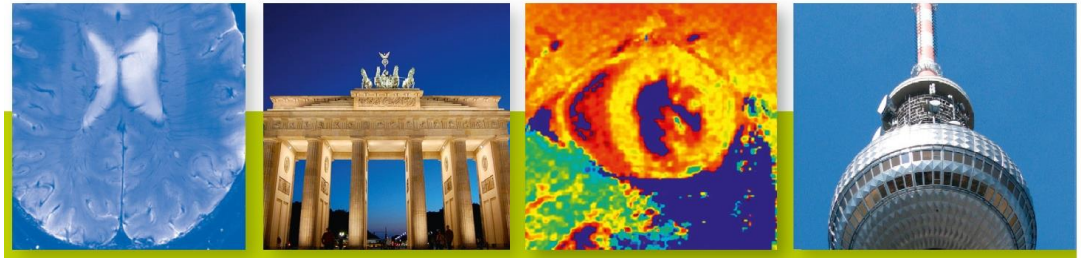


Working Group 4 Update:
Development of Training Programs on Renal MRI

Andreas Pohlmann, Thoralf Niendorf

B.U.F.F. Berlin Ultrahigh Field Facility
MDC MAX DELBRÜCK CENTER FOR MOLECULAR MEDICINE IN THE HELMHOLTZ ASSOCIATION
HELMHOLTZ ASSOCIATION

WG4 Activities in 2019

B.U.F.F. Berlin Ultrahigh Field Facility

- **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

ISMRM Member Initiated Symposium (MIS)

B.U.F.F. Berlin Ultrahigh Field Facility

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 unmeet 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

ISMRM Member Initiated Symposium (MIS)

B.U.F.F. Berlin Ultrahigh Field Facility

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

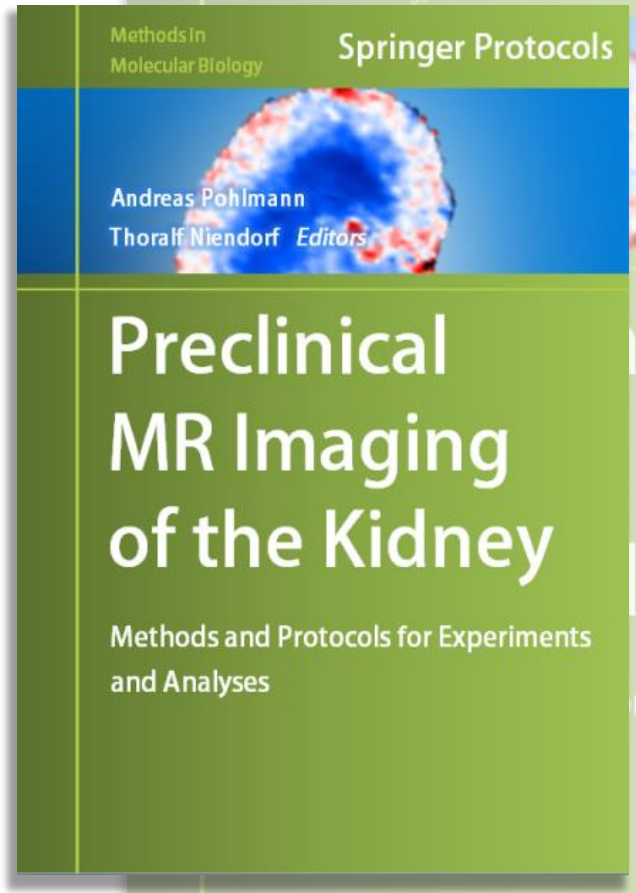
Paul Hockings (Ph.D.), Antaros Medical, Gothenburg, Sweden

MIS was great success and attracted large number of participants

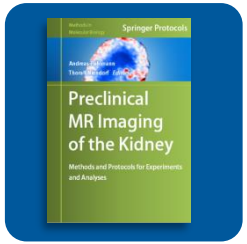
- More than 200 attendees; lively discussions

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
Andreas Pohlmann
Thoralf Niendorf Editors
Preclinical
MR Imaging
of the Kidney
Methods and Protocols for Experiments
and Analyses

Book Project Addresses Two Current Limitations



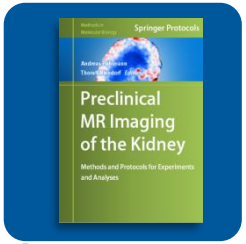
Lack of Training Material

for students and new entrants to the field of renal MRI

Lack of Standardization

Results from studies are difficult to compare

Objectives



WG 4

Training

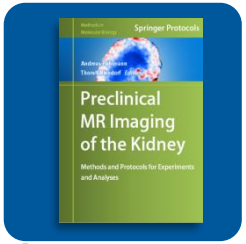
WG 1

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

Objectives



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

What are *Springer Protocols*?

