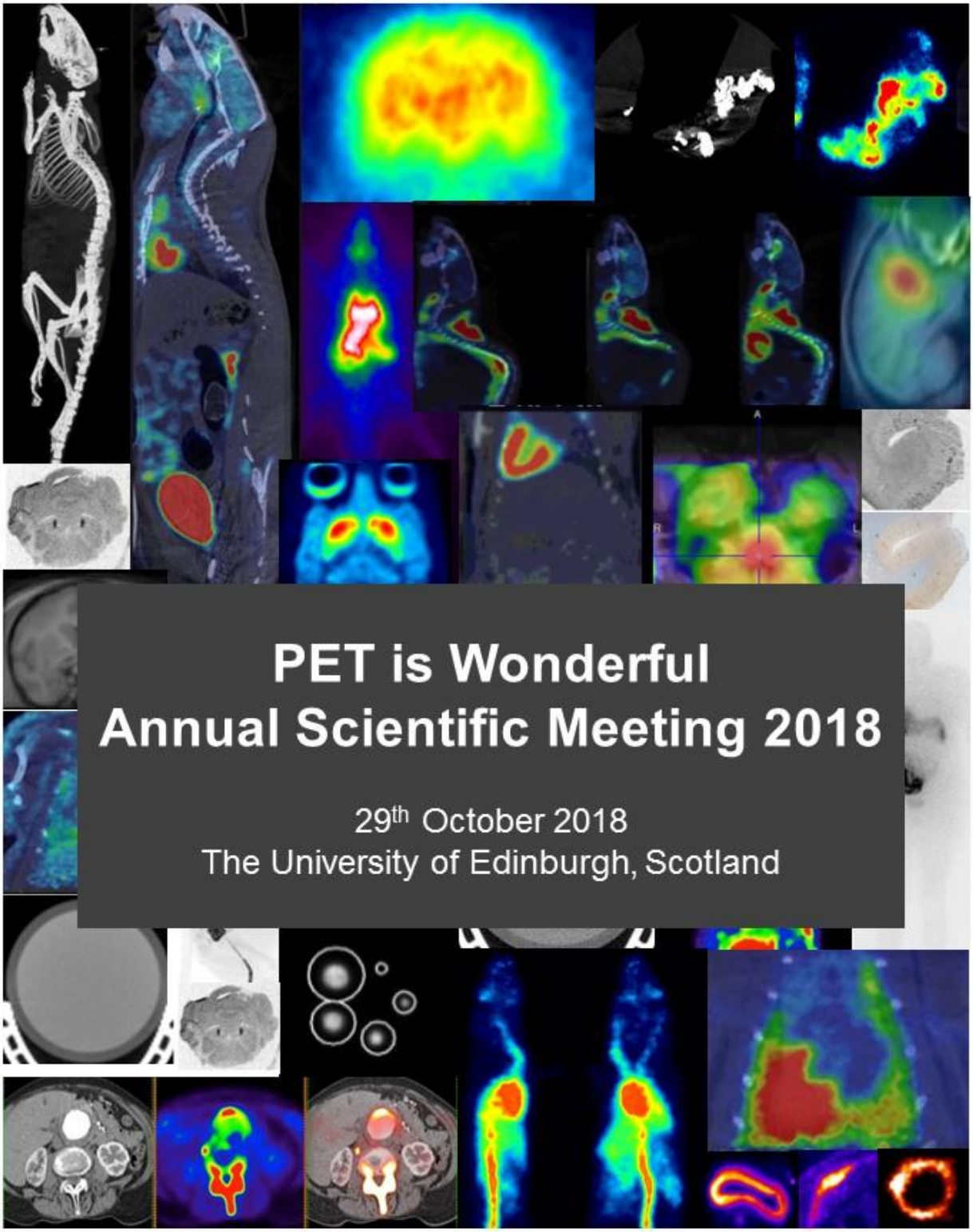

# PET is Wonderful
# Annual Scientific Meeting 2018

29th October 2018
The University of Edinburgh, Scotland

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# Welcome:

Dear PET enthusiasts,

Welcome to the first “PET is Wonderful” Annual Scientific Meeting!

