Comparison of Pulsed Low Dose Rate and Conventional Radiotherapy Using an In-Vivo Model

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INTRODUCTION

Pulsed low-dose-rate (PLDR) has been investigated as a means to spare normal tissue during retreatment. This work studies PLDR treatment, and compares its effectiveness to conventional radiotherapy (CRT).

AIM

- The purpose of this study is to investigate the dose-rate effect on tumor growth with PLDR, consisting of multiple doses of radiation given at short intervals, using a mouse model.
- This study additionally compares cell killing during pulsed low dose rate treatment to conventional treatment.

METHOD

- Male nude mice were injected with human lung cancer (A549) cells subcutaneously bilaterally into their flanks.
- Two experiments were conducted.
  - In the first experiment, mice were irradiated using total body irradiation without anesthesia and treated with 2 Gy daily using 6-MV radiation.
    - Tumors were randomized into six groups: CRT and PLDR treatments, each using three total doses of 12, 14, and 16 Gy.
  - In the second experiment, mice were irradiated using total body irradiation without anesthesia and given 6 Gy in one PLDR irradiation consisting of 24 fractions of 25 cGy.
    - Tumors were divided into three groups by varying the time interval between treatments: 20 s, 1 min, and 3 min.
- Efficacy was monitored with weekly MR scans using a GE Signa 1.5T MR scanner.

RESULTS

- Table 1 displays the average increase in volume, along with the standard deviation of the mean, for tumors treated with CRT and PLDR in 2 Gy/day fractions to various total doses, one and two weeks after treatment, normalized to the volume before treatment.
- Table 2 displays the average increase in tumor volume one and two weeks after treatment, normalized to the volume before treatment, for tumors treated with PLDR using various intervals between treatment.
- The tables show that overall, PLDR does not lead to a statistically significantly greater delay in tumor growth compared to CRT using this mouse model, nor does the dose rate affect tumor growth significantly. To demonstrate tumor growth, Figure 1 shows the growth for two representative tumors in the study.
- Tumors treated with CRT and PLDR showed statistically equivalent increase in size for each dose group examined; two weeks after treatment, tumors treated with CRT and PLDR increased in volume by a factor of 1.33±0.16 and 1.40±0.21 for 12 Gy, 1.25±0.24 and 1.51±0.32 for 14 Gy, 2.13±0.30 and 1.74±0.21 for 16 Gy, respectively.
- Tumors treated to 6 Gy with PLDR showed statistically equivalent increase in size: tumors increased by a factor of 2.79±0.32, 2.40±0.19, 2.73±0.27 for the 20 s, 1 min, and 3 min intervals, respectively.

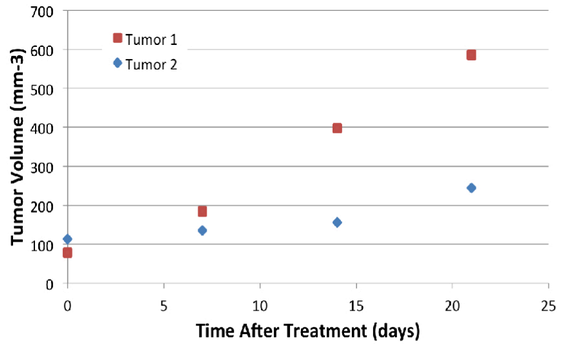

Figure 1. Tumor volume as a function of time for two representative tumors.

Table 1. Average tumor volume increase for tumors treated with CRT and PLDR to various doses.

	CRT, 12 Gy	CRT, 14 Gy	CRT, 16 Gy	PLDR, 12 Gy	PLDR, 14 Gy	PLDR, 16 Gy
Final volume (1 week)/ Initial Volume	1.18 ± 0.15	1.18 ± 0.20	1.57 ± 0.21	1.11 ± 0.21	1.05 ± 0.35	1.52 ± 0.21
Final volume (2 weeks)/ Initial Volume	1.33 ± 0.16 (N=2)	1.25 ± 0.24 (N=5)	2.13 ± 0.30 (N=6)	1.40 ± 0.21 (N=6)	1.51 ± 0.32 (N=4)	1.74± 0.21 (N=10)

Table 2. Average tumor volume increase for tumors treated with PLDR to 6 Gy using various dose rates.

Interval between Irradiation:	20 sec	1 min	3 min
Final volume (1 weeks)/ Initial Volume	1.76 ± 0.17	1.70 ± 0.13	1.56 ± 0.10
Final volume (2 weeks)/ Initial Volume	2.79 ± 0.32 (N=23)	2.40 ± 0.19 (N=26)	2.73 ± 0.27 (N=23)

CONCLUSIONS

There was no statistically significant difference in tumor growth delay between PLDR and CRT using this mouse model. Results suggest that varying the dose rate may potentially produce a more significant tumor effect with better statistics, warranting further studies with more mice.

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