Magnetic Resonance in Drug Research Study Group Newsletter
September 2016

Mission
To facilitate the development and evaluation of MR techniques for drug research and the application of these techniques to study the effects of drugs in humans and animals.

Governing Committee:

Chair: Detlef Stiller, Ph.D.
Vice-Chair: Alexandre J. Coimbra, Ph.D.
Secretary: Catherine D.G. Hines, Ph.D.
Trainee Representative: Georges Hankov, M.Sc.
Past-Chair: Geoffrey J. M. Parker, Ph.D.

Detlef Stiller is the Head of the In Vivo Imaging Laboratory at Boehringer Ingelheim Pharma GmbH & Co. KG. Detlef has over 30 years of experience in multiple areas of imaging in drug development, including MRI, CT, PET, and optical expertise, and has successfully applied imaging to CNS, cardiovascular, metabolic, and respiratory diseases applications. Additional achievements include managing multiple successful collaborations across academic and industrial partners.
(LinkedIn: https://www.linkedin.com/in/detlef-stiller-87a50a1)

Alexandre Coimbra is a Senior Clinical Imaging Scientist in the Clinical Imaging Group at Genentech, Inc., in South San Francisco, California. He has an EE degree from Federal University of Pará, a M.Sc. in Biomedical Engineering from Federal University of Santa Catarina, Brazil, and a Ph.D. in Applied Sciences from the Catholic University of Louvain, Louvain-la-Neuve, Belgium. Alexandre has over 15 years experience in applying imaging in general and MRI in particular in drug research and development. (LinkedIn: https://www.linkedin.com/in/alexandre-coimbra-19460a7)

Catherine Hines is the Director of the MR, CT, US, and Optical Imaging group at Merck Research Labs in West Point, PA. She has a bachelor's degree in Biochemistry from Iowa State University and a Ph.D. in Biomedical Engineering from the University of Wisconsin-Madison. Catherine has over 10 years of experience in abdominal imaging, including fat/water imaging, spectroscopy, elastography, and dynamic contrast enhancement. She has additional expertise towards cardiac imaging, and Discovery and Safety Assessment applications in drug development. (LinkedIn: https://www.linkedin.com/in/catherine-hines-81546678)

Georges started his career in the field of MRI in 2011 with an internship at Stanford University, working on new methods to monitor brain oxygenation. This particular research project led him to his first ISMRM conference in 2012. Later this same year, he joined the imaging department of Genentech as an image analyst where he mainly worked on developing DCE-MRI in the context of oncology and multi-center early phase clinical trials. Early 2014, Georges moved to Switzerland for a joined PhD project, between Roche and ETH Zurich, on brain functional connectivity in rodents. Georges' current role as the MR in Drug Research study group committee is to represent the interests of all trainee members.
(LinkedIn: https://ch.linkedin.com/in/georgeshankov)

Geoff Parker is Professor of Biomedical Imaging at the University of Manchester, UK, and CEO of Bioxydyn, a company specializing in MRI imaging services and software provision. He has a bachelor's degree in Physics from the University of Manchester and a PhD in dynamic contrast-enhanced (DCE) MRI in cancer from the Institute of Cancer Research, London. Geoff has over 20 years of experience in quantitative MRI, including DCE-MRI, diffusion MRI and oxygenation imaging. He has been responsible for several methodological innovations and is active in translating new methods to application in many areas, including oncology, neuroscience, musculoskeletal disease and lung disease.
(LinkedIn: http://www.linkedin.com/in/geoffjmparker)

Table of Contents

In-vitro Studies

Pre-clinical Studies

(1)H-Nuclear magnetic resonance-based metabolic profiling of nonsteroidal anti-inflammatory drug-induced adverse effects in rats.
Um SY, Park JH, Chung MW, Choi KH, Lee HJ.
J Pharm Biomed Anal. 2016 Sep 10;129:492-501. doi: 10.1016/j.jpba.2016.07.045. Epub 2016 Jul 31.

The Cardenolide Glycoside Acovenoside A Affords Protective Activity in Doxorubicin-Induced Cardiotoxicity in Mice.
Ezzat SM, El Gaafary M, El Sayed AM, Sabry OM, Ali ZY, Hafner S, Schmiech M, Jin L, Syrovets T, Simmet T.
J Pharmacol Exp Ther. 2016 Aug;358(2):262-70. doi: 10.1124/jpet.116.232652. Epub 2016 May 31.

