

## German Future Prize 2019

### Ultra-high-field MRI – precision medicine for the benefit of patients

Magnetic resonance imaging (MRI) – also known as magnetic resonance tomography – is now the leading diagnostic imaging method and plays a crucial role in the diagnosis of a large number of diseases. With the development of Siemens Healthineers' Magnetom Terra, the first ultra-high-field MRI system for clinical use, Dr. Christina Triantafyllou, Prof. Mark E. Ladd and Prof. Arnd Dörfler achieved a breakthrough in diagnostic imaging and at the same time established 7 Tesla as a new clinical field strength. The new system is the first in the world to enable the use of ultra-high-field MRI in clinical applications. The research and development team has thus broken new grounds in medical imaging and reached a significant milestone in the history of MRI.

In particular, for diseases of the central nervous system, internal organs, blood vessels and musculoskeletal system, 7 Tesla MRI offers precise visualization of the smallest structures in the human body and thus often the best possible diagnosis. Particularly in the early stages of diseases such as multiple sclerosis (MS) and neurodegenerative diseases, for example dementia and Parkinson's disease, pathological changes are often not sufficiently pronounced to be diagnosed using the clinically established MRI systems at lower field strengths. The image quality and spatial resolution achievable using conventional MRI systems are not always adequate for this purpose. Consequently, before the diagnosis is achieved or the treatment is started, valuable time might be lost. Magnetom Terra from Siemens Healthineers promises a fundamental improvement here: Magnetom Terra's ultra-high-field imaging provides a very high level of detail and is thus able to reveal the slightest changes in the anatomy and even in the function of organs. This helps to enable firstly very early diagnosis and secondly reliable differentiation from other diseases, which was not achievable with previous clinically established field strengths.

In 2017, with Magnetom Terra, the German-Future-Prize-nominated research and development team made possible that ultra-high-field MRI with a field strength of 7 Tesla, which has only been utilized in basic research since the early 2000s, became available for clinical use worldwide, for the first time, as a new and effective diagnostic method – consequently also benefiting patients directly. Christina Triantafyllou leads the global team ‘Ultra-High-Field MRI Solutions’ at Siemens Healthineers, Mark E. Ladd is head of the Division of Medical Physics in Radiology of the German Cancer Research Center in Heidelberg and Arnd Dörfler heads the Neuroradiological Department at the University Hospital of the Friedrich-Alexander University of Erlangen-Nürnberg.

Besides making ultra-high-field MRI at 7 Tesla available for use in a clinical environment, Magnetom Terra also represents an engineering accomplishment that had not previously been achieved: not only new safety concepts have been designed for use on humans, but also a brand new designed, innovative actively-shielded magnet has been developed, which is only half as heavy as the magnets used in previous research systems. Magnetom Terra is therefore much easier to transport and, in particular, easier to integrate into existing hospital infrastructure. Time-consuming and costly construction of new buildings can thus be avoided. A further innovation is Magnetom Terra’s dual-mode functionality, which enables users to switch directly between clinical and research use. The system thus offers the ideal platform for translational research – the latest research developments can therefore be used directly for the benefit of patients.

### **Early diagnosis and more effective countermeasures to combat multiple sclerosis**

The innovative imaging technology of Magnetom Terra can render pathological changes visible at the metabolic level, even before they manifest themselves either morphologically and anatomically. Here, the field strength of 7 Tesla, which is equivalent to approximately 140,000 times the strength of the earth’s magnetic field, produces impressive results. While it was previously only possible to detect pathological changes on clinical images at the advanced stages of MS, for example at 7 Tesla these can often be identified in earlier stages of the disease. Furthermore, smaller lesions in the brain’s gray matter can be detected, which previously was not possible. Particularly for younger people, who make up the majority of MS patients, early diagnosis and swift treatment are key to delaying a subsequent disability or preventing it altogether.<sup>[1], [2]</sup>

**Precise identification of epileptogenic foci**

Epilepsy is one of the most common neurological conditions. In Germany alone, there are around half a million epilepsy patients. Even given the best drug treatment, a considerable proportion of these patients do not remain seizure-free, which greatly restricts the lives of those affected. On the other hand, this patient group may benefit from a higher success rate from epilepsy surgery. This intervention involves the surgical removal of epileptogenic foci from the patient's brain. After complete removal, patients can live seizure-free. Magnetom Terra's outstanding detail resolution makes it possible for epileptogenic foci to be diagnosed more precisely or even initially identified as such. This makes interventions more reliable, enabling those affected to regain their original quality of life.<sup>[3], [4]</sup>

**Sodium imaging for neurodegenerative diseases**

With dementia disorders, a diagnosis can generally be made only in the advanced stages. Morphological damage in the brain will then already have occurred. Here, too, Magnetom Terra offers new possibilities for detecting Parkinson's disease or Alzheimer's disease at an early stage. Using ultra-high-field MRI, the deposits typical of Alzheimer's can be shown better than previously, and in the case of Parkinson's, structural changes in very specific areas of the brain can reliably be detected at an early stage. Here, anatomically visible features play as much a role<sup>[5]</sup> as metabolic changes, which can be shown clearly for example by sodium imaging.<sup>[6]</sup> The release of Magnetom Terra's sodium-based metabolic MRI imaging system for clinical use in Europe and the USA in 2018 was a world's first.

