Magnetic Resonance Fingerprinting – The Future of Quantitative MR Neuroimaging

Gregor Kasprian, M.D.; Victor Schmidbauer, M.D.

Division of Neuroradiology, Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna, Austria

By providing the possibility to acquire a variety of unique tissue contrasts, magnetic resonance imaging (MRI) is the gold standard for diagnostic brain imaging. However, current MRI strategies are compromised by time-consuming image data acquisitions, limitations in the comparability of quantitative imaging data, artifacts, and inter-scanner variability.

Improvements in quantitative imaging techniques will guide us toward a new era in diagnostic neuroradiology. The possibility to complement the subjective assessment of non-invasive brain imaging by quantitative data will lead to better, more reliable, and objectifiable diagnoses of diseases of the central nervous system. Moreover, robust quantitative data will serve as ideal input for artificial intelligence-based algorithms, which – in combination with radiological expertise – will improve diagnostic and prognostic precision and thereby optimize personalized treatment for many patients. To date, quantitative MR techniques have been time consuming and complex in data post-processing, and thus limited to research. To achieve clinical practicability and feasibility, these traditional approaches had to be reinvented.

MR signals translated into tissue-specific fingerprints

Magnetic Resonance Fingerprinting (MRF)[1] is a pioneering approach in the field of MR technology. MRF relies on the principle that each tissue examined evolves its own unique signal – *fingerprint* – after the application of a technically appropriate stimulus [1]. In contrast to conventional MRI, MRF is characterized by variation of the technical parameters, e.g., repetition time, and radiofrequency excitation angle, throughout the sequence acquisition to generate the evolution of the tissue's *fingerprint* [2]. Initially, this tissue fingerprint appears as complex and abstract data, which needs to be translated into an image. As for any translation, a pre-existing standard of reference or dictionary is required. A dictionary-based recognition process connects the acquired signal-derived information to quantitative MR metrics – such as, but not limited to, relaxation parameters and diffusion properties – in a voxel-wise manner [1, 2]. The MRF dictionary contains a collection of simulated fingerprints to represent all tissue-specific properties within the physiological range [3]. Since MRF pattern recognition takes a variety of different parameters into account, the tissue characterization process is considered highly accurate and robust [2]. In summary, three hallmarks characterize the entire MRF process. The first step – signal evolution and acquisition – is MR scanner and sequence dependent. The second and third steps are characterized by automatized data processing: dictionary-based pattern recognition and tissue-specific, property-based visualization [2, 3].

Quantitative MRI and multiple image contrasts in less than eight minutes

Based on a single sequence acquisition of less than eight minutes, MRF provides a variety of multiparametric imaging information for qualitative and quantitative non-invasive neuro MR diagnostics. By choosing physical MR properties as the bedrock of the technical concept, MRF demonstrates excellent inter-scanner reproducibility [4]. This approach allows a robust and objective method to detect, characterize, and quantify physiological and pathological changes of the central nervous system [5, 6]. Furthermore, MRF is regarded as a highly promising technique for eliminating artifacts in MR imaging [2, 7], as each voxel is subjected to the pattern recognition process individually. Overall, MRF is leading the way into the future of MRI, providing structural diagnostic, quantitative, robust, less artifact prone imaging data in a short imaging time.

[1] *MR Fingerprinting is not commercially available in some countries. Due to regulatory reasons its future availability cannot be ensured.*

