24. Moss AH. Integrating supportive care principles into dialysis decision making: a primer for palliative medicine providers. *J Pain Symptom Manage* 2017; 53: 656–662.e651
25. Patel SS, Holley JL. Withholding and withdrawing dialysis in the intensive care unit: benefits derived from consulting the renal physicians association/American Society of Nephrology clinical practice guideline, shared decision-making in the appropriate initiation of and withdrawal from dialysis. *Clin J Am Soc Nephrol* 2008; 3: 587–593
26. Akbar S, Moss AH. The ethics of offering dialysis for AKI to the older patient: time to re-evaluate? *Clin J Am Soc Nephrol* 2014; 9: 1652–1656
27. Ellis G, Whitehead MA, Robinson D *et al.* Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomised controlled trials. *BMJ* 2011; 343: d6553
28. Alfaadhel TA, Soroka SD, Kiberd BA *et al.* Frailty and mortality in dialysis: evaluation of a clinical frailty scale. *Clin J Am Soc Nephrol* 2015; 10: 832–840
29. Negm AM, Kennedy CC, Thabane L *et al.* Management of frailty: a protocol of a network meta-analysis of randomized controlled trials. *Syst Rev* 2017; 6: 130
30. Piers RD, Azoulay E, Ricou B *et al.* Perceptions of appropriateness of care among European and Israeli intensive care unit nurses and physicians. *JAMA* 2011; 306: 2694–2703

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Recent findings on the clinical utility of renal magnetic resonance imaging biomarkers

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A RAPIDLY GROWING FIELD

During the last 15 years, the application of magnetic resonance imaging (MRI) to evaluate the kidneys has evolved dramatically. The interest in renal MRI biomarkers [1, 2] is driven by the potential to quantify morphological, microstructural, haemodynamic and metabolic changes non-invasively and across the entire kidney parenchyma. These ideas have led to a growing excitement within an emerging community of nephrologists, radiologists, surgeons, physicists, computer scientists, pathologists and physiologists. In October 2019, the third international conference on functional renal MRI (Nottingham, UK) attracted around 200 participants across these disciplines, sharing expertise and results in all aspects of this developing field including reproducibility and standardization of methods, preclinical research and multicentre clinical studies.

The origins of MRI date back to the discovery by Damadian in 1971 that certain biophysical quantities, the magnetic relaxation times known as T1 and T2, are able to distinguish benign and malignant tissues [3]. This insight ultimately gave rise to the MRI scanners we know today, where the tissue sensitivities of T1 and T2 are exploited to generate images with exquisite soft tissue contrast. Beyond T1 and T2, advanced MRI techniques have since been developed that can visualize a host of other biophysical tissue properties (Figure 1). Examples are the apparent diffusion coefficient (ADC) of water measured with diffusion-weighted imaging (DWI) [5]; tissue perfusion, which can be measured by magnetically labelling arterial blood [arterial spin labelling (ASL)] [6]; or tissue stiffness, which is measured using MRI elastography [7]. For a detailed overview, see Table 1 in Selby *et al.* [2].

In the past decade, it has become increasingly apparent that the biophysical quantities measurable by MRI can have a utility beyond generating image contrast. In particular, their sensitivity to tissue type should enable them to characterize changes 'within' tissues caused by ageing, disease or intervention [8]. This is a compelling hypothesis in the context of renal medicine because a range of MRI techniques is sensitive to the pathophysiological changes associated with the progression of renal disease. In that sense, MRI may open up a novel source of non-invasive biomarkers to inform on pathogenesis, improve predictions of disease progression and evaluate treatment effects.

RECENT RESULTS ON RENAL MRI BIOMARKERS

A sign of changing attitudes is that renal MRI research is increasingly disseminated beyond MR physics and radiology through the nephrology literature. In September 2018, *NDT* dedicated a special issue entitled *Magnetic Resonance Imaging Biomarkers in Renal Disease* [9]. And over the last year, *NDT* has published four clinical studies exploring a combination of MRI measures in patients with chronic kidney disease (CKD) from which we can learn clear lessons [10–13].

