Traditional Posters: Cancer

Tumor Therapy Response
Hall B Monday 14:00-16:00

Kim Anne Radermacher1, Sébastien Boutry2, Isabelle Mahieu2, Sophie Laurent2, Luce Vander Elst2, Caroline Bouzin1, Julie Magat1, Vincent Grégoire2, Olivier Feron3, Robert N. Muller2, Bénédicte F. Jordan1, Bernard Gallez1
1Biomedical Magnetic Resonance Unit, Catholic University of Louvain, Bruxelles, Belgium; 2NMR and Molecular Imaging Laboratory, University of Mons, Mons, Belgium; 3Unit of Pharmacology and Therapeutics, Catholic University of Louvain, Bruxelles, Belgium; 4Center for Molecular Imaging and Experimental Radiotherapy, Catholic University of Louvain, Bruxelles, Belgium

The aim was to develop a molecular marker for non invasive monitoring of tumor cell death as a response to treatment. The phosphatidylserine-targeted peptide E3 was coupled to ultrasmall particles of iron oxide (USPIO). The USPIO concentration was evaluated in irradiated and untreated tumors by EPR and MRI in vivo. We also compared USPIO-E3 accumulation in three different tumor models presenting different degrees of radiosensitivity (fibrosarcoma is less radiosensitive than hepatocarcinoma which is less radiosensitive than lymphoma). The major finding of the present investigation is that USPIO-E3 allows the sensitive detection of tumor cell death after cytotoxic treatment.

2697. Evaluation of Radiotherapy Using Manganese-Enhanced MRI (MEMRI)
Shigeyoshi Saito1,2, Sumitaka Hasegawa, Takako Furukawa, Tetsuya Suhara, Iwao Kanno, Ichio Aoki
1Graduate School of Medicine, Tohoku University, Sendai, Miyagi, Japan; 2National Institute of Radiological Sciences, Chiba, Japan

Radiotherapy is the use of high-energy x-rays or particles to treat malignancies with the intention of destroying or inactivating cells while preserving normal tissue integrity. We found demonstrated that MEMRI; 1) Cellular viability after radiation exposure could be evaluated using signal enhancement manganese-labeling was reduced after x-ray irradiation for both in-vitro and in-vivo models. MEMRI may be used to evaluate the cellular viability of tumor after radiotherapy.

2698. Dynamic-Contrast-Enhanced-MRI Shows Radiation Resistant Tumor (Nu61) Is Also Resistant to TNFalpha Treatment – Pilot Study
Chad R. Haney1, Xiaobing Fan1, Gregory S. Karčzmar1, Charles A. Pelizzari2, Marta Zamora1, Erica Markiewicz1, Helena J. Mauceri2, Ralph R. Weichselbaum2
1Radiology, University of Chicago, Chicago, IL, United States; 2Radiation & Cellular Oncology, University of Chicago, Chicago, IL, United States

Ionizing radiation is a staple for treating tumors. However, failure to cure tumors is thought to be due to an intrinsic tumor cell radioresistance and its microenvironment. DCE-MRI was used to characterize the response of two tumor cell lines – one radioresistant and the other radioresistant. A genetically modified adenoviral vector was used, which causes infected cells to produce tumor necrosis factor alpha (a potent antivascular agent), only when irradiated. The radioresistant tumors showed no significant changes in the rate transfer constant and fractional volume accessible to the contrast agent. However, the radiosensitive tumors showed significant reduction in both kinetic parameters.

2699. Dichloroacetate Treatment Resulted in Altered Phospholipid Metabolism and Compromised Tumour Bioenergetics in Human Colon Carcinoma Xenografts
Yuen-Li Chung1, Helen Troy1, Geoffrey S. Payne1, Marion Stubbs2, Ian R. Judson1, John R. Griffiths2, Martin O. Leach1
1CR-UK and ESPRC Cancer Imaging Centre, Institute of Cancer Research, Sutton, Surrey, United Kingdom; 2Cancer Research UK Cambridge Research Institute, Cambridge, United Kingdom; 3CR-UK Centre for Cancer Therapeutics, Institute of Cancer Research, Sutton, Surrey, United Kingdom

Dichloroacetate (DCA) is a pyruvate dehydrogenase kinase (PDK) inhibitor and is found to be an anti-cancer agent. The aim of this work was to develop a non-invasive and robust biomarker for tumour response following PDK inhibition. In vivo and in vitro 1H- and 31P-MRS of HT29 xenografts and tumour extracts were used. DCA treatment caused tumour growth inhibition and altered phospholipid metabolism and tumour bioenergetics. The drop in total choline and phosphomonoesters may have potential as non-invasive markers for tumour response following treatment with DCA or other PDK inhibitors.
2700. Resistance and Sensitivity to Docetaxel Treatment of Breast Cancer Tissue in Mice Assessed by Analysis of Choline Compounds with HRMAS NMR Spectroscopy

Jack van Asten1,2, Tone F. Bathen3, Tessa Buckle4, Chantal Beekman4, Ingrid Gribbestad4, Fijs van Leeuwen4, Arend Heerschap1

1Radiology, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands; 2Biophysical Chemistry, Radboud University Nijmegen, Nijmegen, Netherlands; 3Dept. of Circulation and Medical Imaging, Norwegian University of Science and Technology, Trondheim, Norway; 4Radiology and Nuclear Medicine, Division of Diagnostic Oncology, The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital

Breast cancers may be resistant to docetaxel treatment. We investigated the metabolic profile of breast cancer tissue in mouse strains resistant and sensitive to treatment by docetaxel. A typical choline compound profile was found to be predictive for treatment efficiency.

2701. Nitric Oxide Synthase Silencing by Bimodal Liposomes May Reduce Perfusion in Tumours as Assessed by DCE-MRI

Tammy Louise Kalber1, Gavin D. Kenny1, Nazila Kamaly1,2, Willy Gsell3, Marzena Wylesinska-Arridge1, Leigh P. Brody1, Andrew D. Miller2, Jimmy D. Bell1

1Metabolic and Molecular Imaging Group, Imaging Sciences Department, MRC, Imperial College London, Hammersmith Hospital, London, United Kingdom; 2Imperial College Genetic Therapies Centre, Department of Chemistry, Imperial College London, London, United Kingdom; 3The Biological Imaging Centre, Imperial College London, London, United Kingdom

Human colon adenocarcinoma cells, transfected to overexpress inducible nitric oxide synthase (iNOS) were used to characterize the delivery of iNOS siRNA by bimodal liposomes in vitro and in vivo. Incubation in vitro resulted in a significant decrease in nitrite by day 72. Whereas, iNOS overexpressing tumours administered with iNOS siRNA liposomes resulted in decreased T1 over 24 hours, consistent with gradual accumulation within the tumour. Tumour volume measurements showed growth restriction and regression suggestive of siRNA release resulting in gene silencing and therapeutic effect after ~ 5 days. However, DCE-MRI was not able to evaluate changes in tumour perfusion leading.

2702. Early Accumulation of 1H MRS Detected Lipids and Lactate in Rat 9L Glioma to Anti-Angiogenic Treatment

Enrico C. Lallana1, Kyle A. Brong2, Khan Hekmatyar1, Neil Jerome1, Martin Wilson3, Camilo E. Fadul1, Risto A. Kauppinen4

1Dartmouth Medical School; 2Dartmouth College; 3University of Birmingham; 4Dartmouth Medical School, Hanover, NH, United States

A rodent anti-VEGF-antibody, B20-4.1.1, was used to treat orthotopic 9L glioma bearing rats. During the first week of treatment kinetics of T1-weighted signal enhancement following rapid Magnevist iv-bolus slowed down greatly, reflecting reduced vascular leakiness and perfusion. At the same time, 1H MRS showed large increase both in relative lactate and 1.3ppm and 0.9ppm lipids, while water diffusion in treated gliomas was unchanged. These results indicate that 1H MRS provides endogenous imaging biomarkers for tumour cell responses during anti-angiogenic therapy, that are not obtained by contrast enhanced MRI or diffusion.

2703. In Vivo MR Detection of Inhibition of Signaling Transduction in Non-Hodgkin's Lymphoma

Seung Cheol Lee1, Michal Marzec2, Xiabin Liu2, Suzanne Wehrli3, Mariusz Wasik2, Jerry David Glickson1

1Department of Radiology, University of Pennsylvania, Philadelphia, PA, United States; 2Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, PA, United States; 3NMR Core Facility, Children's Hospital of Philadelphia, Philadelphia, PA, United States

More and more drugs for cancer are being developed in the context of signaling transduction. Some of such drugs are already in clinical trial. A noninvasive method to early detect the effect of these drugs is demanding. NMR is a promising candidate to meet this request as it can be applied in vivo to measure metabolic perturbations in tumors following various therapies. We're investigating to see effects of the inhibitor of mammalian target of rapamycin (mTOR) which is a highly conserved serine/threonine kinase that controls cell growth and metabolism in response to nutrients, growth factors, cellular energy, and stress.

2704. Preclinical Therapeutic Sequencing Using a Dual-Tracer Multi-Animal DCE-MRI Platform

James A. Bankson1, David L. Schwartz2, Douglas Webb1, Charles V. Kingsley1, Jorge Delacerda1, Marc S. Ramirez2, Garth Powis1

1Department of Imaging Physics, The University of Texas M.D. Anderson Cancer Center, Houston, TX, United States; 2Department of Radiation Medicine, North Shore-LIJ Health System, New Hyde Park, NY, United States

A dual-tracer multi-animal DCE-MRI platform has been used to compare response of a xenograft model of pancreatic cancer to combinations of radiation therapy and PX-478, a novel selective HIF-1a inhibitor currently in Phase I clinical trial. Six groups of eight animals were administered sham, single-agent, concurrent, or sequential therapies. Dual-tracer multi-animal DCE-MRI evaluation of vascular changes detected most pronounced response in group given combined therapy compared to controls as early as
+3d after completion of therapy, preceding detectable differences in tumor growth by >7d. The dual-tracer multi-animal DCE-MRI platform enabled high-throughput evaluation of response to therapy.

2705. Theranostic Effect of Serial MEMRI on the HESC Induced Teratoma
Jaehoon Chung1, Rajesh Dash1, Kehkooi Kee2, Joelle Barral3, Irving Weissmann4, Dwight Nishimura4, Robert Robbins2, Renee Reijo Pera2, Phillip C. Yang1
1Cardiovascular medicine, Stanford University, Stanford, CA, United States; 2Electrical engineering, Stanford University, Stanford, CA, United States; 3Pathology, Stanford University, Stanford, CA, United States; 4Cardiothoracic surgery, Stanford University, Stanford, CA, United States
Systemic administration of MnCl2 enabled simultaneous monitoring and selective elimination of hESC induced teratoma cells by higher intracellular accumulation of Mn2+. This is the first study to demonstrate MEMRI has a theranostic effect in both detecting and eliminating early teratoma formation.

2706. MRI Molecular Imaging Monitors Downstream Anti-Angiogenic Effects of MTOR Inhibition
Robert Ross1, Jose L. Figueiredo2, Peter Waterman2, Ralph Weissleder3, Alexander R. Guimaraes4,5
1Lank Center for Genitourinary Oncology, Dana Farber Cancer Institute, Boston, MA, United States; 2Center for Systems Biology, Massachusetts General Hospital, Boston, MA, United States; 3Center for Systems Biology, Massachusetts General Hospital, Boston, MA, United States; 4Radiology, Massachusetts General Hospital/Martinos Center for Biomedical Imaging, Charlestown, MA, United States; 5Center for Systems Biology, Massachusetts General Hospital/Martinos Center for Biomedical Imaging, Boston, mA, United States
Inhibitors of the mammalian target of rapamycin (mTOR) are approved in patients with metastatic renal cell cancer (RCC). Our aim was to evaluate in vivo, mTOR inhibition on the vascularity of a RCC mouse model using magnetic nanoparticle enhanced MRI and to compare these effects to the established VEGF inhibitor, sorafenib. There was excellent correlation (R^2 0.95) of MRI measures of vascular volume fraction to histologic microvessel density. VVF in all treatment arms differed from control (p<0.05) at end of therapy. This study demonstrates that MRI can monitor noninvasively, the in vivo antiangiogenic effects of chemotherapeutic agents.

2707. The Effects of SDF-CXCR4 Signaling on Tumor Growth: The Involvement of Neural Progenitor Cells
Nai-Wei Yao1, Chiao-Chi V. Chen1, Chen Chang1
1Functional and Micro-magnetic Resonance Imaging Center, Institution of Biomedical Sciences, Academia Sinica, Taipei, Taiwan
Neural progenitor cells (NPCs) and glioma cells share many common features, including the expression of several cellular markers (such as nestin and CD133), a robust proliferative potential, and pluripotency. The present study demonstrates that tumors exhibited rapid growth following NPCs transplantation while the migration was promoted by the signaling of the stromal cell-derived factor-1 (SDF-1) / CXC chemokine receptor 4 (CXCR4) axis. The finding identified a role of NPCs in tumor expansion.

2708. Optimization of Combined Bevacizumab Plus Irinotecan Therapy in Brain Tumors Using MRI Measures of Relative Cerebral Blood Volume
Kimberly R. Pechman1,2, Deborah L. Donohoe, 2,3, Devyani P. Bedekar, 2,3, Kathleen M. Schmainda, 2,4
1Neurosurgery, Medical College of Wisconsin, Milwaukee, WI, United States; 2Translational Brain Tumor Program, Medical College of Wisconsin, Milwaukee, WI, United States; 3Radiology, Medical College of Wisconsin, Milwaukee, WI, United States; 4Radiology and Biophysics, Medical College of Wisconsin, Milwaukee, WI, United States
Few systematic studies have been performed to determine the optimal timing for combining anti-angiogenic therapy with chemotherapy for the treatment of brain tumors. Standard MRI measures of enhancing tumor volume are not appropriate since anti-angiogenic drugs decrease contrast enhancement. The purpose of this study was to evaluate the utility of using rCBV, derived from DSC imaging, to optimize the combination of bevacizumab and irinotecan for the treatment of brain tumors. The studies, performed in the U87 brain tumor model, demonstrate that the optimal combination, occurs when irinotecan is administered two days before or after treatment with bevacizumab.

2709. Reference Region Based Modeling in DCE-MRI Allows Reliable Therapy Response Monitoring Despite Drug Induced Systemic Changes in a Rat Liver Tumor Model
Andreas Steingoetter1,2, Jonas Svensson1, Yvonne Kosanke1, Ernst Rummery1, Rickmer Braren1
1Institute of Radiology, Klinikum rechts der Isar der TU München, Munich, Germany; 2Institute for Biomedical Engineering, University and ETH Zurich, Zurich, Switzerland; 3Department of Medical Radiation Physics, Malmo University Hospital, Lund University, Malmo, Sweden
A limitation in DCE-MRI is the difficulty of simultaneous measurement of arterial input function and CA concentration in tumor tissue. In this study, two anaesthesia protocols, resulting in a ~ 30% change in heart rate, were used to simulate systemic changes in AIF to analyze the robustness of popAIF vs RR modeling in an orthotopic HCC rat tumor model. Different anaesthesia protocols
resulted in a significant systematic offset for \( \text{popAIF} \) based \( k_{\text{trans}} \) and \( \text{ve} \) modeling compared to RR. This study highlights the robustness and feasibility of the reference region approach.

**2710. Captopril and S-Nitrosoacaptopril as Potent Radiosensitizers: Comparative MR Study and Underlying Mechanisms.**

Benedicte F. Jordan\(^1\), Julie Peeterbroeck\(^1\), Oussama Karroum\(^1\), Caroline Diepart\(^1\), Julie Magat\(^1\), Vincent Gregoire\(^2\), Bernard Gallez\(^2\)

\(^1\)Biomedical Magnetic Resonance Unit, Universite Catholique de Louvain, Brussels, Belgium; \(^2\)IMRE, Universite Catholique de Louvain

EPR and \( 19\text{F-MRI} \) oximetry were used to monitor acute changes in tumor hemodynamics after administration of potential NO-mediated radiation co-treatments. For this purpose, S-nitrosoacaptopril, a converting enzyme inhibitor with vasodilatory properties combined to a nitric oxide donor, was tested in experimental tumors. Tumor oxygenation was significantly increased 30 minutes after administration of the co-treatment. This effect was the result of an increase in tumor blood flow along with a decrease in tumor oxygen consumption by tumor cells. This oxygen effect contributed to the increase in efficacy of radiation therapy with 10 Gy of X-rays, an effect that was not observed with captopril alone.

