Multiparametric Functional MRI of the Kidney: Current State and Future Trends with Deep Learning Approaches

Multiparametrische funktionelle Nierenbildgebung in der MRT: Aktueller Status und zukunftsweisende Entwicklungen mit Deep Learning

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ZUSAMMENFASSUNG

Hintergrund Bis heute stellt die Erfassung der Nierenfunktion eine Herausforderung für die moderne Medizin dar. Oftmals bleiben funktionelle Einschränkungen der Niere unentdeckt und die Ursachen ungeklärt, da weder die Labordiagnostik noch zur Verfügung stehende Bildgebungsmethoden ausreichend Information über den Funktionsstatus der Nieren liefern. In den letzten Jahren haben Entwicklungen auf dem Gebiet der multiparametrischen funktionellen Magnetresonanztomografie (fMRT) mit Anwendung an abdominellen Organen neue Möglichkeiten zur kombinierten Erfassung anatomischer Strukturen und funktioneller Informationen eröffnet. Dieser multiparametrische Ansatz erlaubt die Messung verschiedener Parameter wie der Perfusion, Diffusion, Oxygenierung und Charakterisierung von Gewebeparametern in einem Untersuchungsvorgang, wodurch umfassendere Einblicke in die pathophysiologischen Prozesse verschiedener Nierenerkrankungen und die Wirkung therapeutischer Ansätze ermöglicht werden. Allerdings ist die Anwendung an der Niere noch auf die Forschung beschränkt und der Schritt in die klinische Routinediagnostik ausstehend. Eine der größten Herausforderungen stellt das Fehlen standardisierter Protokolle für die Akquisition und die Datenverarbeitung sowie effizienter Methoden zur Datenanalyse dar. Dieses Review bietet eine Übersicht über die weitverbreitetsten fMRT-Techniken mit Anwendung an der Niere und zeigt neue Ansätze zur Datenverarbeitung und Analyse mittels Deep Learning auf.

Methode Für diesen Artikel wurde eine selektive Literaturrecherche unter Verwendung der Literaturdatenbank PubMed im Mai 2021 durchgeführt und durch eigene Erfahrungen auf diesem Gebiet ergänzt.

Ergebnisse Die multiparametrische funktionelle MRT ist eine vielversprechende Technik zur Erfassung der Nierenfunktion in einem umfassenderen Ansatz durch kombinierte Untersuchung verschiedener Funktionsparameter wie der Perfusion, Diffusion und Oxygenierung in einem Untersuchungsablauf. Neue Entwicklungen auf dem Gebiet des Deep Learning könnten wesentlich bei der Bewältigung der Datenmengen und der Entwicklung effizienterer Methoden zur Datenverarbeitung und Analyse beitragen. Diese Fortschritte lassen hoffen, dass multiparametrische fMRT-Protokolle bald ausreichend optimiert sind, um über die Forschung hinaus auch im klinischen Alltag in der Diagnostik, dem Monitoring und der Behandlung von Nierenerkrankungen eingesetzt zu werden.

Kernaussagen:
▪ Die multiparametrische fMRT umfasst strahlenfreie, nicht invasive und kontrastmittelfreie Techniken.
▪ Durch die kombinierte Aufnahme verschiedener funktioneller und struktureller Gewebeparameter können tie-

fere Einblicke in pathophysiologische Prozesse von Nieren-erkrankungen gewonnen werden.

- Für eine breitere Akzeptanz von MR-Biomarkern in der Zukunft sind die Etablierung von Standards in der Daten-akquisition, -verarbeitung und Analyse sowie prospektive Studien notwendig.

- Deep-Learning-Ansätze könnten einen entscheidenden Beitrag sowohl in der Datenakquisition als auch in der Verarbeitung und Interpretation großer Datenmengen leisten.

ABSTRACT

Background Until today, assessment of renal function has remained a challenge for modern medicine. In many cases, kidney diseases accompanied by a decrease in renal function remain undetected and unsolved, since neither laboratory tests nor imaging diagnostics provide adequate information on kidney status. In recent years, developments in the field of functional magnetic resonance imaging with application to abdominal organs have opened new possibilities combining anatomic imaging with multiparametric functional information. The multiparametric approach enables the measurement of perfusion, diffusion, oxygenation, and tissue characterization in one examination, thus providing more comprehensive insight into pathophysiological processes of diseases as well as effects of therapeutic interventions. However, application of multiparametric fMRI in the kidneys is still restricted mainly to research areas and transfer to the clinical routine is still outstanding. One of the major challenges is the lack of a standardized protocol for acquisition and postprocessing including efficient strategies for data analysis. This article provides an overview of the most common fMRI techniques with application to the kidney together with new approaches regarding data analysis with deep learning.

