UK PET Chemistry Meeting 2025

University of Glasgow

9 September

Abstract Book

Thank you to our generous sponsors

Welcome to the University of Glasgow for UK PET Chemistry Meeting 2025

Dear UK PET Community,

It is with great pleasure that I welcome you to the University of Glasgow for this year's UK PET Chemistry meeting. This event is a celebration of our thriving radiochemistry community, and I am delighted to open our doors to delegates from across the UK and beyond.

At its heart, the UK PET Chemistry meeting is about more than just sharing scientific advancements; it is a platform designed to engage students and early-career researchers (ECRs), sparking their interest and involvement in the field. By fostering meaningful collaborations within the radiochemistry network, this event serves as a catalyst for innovation, connecting seasoned experts with the next generation of radiochemistry pioneers.

This year's meeting offers an exciting scientific agenda with groundbreaking research in radiochemistry and radiopharmaceutical development. Additionally, there will be sessions on clinical management and technical aspects to address the challenges of providing radiopharmaceutical services to patients in the UK. I hope these sessions encourages thoughtful discussions and leads to new collaborations to improve our radiopharmaceutical services.

I would like to acknowledge our sponsors for their invaluable contributions in funding this meeting. I would also like to thank the incredible support I have received from SINAPSE and the local organising committee, whose commitment and hard work have made this conference possible. This committee represents a fantastic Scottish collaboration, bringing together the Universities of Aberdeen Edinburgh, Glasgow, CRUK Scotland Institute and NHS Greater Glasgow and Clyde. Without their dedication and contributions, we would not be able to host this gathering of the UK PET Chemistry community.

Thank you all for taking the time to join us in Glasgow. Your involvement, whether presenting your work, participating in discussions, or simply attending, plays a pivotal role in the success and vibrancy of this conference. It is your enthusiasm and expertise that make our community truly exceptional.

I hope you will enjoy this day of science and networking. Let us make the most of this opportunity to exchange ideas, celebrate our achievements, and chart the way forward for radiopharmaceutical science in the UK.

Have a fantastic time! Warm regards,

Dr Sally Pimlott Chair,
UK PET Chemistry Local Organising Committee

UK PET CHEMISTRY MEETING
Programme

Tuesday 9th Sep 2025 Sir Charles Wilson, University of Glasgow		
09:00 am to 9:40 am	Registration & Poster Set-Up, Tea / Coffee	
9:40am-9:50am	**Welcome/ Peter Horlock** *Sally Pimlott*	
9:50am-10:00am	**Positron Pulse Update/Feedback Session** *Selena Milicevic Sephton*	
10:10am to 10:55am	**Scientific Session 1 – Main Lecture Theatre** **18F Radiochemistry** **Chairs: Helen Betts & Sergio Dall'Angelo** 3 x 12min talks (3 min qs)	**Clinical Manufacture Session A – Rm101B** Workshop style session (45min)
10:10am-10:25am	**O01** Design and Development of PET radiotracers for Imaging Oligodendrocyte Progenitor Cells *Helgi Danielsson, University of Cambridge*	
10:25am-10:40am	**O02** Ethyl Pinacol Boronates as Advantageous Precursors for Copper-Mediated Radiofluorination *Joseph Ford, University of Oxford*	Introduction to Annex 1 *Chair: Sylvain Eschenlauer*
10:40am-10:55am	**O03** Development of a halofluorocarbon, chromatography-free radiosynthesis of fluorine-18 difluorocarbene on the GE TracerLab FXFN module *Catherine Fitzgerald Dickmann, University of Cambridge*	
10:55am to 11:15am	Tea/Coffee	
11:15am to 12:00pm	**Scientific Session 2 – Main Lecture Theatre** **18F and 11C radiochemistry** **Chairs: Andrew Sutherland & Selena Milicevic Sephton** 3 x 12min talks (3 min qs)	**Clinical Manufacture Session B – Rm101B** Workshop style session (45min)
11:15am-11:30am	**O04** The Last Mile in the Qualification Marathon: Analytical Method and Process Validations for [18F]SynVesT-1 *Federico Luzi, King's College, London*	Integration, Integration, Integration *Chair: Ken Wilson and Sue Champion*
11:30am-11:45am	**O05** Silver (I) Oxide Mediated Radiochemical Synthesis of 1,1-[18F] difluoroalkane Derivatives *Pawan Mishra, Cardiff University*	
11:45am-12:00pm	**O06** Docking analysis and preliminary in vitro evaluation of various analogues for PET imaging of AMPAR	

	Shinong Zeng, University of Cambridge
12:00pm to 12:30pm	**Lightning Pitches – Main Lecture Theatre**
12:00pm-12:30pm	***POSTER PRESENTATIONS – 1 min lightning pitches*** *Chairs: Louis Allott & Tim Morgan*
12:30pm to 2:00pm	**Lunch & Exhibitors & Scientific and Technical Poster Session (Rm101A)** Poster presenters please stand by your posters between 1-2pm
2:00pm to 3:40pm	**Keynote and Speak to the Experts Workshop – Main Lecture Theatre**
2:00pm-2:40pm	**Keynote Speaker: ^{89}Zr Radiopharmaceutical Chemistry - Precision Medicine in Cancer Treatment** *Prof Jason Lewis, MSKCC* *Chair: Sally Pimlott*
2:40pm-3:40pm	**Speak to the Experts Workshop: The challenges of producing radiopharmaceuticals for research trials** *Maggie Cooper (20min talk)* **Followed by Panel Discussion (40min)** *Panel: Maggie Cooper (KCL), Jason Lewis (MSKCC), Christophe Lucatelli (University of Edinburgh), Shaun Creasey (Alliance Medical)*
3:40pm to 4:00pm	**Tea/Coffee**
4:00pm to 4:45pm	**Scientific Session 3 – Main Lecture Theatre** **Other Radionuclides** **Stephen Archibald & Dmitry Solovyev** 3 x 12min talks (3 min qs)
4:00pm-4:15pm	**O07** Sustainable chemistry approaches to future responsive metallo-theranostics *Sofia Pascu, University of Bath*
4:15pm-4:30pm	**O08** Novel dual CXCR4 and ACKR3 theranostic agents for PET/SPECT imaging and targeted molecular radiotherapy for cancer *James Wood, King's College London*
4:30pm-4:45pm	**O09** Development of Astatine-211 Production Capability in the UK *Jennifer Young, Queen Mary University of London*
4:45pm to 4:50 pm	***UK PET Chemistry meeting 2026 Announcement***
4:50pm to 5:00 pm	***Prize Awards and Goodbye*** *Sally Pimlott*
5:00pm to 6:00pm	**Post-Meeting Drinks Reception**

Contents

Keynote Talk

Keynote

^{89}Zr Radiopharmaceutical Chemistry – Precision Medicine in Cancer Treatment

Professor Jason Lewis[1*]

[1]Sloan Kettering Institute

The use of Positron Emission Tomography (PET) for cancer imaging is a well-established and widely used molecular imaging modality both in clinical and research settings. Over the last 30 years, our ability to non-invasively diagnose, localize, and treat many forms of cancer has advanced tremendously. These diagnostic tools are now being combined with therapeutic isotopes to create "theranostics" – agents that allow for simultaneous imaging and treatment with the same drug. This talk will include both preclinical and clinical application of these cancer targeting drugs within the central premise of theranostics "see what you treat and treat what you see".

One area of emphasis for the Lewis Lab has been centered around the remarkable specificity and selectivity of antibodies for cancer biomarkers have made immunoglobulins some of the most flexible and adaptable tools in modern medicine. For therapeutic purposes, a wide range of non-labeled antibodies has now entered the clinic. Antibody-based PET and SPECT imaging agents are not far behind. For example, an array of 89Zr-labeled radioimmunoconjugates has shown significant promise in both preclinical and clinical studies. Zirconium-89 has a number of distinct advantages which make it ideal for ImmunoPET including that the radioactive half-life of 78.4 h matches closely the extend times required for optimum biodistribution of intact mAbs. This presentation will review the current state-of-the-art on the use of radiometals with antibody constructs.

Oral Presentations

O01

Design and Development of PET radiotracers for Imaging Oligodendrocyte Progenitor Cells

Helgi V. Danielsson[1*], Nisha K. Ramakrishnan[1,2], Selena Milicevic Sephton,[1] Franklin I. Aigbirhio[1]

[1]Molecular Imaging Chemistry Laboratory, Department of Clinical Neurosciences, University of Cambridge, Cambridge, United Kingdom.
[2]Anne McLaren, Preclinical Imaging Research Laboratory, Department of Radiology, University of Cambridge, Cambridge, United Kingdom.

Contact: hvd24@cam.ac.uk

Keywords: Fluorine-18; Automated Radiosynthesis, Preclinical evaluation

Introduction: Myelin damage is the primary reason for the accumulating neurological disability affecting people with Multiple Sclerosis (MS). Remyelination relies on oligodendrocyte progenitor cells (OPCs) within lesions, and lesions can be OPC *sufficient* or *deficient*, but making this distinction *in vivo* is not possible. We aim to develop a PET radiotracer to quantify OPCs *in vivo*, enabling stratification of individuals, and facilitate assessment of emerging remyelination therapies. The GPR17 receptor is specifically expressed in OPCs and a promising target for small-molecule PET radiotracer development. High affinity GPR17 ligands[1,2] were selected for developing fluorine-18 labelled PET radiotracer analogues.

Methods: Reference compounds were synthesised, as well as tosylate precursors to facilitate one-step radiolabelling *via* nucleophilic substitution with activated [^{18}F]fluoride. Automated radiosynthetic methods were developed on a GE Tracerlab FX_{FN} module, including purification by semi-preparative HPLC and reformulation. Specific binding to GPR17 was assessed by *in vitro* autoradiography in rat brain tissue, by co-incubation with known GPR17 ligands, and stability studies carried out in rat blood plasma. PET studies, with metabolite analysis, were carried out in healthy rats.

Results and conclusions: Reproducible automated radiosynthesis of three PET radiotracers targeting GPR17 was achieved, with high radiochemical purities and reproducible yields, sufficient for biological evaluations (Fig. 1A). Uptake of [^{18}F]HD1-19 and [^{18}F]HD1-69 could be blocked *in vitro* (Fig. 1B). [^{18}F]HD1-19 demonstrated excellent stability, while a PET scan showed minimal brain uptake (peak SUV: 0.8) (Fig. 1C). [^{18}F]HD1-69, however, entered the brain readily (peak SUV: ~1.5, n=2), but was rapidly metabolised *in vivo.* Improved stability was observed for [^{18}F]HD1-69-D_4 *in vitro*, but no improvements in stability or brain uptake were seen *in vivo* (n=3). Newer analogues [^{18}F]HD1-69 and [^{18}F]HD1-69-D_4 show sufficient initial brain uptake, which warrant investigations into further radiotracer analogues from this scaffold, aiming to improve *in vivo* stability and kinetics.