Cannabinoid receptor activation in the juvenile rat brain results in rapid biomechanical alterations: Neurovascular mechanism as a putative confounding factor.
Chatelin S, Humbert-Claude M, Garteiser P, Ricobaraza A, Vilgrain V, Van Beers BE, Sinkus R, Lenkei Z.
J Cereb Blood Flow Metab. 2016 May;36(5):954-64. doi: 10.1177/0271678X15606923. Epub 2015 Oct 2.

MR Studies of Glioblastoma Models Treated with Dual PI3K/mTOR Inhibitor and Temozolomide:Metabolic Changes Are Associated with Enhanced Survival.
Radoul M, Chaumeil MM, Eriksson P, Wang AS, Phillips JJ, Ronen SM.
Mol Cancer Ther. 2016 May;15(5):1113-22. doi: 10.1158/1535-7163.MCT-15-0769. Epub 2016 Feb 16

Non-invasive in vivo imaging of early metabolic tumor response to therapies targeting choline metabolism.
Mignion L, Danhier P, Magat J, Porporato PE, Masquelier J, Gregoire V, Muccioli GG, Sonveaux P, Gallez B, Jordan BF.
Int J Cancer. 2016 Apr 15;138(8):2043-9. doi: 10.1002/ijc.29932. Epub 2015 Dec 9.

The Synergistic Effect of Selumetinib/Docetaxel Combination Therapy Monitored by [(18)F]FDG/[(18)F]FLT PET and Diffusion-Weighted Magnetic Resonance Imaging in a Colorectal Tumor Xenograft Model.
Honndorf VS, Schmidt H, Wiehr S, Wehrl HF, Quintanilla-Martinez L, Stahlschmidt A, Barjat H, Emmas SA, Pichler BJ.
Mol Imaging Biol. 2016 Apr;18(2):249-57. doi: 10.1007/s11307-015-0881-1.

Clinical Studies

Sitagliptin vs. placebo for non-alcoholic fatty liver disease: A randomized controlled trial.
Cui J, Philo L, Nguyen P, Hofflich H, Hernandez C, Bettencourt R, Richards L, Salotti J, Bhatt A, Hooker J, Haufe W, Hooker C, Brenner DA, Sirlin CB, Loomba R.
J Hepatol. 2016 Aug;65(2):369-76. doi: 10.1016/j.jhep.2016.04.021. Epub 2016 May 2.

Rationale and design of the PREFERS (Preserved and Reduced Ejection Fraction Epidemiological Regional Study) Stockholm heart failure study: an epidemiological regional study in Stockholm county of 2.1 million inhabitants.
Linde C, Eriksson MJ, Hage C, Wallén H, Persson B, Corbascio M, Lundeberg J,

Maret E, Ugander M, Persson H; Stockholm County/Karolinska Institutet 4D heart failure investigators.
Eur J Heart Fail. 2016 Jul 7. doi: 10.1002/ejhf.599. [Epub ahead of print]

Adaptive Randomization of Veliparib-Carboplatin Treatment in Breast Cancer.
Rugo HS, Olopade OI, DeMichele A, Yau C, van 't Veer LJ, Buxton MB, Hogarth M, Hylton NM, Paoloni M, Perlmutter J, Symmans WF, Yee D, Chien AJ, Wallace AM, Kaplan HG, Boughey JC, Haddad TC, Albain KS, Liu MC, Isaacs C, Khan QJ, Lang JE, Viscusi RK, Pusztai L, Moulder SL, Chui SY, Kemmer KA, Elias AD, Edmiston KK, Euhus DM, Haley BB, Nanda R, Northfelt DW, Tripathy D, Wood WC, Ewing C, Schwab R, Lyandres J, Davis SE, Hirst GL, Sanil A, Berry DA, Esserman LJ; I-SPY 2 Investigators.
N Engl J Med. 2016 Jul 7;375(1):23-34. doi: 10.1056/NEJMoa1513749.

Adaptive Randomization of Neratinib in Early Breast Cancer.
Park JW, Liu MC, Yee D, Yau C, van 't Veer LJ, Symmans WF, Paoloni M, Perlmutter J, Hylton NM, Hogarth M, DeMichele A, Buxton MB, Chien AJ, Wallace AM, Boughey JC, Haddad TC, Chui SY, Kemmer KA, Kaplan HG, Isaacs C, Nanda R, Tripathy D, Albain KS, Edmiston KK, Elias AD, Northfelt DW, Pusztai L, Moulder SL, Lang JE, Viscusi RK, Euhus DM, Haley BB, Khan QJ, Wood WC, Melisko M, Schwab R, Helsten T, Lyandres J, Davis SE, Hirst GL, Sanil A, Esserman LJ, Berry DA; I-SPY 2 Investigators.
N Engl J Med. 2016 Jul 7;375(1):11-22. doi: 10.1056/NEJMoa1513750.