Clinical experiences in MRF

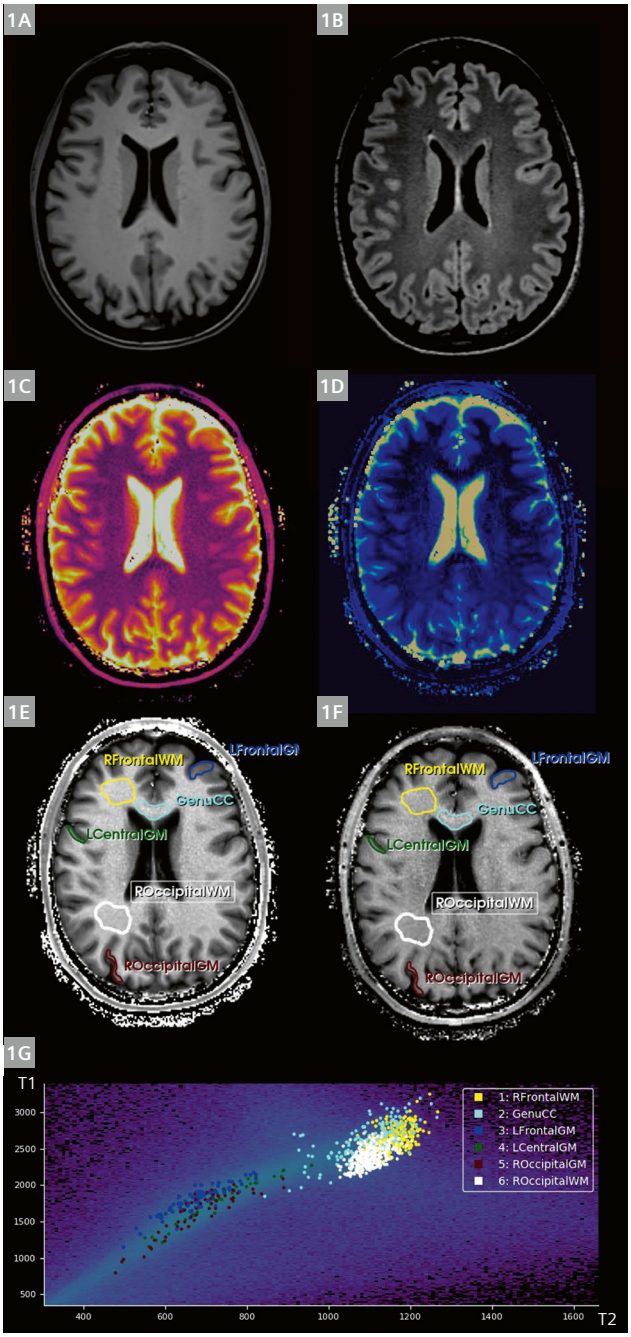
Clinical experiences using this novel approach are still scarce. At the same time, as MRF technology is continuously improving, specific areas of interest in the neuroradiological application of this technology are currently being identified. MRF will be particularly valuable in diagnosing diseases that were previously difficult to assess and evaluate based on the subjective impression of individual radiologists. As MRF is sensitive to multiple MR parameters at once, it offers a variety of in-depth MR imaging markers of pathologically altered brain parenchyma. Pathological brain tissue, which so far might have been categorized as "normal-appearing" brain parenchyma by traditional subjective visual radiological assessment, could be detected more sensitively using MRF. This will allow better quantification and evaluation of the burden of disease in individual patients and will help better understand the current status and progress in a variety of neurological disorders. As a consequence, MRF can help monitor the effect of treatment more reliably than ever before.

Furthermore, time-saving, in-depth multiparametric characterization of pathologically altered brain tissue – after acquisition of a single MRF sequence – may further improve the diagnostic specificity of MRI, allowing to optimize the differentiation of similar-appearing signal changes into specific pathological entities. Ultimately, the resulting reduction in overall MR scan time may also grant easier and faster access to high-end MR diagnostics to the benefit of many patients.

Here, we would like to demonstrate some initial clinicoradiological experiences with MRF in different areas of diagnostic neuroimaging.