*Once upon a time, a group of subjects needed to get PET scans to investigate their brain function. To take on this challenge, a valiant team of two PET researchers was commissioned and the work began. For days, everything went precisely and timely wrong, and the subjects were rather disappointed they did not get their PET scans. However, the valiant team to two PET researchers did not rest until the PET radiotracer could be successfully prepared and used to image the small group of subjects. During the pursuit of that happy ending, several moments of despair occurred, until finally something magical happened: a PET scan! The sky was bluer that day, the grass was greener that day, all planets were aligned that day and the subjects were finally scanned! The moment was gravely recognised by one of the PET researchers who proclaimed: “PET is Wonderful”!*

The story above is based on real events and may be familiar to many (possibly all) of you. If for nothing else, it aims to inspire those going through the “despair phase” into believe that there will be a “PET is Wonderful” moment ahead. And to encourage the use of powerful PET imaging tools, despite the hurdles along the way, to enhance our scientific knowledge of how human diseases develop and progress, to discover new treatments for disease and ultimately to make a real impact on people’s health.

For this first “PET is Wonderful” scientific meeting, we have invited many speakers working in the field of PET imaging research, as well as, applying PET tools to answer their research questions. Our two keynote speakers have a world-wide recognised track-record on using PET imaging to develop new treatments for various human diseases; and have worked for large pharmaceutical companies for over a decade. During this meeting there will also be various opportunities to network with all delegates. We have a small but enthusiastic group of poster presenters who would be delighted to give you a full overview of their research and a raffle ticket! Our meeting sponsors have also been very supportive of this unusually titled meeting (and we thank them for that), which we hope will be the first of many.

We would like to thank all meeting sponsors, speakers, keynote speakers, poster presenters, reviewers and judges for all their contributions to this meeting. And Adriana wants to especially thank Anne for always supporting this meeting - even when Adriana suggested we should have what someone once called “a weird looking logo” on all delegate bags; and thought a “cabaret style room layout” would be just ideal for scientific discussions and networking.

We hope you enjoy the scientific content of this meeting and best of luck with the raffle draw!

*The PiW Meeting Organisers*

**Meeting Organisers:**
Adriana Tavares, Edinburgh Imaging, UK
Anne Grant, Edinburgh Imaging, UK
Catriona Anderson, BHF/University CVS, UK
Christophe Lucatelli, Edinburgh Imaging, UK
Luke Baxter, Edinburgh Imaging, UK
Molly Osborn, BHF/University CVS, UK

**Abstract Review Scientific Committee:**
David Wyper, Neurosciences Foundation, UK
Dan Peters, DanPET, Sweden
Gillian McNaught, Edinburgh Imaging, UK

**Poster Presentation Judges:**
Gilles Tamagnan, XingImaging, USA
Paul Maguire, UCB, Belgium

**Meeting Chairs:**

*Radiochemistry session*
Christophe Lucatelli, Edinburgh Imaging, UK
Gilles Tamagnan, XingImaging, USA

*Central Nervous System & SINAPSE session*
David Wyper, Neurosciences Foundation, UK
Paul Maguire, UCB, Belgium

*Keynote speaker – session 1*
David Wyper, Neurosciences Foundation, UK

*Warburg and Pasteur effects session:*
Adam Waldman, Edinburgh Imaging, UK
Patrick Hadoke, BHF/University CVS, UK

*Bench, bedside and beyond PET session:*
Anthony Gee, King's College, UK
Will Cawthorn, BHF/University CVS, UK

