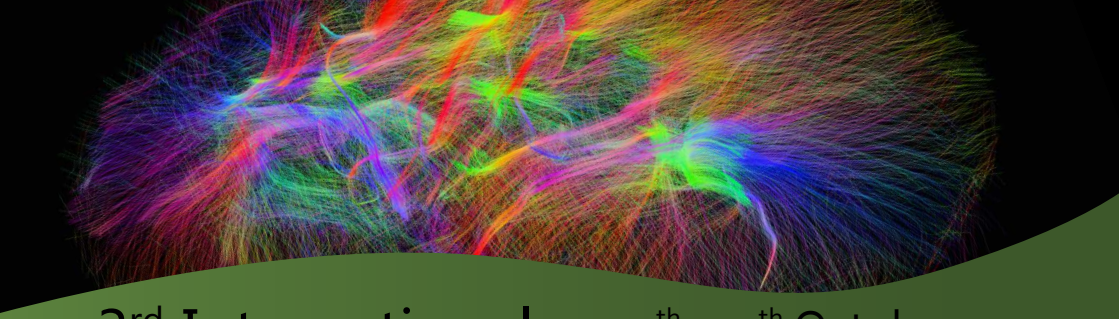


3rd International Conference on Functional Renal Imaging 2019

15th - 17th October

East Midlands Conference Centre,
University of Nottingham,
United Kingdom

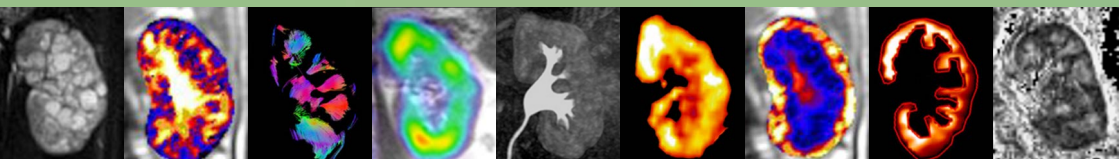
www.nottingham.ac.uk/go/3rdrenalmri

Programme

University of Nottingham
UK | CHINA | MALAYSIA

cost
EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

UK Renal Imaging Network
Transforming kidney health through technology



Message from the Organisers

It is our great pleasure to welcome you to Nottingham for the 3rd International Conference on Functional Renal Imaging. We are excited about the scientific programme and the expertise of invited speakers, as well as opportunities for connecting with friends and colleagues, both new and old. We hope that the conference will stimulate ideas, support collaborations and help advance the application of cutting-edge imaging techniques in research and in the clinic.

This conference builds on the successes of previous meetings in Berlin (2017) and Bordeaux (2015). The ethos from these meetings continues into this conference, in that the programme has been designed to bring together basic scientists, clinical scientists and clinicians from physiology, nephrology, radiology, internal medicine and related fields, as well as experts in imaging sciences and physics. As such, there is a mix of pre-clinical imaging and basic science presentations alongside clinical talks that aim to highlight the important questions that imaging may help address. Bringing those aspects together are updates in the application of functional imaging in renal transplantation, acute and chronic kidney diseases. New this year, we have included sessions that describe the application of imaging techniques outside of the kidney (as many forms of kidney disease have systemic effects), as well as how renal imaging can be used in clinical trials.

The conference is co-organised by the UK Renal Imaging Network (UKRIN) and the COST action "MRI Biomarkers for Chronic Kidney Disease" (PARENCHIMA). PARENCHIMA coordinates the research of leading European groups to improve the reproducibility and standardization of renal MRI biomarkers, increase their availability by developing an open-access toolbox with software and data and demonstrate biological validity and clinical utility in prospective multicentre clinical studies. The main programme is therefore complemented by work group sessions and meetings – on Day 1, updates from Working group 1 will cover consensus recommendations for

the acquisition of MR measures, and a Working group 2 session will comprise of power pitches on computational analysis approaches. On Day 2, there will be brief updates from Working groups 3-5 followed by break-out sessions for Working groups 1 and 3 - all participants are invited to join these meetings! Updates from short term scientific missions that have been supported by PARENCHIMA are scheduled on Day 2.

Abstracts will be presented as power pitches (Days 1 and 2) as well as posters that will be displayed in the exhibition hall for the duration of the conference. The conference dinner will be held on Wednesday evening, in the conference centre, providing a relaxed environment for networking in a more informal setting.

We hope you enjoy your stay in Nottingham - your participation in the conference will undoubtably contribute to its success!

This conference has been approved for 14 Continuous Professional Development points by the Royal College of Physicians and is endorsed by the Renal Association.

Royal College of Physicians

THE RENAL ASSOCIATION founded 1950

Local Organisers


Susan Francis


Nicholas Selby


Charlotte Buchanan


Eleanor Cox


Alexander Daniel

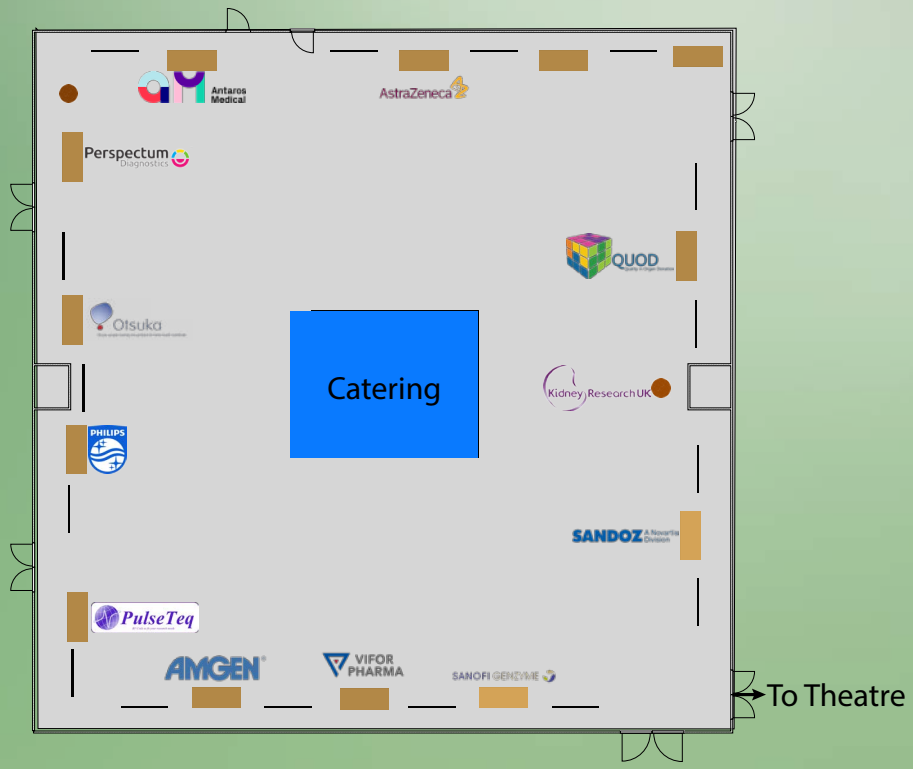

Benjamin Prestwich


Maarten Taal


Lesley Martin

We would also to thank the UKRIN committee - Phil Kalra, Fabio Nery, Iosif Mendichovszky, Steven Sourbron, David Thomas, and Bettina Wilm - for their help with the programme design.

Meeting Layout



Sponsors

We are very grateful to the sponsors of this meeting

Gold Sponsors

Silver Sponsors

Bronze Sponsors

Please note that whilst the sponsors have provided grants towards this independent programme, they have not had any influence or involvement over the agenda, content or organisation of this meeting.

COST

The European Cooperation in Science and Technology (COST) is an EU-funded programme which enables researchers to set up their interdisciplinary research networks in Europe and beyond. Through those networks, called COST Actions, COST provides funds for organising conferences, meetings, training schools, short scientific exchanges and other networking activities in a wide range of scientific topics. While COST does not fund research activities as such, it provides funding for scientific collaboration in the form of conferences, meetings, training schools and scientific exchanges. In this way, it creates open spaces where people and ideas can grow.

Founded in 1971, COST is the longest-running European framework for research collaboration. For nearly 50 years, it has increased the opportunities for researchers and innovators to take part in dynamic science and technology research networks in Europe and across the world. Nowadays, it has established a unique place in the European Research Area (ERA) landscape.

COST Working Groups

Working Group 1

Lead: Christoffer Laustsen
Vice-Lead: Pim Pullens

MRI biomarkers are increasingly used in clinical and preclinical renal research, but results derived by different groups are difficult to compare due to a lack of coherence in the methodology, and different approaches to image acquisition and processing. This is also a barrier to clinical translation, which will require biomarkers that can be compared directly against reference values establishing benchmarks for diagnosis or treatment planning.

Working group 1 will aim to improve the standardisation in the acquisition and analysis of clinical renal MRI data by establishing recommendations that are carried by a broad body of experts, and thus will establish a clear reference baseline for further development and technical and clinical validation. Recommendations will be developed by consensus formation and supported by evidence where available.

In order to avoid different standards emerging in different parts of the world, working group 1 will engage experts beyond Europe and/or coordinate efforts with similar initiatives beyond Europe.

Working Group 2

Lead: Frank Zollner
Vice-Lead: Peter Rogelj

Barriers in the development of renal MRI biomarkers with respect to chronic kidney disease are the limited availability of software tools to analyse and extract the renal data, as well as the lack of access to data from previous studies, which could produce benchmarks for future developments.
Working Group 2 will remove these barriers by delivering an R&D Toolbox consisting of a coherent set of databases and software. It will support the wider adoption of the proposed standards (by working group 1) and reduce future research costs by sharing of resources and preserving of data. The R&D Toolbox will be available to researchers world-wide through a well-supported open-source framework, and a governance structure to ensure self-sufficiency. The software will include a library of core algorithms for the analysis of functional renal MRI, and a graphical user interface for data post-processing and visualisation. The databases will contain an anonymised patient registry with critical phenotyping data, histopathology reports, proteomics, and imaging; and an image bank for benchmarking and quality control with phantom-, volunteer- and patient data.

Working Group 3

Leads: Anna Caroli and Nicholas Selby

Working group 3 joins up clinical sites working on renal MRI, and will pave the way for clinical use of renal MRI by addressing the need for a stronger evidence base.

The standardised methods developed in WG1 and WG2 will be used in large prospective multicentre clinical studies aimed at providing additional evidence of biological and clinical validity (against histopathology and reference methods) and clinical utility (prognostic value) of MRI biomarkers in renal disease.

WG3 Short Term Aims

- Prepare the way for large scale longitudinal multicentre studies aimed at providing additional evidence of biological and clinical validity of MRI biomarkers in CKD (e.g. funding applications, draw up minimum standards for sites to participate in multicentre trials)
- Secure grant funding to further validate MRI biomarkers in ADPKD
- Secure grant funding to validate MRI biomarkers in renal transplantation
- Coordinate smaller scale studies on specific relevant disease areas
- Add MRI to ongoing renal initiatives

Working Group 4

Lead: Thoralf Niendorf

Working Group 4 is developing training materials and workshops on renal magnetic resonance imaging for basic scientists and clinical users. If you would like to join these efforts, please contact the lead of this working group.

Working Group 5

Lead: Marcos Wolf
Vice-Lead: Mitko Kostov

Working Group 5 provides the platform for international stakeholders to merge synergies in the promotion of renal magnetic resonance imaging biomarkers for chronic kidney disease.

Main objectives:

- Organizing annually recurrent plenary and international meetings for the upcoming years
- Optimizing and maintaining the homepage
- Collecting data and distributing them throughout our network
  - Relevant publications
  - News
  - Events
- Providing updates to social media
- Connecting different scientific disciplines and leading industries together
- Providing information for patients

UK Renal Imaging Network

The UK Renal Imaging Network (UKRIN) was established in June 2016, as a Kidney Research UK Research Network. It brings together major UK renal MRI research centres through membership of a national group of MR physicists, radiologists, and clinicians dedicated to developing imaging methods for the study of the kidney. The UKRIN has to date focussed on MRI, but now plans to expand to include other imaging modalities.

Primary Aims of UKRIN are to:

- Co-ordinate ongoing activities in the field of renal imaging research
- Build a shared framework with standardised methods for renal imaging in clinical research. This will be addressed for MRI by the UKRIN-MAPS Partnership grant funded by the Medical Research Council which aims to standardise MRI measures between different centres, MRI vendor platforms and field strengths, to maximise the potential of multiparametric MRI for clinical utility.
- Generate research proposals for multicentre clinical studies involving renal imaging
- Provide imaging expertise and methods for clinical studies that arise from other Clinical Study Groups (CSGs) within the UK Kidney Research Consortium (UKKRC)
- Facilitate collaboration between investigators involved in renal imaging research
- Be inclusive of all imaging modalities

Objectives

- The main purpose of this network is to coordinate ongoing activities in the field of renal imaging research towards the set-up of joint multi-centre clinical studies, to avoid duplication of efforts and promote standardisation by developing shared infrastructures and tools. We will work collaboratively to share expertise, resolve challenges in acquisition and analysis, standardise approaches, and provide technical, biological and clinical validation through multi-centre studies.
- We aim to overcome practical barriers to the setup of studies e.g. new MRI technologies are currently confined to bespoke solutions in dedicated research centres.

To find out more got the website: https://kidneyresearchuk.org/research/research-networks/uk-renal-imaging-network/

To join our mailing list and get involved as a patient or researcher, contact:

Co-chairs:
Susan Francis - susan.francis@nottingham.ac.uk
Nicholas Selby - nicholas.selby@nottingham.ac.uk

Secretaries:
Isky Gordon - i.gordon@ucl.ac.uk
Fabio Nery - fabio.nery.13@ucl.ac.uk

Tuesday 15th

Opening Plenary Session

Moderated by Nicholas Selby and Steven Sourbron

10:30 Introduction to Conference
Susan Francis, Nicholas Selby and Steven Sourbron

10:40 Update from the PARENCHIMA programme
Anna Caroli

10:50 Update from the United Kingdom Renal Imaging Network
Susan Francis

11:00 Perspectives from NIDDK Renal Imaging Workshop
Pottumarth Prasad

11:10 Introduction to MRI techniques
Nicolas Grenier

11:30 Overview of the clinical need for renal MRI
Keith Gillis

12:00 - Lunch and Posters

Chronic Kidney Disease (CKD) and Diabetic Kidney Disease (DKD)

Moderated by Pottumarth Prasad and Nuria García Fernandez

13:00 Clinical overview: CKD and DKD
Phil Kalra

13:20 Pathophysiology of CKD progression
Maarten Taal

13:40 Applications of MRI to CKD: evidence to date
Sophie de Seigneux

14:00 Application of MRI to DKD: evidence to date
Aghogho Odudu

14:20 Panel discussion

14:30 - Coffee

MRI for the Non-Expert

Moderated by David Morris and Anita Harteveld

15:00 Diffusion Imaging
Jean Paul Vallee

15:20 T_1 and T_2 Mapping
Ilona Dekkers

15:40 Arterial Spin Labelling (ASL)
Manuel Taso

16:00 Blood Oxygen Level Dependent (BOLD) Imaging
Menno Pruijm

16:20 - 16:50 - Power Pitches: MRI Methods
16:50 - 17:00 - Coffee

Working Group 1 and 2 Themed Sessions

17:00 Working group 1 update
Improving the standardisation and reproducibility of renal MRI biomarkers through consenus-based technical recommendations.
Christoffer Laustsen

Acquisition recommendations: ASL
María Fernández-Seara

Acquisition recommendations: BOLD
Pottumarthi Prasad

Acquisition recommendations: DWI
Alexandra Ljimani

Acquisition recommendations: T_1/T_2
Susan Francis

17:30 Working group 2 update
Increasing the availability of renal MRI biomarkers by developing an open-access toolbox for research and development.
Frank Zoellner

Power pitches: Image processing and AI

Wednesday October 16th

08:00 - 09:45 - COST management meeting (for COST management committee members only)

Transplantation

Moderated by Isky Gordon and Phil Kalra

10:00 Clinical overview: Transplantation
Cyril Moers

10:20 Pre-clinical transplantation
Bente Jespersen

10:40 Applications of MRI to renal transplantation - evidence to date
Alexandra Ljimani

11:00 Quality in Organ Donation (QUOD)
Maria Kaisar

11:15 - Coffee

11:45 - Power pitches: MRI applications and short term scientific mission presentations

12:45 - Lunch and Posters

Emerging Techniques

Moderated by Christoffer Laustsen and Frank Zoellner

14:00 ^{23}Na MRI
Armin Nagel

14:15 Magnetisation Transfer (MT) and Chemical Exchange Saturation Transfer (CEST)
Dario Longo

14:30 Methods and applications of hyperpolarised ^{129}Xe MRI
Jim Wild

14:45 Magnetic Resonance Elastography (MRE)
Stephan Garcia

15:00 Quantitative Susceptibility Mapping (QSM)
Eric Benchler

15:15 Nephron number and new imaging techniques for histology specimines
Norbert Gretz

15:30 - Coffee

Themed Sessions

16:00 Working Group 3 Update
Joining up clinical sites across Europe to pave the way for clinical use of renal MRI.
Nicholas Selby/Anna Caroli

16:10 Working Group 4 Update
Development of training programs on renal MRI for basic scientists and clinical users.
Andreas Pohlmann

16:20 Working Group 5 Update
Building an international multi-disciplinary community of stakeholders in renal MRI.
Marcos Wolf

Working Group Break Out Sessions

	WG 1 & WG 2	WG 3
16:30	Procedure for updating and maintenance of existing recommendations. Steven Sourbron Formations of new recommendations initiatives. Christoffer Laustsen	Strategy for setup of international studies. Inventory of ongoing studies and document repository. Consensus recommendations in biomarkers. Updates from task forces on ADPK and Transplantation
17:30	Task force 1.1: Procedures for data submission, inventory of candidate databases, planning of meeting in march. - Frank Zoellner Task force 1.2: Redesign and definition of aims around software evaluation. Peter Rogelj	

19:00 - Pre-dinner drinks followed by conference dinner

Thursday October 17th

Acute Kidney Injury (AKI)

Moderated by David Gardner and Valerie Said-Conti

09:00 Clinical Overview
John Prowle

09:20 Histopathology of AKI
Peter Boor

09:40 Preclinical AKI models
Rachel Harwood

10:00 Applications of MRI to AKI - evidence to date
Andrea Fekete

10:20 Panel discussion

10:45 - Coffee

Imaging Outside of the Kidney

Moderated by Jens Jensen and Charlotte Buchanan

11:15 Cardiac and cardiorenal syndrome
Patrick Mark

11:35 Imaging (just) Outside of the Kidney: the Renal Arteries
Annoeles de Boer

11:55 New insights into imaging techniques to improve Arterio-Venous Fistula (AVF) outcome
Michela Bozzetto

12:15 Intradialytic MRI of the Heart and Brain
Eleanor Cox

12:30 - Lunch

MRI in Clinical Research

Moderated by Per Liss and Maarten Taal

13:30 MRI in drug development pathways
Robert Unwin

13:45 Clinical trial design for MRI studies
Richard Haynes

14:00 Radiology - How will functional renal MRI be used in practice?
Doug Pendse

14:15 ADPKD and clinical trials - Progress and future directions
Roz Simms

Closing Plenary: Future Directions of Renal MRI

Steven Sourbron

15:00 - Close

MRI Methods Power Pitches

Tuesday 16:20 - 16:50

Moderated by Pim Pullens

Giulia Villa	Phase contrast magnetic resonance imaging to assess renal perfusion. Current status and practical recommendation
Suraji Serai	DTI based evaluation of renal parenchyma in children: comparison between UPJ obstruction, ARPKD and normal kidneys
Anneloes de Boer	Decreased native renal T_1 one week after gadobutrol administration in healthy volunteers
Manuel Taso	Towards free-breathing volumetric renal ASL with 3D variable dense FSE and compressed-sensing
Rebeca Echeverria-Chasco	Optimization of pseudo continuous arterial spin labeling for renal perfusion imaging
Aaron Oliver-Taylor	A multi-site round robin assessment of ASL using a perfusion phantom
Bashair Alhummiany	Interobserver variability of renal function and volume measurement in MRI renography
Benjamin Prestwich	Optimisation of Renal Sodium MRI
Dmitry Khrichenko	Functional analysis in MR Urography-made simple 2019 update
Dmitry Khrichenko	Multi-parametric 3d rendering to detect crossing vessels with fMRU
Charlotte Buchanan	UK renal imaging network: MRI acquisition and processing standardisation (UKRIN-MAPS)

Image Processing and Artificial Intelligence Power Pitches

Tuesday 17:30 - 18:00

Moderated by Frank Zoellner

Kanishka Sharma	Motion Correction with a Model Target (MoCoMo): A universal approach for quantitative renal MRI?
Joao Periquito	Unbiased MRI assessment of renal tubular volume fraction with data-driven IVIM: initial experience
Lu-Ping Li	Comparison of TLCO and ROI methods for BOLD MRI analysis
Mina Jafari	ASKDCNN: automatic segmentation of kidneys using a novel deep convolutional neural network
David Morris	Segmentation of kidney perfusion maps using K-Means – initial results
Fábio Nery	Quantification of renal microscopic fractional anisotropy using multidimensional diffusion MRI
Alena-Kathrin Schnurr	Comparing sample mining schemes for CNN kidney segmentation in T_1w MRI
Alexander Daniel	Automated renal segmentation in healthy and CKD subjects using fully convolutional neural networks

MRI Applications Power Pitches

Wednesday 11:45 - 12:30

Moderated by Paul Hockings

Alexander Daniel	The Effects of Fixation and Age on MRI Measurements of Ex-Vivo Kidneys
Mohamed Abou El-Ghar	Computer aided diagnosis using BOLD-MRI in early assessment of transplanted kidney
Julia Stabinska	Optimized CEST MRI for functional assessment of transplanted kidney at a clinical 3T MRI system
Praneshan Moodley	Single centre study comparing split function and size disparity of live kidney donors
Pietro Irrera	Mapping the dysregulation of renal acid-base homeostasis upon sepsis-induced shock by CEST-MRI
Rianne Schutter	Ex vivo magnetic resonance imaging during normothermic machine perfusion – developing a novel non-invasive tool to assess donor kidney quality
Pauline Hall Barrientos	Evaluation of transplant renal vascular disease by 4D flow
Keith Gills	Multi-parametric MRI in the early kidney transplant period: Correlation with clinical parameters and follow-up
Anna S. Li	Mapping compensatory renal hypertrophy and hyperfiltration in living kidney donors using multiparametric magnetic resonance imaging
Per Eckerbom	Circadian fluctuations in renal blood flow correlated to urinary output parameters
Christopher Bradley	Renal cortex T_1 for assessment of liver disease severity
Ilona Dekkers	The effect of glycemic control on renal triglyceride content measured by ^{1}H-MRS in patients with type 2 diabetes mellitus

Short Term Scientific Missions

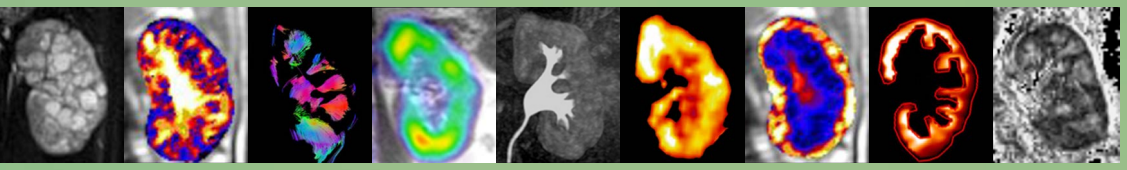
Wednesday 12:30 - 12:45

Moderated by Paul Hockings

Jorge Chacon-Caldera	Dissolved hyperpolarized Xenon-129 MRI in human kidneys
Rebeca Echeverria-Chasco	Implementation of near-identical sequences for renal ASL in scanners from three vendors
Marcos Wolf	Renal magnetic resonance elastography: New gravitational transducer to assess renal stiffness

Invited Speaker Biographies

In alphabetical order



Eric Bechle

Eric Bechler is a third year PhD student in the Department of Diagnostic and Interventional Radiology at the University Hospital Düsseldorf. Mr. Bechler holds a master's degree in medical physics from the Heinrich Heine University in Düsseldorf, Germany.

His doctoral research investigates quantitative susceptibility mapping (QSM). He focuses on the human abdomen, especially the kidney. In his recent work, he determined the best phase unwrapping algorithm for QSM in the abdomen. Currently Mr. Bechler is investigating the usability of QSM to detect different diseases of the kidney.

Peter Boor

Professor Peter Boor received his medical and scientific training at the Medical Schools of Bratislava in Slovakia and Aachen Germany. His focus on kidneys and kidney disease pathology and pathophysiology developed very early during his medical studies and was further expanded in various departments at the Comenius University in Bratislava Slovakia and the RWTH University in Aachen. Peter Boor is a senior pathologist with focus on renal pathology at the Institute of Pathology in Aachen with a dual appointment at the Department of Nephrology in Aachen. Since 2018 he was appointed as chair of Translational Nephropathology at the Institute of Pathology in Aachen.

Professor Boor is a member of several national and international societies of pathology, nephrology and renal pathology. He received several prestigious awards from these societies. His group, the LaBooratory of Nephropathology, was established in 2010 and focuses on in vivo animal modeling of kidney diseases and translational research, with particular focus on diagnostic biomarkers, imaging, digital pathology, and novel treatment targets for CKD, renal fibrosis, renal vasculature and proliferative glomerulonephritides. His scientific work encompasses about 140 original papers, reviews and editorials, and 4 book chapters.

Anneloes de Boer

Anneloes de Boer has a background in both applied physics and medicine. During her medicine studies she was involved in research at the nephrology department on renal denervation as a treatment for hypertension. In the analysis of MRI scans of hypertensive patients, her physics background was of great use. She obtained an Alexandre Suerman stipend which allowed her to continue her research on kidney MRI as part of an MD-PhD project after her graduation. During her PhD, she focused on validation of multiparametric kidney MRI in healthy volunteers and transplant patients.

Currently, she is involved in a study on functional MRI to assess the renal effects of SGLT2 inhibitors in diabetes. She was granted funding by the COST action PARENCHIMA for a research fellowship at Steven Sourbron's group on modelling of DCE MRI.

Michela Bozzetto

Michela Bozzetto was born in Bergamo on January 5th, 1989. She graduated in Biomedical Engineering - Biomechanics and Biomaterials, at Politecnico di Milano in 2014. Her main expertise is in the fields of imaging, 3D model reconstruction, computational fluid dynamics and computational modeling. She is involved in a number of national and international research initiatives aimed at improving surgical planning and surveillance of the vascular access for hemodialysis, as well as elucidating mechanisms driving vascular remodeling. She is the technical expert for the multicentric AVF.SIM clinical study, aimed at assessing the usability and the efficacy of a computational model predicting the clinical outcome of the vascular access for hemodialysis. Between October 2014 and September 2017 she was full-time researcher in the Medical Imaging Unit of the Department of Bioengineering at Istituto di Ricerche Farmacologiche Mario Negri IRCCS.

Since October 2017 she is a PhD student in Engineering and Applied Sciences at University of Bergamo. Besides her research activities, she is involved in the teaching activities for Bachelor students of Engineering and Management for Health. Since 2018, she is member of the Core team of yESAO, the group of young researchers of the European Society of Artificial Organs in charge of the organization and management of the annual meeting of the young group of ESAO Society. She is author of 20 articles and conference papers.

Anna Caroli

Dr Anna Caroli, PhD, graduated in Mathematics cum laude in 2003 from Milan University, Italy, and got her PhD in 2010 from Maastricht University, the Netherlands, at the faculty of Health, Medicine, and Life Sciences. From 2004 to 2015 she worked as researcher at the Lab of Alzheimer's Neuroimaging & Epidemiology of the 'IRCCS San Giovanni di Dio', Brescia, Italy. In 2011 she got a permanent position as senior researcher at the Medical Imaging Unit, Bioengineering Department, 'Istituto di Ricerche FarmacologicheMario Negri IRCCS', Bergamo, Italy, and since 2012 she is leading the Medical Imaging Unit, dealing with medical image processing and analysis, renal imaging biomarkers, multiparametric MRI in Autosomal Dominant Polycystic Kidney Disease (ADPKD) and Chronic Kidney Disease (CKD) patients. Dr Caroli has been involved and is currently involved in a number of clinical trials in ADPKD and CKD (ALADIN, ALADIN2, SIRENA, SIRENA2, TOOL, ACH471-205) as image analysis responsible. Moreover, she has been involved in a number of international initiatives (ARCH-FP7-ICT-2007-2-224390; Trancyst-FP7- PEOPLE-MCA-ITN-317246; ERA-EDTA EuroCYST Initiative). She currently leads the clinical working group (WG3) of the European COST action PARENCHIMA (CA16103), which is paving the way for clinical use of renal MRI in patients with CKD. Since March 2019 she is member of the ESR European Imaging Biomarkers Alliance (EIBALL) Subcommittee. She is author of more than 70 articles and conference papers.

Eleanor Cox

Eleanor Cox is a physicist from the Sir Peter Mansfield Imaging Centre at the University of Nottingham. Her research includes development and optimisation of multiparametric MRI protocols and analysis techniques for application in the abdomen (kidneys and liver) and heart. These protocols have been used to study basic physiology and fluid balance, as well as to understand effect of disease (cardiorenal syndrome, chronic kidney disease, acute kidney injury, compensated liver cirrhosis) and also during pharmacological modulations (dialysis).

Ilona Dekkers

Ilona Dekkers, M.D., MSc, has been working as a radiologist in training at the Leiden University Medical Centre in the Netherlands. Besides clinical work, Ilona is enrolled in a PhD-programme focused on renal and cardiovascular MRI. Her research involves the application of new imaging techniques for renal MRI, as well as epidemiological analyses of associations between renal function and cardiovascular function measured by MRI.