In 2018, Sugiyama *et al.* [12] used a retrospective cohort study design to evaluate the risk of CKD progression in 91 patients with CKD, defined as less than or equal to Stage 3 CKD

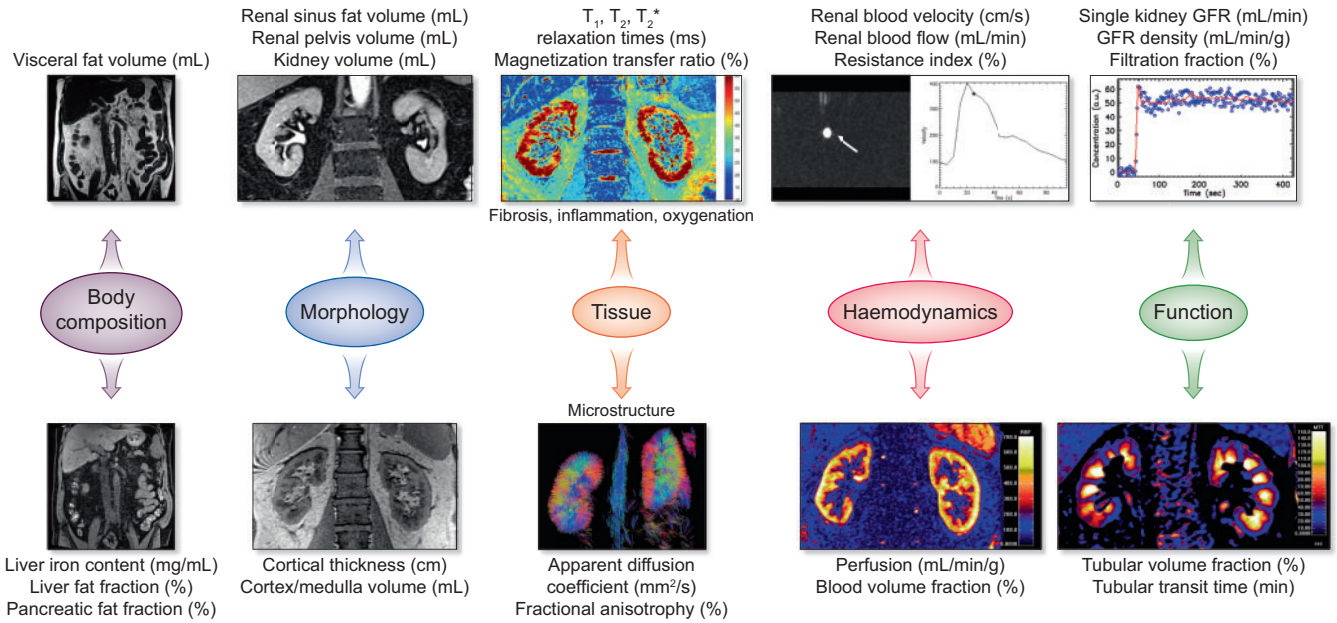

FIGURE 1: The MRI biomarker panel of the ongoing iBEAt study (Prognostic Imaging Biomarkers for Diabetic Kidney Disease) [4] as an illustration of the range of biophysical properties that can be derived from a multi-parametric MRI scan. The iBEAt study is part of the BEAt-DKD project (www.beat-dkd.eu) on prognostic biomarkers for diabetic kidney disease and therefore also incorporates measures of body composition as general risk factors for diabetes. The other measures characterize the kidney and cover gross morphology (red), tissue characterization (orange), haemodynamics (blue) and function (green). All but the functional markers can be measured without the use of MRI contrast agents. Some relevant classes of MRI biomarkers are not included in the iBEAt study, such as those characterizing mechanical properties like stiffness and elasticity (derived from MRE), and molecular markers such as sodium concentration, urea kinetics and metabolism measurable with novel techniques (sodium MRI, hyperpolarized MRI and chemical exchange saturation transfer).

or chronic proteinuria. Blood oxygen level-dependent MRI [14] and DWI were performed at baseline, and patients were followed up with blood tests to measure estimated glomerular filtration rate (eGFR) progression for 5 years. At baseline, the ADC was found to correlate with eGFR. The longitudinal data showed that the baseline relaxation time T2*—sensitive to blood oxygenation—correlated with eGFR slope over the subsequent 5 years.