Methods This article implies a selective literature review using the literature database PubMed in May 2021 supplemented by our own experiences in this field.

Results and Conclusion Functional multiparametric MRI is a promising technique for assessing renal function in a more comprehensive approach by combining multiple parameters such as perfusion, diffusion, and BOLD imaging. New approaches with the application of deep learning techniques could substantially contribute to overcoming the challenge of handling the quantity of data and developing more efficient data postprocessing and analysis protocols. Thus, it can be hoped that multiparametric fMRI protocols can be sufficiently optimized to be used for routine renal examination and to assist clinicians in the diagnostics, monitoring, and treatment of kidney diseases in the future.

Key Points:

- Multiparametric fMRI is a technique performed without the use of radiation, contrast media, and invasive methods.
- Multiparametric fMRI provides more comprehensive insight into pathophysiological processes of kidney diseases by combining functional and structural parameters.
- For broader acceptance of fMRI biomarkers, there is a need for standardization of acquisition, postprocessing, and analysis protocols as well as more prospective studies.
- Deep learning techniques could significantly contribute to an optimization of data acquisition and the postprocessing and interpretation of larger quantities of data.

I. Introduction

All over the world people are suffering from chronic kidney diseases with a high number of unreported incidents [1]. The evaluation of kidney function has remained a huge challenge for modern medicine and nephrologists are repeatedly faced with complex kidney pathologies and pathophysiologies that the diagnostic methods used in the clinical routine, such as laboratory tests, ultrasound, and renal scintigraphy, sometimes do not have sufficient sensitivity or specificity to solve [2–4]. How can we improve diagnostic methods using recent developments in imaging techniques and data analysis to help clinicians in the early detection, monitoring, and treatment of kidney diseases?

In the past decades abdominal imaging with MRI has become a well-established method for detecting various pathologies. Nonetheless, the range of MR imaging techniques used in the clinical routine only represents a portion of the diagnostic potential of MRI. Functional MR imaging (fMRI) is an emerging field with great potential to take diagnostic imaging to the next level. Without the

application of contrast agents, multiparametric fMRI provides non-invasive methods to measure organ perfusion, diffusion, oxygenation and to characterize changes in tissue composition. Especially the assessment of kidney function could become a major area of application, since the complex interaction of blood flow, perfusion, and oxygenation in the renal physiology and pathophysiology of various kidney diseases is still the subject of numerous studies. Additionally, recent advances in the field of deep learning in medical imaging could substantially contribute to coping with data postprocessing and to helping to integrate functional information into the clinical routine for more efficient and feasible diagnostics.

This article outlines the most widely used fMRI techniques and gives an overview of the current state of clinical applications, recent studies, and new developments in data postprocessing with regard to emerging deep learning techniques.

II. Functional MRI Parameters

We can already look back at decades of research on functional imaging with MRI. Since the implementation of MRI scanners for medical diagnostics, MRI has gone far beyond visual imaging [5]. A variety of fMRI techniques have been developed and to some extent applied in the clinical routine. Many promising techniques, however, have remained restricted to research, which also applies to functional imaging of the kidneys [6].

One of the major barriers for broader application and clinical use of renal fMRI is the confusing diversity of fMRI techniques and variations in acquisition, post-processing, and analysis approaches [7]. In order to merge the developments and results of individual studies around the world and standardize clinical research, a multinational group funded by the European Union COST (European Cooperation in Science and Technology) Action called 'PARENCHIMA' was formed [8, 9]. Inspired by the recommendations of this network, this article focuses on the main techniques of fMRI including perfusion, diffusion, and BOLD (blood oxygen level-dependent) imaging added by further MRI techniques such as T1 / T2 mapping and dynamic contrast-enhanced (DCE) MRI, which might also contribute to a more comprehensive understanding of pathological changes in renal structure and function.

