THE ARR

The Association for Radiation Research

9 - 11 June 2025

Lodore Falls Hotel & Spa, Keswick

Abstract Book

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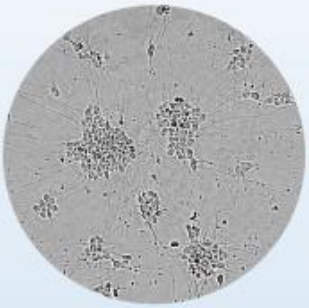

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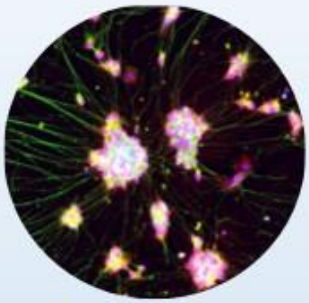

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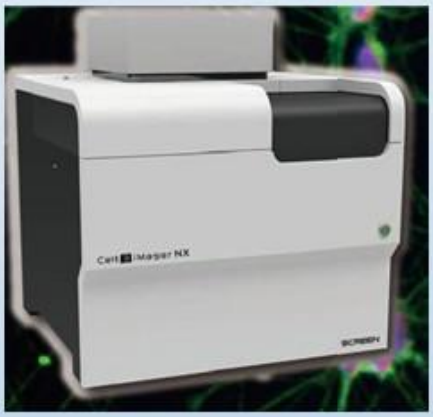

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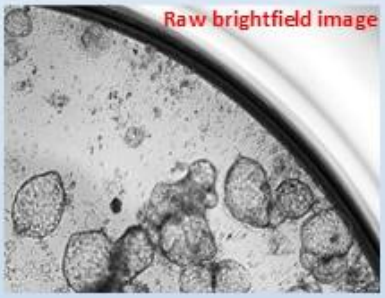

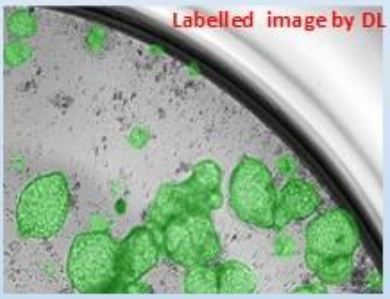

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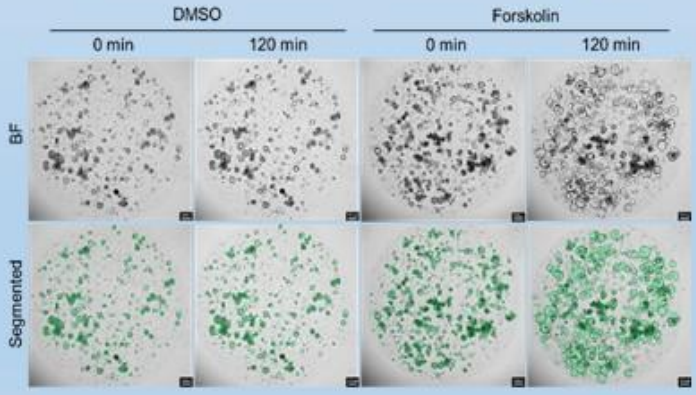

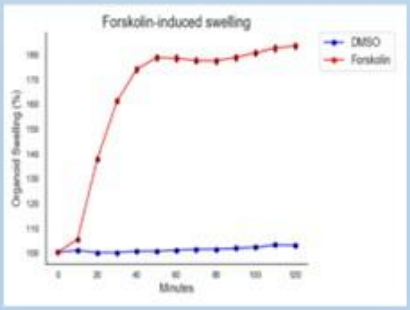

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Welcome

WELCOME TO THE ARR CONFERENCE 2025

On behalf of the Association for Radiation Research (ARR), I am delighted to welcome you to Lodore Falls and Cumbria for the ARR 2025 Conference.

The ARR is a charitable, non-profit organisation which focuses on promoting learning and advancing education in radiation research. It aims to facilitate scientific cooperation and communication among researchers, mainly in the UK but also internationally.

The Society's work encompasses a broad range of topics related to radiation research and it aims to increase and disseminate knowledge of radiation research in the fields of biology, chemistry, physics, medicine and other related disciplines.

We have chosen sessions to reflect these broad topics and have scheduled exciting talks from a variety of experts in the different fields and, importantly, also from many early career researchers.

We hope that this event will provide a valuable and enlightening environment for interdisciplinary exchange and networking, as well as the opportunity to initiate new research collaborations. We greatly value your participation and look forward to an engaging and intellectually stimulating meeting.

Ruth Edge
Chair of ARR 2025

Scientific Committee

- Dr Ruth Edge (Chair, Dalton Cumbrian Facility, The University of Manchester)
- Professor Fred Currell (Dalton Cumbrian Facility, The University of Manchester)
- Dr Alex Baidak (Dalton Cumbrian Facility, The University of Manchester)
- Professor Jason Parsons (University of Birmingham)
- Professor Jonathan Coulter (Queen's University Belfast)

Key Information

Please come to the registration on arrival to register and collect your conference badge.

Day	Opening Times
Monday 9th June	08:00 – 18:30
Tuesday 10th June	08:00 – 22:15
Wednesday 11th June	08:30 – 15:00

Conference Social Events

Event	Date/Time	Venue
Welcome Reception	Monday 9th June - 17:20 - 18:30	Derwent Suite
Tour of DCF	Tuesday 10th June - 13:30 - 16:30	DCF
Conference Dinner	Tuesday 10th June - 19:00 - 22:00	Derwent Suite

Conference Programme

Monday 9th June 2025

Time	Session	Area
08:00 - 09:10	Registration and Arrival Refreshments	Bar Area/Conservatory
09:10 - 09:30	Introduction and Welcome by Ruth Edge & Zara Hodgson	Derwent Suite
09:30 - 11:00	**Session 1 - Space** Session Chair: Fred Currell Invited Speaker **Andrew Coates -** Space weather effects in the solar system Proffered Talks **Adrija Bhowmick -** Molecular Dynamics Simulations of Thermal Cycling Effects on Lunar Construction Materials **Andy Smith -** Creation of a 'Virtual-Moon' in the laboratory – an important step in enabling humanity's return to our satellite world **Jonathan Cousins** - Mechanical and Chemical Evolution of Potential Lunar Construction Materials Under Simulated Lunar Conditions	Derwent Suite
11:00 - 11:20	Refreshments	Derwent Suite/Conservatory
11:20 - 12:50	**Session 2 - Radio Protection** Session Chair: Liz Ainsbury Invited Speaker **Chris Jones -** Future Challenges and Solutions in Defence Radiation Protection Proffered Talks **Rhona Anderson -** Genetic and Cytogenetic Family Trio study of British nuclear test veterans. **Carmel Mothersill -** Approaches to the development of biomarkers for low dose radiation exposure **Jude Ferrier -** Experimental actinide nano-chemistry for the future interim storage of the civil UK plutonium inventory	Derwent Suite
12:50 – 13:00	**Sponsor Talk - Screen Europe (Platinum Sponsor)**	Derwent Suite
13:00 - 14:00	Buffet Lunch & Poster Session	Derwent Suite/Falls Brasserie
13:00 -14:00	Committee Meeting	Boardroom
14:00 - 15:30	**Session 3 - Nuclear/Radiation Chemistry & Physics** Session Chair: Steve Hepworth Invited Speaker **Mats Jonnson -** How ionizing radiation affects the integrity of deep geological repositories for spent nuclear fuel	Derwent Suite

	Proffered Talks **Krasimir Maslarov -** Investigating PVDF radiolysis in aqueous environment **Vasily Sorokin -** Dosimetric and radiobiological characterisation of a 28 MeV proton beam delivered by the MC-40 cyclotron **Marcus Webb -** A New Simulation Toolkit for Radiation Chemistry (MIRaCLE)	
15:30 - 15:50	Refreshments	Derwent Suite/Conservatory
15:50 - 17:20	**Session 4 - Radiation Biology/DNA Damage Repair** Session Chair: Nial Byrne Invited Speaker **Joanne Lysaght -** Radiotherapy as an effective immunomodulator to enhance response rates to immune checkpoint inhibition Proffered Talks **Lydia Mcquoid -** Impact of novel gold nanoparticle formulations on indirect effects of radiation **Morgan Rycroft -** Radiosensitization through CDK12 Inhibition **Tongchuan Wang -** Metabolic effect induced by mannose and related metabolic gene mediated radiosensitisation of HPV negative head and neck Squamous Cell Carcinoma **Fred Currell -** Fast-ion irradiation for rapid vaccine manufacture, getting ready for the next pandemic!	Derwent Suite
17:20 - 18:30	Drinks Reception & Poster Session	Derwent Suite

Tuesday 10th June 2025

Time	Session	Area
08:00 - 09:00	Registration and Arrival Refreshments	Bar Area/Conservatory
09:00 - 10:30	**Session 5 - Medical Isotopes** Session Chair: Adriana Ceruso Invited Speaker **Stephen Archibald -** Radionuclide production, separation and labelling: routes to optimising radiopharmaceutical availability Proffered Talks **Dipak Babar -** Production of Radioactive Nanoparticles of ^{44}Sc and ^{43}Sc: Pioneering the Future of Medicine **Olatunde Michael Oni -** Investigation of the cell chemical definition **Volkan Yasakci -** Radioisotopic-Blended Copper Nanoparticles: Target Development, Separation and Synthesis	Derwent Suite
10:30 - 10:50	Refreshments	Derwent Suite/Conservatory
10:50 - 12:20	**Session 6 - BIR - Radiotherapy** Session Chair: Mike Kirby Invited Speaker **Peter Hoskin -** Reirradiation: Myths and Reality Proffered Talks	Derwent Suite

	Liz Harron - Practical Approaches to Reirradiation **Kristina Small -** SoRTEd: Science of Radiotherapy Education - Improving Patient Understanding and Confidence in Radiotherapy **Jane Shortall -** The implementation of Gaussian Process Regression to Inform Voxel-Based Analysis when Dealing with Sparse and Irregular Time-series Longitudinal Data	
12:20 – 13:30	**Sponsor Talk - RPS (Platinum Sponsor and Sponsor of DCF Tour)**	Derwent Suite
12:30 - 13:30	Sit-down Lunch	Falls Brasserie
13:30 - 14:30	Travel to DCF	
14:30 - 16:30	Tour of DCF	
16:30 - 17:30	Travel back to Keswick/Lodore Falls	
19:00 - Late	Conference Dinner	Derwent Suite

Wednesday 11th June 2025

Time	Session	Area
08:00 - 09:00	Registration and Arrival Refreshments	Bar Area/Conservatory
09:00 - 09:30	AGM	Derwent Suite
09:30 - 10:30	Weiss Medal Winner - Anthony Chalmers	Derwent Suite
10:30 - 10:50	Refreshments	Derwent Suite/Conservatory
10:50 - 12:20	**Session 7 - Clinical/Translational** Session Chair: Asma Sarwar Invited Speaker **Navita Somaiah** – Forward and reverse translation to drive therapeutic advances in breast cancer radiotherapy Proffered Talks **Emily Jessop -** Establishing LGR5 expression levels in Head and Neck Cancer to explore the clinical potential of LGR5-directed therapeutics **Milaan Patel -** Supersonic Gas Curtain Ionization Profile Monitor: A Non-Invasive beam diagnostics for FLASH Proton Therapy **Chris Talbot -** Treatment time and circadian genotype interact to alter the severity of radiotherapy side-effects in prostate cancer patients	Derwent Suite
12:20 - 12:30	Closing remarks	Derwent Suite
12:30 - 13:30	Sit-down Lunch and depart	Falls Brasserie

Invited Speakers

Stephen Archibald

Prof Steve Archibald (King's College London) established an independent career in molecular imaging and drug development at the University of Hull (2000-2023) In 2010, he formed new links to funders, local charities, pharma and the NHS to develop infrastructure for positron emission tomography (PET) imaging and translational capabilities. He secured £4.2 M to build preclinical PET radiochemistry and imaging facilities (the Positron Emission Tomography Research Centre (PETRC), completed in 2014). A concurrent phase of this development was to construct clinical imaging facilities (Jack Brignall PET-CT Centre) to provide improved routine patient care for the NHS with the capacity for future research scanning. A partnership was formed with the Daisy Appeal and a not-for-profit company set up with the charity trustees (Daisy Medical Research Ltd). This further funded infrastructure and a second cyclotron, forming the Molecular Imaging Research Centre (MIRC) for GMP radiopharmaceutical production at Castle Hill Hospital. An innovative approach was taken to utilise the latest compact cyclotron technology and couple this with microfluidic technology for research. The aim was to improve efficiency in molecular imaging research and translational capability, whilst generating intellectual property and commercial value.

From October 2021-May 2023, Archibald was the overall Director of the newly formed Hull Molecular Imaging Centres (HuMIC) development (PETRC, MIRC and Jack Brignall PET-CT Centre), a >£15 M investment in medical imaging and theranostics research infrastructure. Archibald joined King's College London in May 2023 as a Professor of Molecular Imaging and the Head of Department of Imaging Chemistry and Biology. He is now developing new opportunities for research utilising the most comprehensive infrastructure for translational molecular imaging and theranostics research in the UK (PET Centre, CARL laboratories and PERL GMP laboratories all co-located at St Thomas' Hospital).

Abstract: Radionuclide production, separation and labelling: routes to optimising radiopharmaceutical availability

Objective: Reliable and scalable access to a wide range of radionuclides coupled with innovative chemical methodology underpins the development and application of radiotheranostics in cancer diagnosis and therapy.[1] Innovation is required to ensure that there is a step-change in the availability of radiopharmaceuticals in nuclear medicine.

Results: We have carried out development work to optimise cyclotron-based production of a range of radiometals and radiohalides, allowing improved access for radiopharmaceutical development and clinical translation.[2] Selected examples are presented including results from the DESNZ Medical Radionuclide Innovation Programme (MRIP) Innovation project to establish a new production capability for iodine-124 in the UK by: (1) Design and manufacture of [124Te]TeO2 targets; (2) Proton beam irradiation to produce iodine-124 via the 124Te(p,n)124I nuclear reaction; (3) design and construction of an automated processing module to isolate iodine-124 in the form of a [124I]NaI solution; (4) Quality control checks and radiolabelling

reactions. High purity radiometal feedstocks have been shown to offer major improvements in the isolated molar activity of radiopharmaceuticals, we have developed cation exchange monoliths for processing radiometals.[3] Due to its higher permeability and mass transfer, quantitative release of a purified radiometal solution in high concentration can be achieved using weak acidic solutions. Owing to mesoporous structures, monoliths can also potentially act as microreactors to simplify the complete process from radiometal purification to in situ chelator radiolabelling reactions. We have demonstrated this methodology and validated with a clinically used radiopharmaceutical. We have investigated metallo-organic supramolecular cages, to develop a novel reagentless, rapid and simple radiolabelling method (CageTag).[4] We have examined how the functionalisation of the cage vertices influences radiolabelling efficiency with [99mTc]TcO4– along with the in vitro and in vivo properties of the resulting constructs. Encapsulation efficiency of [99mTc]TcO4– was determined in dose-response experiments and in a range of in vitro stability assays biologically-relevant media. The lead candidates were further evaluated in vivo by dynamic planar scintigraphy to access key dynamic information on the biodistribution of the radiolabelled constructs.

Conclusion: Innovative accelerator targetry along with microfluidic separation technologies offer improved access to radionuclides and high-quality feedstocks for radiolabelling reactions. Chemical methods can be used for solid phase labelling or supramolecular encapsulation to offer the potential for step-change improvements to clinical radiopharmaceutical access.

[1] B.P. Burke and S.J. Archibald, Handbook of radiopharmaceuticals (MR Kilbourn and PJH Scott, Editors),, 2nd edition 2021, 291-323.
[2] R. Harper et al. Appl. Rad. Isotop. 2024, 210, 111381.
[3] P. He, et al. React. Chem. Eng., 2016, 1, 361–365.
[4] B. P. Burke, et al. J. Am. Chem. Soc. 2018, 140, 16877

Anthony Chalmers

Anthony Chalmers is Chair of Clinical Oncology at the University of Glasgow, Director of the CRUK RadNet Centre Glasgow and Co-Director of the Scottish Brain Tumour Research Centre of Excellence. His clinical practice at the Beatson West of Scotland Cancer Centre is devoted to the treatment of patients with brain tumours, and he runs the Translational Radiation Biology laboratory in the School Cancer Sciences. His main research ambition is to improve outcomes for patients with glioblastoma by combining radiotherapy with drug therapies that target the DNA damage response, but his interests and activities extend across other cancers of unmet need.