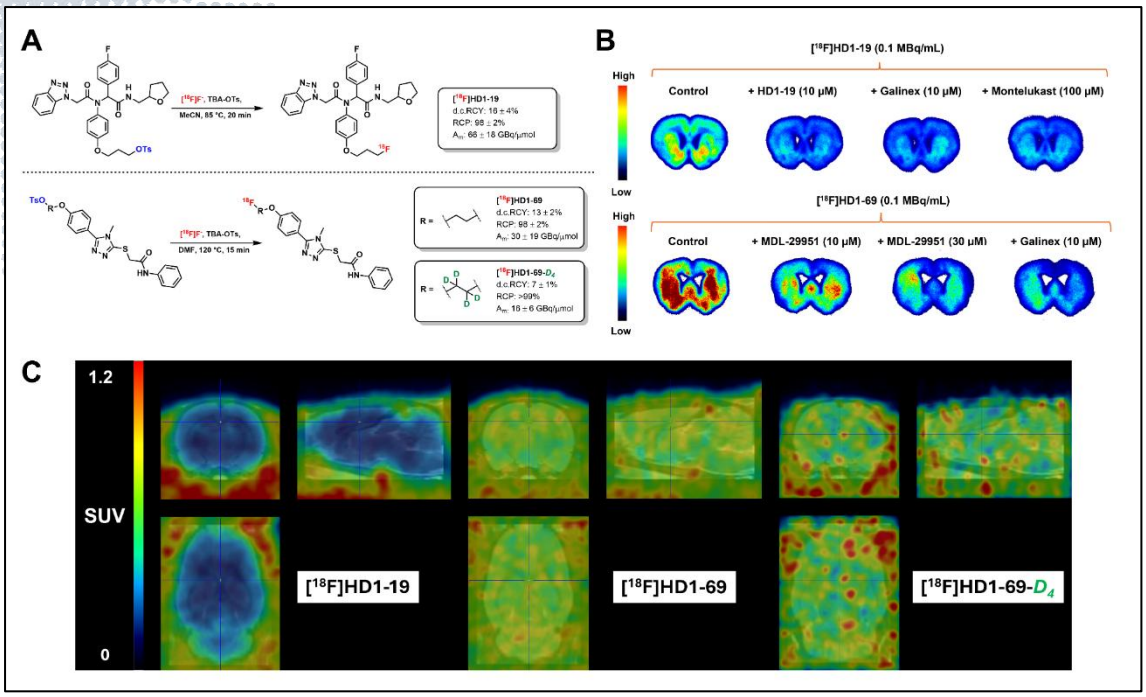

Figure 1*:* Radiosynthesis (**A**), *in vitro* autoradiography (**B**) and summed SUV PET images (0-10 min p.i.) (**C**) for [^{18}F]HD1-19, [^{18}F]HD1-69 and [^{18}F]HD1-69-D_4.

Acknowledgements

This work is supported by the UK MS Society and the Wellcome Trust.

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O02

Ethyl Pinacol Boronates as Advantageous Precursors for Copper-Mediated Radiofluorination

Joseph Ford[1*], Nikolaos Hadjipaschalis[1], Sebastiano Ortalli[1], Zijun Chen[1], Robert S. Paton[2], Matthew Tredwell[3,4] and Véronique Gouverneur[1]

[1]Chemistry Research Laboratory, University of Oxford, United Kingdom.
[2]Department of Chemistry, Colorado State University, United States.
[3]Wales Research and Diagnostic PET Imaging Centre, Cardiff University, University Hospital Wales, United Kingdom.
[4]School of Chemistry, Cardiff University, United Kingdom.

Contact: joseph.ford@chem.ox.ac.uk

Keywords: Fluorine-18 radiochemistry

(Hetero)aryl pinacol boronic esters (Bpin) have been shown to be effective substrates for the ^{18}F-radiolabelling of (hetero)aromatic scaffolds under copper-mediated conditions. These precursors have found wide application, enabling access to various (hetero)aryl ^{18}F-fluorides for use as radiotracers for (pre)clinical imaging.[1] Despite this, several reports indicate that the isolation and purification of some complex (hetero)aryl-Bpins can be challenging, applying silica gel or reverse-phase high-performance liquid chromatography protocols. Such challenges with Bpin precursors complicate their adoption in clinical radiotracer production, despite well-established reactivity.

This work discloses a potential solution to these challenges, by demonstrating that (hetero)aryl boronic esters derived from 3,4-diethylhexane-3,4-diol (BEpins) are a suitable class of substrates for copper-mediated ^{18}F-fluorination (Figure 1).[2] These precursors can be prepared analogously to Bpin precursors, exhibit greater stability to protodeboronation and are easily purified by silica gel chromatography.[3] A comparative reactivity study indicates that (hetero)aryl-BEpin substrates display similar scope and limitations to the equivalent Bpin under established sets of reaction conditions. Finally, the use of a BEpin substrate in radiotracer synthesis is demonstrated, applying an automated programme developed for the preparation of [^{18}F]flumazenil ([^{18}F]FMZ) on a Trasis AllinOne without modification.

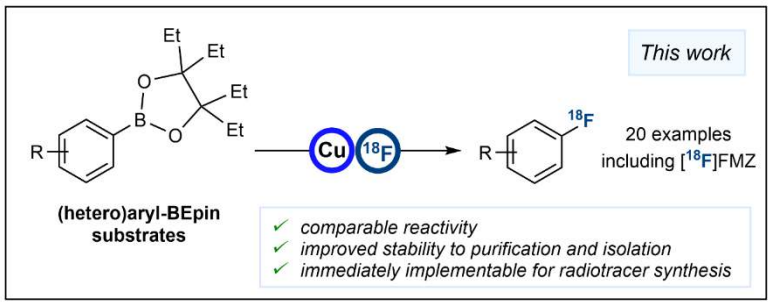

Figure 1. Copper-mediated radiofluorination of (hetero)aryl boronic 1,1,2,2-tetraethylethylene glycol ester (BEpin) reagents.

Acknowledgements
This work is supported by the Biotechnology and Biosciences Research Council (BB/V010999/1), the Engineering and Physical Sciences Research Council (EP/V013041/1), and the National Science

Foundation (CHE-2400056).

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O03

Development of a halofluorocarbon, chromatography-free radiosynthesis of fluorine-18 difluorocarbene on the GE TracerLab FXFN module

C. G. F. Dickmann[1*], S. Milicevic Sephton, [1] F. I. Aigbirhio[1]

[1]Molecular Imaging Chemistry Laboratory, Wolfson Brain Imaging Centre, Department of Clinical Neurosciences, University of Cambridge, Cambridge, CB2 0SZ, United Kingdom

Contact: cgfd2@cam.ac.uk

Background: In recent years, the development of [^{18}F]difluoromethyl radical ([^{18}F]**2**),[1] and [^{18}F]difluorocarbene prosthetic groups ([^{18}F]**4**),[2] has paved the way towards direct [^{18}F]difluoromethylation in routine PET tracer synthesis with high molar activity (Figure 1). Some limitations in their syntheses are perhaps hindering their widespread adoption. These include the requirement of ozone-depleting dibromofluoromethane for the synthesis of precursors **1** and **3** and the lengthy syntheses of both [^{18}F]**2** and [^{18}F]**4** requiring semi-prep purification on cartridge-based radiosynthesis modules. CHDI ligands used.

Aims: The aim of this work was to develop a haloflurocarbon-free, chromatography-free, fully-automated synthesis of [^{18}F]difluorocarbene reagent [^{18}F]**4** on the GE Tracerlab FXFN module.

Methods and Results: Precursor **3** was synthesised in 54% yield from decarboxylative bromination of **5** which circumvented the need for use of the ozone-depleting dibromofluoromethane. Difluorocarbene reagent [^{18}F]**4** was first radiosynthesised on the GE TracerLab FXFN module with semi-prep purification in 2% RCY. The semi-prep purification step was then eliminated in favour of a cartridge-based trapping and elution approach (on an aluminium cartridge loaded in series with a C18 SepPak plus cartridge) to give [^{18}F]**4** in 7.3% ±1.8% (n=6) RCY (97% ± 3% RCP, 1.5 to 11 GBq/µmol). Finally, a fully automated [^{18}F]difluoromethylation radiosynthesis with [^{18}F]**4** was developed on two Tracerlab FXFN modules linked together to yield the model [^{18}F]difluoromethylated compound in adequate amounts for biological studies, include in vivo PET, in under two hours (99.0 MBq, 0.8% RCY, 1.5 GBq/µmol, 103 min total synthesis time). Therefore, we have established a path forward for routine automated synthesis of radiotracers via [^{18}F]difluorocarbene insertion with [^{18}F]**4**.[3]

Conclusions: A halofluorocarbon, chromatography-free synthesis on the GE FXFN Tracerlab module afforded difluorocarbene reagent [^{18}F]**4** in 7.3% ± 1.8% yield. Additionally, a fully-automated three-step [^{18}F]difluorocarbene insertion radiosynthesis is described for the first time.

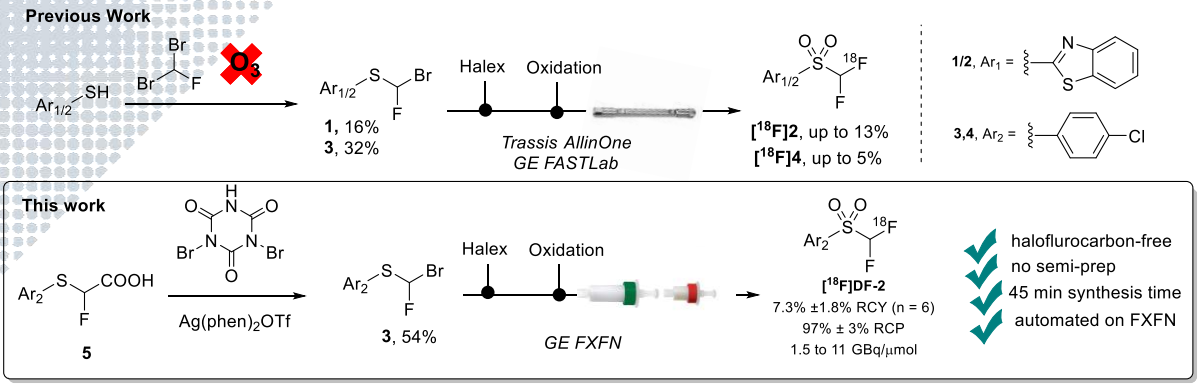

Figure 1. Previous and current radiosynthesis of the [^{18}F]difluoromethyl prosthetic groups.

References

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O04

The Last Mile in the Qualification Marathon: Analytical Method and Process Validations for [^{18}F]SynVesT-1

F.Luzi[1*], R.Hendry[1], C.Steel[1], M.Cooper[1]

[1]Positron Emitting Radipharmaceutical Laboratory (PERL), School of Biomedical Engineering and Imaging Sciences, King's College, London

Contact: federico.luzi@kcl.ac.uk

Keywords: 18-Fluorine; Clinical Manufacture; GMP Validation.

Background: [^{18}F]SynVesT-1 is a small molecule that selectively binds to synaptic vesicle protein 2A (SV2A), a ubiquitous extramembrane protein found on presynaptic vesicles, with potential for imaging several neurological conditions.[1]

Previous efforts from the group enhanced the effectiveness of the production protocol, increasing the $RCY_{n.d.c.}$ from 12 to up to 21%.[2]

The purpose of this abstract is to outline the steps required to successfully validate a radiopharmaceutical for in-human use, in accordance with current GMP regulations.