**2711. In Vivo and In Vitro MR Biomarkers for Choline Kinase Inhibition in Human Colon Cancer HCT-116**

Moses Darpolor\(^1\), Peter Kennealey\(^1\), H. Carl Le\(^1\), Kristen Zakian\(^1\), Ellen Ackerstaff\(^1\), Asif Rizwan\(^1\), Jin-Hong Chen\(^2\), Eliot Sambol\(^2\), Gary Schwartz\(^2\), Samuel Singer\(^2\), Jason Koutcher\(^1,3\)

\(^1\)Medical Physics, MSKCC, New York, NY, United States; \(^2\)Surgery, MSKCC, New York, NY, United States; \(^3\)Medicine, MSKCC, New York, NY, United States

Combined irinotecan and flavopiridol therapy is in clinical trials to treat human colon malignancies. Using in vivo and in vitro MR measurements we report here several critical HCT-116 cellular markers from the treatment. We have shown that flavopiridol is effective in inhibiting choline kinase by lowering phosphocholine/choline levels in vitro, while \( 31\text{P MRSI} \) detected an in vivo transient decrease in phosphocholine level following the treatment with both drugs. Detectable cholesterol/CH\(_3\) levels were observed to increase in tandem with HCT-116 cancer cell apoptotic fraction.

**2712. Early Measures of ADC Response to Radiotherapy And/or Sunitinib in a Murine Intracranial Model of Human Glioblastoma Multiforme**

Warren Foltz\(^1\), Caroline Chung\(^1\), Jesper Kallehauge\(^1\), Kelly Burrell\(^2\), Patricia Lindsay\(^1\), David Jaffray\(^1\), Gelareh Zadeh\(^2\), Cynthia Ménard\(^1\)

\(^1\)Radiation Medicine Program, Princess Margaret Hospital, Toronto, Ontario, Canada; \(^2\)Brain Tumor Research Centre, University Health Network, Toronto, Ontario, Canada

ADC can monitor early tumor response to cytotoxic therapy and predict clinical outcomes. This study monitored early ADC response and tumor growth following sunitinib and or radiotherapy in a murine intracranial model of human glioblastoma multiforme. Imaging proceeded at 3-7 day intervals following base-line MRI and image-based stratification into treatment arms. RT trial arms demonstrated considerable early ADC elevation, and persistent elevation during growth delay. Sunitinib monotherapy maintained ADC below other arms, and constrained tumor growth. Control animals displayed moderate ADC elevation and earliest exponential tumor growth. Early ADC changes may be a useful biomarker of treatment response and growth delay.

**2713. In Vivo Delivery of Liposomal Encapsulated Survivin SiRNA Leads to a Reduction in Tumour Growth Rate**

Gavin David Kenny\(^1\), Tammy Louise Kalber\(^1\), Nazila Kamaly\(^1,2\), Leigh Pauline Brody\(^1\), Andrew David Miller\(^2\), Jimmy David Bell\(^2\)

\(^1\)Metabolic and Molecular Imaging Group, Imperial College, London, United Kingdom; \(^2\)Genetic Therapies Centre, Imperial College, London, United Kingdom

Survivin is a gene upregulated in the majority of cancers, but not expressed in normal tissue and is therefore a possible target for tumour therapy. In this study siRNA targeted to Survivin was encapsulated into liposomes and the delivery to the tumour monitored using MRI and corroborated by fluorescence microscopy. The Survivin siRNA delivered by the liposomes significantly reduced the growth rate of the tumours for at least 72 hours when compared to a control siRNA and therefore could potentially be used as a cancer therapy.

**2714. Evaluation of Diffusion MR as a Biomarker for Nanoparticle Therapy Response in Lymphoma**

Thomas Sheung Chee Ng\(^1,2\), Daniel Procissi\(^1\), Hargun Sohi\(^1\), Andrew A. Raubitschek\(^3\), Russell E. Jacobs\(^1\)

\(^1\)California Institute of Technology, Pasadena, CA, United States; \(^2\)University of Southern California, Los Angeles, CA, United States; \(^3\)Beckman Institute, City of Hope, Duarte, CA, United States

IT-101 is a novel nanoparticle therapy that specifically targets the tumour mass. We evaluated whether diffusion MR is sensitive to early IT-101 response in a mouse model of lymphoma.
2715. **Response of Orthotopic PC3 Prostate Tumors to the HIF Pathway Inhibitor NSC-134754 Assessed by Diffusion Weighted MRI and Immunohistochemistry**

Lauren CJ Baker¹, Jessica KR Boult¹, Yann Jamin¹, Simon Walker-Samuel¹, Margaret A. Ashcroft², Simon P. Robinson¹
¹CR-UK and EPSRC Cancer Imaging Centre, The Institute of Cancer Research and Royal Marsden Hospital, Sutton, Surrey, United Kingdom; ²University College London, London, United Kingdom

The hypoxia-inducible factor pathway (HIF) is a key regulator in tumor cell adaptation to the hypoxic microenvironment. Small molecule HIF inhibitors have been identified and are currently being evaluated in vivo using non-invasive magnetic resonance (MR) methods. In this study, we show that diffusion-weighted magnetic resonance imaging (DW-MRI) can detect tumor response to the HIF pathway inhibitor NSC-134754 24h post administration in a murine orthotopic model of prostate cancer. Complimentary ex vivo histology of parameters including hypoxia, perfused vessels and necrosis further provided an insight into tumor physiology and microenvironment alterations induced by NSC-134754.

2716. **Multi-Parametric Imaging of Tumor Treatment Response to VEGF Blockade**

Benjamin A. Hoff¹, Mahaveer S. Bhojani², Alnawaz Rehemtulla², Brian D. Ross¹, Craig J. Galban¹
¹Radiology, University of Michigan, Ann Arbor, MI, United States; ²Radiation Oncology, University of Michigan

This study investigates permeability and diffusion-weighted imaging as surrogate biomarkers of tumor response to anti-angiogenic therapy. Vascular permeability, and plasma volume fractions and apparent diffusion coefficient (ADC) maps were acquired pre and post treatment initiation of VEGF-Trap, an anti-angiogenic agent, or vehicle in a rodent glioma model. Permeability parameters dropped significantly following treatment, whereas ADC, an indirect measure of cellularity, remained unchanged. Confirmed by histology, tumor cellularity were consistent between groups, whereas, vascular disruption was visible in treated animals resulting in a drop in cell proliferation as determined by ki-67.

2717. **Apparent Diffusion Coefficient as an Early Quantitative Biomarker of Radiation Response in Prostate Cancer**

Warren Foltz¹, Andy Wu¹, Masoom Haider²/³, Peter Chung¹, Andrew Bayley¹, Charles Catton¹, Cynthia Ménard¹
¹Radiation Medicine Program, Princess Margaret Hospital, Toronto, Ontario, Canada; ²Medical Imaging, University Health Network, Toronto, Ontario, Canada; ³Medical Imaging, University of Toronto

Apparent diffusion coefficient (ADC) increases with cytotoxic interventions, and may provide an early response biomarker for prostate radiotherapy. This study evaluated prostate zonal and tumor ADC using clinically normal and high b-values in low/intermediate risk patients at baseline and at 2-week intervals throughout their 8-week radiation treatment. Central gland ADC elevated modestly but significantly throughout treatment, while uninvolved peripheral zone ADC trended towards a late reduction. Tumor ADC was elevated in all follow-ups scans, to 15% at week 8. SNR analysis at each b-value identified the minimum region volume for noise-insensitive measurements, to guide protocol design for future voxel-based assessment.

2718. **Serial R₂* MRI to Evaluate Response to Tumour Vascular Disruptive Treatment in a Clinical Phase I Trial**

Martin Zweifel¹, Daniel Patterson¹, N.J. Taylor², J.J. Stirling², David J. Collins¹, James A. d’Arcy³, Martin O. Leach¹, Gordon J. Rustin¹, Anwar R. Padhani³
¹Medical Oncology, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN, United Kingdom; ²Paul Strickland Scanner Centre, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN, United Kingdom; ³CRUK-EPSRC Cancer Imaging Centre, Institute of Cancer Research & Royal Marsden Hospital, Sutton, Surrey, SM2 5PT, United Kingdom

This is a report of the first, in man study of serial BOLD MRI after a vascular disruptive agent in a translational phase I clinical trial of OXi4503. Changes observed in R₂* were used to define onset of VDA activity and results are compared to DCE-MRI changes at 4 hours. R₂* showed significant VDA within the 1st few hours. Both R₂* and DCE-MRI show positive dose-response relationships. If both R₂* and DCE-MRI parameters are used to assess OXi4503 activity (by significant increases in R₂* and decreases in Ktrans/IAUGC60), then 52% of lesions show MRI changes consistent with VDA effect.

2719. **Comparison of Diffusion and DCE-MRI as Markers for Response to Therapy in HCC Patients**

Edward Andrew Ashton¹, Renuka Iyer²
¹R&D, VirtualScopics, Inc., Rochester, NY, United States; ²Oncology, Roswell Park Cancer Center, Buffalo, NY, United States

This study assessed ADC measurement as a marker for response in oncology trials. An evaluation of variability in ADC in liver tissue was carried out using twelve volunteers. Results showed that ADC can be measured in liver with CoV < 10%. Subsequently, ADC changes from baseline were measured in HCC patients after therapy with an anti-angiogenic agent and/or chemoembolization. Ktrans measurements were also obtained for these patients using DCE-MRI, which is known to be a good marker for changes associated with these therapies. Results show that changes in Ktrans are highly correlated with changes ADC.
When performing dynamic contrast enhanced MRI (DCE-MRI) in the dose-ranging setting, correlating the readout to individual pharmacokinetic (PK) parameters is more informative than relating to dose alone. In a study of the VEGF receptor inhibitor pazopanib in hepatocellular carcinoma (HCC), relationships between image-based measures of vascular function, PK parameters, and clinical activity were observed.

Comparison of Tracer Kinetic Models with DCE-MRI to Evaluate a Phase 1 Anti-Angiogenic Trial
Choon Hua Thng1, Tong San Koh2, Septian Hartono1, Bee Choo Tai1, Puor Sherng Lee1, Helmut Rumpel1, Ai Bee Ong3, Norita Sukri5, Chiung-Ing Wong5, Ross Soo6, Albert Su Chong Low4, Boon Cher Goh5
1National Cancer Centre Singapore, Singapore, Singapore; 2Nanyang Technological University, Singapore, Singapore; 3National University of Singapore, Singapore; 4Singapore General Hospital, Singapore; 5National University Hospital, Singapore; 6Abbott Laboratories, United States

Dynamic contrast enhanced MRI (DCE-MRI) with tracer kinetic modeling has been proposed as a biomarker of angiogenesis imaging. Three tracer kinetic models were studied as methods of angiogenesis assessment: conventional compartmental (model developed by Brix et al. (1)), adiabatic approach to tissue homogeneity model developed by St. Lawrence and Lee (2), and distributed parameter model developed by Koh et al. (3). All models enable derivation of tissue microcirculatory parameters such as blood flow and capillary permeability-surface area product. We aim to examine the association between the above parameters with drug exposure and patient outcome in a Phase I anti-angiogenic trial.

Tumor Perfusion & Permeability
Hall B Tuesday 13:30-15:30

The authors present a method for determining the accuracy of locally estimated arterial input functions in DCE-MRI. Preliminary results from clinical data are presented.

A Versatile 3 T Phantom for Intravoxel-Incoherent Motion (IVIM) Sensitization of Microvascular Flow
Gene Young Cho1, Eric E. Sigmund1, Sungheon Kim1, Jens H. Jensen1, Daniel K. Sodickson1
1Center for Biomedical Imaging, Radiology, NYU School of Medicine, New York, United States

Diffusion-weighted imaging (DWI) can be sensitized to both tissue structure and microvascular flow in tumors. Capillary networks can present intravoxel-incoherent motion (IVIM), creating a pseudodiffusion coefficient that tracks microvascular flow. A versatile flow phantom was constructed for IVIM validation in a full body 3T scanner. This system allows technique optimization for ongoing IVIM-based studies of in vivo tumor pathologies. Biexponential analysis of DWI showed an increase in pseudodiffusivity with increasing flow and a decrease with increased impedance, simulating relevant microvascular processes. Spatial mapping of the IVIM coefficients showed strong contrast between pseudodiffusion and background diffusion. Future applications are discussed.

Study on Effect of Water Exchange in Dynamic Contrast Enhanced MRI and Pharmacokinetic Model Analysis
Jin Zhang1, Sungheon Kim2
1Department of Finance and Risk Engineering, Polytechnic Institute of New York University, New York, NY, United States; 2Center for Biomedical Imaging, Radiology, NYU School of Medicine, New York, NY, United States

Extracting physiologically relevant parameters from DCE-MRI data is still a challenging problem since the effect of contrast agent is indirectly measured in proton MRI. The purpose of the current study was to use a numerical simulation method to generate DCE-MRI data with water exchange effect and to investigate its effects on the pharmacokinetic model parameters. Realistic MRI data were simulated using the BTEX model and a three-site two-exchange model. Two conventional pharmacokinetic models were fitted to the
Dynamic contrast-enhanced magnetic resonance imaging with intravenous Gd-DTPA or Gadomer was used to monitor the selective increase of blood-brain barrier permeability (BBB) at the tumor of glioma-bearing rats, induced by either the natural kinin B1 receptor (B1R) agonist LDBK, or NG29, a synthetic high-affinity agonist. Post-contrast images revealed that only NG29 modulates topographic uptake profiles of both contrast agents within rat glioma and brain tissue surrounding the tumor, as observed by increase of both contrast agents distribution volume and mean Gd concentration in the implanted hemisphere. Our results confirm the use of B1R agonists to permeabilize the BBB around tumors.

Towards Robust and Automated Identification of Vascular Input Function in DCE-MRI

Kim Mouridsen1, Dominique Jennings1, Elisa Gelasca1, Elizabeth Gerstner1, Tracy Batchelor2, Gregory Sorensen2

1Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Charlestown, MA, United States; 2Stephen E. & Catherine Pappas Center for Neuro-Oncology, Massachusetts General Hospital, Boston, MA, United States

Dynamic contrast enhanced MRI (DCE-MRI) holds potential for characterizing key physiological markers of tumor vascularity such as blood brain-barrier-permeability. Reproducibility of pharmacokinetic parameters in multicenter settings is contingent on reliable characterization of the vascular input function (VIF). This is compromised by signal attenuating T2* effects at high concentrations and insensitivity of typical T1-weighted sequences at peak bolus passage, as well as non-reproducible manual identification of VIFs. We demonstrate that a completely automatic VIF identification procedure combined with T2* based estimation of peak concentration yields VIF reproducibility comparable to expert manual selection in two pre-treatment baseline scans of 10 glioblastoma patients.

MRI T2* and T1 Ratio for Assessment of Transport of Macromolecular Contrast Agent in Tumor Interstitium

Ramesh Paudyal1, Hassan Bagher-Ebadian1,2, Swayamprava Panda1, Joseph D. Fenstemacher1, James R. Ewing1,2

1Neurology, Henry Ford Hospital, Detroit, MI, United States; 2Physics, Oakland University, Rochester, MI, United States

Contrast-enhanced (CE-MRI) utilizes T1 and T2* contrast mechanism and paramagnetic labeled contrast agents (CAs) to characterize the resultant kinetic parameters of cerebral tissue. In this study, the dynamic maps of the ratio of T2* and T1, i.e. \( A_2 \), are employed to track the movement of the macromolecular CAs in tumors interstitium. The velocity wave fronts show the redistribution of CAs after extravasation in interstitium which allows monitoring the delivery of the chemotherapeutic agent in tissue.

