Group of Magnetic Resonance (MR)

Department of Magnetic Resonance and Cryogenics

ISI CAS Institute of Scientific Instruments The Czech Academy of Sciences

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THEMATIC RESEARCH FOCUS

Research areas

- Customization and development of methods and applications of ultra-high-field magnetic resonance imaging and spectroscopy of small laboratory animals (mouse, rat, rabbit), excised organs, and in vitro samples for selected areas of multidisciplinary research.
- Quantitative MR imaging of relaxation, diffusion, perfusion, blood flow, metabolites, water/fat:
  - perfusion measurement, mathematical modelling of pharmacokinetics,
  - MR spectroscopic data analysis, MR physics simulation for metabolite quantitation and method development.

Excellence

- In vivo MR spectroscopy – computer simulation of NMR dynamics of coupled spin systems
- In vivo MR measurement of perfusion, and pharmacokinetics modelling

Mission

- Transform own research in MR physics and related areas into progress in quantitative MR imaging and spectroscopy – transform the prevailing MR paradigm of marker detection into quantitative, robust, accurate and precise measurement of well-defined biophysical, biochemical or physiological properties, whose potential of interinstitutional transferability will support biomedical research and development and medical diagnostics and will contribute to better understanding of pathophysiological processes.
- Provide MR measurements implementing the goals stated above, including adequate animal services, to external research and development clients under the framework of large research infrastructures Czech-BioImaging and Euro-BioImaging, and to contribute to the establishment of high-quality standards in these consortia.

UP-TO-DATE ACTIVITIES

Research focus

- MR-data quality improvement by
  - artefact avoidance and quality-assurance filtering of raw data
  - advanced data modelling, robust estimation of model parameters
- Experimental and data-analysis techniques for quantitative MR imaging and spectroscopy – hierarchical data modelling of MR physics and physiology:
  - perfusion measurement protocols, data analysis algorithms for pharmacokinetics modelling, development of web-based perfusion analysis software PerfLab
  - spectroscopy protocols, development of program NMRScopeB for quantum-mechanical simulation, and collaborative improvement of quantitation software jMRUI
- Exploration of the potential of synergies of multiparametric/multimodal imaging
- Method optimization with regard to animal measurement constraints and economics. Extending the current MR spectroscopic simulation possibilities of program NMRScopeB to more complex experiments and improving the utility of

Biomedical 9.4T MR scanner equipped for mouse, rat and rabbit imaging

the current quantitation software jMRUI, based on users' feedback, own testing and using modern computer technology
- Development of perfusion measurement protocols, pharmacokinetic models and data analysis algorithms based on own validation experiments, and development of web-based perfusion analysis software PerfLab

Main capabilities

Basic research

- Development of customized MR protocols (sample preparation, MR measurement, data analysis)
- MR data analysis for the measurement of relaxation, diffusion, perfusion, spectroscopy
- Pulse sequence design and analysis by computer simulation of spin system evolution
- Validation of measurement protocols and data analysis by phantom studies

Applied research

- Support for studies in pathophysiology, development of diagnostics, therapeutic procedures and drugs in translational research in oncology, neurology, cardiology or regenerative medicine by multiparametric MR examinations of small laboratory animals
- Testing of experimental molecule or nanoparticle-based carriers for targeted delivery of imaging markers and drugs by relaxometric in vitro and multiparametric in vivo MR imaging
- Support for plant research, study of the properties of technical and natural gels (e.g. for geology or industries), characterization of porous materials

Sub-fields of group activities

- Biomedical research – (patho)physiology, diagnostics, therapy monitoring
- Nanotechnologies for (bio)medicine
- Pharmaceutics
- Processes in natural and industrial gels