Basic MRF findings in normal subjects

MRF allows characterization of the fingerprint of specific brain compartments. Figure 1 shows the MR images of a 45-year-old normal subject. The upper row depicts sequentially acquired conventional T1-weighted (1A) and fluid-attenuated T2-weighted 3D sequences at 3 Tesla (MAGNETOM Vida, Siemens Healthcare, Erlangen, Germany) totaling an imaging time of up to 8 minutes. The results of a single acquisition using MRF (7 minutes acquisition time) are shown in Figure 1. A T1 map (1C) and a T2 map can be visualized with color coding according to the local T1 and T2 values. Advanced quantitative analysis using the MR Robust Quantitative Tool (MR RoQT) allows characterization of specific gray (dark colors) and white matter (bright colors) compartments, which can be distinguished from each other on the scatterplot graph (bottom row). The scatterplot indicates the T2 (x-axis) and T1 (y-axis) values of the analyzed regions of interest and



1 45-year-old healthy subject. **(1A, B)** T1-weighted (1A) and fluid-attenuated T2-weighted 3D sequences (1B) at 3T. **(1C, D)** MR Fingerprinting acquisition. **(1E, F)** T1 map (1E) and T2 map (1F) with color coding according to the local T1 and T2 values. **(1G)** MR RoQT scatterplot characterizing specific gray (dark colors) and white matter (bright colors) compartments. The scatterplot indicates the T2 (x-axis) and T1 (y-axis) values of the analyzed regions of interest and shows the normal variation of values within one tissue compartment.

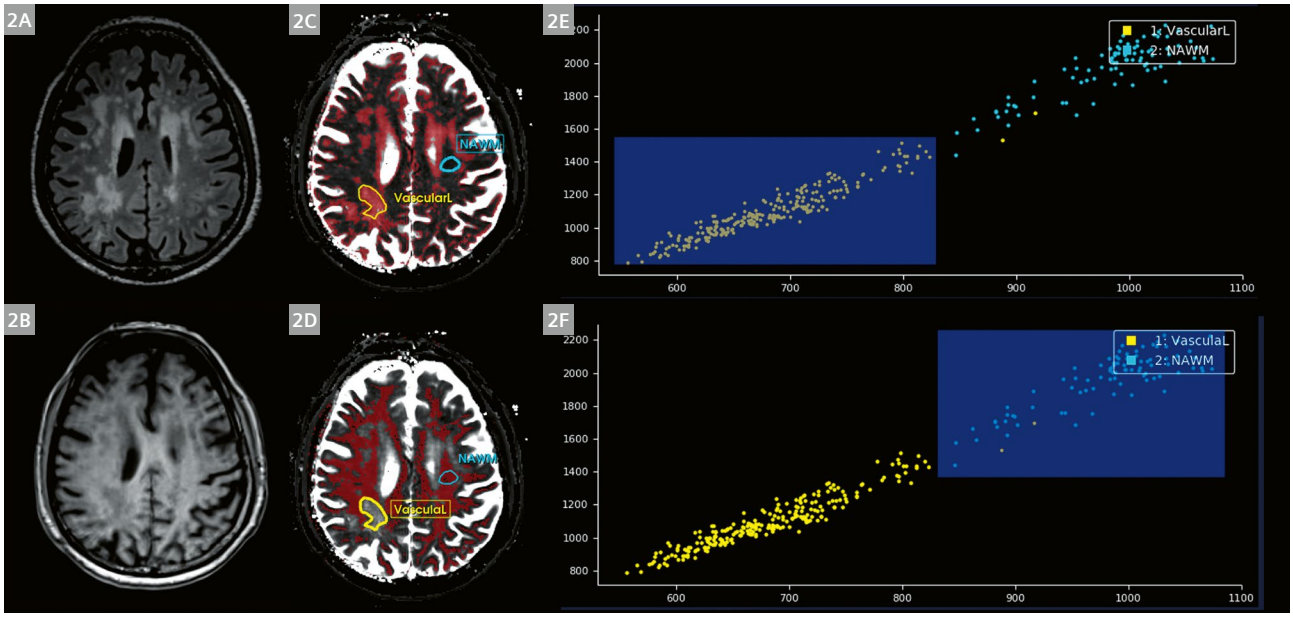
shows the normal variation of values within one tissue compartment. Except for distinct differences between white and gray matter, there are also regional differences in the quantified T1 and T2 values. In addition to structural MR data, MRF also provides quantitative data, which cannot be extracted from conventional T2-weighted and T1-weighted MRI sequences, without investing further acquisition time. MRF is quite a robust quantitative MR technology, which is feasible in a clinical setting.