Using DCE-MRI Model Selection to Investigate the Disrupted Microvascular Characteristics of Tumour-Bearing Livers

Anita Banerji1,2, Josephine H. Naish1,2, Yvon Watson1,2, Giovanni A. Buonaccorsi1,2, Geoff J. Parker1,2

1Imaging Sciences and Biomedical Engineering, School of Cancer and Imaging Sciences, The University of Manchester, Manchester, United Kingdom; 2Biomedical Imaging Institute, Manchester, United Kingdom

Healthy liver tissue has highly leaky sinusoids, a dual blood supply and can be characterised using the one-compartment dual-input Materne model, whereas the two-compartment single-input extended Kety model is often used to describe tumours that contain capillaries and have an arterial supply. We use the Akaike model selection criterion applied to dynamic contrast-enhanced MR data of liver tumours. We demonstrate that the extended Kety model is preferred within the tumour with a trend towards the Materne model within non-tumour liver tissue. This has implications for the identification of tumours in the liver and for partial volume errors.

A Semi-Automated Method for Obtaining the Arterial Input Function in Dynamic Breast Data

Xia Li1,2, E. Brian Welch1, A. Bapsi Chakravarthy1, Ingrid Mayer3, Mark Kelley2, Ingrid Meszoly7, Julie Means-Powell9, John C. Gore2,3, Thomas E. Yankeelov1,2

1Radiology and Radiological Sciences, Vanderbilt University, Nashville, TN, United States; 2Institute of Imaging Science, Nashville, TN, United States; 3Philips Healthcare, Nashville, TN, United States; 4Radiation Oncology, Vanderbilt University; 5Medical Oncology, Vanderbilt University; 6Surgical Oncology, Vanderbilt University; 7Radiology, Vanderbilt University; 8Radiology and Radiological Sciences, Vanderbilt University, Nashville, TN, United States

Quantitative analysis of dynamic contrast enhanced MRI (DCE-MRI) data requires the accurate determination of the time rate of change of the concentration of contrast agent, \( C_p \), in the blood pool; what is typically referred to as the arterial input function, or AIF.
Dynamic contrast enhanced MRI requires an estimate or measurement of the arterial input function (AIF) to model pharmacokinetic behaviour. To reduce the variability in a measured AIF, a population AIF is often used. Alternatively it is possible to obtain an AIF from local tissue. Pharmacokinetic models driven by AIFs extracted from the prostate tissue were compared to a population AIF for 12 prostate cancer patients. Tissue estimated AIFs were found to out perform the population AIF in terms of fitting residuals and variability in KTrans estimates. The results show tissue estimated AIFs can be used to improve DCE-MRI model fitting.

**2731. Identification of Hypoxic Regions In Vivo in the Prostate**

Radka Stoyanova¹, Ellen Ackerstaff¹, HyungJoon Cho², Jason A. Koutcher², Alan Pollack³

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We present an application of Pattern Recognition techniques to identify the characteristic temporal pattern of hypoxia in Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI). The approach is confirmed in DCE-MRI data from an animal model, acquired concurrently with several complementary imaging modalities including pimonidazole staining. The technique is also applied to DCE-MRI data from the tumor of a prostate cancer patient where a similar temporal pattern is uncovered in parts of the tumor. Our results suggest that by applying this approach we can potentially deconvolve the hypoxic temporal pattern in in vivo data from patients with prostate cancer.

**2732. Assessment of Tumor Hypoxia with DCE-MRI: A Preclinical Study on Human Melanoma Tumor Lines**

Tormod André Mjelde Egeland¹, Jon-Vidar Gaustad¹, Berit S. Mathiesen¹, Einar Kåre Rofstad¹

¹Department of Radiation Biology, The Norwegian Radium Hospital, Oslo, Norway

Purpose: To study the potential usefulness of DCE-MRI for assessing the extent of tumor hypoxia. Methods: Gd-DTPA-based DCE-MRI was performed on human melanoma xenografts from 8 different tumor lines grown orthotopically in mice. \( v_e \) and \( K^{trans} \) from Tofts model were obtained on a voxel-by-voxel-basis, and compared with the radiobiologically hypoxic fraction (HFrad). Results: A strong linear correlation between \( v_e \) and HFrad \((p<0.002 \text{ for all quartiles})\) and a non-linear relationship between \( K^{trans} \) and HFrad was found. Conclusions: This study suggests that it may be possible to obtain information on tumor oxygenation in patients from DCE-MRI studies.

**2733. Volume Transfer Constants Spatial Distribution Across Breast Tumors: Evidence of Interstitial Fluid Pressure?**

Pierluigi Di Giovanni¹, Trevor Sean Ahearn¹, Scott I K Semple², Che A. Azlan³, Fiona J. Gilbert¹, Thomas W. Redpath¹

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Among the physiological features found in tumors is the increased interstitial fluid pressure (IFP). Dynamic contrast enhanced MRI (DCE-MRI) can be used to generate a parametric map of the volume transfer constant going from the intravascular space into the lesion interstitial space \((K^{trans})\) and in opposite direction \((K^{out})\). We have studied the spatial distribution of the ratio \(K^{trans}/K^{out}\) in breast cancers. Our parametric maps reveal that those tumors having a central non-enhancing region show a very similar pattern in the imbalance between the two transfer constants. We argue that what we observe is linked to the spatial distribution of IFP.

**2734. A Comparison Between Individual and Population Based Arterial Input Functions in the Analysis of DCE-MRI Breast Cancer Data**

Xia Li¹, E. Brian Welch¹, A. Bapts Chakravarthy¹, Lei Xu¹, Mary Loveless¹, Ingrid Mayer¹, Mark Kelley¹, Ingrid Meszoley¹, Julie Means-Powell¹, John C. Gore¹, Thomas E. Yancelev¹

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The accurate determination of the arterial input function, or AIF, plays an important role to quantitative analysis of dynamic contrast enhanced MRI (DCE-MRI) data. We have proposed (in a separate abstract) a simple and efficient method to obtain the AIF, through tracking an initial seed point placed within the axillary artery. Using this method, we obtain the AIF for each individual patient.
(AIFind) and the population averaged AIF (AIFpop). We apply the AIFs to two DCE-MRI pharmacokinetic models to compare the physiological parameters.

2735. The Relationships Between ADC, $T_1$, and DCE-MRI Tracer Kinetic Parameters in Solid Ovarian Tumors

Caleb Roberts$^{1,2}$, Josephine H. Naish$^{1,2}$, Claire L. Mitchell$^{3}$, Yvonne Watson$^{1,2}$, Sue Cheung$^{1,2}$, Gio A. Buonaccorsi$^{1,2}$, Gordon C. Jayson$^{3}$, John C. Waterton$^{2,4}$, Jean Tessier$^{3}$, Geoff J. Parker$^{1,2}$

$^1$Imaging Science and Biomedical Engineering, School of Cancer and Imaging Sciences, The University of Manchester, Manchester, United Kingdom; $^2$The University of Manchester Biomedical Imaging Institute, The University of Manchester, Manchester, United Kingdom; $^3$Cancer Research UK Dept Medical Oncology, Christie Hospital and University of Manchester, Manchester, United Kingdom; $^4$AstraZeneca, Alderley Park, Macclesfield, Cheshire, United Kingdom

While there is a good understanding of microvascular function and structure described by tracer kinetic model-based analyses of dynamic contrast-enhanced (DCE)-MRI data, the interpretation of apparent water diffusion coefficient (ADC) is less clear. Besides ADC, the parameter that is most sensitive to the water distribution and geometry is $T_1$. In this study, we acquire DCE-MRI and diffusion weighted images from a group of ovarian tumors and find significant relationships between ADC, $T_1$, and $v$, that offer insight into the physiological meaning of these parameters in ovarian tumors.

2736. A Method to Estimate Sample Sizes for DCE-MRI-Based Studies of Heterogeneous Tumors

Chris James Rose$^{1,2}$, James P. O'Connor$^{1,2}$, Caleb Roberts$^{1,2}$, Gio A. Buonaccorsi$^{1,2}$, Yvonne Watson$^{1,2}$, Sue Cheung$^{1,2}$, Gordon Jayson$^{3}$, Geoff J. Parker$^{1,2}$

$^1$Imaging Science and Biomedical Engineering, The University of Manchester, Manchester, United Kingdom; $^2$The University of Manchester Biomedical Imaging Institute, The University of Manchester, Manchester, United Kingdom; $^3$Cancer Research UK and University of Manchester Department of Medical Oncology, The Christie Hospital, Manchester, United Kingdom

DCE-MRI is of great utility for studying tumor microvasculature, particularly in early phase clinical trials. Most analysis methods assume homogeneous tumors, which is often incorrect and a problem when planning trials, because the magnitude of effect observed using DCE-MRI will be attenuated, for example, by contributions from necrotic tissue. By simulating maps of $K^{trans}$ using a model of tumor heterogeneity, we present a method to estimate the distribution of required sample size. We illustrate the method’s application using data from a trial of bevacizumab in CRC metastases and show that by considering heterogeneity, more powerful studies can be planned.

2737. Simultaneous Vessel Size and Blood Volume Measurement in a Human Tumor Outside the Brain

Stefanie Remmele$^1$, Janine Ring$^2$, Julien Sénégas$^1$, Walter Heindel$^2$, Wolfgang E. Berdel$^1$, Christoph Bremer$^4$, Thorsten Persigehl$^2$

$^1$Philips Research Europe, Hamburg, Germany; $^2$Department of Radiology, University of Muenster, Muenster, Germany; $^3$Department of Oncology, University of Muenster, Muenster, Germany; $^4$Department of Radiology, Franziskus Hospital, Muenster, Germany

This work presents results from the first simultaneous steady-state blood volume and vessel size measurement in a human tumor outside the brain (phleomorphic sarcoma in the pubic bone). Images were free of artifacts, sequence timing allowed for appropriate coverage of the signal decays pre and post injection and the dR2*/dR2 values of the tumor were sufficiently high to generate robust physiologic maps, which appeared to be independent from contrast agent washout.

2738. Population-Generalized Vs. Individual-Specific AIF in Human Prostate DCE-MRI

Pharmacokinetic Analysis

Ian Tagge$^1$, Ryan A. Priest$^2$, Tomasz M. Beer$^{3,4}$, Mark G. Garzotto$^{5,6}$, William J. Woodward$^1$, Wei Huang$^1$, Charles S. Springer, Jr.$^{1,4}$, Xin Li$^1$

$^1$Advanced Imaging Research Center, Oregon Health & Science University, Portland, OR, United States; $^2$Radiology, Oregon Health & Science University, Portland, OR, United States; $^3$Hematology/Oncology, Oregon Health & Science University, Portland, OR, United States; $^4$Knight Cancer Institute, Oregon Health & Science University, Portland, OR, United States; $^5$Urology, Oregon Health & Science University, Portland, OR, United States; $^6$Portland VA Medical Center, Portland, OR, United States

Dynamic-contrast-enhanced magnetic resonance imaging (DCE-MRI) has shown promise in diagnostic medicine, particularly as applied to breast cancer screening. Pharmacokinetic parameter determination relies on arterial input function (AIF) validity. However, reliable AIFs are not easily obtained and often cannot be. Thus, it is often necessary to rely on an averaged, population AIF. The latter is also desired for data post processing simplification. Here, the standard model (SM) and first generation “shutter-speed” model (SSM) are used to assess the impact of a generic AIF on the pharmacokinetic parameter Ktrans (volume contrast reagent (CR) transfer constant) estimation in human prostate studies.
Measurement of pharmacokinetic parameters in small animal models of cancer is a frequently-used tool in preclinical investigations of novel interventions. One source of uncertainty from these measurements arises from the challenges of quantifying the concentration time course of a contrast agent in blood. We have proposed performing this measurement in the heart, which allows reduced-artifact high temporal resolution sampling. A pilot study was performed in a thyroid tumor model comparing the inter-subject variation produced by cardiac sampling with conventional sampling in a local blood vessel, and found a large reduction in variation with the proposed approach.

**Perfusion Permeability Methodology**

**Hall B Wednesday 13:30-15:30**

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**Parameter Optimization and Demonstration of Simultaneous Time Resolved Angiography and Perfusion Measurement in the Lower Extremities at Rest and with Exercise**

**Katherine E. Wright**, **Nicole Seiberlich**, **Stephen R. Yutzy**, **Raymond F. Muzic**, **Mark A. Griswold**, **Vikas Gulani**

1Department of Biomedical Engineering, Case Western Reserve University, Cleveland, OH, United States; 2Department of Radiology, Case Western Reserve University/University Hospitals, Cleveland, OH, United States

In this work, Time resolved angiography With Stochastic Trajectories (TWIST) accelerated with parallel imaging, partial Fourier acquisition and view sharing, was used to obtain simultaneous angiography and dynamic contrast enhanced (DCE) perfusion measurements in muscle with a single contrast dose. Parameter optimization was performed to select combinations of undersampling schemes that provided the best temporal resolution while still limiting artifact power and error in perfusion measurements. The results were used to obtain MRA and perfusion exams on volunteer lower extremities during rest and exercise, demonstrating the ability of the technique to measure physiological perfusion changes.

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**W. CBF But Not QOEF Is Affected by HIV Using QBOLD**

Withdrawn by Author

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**Simultaneous Characterization of the Tumor Vascular Permeability, Vessel Size and Density by Using First-Pass Function/Structure MR Imaging**

**Chia-Ming Shih**, **Chien-Yuan Lin**, **Chih-Yuan Chen**, **Tai-Wei Chou**, **Sui-Shan Lin**, **Cheng-Hung Chou**, **Yen-Yu Shih**, **Jyh-Horng Chen**, **Chen Chang**

1Institute of Biomedical Electronics and Bioinformatics, National Taiwan University, Taipei, Taiwan; 2Institute of Biomedical Science, Academia Sinica, Taipei, Taiwan

Two different contrast agents with different approaches were needed for assessing the vascular permeability and structure including vessel size and vessel density. In the present study, First-Pass Function/Structure MR Imaging (First Pass F/S MRI) technique was proposed to simultaneously evaluate vascular function and structure. The proposed technique can reduce scan time and assess the correlation between functional and structural changes in brain tumor.

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**In Vitro Validation of Permeability-Surface Area Product Derived by Distributed Parameter Model with DCE-MRI**

**Septian Hartono**, **Choon Hua Thng**, **Tong San Koh**, **Puor Sherng Lee**, **Fang Keang Lim**, **Theng Boon Lee**, **Helmut Rumpel**, **Quan Sing Ng**

1National Cancer Centre Singapore, Singapore, Singapore; 2Nanyang Technological University, Singapore, Singapore; 3Singapore General Hospital, Singapore

Hollow Fiber Bioreactors (HFBs), typically used for cell culture, mimicks well the human capillary system and thus is ideal to be used to validate the microcirculatory parameters obtained by tracer kinetic modeling. The aim of this study is to validate the permeability-surface area product (PS) obtained by tracer kinetic models with DCE-MRI in a HFB. Linear relationship was found between PS derived from the tracer kinetic models and pore size area of the HFBs.
Preexchange lifetimes of intracellular water (τ in) are of fundamental significance to many experimental and theoretical studies, especially for modeling water behavior in tissue. Many methodologies have been developed to obtain this value for various cell types. Herein, we employed the method of perfusion of microbead-adherent cells, which allowed τ in measurement by highly effective suppression of the extracellular water MR signal and thus selective and direct observation of the intracellular water MR signals. Histologic evaluation confirmed that neurons and astrocytes grown on microbeads maintain key morphologic features. We found that τ in’s for neurons and astrocytes are similar.

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**2745. Quantitative Dynamic 19F MRI Oximetry in a Phantom Simulating Hypoxia**

Steven H. Baete, Yves De Deene

1Laboratory for Quantitative Nuclear Magnetic Resonance in Medicine and Biology, ECNURAD, Ghent University, Gent, Belgium; 2MEDI-SIP-IBBT, Ghent University, Gent, Belgium

Tumor hypoxia is well known to reduce cancer treatment efficacy. Fluor-19 MRI oximetry can be used to map oxygen concentrations in hypoxic tissue. In this study a reproducible phantom which mimics oxygen consuming tissue is used for quantitative dynamic fluor-19 MRI oximetry. The phantom consists of a hemodialysis filter of which the outer compartment is filled with a gelatin matrix containing viable yeast cells and perfluorocarbon vesicles which simulate the absorption of perfluorocarbons from intravenous emulsions in tissue. The phantom can be used for hypoxia simulations and for validating computational biophysical models of hypoxia, as measured with fluor-19 MRI oximetry.