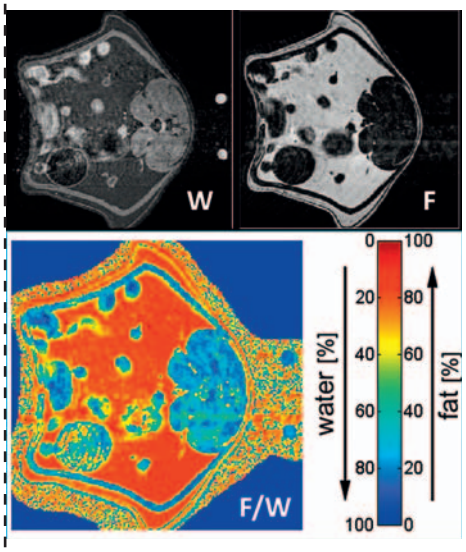
KEY RESEARCH EQUIPMENT

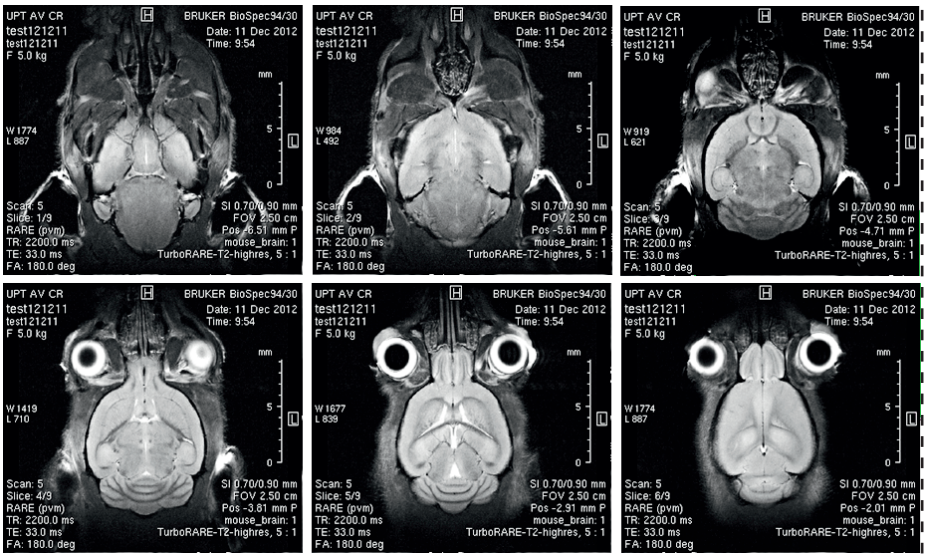
List of devices

- MR scanner 9.4T/30cm Bruker Avance III 94/30 (^{1}H 400 MHz), 200 mT/m gradients, 660 mT/m gradient insert for microimaging, multinuclear equipment (^{31}P, ^{13}C, ^{19}F, ^{23}Na, ^{129}Xe), RF coils for mouse/rat/rabbit measurement, 2 transmit, 4 receive channels, software ParaVision 5.1 and 6.0.1
- general anesthesia (isoflurane, N_2O), vital function monitor SAII 1030, artificial ventilation, animal bed heating
- minisurgery room

Rack for individually ventilated cages for accommodation of mice

Quantification of water and fat fractions in the mouse body





Anatomical T_2 weighted images of a mouse brain

- animal facility for about 200 mice and 100 rats with overpressure and EU14 filtration, animals in individually ventilated cages, hygienic loop, autoclave, UV sterilization chamber, laminar flow boxes for animal handling, minisurgery room
- wet lab with fume chamber, deep freezer (-80° C), cadaver freezer
- MR scanner 4.7T/20cm with magnet Magnex Sci. Ltd., console and electronics MR Solutions MR6000, 1kW RF amplifier CPCAmps 5T1000M, gradients 180 mT/m, Gz insert 1000 mT/m

ACHIEVEMENTS

Ultra-short echo-time spectroscopic techniques exhibiting particularly robust water suppression and low contamination, developed in ISI long ago, have become a worldwide standard and make it possible to reliably determine more than 20 metabolites in brain MR spectra.