Andrea Fekete

Associate Professor, Head of the Diabetes Research Group of the Hungarian Academy of Sciences and Semmelweis University

Scientific interest: diabetes, chronic kidney disease, preclinical drug development, biotech start-ups

Dr. Fekete is a pediatrician with a special interest in experimental diabetology and nephrology at the Semmelweis University, Hungary. She is also a leader of the research group of diabetes at the Hungarian Academy of Sciences and a member of the Hungarian Ethical Committee that supervises human research projects. She is experienced for 15 years in basic science and has more than 70 publications in leading journals of nephrology. With her biotech start-up company, she actively takes part in several drug development and R&D projects.

www.linkedin.com/in/andrea-fekete-ab63b991?trk=hp-identity-name

María Fernández-Seara

María Fernández-Seara, Ph. D., director of the Biomedical Imaging Laboratory at the Radiology Department of the Clínica Universidad de Navarra (Pamplona, Spain).

I am Associate Professor of Biomedical Engineering at the University of Navarra and Adjunct Associate Professor of Radiology at the University of Pennsylvania. I have a broad background in Magnetic Resonance Imaging techniques, with specific training and expertise in Arterial Spin labeling Perfusion MRI. From 2004 to 2006, I was a postdoctoral fellow at the Center for Functional Neuroimaging (University of Pennsylvania, Philadelphia, PA, USA) working with Dr. John Detre, who is a pioneer in the development and applications of ASL. I continue to focus in ASL perfusion MRI as mine main research line. I was the Program Director of the Perfusion Study Group of the International Society of Magnetic Resonance in Medicine (2012-14). I have chaired the ASL expert panel of PARENCHIMA.

Susan Francis

Prof Sue Francis is a physicist with 25 years' experience on developing MRI methods for biomedical applications and translation. She was awarded her PhD from Nottingham in 1998, which focussed on the development of Arterial Spin Labelling methods for studying the brain. In 2016 she was appointed to Professor of Physics. Since 2005, she has led a programme of work exploiting the capabilities of functional and anatomical high and ultra-high field MRI in neuroscience.

In 2009, she developed a programme of imaging in quantitative imaging of the body, and now leads work at Nottingham on the development of MRI methods to study renal and liver function. She is a co-investigator of the Nottingham NIHR Biomedical Research Centre (BRC). She co-chairs the UK Renal Imaging Network (UKRIN) and leads the UKRIN-MAPS MRC Partnership grant to develop a harmonized approach in renal MRI across MR vendors.

Her research interests include the development and application of multiparametric quantitative MRI methods, with a particular interest in Arterial Spin Labelling (ASL) methods to non-invasively assess tissue perfusion in the brain, kidney and liver. She has published widely on the application of renal MRI to study physiological modulations and disease pathophysiology. More recently this includes using sodium MRI to study sodium distribution in the kidney, muscle and skin.

Stephan Garcia

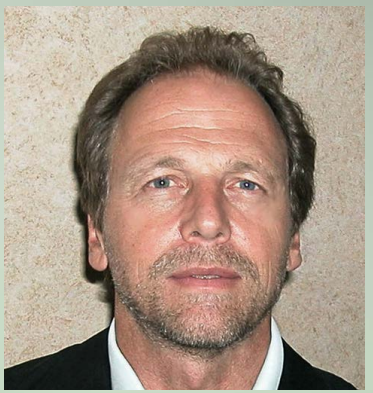
Stephan is a radiologist at Charité – University Hospital Berlin since 2013 and a member of the elastography workgroup under supervision of Prof. Ingolf Sack.

His research focus is on magnetic resonance and ultrasound elastography of abdominal organs, particularly native kidneys and renal transplants. With support of the German Research Foundation (DFG) he developed magnetic resonance and ultrasound elastography setups for kidneys, and their application to clinical research with focus on chronic kidney diseases. He enjoys the challenge to improve multiparametric renal imaging, and to get a better understanding of renal diseases.

Keith Gillis

Keith Gillis is a consultant nephrologist and honorary senior clinical lecturer, working at the Glasgow Renal and Transplant Unit in the Queen Elizabeth University Hospital. Developing an interest in functional renal imaging during his PhD, he has continued his research into the clinical application of multi-parametric renal MRI.

Nicolas Grenier



Nicolas GRENIER is professor of radiology, head of urogenital and vascular radiology in the hospital Pellegrin in Bordeaux.

Prof. Grenier was graduated and completed his residency in radiology at the University of Bordeaux. He did fellowships in pediatric radiology in the Université de Montreal and in MRI in Philadelphia at the University of Pennsylvania.

His main fields of interest have always been MR imaging and ultrasounds in urogenital and vascular domains, with special interest in functional and molecular aspects of renal parenchymal diseases. He developed methods of renal functional MR imaging and of intrarenal cellular targeting with nanoparticles of iron oxide for inflammatory mapping and for tracking labeled mesenchymal stem cells. He also evaluated the role of US-elastography in diffuse renal diseases for the diagnosis of fibrosis.

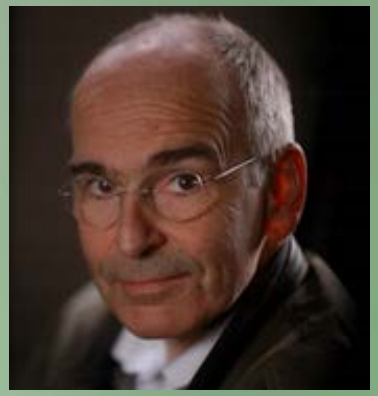
He is also active in the field of urologic oncology with the development of multiparametric MRI of renal tumors and partic-ipates to the development of a new bifunctional instrument for diagnosis of prostate cancer, combining ultrasound and optical imaging, for future innovative theragnostic approaches.

He has authored more than 160 articles in peer-re-viewed journals and 40 book chapters.

Prof. Grenier is a co-funding and past-President of the French Society of Urogenital Imaging. He served as President of the European Society of Urogenital Radiology (ESUR) from 2000 to 2002, and as President of the European Society of Molecular and Functional Imaging in Radiology (ESMOFIR) from 2011 to 2014.

At a national level, he served in the French Academic College of Radiology (CERF) as a board member during nine years, and as President during three years, contributing to improve the structuration of clinical research in radiology and of education for residents.

Norbert Gretz



Professor Norbert Gretz is the head of the Medical Research Center of the Medical Faculty Mannheim, University of Heidelberg, and acting manager of the Institute for Medical Technology, a combined institute of the Medical Faculty Mannheim, University of Heidelberg, and the University of Applied Sciences Mannheim

.

After his medical studies at the Ruprecht-Karls University Heidelberg Norbert Gretz worked as a physician at several hospitals in Germany and abrdoad until he became senior physician at the University Hospital Mannheim. Then he was appointed professor for experimental medicine at the University of Heidelberg and took the management positions in two research institutions. He is project head of several national and international scientific research programmes and is a valuable expert evaluator and consultant for several journals and expert associations. His key research areas are photobiomodulation, chronic wounds, stem cell therapy, optical tissue clearing, gene expression profiling and big data handling.

Rachel Harwood

Rachel is dedicated to improving the health of children through her clinical and academic work. She graduated in Medicine and Surgery with Distinction from Newcastle University in 2008 and went on to apply herself to clinical and surgical training. Throughout this time she took an active interest in clinical research, making international presentations and publications. In 2013 she topped the national interviews for Paediatric Surgery and chose to undertake her training in the North-West, in centres renowned for their high quality training and research. Rachel continues to publish papers on subjects including Mitrofanoff formation and Haemolytic Uraemic Syndrome and has become actively involved with the Stem Cell Research Group of Professor Murray, Mr Kenny and Dr Wilm at the University of Liverpool.

Rachel is currently pursuing her passion for improving children's health outcomes through her PhD which she started in 2017. She is investigating the use of human Umbilical Cord Mesenchymal Stromal cells and their derived extra-cellular vesicles for ischaemic acute and chronic kidney disease. The project is designed to accelerate the translation of these therapies into clinical practice. Key outcomes include the short and long term safety of these therapies; the timing, route and dose of administration; as well as exploring the mechanisms of action, particularly focusing on their interaction with macrophages.

In her spare time Rachel enjoys spending time with her family and friends, doing yoga at sunset, travelling the world and reading a good book!

Richard Haynes

Richard Haynes did his pre-clinical medical studies in Cambridge before moving to Oxford for his clinical studies and qualified in 2000.

He came to CTSU for a period of "out of programme" research in 2006 to work on the HPS2-THRIVE trial with Prof Jane Armitage. He completed his training in renal medicine in 2011 and was appointed as an honorary consultant at the Oxford Kidney Unit. Shortly after that he was appointed to the MRC Programme Leader track and he is now Programme Leader in the MRC Population Health Research Unit for the programme in Randomised Trials in Cardiovascular and Metabolic Disease.

Bente Jespersen

Professor Bente Jespersen is Dept. Chair of Renal Medicine, AU and Aarhus University Hospital.

Initially studying medicine at Aarhus University, Demark. Bente has held several positions including more recently, Consultant and Associate Prof., Dept. of Renal Medicine, Odense University Hospital, DK and Associate Prof., Cardiovascular and Renal Research Unit, University of Southern Denmark. Current appointed as Staff Specialist, Dept. of Renal Medicine, Rigshospitalet, Copenhagen, DK. Bente research areas include both clinical research, e.g. minimisation of drugs and prevention of cancer, infections and cardiovascular disease in renal transplantation, and also experimental research with pig models, presently for prevention of ischaemia reperfusion injury in renal transplantation using mesenchymal stromal cells and machine perfusion of the kidney. Principal investigator and initiator of the finalised multicentre studies SAFIR (angiotensin II receptor antagonist in haemodialysis), CONTEXT (remote ishaemic conditioning in renal transplantation), and the ongoing MePEP study (MEsenchymalstem cell administration and normothermic machine PErfusion in Porcine renal transplantation) with involvement of partners in Oxford, Rotterdam and Groningen. Presently four international PhD students are working with the Jespersen Group in Aarhus with two appointed postdocs.

Maria Kaisar

Dr Maria Kaisar obtained her DPhil in Transplantation Science from the Nuffield Department of Surgical Sciences, University of Oxford. Her interests lie in basic and translational research to better understand the biological mechanisms that lead to organ injury or repair. Her collaborative work, within the National Health Service Blood and Transplant and the University of Oxford, focuses on the development of novel diagnostics of donor organ quality. Maria is a member of the National Management Team and the Steering Committee of the UK Consortium of Quality in Organ Donation (QUOD). She is a Board Member of the Basic Science Committee of the European Society of Organ Transplantation (ESOT) and a member of The Transplantation Society (TTS) Educational Committee.

Phil Kalra

Professor Philip Kalra graduated from Cambridge University and is Professor of Nephrology in Salford and the University of Manchester. He has major research focus on renovascular disease, cardiovascular disease in CKD and CKD progression and he leads the research team in Salford. He was Academic Vice President of the UK Renal Association until September 2019 and was Chair of the UK Kidney Research Consortium and NIHR CRN Renal Disorders group until late 2018. He has been involved in development of several large UK clinical trials in nephrology and cardiology, including the ASTRAL, PIVOTAL and IRONMAN trials, and he has played a role in amalgamating Cardio-Renal education and research within the UK.

Dario Lango

Dario Longo (21/12/1976) received the M.Sc. degree in Chemistry and Pharmaceutical Technologies in 2002 and the Ph.D. degree in Biochemistry Sciences at the University of Turin in 2007. Since 2003 he worked at the Department of Chemistry developing computational approaches for improving the contrast efficiency of MRI Gd-based contrast agents. In 2008 he moved to the Department of Molecular Biotechnology and Health Sciences at the University of Torino developing novel MRI-CEST pH-sensitive contrast agents. In 2014 he become a Junior Group Leader at the Molecular Imaging Center of the University of Torino developing novel contrast agents and procedures for the non invasive assessment of tumor pH and vascularization at preclinical level. In 2018 he got a permanent position as First Researcher at the Institute of Biostructures and Bioimaging (IBB) of the Italian National Research Council (CNR). His research activities deal with the development of new contrast agents (Gd complexes, CEST) and approaches for Magnetic Resonance Imaging (MRI) in-vivo applications at preclinical level focused on i) the characterization of tumor microenvironment (pH, metabolism and vascularization), ii) the non-invasive assessment of treatment response iii) evaluating renal pH imaging to assess kidney diseases. He is coauthor of more than 60 publications and book chapters in peer reviewed international journals and of four patents in developing new agents and procedures for non-invasive in vivo pH measurement and its exploitation. He is a member of the European Society for Molecular Imaging.

Alexandra Ljimani

Alexandra Ljimani is a radiologist at the Department of Diagnostic and Interventional Radiology, University Hospital Düsseldorf.

Alexandra studied medical physics and medicine at Heinrich-Heine-University Düsseldorf. She specialises in modern cross-sectional imaging (3T MRI, MD-CT) and renal imaging and her research interests include functional MR techniques (DWI, DTI, ASL), metabolic MR techniques (CEST, Na-Imaging), fast MR sequences and renal MR imaging.

Alexandra is co-chair of the DWI expert panel (EU PARENCHIMA Project) and is a member of German Society for Radiology (DRG), European Society of Radiology (ESR), Radiological Society of North America (RSNA) and European Society for Magnetic Resonance in Medicine and Biology (ESMRMB).

Partick Mark

Patrick (Paddy) Mark is Professor of Nephrology and Honorary Consultant Nephrologist at the Glasgow Renal and Transplant Unit based at the Queen Elizabeth University Hospital Glasgow.

He was appointed as Clinical Senior Lecturer in 2011 following clinical training in Medicine and Nephrology combined with a Clinical Lecturer post between 2006-2011. He was promoted to Reader in 2015 and to Professor in 2018. He leads the United Kingdom Cardio-Renal Clinical Study Group, as part of the United Kingdom Kidney Research Consortium. He is the Chief Scientist Office Scotland Clinical Lead for Renal Research. His PhD, awarded the Bellahouston Medal for outstanding thesis by medical graduate, was funded by a British Heart Foundation Junior Clinical Fellowship. He graduated in Medicine in 1999 as Brunton Medallist awarded to the highest achieving student that year.

Cyril Moers

Dr. Moers is a transplant surgeon and assistant professor at the University Medical Center Groningen.

His research covers a whole spectrum of clinical and pre-clinical studies in kidney transplantation, focusing on interventions during organ preservation to better conserve organ quality and to quantify the impact that donor characteristics have on post-transplant outcome. He has authored several key publications on the topic of ex vivo renal machine perfusion, two of which appeared in The New England Journal of Medicine. His line of research has a translational character and focuses on pre-transplant organ resuscitation and evaluation. His experimental research has evolved from hypothermic towards normothermic machine perfusion of deceased donor kidneys and the UMCG Surgical Research Laboratory lab is now one of the leading centers in the world for ex vivo renal perfusion. Dr. Moers recently received an ERC Starting Grant to conduct studies which aim to better understand ex vivo renal physiology and discover pre-transplant multi-omics and radiomics (MRI) based biomarkers which can predict post-transplant outcome.

Armin Nagel

Armin Nagel is a professor for functional and metabolic MR imaging at the university of Erlangen-Nürnberg (Germany).

His work focuses on magnetic resonance imaging of non-proton nuclei such sodium, potassium, chloride and oxygen. With his research group Armin Nagel is developing new image acquisition and reconstruction techniques for ultra-high field magnetic resonance imaging. He enjoys working in an interdisciplinary environment with physicists and physicians that fosters fast translation of new technical developments into clinical research applications.

Aghogho Odudu

Dr Aghogho Odudu works as a consultant in acute and renal medicine at Manchester University Hospitals Foundation Trust since 2019.

He graduated in Medicine from the University of Manchester in 2001. He completed the Cambridge University Hospitals Training Rotation in Medicine and became a Member of the Royal College of Physicians in 2004. After training in Paediatric Nephrology and Critical Care Medicine in Manchester he was appointed in 2007 as Registrar in Nephrology and General Medicine in the Yorkshire Deanery. He achieved a Post Graduate Certificate in Education with Merit in 2010, a British Heart Foundation Clinical Research Training Fellowship in 2011 and a PhD in 2013 supervised by Professor Chris McIntyre using cardiovascular magnetic resonance imaging to characterise cardiac disease in haemodialysis patients at the University of Nottingham.

Dr Odudu won the International Society of Blood Purification Best Abstract Prize in 2010 and The University of Manchester's Daniel Turnberg Cup for Trainee Academic Clinicians in 2014. In 2014 he was awarded an National Insitute for Health Research Clinical Lectureship in Nephrology. He has conducted peer review for several journals and been a grant reviewer for Kidney Research UK and the British Heart Foundation. His current research interests include Diabetic Kidney disease and he is conducting a study co-funded by The Academy of Medical Sciences using renal functional MRI in patients with different stages of Diabetic Kidney Disease.

Doug Pendse

Doug Pendse is a Consultant Radiologist at University College London Hospitals and Honorary Associate Professor at UCL.

Doug is a diagnostic and interventional radiologist, specialising in urological imaging. His research interests include minimally invasive treatment of prostate cancer (focal therapy, brachytherapy), prostate MRI and functional imaging in abdominal and urological disease.

Pottumarthi Prasad

Pottumarthi Prasad has a Ph.D. in Radiological Sciences, and is currently a Research Scientist at NorthShore University HealthSystem and holds academic appointments of Professor at University of Chicago (Radiology) and Northwestern University (Biomedical Engineering).

He is a Fellow of the International Society of Magnetic Resonance in Medicine and certified by the American Board of Medical Physics in MRI. In the last two decades, his primary research interest has been functional renal MRI. He has applied these methods to pre-clinical models, healthy human individuals and some of the early translational studies to patients. He serves as an International Observer on the PARENCHIMA Management Committee.

John Prowle

Dr Prowle is a Senior Clinical Lecturer in Intensive Care Medicine within the Critical Care and Perioperative Medicine Research Group at Barts and the London School of Medicine and Dentistry, Queen Mary University of London and is an Honorary Consultant Physician in Intensive Care Medicine and Nephrology at the Royal London Hospital, Barts Health NHS Trust, London, UK.

Dr Prowle graduated in medicine from the University of Cambridge in 1999 and undertook Doctoral Research under the supervision of Prof Rinaldo Bellomo in Melbourne, Australia leading to the award of his research doctorate in 2013.

Dr Prowle's academic interests include the Pathogenesis, Diagnosis and Treatment and Outcomes of Acute Kidney Injury, Continuous Renal Replacement Therapies in the ICU, Fluid Therapy and Medical Complications of Major Surgery. He has co-authored over 100 peer-reviewed publications and book chapters, including chapters related to Acute Kidney Injury in the latest editions of the Oxford Textbook of Clinical Nephrology and the Oxford Textbook of Critical Care.

Menno Pruijm

Dr Menno Pruijm is full time staff member and head of the dialysis unit of the Service of Nephrology and Hypertension of the University Hospital of Lausanne, Switzerland. He is also Privat Docent at the Division of Medical Sciences at the University Hospital of Lausanne.

Dr Pruijm obtained his Medical Degree summa cum laude in 1998 in Leuven, Belgium, specialized in Internal Medicine in Leiden, the Netherlands and in Nephrology in Lausanne. He is past president of the ultrasound committee and member of the dialysis committee of the Swiss Society of Nephrology. He is one of the main drivers of several cohort studies, and has a large expertise in renal imaging, including renal ultrasound and functional renal MRI. He is an international leader in the field of BOLD-MRI and part of the European Union COST Action ('PARENCHIMA'). Since 2010, he receives support from the Swiss National Science Foundation, Swiss Society of Nephrology, and the Swiss and European Society of Hypertension for his work on renal MRI. Dr Pruijm is also involved in many industry-driven studies, focusing on the influence of drugs on renal hemodynamics. He has published more than 100 peer-reviewed papers.

Sophie de Seigneux

Sophie de Seigneux is a nephrologist MD PhD trained in Switzerland, Denmark and France. She is currently assistant professor at Geneva University Hospital.

Her research interests are kidney disease pathophysiology and diagnosis. Together with Jean-Paul Vallee in Geneva, she started a program on the use of MRI fort he diagnosis and prediction of fibrosis and renal function evolution in CKD patients.

Nicholas Selby

Dr Selby studied medicine at the University of Nottingham, graduating in 1998, and after completing post-graduate training in the East Midlands was appointed a full-time NHS consultant nephrologist at the Royal Derby Hospital in 2009. In 2015 he was appointed Associate Professor of Nephrology at the University of Nottingham, based in the Centre for Kidney Research and Innovation (www.nottingham.ac.uk/research/groups/renal), Royal Derby Hospital Postgraduate Medical School.
Dr. Selby is a clinical academic with primary interests in Acute Kidney Injury (AKI), Magnetic Resonance Imaging (MRI) of the kidney and the haemodynamic consequences of dialysis. He led the development of one of the first e-alert systems for AKI in the UK and is CI on several investigator-instigated studies in these areas including the Tackling AKI study. Since 2011 Dr Selby has been awarded peer reviewed grant funding from MRC, the Health Foundation, Kidney Research UK and British Renal Society. He has published over 75 peer-reviewed articles. Dr Selby has several national AKI roles, including leadership of the AKI Clinical Study Group that sits within the UK Kidney Research Consortium, the co-chair of the UK Renal Imaging Network and programme board of the NHS England ‘Think Kidneys’ programme.

Roz Simms

Roslyn Simms is a Consultant Nephrologist in Sheffield Kidney Institute and Honorary Senior Lecturer in the University of Sheffield.

Her specialist interest is in inherited kidney diseases, particularly autosomal dominant polycystic kidney disease (ADPKD). She also shares a specialist regional treatment clinic for patients with renal angiomyolipomas and tuberous sclerosis. Her qualifications include an intercalated B.Sc and MBChB (University of Glasgow) and a PhD in zebrafish models of inherited cystic kidney disease (Newcastle University 2013). During the last five years her research has translated into clinical work focusing on defining progression in patients with early ADPKD involving structural and functional magnetic resonance imaging (fMRI). Currently she is a member of the steering group for the James Lind Alliance for the ADPKD Priority Setting Partnership.

Steven Sourbron

Steven Sourbron is a Lecturer in Medical Physics at the University of Leeds since 2009 and heads the Leeds Imaging Biomarkers Group which focuses on development, validation and translation of MRI biomarkers.

Current projects focus mostly on applications in liver and kidney and include for instance the BEAt-DKD project (www.beat-dkd.eu) on predicting disease progression in diabetic kidney disease, the TRISTAN project (www.imi-tristan.eu) on imaging biomarkers of drug toxicity, the UKRIN-MAPS project which will develop a UK-wide national infrastructure for advanced renal MRI in clinical trials, and the HEPARIM project on risk assessment for major hepatectomy. He is also chair of the COST action project PARENCHIMA on imaging biomarkers for chronic kidney disease (www.renalmri.org). Prior to Leeds, he worked as post-doc in the Radiology department of the Ludwig-Maximilian University of Munich (2005-2010), and as PhD student in the radiology department of the Vrije Universiteit Brussel (VUB , 2001-2005). He studied physics at the VUB and industrial design at the University of Antwerp. From 4 November 2019 onwards he will be taking up a Chair in Medical Imaging Physics at the University of Sheffield.

Maarten Taal

Maarten Taal graduated from the University of Cape Town Medical School, South Africa, in 1987. After completing his post-graduate training in internal medicine and nephrology at Groote Schuur Hospital, Cape Town, he joined the Laboratory of Kidney and Electrolyte Physiology at Brigham and Women's Hospital, Boston, USA under the directorship of Barry M. Brenner, MD.

His research focused on mechanisms underlying the progression of chronic kidney disease and earned him a Doctor of Medicine degree. He subsequently moved to the United Kingdom where he was appointed a Consultant Renal Physician at Derby City General Hospital (now Royal Derby Hospital) in 2002 and Honorary Associate Professor at the University of Nottingham in 2011. He was appointed Professor of Medicine in the Division of Medical Sciences and Graduate Entry Medicine, University on Nottingham in April 2014, where he leads the Centre for Kidney Research and Innovation. His current research interests include Chronic Kidney Disease Progression, Diabetic Nephropathy, Renal Osteodystrophy and Cardiovascular Disease in CKD patients. He has a career-long interest in Chronic Kidney Disease (CKD) and co-authored the Renal Association's Clinical Practice Guidelines for CKD. He serves as an Editor for "Brenner and Rector's The Kidney", Section Editor for "Current Opinion in Nephrology and Hypertension" and Academic Editor for "PLOS Medicine". He is Chair of the UK Kidney Research Consortium CKD Clinical Study Group and Immediate Past President of the British Renal Society.

Manuel Taso

Dr. Taso was trained in Physics and Chemistry before obtaining his Ph.D. from Aix-Marseille University (Marseille, France), focused on characterization of the spinal cord morphology and microstructure using multi-parametric MRI (diffusion, magnetization transfer) and original image analysis tools dedicated to spinal cord imaging (templates, segmentation tools). Since 2016, he has been a research fellow under the supervision of Dr. David Alsop in the Radiology department at the Beth Israel Deaconess Medical Center and Harvard Medical School in Boston. His research interests are geared towards non-contrast perfusion imaging using Arterial Spin Labeling (ASL) with a focus on abdominal applications (kidneys, pancreas). Some of his work include pulse-sequence development for improved ASL robustness, but also image acceleration using parallel-imaging and Compressed-Sensing for motion mitigation to enable free-breathing abdominal acquisitions and facilitate translation into clinical practice.

Robert Unwin

I am a University of Southampton medical graduate, and I was an MRC Training Fellow and later Wellcome Trust Senior Clinical Research Fellow at St Mary's Hospital Medical School in London, and a Research Affiliate in the Department of Cellular and Molecular Physiology at Yale University, New Haven. On returning to the UK, I was appointed a Senior Lecturer in Clinical Pharmacology at the Royal Postgraduate Medical School (Hammersmith Hospital) and I later moved to UCL, eventually becoming Professor of Nephrology and Physiology in 1997. I have since been Head of the UCL Centre for Nephrology, Middlesex Hospital, and later at the Royal Free Hospital, and also Head of the Research Department for Internal Medicine. Since 2017 I have been working in AstraZeneca Biopharmaceuticals R&D in both the renal science and early clinical development groups for kidney disease as a Senior Medical Director, and prior to that, from 2014-17, I was on secondment from UCL as a Chief Scientist in Cardiovascular, Renal & Metabolism (CVRM) bioscience. My clinical interests have been mainly in renal tubular disorders and renal stone disease, as well as renal tubular GI transport physiology, and more recently in early drug development. I have published on various aspects of renal physiology and pathophysiology, hypertension, renal tubular disorders, and renal stone disease.

Jean Paul Vallee

JP Vallée MD, PhD is currently the head of the unit of cardiovascular radiology of the diagnostic department of the Geneva University Hospital which is performing cardiac MRI including stress perfusion imaging as well cardiac CT.

Apart from his clinical activity, JP Vallée is leading a translational research group on the development of new quantitative methods in the cardiovascular and renal field. His group has developed a strong expertise in imaging small animals on clinical MR systems particularly to measure cardiac function and infarct size in rodents. They have developed a DWI method to measure renal fibrosis using the RESOLVE sequence that has been successfully validated on rodent and on patients. This method is based on a new parameter ΔADC corresponding to cortico-medullary difference of the apparent coefficient diffusion ADC that is highly correlated to fibrosis observed on the biopsy specimens (L. Berchtold et al., Nephrology, dialysis, transplantation, in press, (2019))

Jim Wild

Professor Jim Wild joined the University of Sheffield in 2000 to set up the technology of Hyperpolarised gas lung Magnetic Resonance Imaging (MRI). Before that he was a postdoctoral researcher at the NMR group at the University of Alberta (1998-2000) working on high field strength imaging and spectroscopy methods. His PhD was in ^{1}H MR spectroscopy at the University of Edinburgh (1995-1998).

His research interest is the physics and engineering and clinical applications of hyperpolarised gas (^{3}He and ^{129}Xe) and proton MRI in the lungs and pulmonary vasculature.

Physics and engineering projects include:

- Rapid acquisition methods for imaging of inhaled hyperpolarised gases using compressed sensing, steady state free precession and parallel imaging.
- Techniques for simultaneous imaging of ^{1}H, ^{3}He and ^{129}Xe in the lungs.
- RF coil hardware engineering for ^{3}He and ^{129}Xe lung MRI.
- ^{3}He and ^{129}Xe MRI at different magnetic field strengths.
- Spin exchange optical pumping physics for polarisation of ^{3}He and ^{129}Xe.
- Measuring and modelling gas flow and diffusion in the lungs; physiological models of alveolar geometry and gas exchange.

Frank Zoellner

Frank Zöllner received the diploma and a PhD degree (Dr.-Ing.) in computer science from the University of Bielefeld, Germany,in 2001 and 2004,and the venia legendi in medical physics from the Heidelberg University in 2014, respectively. In 2017 he became adjunct Professor for medical physics at the University of Heidelberg.

After his undergraduate studies in computer sciences he joined the Applied Computer Science group in 2001 and worked towards his PhD within the bioinformatics graduate program (Graduiertenkolleg 'Bioinformatik') until 2004. From 2004 until 2006 he worked as a post-doctoral researcher in the BMBF project ALPIC . From 2006 until 2007 he was a researcher at the Section of Radiology , Institute for Surgical Sciences, Haukeland University Hospital and the Neuroinformatics and Image Analysis Group , Section for Physiology, Department of Biomedicine at the University of Bergen, Norway.

In 2008, Dr. Zöllner joined the Chair of Computer Assisted Clinical Medicine as a post-doctoral researcher. He leads the research group MRI and Medical Image Analysis and since 2014 he is deputy chair of Computer Assisted Clinical Medicine.