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**2746. Detection of Skeletal Muscle Perfusion Differences with DCE-MRI: Contrast Agent and Pharmacokinetic Model**

Karolien Jaspers, Tim Leiner, Petra Dijkstra, Marlies Oostendorp, Jolanda MCG van Golde, Mark J. Post, Walter H. Backes

1Cardiovascular Research Institute Maastricht, Maastricht, Netherlands; 2Radiology, Maastricht University Medical Centre, Maastricht, Netherlands; 3Central Animal Facilities, Maastricht University, Maastricht, Netherlands; 4Internal Medicine, Maastricht University Medical Centre, Maastricht, Netherlands; 5Physiology, Maastricht University, Maastricht, Netherlands

Adequate introduction of therapeutic neovascularization in patients with peripheral arterial disease requires functional monitoring of vascular responses. The potential of the medium-sized contrast agent Gadomer for detecting (patho-)physiological perfusion differences with DCE-MRI was tested in a rabbit hind limb ischemia model. The lower extravasation rate of Gadomer requires a pharmacokinetic model that includes the blood plasma fraction vp rather than a model that accounts for reflux. Gadomer proved equally successful as Gd-DTPA in detecting flow differences between red (soleus) and white (tibialis) muscle, and between ischemic and normal soleus muscle tissue, while facilitating better image quality.

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**2747. Hybrid Reference Tissue Calibrated Dual-Bolus 3D Quantitative Dynamic Contrast-Enhanced MRI in a Rabbit VX2 Tumor Model**

Alexander Yowei Sheu, Dingxin Wang, Johnathan Chung, Robert K. Ryu, Reed A. Omary, Debiao Li, Andrew C. Larson

1Departments of Radiology and Biomedical Engineering, Northwestern University, Chicago, IL, United States; 2Department of Radiology, Northwestern University, Chicago, IL, United States; 3Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL, United States

Quantitative DCE-MRI can be used to measure pharmacokinetic parameters (Ktrans, ve, and vp) that indicate tumor angiogenesis and perfusion. The purpose of this study was to develop an innovative hybrid reference tissue calibrated dual-bolus 3D quantitative DCE-MRI method. Tissue contrast enhancement was quantified using 3D GRE DCE-MRI during first-bolus, AIF was monitored using 2D SR GRE DCE-MRI during second-bolus, and reference tissue (back muscle) was used to provide the final calibration. Our results support the use of quantitative DCE-MRI to differentiate hypervascular tumor tissue from the necrotic core, providing valuable diagnostic information about the stage and segmentation of a tumor.

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**2748. Phase Contrast Velocity Imaging Using Compressed Sensing**

Daniel J. Holland, Dmitry M. Maliourov, Andrew Blake, Lynn F. Gladden, Andrew J. Sederman

1Department of Chemical Engineering and Biotechnology, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom; 2Microsoft Research Cambridge, Cambridge, United Kingdom

This work describes a method for accelerating the acquisition of phase-encoded velocity images using compressed sensing. Results are shown for both experimental and simulated measurements of liquid and gas flow through a model porous material. Using this approach, acceleration factors for Cartesian data of between 2 and 5 are achieved with minimal reconstruction error. By combining this reconstruction algorithm with a variable density spiral acquisition, a full order of magnitude decrease in imaging time is achieved. This approach is applicable to MR angiography and perfusion studies in clinical MRI and to other phase imaging techniques.
Intravoxel Incoherent Motion (IVIM) Imaging at Different Field Strengths – What Is Feasible?
Anna Rydhög1, Matthias J. P. van Osch2, Markus Nilsson1, Jimmy Lätt1, Freddy Stålhberg1,4, Ronnie Wiresam1, Linda Knutsson1
1Department of Medical Radiation Physics, Lund University, Lund, Sweden; 2Department of Radiology, LUMC, Leiden, Netherlands; 3Department of Image and function, University Hospital Lund, Lund, Sweden; 4Department of Diagnostic Radiology, Lund University, Lund, Sweden

Intravoxel Incoherent Motion (IVIM) is a non-invasive method which has the potential to quantify perfusion parameters such as CBV and CBF from signal-versus-b data. Simulations was performed using synthetics voxel consisting of four different compartments (tissue, CSF, arterial and venous blood) for comparison of the expected signal curves at three field strength (1.5, 3 and 7 T). Confirmation of the simulated results was obtained from in vivo measurements on a volunteer. We conclude that for higher field strengths the relative contribution from venous blood decreases suggesting that IVIM at 7 T would primarily reflect arterial blood volume.

The Detection of Tumor Sub-Regions Based on $T_1$ and ADC Clustering
Caleb Roberts1,2, Chris Rose3, Josephine H. Naish1,2, Yvonne Watson1,2, Sue Cheung1,2, Gio A. Buonaccorsi1,2, Gordon C. Jayson1, John C. Waterton2,4, Jean Tessier4, Geoff J. Parker1,2
1Imaging Science and Biomedical Engineering, School of Cancer and Imaging Sciences, The University of Manchester, Manchester, United Kingdom; 2The University of Manchester Biomedical Imaging Institute, The University of Manchester, Manchester, United Kingdom; 3Cancer Research UK Dept Medical Oncology, Christie Hospital and University of Manchester, Manchester, United Kingdom; 4AstraZeneca, Alderley Park, Macclesfield, Cheshire, United Kingdom

Tracer kinetic model-based analyses of dynamic contrast-enhanced (DCE)-MRI data typically report summary statistics that treat tumors as being homogeneous. However, since anti-angiogenic therapies often preferentially affect certain parts of heterogeneous tumors there is interest in the development of methods to provide insight into regional changes. We present a method that uses $k$-means clustering of $T_1$ and the apparent water diffusion coefficient (ADC) measured in a group of ovarian tumors to sub-divide tumors into distinct regions and demonstrate that differences in tracer kinetic parameters exist between these regions and the overall tumor median statistic.

Maximizing Accuracy and Precision on Pharmacokinetic Parameter Estimates in DCE-MRI: What Is the Optimal Flip Angle?
Olivier Maciej Girard1, Paul O. Scheibe2, David R. Vera1, Robert F. Mattrey1
1Department of Radiology, University of California, San Diego, CA, United States; 2Ixzar, Inc., Arroyo Grande, CA, United States

Dynamic Contrast Enhanced (DCE) MRI is a promising tool to investigate microvascular tissue properties. Although it has been applied in various clinical studies its accuracy still remains subject to debate since numerous errors may bias the pharmacokinetic (PK) parameter estimates. Here we propose to study the propagation of measurement noise and flip angle (FA) uncertainty up to the parameter accuracy for the AATH model, which allows separate measurements of flow and permeability. This simulation study investigated parameter accuracy for the AATH model, which allows separate measurements of flow and permeability. The influence of three key factors was assessed: temporal resolution, signal to noise ratio and error in the AIF peak height measurement. Results showed that a high temporal resolution is the most critical factor in ensuring parameter accuracy but this requirement can be relaxed if larger biases can be permitted and T2 need not be accurately measured. An error of 10 % in the measurement of the AIF peak height resulted in an error of at most 10 % in each parameter.

A General Dual-Bolus Approach for High Resolution Quantitative DCE-MRI
Lucy Elizabeth Kershaw1, Marine Beaumont1, Hai-Ling Margaret Cheng2
1The Research Institute and Diagnostic Imaging, The Hospital for Sick Children, Toronto, Ontario, Canada; 2Department of Medical Biophysics, The University of Toronto, Toronto, Ontario, Canada

This study presents a dual-bolus technique to measure the arterial input function (AIF) for DCE-MRI. A low-dose prebolus was used to estimate the AIF for a tissue uptake curve measured from a second high-dose injection. AIFs were measured in the rabbit aorta using a high temporal resolution TRICKS acquisition. The scaled prebolus AIF was shown to match the main bolus AIF closely. Measurement of the AIF in a separate acquisition allows the tissue of interest to be imaged at high spatial resolution in a DCE-MRI experiment.
2754. Scope and Interpretation of the Modified Tofts Model

Steven Sourbron1
1Ludwig-Maximilian-University Munich, Munich, Bavaria, Germany

We present a theoretical analysis which shows that the modified Tofts model only applies to tissues that are weakly vascularized and permeability-limited. In other regimes, a model of exactly the same form applies, but the parameter typically interpreted as plasma volume has a mixed interpretation. Hence, if a modified Tofts model is found to describe the data well, none of the physical parameters are measurable without further assumptions on the state of the tissue. These ambiguities can only be resolved by sampling the data fast and precisely enough, so that the complete two-compartment exchange model can be fitted.

2755. Improved Correlation to Quantitative DCE-MRI Pharmacokinetic Parameters

Using a Modified Initial Area Under the Uptake Curve (MIAUC) Approach

Hai-Ling Margaret Cheng1,2
1Research Institute & Diagnostic Imaging, The Hospital for Sick Children, Toronto, Ontario, Canada; 2Medical Biophysics, University of Toronto, Toronto, Ontario, Canada

Non-model DCE-MRI parameters such as the initial area under the uptake curve (IAUC) do not require arterial input function (AIF) measurement or model-fitting, and can hence be more robust than pharmacokinetic modeling. However, the IAUC is intractably correlated with biological parameters such as the transfer constant Ktrans and interstitial space ve. Herein, a modified IAUC (mIAUC) method is presented. The mIAUC parameters are strongly correlated with true Ktrans and ve, and are outperformed by pharmacokinetic parameters only when a rapidly sampled AIF is used. The proposed mIAUC method retains advantages of non-model DCE-MRI while providing stronger correlation with underlying physiology.

Cancer: Cells Biopsies & Biofluids

Hall B Thursday 13:30-15:30

2756. MEK1/2 Signalling Inhibition in Human Melanoma Cells Leads to Reduced Lactate Production Via Inhibition of Glucose Uptake and Lactate Dehydrogenase Activity

Maria Falck Miniotis1, Thomas R. Eykyn1, Paul Workman2, Martin O. Leach1, Mountia Beloueche-Babari1
1CRUK and EPSRC Cancer Imaging Centre, The Institute of Cancer Research & The Royal Marsden Hospital, Sutton, Surrey, United Kingdom; 2CRUK Centre for Cancer Therapeutics, The Institute of Cancer Research & The Royal Marsden Hospital, Sutton, Surrey, United Kingdom

Deregulated RAS-BRAF-MEK1/2-ERK1/2 signalling is frequently observed in cancer and considerable effort is focused towards developing MEK1/2-targeted therapy. We previously reported that MEK1/2 inhibition causes a reduction in 1H MRS-detectable lactate in human cancer cells. Here we analyse the time-course of the response and investigate the mechanism behind this effect by assessing glucose uptake and lactate dehydrogenase (LDH) activity. We demonstrate that MEK1/2 inhibition leads to decreased lactate production through down-regulation of both glucose uptake and LDH activity. These results show lactate as a potential non-invasive MRS biomarker of response to MEK1/2-targeted therapeutics.

2757. Metabolic Consequences of Perifosine Treatment

Judy S. Hwang1, Sabrina M. Ronen1
1Radiology and Biomedical Imaging, University of California, San Francisco, San Francisco, CA, United States

Perifosine is a novel anticancer alkylphospholipid that is in clinical trials for treatment of cancer. This study investigates the changes in choline metabolism of MCF-7 human breast cancer cells modulated by perifosine treatment. Cells were incubated with 13C labeled choline and 1H, 13C, and 31P MR spectra of cell extracts were recorded. The overall inhibition of phosphatidylcholine synthesis via the Kennedy pathway was observed upon treatment. The accumulation of perifosine was also detected in the cell membrane. The observed changes in choline metabolism upon perifosine treatment could reflect its mechanism of action or its effect on PI3K signaling.

2758. Changes in Choline Metabolism as Potential Biomarkers of HSP90 Inhibition in NEU/HER2-Driven Mammary Carcinoma Oncomouse® Cells

Nada M.S. Al-Saffar1, Laura L. Jackson1, Swee Sharp2, Loreta Rodrigues3, John R. Griffiths1, Paul Workman2, Martin O. Leach1
1CR-UK and EPSRC Cancer Imaging Centre, Institute of Cancer Research, Sutton, Surrey, United Kingdom; 2CR-UK Centre for Cancer Therapeutics, Institute of Cancer Research, Sutton, Surrey, United Kingdom; 3CR-UK Cambridge Research Institute, Cambridge, United Kingdom

17-AAG is a novel anticancer drug that inhibits heat shock protein 90 (HSP90) leading to combinatorial degradation of many oncogenic client proteins including NEU/HER2 and its downstream proteins, which have key roles in cell growth and survival. NEU/HER2 is overexpressed in 25% of human breast cancers. In this study, we have used 1H and 31P-MRS to establish biomarkers for HSP90 inhibition in cells isolated from a NEU/HER2-driven mammary carcinoma Oncomouse®. We report a 2-fold increase in choline-containing metabolites which was associated with a decrease in NEU/HER2 expression. Hence these MRS changes could serve as biomarkers for HSP90 inhibition in cells/tumors driven by NEU/HER2.

Hitoshi Kubo\(^1\), Masafumi Harada\(^1\), Takamasa Abe\(^2\), Hiroshi Maezawa\(^3\), Hiromu Nishitani\(^4\)

\(^1\)Department of Medical Imaging, University of Tokushima, Tokushima, Japan; \(^2\)SBD/MR Division, Oxford Instruments KK., Tokyo, Japan; \(^3\)Department of Radiation Physics, Engineering and Biology, University of Tokushima, Tokushima, Japan; \(^4\)Department of Radiology, University of Tokushima, Tokushima, Japan

The early metabolic response of pyruvate and lactate induced by 5-fluorouracil (5FU) on mouse mammary cancer cells under normal and fasting conditions was evaluated by NMR measurement using hyperpolarized 1-13C-pyruvate and absorption spectroscopy. This study measured four combinations of nutritional status and treatment with 5FU. The rate constant of pyruvate-lactate metabolism was changed by the nutritional conditions without and with 5FU treatment. The results suggested that this technique allows the detection of the early metabolic response induced by an anticancer agent.

2760. Metabolic Changes in Luminal-Like Orthotopic Breast Cancer Xenografts Following Estrogen Supplement Withdrawal

Siver Andreas Moestue\(^1\), Vickie Yi Zhang\(^2\), Else Marie Huuse\(^3\), Beathe Sitter\(^4\), Gunhild Mari Melandsmo\(^5\), Olav Engebretsen\(^6\), Ingrid Susann Gribbestad\(^7\)

\(^1\)Department of Circulation and Medical Imaging, Norwegian University of Science and Technology, Trondheim, Norway; \(^2\)Department of Radiology and Biomedical Imaging, UCSF, San Francisco, United States; \(^3\)Department of Tumor Biology, Institute for Cancer Research, Oslo, Norway

An estrogen-dependent luminal-like breast cancer xenograft model was used to study choline metabolites after endocrine therapy using HR MAS MRS. The data suggested that choline metabolite concentrations do not change following endocrine therapy whereas taurine and lactate do change.

2761. Myc Regulates a Transcriptional Program That Stimulates Glutaminolysis

David R. Wise\(^1\), Anthony Mancuso, Ralph Deberardinis\(^2\), Sayed Nabil, Xiao-Yong Zhang\(^3\), Harla K. Pfeiffer\(^4\), Ilana Nissim\(^5\), Evgueni Daikhind\(^6\), Marc Yudkoff\(^7\), Steven B. McMahon\(^1\), Craig B. Thompson

\(^1\)Cancer Biology, University of Pennsylvania, Philadelphia, PA, United States; \(^2\)University of Texas South Western Medical Center; \(^3\)Thomas Jefferson Medical College; \(^4\)Children's Hospital of Philadelphia

High levels of both glucose and glutamine consumption are required for rapid proliferation of most cancer cells. In this work, the role of myc in regulating the transcriptional control of glutaminolysis was examined. Two different models were used: immortalized mouse embryo fibroblasts (MEF) with inducible myc activity and human glioma cells with naturally high myc levels that were knocked down with short-hairpin RNA. Elevated myc activity was associated with increased glutamine transport, glutaminase activity and lactate dehydrogenase activity as demonstrated by PCR. It was also associated with increased overall glutimolytic flux as evidenced by \(^1\)C NMR.