Methods and Results: The validation covered three main points: aseptic dispensing, analytical method validation, and bioburden/sterility of the sample.
Aseptic dispensing, carried out using a KLAR dispenser and dedicated sterile kits, showed initial incompatibility due to the unmatching viscosity of the matrix and retention of the product. The problem was solved by mounting a different dispensing filter onto the KLAR kit, resulting in homogeneous and reproducible batches.

The strict limits on chemical purity complicated the analytical method validation, which however was accomplished by adjusting the maximum injectable volume.

Bioburden and sterility validation batches were successfully executed and submitted for analysis to external contractors. Execution of these batches also allowed for training of staff.

Conclusions and Future Work: With a robust synthesis method at hand (5 operators had RCY > 20%), the final steps for the validation of [^{18}F]SynVesT-1 were successfully carried out at PERL to allow in-human use of the radiopharmaceutical. The product is aseptically and homogenously dispensed in up to three product vials, ensuring a high dose coverage. The proposed analytical methods are fit for purpose and with great tolerance towards potential impurities. Bioburden and sterility validation batches were executed and results are awaited.
Future work will see the validated method being used for clinical trials using a Quadra™ Total Body PET/CT scanner, in collaboration with Imperial College, London.

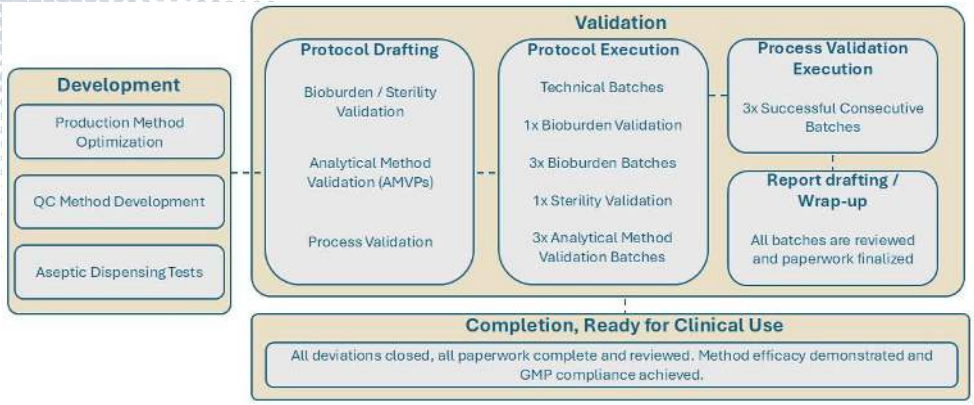

Figure 1. Flowchart describing the full validation process for a novel radiopharmaceutical.

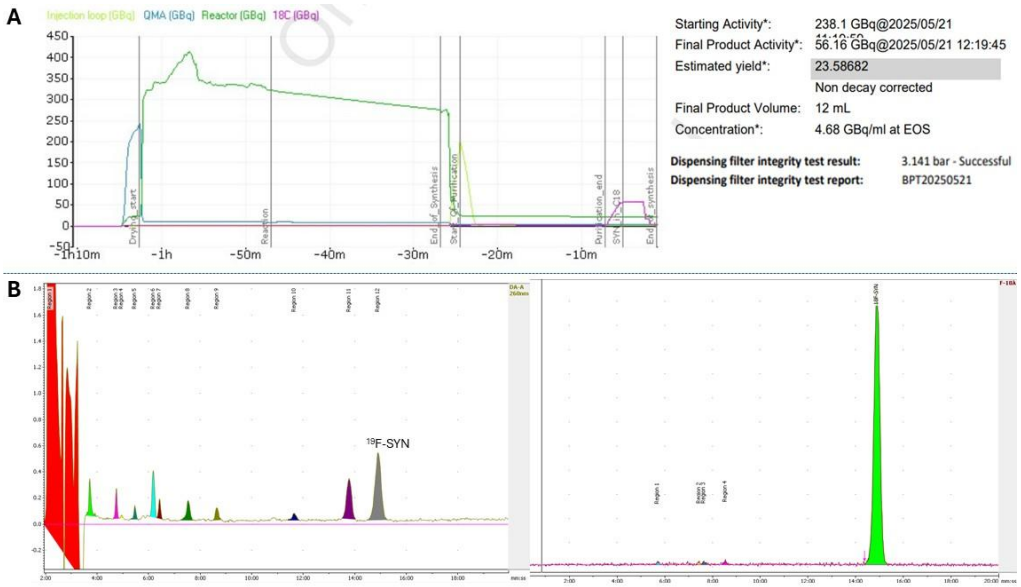

Figure 2. Snapshots from different timepoints of the process validation execution: **A.** Synthesis completion with RCY and filter integrity testing; **B.** Chemical and radiochemical purity confirmed via HPLC.

Acknowledgements

The authors acknowledge the contribution of Prof. Paul Edison and Prof. Federico Turkheimer that will conduct the clinical trials. The authors also thank University of Edinburgh and KU Leuven for the help during the development of the synthesis method.

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O05

Silver (I) Oxide Mediated Radiochemical Synthesis of 1,1-[18F] difluoroalkane Derivatives

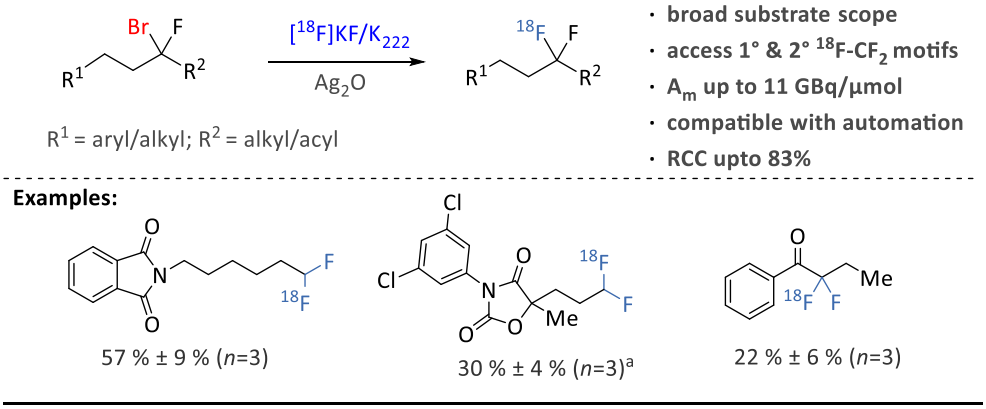
Pawan Mishra[1*], Jasmine Hind[1], Ian Fallis[1] and Matthew Tredwell[1,2]

[1]School of Chemistry, Cardiff University, Main Building, Park Place, Cardiff CF10 3AT, U.K.
[2]Wales Research and Diagnostic PET Imaging Centre, Cardiff University, University Hospital of Wales, Heath Park, Cardiff CF14 4XN, U.K.

Contact: Mishrap2@cardiff.ac.uk

Keywords: 18-Fluorine, PET imaging, Gem-difluoroalkane

Selective and specific ^{18}F-radiotracers are required for use in positron emission tomography (PET) imaging for medical diagnosis and drug development. In this context, several synthetic methods for access to ^{18}F-labelled organic molecules are well-documented in the literature. However, the synthesis of ^{18}F-difluorinated functional groups is highly limited in scope and often results in radiotracers with low molar activities (A_m). Here we disclose the radiochemical synthesis of a wide variety of ^{18}F-difluoroalkyl groups through nucleophilic substitution of geminal bromofluoroalkyl electrophiles with [^{18}F]fluoride mediated by Ag_2O. The utility of this transformation to support (pre)clinical imaging is demonstrated by translation onto an automated synthesizer.



Acknowledgements
Financial support for this was provided by the EPSRC (EP/T031220/1 and EP/T517951/1)

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O06

Docking analysis and preliminary *in vitro* evaluation of various analogues for PET imaging of AMPAR

Shinong Zeng[1*], NishaKuzhuppilly-Ramakrishnan[1], Franklin Aigbirhio[1], Matija Zlatar[2], Yanyan Zhao[1], Selena M. Sephton[1]

[1] University of Cambridge, Molecular Imaging Chemistry Laboratory, Department of Clinical Neurosciences, Cambridge, United Kingdom

[2] University of Belgrade, Institute of Chemistry, Technology and Metallurgy, Njegoseva 12, Belgrade, Serbia

Contact: sz480@cam.ac.uk

Keywords: AMPA Receptors; PET tracers; *in vitro* Evaluation

Neurodegeneration is a key pathological hallmark of disorders, such as Alzheimer's disease (AD). It is a complex interplay of various factors, including glutamatergic neurotransmission via α-amino-3-hydroxy-5-methyl-4- isoxazole propionic acid receptors (AMPAR). Currently, research is focusing on investigating early synaptic plasticity impairments that precede neurodegeneration in various AD mouse models. However, relatively few studies have explored AMPARs as a direct target for the quantification of AD diseases. Therefore, we envisioned using PET to enable the visualisation of AMPAR in the living human brain. In this work, we designed suitable AMPA PET radiotracer candidates based on 4-[2- (phenylsulfonylamino)ethylthio]-2,6-difluoro- phenoxyacetamide (PEPA) structural motifs using docking studies to predict their binding properties. Theoretically, PEPA exhibited a binding affinity of -8.7 kcal/mol, and out of 344 analysed molecules, 199 analogues had an equal or higher theoretical binding affinity. From them 15 candidates were better than –10.5 which was selected as criteria for subsequent in vitro analysis. For the chemical selection, we synthesized PEPA, K-2, and K-2_{OH} as reference compounds. Moreover, we conducted the in vitro evaluation of selected analogues to establish the binding affinity of the tested analogues to one of the AMPAR subunits, GluA2, using the Surface Plasmon Resonance method. The K_D of the PEPA- and K-2-GluA2 interaction was calculated as 154 nM and 24 nM using a steady-state fit model. Furthermore, 10 analogues with theoretically good binding affinities were identified in the fragment screening process. Among these, four compounds showed promising binding to AMPAR GluA2. This novelty stems from the role of AMPAR in modulating synaptic plasticity, hence the need for a suitable PET probe in many neurological disorders.

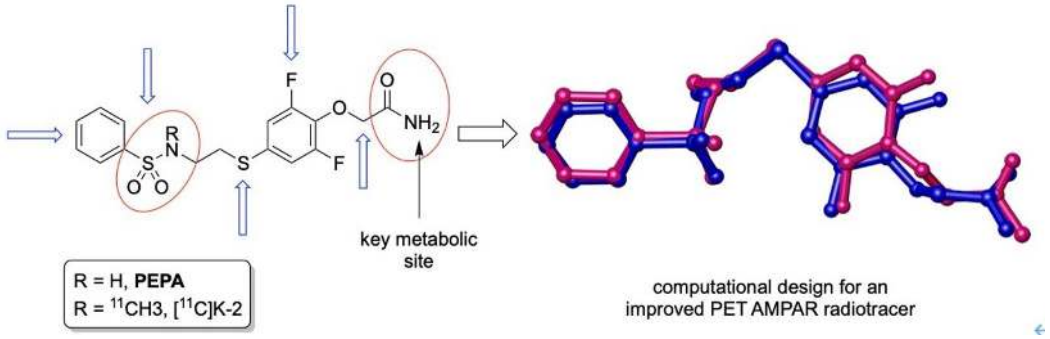

Figure 1: Chemical Structure and Computational Design of PET AMPAR Radiotracer

Previously reported analogue of PEPA, [^{11}C]K-2, showed rapid metabolism in vivo, resulting in a hydrolyzed [^{11}C]K-2_{OH} radio-metabolite, which itself binds to AMPAR with higher affinity. Our docking

study aimed to increase its metabolic stability while preserving its binding properties.