Measuring perfusion with ASL

Renal perfusion is expected to be one of the main elements of renal function, and changes in kidney perfusion might significantly impact the progression of acute kidney injury and chronic kidney diseases. Beside different methods measuring renal blood flow, the assessment of renal perfusion is far more complicated and difficult to perform non-invasively. Arterial spin labeling (ASL) is a technique for the non-invasive imaging and quantification of perfusion without the administration of contrast media using the water molecules of the blood as endogenous tracers. Therefore, the blood has to be prepared and "labeled" magnetically before entering the imaging plane, which is performed by implementing radiofrequency pulses to change the longitudinal magnetization of the water protons. After generating two images, a "control" image without labeled blood and a "label" or "tag" image with labeled blood, the relative perfusion can be calculated by subtraction. The result depicts a perfusion-weighted image, where signal intensity is proportional to the perfusion. Using kinetic models, quantitative perfusion maps can be computed and the perfusion can be measured in mL/100 g/min [10].

There are different schemes for labeling the blood with flow-sensitive alternating inversion recovery (FAIR) pulsed ASL and pseudocontinous ASL being the most widely used [11]. In recent years, faster readout strategies such as 3 D gradient and spin echo (GRASE) sequences contributed to faster image acquisition and improvement of the intrinsic low signal-to-noise ratio (SNR) of ASL. Motion correction tools and suppression of background tissue compartments can additionally help to optimize image quality [12].

A shortcoming of renal ASL is the problem of validation due to the lack of a gold-standard technique for perfusion measurement. ASL has been validated against para-aminohippurate clearance, ultrasound flowmetry, microspheres, and scintigraphy [13]. There were also numerous studies testing the reproducibility of renal ASL, though with different technical implementations [13]. The clinical applications of ASL encompass diagnostics for renal transplant recipients, living kidney donors, acute kidney injury, and chronic kidney diseases, showing a correlation of decreasing GFR with a reduced perfusion signal [14]. ASL was also tested under the influence of various drugs affecting renal perfusion [15].

Assessing renal microstructure with DWI

In the clinical routine, the only way to assess changes in the renal interstitium to date is renal biopsy. But there is a promising non-invasive alternative to make microstructural changes visible and measurable with diffusion-weighted imaging (DWI).

DWI is sensitized to the Brownian motion of water molecules, making it possible to draw conclusions concerning renal microstructure and the degree of renal fibrosis. Strong additional bipolar gradients are applied with varying gradient strengths and durations constituting different diffusion-weighting, which is summarized in b-values. As a quantitative parameter for diffusion, the apparent diffusion coefficient (ADC) is calculated from DW images to indicate the degree of water displacement [16]. Beside the diffusion of water molecules, an effect called pseudodiffusion can be observed at lower b-values, which results from water motion in preformed structures, i. e., perfusion. With the intra-voxel incoherent motion (IVIM) approach, pseudodiffusion and "real" diffusion can be distinguished by using a biexponential model [17]. In order to investigate the spatial dependence of diffusion and quantify the degree of the well-known spatial anisotropy of the renal medulla, a larger number of non-collinear diffusion directions than the three directions usually used for the calculation of ADC can be acquired. This technique called diffusion tensor imaging (DTI), however, is accompanied by a high expenditure of time [17]. The majority of studies applying renal DWI simply use ADC, despite the advantage of additional information from IVIM and DTI [18].

Similar to renal ASL, validation studies with renal DWI also lack a standardized acquisition and analysis protocol. For biological validation, again no gold standard is available. Renal DWI has been technically validated in numerous reproducibility studies and applied in various clinical studies, including acute graft dysfunction, acute pyelonephritis, polycystic disease, and chronic kidney disease [19].

BOLD MRI to reflect renal tissue oxygenation

Blood oxygenation level-dependent (BOLD) MRI is the first method to non-invasively estimate the oxygenation status of blood and to evaluate tissue oxygenation. This is made possible by the change of the magnetic properties of hemoglobin (HB) with oxygen saturation, which leads to a decrease or increase in free induction signal decay time constant T_2^* resulting in a measurable contrast in BOLD imaging [20]. A decrease in tissue oxygenation is assumed to play a major role in the progress of chronic kidney disease and acute kidney injury. The information about the ratio of oxy- and desoxy-HB in correlation to perfusion could help to gain more comprehensive insight into pathophysiological processes and to determine between causes and consequences of renal hypoxia [21].