2762. MR Determined Metabolites May Serve as Prognostic Factors in Breast Cancer

Tone Frost Batten\(^1\), Beathe Sitter\(^2\), Guro F. Giskeodegård\(^3\), Lutgarde Buydens\(^4\), Geert Postma\(^5\), Hans Fjosne\(^6\), Steinar Lundgren\(^7\), Ingrid S. Gribbestad\(^8\)

\(^1\)Dept. of Circulation and Medical Imaging, NTNU, Trondheim, Norway; \(^2\)Dept. of Analytical Chemistry, Radboud University Nijmegen, Nijmegen, Netherlands; \(^3\)Dept. of Surgery, St. Olavs University Hospital, Trondheim, Norway; \(^4\)Dept. of Oncology, St.Olavs University Hospital, Trondheim, Norway

The purpose of the current study was to define new prognostic factors for breast cancer based on HR MAS MRS. Proton MR spin echo spectra were acquired from excised breast cancer tissue. 5-years follow-up data were available for all included patients. The spectra were analysed with PCA. Using ROC and Kaplan-Meyer survival analysis of score values, two groups with significant different cumulative survival were defined. Higher levels of glycerophosphocholine, betaine and creatine, and lower levels of lactate and glycine were associated to good prognosis. A combination of MR determined metabolites may serve as an additional prognostic factor in breast cancer.

2763. \(^{31}\)P NMR of Phospholipid Metabolites in Prostate Cancer and Benign Prostatic Hyperplasia

Richard A. Komoroski\(^1\), John C. Holder\(^2\), Alex A. Pappas\(^2\), Alex E. Finkbeiner\(^2\), Sadhna Verma\(^3\)

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Although \(^{31}\)P NMR is an excellent method for probing the phospholipid (PL) metabolites in prostate cancer, it has been little used recently. We report an \textit{in vitro} \(^{31}\)P NMR comparison of prostate cancer and benign prostatic hyperplasia (BPH), focusing on the levels of major PL metabolites. Unlike phosphocholine (pc) and glycerophosphocholine (gpc), phosphoethanolamine (pe) and glycerophosphoethanolamine (gpe) (and their ratio) were significantly different between cancer and BPH. The levels of pe and gpe relative to those of pc and gpc are consistent with the former being major contributors to the “total choline” resonance observed by \(^1\)H MRS \textit{in vivo}.
Detection Of Cancer In Cervical Tissue Biopsies Using Mobile Lipid Resonances Measured With Diffusion-Weighted 1H Magnetic Resonance Spectroscopy
Dominik Zietkowski1, Robert L. Davidson1, Thomas R. Eykyn1, Sonali S. De Silva1, Nandita M. deSouza1, Geoffrey S. Payne1
1CR-UK and EPSRC Cancer Imaging Centre, The Institute of Cancer Research, Sutton, Surrey, United Kingdom

An optimised diffusion-weighted stimulated echo sequence with bipolar gradients attenuated low molecular weight metabolites in cervical cancer tissue samples giving improved visibility and characterisation of mobile lipid resonances (MLR). Linear discriminant analysis (LDA) of MLR peaks almost completely separated cervical biopsies containing cancer from those that did not, reflecting underlying differences in MLR composition. Generated Receiver Operating Characteristic (ROC) curves and calculated area under the curve (0.962) validated high sensitivity and specificity of the technique.

Choline Metabolite Ratios from NMR as Markers of Human Breast Cancer
Mary C. Mahoney1, Jing Huei Lee2, Wen Jang Chu2, John M. Pearce2, Kim M. Cecil3, Stephen M. Strakowski2, Richard A. Komoroski2
1Radiology, University of Cincinnati, Cincinnati, OH, United States; 2Center for Imaging Research, University of Cincinnati, Cincinnati, OH, United States; 3Radiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, United States

In vivo 1H MRS of breast cancer lesions can detect a signal assigned to total choline (tCho), which arises from a variety of choline-containing metabolites. The contribution of each metabolite to the increased tCho peak in vivo is not known. Here we report in vitro 1H NMR spectroscopy results on fine-needle aspirate (FNA) biopsies of lesions from breast cancer patients, several of whom were also studied by in vivo MRS. Phosphocholine was usually the major metabolite, whereas the contribution of glycerophosphocholine varied substantially, and that of Cho was always minor.

Role of Choline Kinase and Phosphatidylcholine Phospholipase C in Aberrant Choline Metabolism in Human Epithelial Ovarian Cancer
Égidio Iorio1, Marina Bagnoli2, Alessandro Ricci3, Maria Elena Pisani1, Kristine Glunde4, Giancarlo Castellano5, Elisa Venturini6, Zaver M Bhujwalla7, Delia Mezzanzanica2, Silvana Canevari2, Franca Podo1
1Istituto Superiore di Sanità, Roma, Italy; 2Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; 3Johns Hopkins University School of Medicine, Baltimore, MD, United States; 4Cogentech-Consoritium for Genomic Technologies, Milano, Italy

Altered phosphatidylcholine (PC) metabolism in epithelial ovarian cancer (EOC) can provide choline-based imaging approaches as powerful tools to improve diagnosis and identify new therapeutic targets. Measurements are reported on protein expression and enzyme activation of choline kinase (ChoK) and PC-specific phospholipase C (PC-plc) in EOC cell lines compared with non-tumoral counterparts. The role of ChoK and PC-plc in the intracellular accumulation of PCho in EOC cells was investigated by RNA silencing and pharmacological inhibition respectively. Analyses are also reported on ChoK mRNA expression and on ChoK and PC-plc protein expression in a set of surgical specimens from EOC patients.

Comparison of Fatty Acid and Phosphatidylcholine Levels in Breast and Prostate Cancer Cells and Tumors
Noriko Mori1, Flonne Wides2, Tomoyo Takagi3, Kristine Glunde2, Zaver M. Bhujwalla2
1JHU ICMIC Program, The Russell H. Morgan Department of Radiology and Radiological Science, The Johns Hopkins University School of Medicine, Baltimore, MD, United States; 2JHU ICMIC Program, The Russell H. Morgan Department of Radiology and Radiological Science, The Johns Hopkins University School of Medicine, Baltimore, MD, United States

Elevated lipogenesis is a characteristic feature of cancer. Fatty acid synthase overexpression has been found in many human cancers. Both tumor cells in culture and solid tumor models are essential tools to study cancer biology. To understand the differences in lipid components between tumor cells in culture and solid tumors, we compared fatty acid and phosphatidylcholine levels with 1H MRS of lipid-soluble cell or tumor extracts derived from prostate and breast cancer cell lines. Significantly different patterns of fatty acid levels between cells in culture and in tumors, demonstrate the importance of the tumor microenvironment in lipid metabolism.

Metabolic Profile of Lipid Extracts Obtained by Astrocytic Brain Tumors
Frauke Nehen1, Wieland Willker1, Laura Columbano2, Rudolf Fahrbusch2, Dieter Leibfritz1
1Institute of Organic Chemistry, University of Bremen, Bremen, Germany; 2International Neuroscience Institute Hannover, Hannover, Germany

Lipophilic tissue extracts of astrocytic brain tumors were analyzed by 1H-NMR spectroscopy. Tumor core, tumor margin and reference tissue differ significantly with respect to their content of galactosyl cerebrosides and one unknown metabolite. Lipid separation with solid phase extraction of eight lipid extracts, enrichment by combining fractions in which the unknown metabolite was observed and analysis by various 2D-NMR methods revealed that the unknown metabolite is an isoprene derivative.
Peak Alignment of MR Spectra

Guro Fanneløb Giskeødegård¹, Tom Bloemberg², Lutgarde Buydens², Geert Postma², Ingrid Susanne Gribbestad¹, Tone Frost Bathen¹
¹Dept. of Circulation and Medical Imaging, Norwegian University of Science and Technology (NTNU), Trondheim, Norway; ²Dept. of Analytical Chemistry, Radboud University Nijmegen, Nijmegen, Netherlands

Correction of misaligned peaks is an important part of multivariate preprocessing of MR spectra. In this study, three different peak alignment algorithms were tested on HR MAS MRS data from breast cancer tissue. The datasets were used to predict the prognostic factor ER status, which is shown to be related to metabolic profile. Correlation optimized warping (COW) and peak alignment by genetic algorithm (PAGA) resulted in greatly improved PLS-DA classification of ER status compared to unaligned data. Parametric time warping (PTW) did not improve the classification error, indicating that PTW may not be as suitable for metabolomic MR data.

Magnetic Resonance Spectroscopy-Based CTP:choline-Phosphate Cytidylyltransferase Activity Measurement Technique

Christopher S. Ward¹, Sabrina M. Ronen¹
¹Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, CA, United States

CTP:choline-phosphate cytidylyltransferase (CCT) is the enzyme responsible for catalyzing the addition of CTP to phosphocholine to form CDP-choline, which is generally accepted to be the rate-limiting reaction in the formation of phosphatidylcholine. This study introduces a dynamic \(^{31}\)P MR-based means to measure the kinetics of the cytidylyltransferase-catalyzed reaction. The results suggest the potential of this technique to quantitatively assess modulations in CCT activity.

Metabolic Changes Associated with HPV Infection in Cancer Cells Observed with \(^1\)H MRS

Dominik Zietkowski¹, Geoffrey S. Payne¹, Nandita M. deSouza¹
¹CR-UK and EPSRC Cancer Imaging Centre, The Institute of Cancer Research, Sutton, Surrey, United Kingdom

This study investigates the metabolic effects of HPV infection and tests whether \(^1\)H MRS can detect these in a model consisting of isogenic HPV-16 E6 transfected derivatives of A2780 ovarian cell line (E6 is the key cancer-causing HPV protein). It was possible to observe in the HPV-E6 transfects higher cholines, lower lactate, glycine, lipids and their (poly-) unsaturation. These changes seem to be related to changes in E6 transfects proliferation. Similar changes may also apply to HPV infection in cervix and documenting these may provide insights to understand the metabolic ‘field effect’ observed around cervical tumor and into viral oncogenesis.

Detection of Apoptotic Cell Death in Vitro Using Quantitative Magnetization Transfer

Colleen Bailey¹,², Kimberly L. Desmond¹,², Gregory J. Czarnota¹,², Greg J. Stanisz¹,²
¹Sunnybrook Health Sciences Centre, Toronto, ON, Canada; ²University of Toronto, Toronto, ON, Canada

Acute myeloid leukemia cells were treated with cisplatin to induce apoptosis and spun into a cell sample for imaging. Magnetization transfer scans were performed at 427 and 243 Hz peak power, for sixteen offset frequencies logarithmically spaced from 0.12 to 200 kHz. The magnetization transfer ratio at 2320 Hz showed a statistically significant increase from 24.8% in control cells to 28.0% thirty-six hours after cisplatin treatment and 30.3% forty-eight hours after cisplatin treatment, preceding T1 changes. Quantitative fitting showed an increase macromolecular/free water proton exchange and a decrease in T2B, which characterizes the width of the macromolecular lineshape.

Animal Models of Cancer

Hall B Monday 14:00-16:00

Hyperpolarized \(^{13}\)C Biomarkers of Androgen Independent Prostate Cancer

Paniz Vafaei¹, Robert Bok¹, Lynn DeLosSantos, Vicki Zhang, Phillip Guan, Dan Vigneron, John Kurhanewicz
¹Radiology, University of California, San Francisco, San Francisco, CA, United States

Androgen independence of prostate cancer is an important clinical status to identify, but no well-defined biomarkers for this state exist. In this study we used fast \(^{13}\)C-MRSI after injection of hyperpolarized [1-\(^{13}\)C] pyruvate and pathological and biochemical analysis of the tumor to determine hyperpolarized (HP) biomarkers of androgen dependent and androgen independent prostate cancer. Androgen independent phenotype had a significantly higher HP lactate/noise, Total Hyperpolarized Carbon, HP lactate/pyruvate, and LDH activity relative to the androgen dependent phenotype.

Multi-Parametric Characterization of an Experimental Model of Cancer Cachexia

Marie-France Penet¹, Sridhar Nimmagadda¹, Mayur Gadiya¹, Balaji Krishnamachary¹, Martin G. Pomper¹, Zaver M. Bhujwalla¹
¹JHU ICMIC Program, Russell H. Morgan Department of Radiology and Radiological Science, The Johns Hopkins University School of Medicine, Baltimore, MD, United States

Cachexia is a life-threatening syndrome of progressive weight loss that occurs with a high frequency in several cancers. A better in vivo characterization of cachectic tumors is important to identify new targets and improve treatment to arrest or reverse this condition.
Here we have characterized differences in vascular properties, quantified by 1H magnetic resonance imaging of the intravascular agent albumin-GdDTPA, between cachectic and non-cachectic tumors. We also performed 18F-deoxyglucose PET imaging to study the glycolytic activity of those tumors. We found significantly less permeable vasculature and increased glycolytic activity in the cachectic tumors compared to the non-cachectic ones.

2775. Adjustable Curie-Temperature Nanoparticles for Imaging and Highly Controllable Hyperthermia Cancer Therapy

Boris Odintsov1, Vadim Aleksandrovich Atsarkin2, Viktor Demidov3, Andrey Kaul4, Mariya Popova5, Carolina Soto6, Edward Roy6

1Biomedical Imaging Center, University of Illinois, Urbana-Champaign, IL, United States; 2IRE RAN, Moscow, Russian Federation; 3IRE RAN, Russian Federation; 4Moscow University, Russian Federation; 5UIUC, IL, United States; 6University of Illinois, Urbana-Champaign, IL, United States

New nanomaterials recently synthesized in our group are lanthanum manganite doped with silver ions. The unique feature of the doped mangantites is the possibility to control their Curie temperature in the range of tumor hyperthermia interest (41–43oC). At its Curie temperature, a ferromagnetic particle loses its magnetic properties; this metal-insulator phase transition is tunable and reversible. New ferromagnetic particles adopt the superparamagnetic behavior and are comparable to iron oxide as an MRI contrast agents. The goal of this presentation is to introduce newly synthesized nanomaterials and create a new platform for highly controllable hyperthermia cancer therapy and imaging.

2776. High Resolution MRI of Tumors in the Smo/Smo Mouse Medulloblastoma Model

Donghoon Lee1, Stacey Hansen1, Richard Ellenbogen1, Miqin Zhang1, James Olson1

1University of Washington, Seattle, WA, United States; 2Fred Hutchinson Cancer Research Center, Seattle, WA, United States

This work describes MRI methods for diagnosis and staging of tumors in the Smo/Smo genetically engineered mouse model of medulloblastoma. High resolution MRI was performed to attain T2 weighted imaging to screen tumors, T1 weighted imaging to examine the blood brain barrier integrity, and diffusion weighted imaging to improve tumor delineation. Sub-millimeter sized tumors in mice as young as 2 months were imaged even though animals were asymptomatic by other criteria. MRI findings were well correlated with histopathology. Thus, high resolution MR imaging is an excellent way to detect and stage tumors in mouse medulloblastoma models.

2777. Fast, High-Resolution, 3-Dimensional Imaging of the Mouse Prostate with BSSFP

Christiane L. Mallett1,2, Paula J. Foster1,2

1Imaging Research Laboratories, Robarts Research Institute, London, Ontario, Canada; 2Medical Biophysics, The University of Western Ontario, London, Ontario, Canada

Purpose: To obtain high-quality images of the mouse prostate for studies of prostate cancer. Methods: Mice were imaged with balanced steady state free precession (bSSFP), T1- and T2-weighted spin-echo sequences. Results: We obtained whole-body images at 200 micron resolution that included the prostate, popliteal and inguinal lymph nodes in ~25 mins. 2D T1- and T2-weighted SE sequences had inferior SNR per slice thickness and prostate-fat CNR relative to bSSFP. Conclusion: bSSFP gives fast, high resolution, 3D mouse prostate and body imaging with high SNR and CNR. This will be used in studies of prostate cancer and metastasis.