Neurofunctional Reward Processing Changes in Cocaine Dependence During Recovery.
Balodis IM, Kober H, Worhunsky PD, Stevens MC, Pearlson GD, Carroll KM, Potenza MN.
Neuropsychopharmacology. 2016 Jul;41(8):2112-21. doi: 10.1038/npp.2016.11. Epub 2016 Jan 21.

METastasis Reporting and Data System for Prostate Cancer: Practical Guidelines for Acquisition, Interpretation, and Reporting of Whole-body Magnetic Resonance Imaging-based Evaluations of Multiorgan Involvement in Advanced Prostate Cancer.
Padhani AR, Lecouvet FE, Tunariu N, Koh DM, De Keyzer F, Collins DJ, Sala E, Schlemmer HP, Petralia G, Vargas HA, Fanti S, Tombal HB, de Bono J.
Eur Urol. 2016 Jun 14. pii: S0302-2838(16)30241-X. doi: 10.1016/j.eururo.2016.05.033. [Epub ahead of print]

MRI and MRE for non-invasive quantitative assessment of hepatic steatosis and fibrosis in NAFLD and NASH: Clinical trials to clinical practice.
Dulai PS, Sirlin CB, Loomba R.
J Hepatol. 2016 Jun 14. pii: S0168-8278(16)30267-7. doi: 10.1016/j.jhep.2016.06.005. [Epub ahead of print] Review.

Length of optic nerve double inversion recovery hypersignal is associated with retinal axonal loss.
Hadhoum N, Hodel J, Defoort-Dhellemmes S, Duhamel A, Drumez E, Zéphir H, Pruvo JP, Leclerc X, Vermersch P, Outteryck O.
Mult Scler. 2016 Apr;22(5):649-58. doi: 10.1177/1352458515598021. Epub 2015 Jul 30.

Reviews/Guidelines/Meta-analyses

Glial biomarkers in human central nervous system disease.

Garden GA, Campbell BM.
Glia. 2016 Oct;64(10):1755-71. doi: 10.1002/glia.22998. Epub 2016 May 26. Review.

Dynamic contrast-enhanced MRI for oncology drug development.
Sung YS, Park B, Choi Y, Lim HS, Woo DC, Kim KW, Kim JK.
J Magn Reson Imaging. 2016 Aug;44(2):251-64. doi: 10.1002/jmri.25173. Epub 2016 Feb 8. Review.

The clinical perspective: How to personalise treatment in MS and how may biomarkers including imaging contribute to this?
Vermersch P, Berger T, Gold R, Lukas C, Rovira A, Meesen B, Chard D, Comabella M, Palace J, Trojano M.
Mult Scler. 2016 Aug;22(2 Suppl):18-33. doi: 10.1177/1352458516650739.

METastasis Reporting and Data System for Prostate Cancer: Practical Guidelines for Acquisition, Interpretation, and Reporting of Whole-body Magnetic Resonance Imaging-based Evaluations of Multiorgan Involvement in Advanced Prostate Cancer.
Padhani AR, Lecouvet FE, Tunariu N, Koh DM, De Keyzer F, Collins DJ, Sala E, Schlemmer HP, Petralia G, Vargas HA, Fanti S, Tombal HB, de Bono J.
Eur Urol. 2016 Jun 14. pii: S0302-2838(16)30241-X. doi: 10.1016/j.eururo.2016.05.033. [Epub ahead of print]

MRI and MRE for non-invasive quantitative assessment of hepatic steatosis and fibrosis in NAFLD and NASH: Clinical trials to clinical practice.
Dulai PS, Sirlin CB, Loomba R.
J Hepatol. 2016 Jun 14. pii: S0168-8278(16)30267-7. doi: 10.1016/j.jhep.2016.06.005. [Epub ahead of print] Review.

Methodology - MRI

Dynamic contrast-enhanced MRI for oncology drug development.
Sung YS, Park B, Choi Y, Lim HS, Woo DC, Kim KW, Kim JK.
J Magn Reson Imaging. 2016 Aug;44(2):251-64. doi: 10.1002/jmri.25173. Epub 2016 Feb 8. Review.