Berchtold *et al.* [13] reported a larger cross-sectional study of 164 patients with CKD undergoing a native (46) or transplant (118) renal biopsy who had an MRI biomarker study within 1 week of the biopsy. ADC, T2* and T1 were found to correlate with eGFR. The corticomedullary difference (CMD) in ADC and T1 correlated with the gold standard measurement of interstitial fibrosis (IF) on renal biopsy. The results confirmed previous pilot work in animal models and a smaller case series [15]. More recently, the authors presented longitudinal data in a small set of 19 renal transplant patients with a repeat MRI/biopsy examination [16]. The data demonstrated a correlation between the change in CMD ADC and the change in IF, but not between the change in eGFR and the change in IF. This could indicate that ADC can pick up disease progression earlier than eGFR.

Brown *et al.* [10] pursued another approach for assessing fibrotic changes in diabetic nephropathy. In a pilot cohort study of 30 diabetics with Stage 0–5 CKD and 13 healthy volunteers, they measured both tissue stiffness (with MRE) and perfusion (with ASL). Since perfusion affects tissue stiffness directly, their hypothesis was that this combination would improve the specificity to fibrosis. They reported positive correlations between eGFR and shear stiffness, cortical perfusion and a surrogate filtration fraction showing that all three quantities decrease with advancing diabetic nephropathy. In the small number of cases with a renal biopsy (5/30), the stiffness did not show an obvious change with fibrosis grade, potentially due to the masking effect of perfusion changes [7].

The case–control study by Buchanan *et al.* [11] involved a multiparametric MRI evaluation in 22 patients with CKD and 22 age-matched healthy volunteers. Patients also had a measured GFR, a renal biopsy within 3 months prior to MRI and a repeat MRI within 1 week to determine reproducibility. They observed that MRI measures have variable reproducibility with coefficients of variation (CoV) in the range of 2.4–23%. Cortical perfusion, renal artery flow, kidney volume, medullary and cortical ADC, and cortical T1 all correlated with eGFR. A multivariate analysis showed that a combination of two MRI measures, cortical T1 and perfusion, provided the best prediction of eGFR ($R = 0.87$).

POPULATION HETEROGENEITY OR MEASUREMENT ERROR?

While all four studies identified multiple MRI measures that correlate with eGFR, the correlation coefficients covered a large range from 0.2 to 0.8 showing substantial variability even within given CKD stages. This could be seen as indirect evidence that

MRI measures show the heterogeneity of individuals with different causes of kidney disease or pick up progressive disease that has not yet affected current measures such as eGFR. If confirmed this would have major implications for their clinical utility. For that conclusion to be valid, however, it is essential to rule out that the observed variability is due to measurement uncertainty.

The repeatability data provided by Buchanan *et al.* [11] offer some assurance that at least a part of the heterogeneity reflects actual differences within the population. For instance, cortical T1 has the best precision with a CoV of 2.4%, but the heterogeneity in patients is larger (4.7%)—indicating that some of the heterogeneity is real rather than a measurement artefact. At the other end of the spectrum, cortical perfusion has a CoV of 23%, but the population has again a larger heterogeneity of 69%, so this cannot be explained by measurement error alone.

