A Nomogram for Predicting the Expected Seed Count for Diffusing Alpha-Emitters Radiation Therapy (Alpha DaRT) Treatment Planning

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BACKGROUND

- ***Alpha DaRT*** (Diffusing Alpha-emitters Radiation Therapy) delivers highly localized radiation via ***intratumoral placement of radium-224*** sources, which emit short-range, high-LET alpha particles depositing dose within several millimeters of each seed. Clinical studies have demonstrated its safety, efficacy, and favorable toxicity profile in ***head and neck*** squamous cell carcinoma[1] and in recurrent or unresectable ***skin cancers[2]***.
- In contrast to external beam radiotherapy, treatment planning for Alpha DaRT is dominated by ***geometric considerations***, as dose deposition is governed primarily by ***seed placement, inter-seed spacing, and target boundaries***. As such, determining the feasible number and spatial arrangement of seeds within a tumor volume is a central planning challenge. Additionally, because DaRT seeds must be ordered prior to implantation, accurate pre-implant modeling of how many seeds can be safely and effectively placed within a given tumor volume is essential.
- This work addresses this unmet need by introducing a ***rigorous, geometry-aware nomogram*** framework that quantifies achievable ***seed-packing densities in arbitrarily shaped targets***, enabling more reliable treatment planning, improved reproducibility, and better alignment between pre- and post-procedural planning.

REFERENCES

1. Popovtzer A, et al. Int J Radiat Oncol Biol Phys. 2020 Mar 1;106(3):571-578.
2. D'Andrea MA, et al. JAMA Netw Open. 2023 May 1;6(5):e2312824.

OBJECTIVES

To develop, compare, and validate a nomogram that uses tumor shape and size to predict seed density for Diffusing Alpha-emitters Radiation Therapy (Alpha DaRT) treatment planning with flexible and needle applicators.

