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# **High-Contrast Imaging for Cancer Therapy with Protons**

Medical physicist Dr. Aswin Hoffmann and his team from the Institute of Radiooncology – OncoRay at the Helmholtz-Zentrum Dresden-Rossendorf (HZDR) are the first researchers worldwide to combine magnetic resonance imaging (MRI) with a proton beam, thus demonstrating that in principle, this commonly used imaging method can indeed work with particle beam cancer treatments. This opens up new opportunities for targeted, healthy tissue-sparing cancer therapy. The researchers have published their results in the journal *Physics in Medicine and Biology* (DOI: <u>10.1088/1361-6560/aaece8</u>).

Radiation therapy has long been part of the standard oncological treatment practice. A specific amount of energy, called dose, is deposited into the tumor tissue where it will damage the cancer cells' genetic material, preventing them from dividing and ideally, destroying them. The most commonly used form of radiation therapy today is called photon therapy, which uses high-energy x-ray beams. Here, a substantial portion of the beam penetrates the patient's body, while depositing harmful dose in healthy tissue surrounding the tumor.

## Atomic nuclei as weapons against cancer

An alternative is radiation therapy with charged atomic nuclei, such as protons. The penetration depth of these particles depends on their initial energy. They release their maximum dose at the end of their trajectory. No dose will be deposited beyond this so-called "Bragg peak". The challenge for physicians administering this kind of therapy is to control the proton beam to exactly match the shape of the tumor tissue and thus spare as much of the surrounding normal tissue as possible. Before the treatment, they conduct an x-ray-based computed tomography (CT) scan to select their target volume.

"This has various disadvantages," Hoffmann says. "First of all, the soft-tissue contrast in CT scans is poor, and secondly, dose is deposited into healthy tissue outside of the target volume." On top of this, proton therapy is more susceptible to organ motion and anatomical changes than radiation therapy with x-rays, which impairs the targeting precision when treating mobile tumors. At present, there is no direct way of visualizing tumor motion during irradiation. That is the biggest obstacle when it comes to using proton therapy. "We don't know exactly whether the proton beam will hit the tumor as planned," Hoffmann explains. Therefore, physicians today have to use large safety margins around the tumor. "But that damages more of the healthy tissue than would be necessary if radiation were more targeted. That means we are not yet exploiting the full potential of proton therapy."

# First prototype for MR-guided particle therapy

Hoffmann and his team want to change that. In cooperation with the Belgian proton therapy equipment manufacturer IBA (Ion Beam Applications SA), his research group's objective is to integrate proton therapy and real-time MR imaging. Unlike x-ray or CT imaging, MRI delivers excellent soft-tissue contrast and enables continuous imaging during irradiation. "There are already two such hybrid devices for clinical use in MR-guided photon therapy; but none exists for particle therapy."

This is mainly due to electromagnetic interactions between the MRI scanner and the proton therapy equipment. On the one hand, MRI scanners need highly homogeneous magnetic fields in order to generate geometrically accurate images. The proton beam, on the other hand, is generated in a cyclotron, a circular accelerator in which electromagnetic fields force charged particles onto a circular trajectory and accelerate them. The proton beam is also steered and shaped by magnets, whose magnetic fields can interfere with the MRI scanner's homogeneous magnetic field.

"When we launched the project three and a half years ago, many international colleagues were skeptical. They thought it was impossible to operate an MRI scanner in a proton beam because of all the electromagnetic disturbances," Hoffmann explains. "Yet we were able to show in our experiments that an MRI scanner can indeed operate in a proton beam. High-contrast real-time images and precise proton beam steering are not mutually exclusive." Many experts predicted another difficulty to occur from proton beam behavior: when electrically charged particles move in the magnetic field of an MRI scanner, Lorentz forces will deflect the beam from its straight trajectory. However, here, as well, the researchers were able to demonstrate that this deflection can be anticipated and thus corrected for.