He is Chief Investigator for a portfolio of early phase clinical trials evaluating the PARP inhibitor olaparib and the ATM inhibitor AZD1390 in combination with radiotherapy and/or chemotherapy in the treatment of glioblastoma and collaborates with other UK investigators on novel clinical trial platforms including BRAIN-MATRIX and the CONCORDE study in non-small cell lung cancer.

From 2016-19 he was Chair of the UK's Clinical and Translational Radiotherapy Research Working Group (CTRad) and in 2020 he co-founded the CRUK RadNet Radiotherapy-Drug Combinations Working Group. From 2020-24 he was an Executive Board Member of the European Association for Neuro-Oncology (EANO) and a member of the Medical Research Council's Molecular and Cellular Medicine Board.

He was a co-recipient of the BIAL Award in Biomedicine 2023 and received the European Society of Radiotherapy and Oncology (ESTRO) Interdisciplinary Award in May 2024.

Abstract: Chipping away at the therapeutic ratio: can inhibitors of the DNA damage response improve outcomes for patients with brain tumours?

Inhibition of components of the DNA damage response (DDR) has been shown to enhance radiation sensitivity in multiple cancer models, both in vitro and in vivo. While numerous early phase clinical trials of DDR inhibitors in combination with radiation have now been successfully completed, there is still no conclusive evidence that these agents improve outcomes for patients treated with radiotherapy. Our early observation that the radiosensitizing properties of PARP inhibitors are most pronounced in rapidly proliferating cells has been validated by early phase clinical trial data showing exacerbation of acute radiation toxicity in rapidly proliferating tissues such as oropharyngeal and oesophageal mucosa. Lack of radiosensitisation in non-proliferating cell populations raises that prospect that PARP inhibitors might be more effectively combined with radiation therapy in patients with brain tumours, where the critical normal tissues are non-replicating. ATM inhibitors are much more potent radiosensitizers than PARP inhibitors, but less is known about their impact on normal tissue toxicity since they have only recently progressed to the clinic, although preclinical in vivo data are encouraging.

In this presentation I will review the key preclinical and clinical data relating to the use of PARP and ATM inhibitors in glioblastoma, the most prevalent and aggressive primary brain tumour. Since brain radiotherapy is associated with significant neurocognitive toxicity, I will consider the relative impact of these DDR inhibitors on late radiation responses in the brain as well as effects on tumours. Exploration of the mechanisms underlying the multifaceted effects of these inhibitors has taken us into the realm of radiation induced neuroinflammation and a variety of different cell types within the microenvironment of glioblastoma and the normal brain.

Peter Hoskin

Peter Hoskin trained in clinical oncology at the Royal Marsden Hospital London and has been consultant in clinical oncology at Mount Vernon Cancer Centre, Northwood UK since 1992. He is Professor in Clinical Oncology in the University of Manchester, Honorary Professor in Clinical Oncology at University College London and honorary consultant in clinical oncology at the Christie Hospital, Manchester and University College Hospital, London. In Manchester he leads the Radiotherapy Related Research Group (RRR) and personal research interests focus on brachytherapy, radiosensitisation, biomarkers, radiotherapy quality assurance and palliative radiotherapy. He has published extensively and was Editor of Clinical Oncology for 15 years. He is now Clinical Editor for Radiotherapy and Oncology and sits on several journal editorial boards including Brachytherapy and the Journal of Contemporary Brachytherapy.

Abstract: Reirradiation: Myths and Reality

The ESTRO/EORTC consensus on re-irradiation has defined a number of scenarios in which this may occur. Type I reirradiation is defined by a second (or more) course of radiotherapy to the same site as previous with clear overlap. In type 2 reirradiation there is no overlap but reirradiation in the same or a different organ. When considering a course of re-irradiation there are a number of parameters to consider including patient and tumour characteristics, previous and current oncological treatments including radiotherapy details, assessment of the cumulative doses and indications for reirradiation. There is a clear difference between palliative re-irradiation aiming to control symptoms with relatively low doses and radical re-irradiation aiming to achieve local control requiring high dose radiation.

Common examples of radical retreatment include head and neck cancers, lung cancer, prostate cancer and uterine and vulvovaginal cancers; examples of palliative reirradiation are metastatic bone pain and spinal metastases.

In general, a primary course of radiotherapy will have delivered a dose of radiation at or close to tolerance of surrounding organs at risk (OARs) and therefore re-irradiation will inevitably exceed conventional tolerance if a similar dose is given again and simple summation of doses is used. In practice this does not seem to be as big a problem as a theoretical consideration would suggest.

Much will depend upon the ability of normal tissues to recover radiation tolerance, likely to be high in rapidly dividing tissues such as bowel and low in CNS and kidney. There is little radiobiological data on which to base this but clearly the longer the period between primary and re-irradiation the better the chances or recovery and low toxicity. However, there will always be a compromise between maximising recovery and minimising opportunity for further tumour regrowth.

This does mean that there will inevitably be a higher risk of normal tissue damage with re-irradiation and a clear but sensitive discussion with the patient regarding the likelihood of severe toxicity balanced by the likelihood of tumour control is vital when undertaking these procedures. Thresholds for what is acceptable to the clinician and what is acceptable to patients and carers will vary.

Chris Jones

Chris is Principal Technical Authority for Radiation Protection and Regulatory Sciences at AWE Nuclear Security Technologies, a non-departmental public body tasked with protecting the UK against nuclear and radiological threats. In this role, he is responsible for the technical leadership, policies and strategies of a team of about 200 radiation protection professionals who provide health physics, dosimetry, instrumentation, radiometrology and environmental monitoring services for civilian and military personnel across the Defence Nuclear Enterprise, Homeland Security, and conventional defence sectors. Chris has been working as an operational radiation protection professional since 2009 and has been an accredited Radiation Protection Adviser since 2014.

He is a Fellow of the Society of Radiological Protection, a Chartered Radiation Protection Professional, Chair of the Defence Community of Action on RP Skills and a member of ICRP Task Group 127 which considers exposure situations and categories of exposure.

Abstract: Future Challenges and Solutions in Defence Radiation Protection

There are a wide range of scenarios in which people, be that workers or the public, may encounter radiological hazards as a result of a 'defence' or 'homeland security' activity. Defence personnel use X-ray generators and radioactive materials (such as tritium light sources in gun sights) during their day-to-day work; the defence nuclear programme utilises fissile material to power nuclear submarines and within the nuclear deterrent; and defence and security personnel can be tasked to respond into environments in which radioactive material has been accidently or deliberately released. It is therefore important to have an enduring and effective radiation protection capability to ensure exposure to ionising radiation is kept as low as reasonably practicable for everyone who could potentially be exposed in any of these scenarios.

Efforts to maintain that enduring and effective capability will face a number of challenges over the coming years. There is a growing UK-wide shortage of radiation protection professionals, caused by a perfect storm of a rapidly growing demand from new civil nuclear builds, fusion power research, decommissioning and waste management, the medical sector as well as growing defence programmes, at exactly the same time as the demographics of the profession are meaning a large percentage of the workforce are nearing retirement. There are new technologies being implemented which will present new radiological hazards in the workplace but also opportunities to improve radiation protection controls if they can be properly harnessed. Societal expectations regarding a tolerable level of risk and the technologies people expect to be used to protect them will continue to evolve, which in time will drive changes in legislation and regulatory expectations. The lack of research over several decades into many of the underpinning data and assumptions used to specify required controls will become increasingly apparent as the scenarios encountered move further away from those seen in the 1950s and 1960s when the data was originally gathered.

To counter these challenges, a number of new initiatives have been implemented or planned, central to which is a much more collaborative approach across and outside defence than has been seen for many years; including joint training initiatives across the Defence Nuclear Enterprise and research collaborations with academia and national laboratories. It will take a UK-wide effort to meet the challenges of the defence sector, but hopefully with benefits that will spread well beyond it.

Mats Jonsson

Mats Jonsson received his MSc-degree in Chemistry and Chemical Engineering at the Royal Institute of Technology (KTH) in Stockholm, Sweden, in 1991 and his PhD-degree in Nuclear Chemistry at the same university in 1995. After one year as a postdoc at NRC Canada in Ottawa (Steacie Institute for Molecular Science) followed by one year as a research engineer at ABB Corporate Research in Västerås, Sweden, he returned to the Royal Institute of Technology as assistant professor in nuclear chemistry in 1997. He was promoted to associate professor in 2003 and to full professor in 2005.

He was head of the department of chemistry from 2009 to 2011 and vice dean of the School for Chemical Science and Engineering from 2011 to 2017. He was also director of undergraduate studies from 2016 to 2017. Since July 2023, he is the deputy head of the School of Engineering Sciences in Chemistry, Biotechnology and Health at the Royal Institute of Technology.

His research is focused on interfacial radiation chemistry with particular focus on radiation induced dissolution of spent nuclear fuel and radiation induced corrosion of metallic materials (e.g., copper). He is also active in the fields of heterogeneous photocatalysis and radiation and radical chemistry of polymers in solution. Since 2009 he was a member of the Miller Trust Committee (organizing international conferences in radiation chemistry). Between 2013 and 2017 he was the vice chair of the trust and between 2017 and 2023 he was the chair of the trust.

Abstract: How ionizing radiation affects the integrity of deep geological repositories for spent nuclear fuel.

Several countries operating nuclear power plants plan to place the spent nuclear fuel in geological repositories. In these repositories, the highly radioactive spent nuclear fuel is isolated from the biosphere through natural and engineered barriers. Before building and taking a geological repository into use, thorough safety assessments are required. Given the extremely long time-spans that must be covered by such assessments (100 000 – 1 000 000 years), it is a very challenging task to provide accurate mechanistic descriptions of the processes that could occur in the repository. In addition to the geological and geochemical processes that can be foreseen to occur at a repository site, the impact of the inherent radioactivity of the spent nuclear fuel on the integrity of the barriers as well as on the fuel itself must be accounted for.

In this presentation, the impact of ionizing radiation emitted from spent nuclear fuel on the engineered barriers of the Swedish and Finish repository concept (KBS-3) is discussed. The engineered barriers according to this concept are a copper-coated cast iron canister containing the fuel and a layer of bentonite clay embedding the canister inside drilled holes in the bedrock. Under normal operating conditions, both these barriers are exposed to ionizing radiation during the initial phase of the repository life time. Hence, they could potentially be affected by radiation-induced processes. In the event of a complete barrier failure, the spent nuclear fuel will come in contact with groundwater. This will have a direct impact on the dissolution of the fuel and the subsequent release of radionuclides into the biosphere.

In this presentation, radiation-induced process in the bentonite clay, on the surface of the copper-coated canister and on the surface of the spent nuclear fuel itself will be presented and discussed in view of their impact on the long-term safety of a geological repository.

Joanne Lysaght

Joanne Lysaght is Professor in Cancer Immunology and Immunotherapy in Trinity College Dublin. She is the Research Theme Lead for Cancer Immunology at the Trinity St. James's Cancer Institute and President of the Irish Society for Immunology. Prof. Lysaght's research group focus on a number of different areas around the central theme of cancer immunology and immunotherapy. Currently, a major research focus is investigating the impact of chemotherapy and radiotherapy to enhance anti-tumour immunity when used in combination with immunotherapies, namely immune checkpoint inhibitors.

The majority of research in the cancer immunology and immunotherapy group is focused on upper gastrointestinal cancer, particularly oesophageal cancer but also gastric, pancreatic and ovarian cancer.

Abstract: How ionizing radiation affects the integrity of deep geological repositories for spent nuclear fuel.

Oesophageal adenocarcinoma (OAC) presents a significant challenge in oncology, with a five-year survival rate of just 20% due to its aggressive nature, late-stage diagnosis and intrinsic resistance to standard treatments. The rising incidence of OAC in Western countries, driven by increasing incidence of obesity, gastroesophageal reflux disease and Barrett's oesophagus, underscores the urgent need for more effective therapies. The advent of immune checkpoint inhibitors (ICI's) as a cancer therapy has revolutionised the management of many advanced malignancies, however their impact is limited by intrinsic immune suppression and resistance mechanisms. These immunotherapies attempt to counteract this malignant-mediated immune suppression.

The first FDA approved immune checkpoint inhibitor was anti-CTLA-4 (ipilimumab) in 2011 and since then approval has been granted for antibodies targeting PD-1, PD-L1 and LAG-3 for a wide range of cancer types. With a better understanding of the tumour microenvironment, its impact on local immunity and how these immunotherapies work has led to studies assessing the role of radiotherapy as an immunomodulatory adjuvant to ICIs. We and others have assessed dosing and scheduling of radiotherapy and/or chemoradiotherapy in combination with ICIs in the neoadjuvant or first line setting both in vitro and in the ex vivo setting in upper gastrointestinal cancers. In addition, we have also assessed the introduction of HDACi with radiotherapy to enhance the efficacy of ICIs and the immunogenicity of tumour cells in vitro, in order to provide clinical rationale for this multi-pronged approach to enhance response rates to ICIs.

Navita Somaiah

Dr Navita Somaiah is a Clinician Scientist and Group Leader (Translational Breast Radiobiology) in the Division of Radiotherapy and Imaging at the ICR and an Honorary Consultant Clinical Oncologist in the Breast Unit at The Royal Marsden NHS Foundation Trust.After completing her DPhil in radiation biology at the University of Oxford, she became the first recipient of an ICR Clinician Scientist Fellowship award. Her research focuses on biological optimisation of radiotherapy by improving tumour response whilst minimising normal tissue toxicity, for a truly personalised approach.

Her team leads innovative, biology-driven clinical trials in patients with high-risk breast cancers, with linked translational research. She is the chief investigator of the international Phase I/II KORTUC trial that is looking at innovative approaches to tackling tumour hypoxia and radiosensitisation. She is the translational lead for two neoadjuvant breast radiotherapy trials at RM/ICR aimed at defining the radiation-induced immune landscape in primary breast cancers for optimal radio-immunotherapy combinations. Alongside this, her team are involved in developing more sensitive imaging technologies and novel biomarkers to monitor response to therapy, pick up early relapse/resistance and predict treatment responsiveness in high-risk breast cancers.

Abstract: Forward and reverse translation to drive therapeutic advances in breast cancer radiotherapy

High-risk or locally advanced breast cancer (BC) patients who either do not achieve radiological/pathological complete response (CR) to neo-adjuvant treatment or are inoperable due to extent of disease or medical co-morbidities, continue to remain at high risk of loco-regional and distant relapse despite current therapy options. These patients represent an area of unmet need where novel approaches to better loco-regional control are required to improve outcomes. Alongside this, more sensitive imaging technologies and novel biomarkers are needed to i) monitor response to therapy, ii) pick up early relapse/radioresistance and iii) predict treatment responsiveness.

In this talk I will share some of the forward and reverse translational approaches that my team are using to drive therapeutic advances in BC radiotherapy (RT), using the KORTUC phase 2 trial testing a novel radiosensitiser (H2O2) in locally advanced BC as an example. KORTUC patients undergo pre-RT, 2W and 12M post-RT biopsies and longitudinal DCE/DW-MRI to assess response. Super-resolution ultrasound scans of tumours are also performed, allowing visualisation of microvasculature changes in response to RT at an unprecedented micrometre resolution, while extracting quantitative biomarkers (eg. vessel density/diameter). This trial therefore gives us a unique opportunity to understand radiation-induced changes in the tumour immune microenvironment and their relationship with hypoxia and angiogenesis. Pilot results from gene set enrichment analysis of bulk RNA sequencing from paired pre- and 2W post-RT biopsies showed upregulation of immune and stromal pathways after RT. Immune cell populations derived via xCell showed significant increases in fibroblasts, dendritic cells and macrophages at 2W post-RT. Partial least squares discriminant analysis and gene weightings to separate groups based on 12M MRI responses identified MB21D2 as an important gene separating complete response and progressive disease. Our early data suggests baseline immune activity and immune responses to RT are important determinants of long-term response.