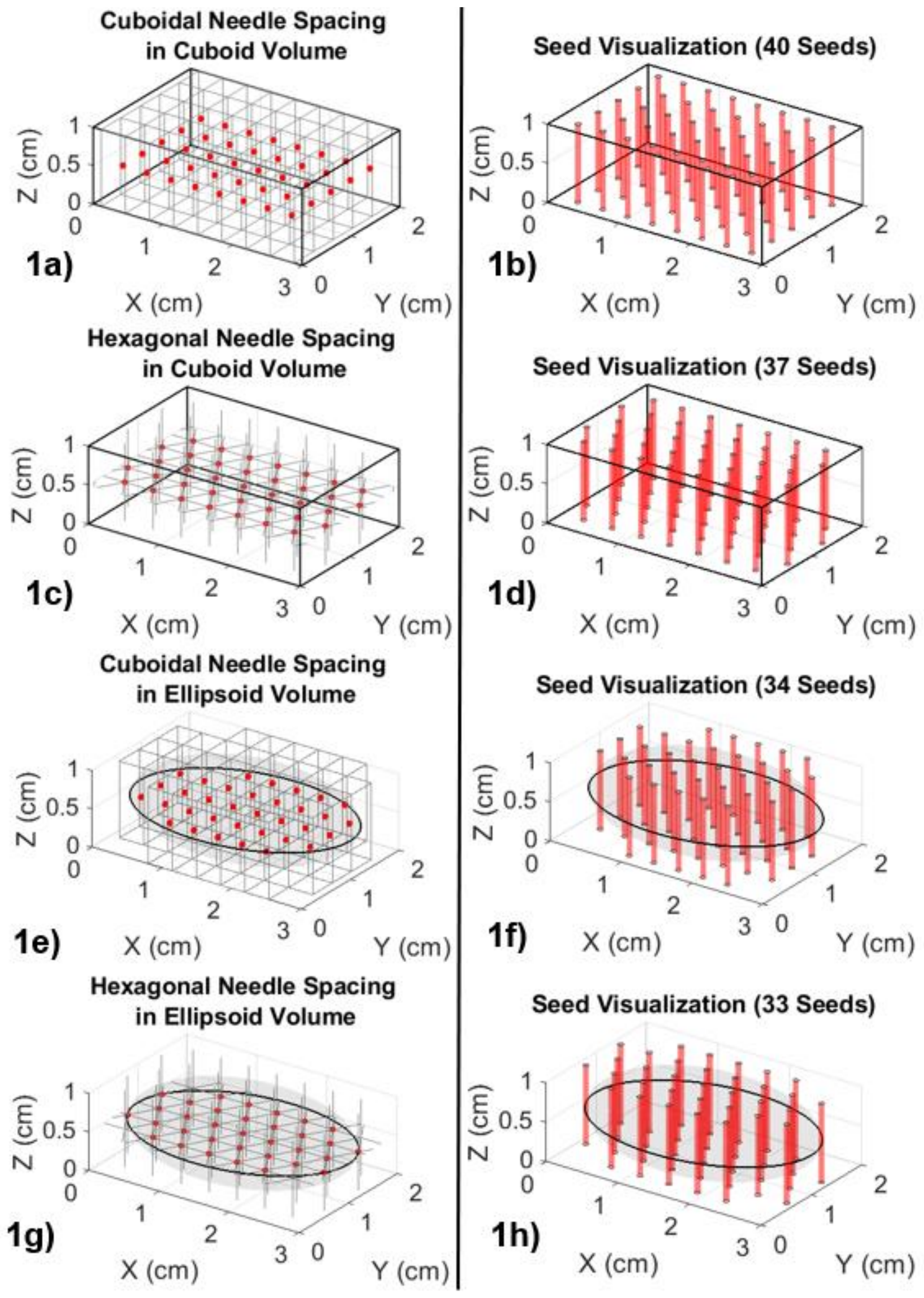

Figure 1. Seed packing for cuboid (a–d) and ellipsoidal (e–h) tumor geometries with principal axes of x = 3 cm, y = 2 cm, and z = 1 cm. Seed centers correspond to hexagonal lattice nodes and cubic lattice cell centers, shown as red dots in the left four geometric visualizations.

METHODS 1

- DaRT seed densities were evaluated using four geometry-based nomogram models differing by **tumor shape (cuboid or ellipsoid)** and needle **row offset pattern (cubic or hexagonal lattice).**
- All models assumed **parallel** needle insertion with **uniform inter-needle spacing**. A seed was counted as included if its geometric center lay within the tumor volume.

