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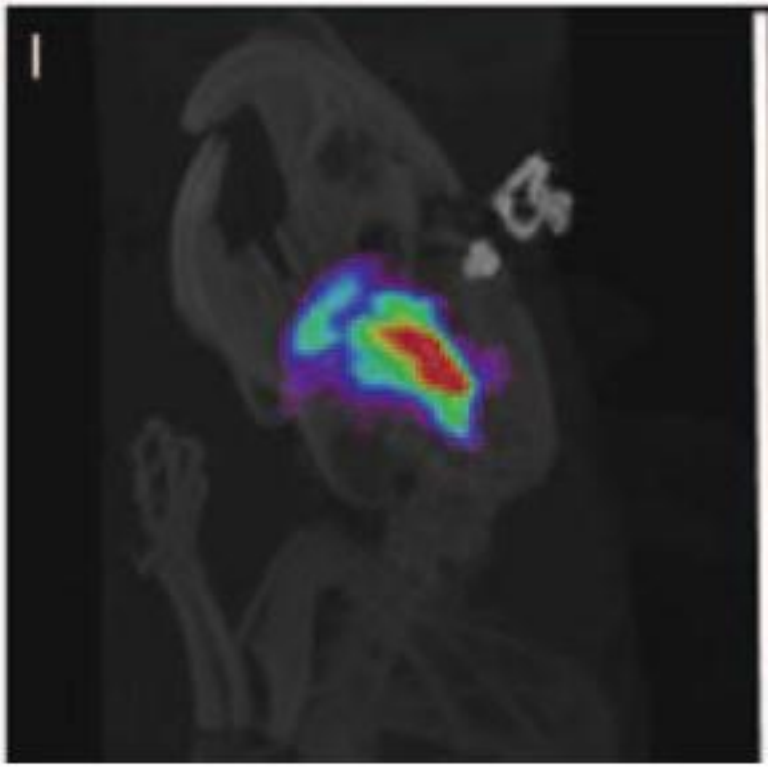
Rhenium-186 liposomes as convection-enhanced nanoparticle brachytherapy for treatment of glioblastoma

William T. Phillips, Beth Goins, Ande Bao, Daniel Vargas, Juan E. Guttierez, Abram Trevino, Jessica R. Miller, James Henry, Richard Zuniga, Giacomo Vecil, and Andrew J. Brenner

Although external beam radiation is an essential component to the current standard treatment of primary brain tumors, its application is limited by toxicity at doses more than 80 Gy. Recent studies have suggested that brachytherapy with liposomally encapsulated radionuclides may be of benefit, and we have reported methods to markedly increase the specific activity of rhenium-186 (186Re)–liposomes. To better characterize the potential delivery, toxicity, and efficacy of the highly specific activity of 186Re-liposomes, we evaluated their intracranial application by convection-enhanced delivery in an orthotopic U87 glioma rat model. After establishing an optimal volume of 25 mL, we observed focal activity confined to the site of injection over a 96-hour period. Doses of up to 1850 Gy were administered without overt clinical or microscopic evidence of toxicity. Animals treated with 186Re-liposomes had a median survival of 126 days (95% confidence interval [CI], 78.4– 173 days), compared with 49 days (95% CI, 44–53 days) for controls. Log-rank analysis between these 2 groups was highly significant (P 5 .0013) and was even higher when 100 Gy was used as a cutoff (P < .0001). Noninvasive luciferase imaging as a surrogate for tumor volume showed a statistically significant separation in Bioluminescence by 11 days after 100 Gy or less treatment between the experimental group and the control animals (MRI also supported this difference in tumor size. Duplication of tumor volume differences and survival benefit was possible in a more invasive U251 orthotopic model, with clear separation in bioluminescence at 6 days after treatment; median survival in treated animals was not reached at 120 days because lack of mortality, and log-rank analysis of survival washighly significant (P 5% < .0057). Analysis of tumors by histology revealedminimal areas of necrosis and gliosis. Theseresults support the potential efficacy of the highly specific activity of brachytherapy by 186Re-liposomes convection enhanced delivery in glioma.



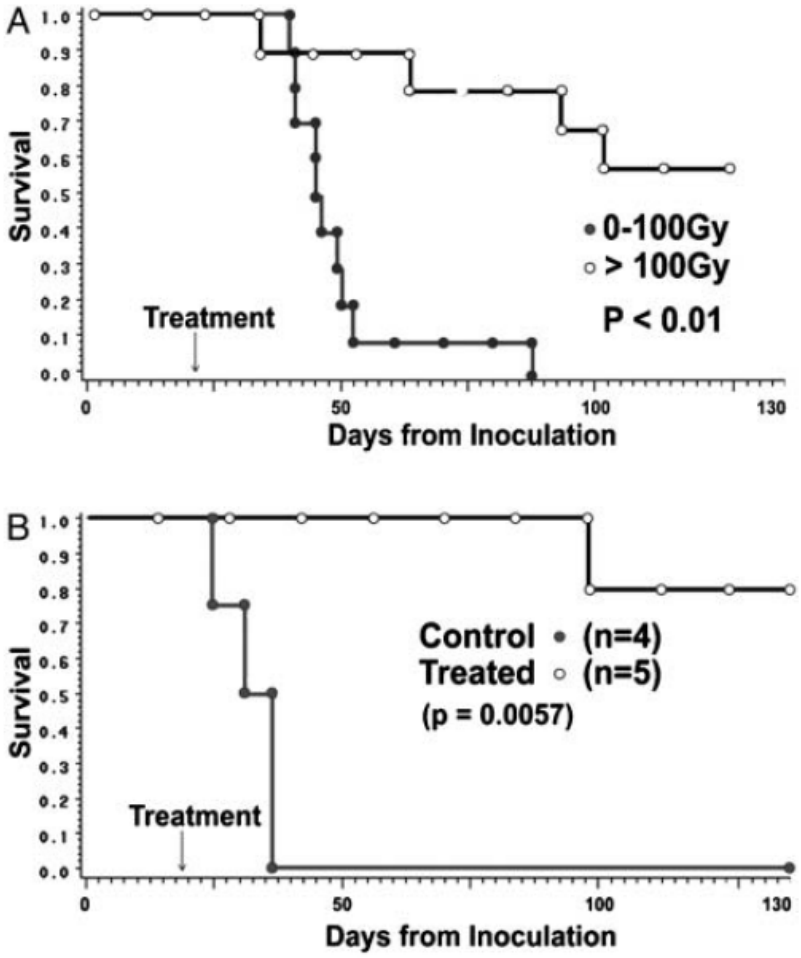


Fig. 6. Animal survival (A) from rats bearing U87 xenografts as a function of treatment of less than or greater than 100 Gy and (B) from animals bearing U251 xenografts.