MRF findings in brain pathologies

In addition to the quantitative characterization of regional variations of brain tissue fingerprints, a detailed analysis of the MR characteristics of abnormal brain regions is also possible. Figure 2 depicts a 67-year-old patient with severe vascular leukoencephalopathy. Conventional FLAIR (2A) sequences depict the T2-weighted hyperintense white matter alterations, which are less conspicuous on T1-weighted sequences (2B). By using MRF and generating T2 maps (2C, D), lesional (yellow) and non-lesional (turquoise) brain regions can be automatically segmented based on their T1 and T2 quantitative characteristics, shown in the scatterplots (2E, F). By either selecting the lesional (yellow) or non-lesional (turquoise) range of T1/T2 values, these tissue types can be distinguished and separated as well as quantified. This will allow a more accurate semi-automated follow-up analysis of brain imaging data, and allows better monitoring of the course of a disease or the effectiveness of therapeutic measures.

MRF in amyotrophic lateral sclerosis

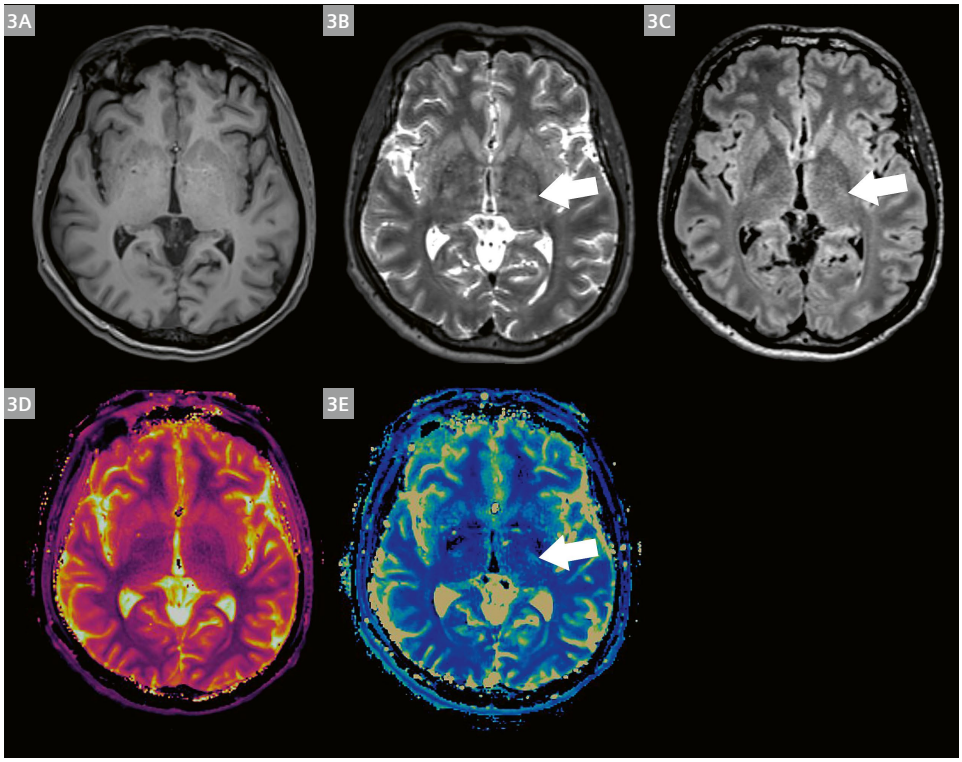
MRF can be particularly valuable if qualitative findings need to be objectified. This may be especially important in cases of neurodegenerative disorders such as amyotrophic lateral sclerosis (ALS). The hyperintense T2-weighted signal change of the corticospinal tract has been a useful sign of Wallerian degeneration in ALS. However, the sign is often subtle and sometimes non-specific. A reliable quantitative analysis of these changes might help to identify this sign with greater confidence and diagnostic certainty. Figure 3 shows the results of an MRI examination of a 71-year-old patient with clinically suspected ALS: The T1-weighted (3A), T2-weighted (3B), and FLAIR (3C) 3D sequences were sequentially acquired at 3 Tesla. The second row shows the results of the MRF analysis in the same patient, depicting the T1 map (3D) and the T2 map (3E). The arrows point to the left internal capsule. Please note the slight T2-weighted hyperintense signal alteration of the