Since no gold-standard for non-invasive measurement of tissue oxygenation is available, BOLD MRI has only been validated against micropuncture techniques in animals [22]. Various studies have demonstrated the reproducibility of this technique in humans as well as its potential to detect changes in human renal tissue oxygenation in patients with chronic kidney diseases, renal artery stenosis, and transplant kidneys. Moreover, BOLD-MRI has been proven to be a useful tool for evaluating drug effects on kidney function and for estimating its potential nephrotoxicity. [20]

Similar to ASL and DWI, BOLD MRI lacks standardization in image acquisition and analysis. It is most frequently performed with multiple gradient echo (GRE) sequences at 3 T as the preferred field strength. It is recommended to standardize the physiological status of the patient regarding hydration and salt intake, since these exogenous factors have been shown to significantly influence tissue oxygenation [9]. In research settings, regions of interest (ROIs) have been a widely used technique for image analysis, whereas for clinical settings a whole kidney analysis encompassing the cortex and medulla should be performed. The gain of information could be increased using BOLD in combination with other fMRI techniques such as ASL and DWI [23].

Tissue characterization with T1 and T2 Mapping

Tissue changes caused by inflammation, edema, fibrosis, or necrosis lead to changes in relaxation times which can be imaged and quantified by T1 or T2 mapping [24]. For T_1 mapping, the established method is the inversion recovery (IR) technique. The IR preparation is repeated several times while increasing inversion time to acquire multiple data points using a single-shot imaging module (e. g., echo planar imaging (EPI), steady state free precession (SSFP)) with long repetition time (TR). Recently published techniques such as the variable flip-angle (VFA) or modified Look-Locker imaging (MOLLI) are possible alternatives. [25]. Due to differences in the content of free water between the medulla and the cortex, T1 mapping allows pronounced corticomedullary differentiation (CMD) [26]. In renal transplants, however, cortical and medullary T1 relaxation times seem to be higher than in healthy subjects [24]. Various studies also depicted a correlation of T1 relaxation times and the degree of renal impairment and GFR in patients with renal insufficiency [26, 27].

T2 mapping is usually performed with multi-echo(fast) spin-echo sequences and enables full kidney coverage within a short period of time. Image quality can be influenced by susceptibility artifacts due to blood flow, tissue diffusivity, magnetic field inhomogeneities, and imperfect slice selection pulse profiles [25]. To mitigate these problems, special T2 preparation pulses (e. g., CPMG) can be used in combination with a fast single-shot readout (similar to the application of an inversion pulse in T1 mapping) [28]. In cardiac imaging, T2 mapping is an established technique to detect edema after myocardial infarction or inflammation [29]. Beside several animal studies examining T2 sensitivity to ischemia-reperfusion injury [24], T2 mapping might have the potential to detect early stages of autosomal dominant polycystic kidney disease (ADPKD) in the future [30]. Larger studies evaluating the value of T2 mapping of the kidneys in humans are still missing.

Dynamic contrast-enhanced MRI

Dynamic contrast-enhanced (DCE) MRI implies the administration of gadolinium-containing contrast agents. They enter the kidney's capillary system and undergo glomerular filtration and tubular excretion before being eliminated in the urine. By analyzing the contrast enhancement in the tissue of interest, DCE offers the possibility to describe the glomerular filtration rate (GFR) by measuring tubular flow and tubular transit time as well as vascular parameters such as permeability, renal blood flow, and blood volume [31]. DCE MRI has been validated in several studies against different methods and in patients with acute kidney injury, renal tumors, and kidney transplants [32–34], where it has been found valuable for assessing renal perfusion and filtration. The main drawback of DCE is the application of a gadolinium-containing contrast medium, which entails increased risk for developing NSF [35] and gadolinium retention in the brain [36], especially in patients with impaired kidney function.

Multiparametric fMRI protocols and applications

Apart from ASL, DWI, BOLD MRI, T1 and T2 mapping, and DCE MRI, there are further techniques providing valuable information about pathological processes in the kidneys. According to a position paper from the COST Action PARENCHIMA, further commonly available MRI biomarkers are renal volumetry, phase-contrast MRI, and magnetization transfer (MT) [37]. Most recent studies implementing multiparametric fMRI techniques comprise a combination of ASL, DWI, BOLD, and T1 and T2 mapping. Sometimes volumetric analysis and phase-contrast MRI are added [38]. A few include DCE or fat quantification with Dixon MRI [39]. Obviously, the choice of MRI biomarkers depends on the clinical question. Multiparametric fMRI offers the possibility to select from a range of MRI biomarkers that address the study hypothesis and kidney pathology. Especially the examination of transplant kidneys with multiparametric fMRI protocols is of great interest, since there are a lack of sensitive monitoring techniques for the evaluation of kidney function and early detection of kidney failure. The combination of functional parameters assessing changes in perfusion, diffusion, oxygenation, kidney volume, and tissue structure is a promising approach to gain deeper insight into the biological process of acute rejection of kidney transplants and prediction of long-term complications [40]. Multiparametric fMRI has recently been applied to examine patients with chronic kidney diseases [41, 42], acute kidney injury [38], IgA nephropathy [43], polycystic kidney disease [44], and interstitial renal fibrosis [45]. ▶ **Fig. 1** shows examples of a multiparametric fMRI protocol for kidney examination comprising T1 mapping, BOLD, DWI, and ASL.

