the course of a fractionated radiotherapy treatment or during a PET study. This work examines how transient perfusion of vessels may influence tissue radiosensitivity (including reoxygenation) and FMISO image contrast, as a guide for dose painting.

Material and Methods: Microscopic oxygen and FMISO distributions are simulated in tissue using bespoke MATLAB software which solves coupled partial differential equations by finite difference methods. Dynamic vasculature is modelled by opening and closing individual vessels at random, with time spent in each state sampled from a normal distribution. Oxygen enhancement ratios are calculated from the resulting PO2 maps. The optimal prescription dose is found by simulating a range of dose levels and determining radiobiological cell kill using the linear-quadratic model with repopulation. A novel approach to modelling reoxygenation is adopted in which a tissue's oxygen consumption in one fraction is reduced by the cell kill in previous fractions.

Results: Predicted FMISO tissue-to-muscle ratios (TMR) are in the range 1.0-2.3, increasing as PO2 decreases to a peak at ~7 mmHg. At very low vascularity, FMISO uptake is limited by perfusion of tracer into the tissue, rather than the oxygen-dependent binding characteristic. No gross differences are observed in TMRs simulated with static or dynamic vascular models. For a representative hypoxic tumour (10 mmHg, intrinsic α=0.3) surviving fractions of 10^-9 are predicted at doses of: 110 Gy (static vasculature, no reoxygenation), 87 Gy (dynamic vasculature changing every fraction) and 71 Gy (reoxygenation by reduced consumption). The effect of vessel dynamics is negligible if significant reoxygenation of chronic hypoxia occurs.

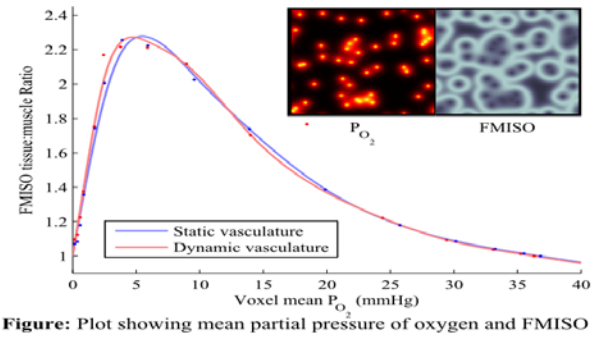

Figure: Plot showing mean partial pressure of oxygen and FMISO tissue:muscle ratio at 4 hrs for simulations with static vascular model and a dynamic model in which vessels randomly open and close. *Inset:* Simulated miscroscopic distributions of oxygen and FMISO at 4 hours in the same 1 mm^2 of tissue with mean PO_2 = 5 mmHg.

	Static Vessels		Dynamic Vessels		Rexoygenation	
Dose	P_{O_2}	SF	P_{O_2}	SF	P_{O_2}	SF
0 Gy	3.8	1	3.8	1	3.8	1
10 Gy	3.8	2.3×10^{-1}	4.1	2.3×10^{-1}	14.8	2.0×10^{-1}
20 Gy	3.8	6.0×10^{-2}	3.8	5.5×10^{-2}	35.2	2.5×10^{-2}
30 Gy	3.8	1.6×10^{-2}	3.8	1.3×10^{-2}	39.4	2.8×10^{-3}
40 Gy	3.8	1.1×10^{-2}	3.8	8.1×10^{-3}	39.9	8.3×10^{-4}
50 Gy	3.8	8.4×10^{-3}	3.5	5.0×10^{-3}	40.0	2.5×10^{-4}
60 Gy	3.8	6.2×10^{-3}	3.6	3.2×10^{-3}	40.0	7.3×10^{-5}

Table: Simulated surviving fraction (SF) and oxygen partial pressure (PO_2) in mmHg for varying dose delivered in 2 Gy fractions with a static vascular model, a dynamic vascular model and the reduced consumption reoxygenatio model. Parameters: intrinsic radiosensitivity α = 0.3, repopulation kick-off time 21 days and doubling time 5 days.