*Keynote speaker – session 2*
David Wyper, Neurosciences Foundation, UK

**VIP PET Prize Judges:**
Adriana Tavares, Edinburgh Imaging, UK
Christophe Lucatelli, Edinburgh Imaging, UK


South Hall Complex, The University of Edinburgh, UK

## Meeting Sponsors:

**Diamond:**

**Gold:**

PET is Wonderful
Est. 2015

| FINAL MEETING PROGRAMME | |
|---|---|
| **9:00 – 9:30** | Welcome and registration |
| **9:30 – 9:40** | **Prof David Wyper**<br>Opening of PiW Annual Meeting 2018 |
| **9:40 – 10:00** | **Dr Adriana Tavares**<br>Why “PET is Wonderful”? |
| **10:00 – 11:00** | **What is new in (radio)chemistry?** |
| | **Dr Andrew Sutherland, University of Glasgow, UK**<br>New Molecular Tracers for PET Imaging of the Translocator Protein (TSPO) |
| | **Dr Paul Lusby, University of Edinburgh, UK**<br>Novel Platforms for Molecular Imaging using Encapsulation Methods |
| | **Prof Anthony Gee, King’s College London, UK**<br>What is special about being alive? …. Discrepancies between *in vivo* and *in vitro* binding of radiotracers |
| **11:00 – 11:20** | **Tea and coffee morning break** |
| | Exhibitors and poster browsing. Delegate Engagement Prize. |
| **11:20 – 12:05** | **Central nervous system and the origins of SINAPSE** |
| | **Dr Tilo Kunath, University of Edinburgh, UK**<br>$^{18}$F-DOPA PET imaging of a novel CRISPR-engineered rat model of Parkinson’s |
| | **Prof Adam Waldman, University of Edinburgh, UK**<br>PET of glioma metabolism - even more wonderful with a bit of MRI? |
| | **Prof Alison Murray, University of Aberdeen, UK**<br>The power of 3: SINAPSE, PET and industry |
| **12:05 – 12:50** | **Keynote speaker talk 1:** |
| | **Dr Gilles Tamagnan, XingImaging, USA**<br>Clinical trials of radiotracers for brain imaging: Translating an imaging agent to the clinic? |
| **12:50 – 13:40** | **Lunch and poster session** |
| | Exhibitors and poster browsing. Delegate Engagement Prize.<br>*Bartec and SouthernScientific 5 minute sponsor pitch.* |

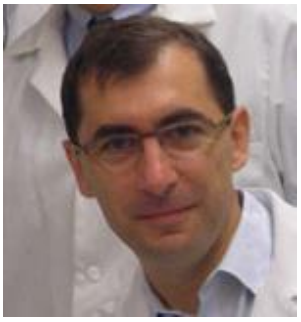
| | |
|---|---|
| **13:40 – 14:25** | **The Warburg and Pasteur effects: new ideas and old-school PET** |
| | **Dr Will Cawthorn, University of Edinburgh, UK**<br>Using PET/CT to dissect the metabolic functions of adipose tissue |
| | **Dr Roland Stimson, University of Edinburgh, UK**<br>Imaging brown adipose tissue in humans – a hot topic |
| | **Prof Sarah Walmsley, University of Edinburgh, UK**<br>Hypoxia and the innate immune response |
| **14:25 – 14:45** | **Afternoon break and refreshments** |
| | Exhibitors and poster browsing. Delegate Engagement Prize. |
| **14:45 – 15:30** | **Bench, bedside and beyond PET imaging** |
| | **Dr Patrick Hadoke, University of Edinburgh, UK**<br>Do they stay or do they go? Tracking the fate of cells administered during ischaemia-induced angiogenesis |
| | **Dr Shareen Forbes, University of Edinburgh, UK**<br>Applications of PET imaging to understand and optimise islet transplantation in Man |
| | **Prof David Newby, University of Edinburgh, UK**<br>Non-invasive imaging of cardiovascular disease: it's chalk and cheese |
| **15:30– 16:15** | **Keynote speaker talk 2:** |
| | **Dr Paul Maguire, UCB, Belgium**<br>Using PET to develop novel medicines |
| **16:20 – 17:00** | **Prof David Wyper**<br>Meeting Prizes:<br>- Announcement of the "Best Poster Prize" winner<br>- Announcement of the "Delegate Engagement Prize" winner<br>- Announcement of the "VIP PET Prize" winner |