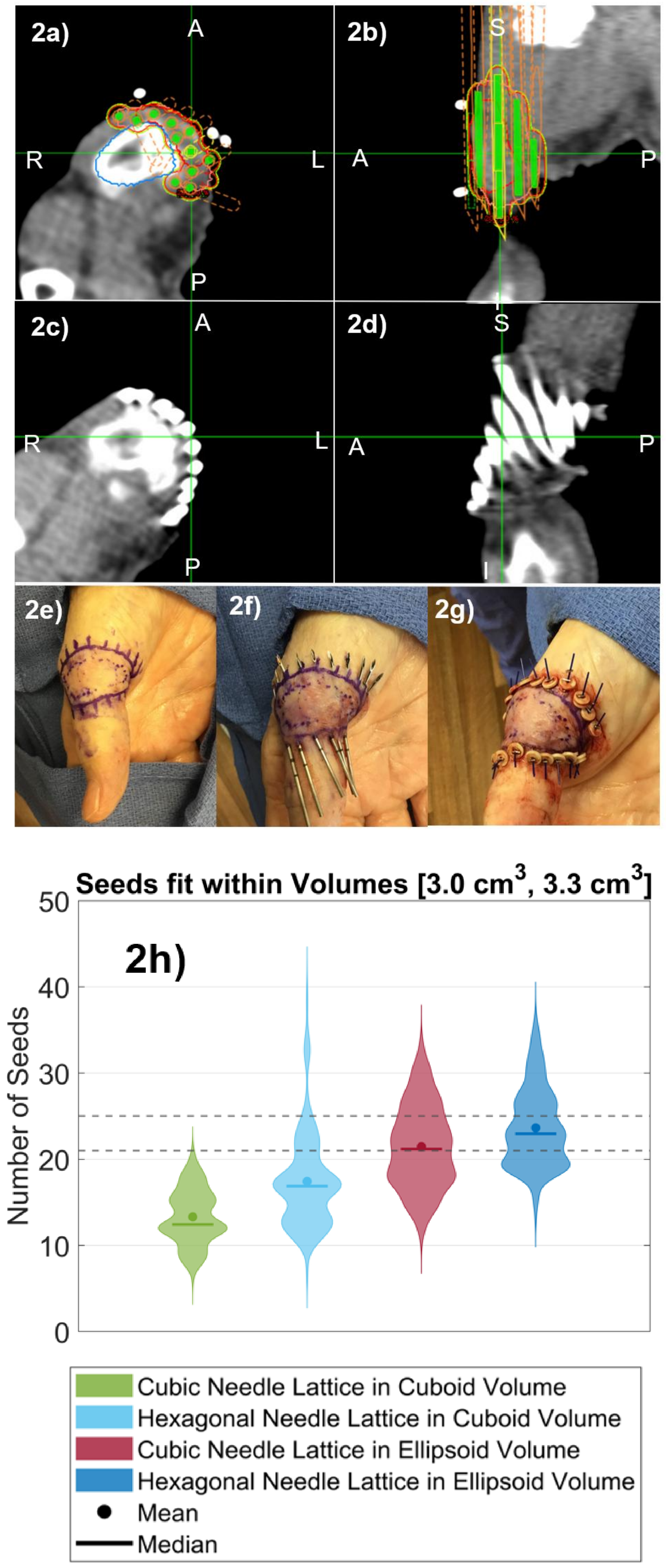

Figure 2. First Alpha DaRT patient treated at our institution. Pre-plan (a–b) and post-insertion (c–d) needle placements are shown. Procedure photographs (e–g) illustrate delineation of the treatment target and needle insertion for seed implantation. Subplot (h) shows violin plots of seed number predictions from the nomogram models.

Needles were spaced 4 mm apart in a hexagonal grid to deliver 10 Gy to the clinical target volume (3.14 cm³). Seeds were secured with protective caps on each end to prevent slippage. Nomogram results for volumes of 3.14 ± 0.15 cm³ were used to ensure adequate statistical power. Dashed lines indicate the actual pre-plan and post-insertion seed counts (25 and 21, respectively). Models using the ellipsoidal tumor shape showed the closest agreement.

METHODS 2

- Tumor volumes ranging from 1 to 40 cm³ were generated by independently varying each tumor axis dimension from 1 mm upward in 0.5 mm increments. Seed density was compared for: (1) ***cubic*** *needle lattice in a* ***cuboid*** *volume*, (2) ***hexagonal*** *needle lattice in a* ***cuboid*** *volume*, (3) ***cubic*** *needle lattice in an* ***ellipsoidal*** *volume*, and (4) ***hexagonal*** *needle lattice in an* ***ellipsoidal*** *volume*.

RESULTS

- The ***highest*** seed density was observed for the ***hexagonal needle lattice within an ellipsoidal treatment*** volume (7.2 ± 1.0 seeds/cm³), whereas the ***lowest*** occurred for the ***cubic needle lattice within a cuboidal treatment volume*** (4.7 ± 1.0 seeds/cm³).
- The remaining two configurations yielded comparable densities (6.6 ± 2.1 and 6.8 ± 1.1 seeds/cm³). These values agree with the first-in-human Alpha DaRT clinical trial by Popovtzer *et al.*, which reported approximately 7 seeds/cm³.[1]
- For our first clinical case (CTV = 3.14 cm³), both the pre-implant plan (25 seeds) and post-implant outcome (21 seeds) were ***most consistent with ellipsoidal treatment*** volumes using either a ***cubic*** (21.5 ± 5.8 seeds) or a ***hexagonal*** needle lattice (23.6 ± 4.5 seeds).

CONCLUSIONS

This work demonstrates that geometry-based nomograms capture the influence of tumor shape and packing geometry on achievable seed distributions, enabling more reproducible and personalized Alpha DaRT treatment planning quality assurance prior to seed order placement.