Oral Presenter Abstracts

O1 - Molecular Dynamics Simulations of Thermal Cycling Effects on Lunar Construction Materials

In addition to the oral presentation, this abstract will also be displayed as a poster on posterboard 2

Miss Adrija Bhowmick[1], Mr. Caue P. De Souza[2], Prof. Nigel J. Mason[1], Dr. Felipe Fantuzzi[2]
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The pursuit of lunar settlements marks a significant milestone in humanity's exploration of space. With NASA's Artemis programme, we are embarking on a transformative era of lunar exploration aimed at advancing scientific knowledge and providing habitable infrastructure to support astronauts during extended lunar missions [1,2]. The Moon endures relentless environmental challenges, including high-energy radiation, temperature fluctuations ranging from 100 K to 400 K, and a lack of atmospheric protection [3,4]. Ensuring the well-being of astronauts in such a harsh environment necessitates the development of innovative materials capable of withstanding extreme conditions. These advancements will facilitate the construction of durable lunar habitats and foster sustainable human settlement expansion. The goal of the present work is to employ molecular dynamics (MD) simulations to investigate the structural stability and performance of candidate materials for space applications under extreme environmental conditions. Specifically, we simulated thermal cycling in the range of 100 K to 400 K to mimic the dramatic temperature changes on the lunar surface. This study primarily focuses on silica (SiO_2), the primary component of glass used in space missions [5] and a material abundantly found on the Moon [6], and polyethylene, a widely studied polymer binder for lunar concrete [7,8]. Our simulations utilise the Meso-Bio-Nano (MBN) Explorer software [9] and the reactive CHARMM force field [10,11], enabling detailed modelling of molecular behaviour under these conditions. Preliminary results reveal that the crystalline form of SiO_2 possesses remarkable stability against temperature cycling, attributed to its high melting point and highly crystalline structure. The amorphous form of SiO_2, was created by melting and rapidly quenching into glass, also exhibits significant resilience. The initial pre-optimised geometry of a box of polyethylene was created using CHARMM-GUI [12] and a temperature cycle was performed on the optimised system using MBN Explorer. To further explore the effects of the temperature cycle, recent efforts have focused on introducing nanoscale defects [13], such as nano-cracks, within the amorphous SiO_2 structure to evaluate their behaviour under thermal stress. This follows experimental findings where polyethylene samples, after experiencing irradiation-induced cracks, demonstrated healing when subjected to temperature cycling. By simulating a similar phenomenon in amorphous SiO_2, we aim to assess its potential for self-repair or improved resilience under thermal stress. This work underscores the value of MD simulations in narrowing down potential experimental setups. Future research will expand on this work by integrating Irradiation Driven Molecular Dynamics (IDMD) method [14] available in MBN into simulations, refining defect modelling, increasing simulation scale, and broadening the directory of suitable materials for lunar habitat construction. These computational insights aim to complement ongoing experimental work and accelerate the development of robust materials for extraterrestrial applications.

O2 - Creation of a ‘Virtual-Moon’ in the laboratory – an important step in enabling humanity’s return to our satellite world

Dr Andy Smith[1], Dr Ruth Edge, Dr Kay Dewhurst, Dr Mel O'Leary, Dr Aidan Milston, Dr Samir Shubeita, Professor Fred Currell
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The Moon is a harsh mistress. Human engineering structures – from rovers to personnel habitats – built on the lunar surface will have to endure an extremely hostile environment for many years, probably decades. Constantly bombarded by radiation from the solar wind, they will experience wide temperature swings, from < -150 °C in the depths of a lunar night, to > +150 °C in the middle of the lunar day.

Radiation damage, particularly from ions, is known to cause mechanistic failure – similar to ‘work-hardening’ – which can lead to deleterious effects such as embrittlement. Without the benefits of high temperatures to enable self-annealing to help cure such defects, these mechanical consequences of radiation damage can lead to accelerated structural failure of materials.

Adapting the methodology developed for understanding the effects of extreme radiation levels experienced by structural materials deployed in nuclear reactors, DCF plans to combine radiation from its ion beam accelerators – mimicking the solar wind – with a new temperature controlled sample stage that can repeatedly take the sample from lunar day to lunar night and back again in a matter of hours. Using this combination we can test structural material candidates for their resilience to the harsh lunar environment in a practically short time.

This paper describes both the problem, and how such a ‘virtual-moon’ can be created in the laboratory in order to test candidate materials for lunar structural materials – here on Earth – to perfect those required for construction of future lunar bases to support humanity’s return to the Moon.

O3 - Mechanical and Chemical Evolution of Potential Lunar Construction Materials Under Simulated Lunar Conditions

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[1]University Of Kent, Canterbury, United Kingdom

Establishing a sustainable and continuous Lunar presence hinges on identifying the most suitable materials for Lunar habitats to be constructed from. Any habitat constructed on the Lunar surface would be exposed to extreme temperatures, radiation, vacuum and meteorite impacts. Not only will the mechanical and chemical properties of these materials need to remain stable against this harsh Lunar environment, but they must also protect its inhabitants whilst doing so.

To ensure cost-effectiveness and sustainability, it is crucial to utilize lunar resources as much as possible, and lightweight material when not, in building these structures. The selection of materials will be pivotal for long-term human habitation on the Lunar surface. The chosen materials must withstand the challenges of the Lunar environment; therefore, their structural and protective properties must be tested over extended periods, ensuring their reliability for 10+ years.

This work aims to inform on the most suitable Lunar habitat construction materials. By experimentally exposing various materials to 20+ years of simulated Lunar environment to identify how their properties change.

O4 - Genetic and Cytogenetic Family Trio study of British nuclear test veterans.

Prof Rhona Anderson[1]
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Veterans of the British nuclear testing programme represent a population of ex-military personnel who had the potential to be exposed to ionising radiation through their participation at nuclear testing sites in the 1950s and 1960s. In the intervening years, members of this population have raised concerns about the status of their health and that of their descendants, as a consequence. Radiation dose estimates based on film badge measurements of external dose recorded at the time of the tests suggest any exposure to be limited for the majority of personnel, however, only ~20% of personnel were monitored and no measurement for internalised exposure are on record. Here, we assay for chromosomal evidence of historical radiation exposure in a group of aged nuclear test veterans, using multiplex in situ hybridisation (M-FISH), for comparison with a matched group of veterans who were not present at nuclear test sites. In total, we analysed 9379 and 7698 metaphase cells using M-FISH (24-colour karyotyping) from 48 nuclear test and 38 control veteran samples, representing veteran servicemen from the army, RAF and Royal Navy. We observed stable and unstable simple- and complex-type chromosome aberrations in both nuclear test and control veterans' samples, however find no significant difference in yield of any chromosome aberration type between the two cohorts. We do observe higher average frequencies of complex chromosome aberrations in a very small subset of veterans previously identified as having a higher potential for radiation exposure, which may be indicative of internalised contamination to long-lived radionuclides from radiation fallout. By utilising published whole genome sequence analysis data of a sub-set of the same family groups, we examined for but found no relationship between paternal chromosome aberration burden, germline mutation frequency and self-reported concerns of adverse health in family members, suggesting that the previously reported health issues by participants in this study are unlikely to be associated with historical radiation exposure. We did observe a small number of families, representing both control and nuclear test cohorts, showing a relationship between paternal chromosome aberrations and germline mutation sub-types. A final part of the GCFT study involves examining for any chromosomal instability in the unexposed adult children and this data is similarly being integrated to examine for any relationship in genetic and/or cytogenetic aberrations between the veteran father and their child.

O5 - Approaches to the development of biomarkers for low dose radiation exposure

Professor Carmel Mothersill[1], Dr Aftab Taiyab[1], Professor Colin Seymour[1], Dr David Williams[2]
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One of the major issues in radiation protection is predicting the impact of widespread exposure of people and the environment to low doses of radiation. It is now well accepted that the mechanisms induced by low dose exposures to ionising radiation (LDR) are different to those occurring after high dose exposures. However, the downstream effects of these mechanisms are unclear as are the quantitative relationships between exposure, effect, harm and risk. In this presentation we will discuss the mechanisms known to be important with an overall emphasis on how so-called “non-targeted effects” (NTE) communicate and coordinate responses to LDR. Targeted deposition of ionising radiation energy in cells causing DNA damage, is still regarded as the dominant trigger leading to all downstream events whether targeted or non-targeted. We regard this as an over-simplification dating back to formal target theory. It ignores that last 100 years of biological research into stress responses and signalling mechanisms in organisms exposed to toxic substances including ionising radiation. We will provide evidence for situations where energy deposition in cellular targets alone cannot be plausible as a mechanism for LDR effects. An example is where the energy deposition takes place in an organism not receiving the radiation dose. We will also discuss how effects after LDR depend more on dose rate and radiation quality rather than actual dose, which appears rather irrelevant. Finally, we will use recent evidence from studies of cataract and melanoma induction to suggest that after LDR, post-translational effects such as protein mis-folding, or defects in energy metabolism or mitochondrial function may dominate the aetiology and progression of disease. A focus on such novel pathways may open the way to successful prophylaxis and development of new biomarkers for better risk assessment after low dose exposures.

O6 - Experimental actinide nano-chemistry for the future interim storage of the civil UK plutonium inventory

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During the reprocessing of spent nuclear fuel, valuable Pu and U is separated from waste fission products. This material is safely and securely stored in sealed packages under inert atmospheres as actinide oxide nanopowders, either as PuO2 or as a mixture of UO2 and PuO2 known as MOX.[1] PuO2 is associated with a variety of storage challenges due to the radiation emitted, radiolysis of atmospheric contaminants such as water to produce H2, and the heat generated by radioactive decay.[2] It is also known that industrial interim storage conditions could promote undesirable adventitious reactions with contaminant gases present in the storage atmospheres including H2, however this reactivity is not currently well understood.[3] This work supports the development of industrial nuclear safety-cases by exploring the catalytic behaviour of nuclear materials under realistic storage conditions. As Pu cannot be studied within the university setting, surrogate materials (UO_2, ThO_2) have been synthesised using the industrial routes. The effects of Pu radioactivity on the surface chemistry of the surrogate materials can be simulated using the alpha beamline at the Dalton Cumbrian Facility and preliminary work to build a suitable reaction cell will be discussed. This poster will present initial work including the design of a reactor to perform in-situ reactivity studies using Diffuse Reflectance Infrared Fourier Transform Spectroscopy (DRIFTS) coupled with mass spectrometry. DRIFTS has been used to interrogate the reactivity of surrogate materials with contaminant gases and early results relating to reactivity with water will be presented. In addition, method development and initial results from the analysis of radioactive and highly air/moisture-sensitive samples using vibrational spectroscopy, surface area analysis and powder x-ray diffraction will be presented.

O7: Investigating PVDF radiolysis in aqueous environment

In addition to the oral presentation, this abstract will also be displayed as a poster on posterboard 6

Mr Krasimir Maslarov[1], Dr Aliaksandr Baidak[1]
[1]University of Manchester, Manchester, United Kingdom

Purpose/Objective: PVDF was one of the first fluoropolymers to be discovered and is widely used in consumer products from paints to seals. Its radiolysis primarily leads to dehydrofluorination. As such, most studies of PVDF radiolysis have focused on changes in mechanical properties or on the HF yield, especially when looking at irradiation in water. Chain-scission products, when reported, are typically only mentioned in reference to their very low yield.

However, with PFAS coming under ever-increasing scrutiny, and a potential ban on all PFAS compounds in the EU, identifying potential sources of toxic short-chain PFAS grows ever more important.

Material/Methods: PVDF powder, pellets & films were placed in a vial partially filled with 1 mM NaOH. The samples were then irradiated in a Gamma irradiator (Foss Therapy Services Model 812). The supernatant was analyzed using ion-selective electrodes, LC-MS & 19F NMR to determine fluoride release and determine the presence and identity of any short-chain PFAS released. The gas in the headspace was analyzed using GC-MS to identify the volatiles released, and the solid polymer with IR & UV-vis spectroscopy to observe structural changes in the polymer.

Results: Fluoride yield was calculated over a range of doses (0-100 kGy), and was in line with previous values in literature (2-3 molecules/100 eV). Said yield has been found to decrease with dose, again matching what had been previously reported. A linear relationship between transmittance at certain wavenumbers and dose was established, with changes in the spectrum corresponding to expected structural changes (C=C bond formation, O-H bond formation). Short-chain fluorocarbons were identified in the headspace, even at low doses. These were primarily fluoropropanes, both saturated and unsaturated, hydrogenated and unsaturated. The supernatant was further studied with LC-MS.

Conclusions: This study investigated the radiolysis of PVDF, confirming previous results about fluoride release, and giving new insight into the formation of short-chain PFAS under gamma irradiation. The fluoride yield decreased with increasing dose, consistent with prior research. Structural changes in PVDF were observed via spectroscopy. These results show the potential for toxic short-chain PFAS formation during PVDF degradation. With increasing regulatory scrutiny on PFAS, understanding the full suite of PVDF's decomposition products is necessary for understanding the potential environmental and health risks associated with its use.

O8 - Dosimetric and radiobiological characterisation of a 28 MeV proton beam delivered by the MC-40 cyclotron

In addition to the oral presentation, this abstract will also be displayed as a poster on posterboard 6

Mr Vasily Sorokin[1], Dr Ben Phoenix[3], Dr Maria Fabbrizzi[2], Professor Jason Parsons[2,3], Dr Mark Hill[1]
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Proton beam therapy (PBT) is an advanced radiotherapy technique capable of precisely delivering radiation doses to tumours due to the physical characteristics of the proton beam, notably the Bragg peak phenomenon. However, uncertainties in clinical effectiveness arise because of increases in linear energy transfer (LET) around the Bragg peak region. In this study, comprehensive Monte Carlo simulations using Geant4 were conducted to characterise a pristine proton beam with an initial energy of (27.90 ± 0.05) MeV across multiple absorber configurations. These configurations included no absorber, and various combinations of polymethyl methacrylate (PMMA) and polypropylene (PP) blocks to degrade beam energy. Track-averaged and dose-averaged LET values were meticulously calculated following established protocols, revealing significant increases in LET as proton energy decreased near the Bragg peak. The variation in DNA damage complexity as a function of the resulting energy spectra was also calculated using Monte Carlo Damage Simulation (MCDS) software (Stewart et al 2011 Radiat. Res. 176:587).

Experimental validation involved assessing the biological impact of the proton beam on head and neck squamous cell carcinoma (HNSCC) and HeLa cell lines. A noticeable reduction in cell survival correlated strongly with increasing LET values. Detailed analyses of DNA damage, performed via gammaH2AX/53BP1/OGG1 immunofluorescence microscopy and multiple comet assay methods, indicated that higher LET values were predominantly associated with persistent single-strand DNA breaks and complex DNA damage types that were markedly resistant to repair mechanisms. Furthermore, increasing LET was associated with higher frequencies of micronuclei formation, indicative of substantial chromosomal damage.

This integrated physical and biological characterisation underscores the importance of LET variations across the Bragg peak, demonstrating their direct influence on the DNA damage profile, biological effectiveness, and therapeutic efficacy of PBT. These findings support the need for careful consideration of LET distribution in clinical proton therapy planning to enhance treatment outcomes.

O9 - A New Simulation Toolkit for Radiation Chemistry (MIRaCLE)

In addition to the oral presentation, this abstract will also be displayed as a poster on posterboard 8

Dr Marcus Webb[1], Professor Fred Currell[2]
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Purpose/Objective: The Manchester Inhomogeneous Radiation Chemistry by Linear Expansions (MIRaCLE) toolkit will be introduced. This toolkit offers a fast and user-friendly means to solve radiation chemistry problems by solving the reaction-diffusion equation for user-specified chemical reactions. It accounts for the inhomogeneous spatial distributions of chemical species over time. The toolkit is applicable to various areas of radiation science, including radiobiology, radiation therapy, nuclear medicine, nanoparticle dose enhancement, nuclear waste management, and handling of special nuclear materials. Its ability to include interactions at solid-fluid boundaries enables the solution of many critical problems in these domains.