# Keynote Speakers:

**Dr Paul Maguire**

Paul is Senior Director and Molecular Imaging Lead in UCB Pharma Translational Medicine Neuroscience, Braine l'Alleud, Belgium. He received his BSc. from Paisley College of Technology and PhD from University of Surrey, UK and is MIPEM, MInstP and UK clinical scientist. He was previously Director and Head of Clinical Imaging at Novartis Basel, Switzerland and Director of Neuroimaging at Pfizer Global R&D, Groton, US. He has been leading the application of imaging and biomarkers in translational neurosciences for the past 14 years. His research interests include PET-PK modeling, molecular imaging probe development, neuronal activation as a target and mechanism biomarker, and atrophy measurements using structural MRI. In his earlier career 1990-2004 Paul was physicist in the PET program, Paul Scherrer Institute PET research program in Villigen, Switzerland, assistant professor and medical physicist at University Medical Center Groningen / University of Groningen.

**Dr Gilles Tamagnan**



Gilles D. Tamagnan, PhD, received his doctorate in medicinal chemistry at the University Joseph Fourier in Grenoble, France in 1993. After a postdoctoral fellowship spent on the crystallization of protein, Dr. Tamagnan completed a second postdoctoral fellowship at RBI in Boston, Massachusetts. His research was focused on developing new radioligands for the diagnosis of Parkinson's disease, and Dr. Tamagnan is a co-inventor of DatScan. He joined the Neuroimaging Program at Yale University in June 1997 to work on the development of new radioligands to study neurodegenerative diseases. Later he moved to Molecular NeuroImaging (MNI) LLC and the Institute for Neurodegenerative Disorders (IND) in 2003, where he worked as Vice President of Chemistry and Translational Research and Laboratory Research and Development Director for several years. Recently Dr Tamagnan has found and is the current Chief Executive Officer of XingImaging LLC, a company focused on developing new radiotracers and providing imaging services.

# Meeting Poster Abstracts:

## Abstract 1

**Title:** Non-invasive parametric mapping of binding in mouse brain-PET studies: a validation

**Authors:** Catriona Wimberley[1,2], Duc Loc Nguyen[2], Charles Truillet[2], Zuhal Gulhan[3], Yoann Fontyn[2], Raphael Boisgard[2], Sylvie Chalon[3], Viviane Bouilleret[4], Irene Buvat[2]

**Affiliations:** [1.] Edinburgh Imaging, Queen's Medical Research Institute, Little France, Edinburgh
[2.] I2BM/SHFJ/IMIV, INSERM/CEA, Orsay, France
[3.] UMR 1253, iBrain, Université de Tours, Inserm, Tours, France
[4.] Hôpital Bicêtre,Le Kremlin Bicetre, France

**Abstract:**

TSPO PET imaging can follow neuroinflammation associated with neurodegenerative disorders using [$^{18}$F]DPA-714, but there are quantification challenges for mouse studies because arterial sampling is nearly impossible. Due to the ubiquitous expression of TSPO, no reference region is available. The aim of this study was to use a previously described method for the extraction and use of an image derived input function (IDIF) using factor analysis (FA) which was input to a voxel-wise Logan plot for parametric binding maps. The maps were validated against quantified autoradiography within the same animal.

The model was induced by injection of kainic acid into the right hippocampus of adult male C57/Bl6 mice (n=4). A dynamic [$^{18}$F]DPA-714 PET/CT (60min) was performed 1 month and 6 months post KA injection. FA was applied to all images using 4 factors to extract the IDIF. The normalised curve was used in a voxel wise Logan plot to estimate the total volume of distribution, $V_T$. Each animal was sacrificed after the scan and the brain underwent autoradiography with $^3$H-DPA-714 (4 slices starting at the hippocampus). Regions of interest were manually drawn over brain regions on each slice and equivalent regions were drawn on the $V_T$ map. The average regional binding values were extracted and correlations were generated for each mouse.