**Improved treatment monitoring in oncology**

In oncology, Magnetom Terra also offers new opportunities for early treatment and better monitoring. While cancers can frequently be diagnosed using previously clinically established field strengths, weeks can often pass until it is clear whether a treatment has been effective. Using biomarkers, ultra-high-field MRI has succeeded in clinical research in characterizing brain tumors in a way that enables improved prognosis of disease outcome and especially individualized treatment – in line with the goals of precision medicine.<sup>[7]</sup> The formation of new blood vessels typical of aggressive tumors can be rendered visible at 7 Tesla and used clinically in diagnostics and treatment monitoring. Furthermore, the examination of metabolic processes by means of spectroscopic methods, as well as imaging with sodium, also open up new possibilities for characterizing tumors.<sup>1, [8], [9]</sup>

The physicist Christina Triantafyllou was a driving force behind the development of Magnetom Terra, the first system in the world to establish the technical prerequisites for the clinical application of 7 Tesla imaging. Mark E. Ladd, senior physicist at the German Cancer Research Center in Heidelberg, played a prominent part in the research developments of the first 7 Tesla MRI systems installed at the University Hospital in Essen and in Heidelberg in the 2000s. He also played a significant role in Magnetom Terra's clinical approval process. The radiologist and neuroradiologist Arnd Dörfler was involved in the development phase: in particular, he played a key role in the clinical implementation and validation of the world's first 7 Tesla MRI system designed for clinical operation at the University Hospital of Erlangen and in the clinical approval of Magnetom Terra.

<sup>1</sup> Research mode is still under development and not commercially available in the U.S. and other countries. Its future availability cannot be ensured.

Further information and pictures are available at <https://www.siemens-healthineers.com/press-room/press-features/pf-zukunftspreis2019.html>.

### Contact for journalists

Ulrich Kuenzel

Phone: +49 162 2433492; E-mail: [Ulrich.Kuenzel@siemens-healthineers.com](mailto:Ulrich.Kuenzel@siemens-healthineers.com)

### Bibliography

- <sup>[1]</sup> Springer E, Dymerska B, Cardoso PL, Robinson SD, Weisstanner C, Wiest R, Schmitt B, Trattning S (2016): Comparison of Routine Brain Imaging at 3 T and 7 T. *Invest Radiol.* 51(8), p. 469-82: <https://www.ncbi.nlm.nih.gov/pubmed/26863580>.
- <sup>[2]</sup> Obusez EC, Lowe M, Oh SH, Wang I, Jennifer Bullen, Ruggieri P, Hill V, Lockwood D, Emch T, Moon D, Loy G, Lee J, Kiczek M, Manoj Massand, Statsevych V, Stultz T, Jones SE (2018): 7T MR of intracranial pathology: Preliminary observations and comparisons to 3T and 1.5T. *Neuroimage*, 168, p. 459-476: <https://www.ncbi.nlm.nih.gov/pubmed/27915116>.
- <sup>[3]</sup> Davis KA, Nanga RP, Das S, Chen SH, Hadar PN, Pollard JR, Lucas TH, Shinohara RT, Litt B, Hariharan H, Elliott MA, Detre JA, Reddy R. (2015): Glutamate imaging (GluCEST) lateralizes epileptic foci in nonlesional temporal lobe epilepsy. *Sci Transl Med*, 7(309):309ra161: <https://www.ncbi.nlm.nih.gov/pubmed/26468323>.
- <sup>[4]</sup> Veersema TJ, Ferrier CH, van Eijsden P, Gosselaar PH, Aronica E, Visser F, Zwanenburg JM, de Kort GAP, Hendrikse J, Luijten PR, Braun KPJ (2017): Seven tesla MRI improves detection of focal cortical dysplasia in patients with refractory focal epilepsy. *Epilepsia Open*, 2(2), p. 162-171: <https://www.ncbi.nlm.nih.gov/pubmed/29588945>.
- <sup>[5]</sup> Schmidt M, Engelhorn T, Marxreiter F, Winkler J, Lang S, Kloska S, Goelitz P, Doerfler A (2017): Ultra high-field SWI in the substantia nigra at 7T: reliability and consistency of the swallow-tail sign. *BMC Neurology* 17:194: <https://www.ncbi.nlm.nih.gov/pubmed/29073886>.