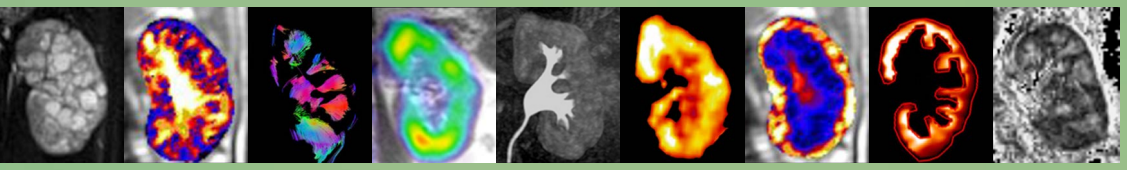
Since 2019 he leads the joint project "Molecular Innovative Imaging for Individualized Diagnostics" (M2IBID) within the "Mannheim Molecular Intervention Environment (M²OLIE)" Research Campus which is one of nine currently funded research projects as part of the "Forschungscampus – Public-Private Partnership for Innovation" competition awarded from the German Ministry of Education and Research.

His research interests lie in the fields of pattern recognition, image processing and imaging techniques. In particular, he is interested in applying computational methods from pattern recognition, image analysis to the fields of molecular imaging and medical image analysis.

Dr. Zöllner is a member of the IEEE EMBS Society and International Society for Magnetic Resonance in Medicine (ISMRM).

Invited Speaker Abstracts

In order of the talks in the program schedule



Update from the PARENCHIMA programme

Anna Caroli
Istituto di Ricerche FarmacologicheMario Negri IRCCS

The COST Action PARENCHIMA coordinates the research of European groups working on renal MRI, trying to unlock renal MRI biomarker potential by improving their standardisation and availability, and by generating strong multicentre clinical evidence of biological validity and clinical utility. PARENCHIMA is an open and growing network, counting to date more than 230 researchers from 26 countries.

To improve the standardisation in the acquisition and analysis of renal MRI data and establish clear reference baseline for further development and technical and clinical validation, WG1 wrote a comprehensive book on preclinical renal MRI and developed detailed recommendations on clinical renal MRI acquisition protocols, based on consensus among international experts.

To answer the need for software tools to analyse renal MRI data and lack of access to data, WG2 is implementing an open-source toolbox consisting of a coherent set of software and data.

After publishing a series of papers on MRI biomarkers in renal disease, WG3 set up a study documentation repository to help designing new study protocols and is coordinating smaller scale studies, with special focus on ADPKD, transplantation, and CKD.

Moreover, PARENCHIMA is trying to introduce renal MRI to a wider audience by organising specific workshops and international conferences.

Update from the United Kingdom Renal Imaging Network

Susan Francis
University of Nottingham

The UK Renal Imaging Network (UKRIN) was formally set up in 2016 in collaboration with Kidney Research UK (KRUK), to bring together UK centres dedicated to the development and application of MRI methods for the study of the kidney. This talk will outline the ongoing programme of work of UKRIN and its goal. Further, UKRIN-MAPS (MRI Acquisition and Processing Standardisation), an MRC Partnership framework of UKRIN sites, which aims to share expertise and build capacity in renal MRI by developing harmonized protocols across MR field strengths (1.5 and 3T) and MR vendors will be presented.

UKRIN-MAPS aims to set up harmonised acquisition protocols, acquire normative renal MRI data in a healthy subject cohort, develop data analysis methods and implement an online data sharing platform (XNAT). We will develop and validate a software framework for analysis and quality assurance (QA) of multi-parametric renal MRI data and its cross-site sharing. The repeatability of the multi-parametric protocol will be assessed using a "travelling kidney" study, scanning healthy subjects across multiple sites, as well as performing repeat scans at their home site. This will allow determination and calibration of any between-site differences and assessment of within-site stability. Phantom QA data will also be acquired on each scan day. Additional healthy subject data will be acquired which, when pooled with the travelling kidney study, will result in 50 healthy subjects' data at both 1.5 T and 3T.

For more information see poster 11.

Perspectives from NIDDK Renal Imaging Workshop

Pottumarth Prasad
NorthShore University HealthSystem

National Institute of Diabetes and Digestive and Kidney Diseases organized a Renal Imaging Workshop in July 2018 with a primary goal of charting a path forward for functional renal imaging. It was meant to provide an overview of current capabilities, learn about opportunities from other field and discuss challenges in translation to the clinic.

The program committee included investigators active in the field of renal imaging and imaging experts at the National Institutes of Health. The two day program was constructed with a combination of talks by international experts, poster sessions, and breakout sessions. The breakout sessions offered the opportunity for open discussions with all the attendees which were then summarized by the session leads.

The two day workshop on the NIH campus was attended by about 150 members including imaging scientists, nephrology investigators, trainees and young investigators. The agenda can be accessed at: https://www.niddk.nih.gov/news/meetings-workshops/renal-imaging-workshop?agenda . Some of the speakers had consented for their presentations to be made available and so you can see the links.

This presentation will provide you a broad overview of the program and summarize some take home messages that may be relevant to the PARENCHIMA members.

Acknowledgements

Daniel Gosset of NIDDK for providing draft report

Introduction to MRI techniques (MRI for the non-expert)

Nicolas Grenier
Service de Radiologie, CHU de Bordeaux, Université de Bordeaux

Renal physiology is complex with two compartments functioning under highly different conditions. The cortex is highly perfused with a high level of oxygen whereas medulla shows a poor perfusion level and works under hypoxic conditions. Water movements are multiple along the nephrons to maintain normal homeostasis. Glomerular filtration rate is a major marker of renal function, but its measurement is complex to obtain in clinics.

Renal MR imaging has the potential to provide several functional and structural biomarkers useful for patient management in acute and chronic diseases developed in native and transplanted kidneys. Compared to ultrasound and computed tomography MRI is the most flexible technique with the highest range of applications, evidencing many types of tissue changes such as perfusion, oxygenation, water diffusibility, cellular phagocytic activity, tissue stiffness, and level of filtration function. Most of these functional parameters can be approached using MRI with DCE, DWI, BOLD. Some other techniques may reflect structural changes within extracellular matrix of renal tissue during process of renal scarring such as MR-elastography. Many of these methods are still in development phases, requiring more clinical experience with harmonization of technical procedures and evaluation of their reliability and validity on larger scales. Their impact on patient management also requires further prospective studies.

Overview of the clinical need for renal MRI

Keith Gillis
Queen Elizabeth University Hospital, Glasgow

Multi-parametric magnetic resonance imaging (MRI) provides the ability to evaluate kidney structure and function in a single imaging session. Whilst estimated glomerular filtration rate and proteinuria estimate risk of progression to end stage kidney disease, novel biomarkers are required to more accurately risk stratify patients. Similarly, in patients with inflammatory disorders, existing parameters often fail to discriminate patients with active inflammation, who may respond to augmented immune therapy, from those with kidney scarring, in whom increased immune therapy would not be helpful. Finally, renal vascular pathology represent a unique quandary, for which new imaging methods are required.

Clinical overview: CKD and DKD

Phil Kalra
Salford and the University of Manchester

Chronic kidney disease (CKD) is very common, affecting around 10% of adult Western populations, and Diabetic nephropathy is the commonest individual cause, being responsible for 20% of CKD in the UK, but 40% in the US. However, in the Indian sub-continent diabetes is the cause of up to 60% of CKD. The prevalence of CKD increases with age, but many elderly patients are labelled with the condition yet have little risk of progressive loss of kidney function. At all stages of CKD there is increased risk of cardiovascular disease, a risk that is accentuated by the presence of albuminuria (or proteinuria).

The key aims of treatment are to :

1. Reduce cardiovascular risk
2. Slow progression of renal functional loss
3. Control endocrine complications (anaemia, metabolic bone abnormalities) in later stages
4. Prepare patients for renal replacement therapy (dialysis, transplantation or conservative care) in stage 5 (end-stage kidney disease) CKD

Hence blood pressure control, especially with ACE-inhibitors or angiotensin receptor blockers, glycaemic control in diabetics, and statins are commonly used treatments in the CKD life course. Within the last few years there have been exciting developments with SGLT-2 inhibitors and GLP-1 agonists, agents developed primarily to control glycaemic status; large trials have shown specific benefits to renal outcomes.

Pathophysiology of CKD progression

Maarten Taal
Royal Derby Hospital and the University of Nottingham

Chronic kidney disease (CKD) is characterised by progressive kidney damage that eventually results in kidney failure. This observation led to the hypothesis that a common pathway of mechanism drives progressive kidney damage once a critical number of nephrons is lost. This talk will describe these proposed mechanisms of CKD progression and consider how multiparametric renal MRI could be used to characterise the relative importance of difference mechanisms in an individual to facilitate a personalised medicine approach to therapy.

Applications of MRI to CKD: evidence to date

Sophie de Seigneux
Geneva University Hospital

MRI is emerging as an important tool for the identifications and follow up of chronic kidney disease (CKD) patients. Important aims in CKD patients are to assess histological lesions such as interstitial fibrosis and inflammation, to be able to follow a patient over time, and to classify patients in high or low risk of end stage renal disease. Different MRI sequences are used to this target, and a combination of modalities will probably be needed. Current challenges include standardization of techniques, and implementaion in routine clinical care.

Application of MRI to DKD: evidence to date

Aghogho Odudu
Manchester University Hospitals Foundation Trust

Diabetic kidney disease (DKD) is the main cause of end-stage kidney disease in the UK and the main cause of death in those with type 2 diabetes. Current markers of DKD such as proteinuria are unpredictable surrogate markers in clinical trials whilst other markers identify disease late. Thus, there is considerable interest in developing validated surrogate markers of DKD. Few data explore the potential of renal imaging in DKD.

Renal hypoxia is an early change in DKD preceding microstructural change and in experimental models, hypoxia represents a final common pathway for progression of DKD. To understand renal oxygenation in DKD and develop new treatments, non-invasive measures of renal haemodynamics and oxygenation are needed. This is challenging and Blood Oxygen Level-Dependent Magnetic Resonance Imaging (BOLD-MRI) is the best described technique. BOLD-MRI uses magnetic effects of deoxygenated hemoglobin to generate renal oxygenation maps that were validated against implanted oxygen-sensitive microelectrodes. BOLD-MRI successfully distinguished different stages of DKD in some studies with standardized imaging protocols but larger multicenter studies, grouping several causes of Chronic Kidney Disease (CKD) showed no differences. Arterial spin-labelling (ASL) has been validated against radiolabelled microspheres for absolute quantification of perfusion but the utility in DKD is uncertain. Measuring regional renal perfusion is likely to be complementary to measuring renal oxygenation but few longitudinal studies combined these techniques. We are conducting a study using multiparametric renal MRI (BOLD with furosemide challenge, ASL, T_1-mapping) to measure renal oxygenation in patients with DKD and measured glomerular filtration rate (GFR) to explore whether renal haemodynamics can separate those with rapid and slower rates of disease progression.

Diffusion Imaging

Jean Paul Vallee
Geneva University Hospital

Diffusion-weighted magnetic resonance imaging (DWI) is a non-invasive method to assess local water motion in the tissue that can probe the renal microstructure, including the presence and the degree of renal fibrosis. The physical principle behind DWI acquisition will be explained with an emphasis on the different type of MR sequences. Regarding the analysis, 3 different types of DWI biomarkers can be measured: (i) the apparent diffusion coefficient—an overall measure of water diffusion and microcirculation in the tissue; (ii) true diffusion, pseudodiffusion and flowing fraction— providing separate information on diffusion and perfusion or tubular flow; and (iii) fractional anisotropy—measuring the microstructural orientation. Finally, the current status of renal DWI in diffuse renal diseases will also be discussed.

T_1 and T_2 Mapping

Ilona Dekkers
Leiden University Medical Centre

There is an increasing need for the development of non-invasive imaging biomarkers to assess the influence of fibrosis and inflammation in the kidney. The application of MRI for non-invasive tissue characterization by voxel-wise mapping of longitudinal (T_1) and transverse (T_2) relaxation time of the kidney without contrast media, referred to as native T_1 and T_2 mapping, is a promising tool for predicting clinical outcomes in renal disease. This talk will provide an overview of technical considerations of T_1 and T_2 mapping, and its potential for non-invasive detection and quantification of renal fibrosis.

Arterial Spin Labelling (ASL)

Manuel Taso
Beth Israel Deaconess Medical Centre and Harvard Medical School

This talk will give an overview of Arterial Spin Labeling (ASL), a non-invasive MRI method for measuring tissue perfusion. While the first report of renal ASL was more than 20 years ago, its clinical translation is still lagging outside of the brain mainly because of additional challenges associated to abdominal MR imaging.

After a brief introduction on perfusion imaging, we will review the basic mechanism of ASL showing how arterial blood water can be used as an endogenous tracer. Various labeling methods that have been developed and applied in renal imaging will be presented (e.g. FAIR, PCASL, velocity-selective) showing potential benefits and pitfalls of each method, as well as the specific challenges with regards to ASL labeling in the abdomen.

Strategies to address motion (background suppression, prospective/retrospective motion compensation) will then be addressed as well as imaging sequences.

Finally, an overview of ASL applications in renal diseases will be presented, mainly chronic kidney disease, renal transplantations.

Blood oxygenation level-dependent (BOLD) MRI to measure renal tissue oxygenation: too bold to be true?

Menno Pruijm
University Hospital of Lausanne

The maintenance of renal tissue oxygenation is vital to assure optimal functioning of the kidneys. Blood oxygenation level-dependent (BOLD) MRI is an interesting tool to measure renal tissue oxygenation, especially in CKD patients, as there is no need for contrast products or invasive procedures.

Renal BOLD-MRI has been used for more than twenty years in the research setting; over the years, much has been learned on the factors that influence the BOLD-signal. Progresses in the acquisition and analysis of the images have improved its reproducibility and increased the information obtained with one exam. Clinical studies have shown that high cortical R2* values (corresponding to low oxygenation) predict adverse renal outcome in CKD patients. BOLD-MRI-alone or in combination with other functional MRI methods- can now be used to monitor the renal effects of drugs, and is increasingly used in the preclinical setting.

Theoretical background, practical aspects, pitfalls and perspectives of this exciting technique will be presented in this review.

Acquisition recommendations: ASL

María Fernández-Seara
Clínica Universidad de Navarra

The Arterial Spin Labeling (ASL) expert panel in Working Group 1 of the PARENCHIMA COST action has developed technical recommendations for acquisition, analysis and reporting of ASL data in the human kidney. These recommendations have been formulated as a set of 59 consensus statements, regarding patient preparation, hardware, acquisition protocol, analysis steps and data reporting. Consensus was achieved through a modified Delphi process and was based on available evidence and expert opinion.

As a default protocol, the panel recommends the use of FAIR or PCASL labeling, followed by a single slice SE-EPI readout, with background suppression of the static tissue signal, and a single-compartment quantification model. This approach was selected as it is expected to provide renal perfusion maps of adequate quality and SNR. If extended kidney coverage is desirable for a specific clinical application, 2D multi slice SE-EPI is the preferred readout.

The purpose of these recommendations is to promote standardization of renal ASL perfusion measurements and improve comparability of results across scanners and in multi-centric clinical studies. However, they are expected to be updated as more clinical data become available.

Acquisition recommendations: BOLD

Pottumarth Prasad
NorthShore University HealthSystem

Harmonization of acquisition and analysis protocols is an important step in the validation of BOLD MRI as a renal biomarker. This harmonization initiative provides technical recommendations based on a consensus report with the aim to move towards standardized protocols that facilitate clinical translation and comparison of data across sites.

Survey data were collected via the Delphi consensus process from 24 researchers on renal BOLD MRI exam preparation, data acquisition, data analysis, and interpretation. Consensus was defined as ≥ 75% unanimity in response.

Among 32 survey questions, 14 achieved consensus resolution, 13 showed clear respondent preference (65-74% agreement), and 5 showed equal (50/50%) split in opinion among respondents. Recommendations for subject preparation, data acquisition, processing and reporting are given based on the survey results and review of the literature.

These technical recommendations are aimed towards increased inter-site harmonization, a first step towards standardization of renal BOLD MRI protocols across sites. We expect this to be an iterative process updated dynamically based on progress in the field.

Acquisition recommendations: DWI

Alexandra Ljimani
Heinrich Heine University Düsseldorf

Standardization is an important milestone in the validation of diffusion-weighted imaging (DWI) as renal MR-biomarker. As the first step in the standardization process technical recommendations are offered in three varieties of renal DWI (monoexponential apparent diffusion coefficient (ADC), intravoxel incoherent motion (IVIM) and diffusion tensor imaging (DTI)) and associated metrics. This standardization process is initiated by 'PARENCHIMA' project funded by European Union European Cooperation in Science and Technology Action (COST).

Reported DWI metrics from a host of prior renal DWI studies (194 studies in total) were extracted. Following data extraction, correlations between quantitative diffusion parameters and all possible products or ratios of the DWI protocol parameters (52 combinations in all) were computed via Pearson correlation coefficients.

Based on the results of this analysis, two rounds of survey were performed consistent with the consensus-building goals of the Delphi process including a range of renal imaging researchers with experience in renal diffusion imaging (21 researchers from 21 institutions in 8 different countries on 3 continents).

The given technical recommendations on DWI might yield tremendous benefits to the field of functional renal MRI as a whole and increase chances of clinical impact on a larger scale.

Acquisition recommendations: T_1/T_2

Susan Francis
University of Nottingham

An expert panel in Working Group 1 of the PARENCHIMA COST action reviewed and developed technical recommendations for the current status of acquisition, analysis and reporting of renal longitudinal (T_1) and transverse (T_2) relaxation time mapping.

Recent literature and accumulated experience with local scan protocols of the expert panel were used to construct a survey to define consensus recommendations using an approximation of a two-step modified Delphi method. The first survey consisted of 56 items on T_1 mapping, of which 4 reached the pre-defined consensus threshold of 75% or higher. The second survey was expanded to include both T_1 and T_2 mapping, and consisted of 54 items of which 32 reached consensus.

Consensus-based technical recommendations for renal T_1 and T_2 mapping derived from the survey results were formulated on hardware, patient preparation, acquisition, analysis and reporting. Surprising, considering the long history of relaxometry in MRI, the process showed that currently there is limited consensus within the community on fundamental measures of renal T_1 and T_2 mapping. This process identified the knowledge gaps, areas in which commercial packages are limited, as well as priorities for future research for the harmonization of scan protocols across sites, and ultimate facilitation of clinical implementation.

Working group 2 update

Frank Zoellner
University of Heidelberg

Parenchima Working Group 2 "R&D Toolbox" will remove these barriers by delivering an R&D Toolbox consisting of a coherent set of databases and software. The aim is to establish a library of core algorithms for the analysis of functional renal MRI, and a graphical user interface for data post-processing and visualization. The databases will contain an anonymized patient registry with critical phenotyping data, histopathology reports, proteomics, and imaging; and an image bank for benchmarking and quality control with phantom-, volunteer- and patient data.

In this talk we will present the progress towards establishing a database and software library.

We will also present an outline for the breakout sessions of the WG2 taking place on Wednesday.

Clinical overview: Transplantation

Cyril Moers
University Medical Center Groningen

There is a considerable shortage of kidneys recovered from deceased donors, which are essential to save lives of critically ill patients who suffer from renal failure. Hence, more kidneys of marginal quality need to be considered for transplantation. Reliable pre-transplant assessment of organ quality has become a top priority, to prevent transplantation of organs with very poor or even no function. Currently, decisions on organ acceptance or discard rely on the professional opinion the organ recipient's physicians. Their judgment tends to be on the safe side. Nevertheless, up to 30% of kidneys that do pass clinical assessment will not show acceptable outcome after all.

As a transplant surgeon, I am regularly confronted with the limitations of this subjective clinical judgment and determined to improve the way we assess the quality of donor organs. Attempts at developing more objective diagnostic tools have failed so far. Highly innovative methods need to be explored in order to develop truly and independently predictive pre-transplant assessment tools for donor kidneys, as well as non-invasive diagnostic modalities to identify post-transplant complications at a very early stage. Transplant centers are increasingly interested in utilizing ex vivo organ perfusion to presumably better preserve, improve and assess donor kidneys prior to transplantation. To ultimately identify relevant prognostic markers during ex vivo perfusion, it is essential to first obtain a deep understanding of molecular mechanisms during perfusion and how these differ from such processes in vivo.

Magnetic resonance imaging (MRI) provides a promising non-invasive tool to obtain a wealth of additional tissue-specific information about kidney quality and viability, both prior to and post-transplantation. So far, innovative MRI techniques have not been applied to image and characterize ex vivo perfused donor kidneys. Post-transplant MRI of the graft is also still in its infancy. Currently, it remains unknown which measurements during ex vivo kidney perfusion are relevant predictors of post-transplant outcome, or which imaging biomarkers are indicative of specific post-transplant allograft pathology. Hence, there is an urgent need to better understand this relationship and discover the true diagnostic potential of renal MRI in the transplantation setting. My research aims to utilize innovative multi-omics and radiomics methodology to address these issues.

Pre-clinical transplantation

Bente Jespersen
AU and Aarhus University Hospital

The pig has renal anatomy and physiology like the human.

The talk will go through porcine experimental models for donation after brain death and donation after circulatory death including the care of the pigs before surgery, during repetitive surgery and during observation with measurement of kidney function and structure.

Induction of renal ischaemia as well as strategies to limit ischaemia-reperfusion injury such as remote ischaemic conditioning, mesenchymal stromal cell therapy and normothermic machine perfusion will be described. In addition limitations of this large animal model will be elucidated.

Applications of MRI to renal transplantation - evidence to date

Alexandra Ljimani
Heinrich Heine University Düsseldorf

Renal transplantation is the therapy of choice for patients with end-stage renal diseases. Although the improvement of immunosuppressive therapy has significantly increased the half-life of renal allografts over the past decade. However, complications still occur. Therefore, an early detection of allograft dysfunction is mandatory for its durability. Non-invasive MRI techniques have the potential to enable the assessment of different functional renal parameters in addition to anatomic imaging.

Diffusion-weighted imaging (DWI) provides information on renal diffusion and perfusion. Diffusion-tensor imaging (DTI) accounts for the directionality of diffusion and gives information on the integrity of tissue structures. Blood oxygen level-dependent MR (BOLD) evaluates renal tissue oxygenation. Arterial spin labelling (ASL) offers information on tissue perfusion. T_1 and T_2 mapping can offer information on renal fibrosis. Other functional MRI technologies, such as CEST and sodium MRI, are promising to provide further important information on renal allografts.

Considering the risk of NSF and gadolinium deposits in the brain, contrast agent - free methods should be preferred for the MRI examination of transplanted patients. All the new, advanced MRI techniques can provide information without administration of contrast agents and might extend the possibilities of current clinical diagnostic significantly.

Quality in Organ Donation (QUOD)

Maria Kaisar
University of Oxford and NHS Blood and Transplant

Organ transplantation saves thousands of lives every year and is the treatment of choice for end stage organ failure. Despite an increase in donation rates, the gap remains between the supply and the need for life-saving organs. This is predicted to worsen over the next decades, making this disparity a key challenge facing the transplant community today.

The Quality in Organ Donation (QUOD) program is a national consortium that led to the establishment of the QUOD biobank and the development of a unique collaborative research infrastructure.

The QUOD biobank collects and stores clinical samples from all the deceased donors across the UK. Longitudinal blood and urine samples, in addition to biopsies from abdominal and cardiothoracic organs, are collected and centrally stored. All the QUOD samples are linked to donor and recipient demographic and clinical data from the NHSBT transplant registry. Retrieved but not transplanted whole organs are also collected and stored according to pre-defined standard operational protocols.

To date, more than 80,000 bio-banked samples have been collected from 4,500 deceased donors. Samples have been allocated for research to more than 70 research applications submitted to QUOD from academic and research institutions across the UK.

This unique bio-resource has been invaluable in the study of the biological mechanisms that lead to donor organ injury and the discovery of novel biomarkers for better donor and organ assessment. On-going work on the integration of novel analytical technologies using whole organs will allow the creation of tissue and single cell atlases.

My talk will provide an overview of the QUOD biobank and an insight into the research work our group undertakes to identify new biomarkers of donor organ quality and to better understand some of the mechanisms that are involved in the development of kidney injury. These biological processes can be further targeted during donor management or organ perfusion to repair and recondition donor organs. To this end, the QUOD biobank provides the infrastructure to increase donor organ utilization and improve transplant outcomes for organ recipients.

For more information see poster 32

^{23}Na MRI

Armin Nagel
University of Erlangen-Nürnberg

Besides protons (1H) – which are used for conventional MRI – sodium (^{23}Na) is the nucleus that is best suited for in vivo MRI, due to its physical properties and its high natural abundance. However, ^{23}Na MRI is challenging, since the in vivo signal-to noise ratio (SNR) of ^{23}Na MRI is approximately three orders of magnitude lower than the SNR of 1H MRI. To compensate for this, usually larger voxel volumes and longer acquisition times are used. In addition, dedicated hardware and acquisition techniques are required.

Sodium ions (Na+) play an important role in many cellular processes such as the maintenance of the homeostasis if the body's fluid and electrolyte balance, which are regulated by the kidneys. ^{23}Na MRI allows for the quantification of the tissue sodium concentration (TSC), which is a volume-weighted average of the intra- and extracellular sodium concentration. In contrast, in routine clinical diagnostics only extracellular ion concentrations can be analyzed. Thus, ^{23}Na MRI may add valuable additional information for the characterization of renal diseases.

In this presentation, the basic principles of ^{23}Na MRI will be briefly explained and clinical research applications of ^{23}Na MRI in the fields of renal imaging and kidney disease will be discussed.

Magnetisation Transfer (MT) and Chemical Exchange Saturation Transfer (CEST)

Dario Longo
Institute of Biostructures and Bioimaging

Current clinical tests are insufficient for assessing several renal pathologies, including acute kidney injury and progressive renal disease, including fibrosis. Moreover, although the principal role of the kidney is the maintenance of acid-base balance, present imaging approaches are unable to assess this important parameter. Therefore, novel noninvasive imaging approaches are needed to improve the in vivo assessment of kidney damage and of disease progression.

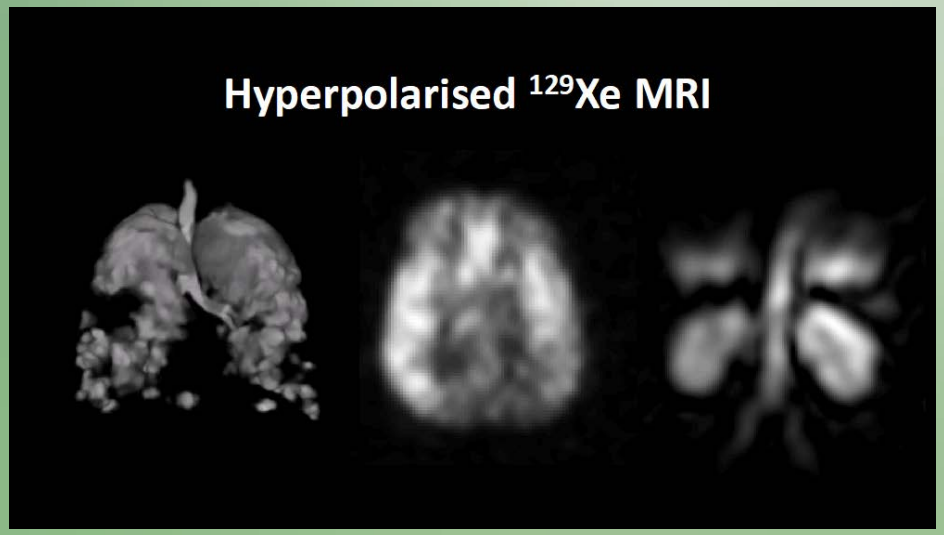
Magnetization Transfer (MT) and Chemical Exchange Saturation Transfer (CEST) imaging are two MRI approaches that exploit the exchange of proton pools in different environments to generate contrast. MT approaches can evaluate the macromolecular content of tissues, whereas MRI-CEST has been shown to report on the tissue pH.

We will discuss different MRI-based MT and CEST approaches to assess kidney functionality and for monitoring disease progression, using examples from our own research and from recent literature. Based on these data, both MT and CEST approaches might be considered potential innovative diagnostic tools for characterizing renal diseases.

Methods and applications of hyperpolarised ^{129}Xe MRI

Jim Wild
University of Sheffield

The talk will cover the methodology for hyperpolarised ^{129}Xe MRI in humans including, polariser physics, regulatory aspects, RF coils, pulse sequence design and functional imaging methods for clinical applications in the lungs, brain and more recent work in the kidneys.



Magnetic Resonance Elastography (MRE)

Stephan Garcia
University Hospital Berlin

Magnetic resonance elastography (MRE) is a quantitative, phase-contrast based magnetic resonance imaging (MRI) technique that uses propagating shear waves to generate viscoelastic parameters maps.

MRE is based on three technical key components: (I) generation of mechanical waves by (multiple) external vibration drivers, (II) magnetic resonance pulse sequence combined with motion encoding gradients, and (III) post processing for computing viscoelastic parameter maps by inversion algorithms.

A powerful, multifrequency variant of MRE is tomoelastography which has been successfully applied to the kidneys under physiological and pathological conditions. Tomoelastography has demonstrated the sensitivity of viscoelastic parameters in renal tissue to vascularization and blood perfusion. Consequently, dysfunctional kidneys were reported as being softer than functional kidneys making MRE a promising quantitative imaging marker for renal function at early disease stages. The fact that MRE does not require contrast-agents makes it particularly useful for renal disease characterization by MRI.

Quantitative Susceptibility Mapping (QSM) of the kidney - Technical challenge and potential diagnostic value

Eric Benchler
University Hospital Düsseldorf

Quantitative Susceptibility Mapping (QSM) is a current technique that calculates tissue magnetic susceptibility from gradient-echo phase images. It is commonly applied in neuroimaging to study iron deposition in different diseases of the human brain [1–3]. Recent mice studies showed that QSM could be a viable tool for clinical applications as it detects subtle differences in the tissue architecture of the kidney and is able to detect inflammation and fibrosis [4–6].
However, QSM in the abdomen has many potential pitfalls making it a challenging task. The large difference in susceptibility between air and tissue in the abdomen leads to streaking-artefacts and wrongly estimated susceptibility values [7]. Novel literature suggests that QSM algorithms have to be carefully chosen, to tackle the large changes in susceptibility [8]. Furthermore, the contribution of fat influences the susceptibility calculation and has to be removed from the MRI signal. In addition, the necessity of breath-hold imaging limits the spatial resolution, which in turn leads to erroneous susceptibility values [9].
All of the above-mentioned pitfalls and challenges make QSM in the kidney a difficult but not impossible task. Preliminary results indicate that QSM might be able to detect structural changes in kidneys.