The four mice showed strong correlations between the average $V_T$ extracted from the PET and autoradiography: 1 month: $r^2$=0.62 and 6 months $r^2$ =0.75, 0.68 and 0.77. The coefficient of determination for all regions within all mice together was 0.59.

This study showed strong regional correlations between $V_T$ maps and autoradiography, and the maps showed strong visual similarities. These results validate the use of an IDIF extracted using FA to produce parametric maps. This method will be useful for longitudinal studies within rodents and for studies using whole body PET.

## Abstract 2

**Title:** Network analysis of dynamic whole-body PET images can cluster radiotracer tissue uptake kinetics

**Authors:** Carlos J. Alcaide-Corral[1,2], Tashfeen Walton[1,2], Christophe Lucatelli[2], Tom C. Freeman[3], Adriana A. S. Tavares[1,2]

**Affiliations:** [1.] British Heart Foundation/University of Edinburgh Centre for Cardiovascular Science, Queen's Medical Research Institute, Little France Campus, Edinburgh, EH16 4TJ, UK.
[2.] Edinburgh Imaging, University of Edinburgh, Little France Campus, Edinburgh, EH16 4TJ, UK.
[3.] The Roslin Institute and Royal (Dick) School of Veterinary Studies, University of Edinburgh, Easter Bush, Edinburgh, EH25 9RG, UK.

**Abstract:**

Whole-body dynamic Positron Emission Tomography (PET) imaging can aid disease diagnosis and enhance drug candidate' selection by characterizing target/off-target engagement. PET studies generate multiparameter and multidimensional datasets, which are frequently minimally explored due to limitations in current analysis methods for mining these complex data. With the upcoming advent of the first clinical whole-body PET scanner, the sizes of PET datasets is due to further exponentially expand, as the community will access, for the first time, truly PET whole-body human dynamic datasets – something only currently available for small animals. Here we report on a new set of experiments designed to investigate correlation network analysis as a model for mining multi-organ dynamic PET data.

Methods: Whole-body dynamic PET mice imaging with $^{18}$F-sodium fluoride over 1 hour was used in this study. The radiotracer was administered using four different routes (femoral artery, femoral vein, tail vein and intraperitoneal injection) to probe ability of network analysis for detection of subtle and gross changes in tissue kinetics. Logan and Patlak ($t^*$=15min) analysis was used for conventional quantification of the data. Pearson correlation and the Markov cluster algorithm were used for network analysis of the raw dynamic PET datasets.

Results: Femoral vein, tail vein and intraperitoneal injections highly correlate ($r^2$>0.9) but underestimate kinetic outcomes in tissues with reversible uptake compared with femoral artery injection (7, 9 and 16% underestimation bias, respectively). Network analysis showed differences in the grouping of the three intravascular administrations investigated here; and the intraperitoneal nodes and edges for tissues with reversible kinetics were clustered independently from intravascular injections.

Conclusion: This study demonstrates network analysis can provide a complementary new approach to mine, classify and rank multi-organ kinetics of dynamic whole-body PET data that is rapid, robust, sensitive and scalable.

## Abstract 3

**Title:** Why do the metabolic effect of calorie restriction differ between males and females? Use of PET/CT imaging to identify systemic and tissue-specific differences

**Authors:** Benjamin Thomas, Karla Suchacki, Andrea Lovdel, Domenico Mattiucci, Richard Sulston, Carlos Alcaide-Corral, Nik Morton, Adriana Tavares, Will Cawthorn.

**Affiliations:** British Heart Foundation Centre for Cardiovascular Science, The Queen's Medical Research Institute, University of Edinburgh, 49 Little France Crescent Edinburgh, EH16 4SB, UK.

**Abstract:**

Chronic diseases are the leading cause of mortality worldwide, accounting for over 60% of all deaths; metabolic dysfunction is central to chronic diseases such as obesity. The need to treat metabolic dysfunction has dramatically increased in recent decades, and the ability of caloric restriction (CR) to prevent these is well established. Recent published and unpublished work indicates a metabolic sexual dimorphism in response to CR; it significantly reduces adiposity and improves glucose tolerance in males, but not in females. The basis for these sex differences remains unknown but may be related to enhanced glucose uptake.

