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RESEARCH

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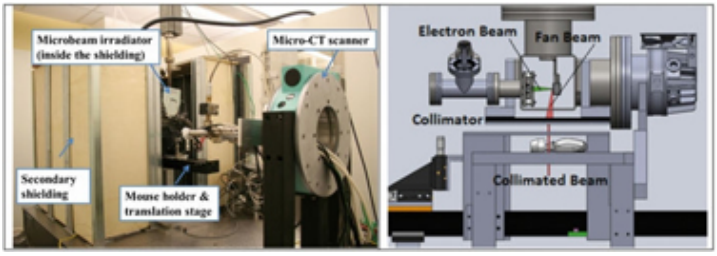
Tabletop source eyes microbeam therapy

Microbeam radiation therapy (MRT), in which a tumour is irradiated with an array of high-dose, microscopically thin X-ray beams, shows great promise for brain tumour treatments. Studies in animal models demonstrate that MRT can selectively eradicate tumour cells while sparing normal tissue. However, the technique's current reliance on a synchrotron radiation source is a major roadblock for potential clinical translation.



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The microbeam radiotherapy system (http://images.iop.org/objects/med/news/9/3/48/pic1.jpg)

In a quest for an alternative X-ray source for microbeam radiation, researchers from the University of North Carolina (http://unc.edu/) (UNC) at Chapel Hill have developed a tabletop MRT system based on a carbon nanotube (CNT) field emission source array technology (invented in the laboratory of Jianping Lu and Otto Zhou (http://research.physics.unc.edu/project/zhou/) at UNC and commercialized by start-up XinRay Systems). Using a hybrid image-guided MRT protocol, they have determined the microbeam targeting accuracy in mice bearing small brain tumours (*Phys. Med. Biol.* **59** 1283 (http://iopscience.iop.org/0031-9155/59/5/1283/article)).

"Instead of a single small focal spot, a distributed CNT X-ray source array spreads the thermal power over a long narrow focal track on the anode. It's equivalent to having a large number of high-power X-ray tubes irradiating the target at the same time," explained first author Lei Zhang, a graduate student working in the laboratory of Sha Chang and Otto Zhou. "In this way, a CNT field emission cathode can generate higher microbeam flux than conventional X-ray tubes."

System testing

The prototype MRT system includes the CNT-based irradiator and a high-resolution CNT-based micro-CT scanner, also developed by the team. The irradiator comprises a linear CNT field emission cathode array, an electrostatic focusing lens and a tungsten anode. For this study, the X-rays were collimated into a 280 μm wide microbeam.

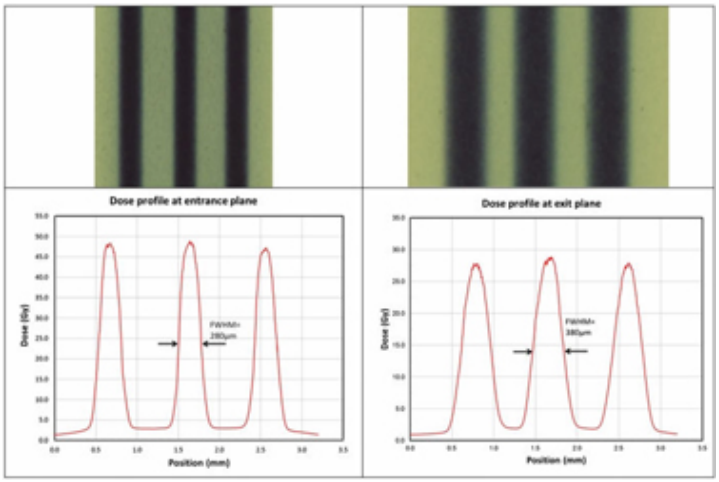
Zhang and colleagues studied 14 tumour bearing mice. To identify the tumour location with respect to the microbeam position, they proposed an image guidance protocol based on registration of X-ray images

with MR images. One day before treatment, the mice were imaged with a 9.4 T MR scanner. The 2D shape, size and location of the tumour were clearly visualized in the MR image and the average tumour size was measured as 1.4 × 2.2 mm.

On the day of irradiation, the mice were anaesthetized and immobilized in customized holders using hardware including two ear bars. Two-dimensional X-ray projections recorded by the on-board micro-CT scanner showed bone structures such as the skull, jaw and spinal cord, as well as the ear bars. These images were scaled and aligned manually with the sagittal MR images. The researchers then used the registered image to calculate the distance from the tumour centre to the ear bars.