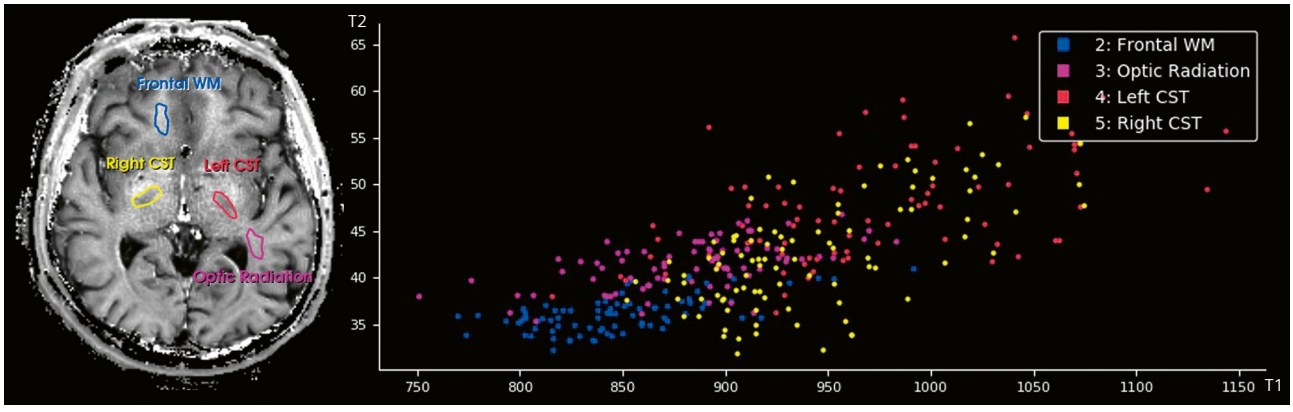
2 A 67-year-old patient with severe vascular leukoencephalopathy. **(2A)** Conventional FLAIR depict the T2-weighted hyperintense white matter alterations, which are less conspicuous on **(2B)** T1-weighted sequences. **(2C, D)** By using MRF lesional (yellow) and non-lesional (turquoise) brain regions can be automatically segmented based on their quantitative R1 (x-axis) and R2 (y-axis) characteristics, shown in the scatterplots **(2E, F)**.

corticospinal tract, which is confirmed on the T2 map of the MRF analysis.

If the local T1 (x-axis) and T2 (y-axis) values are analyzed using the postprocessing software MR RoQT, an unequivocal difference between the corticospinal tract fingerprints (red and yellow) and those of the optic radiation (pink) or the frontal white matter (blue) can be identified (Fig. 4). This improves the diagnostic confidence of the radiologist and leads to a smaller interrater variability in the imaging assessment of this disorder. Further, these findings can be combined with diffusion tensor imaging (DTI) based parameters (FA, diffusivity) or diffusion-weighted imaging (DWI) based ADC measurements to increase the diagnostic sensitivity of this sign.