Nine-week-old Male and female C57BL/6J mice were calorie restricted to 70% or fed ad-libitum for 6 weeks, during which time: they were regularly assessed for fasting blood glucose, body composition using TDNMR, and weighed; glucose tolerance was assessed with an oral glucose tolerance test. Finally, mice underwent PET/CT imaging with 2-Fluoro-2-deoxy-D-glucose ($^{18}$F-FDG) to assess tissue specific uptake.

CR improves fasting blood glucose and area-under-the-curve on an oral glucose tolerance test in males, but not females. CR reduced lean and fat mass of male mice, but only lean mass of female mice. CR preferentially reduces gonadal adipose tissue as a percent of whole body mass in males, but no specific investigated depot in females. CR induces significant $^{18}$F-FDG uptake in the brain of male mice relative to ad libitum-fed mice; other adipose depots trend towards increased $^{18}$F-FDG uptake. No tissue specific difference in uptake was observed in female mice, except decreased $^{18}$F-FDG uptake in brown adipose in CR compared to ad-libitum-fed mice was seen.

CR induces preferential loss of gonadal adipose tissue in male mice. CR increases glucose uptake in adipose depots and brain in male mice, but reduces glucose uptake in brown adipose in female mice, relative to other tissues, upon receiving a glucose load.

## Abstract 4

**Title:** Rapid and reproducible method for measurement of pharmacokinetics/ pharmacodynamics (PK/PD) of drugs to support quantification of Positron Emission Tomography (PET) receptor-occupancy data

**Authors:** Agne Stadulyte[1], Carlos José Alcaide-Corral[1], Tashfeen Walton[2], Christophe Lucatelli[2], Adriana Alexandre S. Tavares[1]

**Affiliations:** [1.] Edinburgh Preclinical Imaging (EPI), University of Edinburgh, Scotland
[2.] Edinburgh Imaging, Queen's Medical Research Institute, University of Edinburgh, Scotland

**Abstract:**

In Positron Emission Tomography (PET) research, it is important to assess not only pharmacokinetics of a radiotracer, but also of the drugs used in blocking/displacement studies. Typically, pharmacokinetic/pharmacodynamic (PK/PD) analysis of drugs used for rodent PET work is based on population average pharmacokinetic profiles of the drugs. This can result in bias of PET data quantification, including bias in occupancy measurements. Such bias is unknown or is poorly studied in the field of small animal PET imaging.

This study aims to develop a High Performance Liquid Chromatography (HPLC) method for quantification of PK/PD of drugs for use in preclinical rodent PET research. This work was piloted with the translocator 18 kDa protein (TSPO) selective drug, PK11195.

Adult Sprague-Dawley male rats (n=6) were anaesthetised and the femoral artery was cannulated for collection of blood samples. PK11195 (5mg $kg^{-1}$) was administered via tail vein (bolus i.v.) using two different formulations. Arterial blood samples (1mL) were collected at 0.5, 1, 2, 3, 5, 15, 30 and 60 minutes as well as heart, brain, lungs and spleen at 3 and 60 min post-injection, and then processed using the HPLC method developed in our lab. Concentration of PK11195 was determined using a calibration curve which was generated prior to blood and tissue sample analysis. Measured average inter-sample variability was equal to 15.5%. Individual PK/PD measurements were significantly different when compared to the value calculated from population average PK/PD curve ($p<0.05$). Also, the PK/PD analysis of PK11195 in rats suggested active clearance from the blood and kinetic transfer into the organs, with approximately 50% less PK11195 exposure levels in brain compared with peripheral tissues.

Here we report a rapid and reproducible method to measure PK/PD of drugs in rodents using analytical HPLC. This study highlights the importance of PK/PD studies when conducting blocking/displacement rodent PET experiments.

