

This site uses cookies. By continuing to use this site you agree to our use of cookies. To find out more, see our [Privacy and Cookies policy](#).



MedicalPhysicsWeb

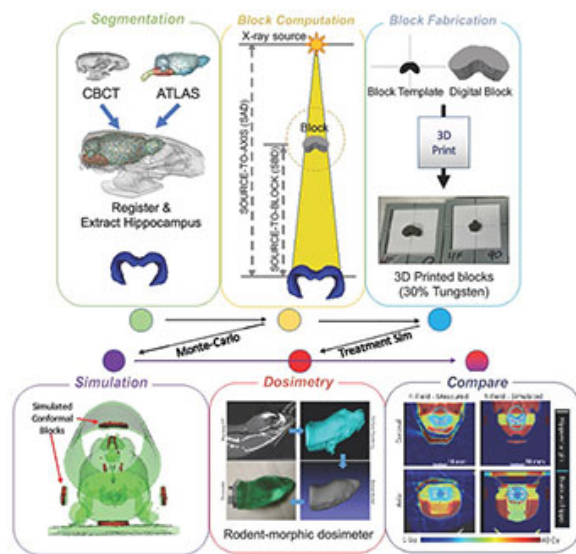
RESEARCH

Nov 10, 2017

Radiotherapy scheme spares hippocampus in rats

Avoiding the hippocampus when administering whole-brain radiotherapy (WBRT) to treat brain metastases may reduce neurocognitive decline following treatment. This finding was revealed by preliminary data from the RTOG 0933 clinical trial, which compared memory decline in patients treated with and without hippocampal avoidance.

Paving the way for future studies on brain treatments with reduced neurotoxicity, researchers at [Duke University Medical Center](https://medschool.duke.edu/) (<https://medschool.duke.edu/>) have developed a novel 3D conformal treatment technique to deliver WBRT in laboratory rats. Their most recent implementation of this technique incorporates several innovations, including high-precision 3D-printed immobilization and conformal radiation blocks and high-resolution MRI atlases, to achieve hippocampal avoidance (HA) WBRT (*Med. Phys.* doi: 10.1002/mp.12533 (<http://onlinelibrary.wiley.com/doi/10.1002/mp.12533/full>)).



(<http://images.iop.org/objects/med/news/12/11/30/pic1.jpg>)

Conformal hippocampal-avoidance whole-brain radiotherapy (<http://images.iop.org/objects/med/news/12/11/30/pic1.jpg>)

"The aim of creating a more accurate animal model of hippocampal sparing was to facilitate basic research to parallel the ongoing clinical trials of hippocampal sparing in patients with brain metastases," explained co-lead author [Christina Cramer](http://www.wakehealth.edu/Faculty/Cramer-Christina-Kehl.htm) (<http://www.wakehealth.edu/Faculty/Cramer-Christina-Kehl.htm>), currently at [Wake Forest Baptist Health](http://www.wakehealth.edu/) (<http://www.wakehealth.edu/>). "Radiation-induced cognitive decline is a substantial quality-of-life issue for patients treated with whole-brain radiotherapy."

"The concept for this project grew from my interest in the role of the hippocampus in memory and neuroanatomic target theory of radiation-induced cognitive decline," Cramer added. "The role of hippocampal avoidance is still emerging with multiple active trials currently ongoing, but the initial data from RTOG 0933 are encouraging, showing less decline relative to historical controls. Basic science research exploring the mechanisms of radiation-induced cognitive decline and the potential benefit of hippocampal avoidance needs to keep pace with the rapidly expanding clinical data in this field."

Studying the plans

The research team generated four conformal avoidance plans that delivered a high mean dose to the brain of 22.5–26.2 Gy at a mean hippocampal-avoidance dose of 7 Gy. The plans, which consisted of equi-angularly spaced coplanar axial beams, contained two, four, seven or eight fields. Based on simulation results, Cramer, co-lead author Suk Yoon and colleagues determined that the 4-, 7- and 8-field plans achieved similar hippocampal sparing, with the 7- and 8-field plans only yielding marginal improvements in planning target volume coverage.

The researchers generated dose-volume histograms based on segmented whole-brain and hippocampal values extracted from the MRI atlas, for all conformal HA-WBRT plans, with a 1-mm margin for the hippocampus. They ultimately selected the 4-field HA-WBRT plan for *in vivo* dosimetry and treatment verification. Using this plan, the researchers irradiated two Wistar rats with a single 4 Gy radiation dose.

A subsequent investigation using immunohistochemistry revealed a significant reduction in DNA double-strand breaks within the spared region of the hippocampus, compared with rats that had received a similar radiation dose using a standard treatment plan.

To immobilize the rats, the researchers developed a custom 3D bite block that angled the animal's head in a supine position to expose the central diencephalon to radiation. They used in-house software to calculate precise 3D conformal radiation block shapes for arbitrary gantry angles, based on the segmented volumes to be spared. The software utilized data from a low-dose, bone-contrasted cone-beam CT scan of the brain of an 8-week Wistar rat, with the hippocampus segmented via registration to an MRI atlas in 3D slices. The computed block dimensions were then 3D printed.

While immunohistology studies confirmed that this set-up was valid for *in vivo* radiotherapy of rats with hippocampal avoidance, the authors reported that radiation coverage of the whole brain was low for all plans. In simulations, 48.5–57.8% of the volume received 30 Gy, while only 46.7–52.5% received 30 Gy in dosimetric measurements. The authors attributed this to the shape of the rat hippocampus and the inability of the treatment platform to employ non-coplanar beams.

The authors stated that this represented suboptimal whole-brain target coverage, and that non-coplanar beams and intensity-modulated radiation therapy (IMRT) may be required to meet the stringent dose criteria associated with current human RTOG clinical trials.



Suk Whan Yoon, Christina Cramer, David Kirsch and Mark Oldham (<http://images.iop.org/objects/med/news/12/11/30/pic2.jpg>)

"A long-term goal of this research is to develop and optimize advanced pre-clinical radiotherapy treatment plans that mimic human treatment plans for other sites as well, including lung cancer, sarcoma and brainstem glioma," added Mark Oldham (<https://www.radonc.duke.edu/about-us/teams/research-staff/mark-oldham-phd>), director of Duke's Optical Biophysics and 3D Dosimetry Lab (<https://radonc.duke.edu/research-education/research-labs/radiation-physics/oldham-lab/research>). "These will require conformal dose distributions to irregular targets over very small spatial dimensions to mimic human treatments."

He explained that pre-clinical radiation therapy requires precision immobilization and segmentation of targets and organs-at-risk, using accurate registration and deformation of micro-CT, micro-MRI and anatomical templates. IMRT treatment planning capability will also be needed for the micro-

irradiator. "Substantial development is required to enable treatment planning on such a small spatial scale, which may be facilitated by advances in 3D printing, and which will need verification by our high-resolution dosimetry techniques," Oldham told *medicalphysicsweb*.

About the author

[Cynthia E Keen](#) is a freelance journalist specializing in medicine and healthcare-related innovations.