References

1. Li DTH, Hui ES, Chan Q, et al. Quantitative susceptibility mapping as an indicator of subcortical and limbic iron abnormality in Parkinson's disease with dementia. NeuroImage Clin. 2018;20:365–373 doi: 10.1016/J.NICL.2018.07.028.
2. Zivadinov R, Tavazzi E, Bergsland N, et al. Brain Iron at Quantitative MRI Is Associated with Disability in Multiple Sclerosis. Radiology 2018:180136 doi: 10.1148/radiol.2018180136.
3. Sun H, Klahr AC, Kate M, et al. Quantitative Susceptibility Mapping for Following Intracranial Hemorrhage. Radiology 2018;288:830–839 doi: 10.1148/radiol.2018171918.
4. Xie L, Layton AT, Wang N, et al. Dynamic contrast-enhanced quantitative susceptibility mapping with ultrashort echo time MRI for evaluating renal function. Am. J. Physiol. Renal Physiol. 2016;310:F174-82 doi: 10.1152/ajprenal.00351.2015.
5. Xie L, Sparks MA, Li W, et al. Quantitative susceptibility mapping of kidney inflammation and fibrosis in type 1 angiotensin receptor-deficient mice. NMR Biomed. 2013;26:1853–1863 doi: 10.1002/nbm.3039.
6. Xie L, Dibb R, Cofer GP, et al. Susceptibility tensor imaging of the kidney and its microstructural underpinnings. Magn. Reson. Med. 2015;73:1270–81 doi: 10.1002/mrm.25219.
7. Haacke EM, Liu S, Buch S, Zheng W, Wu D, Ye Y. Quantitative susceptibility mapping: current status and future directions. Magn. Reson. Imaging 2015;33:1–25 doi: 10.1016/J.MRI.2014.09.004.
8. Bechler E, Stabinska J, Wittsack H-J. Analysis of different phase unwrapping methods to optimize quantitative susceptibility mapping in the abdomen. Magn. Reson. Med. 2019 (in press).
9. Karsa A, Punwani S, Shmueli K. The effect of low resolution and coverage on the accuracy of susceptibility mapping. Magn. Reson. Med. 2019;81:1833–1848 doi: 10.1002/mrm.27542.

Nephron number and new imaging techniques for histology specimines

Norbert Gretz
University of Heidelberg

MRI protocols for counting and sizing of glomeruli have been established both in ex vivo and in vivo analysis of mice and rats. The protocols are using cationic ferritin that binds to the anionic, highly charged glomerular basal membrane.

The first papers describing sizing and counting of glomeruli date back to 2011/2012. Although the counting is very well in agreement with stereological counting the disadvantage of MRI-based counting and sizing is a) the expensive ferritin, b) the expensive MRI-machine, c) the expensive maintenance of the MRI-machine.

An interesting alternative to MRI-based counting and sizing of glomeruli is the 3D imaging of kidneys after optical tissue clearing/expansion (OTC). OTC dates back to the work of Spalteholz (1911). Only recently new protocols for different organs were published. The principal of all of them is lipid removal and refractive index adjustment. Furthermore, new dyes and procedures for whole animal staining were introduced. Initially the OTC sample preparation was very long lasting (up to 1 month). In the meantime, fast protocols have been published (~4 hours). In addition, even 20-year-old paraffin blocks have been successfully imaged as a 3D block. Even immunohistochemistry in these blocks is possible.

Clinical Overview: AKI

John Prowle
Queen Mary University of London

An overview of the definition, aetiology, pathophysiology, epidemiology and outcomes of acute kidney injury as encountered in clinical practice, both in the ICU, in hospital and in the community. Background will be provided into the role of global and regional changes in renal perfusion in the development and maintenance of renal dysfunction in AKI. This will provide context to discussion of renal imaging modalities that may be applied to patients with or at risk of AKI in subsequent talks.

Histopathology of AKI

Peter Boor
Institute of Pathology in Aachen and Department of Nephrology in Aachen

Acute Kidney Injury (AKI) is a serious medical conditions with high morbidity and mortality that can also lead to chronic kidney disease (CKD). AKI is a frequent condition occurring in approx. 20% of hospitalized patients worldwide with an increasing incidence and disappointing outcomes. A multitude of etiologically distinct underlying diseases lead to AKI, suggesting that identification of common pathological processes would be of upmost importance.

In this lecture I will discuss the pathological findings in AKI and particularly focus on aspects and opened questions linking these to the clinical medicine and preclinical translational research. I will exemplify some molecular mechanisms involved in AKI, with particular focus on renal tubular epithelial cell injury, a major common pathological finding in AKI.

Preclinical AKI models

Rachel Harwood
University of Liverpool

Renal ischaemia reperfusion injury (IRI) can be seen in a wide variety of disease processes: cardiac bypass; renal pedicle clamping during partial nephrectomy; hypotension due to blood loss; dehydration and heart failure, to name but a few. Acute kidney injury (AKI) is commonly seen, but it is becoming increasingly recognised that there is a much higher propensity for developing chronic kidney disease (CKD). This is particularly true for children with congenital heart disease for whom CKD is independently associated with a higher mortality rate.

This talk will describe the pre-clinical methods that can be used to longitudinally monitor the renal function of rodents using transcutaneous FITC-Sinistrin clearance time and multi-spectral optoacoustic tomography (MSOT). The application of these technologies has enabled the classically variable IRI model to be refined, enabling future efficacy studies to be confidently undertaken.

Applications of MRI to AKI - evidence to date

Andrea Fekete
Hungarian Academy of Sciences and Semmelweis University

Acute kidney injury (AKI) and associated complications including chronic kidney failure or cardiovascular disease remains devastating illnesses with unacceptably high rates of morbidity worldwide.

Diagnosis of AKI is mainly based on increased level of serum creatinine, however this is an unspecific marker. SeCr is poorly sensitive to rapid changes and depends on various factors including age, state of hydration and others, which delays the diagnosis and early intervention of AKI.

Renal functional MR imaging (fMRI) has rapidly grown to be a valuable tool to evaluate renal function, perfusion, oxygenation or inflammation non-invasively and real-time. The presentation briefly summarizes MRI basics for BOLD, ASL and DWI and review latest preclinical experiments and clincial studies of recent years.

Cardiac and cardiorenal syndrome

Patrick Mark
Queen Elizabeth University Hospital, Glasgow

Patients with advanced chronic kidney disease have a dramatically elevated risk of premature cardiovascular disease. Although these patients have multiple cardiovascular risk factors such as diabetes, hypertension and dyslipidaemia, this does not fully explain the excess in cardiovascular mortality.

It is now widely recognised that functional and structural cardiac abnormalities specifically left ventricular hypertrophy and dysfunction are strongly associated with adverse cardiovascular outcomes in patients with CKD.

Cardiovascular MRI (CMR) has been used to interrogate the myocardium of patients with CKD and offers insights into the mechanisms behind premature cardiovascular death and heart failure in CKD. The talk will review developments in CMR specific to patients with CKD.

Imaging (just) Outside of the Kidney: the Renal Arteries

Annoeles de Boer
University Medical Centre Utrecht, Utracht University

This talk aims to cover both the clinical rationale behind imaging of the renal arteries, as well as recent advances in imaging techniques with a focus on MRI.

The traditional indication for imaging of the renal artery was suspected renovascular hypertension. Already in 1934, Goldblatt described the phenomenon of increased blood pressure in response to clipping of one of both renal arteries. [1] Later, the role of the renin-angiotensin-aldosterone system was discovered. In practice, renal artery stenosis appears to be only one of multiple factors contributing to "renovascular" hypertension, but detection of renal artery stenosis remains relevant. Imaging of the renal vasculature has gained further interest thanks to the ever-growing number of kidney transplantations. Vascular imaging is performed to test eligibility of both donor and receiver, plan surgery and to detect vascular complications post-transplantation. In addition, imaging of the renal artery is crucial prior to renal denervation, an experimental treatment for resistant hypertension.

The renal artery is usually assessed by four different modalities: ultrasound, conventional angiography (digital subtraction angiography or DSA), CT angiography (CTA) and MR angiography (MRA). Ultrasound is cheap and quick, but its success and accuracy depend on patient habitus and operator experience. Conventional angiography is considered the gold standard, but the procedure is invasive. CTA and MRA are considered equally accurate [2,3], but both have their own limitations and advantages. CTA is quick, but it exposes the patient to radiation and iodinated contrast agent. MRA is more time consuming, but it has some crucial advantages. It does not expose the patient to radiation, and even more important: recent advances in imaging techniques make administration of contrast agent superfluous. Especially inflow dependent inversion recovery (IFDIR) is promising as a reasonably quick and reliable sequence to assess the renal arteries in a completely non-invasive manner. [4] Another emerging technique, 4D phase contrast MRI, allows for assessment of renal blood flow characteristics throughout the larger branches of the renal artery, including flow velocity and total flux.[5]

1. Goldblatt H, Lynch J, Hanzal RF, Summerville WW. STUDIES ON EXPERIMENTAL HYPERTENSION : I. THE PRODUCTION OF PERSISTENT ELEVATION OF SYSTOLIC BLOOD PRESSURE BY MEANS OF RENAL ISCHEMIA. J Exp Med. 1934;59(3):347-79.

2. Gaddikeri S, Mitsumori L, Vaidya S, Hippe DS, Bhargava P, Dighe MK. Comparing the diagnostic accuracy of contrast-enhanced computed tomographic angiography and gadolinium-enhanced magnetic resonance angiography for the assessment of hemodynamically significant transplant renal artery stenosis. Curr Probl Diagn Radiol. 2014;43(4):162-8.

3. Eklöf H, Ahlström H, Magnusson A, Andersson LG, Andrén B, Hägg A, Bergqvist D, Nyman R. A prospective comparison of duplex ultrasonography, captopril renography, MRA, and CTA in assessing renal artery stenosis. Acta Radiol. 2006;47(8):764-74.

4. Edelman RR, Koktzoglou I. Noncontrast MR angiography: An update. J Magn Reson Imaging. 2019;49(2):355-373.

5. Motoyama D, Ishii Y, Takehara Y, Sugiyama M, Yang W, Nasu H, Ushio T, Hirose Y, Ohishi N, Wakayama T, Kabasawa H, Johnson K, Wieben O, Sakahara H, Ozono S. Four-dimensional phase-contrast vastly undersampled isotropic projection reconstruction (4D PC-VIPR) MR evaluation of the renal arteries in transplant recipients: Preliminary results. J Magn Reson Imaging. 2017;46(2):595-603.

New insights into imaging techniques to improve Arterio-Venous Fistula (AVF) outcome

Michela Bozzetto
University of Bergamo

Native arteriovenous fistula (AVF) is the preferred vascular access for hemodialysis, but it still has high rate of failure due to vascular stenosis. There is a urgent need of novel strategies to predict and possibly reduce AVF non-maturation and long-term dysfunction.

In the past years, our group developed a computational modelling tool providing a prediction of AVF blood flow at 40 days after surgery to improve surgical planning and reduce AVF non-maturation rate. Convincing evidence supports a key role of local unsteady and disturbed flow in stenosis formation. To elucidate the role of local hemodynamics, we performed a feasibility longitudinal study coupling imaging techniques with computational fluid dynamic (CFD) simulations. We optimized CUBE T_1 sequence for contrast-free MR imaging of the AVF and we scanned 3 patients at 1 week, 6 weeks, 6 months and 1 year after AVF creation; we segmented the vessel lumen and generated patient-specific 3D AVF model from MR images. AVF color-doppler Ultrasound provided blood flow boundary conditions for the CFD simulations.

The developed MRI-to-CFD pipeline allowed to detect AVF morphological changes and corresponding local hemodynamic changes over time, paving the way to future prospective clinical investigations aiming at identifying hemodynamic predictors of AVF stenosis.

Intradialytic MRI of the Heart and Brain

Eleanor Cox
University of Nottingham

End stage renal disease can have potential implications on almost any part of the body. Repetitive circulatory stress caused by haemodialysis (HD) plays a central role in the pathophysiology of multi organ system dysfunction in HD patients, but the full extent of organ dysfunction brought about by HD is not fully understood. This talk will give an overview of the intradialytic MRI studies of the heart, brain and kidneys that we have performed in Nottingham.

MRI in drug development pathways

Robert Unwin
AstraZeneca Biopharmaceuticals

Medical imaging, including MRI, can help to address several key issues that arise during drug development. These may include patient stratification (e.g., identifying likely treatment responders), detection and diagnosis of disease-related abnormalities, assessment of severity (grade), therapeutic monitoring, and longer-term follow-up of trial subjects.

In clinical trials of drug efficacy, imaging biomarkers and imaging surrogate end-points have the advantage of being quantifiable and potentially more objective (use of independent external observers and potential for application of machine learning techniques), and are usually quicker to measure than clinical outcomes. This is particularly true in renal medicine, where the currently accepted (for drug approval) clinical trial end-points can take many years to reach, making such trials prohibitively expensive and high risk, which has been a major barrier to trials in nephrology when compared with other clinical specialties (e.g., oncology and cardiovascular diseases). As examples, MRI imaging has already proved valuable in a clinical trial setting in oncology (tumour size), dementia (regions of brain atrophy), multiple sclerosis (T_2-weighted imaging), and erosive arthropathies.

Many organs, including the kidney, have a 'functional reserve', meaning that blood or urine biomarkers can be normal in the presence of established and even advanced disease. MRI imaging offers the possibility of providing whole organ (anatomical), region- and tissue-specific information. The kidney is a case in point, because its reserve can compensate for around 75% of functional loss, which makes current biomarkers - serum creatinine and urinary albumin - relatively insensitive for early kidney damage.

Three measures of functional MRI imaging are currently being used and explored in renal medicine, which could be incorporated in future clinical trials in nephrology, if sufficiently well-validated and shown to be predictive of disease progression: apparent diffusion coefficient (fibrosis), arterial spin labelling (perfusion), and BOLD imaging (oxygenation). However, while imaging surrogates such as these can be particularly helpful when clinical outcome is difficult to assess, any changes detected may not always reflect (or predict) clinical outcome, which will always needs to be established before they can be used in a clinical trial.

Clinical trial design for MRI studies

Richard Haynes
Nuffield Department of Population Health, University of Oxford

Randomized trials are the best method for determining the effects of treatments on clinical outcomes. There is considerable interest in identifying biomarkers that predict clinical outcomes and also the effects of treatments in a shorter timeframe than clinical outcome trials. This talk will discuss the potential application of renal MRI to this problem and some of the issues involved.

Radiology - How will functional renal MRI be used in practice?

Doug Pendse
University College London

For more than a century radiologists have been using medical imaging to diagnose disease. In the last hundred years radiology has evolved from the humble first radiograph of 1895 to the advanced multimodality imaging techniques of today. Despite these huge technological advances, the use of medical imaging today still relies on the subjective interpretation of images by a radiologist. In the era of quantitative imaging, radiomics and machine learning, we explore how functional renal MRI may be used in clinical practice.

ADPKD and clinical trials - Progress and future directions

Roz Simms
Sheffield Kidney Institute and the University of Sheffield

Autosomal dominant polycystic kidney disease (ADPKD) is the commonest inherited kidney disease worldwide and the third commonest cause of established kidney failure in the UK accounting for 10% of adults requiring renal replacement therapy. Developing treatments to delay the relentless disease progression is a priority in ADPKD, however there are challenges related to the design of clinical trials. Progress related to approval of Total Kidney Volume (TKV) the first prognostic imaging biomarker for use in clinical trials for ADPKD and future directions for MRI research in ADPKD will be discussed.

Closing Plenary: Future Directions of Renal MRI

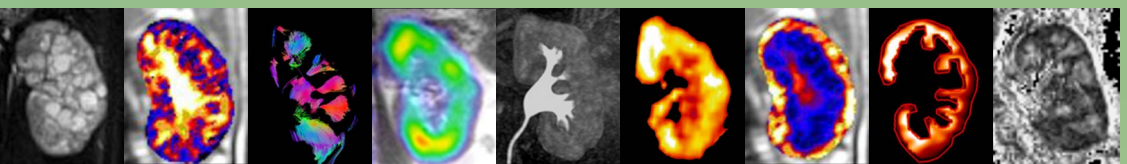
Stephen Sourbron
The University of Leeds

Renal MRI research has experienced an explosive growth over the past few years, driven to a large extent by increasing interest from the nephrology community in imaging biomarkers that can help to diagnose kidney disease, stratify patients for treatment and monitor response. Imaging biomarkers provide the only means of tracking disease and treatment effects non-invasively and in-situ, as opposed to biomarkers in blood- and urine tracing downstream effects that may not be specific to the kidney and tend to respond late.

In this talk I will review the trajectory of the field over the past 5 years as well as current ongoing initiatives and research programmes that are likely to deliver new insights over the next decade. I will also aim to identify the key open questions and bottlenecks that still exist, emerging solutions and areas where more investment is needed to fully establish renal MRI biomarkers as a routine tool in nephrology, drug development and basic research on renal disease.

Poster Abstracts

In order of the power pitches in the program schedule



Phase contrast magnetic resonance imaging to assess renal perfusion: current status and practical recommendations

Villa G[1], Ringgaard S[2], Hermann I[3], Noble R[4], Brambilla P[5], Khatir DS[6], Zöllner FG[3], Francis ST[4], Selby NM[4], Remuzzi A[1,7], Caroli A[1]

[1]Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Bergamo, Italy; [2]Aarhus University, Aarhus, Denmark; [3]Heidelberg University, Mannheim, Germany; [4]University of Nottingham, Nottingham, UK; [5]ASST Papa Giovanni XXIII, Bergamo, Italy; [6]Aarhus University Hospital, Aarhus, Denmark; [7]University of Bergamo, Dalmine, Italy

Introduction

Phase-contrast magnetic resonance imaging (PC-MRI) is a non-invasive method used to compute blood flow velocity and volume [1,2]. This study aims to discuss the current status of renal PC-MRI and provide practical recommendations which could inform future clinical studies and its adoption in clinical practice.

Methods

A comprehensive search of all the PC-MRI studies in human healthy subjects or patients related to the kidneys was performed.

Results

A total of 39 studies were included in which PC-MRI was used to measure renal blood flow (RBF) alongside other derivative hemodynamic parameters. PC-MRI has been technically validated in a number of studies both in vitro and in vivo, generally showing good correlation with gold standard methods of RBF measurement. Moreover, a large number of studies have investigated the reproducibility, and intra- and inter- observer variability of RBF measures obtained by PC-MRI, showing an overall good reproducibility. PC-MRI has been biologically validated against alternative techniques in humans, showing an overall good agreement.

Despite renal PC-MRI not being routinely used in clinics, there are a number of clinical studies showing its potential to support diagnosis and monitoring of renal diseases, in particular chronic kidney disease, renovascular disease, and autosomal dominant polycystic kidney disease, particularly in the earlier stages. In healthy volunteers the variability in RBF values, both in individual studies and across studies, is rather large, making the definition of normative ranges not possible yet.

Discussion

There are a few key recommendations to be followed to accurately measure RBF, possibly reducing the wide variability in the measurements reported so far. The acquisition slice should be placed perpendicularly to the vessel direction, and prior to any bifurcation; to this purpose, a good survey scan is extremely helpful. TR and TE should be minimum, velocity encoding should be higher than the peak velocity, and spatial resolution should be sufficient to reliably identify vessels. Motion compensation and cardiac gating should be performed. Once acquired, PC-MRI should undergo a careful visual inspection, and images with artefact should be discarded. To quantify RBF, ROIs should cover the vessel lumen only, and should be adjusted to account for vessel movement during the cardiac cycle. Since PC-MRI acquisition and processing are quite straightforward, there is no need for a high-level of technical expertise.

Conclusion

The current published literature supports PC-MRI as a feasible and valid non-invasive technique to reliably measure renal blood flow, alongside a number of derivative hemodynamic parameters, in both healthy volunteers and patients with renal disease. Future multicentric studies are needed to provide definitive normative ranges and to demonstrate the clinical potential of PC-MRI, likely as part of a multi-parametric renal MRI protocol. International collaborative efforts such as the COST action PARENCHIMA may help in answering this need.

References

[1] Nayak et al. J Cardiovasc Magn Reson 2015; 17:71. [2] Lotz et al. RadioGraphics 2002; 22:651–671.

Acknowledgements

This article is based upon work from COST Action Magnetic Resonance Imaging Biomarkers for Chronic Kidney Disease (PARENCHIMA), funded by COST (European Cooperation in Science and Technology). www.cost.eu.

DTI based evaluation of renal parenchyma in children: comparison between UPJ obstruction, ARPKD and normal kidneys.

Suraj D Serai [1], Ph.D.; Juan S. Calle-Toro [1], MD; Erum A. Hartung [1], MD; Kassa Darge [1], MD, PhD; Hansel J. Otero [1], MD

[1] The Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine, Philadelphia, USA.

Objective/ Introduction

To compare renal diffusion tensor imaging (DTI) based metrics in children with ureteropelvic junction (UPJ) obstruction and children with autosomal recessive polycystic kidney disease (ARPKD) to normal kidneys.

Methods

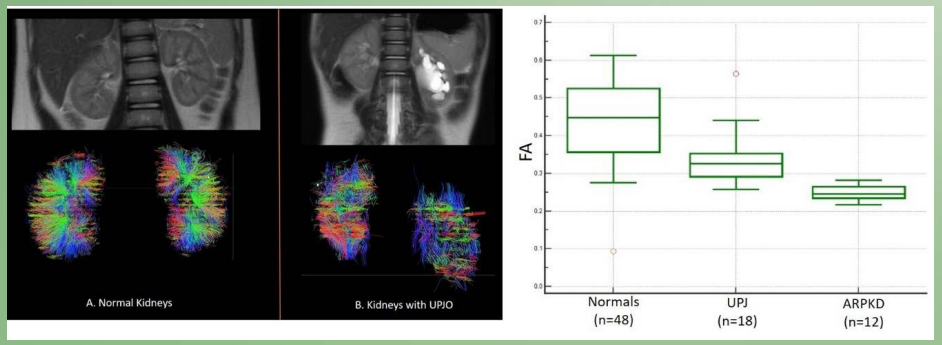
18 kidneys from 16 patients with morphologic and functional findings of UPJ obstruction; and 8 patients with ARPKD were selected for the final sample. For normal controls, 8 children with no history of renal disease were recruited and imaged prospectively; and were grouped with additional 16 retrospectively selected patients that underwent functional MR urography (MRU) with renal DTI and were deemed normal on T_2-weighted images and functional parameters. DTI acquisition sequence included a 20-direction DTI with b-values of b=0 s/mm^2 and b=400 s/mm^2. Diffusion Toolkit and TrackVis were used for analysis and segmentation. TrackVis was used to draw regions of interest (ROI) covering the entire volume of the renal parenchyma, excluding the collecting system. Fibers were reconstructed using a deterministic fiber tracking algorithm. Whole kidney ROI based analysis was performed to obtain cortico-medullary fractional anisotropy (FA), apparent diffusion coefficient (ADC) and track length (TL) measurements for each kidney. T-tests were performed to compare means and statistical significance was defined at p<0.05.

Results

48 normal kidneys from 24 patients (mean age 10.6 ± 4.1 years; 4/24 males) were compared to 18 kidneys from 16 patients (10.4 ± 6.8 years; 9/16 males) with UPJ obstruction and 12 kidneys from 6 patients with ARPKD (mean age = 13.8 years ± 8.5; 5/6 males). Mean FA values were significantly lower (0.31 ± 0.07; n=22) in kidneys with UPJ obstruction, and in kidneys of patients with ARPKD (0.25 ± 0.02; n=12) than normal kidneys (0.44 ± 0.09; n=48) (p<0.001). No significant difference was found between ADC and TL.

Conclusion

DTI of the kidney offers a novel approach for characterizing renal disease based on changes in diffusion anisotropy and kidney structure. DTI derived FA is able to discriminate between normal kidneys and those with UPJ obstruction and in children with ARPKD.



Decreased native renal T_1 one week after gadobutrol administration in healthy volunteers

A. de Boer[1], A. A. Harteveld[1], P. J. Blankestijn[2], C. Bos[1], M. Froeling[1], J.A. Joles[2], M.C. Verhaar[2], J.M. Hoogduin[1], T. Leiner[1]

[1.] Department of Radiology; [2.] Department of nephrology and hypertension, University Medical Center Utrecht, The Netherlands

Introduction

Gadolinium based contrast agents (GBCA) are widely used in MRI. In a reproducibility study on multiparametric renal MRI, we found persistently decreased T_1 values during the retest ~7 days after the initial session. This might be explained by the presence of minute amounts of contrast agent from GBCA injection during the first session. Here, analyses to support this hypothesis are presented.

Methods

23 healthy volunteers were included (estimated glomerular filtration rate (eGFR) range: 103-163ml/min/1.73m^2). Median time between both MRI sessions was 7 days (range: 4-16 days). Data of 21 volunteers was used for analysis, and in 16 of those volunteers contrast enhanced (DCE) imaging was performed. One was excluded because of insufficient image quality and one because of the GBCA dose received was uncertain due to problems with intravenous access. T_1 mapping was performed before contrast enhanced imaging (dose 0.05mmol/kg gadobutrol). Linear regression was used to relate both the time interval between the two sessions and eGFR from a blood sample to T_1 differences between sessions (ΔT_1).

Results

The ΔT_1 differed significantly between subjects scanned with and without contrast agent: median ΔT_1 cortex -98 vs 7ms ($p<0.001$) and medulla -68ms vs 19ms ($p=0.001$, Mann-Whitney-U test). The ΔT_1 corresponds to a gadobutrol concentration of 10ng/g (cortex) and 5ng/g tissue (medulla), or ~2µmol (0.01% of original dose). ΔT_1 correlated with interval between acquisitions for both cortex (regression coefficient (β) 16.5ms/day, R_2 0.50, $p<0.001$) and medulla (β 11.5ms/day, R_2 0.32, $p<0.001$) (figure 1). Medullary ΔT_1 correlated with eGFR (β 1.13ms/(ml/min), R_2 0.32, $p=0.003$).

Discussion

For this reproducibility study, the design aimed to rule out systematic differences between sessions. The only reasonable remaining cause for the T_1 bias was the GBCA administration during the first session, which is confirmed by the significant difference in ΔT_1 between subjects scanned with and without contrast agent. Delayed excretion of GBCAs has been modelled on retrospective data.(1) In this model, phases of distribution and elimination are followed by a slow residual excretion phase from a deep compartment, probably bone, with time constants ranging from 6-102 hours.(1) To ultimately confirm the delayed excretion, future work should include repeated T_1 measurements in the same individual. Without tissue samples, it cannot be ruled out that another process caused the T_1 bias.

Conclusion

This study adds to existing reports of gadolinium retention in brain, bone and skin. Even in this healthy population, excretion delay increased with decreasing kidney function. We underline that there are no reports of adverse effects of macrocyclic GBCAs in subjects with normal renal function,(2) but studies on long term safety are lacking. Moreover, MRI based T_1 mapping may prove to be a valuable tool to detect biodistribution of GBCA in vivo.

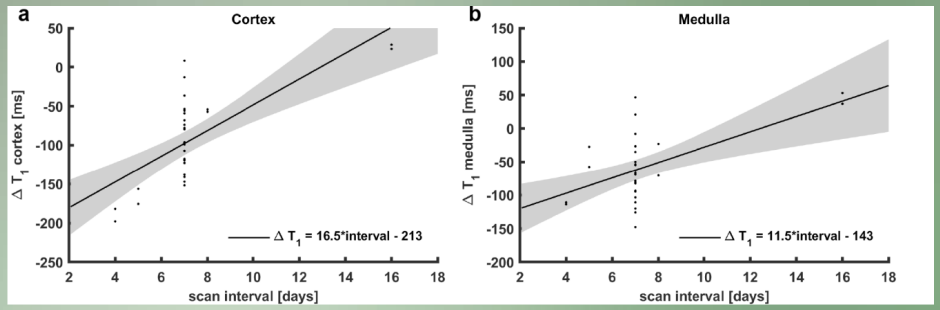


Figure 1: Regression analysis of the dependence of ΔT_1 on scan interval of subjects scanned with contrast agent. Shaded areas denote the 95% confidence interval of the regression line. a Cortical ΔT_1 values, R2 0.50, p<0.001; b Medullary ΔT_1 values, R_2 0.32, p<0.001.

References

1. Lancelot E. Invest. Radiol. 2016;51(11):691-700; 2. McDonald RJ, et al. Radiology. 2018;289(2):517-34.

Towards free-breathing volumetric renal ASL with 3D variable density FSE and compressed-sensing

Manuel Taso[1], Arnaud Guidon[2], Daniel V. Litwiller[2], David C. Alsop[1]

[1]Radiology, division of MRI Research, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA [2]Global MR Applications and Workflow, GE Healthcare

Introduction

While renal perfusion assessment using Arterial Spin Labeling (ASL) is gaining more and more traction, most implementations still rely on imaging sequences with limited slice coverage. But volumetric encoding combined with free-breathing acquisition help advance the use of ASL for broader abdominal applications. We report here on some early results of a variable-density Fast-Spin-Echo sequence[1] that we optimized for motion robustness to enable free-breathing volumetric renal ASL.