- I. Tkáč, Z. Starčuk, I.-Y. Choi, R. Gruetter: "*In Vivo 1H NMR Spectroscopy of Rat Brain at 1 ms Echo Time",* Magnetic Resonance in Medicine **41**, 649–656, 1999

A simulator of coupled spin systems undergoing relaxation and spatially/frequentially-inhomogeneous excitation (NMRScopeB) has been developed and integrated into jMRUI software, used at over 2500 institutions worldwide.

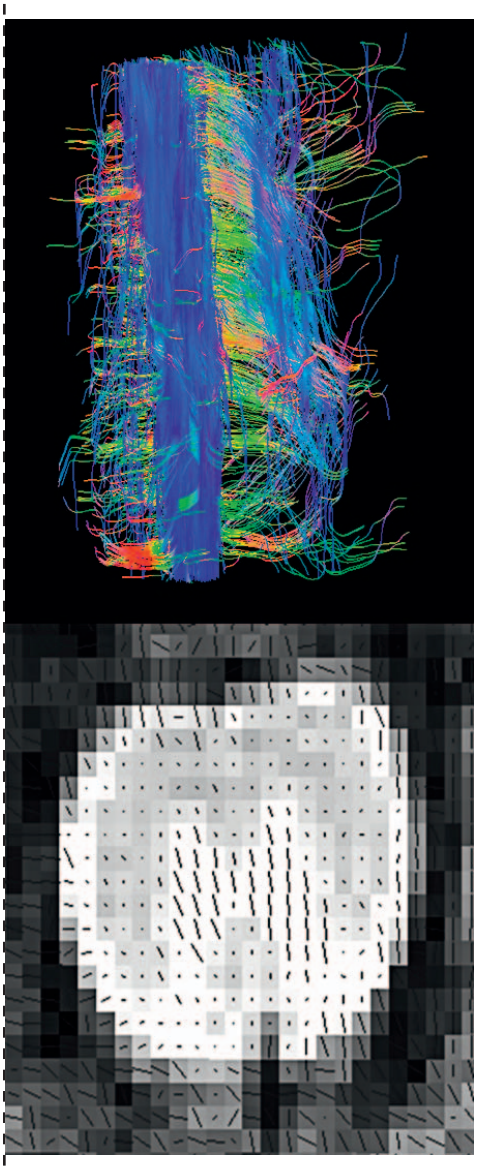
- D. Stefan, F. Di Cesare, A. Andrasescu, E. Popa, A. Lazariev, E. Vescovo, O. Strbak, S. Williams, Z. Starčuk, M. Cabanas, D. van Ormondt, D. Graveron-Demilly: "*Quantitation of magnetic resonance spectroscopy signals: the jMRUI software package*", Meas. Sci. Technol. **20**, 104035, 9p., 2009
- Z. Starčuk, J. Starčuková: "*Quantum-mechanical simulations for in vivo MR spectroscopy: principles and possibilities demonstrated with the program NMR-ScopeB*", Analytical Biochemistry **529**, 79–97, 2017

Techniques or protocols for accurate measurement of material properties (magnetic susceptibility, relaxivity) have been developed and applied in practical studies.

- J. Tuček, Z. Sofer, D. Bouša, M. Pumera, K. Holá, A. Malá, K. Poláková, M. Havrdová, K. Čépe, O. Tomanec, R. Zbořil: "*Air-stable superparamagnetic metal nanoparticles entrapped in graphene oxide matrix",* Nature Communications **7**, DOI: 10.1038/ncomms12879, 2016
- J. Starčuková, Z. Starčuk, H. Hubálková, I. Linetskiy: "*Magnetic susceptibility and electrical conductivity of metallic dental materials and their impact on MR imaging artifacts",* Dental materials **24**, 715–723, 2008
- R. Kořínek, J. Vondrák, K. Bartušek, M. Sedlaříková: "*Experimental investigations of relaxation times of gel electrolytes during polymerization by MR methods",* J. Solid State Electrochem DOI 10.1007/s10008-012-1715-6, 2012

Models and algorithms have been developed for the analysis of perfusion based on MR measurement in animals and humans. This development aids the diagnostics, therapy development, and basic research of pathophysiology.