2778. MRI Characterisation of a Novel Transgenic Mouse Model of Neuroblastoma

Yann Jamin1, Elizabeth Ruth Cullis2, Lynsey Vaughan2, Dow-Mu Koh1, Louis Chesler2, Simon P. Robinson1

1Cancer Research UK and EPSRC Cancer Imaging Center, The Institute of Cancer Research and Royal Marsden NHS Trust, Sutton, Surrey, United Kingdom; 2Section of Paediatric Oncology, The Institute of Cancer Research, Sutton, Surrey, United Kingdom

This study characterises the novel transgenic murine TH-MYCN model of high-risk human neuroblastoma, the most common extracranial childhood solid tumour, with MRI, especially the anatomical presentation, the longitudinal development of the tumour in situ, and its established response to the chemotherapeutic agent cyclophosphamide in vivo. In addition, quantitative MRI parameters, and interrogation of the tumour vasculature by DCE-MRI, are also reported. We demonstrate that MRI screening would be a crucial asset in the development of novel MYCN-targeted therapies for neuroblastoma and would accelerate their clinical development by allowing simultaneous evaluation of preclinical MRI biomarkers of treatment response.

2779. Interstitial Fluid Pressure Correlates with Water Diffusion Coefficient in Mouse Mammary Tumor Model

Sungheon Kim1, Lindsey DeCarlo2, Gene Young Cho1, Jens H. Jensen1, Daniel K. Sodickson1, Linda Moy1, Silvia Formenti1, Robert J. Schneider2, Eric E. Sigmund1

1Center for Biomedical Imaging, Radiology, New York University, New York, NY, United States; 2Microbiology, New York University, New York, NY, United States; 3Radiation Oncology, New York University, New York, NY, United States

Effective delivery of therapeutic drug is often impeded by physiological barriers including elevated interstitial fluid pressure (IFP). In this study, we investigated the feasibility of using Intra-Voxel-Incoherent-Motion (IVIM) diffusion weighted imaging (DWI) to measure tumor blood flow and the association of IVIM diffusion coefficients with IFP. From a study of 10 mice with 4T1 mouse mammary tumor model, strong correlations (R^2 > 0.64) were observed between the elevated IFP (> 5 mmHg) and diffusion coefficients estimated using monoexponential as well as biexponential diffusion models. This result suggests a high potential of DWI parameters as surrogate markers for IFP.
2780. Multi-Modal Assessment of Longitudinal Growth of Liver Metastases in a Mouse Model of Colon Carcinoma
    Prachi Pandit1,2, Samuel M. Johnston1,2, Yi Qi2, Jennifer Story3, Beth Hollister3, G A. Johnson1,2
    1Biomedical Engineering, Duke University, Durham, NC, United States; 2Center for In Vivo Microscopy, Duke University, Durham, NC, United States; 3Piedmont Research Center, Morrisville, NC, United States

In this work we present a longitudinal, multi-modality study to monitor the growth of liver metastases in mouse model of colon carcinoma. We have compared the relative merits of using high-field T2-weighting MRI and contrast-enhanced microCT as a preclinical cancer imaging technique in free-breathing mice. The advantages of microCT lie in the fast acquisition of high-resolution isotropic datasets. MRI, on the other hand has higher contrast resolution, and requires neither contrast injection nor radiation dose. Both techniques, ungated MRI and respiratory-gated MicroCT, perform well in the presence of motion, and are sufficiently fast and non-invasive to allow repeated scanning.

2781. Imaging of Tumor Angiogenesis in a Novel Skin Chamber Using MRI and Optical Imaging
    Tobias Bäuerle1, Clarissa Gillmann2, Reiner Umathum1, Margareta M. Müller3, Michal Neeman4, Wolfhard Semmler2, Michael Bock1
    1Medical Physics in Radiology, German Cancer Research Center, Heidelberg, Germany, Germany; 2Medical Physics in Radiology, German Cancer Research Center, Heidelberg, Germany, Germany; 3Tumor- and Microenvironment, German Cancer Research Center, Heidelberg, Germany, Germany; 4Biological Regulations, The Weizmann Institute of Science, Rehovot, Israel

Tumor angiogenesis in animal models is often visualized using optical imaging or MRI. In this work we present a subcutaneous skin chamber for simultaneous optical and MR imaging to study the tumor-induced growth of blood vessels in vivo. The fully MR-compatible chamber features an optical window, and can be combined with a dedicated external loop coil.

2782. MR Characterization of the Tumor Microenvironment After Arsenic Trioxide Treatment: Evidence for an Effect on Oxygen Consumption That Radiosensitizes Solid Tumors
    Caroline Diepart1, Oussama Karroum, Julie Magat, Olivier Feron, Bénédicte Jordan, Bernard Gallez
    1UCL, Brussels, Belgium

As2O3 inhibits mitochondrial respiratory function in human leukemia cells. We hypothesized that As2O3 could also be an important modulator of tumor oxygenation by affecting the oxygen consumption of solid tumors. We observed an increase in tumor pO2 in two tumor models after arsenic treatment using oximetry techniques based on EPR and 19F NMR relaxometry. This effect was explained by a decrease in oxygen consumption of the tumors. Finally, the irradiation of tumors showed a regrowth delay that was significantly increased in arsenic-treated mice. As2O3 is an important modulator of pO2 by decreasing oxygen consumption and enhances the response of tumors to radiotherapy.

2783. Improving Tumour ADC Estimates and Elucidating Tumour Heterogeneity Using Adaptive Bayesian Markov Random Field Monte Carlo
    Simon Walker-Samuel1, Matthew Orton1, Jessica K R Boul1, Simon P. Robinson1
    1Cancer Research UK & EPSRC Cancer Imaging Centre, The Institute of Cancer Research, Sutton, Surrey, United Kingdom

A method for improving ADC estimates using an adaptive Bayesian Markov random field analysis is described and evaluated using simulations and in vivo tumour models. Via the sharing of information between neighbouring pixels, the uncertainty and error in ADC estimates are significantly reduced by a factor of up to 80%. The approach also enables the segmentation of homogeneous tissue components and a novel measure of tissue (tumour) heterogeneity is described.

2784. Serial Multiparametric MRI in Study Design and Response Evaluation of Radiation and Antiangiogenic Therapy in an Intracranial Murine Glioblastoma Model
    Caroline Chung1, Warren Foltz2, Petra Wildgoose1, Kelly Burrell1, Patricia Lindsay1, Andrea Kassner2, David Jaffray1, Gelareh Zadeh3,5, Cynthia Menard1
    1Radiation Medicine Program, Princess Margaret Hospital, Toronto, Ontario, Canada; 2SickKids Hospital, Toronto, Ontario, Canada; 3SickKids Hospital, Toronto, Ontario, Canada; 4Brain Tumour Research Centre, Toronto, Ontario, Canada; 5Toronto Western Hospital, Canada

This study demonstrates feasibility of using multiparametric micro-MRI to overcome the challenges of intracranial mouse tumour models. Baseline T2w images were used to select mice with visible tumours and to stratify mice to treatment arms based on tumour size. Serial multiparametric MRI was used to measure tumour growth and vascular changes on DCE-MRI (iAUC60) with radiation (RT) and/or sunitinib (SU) anti-angiogenic treatment. Early rises in iAUC60 were noted following both RT and SU monotherapy, while the combination of RT and SU resulted in an early significant decrease in iAUC60. These early measured DCE-MRI changes show promise as useful early biomarkers for treatment response.
2785. A Multiple Coil Array Approach for Mouse Brain Tumor Imaging

Lilia V. Ilieva1, Marcelino Bernardo2, Diane Palmieri3, Patricia Steeg4, Joseph Kalen1, Peter Choyke2
1Small Animal Imaging Program, SAIC-Frederick, NCI-Frederick, Frederick, MD, United States; 2Molecular Imaging Program, NCI, NIH, Bethesda, MD, United States; 3Imaging Physics, SAIC-Frederick, NCI-Frederick, Frederick, MD, United States; 4Laboratory of Molecular Pharmacology, NCI, NIH, Bethesda, MD, United States

Multiple mouse MRI is of critical importance in preclinical cancer research when longitudinal studies with multiple animals is required. This work presents a four-mouse brain imaging coil system and its application in the development of a breast cancer brain metastasis mouse model. The four-mouse SENSE array is integrated in a single platform with physiological support system. Six imaging sessions on 18 mice were performed weekly to monitor the initiation and progression of the brain metastases. The usage of the multiple mouse brain coil system significantly improved the efficiency of MRI studies involving serial imaging of multiple small animals.

2786. 13C HR MAS MRS Reveals Differences in the Glucose Metabolism Between Two Breast Cancer Xenograft Models with Different Gene Expression Pattern

Maria Tunset Grinde1, Siver Andreas Moestue1, Øystein Risa1, Olav Engebråten1, Ingrid Susann Gribbestad1
1Department of Circulation and Medical Imaging, NTNU, Trondheim, Norway; 2Department of Tumor Biology, Cancer Research Institute, Oslo University Hospital, Oslo, Norway

13C HR MAS MR spectroscopy has been used to study two breast cancer xenograft models, representing a human luminal-like and a basal-like genetic profile. The models received a bolus injection of [1-13C]glucose and the conversion from glucose to lactate and alanine was observed 10 or 15 minutes after. The luminal-like model showed a significantly lower ratio of glucose/alanine and glucose/lactate compared to the basal-like model. This can be explained by a lower uptake of glucose and/or a higher rate of glucose metabolism towards alanine and lactate in the luminal-like compared to the basal-like model.

2787. DMSO as a Potential Contrast Agent for Brain Tumours

Teresa Delgado-Goni1,2, Rui V. Simoes3, Milena Acosta3, Juana Martin-Sitjar1,2, Silvia Lope-Piedrafita3, Carles Arus1,2
1Bioquimica i Biologia Molecular, Universitat Autonoma de Barcelona, Cerdanyola del Valles, Barcelona, Spain; 2CIBER-BBN, Zaragoza, Spain; 3Servei de Ressonancia Magnetica Nuclear, Universitat Autonoma de Barcelona, Cerdanyola del Valles, Barcelona, Spain

We describe here the application of Dimethyl Sulfoxide (DMSO) as a potential contrast agent for brain tumour imaging. DMSO crosses the blood-brain-barrier, but its differential wash-out kinetics produces a clear contrast enhancement in mouse brain glioblastoma compared to nearby/peritumoral brain parenchyma, measured by SV MRS and MRSI sequences.

2788. Predicting and Monitoring Response to Chemotherapy by Benzamide Riboside in Hepatocellular Carcinoma Using Apparent Diffusion Coefficient of Water

Andriy Babsky1, Shenghong Ju2, Beena George, Stacy Bennett, Mingsheng Huang, Hiremagalur N. Jayaram, Gordon McLennan, Navin Bansal1
1Radiology, Indiana University, Indianapolis, IN, United States; 2Indiana University

Implantation of N1S1 cells in the rat liver can be studied as an intrahepatic hepatocellular carcinoma (HCC) model for pre-clinical study of transarterial therapy with the apoptotic agent benzamide riboside (BR). Water apparent diffusion coefficient (ADC) in HCC was higher than in nearby normal liver tissue. Intrahepatic infusion of BR was a semi-effective treatment of HCC in rats. BR therapy did not change the water ADC value, regardless of tumor sensitivity. A higher initial ADC level could be a promising sign for effective BR treatment, and in contrast, tumors with a lower initial ADC value are most likely to be resistant to BR-treatment.

2789. Dynamic Contrast-Enhanced Magnetic Resonance Imaging Reveals Differences in Xenografts with Luminal Like and Basal Like Gene Expression Pattern

Else Marie Huuse1, Siver Andre Moestue1, Olav Engebråten3, Tone Frost Bathen1, Ingrid Susann Gribbestad1
1Department of Circulation and Medical Imaging, Norwegian University of Science and Technology (NTNU), Trondheim, Norway; 2Department of Tumor Biology, Institute for Cancer Research, Oslo, Norway; 3Oslo University Hospital , Oslo, Norway

Molecular sub-classification of breast cancer based on gene expression pattern represents clinically distinct patient groups with different outcome. Two breast cancer xenograft models reflecting two of these groups: Basal like (ER-, poor prognosis) and luminal like (ER+, better prognosis), were characterized using DCE-MRI. Our results shows a significant higher Ktrans in basal like than in luminal like small tumors, however, this difference disappears for large tumors. Estradiol withdrawal had minor effect on growth and DCE-MRI derived parameters for the basal like tumors. The luminal like tumors ceased to grow and had a significant increase in Ktrans and ve .
Comparative Analysis of Gd Vs Dy in DSC-MRI Studies of a High Grade Glioma Murine Model
Rocio Perez-Carro1, Jesus Pacheco-Torres1, Sebastian Cerdan1, Pilar Lopez-Larrubia1
1Instituto de Investigaciones Biomedicas, CSIC/UAM, Madrid, Spain

Gd(III) is the lanthanide ion more widely used as longitudinal relaxation enhancer due to its long electronic relaxation time. Stable Gd complexes are the T1 contrast agents more used for MRI studies. Other paramagnetic lanthanides as Dy(III) are also employed as contrast agents in dynamic susceptibility contrast MRI. We used both Gd and Dy containing chelates in perfusion studies to yield parametric maps (CBF, CBV and MTT) in a high grade glioma rat model. The goal is to establish an optimal method to delimit and characterize brain regions in the murine model to test the effectiveness of antiangiogenic therapies.

Modulations of Intra and Extracellular pH in Tumor Variants Defective in Either Respiration or Glycolysis, Observed by In Vivo MRS
Norbert W. Lutz1, Johanna Chiche2, Yann Le Fur1, Christophe Vilmen1, Frederic Frassinetti1, Laurent Daniel1, Jacques Pouysségur2, Patrick J. Cozzone2
1CRMBM UMR 6612 CNRS, Aix-Marseille University, Medical School, Marseille, PACA, France; 2Institute of Developmental Biology and Cancer Research CNRS UMR 6543, Centre A. Lacassagne, Nice; 3Inserm UMR 911-CRO2, Aix-Marseille University, Medical School

The current use of angiogenesis inhibitors for cancer treatment requires further modifications of the hypoxic tumor microenvironment to achieve complete tumor regression. To contribute to the development of a new treatment strategy, we investigated effects of modulations of multiple mechanisms of glycolytic activity and pH regulation on intracellular and extracellular pH (pHi, pHe) by 31P NMR spectroscopy of tumor xenografts in nude mice. Three ras-transformed fibroblast variants were compared: wild-type CCL39, and mutants defective in either glycolysis or respiration. Compared to CCL39, pHi was increased in either mutant, and pHe was less heterogeneous due to a reduction of low-pH regions.

Single Dose (0.1mmol/kg) Brain Magnetic Resonance Imaging with Gadobutrol at 1.5T and 3.0T: Comparison to 0.15mmol/kg Gadoterate Meglumine
Harald Kramer1, Val M. Runge2, L Gill Naul2, Alan T. Loyenhahn3, Maximilian F. Reiser1, Bernd J. Wintersperger1
1Department of Clinical Radiology, University Hospital Munich, Munich, Germany; 2Scott and White Memorial Hospital, TX, United States; 3University of Kentucky, KY, United States

The detection of a link between the application of Gd contrast agents highlights the need for dedicated application protocols. The purpose of the study was to evaluate the efficacy of single dose gadobutrol compared to a substantially higher dose gadoterate meglumine in a tumor model at 1.5T and 3.0T. All animals were implanted Glioma cells using an implanted plastic brain cannula. After 7 days brain MR exams were performed whether with gadobutrol or gadoterate meglumine with a 24h interval. After the second MRI brains harvested for histopathologic assessment. Data were evaluated regarding SNR, CNR and lesion enhancement (LE).