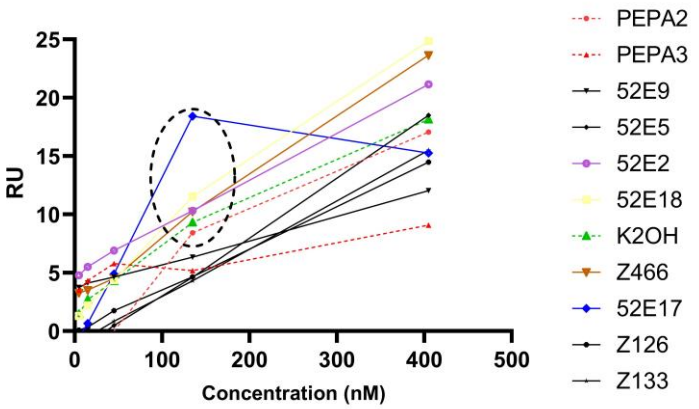

Figure 2: Response signal for the selected analogues binding to AMPAR

Ten compounds, including K-2_{OH}, were identified during the fragment screening process. All compounds exhibited a concentration-dependent increase in response. Analysis was focused on the response at 135 nm, corresponding to the approximate affinity K_D of PEPA. Among these, four compounds demonstrated promising binding to AMPAR. Notably, compound 52E17 displayed a marked increase in response, showing the highest signal at 135 nm.

Acknowledgements
This work is supported through the ARUK Pump Priming Scheme. The authors would like to thank Dr. Katherine (Department of Biochemistry, University of Cambridge)and Dr. Stephen McLaughlin (MRC Laboratory of Molecular Biology) for insightful discussion and the SPR technique.

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O07

Sustainable chemistry approaches to future responsive metallo-theranostics

Sofia Pascu[1*], Ruediger Exner[1], Fernando-Cortezon Tamarit[1,2], Haobo Ge[1,2], Stan Botchway[3], Stephen Paisey and Charareh Pourzand[1]

[1]Department of Chemistry, University of Bath

[2]Department of Life Sciences, University of Bath

[3] STFC Research Complex at Harwell, Harwell Campus, Oxon

[4] PETIC, Medical School, University of Cardiff

Contact: s.pascu@bath.ac.uk

Keywords: multimodal imaging applications, NIR emitting fluorophors, PET with Ga-68, Zr-89, Cu-68; SPECT with In-111

This work presents our recent advances in the synthesis, radiolabelling, and cellular imaging of new fluorescent probes, including near-infrared (NIR) dyes-targeting in cancer cells. Applying sustainable synthetic protocols, notably microwave-assisted methods, we developed a new class of emissive compounds functionalised with N- and N/S-based chelators. These were radiolabelled with Ga-68, Zr-89, Cu-68, and In-111, supporting both PET and SPECT applications. Then, our general design employed symmetrical cyanine dyes as bifunctional fluorescent linkers connecting biological vectors and radioligands (Figure 1). Straightforward nucleophilic substitution enabled the conjugation of fluorophores with DFO or acetylacetone, yielding NIR-emitting probes radiolabelled with Zr-89. Radiochemistry results and optical imaging assays in prostate and other cancer cell lines are presented for a range of synthetic frameworks. Investigations into sulfonated indocyanine dyes revealed their suitability for NIR imaging of living prostate cancer cells. Our far-red probes exhibited promising fluorescence lifetimes and lysosomal localisation, supported by FLIM and TCSPC data. Conjugation with small-molecule targeting vectors, including D-biotin, LysUreaGlu (PSMA-targeting) and the [7,13] bombesin fragment (GRPR-targeting) will also be discussed hereby. To this end, their potential use towards PET/optical and SPECT/optical imaging and the possibility of coupling with optoacoustic imaging and (radio)therapy are of future research interest.

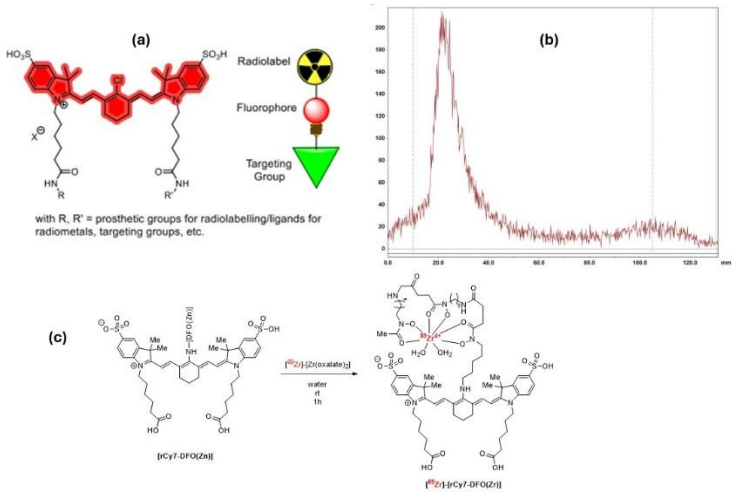

Figure 1. (a) Schematic representation of multimodal, targeted imaging agents as scaffolds for future theranostics. (b) Radio-iTLC of the zirconium-89 complex of the DFO-derivative, synthesized as shown in (c).

Acknowledgements
This work was supported by ERC and EPSRC IAA.

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O08

Novel dual CXCR4 and ACKR3 theranostic agents for PET/SPECT imaging and targeted molecular radiotherapy for cancer

James Wood[1*], Isaline Renard[1,2], John D. Wright[1,2], Juozas Domarkas[2], Benjamin P. Burke[2], Dominique Schols[3], Thomas D'Huys[3], Tom Van Loy[3], Timothy J. Hubin[4] and Stephen J. Archibald[1,2]

[1]Department of Imaging Chemistry and Biology, King's College London, SE1 7EH, London, UK.
[2]Department of Chemistry and Positron Emission Tomography Research Centre, University of Hull, HU6 7RX, Hull, UK.
[3]Rega Institute for Medical Research, KU Leuven, 3000 Leuven, Belgium.
[4]Department of Chemistry and Physics, Southwestern Oklahoma State University, OK 73096, USA.

Contact: James.g.wood@kcl.ac.uk

Keywords: Chemokine, Bicyclam, Copper

The chemokine receptors CXCR4 and ACKR3 (previously CXCR7) have been shown to be overexpressed in many different cancers[1] and usually indicate a poor prognosis. Many imaging agents and therapeutic compounds have been studied for the targeting of CXCR4; however, few exist for ACKR3. Due to the collaborative nature of CXCR4 and ACKR3, targeting both receptors simultaneously could lead to preferable therapeutic outcomes.

[^{64}Cu]CuCB-Bicyclam is a high-affinity radiotracer for the PET imaging of CXCR4-overexpressing tumours[2,3]. Copper(II) and zinc(II) analogues of this compound have been developed in our research group, showing high affinity for both CXCR4 and ACKR3. Radiolabelling selected candidates with ^{64}Cu (PET) and ^{67}Cu (SPECT and radionuclide therapy) has shown promising preliminary results for the dual therapy and imaging of these chemokine receptors.

The lead candidates present with high affinity for the two chemokine receptors, with IC_{50} values as high as 5 nM and 40 nM for CXCR4 and ACKR3, respectively. The successful ^{67}Cu radiolabelling of novel dual CXCR4/ACKR3-targeting agents is reported here with subsequent *in vitro* and *in vivo* evaluation. SPECT/CT imaging of the lead candidate, [^{67}Cu]SJA999, showed significant tumour uptake in animals implanted withCXCR4- and ACKR3-overexpressing xenografts, with high tumour uptake maintained at least 3 days post-injection. Specificity of [^{67}Cu]SJA999 for CXCR4 was confirmed in blocking studies using the high-affinity CXCR4 antagonist, Cu_2CB-Bicyclam.

Future work will focus on extending the *in vivo* validation of our novel dual inhibitor to ACKR3 to better understand the interactions of this type of derivative with the two chemokine receptors of interest. Further evaluation will be carried out in a range of tumour models with different expression levels of CXCR4 and ACKR3, as well as in radiopharmaceutical therapy experiments.

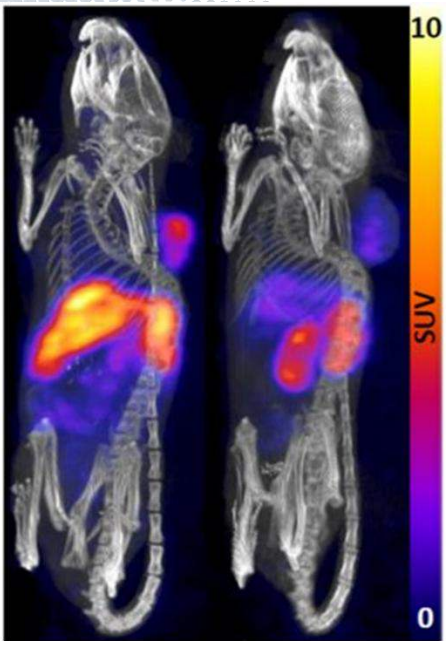

Figure. Representative 30 min SPECT/CT scan of ^{67}Cu-radiolabelled CXCR4/ACKR3 dual inhibitor in U87-CXCR4 tumour-bearing mice, unblocked (left) and blocked with 5 mg/kg (i.p.) of Cu_2CB-Bicyclam (right), imaged at 3 d post-injection.

Acknowledgements

This work is supported by the EPSRC Doctoral Training Programme (Grant number 2904200).

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O09

Development of Astatine-211 Production Capability in the UK

Jennifer Young[1,2]*, Max Palmer[1], Charlotte Rivas[1], Stephen Archibald[2], Zilin Yu[2], Colin Steel[2], Steven Kealey[2], Sean Collins[3], Ben Phoenix[4], Dawid Hampel[4], Tzany Kokalova-Wheldon[4], Carl Wheldon[4], Jane Sosabowski[1]

1. Centre for Cancer Biomarkers and Biotherapeutics, Barts Cancer Institute, John Vane Science Centre, Queen Mary University of London, London, UK.
2. School of Biomedical Engineering & Imaging Sciences, King's College London, London, UK.
3. National Physical Laboratory, Teddington, London, UK.
4. School of Physics and Astronomy, University of Birmingham, Birmingham, UK.