3 A 71-year-old patient with clinically suspected ALS. T1-weighted **(3A)**, T2-weighted **(3B)**, and FLAIR **(3C)** 3D sequences sequentially acquired at 3T. (3D, E) show the results of the MRF analysis in the same patient, depicting the T1 map **(3D)** and the T2 map **(3E)**. The arrows point to the left internal capsule. The slight T2-weighted hyperintense signal alteration of the corticospinal tract is confirmed on the T2 map of the MRF analysis.

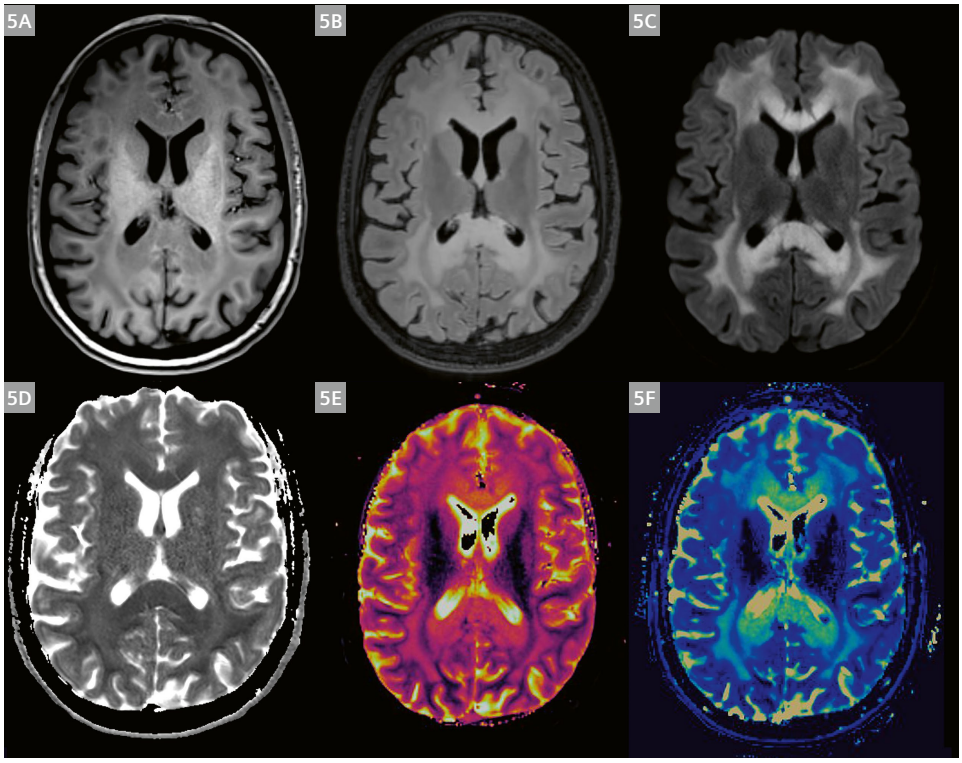


4 Postprocessing of the patient data shown in Figure 3 using the MR Robust Quantitative Tool (MR RoQT). T1 values are indicated on the x-axis, T2 values are plotted on the y-axis. The left and right corticospinal tracts show a distinctive difference in their T1 and T2 fingerprints compared to other white matter regions.