When comparing results 'between' studies, the MRI acquisition and analysis method is an additional source of variability. For instance, three of the four studies measure ADC but the findings are not completely aligned. Buchanan *et al.* [11] found that cortical ADC correlates with eGFR whereas the CMD in ADC does not. Berchtold *et al.* [13] found the opposite: the CMD in ADC correlates with eGFR but cortical ADC does not. To a large extent, these differences may be due to the different patient populations, as the cause of CKD or of transplant dysfunction is likely to influence these variables. However, an effect of the MRI method cannot be ruled out at this stage. MRI biomarker assays are not standardized and have different levels of systematic error—an issue that is well-recognized and currently being addressed [17].

Clearly, the accuracy of MRI measures needs to be better characterized before we can determine exactly to what extent the differences within and between populations reflect meaningful heterogeneity. Nevertheless, the cross-sectional analyses in Brown *et al.*, Buchanan *et al.*, Sugiyama *et al.* and Berchtold *et al.* [10–13] combined with the known repeatability data do support the hypothesis that MRI measures are complementary to current diagnostics and can, therefore, provide added value in patient management.

THE ISSUE OF BIOLOGICAL SPECIFICITY

The literature on renal MRI, especially when directed at a nephrology audience, often implicitly or explicitly equates MRI measures such as T2*, T1 or ADC with pathophysiological variables associated with CKD progression such as oxygenation or fibrosis. While recognizing the need for adapting technical language in a multidisciplinary audience, it is important to be aware of the limitations of such interpretations. The relationship between most MRI measures and quantities of interest in CKD pathogenesis is complex and dependent on multiple unknown factors. They are sensitive to many pathophysiological processes but for the same reason they are also inherently nonspecific.

Oxygenation and IF are two examples of properties that cannot (yet) be derived from an individual MRI measure. For instance, the transverse relaxation time T2* is sensitive to the oxygenation of blood due to the paramagnetic properties of deoxygenated haemoglobin. It is therefore tempting to interpret the findings in Sugiyama *et al.* [12] as confirming that hypoxia is a driver for CKD progression. However, T2* is also strongly sensitive to microstructure [18] and this is likely to play a role in the differences between individuals. Another example that appears in the papers above [11–13] is the ADC of water [9]. In many tissues, IF reduces ADC by creating barriers to water mobility in the extracellular space. Unfortunately, this does not necessarily translate to the kidneys, which under normal conditions have a very small cortical interstitium [19]. Without a better understanding of these complex relationships, it is difficult to justify an interpretation of ADC in terms of IF.

A priority in renal MRI research must, therefore, be to improve the specificity to individual biological processes and understanding of how these interact. One approach is to build a discrete signature for pathological processes derived from a combination of the many available MRI contrast techniques. Apart from the aforementioned relaxation times, DWI, ASL and MRE, this can include other biophysical tissue properties such as magnetization transfer [20], more advanced microstructural methods such as susceptibility mapping [21] and diffusion tensor imaging [22], morphological measures such as kidney volume [23] or cortical thickness, and functional techniques such as MR renography or sodium MRI. Naturally, all of these can be further combined with blood- and urine-based biomarkers and clinical information, building a set of signatures that incorporate all available information.

The publications discussed herein provide some indications that, at least for the case of IF, combinations of multiple MRI measures with blood- or urine-based markers can indeed improve their specificity. Buchanan *et al.* [11] show that ADC, T1 and cortical perfusion are all associated with IF. In a much larger dataset, Berchtold *et al.* [13] found that CMD in ADC, CMD in T1 and eGFR were independently correlated with IF. Combining all three in a single score led to a good prediction of IF and produced a test with AUC = 0.84 for identifying patients with IF <25%. Since properties such as cortical perfusion, magnetization transfer and diffusion tensor imaging are all correlated with IF, they could potentially improve the specificity further.

DOES MRI IMPROVE PREDICTIONS OF CKD PROGRESSION?

The longitudinal data in Sugiyama *et al.* [12] support a hypothesis that multiparametric signatures not only improve specificity but also can lead to added clinical utility. In a multivariate analysis, baseline eGFR, level of proteinuria and the MRI measure T2* were independent predictors of the eGFR slope. Interestingly, the imaging measure that was predictive of eGFR decline (T2*) did not correlate well with eGFR at baseline, whereas the imaging measure that correlated best with eGFR (ADC) was 'not' predictive of eGFR decline. This shows that cross-sectional analyses should evaluate measures that are orthogonal as well as correlated with eGFR.

