Monte Carlo Simulation for Radioisotope Composite Injection in Skin

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1. Introduction

Radiation therapy is a cornerstone of cancer management. In addition to external-beam modalities, radiopharmaceutical or radioligand therapies have expanded rapidly, with approved agents such as Novartis' Lutathera (^{177}Lu-DOTATATE) and Pluvicto (^{177}Lu-vipivotide tetraxetan) [1]. Local intra-arterial or intralesional delivery is also clinically established; for example, Boston Scientific's TheraSphere (Y-90 glass microspheres) is infused selectively to achieve high tumor dose while limiting normal-tissue exposure. Local delivery strategies can, in principle, reduce whole-body exposure and the total administered activity needed to achieve therapeutic dose at the target.

We are developing a microneedle-based local injection approach for skin tumors (e.g., keloids), using a radioactive nanocomposite in which nanoparticles are radiolabeled. In this work, we estimate the minimum initial activity required for treatment by Monte Carlo (MC) simulation, imposing a conservative planning goal that every voxel within the target volume should receive at least 20 Gy [2].

2. Materials and Methods

2.1. Simultaion Parameters

Simulations were performed with Geant4 v11.0.3. To model low-energy electron–photon interactions in soft tissue, we employed G4EmLivermorePhysics. Production cuts were tuned so that the effective secondary-production thresholds corresponded to ~10 keV in soft tissue. The source particle spectrum followed the β−emission of phosphorus-32 (P-32; $E_{max} \approx 1.71$ MeV). A total of 1.0×10^6 histories were tracked per run. As usual for P-32, emitted neutrinos were neglected because they do not contribute to local dose deposition.

2.2. Simulation Geometry

The skin phantom was a 30 mm × 30 mm slab with 4 mm thickness. The target volume was centered within the phantom and defined as 5 mm × 5 mm × 2 mm. For dose scoring, the target was voxelized into 0.1 mm × 0.1 mm × 0.1 mm cubes. The radioactive nanocomposite was modeled as a 5×5 array of spherical sources with 2 mm center-to-center spacing; two sphere diameters were studied (1 mm and 2 mm). All test conditions used the same depth setting to isolate the effects of source size and array geometry.

2.3. Activity required for therapy

We first computed the energy deposition–per-history in each voxel and converted it to dose-per-history. The minimum-dose voxel within the target then defined the required number of emitted electrons (equivalently, decays) to reach 20 Gy at that voxel. Finally, accounting for radioactive decay of P-32 ($T_{1/2}$ = 14.3 days) and integrating activity over a 42.9-day window (three half-lives), we converted the required number of decays into the initial activity A_0.

$$\frac{20\ Gy}{x\ [Gy/particle]} = N\ [\text{particles}] \quad (1)$$

$$A_{total} = A_0 \int_0^{42.9} e^{-\lambda t} dt = A_0\left(\frac{1-e^{-\lambda t}}{\lambda}\right) \quad (2)$$

$$A_0 = \frac{A_{total} \cdot \lambda}{1-e^{-\lambda t}} \quad (3)$$

3. Results and Discussion

Fig. 1. visualizes the voxelized energy-deposition maps for two source diameters (1 mm and 2 mm) and two axial layers: the source plane (iZ = 0) and a layer 1 mm above the source centers (iZ = 10; voxel size 0.1 mm). In each panel, the cyan star marks the coldest voxel within the target, which determines the prescription-limiting activity because our goal is ≥ 20 Gy in every voxel.

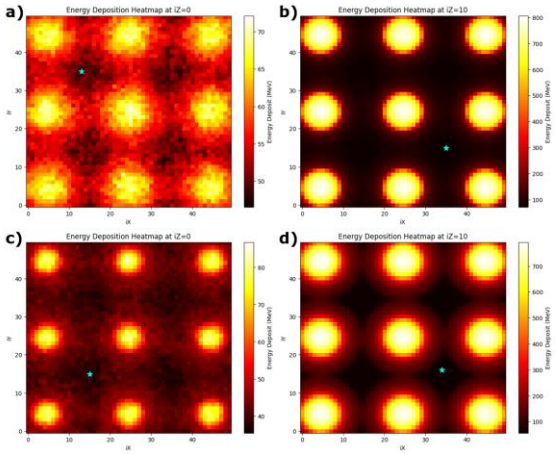

Fig. 1. Energy-deposition maps for a 5×5 array of spherical sources (2-mm spacing): (a,b) 1-mm spheres; (c,d) 2-mm; (a,c) iZ=0 (source plane); (b,d) iZ=10 (1 mm above). The cyan star marks the coldest voxel.

Using the activity formulation in §2.3, we determined that—to raise the coldest voxel to 20 Gy—the required initial activity for the 1-mm spheres was 10.23 μCi at the off-plane layer (iZ = 10) and 0.59 μCi at the source plane (iZ = 0), whereas for the 2-mm spheres the corresponding activities were 13.43 μCi and 0.60 μCi at iZ = 10 and iZ = 0, respectively.

Because clinical planning must satisfy the worst-case voxel, the relevant values are the off-plane minima (10.23 μCi for 1 mm spheres; 13.43 μCi for 2 mm spheres). The much smaller activities obtained on the source plane (~0.6 μCi) reflect the strong dose peaks near the sphere centers and would underestimate the dose needed to cover the entire target thickness. Increasing the source diameter from 1 mm to 2 mm increased the prescription-limiting activity by ~31%, consistent with deeper but more spatially separated high-dose lobes that leave slightly colder interstitial regions between neighboring sources (2 mm center-to-center spacing).

Interpreted per particle for the 5×5 array (uniform labeling assumed), the prescription-limiting activities correspond to approximately 0.41 μCi/sphere (10.23 μCi/25) for 1 mm spheres and 0.54 μCi/sphere (13.43 μCi/25) for 2 mm spheres. For context, TheraSphere employs ~25 μm Y-90 glass microspheres at roughly 0.108 μCi per sphere. Although the isotopes, sizes, and delivery sites differ, our estimates fall in the same order of magnitude (∼ 0.1–0.5 μCi per particle), suggesting that per-particle activities required for microneedle-delivered radioactive nanocomposites are comparable to those used in an established local radiotherapy product.

Practically, these results highlight that (i) axial coverage dictates the administered activity in this geometry, and (ii) modest geometric adjustments—e.g., reducing source spacing, employing two staggered planes, or optimizing injection depth—should further mitigate cold spots and lower the activity needed to meet a 20 Gy minimum throughout the target.

4. Conclusions

This pilot Monte Carlo study outlines a practical method to size the initial activity for a microneedle-delivered P-32 nanocomposite to achieve full minimum-dose coverage in a skin-lesion target. Simulations indicate that axial coverage—rather than on-plane hotspots—governs the prescription, and that modest geometric refinements (tighter spacing, staggered planes, optimized depth) can mitigate cold voxels and reduce the required activity. The per-particle activity estimate is on the same order as established local radiotherapy products, supporting translational plausibility. These findings provide a concise quantitative basis for sensitivity analyses and benchtop/phantom validation toward in-vivo feasibility.

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