III. Data postprocessing and analysis: new strategies with deep learning

With multiparametric fMRI a vast amount of data can be generated. How should this quantity of data be handled? How can this information be directly extracted?

Data postprocessing and analysis is a topic rarely described in detail in most clinical studies regarding functional renal imaging.
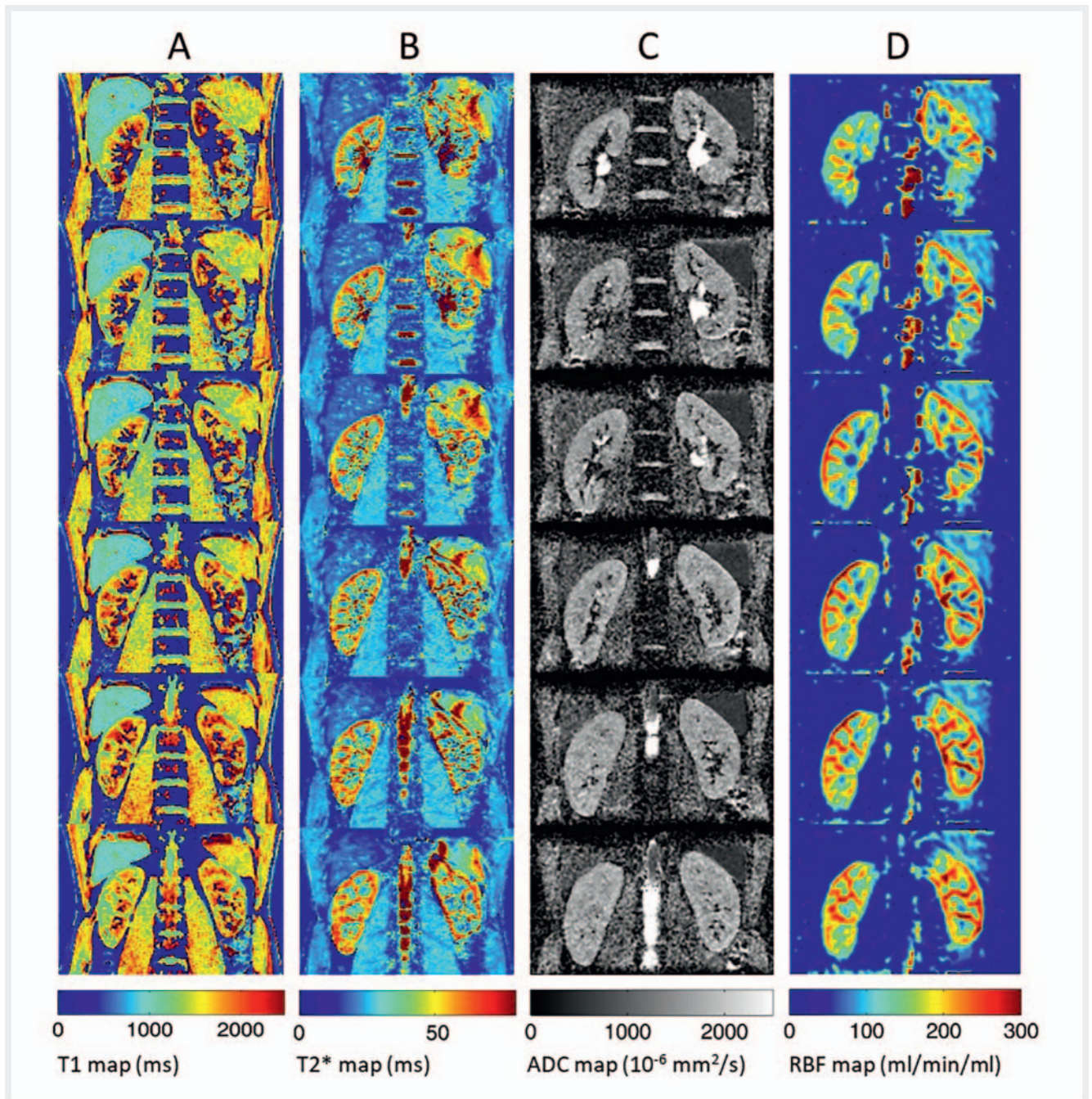
► **Fig. 1** Multiparametric renal functional imaging of a volunteer showing multiple slices of different functional parameters. **A** Tissue characterization with T1 mapping. **B** BOLD MRI with T2* mapping. **C** Assessing microstructure with ADC mapping. **D** Perfusion imaging with ASL (renal blood flow (RBF) mapping).