Contact: jennifer.young@qmul.ac.uk

Keywords: Alpha Radionuclides, Astatine-211, Radiohalogens

Astatine-211 is an alpha-particle emitting radiohalogen which displays particularly good characteristics for clinical use in molecular radiotherapy. It has a 7.2 hour half-life, which requires it to be produced in the same country in which it will be used. The production process ^{211}At is well reported, using the nuclear reaction ^{209}Bi(α,2n)^{211}At (1,2), but requires a high energy cyclotron with the capability to produce an alpha beam. There is one such cyclotron in the UK, the Scanditronix MC40 at the University of Birmingham.

In 2023 Queen Mary University of London (QMUL) with collaborators, the University of Birmingham (UoB), King's College London (KCL), and the National Physical Laboratory secured funding from the UK Government's Medical Radionuclide Innovation Programme to establish new UK production capability for ^{211}At.

Project achievements to date include: (1) modification of the MC40 cyclotron solid target holder for Bi-209 targets; (2) the first irradiations of Bi-209 to produce ^{211}At; (3) the design and build of an automated processing rig to purify the ^{211}At; (4) demonstration that the rig can process ^{211}At into a form suitable for radiolabelling.

Next steps in the project include: (1) metrology and quantification of the ^{211}At produced; (2) radiolabelling of a range of precursors with ^{211}At; (3) scale-up of production activity at UoB; (4) optimisation and scale-up of processing at both KCL and QMUL.

This demonstration of UK production of ^{211}At will enable and accelerate research with this new radionuclide and is the first step to enable clinical trials of astatine-211-labelled radiopharmaceuticals in the UK.

Acknowledgements
This work was funded by the Medical Radionuclide Innovation Programme from the Department for Energy Security and Net Zero.

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Poster Presentations

P01

Radiosynthesis of 14-(R,S)-[18F]fluoro-6-thia-heptadecanoic acid

G. Brown[1]*, F. Edgar[1]R. Bielik[1], D. Soloviev[2], D. Lewis[1,2]

[1]Cancer Research UK Scotland Institute, Garscube Estate, Switchback Road, Glasgow, G61 1BD, UK.
[2]School of Cancer Sciences, University of Glasgow; Glasgow, G61 1QH, UK

Contact: g.brown@crukscotlandinstitute.ac.uk

Purpose: Free fatty acids are a key source of energy via non-glycolytic metabolic pathways and 14-(R,S)-[^{18}F]fluoro-6-thia-heptadecanoic acid (FTHA) is a long chain fatty acid analogue used as a PET biomarker to assess mitochondrial fatty acid beta-oxidation. It has previously been used to image energy metabolism in the myocardium and adipose tissue. We propose a new application of PET imaging with [^{18}F]FTHA to trace fatty acid oxidation in NSCLC cancer.

Procedures: The radiosynthesis of [^{18}F]FTHA was performed using a customised RNPlus Research automated radiosynthesis system (Synthra GmbH, Hamburg, Germany). [^{18}F]FTHA was labelled with fluorine-18 via substitution of nucleophilic [^{18}F]fluoride with a 14-(R,S)-benzyl-tosyloxy-6-thiaheptadecanoate precursor. The [^{18}F]product was purified by reverse phase HPLC, isolated by solid phase extraction on a C-18 stationary phase support then formulated in 0.9% saline (containing 6 % ethanol). Radiochemical purity of the final [^{18}F]FTHA formulation was determined by radio-HPLC.

Results: The average radioactivity yield of [^{18}F]FTHA was 10.2 GBq (range 8.4 - 12.8 GBq) at the end of synthesis (EOS) starting from 34 - 40 GBq of [^{18}F]fluoride at the end of bombardment. The synthesis time was 56 minutes. The average radioactivity volumetric concentration at EOS was 988 - 1424 MBq mL^{-1}. The radiochemical purity of the formulated product was 93 - 97 %. A stability test using a 12.0 GBq sample dose with a radioactivity volumetric concentration of 1600 MBq mL^{-1} at EOS showed a small amount of radiolysis 6.5 hours post-synthesis. At t = 0 hrs, the radiochemical purity of the dose was 95.2 % whereas at t = 6.5 hrs the radiochemical purity was 93.2 %.

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P02

Fluorine-18 Labelled D-Amino Acids for PET Imaging of Bacterial Infections

Ishbel Cooke[1], Helen M. Betts[2,3], Jeni C. Luckett[4], Miriam O'Duill[1]

[1]School of Chemistry, University of Nottingham, GSK Carbon Neutral Laboratories, Jubilee Campus, NG8 1BB

[2]Department of Nuclear Medicine, Nottingham University Hospitals NHS Trust, Queen's Medical Centre, Nottingham, NG7 2UH, UK

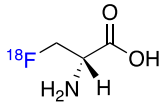
[3]School of Medicine, University of Nottingham, Queen's Medical Centre, Nottingham, NG7 2UH, UK

[4]School of Life Sciences, University of Nottingham, Biodiscovery Institute, University Park, Nottingham, NG7 2RD, UK

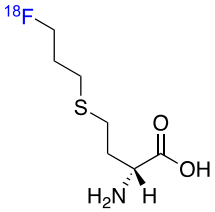
Contact: pcyic6@nottingham.ac.uk

Keywords: Fluorine-18, Bacterial Infection, D-amino acids

Antimicrobial resistance is a growing concern, with recent UK figures reporting a rise in resistant infections, deaths due to resistant infections and the use of antibiotics. PET imaging of bacterial infections holds potential to aid in diagnosis and treatment planning for patients with suspected infection. Currently there is no ideal radiotracer for this purpose. The use of carbon-11 and fluorine-18 radiolabeled D-amino acids have been explored due to their selective uptake in bacterial cell peptidoglycan and not in human cells.[1] This poster details the synthesis, radiosynthesis and *in vitro* evaluation of D-amino acid radiotracers D-[^{18}F]FPHCys and D-[^{18}F]FAla.[2,3] The radiotracers were evaluated in *S. aureus*, *P. aeruginosa* and *E. coli*, using heat killed bacteria as controls.



D-[^{18}F]FAla



D-[^{18}F]FPHCys

Acknowledgements

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P03

Multi-patient dose synthesis of [^{18}F]Flumazenil via a copper-mediated ^{18}F-fluorination

Thibault Gendron[1*], **Gianluca Destro[2*]**, Natan J. W. Straathof[2], Jeroen B. I. Sap[2], Florian Guibbal[2], Charles Vriamont[1], Claire Caygill[3], John R. Atack[3], Andrew J. Watkins[4], Christopher Marshall[4], Rebekka Hueting[4], Corentin Warnier[1], Véronique Gouverneur[2] & Matthew Tredwell[4,5]

[1]Trasis, Rue Gilles Magnée, 90, 4430, Ans, Belgium
[2]Chemistry Research Laboratory, University of Oxford, 12 Mansfield Road, Oxford, OX1 3TA, UK
[3]Medicines Discovery Institute, Cardiff University, Main Building, Park Place, Cardiff, CF10 3AT, UK
[4]Wales Research and Diagnostic PET Imaging Centre, Cardiff University, University Hospital of Wales, Heath Park, Cardiff, CF14 4XN, UK
[5]School of Chemistry, Cardiff University, Main Building, Park Place, Cardiff, CF10 3AT, UK

Contact: gianluca.destro@ed.ac.uk

Keywords: 18-Fluorine, Copper Mediated Radiofluorination, GMP.

Flumazenil (FMZ) is a functionally silent imidazobenzodiazepine which binds to the benzodiazepine binding site of approximately 75% of the brain γ-aminobutyric acid-A receptors (GABAARs). Positron Emission Tomography (PET) imaging of the GABAARs with [^{11}C]FMZ has been used to evidence alterations in neuronal density, to assess target engagement of novel pharmacological agents, and to study disorders such as epilepsy and Huntington's disease. Despite the potential of FMZ PET imaging the short half-life ($t_{1/2}$) of carbon-11 (20 min) has limited the more widespread clinical use of [^{11}C]FMZ. The fluorine-18 (^{18}F) isotopologue with a longer $t_{1/2}$ (110 min) is ideally suited to address this drawback. However, the majority of current radiochemical methods for the synthesis of [^{18}F]FMZ are non-trivial and low yielding (Figure 1). We report a robust, automated protocol that is good manufacturing practice (GMP) compatible, and yields multi-patient doses of [^{18}F]FMZ. The fully automated synthesis was developed on the Trasis AllinOne (AIO) platform using a single-use cassette. [^{18}F]FMZ was synthesized in a one-step procedure from [^{18}F]fluoride, via a copper-mediated ^{18}F-fluorination of a boronate ester precursor. Purification was performed by semi-preparative radio-HPLC and the collected fraction formulated directly into the final product vial (Figure 2). The overall process from start of synthesis to delivery of product is approximately 55 min. Starting with an initial activity of 23.6 ± 5.8 GBq (n = 3) activity yields of [^{18}F]FMZ were 8.0 ± 1 GBq (n = 3). The synthesis was successfully reproduced at two independent sites, where the product passed quality control release criteria in line with the European Pharmacopoeia standards and ICH Q3D(R1) guidelines to be suitable for human use. Reported is a fully automated cassette-based synthesis of [^{18}F]FMZ that is Good Manufacturing Practice (GMP) compatible and produces multi-patient doses of [^{18}F]FMZ.