Integrated MRI Approaches to Interrogate Tumor Oxygenation and Vascular Perfusion of Orthotopic Brain Tumors in a Mouse Model
Heling Zhou1, Amyn A. Habib1, Ralph P. Mason1, Dawen Zhao1
1Radiology, UT Southwestern Medical Center, Dallas, TX, United States

Glioma is a lethal cancer. It is imperative to non-invasively evaluate intracranial tumor microenvironment. We applied multiple MRI approaches to evaluate tumor microenvironment in orthotopic gliomas in a mouse model. An interleaved T2*-weighted and T1-weighted sequence, sensitive to both blood and tissue oxygen tension, was applied to assess tumor oxygenation. Our results showed significantly increased signal intensity in intracranial tumors with oxygen inhalation. Dynamic susceptibility contrast MRI was used to evaluate vascular perfusion and correlate with change in oxygenation. Our study suggests the integrated MRI approaches will be useful to evaluate interplay of tumor oxygenation and hemodynamics.

Intrinsic Susceptibility Contrast (R2*) in the Evaluation of Tumour Oxygenation at Baseline and in Response to Neoadjuvant Chemotherapy in Breast Cancer
Sonia P. Li1, N J. Taylor2, J J. Stirling3, Mei-Lin W. Ah-See1, Mark J. Beresford1, David J. Collins3, James A. d'Arcy1, Andreas Makris1, Anwar R. Padhani2
1Mount Vernon Hospital, Northwood, Middlesex HA6 2RN, United Kingdom; 2Paul Strickland Scanner Centre, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN, United Kingdom; 3CR-UK Clinical MR Research Group, Royal Marsden Hospital, Sutton, Surrey, SM2 5PT, United Kingdom

R2* has potential to provide information about tumour oxygenation but is underexplored in breast cancer. Here, primary carcinomas were imaged with multiparametric MRI before and after 2 cycles of neoadjuvant chemotherapy. Correlations between R2* and kinetic parameters were investigated. R2* as a predictor of pathological benefit was compared with DCE/DSC-MRI parameters. Significant inverse correlations between R2* and blood flow/volume in untreated cancers confirm that R2* reflects blood oxygenation; however
Improving temporal resolution without compromising spatial resolution has the potential to improve differential diagnosis in breast cancer. Several accelerated imaging methods exist that may aid in this endeavor but it is difficult to quantitatively measure and compare their respective performance. To address this problem, we have created a digital breast phantom comprised of enhancing and non enhancing lesions surrounded by normal background breast tissue. This phantom provides realistic, simulated k-space data for both Cartesian and non Cartesian acceleration methods. We describe the creation of this phantom and demonstrate its use.

Quantification of total Choline compounds in breast spectra is challenging due to the contamination of unsuppressed lipids. In vivo breast spectra in healthy controls were acquired using proton echo planar spectroscopic imaging. Localized spectra were fitted across the 4.0-2.0ppm range by LCModel using a basis-set with singlet resonances for tCho and lipid peaks. LCModel fitting enables identification of the tCho baseline and quantification of the peak area by spectral integration. In vivo tCho concentrations were consistent with literature values. This method is suitable for automatic tCho quantification of breast spectroscopic imaging data of low quality.

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Qualitative and Quantitative Assessment of Breast Tumour Appearance in Diffusion-Weighted Imaging and Correlation with Molecular Prognostic Factors

Giuseppe Petralia\(^1\), Luke Bonello\(^1\), Paul Summers\(^1\), Sara Raimondi\(^1\), Ala Malasevschi\(^1\), Roberto Di Filippi\(^1\), Dow-Mu Koh\(^1\), Marzia Locatelli\(^1\), Giuseppe Curigliano\(^4\), Massimo Bellomi\(^1\)

\(^1\)Radiology, Istituto Europeo di Oncologia, Milan, Lombardia, Italy; \(^2\)Epidemiology and Biostatistics, Istituto Europeo di Oncologia, Milan, Lombardia, Italy; \(^3\)Radiology, Royal Marsden Hospital, Sutton, United Kingdom; \(^4\)Medical Oncology, Istituto Europeo di Oncologia, Milan, Lombardia, Italy

We performed a qualitative analysis of diffusion weighted magnetic resonance imaging (DW-MRI) of breast tumours to identify common semiotic characteristics, and a quantitative analysis in 28 patients to examine the correlation of DW-MRI with molecular prognostic factors, and to assess the interobserver variability in the calculation of ADC values. Hyper-intensity in DW images and low ADC values (mean 1.1 x 10^{-3} mm^2/sec) were common characteristics in the breast tumours studied. Interobserver variability was 20%. A marginally significant correlation between ADC value and percentage of PgR and possible higher mean ADC values for the LUMINAL A subtype warrant further study.

Prostate Cancer - Clinical

Hall B Wednesday 13:30-15:30

DCE-MRI at 3T in Patients with Advanced Prostate Cancer Undergoing Androgen Deprivation Therapy

Tristan Barrett\(^1\), Andrew Gill\(^1,2\), Masako Kataoka\(^1\), Vincent J. Gnanapragasam\(^1\), Andrew Priest\(^1,3\), Ilse Joubert\(^1\), Mary McLean\(^1,4\), Martin J. Graves\(^1\), David J. Lomas\(^1\), John R. Griffiths\(^1\), David Neal\(^5\), Evis Sala\(^1\)

\(^1\)Radiology, Addenbrooke's Hospital, Cambridge, United Kingdom; \(^2\)Medical Physics, Addenbrooke's Hospital, Cambridge, United Kingdom; \(^3\)Urology, Addenbrooke's Hospital, Cambridge, United Kingdom; \(^4\)Cambridge Research Institute, Cancer Research UK, Cambridge, United Kingdom; \(^5\)Cambridge Research Institute, Cancer Research UK, Cambridge, United Kingdom

Prostate cancer is the commonest malignancy in UK men. Androgen deprivation therapy (ADT) remains an important treatment. However, 51% eventually develop resistance, making it necessary to identify quantitative markers that demonstrate ADT response. We used dynamic-contrast-enhancement (DCE)-MRI to measure permeability parameters before and 3 months after ADT in 12 patients with biopsy-proven prostate cancer. There was a significant reduction in all parameters measured (Ktrans, kep, Ve, IAUGC-90), whereas ‘normal’ tissue showed no significant change. These results suggest that DCE-MRI has potential to monitor ADT response and select patients with AD resistance at early time-points, allowing consideration of other treatments.

Can Ex-Vivo MRI Be Used for Correlating Diffusion Weighted Imaging Parameters to Pathology for Validation of In-Vivo Multiparametric MRI

Michael A. Jacobs\(^1,2\), Vadappuram Chacko\(^1\), Baasil Okolli\(^1\), Tamara Lotan\(^1\), Katarzyna J. Macura\(^1\)

\(^1\)The Russell H. Morgan Department of Radiology and Radiological Science, The Johns Hopkins University School of Medicine, Baltimore, MD, United States; \(^2\)Sidney Kimmel Comprehensive Cancer Center, The Johns Hopkins University School of Medicine; \(^3\)Pathology, The Johns Hopkins University School of Medicine, Baltimore, MD, United States

By using a multiparametric approach to investigate the in-vivo and ex-viso characteristics of prostate cancer a better understanding of prostate cancer aggressiveness and tumor staging can be realized. This radiological-pathological correlation will assist in detection, localization, assessment of the tumor microenvironment. Such a comprehensive approach offers more power to evaluate prostate disease than any single measure alone.

The Effect of Spatial Resolution on the Correspondence Between Hematoxylin-Eosin Stained Sections and MR Images for Prostate Cancer

Greetje Groenendaal\(^1\), Maaike R. Moman\(^1\), Johannes G. Korparaal\(^1\), Paul J. van Diesel\(^2\), Marco van Vulpen\(^1\), Marielle E.P. Philippens\(^1\), Uulke A. van der Heide\(^1\)

\(^1\)Radiotherapy, University Medical Center Utrecht, Utrecht, Netherlands; \(^2\)Pathology, University Medical Center Utrecht, Utrecht, Netherlands

Sensitivity and specificity values of DW-MRI and DCE-MRI for prostate cancer are often based on the correspondence of imaging and pathology within relatively large volumes inside the prostate. However, for prognosis, therapy selection and focal therapy, decisions on a voxel level are required. We investigated at which spatial resolution validation of MR images with hematoxylin-eosin stained sections is meaningful. We found that the chance is small that matching tumor voxels are found on the MR images and pathology within a volume smaller than 0.4 cc. This puts limitations on the accuracy at which tumor volume and extent can be determined.
2804. Echo Planar Spectroscopic Imaging with Peak-Enhanced 2D-Capon Analysis for Prostate Studies
Fred J. Frigo1, Andreas Ebel1
1GE Healthcare, Waukesha, WI, United States

Two-dimensional echo planar spectroscopic imaging (EPSI) may be used for clinical evaluation of the human prostate. The results of EPSI studies are typically represented as the set of MRS absorption spectra in which the concentration of each metabolite can be determined on the basis of its frequency representation in the voxel of interest. In addition to frequency information, the damping characteristics of each metabolite can also be determined by using two-dimensional Capon analysis. This damping information may be used in conjunction with the frequency information to more easily identify metabolites during clinical diagnosis of EPSI prostate studies.

2805. 31P MR Spectroscopy for Prostate Cancer Characterization at 7Tesla
Catalina Arteaga1, Uuile A. van der Heide1, Marco van Vulpen1, Peter R. Luijten2, Dennis W.J. Klomp2
1Radiotherapy, UMC Utrecht, Utrecht, Netherlands; 2Radiology, UMC Utrecht, Utrecht, Netherlands

We showed the feasibility of obtaining 31P MRS in the prostate area at 7T with the use of anatomy imaging and optimized B0 shimming. Individual detection of PC, GPC, GPE and GPC was feasible, illustrating the benefit of going to higher spectral resolutions that can be obtained at higher fields like 7T.

2806. Signal Characterization of a Novel Two-Channel Rigid Endorectal Coil for MR Imaging of the Prostate
Niranjani Venugopal1, Axel Krieger1, Herve Momo Jeunfack1, Ken Bradshaw1, Boyd McCurdy1, Lawrence Ryner2
1Physics and Astronomy, University of Manitoba, Winnipeg, MB, Canada; 2Medical Physics, CancerCare Manitoba, Winnipeg, MB, Canada; 3Sentinelle Medical, Toronto, Ontario, Canada; 4Sentinelle Medical Inc.; 5Medical Physic, CancerCare Manitoba, Winnipeg, MB, Canada; 6National Research Council Institute for Biodiagnostics, Winnipeg, MB, Canada

We present a comparison of a newly designed dual-channel, rigid endorectal coil for both imaging and spectroscopic imaging of the prostate with a standard, single-channel, inflatable endorectal coil, demonstrating a SNR improvement of up to ~500% in the near-coil area (where the prostate peripheral zone is located), and up to ~150% at depth (where the prostate central zone is located). This huge SNR improvement allows for greatly improved MR/MRSI imaging of the prostate.

2807. Short Echo Time in Vivo Prostate MRSI
Niranjani Venugopal1, Boyd McCurdy1, Darrel Drachenberg3, Salem Al Mehari3, Aziz Alamri3, Gurudarshan Sandhu3, Sri Sivalingam3, Lawrence Ryner4
1Physics and Astronomy, University of Manitoba, Winnipeg, MB, Canada; 2Medical Physics, CancerCare Manitoba, Winnipeg, MB, Canada; 3Sentinelle Medical, Toronto, Ontario, Canada; 4National Research Council Institute for Biodiagnostics, Winnipeg, MB, Canada

We present a robust method improve the quality of in vivo prostate MRSI data acquisition by utilizing an optimized conformal voxel technique coupled with a spatial-spectral excitation PRESS pulse sequence for short echo time acquisitions. The PRESS pulse sequence was modified to include the optimized conformal voxel MR spectroscopic imaging technique (CV-MRSI). In vivo implementation of this optimized MRSI technique confirms the reduction in peripheral lipid contamination, and improved the quality of spectra throughout the prostate. In summary we have demonstrated the utility of short TE in vivo prostate MRSI acquisitions, which provides significant signal increase and reveal short TE metabolites to potentially improve prostate cancer detection.

2808. Clinical Prostate T1 Quantification Using a Magnetization-Prepared Spiral Technique
Warren Foltz1, Masoom Haider2, Peter Chung1, Andrew Bayley1, Charles Catton1, Venkat Ramanan1, David Jaffray1, Graham Wright2, Cynthia Ménard2
1Radiation Medicine Program, Princess Margaret Hospital, Toronto, Ontario, Canada; 2Medical Imaging, University Health Network, Toronto, Ontario, Canada; 3Medical Imaging, University of Toronto; 4Sentinelle Medical, Toronto, Ontario, Canada; 5Sentinelle Medical Inc.; 6National Research Council Institute for Biodiagnostics, Winnipeg, MB, Canada

A magnetization-prepared spiral imaging strategy with RF cycling has been adapted for time-efficient multi-slice clinical prostate T1 quantification at 1.5T. In vitro testing validated an overall robustness to RF offsets. Pilot studies in patients without prior external beam radiation demonstrated an equivalence between zonal T1, with reduced T1 in peripheral zone tumors. Intra-patient zonal T1 variabilities motivate individual measurements for dynamic studies of vascular metrics. SNR analysis identified useful region volumes for thermal-noise insensitive measurements, to guide protocol design for future voxel-based prostate T1 mapping. High RF insensitivity combined with time-efficiency suggests method potential for robust implementation on stronger magnets.

2809. Multi-Slice Parametric Mapping in Prostate DCE-MRI
Ryan Alexander Priest1, Xin Li2, Ian J. Tagge1, William J. Woodward2, Tomasz M. Beer3,4, Charles S. Springer, Jr.2,4, Mark G. Garzotto5,6
1Diagnostic Radiology, Oregon Health & Science University, Portland, OR, United States; 2Advanced Imaging Research Center, Oregon Health & Science University, Portland, OR, United States; 3Hematology/Oncology, Oregon Health & Science University, Portland, OR, United States; 4Knight Cancer Institute, Oregon Health &
Pharmacokinetic analysis of data generated using Dynamic-Contrast-Enhanced MRI (DCE-MRI) has proven to be a valuable tool in the evaluation of the vascular pathophysiology of prostate adenocarcinoma. With improved hardware, multi-slice parametric mapping has become feasible and could provide valuable insight to complement conventional T2*-weighted images. In this study multi-slice parametric mapping was performed with DCE-MRI data using both the standard model (SM) and the first generation shutter-speed model (SSM). Parametric maps were then compared with biopsy results.

2810. Ability of Combined DTI and DCE MRI to Predict Pathologic Gleason Score

Piotr Kozlowski1, Silvia D. Chang1, Edward C. Jones2, Ran Meng3, Nicholas Buchan4, S Larry Goldenberg, 4,5
1UBC MRI Research Centre, Vancouver, BC, Canada; 2Radiology, University of British Columbia, Vancouver, BC, Canada; 3Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada; 4Vancouver Prostate Centre, Vancouver, BC, Canada; 5Urologic Sciences, University of British Columbia, Vancouver, BC, Canada

DTI and DCE MRI were carried out in 27 prostate cancer patients. Mean diffusivity, fractional anisotropy and pharmacokinetic modeling parameters calculated from MRI data were correlated with Gleason score determined by biopsy and prostatectomy specimens. Mean diffusivity and fractional anisotropy correlated significantly with Gleason score, as demonstrated by the Spearman’s rank correlation test and the ordinal logistic regression modelling. These results strongly suggest that DTI MRI is capable of non-invasively grading prostate tumours.

2811. Investigation of Prostate Cancer Using Diffusion Weighted IVIM Imaging

Jörg Döpfert1, Andreas Lemke1, Anja Weidner1, Lothar Rudi Schad1
1Department of Computer Assisted Clinical Medicine, Heidelberg University, Mannheim, Germany; 2Institute of Radiology and Nuclear Medicine, Heidelberg University, Mannheim, Germany

In this work, the decrease of the apparent diffusion coefficient (ADC) in cancerous prostate tissue compared to healthy prostate tissue is investigated using the Intravoxel Incoherent Motion (IVIM) Theory. Moreover, the extracted parameters and the calculated parameter maps are analyzed with regard to the differentiation between cancerous and healthy tissue. Therefore, diffusion weighted images of the prostate of 9 patients with prostate carcinoma were acquired and evaluated, yielding a significant decrease of the ADC and the perfusion fraction in cancerous tissue compared to healthy tissue. The results suggest that the decrease of the ADC primarily comes from perfusion effects.