Material/Methods: Our method efficiently solves the reaction-diffusion equation using spectral methods, representing species concentrations through linear expansions in spectral functions. The time-evolution is split into sequential diffusion and reaction steps, with the diffusion steps solved exactly and the reaction steps solved numerically to second-order accuracy in the timestep. A second-order splitting method alternates between diffusion and reaction steps, resulting in a fast, stable, and accurate method. By selecting appropriate spectral functions, interactions with bounding surfaces (solid-fluid interfaces) are naturally included without performance penalties.

Although the software handles three-dimensional spatial problems, its architecture and underlying mathematics exploit spherical, cylindrical, or translational symmetries for more compact problem representations and increased performance. The entire toolkit can be run using Jupyter notebooks, providing a simple and intuitive user experience, which will be valuable for widespread use.

Results and Conclusion: MIRaCLE has demonstrated its value to the nuclear industry by solving 600 different versions of a radiolysis problem relevant to the safe storage of plutonium. These solutions, representing various physical conditions, were explored on a laptop within hours, compared to days of super-compute time required by Monte Carlo approaches.

We will present recent work comparing MIRaCLE simulations of radiation chemistry problems to Monte Carlo simulations. Water radiolysis examples will demonstrate that MIRaCLE achieves similar modeling outcomes as Monte Carlo methods but in a faster and more user-friendly package. MIRaCLE significantly reduces computational time and resource requirements, achieving results in hours on a laptop compared to days on supercomputers using Monte Carlo methods.

References:

- Bradshaw et al., "A new approach for simulating inhomogeneous chemical kinetics," Scientific Reports, 2023.
- Tran et al., "Geant4-DNA modeling of water radiolysis beyond the microsecond: An on-lattice stochastic approach," International Journal of Molecular Sciences, 2021.

O10 - Impact of novel gold nanoparticle formulations on indirect effects of radiation

In addition to the oral presentation, this abstract will also be displayed as a poster on posterboard 19

Miss Lydia Mcquoid[1], Professor Jonathan Coulter[1]
[1]Queen's University Belfast, Belfast, United Kingdom

Introduction: Ionising Radiation (IR) is a widely used treatment modality for various forms of cancer, however, off-target radiation damage is a common occurrence complicating therapeutic responses. Irradiated cells can release factors that propagate radiation damage to neighbouring unirradiated cells, an effect termed the radiation-induced bystander effect (RIBE)[1_2]. Understanding the impact of radiotherapy-enhancing agents on the RIBE is important to maximise their full clinical impact – whether they enhance tumour cell kill beyond the irradiated volume or stimulate proliferation in neighbouring cells. Further to local bystander effects, increasing evidence suggests that radiotherapy in combination with immunotherapy can promote a systemic immune response capable of reducing the growth of untreated secondary tumours – the radiation induced abscopal effect (RIAE)[3_5]. Two novel chemokine-targeting gold nanoparticles (AuNPs), antagonising CXCR2 and CXCR4 have proven to act as effective radiosensitisers. Both AuNP formulations were examined for potential RIBE impacts in models of prostate (PCa) and head and neck cancer (HNSCC), with initial studies underway investigating RIAE in vivo.

Methods: Direct radiation sensitivity (0-6 Gy) and bystander effects (transfer of conditioned media from irradiated cells) were evaluated in DU145 (PCa), FaDu (HNSCC), and MOC1 (HNSCC) cell lines using micronuclei formation, clonogenic, and apoptosis assays. The secretion of RIBE-inducing factors was measured in FaDu cells using a cytokine array. A murine model of HNSCC using subcutaneously implanted MOC1 cells was used to investigate the ability of IR, AuNP, and immunotherapy (anti-PD1) to prime an immune response towards primary tumours. One dose of AuX2R treatment was administered directly to tumours 24 h prior to radiation treatment (x2 8 Gy fractions), with anti-PD1 administered twice weekly for 4 weeks.

Results: Treatment of unirradiated bystander cells with conditioned media from AuNP and IR-treated cells resulted in significant increases (>50%) in the formation of micronuclei representing an inhibitory RIBE ($p<0.001$). Clonogenic and apoptotic assays confirmed strong radiosensitisation by both AuNP formulations ($p<0.01$). Analysis of cytokine release from AuNP treated and irradiated FaDu cells indicates that IR causes an increase in pro-survival cytokines, but AuNPs abolish this effect. Initial observations from an ongoing in vivo study indicate that triple combination therapy (IR, AuX2R, anti-PD1) promotes survival compared to groups with a single or double treatment combination.

Discussion: Enhancement of inhibitory bystander effects in unirradiated cells receiving media from AuNP-treated irradiated cells suggests that the AuNP formulations are capable of propagating damage further than the irradiated volume. In a clinical setting this could mean targeting a smaller tumour area might achieve the same amount of tumour damage, thus reducing the likelihood of damaging off-target effects to healthy tissue. Results from the cytokine array might suggest that different mechanisms of action are at work in IR-induced and AuNP/IR-induced bystander effects.

O11 - Radiosensitization through CDK12 Inhibition

In addition to the oral presentation, this abstract will also be displayed as a poster on posterboard 20

Miss Morgan Rycroft[1], Dr Helen Bryant[1]
[1]University of Sheffield, Sheffield

Resistance to radiotherapy is an ongoing problem in the treatment of many cancers, specifically those with sophisticated DNA damage response (DDR) mechanisms, such as Non-small cell lung cancer (NSCLC). New treatment regimes that can target the DDR in combination with radiotherapy are therefore of utmost interest. CDK12 is a transcription regulating kinase thought to be involved in the expression of long genes, including many involved in the Homologous Recombination (HR) repair pathway. The enzymatic activity of CDK12 is controlled by Cyclin K, a 70kDa protein subunit. The novel compound CT7439 is a Cyclin K degrader developed by Carrick Therapeutics, previously shown to display inhibitory activity against CDK12. We report that molecular degradation of Cyclin K with CT7439 induces an increase in sensitivity to radiotherapy across a range of cell lines, and that this occurs as a consequence of altered DDR pathway utilisation. Using clonogenic and cell survival assays, we tested the sensitization abilities of CT7439 in a range of NSCLC and other cancer cell lines. A decrease in expression of HR proteins was observed using RT-PCR and western blot analysis, and further immunofluorescence assays indicated an increase in error prone NHEJ-mediated repair. These results provide strong rationale for the inhibition of CDK12 in radiotherapy resistant cancers.

O12 - Metabolic effect induced by mannose and related metabolic gene mediated radiosensitisation of HPV negative head and neck Squamous Cell Carcinoma

Dr Tongchuan Wang[1], Dr. Connor Brown[1], Ms Meabh Doherty[1], Dr. Niall Byrne[1], Dr. Rayhanul Islam[1], Dr Jie Feng[1], Dr. Cancan Yin[1], Dr Sarah Chambers[1], Miss Lydia Mcquoid[1], Dr Letitia Mohamed-Smith[1], Dr. Karl Butterworth[1], Dr. Emma Kerr[1], Professor Jonathan Coulter[1]
[1]Queen's University Belfast, Belfast, UK

Radiotherapy (RT) is a cornerstone of multidisciplinary cancer treatment, particularly for HPV-negative head and neck squamous cell carcinoma (HNSCC), a subtype with poor prognosis1. However, the severe adverse effects of RT pose significant clinical challenges. This study investigates the potential of mannose, a safe and natural monosaccharide, to enhance the radiosensitivity of HPV-negative HNSCC by targeting phosphomannose isomerase (PMI), a key enzyme in mannose metabolism. Using CRISPR/Cas9 technology, PMI was knocked out (PMI KO) in HNSCC cells, resulting in a 20-fold increase in sensitivity to mannose, as shown by cell viability assays. In an in vivo model, PMI KO combined with mannose significantly delayed tumor growth by 16 days compared to controls. Seahorse assays, ATP measurements, and 13C-glucose labeling LC-MS revealed reduced oxygen consumption rates (OCR), extracellular acidification rates (ECAR), metabolic quiescence, and decreased ATP levels in PMI KO cells treated with mannose. Clonogenic assays demonstrated that PMI KO combined with mannose enhanced radiosensitivity, with a sensitizer enhancement ratio (SER) of 1.51 under normoxia (21% O_2) and 1.35 under hypoxia (0.2% O_2). Additionally, mannose increased radiation-induced unresolved DNA double-strand breaks (2-fold) and reactive oxygen species (ROS) in PMI KO cells. Under hypoxic conditions, a major contributor to radiation resistance, mannose treatment combined with PMI ablation reduced succinate levels, leading to HIF-1α destabilization and enhanced radiosensitivity. 3D tumor sphere models confirmed that mannose-induced metabolic suppression, coupled with PMI depletion, improved oxygen levels within the tumor spheres, facilitating oxygen-dependent radiosensitization. These findings highlight the radiosensitizing potential of mannose and uncover its novel mechanisms, including metabolic reprogramming and HIF-1α downregulation. Mannose shows promise as a clinically significant adjuvant to radiotherapy for HPV-negative HNSCC, addressing a critical need for effective, less toxic treatments.

O13 - Fast-ion irradiation for rapid vaccine manufacture, getting ready for the next pandemic!

In addition to the oral presentation, this abstract will also be displayed as a poster on posterboard 18

Professor Fred Currell[1], Mr Jordan Elliot[1], Dr Ruth Edge[1], Dr Mel O'Leary[1], Dr. Mustafa Ozan Atasoy[2], Prof Muhammad Munir[2]
[1]Dalton Cumbrian Facility, University of Manchester, Westlakes Science & Technology Park, Moor Row, UK,
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Purpose/Objective: The COVID-19 pandemic showed the need for safe handling of dangerous viruses and rapid vaccine development. Currently, handling such pathogens requires costly, specialized facilities. This project aims to address this by developing a method to make high-risk virions safe, using fast ion radiation. The track structure of fast ions suggests that they are an excellent choice for doing this whilst keeping external structural integrity [1]. Virions are the fully formed, version of a virus outside of a host cell. Upon entering a host they interfere with its mechanisms, using their nucleic acid payload to reproduce. However, once properly inactivated through damage to this payload, they can be safely handled at a significantly lower cost, enabling broader research into viral biology. These inactivated virions could also provide feedstock for rapidly manufactured vaccines. Minimising alteration to the outer structure of these inactivated virions will result in better vaccines. Hence understanding and limiting changes to virions' outer structures whilst inactivating them is important to both deliver useful mimics into laboratories for measuring structure or mechanistic effects and to deliver the most effective inactivated vaccine feedstock. Using a radiation transport and genomic damage model [1], projections suggest that fast ions from a facility such as the Dalton Cumbrian Facility (DCF) could make sufficient vaccine feedstock for the entire UK population in about 20 days.

Material/Methods: MS2 bacteriophage is a small, non-enveloped RNA virus that infects bacteria, making it a well-studied model for RNA virus behaviour. Its structural similarities to coronaviruses, including its RNA genome and capsid-based stability, make it a useful model for testing viral inactivation methods in a safe and cost-effective manner. 5 MeV helium ions were used to irradiate MS2 bacteriophage, using DCF's spinning wineglass sample handling system [2]. Samples, each with a known number of proliferating units, were irradiated to various doses. In some cases, these samples were additionally stabilised with glycerol. A colony-forming assay was used to assess the number of active bacteriophages remaining in the samples.

Results: For samples both with and without glycerol stabilisation, first-order inactivation kinetics was observed, i.e. the number of detected active virions decreased exponentially with the dose used. This trend is indicative of a single-hit inactivation model, as would be expected [1]. The rate of loss was consistently greater in the samples without glycerol stabilisation, suggesting indirect damage mechanisms by radiolysis were involved in these samples alongside the direct damage mechanism. Transmission electron microscopy of samples irradiated to levels where less than 1/1000th of the bacteriophage remain active showed many intact virions, validating the idea that fast ions can inactivate virions without significantly damaging the outer capsid.

Conclusions: Helium ion irradiation has demonstrated both the expected first-order inactivation kinetics and the maintaining of intact capsids in MS2 bacteriophage, giving confidence in the concept of fast ion virion inactivation for both safe use of otherwise high containment viruses in low containment level laboratories and as potential vaccine feedstock.

O14 - Production of Radioactive Nanoparticles of ^{44}Sc and ^{43}Sc: Pioneering the Future of Medicine

In addition to the oral presentation, this abstract will also be displayed as a poster on posterboard 23

Dr Dipak Babar[1], Mr Volkan Yasakci[1], Dr Aidan Milston[1], Dr Ruth Edge[1], Dr Robert Jones[1], Professor Fred Currell[1]
[1]The Dalton Cumbrian Facility, The University of Manchester, Westlakes Science & Technology Park, Moor Row, United Kingdom

Objectives: Radioactive scandium isotopes, particularly Scandium-44 (^{44}Sc) and Scandium-43 (^{43}Sc), have gained significant attention in recent years due to their promising applications in nuclear medicine, targeted radiotherapy, and imaging techniques. These isotopes exhibit favourable half-lives, decay properties, and chemical stability, making them ideal candidates for diagnostic and therapeutic applications. On the other hand, Nanomaterials have revolutionized cancer research by their high surface area, tunable size, and functionalization capabilities. Considering these effective properties of radioactive materials and nanomaterials, we have synthesized Radioactive nanoparticles of Sc isotopes. The whole process has been carried out in fully automated fashion.

Method: We investigated the production of ^{44}Sc via the ^{44}Ca(p,n)^{44}Sc and ^{43}Sc via the ^{43}Ca(p,n)^{43}Sc nuclear reaction using a proton beam. A 50 µm thick ^{44}Ca/^{43}Ca target was irradiated with an 8 MeV proton beam at a current of 1 µA for a duration of 1 hour. Post-irradiation, the produced scandium isotopes were analysed using gamma-ray spectroscopy (HPGe detector) to determine radionuclidic purity and activity. The DGA and DOWEX-50 resins were used for the separation of Sc radioisotopes from parent material. Radioactive nanoparticles were synthesized via the co-precipitation method by reacting separated Sc radioisotopes with ammonium bicarbonate, facilitating controlled precipitation and nanoparticle formation. Synthesized radioactive nanoparticles again analysed using gamma-ray spectroscopy to confirm the activity.

Results: The separation of radioactive Sc from Ca was successfully confirmed using Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES), demonstrating a 98% purity of Sc with a recovery rate of 90%. The successful synthesis of radioactive Sc nanoparticles was validated through High-Resolution Transmission Electron Microscopy (HRTEM) and Scanning Electron Microscopy (SEM), providing detailed insights into their morphology and size distribution. HRTEM analysis confirmed the formation of ultrafine nanoparticles with an average diameter of ~1 nm, while SEM measurements indicated a diameter of ~5 nm. More importantly, the radioactive nanoparticles of Sc exhibited expected radioactivity, which was quantified using gamma spectroscopy.

Conclusion: The synthesis of radioactive nanoparticles of ^{44}Sc and ^{43}Sc was successfully carried out using an automated process, ensuring precision and reproducibility. The procedure effectively confirmed successful dissolution and separation. Additionally, the measured radioactivity of the produced radioactive nanoparticles exhibited strong agreement with theoretical cross-section calculations, validating the efficiency and reliability of the production method.

The synthesized radioactive nanoparticles exhibit significant potential for applications in cancer treatment, offering a promising avenue for targeted delivery to brain and enhanced therapeutic efficacy. Future research will focus on further optimizing target preparation, improving surface functionalization of nanoparticles for enhanced tumor specificity, and conducting comprehensive in vivo stability and biodistribution assessments.