Next, they irradiated the mice in seven groups. The first two mice were irradiated by a single microbeam of 138 Gy entrance dose. The second pair was irradiated by two parallel microbeams with centre-to-centre distance of 900 μm and an entrance dose of 108 Gy per beam. The remaining five pairs of mice were irradiated by three microbeams, with a 900 μm pitch, delivering 48 Gy each. The average dose rate at the mouse head entrance plane was 1.16 Gy/min.

To verify beam delivery, the researchers placed Gafchromic films at the entrance and exit planes of the mouse head during irradiation. Selected films were scanned and analysed to create dose profiles, which were then compared with the prescribed treatment plans.



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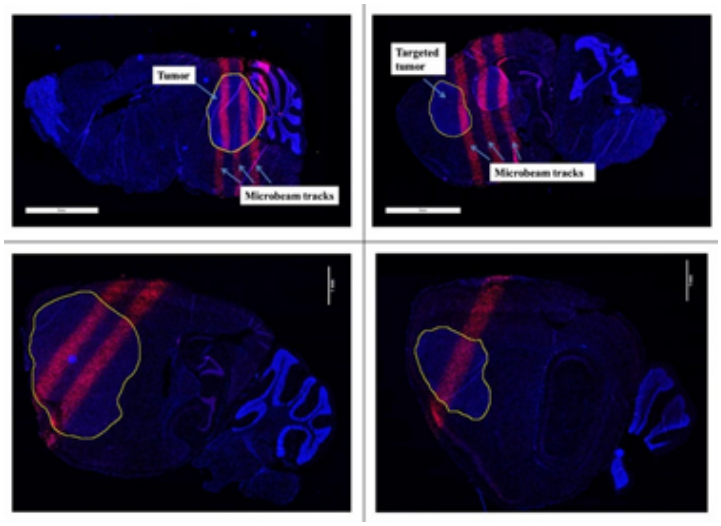
Beam delivery verification (http://images.iop.org/objects/med/news/9/3/48/pic2.jpg)

An example analysis of films from a mouse treated with three microbeams showed an entrance beam width of 280 μm, consistent with tube calibration results. The beams broadened to 380 μm at the exit plane. The measured peak dose of each beam was also consistent with the prescribed value. The peak-to-valley-dose-ratio (PVDR, the average peak dose divided by the average valley dose) for this animal was roughly 16 at the entrance plane, and 15 at the exit plane – values well within the range of synchrotron-based MRT.



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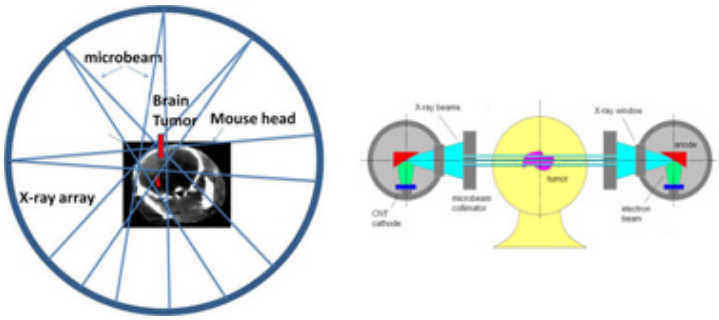
Visualizing double-strand breaks (http://images.iop.org/objects/med/news/9/3/48/pic3.jpg)

The researchers also used γ-H2AX immunofluorescence staining as a quantitative biomarker of radiation-induced DNA double-strand breaks (DSB). Stained images of irradiated mouse brain tissue slices showed DSBs as pink strips corresponding to the microbeam path. Of 13 mice analysed (one was excluded due to staining errors), 11 received the prescribed number of microbeams on the tumour, while two received one of three planned microbeams.

The team used the stained sections to measure the displacement from the centre of the microbeam to the centre of the tumour. The average localization accuracy for the 13 mice was 454 μm. They also manually registered the stained image back to the corresponding pre-treatment MR image and measured an average targeting error of 537 μm. Such values are comparable with the targeting accuracy reported for other (non-microbeam) image-guided small-animal irradiators.



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Flexible treatment configurations (http://images.iop.org/objects/med/news/9/3/48/pic4.jpg)

The authors conclude that their first-generation image-guided MRT system can generate microbeams with the necessary energy, beam width and PVDR to produce similar therapeutic effects to those seen in synchrotron MRT studies. They note, however, that the delivered dose rate is too low for tumour eradication within a reasonable time.

To address this limitation, the researchers are now constructing a second-generation CNT irradiator that will increase the average dose rate by a factor of 20, enabling targeted delivery of microbeams with peak dose matching the lower end of doses used in synchrotron MRT. "The second-generation CNT-MRT system is under construction. We expect it to be coming on line soon," said Zhang.

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About the author

Tami Freeman is editor of *medicalphysicsweb*.