2812. Comparison of HASTE & EPI Diffusion Weighted Images in the Prostate

Ben Babourina-Brooks1, Gary Cowin1, Deming Wang1
1Centre for Magnetic Resonance, University of Queensland, Brisbane, Queensland, Australia

A comparison of two diffusion weighted imaging sequences, Echo Planar Imaging (EPI) and Half fourier Acquisition Single shot Turbo spin echo (HASTE), was conducted in the prostate. EPI, which is currently the main DWI method, is highly susceptible to artifacts, namely magnetic susceptibility and chemical shift. We propose to use a HASTE sequence, which is less affected by these artifacts, to gain more reproducible Apparent Diffusion Coefficient (ADC) values and increase ADC map quality. Advancements in this area will lead to more accurate prostate cancer localisation.

2813. 3T MR Spectroscopic Imaging with and without Endorectal Coil in Localizing Prostate Cancer: An Initial Experience

Derya Yakar1, Stijn Heijmink, Jelle Barentsz, Christina Hulsbergen - Van de Kaa, Jurgen Fütterer, Tom Scheenen
1Radboud University Nijmegen Medical Centre, Nijmegen, Gelderland, Netherlands

Currently used techniques in localizing prostate cancer (Pca) have definite shortcomings. We studied the potential of 3D-magnetic resonance spectroscopic imaging (MRSI) with and without an endorectal coil (ERC) at 3T in improving the localization of Pca. Eighteen patients with histologically proven Pca underwent an MRSI examination with and without the use of an ERC. The areas under the receiver operating characteristic curve were improved for all of the readers with the use of an ERC. For one reader this improvement was statistically significant (p< .05). Overall the AUC for all readers was quite low, with and without the use of an ERC. Emphasis have to be made on the fact that these results concern an initial experience based on a first cohort of patients examined at 3T with 3D-MRSI in our institution. In our experience more recent data of patients examined with 3D-MRSI at 3T in our institution are far more promising due to higher signal-to-noise ratios resulting in better fitted spectra and less non ratable ROIs.

2814. Clinical Prostate T2 Quantification Using a Magnetization-Prepared Spiral Technique

Warren Foltz1, Supriya Chopra1, Peter Chung1, Andrew Bayley1, Charles Catton1, David Jaffray1, Graham Wright1, Masoom Haider2,3, Cynthia Ménard1
1Radiation Medicine Program, Princess Margaret Hospital, Toronto, Ontario, Canada; 2Sunnybrook Research Institute, Toronto, Ontario, Canada; 3Medical Imaging, University Health Network, Toronto, Ontario, Canada; 4Medical Imaging, University of Toronto

A magnetization-prepared spiral imaging technique, termed T2prep, was adapted for robust time-efficient clinical prostate evaluation, and piloted in two prostate cancer cohorts. The patient groups presented with: (A) no prior history of external beam radiation; and (B) biochemical failure after radiotherapy. Cohorts were scanned (A) without and (B) with an endo-rectal coil in tandem with a torso
phased-array, respectively. Prostate zonal and tumor T2 values supported known trends. For each cohort, an SNR analysis was performed to identify minimum region volumes for thermal-noise insensitive measurements, and to guide protocol design for future voxel-based analysis.

**2815. Early Quantitative T1 and T2 Response of the Prostate Gland During Radiotherapy**

Warren Foltz1, Andy Wu1, Anna Kirsilova1, Peter Chung1, Andrew Bayley1, Charles Catto1, David Jaffray1, Masoom Haider2, Cynthia Ménard1

1Radiation Medicine Program, Princess Margaret Hospital, Toronto, Ontario, Canada; 2Medical Imaging, University Health Network, Toronto, Ontario, Canada

Magnetization-prepared spiral imaging techniques were adapted for quantitative T2 and T1 characterization of early radiation response in patients with low/intermediate risk of localized cancer throughout 8-weeks of radiotherapy. Early central gland T2 elevation preceded persistent tumor T2 elevation, and late reduction in peripheral zone T2; observations which support a known loss of contrast in diagnostic images, and a complementary role for T2 in ADC and DCE radiation response evaluation. Zonal and tumor T1 measures were insensitive to radiotherapy. However, considerable inter-patient but minor intra-patient T1 heterogeneities support a sufficiency of baseline T1 scanning for serial quantitative perfusion analysis during radiotherapy.

**Cancer (Miscellaneous)**

**Hall B Thursday 13:30-15:30**

**2816. MRI-Based ‘Wait-And-See’ Policy in Clinical Complete Responders to Chemoradiation in Rectal Cancer: A Promising Alternative**

Monique Maas1, Doenja Lambregts1, Ronald van Dam1, Patty Nelemans3, Guido Lammering3, Rob Jansen3, Regina Beets-Tan1, Geerard Beets2

1Radiology, Maastricht University Medical Center, Maastricht, Limburg, Netherlands; 2Surgery, Maastricht University Medical Center, Maastricht, Limburg, Netherlands; 3Epidemiology, Maastricht University Medical Center, Maastricht, Limburg, Netherlands; 1Radiotherapy, Maastricht University Medical Center, Maastricht, Limburg, Netherlands; 3Medical Oncology, Maastricht University Medical Center, Maastricht, Limburg, Netherlands

When - after neoadjuvant chemoradiation for rectal cancer - imaging could accurately select the complete responders, surgery might safely be omitted and patients can undergo a wait-and-see policy. This study aims to evaluate whether MRI at 1.5T is accurate enough to select patients for wait-and-see and can safely be used as a follow-up tool.

**2817. N-Stage Assessment in Non-Small Cell Lung Cancer Patients: Comparison of Capability Among STIR Turbo SE Imaging, Diffusion-Weighted Imaging and FDG-PET/CT**

Daisuke Takenaka1, Yoshiharu Ohno1, Keiko Matsumoto1, Hisanobu Koyama1, Yumiko Onishi1, Munenobu Nogami1, Nobukazu Aoyama1, Hideaki Kawamitsu1, Kazuro Sugimura1

1Radiology, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan; 1Division of Radiology, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan

FDG-PET/CT can assess morphological and metabolic information at same time, and widely utilized for N-stage assessment in non-small cell lung cancer (NSCLC) patients. In the last decade, short inversion time inversion recovery (STIR) turbo spin-echo (SE) imaging has been determined at least as valuable as PET/CT in this setting. Recently, diffusion-weighted image (DWI) is suggested as new technique for differentiation of metastatic lymph nodes from non-metastatic lymph nodes. The purpose of this study was to prospectively and directly compare capability of N-stage assessment among integrated FDG-PET/CT, STIR turbo SE imaging and DWI in NSCLC patients.

**2818. Assessment of the Early Response to Chemotherapy with Diffusion-Weighted MRI in Advanced Lung Cancer Patients-Comparison with FDG-PET**

Tatsuro Tsuchida1, Miwa Morikawa2, Yukihiro Umeda2, Masato Sasaki3, Tomohito Kamibayashi1, Hirohiko Kimura1

1Dept. of Radiology, University of Fukui, Fukui, Japan; 2Dept. of Respiratory Medicine, University of Fukui, Fukui, Japan; 3Dept. of Thoracic Surgery, University of Fukui, Fukui, Japan

The purpose of this study was to examine the utility of DWI-MRI for the assessment of early response to chemotherapy in patients with advanced lung cancer by comparing FDG-PET. Twenty-two lung cancer patients received MRI, FDG-PET, and CT examination before and after 1 cycle of chemotherapy. Progression-free survival (PSF) between responder and non-responder against chemotherapy was compared by means of % change of ADC and SUV. Both index indicated that responder demonstrated significant longer PSF and DWI-MRI will be a promising tool for the assessment of the early response to chemotherapy.
2819. **Perfusion MRI of Solitary Pulmonary Nodules at 3T: Assessment of Perfusion Parameters and Correlation with Histology**

Hatsuho Mamata1, Junichi Tokuda1, Ritu Gill2, Robert F. Padera2, Robert E. Lenkinski3, David J. Sugarbaker4, Hiroto Hatabu1

1Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States; 2Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States; 3Radiology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, United States; 4Thoracic surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States

Solitary pulmonary nodule (SPN) is one of the most common findings in chest imaging. It is important to avoid unnecessary intervention for benign lesions, thereby lowering the associated mortality / morbidity. In this study, we applied perfusion MRI to evaluate perfusion characteristics of SPN and feasibility of perfusion MRI as a diagnostic tool to differentiate malignant from benign SPN. Perfusion MRI parameters and T1 curve has great potential to differentiate malignant vs. benign SPN, thus to avoid unnecessary surgical interventions.

2820. **Feasibility of Detecting Radiation-Induced Lung Injury in Non-Small Cell Lung Cancer Patients Using Hyperpolarized Helium-3 MRI**

Rob H. Ireland1,2, Omar S. Din2, James A. Swinscoe2, Edwin JR van Beek3, Matthew QF Hatton2, Jim M. Wild1

1Academic Unit of Radiology, University of Sheffield, Sheffield, United Kingdom; 2Academic Unit of Clinical Oncology, University of Sheffield, Sheffield, United Kingdom; 3Department of Radiology, University of Iowa, Iowa, IA, United States

This preliminary work demonstrates the feasibility of pre-treatment assessment of lung ventilation and post-treatment detection of radiation-induced lung damage using 3He-MRI for NSCLC patients.

2821. **Intracellular Acidification of Human Melanoma Xenografts by the Respiratory Inhibitor Lonidamine Plus Hyperglycemia: A 31P Magnetic Resonance Spectroscopy Study**

Kavindra Nath1, Elliott C. Woods1, Seung Cheol Lee1, David S. Nelson1, Dennis B. Leeper2, Rong Zhou1, Lin Li1, Jerry D. Glickson1

1Radiology (Molecular Imaging Section), University of Pennsylvania, Philadelphia, PA, United States; 2Radiation Oncology, Thomas Jefferson University, Philadelphia, PA, United States

In vivo 31P magnetic resonance spectroscopy illustrates that human melanoma xenografts can be acidified by induction of hyperglycemia combined with administration of lonidamine, an inhibitor of mitochondrial respiration. In melanoma xenograft (10-13 mm diameter), intracellular pH (pHi, measured by chemical shift of the Pi resonance) was reduced by ~0.7 unit during i.v. infusion of glucose (0.6 M) for 120 min along with administration of lonidamine (50 mg/kg). Preliminary result of this study shows that lonidamine combined with hyperglycemia acidified human melanoma xenografts by reducing pHi, a more critical parameter for thermosensitization to improve tumor response to alkylating agents.

2822. **Monitoring Bone Marrow Changes During Chemoradiotherapy Using MRI Fat Quantification**

Mark Bydder1, Yun Liang2, Huanzhou Yu1, Ann Shimakawa1, Jean Brittain3, Graeme Bydder1, Loren Mell2

1Radiology, University of California San Diego, San Diego, CA, United States; 2Radiation Oncology, University of California San Diego, San Diego, CA, United States; 3GE Healthcare, Applied Science Lab, United States

The goal of this study was to evaluate a non-invasive magnetic resonance imaging method of fat quantification as a measure of yellow bone marrow in the pelvis and spine. This is a new technology that will enable monitoring of response to therapy and assessment of the effectiveness of strategies to reduce hematologic toxicity.

2823. **Motion-Sensitized Driven-Equilibrium (MSDE) Turbo Spin-Echo Sequence Increases Radiologists' Diagnostic Performance in Detection of Brain Metastasis**

Eiki Nagao1, Takashi Yoshiura1, Akio Hiwatashi1, Koji Yamashita1, Hironori Kamano1, Yukihisa Takayama1, Tuvshinjargal Dashjants1, Makoto Obara2, Tomoyuki Okuaki2, Hiroshi Honda1

1Clinical radiology of Kyushu-university, Fukuoka, Japan; 2Philips Electoronics Japan

Motion-sensitized driven-equilibrium (MSDE) sequence has been reported to effectively suppress signals from flowing blood in vessels that can mimic the brain metastases on post-contrast T1-weighted images. We performed an observer test to determine whether use of a 3D turbo spin-echo (TSE) sequence with MSDE increases radiologists’ diagnostic performances in detecting brain metastases comparing to a conventional 3D gradient-echo sequence (MPRAGE). A jackknife free-response receiver operating characteristic (JAFROC) analysis showed that TSE with MSDE increases radiologists’ diagnostic performances compared to MPRAGE. The reading time was also significantly shortened by use of MSDE.
2824. **Correlation of a Priori DCE-MRI Data with Ki-67 and HIF-1α Expression Levels in Neck Nodal Metastases: Initial Analysis**

Jacobus FA Jansen¹, Diane Carlson¹, Bhuvanesh Singh¹, Hilda Stambuk¹, Ya Wang¹, Dennis Kraus¹, Richard Wong¹, Snehal Patel¹, Jatin Shah¹, Jason Koutcher¹, Amita Shukla-Dave¹

¹MSKCC, NY, United States

Pretreatment DCE-MRI was performed on neck nodal metastases of 12 patients who underwent surgery. Surgical specimens were analyzed with immunohistochemistry (IHC) assays for Ki-67 (reflecting cellular proliferation) and HIF-1α (hypoxia inducible transcription factor). Spearman correlation was used to correlate DCE-MRI and molecular marker data. Significant correlation results were observed between DCE-MRI data (Ktrans and ve) and tumor hypoxia, and proliferation as measured by Ki67 and HIF-1α expression levels, respectively. Future studies with larger patient populations need to be carried out to confirm pretreatment DCE-MRI findings and molecular marker results in biopsy samples for better patient management.

2825. **Focused Primary Tumour Staging and WB-MRI Distant Disease Assessment: A Potential All-In-One Staging Tool**

Martin D. Pickles¹, Lindsay W. Turnbull¹

¹Centre for MR Investigations, University of Hull, Hull, East Yorkshire, United Kingdom

Oncology patients undergo multiple imaging investigations to stage their disease. The aim of this study was to investigate the feasibility of a focused primary tumour (breast or prostate) examination in combination with a WB-MRI for staging of distant disease. If successful we propose the addition of this technique would allow the omission of other examinations, such as radionuclide imaging, thereby streamlining the current imaging pathway. We conclude that focused primary tumour examinations in combination with a WB-MRI for staging of distant disease is feasible. However, the technique needs to validated in a much larger cohort than the one studied.

2826. **Imaging Characteristics of Metastasis in Whole Body Diffusion Weighted imaging of Renal Clear Cell Carcinoma**

Jing Liu¹, XiaoYing Wang¹, XueXiang Jiang¹

¹Department of Radiology, Peking University First Hospital, Beijing, China

The study aimed to explore the role of Whole-body DWI in clear cell renal cell carcinoma (RCC) and obtain the imaging characteristics of metastases. Ten patients with histologically confirmed clear cell RCC and possible metastatic lesions were underwent standard Whole-body DWI, chest CT and routine MR examinations before chemotherapy. The results showed that the whole body DWI was very sensitive to the metastatic lesions in clear cell RCC and DWI showed its high rate of detection in pulmonary metastases. Whole body DWI had revealed great potential in metastatic screening of clear cell RCC.

2827. **Whole Body Imaging Multiparametric (T2/DWI/DCE) and Advanced Multimodality (PET/CT) for Detection of Recurrent Metastatic Cancer**

Michael A. Jacobs¹, Li Pan², Katarzyna J. Macura¹, Thorsten Feiweier³, Wilhelm Horger³, Richard L. Wahl¹

¹The Russell H. Morgan Department of Radiology and Radiological Science, The Johns Hopkins University School of Medicine, Baltimore, MD, United States; ²Center for Applied Medical Imaging, Siemens Corporation, Corporate Research, Baltimore, MD, United States; ³Siemens AG, Healthcare Sector, Magnetic Resonance, Germany

By using Whole Body MR and PET/CT approach to investigate metastatic disease can lead a better understanding of cancer aggressiveness. Functional imaging such as DWI/ADC, DCE-MRI and 11C Choline PET is feasible and thus, combined DWI/ADC mapping, and PET/CT provides radiological biomarkers of molecular environment and could provide targets imaging treatment response.