<sup>[6]</sup> E.A. Mellon, D.T. Pilkinton, C.M. Clark, M.A. Elliott, W.R. Witschey 2nd, A. Borthakur, R. Reddy (2009): Sodium MR imaging detection of mild Alzheimer disease: preliminary study. *AJNR* 30(5):978-984:

<https://www.ncbi.nlm.nih.gov/pubmed/19213826>.

<sup>[7]</sup> Choi C, Ganji SK, DeBerardinis RJ, Hatanpaa KJ, Rakheja D, Kovacs Z, Yang XL, Mashimo T, Raisanen JM, Marin-Valencia I, Pascual JM, Madden CJ, Mickey BE, Malloy CR, Bachoo RM, Maher EA (2012): 2-hydroxyglutarate detection by magnetic resonance spectroscopy in subjects with IDH-mutated gliomas. *Nature Medicine* volume 18, p. 624–629:

<https://www.ncbi.nlm.nih.gov/pubmed/22281806>.

<sup>[8]</sup> Paech D, Windschuh J, Oberhollenzer J, Dreher C, Sahn F, Meissner

JE, Goerke S, Schuenke P, Zaiss M, Regnery S, Bickelhaupt S, Bäumer P, Bendszus M, Wick W, Unterberg A,

Bachert P, Ladd ME, Schlemmer HP, Radbruch A. (2018): Assessing the predictability of IDH mutation and MGMT methylation status in glioma patients using relaxation-compensated multipool CEST MRI at 7.0 T. *Neuro Oncol* 20(12):1661-1671:

<https://www.ncbi.nlm.nih.gov/pubmed/29733378>.

<sup>[9]</sup> Biller A, Badde S, Nagel A, Neumann JO, Wick W, Hertenstein A, Bendszus M, Sahn F, Benkhedah

N, Kleesiek J. (2016): Improved Brain Tumor Classification by Sodium MR Imaging: Prediction of IDH Mutation Status and Tumor Progression. *AJNR* 37(1):66-73: <https://www.ncbi.nlm.nih.gov/pubmed/26494691>.

**Siemens Healthineers** enables healthcare providers worldwide to increase value by empowering them on their journey towards expanding precision medicine, transforming care delivery, improving patient experience and digitalizing healthcare. A leader in medical technology, Siemens Healthineers is constantly innovating its portfolio of products and services in its core areas of diagnostic and therapeutic imaging and in laboratory diagnostics and molecular medicine. Siemens Healthineers is also actively developing its digital health services and enterprise services. In fiscal 2018, which ended on September 30, 2018, Siemens Healthineers generated revenue of €13.4 billion and adjusted profit of €2.3 billion and has about 50,000 employees worldwide. Further information is available at [www.siemens-healthineers.com](http://www.siemens-healthineers.com).

The **German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ)** with its more than 3,000 employees is the largest biomedical research institution in Germany. At DKFZ, more than 1,300 scientists investigate how cancer develops, identify cancer risk factors and endeavor to find new strategies to prevent people from getting cancer. They develop novel approaches to make tumor diagnosis more precise and treatment of cancer patients more successful.

DKFZ's Cancer Information Service (KID) provides individual answers to all questions about cancer for patients, the general public, and health care professionals. Jointly with partners from Heidelberg University Hospital, DKFZ runs the National Center for Tumor Diseases (NCT) located in Heidelberg and Dresden, and, also in Heidelberg, the Hopp Children's Cancer Center (KiTZ). In the German Cancer Consortium (DKTK), one of six German Centers for Health Research, DKFZ maintains translational centers at seven university partnering sites. Combining excellent university hospitals with high-profile research at a Helmholtz Center at the NCT and DKTK sites is an important contribution to the endeavor of translating promising approaches from cancer research into the clinic in order to improve the chances of cancer patients.

DKFZ is a member of the Helmholtz Association of National Research Centers, with ninety percent of its funding coming from the German Federal Ministry of Education and Research and the remaining ten percent from the State of Baden-Württemberg.

With its 50 departments and institutes, **Universitätsklinikum (University Hospital) Erlangen** covers all areas of modern medicine. The majority of buildings of the University Hospital are located centrally by the Schlossgarten and house approximately 1350 beds. Patient care, research and teaching are interconnected on a highly sophisticated level. Patients benefit from state-of-the-art treatment methods that are often not yet available at other facilities. In 2018 over 545.000 outpatients have been treated, as well as 65.000 inpatients. Comprehensive quality assurance systems ensure optimal patient care from arrival to discharge. More than 7700 employees in interdisciplinary teams are committed to this goal. They are united in what they strive to achieve: to alleviate suffering and to heal diseases.