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JOINT AAPM | COMP MEETING
MEDICAL PHYSICS COMMUNITY · INSPIRATION · INNOVATION · IMPACT

Volumetric Dose Enhancement Due to Time-Dependent Diffusion of Gold Nanoparticles Eluted from Loaded Spacers in Nanoparticle-Aided Brachytherapy

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Purpose

Investigate the impact of spatiotemporal distributions of gold nanoparticles (AuNPs) released from loaded brachytherapy spacers on Iodine-125 brachytherapy treatment dose distributions.

Methods

- A second-order finite difference model
- Intercellular space
- Two geometries
  - spacer-seed pairs (1S)
  - spacer-spacer-seed triplets (2S)
- Four pairs/triplets were placed 5 mm apart in opposite alignments to adjacent pairs/triplets
- Periodic boundaries in three dimensions.
- Each spacer was loaded with 30 mg gold/g of spacer.
- Three different time release patterns
- Dose enhancement factor was found from AuNP concentration using previously published results
- Iodine-125 dose distribution was calculated using AAPM TG-43 formalism.

Conclusions

- When one spacer is used the impact on dosimetric values is dominated by the diffusion coefficient
- There is greater complexity and interplay when multiple spacers are used
- Larger AuNPs provide a more homogeneous dose distribution and smaller AuNPs provide a more homogeneous dose enhancement
- Slower release rate generally have lower dosimetric values but could benefit in systems with higher clearance rates
- Same D90 and D50 with 11.4% and 8.2% lower air kerma strength in 1S
- Same D90 and D50 with 14.1% and 11.5% lower air kerma strength in 2S

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METHODS AND MATERIALS

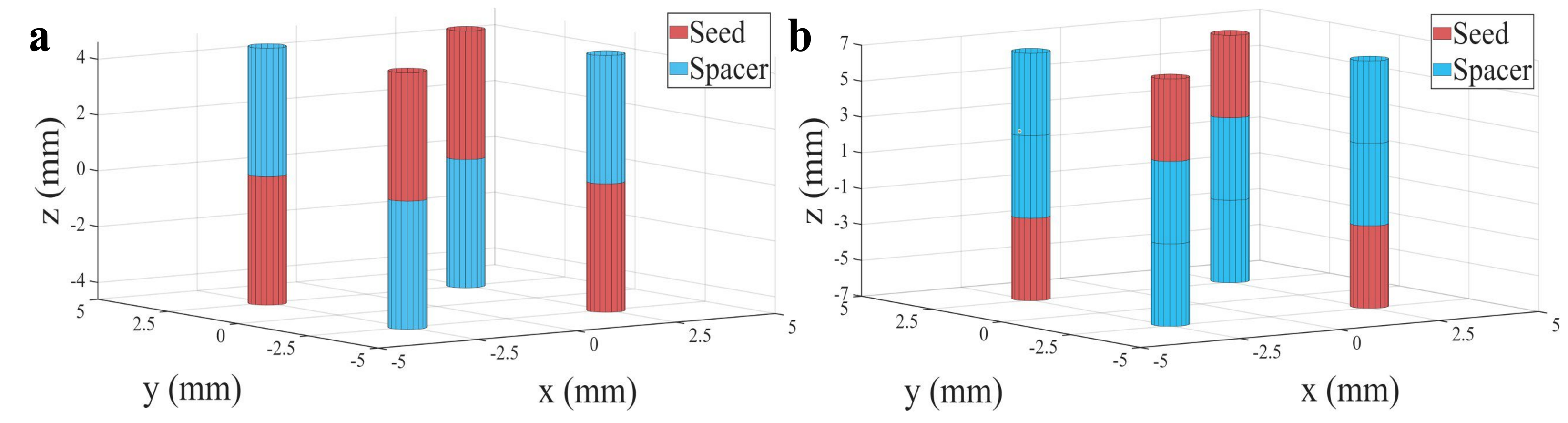

Figure 1. Simulation Geometries. The spacer-seed (blue-red) a) pairs (1S) and b) triplets (2S) are arranged parallel to the z-axis and centered at combinations of (±2.5 mm, ±2.5 mm) on the x-y plane..