B.U.F.F. Berlin Ultrahigh Field Facility

- ***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 

- 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 Structure

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

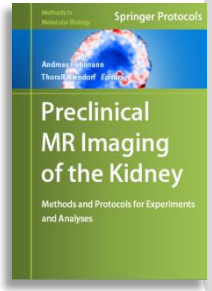
Unique features of this Springer Protocols book

B.U.F.F. Berlin Ultrahigh Field Facility

- 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

TOC



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

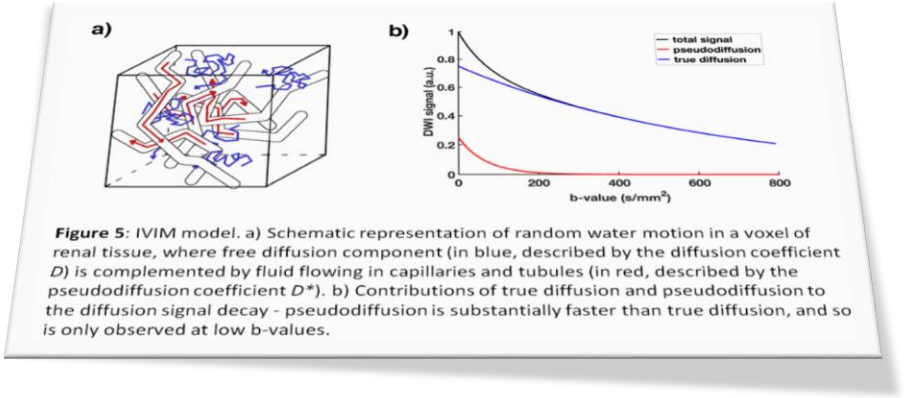
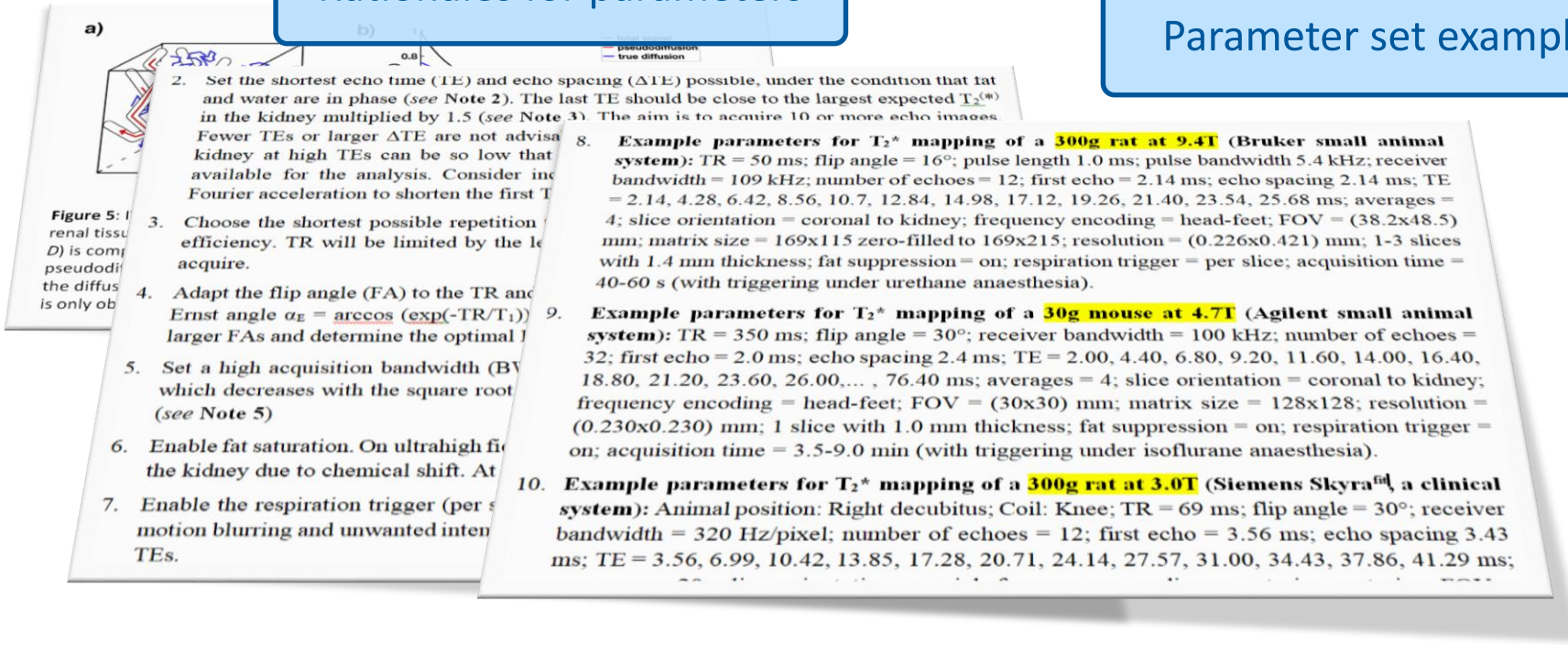