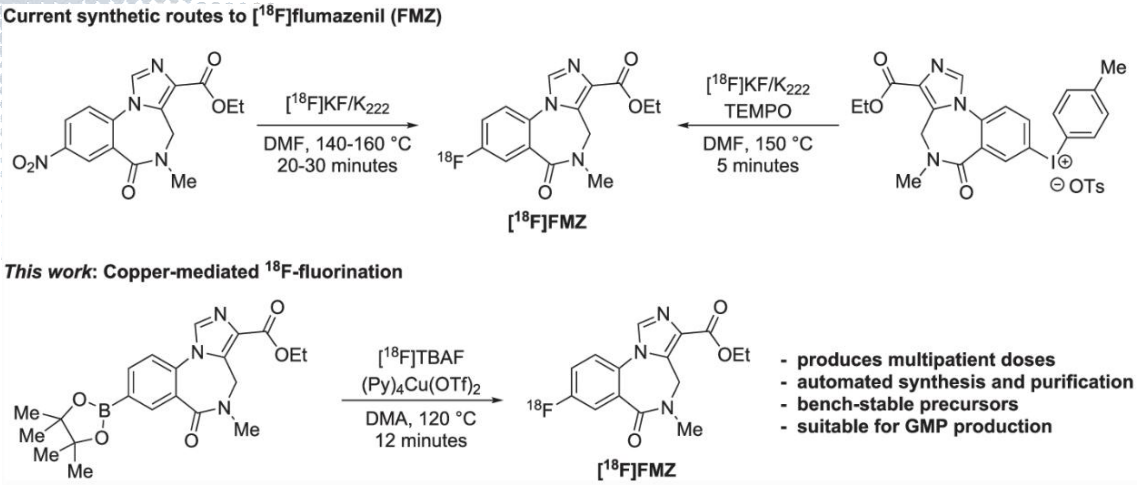

Figure 1: Existing protocols and new copper-mediated 18F-fluorination approach

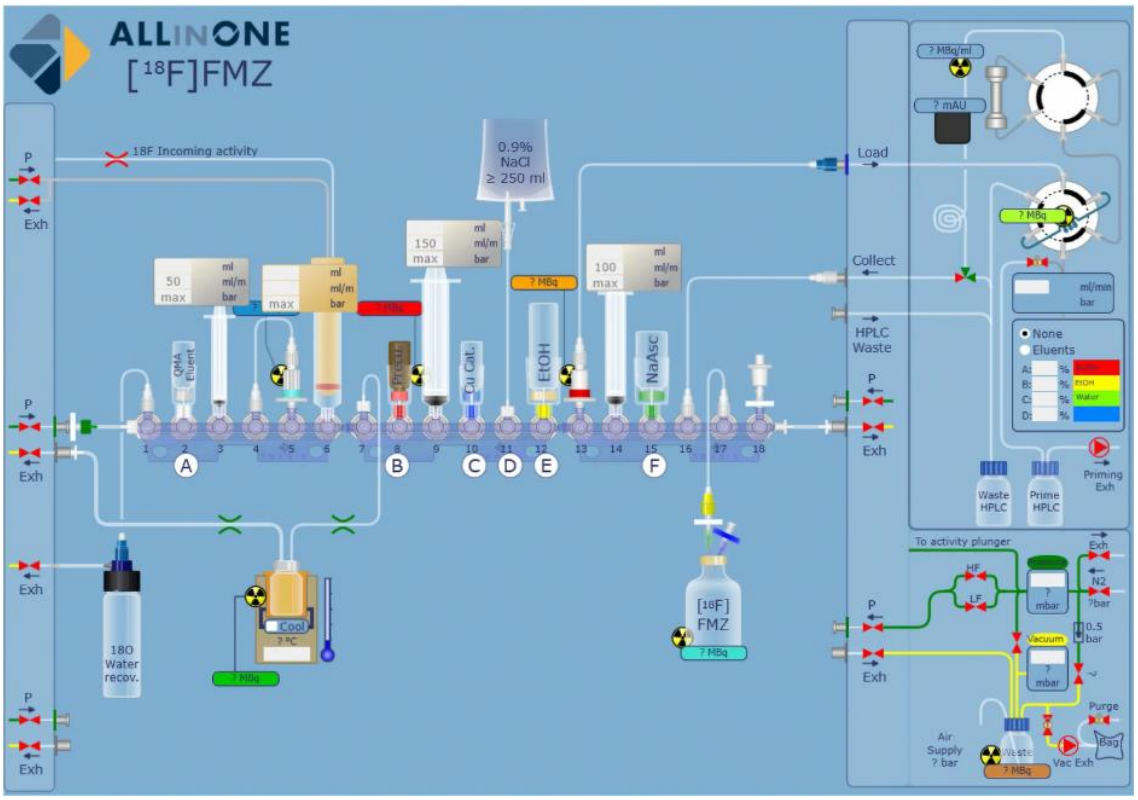

Figure 2: Cassette layout

Acknowledgements

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P04

Organocatalytic Asymmetric Synthesis of SynVesT-1, a PET Imaging Agent of the SV2A Receptor

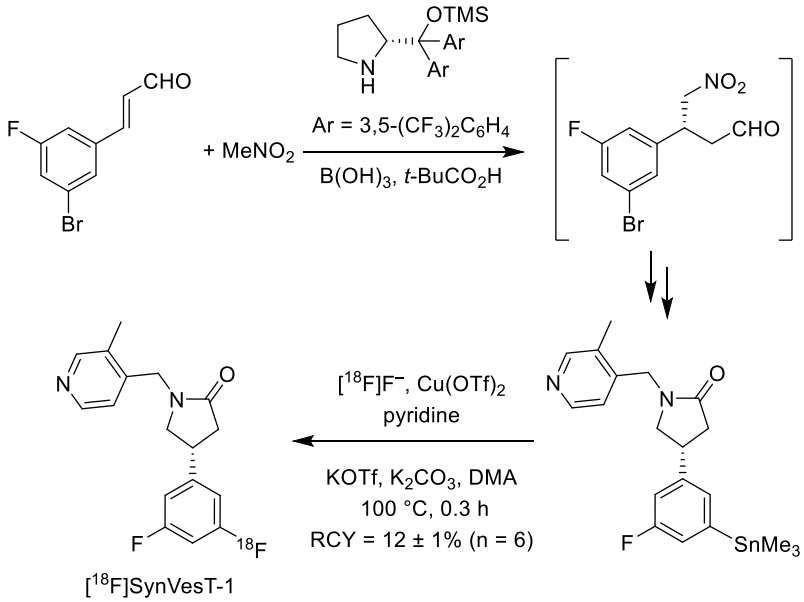
Valeria Burianova[1], **Holly McErlain[1*],** Timaeus E. F. Morgan[2], Adriana A. S. Tavares[2], and Andrew Sutherland[1]

[1]School of Chemistry, University of Glasgow, Glasgow, G12 8QQ, U.K.
[2]BHF-University Centre for Cardiovascular Science, University of Edinburgh, Edinburgh EH16 4TJ, U.K.

Contact: holly.mcerlain@glasgow.ac.uk

Keywords: SV2A; [^{18}F]SynVesT-1; asymmetric organocatalysis.

[^{18}F]SynVesT-1 is a potent and selective positron emission tomography imaging agent for synaptic vesicle glycoprotein 2 (SV2A).[1] SV2A is an integral transmembrane glycoprotein widely expressed in the brain. Although the exact role of SV2A has not been confirmed, it is known that SV2A participates in key vesicular processes. Furthermore, SV2A is a validated target for epilepsy and a biomarker of synaptic density. The established synthetic strategy to obtain [^{18}F]SynVesT-1 involves the multistep synthesis of a racemic intermediate, requiring late-stage separation of the two enantiomers via chiral HPLC.[2] Our aim was to develop an asymmetric synthetic route to access [^{18}F]SynVesT-1. In this work, we optimised a seven-step route to an organotin precursor of [^{18}F]SynVesT-1 starting with a Wittig reaction of 3-bromo-5-fluorobenzaldehyde.[3] This was followed by the asymmetric conjugate addition of nitromethane to the resulting cinnamaldehyde utilising the Hayashi-Jørgensen organocatalyst (Scheme 1). Subsequently, a number of standard transformations facilitated the synthesis of the organotin precursor which was then subjected to automated copper(II)-mediated fluoro-destannylation for the preparation of [^{18}F]SynVesT-1. This work will be discussed, along with a second-generation route detailing the synthesis of a boronic ester-derived precursor to [^{18}F]SynVesT-1.



Scheme 1. Asymmetric synthetic route for the synthesis of [^{18}F]SynVesT-1.

Acknowledgements
This work is supported by a Welcome Trust Technology Development Award (221295/Z/20/Z) and via the Medical Research Council funded Total Body PET Infrastructure Project (MR/Y008944/1).

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P05

^{18}F-Difluoromethyl(ene) Motifs via Oxidative Fluorodecarboxylation with [^{18}F]Fluoride

Sebastiano Ortalli[1*], Joseph Ford[1], Robert Szpera[1], Barbara Stoessel[1], Andrés A. Trabanco[2], Matthew Tredwell[3,4], Véronique Gouverneur[1*]

[1]Chemistry Research Laboratory, University of Oxford, Oxford OX1 3TA, United Kingdom
[2]Global Discovery Chemistry, Therapeutics Discovery, Johnson & Johnson Innovative Medicine, E-45007 Toledo, Spain
[3]Wales Research and Diagnostic PET Imaging Centre, Cardiff University, University Hospital of Wales, Cardiff CF14 4XN, United Kingdom
[4]School of Chemistry, Cardiff University, Cardiff CF10 3AT, United Kingdom

Contact: sebastiano.ortalli@chem.ox.ac.uk

Keywords: Fluorine 18, ^{18}F-Difluoromethyl(ene), Automation

The geminal difluoro motif is highly prevalent in bioactive compounds owing to its uniquely favourable physicochemical properties, capable of influencing key pharmacokinetic parameters such as lipophilicity, metabolic stability, and the pKa of neighbouring functional groups.[1] However, whilst the synthesis of aryl and α-heteroatom ^{18}F-difluoromethyl compounds has been well explored, access to molecules featuring the *gem*-^{18}F-difluoromethyl(ene) motif at less activated positions remains a significant challenge in radiochemistry.[2]
Herein, we describe the radiosynthesis of biorelevant ^{18}F-difluoromethyl(ene)-containing compounds *via* the manganese-mediated ^{18}F-fluorodecarboxylation of α-fluorocarboxylic acid precursors.[3] This direct process provides a solution to a long-standing challenge in ^{18}F-radiochemistry and broadens the accessible radiochemical space for positron emission tomography (PET) ligand discovery. Furthermore, scalability on a fully automated radiosynthetic platform is exemplified with the synthesis of [^{18}F]4,4-difluoropiperidine, a versatile building block amenable to a variety of post-labelling diversification reactions.

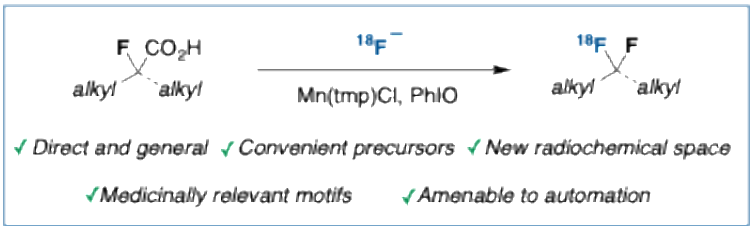

Figure 1. This work: Radiosynthesis of ^{18}F-Difluoromethyl(ene) Motifs via Oxidative Fluorodecarboxylation with [^{18}F]Fluoride.

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P06

Ultrasmall Gold Nanoparticles for the targeted PET Imaging of Prostate Cancer

Rabeeha Al-Zuhairi[1,2*], Juozas Domarkas[1,2], John Wright[1,2,3], Isaline Renard[1,2,3], Georgios Efthimiou[2], Bassim Abdulwahaab[1,2] and Stephen J. Archibald[1,2,3]

[1]PET Research Centre, University of Hull;
[2]Centre for Biomedicine, Hull York Medical School; [3]School of Biomedical Engineering and Imaging Sciences, King's College London.

Contact: R.M.AL-ZUHAIRI-2020@hull.ac.uk

Keywords: Ultrasmall, gold, nanoparticle, PSMA and PET imaging

Background

Prostate cancer PET imaging with gold nanoparticles can utilise functionalisation of the particle surface to target PSMA expressing cancer cells and drive tumour accumulation. [1] When combined with radionuclides, attached to the surface through chelating groups, these nanoparticles can be detected using PET scanning.[2] PET imaging of PSMA expressing tumours already shows promise for early detection, personalised treatment, and more accurate monitoring of cancer progression.[3]

Development and in vitro characterisation

Different novel types of ultrasmall gold nanoparticles were designed include: PSMA1-AuNP, NODAGA-PSMA1-AuNP, NODAGA-PSMA1-PEG4-AuNP, NODAGA-PSMA1-CIP-AuNP, NODAGA-PSMA1-PEG4-CIP-AuNP. After PSMA extension by PEG-6, PSMA2-AuNP, NODAGA-PSMA2-AuNP, NODAGA-PSMA2-PEG4-AuNP, NODAGA-PSMA2-CIP-AuNP and NODAGA-PSMA2-PEG4-CIP-AuNP were synthesised. The characterisation of the gold nanoparticles was carried out using DLS, UV-vis. and ICP, showing a size range from 1.6 to 3 nm and a zeta potential from –27 to –11. Concentration and size characteristics were also investigated using UV-vis. spectroscopy.