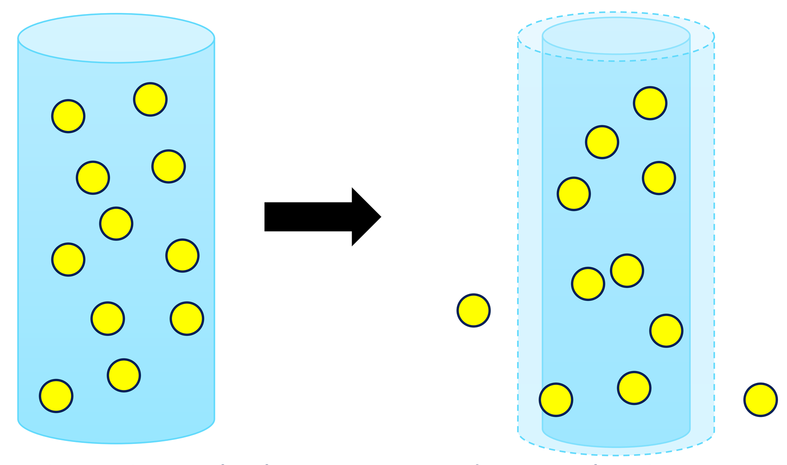

Figure 2: Brachytherapy spacer decays releasing AuNPs over time

$$\frac{\partial C}{\partial t} = D\nabla^2 C - kC + S$$

Equation used to model the concentration of AuNPs in extracellular space.

- D is Diffusion coefficient
- k is first order removal from extracellular space via endocytosis
- S is a source term representing the release of AuNPs from Brachytherapy spacers.
- C is concentration of AuNPs
- t is time

RESULTS

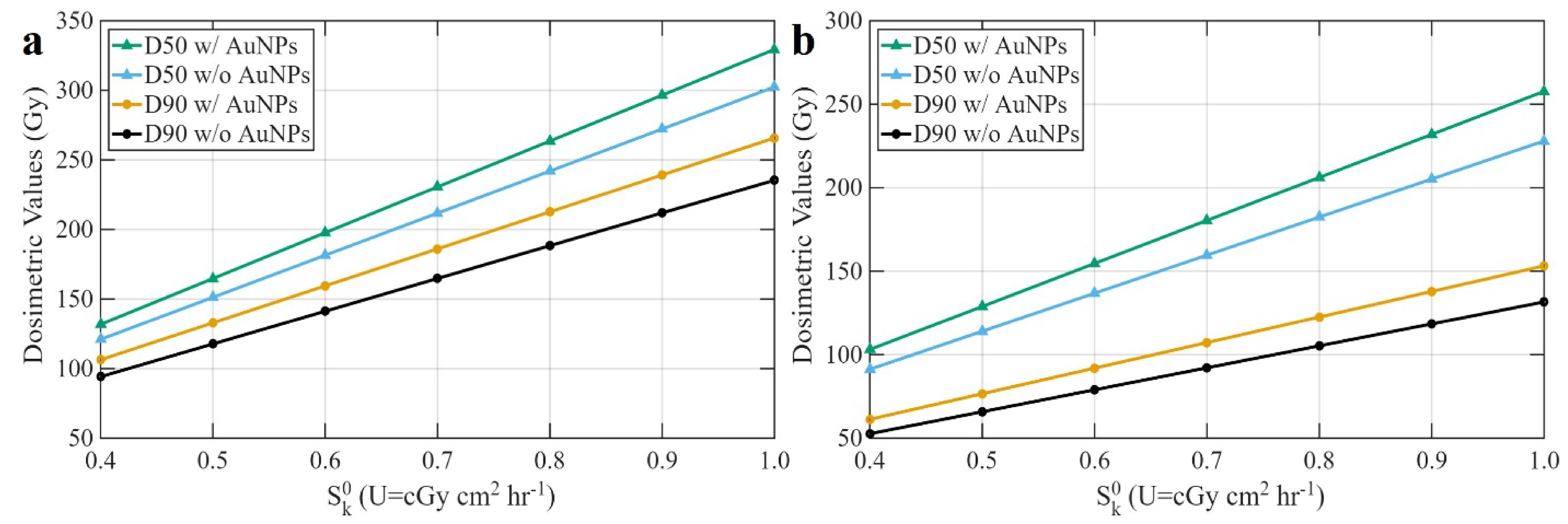

Figure 3. D90 and D50, with and without 14 nm AuNPs being released from the spacers in the a) spacer-seed pairs (1S) ($D50$ w/ AuNPs $= 329.4 \cdot S_k^0$, $D50$ w/o AuNPs $= 302.4 \cdot S_k^0$, $D90$ w/ AuNPs $= 265.7 \cdot S_k^0$, $D90$ w/o AuNPs $= 235.4 \cdot S_k^0$) and in the b) spacer-seed triplets (2S) ($D50$ w/ AuNPs $= 257.7 \cdot S_k^0$, $D50$ w/o AuNPs $= 228 \cdot S_k^0$, $D90$ w/ AuNPs $= 153.2 \cdot S_k^0$, $D90$ w/o AuNPs $= 131.6 \cdot S_k^0$) ($U = \mathrm{cGy\ cm^2\ hr^{-1}}$).