Methods

We developed a sequence combining a background-suppressed pseudo-continuous ASL preparation (500µs Hanning pulses, $B_{1,av}$=1.4µT, G_{max}/G_{av}=3.5/0.5 mT/m, labelling/PLD=1.5/1.5s) with a variabledensity FSE readout. The readout was designed as a variable density Poisson-disk sampling with a fully sampled (10^2) and oversampled (6^2) k-space center region (10^2). The oversampled region was acquired at the beginning of each echo-train followed by pseudo-random outer k-space sampling on a Cartesian grid (minimizing distance between successive echoes to minimize potential eddy-currents while maximizing sampling incoherency). **Experiments** were carried out on a GE Discovery MR750 3T scanner with a 32-ch body array. We compared the 3D-VDFSE sequence acquired under free-breathing and timed-breathing (TR/TE_{eff}=6200/5ms, Mtx=128x128x64, ETL=120, VFA) with our gold-standard single slice

single-shot FSE with retrospective motion-correction[2] in healthy volunteers. **All reconstructions** were performed offline using the BART[3] toolbox under MATLAB. After ESPIRiT[4] coil sensitivity estimation using the PD-w reference volume, we first reconstructed heavily undersampled single-shot volumes (each excitation) using an L_1-wavelet regularized CS reconstruction (10 iterations, λ_1=0.001). Although extremely blurred, we used those singleshot data to discard motion or otherwise corrupted datasets to keep only volumes within ± 2 standard deviations of the average ASL signal. We then reconstructed an average ASL volume with the remaining excitations using a 4D-CS reconstruction using spatial wavelets and temporal total-variation (TV) as sparsifying transforms[1].

Results

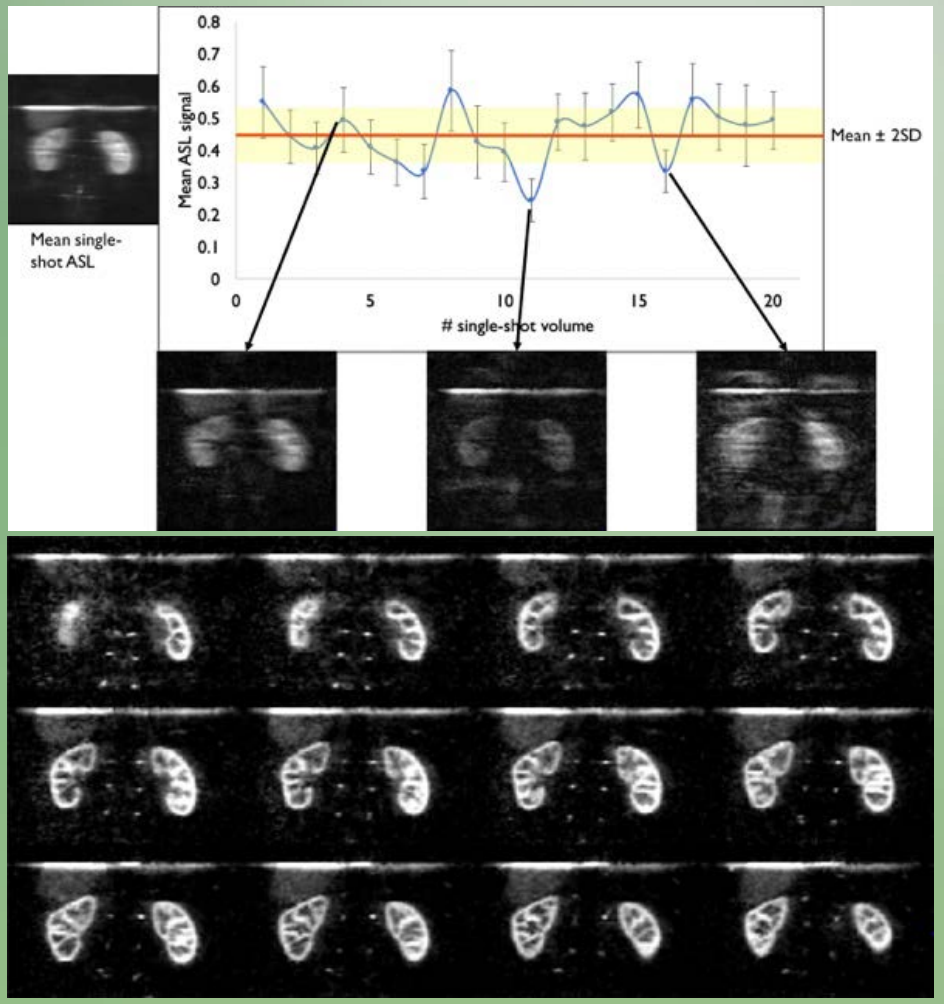
The figure to the right illustrates the reconstruction strategy from the VD-FSE data on a timed-breathing dataset. By reconstructing single-shot volumes, we could highlight significantly degraded excitations because of motion, reduced labelling efficiency or other causes that when discarding prior to 4D-CS reconstruction allowed collecting high-quality isotropic whole kidneys ASL data.

Discussion and Conclusion

We report here preliminary results with a motion-robust sequence for volumetric ASL perfusion imaging in the abdomen. While not providing true motion compensation, we have seen benefits of the sampling and reconstruction strategy in terms of image quality of volumetric renal ASL. Future developments will be focused on resolving respiratory motion either with external sensors (bellows) or using the single-shot data for such purpose. As ASL is a low resolution technique, the constraints on the motion compensation are likely to be less demanding than for anatomical imaging. The use of heavy background suppression further reduces the demands on motion compensation. These developments should enable motion-compensated whole abdomen ASL that could be readily transferrable into clinical routine.

References

1. Taso, M. et al., Magn. Reson. Med. 82, 680–692 (2019). 2. Taso, M. et al., Magn. Reson. Med. 81, 2439–2449
(2019). 3. Uecker, M. et al., Proc. Intl. Soc. Mag. Reson. Med 2486 (2015). 4. Uecker, M. et al., Magn. Reson.
Med. 71, 990–1001 (2014).



Optimization of pseudo continuous arterial spin labeling for renal perfusion imaging

Rebeca Echeverria-Chasco[1], Marta Vidorreta[3], Verónica Aramendía-Vidaurreta[1], Nuria Garcia-Fernandez[2], Gorka Bastarrika[1], and María A. Fernández-Seara[1]

[1]Radiology, [2]Nephrology, Clínica Universidad de Navarra, Pamplona, Spain; [3]Siemens Healthineers, Madrid, Spain

Introduction

Arterial Spin Labeling (ASL) is a non-invasive MR imaging technique to measure perfusion, which uses arterial blood as endogenous tracer. Pseudo Continuous Arterial Spin Labeling (pCASL)[1] is the recommended implementation for brain ASL[2]. The efficiency of pCASL is sensitive to arterial blood velocities and magnetic field variations at the labeling plane, which can be accentuated in renal ASL. The main goal of this work was to improve the robustness of pCASL for renal perfusion imaging.

Methods

Arterial blood flow was characterized at the labeling plane location in 8 healthy volunteers (age=29±3y) and 4 stage-3 chronic kidney disease (CKD) patients (age=78.5±7.5y), using a PC sequence. Numerical simulations based on a Bloch Equations approach[2] were performed to evaluate the pCASL inversion efficiency over a wide range of sequence parameters, artefactual off-resonance frequencies[3] and considering aortic blood velocities for both groups. The results in healthy volunteers were validated experimentally in 5 subjects (age=33±9y), studying 8 unbalanced pCASL configurations with four average gradients (Gave) and two ratios (R=Gmax/Gave) (Fig 1,i). A two-way ANOVA was used to evaluate the relationship between ASL signal (which depends on pCASL efficiency) and gradient configurations.

Results

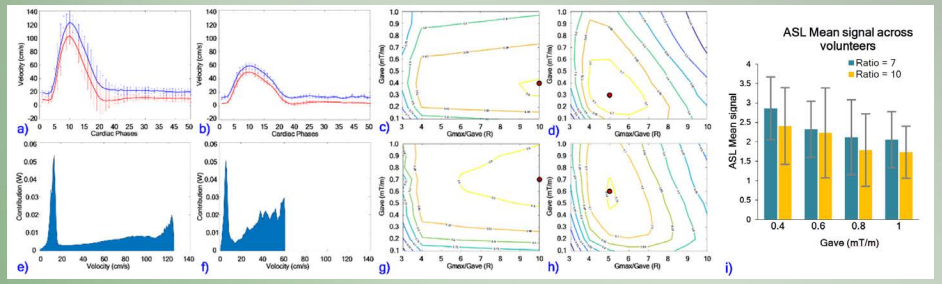


Fig 1: Blood velocity profiles in the aorta and contribution curves of healthy volunteers (a, e) and CKD patients (b, f). Simulation results for on-resonance and off-resonance conditions (considering off-resonance frequencies up to 500Hz), for healthy volunteers (c, d) and CKD patients (g, h). i) Results of the pCASL experiment in healthy volunteers for the eight tested scenarios. A p-value of 0.04 confirmed that there were significant differences in the efficiency across Gave values.

Conclusion and Discussion

The experimental data in healthy subjects demonstrated the validity of the simulations to evaluate pCASL labeling efficiency. Thus, the results of the simulations in CKD patients can be useful to configure the pCASL parameters in this group of subjects. On-resonance, high efficiency values are achieved for a wide range of parameters. Off-resonance, the range of parameters that provide high efficiency is narrower, although, interestingly, efficiency in CKD patients is less sensitive to offresonance effects than in the young healthy volunteers, due to their lower blood velocities.

The pCASL parameters which maximize the labeling robustness are low ratios of 5-7 and Gave of 0.3 - 0.5 mT/m for young healthy subjects and similar ratios but higher Gave of 0.5-0.7 for CKD patients. Future work will evaluate aortic blood velocities in elderly healthy subjects (which are likely to be used as controls in CKD studies).

References

[1] Dai W et al. Magn Reson Med. 2008 Dec;60(6):1488-97. [2] Alsop DC et al. Magnetic Resonance in Medicine, 2015:73(1):102-16. [3] Zhao L et al. Magn Reson Med. 2017;78(4):1342–51.

Acknowledgements.

Rebeca Echeverria-Chasco received Ph.D. grant support from Siemens Healthcare Spain.

A multi-site round robin assessment of ASL using a perfusion phantom

A. Oliver-Taylor[1], T. Hampshire[1], H.J. Mutsaerts[2,3,4], P. Clement[5], E. Warnert[6], J.P.A. Kuijer[2], K. Baas[3], J. Petr[7,8], J.C.W. Siero[4,9], J.P. Marques[10], S. Sunaert[11], R.J.H. Borra[12], M.J.P. van Osch[13], X. Golay[1,14], and E. Achten[5]

[1]Gold Standard Phantoms Limited, London, UK, [2]VUmc, Amsterdam, Netherlands, [3]AMC, Amsterdam, Netherlands, [4]UMCU, Utrecht, Netherlands, [5]Ghent University, Ghent, Belgium, [6]Erasmus MC, Rotterdam, Netherlands, [7]HZDR, Dresden, Germany, [8]RIT, Rochester NY, USA, [9]Spinoza Centre for Neuroimaging, Amsterdam, Netherlands, [10]Donders Institute, Nijmegen, Netherlands, [11]KULeuven, Leuven, Belgium, [12]MIC, UMCG, Groningen, Netherlands, [13]LUMC, Leiden, Netherlands, [14]ION, UCL, London, United Kingdom

Introduction

Perfusion, the delivery rate of arterial blood to an organ, can be non-invasively measured using Arterial Spin Labelling (ASL) MRI. Since the publication of the consensus paper on brain perfusion[1] there are now clear recommended guidelines on how to perform a brain ASL experiment, however, while there have been numerous reproducibility studies[2] and sources of potential physiological confounds are well established[3], it has so far not been possible to compare various ASL implementations depending on hardware differences only. In addition, no recommendation exist for kidney perfusion.

In this study we set out to assess the effective reproducibility of CBF estimates by ASL using a recently developed organ-independent perfusion phantom[4] at 11 different sites with a range of scanner manufacturers (17 systems total). We present here data from 5 Philips 3T MRI systems across 3 sites.

Methods

A perfusion phantom was transported by car to 3T MRI imaging centres in the Netherlands over the course of a week and scanned on five 3T Philips MRI systems (3 Ingenia, 2 Achieva) running software release 5.3. ASL measurements were made using the vendor supplied sequence, comprising of pCASL labelling with a 4-shot 2D-EPI segmented acquisition, comprising an acquisition with a long-TR and without background suppression or labelling pulses for an M_0 image, followed by 3 repetitions of control-label pairs. Measurements were made at 2 phantom flow rates, 200ml/min and 350ml/min.

CBF maps were calculated in Matlab using the single-subtraction equation for pCASL. Images were registered to a structural atlas image produced from the CAD model of the phantom, from which an ROI mask of the capillary-simulating porous material was generated. The mean and standard deviations of the perfusion rate within this mask were then calculated.

Results

Figure 1.a shows representative perfusion maps of the fifth slice from each data set. Figure 1.b and c show the CBF value distributions for MRI system 5. The mean CBF values and standard deviations for each system are shown in Figure 4. Across all systems the mean CBF was 33.7±3.1ml/100g/min at 200ml/min and 76.7±9.0ml/100g/min at 350ml/min.

Discussion

Mean CBF values were reasonably consistent at both flow rates, with coefficient of variance CoV of the mean CBF was 9.2%/11.7% at 200/350ml/min. As image quality, including artefacts and distortion is qualitatively comparable across all systems, a potential cause of the differences in the measured CBF is due to differences in labelling efficiency, which would also explain the increased CoV at the higher flow rate. However, no repeat measurements were made, so there is no metric of intra-session variability which might also explain some of the variations observed between systems.

Conclusion

We have presented a multi-site assessment of 2D-EPI pCASL measurements on Philips 3T MRI systems running the same software version, using a perfusion phantom. In general, results across systems are in good agreement with each other, however, further measurements and more sophisticated analyses are required to determine statistical significance.

References

1. Alsop DC, et al. MRM 2015; 73: 102-116. 2. Mutsaerts, et al. Neuroimage 113, 2015. 3. Clement, et al. JCBFM, 2018 Sep;38(9):1418-1437. 4. Oliver-Taylor A et al. Proc. ISMRM, 2017, Abstract #0681

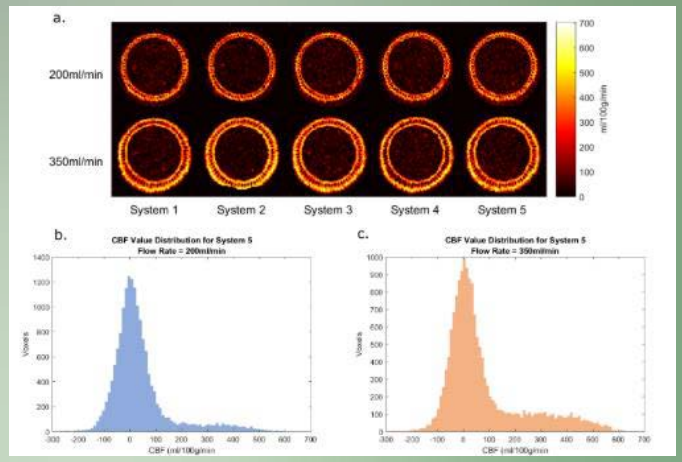


Figure 1

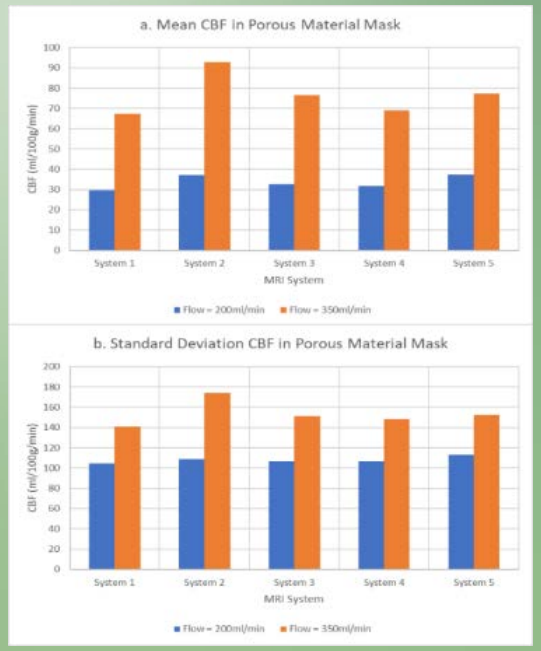


Figure 2

Inter-observer Variability of Renal Function and Volume Measurement in MRI Renography

Bashair Alhummiany, David Shelley, Margaret Saysell, Steven Sourbron, Kanishka Sharma

Biomedical Imaging Sciences Department, LICAMM, University of Leeds

Introduction

MR Renography (MRR) produces biomarkers of renal tissue perfusion and glomerular filtration[1], serving as a potential tool for diagnosis in diabetic kidney disease (DKD). This study aims to determine the inter-observer variability of MRR biomarkers in a population of DKD patients with a state-of-the-art MRR protocol developed for the iBEAt study[2].

Methods

MR renography was performed with a 2D Turbo-FLASH sequence on 11 patients with type-2 diabetes and eGFR >= 30 ml/min at 3T Siemens PRISMA MRI scanner (Free- Breathing; Acq time 7:07min, Temporal resolution 1.6s; FOV 400mm; Voxel size 2.78x2.08x7mm; 1 axial slice and 8 coronal-oblique slices; TR 179ms; TE 0.97ms; FA 10°; TI 85ms; GRAPPA 2). A quarter dose of Dotarem (0.05 ml/kg) was injected at 2ml/sec.

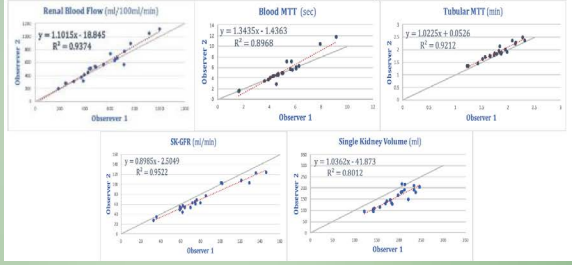
Post-processing was performed using in-house software PMI[3]. A semi-automated thresholdbased method was used for AIF selection (axial slice) and whole kidney ROI measurement (coronal-oblique slices). Renal perfusion and filtration parameters were then computed using the two-compartment filtration model[4] (2CFM) with bolus delay.

Two independent observers were trained on the PMI software using a training dataset that was not utilised for testing. Observer

2 (post-doc computer science, 2 years experience in MRR) was trained by the PI (MR physics, >15 years experience in MRR), and trained observer 1 (PhD student radiography, no experience in MRR). Analysis of the 11 test-cases was performed independently. Inter-observer effects were assesed using linear regression analysis, and mean and relative differences for each quantified parameter.

Results

Figure 1 shows the scatter plot with linear regression analysis; Table 1 summarises the inter-observer agreement in all 5 independent parameters.



Observer 1 vs Observer 2	Mean Difference (mean ± SD)	Relative Difference (mean ± SD)
Renal Blood Flow (ml/100ml/min)	-34.75 ± 64.87	0.10 ± 0.07
Blood MTT (sec)	-0.28 ± 0.96	0.09 ± 0.12
Tubular MTT (min)	-0.09 ± 0.09	0.06 ± 0.04
SK-GFR (ml/min)	10.72 ± 6.81	0.15 ± 0.08
Single Kidney Volume (ml)	35.03 ± 18.80	0.23 ± 0.11

Discussion

The reported results demonstrate high correlation between observers in all the measured parameters, but KV (Kidney volume) and SK-GFR showed a systematic difference. Analysis of the data showed that this was due to the subjective choices in the segmentation thresholds by the two observers leading to a systematic difference in kidney ROI size that propagates into SK-GFR.

Conclusion

MRR biomarkers are generally robust against inter-observer effects but there is a need for a more automated approach to kidney ROI selection in order to eliminate systematic errors in volume-dependent parameters.

References

[1] Notohamiprodjo M, et al. Eur J Radiol. 2010; 76(3):337-47. [2] www.beat-dkd.eu/project/. [3] Sourbron S, et al. Magn Reson Mater Phy. 2009; 22(1):539. [4] Sourbron S, et al. Invest Radiol 2008; 43:40–48.

Acknowledgments

K. Sharma and S. Sourbron are supported by the BEAt-DKD project that received funding from the IMI2-JU (No 115974) and JDRF. B. AlHummiany receives funding from the Department of Diagnostic Radiology, Taibah University, Medina, Saudi Arabia.

Optimisation of Renal Sodium MRI

Benjamin. L. Prestwich[1], Matthew. Clemence[2], Susan. T. Francis[1]

[1]Sir Peter Mansfield Imaging Centre, University Park, University of Nottingham, UK. [2]Philips Clinical Science Group, Philips Healthcare, Guildford, UK.

Introduction

Sodium (^{23}Na) is the second most abundant NMR sensitive nucleus in the human body. ^{23}Na MRI has the potential to provide complementary quantitative measures to ^{1}H MRI. However, the low sensitivity of ^{23}Na MRI in the body and need for additional hardware has limited its use. ^{23}Na MRI of the kidney has been shown to provide the sensitivity to measure the corticomedullary sodium gradient (CMSG), which serves to regulate homeostasis, and has been demonstrated to be reduced in kidney disease and transplanted kidneys[1–3]. This work explores the optimisation of ^{23}Na MRI of the kidney and its combination with ^{1}H MRI. There are several challenges associated with ^{23}Na MRI, due to its low sensitivity (3,000-20,000 times less than ^{1}H MRI) and the quadrupolar moment of sodium leading to short relaxation times. In order to maximise the ^{23}Na MRI signal the scan parameters must be optimised. For a gradient echo technique, the signal is primarily dependent on flip angle (FA), repetition time (TR) and echo time (TE) however there are several limiting factors that will dictate the possible values these scan parameters can take in practice. These limitations are mainly imposed by the scanner and RF coil hardware, the two main factors are the *average RF* power and *maximum* B_1 delivered by the RF coil. The work shown here aims to determine the optimal scan parameters to work within the scanner hardware limitations. This is done initially by simulation then confirmed with phantom and *in-vivo* data. Finally, the further benefit of ^{23}Na MRI comes with the fusion of ^{23}Na images with ^{1}H morphological and functional images to produce co-located complementary information, for this the collection of ^{23}Na and ^{1}H images within a single scan session without moving the patients is ideal.

Methods

Scans were acquired using a Philips 3T Ingenia DDAS scanner using a Pulseteq 13cm dual loop ^{23}Na coil. In order to ascertain the optimal combination of parameters a series of scans on a ^{23}Na phantom were carried using pulses with B_1 = 5, 7.5, 10, 15, 20, 30, 40 mT at the maximum Ernst angle the average RF power limit would allow. Scan were collected for a single average and multiple averages within average RF power limits in a total acquisition time of 3 minutes. Identical scans were collected *in-vivo* in a healthy subjects, in addition ^{1}H MRI images were collected using the Q-body coil.

Results

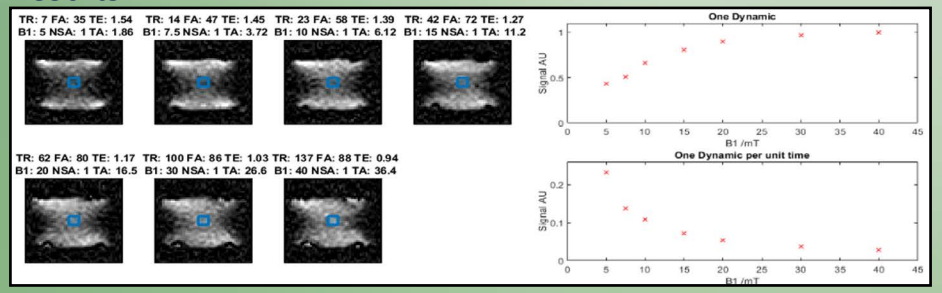


Figure 1: Left: Single slice sodium MRI scan with increasing B_1. Right: Top - Mean signal intensity from the blue square ROI, Bottom–signal intensity per unit time from sodium MRI scan.

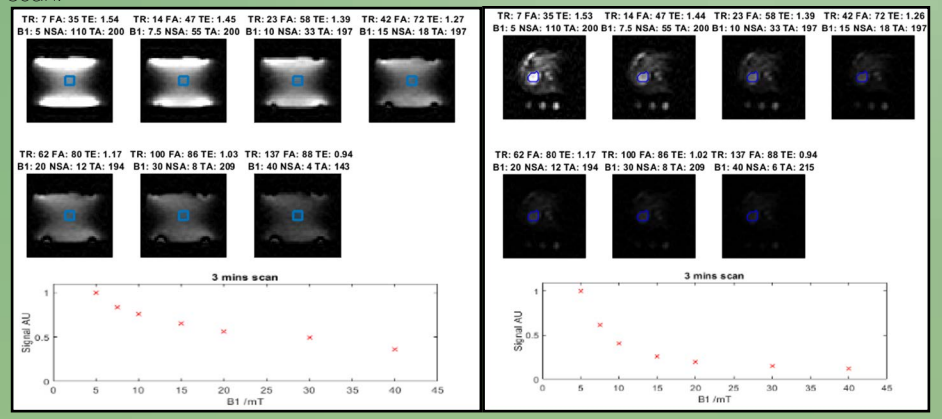


Figure 2: Left – Identical scan as in Fig.1 with an increased number of averages to result in a total scan time of approximately 200 seconds, and mean signal intensity from the blue square ROI in the phantom. Right -identical scan carried out in vivo, showing an axial slice and associated signal intensity.

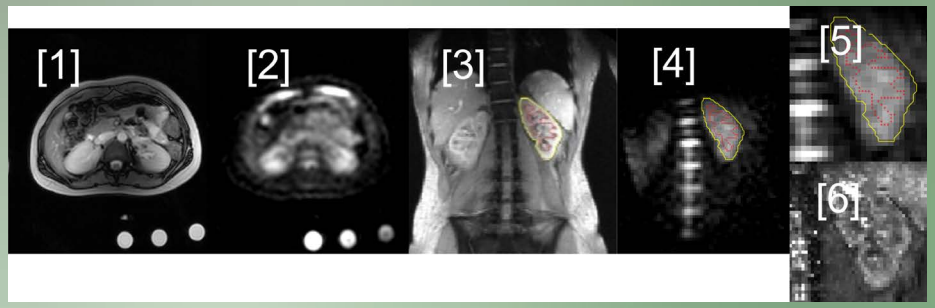


Figure 3: Renal images: 1) Axial proton localiser and corresponding 6x6x20mm axial ^{23}Na image. 3) Coronal T_1-weighted ^{1}H scan to segment the cortex and medulla and 4) 6x6x20 mm coronal ^{23}Na image with the regions from 3) overlaid. 5) Enlarged ^{23}Na image and 6) associated T_2^* map.

Discussion

The single average measurements in Figure [1] show that, as expected, there is less signal from a short TR, as due to incomplete recovery of the longitudinal magnetisation. However, a short TR allows for multiple averages in a given time as shown in Figure [2], optimal signal per unit time is obtained using a TR of 7 ms in both phantom and *in vivo* scans.

Conclusion

The optimal ^{23}Na scan parameters were found.

References

1.Haneder, S. et al, Strahlenther Onkol 188, 1146–1154 (2012). 2. Haneder, S. et al, . Magn. Reson. Mater. Physics, Biol. Med. 27, 47–52 (2014). Moon, C. H. et al Eur. Radiol. 24, 1320–1326 (2014).

Acknowledgements

This work is funded by MRC Discovery Grant MC/PC/15074.

Multi-parametric 3d rendering to detect crossing vessels with fMRU

Dmitry Khrichenko, Hansel Otero, Kassa Darge
Division of Pediatric Radiology at Children's Hospital of Philadelphia

Introduction

In addition to calculating split renal function, functional MR urography (fMRU) has been used to identify crossing vessels [1,2]. A split dose [3] and temporal projections [4] have been suggested to assist with visualization. A new fMRU post processing technique is presented here to further enhance crossing vessel visualization and localization. The arterial, venous and excretion phases are distinguished and depicted in 3 dimensions.

Methods

FMRU dynamic images were processed with pMRI (www.parametricmri.com, Philadelphia, PA, USA). Tabulated results, enhancement and excretion plots, as well as parametric maps were generated during the analysis. Various parametric maps were used to visualize the urinary tract in 3 dimensions (fig 1).

Results

The excretion phase (yellow) was rendered from a temporal subtraction maximal intensity projection (post arterial phase until end of scan). The arterial phase (red) was rendered from the blood volume parameter of a bi-directional two compartment permeability model [5]. Other surfaces included left and right parenchyma and the venous phase. The relative opacities, color, zoom and rotation were adjusted for best visualization.

Discussion

Surface rendering in MRI can be challenging due to noise and the ambiguity of signal intensity value vs structure relationship. The advantage of using multiple parametric maps for 3-dimensional rendering is the ability to differentiate between different types of crossing structures and also to visualize simultaneously the dilated renal pelvis and the pelviureteric junction.

Conclusion

Multi-parametric 3D rendering is able to differentiate between renal arteries and ureters, and display them in a 3-dimensional model in relation to the pelviureteric junction, facilitating the depiction of the crossing vascular structures. Further, research is needed to determine clinical utility.

References

1. Parikh, Kushal R., Matthew R. Hammer, Kate H. Kraft, Vesna Ivančić, Ethan A. Smith, and Jonathan R. Dillman. Pediatric radiology 45, no. 12 (2015): 1788-1795.
2. Weiss, Dana A., Sagar Kadakia, Rebecca Kurzweil, Arun K. Srinivasan, Kassa Darge, and Aseem R. Shukla. Journal of pediatric urology 11, no. 4 (2015): 173-e1.
3. Kocaoğlu, Murat Pediatr Radiol. doi 10 (2015).
4. Khrichenko, Dmitry, Susan J. Back, Dana A. Weiss, and Kassa Darge. Pediatric radiology 46, no. 9 (2016): 1358-1359.
5. Roberts, Timothy PL, Dmitry Khrichenko, and Arastoo Vossough. Clinical MR Neuroimaging: Physiological and Functional Techniques (2009): 369.