Nonetheless, it is one of the main limiting factors for use in clinical practice, since it can have a significant impact on data interpretation. For successful application of multiparametric fMRI protocols in the clinical routine and studies of large patient cohorts in the future, standardized data postprocessing and data analysis workflows are needed.

Over the last few years impressive developments in deep learning (DL) have aroused great interest across a variety of areas including healthcare applications [46]. Recent advances in artificial neural networks show great potential for medical imaging technology, data analysis, and diagnostics and might substantially impact the future of healthcare. MRI could take advantage of these advances by implementing DL techniques for the optimization of data acquisition, postprocessing, and analysis [47]. There are also efforts by the European Union COST to form a database for machine learning applications on renal MRI and for "bridging the gap between data and technology" [48].
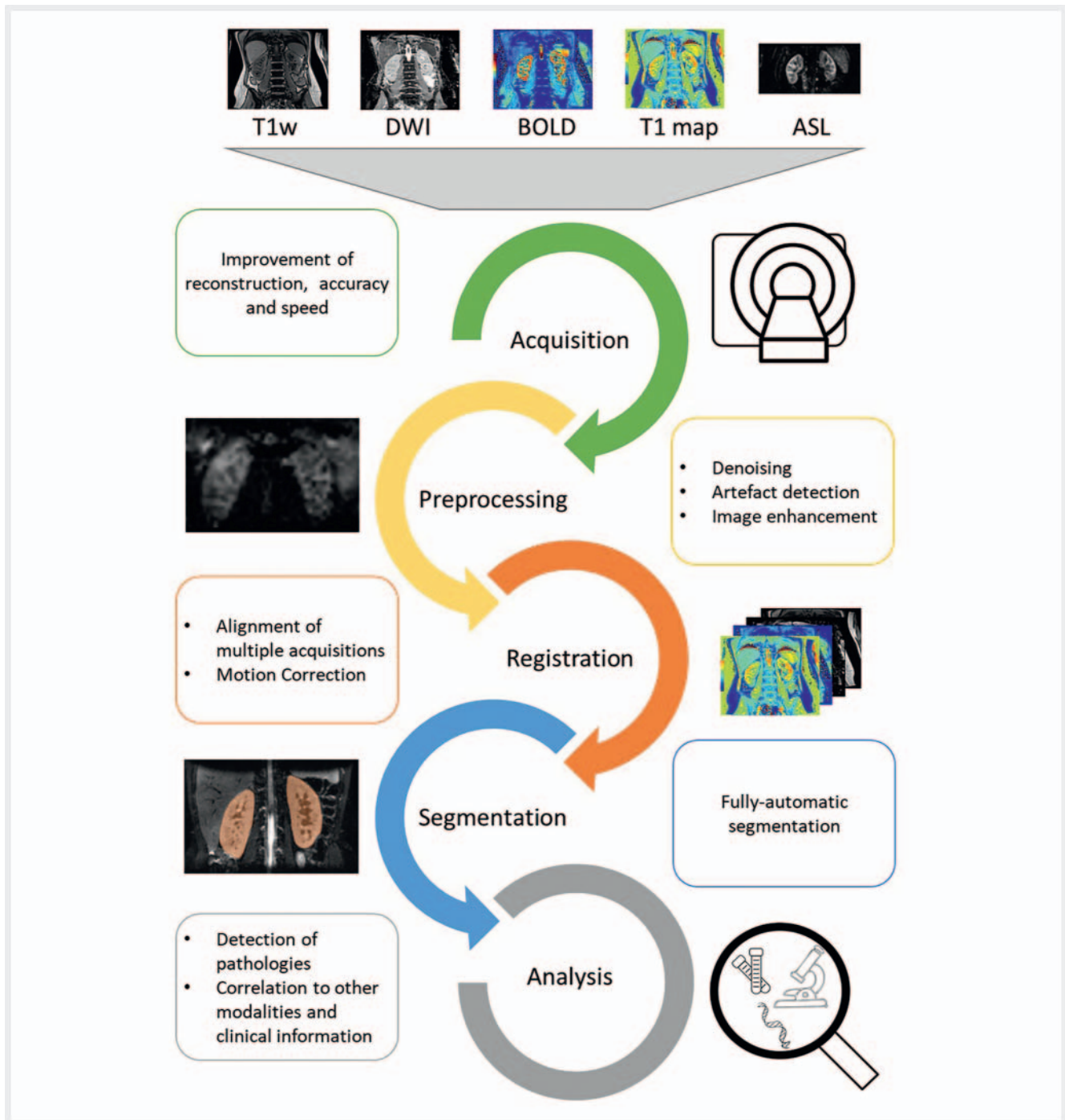
▶ **Fig. 2** Image processing pipeline depicting different application steps for deep learning approaches in multiparametric renal MRI.