The findings in Sugiyama *et al.* [12] as regards the role of MRI in predicting progression rates are promising but obviously require further validation. The multivariate model was

trained on the full dataset and no separate dataset was available to test it. Separate predictions without MRI were not performed and therefore it is not clear how much T2* adds to the prediction. The univariate correlation of T2* with the eGFR slope was weak ($r = 0.27$), suggesting any improvement is marginal. The population was also heterogeneous and a sub-analysis of the 38 diabetic patients suggested there may be a benefit in considering more well-defined phenotypes. This retrospective study was not controlled for variables that can influence oxygenation, including participant hydration, fasting and smoking status [24]. Finally, in view of the high cost of MRI, the cost-effectiveness of MRI measures and the additional information they provide are key factors in determining their eventual utility in clinical practice. In the context of identifying at-risk patients, who may benefit from targeted therapy to slow progression of kidney disease, a health economic analysis would be required to evaluate the use of MRI screening to potentially identify those at risk of rapid progression.

These limitations notwithstanding, the findings do support the hypothesis that there may be a role for MRI in selecting at-risk patients for more aggressive management. Indeed, in the most common inherited cause of kidney failure, autosomal dominant polycystic kidney disease (ADPKD), total kidney volume (TKV) measured using MRI inversely correlates with eGFR [25]. The increase in TKV occurs before the decline in eGFR [26], which means that TKV identifies progression at an earlier stage. TKV has been approved by the European Medicines Agency (2015) and the US Food and Drug Administration (FDA, 2016) as a prognostic enrichment biomarker to identify patients at high risk of disease progression and to identify those who could be included in clinical trials of novel treatments. Furthermore, when NICE approved tolvaptan as the first disease-modifying treatment for patients with ADPKD they recommended patients be eligible if they had Stage 2–3 CKD and evidence of rapidly progressive disease. Subsequently 'rapidly progressive disease' in ADPKD has been identified by 1- and 5-year percentage rates of decline in eGFR 'or' an annual percentage increase in TKV [27] linked to an imaging classification [28].

It is difficult to predict when MRI biomarkers will become available for clinical use. Individual institutes with capacity for in-house development are already offering TKV for local clinical use (https://www.mayo.edu/research/centers-programs/imaging-core/services/image-analysis; https://sheffield3dlab.com/services/) and one may expect that such solutions will be available more widely in the very near future. However, the step from simple volumetric measures such as TKV to more elaborate functional or structural measures such as ADC or perfusion is major. In other application areas of MRI biomarkers, such as diffusion and perfusion MRI to select acute stroke patients for revascularization, it has taken 30 years to move from invention to clinical practice [29]. But there are signs that the process is speeding up as the field of MRI biomarker research is maturing and increasing numbers of small- and medium-sized enterprises are offering imaging biomarkers for drug trials or clinical practice. For instance, an MRI-based surrogate for liver biopsy has become available commercially <5 years after publication of the supporting clinical data [30]. The FDA has currently qualified only one imaging biomarker out of eight (12.5%), but 23% of all the accepted letters of intent are for imaging biomarkers, often submitted by companies (https://www.fda.gov/drugs/cder-biomarker-qualification-program/biomarker-qualification-submissions). These developments offer hope that the clinical translation of renal MRI biomarkers will be significantly faster than that of historical biomarkers in acute stroke.

FUTURE RESEARCH PRIORITIES

In conclusion, recent research by independent groups supports the working hypotheses of the renal imaging community that MRI measures have great potential to impact in various areas of renal medicine. Future research should focus on improving the characterization of measurement uncertainty, standardization of measurement methods, larger and longitudinal clinical studies in well-defined phenotypes, improving specificity by multi-parametric and multi-modal signatures, and modelling of potential cost-effectiveness. We look forward to following the continuous development and evolving role of renal MRI biomarkers in nephrology.

