

Working Group 4 Update: Development of Training Programs on Renal MRI

Andreas Pohlmann, Thoralf Niendorf

- **Organization of ISMRM Member Initiated Symposium (MIS):**
Frontiers in Magnetic Resonance Imaging Biomarkers of Renal Disease
ISMRM Montreal 2019
- **Writing & editing of Springer Protocols book:**
*Preclinical MR Imaging of the Kidney:
Methods and Protocols for Experiments and Analyses*
Publication mid 2020

Frontiers in Magnetic Resonance Imaging Biomarkers of Renal Disease

Organizers:

- Thoralf Niendorf, Max-Delbrueck Center for Molecular Medicine, Berlin, Germany
- Octavia Bane, Icahn School of Medicine at Mount Sinai Hospital, New York, USA

Format: 7 presentations (each 14 min + 3 min discussion)

Targets:

- raise awareness for renal MRI
- outline opportunities, challenges, future directions of renal MRI
- attract young scientists and new entrants into the field

1) **The Link to Biology and Renal Physiology: The Physiologist's Perspective**

Erdmann Seeliger (M.D.), Charité University Medicine, Berlin, Germany

- outline fundamentals of renal biology and renal physiology

2) **Renal Diseases and Pathophysiology: The Nephrologist's Perspective**

Madhav Menon (M.D.), Icahn School of Med. at Mount Sinai Hospital, New York

- presents unmet clinical needs in nephrology

3) **Emerging Renal MRI Biomarkers or Measurement Approaches: The MR Physics Perspective**

Charlotte Buchanan (Ph.D.), Sir Peter Mansfield Imaging Centre, Nottingham, UK

- outlines current concepts and the physics of parametric MRI

4) **Technical Validation: Demonstrating Accuracy, Precision and Quality Assurance of Renal MR Biomarkers**

Ilona Dekkers (M.D.), Leiden University Medical Center, The Netherlands

- highlights the challenges en route to MRI biomarkers of renal disease

5) Computational Models, Predictive Analytics and Machine Learning for Advancing Renal Diagnostics and Therapies

Satish Viswanath (Ph.D.), Case Western Reserve University, Cleveland, Ohio, USA

- highlights the improvements in computational models and predictive analytics

6) Potential Added Value of Novel Renal MR Biomarkers in Drug Development or Patient Management

Lilach Lerman (M.D.), Mayo Clinic, Rochester, Minnesota, USA

- discuss value of novel renal MRI biomarkers

7) Practical Challenges of Multi-center Studies and Clinical Renal MRI Trials

Paul Hockings (Ph.D.), Antaros Medical, Gothenburg, Sweden

MIS was great success and attracted large number of participants

- More than 200 attendees; lively discussions

Motivated our plan for an *ISMRM workshop on Renal MRI* in April 2021

- This was made part of the work program and deliverables of WG4

Methods in
Molecular Biology

Springer Protocols

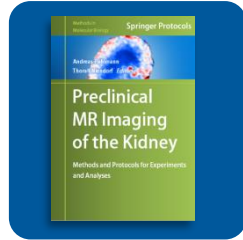
Methods in
Molecular Biology

Springer Protocols

Andreas Pohlmann
Thoralf Niendorf *Editors*

Preclinical MR Imaging of the Kidney

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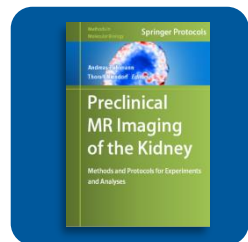


Lack of Training Material

for students and new entrants to the field of renal MRI

Lack of Standardization

Results from studies are difficult to compare



WG 4

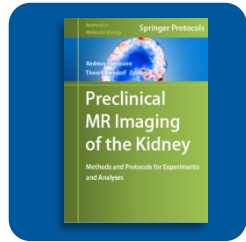
Training

WG 1

Standardization

One-stop source for learning preclinical renal MRI

- Create library of protocols for a range of renal MR methods
- Protocols give detailed step-by-step instructions
- Complement experimental protocols with:
 - Advice on animal preparation & monitoring
 - Explanation of MRI method's basic concept
 - Instructions for data analysis



WG 4



Training

WG 1

Standardization

Recommendations for preclinical renal MRI

- First step towards harmonizing protocols
- MR parameter sets with rationales are convincing
- Supported by authors of several labs & PARENCHIMA
- Access to working protocol reduces need to “play-around”
- Paves the way for consensus-based recomm. in about 5yrs

- ***Methods in Molecular Biology (MIMB)*** is a critically acclaimed books series, part of the Springer Protocols
- Exists for 35 years: >2,100 books  with >47,000 protocols  PDF
- Each chapter (protocol) is provided in **readily reproducible step-by-step** fashion
 1. Short **introduction**
 2. List of **materials** needed
 3. Detailed **procedure**
 4. Comprehensive **notes** section (tips & tricks, troubleshooting advice)
- Each chapter is listed in **PubMed**:

Assessment of **Renal** Hemodynamics and Oxygenation by Simultaneous **Magnetic Resonance Imaging (MRI)** and Quantitative Invasive Physiological Measurements.