Figure 5: IVIM model. a) Schematic representation of random water motion in a voxel of renal tissue, where free diffusion component (in blue, described by the diffusion coefficient *D*) is complemented by fluid flowing in capillaries and tubules (in red, described by the pseudodiffusion coefficient *D**). 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.

Preview

Rationales for parameters

Parameter set examples



a)

b)

pseudodiffusion
true diffusion

Figure 5: I
renal tissu
D) is com
pseudodif
the diffus
is only ob

2. 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 $T_2^{(*)}$ 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 advisa kidney at high TEs can be so low that available for the analysis. Consider inc Fourier acceleration to shorten the first T

3. Choose the shortest possible repetition efficiency. TR will be limited by the le acquire.

4. Adapt the flip angle (FA) to the TR and Ernst angle $\alpha_E = \arccos(\exp(-TR/T_1))$ larger FAs and determine the optimal

5. Set a high acquisition bandwidth (BV which decreases with the square root (*see* **Note 5**)

6. Enable fat saturation. On ultrahigh fi the kidney due to chemical shift. At

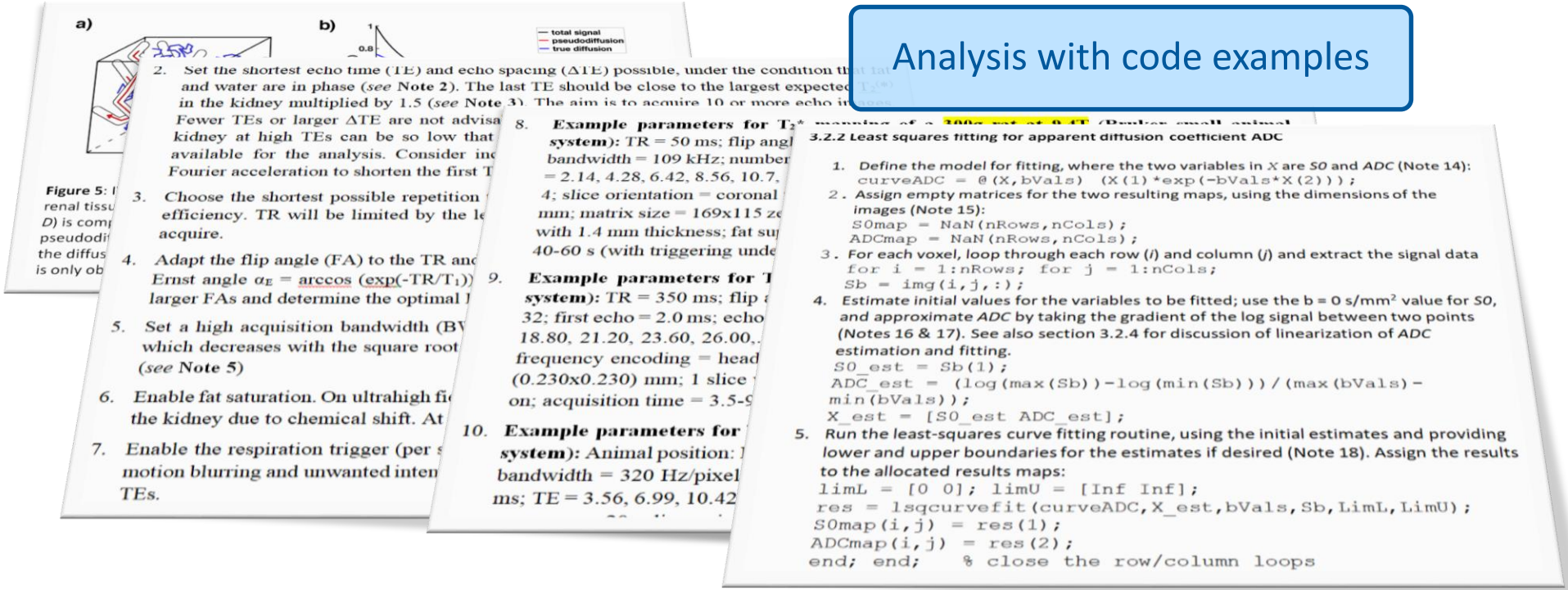
7. Enable the respiration trigger (per s motion blurring and unwanted inten TEs.