O15 - Investigation of the cell chemical definition

In addition to the oral presentation, this abstract will also be displayed as a poster on posterboard 21

Mr Olatunde Michael Oni[1], Dr Tessa Davey[1], Dr Tim Smith[1]
[1]Bangor University, Bangor, United Kingdom

Targeted radionuclide therapy (TRT), with alpha and auger electron emitters has lately been noted as a mode of treating cancer with high efficacy. Many radioisotopes are being studied computationally and experimentally for both tumour diagnostic and therapeutic applications. Monte Carlo (MC) simulation toolkits play a key role in optimisation to address problems of dose localisation and internalisation of radioisotopes in TRT. The chemical makeup of the cell is fundamental in MC simulation thus it is imperative to consider the effect of the chemical makeup while simulating cellular absorbed dose and other dosimetry parameters. Cells are generally assumed to have the density of water, and as such are theoretically assigned water values especially in the computation of medical internal radiation dosimetry (MIRD) parameters. This study employed the simulation toolkits of Geant4 application for tomographic emissions (GATE), to study the effect of chemical definition of individual cancer cell on the absorbed dose to the nucleus by different therapeutic radioisotopes. Results of the study employing Wilcoxon signed rank test and analysis of variance (ANOVA) revealed a close agreement with no significant difference of the absorbed dose to the nucleus of spherical water-considered cell and cell nucleus with chemically defined material composition. Cells with water definition presented higher mean absorbed dose than the chemically defined cells for some of the radioisotopes considered. The mean absorbed dose to a 4µm nucleus from a uniformly distributed radioisotope investigated in this study revealed an inverse relationship with the radius of the source distribution (0 µm to 4 µm) within the nucleus, leading to a more than 10-fold reduction in the mean absorbed dose.

O16 - Radioisotopic-Blended Copper Nanoparticles: Target Development, Separation and Synthesis

In addition to the oral presentation, this abstract will also be displayed as a poster on posterboard 22

Mr Volkan Yasakci[1], Dr Dipak Babar[1], Dr Aidan Milston[1], Dr Aliaksandr Baidak[1], Professor Fred Currell[1]
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Objective: The global rise in cancer incidence has led to ongoing advancements in diagnostic and therapeutic agents with notable success. In this context, researchers are synthesising a range of radionuclides, typically using medical cyclotrons or nuclear reactors. Ideally, these radionuclides should be suitable for both imaging and treatment, and their half-lives must be adequate for labelling, visualisation, and therapeutic procedures. In addition, the target material should be readily available, cost-effective, and capable of yielding high-quality outcomes [1–3]. Recently, theragnostic applications have expanded rapidly. This work is carried out within the broader 'Optimised Production of Theragnostic Isotopes of Copper and Scandium (OPTICS)' project, which aims to implement an automated, modular process—spanning transmutation through to synthesis—for radiopharmaceutical production. My project specifically involves the use of blended copper radioisotopes (natCu/61Cu, natCu/64Cu, 64Cu/67Cu). By performing transmutations at the Dalton Cumbrian Facility, we seek to develop these copper-based nano-pharmaceuticals within a fully automated system that includes dissolution and separation, nanoparticle synthesis, and antibody labelling.

Materials and Methods: For the production of copper radioisotopes, natural nickel (natNi) and enriched 60/61/64Ni isotopes were selected as target materials. The solid nickel isotopes were dissolved in concentrated HCl with a few drops of 30% H2O2. The pH of the resulting solution was then adjusted to 9 using ammonia, diluted with deionized water, and subjected to electrodeposition at 4.5 V and 50 µA. Nickel targets were transmuted using protons at energies up to 10 MeV and alpha particles at energies up to 15 MeV between 1 and 2 hours. A Dowex 1x8 chloride resin was used for the separation process. First, the column was conditioned with 9 M HCl, after which the nickel fraction was eluted with 9 M HCl, and the copper fraction was subsequently eluted with 0.1 M HCl. Copper nanoparticles were then synthesized at 30°C for one hour under a nitrogen flow using catechin. All procedures were conducted in a fully automated, computer-controlled system comprising three units: the Target Head (Unit 1), the Separation Board (Unit 2) located inside the hot cell, and the Vortex Mixer (Unit 3).

Results and Discussion: The gamma counter results obtained indicate that the transmutation of 61/64/67Cu was successfully achieved. Furthermore, based on the size measurements and electron microscopy findings, the Cu nanoparticles range from 1 to 50 nm in diameter.

O17 - Practical Approaches to Reirradiation

Miss Elizabeth Harron[1]
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Reirradiation after previous radiotherapy has long been an area of uncertainty and cautiousness. In the past at Nottingham, calculations were done on an individual ad-hoc basis, generally by the treating clinician, based on their experience and knowledge of the patient. Requests for therapeutic reirradiation have dramatically increased in recent years at Nottingham, since stereotactic ablative body radiotherapy (SABR), including pelvic reirradiation, was commissioned in England in 2020. This has led to a need to change ways of working and formalise radiobiology calculations in order to provide goals for treatment planning and advise on dose and/or fractionation for the reirradiation. In this presentation, the challenges of implementing this will be presented, along with the practical solutions adopted at our centre using Excel and Raystation radiotherapy treatment planning system. This includes the development of an issued in-house spreadsheet and the commissioning of a commercially available 2Gy per fraction equivalent dose (EQD2) calculation tool. Several interesting case studies will be presented, and remaining challenges in the workflow will be discussed.

O18 - SoRTEd: Science of Radiotherapy Education - Improving Patient Understanding and Confidence in Radiotherapy

In addition to the oral presentation, this abstract will also be displayed as a poster on posterboard 28

Dr Kristina Small[1]
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The availability of clear and comprehensive information is a key aspect of cancer patient support to relieve anxieties and allow better understanding of treatments[1] [2].

This is particularly relevant for radiotherapy, with patients and indeed the general public typically having a lower awareness of the treatment compared with chemotherapy or surgery[3] [4]. Furthermore, patients may also negatively associate radiotherapy with the dangers of radiation[5] – potentially compounded by misinformation and negative media portrayals[6].

The primary focus of radiotherapy information is on patient experience, including planning and delivery as well as potential side effects. Information on the basic science of radiotherapy – how it works, descriptions of technical, biological and physical terms – is under-represented in-patient literature. This project therefore aims to determine interest in learning about the science of radiotherapy with a view to developing resources based on patient feedback.

Here, we will present the results of a survey investigating patients' views and opinions on learning about the science of radiotherapy treatment. Patient experiences in accessing information and other aspects of cancer treatment that they are interested in learning about were also included in the survey. Demographic information was recorded, including age, ethnic background, gender and highest level of education – both general and more specifically a participant's highest science qualification.

Patients were recruited through a number of local and national cancer charity and support groups, either offering general support or focusing on a particular type or types of cancer. In total, 259 participants submitted a completed survey.
The two key questions within the survey asked patients if they were interested in learning about the science of radiotherapy and, if such information was available, how likely they would be to access it. Responses were overwhelmingly positive, with 83% of participants indicating interest in the science of radiotherapy and 88% responding that they would be 'likely' or 'very likely' to access such resources.

Participants had numerous reasons for wanting to learn about the science of radiotherapy, including simple curiosity and wanting to expand upon the information given by clinicians before or during their treatment. A significant proportion highlighted mental health and anxieties surrounding the treatment, indicating that an improved understanding of the more technical aspects of radiotherapy could make them feel more at ease throughout their treatment.

Aside from radiotherapy, the survey results also indicated that cancer patients are interested in learning about other aspects of cancer diagnosis and treatment. In particular, significant numbers of participants highlighted chemotherapy, immunotherapy and medical imaging as areas they would be keen to learn more about.

In conclusion, the SoRTEd project has thus far demonstrated clear interest among cancer patients in learning about the science of radiotherapy. The next planned steps involve interaction with patient focus groups to gain a deeper understanding of how they would like to access such information. This will feed into the development and testing of educational resources, with the long-term aim of making these available to radiotherapy patients – satisfying curiosities and allaying fears or anxieties during cancer treatment.

O19 - The implementation of Gaussian Process Regression to Inform Voxel-Based Analysis when Dealing with Sparse and Irregular Time-series Longitudinal Data

In addition to the oral presentation, this abstract will also be displayed as a poster on posterboard 27

Dr Jane Shortall[1], Dr Eliana Vasquez Osorio[1], Dr Andrew Green[2], Professor David Wong[3], Dr Tanuj Puri[1], Professor Peter Hoskin[1,4], Professor Ananya Choudhury[1,4], Professor Marcel van Herk[1], Dr Alan McWilliam[1]
[1]Division of Cancer Sciences, The University of Manchester, Manchester, United Kingdom, [2]EMBL's European Bioinformatics Institute, Cambridge, United Kingdom, [3]School of Medicine, University of Leeds, Leeds, United Kingdom, [4]Clinical Oncology, The Christie NHS Foundation Trust, Manchester, United Kingdom

Purpose: One in three prostate cancer patients will experience biochemical recurrence (BCR), detected via rises in Prostate Specific Antigen (PSA). Routine post-radiotherapy follow-up consists of six-monthly PSA monitoring, and measurements are often irregular and sparse. Consequently, BCR can remain undetected for months and the opportunity for early intervention missed.

Short-term post-radiotherapy PSA data could act as an early surrogate of BCR, which has been linked to too low dose in certain anatomy via voxel-based analysis (VBA).

We aim to identify associations between radiotherapy dose and dynamic short-term follow-up PSA. We implement Gaussian Process (GP) regression to interpolate regularly sampled PSA values, to inform VBA testing the association of post-radiotherapy PSA with radiotherapy dose over time.

Methods: Planning CTs, dose distributions and clinical information, including repeat post-radiotherapy PSA measurements, were collected for 219 prostate cancer patients treated with conformal hypo-fractionated radiotherapy (2005-2007) at a single academic centre. Patients had at least two post-radiotherapy readings, and did not experience BCR within three-years of follow-up.

A population-based GP model was produced using log-transformed PSA trajectories (MagmaClustR). The posterior mean for each patient was sampled at 6-monthly time-points between 0 and 48-months, for use in VBA.

CTs were deformably registered to an arbitrarily chosen reference patient and dose distributions mapped to the same anatomy (in-house software). Dose distributions were flipped in the left-right direction and included in analysis twice. Target Registration Error analysis was performed to account for registration uncertainty. Dose distributions were blurred using a 3D Gaussian filter corresponding to the variation of landmarks made at the seminal vesicles and apex (≤0.9cm).

A Spearman's rank test was performed between PSA and dose in each voxel of the dose distribution, at each 6-monthly time-point (in-house software). Correlation coefficients (ρ) for each voxel were collected to create ρ-maps. Permutation testing was performed (n=1000) to correct for multiple comparisons and determine regions of significant correlation. ρ values corresponding to $p \leq 0.05$ were identified from the distribution of extreme ρ-statistics, and iso-ρ levels plotted on the observed ρ-map. Time-points were analysed separately.

Results : A large region superior to the prostate, covering the seminal vesicles, of significant association between planned radiotherapy dose and PSA was identified for all time-points up to 36-months ($p \leq 0.05$). This region indicated where lower dose was correlated with higher PSA (indicative of higher BCR).

The region changed over time, growing from approximately 500cm3 at 0-months, to approximately 900cm3 at 24-months follow-up. After 24-months, the region rapidly decreased in volume, reaching 600cm3 at 30-months follow-up. This could indicate that PSA within two-years of follow-up is most informative of potential treatment failure.

Conclusion: We present a method to successfully incorporate sparse time series data into GP informed VBA to inform of early outcome prediction for prostate cancer patients treated with radiotherapy. Our results suggest that radiotherapy dose could be influencing post-radiotherapy PSA. Once validated in other external datasets, these results could be used to re-stratify patients after radiotherapy, allowing for more informed follow-up schedules, earlier intervention, and refined target volumes.

O20 - Establishing LGR5 expression levels in Head and Neck Cancer to explore the clinical potential of LGR5-directed therapeutics

Miss Emily Jessop[1], Mrs Amy Bates[2], Miss Inês Ferreira[1], Mr Jakub Mieczysław Pęczek[1], Dr Jose Valverde Lopez[1], Mr Glenn Harden[2], Dr John Tadross[2], Mr Malcolm Cameron[2], Mr Chang Bon Man[2], Miss Phoebe Roche[2], Miss Theofano Tikka[3], Dr William Ince[2], Profesor Rajesh Jena[1,2], Dr Maike de la Roche[1], Dr David Fernandez-Antoran[1], Dr Gillian Barnett[1,2], Dr Marc de la Roche[1]
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Objective: Head and Neck Cancer (HNC) patients frequently develop locoregional recurrence or distant metastases following (chemo)radiotherapy, highlighting the need for more effective treatment strategies. A novel, highly specific antibody to the stem cell marker LGR5 (α-LGR5) has previously been validated for detection of high expression levels in colorectal and hepatocellular carcinoma; and B cell acute lymphoblastic leukaemia relative to healthy tissue (1). Moreover, α-LGR5 has been validated in multiple therapeutic modalities such as an antibody drug conjugate version (α-LGR5-ADC) that shows remarkable efficacy in specifically targeting these cancer types.

In this study we aimed to identify levels of LGR5 expression in HNC squamous cell carcinoma (SCC) cells and cell lines and to determine the therapeutic efficacy of α-LGR5-ADC in targeting HNC cell lines.

Methods: GR5 expression was measured in 2 HNC cell lines (FaDu, hypopharyngeal SCC and SCC-61 from oral tongue) in addition to LoVo (colorectal carcinoma) and HEK293T cells (human embryonic kidney). Reverse transcription-quantitative polymerase chain reaction (RT-qPCR) was performed. Cells were fixed, permeabilised, blocked and immunostained with α-LGR5 or α-cytokeratin 5/6 primary antibodies and then with a secondary antibody, and imaged by immunofluorescence.

The cleavable linker ADC (α-LGR5-ADC) and non-cleavable control linker ADC (α-LGR5-ADCNC) were generated (1) and used to treat cells at varying concentrations. The level of metabolically active cells was measured, and the luminescent signal quantified.

Tumours and a segment of surrounding healthy tissue were harvested from patients with primary HNSCC undergoing surgical resection prior to radiotherapy at Cambridge University Hospitals as part of the Hamlet.rt Collect study. Immunofluorescence was performed on normal and tumour tissue paraformaldehyde-fixed paraffin-embedded (FFPE) biopsies.

Results: The two HNC cell lines expressed very low LGR5 levels relative to the LGR5-high LoVo cell line and LGR5-low HEK293T cells. These levels reflected sensitivity to α-LGR5-ADC treatment with LoVo cells being particularly sensitive (EC50 values for killing = 9 nM) and little to no treatment sensitivity displayed by the HNC cell lines and HEK293T cells.

Additionally, very few of the biopsies from HNC patients demonstrated LGR5 expression, <5% of carcinoma cells expressed detectable LGR5 levels, and this was consistent with LGR5 expression in healthy tissues. Interestingly, high levels of cellular LGR5 were confined to a lymphocyte population present in certain HNC tumours. The number of tumour-infiltrating LGR5high lymphocyte was consistent between matched healthy and malignant tissues.

Conclusion: Given the minimal levels of LGR5 detected in HNSCC cell lines and patient tissue, our results indicate that targeting LGR5 expressing cells in HNSCC tumours is not an effective therapeutic strategy. In

fact, if high LGR5 expression in tissue- and tumour-infiltrating lymphocytes is confirmed, LGR5-targeting therapeutics may negatively impact patient outcome. Further study of LGR5 expression on a larger subset of pre- and post-radiotherapy patients is ongoing.

We hypothesise that α-LGR5 can be used to identify the presence of LGR5-high lymphocytes and may be a predictor of HNC tumours that are responsive to checkpoint inhibition. Ultimately, HNSCC patients should be further stratified for LGR5 expression to identify individuals more likely to respond to LGR5-targeting therapeutics.

O21 - Supersonic Gas Curtain Ionization Profile Monitor: A Non-Invasive beam diagnostics for FLASH Proton Therapy

In addition to the oral presentation, this abstract will also be displayed as a poster on posterboard 31

Dr Milaan Patel[1,2], Dr Narender Kumar[1,2], Mr William Butcher[1,2], Mrs Farhana Thesni[1,2], Prof. Carsten Welsch[1,2]
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Introduction: Proton beam therapy enables conformal dose delivery due to the advantages of the Bragg peak. Real-time measurement of beam profile, position, current, and energy (dose) without disrupting the beam can enhance treatment efficacy in both preclinical and clinical settings. While existing devices provide real-time monitoring at conventional dose rates, achieving the same at FLASH dose rates remains a significant challenge. This presents an opportunity for novel real-time diagnostic approaches in FLASH proton beam therapy. This contribution presents the Supersonic Gas Curtain Ionization Profile Monitor (SGC-IPM), a non-invasive, two-dimensional beam profile and position measurement system, and explores its performance and the challenges of implementation in medical accelerators.