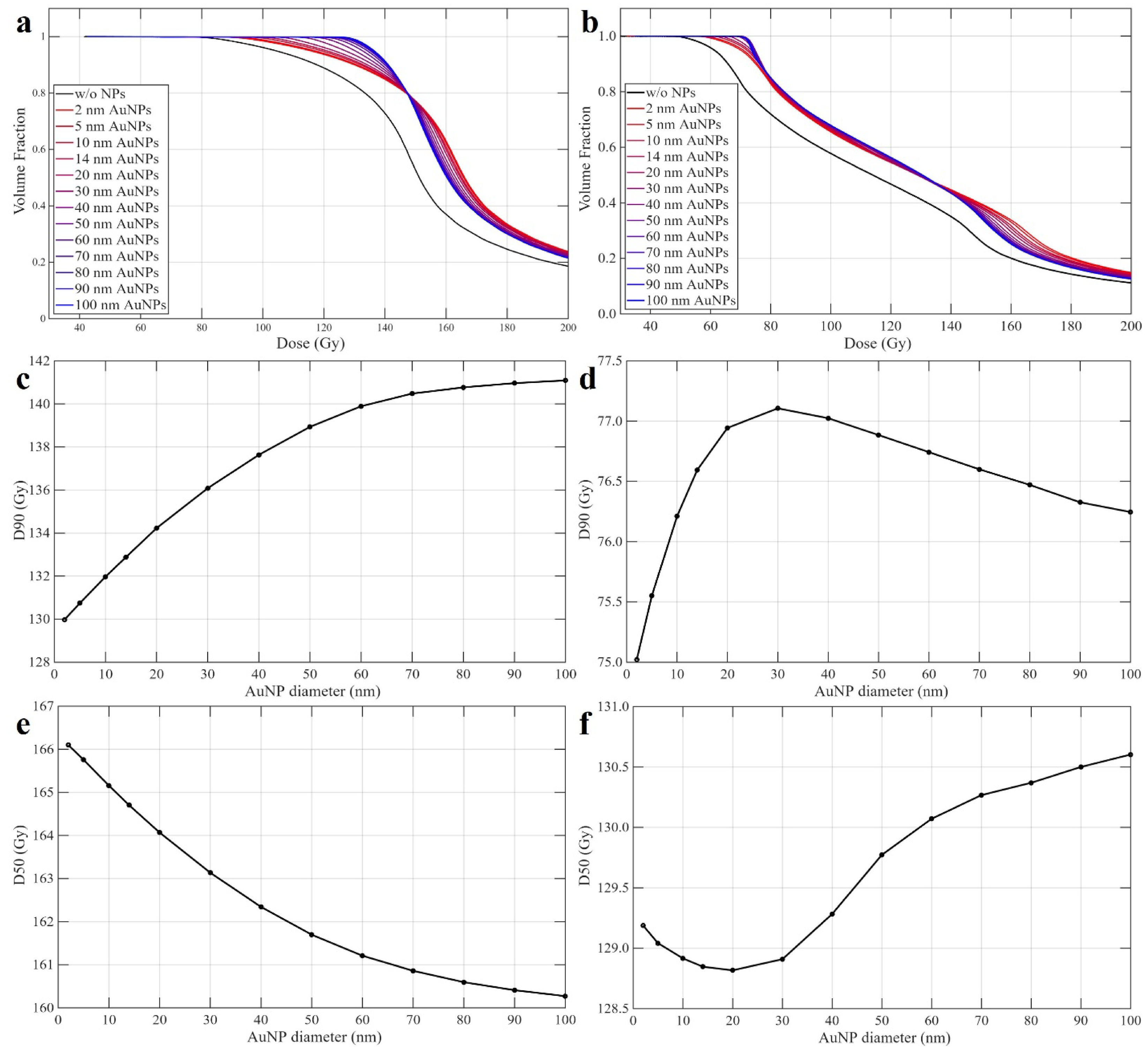

Figure 4. Dose Volume Histogram for a) spacer-source pair (1S) and b) spacer-spacer-source triplet (2S) for zero nanoparticles and various sized AuNPs. D90 vs AuNP diameter in c) 1S and d) 2S. D50 vs AuNP diameter in e) 1S and f) 2S. ($S_k^0 = 0.5$ U)

