field along the stent axis, increase the surface dose of beta-emitting stents and it is up to 60% for 3 Tesla magnetic field. Therefore, patients treated with beta-emitting stents should not be placed in the magnetic field for a long time.

One important issue in clinical studies about stent implants is the stent restenosis. It happens due to tissue hyperplasia on the upper edge of the stents that constitutes a common long-term complication and presents major limitation for interventional therapies [11]. The axial dose distribution of beta-emitting stents in figure 4 shows that the edge hotspots in beta-emitting stents are more prominent with due to their long half-life compared to the stent endges. Therefore, utilization of beta-emitting stents as well as seed-loaded with more than 20 mm, seems not to be advisable in the case of advanced esophageal cancer.