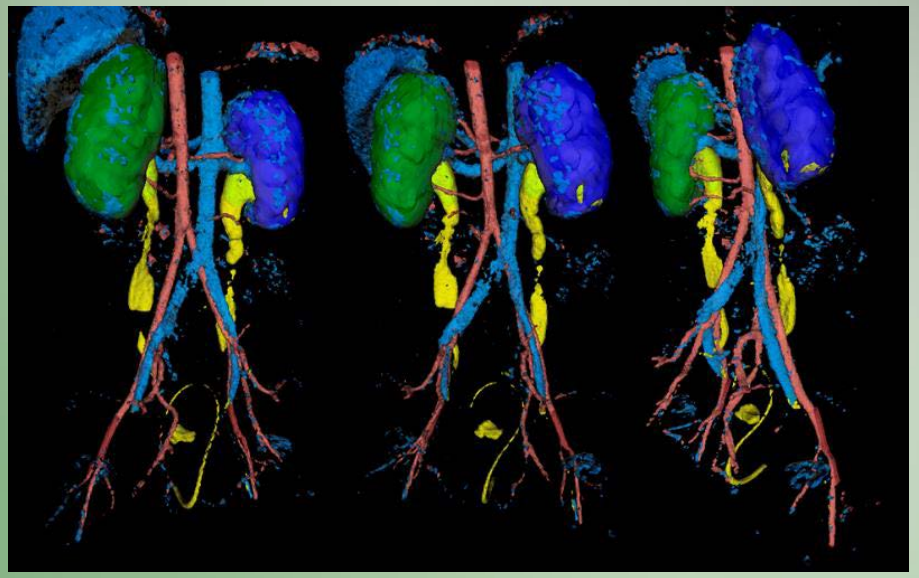


Figure 1

Functional analysis in MR Urography-made simple 2019 update

Dmitry Khrichenko
Division of Pediatric Radiology at Children's Hospital of Philadelphia

Introduction

Functional analysis in MR Urography-made simple [1] was published in 2010 and introduced the CHOP-fMRU (www.chop-fmru.com, Philadelphia, PA) post-processing software. Computer technology has made significant advances since, providing many new opportunities for software development. PMRI (www.parametricmri.com, Philadelphia, PA), presented here, continues where CHOP-fMRU left off, utilizing modern computer languages and technology.

Methods

PRMI was developed in a Windows environment (Microsoft, Redmond, WA) in C#, C++, LINQ, SQL and XAML. It runs on 32- and 64-bit Windows computers utilizing the Microsoft .NET framework (Microsoft, Redmond, WA).

Results

PMRI performs the same post-processing techniques as CHOP-fMRU, as well as bi-directional mapping, dynamic histograms, functional 3D rendering, functional 3D volume projections, improved segmentation, improved user interface, PACS integration, and a 500-5000X performance increase (figure 1). DWI analysis, T_2 [2] and T_1 mapping are built in, allowing for a detailed, multi-parametric analysis of the kidneys. Hundreds of MR Urograms have been analysed with pMRI in a clinical and research setting.

Discussion

PACS integration and performance and usability improvements increase productivity relative to the previous software. Parenchymal segmentation is faster and appears more accurate due to the new segmentation tools [3]. 3D projections and rendering allow for better visualization of the urinary system. Batch processing keeps track of all analyses performed in a central database allowing for recall of past cases and bulk research analysis.

Conclusion

PMRI introduces many new post-processing techniques, some of which have been utilized clinically and in research [2-4]. More applications are expected in the future as the software continues to mature.

References

1. Khrichenko, Dmitry, and Kassa Darge. Pediatric radiology 40, no. 2 (2010): 182-199.
2. Calle-Toro, Juan S., Christian A. Barrera, Dmitry Khrichenko, Hansel J. Otero, and Suraj D. Serai. Abdominal Radiology (2019): 1-11.
3. Didier, Ryne A., Dmitry Khrichenko, Christian A. Barrera, Carolina Maya, Ann M. Johnson, Edward R. Oliver, Julie S. Moldenhauer, and Teresa Victoria. American Journal of Roentgenology (2019): W1-W4.
4. Barrera, Christian A., Dmitry Khrichenko, Suraj D. Serai, Helge D. Hartung, David M. Biko, and Hansel J. Otero. Journal of Magnetic Resonance Imaging (2019).

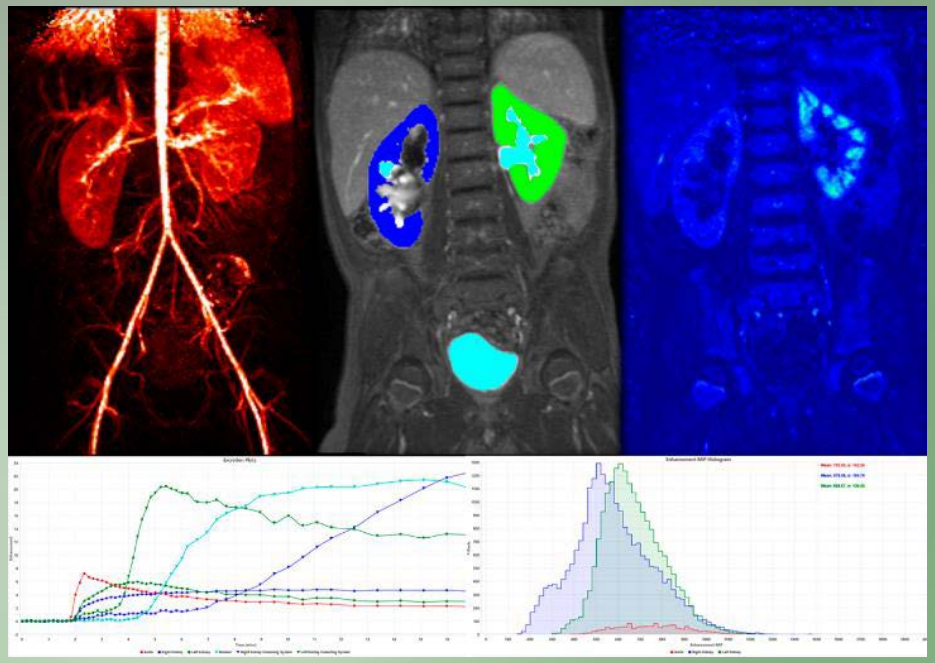


Figure 1

UK Renal Imaging Network: MRI Acquisition and Processing Standardisation (UKRIN-MAPS)

C.E. Buchanan[1*], F. Nery[2*], A.N. Priest[3], J. Sousa[4], M. Nation[5], I.A. Mendichovszky[3], S. Sourbron[4], D.L. Thomas[2,6], S.T. Francis[1] (*joint first authors)

[1]Sir Peter Mansfield Imaging Centre, University Park, University of Nottingham, UK, [2]Developmental Imaging and Biophysics Section, UCL Great Ormond Street Institute of Child Health, London, UK, [3]Department of Radiology, Cambridge University Hospitals NHS Foundation Trust, Addenbrooke's Hospital, Cambridge, UK, [4]Imaging Biomarkers Group, Department of Biomedical Imaging Sciences, University of Leeds, [5]UK, Kidney Research UK, Peterborough, [6]UCL Queen Square Institute of Neurology, London, UK.

Introduction

Renal MRI has undergone significant developments in recent years. Standardisation and multicentre evaluation of methods is now crucial for clinical translation. The UK Renal Imaging Network (UKRIN)[1] was set up in 2016 in collaboration with Kidney Research UK (KRUK), to bring together UK centres dedicated to the development and application of MRI methods for the study of the kidney. Here, we present UKRIN-MAPS (MRI Acquisition and Processing Standardisation)[2], an MRC Partnership framework of 13 existing UKRIN sites[2], which aims to share expertise and build capacity in renal MRI by developing harmonized protocols across MR field strengths (1.5 and 3T) and MR vendors.

Methods

This project aims to set up harmonised, consensus acquisition protocols, acquire normative renal MRI data in a healthy subject cohort, develop data analysis methods and implement an online data sharing platform (XNAT). We will develop and validate a software framework for analysis and quality assurance (QA) of

multi-parametric renal MRI data and its cross-site sharing. The repeatability of the multi-parametric protocol will be assessed using a "travelling kidney" study, scanning healthy subjects across multiple sites, as well as performing repeat scans at their home site. This will allow determination and calibration of any between-site differences and assessment of within-site stability. Phantom QA data will also be acquired on each scan day. Additional healthy subject data will be acquired which, when pooled with the travelling kidney study, will result in 50 healthy subjects' data at both 1.5 T and 3T.

Results

Optimisation and harmonisation of multiparametric renal MRI protocols, including morphological images, BOLD R_2^*, DWI, Phase Contrast MRI, T_1 mapping and ASL is currently underway, across GE, Philips and Siemens MR platforms. We have focused on harmonisation of B_0 and B_1 mapping schemes, T_2^* BOLD, T_1 mapping and DWI techniques, including the use of the NIST T_1 and Qalibre Diffusion phantoms. Example data is shown in Figure 1.

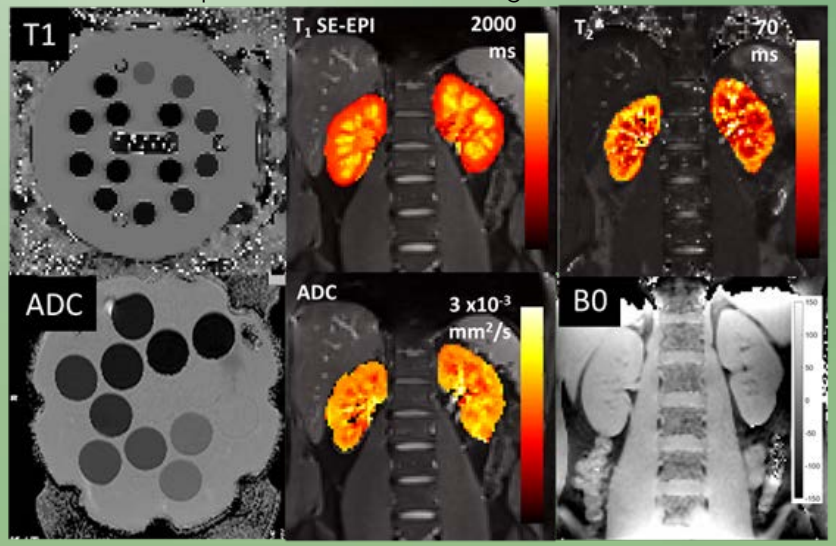


Figure 1: Example maps from phantom and in vivo kidney data, acquired using harmonised UKRIN acquisition protocols.

Discussion

While various single centre renal MRI studies have been performed in recent years, UKRIN-MAPS is the first multicentre effort aiming to generate reference standardised renal MRI acquisition and processing methods, and a streamlined data management and sharing system to serve as a platform to enable large-scale clinical trials. The multi-parametric normative dataset that will be generated within this project will establish reproducibility and biological variance of renal MR biomarkers in a multicentre and multivendor context.

Conclusion

UKRIN-MAPS aims to enable clinical translation of MRI for renal disease via multi-centre validation of multi-parametric acquisition protocols and analysis pipelines.

References

[1] Francis, S. & Selby, N. The UK Renal Imaging Network. (2016). Available at: https://www.kidneyresearchuk.org/research/uk-renal-imaging-network. (Accessed: 10th July 2019).
[2] Francis, S. et. al. UK Renal Imaging Network (UKRIN): MRI Acquisition and Processing Standardisation (MAPS). (2018). Available at: https://www.nottingham.ac.uk/research/groups/spmic/research/uk-renal-imaging-network/ukrin-maps.aspx. (Accessed: 10th July 2019)

Acknowledgements

This work is funded by MRC Partnership grant MR/R02264X/1.

Motion Correction with a Model Target (MoCoMo): A universal approach for quantitative renal MRI

Fotios Tagkalakis[1], Kanishka Sharma[1], Susmita Basak[1], Christopher Kelly[2], David Shelley[3], Irvin Teh[2], Jehill Parikh[4], Peter Thelwall[4], Neil Sheerin[5], and Steven Sourbron[1]

[1]Leeds Imaging Biomarkers Group, Biomedical Imaging Science Department, University of Leeds, Leeds, United Kingdom, [2]Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, Leeds, United Kingdom, [3]Advanced Imaging Centre, University of Leeds, Leeds, United Kingdom, [4]Newcastle Magnetic Resonance Centre, Newcastle University, Newcastle, United Kingdom, [5]Institute of Cellular Medicine, Newcastle University, Newcastle, United Kingdom

Introduction

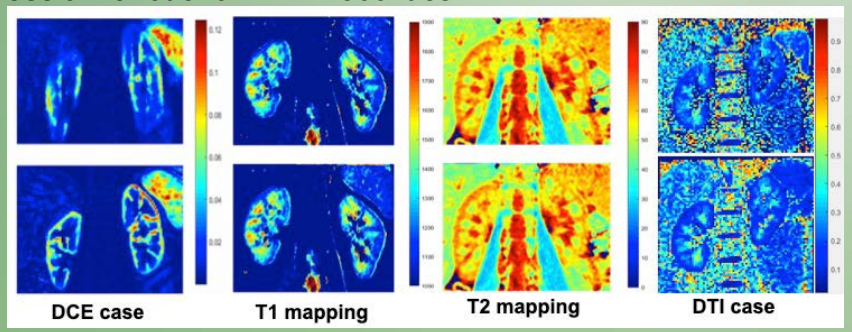
Motion correction in quantitative MRI is challenging due to changes in contrast introduced by varying parameters such as inversion time, echo time, diffusion weighting or contrast agent concentration. An elegant solution is Motion Correction with a Model Target (MoCoMo), which utilizes the MRI signal model to build registration targets of variable contrast, effectively performing a joint optimisation of the deformation fields and the quantitative MRI maps. The aim of this study is to investigate whether MoCoMo is an effective motion correction approach across multiple quantitative MRI modalities.

Method

Test data were drawn from renal pilot studies for 4 different contrast mechanisms, measured in 3 centres, on 2 different 3T scanners (Siemens, Philips). 2D registrations of a single slice were performed with a pixel-by-pixel model fitting using a linear 2-compartment model fit for DCE-MRI[(1)], mono-exponential recovery for T_1[(2)], mono-exponential decay for T_2[(3)], and a diffusion tensor model for DTI[(4)]. Frame-by-frame image co-registration was implemented in Elastix[(5)] following a multiresolution scheme, using the mutual information metric with adaptive stochastic gradient descent[(6)]. Each registration was performed with a combination of rigid body registration and free-form registration (B-spline).

Results and Conclusion

Figure below shows results without motion correction (top row) and with motion correction (bottom row) for each of the four contrast mechanisms (DCE: Renal Blood Flow; T_1 map; T_2 map; Fractional Anisotropy, respectively). This preliminary study suggests that MoCoMo is a suitable candidate for universal motion correction across all functional MRI modalities.



References

1. Flouri D, et al., Magn Reson Med. 2016;76(3):998-1006.
2. Messroghli DR, et al., Magn Reson Med. 2004;52(1):141-6.
3. De Bazelaire CM, et al., Radiology. 2004;230(3):652-9.
4. Kingsley PB. Concepts in Magnetic Resonance Part A. 2006;28A(2):123-54.
5. Klein S, et al., IEEE Trans Med Imaging. 2010;29(1):196-205.
6. Staring M, et al., Medical Image Analysis for the Clinic: A Grand Challenge. 2010:73-9.

Acknowledgements

This project has received funding from the IMI2-JU (No 115974) and JDRF.

Unbiased MRI Assessment of Renal Tubular Volume Fraction with Data-Driven IVIM: Initial Experience

Joao Periquito[1], Min-Chi Ku[1], Kathleen Cantow[2], Erdmann Seeliger[2], Bert Flemming[2], Thomas Gladytz[3], Dirk Grosenick[3], Thoralf Niendorf[1], Andreas Pohlmann[1]

[1]Berlin Ultrahigh Field Facility, Max Delbrueck Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany, [2]Institute for Vegetative Physiology, Charité Universitaetsmedizin Berlin, Berlin, Germany, [3]Physikalisch-Technische Bundesanstalt (PTB), Berlin, Germany

Introduction

Tubular volume fraction (TBF) is a potential confounding factor whose estimation might be helpful for the interpretation of renal T_2^*.[1,2] Diffusion-weighted imaging (DWI) provides a method for in-vivo evaluation of renal water mobility, which can be linked to three different sources: i) tissue water diffusion, ii) blood flow, and iii) tubular flow. To account for the TBF in renal diffusion assessment the commonly used bi-exponential intravoxel incoherent motion (IVIM) modelling,[3] was recently extended to a tri-exponential approach.[4] Here we explored the feasibility of assessing TBF changes using the non-negative least squares (NNLS) approach that is data-driven and requires no a priori knowledge.[6,7]

Methods

In-vivo experiments with adult female Wistar rats were performed on a 9.4T small animal-scanner (Bruker Biospec, Ettlingen, Germany). A bolus of glucose solution was administered i.v. to induce changes in the TBF. We employed a diffusion-sensitized split-echo RARE variant to ensure renal-DWI free of geometric distortion. ROIs were defined in the cortex (COR), outer medulla (OM) and inner medulla (IM) using semi-automated kidney segmentation[8]. The NNLS method[6] was implemented by adapting an open-source toolbox[7]. The NNLS analysis yields a spectrum of detected exponential components, where each peak represents a (pseudo)diffusion compartment with a mean diffusivity (MD; geometric mean of peak) and volume fraction (area-under-the-curve).

Results

Split-RARE DWI provided excellent image quality with anatomic fidelity and ample diffusion contrast in the rat kidney (Fig.1-A). NNLS revealed 3 distinct components for all renal layers, at baseline as well as during hyperglycemia (Fig.1-B). At baseline slow: (MD_{slow}= 1.78–2.34x$10^{-3}$$mm^2$/s, f_{slow}= 0.76–0.83), intermediate: ($MD_{intermediate}$= 9.15–9.68x$10^{-3}$$mm^2$/s, $f_{intermediate}$= 0.14–0.22) and fast:(MD_{fast}= 181–184x$10^{-3}$$mm^2$/s, f_{fast}= 0.02–0.03). During hyperglycemia significant alterations in the MDs and fractions were observed in all renal layers. While the f_{slow}= 0.14–28 decreased, $f_{intermediate}$= 0.40–0.73 and f_{fast}= 0.11–013 increased. Furthermore, the MD_{slow}= 0.56–0.87 x$10^{-3}$$mm^2$/s decreased in all regions.

Discussion & Conclusion

These initial results obtained with an unbiased model-free approach support the hypothesis of 3 distinct exponential components in renal DWI data. Baseline MD_{slow} and $MD_{intermediate}$ are in the range of diffusivities reported in previous studies[5,9] The obtained diffusivities, fractions and their changes during hyperglycemia support the interpretations of slow, intermediate, and fast components as representing tissue diffusion, tubular flow, and blood flow respectively. Acute hyperglycemia induces osmotic diuresis and increases GFR and renal blood flow[10], which is reflected by the increase in $f_{intermediate}$ and f_{fast}, respectively[10]. This novel approach requires further studies but it might be a promising refinement of the common IVIM analysis for the unbiased MRI assessment of renal TBF.

References

[1] Pohlmann et al., Acta Physiologica (2013) 8(2):673-689; [2] Pohlmann et al., Invest. Radiol. (2014) 49(8):547-60; [3] Le Bihan et al. Radiology (1988) 168(2):497-505; [4] van Baalen et al., Magn Reson

Med. (2017) 46(1):228-239; [5] van der Bel et al., European Journal of Radiology (2017) 91(3) 168-174; [6] Lawson et al., 1974; [7] Bjarnason et al., JMR 206(2):200-204; [8] Pohlmann et al., Tomography (2017) 3(4):188-200; [9] Zhang et al., Abdominal Radiology (2018) 43(3):655-662; [10] Woods et al., The American journal of physiology (1987) 252(1):65-73

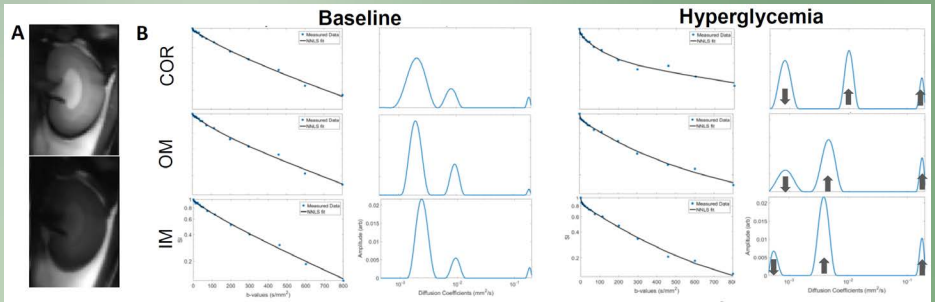


Figure 1: A. Diffusion-weighted images with some of the acquired b-values: 0 (top) and 460 s/mm^2 (bottom). B. NNLS Analysis with the diffusion decay and the NNLS spectrum, baseline (left) and hyperglycemia (right).The top, middle and bottom rows refer to: cortex, outer medulla and inner medulla respectively.

Comparison of TLCO and ROI Methods for BOLD MRI Analysis

Lu-Ping Li[1], Bastien Milani[2], Menno Pruijm[2], and Pottumarthi Prasad[1]

[1]Northshore University HealthSystem, Evanston, IL, USA; [2]Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland

Introduction

We recently reported renal BOLD MRI data in individuals with diabetes and moderate Chronic Kidney Disease (CKD, stage 3.a) [PMID: 30669143] where we had used manually defined regions of interest (ROI) for the analysis of renal BOLD MRI (Figure 1.d). When compared to a healthy control group, we did not find significant differences in individuals with CKD in regional R_2^* or response to furosemide. With the recent introduction of 12 layer concentric objects (TLCO) [PMID: 27798200] method (Figure 1.a-b), we wanted to evaluate its relative performance in terms of demonstrating differences between the two groups.

Methods

Data in 36 subjects (23 CKD and 13 control) were analysed by TLCO. Data for pre- and postfurosemide scans were analysed. To compare measurements between TLCO and ROI methods, we assumed (Figure 1): Inner = Medulla; Outer = Cortex; Mean of 12 layers = Kidney; Slope = (Medulla – Cortex). The level of agreement between the two methods of analysis was assessed using Pearson correlation coefficient. The different measured values between CKD and control groups were compared using Student's T test.

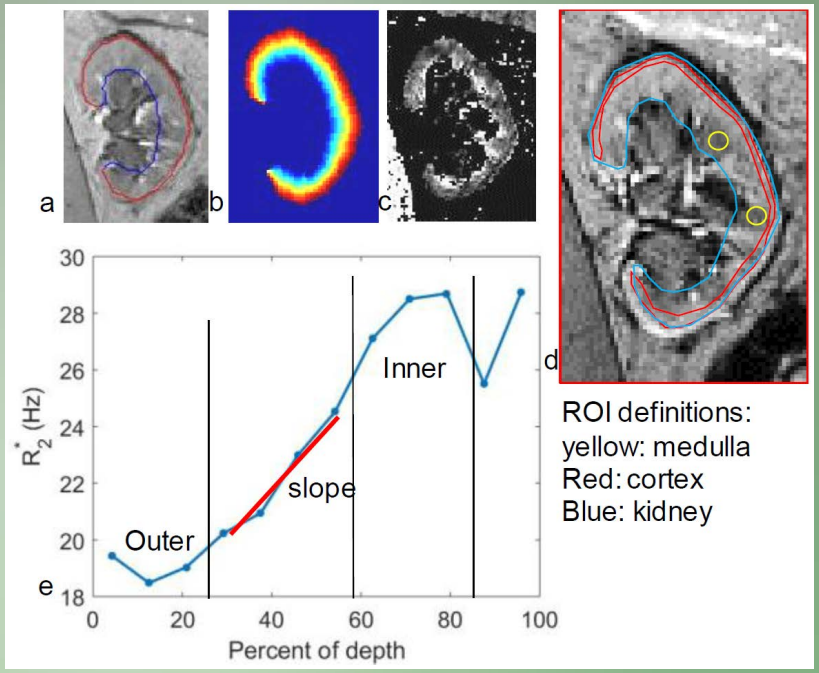


Figure 1: Illustration of TLCO and ROI methods

Results and Discussion

	pre-cortex (n=36)	pre-medulla (n=36)	pre-kidney (n=36)	ΔCortex (n=30)	ΔMedulla (n=30)	ΔKidney (n=30)
R value	0.73	0.85	0.81	0.32	0.54	0.66
p value	*< .00001*	*< .00001*	*< .00001*	*0.0805*	*0.0019*	*0.0001*

Table 1: Pearson Correlation Coefficient between TLCO and ROI

TLCO				ROI		
	ΔR2*_inner	pre_slope	Δslope		ΔR2*_medulla	R2*(M-C)
Control	4.3 ± 1.5	18.0 ± 5.5	8.3 ± 4.5	**Control**	6.2 ± 3.6	10.9 ± 4.1
CKD	2.2 ± 2.0	14.1 ± 4.2	4.7 ± 2.5	**CKD**	4.5 ± 3.6	8.6 ± 4.2
p value	*0.003*	*0.035*	*0.010*	***p value***	*0.218*	*0.147*

Table 2: Response to Furosemide

There was significant correlation between R_2^* measurements by both methods (Table 1). The level of agreement was considered large for R_2^* ($\rho > 0.6$) and moderate for ΔR_2^*. Both methods showed no significant differences between control and CKD with any of the regional R_2^* measurements (data not shown). TLCO demonstrated a significant difference in $\Delta R_{2\ inner}^*$ between controls and CKD, while $\Delta R_{2\ Medulla}^*$ by ROI analysis did not (Table 2).

In addition to providing regional estimates, TLCO offers a unique "slope" parameter, as defined in Figure 1.e. Slope is thought to be related to cortico-medullary difference, however ROI analysis failed to show a difference. There is recent interest in using C-M difference as an imaging marker with other MRI measurements [PMID: 30608554]. Consistent with $R_{2\ inner}^*$, Δslope showed significant difference between CKD and control group.

Conclusion

In conclusion, there was good agreement between ROI and TLCO measurements for regional assessments. But TLCO demonstrated response to furosemide both by $\Delta R_{2\ inner}^*$ and Δslope.

Acknowledgment

Work supported in part by grants from the National Institute of Diabetes Digestive and Kidney Diseases, R01-DK093793.

ASKDCNN: Automatic Segmentation of Kidneys using A Novel Deep Convolutional Neural Network

Mina Jafari[1], Susan Francis[2], Charlotte Buchanan[2], Jonathan Garibaldi[1], Xin Chen[1]

[1]School of Computer Science, University of Nottingham, UK [2]Sir Peter Mansfield Imaging Centre, University of Nottingham, UK

Introduction

Precise segmentation of kidney in magnetic resonance images (MRI) continues to be a challenging and active research area, due to difficulties caused by different MRI scanners and protocols, and similarities in intensity between the kidney and surrounding organs. Manual and semi-automatic, and a small number of automatic methods have been developed. A generic and efficient kidney segmentation framework is highly desirable. In this work, we propose an efficient fully automated method for high accuracy kidney segmentation of localizer scans collected in multiparametric MRI datasets.

Methods

Image segmentation based on deep convolutional neural network (DCNN) has achieved predominant performance over other classical methods in many medical applications. Our proposed method is adapted from a state-of-the-art DCNN method based on an encoder-decoder architecture (known as U-net [1]). It consists of an encoding path to extract image features in multiple image scales and a decoding path to produce a high resolution pixel-wise segmented image. Inspired by the dense net [2] and residual net [3] which have significantly increased the efficiency for training of DCNNs in object classification tasks, we propose a more efficient DCNN segmentation method than the original U-net. This enables rich feature information to be efficiently passed between consecutive layers in both the encoding and decoding paths, resulting in high segmentation accuracy.

Materials

Balanced turbo field echo (bTFE) coronal localizer scans were used to quantify kidney volume (400 mm x 400 mm x 91 mm field-of-view with 1.56 mm x 1.56 mm in-plane resolution and 7 mm slice thickness). Kidney volume masks were generated by manually tracing the kidney on the bTFE localizer images (Analyze9VR, AnalyzeDirect, Overland Park, KS, USA). In total, 230 3D images were available.

Results

Our method was evaluated based on the localizer dataset. 10 images were randomly selected for model validation. The remaining 220 images were randomly and evenly divided into a training and a testing group and cross validated in a 2-fold cross validation manner. All the images were 256x256x13, and zero-median normalization was applied to minimise the intensity variations. We assess the segmentation accuracy by comparing the segmented output of our DCNN method with manual annotations by experts. The dice coefficient of the 2-fold cross validation was 0.87±0.06 for both left and right kidneys. Training time was 90 hours and test time for each image was less than 10 seconds. An example image is shown in Fig. 1.

Discussion

The best reported dice value in literature for automatic kidney segmentation is 0.86±0.07 using a DCNN network on CT images in Autosomal Dominant Polycystic Kidney Disease [4]. However, CT images is arguably an easier task compared to MRI due to more consistent intensity values across images. Our goal is to increase the generalizability of our method e.g. train on one set of images, and test on other MRI images acquired using other protocols and field strengths (i.e. 1.5 T, T_1/T_2, etc.).

Conclusion

In this work, we propose a new DCNN network that takes advantages of state-of-the-art methods and escalates the performance without increasing the number of parameters and training time. Although we only focus on segmentation of kidney in MRI in this study, the proposed method is generic and flexible, and can be applied to many different imaging modalities, 2D/3D and other clinical applications. We are working towards a solution to improve the method for training, as accurate manual annotation of a large dataset is extremely labour intensive and expensive in medical applications.

References

[1] Ronneberger, O., et al. International Conference on Medical image computing and computer-assisted intervention. 2015. Springer. [2] Huang, G., et al. Proceedings of the IEEE conference on computer vision and pattern recognition. 2017. [3] Veit, A., et al. Advances in neural information processing systems. 2016. [4] Sharma, K., et al. Nature, 2017.