Methods: SGC-IPM uses a gas screen positioned in front of the beam on the vacuum side. Interaction with the beam ionizes the gas atoms which are then extracted maintaining their relative spatial distribution to reconstruct the 2D beam profile. The device was tested at a DC Pelletron accelerator at the Dalton Cumbria Facility in Whitehaven, UK, and the MC40 Cyclotron at the University of Birmingham, UK. Beam profiles were recorded across a range of energies (4–28 MeV) and currents (1–100 nA) with various beam sizes and shapes.

Results: The study presents 2D beam profile measurements, detailing data processing and improvements in detection time achieved across two experimental campaigns. The detector’s response to beam energy and current was analysed using a mathematical model based on beam fluence. This relationship was used to estimate the minimum detection time required to measure a beam profile, expressed in terms of the total dose delivered before detection. The device’s performance is assed using an example case study of dose delivery to a standard 1-liter clinical volume at a 15–20 cm depth in water.

Conclusion: This study demonstrates two-dimensional beam profile measurements using a detector whose response scales with beam fluence; a quantity independent of dose rate. This ensures consistent performance across both conventional and FLASH dose rates. The detector's unique response to beam current and energy suggests its potential for calibration-based predictions of these parameters. However, improving sensitivity and reducing the device's size remain key challenges. Addressing these issues is essential for successful integration with medical accelerators.

O22 - Treatment time and circadian genotype interact to alter the severity of radiotherapy side-effects in prostate cancer patients

In addition to the oral presentation, this abstract will also be displayed as a poster on posterboard 32

Prof Chris Talbot[1]
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Purpose: Circadian rhythm influences a wide range of biological processes, including efficacy and side effects of cancer treatment. Earlier evidence disagreed on whether risk of radiotherapy side-effects is affected by treatment time, probably due to differences in organs irradiated and time analysis methods. We previously showed an interactive effect of time and genotype of circadian rhythm genes on late toxicity after breast radiotherapy (1-3). This study aimed to replicate those results in a different cancer type.

Materials and Methods: We collected time of each radiotherapy fraction from patients in REQUITE prostate cancer cohorts. REQUITE was a multi-centre, prospective study in Europe and US (www.requite.eu). Enrolment was open for two and a half years through 26 centres in eight countries. Radiotherapy toxicity data was collected at baseline, after radiotherapy and one & two years later. Genome-wide SNP data was available typed with Illumina OncoArrays. The primary endpoints used were late rectal bleeding and urinary incontinence assessed by CTCAE v4. 861 prostate cancer patients with complete clinical and SNP data were included in the analysis. Local date-times for each fraction were converted into solar times as continuous predictors. Genetic chronotype markers were included in LASSO regression analyses with random forest feature selection to identify predictors of each end-point.

Results: For rectal bleeding at 24m, significant predictors include spread of treatment times across fractions (OR=1.57, 95%CI=1.2-2), BMI (OR=0.9, 95%CI=0.85-0.96), use of alpha blockers (OR=2.3, 3 95%CI=1.2-4.2) and PER3 circadian SNP rs696305 (OR=0.37, 95%CI=0.16-0.84). Treatment time (hours after sunrise) alone was non-significant but a significant interaction exists between the SNP and treatment time ($P < 0.001$) suggesting that circadian genotype modifies the time of peak radiotoxicity risk. Models achieve a ROC AUC of 0.66.

For urinary incontinence at 24m, significant predictors include radical prostatectomy (OR=3.2 95%CI=2.1-4.9), spread of treatment times across all fractions (sd, OR=1.5 95%CI=1.2-1.9), treatment time (hours before or after 1pm), OR=1.5 95%CI=0.3-0.7) and PER3 SNP rs172933 (OR=0.45 95%CI=0.25-0.82). A significant interaction exists between the SNP and treatment time ($P<0.001$) suggesting that circadian genotype modifies the time of peak radiotoxicity risk. Models have a ROC AUC of 0.67.

Conclusion: Both rectal and urinary side effects could be reduced by selecting the optimal treatment time based on the genotypes of circadian genes. Model-based predictions show 44% of patients could reduce their risk of rectal bleeding from 11% when treated at 9am to 5% when treated at 5pm, and predict a significant reduction in risk of urinary incontinence from 15% to 5% by avoiding treatment in the middle of the day.

Future clinical trials could stratify patients treated at optimal times compared to those scheduled conventionally to show that chronoradiotherapy is a cost-effective method of reducing side effects and improving quality-of-life.

P1 - Space, the final frontier – radiation implications of living on the moon

Mr Edwin Hsu[1,2], Mr Jordan Elliot[1,2], Mr Volkan Yasakci[1,2], Mr Alan Cross[3], Professor Fred Currell[1,2]
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"We choose to go to the Moon in this decade and do the other things, not because they are easy, but because they are hard, because that goal will serve to organize and measure the best of our energies and skills…" [1]. This famous challenge from President J. F. Kennedy's 1962 address continues to underscore the spirit behind current efforts to return to the lunar surface – this time we go with the aim of establishing a permanent base on the moon. And then on to Mars.

Just as metabolic function is vital to every living organism, robust energy systems are fundamental to space exploration. For a lunar base, these systems must reliably supply power even through the 14 Earth-day-long lunar night, ensuring all mission-critical operations continue uninterrupted.

Advanced nuclear technologies—such as nuclear batteries (radioisotope thermoelectric generators) and compact nuclear reactors—offer both reliable and long-duration energy solutions, ensuring continuous power where solar resources cannot serve. However, the harsh radiation and thermal cycling environment of space and the Moon itself necessitates thorough pre-flight testing of these systems to protect both equipment and crew, making radiation testing a critical step in mission planning. Rigorous ground-based assessments can help validate shielding, hardness of electronics, and related safety protocols—all essential elements to fulfil Kennedy's vision for bold exploration while maintaining the highest standards of safety and reliability.

But do we have the right testing capabilities and if not, what would they look like? Here we report how the UK is positioned to support the necessary tests.

Material/Methods: Using a combination of desk-based research, first-principles analysis and simulations, we are formulating descriptions of the various radiation environments experienced by power systems, their support electronics and shielding on journeys from the Earth to the Moon and Mars. A combination of further desk-based research and interviews with radiation facility managers have been/will be undertaken to assess the current capabilities and assess gaps in the UK's provision.

Results: By the time of the conference, we will be able to report on the expected range of radiation insults power systems intended for space applications can be expected to endure. Although the implications of these insults on living systems lies outside of the scope of this study, the data reported is likely to be of interest to the radiation protection and biological effects communities represented at the conference. An assessment of available testing facilities, ongoing upgrade activities and requirements not currently being met will be presented. Preliminary results show the Northwest and Midlands regions of England to have over 50% of relevant radiation sources, suggesting this might be a good area to locate future activities.

Conclusions: Returning to the moon and establishing a base there offer significant challenge but one which can inspire us to give the best of ourselves. The UK radiation science community has a clear role to play and has several key facilities available to it to pursue the ground-based preflight testing required.

P2 - Occupational radiation exposure to UK Orthopaedic Surgeons: A dose monitoring exercise

Miss Hannah Mancey[1], Kinga Zmijewska[1], Deborah Eastwood[2], Lynn Hutchings[3], Nicky Gibbens[1], Charlotte Lewis[4], Stephen Barnard[1]
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Breast cancer is the most common female cancer in the UK, accounting for 11,500 deaths per year, with around 1% of UK breast cancer incidences attributed to ionising radiation exposure [1, 2, 3] . A recently published epidemiological study reported an increased prevalence of breast and all-cause cancer among female orthopaedic surgeons compared to an age-matched female population, causing significant concern amongst the orthopaedic workforce [4]. The study was conducted using self-reported survey data from 672 surgeons across the United States and found a 2.9-3.9 fold excess risk of breast cancer within the female orthopaedic surgeon population [4]. Orthopedic surgeons are occupationally exposed to ionising radiation, with the majority of orthopaedic surgeons thought to be receiving an annual radiation dose of less than 2 mSv/year [5], which is below the 20 mSv/year occupational dose limit set for radiation workers in the UK. As a result of the concerned workforce, the British Orthopaedic Association approached UKHSA to assist in undertaking a radiation dose monitoring exercise. This monitoring exercise aimed to provide insight into the radiation doses received by orthopaedic surgeons in the UK during routine activities and identify any significant correlations with demographic factors.

The total radiation dose received by orthopaedic surgeons was monitored over 3 months using thermoluminescent dosemeters (TLDs) issued by the UKHSA, Personal Dosimetry Service. Participating surgeons were also sent an electronic questionnaire to capture self-reported information on the use and availability of Personal Protective Equipment (PPE) (including lead thickness, styles and sizes), biological sex, career stage and the approximate number and type of radiation-related procedures they perform. The survey also requested information regarding what recent (within in the past three years) radiation safety or protection training they had received.

A total of 189 surgeons were monitored for a continuous 3-month period. Our findings suggest that whilst these surgeons, as with the majority of radiation workers, likely receive a radiation exposure greater than that of the general population, none were found to have received a dose that would put them at risk of exceeding the 20 mSv yearly dose limit set by HSE's Ionising Radiations Regulations 2017. The highest recorded whole-body dose was 1.84mSv in the three-month wear period, equivalent to a 7.3mSv yearly exposure dose. Following personal dose monitoring and information collated from the self-reporting survey, no factor included in the survey was found to significantly influence radiation exposure dose. We report a lack of radiation protection training in the orthopaedic workforce surveyed, with 58.8% of respondents not having had any form of radiation protection training in the past three years. The BOA have created a working group aimed at identifying and understanding radiation exposure risks and improving protective measures in orthopaedic surgeons. The results of this exercise will help to inform as to future recommendations made by the BOA to ensure that the UK orthopaedic workforce remains appropriately educated and protected.

P3 - Low dose radiation effects are inherently unpredictable

Professor Colin Seymour[1], Pofessor Carmel Mothersill[1]
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Low dose radiation effects usually result from deliberate or accidental releases into the environment. Thus, the primary source of radiation is a radioactive isotope. The radiation dose rate is usually chronic, and the effects can be complicated by the speciation of the isotope due to other environmental conditions such as acidity, or other pollutants. In a previous paper our group has argued that because of this complexity, the dose rate is more relevant to the radiation response than the total dose absorbed by the organism or ecosystem under investigation. This can be clearly seen when classical survival curves are generated using chronic rather than acute doses. The “shoulder” of the survival curve which after high acute doses represents both the well understood, accumulation of damage but also the occurrence of communication (e.g. bystander signalling). In cell cultures following attenuated dose rates, the “shoulder” as a measurable parameter, effectively disappears due to the attenuation of the low dose responses. However, in the whole organism, these low dose responses occur at the system level and become complex and therefore inherently unpredictable. The lower the dose rate, the longer the communication/signalling window remains open, while very high dose rates may reduce the initial intercellular communication. We will argue, in this presentation, using data from our laboratory and others, that within any radiation dose, there is an element of unpredictability and that this is dictated more by the dose rate than to total dose.

P4 - Radiation Effects on Polymeric Food Packaging Materials with Antimicrobial and Antioxidant Properties

Dr Aliaksandr Baidak[1,2], Ms Yulia Sorokina[1], Dr William Leising[2], Dr Ruth Edge[2], Dr Fabiana Tescione[3], Dr Mariamelia Stanzione[3], Dr Giovanna Buonocore[3]
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Motivation: Incorporating antimicrobial and antioxidant agents into thermoplastic polyurethane (TPU) films presents a promising strategy for active food packaging, aiming to extend the shelf life of food products and thereby reduce food waste. This approach leverages the controlled release of natural compounds, such as α-tocopherol and eugenol, to inhibit microbial growth and oxidative processes that lead to food spoilage. Additionally, the integration of these bioactive agents into TPU films holds significant potential for healthcare applications, including antimicrobial wound dressings and medical device coatings, where preventing infection and promoting healing are paramount.

Purpose and Objectives: This study investigates the effects of gamma irradiation on TPU films embedded with α-tocopherol and eugenol, focusing on their release kinetics, thermal stability, optical properties, and chemical structure. The goal is to assess the suitability of these films for active food packaging applications aimed at reducing food waste and to explore their potential in healthcare settings.

Materials and Methods: TPU films containing 2.5% and 5% concentrations of α-tocopherol or eugenol were subjected to gamma irradiation at doses of 10 and 25 kGy. Release kinetics of the additives were analysed using both manual and automated extraction methods to determine diffusion coefficients. Thermal properties were assessed via thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC). Optical properties were examined using UV-Vis spectroscopy, while Fourier transform infrared (FTIR) and FT Raman spectroscopy were employed to detect any chemical modifications in the films.

Results: The release profiles of α-tocopherol and eugenol exhibited an initial rapid release phase (0–90 minutes) followed by a plateau, indicating complete diffusion. Diffusion coefficients ranged from 5.81×10^{-9} cm^2/s (2.5% α-tocopherol, 0 kGy) to 10.7×10^{-9} cm^2/s (5% α-tocopherol, 10 kGy), with no significant differences observed between irradiated and non-irradiated samples. This suggests that industry-standard irradiation doses do not adversely affect the diffusion of active agents, ensuring their efficacy in inhibiting microbial growth and oxidation.

Thermal analyses indicated that TPU films maintained their structural integrity at irradiation doses up to 25 kGy, with no significant changes in melting points or decomposition temperatures. However, exposure to 755 kGy resulted in decreased melting points and altered decomposition temperatures, suggesting potential degradation at higher doses. UV-Vis, FTIR, and FT Raman spectroscopy analyses revealed no significant chemical changes in films irradiated up to 25 kGy, while higher doses led to detectable structural modifications.

Conclusion: TPU films incorporating α-tocopherol and eugenol demonstrate robust thermal and chemical stability under industry-standard gamma irradiation doses (10 kGy and 25 kGy), making them viable candidates for active food packaging solutions aimed at extending shelf life and reducing food waste. The controlled release of these natural antimicrobial and antioxidant agents can effectively inhibit spoilage, thereby enhancing food preservation. Moreover, the antimicrobial properties of these films suggest potential applications in healthcare, such as in antimicrobial wound dressings and medical device coatings, where maintaining sterility and preventing infection are critical.

P5 - Containerless Chemistry: Direct radiation on liquid samples with ultrasonic acoustic levitation

Dr William Leising[1,2], Mr George Tucker[3], Mr Kacper Burczyk[4], **Dr Kay Dewhurst**[1], Professor Fred Currell[1,2], Dr Aliaksandr Baidak[1,2]
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Purpose: Radiation chemistry dose measurements can be complicated by the effects of the interface between a liquid sample and its solid container, requiring the use of dose correction factors that may not be well known for certain sample-container material combinations. This study utilises ultrasonic acoustic levitation of liquid droplets to remove the liquid-container interface and enable accurate dose measurements for small-volume liquid samples.

Methods: The well characterised dose indicator Fricke (acidified and aerated ammonium ferrous sulphate solution) was used to assess the effectiveness of the container-less irradiation approach. An ultrasonic levitator based on the TinyLev [1] system was used to suspend 15µL droplets of Fricke solution inside a Co-60 gamma irradiator. The droplets received controlled doses of 0 to150 Gy and were analysed for Fe3+ content using a UV-Vis spectrometer. To obtain a sufficiently large sample for the UV-Vis analysis, three droplets at each dose level were combined.

Results: The results show a linear correlation between Fe3+ concentration in irradiated Fricke samples with dose, yielding a g-value of 1.58 µmol/J, calculated without the need for an interface dose correction factor. The results are in line with accepted value from literature of 1.61 µmol/J [2].

Conclusion: In conclusion, the approach of using acoustic levitation to irradiate small-volume liquid samples is an effective method for dose measurement which does not require dose correction factors. This study paves the way for future container-less radiation chemistry experiments.