- M. Bartoš, R. Jiřík, J. Kratochvíla, M. Standara, Z. Starčuk, T. Taxt: "*The precision of DCE-MRI using the tissue homogeneity model with continuous formulation of the perfusion parameters*", Magnetic Resonance Imaging **32**, 505-513, 2014
- J. Kratochvíla, R. Jiřík, M. Bartoš, M. Standara, Z. Starčuk, T. Taxt: "*Distributed capillary adiabatic tissue homogeneity model in parametric multi-channel blind AIF estimation using DCE-MRI",* Magnetic Resonance in Medicine **75**, 1355-1365, 2016
- E. Eskilsson, G.V. Rosland, K.M. Talasila, S. Knappskog, O. Keunen, A. Sottoriva, S. Foerster, G. Solecki, T. Taxt, R. Jiřík, S. Fritah, P. N. Harter, K. Välk, J. Al Hossain, J. V. Joseph, R. Jahedi, H. S. Saed, S. G. Piccirillo, I. Spiteri, P. Euskrichen, G. Graziani, T. Daubon, M. Lund-Johansen, P. Ø. Enger, F. Winkler, C. A. Ritter, S. P. Niclou, C. Watts, R. Bjerkvig, H. Miletic: "*EGFRvIII mutations can emerge as late*



Neuronal fibre tracking based on diffusion tensor imaging in rat spinal cord

and heterogenous events in glioblastoma development and promote angiogenesis through Src activation", Neuro-Oncology DOI: 10.1093/neuonc/now113, 2016

Diffusion measurement has been applied in the search for potential early-stage markers of Parkinson's disease

- A. Khairnar, P. Latta, E. Dražanová, J. Rudá-Kučerová, N. Szabó, A. Arab, B. Hutter-Paier, D. Havas, M. Windisch, A. Šulcová, Z. Starčuk, I. Rektorová: "*Diffusion Kurtosis Imaging Detects Microstructural Alterations in Brain of α-Synuclein Overexpressing Transgenic Mouse Model of Parkinson's Disease: A Pilot Study",* Neurotoxicity Research **28**, 281–289, 2015
- A. Khairnar, J. Rudá-Kučerová, E. Dražanová, N. Szabó, P. Latta, A. Arab, B. Hutter-Paier, D. Havas, M. Windisch, A. Šulcová, Z. Starčuk, A. Király, I. Rektorová: "*Late-stage α-synuclein accumulation in TNWT-61 mouse model of Parkinson's disease detected by diffusion kurtosis imaging",* Journal of Neurochemistry **136**, 1256–1269, 2016

MAIN COLLABORATING PARTNERS

Collaboration with academic partners

- Masarykova univerzita (Brno, CZ), Vysoké učení technické (Brno, CZ), Fakultní nemocnice u sv. Anny – ICRC (Brno, CZ), Biofyzikální ústav AV ČR (Brno, CZ), Univerzita Palackého (Olomouc, CZ), Veterinární a farmaceutická univerzita (Brno, CZ), Ústav makromolekulární chemie AV ČR (Praha, CZ), Ústav živočišné fyziologie a genetiky AV ČR (Brno, CZ), Ústav molekulární genetiky AV ČR (Praha, CZ), Výzkumný ústav veterinárního lékařství (Brno, CZ)
- Katholieke Universiteit Leuven (Leuven, BE), Ecole Polytechnique Fédérale de Lausanne (Lausanne, CH), Université Claude Bernard Lyon 1 (Lyon, FR), University of Manchester (Manchester, UK), Max Planck Institute for Human Cognitive and Brain Sciences (Leipzig, DE), Radboud University Nijmegen Medical Centre (Nijmegen, NL), Universitat Autonoma de Barcelona (Barcelona, ES), Universitat de Barcelona (Barcelona, ES), University of Bern (Bern, CH), University of Bergen (Bergen, NO)