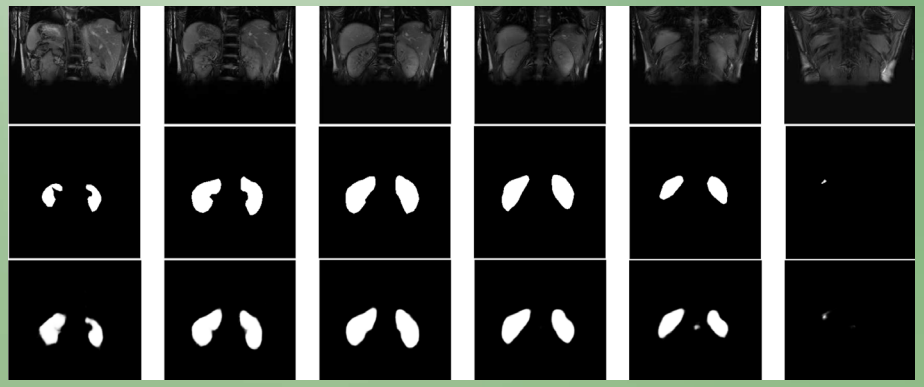


Figure 1: Qualitative results of a challenging subject from slice 8 to 13. First row: original image. Second row: ground truth. Third row: output of our method.

Segmentation of Kidney Perfusion Maps using K-Means – Initial results

DM Morris[1], M Donnelly[2], FJ Gifford[1], P Dunne[2], PC Hayes[2], KJ Simpson[2], JA Fallowfield[1] and SIK Semple[3]

[1]MRC Centre for Inflammation Research & [3]BHF Centre for Cardiovascular Science, University of Edinburgh and [2]Liver Unit, Royal Infirmary of Edinburgh all Edinburgh Bioquarter, Edinburgh, United Kingdom

Introduction

Magnetic Resonance Imaging (MRI) Arterial Spin Labelling (ASL) non-invasively measures perfusion which provides functional information across the kidney as a biomarker map. Segmentation of the cortex and medulla of the kidney is important as they have different functions and perfusion values. Segmentation has been previously done by identifying two distributions in the whole kidney T_1 and B_0 histograms[1] or by defining cortex and medulla on a structural image[2]. Both these methods require acquisition of additional images and registration. We propose the application of k-means clustering for segmentation of individual perfusion maps.

Methods

All data was acquired on a 3.0 T Siemens Prisma Scanner (Siemens Healthineers, Erlangen, Germany). 15 subjects were scanned to evaluate this approach, 7 with normal kidney function and 8 suffering from renal impairment. The perfusion maps were generated on the console and segmentation was carried out in MATLAB 2016b (The Mathworks Inc. Natick MA USA). The segmentation first smoothed a single slice of the maps with a 3 x 3 kernel before an initial region was defined to encompass the whole kidney. Clustering was then applied to identify two distributions based on the perfusion values and their position. Segmentations were projected back into image space and checked for physiological sense before the mean perfusion of each region was determined. SPSS 24 (IBM, Armonk, NY, USA) was used to carry out Mann–Whitney U tests to identify significant differences

between groups.

Results

Table 1 summarises the perfusion values (mean ± STDEV) for the whole kidney, cortex and medulla with significant ($p < 0.05$) differences between whole kidney and cortex/medulla indicated with * and differences in regions between normal/impaired kidneys with °.

Region \ Group	All Subjects	Normal Kidney Function	Impaired Kidney function
Whole Kidney	236 ± 75	263 ± 47	201 ± 92
Cortex	278 ± 88 *	314 ± 62 °*	237 ± 99 °*
Medulla	162 ± 68 *	186 ± 44 °*	144 ± 83 °*

Table 1 Perfusion values in units of ml/100 g tissue/min

Discussion

The clustering algorithm has identified segmentations that are meaningful given kidney anatomy which identify significantly different regions of tissue perfusion. Differences between healthy and compromised patients in the cortex and medulla were not observed at the whole kidney level. However, the absolute values for medulla perfusion are higher than expected[3]. On investigation this was a result of the lower resolution, compared to structural MRI, of ALS images (4.7 x 4.7 x 4.7 mm) which resulted in partial volume voxels which were clustered into the smaller medullary regions.

Conclusion

K-means clustering has been successfully applied to ASL perfusion maps of the kidneys giving physiologically appropriate segmentations with reduced operator involvement but this technique has dependencies on the data quality requiring imaging optimisation and further investigation.

References

1. Cox et al. Frontiers in Physiology (2017) vol. 8 696. doi:10.3389/fphys.2017.00696
2. Gillis et al. BMC Nephrology (2014) 15(23), 2014 (doi:10.1186/1471-2369-15-23)
3. Odudu et al. Nephrol Dial Transplant (2018) 33: ii15–ii21 doi: 10.1093/ndt/gfy180

Acknowledgements

We acknowledge the support provided by Siemens in the form of sequence and analysis provided in the Works In Progress package ASP 1023 E as part of the research agreement with the University of Edinburgh.

Quantification of renal microscopic fractional anisotropy using multidimensional diffusion MRI

Fabio Nery[1], Filip Szczepankiewicz[2,3,4], Leevi Kerkelä[1], Matt G. Hall[1,5], Enrico Kaden[6], Isky Gordon[1], David L. Thomas[7,8], Chris A. Clark[1]

[1] Developmental Imaging and Biophysics Section, UCL Great Ormond Street Institute of Child Health, London, UK [2] Department of Radiology, Brigham and Women's Hospital, Boston, Massachusetts [3] Harvard Medical School, Boston, Massachusetts [4] Medical Radiation Physics, Clinical Sciences, Lund, Lund University, Lund, Sweden [5] National Physical Laboratory, Teddington, United Kingdom [6] Centre for Medical Image Computing, University College London, London, United Kingdom [7] Leonard Wolfson Experimental Neurology Centre, UCL Queen Square Institute of Neurology, London, UK [8] Department of Brain Repair and Rehabilitation, UCL Queen Square Institute of Neurology, London, UK

Introduction

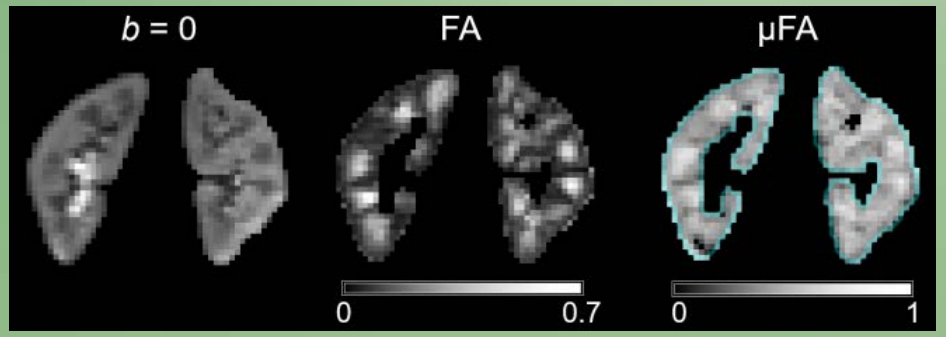
Diffusion MRI (dMRI) enables non-invasive assessment of tissue microstructure. Fractional anisotropy (FA) is a widely dMRI biomarker used but is confounded by orientation dispersion [1]. Multidimensional (MD)-dMRI provides novel microstructural parameters, such as microscopic fractional anisotropy (μFA) which disentangles anisotropy and orientation dispersion [1]. Nevertheless, MD-dMRI has not yet been harnessed to assess kidney microstructure [2]. Here we report on the feasibility of in vivo quantification of renal μFA in healthy subjects.

Methods

Ten healthy volunteers (age 31±6 years) were scanned on a 3T Siemens Prisma system using a spin-echo EPI sequence with linear (LTE) and spherical tensor diffusion encoding (STE). Encoding waveforms were optimized numerically [3]. Diffusion encoding parameters were: b-values(s/mm^2)/averages=[0,250,500,750,1000]/[4,2,2,2,2]; 12 directions. Other sequence details: FOV=288x288mm^2; voxel size=3x3x(4–4.6)mm^3; 11 slices; TR/TE=3000/87ms. Respiratory triggering and image registration (elastix [4]) were used for motion compensation. Calculation of μFA was performed using a single-shell approach [1, 2] using the highest b-value data.

Results and discussion

The hallmark of μFA (divergence of LTE and STE signal) was observed in all subjects. Powder-averaged LTE signal was higher than STE signal from b=500s/mm^2 in the medulla and b=750s/mm^2 in cortex (t-test, $p<0.05$) with the largest relative LTE-STE difference found at the highest b-value sampled (b=1000s/mm^2). ROI-based cortical and medullary μFA were, respectively, 0.53 ± 0.09 and 0.65 ± 0.05 (two-tailed paired t-test, $P < 10^{-4}$), significantly higher than conventional FA in both the cortex and medulla (0.19 ± 0.02 and 0.40 ± 0.03, respectively) (2-tailed paired t-tests, $P < 10^{-5}$) (see figure). The lower cortico-medullary (CMD) differentiation in μFA (compared to conventional FA) suggests orientation dispersion in cortex enhances CMD seen in conventional FA.



Central b=0 s/mm^2 slice, conventional FA and μFA maps

Conclusion

This study provides pilot data in healthy volunteers suggesting feasibility of renal μFA quantification, which may provide a new MRI biomarker to characterise renal tissue microstructure. Future studies are warranted to ascertain the clinical utility of μFA quantification.

References

[1] Lasič, S., et. al., 2014. Front. Phys., 2, pp.1–14; [2] Nery, F., et. al., 2019, MRM, doi: 10.1002/mrm.27869, [3] Sjölund, J., 2015, doi: 10.1016/j.jmr.2015.10.012; [4] Klein, S., 2010, IEEE TMI, doi: 10.1109/TMI.2009.2035616

Acknowledgements

Funding by Great Ormond Street Hospital Children's Charity (V0318) and support by NIHR Great Ormond Street Hospital Biomedical Research Centre.

Comparing sample mining schemes for CNN kidney segmentation in T_1w MRI

Alena-Kathrin Schnurr, Christian Drees, Lothar R. Schad, Frank G. Zöllner

Computer Assisted Clinical Medicine, Medical Faculty Mannheim, Heidelberg University

Introduction

Exact delineation of the kidney contour is an important step in therapy and diagnostics of renal diseases [1]. Manual annotation is time consuming and suffers from high observer-variability, thus a fast and fully automatic segmentation of the kidneys is required. We investigate how different sample mining schemes during the training of convolutional neural networks influence the segmentation quality on T_1w MRIs.

Methods

We used 18 T_1w coronal whole body MRI scans from the Visceral Anatomy 3 challenge data set [2] with voxel size of 1.25 x 1.25 x 5 mm. As renal MRIs usually have a smaller field of view the images were cropped to a 256 x 256 in plane. For training we additionally used the 11 T_1w scans from the Visceral Silver Corpus data set [2].

We used a U-Net architecture with additional residual connections and batch normalization [3]. The networks were trained using the weighted cross entropy loss. The loss was based on the dilated kidney masks and a thresholding of the background. Image intensities were normalized based on the 5th and the 95th percentile. Each network trained for 50 epochs on 128 x 128 patches with a learning rate of 0.001 and batch size = 8.

We compared three different sample mining schemes. Random: patches are randomly selected from each slice. μ ± 3Std: patch centers are constrained to the average label position ± three times the standard deviation. Label: patch centers are constrained to label

positions. We performed 3-fold cross validation on the Anatomy 3 data and extended the training for each fold with the Silver Corpus data.

Results

	Random	μ ± 3Std	Label
Left Kidney - Dice	**0.885 ± 0.046**	0.877 ± 0.053	0.879 ± 0.053
Right Kidney - Dice	**0.863 ± 0.076**	0.835 ± 0.115	0.836 ± 0.130
Left Kidney - MSSD (mm)	3.521 ± 4.114	2.918 ± 3.913	**1.852 ± 2.052**
Right Kidney - MSSD (mm)	1.823 ± 2.724	1.264 ± 1.236	**1.031 ± 0.932**

Discussion

There seems to be no benefit in stirring the sample selection into the general area of the kidney using μ ± 3Std. Random sampling did perform best according to the Dice. However, according to the Mean Symmetric Surface Distance, which is more sensitive to outliers, the best segmentation is achieved when training patches are centered on the label voxels.

Conclusion

Segmentation quality differs based on the selected sampling scheme. When the exact contour of the object is required a label based scheme leads to an enhanced segmentation quality.

References

[1] O. Jimenez-del-Toro et al., IEEE Trans Med Imaging, 35(11), 2459-2475 (2016)
[2] F. Zöllner et al., Am J Roentgenol, 199 (5), 1060-1069 (2012)
[3] O.Ronneberger et al., MICCAI, 9351, 234-241 (2015)

Acknowledgements

This research project is partly supported of the Research Campus M2OLIE funded by the German Federal Ministry of Education and Research (BMBF) within the Framework “Forschungscampus: public-private partnership for Innovations” under the funding code 13GW0388A. We gratefully acknowledge the support of NVIDIA Corporation with the donation of the NVIDIA Quadro P5000 used for this research.

Automated Renal Segmentation in Healthy and CKD Subjects Using Fully Convolutional Neural Networks

Alexander J Daniel[1], Charlotte E Buchanan[1], Susan T Francis[1]

[1]Sir Peter Mansfield Imaging Centre, University of Nottingham

Introduction

Segmentation of kidneys in MR images is a vital yet time consuming aspect of many studies. These segmentations can be used to produce a measure of total kidney volume (TKV), to increase the accuracy of other pipelines or reduce computation times by only carrying out calculations for a relevant region of interest (ROI). The gold standard for segmentation is manual ROI definition by an experienced and skilled person, but this is a time consuming process. The development of a fully automated method is highly desirable. Such methods have been proposed but are limited to use with a single pathology[1]. Deep learning allows a single method to be written and trained on datasets, as more data becomes available, the algorithm can become more accurate and generalised without the need to rewrite the underlying methods. Here a fully convolutional neural network (FCN) is used to segment the kidneys.

Methods

T_2-weighted images (half-Fourier single-shot turbo spin echo (HASTE) sequence: TR = 1800 ms, echo time TE = 60 ms, bandwidth BW = 792.3 Hz/pixel, field of view FOV = 350x350 mm^2, 13 slices and voxel size of 1.5x1.5x5mm^3) were acquired on a 3T Philips Ingenia system in a single breath hold . A total of 60 subjects were scanned with 10 being scanned 5 times on the same day to allow the repeatability of TKV to be assessed. This repeatability data was used for validation while 80% of the remaining subjects were used for training and 20% used for testing. Subjects were an even split of healthy control (HC) participants and Chronic Kidney Disease (CKD) patients. A ground truth segmentation was made for each scan. The network architecture is shown in Figure 1.

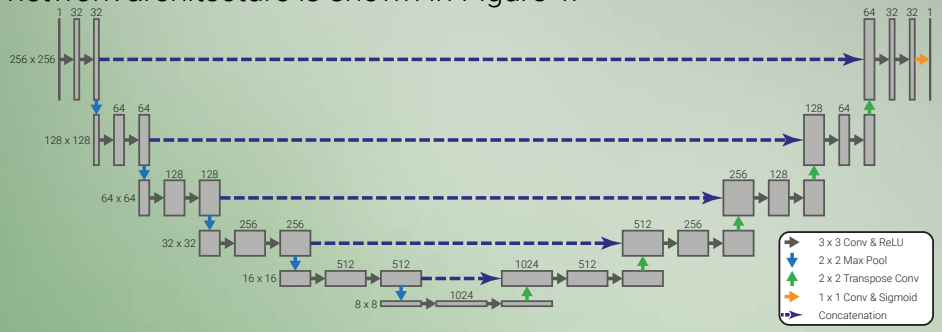


Figure 1: An overview of the fully convolutional neural networks architecture.

Results

Using the network to predict the TKV of each of the unseen validation volumes, produces a Dice coefficient of 0.93±0.02, with a mean underestimation of -2.0±16.5 ml. The underestimation of TKV was slightly greater in the CKD group than the HC group (-7.7±9.4 ml in CKD and +3.6±20.1 ml in HCs respectively).

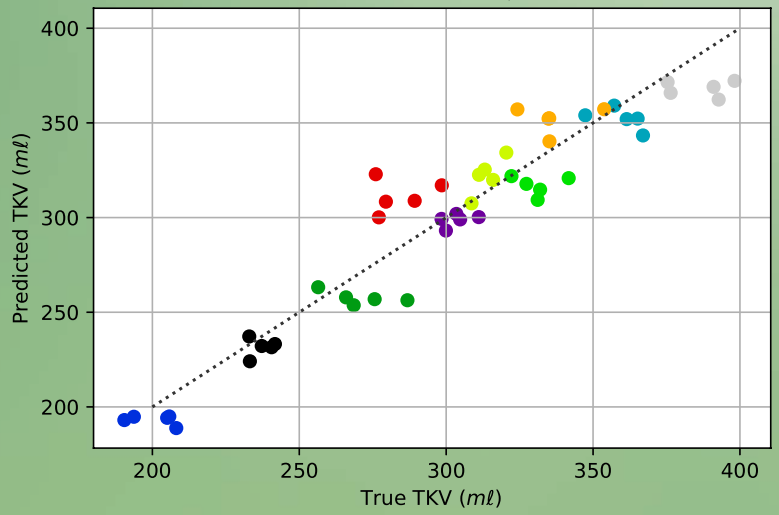


Figure 2 The TKV predicted by the FCN plot against the manually segmented true TKV. Each subject is shown in a different colour.

Discussion
In eight out of the ten validation subjects, the network produced more consistent predictions of TKV than the manual segmentation, this can be seen in Figure 2. Given we know the TKV of each subject did not change between scans, this indicates that the network may be outperforming the humans.

Conclusion
We have developed an algorithm to accurately and quickly segment the kidneys in MRI data with no user input. This method works well for healthy participants and CKD subjects and can easily be modified to work with any group where sufficient training data exists.

References
1. Zöllner, F. G. et al. American Journal of Roentgenology (2012)

Acknowledgements
We gratefully acknowledge the support of NVIDIA Corporation with the donation of the Titan Xp GPU used for this research.

The Effects of Fixation and Age on MRI Measurements of Ex-Vivo Kidneys

Alexander J Daniel[1], Charlotte E Buchanan[1], Isma Kazmi[2], Eleanor F Cox[1], Nicholas M Selby[2], David S Gardner[3], and Susan T Francis[1]

[1]Sir Peter Mansfield Imaging Centre, University of Nottingham, [2]Centre for Kidney Research and Innovation, University of Nottingham, [3]School of Veterinary Medicine and Science, University of Nottingham

Introduction
Renal pathologies are currently assessed via biopsy and histological staining, an invasive process that is not representative of the entire kidney. Multiparametric MRI has been suggested as an alternative method of assessing the underlying pathology[1]. By comparing whole organ histology, in-vivo MRI and high SNR ex-vivo MRI, the effectiveness of MRI as a replacement for renal biopsy can be evaluated. To scan the kidneys ex-vivo requires fixing them in formalin, the effect of this process upon renal tissue is not known. Here we study these effects in a porcine model to facilitate future ex-vivo studies in human kidneys.

Methods
Porcine kidneys were fixed in Neutral Buffered Formalin for twenty-four-hours then washed in phosphate-buffered saline[2]. The samples were then scanned at 3T and 7T, with a T_1 and T_2^* map being produced at each field strength. Samples were scanned over a ten-week period post fixation. To study renal inflammation and fibrosis, samples from a 0.5 and 2.5 year old pig were scanned and histology was performed on the renal cortex.

Results
Figure 1 shows how the T_1 and T_2^* of the kidney change over the ten-week window. It can be seen that the parameters are similar to

those of unfixed kidneys between twenty-four-hours and one-week. A second kidney was scanned over the first twenty four hours after fixation and showed no significant change in MRI measurements.

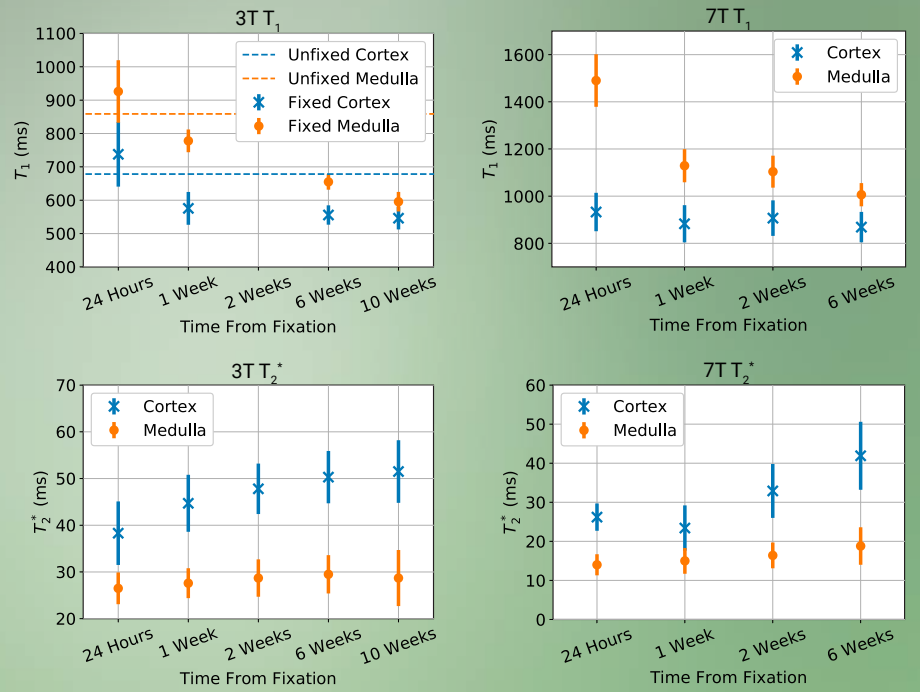


Figure 1: The effects of fixation of T_1 and T_2^* on a porcine kidney

No significant change was seen between the 0.5 year old and 2.5 year old pigs kidneys when analysing the histology of the cortex. This is also reflected in the MRI measurements of the cortex.

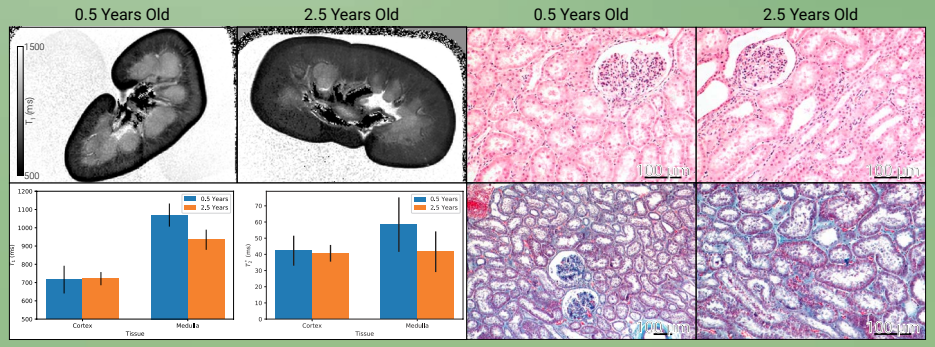


Figure 2: Comparing histology and MRI of kidneys of different age pigs.

Discussion

As the properties of the kidneys were similar to those of un-fixed kidneys in the first twenty-four-hours and were stable over this period, it is advisable that any future fixed samples are scanned in this window. The agreement between the histology and MRI data between the two ages of pigs is a promising indication.

Conclusion

We have shown that the optimum time to scan formalin fixed kidney samples is within twenty-four-hours of rehydration.

References

1. Cox, E. F et al. Front. Physiol. 8, (2017)
2. Sengupta, S. et al. NeuroImage (2017)

Computer aided diagnosis using BOLD-MRI in early assessment of transplanted kidney

Mohamed Abou EL-Ghar[1], Mohamed Shehata[2] , Mohamed Badawy[1], Ayman Elbaz[2]

[1]Radiology Department, Urology and Nephrology Center, Mansoura University, Mansoura, Egypt. [2]BioImaging Lab, Bioengineering Department, University of Louisville, Louisville, KY, USA.

Introduction

Non-invasive evaluation of renal transplant function is essential to minimize and manage acute renal rejection (AR). A computer assisted diagnostic (CAD) system is developed to evaluate kidney function post-transplantation. The developed CAD system utilizes the amount of blood-oxygenation extracted from 3D (2D + time) blood oxygen level-dependent magnetic resonance imaging (BOLD-MRI) to estimate renal function.

Methods

BOLD-MRI scans were acquired at five different echo-times (2, 7, 12, 17, and 22) ms from 15 transplant patients. The developed CAD system first segments kidneys using the level-sets method followed by estimation of the amount of deoxyhemoglobin, also known as apparent relaxation rate (R_2^*). These R_2^* estimates are used as discriminatory features (global features (mean R_2^*) and local features (pixel-wise R_2^*)) to train and test state-of-the-art machine learning classifiers to differentiate between non-rejection (NR) and AR.

Results

Patients were divided into two groups – normal kidney function group (10 patients) and AR group (5 patients). Using a leave-one-out cross-validation approach along with a multi-layer preceptron neural network (MLP-NN) classifier, the CAD system demonstrated 93.3% accuracy, 100% sensitivity, and 90% specificity in distinguishing AR from normal kidney.

Discussion

BOLD-MRI has the unique advantage of having a higher SNR while avoiding the use of CAs. Therefore, it has been recently used by researchers to study renal rejection [1–4], using the amount of the deoxygenated hemoglobin in the kidney to quantify renal function. It has been reported that the R_2^* in medulla is higher in both healthy transplants and native kidneys compared to AR [1–4], while cortical R_2^* values were reported to be similar [1, 4]. These BOLD-MRI studies have several limitations including (1) manual delineation of the kidney using a 2D ROI, which makes this delineation subjective, (2) only performed statistical analyses to investigate the significant differences between different groups, and (3) none of these studies developed a fully automated CAD system for the early detection of AR renal transplants.

So' development of a fully automated CAD system, to make an early and accurate diagnosis of acute rejection renal transplants is warranted , our system has ability to: (i) delineate the kidney at different echo-times; (ii) extract global features and local features from the segmented kidney at different echo-times; and (iii) implement a classification model using the global and local features to assess the renal transplant status.

Conclusion

A non-invasive CAD system for early diagnosis of AR using BOLD-MRI provided high classification accuracy, sensitivity, and specificity. The CAD system incorporates global and local features to better characterize renal function and evaluate AR.

References

1- G. Liu et al., BMC Nephrology, vol. 15, no. 1, pp. 158, 2014.
2- F. Han et al., Nephrology Dialysis Transplantation, vol. 23, no. 8, pp. 2666–2672, 2008.
3- E. A. Sadowski et al., Magnetic Resonance Imaging, vol. 28, no. 1, pp. 56–64, 2010.
4- A. Djamali et al., Transplantation, vol. 82, no. 5, pp. 621– 628, 2006.

Optimized CEST MRI for functional assessment of transplanted kidney at a clinical 3T MRI system

Julia Stabinska[1], Alexandra Ljimani[1], Eric Bechler[1], Christian Tell[2], Helge Jörn Zöllner[1,3], Hans-Jörg Wittsack[1], Anja Müller-Lutz[1]

[1] Heinrich Heine University Dusseldorf, Medical Faculty, Department of Diagnostic and Interventional Radiology, D-40225 Dusseldorf, Germany, [2] Heinrich Heine University Dusseldorf, Medical Faculty, Department of Nephrology, D-40225 Dusseldorf, Germany, [3] Heinrich Heine University Dusseldorf, Medical Faculty, Institute of Clinical Neuroscience and Medical Psychology, D-40225 Dusseldorf, Germany

Introduction

CEST-MRI in kidney is technically challenging due to large B_0 inhomogeneity and presence of fat[1]. In this preliminary work, we demonstrate that the combination of dual-echo CEST acquisition and Dixon method allows an effective fat signal removal and therefore, more accurate quantification of the CEST effects in transplanted kidney.

Methods

All experiments were performed on a 3T Siemens Prisma MRI system. Fourteen renal transplant recipients were examined with a dual-echo CEST sequence. The two-point Dixon technique was used to generate water-only and fat-only images for each frequency offset[2]. B_0 maps were obtained using the water shift referencing (WASSR) method[3].

Results and Discussion

Figure 1 shows the z-spectra obtained for a single pixel placed in renal cortex/renal capsule and renal medulla. Note that the lipid artefact is successfully removed in the lipid abundant region such as renal cortex/renal capsule (Fig. 1a). On the other hand, there is nearly no difference between the z-spectra calculated with and without

Dixon in renal medulla (Fig. 1b).

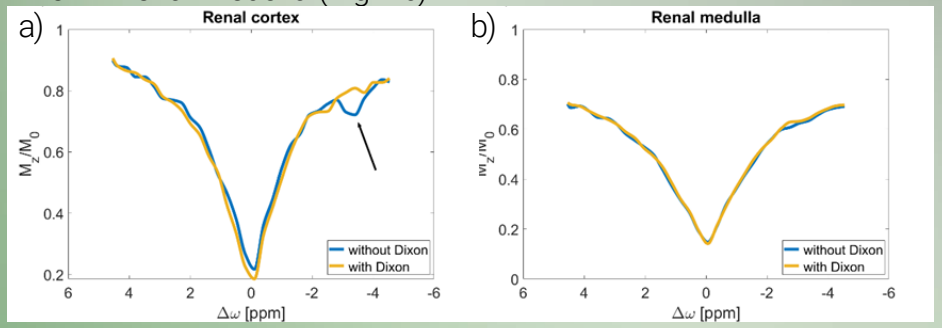


Figure 1. The z-spectra obtained for a single pixel in renal cortex (a) and renal medulla (b). Black arrow indicates the lipid peak, which is clearly visible in the z-spectrum without Dixon.

Conclusion

We have demonstrated that the 2-pt Dixon method is able to effectively suppress the lipid signals that may lead to erroneous CEST contrast in kidney. A larger patient collective is needed to evaluate the feasibility of CEST MRI at 3T in the functional assessment of renal allografts.

