4/25/2011

Interleaved carbon minibeams: An experimental radiosurgery method with clinical potential

F. Avraham Dilmanian[1,4,5], Adam Rusek[2], Giovanna R. Fois[1,6], John Olschowka[7], Nicolle R. Desnoyers[1*], Jane Y. Park[1], Istvan Dioszegi[3], Ruiliang Wang[1], Dardo Tomasi[1,7], Hedok Lee[1], Sean D. Hurley[7], Patricia K. Coyle[5], Allen G. Meek[3], and M. Kerry O'Banion[7]

[1]Medical Department, [2]NASA Space Radiation Laboratory Brookhaven National Laboratory, and the [3]Nonproliferation and National Security Department, Upton, NY 11973, U.S.A.

[4]Department of Radiation Oncology, Stony Brook University Medical Center, NY 11794, U.S.A.

[5]Department of Neurology, Stony Brook University Medical Center, NY 11794, U.S.A

[6]Physics Department, University of Cagliari, Sardinia 09042, Italy

[7]Departments of Neurobiology and Anatomy, University of Rochester, Rochester, NY 14642, U.S.A.

[8]National Institute on Alcoholism and Alcohol Abuse, Bethesda, MD 20892, U.S.A.

[*]Present address:
Ross University School of Veterinary Medicine
P.O. Box 334
Basseterre, St. Kitts
West Indies

Author contributions: F.A.D., A.R., A.G.M., and M.K.O. designed research; F.A.D., A.R., G.R.F., N.R.D., J.Y.R., I.D., D.T., R.W., S.D.H., J.O., and M.K.O. performed research; F.A.D., I.D., D.T., R.W., S.D.H., J.O., and M.K.O analyzed data; and F.A.D., A.R., G.R.F., P.K.C., A.G.M, and M.K.O. wrote the paper.

Abstract

Radiation therapy and radiosurgery for the CNS tumors, head-and-neck tumors, and benign neurological targets have well known limitations. Interleaved carbon minibeams is a novel experimental radiosurgery method that uses arrays of parallel, thin planes of carbon ion beams (minibeams). These minibeam arrays (300 µm or thicker), as their synchrotron-generated x-ray minibeam counterparts, are tolerated by normal tissues, including the CNS, at extraordinary high doses. The effect was first established with 25-37 µm x-ray beams (microbeams, <300 µm). Single-dose-fraction exposures of about 250 Gy in-beam in-depth doses produced no short- or long-term histological effects to the rat brain. Subsequently, x-ray minibeams as thick as 0.68 mm retained much of this tissue-sparing effect, and two arrays of such thick horizontal minibeams aimed at 90º to each other could be interleaved (or "interlaced") to produce a solid beam at the target. In the present study four arrays of 0.3 mm carbon minibeams administered from 90° angles interleaved to ablate a 6.5-mm target in the rabbit brain. A single-fraction of 46.3 Gy physical target dose, relating to 139 photon-equivalent Gy (GyE) was produced, using an average 3.0 relative biological effectiveness (RBE). Contrast MRI at 65 days and 6 months, and H&E histology at 6 months, showed little to no damage in surrounding brain. These results indicate the method's potential for clinical use. Advantages over conventional techniques include carbon therapy's Bragg-peak dose deposition, high RBE culminating at the target, and sharp dose falloff, together with the minibeams' sparing of non-targeted tissues and single-dose-fraction feature.

Key words: carbon therapy, minibeams, tissue sparing, tissue repair, high RBE radiation, single dose-faction therapy, radioresistant tumors, sharp dose falloff, radiosurgery

Acknowledgements

We thank Charles Pearson for his help in designing and assembling the rabbit holder and the multislit collimator, I Hung Chiang and Michael Sivertz for technical assistance at the beamline and the accelerator control room, Tom Zimmerman for veterinary supervision and advice, MaryAnn Petry and Kerry Bonti for advice and assistance with rabbit husbandry, Tiffany Bowman for preparing the drawings presented here, Joseph Gatz III for designing and manufacturing mechanical components, Peggy L. Micca for laboratory assistance, Shravan Cheruku and Lynda Nwabuobi for help with rabbit handling and husbandry, Benjamin D. Greenberg, Al Musella, Steven Rasmussen, Stanislaw Sobotka, and Wojtek Sobotka for assistance with the manuscript, and Derek I. Lowenstein for beam time allocation and advice at the NSRL. Research was supported by grants Musella Brain Tumor Foundation, Brain Tumor Foundations of “Lauren's First and Goal” and “Have a Chance”, Voices against Brain Cancer, Stony Brook Foundation (Allen G. Meek MD, PI), Stony Brook’s School of Medicine and the Office of Vice President for Research, and Stony Brook’s Targeted Research Opportunities program. NSRL is operated by NASA under a contract with BNL and the U.S. Department of Energy.