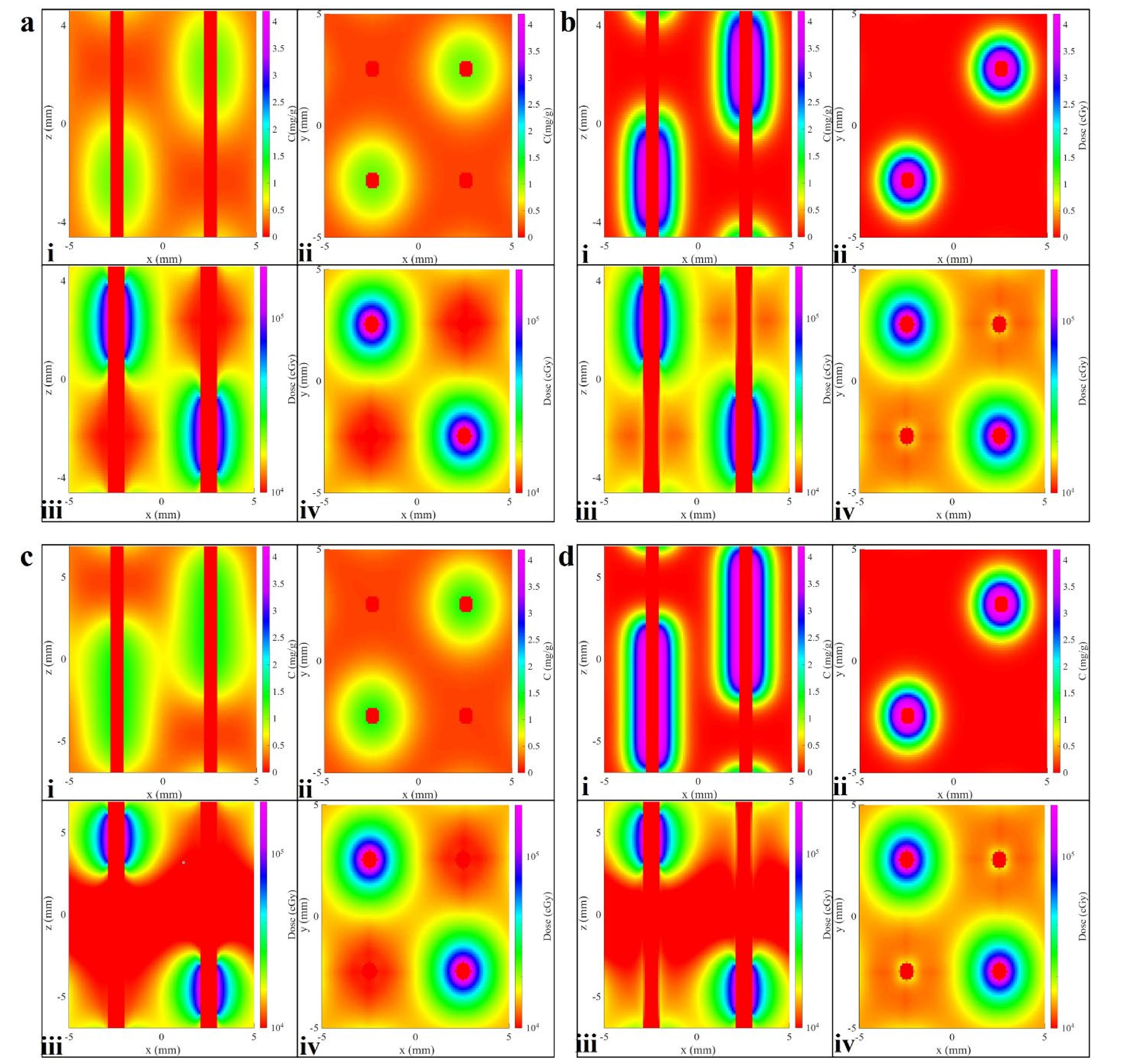

Figure 5. Figure 5: Distribution of AuNP concentration after 20 days for 20 nm (a,c) and 80 nm (b,d) in the i) x-z plane at y=-2.5 mm and ii) x-y plane at z=-4.6 mm and the total dose distribution in the iii) x-z plane at y=-2.5 mm and iv) x-y plane at z=-4.6 mm in the spacer-source pair (1S) (a,b) spacer-source triplet (2S) geometry (c,d).