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CONFLICT OF INTEREST STATEMENT

None declared.

(See related articles by Berchtold *et al.* Validation of the corticomedullary difference in magnetic resonance imaging-derived apparent diffusion coefficient for kidney fibrosis detection: a cross-sectional study. *Nephrol Dial Transplant* 2020; 35: 937–945; Buchanan *et al.* Quantitative assessment of renal structural and functional changes in chronic kidney disease using multi-parametric magnetic resonance imaging. *Nephrol Dial Transplant* 2020; 35: 955–964; Sugiyama *et al.* Reduced oxygenation but not fibrosis defined by functional magnetic resonance imaging predicts the long-term progression of chronic kidney disease. *Nephrol Dial Transplant* 2020; 35: 964–970; Brown *et al.* The utility of magnetic resonance imaging for non-invasive evaluation of diabetic nephropathy. *Nephrol Dial Transplant* 2020; 35: 970–978)

REFERENCES

1. Ebrahimi B, Textor SC, Lerman LO. Renal relevant radiology: renal functional magnetic resonance imaging. *Clin J Am Soc Nephrol* 2014; 9: 395–405
2. Selby NM, Blankestijn PJ, Boor P *et al.* Magnetic resonance imaging biomarkers for chronic kidney disease: a position paper from the European Cooperation in Science and Technology Action PARENCHIMA. *Nephrol Dial Transplant* 2018; 33: ii4–ii14
3. Damadian R. Tumor detection by nuclear magnetic resonance. *Science* 1971; 171: 1151–1153