References

[1]Zhang et al. Proc. Int. Soc. Magn. Reson. Med., Paris, France, 2018; [2]Liu et al. Magn Reson Med. 2016; 78(5); [3]Kim et al. Magn Reson Med. 2009; 61(6):14441-50

Does Size Matter? Single centre study comparing split function and size disparity of live kidney donors

Praneshan Moodley[1], Arvind Singh[1], Thomas Gruning[1], Brent Drake[1], Imran Saif[1], Ismaa Kiani[1], Richard Powell[1]
[1]Derriford Hospital NHS trust, Plymouth, United Kingdom

Introduction

In potential live donors, if there is a size disparity between the 2 kidneys (>10%) then divided renal function (or split kidney function) can be measured by combining 51Cr-ethylenediamine tetra-acetic acid (EDTA) and 99m Tc-dimercaptosuccinic acid (DMSA) or using Mercaptoacetyltriglycine (MAG3) scan. The kidney with the lower function will usually be donated. The British Transplant Society recommends initial evaluation of donor candidates using eGFR computed from a creatinine assay standardised to the international reference standard. GFR must then be assessed by a reference measured method (mGFR) such as 51Cr-EDTA, 125iothalamate or iohexol performed according to guidelines published by the British Society of Nuclear Medicine. Differential kidney function, determined by the 99mTcDMSA scanning is recommended where there is >10% variation in kidney size or significant renal anatomical abnormality. However, we noticed a significant difference in split function between kidneys despite US/CT showing almost identically sized kidneys. We aimed to determine whether differences between kidney sizes in the donor was useful in predicting which potential donors should undergo differential kidney function testing.

Methods

We performed a retrospective study including 63 donors who were investigated in 2017 and the first half of 2018. The results of the investigations were pulled out using local data records. Kidney size measured either by US/CT scan was compared to the split kidney function measured by DMSA scan.

Results

We divided the living donors into 3 different categories:
Category 1 - based on split kidney function. 6 donors had a difference in differential function
measured with MAG3 of atleast 8 percentage points. None were less than 30 years of age. Only 2 had a size difference >= 1cm.
Category 2 - based on kidney size. 8 donors had a size difference >= 1cm. 2 had a difference of atleast 8% in differential function measured with MAG3.
Category 3 - based on significantly lower differential function. 3 donors had one kidney with a differential function of < 43%. None had size difference.

Conclusion

We concluded that patients can have significant variation in their split kidney function. CT/US scans, though helpful, are not the most reliable modality for assessment when it comes to kidney donation. We propose that all potential living donors should be considered for MAG3 or 99mTc-DMSA to guide us better in deciding which kidney is suitable for donation.

Resources

https://www.bnms.org.uk/

Mapping the dysregulation of renal acid-base homeostasis upon sepsis-induced shock by CEST-MRI

Lorena Consolino[1], Alice Antonello[1], Amerigo Pagoto[1], Pietro Irrera[2], Laura Conti[1], Elisabetta Bolli[1], Dario Livio Longo[3]

[1] University of Torino, Dept. of Molecular Biotechnology and Health Sciences, Torino, Italy [2] University of Campania "Luigi Vanvitelli", Napoli, Italy [3] Institute of Biostructures and Bioimaging, National Research Council of Italy, Torino, Italy

Introduction

Sepsis is a systemic inflammatory response to a suspected infection that often leads to multi-organ dysfunction. Among the different clinical signs, metabolic acidosis is mainly a consequence of renal failure that impairs the homeostasis of the systemic acid-base regulation [1]. Recently, several MRI approaches have been proposed to monitor sepsis-induced changes in renal physiology [2,3]. In this work, MRI-pH mapping was applied to investigate whether variations of pH balance in kidneys might be a predictive and specific biomarker for early diagnosis of sepsis-induced shock.

Methods

Male C57BL/6J mice (n=12) were i.p. administered with 10 mg/kg body weight (b.w).of LPS from E. coli to induce sepsis condition or with 1 ml of 4% thioglycollate (TG) broth as a control model of local inflammation. After 18 hours, MR images were acquired on kidney coronal sections on a 7T Bruker MRI scanner (FOV: 3 cm, in-plane resolution: 234 µm, slice thickness: 1.5 mm). MRI-CEST pH mapping [4] was performed using a fast spin-echo sequence with a RF saturation pulse of 3 µT x 5s and Z-spectra acquired before and after i.v injection of 1.5 g I/kg b.w. iopamidol. Mice were then sacrificed, several organs collected and stained with H&E. Concentration of cyto/chemochines and creatinine were detected in mouse sera by cytometric beads and ELISA kits.

Results

T_2w MR-images of kidneys failed to report macroscopic lesions in both LPS and TG mice. Conversely, extracellular pH values significantly raised upon LPS, whereas any pH changes were reported in TG and vehicle (mean pH: 6.48 and 6.83, $p<0.001$ for LPS; 6.65 and 6.70 for TG; 6.55 and 6.64 for vehicle, before and after treatment). Besides common sepsis-induced systemic signs (dishevelled hair, reduced mobility, diarrhoea), LPS-endotoxic shock stimulated a marked recruitment of proinflammatory mediators, as IL-6 and MCP-1, whereas a marginal increase was detected in TG mice (Fig.2A). In addition, only LPS mice reported a strong body weight loss (Δweight= -2.2 g), which variation significantly correlated with ΔpH changes ($r=-0.77$, $P<0.05$). Increased concentration of serum creatinine (5.52 mg/µL) confirmed LPS-induced renal functional impairment in comparison to TG (0.46 mg/µL) and vehicle (1.2 mg/µL)

Discussion

The proposed MRI-pH-CEST approach reported specific alterations of renal pH balance towards more basic values in a systemic model of sepsis. These alterations, not detected in a local inflammation model induced by TG, could be associated to reduced GFR and functional renal impairment, as evidenced by increased serum level of creatinine, that may affect the regulation of acid-base balance in kidneys with subsequent influences on renal pH changes [4].

Conclusion

These results showed that renal pH variations occur in LPS-treated mice and can be non-invasively visualized by the proposed CEST-MRI approach. Therefore, this study suggests that further evaluation of renal pH mapping might be considered as a potential tool for diagnosis of sepsis.

References

1. Kellum JA., Critical care and resuscitation 2004, 6:197-203
2. Tran M. et al., Clin Invest. 2011,121 :4003–4014
3. Liu J. et al., NMR in Biomed 2018, 31:e3942
4. Longo DL et al., NMR in Biomedicine. 2017;30:e3720

Acknowledgements

Framework of the EU COST Action CA16103-PARENCHIMA "Magnetic Resonance Imaging Biomarkers for Chronic Kidney Disease"

Ex vivo magnetic resonance imaging during normothermic machine perfusion – developing a novel non-invasive tool to assess donor kidney quality

R. Schutter[1], V.A. Lantinga[1], O.C. van Varsseveld[1], H.G.D. Leuvenink[1], R.J.H.Borra[2], C. Moers[1]

[1]Dept of Surgery, University Medical Center Groningen, University of Groningen, The Netherlands [2]Dept of Radiology, University Medical Center Groningen, University of Groningen, The Netherlands

Introduction

The typical deceased donor kidney nowadays is of inferior quality compared to renal grafts a decade ago. Pre-transplant prognostic models and diagnostic tools that are currently available have insufficient independent predictive value to be used for decisions regarding organ acceptance or discard. As a result, such decisions are largely based on the subjective opinion of transplant clinicians involved. Normothermic machine perfusion (NMP) of renal grafts at 37°C provides an ideal platform for isolated organ imaging prior to transplantation, to assess whether a particular kidney is expected to show adequate post-transplant function and longevity. In recent years, novel magnetic resonance imaging (MRI) techniques have been developed, which can quantify important determinants of allograft quality, such as endothelial integrity, mitochondrial function and tissue stiffness, however it remains unclear if these novel imaging biomarkers correlate with outcome after transplantation. The overall aim of the this project is to provide evidence for the predictive value of existing and novel imaging biomarkers from ex-vivo non-invasive MRI assessment of kidney grafts during normothermic machine perfusion prior to transplantation. Here we present the results of first series of pilot experiments assessing the overall feasibility of this approach.

Methods

Five porcine slaughterhouse kidneys were used to optimize the setup and evaluate several MR sequences for their ability to show relevant tissue and vascular changes. NMP was performed with autologous red blood cells in Williams' Medium E with the addition of creatinine, bovine serum albumin and amoxicillin with clavulanic acid. Segmental ischemia/reperfusion injury was induced by inflating and deflating a balloon catheter in one of the main branches of the renal artery. Imaging sequences were performed during different stages of the perfusion. Blood and urine samples were obtained, as well as histological samples at the end of the perfusion.

Results

A stable and reliable NMP setup for isolated kidneys inside a clinical MRI scanner was obtained. Pilot experiments were mainly performed to develop and optimize the NMP setup. Experience was gained in developing a smooth logistical procedure and optimization of image quality and other technical aspects regarding MRI sequences applicable to an ex vivo perfused kidney. Optimal MRI quality was observed when using a 64-channel coil allowing for highly accelerated imaging approaches. Ultra-high resolution (0.6 mm, isotropic) zoomed T_2-weighted imaging provided a clear 3D overview of ischemic areas and high resolution 3D arterial spin labeling (ASL) was able to accurately observe changes in regional blood flow.

Conclusion

This pilot study showed that it is logistically and technically feasible to combine the promising (pre-transplant) evaluation of normothermic machine perfusion with ex vivo magnetic resonance imaging. Several important aspects of allograft quality could be imaged. After finalizing the optimization phase with porcine grafts, human discarded kidneys will be evaluated for allograft quality, allowing for the method to be tested in a typical clinical transplantation setting. Ultimately, we aim to image human donor kidneys that have been accepted for transplantation and correlate ex vivo MRI data with transplant outcomes to develop a unique pre-transplant organ assessment tool.

Evaluation of transplant renal vascular disease by 4D flow

Pauline Hall Barrientos[1], Alastair J Rankin[2], Giles Roditi[3], Patrick B Mark[2], Keith A Gillis[2]

1. Department of Clinical Physics and Bioengeering, NHS Greater Glasgow and Clyde, UK 2. Institute of Cardiovascular and Medical Sciences, University of Glasgow, UK 3. Department of Radiology, NHS Greater Glasgow and Clyde, UK

Introduction

Investigation for transplant renal artery stenosis can be challenging given that doppler ultrasound is highly user dependent and given the issues with both iodinated and gadolinium contrast in renal impairment. We aimed to evaluate the use of 4D flow to measure parameters in renal transplant arteries.

Methods

4D flow data were acquired over the renal and iliac/aortic arteries. Conventional 2D phase contrast magnetic resonance imaging slices were acquired along the aorta for native kidneys, and iliac artery for transplant kidneys.

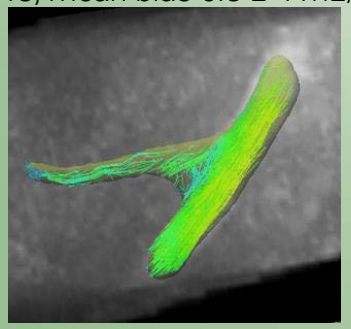
Studies were performed on a 3 T Siemens Prisma with a body array coil and ECG gating. The sequences used were as follows: 4D flow WIP 785k: TR/TE 45.92/3.19 ms, spatial resolution 1.5 x 1.5 x 1.5 mm, flip angle = 7°, venc = 100 cm/s and 30-50 cm/s, ~20 cardiac phases, scan duration ~8 minutes. 2D: TR 51.9 ms, TE 5.1 ms, spatial resolution 0.8 x 0.8 x 5 mm, flip angle = 20°, venc 100 cm/s, ~30 cardiac phases, scan duration 9 s. 4D flow datasets were analysed using a work-in-progress package supplied by Siemens. 2D datasets were analysed using Argus by Siemens.

Results

5 participants were recruited: 4 patients with kidney transplants, and 1 healthy volunteer. Table 1 demonstrates the results of net flow and peak velocities with the renal artery.

	Volunteer 1	Patient 1	Patient 2	Patient 3	Patient 4
Net flow (mL/s)	L 2.7 R 3.7	2.3	13.2	5.3	7.4
Peak velocity (cm/s)	L 58 R 53	66	81	68	66
Area (mm^2)	L 11 R 16	9.2	43.7	25	75

There were no significant differences between 2D and 4D net flow measurements (p=0.48, mean bias 0.8 ± 4 mL/s).



Discussion

Renal artery blood flow measured by 4D flow was variable, in both kidney transplant recipients and in the native kidneys of a healthy volunteer. Turbulent flow, suggestive of stenosis, was not identified in any of the participants.

Conclusion

4D flow allows measurement and visualisation of renal artery flow in transplant and native kidneys. Further studies are required to fully understand flow dynamics and normal range of renal artery velocities in native and transplant kidneys.

Multi-parametric MRI in the early kidney transplant period: Correlation with clinical parameters and follow-up

Keith A Gillis[1], Alastair J Rankin[1], Sarah Allwood-Spiers[5], Rosemary Woodward[3], Giles Roditi[3], Aleksandra Radjenovic[1], Bernd Kuehn[4], Rajan K Patel[2], Patrick B Mark[1]

[1.] Institute of Cardiovascular and Medical Science, University of Glasgow, UK [2.] Glasgow Renal and Transplant Unit, NHS Greater Glasgow and Clyde, UK [3.] Department of Radiology, NHS Greater Glasgow and Clyde, UK [4.] Siemens Healthineers, Erlangen, Germany [5.] Department of clinical physics, NHS Greater Glasgow and Clyde, UK

Introduction

Kidney transplant function is routinely measured using estimated glomerular filtration rate (eGFR) and proteinuria. However, these measures do not provide comprehensive information regarding allograft structure, function, nor prognosis. Earlier studies have demonstrated correlation of clinical and histopathological measures with MRI measurements[1], including diffusion-weighted imaging[2]. Use of multi-parametric magnetic resonance imaging (MRI) may yield novel biomarkers for prediction of outcome and response to therapy in renal transplantation.

Methods

Patients undergoing kidney transplant for end-stage kidney disease underwent multi-parametric MRI at 6 weeks post operatively. Clinical and biochemical measures were made at baseline and 1 year. Imaging was performed on a 3T Siemens MAGNETOM Prisma system, with the protocol entailing kidney volume, arterial spin labelling perfusion, T_1 relaxation time, R_2^*, apparent diffusion coefficient (ADC) and fractional anisotropy. Pearson correlation coefficient was used to evaluate relationships between variables; where required, data were log transformed to achieve a normal distribution.

Results

20 participants were recruited: 16 male, mean age 55.5 ± 12.8 years, baseline eGFR 54.0 ± 23.6 ml/min/1.73m^2, and blood pressure 146/80 ± 15/15 mmHg. At 1-year eGFR was 52.0 ± 27.6 ml/min/1.73m^2. There was correlation between baseline eGFR and cortical ADC (r=0.52, p=0.02). There was no correlation between baseline eGFR and other MRI parameters. There was significant correlation between one-year eGFR and whole kidney (r=0.47, p=0.04) and cortical (r=0.52, p=0.02) ADC.

Discussion

We investigated the correlation between multi-parametric MRI parameters and clinical measures at baseline and at 1 year of follow-up. Limitations include small sample size, propensity of male gender, and lack of correlation with histopathological measures. Nevertheless, there was association between ADC and renal function. This requires confirmation in a larger cohort, including comparison of MRI parameters to histopathological changes on kidney biopsy.

Conclusion

Measurement of ADC may yield novel biomarkers with prognostic ability in kidney transplantation.

References

1. Buchanan et al, NDT 2019
2. Friedli et al, Scientific Reports 2016

Acknowledgements

Many thanks to Peter Weale and Tao Yuehui from Siemens for ongoing support.

Mapping compensatory renal hypertrophy and hyperfiltration in living kidney donors using multiparametric magnetic resonance imaging

Anna S. Li[1,2], Josephine H. Naish[1], Penny L. Hubbard Cristinacce[1], Alastair J. Hutchison[1], Sandip Mitra[1,2], Rachel Lennon[1,2]

[1.] University of Manchester, Manchester, UK [2.] Manchester University NHS Foundation Trust, Manchester, UK

Introduction

Despite sustained glomerular hypertrophy and hyperfiltration, the vast majority of living donors do not develop hyperfiltration injury with fibrosis and progressive GFR decline. Our study uses serial multiparametric MRI to assess volume and blood flow of the remaining kidney in the first month post-donor nephrectomy. Relationships between changes in kidney volume (KV), blood flow (BF) and single kidney GFR (SKGFR) may reflect functional reverse of the remaining kidney and provide insight into the early stages of nephron loss in the development of CKD.

Methods

18 living kidney donors underwent 3 sessions of MRI and creatinine-based eGFR measurements prior to, 4-7 days after, and 4 weeks after nephrectomy. MRI scans were performed on a 3T Philips Ingenia scanner. The non-contrast multi-parametric MR protocol includes: whole kidney volumetric assessment by manual delineation using a multi-slice T_1-weighted (inversion-recovery) turbo-spin echo; assessment of renocortical BF using a FAIR arterial spin labelling (FAIR-ASL) technique; and quantitative T_1-mapping using a MOLLI technique adapted for use in the kidney.

Results

Median age of the donors was 55 (44.5 to 64); baseline KV was 145±36mL, increasing to 181±46mL at Day 4 and 175±41mL at week 4. SKGFR was 47±5 mL/min/1.73m^2 at baseline, increasing to 61±12 mL/min/1.73m^2 at Day 4 and 61±10 mL/min/1.73m^2 at week 4. RBF per unit weight did not change at either Day 4 (393±134 mL/100g/min) or week 4 (402±78 mL/100g/min) post-donation compared to baseline (400±88 mL/100g/min).

Conclusion

The results show that compensatory hypertrophy and hyperfiltration started rapidly following renal tissue loss, became established within a few days, and remained sustained over the next 4 weeks. Given adult glomerular number does not increase in compensatory hypertrophy, our preliminary findings indicate that average single glomerular volume and GFR rose post-donation. As BF per unit weight did not change post-nephrectomy in our cohort, with an increase in overall KV, this suggests that the overall kidney BF would also increase. Further study into this growth of normal tissue is required to identify imaging biomarkers for nephron reserve and capacity for compensation before the onset of hyperfiltration injury.

References

Lenihan et al. Curr. Transplant. Reports (2016); Song et al. Int. Urol. Nephrol. (2014)

Cutajar et al. Eur. Radiol. (2015); Niles et al. Invest. Radiol. (2016)

Circadian fluctuations in renal blood flow correlated to urinary output parameters.

P Eckerbom[1], P Hansell[2] , E Cox[3], C Buchanan[3], J Weis[4], F Palm[2], S Francis[3], P Liss[1]

[1]Institution for Surgical Sciences, Dept of Radiology, Uppsala University, Uppsala, Sweden [2]Institution for Medical Cell Biology , Dept of Physiology, Uppsala University, Uppsala, Sweden [3]The Sir Peter Mansfield Imaging Centre, University of Nottingham, Nottingham, UK [4]Institution for Surgical Sciences, Dept of Med Physics, Uppsala University, Uppsala, Sweden.

Introduction

In humans, a number of biological processes throughout the body including the kidneys show circadian variations and there is a rapidly growing interest in this field. Non-invasive MRI techniques Phase contrast (PC), Arterial Spin Labelling (ASL) and Blood Oxygen Level Dependent (BOLD) make it possible to study renal perfusion and oxygenation without risk for contrast induced conditions and with the advantage of short-time repeatability. In this study we studied total and regional renal perfusion and regional renal oxygenation in healthy volunteers over 24 hours and correlated it to urinary output parameters.

Methods

During 24 hours, eight female and eight male healthy volunteers, mean age 23 years were scanned every fourth hour at 3T using a scan protocol comprising PC, ASL and BOLD sequences. The subjects received a urinary catheter to measure urine output parameters (urine production, excretion of Na+, K+, protein, creatinine and urea) during the study. Total renal blood flow, regional (cortex, outer and inner medulla) perfusion and regional oxygenation were analyzed using PC, ASL and BOLD respectively. For regional measurements, cortex was analyzed using a single ROI encompassing as much cortex as possible while outer and inner medulla was measured by the mean value of four smaller ROI´s from different parts of the kidney.

Results

Significant circadian fluctuations were found for total renal blood flow with increasing flow from noon to midnight and thereafter decreasing flow towards the morning hours. Regional renal perfusion showed no significant circadian variations although a similar pattern as for total renal blood flow was noticed for cortical perfusion. Also for oxygenation, no significant circadian fluctuations could be seen. Regarding urinary parameters significant circadian oscillations could be seen for urine production, excretion of Na+, K+, Creatinine and Urea, all of them showing decreasing values during the night hours.

Discussion

The finding that renal blood flow exhibits a circadian pattern is not surprising given the well known decrease in cardiac output during the night hours. To our knowledge this is though the first time this has been shown using non-invasive methods. The finding that regional renal blood flow does not show significant circadian fluctuations is though a bit surprising since it could be expected to follow the pattern of total renal blood flow. The reason for this might be that ASL is not sensible enough to pick up small differences in small ROI´s. Renal oxygenation could be expected to be relatively stable

due to the continuous need of high oxygen supply to the kidney in which the medulla is at the brink of hypoxia even under normal conditions. Combining measurements of renal blood flow/oxygenation and excretion parameters might add important information in further studies under pathological conditions.

Conclusion

This study has shown circadian fluctuations in total renal blood flow measured by non-invasive PC MRI correlating well to the circadian pattern of urinary parameters also measured. No significant circadian fluctuations could be detected for regional renal perfusion and oxygenation. Knowledge of circadian variations of renal blood flow could be important for future studies/clinical applications dealing with renal blood flow alterations.

Renal cortex T_1 for assessment of liver disease severity

C. R. Bradley[1, 2], E. F. Cox[1, 2], R. A. Scott[2], M. W. James[2], G. P. Aithal[2], I. N. Guha[2], S. T. Francis[1, 2]

[1]Sir Peter Mansfield Imaging Centre, University Park, University of Nottingham, UK, [2]Nottingham Biomedical Research Centre, Nottingham University Hospitals NHS Trust and University of Nottingham, Queen's Medical Centre, Nottingham, UK.

Introduction

Non-invasive markers are now commonly used in clinical practice to help understand the progression or regression of disease. Here, we assess whether renal cortex T_1 can delineate liver disease severity, and whether renal cortex T_1 could be used as a predictor of liver related outcome (LRO) - defined as ascites, variceal bleed, jaundice, or encephalopathy. Finally in stable Compensated Cirrhosis (CC) patients we assess renal cortex T_1 over time, allowing a coefficient of variation (CoV) in a stable group to be determined as a benchmark for tracking disease progression.

Methods

40 Healthy volunteers (HV), 60 CC patients, and 7 Decompensated Cirrhosis (DC) patients had renal cortex T_1 measured as part of a multi-organ protocol (comprising renal, liver and cardiac measures). Renal cortex T_1 was compared between the three patient groups, and between CC patients with and without a LROs up to 2304 days after their baseline scan. A subset of CC patients (n=11) were scanned annually for a further 3 years, these were all subsequently shown to be stable from clinical biomarkers.

Renal cortex T_1 was assessed using a respiratory triggered multislice inversion-recovery scheme with a balanced FFE readout, images were collected at 9 inversion times (TIs: 100–900 ms in 100 ms steps) with minimal temporal slice spacing (144 ms). Ascend and descend slice order acquisitions were acquired to increase the

dynamic range of inversion times, total scan time was ~3 min [1]. Data were fit to a two-parameter model to generate T_1 and M_0 maps. From a kidney mask, a histogram of T_1 values was formed to yield two peaks originating from the renal cortex and medulla, and the median T_1 values of the renal cortex calculated.

Results

There was a significant difference in renal cortex T_1 between HVs, CC and DC patients (P<0.001, Fig.1). Of the 60 CC patients, 11 had a LRO up to 2304 days after their baseline scan, these had a significantly reduced renal cortex T_1 (P<0.01, Fig.2a). Tertile cut-off points of renal cortex T_1 were used to compute Kaplan-Meier survival curves with a significant difference observed for patients with renal cortex T_1 <958ms (P<0.00001, Fig.2b) [2]. In the stable CC group, year-on-year there was no difference in renal cortex T_1, with a low CoV of 3.5±2.5%, close to the CoV of a healthy control group scanned 1 week apart (shown by grey dashed line, Fig.3).

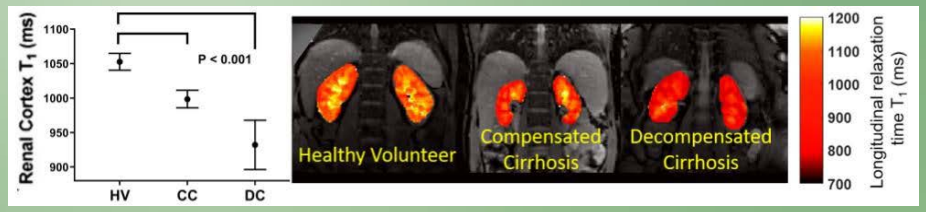


Figure 1

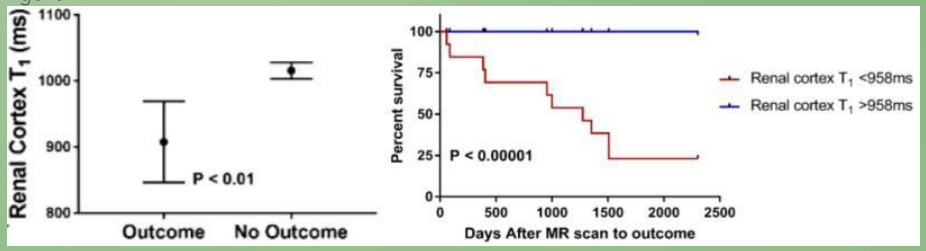


Figure 2

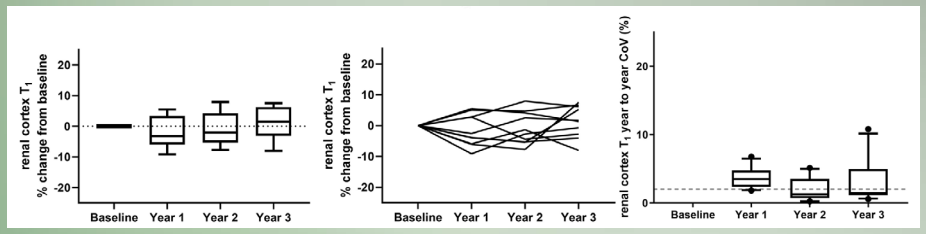


Figure 3

Discussion and Conclusion

We have shown that renal cortex T1 decreases with disease severity and can predict LRO in the CC group. The year-on-year CoV for renal cortex T1 in a stable CC group is very low, therefore renal cortex T1 can be used to detect subtle changes in renal tissue due to intervention or disease progression.

References

[1] E.F. Cox et. al, Front. Physiol. 8,696 (2017). [2] C.R. Bradley et. al, J. Hepatol. 69,1015-24 (2018).

The effect of glycemic control on renal triglyceride content measured by ^{1}H-MRS in patients with type 2 diabetes mellitus

Ilona A. Dekkers[1], MD, MSc, Maurice B. Bizino[1,2] MD, Elisabeth H. M. Paiman[1] MD, Johannes W Smit[4] MD, PhD, Ingrid M. Jazet[2] MD PhD, Aiko P.J. de Vries[3], MD, PhD, Hildo J. Lamb[1], MD, PhD

[1.] Dep. of Radiology, Leiden University Medical Center, Leiden, the Netherlands [2.] Dep. of Endocrinology, Leiden University Medical Center, Leiden, the Netherlands [3.] Dep. of Nephrology, Leiden University Medical Center, Leiden, the Netherlands [4.] Dep. Internal Medicine, Radboud University Medical Center, Nijmegen, the Netherlands

Introduction

Renal steatosis is a potential driver of diabetic kidney disease [1], and tight glycemic control can reduce risk of diabetic nephropathy. Recent technical developments have showed that in-vivo measurement of renal triglyceride content (RTGC) is technically feasible using ^{1}H-MRS [2,3]. We aimed to assess whether glycemic control influences. In adddition, we compared glucagon-like peptide-1 receptor agonists receptor agonist (GLP1-RA) liraglutide liraglutide to standard glucose-lowering therapy.

Methods

In this single-center parallel-group trial T2DM patients were randomized to liraglutide or placebo added to standard care (metformin/sulfonylurea-derivative/insulin). Baseline and follow-up ^{1}H-MRS was performed using single voxel Point Resolved Spectroscopy (PRESS) and Multiply Optimized Insensitive Suppression Train (MOIST) for water suppression. Patients with ^{1}H-MRS spectra that met the quality criteria were included. Change in RTGC after 26 weeks of glycemic control and difference of RTGC change between treatment groups was analyzed using ANCOVA while adjusting for baseline differences. Between-group differences in RTGC were tested using non-parametric tests.

Results

Baseline study population consisted of 50 T2DM patients (mean age 56.5±9.1 years; range 33–73 years; 46% males). Baseline median RTGC was 0.23% [25th,75thpercentile; 0.12,0.36] compared to 0.14% [0.09,0.23] (p=0.06) at follow-up. Mean HbA1c at baseline was 61.6±8.4 mmol/mol, which changed to 56.3±9.5 mmol/mol (p=0.046) at follow-up. No significant differences were found in median RTGC reduction in the liraglutide group (n=9) versus standard glucose-lowering therapy group (n=8) (p=0.33).

Discussion

We found a near significant reduction in RTGC after 26-weeks of glycemic control (irrespective of randomized treatment group). When comparing glycemic control via the GLP-1RA liraglutide to placebo for 26 weeks, added to standard glycemic control, we showed that RTGC reduction was more pronounced in the liraglutide group than in the standard glucose lowering therapy group, however no statistically significant differences were found when taking baseline differences into account. Although our subgroup analysis should be considered cautiously with regard to the size and exploratory character of our study, our findings suggest that glycemic control, via GLP-1RA or standard glucose lowering therapy, might potentially beneficially influence renal steatosis.

Conclusion

Although this exploratory study showed lower RTGC after 26-weeks of glycemic control this finding did not reach statistical significance, warranting the need for larger clinical studies on glycemic control and renal steatosis.

References

1. de Vries APJ, et al. Lancet Diabetes Endocrinol 2014;2:417–26.
2. Dekkers IA, et al. J Magn Reson Imaging 2018.