The term "deep learning" refers to a deep network of multilayer neural networks to analyze data. The main difference of the DL approach compared to other machine learning techniques is its ability to learn feature representation and classification in the same process, thus optimizing both simultaneously [49]. DL techniques with application in medical imaging are mostly based on convolutional neural networks (CNNs) to learn useful representations of images and other structured data [50]. The multitude of options to implement DL in the process of data analysis ranges from data acquisition to computer-aided diagnosis. ▶ **Fig. 2** gives an overview over the different application steps for deep learning approaches.

Starting from MR image acquisition, DL can be implemented in the process of image reconstruction to significantly improve robustness, accuracy, and image quality from undersampled k-space data as well as to optimize speed compared to conventional reconstruction approaches [51–56]. Impressive results have been seen for instance in dynamic MR image reconstruction

of cardiac MRI, where real-time image reconstruction [57] and 4 D DL reconstruction networks have been developed [58]. Also, CNN-based methods can assist in the detection of artifacts [59], prospective motion correction [60], and image denoising [61–63]. In image super-resolution, deep learning techniques are implemented for reconstruction of higher-resolution images or image sequences from low-resolution images [64–66]. Further areas of application include image synthesis to derive new parametric images of tissue contrast from a collection of MR acquisitions [67, 68], quantitative susceptibility mapping (QSM) to non-invasively estimate magnetic susceptibility of biological tissue [69, 70], and MR fingerprinting (MRF) [71].

Multiparametric renal fMRI poses several challenges for data analysis regarding registration and segmentation, where DL seems especially promising to boost further development and the path to the clinical routine. First, renal parenchyma is difficult to differentiate from the surrounding organs and structures only by signal intensity. Secondly, multiparametric fMRI encompasses heterogenous signal contrasts and image qualities. Furthermore, kidneys can vary dramatically in their anatomical position, size, and features, such as cysts. Last but not least, motion due to breathing leads to a considerable variation in the position of the kidneys not only between but also within measurements. Image registration and segmentation, therefore, are a precondition for efficient analysis of multiparametric fMRI data.

Image registration implies spatial alignment of intra- and inter-subject kidney images to enable further processing steps. There is a range of strategies for image registration with different approaches, which can be grouped into image acquisition techniques and post-processing methods [72]. The emerging use of DL shows the greatest potential to contribute to more efficient image registration, thereby surpassing standard deformable registration algorithms in accuracy and speed. Still, application to renal MRI is pending, which might also be attributed to the lack of public datasets and validation protocols. The application of newly developed methods to other imaging modalities and organs, however, seems promising for the transfer to renal MRI [50].

For quantitative analysis of multiparametric fMRI in the kidneys, organ segmentation for the assessment of total kidney volume (TKV) but also kidney compartments including the cortex and medulla is an essential step. Due to the challenges of renal multiparametric fMRI as described above, manual segmentation has been the prevalent segmentation technique in renal MRI studies. However, for clinical use of renal fMRI, this time-consuming and laborious method needs to be replaced by more efficient segmentation techniques. Beside other semi-automatic and automatic segmentation techniques such as image processing and model-based image segmentation, machine learning and especially deep learning approaches have again been shown to be the most promising to deal with the more complex multiparametric datasets [73]. DL has already been applied in a few studies for segmentation of the kidneys to estimate TKV [74–78].

Going even further beyond the tasks of image pre- and post-processing, DL can be implemented for computer-aided diagnosis. By combining the ability to analyze imaging data and retrieve clinical information, automated classification systems can be developed to assist clinical diagnostics, as has been successfully shown in the diagnosis of prostate cancer, for example [79, 80]. In kidney diagnostics, DL methods have been demonstrated to assist in the diagnosis of transplant rejection with fMRI and the integration of clinical data, thereby forming a computer-assisted diagnostic (CAD) system for the assessment of kidney function including DWI, BOLD, and creatinine clearance [81–83]. Another application of DL is the differentiation of renal cell carcinoma [84, 85].