Binding affinity (FACS) was determined using flow cytometry experiments with PSMA expressing cell lines, the maximum inhibition of anti-PSMA antibody in the competition assay for the PSMA1 derivatives was observed for PSMA1-AuNP (89%) followed by NODAGA-PSMA1-AuNP and NODGA-PSMA1-PEG-CIP-AuNP (68%). This could be compared with the second generation PSMA2 derivatives, where the maximum binding inhibition observed was for NODAGA-PSMA2-AuNP (89%) and NODAGA-PSMA2-CIP-AuNP (86%). Cytotoxicity was investigated using the MTT assay. LNcap cells was exposed to different concentrations of PSMA1-AuNP giving IC_{50} = 175 µg/mL .

The novel PSMA1-AuNPs and PSMA2-AuNPs were radiolabelled with ^{68}Ga. The tange of radiochemical yields was from 11-19% with a radiochemical purity of 99% (by radio-TLC) achieved after purification using 10k and 5k spin filters. Serum stability assays of functionalised NODAGA-PSMA1-AuNPs with ^{68}Ga NODAGA-PSMA1-AuNPa were carried out in bovine serum at 37°C, demonstrating high stability for all constructs. LNCaP prostate cancer cell uptake of ^{68}Ga-labelled NODAGA-PSMA1-AuNP and NODAGA-PSMA2-AuNP was investigated *in vitro* at three timepoints, showing maximum uptake up of 6% and 12%, respectively.

In vivo imaging studies

The biodistribution of [^{68}Ga]GaNODAGA-CIP-AuNP was assessed in naïve animals in PET/CT studies, showing rapid renal excretion with limited tissue retention. Xenograft tumour models (LNCaP) were imaged using PET/CT for [^{68}Ga]GaNODAGA-CIP-AuNP, [^{68}Ga]GaNODAGA-PSMA1-AuNP and [^{68}Ga]GaNODAGA-PSMA1-PEG-AuNP, again showing rapid renal excretion with no tumour uptake observed for any of the compounds.

Conclusion

A range of ultrasmall gold nanoparticles was synthesised, characterised and radiolabelled. This phase of the research work assessed the characterised nanoparticles *in vivo* and demonstrated a desirable excretion profile but poor tumour uptake. The next step is to investigate the PSMA2-AuNP compounds which have been designed to improve the capability to penetrate and bind to tumour cell expressed PSMA. The original design may have resulted in too short a circulation time for tumour uptake. Modification of the PSMA binding group is expected to address this issue.

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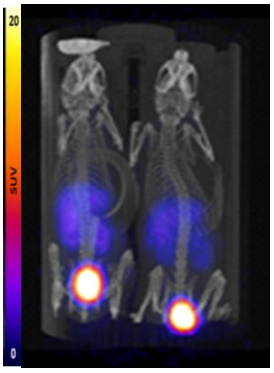
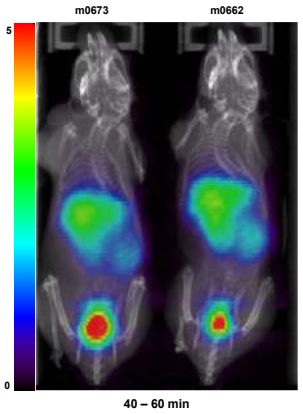
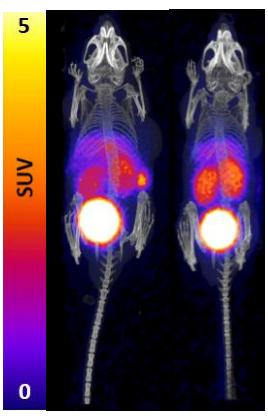
(A) Biodistribution [^{68}Ga]GaNODAGA-CIP-AuNP



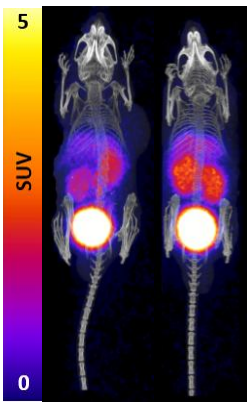
(B) Tumour model PET [^{68}Ga]GaNODAGA-CIP-AuNP



(C) Tumour model PET [^{68}Ga]GaNODAGA-PSMA1-AuNP



(D) Tumour model PET [^{68}Ga]GaNODAGA-PEG-PSMA1-AuNP



P07

Automating Zirconium-89 Radiopharmaceutical production using commercially available cassette-based platforms.

Marshall, N; Domarkas, J; Wright, S; Archibald, S. J.; Allott, L*

Contact: louis.allott@kcl.ac.uk

Positron Emission Tomography (PET) is a clinical functional imaging technique used in the assessment and monitoring of diseases like cancer, to understand the biology driving the disease phenotype. There is growing interest in developing radiopharmaceuticals from large proteins like antibodies (150 kDa) due to their high target affinity and specificity. This is known as immunoPET and utilises the isotopes like zirconium-89 (^{89}Zr), due to its long radioactive half-life (3.3-day half-life) which is compatible with the slow pharmacokinetics of antibodies (24 – 72h). [1]

The production of ^{89}Zr-immunoPET radiopharmaceuticals for small clinical trials is currently performed by manual hands-on processes following good manufacturing practices (GMP); however, the larger scale production of multi-patient doses, or the production of ^{89}Zr-immunoconjugates in facilities which cannot accommodate hands-on processes, are current roadblocks to implementing ^{89}Zr production for clinical studies.

Automated methodologies could improve access to immunoPET, and bring benefits such as standardisation of synthesis, batch reproducibility, and better radiation protection to those manufacturing radiopharmaceuticals.

Some automated methodologies have been reported in the literature, for example the work of Poot et al (2019) [2], however our work represents the first ^{89}Zr-radiolabelling procedure using a fully cassette-based platform, the GE FASTLab™ (GE HealthCare). The FASTLab™ is commercially available and installed in >1000 radiopharmaceutical manufacturing sites worldwide, which could expedite worldwide accessibility to ^{89}Zr radiopharmaceuticals as well as our ambition to deliver immunoPET clinical trials at the Molecular Imaging Research Centre (MIRC), Castle Hill Hospital, Hull.

Model bioconjugates DFO-Trastuzumab and DFO-BSA (bovine serum albumin) have been synthesised in our laboratory in good yields (ca. 83.2 %). Both [^{89}Zr]Zr-DFO-Trastuzumab and [^{89}Zr]Zr-DFO-BSA have been radiolabelled using a hands-on approach, in good radiochemical yield (41.8% and 60.2%, respectively) and purified by size exclusion PD-10 columns (>98% radiochemical purity). The radiolabelling is now being translated into a fully automated procedure using the FASTLab. A cassette has been designed, and a sequence is currently in advanced stages of development.

Once the method has been developed, it will be validated at the MIRC with a view to seek Medicines and Healthcare Products Regulatory Agency (MHRA) approval for its use in the clinical production of ^{89}Zr immunoconjugates.

Figure 1: Schematic showing the aims of the project. *Monoclonal antibodies (mAbs) are conjugated to DFO (DFO-NCS). mAb-DFO precursors undergo an automated radiolabelling procedure using the GE FASTLab platform. The outcome of this will be a ^{89}Zr radiolabelled radiopharmaceutical. Figure adapted from Zeglis and Lewis (2015).*

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P08

Bicycle Radionuclide Conjugates for radioisotope delivery to solid tumors

Gemma Mudd[1], Johanna Lahdenranta[2], Anusha Regupathy[1], Ben Blakeman[1], Francesca Wood[1], Philip Huxley[1]

[1]BicycleTx Ltd, Portway Building, Granta Park, Cambridge, CB21 6GS
[2]Bicycle Therapeutics Inc, 35 Cambridgepark Drive, Cambridge, MA, 02140, United States

Contact: gemma.mudd@bicycletx.com

Keywords: 68-Gallium, 177-Lutetium, Clinical Manufacture

Bicycle Therapeutics is developing a unique class of chemically synthesised medicines. Bicycle® molecules are a novel peptide-based modality consisting of entropically constrained short peptides stabilized in a bi-cyclic structure using a central chemical scaffold. De novo identification of Bicycles that bind to biological targets, including proteins overexpressed in tumors, can be performed using the Bicycle® phage display platform.

Bicycle molecules have potential broad utility, allowing efficient and targeted delivery of different classes of payloads into tumors, for example cytotoxic agents, radioisotopes, and immune modulators. Bicycle® molecules are currently being explored in the clinic as Bicycle drug conjugates (BDCs) for targeted delivery of cytotoxic payloads into tumors. In an alternative approach, we are developing Bicycle Radionuclide Conjugates (BRCs), in which Bicycle® molecules are employed as targeting vectors to deliver radioisotopes to tumors for cancer imaging and therapy.

The inherent properties of Bicycle® molecules, namely their small size (compared to biologics) and hydrophilic nature, make them an ideal modality for radionuclide delivery. These characteristics, combined with exquisite binding specificity and high binding affinity, allow for rapid extravasation and tumor penetration, resulting in high accumulation of payload in the tumor. Their short biological half-life allows high contrast imaging at early timepoints and limits the exposure of normal tissue to payload.

Chemical optimization can be utilized to further improve binding affinity, in vivo stability and biodistribution. In this body of work, we used in vitro cell binding assays and mouse cell line derived xenograft models for:

1) Characterization of early BRCs to establish binding properties and in vivo biodistribution
2) Optimization of BRCs to improve their biodistribution profiles.

Here, we show that BRCs efficiently deliver radioisotopes to tumors in preclinical models, and that lead optimization of BRCs can produce molecules with improved in vivo behaviour.

