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Abstract

A Mouse Model Is Useful For Evaluating Different Approaches of High-Dose Radiotherapy

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OBJECTIVES: High-dose radiotherapy has merits in treating bulky human tumors. Three different approaches were evaluated by using an animal model.

METHODS: The dorsal skin of C3H/HeJ mice was shaved, lifted, and sutured on a titanium holder to fix the skin for a known geometry. The holder has an oblique open window (16x14 mm), where pluripotent mouse NE cells were injected into the skin. Tumor growth was monitored by using a caliper.

RESULTS: To simulate stereotactic body radiation therapy (SBRT), tumors grown to 5-10 mm in diameter were irradiated with 13 Gy daily for 4 days for a total of 52 Gy of 250 Kv X-rays (2.2 Gy/min). Among 14 tumors exposed, 13 of them were not regrown during 36 days of observation period. The cure rate for SBRT was 13/14 (93%).

A miniature version of existing MLC grid was milled with copper blocks to make 25 holes of 2.0 mm squares (1:3 open-to-closed ratio), which was converged from the source of the X-rays. This grid allows ¼ of target area (oblique window) to be exposed. The 52 Gy (SBRT dose) was delivered to each quarter daily for 4 consecutive days to cover the whole 4 quarters of target area exposed, which is called quadruple grid radiotherapy (QGRT). The cure rate for QGRT was 9/12 (75%).

When skin fur regrowth in irradiated area was quantified as a sign of recovery, a Student's t-test showed that the regrowth for QGRT was much greater (p=0.0003) than that for SBRT.

In QGRT trials, some low-dose pockets were noted, so that the grid opening was widened from 2.0 to 2.4 mm squares, in which beam overlap was inevitable. To compensate the dose (9.7%) caused by overlaps, a priming dose (8-12 Gy) was adopted prior to quadruple grid exposures. This modified treatment plan is named as wQGRT. The cure rate for wQGRT was 13/15 (87%).

Chi-squared test shows that tumor cure rates among SBRT, QGRT and wQGRT are not different (p=0.431).

CONCLUSIONS: Our mouse model appears to be useful in evaluating that wQGRT offers tumor

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cure rates equivalent to SBRT, and with reduced normal tissue damage.