

Purpose: To study the potential advantage of space-fractionation (SF) over time-fractionation (TF) in radiotherapy.

Methods: The back skin of mouse was stretched and fixed with two thin titanium plates, exposing a circular window of 1.5cm in diameter. Tumor cells were implanted at the center of the window. When the tumor grew to 6mm, the window was irradiated with either TF or SF schemes: open field irradiation of 13Gy per fraction each day for four days for 52Gy total dose; or 52Gy per fraction through 2mmx2mm grid covering 25% of the open field, but then shifting the grid each day to a previously untreated area so that the entire window received an acute dose of 52Gy over four days. The animals were observed for 51 days and the number of hair within the irradiation window was counted after the mice were euthanized.

Results: 17 animals in the TF arm and 12 in the SF arm completed the study. After four days of irradiation, the tumors shrank to completely disappear within 2-3 days for both cohorts. Similar skin reaction and complete fur loss on both sides of the window were observed for both arms. The fur started to grow back at 4 weeks and was white rather than the original gray color. On the beam entry side, the average number of fur was 452 for the TF arm and 860 for the SF arm ($p=0.0003$). On the beam exit side, the number of fur strands was 223 for the TF arm and 730 for the SF arm ($p=0.0001$). These results strongly indicate less skin damage with SF.

Conclusion: SF allowed us to deliver a higher acute dose but showed much less late-term normal tissue toxicities. The results show strong evidence that SF has protective effects to normal structures.