IV. Discussion

Renal MRI is an emerging technique that has not yet been established in the clinical routine. Several other more established imaging techniques with different strengths and weaknesses are usually preferred by clinicians.

The most commonly applied method for renal imaging is ultrasonography. It is also a non-invasive, non-ionizing technique, which provides the ability to dynamically image morphological abnormalities with high resolution, to measure blood flow with the Doppler method, and to apply a safe contrast agent to visualize perfusion without harming the kidney [86–89]. In contrast to MRI, it is widely available and cost-efficient [90]. However, image quality is operator-dependent and can be considerably reduced by gas between the transducer and the organ of interest or by the obesity of subjects. Measurements and images are more difficult to reproduce and quantification is feasible only to a limited extent [2, 91, 92].

Like MRI, CT is a tomographical imaging technique that uses radiation to obtain images. Even though MRI techniques have become a lot more time-efficient in the past decades, CT is still much faster than MRI and is more cost-effective [93, 94]. Apart from morphological and angiographical imaging, CT has the ability to measure renal blood flow and perfusion as well as GFR and tubular function [2]. The major drawback of CT is the need for nephrotoxic contrast agent for most tasks besides detecting renal obstruction, which limits its use for kidney diseases [95].

Functional renal imaging in the clinical routine also includes renal scintigraphy. It is the gold standard for measuring glomerular filtration and tubular function [92] and enables accurate evaluation of split function and renal obstruction. Nonetheless, image resolution and quality are very poor in comparison to other imaging modalities and diagnostic value is limited.

Most clinicians are not aware of the potential of MRI to offer functional imaging of the kidneys even without the administration of contrast media. But there are also several disadvantages to using MRI that might present an obstacle to broader application. The leading drawback of MRI is the limited availability, especially in smaller hospitals, and the cost expenditure associated with purchase and maintenance [90]. Renal MRI can be performed with 1.5 and 3 Tesla, although studies have shown the benefits of 3 Tesla for SNR, examination time, and spatial resolution [9]. Moreover, the use of MRI needs experienced operators. When using multiparametric fMRI protocols to examine kidneys, there is still a need for standardized procedures, protocols, and postprocessing as well as more offers by medical technology companies [6]. Contrary to general belief, the examination time of MRI has

been reduced significantly in the past decades and single parameters can be measured in a few minutes. Furthermore, breathing strategies such as breath-hold, respiratory-triggered, or free-breathing imaging can be adapted to patient condition for most sequences [9]. Last but not least, relative contraindications such as pacemakers and cochlear implants have to be considered.

Nonetheless, MRI has a lot to offer and might help to even reduce the costs of multiple sometimes even invasive diagnostic examinations. Beside high-resolution anatomical imaging, the range of functional parameters offered by MRI is exceptional and can be achieved mainly without the use of contrast agent. Examination protocols can be adapted to the clinical issue, kidney disease, and patient condition and are suited for both short-term and long-term monitoring. Eventually, the aim of developing multiparametric fMRI for the kidneys is not to replace established techniques such as ultrasonography and renal scintigraphy, but to broaden and improve renal imaging and help clinicians and patients in the treatment of kidney diseases.

V. Summary

Multiparametric functional MRI of the kidneys is a promising approach for assessing renal function and pathophysiology. Combinations of perfusion, diffusion, and BOLD imaging together with techniques for tissue characterization such as T1 and T2 mapping and further MR biomarkers can be selected depending on the clinical question and the kidney pathology to gain more comprehensive insight into the cause and consequences of diseases and the effect of therapeutic interventions. However, several obstacles have to be overcome before the method can be implemented in the clinical routine. On the one hand, there is a need for standardization of fMRI protocols to enable comparability of studies and to facilitate clinical application. On the other hand, new strategies for handling the emergence of huge amounts of data are necessary. Recent advances in DL techniques open new possibilities for data postprocessing and analysis and might give clinical use of renal fMRI a decisive push forward. More studies examining different kidney pathologies with larger cohorts and longitudinal design with implementation of a standardized workflow for data acquisition, postprocessing, and analysis are needed to further improve and at the same time demonstrate the ability of multiparametric fMRI to enhance diagnostic imaging of the kidneys.

Conflict of Interest

The authors declare that they have no conflict of interest.

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