P6 - Radiation Effects on 3D Printed Polypropylene

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Purpose/Objective: Advanced manufacturing, particularly 3D printing, offers significant opportunities for innovation, enhancing supply chain resilience and reducing costs. While previous studies have examined the mechanical degradation of 3D-printed polymers exposed to radiation [1], the effects of water exposure and variations in radiation conditions remain underexplored. This factor is important since many nuclear industry applications involve exactly this scenario and just-in-time manufacture could offer far less plant downtime, faster prototype turnaround and commensurate decreased costs. Furthermore, 3D-printed set-ups are becoming increasingly used in radiation research laboratories and other industries where the same types of scenario can be expected to occur.

This study investigates the impact of gamma radiation on 3D-printed polypropylene under different environmental and dose rate conditions, comparing its performance to that of machined polypropylene as a control.

Materials/Methods: Samples of 3D-printed polypropylene were exposed to gamma radiation at doses ranging from 50 to 200 kGy under different dose rates, both in air and in water. For comparison, machined polypropylene samples were also irradiated under similar conditions. The bulk mechanical properties of the irradiated samples were assessed through measurement of stress-strain curves to evaluate degradation patterns and structural integrity.

Results: 3D-printed polypropylene exhibited degradation in mechanical performance comparable to machined polypropylene when exposed to gamma radiation. Irradiation in water was observed to mitigate mechanical deterioration to a certain extent. Dose rate effects suggest a role for cross-linking in maintaining material integrity. A strand-wise failure mode observed in 3D-printed polypropylene presents a potential early detection system for structural failure, which could be leveraged in future applications of additively manufactured components in radiation environments.

Conclusions: Key differences between the expected performance of bulk manufactured and 3D printed polypropylene have been demonstrated. The results demonstrate that radiation-induced degradation in 3D-printed polypropylene is influenced by environmental conditions and dose rate. These findings have implications for the deployment of just-in-time manufactured components in both radiation lab environments and on nuclear plants and in radiation industries.

P7 - Investigating damage to folded RNA using X-ray radiation

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Purpose/Objective: Although the contribution of DNA and protein damage to many diseases, including cancer [1], is well established, the impact of RNA is often neglected. RNAs' form and function are inherently linked and consequently, any alteration to RNA structure can disrupt its function and lead to negative downstream effects, as many critical biochemical interactions rely on RNA having its optimal structure [2]. Damage that can disrupt this structure can come from both internal and external sources, with RNA being especially vulnerable to damage from reactive oxygen species and ionizing radiation due to some key features including possessing a hydroxy (OH) group on the second and third carbon of the ribose sugar [3]. This study examines how x-ray radiation damages RNA and evaluates the ability of antioxidants to prevent such damage. A single source of RNA, a single-stranded RNA ladder, containing multiple different lengths was chosen as the target for this study and based on prior literature, ascorbic acid, HEPES, tris and phosphate [4][5] were chosen as the antioxidants as they all have been used in preventing RNA degradation in other biological systems.

Material/Methods: The RNA samples were mixed with an equal volume of either nuclease-free water or a chosen antioxidant, at 0.1 M concentration, and the samples were irradiated to various doses using a MultiRad350 X-ray cabinet. The samples were analysed after irradiation using TAE agarose gel electrophoresis and gel imaging to confirm RNA damage. The imaged gels were analysed further using ImageJ and a bespoke Mathematica programme to obtain the decay rate constant of each RNA length in each radioprotective environment.

Results: Predictably, longer RNA lengths are more prone to ionizing radiation damage. This study shows that the damage is stochastic with all the lengths of RNA being damaged. The longer the length of RNA, the easier it is to be degraded by ionizing radiation. However, this is due to the longer RNAs' being a physically bigger target; damage is in proportion to the strand length. The loss of RNA is also consistent with first order damage kinetics, i.e. a single photon can stochastically cause a break either through direct or indirect processes. Ascorbic acid was the most effective radical scavenger, as expected each scavenger corresponded with its scavenging potency. Under high scavenging conditions the damage is almost completely removed, indicating indirect damage is by far the dominant process.

Conclusions: As expected, it is shown that as total dose increases so does the damage to RNA, however, longer lengths of RNA are degraded at a faster rate. This is not a priory obvious as the RNA was in its native folded structure. X-rays form single strand breaks on RNA mostly via the indirect damage pathway as the antioxidants were effective at preventing the indirect damage showing that the direct damage caused by x-rays is a much smaller effect.

P8 - FLASH-induced damage reduction measured in-vitro correlates with effective oxygen-depletion determined in-silico: support for oxygen-depletion contributing to FLASH's reduced damage burden.

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Objectives: FLASH irradiation demonstrates preferable normal-tissue protection, including a reduced damage component witnessed in vitro. Radiochemical mechanisms proposed include radical-radical recombination and transient oxygen depletion (TOD), with both being proposed to lead to lower levels of FLASH-induced damage, but their respective contributions remain unclear.

Previously we reported that FLASH irradiation at low oxygen tension induces lower levels of DNA damage in whole-blood peripheral blood lymphocytes (PBLs) irradiated ex vivo, an effect modulated by oxygen tension, dose, and dose rate. This supports the concept of an oxygen-related mechanism contributing to the damage-sparing effect of FLASH irradiation in vitro (1), but this study failed to distinguish between RRR and TOD as being the mechanism(s) responsible. However, further comet assay analysis was undertaken to assess crosslink formation as a putative marker of RRR (particularly, if any radiation-induced secondary or tertiary organic radicals recombine) and also to assess anoxic DNA damage formation as an indicative marker of TOD (2). The findings of this study were that, following FLASH irradiation, there was no evidence of any crosslink formation, so no experimental evidence of RRR; however, FLASH irradiation induced a more anoxic profile of damage, supporting the TOD mechanism as being a key driver of the reduced damage burden witnessed.
In parallel studies, Rothwell et al. reported an in silico model to determine the parameters for oxygen depletion from FLASH-radiotherapy (3). This used an eight-dimensional parameter space to demonstrate conditions under which radiation may induce effective depletion of oxygen, sufficient to enable a diffusion-limited hypoxic cellular response. Findings suggest that FLASH sparing by oxygen depletion is best achieved using higher doses, delivered at dose rates of tens of Gy/s or higher, but only for systems of limited oxygen tension at the time of irradiation.

In an attempt to further establish the involvement of TOD in FLASH's reduced damage component, this study compares FLASH-mediated DNA damage reduction in vitro with oxygen depletion for FLASH radiotherapy modelled in silico, to i) investigate the contribution of TOD towards the reduced damage burden in vitro, and ii) evaluate its contribution to the broader FLASH effect in vivo.

Methods: An in silico model was used to identify and compare the parameter space for FLASH-induced oxygen depletion in an in vitro setup with experimental DNA damage reduction data, previously determined using the alkaline comet assay.

Results: Correlation analysis revealed a strong relationship between model-predicted oxygen depletion and experimentally-observed DNA damage reduction (Spearman's = 0.87, p = 2 x 10-6; Pearson's = 0.85, p = 4 x 10-6).

Conclusions: Our findings support a significant role for TOD in the FLASH-induced reduction in damage in vitro at low oxygen tensions in vitro. However, the parameter spaces identified, for both oxygen depletion in silico and DNA damage reduction in vitro, suggest that TOD may only partially contribute to the wider-ranging FLASH sparing effects in vivo. Further work is required to demarcate the sparing effects of FLASH in vivo.

P9 - Realizing the radiobiological impact of protons in glioblastoma models

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Glioblastoma multiforme (GBM) is the most common primary brain tumour in adults and has dismal survival prospects (median of ~14.6 months). Conventional X-ray (photon) radiotherapy or chemotherapy have limited efficacy, therefore there is an urgent need for more effective but safer therapeutics. Proton beam radiotherapy has the significant advantage over photons of delivering the maximum energy targeted to the solid tumour with a low entrance dose sparing the healthy tissues and organs at risk. Additionally, by taking advantage of the Bragg-peak to deliver a higher LET (linear energy transfer), this will also generate a higher biological effectiveness due to increased ionisation density and therefore cellular damage. However, the optimal use of protons in GBM treatment has yet to be realised.

GBM is thought to be driven by a small niche of cancer stem cells which have unlimited proliferative capability. GBM stem-like cells (GSCs) which express stem cell markers CD133, SOX2 and nestin have been demonstrated to be more radioresistant than their paired bulk non-stem cells. Given this, it is hypothesised that radiosensitising strategies are required to effectively target this population leading to tumour cell death, and therefore increasing the survival of GBM patients. Another important factor in solid tumours such as GBM is hypoxia, which generates a more radioresistant phenotype, particularly in response to conventional X-ray radiotherapy treatment.

Our data shows that inhibition of key DNA damage response (DDR) pathway proteins, particularly ATM and DNA-PKcs, combined with low LET photons and protons can significantly reduce GBM cell survival compared to radiation alone in both bulk and stem like populations. We also demonstrate in mild hypoxic conditions (1 % oxygen) that some GBM cell lines gain further radioresistance to proton and photon radiation treatment. However, the combination of DDR inhibition with photons/protons is still effective in radiosensitising GBM cells, which has been observed in both monolayer and 3D spheroid models. We have furthermore investigated the molecular mechanisms that may underpin the altered GBM cellular hypoxic response to irradiation, and are in the process of validating possible targets for combination therapy to further enhance cellular radiosensitisation.

Our work has indicated the exciting prospect of improving the GBM cellular response to the current standard of care radiotherapy. In particular, this can be achieved through the combination of protons and DDR inhibition, taking into account important factors such as the GBM cancer stem cell population and inherent radioresistance caused by hypoxic conditions.

P10 - Determinants of Cellular Vulnerability and Resistance to Radioligand Therapeutics

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Radioligand therapeutics (RLTs) represent a promising modality for targeting cancer by conjugating beta- or alpha-particle emitters to ligands that selectively bind tumor-associated antigens. These agents not only induce potent DNA damage in targeted cells but can also be visualized for real-time patient monitoring, offering both therapeutic and diagnostic benefits. Clinically, RLTs such as lutetium-177 (^{177}Lu)-conjugated DOTATATE and PSMA ligands have demonstrated efficacy in treating refractory neuroendocrine and prostate cancers. Beta-particles, such as those emitted by ^{177}Lu, offer broader tissue penetration over tens to hundreds of cells, enabling damage across a larger field. In contrast, alpha-particle emitters induce highly localized, complex DNA double-strand breaks (DSBs) due to their short-range, high linear energy transfer (LET) properties. Traditional cancer treatments using external beam ionizing radiation (X-rays) remain a cornerstone of clinical oncology, though they primarily cause sparsely ionizing damage and rely heavily on cellular oxygenation and cell cycle phase. Despite their clinical utility, the distinct DNA damage landscapes and cellular responses elicited by RLTs and conventional radiotherapy remain incompletely understood. To systematically define shared and distinct cellular pathways influencing sensitivity and resistance to different sources of ionizing radiation, we will conduct focused and genome-wide CRISPR-Cas9 knockout screens in prostate, neuroendocrine, and breast cancer cell lines treated with RLTs or X-rays. Hits from these screens will undergo validation and mechanistic follow-up to refine our understanding of therapeutic vulnerabilities. Additionally, we will explore the radiation-induced bystander effect (RIBE)—where non-irradiated cells exhibit impaired viability due to signals from irradiated neighbors—in the context of RLT exposure. Collectively, these efforts will provide a greater understanding of the differences in cellular responses to ionizing radiation treatments as well as the potential bystander effects induced by these therapies. The targets identified in these screens may inform personalized combination therapies involving RLTs and improve patient outcomes.

P11 - Countering the proteinase activated receptor 1 (PAR-1) pro-tumour phenotype using a novel nanotherapeutic approach

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Background: Pancreatic cancer (PDAC) caused 432,000 deaths in 2018, with tumour resection as the only curative option.1 Over 80% of patients are diagnosed with unresectable tumours, while others with borderline resectable disease undergo neoadjuvant chemotherapy or chemoradiotherapy (CRT) to improve surgical success.2 The efficacy of radiotherapy is limited by the proximity of the pancreas to sensitive organs and high intrinsic radioresistance.3 A targeted radiosensitiser, such as a gold nanoparticles (AuNPs), could enhance the impact of radiotherapy while minimising damage to surrounding tissues. Proteinase-activated receptor 1 (PAR-1), often overexpressed in PDAC, promotes tumour growth, migration, EMT, and survival, making it a promising therapeutic target.4
This project investigates the molecular impact of PAR-1 signaling in PDAC comparing PAR-1 antagonistic peptides against the small molecule inhibitor vorapaxar, assess the impact of antagonism on key oncogenic and pro-survival traits, in addition to any alteration of the radiation response. In parallel, we have developed a PAR-1 targeting, antagonistic AuNP, designed to increase the radiation sensitivity of PDAC tumour models.

Results: Alamar blue cytotoxicity studies indicate no direct impact on PDCA survival following PAR-1 inhibition, either with vorapaxar or PAR-1 targeting pepducins ($p<0.05$). Similarly, PAR-1 inhibition alone had no direct impact on modulating radiation sensitivity. Irrespective, overexpression of the PAR-1 receptor in PDAC tumour models, provide a means of promoting targeted AuNP internalisation. AuNP-PAR1 was synthesised using the Turkevich method, with the final nanoparticle possessing a hydrodynamic size of 38 nm, charge of 15.53 mV and a polydispersity index of 0.15. Importantly, the formulation proved stable both over time, and under conditions of stress, with no significant increase in size under salt or serum protein stress. AuNP-PAR1 was avidly internalised resulting within 24 h, reaching 31.57 and 59.29 pg/cell in BXPC and PANC-1 cells respectively. Importantly, target specificity was confirmed by pre-blocking the PAR-1 pepducin binding site, attenuating AuNP-PAR-1 uptake by 47%.

Conclusions: PAR-1 specific, pepducin-functionalised AuNPs exhibit good stability under physiological stress, with the ability to be avidly internalised into in vitro cell models of PDAC. Importantly, we have demonstrated specificity for the PAR-1 receptor, a result that will help minimise uptake in low PAR-1 expressing normal cells. PAR-1 inhibition alone confers no intrinsic radiosensiting properties, however, clonogenic assays underway to establish the radiation dose modifying potential of the fully functionalised PAR-1 AuNP.

P12 - Understanding the biological response of head and neck cancer to boron neutron capture therapy

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Boron neutron capture therapy (BNCT) is a tumour-targeted radiotherapy technique that enables the delivery of high LET particles directly to tumour cells, thus sparing the normal cells/tissues, leading to increased biological effectiveness, and also safety, compared to conventional X-ray radiotherapy. Boron containing drugs are designed to be specifically and preferentially taken up by tumour cells before irradiation with thermal energy neutrons, resulting in a boron fission reaction that releases high LET helium and recoiled lithium ions that inflict cellular damage within boron containing cells [1]. Although high LET radiation has been shown to produce more complex DNA damage (CDD) than lower LET sources [2], the profile of DNA damage produced and the cellular responses to this following BNCT has yet to be fully elucidated.

Utilising the UK's only high flux accelerator-driven neutron facility at the University of Birmingham, we are investigating the cellular effects of BNCT on head and neck squamous cell carcinoma (HNSCC) cell models utilising two boron-containing compounds, boric acid and boronophenylalanine (BPA), that latter of which has been shown to be effective at treating various cancers, particularly recurrent HNSCC, in clinical trials in Japan and China. BPA uptake requires expression of the LAT1 amino acid transporter in contrast to boric acid which is freely diffusible. Our investigations show that LAT1 expression is variable across HNSCC cell lines, likely resulting in differential BPA uptake and treatment effectiveness. We investigated whether short (2 hour) or long (24 hour) incubation with boron-containing compounds affected the efficacy of BNCT treatment. Clonogenic survival assays demonstrate the propensity of both boron-containing compounds to induce significant HNSCC cell death in combination with neutrons, whilst remaining non-toxic to cells without neutron exposure. Interestingly, 24h boron-compound incubation showed little difference in BNCT efficacy between boric acid and BPA despite differing LAT1 expression across cell lines. Alternatively, in 3D HNSCC spheroid models, BPA treatment increased the sensitivity of spheroids to neutron irradiations compared to boric acid, indicating a greater penetrance of BPA into the spheroid. We are also now examining how hypoxia affects cell sensitivity to BNCT and have observed a reduction in LAT1 expression in cells cultured at low oxygen tensions (0.1% and 1% O_2) compared to cells cultured in normoxic conditions (21% O_2).