4. Gooding KM, Lienczewski C, Papale M *et al*. Prognostic Imaging Biomarkers for Diabetic Kidney Disease (iBEAt): Study protocol. *medRxiv* 2020; https://www.medrxiv.org/content/10.1101/2020.01.13.20017228v1 (18 May 2020, date last accessed)
5. Caroli A, Schneider M, Friedli I *et al*. Diffusion-weighted magnetic resonance imaging to assess diffuse renal pathology: a systematic review and statement paper. *Nephrol Dial Transplant* 2018; 33: ii29–ii40
6. Odudu A, Nery F, Harteveld AA *et al*. Arterial spin labelling MRI to measure renal perfusion: a systematic review and statement paper. *Nephrol Dial Transplant* 2018; 33: ii15–ii21
7. Kirpalani A, Hashim E, Leung G *et al*. Magnetic resonance elastography to assess fibrosis in kidney allografts. *Clin J Am Soc Nephrol* 2017; 12: 1671–1679
8. O'Connor JPB, Aboagye EO, Adams JE *et al*. Imaging biomarker roadmap for cancer studies. *Nat Rev Clin Oncol* 2017; 14: 169–186
9. Caroli A, Pruijm M, Burnier M *et al*. Functional magnetic resonance imaging of the kidneys: where do we stand? The perspective of the European COST Action PARENCHIMA. *Nephrol Dial Transplant* 2018; 33: ii1–ii3
10. Brown RS, Sun MRM, Stillman IE *et al*. The utility of magnetic resonance imaging for noninvasive evaluation of diabetic nephropathy. *Nephrol Dial Transplant* 2020; 35: 970–978
11. Buchanan CE, Mahmoud H, Cox EF *et al*. Quantitative assessment of renal structural and functional changes in chronic kidney disease using multiparametric magnetic resonance imaging. *Nephrol Dial Transplant* 2020; 35: 955–964
12. Sugiyama K, Inoue T, Kozawa E *et al*. Reduced oxygenation but not fibrosis defined by functional magnetic resonance imaging predicts the long-term progression of chronic kidney disease. *Nephrol Dial Transplant* 2020; 35: 964–970
13. Berchtold L, Friedli I, Crowe LA *et al*. Validation of the corticomedullary difference in magnetic resonance imaging-derived apparent diffusion coefficient for kidney fibrosis detection: a cross-sectional study. *Nephrol Dial Transplant* 2020; 35: 937–945
14. Pruijm M, Milani B, Pivin E *et al*. Reduced cortical oxygenation predicts a progressive decline of renal function in patients with chronic kidney disease. *Kidney Int* 2018; 93: 932–940
15. Friedli I, Crowe LA, Berchtold L *et al*. New magnetic resonance imaging index for renal fibrosis assessment: a comparison between diffusion-weighted imaging and T1 mapping with histological validation. *Sci Rep* 2016; 6: 30088
16. Berchtold L, Crowe LA, Friedli I *et al*. Diffusion magnetic resonance imaging detects an increase in interstitial fibrosis earlier than the decline of renal function. *Nephrol Dial Transplant* 2020; doi:10.1093/ndt/gfaa007
17. Mendichovszky I, Pullens P, Dekkers I *et al*. Technical recommendations for clinical translation of renal MRI: a consensus project of the Cooperation in Science and Technology Action PARENCHIMA. *MAGMA* 2020; 33: 131–140
18. Niendorf T, Pohlmann A, Arakelyan K *et al*. How bold is blood oxygenation level-dependent (BOLD) magnetic resonance imaging of the kidney? Opportunities, challenges and future directions. *Acta Physiol* 2015; 213: 19–38
19. Zeisberg M, Kalluri R. Physiology of the renal interstitium. *Clin J Am Soc Nephrol* 2015; 10: 1831–1840
20. Jiang K, Ferguson CM, Ebrahimi B *et al*. Noninvasive assessment of renal fibrosis with magnetization transfer MR imaging: validation and evaluation in murine renal artery stenosis. *Radiology* 2017; 283: 77–86
21. Xie L, Bennett KM, Liu C *et al*. MRI tools for assessment of microstructure and nephron function of the kidney. *Am J Physiol* 2016; 311: F1109–F1124
22. Hueper K, Hartung D, Gutberlet M *et al*. Magnetic resonance diffusion tensor imaging for evaluation of histopathological changes in a rat model of diabetic nephropathy. *Invest Radiol* 2012; 47: 430–437
23. Bae KT, Commean PK, Lee J. Volumetric measurement of renal cysts and parenchyma using MRI: phantoms and patients with polycystic kidney disease. *J Comput Assist Tomogr* 2000; 24: 614–619
24. Evans RG, Ince C, Joles JA *et al*. Haemodynamic influences on kidney oxygenation: clinical implications of integrative physiology. *Clin Exp Pharmacol Physiol* 2013; 40: 106–122
25. Chapman AB, Guay-Woodford LM, Grantham JJ *et al*. Renal structure in early autosomal-dominant polycystic kidney disease (ADPKD): the Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP) cohort. *Kidney Int* 2003; 64: 1035–1045
26. Chapman AB, Bost JE, Torres VE *et al*. Kidney volume and functional outcomes in autosomal dominant polycystic kidney disease. *Clin J Am Soc Nephrol* 2012; 7: 479–486
27. Gansevoort RT, Arici M, Benzing T *et al*. Recommendations for the use of tolvaptan in autosomal dominant polycystic kidney disease: a position statement on behalf of the ERA-EDTA Working Groups on Inherited Kidney Disorders and European Renal Best Practice. *Nephrol Dial Transplant* 2016; 31: 337–348
28. Irazabal MV, Rangel LJ, Bergstralh EJ *et al*.; the CRISP Investigators. Imaging classification of autosomal dominant polycystic kidney disease: A simple model for selecting patients for clinical trials. *J Am Soc Nephrol* 2015; 26: 160–172
29. Powers WJ, Rabinstein AA, Ackerson T *et al*.; on behalf of the American Heart Association Stroke Council. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2019; 50: e344–e418
30. Banerjee R, Pavlides M, Tunnicliffe EM *et al*. Multiparametric magnetic resonance for the non-invasive diagnosis of liver disease. *J Hepatol* 2014; 60: 69–77

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