Cantow K, Arakelyan K, Seeliger E, Niendorf T, Pohlmann A.

Methods Mol Biol. 2016;1397:129-154. doi: 10.1007/978-1-4939-3353-2_11.

PMID: 26676132

Book consists of **4 parts** and **39 chapters** (articles)

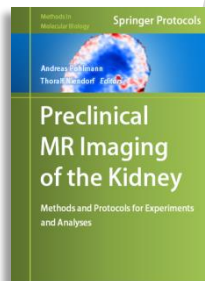
PART I Animal Models, Preparation, Monitoring and Physiological Interventions
3 chapters

PART II Measurement Techniques
12 chapters (Introductions the concepts and gives application examples)

PART III Experimental Protocols
13 chapters (Descriptions of experimental steps)

PART IV Protocols for Advanced Analyses
11 chapters

- Experimental steps are described in generic terms
 - Rationale for choice of acquisition parameters is explained
 - Examples of specific parameter choices are given in *Notes* section
 - mouse & rat
 - animal & clinical scanner
 - different field strenghts
- Each chapter/protocol is written by authors from several labs



Topics	PART I	PART II	PART III	PART IV
Animal Models of Renal Pathophysiology and Disease	Intro			
Preparation & Monitoring of Small Animals	Intro			
Reversible Physiological Interventions	Intro			
Invasive Probes for Quantitative Asst. of Renal Physiology		Concept	Exp. Prot.	
Multi-Modality Imaging (US, PET, Photoacoustic)		Concept		
MRI Hardware Considerations		Concept		
Essential Practical Steps (Slice planning, Shimming, TOF)			Exp. Prot.	
Renal Volume Measurement			Exp. Prot.	
T1 mapping		Concept	Exp. Prot.	Analysis
T2* & T2 mapping		Concept	Exp. Prot.	Analysis
DWI for ADC and IVIM		Concept	Exp. Prot.	Analysis
DCE -derived Perfusion and Filtration		Concept	Exp. Prot.	Analysis
ASL		Concept	Exp. Prot.	Analysis
CEST for Mapping of pH and Perfusion		Concept	Exp. Prot.	Analysis
²³ Na MRI		Concept	Exp. Prot.	Analysis
¹³ C MR (Hyperpolarized)		Concept	Exp. Prot.	Analysis
¹⁹ F Cell Tracking for Inflammatory Cell Migration		Concept	Exp. Prot.	Analysis
¹⁹ F Oximetry			Exp. Prot.	
Subsegmentation of the Kidney (SOMBRERO, TLCO)				Analysis
Image Denoising for Parametric Mapping (NLM filter)				Analysis
	3	12	13	11

Basic Concepts

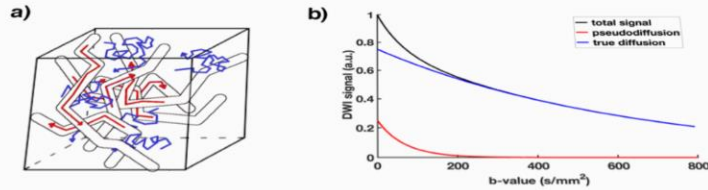
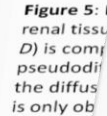


Figure 5: IVIM model. a) Schematic representation of random water motion in a voxel of renal tissue, where free diffusion component (in blue, described by the diffusion coefficient D) is complemented by fluid flowing in capillaries and tubules (in red, described by the pseudodiffusion coefficient D^*). b) Contributions of true diffusion and pseudodiffusion to the diffusion signal decay - pseudodiffusion is substantially faster than true diffusion, and so is only observed at low b-values.

Parameter set examples



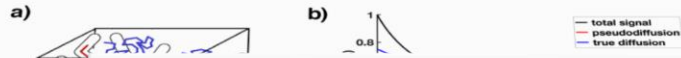


Figure 5: (a) Schematic of a 3D volume element in renal tissue. (b) Graph showing the total signal (black line), pseudodiffusion (red line), and true diffusion (blue line) components of the signal decay over time.