8. ***Example parameters for T_2* mapping of a 300g rat at 9.4T (Bruker small animal system):*** *TR = 50 ms; flip angle = 16°; pulse length 1.0 ms; pulse bandwidth 5.4 kHz; receiver bandwidth = 109 kHz; number of echoes = 12; first echo = 2.14 ms; echo spacing 2.14 ms; TE = 2.14, 4.28, 6.42, 8.56, 10.7, 12.84, 14.98, 17.12, 19.26, 21.40, 23.54, 25.68 ms; averages = 4; slice orientation = coronal to kidney; frequency encoding = head-feet; FOV = (38.2x48.5) mm; matrix size = 169x115 zero-filled to 169x215; resolution = (0.226x0.421) mm; 1-3 slices with 1.4 mm thickness; fat suppression = on; respiration trigger = per slice; acquisition time = 40-60 s (with triggering under urethane anaesthesia).*

9. ***Example parameters for T_2* mapping of a 30g mouse at 4.7T (Agilent small animal system):*** *TR = 350 ms; flip angle = 30°; receiver bandwidth = 100 kHz; number of echoes = 32; first echo = 2.0 ms; echo spacing 2.4 ms; TE = 2.00, 4.40, 6.80, 9.20, 11.60, 14.00, 16.40, 18.80, 21.20, 23.60, 26.00,... , 76.40 ms; averages = 4; slice orientation = coronal to kidney; frequency encoding = head-feet; FOV = (30x30) mm; matrix size = 128x128; resolution = (0.230x0.230) mm; 1 slice with 1.0 mm thickness; fat suppression = on; respiration trigger = on; acquisition time = 3.5-9.0 min (with triggering under isoflurane anaesthesia).*

10. ***Example parameters for T_2* mapping of a 300g rat at 3.0T (Siemens Skyra[fd], a clinical system):*** *Animal position: Right decubitus; Coil: Knee; TR = 69 ms; flip angle = 30°; receiver bandwidth = 320 Hz/pixel; number of echoes = 12; first echo = 3.56 ms; echo spacing 3.43 ms; TE = 3.56, 6.99, 10.42, 13.85, 17.28, 20.71, 24.14, 27.57, 31.00, 34.43, 37.86, 41.29 ms;*

Preview

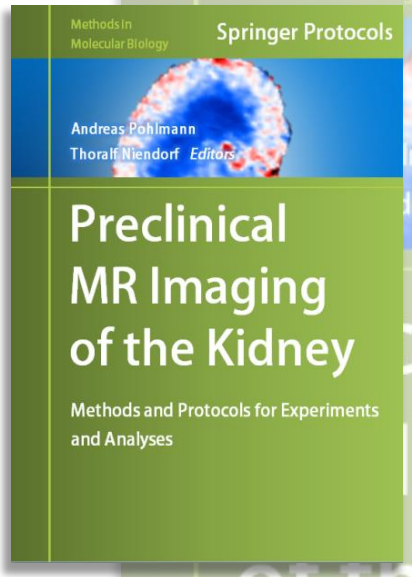


Analysis with code examples

We are Close to the Finish Line!

B.U.F.F. Berlin Ultrahigh Field Facility

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**



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… in 14 countries

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Denmark
France
Germany
Hungary
Italy
Netherlands
Norway
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