### Competence center featuring a cyclotron and a large experimental room

To explore these mutual interactions, Hoffmann and his team used the experimental room at the National Center for Radiation Research in Oncology – OncoRay. This joint research platform operated by HZDR, TU Dresden and University Hospital Carl Gustav Carus was founded in 2005 as an innovative center of excellence. Since the UPTD (University Proton Therapy Dresden) was established in 2014, patients have been receiving proton therapy in the OncoRay facility. Today, more than 120 scientists at OncoRay conduct research on innovative approaches and technologies for radiation therapy.

"Our mission is to individualize proton therapy biologically and to optimize it technologically towards its physical limits," says Hoffmann, head of the research group on MR-guided radiation therapy at the HZDR. OncoRay has its own cyclotron to deliver the proton beam into the therapy room as well as into the experimental room. Hoffmann and his colleagues used the latter for their research activities. With the support of IBA and the Paramed MRI Unit of ASG Superconductors SpA, they installed an open MRI scanner in the path of the proton beam, realizing the world's first prototype of MR-guided particle therapy. "We are lucky to have an experimental room that is large enough to accommodate an MRI scanner. That is one of OncoRay's unique features."

### Knee phantom, mixed sausage and predictable diversion

For their experiments on this first prototype, they initially used what is called a knee phantom, a small plastic cylinder filled with an aqueous contrast liquid and a variety of differently shaped plastic pieces. Hoffmann and his team used it to conduct quantitative analyses of image quality. In a second series of experiments, the researchers used a piece of Dresden mixed sausage. "When the Dutch research group studied imaging for their MR-guided photon therapy device in 2009, they used pork chop," Hoffmann says. "In 2016, Australian researchers demonstrated their MR-photon therapy device on a Kangaroo steak. Since we also wanted to go regional for our prototype in MR-guided particle therapy, we used Dresden mixed sausage." Both the series of experiments with the phantom and with the sausage showed that the magnetic fields from proton therapy did not distort the image. They merely caused minor shifts in the MR image, which can be corrected for.



The project is currently entering its next phase. The goal is to develop the world's first prototype for MR-guided particle therapy that is applicable for clinical use.

#### Caption:

Dr. Aswin Hoffmann and his team installed an open MR scanner in the experimental room at the National Center for Radiation Research in Oncology – OncoRay. Conducting various experiments, the HZDR researchers were able to demonstrate that MRI can be combined with a proton beam. Source: HZDR / R. Weisflog

#### **Publication:**

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The National Center for Radiation Research in Oncology – OncoRay is a cross-institutional research platform with a special focus on translational research. This means that results from fundamental research should be further developed specifically for the benefit of patients and tested in clinical trials. The aim is to significantly improve the treatment of cancer by administering radiation therapy that is biologically personalized and technically optimized. For this, OncoRay combines the strengths of its three participating institutes – University Hospital Carl Gustav Carus, Technische Universität Dresden and Helmholtz-Zentrum Dresden-Rossendorf (HZDR). Around 120 scientists from all over the world work at OncoRay in interdisciplinary programs, combining the research fields of medicine, physics, biology and information science.

The **Helmholtz-Zentrum Dresden-Rossendorf (HZDR)** performs – as an independent German research center – research in the fields of energy, health, and matter. We focus on answering the following questions:

- How can energy and resources be utilized in an efficient, safe, and sustainable way?
- How can malignant tumors be more precisely visualized, characterized, and more effectively treated?

• How do matter and materials behave under the influence of strong fields and in smallest dimensions? To help answer these research questions, HZDR operates large-scale facilities, which are also used by visiting researchers: the Ion Beam Center, the High-Magnetic Field Laboratory Dresden, and the ELBE Center for High-Power Radiation Sources.

HZDR is a member of the Helmholtz Association and has five sites (Dresden, Freiberg, Grenoble, Leipzig, Schenefeld near Hamburg) with almost 1,200 members of staff, of whom about 500 are scientists, including 150 Ph.D. candidates.