Rationale and design of the PREFERS (Preserved and Reduced Ejection Fraction Epidemiological Regional Study) Stockholm heart failure study: an epidemiological regional study in Stockholm county of 2.1 million inhabitants.
Linde C, Eriksson MJ, Hage C, Wallén H, Persson B, Corbascio M, Lundeberg J, Maret E, Ugander M, Persson H; Stockholm County/Karolinska Institutet 4D heart failure investigators.
Eur J Heart Fail. 2016 Jul 7. doi: 10.1002/ejhf.599. [Epub ahead of print]

METastasis Reporting and Data System for Prostate Cancer: Practical Guidelines for Acquisition, Interpretation, and Reporting of Whole-body Magnetic Resonance Imaging-based Evaluations of Multiorgan Involvement in Advanced Prostate Cancer.
Padhani AR, Lecouvet FE, Tunariu N, Koh DM, De Keyzer F, Collins DJ, Sala E, Schlemmer HP, Petralia G, Vargas HA, Fanti S, Tombal HB, de Bono J.
Eur Urol. 2016 Jun 14. pii: S0302-2838(16)30241-X. doi: 10.1016/j.eururo.2016.05.033. [Epub ahead of print]

MRI and MRE for non-invasive quantitative assessment of hepatic steatosis and fibrosis in NAFLD and NASH: Clinical trials to clinical practice.
Dulai PS, Sirlin CB, Loomba R.
J Hepatol. 2016 Jun 14. pii: S0168-8278(16)30267-7. doi: 10.1016/j.jhep.2016.06.005.

[Epub ahead of print] Review.

Perfusion MRI as the predictive/prognostic and pharmacodynamic biomarkers in recurrent malignant glioma treated with bevacizumab: a systematic review and a time-to-event meta-analysis.
Choi SH, Jung SC, Kim KW, Lee JY, Choi Y, Park SH, Kim HS.
J Neurooncol. 2016 Jun;128(2):185-94. doi: 10.1007/s11060-016-2102-4. Epub 2016 Apr 23. Review.

Non-invasive in vivo imaging of early metabolic tumor response to therapies targeting choline metabolism.
Mignion L, Danhier P, Magat J, Porporato PE, Masquelier J, Gregoire V, Muccioli GG, Sonveaux P, Gallez B, Jordan BF.
Int J Cancer. 2016 Apr 15;138(8):2043-9. doi: 10.1002/ijc.29932. Epub 2015 Dec 9.

Length of optic nerve double inversion recovery hypersignal is associated with retinal axonal loss.
Hadhoum N, Hodel J, Defoort-Dhellemmes S, Duhamel A, Drumez E, Zéphir H, Pruvo JP, Leclerc X, Vermersch P, Outteryck O.
Mult Scler. 2016 Apr;22(5):649-58. doi: 10.1177/1352458515598021. Epub 2015 Jul 30.

Methodology - MRS

(1)H-Nuclear magnetic resonance-based metabolic profiling of nonsteroidal anti-inflammatory drug-induced adverse effects in rats.
Um SY, Park JH, Chung MW, Choi KH, Lee HJ.
J Pharm Biomed Anal. 2016 Sep 10;129:492-501. doi: 10.1016/j.jpba.2016.07.045. Epub 2016 Jul 31.

Interventional Study

Sitagliptin vs. placebo for non-alcoholic fatty liver disease: A randomized controlled trial.
Cui J, Philo L, Nguyen P, Hofflich H, Hernandez C, Bettencourt R, Richards L, Salotti J, Bhatt A, Hooker J, Haufe W, Hooker C, Brenner DA, Sirlin CB, Loomba R.
J Hepatol. 2016 Aug;65(2):369-76. doi: 10.1016/j.jhep.2016.04.021. Epub 2016 May 2.

The Cardenolide Glycoside Acovenoside A Affords Protective Activity in Doxorubicin-Induced Cardiotoxicity in Mice.
Ezzat SM, El Gaafary M, El Sayed AM, Sabry OM, Ali ZY, Hafner S, Schmiech M, Jin L, Syrovets T, Simmet T.
J Pharmacol Exp Ther. 2016 Aug;358(2):262-70. doi: 10.1124/jpet.116.232652. Epub 2016 May 31.