Analysis with code examples

- Set the shortest echo time (TE) and echo spacing (ΔTE) possible, under the condition that fat and water are in phase (see Note 2). The last TE should be close to the largest expected TE in the kidney multiplied by 1.5 (see Note 3). The aim is to acquire 10 or more echo images. Fewer TEs or larger ΔTE are not advisable. At high TEs, the signal-to-noise ratio in the kidney can be so low that it is not available for the analysis. Consider increasing the acquisition time or using Fourier acceleration to shorten the first TE.
- Choose the shortest possible repetition time (TR) and flip angle (FA) for the desired efficiency. TR will be limited by the length of the acquisition.
- Adapt the flip angle (FA) to the TR and Ernst angle $\alpha_E = \arccos(\exp(-TR/T_1))$. Larger FAs and determine the optimal FA.
- Set a high acquisition bandwidth (BW) which decreases with the square root of the SNR (see Note 5).
- Enable fat saturation. On ultrahigh field, fat saturation is necessary to suppress the fat signal in the kidney due to chemical shift. At high TEs, fat saturation is only observed in the kidney.
- Enable the respiration trigger (peristaltic motion blurring and unwanted intensity changes).
- Example parameters for T_2^* mapping:** TR = 50 ms; flip angle = 12°; bandwidth = 109 kHz; number of slices = 2, 14, 4.28, 6.42, 8.56, 10.7, 12.8, 15.0; slice orientation = coronal; matrix size = 169x115 zero-padded; fat suppression with 1.4 mm thickness; fat suppression time = 40-60 s (with triggering under 100 ms).
- Example parameters for T_2 mapping:** TR = 350 ms; flip angle = 12°; first echo = 2.0 ms; echo spacing = 18.80, 21.20, 23.60, 26.00, 28.40, 30.80, 33.20, 35.60, 38.00, 40.40, 42.80, 45.20, 47.60, 50.00, 52.40, 54.80, 57.20, 59.60, 62.00, 64.40, 66.80, 69.20, 71.60, 74.00, 76.40, 78.80, 81.20, 83.60, 86.00, 88.40, 90.80, 93.20, 95.60, 98.00, 100.40, 102.80, 105.20, 107.60, 110.00, 112.40, 114.80, 117.20, 119.60, 122.00, 124.40, 126.80, 129.20, 131.60, 134.00, 136.40, 138.80, 141.20, 143.60, 146.00, 148.40, 150.80, 153.20, 155.60, 158.00, 160.40, 162.80, 165.20, 167.60, 170.00, 172.40, 174.80, 177.20, 179.60, 182.00, 184.40, 186.80, 189.20, 191.60, 194.00, 196.40, 198.80, 201.20, 203.60, 206.00, 208.40, 210.80, 213.20, 215.60, 218.00, 220.40, 222.80, 225.20, 227.60, 230.00, 232.40, 234.80, 237.20, 239.60, 242.00, 244.40, 246.80, 249.20, 251.60, 254.00, 256.40, 258.80, 261.20, 263.60, 266.00, 268.40, 270.80, 273.20, 275.60, 278.00, 280.40, 282.80, 285.20, 287.60, 290.00, 292.40, 294.80, 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We are Close to the Finish Line!

Jan-Apr 2018 • Finalizing concept → proposal to *Springer* → contract

May 2018 • Assembling editorial team

Jul 2018 • Editorial meeting via Skype

Jul-Aug 2018 • Section editors identify & contact potential authors

Sept 2018 • Disseminate chapter templates to authors

4 Oct 2018 • Editors meeting @ Prague COST action meeting

4-5 Apr 2019 • **Editorial review meeting** in Cavtat (Dubrovnik), Croatia

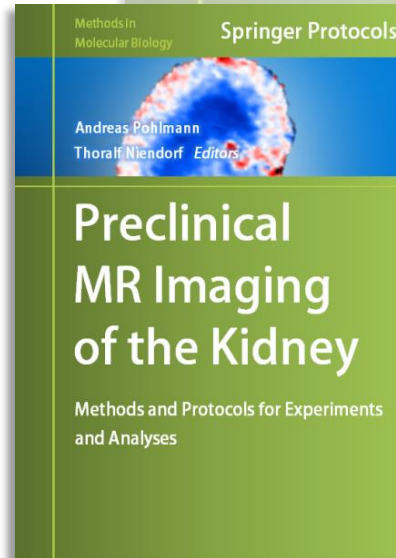
Apr - Sept 2019 • Review process

Oct 2019 • **Formatting of chapters**

Nov 2019 • Submission to Springer

Mid 2020 • **Publication**





Acknowledgment

Andrea Fekete, Semmelweis University Budapest, Hungary

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Christoffer Laustsen, Aarhus University Hospital, Denmark

Dario Livio Longo, University of Torino, Italy

Iris Friedli, Antaros Medical, Mölndal, Sweden

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Australia
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Netherlands
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Portugal
Spain
Sweden
Switzerland
UK
USA



...to everyone who helped turning
this vision into reality!

*) <https://discuss.phplist.org/t/big-thanks-to-duncan-this-month/849>