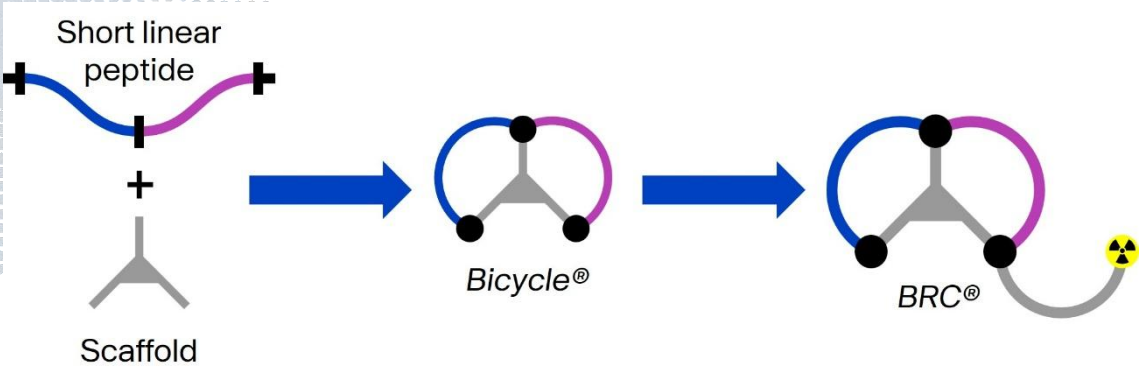


Figure 2: The Bicycle Radionuclide Conjugate® (BRC®) concept

P09 – Abstract withdrawn by author

P10

Gallium-68 Encapsulated Inorganic Nanoparticles for PET and Fluorescence Imaging

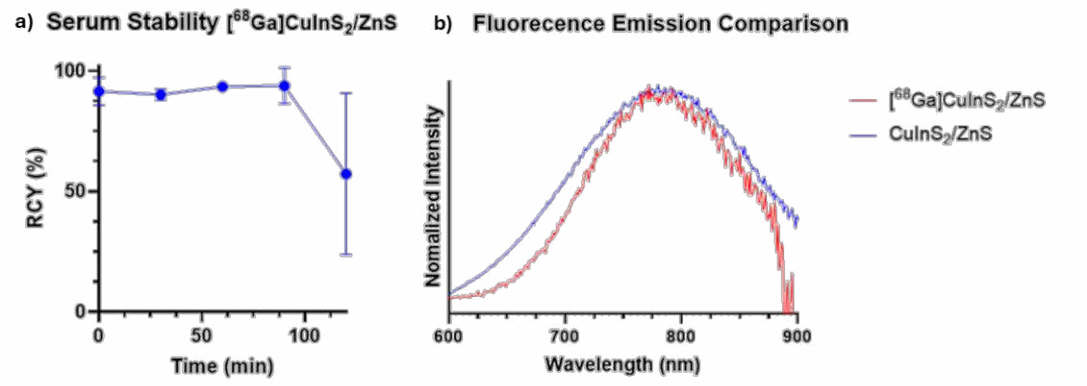
Aisleen S. Whelan[1,2], Thomas W. Price[1], Hélio M. Gil[1], Laurène Wagner[1], Samantha Y.A. Terry[1], Mark Green[2], Sean Woodall[3], Graeme J. Stasiuk[1]

[1]Kings College London, Department of Imaging Chemistry and Biology, London, United Kingdom
[2] Department of Physics, Faculty of Natural, Mathematical & Engineering Sciences, King's College London, London, WC2R 2LS
[3]United Kingdom National Nuclear Laboratory, Central Laboratory, Cumbria, United Kingdom

Contact: aisleen.whelan@kcl.ac.uk

Keywords: Other Positron Emitters, 68-Gallium, Nanoparticles

Dual-modal imaging, combining PET and fluorescence, offers great potential for enhancing tumour detection and image-guided surgery using one molecule. Quantum dots (QDs), with their high brightness, stability, and tuneable optical properties, serve as an ideal platform for these applications.[1,2] This work focuses on encapsulating gallium-68 within Copper Indium Sulphide/Zinc Sulphide ($CuInS_2$/ZnS) QDs to enable simultaneous PET and fluorescence imaging, allowing for staging and surgical guidance on the same day. $CuInS_2$/ZnS QDs were synthesised using a microwave method, which ensures rapid and uniform heating for efficient core-shell formation. Gallium-68 was incorporated into the QD core during synthesis. The QDs were characterized using fluorescence analysis, UV-Vis absorbance, and dynamic light scattering to confirm optical properties and size distribution. Serum stability was assessed via instant thin-layer chromatography (iTLC). The emission peaks of $CuInS_2$/ZnS and [^{68}Ga]$CuInS_2$/ZnS QDs remained at approximately 780 nm, indicating that gallium-68 integration preserved fluorescence properties. iTLC demonstrated effective gallium-68 encapsulation with a radiochemical conversion of 44%. Serum stability studies revealed gallium-68 retention above 90% for over 90 minutes (92% at 0 min, 94% at 90 min) before decreasing to 58% at 120 minutes, maintaining robust stability over two half-lives. This work successfully demonstrates gallium-68 encapsulation within $CuInS_2$/ZnS QDs for dual-modal imaging. The preserved fluorescence and high stability highlight their potential for improving tumour detection and surgical outcomes, streamlining imaging procedures, and reducing patient burden.



a) Serum Stability of gallium-68 Encapsulated QDs Over Two Half-Lives b) Comparison of Normalized Fluorescence Emission for QDs and gallium-68 Encapsulated QDs

Acknowledgements

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P11

Production of [^{11}C]PK11195 on Synthra MeI plus in a GMP environment

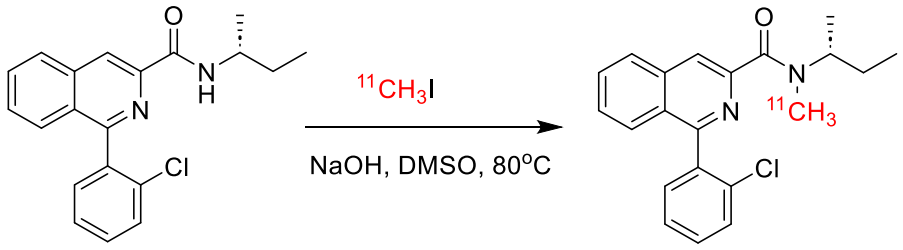
Matthew Hird[1*], Lydia Ward[1], Aniruddha Doke[1] and Graham Smith[1].

[1]Radiopharmaceutical Unit, Wolfson Brain Imaging Centre, School of Clinical Medicine, University of Cambridge.

Contact: mh910@cam.ac.uk

Introduction: [^{11}C]PK11195, is a PET is a first-generation translocator protein (TSPO) PET radiopharmaceutical revalidated at the Radiopharmaceutical Unit (RPU). Exempt from the issues associated with RS6971 polymorphism, it is used in clinical settings for diagnosis of neuroinflammation related disorders.

Materials and Methods: The Synthra MeI plus is used for the synthesis of [^{11}C]PK11195 via semi preparative HPLC purification. [^{11}C]CO_2 is produced from the GE PETtrace 800 cyclotron in 50-60 min. Irradiation produces ~45 GBq of starting [^{11}C]CO2 radioactivity which on the module is converted via [^{11}C]CH_4 to [^{11}C]CH_3I. The radiosynthesis of [^{11}C]PK11195 proceeds via methylation of the PK11195 precursor (2 mg) in DMSO. After a 6-minute delivery to the reactor, the reaction is heated at 80°C for 3 minutes. The solution is cooled and diluted with water before being injected onto the semi-preparative column. The product peak is collected in 17mL of water and then trapped on an Oasis MCX cartridge. The cartridge is washed with water for injection (WFI) to wash off solvents and impurities into the waste bottle. [^{11}C]PK11195 is eluted from the cartridges with ~1 mL of Ethanol and 2 mL of PBS into a solution of 10 mL 0.9 % NaCl, then delivered to the dispensing system (Clio dispenser).



Scheme 1. Radiosynthesis of [^{11}C]PK11195

Results: Currently in routine production at the RPU for one patient dose at a time. Typical synthesis time was 48 minutes, and average radiochemical yield was 10 %, 1.4 GBq (n = 5), with a molar activity average of 83.8 GBq/µmol (n= 5). This provides sufficient dose for imaging studies on site. A large percentage of [^{11}C]PK11195 (~40%) is currently stuck on the dispensing kit (due to lipophilicity of PK).

Conclusions: [^{11}C]PK11195 has been validated for clinical production in RPU. The manufacturing process is reasonably robust, semi-automated with minimal user interaction and provides enough radiotracer for 1 patient doses on-site.

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P12

Synthesis of [^{11}C]HCN for clinical production of L-[^{11}C]Leucine

João Louçano[1*], Simon Zientek[1], Matthew Hird[1], Sebaey Mahgoub[1], Aniruddha Doke[1], Graham Smith[1]

[1]Radiopharmaceutical Unit, Wolfson Brain Imaging Centre, Department of Clinical Neurosciences, University of Cambridge

Contact: jl2559@cam.ac.uk

Keywords: Carbon-11; automation; cyanide**.**

[^{11}C]HCN is a pivotal precursor in the synthesis of 11C-labelled radiotracers, widely utilized in the production of amino acids, deoxyglucose, glucose, and amines. Its versatility and importance in radiochemistry are well-documented, facilitating the development of numerous clinically significant radiotracers [1]. One such tracer is L-[^{11}C]Leucine ([^{11}C]Leu), which is currently being tested to study the pathophysiology of Alzheimer's disease. Here, we report the automated synthesis of [^{11}C]HCN from cyclotron produced [^{11}C]CO2, and it's subsequent use for the synthesis of [^{11}C]Leu.

In a typical run, [^{11}C]CO_2 is produced from a GE PETtrace 800 cyclotron and delivered to a modified Synthra MeI module. Catalytic reduction by H_2 over Ni generates [^{11}C]CH_4, which is converted to cyanide by reaction with gaseous NH_3 over Pt catalyst at 950°C. The resulting [^{11}C]HCN is directed to a second radiosynthesis module for the production of L-[11C]Leucine via a Bucherer-Strecker reaction [2]. In parallel, isovaleraldehyde bisulfite is reacted with ammonium hydroxide in the second radiosynthesis module. The resulting aminosulfonate reacts with [^{11}C]HCN to give the aminonitrile, which in turn is hydrolysed to give racemic [^{11}C]leucine. The L form is obtained by chiral HPLC purification.

Four independent productions yielded 13-20 GBq of [^{11}C]HCN (corresponding to 31–45% radiochemical yield from [^{11}C]CO2, not decay corrected). Subsequent [^{11}C]Leu synthesis yielded 0.6-1.1 GBq of purified tracer, consistently meeting clinical standards for chemical, radiochemical, and enantiomerical purity.

The process has been validated for clinical production of L-[^{11}C]Leucine which is now being used in clinical trials. The synthesis and validation of [^{11}C]HCN for the clinical production of L-[^{11}C]Leucine demonstrate the potential for robust and efficient ^{11}C radiotracer production, paving the way for advanced PET imaging applications.

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Clinical Manufacture Sessions

SESSION A

An Introduction To Annex 1

Sylvain Eschenlauer[1]

[1]West of Scotland PET Centre, Gartnavel General Hospital, NHS Greater Glasgow and Clyde, Glasgow, G12 0YN, U.K.

Contact: Sylvain.Eschenlauer@nhs.scot

The aim of this session is to present the key changes in the new version of Annex 1. We will look at how to assess current practice against new Annex 1 and how to implement the necessary changes to ensure continued compliance.

SESSION B

Integration, Integration, Integration

Ken Wilson[1], Sue Champion[2]

[1]Edinburgh Imaging PET Radiochemistry, University of Edinburgh, Edinburgh, EH16 4TJ, U.K.

[2]West of Scotland PET Centre, Gartnavel General Hospital, NHS Greater Glasgow and Clyde, Glasgow, G12 0YN, U.K.

Contact: kenneth.wilson@ed.ac.uk

The aim of this session is to look at how we approach chromatographic integration, the specific challenges encountered in the PET Radiochemistry environment and look into the enigma that is 'A Peak'.

Thank you to our generous sponsors