Adaptive Randomization of Veliparib-Carboplatin Treatment in Breast Cancer.
Rugo HS, Olopade OI, DeMichele A, Yau C, van 't Veer LJ, Buxton MB, Hogarth M, Hylton NM, Paoloni M, Perlmutter J, Symmans WF, Yee D, Chien AJ, Wallace AM, Kaplan HG, Boughey JC, Haddad TC, Albain KS, Liu MC, Isaacs C, Khan QJ, Lang JE, Viscusi RK, Pusztai L, Moulder SL, Chui SY, Kemmer KA, Elias AD, Edmiston KK, Euhus DM, Haley BB, Nanda R, Northfelt DW, Tripathy D, Wood WC, Ewing C, Schwab R, Lyandres J, Davis SE, Hirst GL, Sanil A, Berry DA, Esserman LJ; I-SPY 2 Investigators.
N Engl J Med. 2016 Jul 7;375(1):23-34. doi: 10.1056/NEJMoa1513749.

Adaptive Randomization of Neratinib in Early Breast Cancer.
Park JW, Liu MC, Yee D, Yau C, van 't Veer LJ, Symmans WF, Paoloni M, Perlmutter J, Hylton NM, Hogarth M, DeMichele A, Buxton MB, Chien AJ, Wallace AM, Boughey JC, Haddad TC, Chui SY, Kemmer KA, Kaplan HG, Isaacs C, Nanda R, Tripathy D, Albain KS, Edmiston KK, Elias AD, Northfelt DW, Pusztai L, Moulder SL, Lang JE, Viscusi RK, Euhus DM, Haley BB, Khan QJ, Wood WC, Melisko M, Schwab R, Helsten T, Lyandres J, Davis SE, Hirst GL, Sanil A, Esserman LJ, Berry DA; I-SPY 2 Investigators.
N Engl J Med. 2016 Jul 7;375(1):11-22. doi: 10.1056/NEJMoa1513750.

Neurofunctional Reward Processing Changes in Cocaine Dependence During Recovery.
Balodis IM, Kober H, Worhunsky PD, Stevens MC, Pearlson GD, Carroll KM, Potenza MN.
Neuropsychopharmacology. 2016 Jul;41(8):2112-21. doi: 10.1038/npp.2016.11. Epub 2016 Jan 21.

Cannabinoid receptor activation in the juvenile rat brain results in rapid biomechanical alterations: Neurovascular mechanism as a putative confounding factor.
Chatelin S, Humbert-Claude M, Garteiser P, Ricobaraza A, Vilgrain V, Van Beers BE, Sinkus R, Lenkei Z.
J Cereb Blood Flow Metab. 2016 May;36(5):954-64. doi: 10.1177/0271678X15606923. Epub 2015 Oct 2.

MR Studies of Glioblastoma Models Treated with Dual PI3K/mTOR Inhibitor and Temozolomide:Metabolic Changes Are Associated with Enhanced Survival.
Radoul M, Chaumeil MM, Eriksson P, Wang AS, Phillips JJ, Ronen SM.
Mol Cancer Ther. 2016 May;15(5):1113-22. doi: 10.1158/1535-7163.MCT-15-0769. Epub 2016 Feb 16.

The Synergistic Effect of Selumetinib/Docetaxel Combination Therapy Monitored by [(18)F]FDG/[(18)F]FLT PET and Diffusion-Weighted Magnetic Resonance Imaging in a Colorectal Tumor Xenograft Model.
Honndorf VS, Schmidt H, Wiehr S, Wehrl HF, Quintanilla-Martinez L, Stahlschmidt A, Barjat H, Emmas SA, Pichler BJ.
Mol Imaging Biol. 2016 Apr;18(2):249-57. doi: 10.1007/s11307-015-0881-1.

Observational Study

Rationale and design of the PREFERS (Preserved and Reduced Ejection Fraction Epidemiological Regional Study) Stockholm heart failure study: an epidemiological regional study in Stockholm county of 2.1 million inhabitants.
Linde C, Eriksson MJ, Hage C, Wallén H, Persson B, Corbascio M, Lundeberg J, Maret E, Ugander M, Persson H; Stockholm County/Karolinska Institutet 4D heart failure investigators.
Eur J Heart Fail. 2016 Jul 7. doi: 10.1002/ejhf.599. [Epub ahead of print]

Length of optic nerve double inversion recovery hypersignal is associated with retinal axonal loss.
Hadhoum N, Hodel J, Defoort-Dhellemmes S, Duhamel A, Drumez E, Zéphir H, Pruvo JP, Leclerc X, Vermersch P, Outteryck O.
Mult Scler. 2016 Apr;22(5):649-58. doi: 10.1177/1352458515598021. Epub 2015 Jul 30.