Collaboration with companies

- Philips Healthcare (Nijmegen, NL), Siemens Healthcare (Erlangen, DE), GE Healthcare (USA), icoMetrix (Leuven, BE)

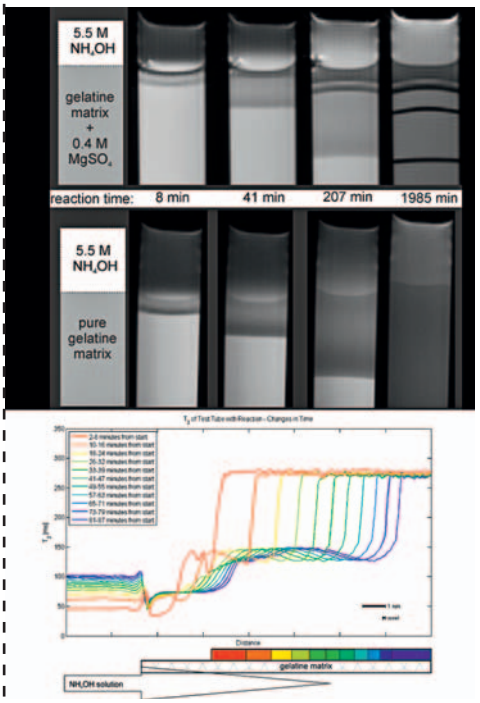
EXPECTATIONS

Offers

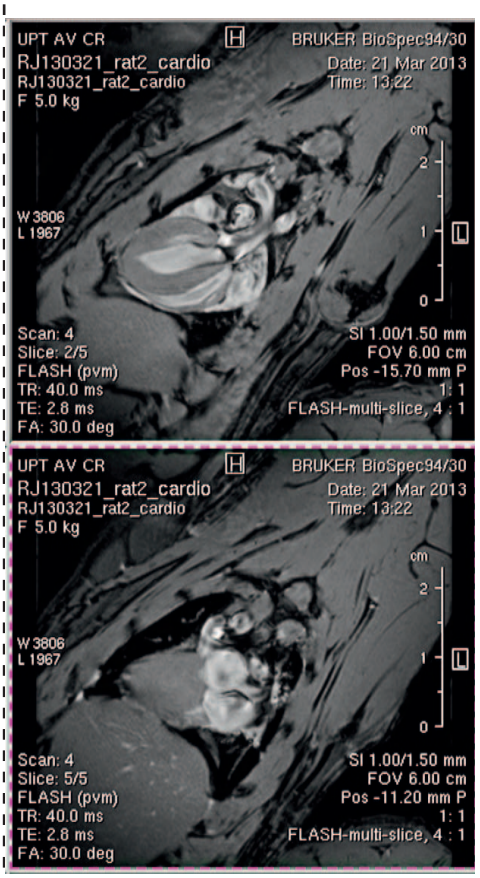
- Development and execution of MR measurement protocols and data analysis methods for specific applications (multiparametric testing of contrast agents, pharmacokinetics, pharmacodynamics, therapeutic procedures in animal models, characterization of gels or porous materials, MR imaging of small diamagnetic objects)
- Collaboration in development, preparation, validation of an animal model, assistance in animal use protocol preparation, arrangement of complementary examinations
- Open access via Czech-BioImaging (www.isibrno.cz/czbi, www.czech-bioimaging.cz)

Requirements

- We seek scientifically interesting applications with societal impact on medicine or industry.
- We offer collaboration in MR technology development.



Dynamic study of the formation of Liesegang rings in a reaction-diffusion process in a gel modelling a natural geologic process; MR-observation of changes in T_2 relaxation



T_1-weighted images of rat heart