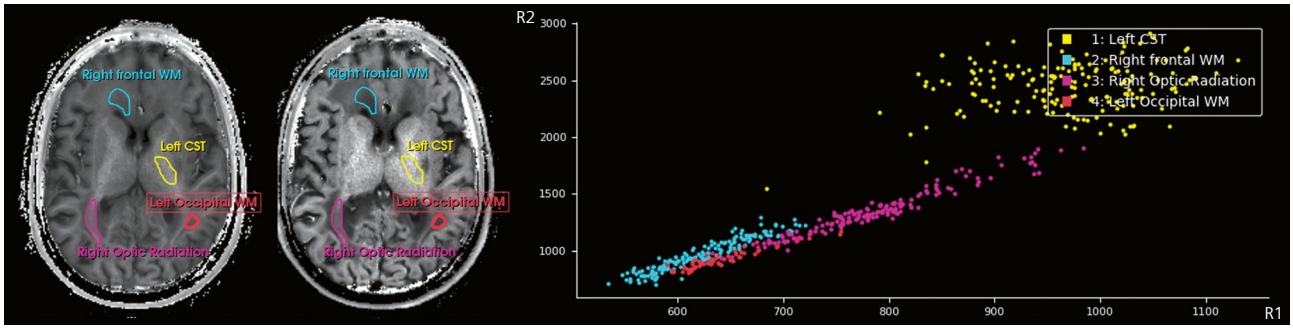
MRF in metabolic disorders or leukodystrophies

MRF may also be beneficial in neurological disorders, characterized by widespread signal alterations of the gray and white matter, such as leukodystrophies or mitochondriopathies. Figure 5 shows the MR images of a 6-year-old girl with glutaric aciduria type I – a metabolic disorder/mitochondriopathy. Please note the extensive white matter signal alterations on T1 (5A) FLAIR (5B) and DWI (5C, D). There is extensive white matter diffusion restriction. MRF (5E, F) quantifies the regional signal changes on T1 (5E) and T2 (5F) maps, indicating the relative sparing of the corticospinal tract and basal ganglia.

Using MRF-based quantification on T1 and T2 maps (Figure 6), regional variations in the pathology associated fingerprints can be identified. There is massive T1 and T2 shortening (turquoise) of the right frontal white matter. The optic radiation (pink) is less severely affected and the left corticospinal tract shows T2 (x-axis) and T1 (y-axis) values, which are in the normal range (compare Fig. 1). Combined with semiautomated segmentation tools (MR RoQT), this approach helps monitor disease progression and further refine specific disease-related patterns and fingerprints.



5 A 6-year-old girl with glutaric aciduria. Extensive white matter signal alterations on T1 **(5A)** FLAIR **(5B)** and DWI **(5C, D)**. MRF **(5E, F)** quantifies the regional signal changes on T1 (5E) and T2 (5F) maps indicating the relative sparing of the corticospinal tract and basal ganglia.



6 MRF-based quantitative R1 (x-axis) and R2 (y-axis) values show a severe shortening of the right frontal WM (turquoise). The right optic radiation (pink) as well as the left occipital WM (red) are less affected. Normal-appearing R1 and R2 values can be found in the left corticospinal tract (yellow).

Summary

MRF leads the way into a new era of neuro MRI. The possibility to provide multiple quantitative MR parameters based on a single data acquisition in less than 8 minutes results in quantitative data suitable for characterizing normal and pathologically altered tissue compartments of the central nervous system. As the regional neuroanatomical tissue diversity can be mapped non-invasively, MRF opens new possibilities in the non-invasive characterization of normal brain structure and its developmental changes across human lifespan. Further, pathological processes can be objectified and quantified, leading to greater confidence in the diagnosis of metabolic and neurodegenerative disorders. The extent of tissue pathology can be mapped and monitored over time, which is helpful in neurovascular disorders and inflammatory and/or demyelinating conditions. Lastly, disease-specific fingerprints of metabolic disorders and abnormal myelination processes are quantifiable and will be easier to identify. In the future, MRF will serve as an important backbone for artificial intelligence-based algorithms, aiming to automatically identify lesion-specific fingerprints. This will ultimately change the daily practice of neuroradiology.

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Contact

Associate Professor Gregor Kasprian, M.D., MBA
Department of Biomedical Imaging and Image-guided Therapy
Medical University of Vienna
Währinger Gürtel 18-20
1090 Vienna
Austria
Tel.: (+43) 1 40400 48950
gregor.kasprian@meduniwien.ac.

Gregor Kasprian

Victor Schmidbauer