Using neutral comet assays, we have seen a differential DNA damage profile in cells treated with BNCT compared to conventional X-ray radiation. Initially following BNCT, a limited number of DNA double strand breaks are formed, the quantity of which increases 4h post-treatment, whereas X-ray radiation results in initial double strand break damage that is fully repaired by 4h post irradiation. Enzyme modified comet assays [3] will be utilised to investigate the production of complex DNA damage alongside immunostaining to assess γH2AX and OGG1 foci formation. Additionally, we have been utilising a chick embryo model to investigate BNCT in vivo, to facilitate our understanding of drug uptake and tumour specificity of the treatment. This study will provide a deeper understanding of the cellular response mechanisms in HNSCC following high-LET BNCT treatment.

P13 - NAMPT inhibition enhances sensitivity of glioblastoma cells to radiation.

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Purpose: Targeting the altered metabolism of cancer cells presents a promising approach to overcoming radioresistance in glioblastoma, a leading cause of tumour recurrence and patient mortality. This in vitro study aimed to investigate the interaction between radiation and FK866 (Daporinad), a highly specific inhibitor of nicotinamide phosphoribosyltransferase (NAMPT), a key enzyme in nicotinamide adenine dinucleotide (NAD) salvage biosynthesis pathway.

Materials and Methods: The effects of FK866 were evaluated in vitro on cell proliferation, survival, cell cycle, gene expression, and radiosensitization using genetically heterogenous human glioblastoma stem-like cells (GSCs), each exhibiting varying levels of NAMPT expression and activity.

Results: Treatment with FK866 significantly reduced total cell numbers across all ten GSC lines tested, with IC50 values ranging from 0.25 nM to 8.8 nM. Notably, this single agent activity was consistent irrespective of genetic subtype, O6-methylguanine-DNA methyltransferase (MGMT) methylation status, or baseline NAMPT expression and activity levels. The specificity of FK866 was confirmed by rescue experiments, wherein supplementation with NAD or nicotinamide mononucleotide (NMN) effectively reversed drug-induced cytotoxic effects in two representative GSC lines, validating on-target NAMPT inhibition and subsequent NAD depletion as the primary mechanisms involved. Time-course analysis revealed a delayed onset of cytotoxicity, correlating with progressive alterations in metabolic and gene expression profiles detected up to 72 hours of FK866 exposure, even though NAD levels were depleted within 24 hours. Furthermore, FK866 demonstrated cytotoxic efficacy as a single agent and functioned as a potent radiosensitizer in two- and three-dimensional glioblastoma cell culture models when added 2 hours prior to radiation. This radiosensitising effect was confirmed in four distinct GSC lines via clonogenic survival assays (2D) and spheroid growth delay analyses (3D).

Given the crucial role of NAD in DNA repair processes, FK866-induced changes in DNA damage response were examined by evaluating γH2AX formation. Results indicated a synergistic interaction when FK866 was combined with radiation. FK866-induced cytotoxicity was further characterized by cell cycle alterations, including G2/M accumulation and mitotic block.

Conclusions: Targeting NAMPT with FK866 has therapeutic potential in glioblastoma both as a single agent and a potent radiosensitiser.

P14 - Automated Production of Radionuclide Nanoparticles for Medical Applications

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Purpose/Objective: The Dalton Cumbrian Facility (DCF) has developed an automated platform for synthesizing active nanoparticles using copper and scandium radionuclides. These radionuclides, produced via transmutation of nickel and calcium, have potential applications in radiotherapy and theragnostics. The primary objective of this work is to establish a fully automated beamline end-station for the efficient and safe production of these nanoparticles, enhancing research capabilities and scalability. This end-station facilitates all steps from transmutation, dissolution, isotope separation and nanoparticle synthesis without a human in the room. This end-station will be available for collaborative use at DCF.

Materials/Methods: A solid target of nickel or calcium carbonate is aligned with a proton or alpha particle beam using a computer-controlled stage with three degrees of freedom (two positional and one rotational). The target can either contain natural nickel or calcium or isotopically enriched 60Ni, 61Ni, 64Ni, 40Ca, 43Ca, or 44Ca, allowing for production of 60Cu, 61Cu, 64Cu, 67Cu, 43Sc, 44Sc, 47Sc, depending on the choice of proton or alpha particle beams. The target is irradiated, resulting in partial transmutation of the target to produce radionuclides. After activation, the target is dissolved, and the solution is transferred into a hot-cell for radionuclide separation using an ion exchange resin and peristaltic pumps under computer control. The isolated radionuclides are then introduced into a computer-controlled nanoparticle synthesis unit, which precisely regulates temperature and key reaction parameters. The system incorporates an array of sensors and cameras, enabling remote monitoring and fully autonomous operation. The system has been constructed so that the original Ni or Ca isotopes can be recovered in enriched form for reuse while the Cu or Sc product isotopes can be blended as required. Since the resultant nanoparticles of either Cu or Sc2(CO3)3 across different blends are chemically identical but radiologically distinct this approach opens the way to personalised radiopharmaceutical delivery in an entirely new way.

Results: The development of the automated beamline end-station has been completed. It significantly enhances safety by reducing operator exposure to radiation and hazardous materials. The automated workflow also increases throughput by eliminating manual intervention and enabling asynchronous operation. Trials have demonstrated successful transmutation, dissolution, separation and automated nanoparticle synthesis. Because the system is highly modular, it is possible to reconfigure it for a wide range of radiopharmaceutical productions and is not limited to nanoparticles alone. Small molecule chelation approaches are also possible.

Conclusions: This automated production system offers a scalable and reproducible method for synthesizing radionuclide nanoparticles, addressing key challenges in radionuclide availability for medical research. The system will facilitate investigations into a wider range of activated materials, expanding the portfolio of radionuclides available for radiotherapy and theragnostic applications. Interested users are encouraged to approach the team to discuss future collaborative use.

P15 - Five years of BIR Radiotherapy and Oncology Annual Meetings – Room for more Radiation Research?

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Introduction: The British Institute of Radiology (BIR) began focused two-day Radiotherapy and Oncology (BIRTO) international meetings, following several requests for something in the UK, where there was an absence of such meetings directed solely towards Radiotherapy and Oncology; especially from a fully multidisciplinary perspective. 2025 saw the fifth such meeting delivered successfully in London in March. This paper examines all these meetings with a view to asking the question as to whether there is scope for further radiation research to be added into the subject arena.

Methods: All five BIR annual Radiotherapy and Oncology meetings have been examined thematically in terms of session themes, plenary talks and discussions, teaching sessions, invited and proffered materials.

Results and discussion: Excluding the first meeting (BIRTO21) (because it's delivery was online only, distributed over two separate weeks, and with teaching sessions as separate lunchtime webinars (across 6 weeks)), most two-day in-person meetings were composed of 12 separately themed sessions, with an average of 42 talks presented per meeting in the main sessions. In the two most recent BIRTO meetings, some sessions were double/treble length, to concentrate on subject topics such as Patient Voice, International Collaborations/initiatives and Artificial Intelligence. Plenary keynote presentations ranged from 2 to 5 talks per meeting; the most when extra talks were scheduled over lunchtimes. Four teaching sessions were included in the 2021 and 2022 meetings.

Most sessions have focused on Clinical Practice and new/developing modalities (such as PBT). The most consistent sessions (taking place at every meeting) have been Adaptive RT, Safety and Regulation (usually led by the UKHSA) and Manufacturer's talks. Radiobiology and related topics have featured in three invited talks and in proffered materials too. Plenaries and keynote/prize talks have included topics such as personalised radiation oncology, FLASH RT, Re-irradiation, particle therapy, imaging developments, AI and patient experiences. Some of the most powerful presentations have come from patients themselves, giving all present a sense of focus and purpose for sharing experiences, research and development at all levels. For the 2021/2022 meetings, teaching sessions covered topics such as IGRT, PBT, dosimetry and radiation detectors, radiomics, adaptive RT and Brachytherapy.

Conclusions: A key feature, shown by the range of sessions across the five meetings, is the variety of subject matter; a feature often highlighted in feedback. But there is scope to introduce further radiation research with direct applicability to translational and clinical Radiotherapy, as well as research into radiation detection/image formation. More creative, online content could be utilised as well as re-enabling teaching sessions within the main two-day meeting. Webinars and other online opportunities could also be explored. A highly successful online meeting on Practical Radiobiology for everyday modern Radiotherapy was organised in 2021 during the pandemic; therefore, specific ARR/BIR webinars are now being explored, together with a specific session to be organised by the ARR for BIRTO26, which we hope will attract more papers on Radiobiology and fundamental research pertinent to clinical Radiotherapy and Imaging, especially from early career researchers.

P16 - Phosphomannose-isomerase gene expression as a novel radiosensitising target in Pancreatic cancer

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Introduction: Pancreatic ductal carcinoma (PDAC), one of the most serious gastrointestinal cancers, ranked 7th for mortality in China and 3rd in the United States, with a five-year overall survival rate of only 13%.[1 2] The role of radiation therapy in treating PDAC has been controversial, but it has been used to treat borderline resectable PDAC providing a survival benefit to patients.[3] Compared to multiple chemotherapy strategies including FOLFORINOX, and gemcitabine combined with Nab-paclitaxel, commonly used for PDAC treatment, only a few radiosensitising-based drugs have been successfully developed, still at a nascent developmental stage due to the low specificity and undesirable side effects.[4] A 2018 Glasgow study reported the chemotherapy-sensitising potential of mannose indicating that the magnitude of effect could be influenced by phosphomannose isomerase activity (PMI).[5] The aim of this project was to determine whether mannose holds the potential to radiosensitise PDAC tumour models and explore further the relationship PMI function and observed biological and therapeutic effects.

Method: PDAC cell line models Panc-1 and BxPC-3 were used for in vitro studies. Alamar blue assay were used to assess direct cytotoxicity. Western blots were performed assess the expression of PMI, with CRISPR-Cas9 technology used to construct stable PMI knock out models. Poly(amidoamine) based pABOL-EDA nanoparticles were synthesised as an siRNA delivery vehicle, designed to transiently supress PMI expression. Finally, the impact of radiation plus PMI knockout or knockdown was determined by clonogenic assay.
Results: PMI was expressed by both PDAC tumour models. The direct cytotoxic effect of mannose (20 mM) was inversely correlated with the PMI expression. Long term mannose (20 mM) exposure (throughout the duration of the clonogenic assay) sensitised both BXPC3 and PANC-1 cells yielding respective mean sensitiser enhancement ratio (SER) of 1.14 and 1.16. Importantly, in PMI knockout models, sensitivity to mannose was increased by 2.24 fold and 6.38 fold, with an increased SER of 1.20 for BxPC-3 cell model.

Discussion: PMI represents a potential target to enhance the radiosensitising effects of mannose, a response likely attributable to metabolic reprogramming of cells. In PDAC cells, nucleotides are synthesised via salvage and de novo pathways, both requiring ribose-5-phosphate (R-5-P) from glucose metabolism. Autophagy also contributes to nucleotide supply. Mannose, a glucose analogue, has been reported to disrupt glucose metabolism in head and neck cancer models, an effect that potentially impairs R-5-P production and nucleotide biosynthesis in PDAC.[3] This disruption may affect PDAC cell proliferation and survival by altering essential metabolic pathways. Further investigation will explore the metabolic mechanisms underlying the observed mannose radiosensitising effect.

P17 - Hypoxia-driven Changes in Plasma Membrane Protein Expression Reveal Molecular Radiotherapy Targets

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Introduction: Molecular radiotherapy (MRT) selectively targets receptors upregulated on cancer cells, offering effective treatment for lymphoma [1] and prostate cancers [2]. Plasma membrane proteins (PMPs) play a key role in cellular function and serve as accessible MRT targets [3, 4]. Hypoxia, common in solid tumours like cervical cancer, alters PMP expression and impacts radiotherapy response [5, 6]. Locally advanced cervical cancer has a five-year survival rate of ~58% [7], with recurrence in 30-50% of cases, often as therapy-resistant metastases [8]. Identifying hypoxia-upregulated PMPs may reveal novel imaging and therapeutic targets [9, 10]. Here, we report the proteomic characterization of PMPs in the SiHa cervical cancer cell line under hypoxia.

Method: SiHa cells were cultured under hypoxic (0.1% O_2) and normoxic (21% O_2) conditions for 48h. Cells underwent surface biotinylation with sulpho-NHS-SS-biotin (Thermo Scientific, USA), and biotinylated PMPs were isolated using NeutrAvidin agarose. Samples were alkylated, trypsinised, and cleared of peptides using the EasyPep™ Mini MS Sample Prep Kit (Thermo Scientific, USA). Samples were analysed using LC-MS/MS on a Thermo Scientific Q Exactive HF system, with protein identification was performed by searching the data against the SwissProt database. In silico analysis was performed in R using clusterProfiler package. Proteins detected in ≥30% of samples were included to balance reliability and biological relevance.

Results: Proteomic analysis of 18 samples revealed consistent protein abundance before and after normalisation, with clustering based on oxygen conditions. A total of 5,164 proteins were identified, with enrichment analysis highlighting focal adhesion and cell-substrate junction as the top two categories. PMPs accounted for ≈30% of the identified proteins based on the UniProt database. Among these, 55 PMPs exhibited significant differential expression (FDR < 0.05, |log2FC| ≥1). The top five upregulated PMPs under hypoxia were Integrin beta-2 (ITGB2), Jagged1 (JAG2), Transforming growth factor-beta-induced (TGFBI), Serpin Family E Member 1 (SERPINE1), and Integrin alpha-7 (ITGA7).

Conclusion: This pilot study identified hypoxia-upregulated PMPs, including ITGB2, linked to poor prognosis, and TGFBI, associated with macrophage polarisation and chemotherapy resistance in pancreatic cancer [11,12]. Future work will characterise PMPs in cervical cancer panels and conduct in silico prognostic analysis to identify MRT targets.

P18 - A Novel Proteomic Pipeline for the Identification of Hypoxia-Sensitive Plasma Membrane Proteins.

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Introduction: Hypoxia (≤2% O_2) is a hallmark of solid tumours, including bladder cancer (BlCa), contributing to radioresistance. It alters plasma membrane proteins composition (PMPs), which can serve as targets. Hypoxia-modifying therapy (carbogen and nicotinamide [CON]) when combined with radiotherapy can improve survival by up to 20% in patients with hypoxic cancers. However, there are no biomarkers used clinically to identify patients with hypoxic tumour. Proteomic analysis of PMPs can reveal novel targets for imaging and treatment. However, detection is obscured by abundant cytosolic proteins. This study introduces a novel pipeline to identify hypoxia-induced PMPs.

Method: UMUC3 cells were cultured under normoxia (21% O_2) and hypoxia (0.1% O_2) for 48h. PMPs were isolated using the Pierce™ Cell Surface Protein Biotinylation and Isolation Kit. Cells were biotinylated with 0.25mM sulpho-NHS-SS-biotin, lysed, and incubated with NeutrAvidin agarose. Bound proteins were reduced, alkylated, digested, and analysed via LC-MS/MS on a Q-Exactive HF system. Protein identification was performed by searching the data against the SwissProt database. In silico analysis was performed in R using clusterProfiler package. For biological relevance, only proteins detected in ≥30% of samples were included.

Result: Twenty-four samples were analysed, demonstrating condition-dependent clustering with minimal technical variation. A total of 5,963 proteins were identified, with enrichment analysis highlighting focal adhesion and cell-substrate junction as PMP-associated cellular component. A total of 1,332 proteins were MPs based on UniProt annotations, with 107 significantly affected by hypoxia (false discovery rate 0.05, absolute fold change > 1). Significant PMPs include ITGA5, L1CAM, and SLC2A1, all previously linked to hypoxia.

Conclusion: This pipeline isolates and identifies hypoxia-driven PMPs in BlCa while minimising cytosolic contamination, including ITGA5 (hypoxia-induced, linked to migration and invasion), SLC2A1 (prognostic marker), and L1CAM (chemoresistance-associated). Future work will characterise BlCa PMPs and validate targets using immunofluorescence to assess expression and localisation in tissue samples.

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