Conclusion: A model has been demonstrated that predicts realistic FMISO uptake in hypoxic tissue and provides a method for calculating prescription doses with reoxygenation. Individual vessel dynamics do not affect FMISO image contrast at 4 hours, or the prescription dose if global reoxygenation occurs.

OC-0529

A MR-based IGRT platform using the KPC transgenic mouse model of pancreatic cancer

J. Thompson[1], J. Beech[1], D. Allen[1], S. Gilchrist[1], R. Newman[1], P. Kinchesch[1], A. Gomes[1], Z. D'Costa[1], L. Bird[1], K. Vallis[1], R. Boghozian[1], A. Kavanagh[1], O. Sansom[2], I. Tullis[1], R. Muschel[1], M. Hill[1], B. Vojnovic[1], S. Smart[1], E. Fokas[1]
[1]*CRUK/MRC Institute for Radiation Oncology University of Oxford, Department of Oncology, Oxford, United Kingdom*
[2]*Cancer Research UK Beatson Institute- Glasgow, Institute of Cancer Sciences- University of Glasgow, Glasgow, United Kingdom*

Purpose or Objective: With a 5-year survival rate of 5%, pancreatic ductal adenocarcinoma (PDAC) is considered a disease of unmet-need. Preclinical radiobiological research in PDAC has been limited by mouse models that do not recapitulate the human biology and, more importantly, the immense technical challenges in establishing a platform that enables precise irradiation of pancreatic tumours in mice

Material and Methods: Herein we describe the key steps in the development of a state-of-the-art preclinical image-guided radiotherapy (IGRT) platform that enables precise planning and dose delivery in the KRASLSL.G12D/+; p53R172H/+; PdxCretg/+ (KPC), a genetically-engineered mouse model (GEMM) of PDAC. CT (x-ray computerised tomography) does not provide the soft tissue contrast required for accurate and precise RT planning in the mouse. We demonstrate the use of magnetic resonance Imaging (MRI) for RT planning in the mouse abdomen. KPC mice with spontaneous pancreatic tumours were anaesthetised and placed in an MR-CT compatible cradle. A newly-developed respiratory-gated multiple echo contrast scan (8 echoes, TE 6-50 ms) operating at constant TR=3600, was run at 150x150x300 um resolution in a scan time of ca. 9 minutes.

Results: Tumours were undetectable using CT but showed as bright regions on T2-weighted images, as described previously. After registration of the MRI to the CT images RT planning was quite straightforward and beam trajectory and RT dose estimations were performed for a conical arc trajectory. MRI can be used with CT-guided RT system to give soft tissue contrast and enable RT planning. The respiratory gated T2-weighted scans acquired using multiple echoes gave very good contrast, though the scan time was relatively long (ca. 9 minutes). At the expense of SNR this can be reduced to ca. 2 minutes through use of fast spin echo. The different steps will be discussed in detail. Precise beam delivery was confirmed using immunohistochemical staining for γH2AX foci.

Conclusion: Altogether, our IGRT platform represents a novel tool to explore the effects of RT on the biology of PDAC and investigate the mechanisms of treatment resistance. To our best of knowledge, no studies to date have reported such a precise MR-based IGRT platform for preclinical radiobiological research in the KPC model. This platform will enable exploration of the mechanisms of treatment resistance and is expected to provide important radiobiological insight to guide successful future clinical trials that will directly benefit patients with PDAC.

OC-0530

Nanoparticle-enhanced MRI-guided radiation therapy

A. Detappe[1,2], S. Kunjachan[1], O. Tillement[2], R. Berbeco[1]
[1]*Dana Farber Cancer Institute, Radiation Oncology, Boston, USA*
[2]*Institut Lumiere Matiere, Universite Claude Bernard, Lyon, France*

Purpose or Objective: MRI is increasingly used in radiation oncology for target delineation and real-time treatment guidance. The gadolinium-based nanoparticles (GdNP) used in this study are a dual modality probe with MRI contrast and radiosensitization properties. We use a mouse model of pancreatic cancer to demonstrate *in vivo* contrast enhancement, quantification of GdNP concentration, and