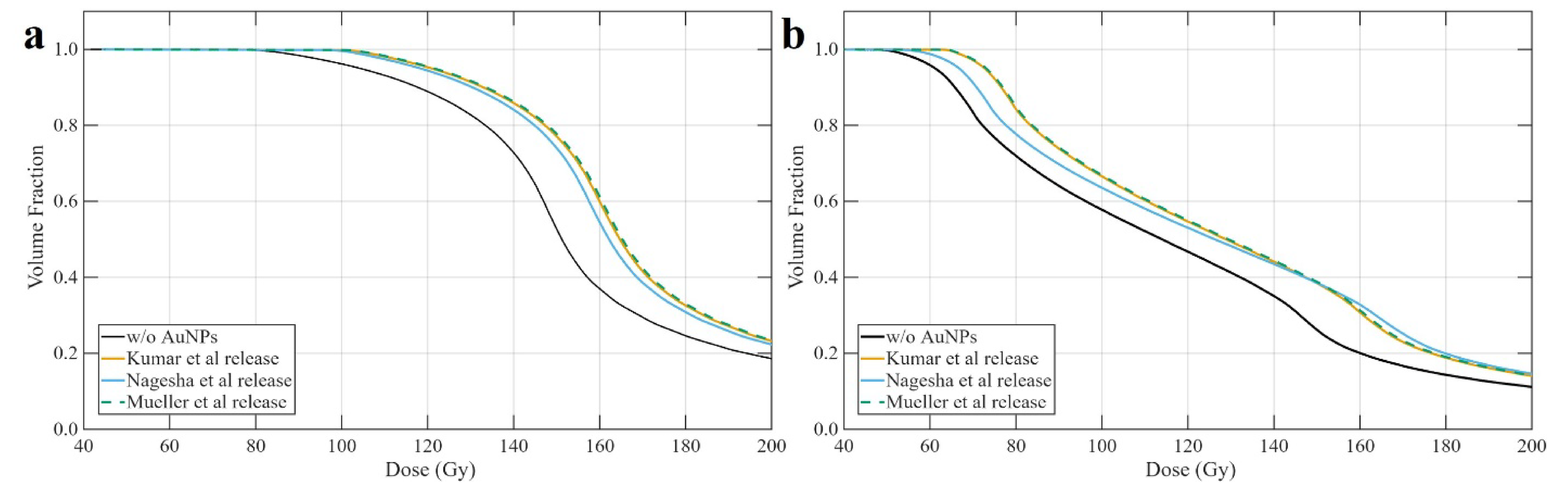

Figure 6. Dose Volume Histogram (DVH) for three different experimental nanoparticles release patterns from Kumar et al (1) (constant release for 14 days), Nagesha et al (2) (63% release in first 20 days then remaining 37% in the next twenty days) and Mueller et al (3) (Weibull model) in a) spacer-source pair (1S) geometry and (b) spacer-source triplet (2S) geometry. (AuNP d=14 nm, $S_k^0 = 0.5$ U)

References

[1] Kumar R, Belz J, Markovic S, et al. Nanoparticle-Based Brachytherapy Spacers for Delivery of Localized Combined Chemoradiation Therapy. International Journal of Radiation Oncology*Biology*Physics. 2015;91(2):393-400. doi:10.1016/j.ijrobp.2014.10.041.
[2] Nagesha DK, Tada DB, Stambaugh CKK, et al. Radiosensitizer-eluting nanocoatings on gold fiducials for biological in-situ image-guided radio therapy (BIS-IGRT). Phys Med Biol. 2010;55(20):6039. doi:10.1088/0031-9155/55/20/001.
[3] Mueller R, Moreau M, Yasmin-Karim S, et al. Imaging and Characterization of Sustained Gadolinium Nanoparticle Release from Next Generation Radiotherapy Biomaterial. Nanomaterials 2020, Vol 10,. 2020;10(11):1-13. doi:10.3390/NANO10112249.