## Abstract 5

**Title:** [$^{18}$F]-FDG PET/CT imaging: A tool to reveal the metabolic functions of bone marrow adipose tissue in mice and men

**Authors:** Karla Suchacki[1], Adriana Tavares[1], Domenico Mattiucci[1,2], Andrea Lovdel[1], Richard Sulston[1], Benjamin Thomas[1], Matthew Sinton[1], Bonnie Nicholson[1], Carlos Alcaide[1], Diana Said[1], Antonella Poloni[2], Saverio Cinti[2], Gavin MacPherson[3], Anish Amin[3], Michelle Williams[4], Calum Gray[4], Robert Wallace[5], Erica Scheller[6,7], Ormond MacDougald[8], Roland Stimson[1], Nik Morton[1], William Cawthorn[1]

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[2.] Dipartimento di Scienze Cliniche e Molecolari, Clinica di Ematologia, Università Politecnica delle Marche, Ancona, Italy.
[3.] Department of Orthopaedic Surgery, Royal Infirmary Edinburgh, Scotland, UK.
[4.] Clinical Research Imaging Centre, Queen's Medical Research Institute, University of Edinburgh, UK
[5.] Department of Orthopaedics, The University of Edinburgh, UK.
[6.] Division of Bone and Mineral Diseases, Department of Medicine, Washington University, St. Louis, MO, USA.
[7.] Department of Cell Biology & Physiology, Washington University, St. Louis, MO, USA.
[8.] Department of Molecular & Integrative Physiology, University of Michigan, Ann Arbor, MI, USA.

**Abstract:**

Introduction: Bone marrow adipose tissue (BMAT) is a major adipose tissue subtype. However, it remains unclear if BMAT has properties of white or brown adipose tissue (WAT or BAT) and thereby influences metabolic homeostasis.

Objectives: Assess [$^{18}$F]-Fludeoxyglucose (FDG) uptake into bone and the marrow cavity (MC) following: 1) insulin treatment in mice, 2) acute and chronic cold (CC) exposure in mice, or 3) conditions of BAT activation in humans.

Methods: Objective-1: mice were fasted for 4h and then treated with insulin (0.75IU/g) or saline, immediately with [$^{18}$F]-FDG, and housed at room temperature (RT) for 1h before scanning. Objective-2: prior to [$^{18}$F]-FDG administration mice were fasted for 4h at RT (control) or 4°C (acute or CC). CC mice were housed at 4°C for 72h before fasting. Objective-3: human subjects were exposed to mild cold (16°C) for 2h before [$^{18}$F]-FDG PET/CT scanning in 1) participants who received no medication or 2) three doses of prednisolone or placebo prior to attendance. Scans were analysed using PMOD software and measured activities of target tissues expressed as standard uptake values (SUV).

Results: The marrow cavity (MC) is the predominant site of [$^{18}$F]-FDG skeletal uptake. Insulin stimulated [$^{18}$F]-FDG uptake in the femur and the heart, as previously reported, but did not affect [$^{18}$F]-FDG uptake in the bone or MC at other skeletal sites. Despite suggestions that MAT is BAT-like, we found that neither bone nor the MC was cold-responsive during acute cold exposure. In cold-exposed humans, [$^{18}$F]-FDG uptake in the MC of the humerus and clavicle occurred at 10% and 28% of the level in BAT. Despite acutely increasing BAT activity, glucocorticoids decreased [$^{18}$F]-FDG uptake into the bone and had no effect of [$^{18}$F]-FDG uptake into the MC.

Conclusion: BMAT of mice and humans is functionally distinct from WAT and BAT but is a significant site of basal glucose uptake.

## Abstract 6

**Title:** Multi-centre standardization of preclinical PET/CT imaging: a necessary step towards achieving translational imaging datasets

**Authors:** Wendy McDougald[1,2], Christian Vanhove[3], Barbara Lewellen[4], Adrienne Lehnert[4], John Wright[5], Marco Mingarelli[6], Carlos Alcaide Corral[1,2], Jurgen E. Schneider[5], Sven Plein[5], Andy Welch[6], Robert Miyaoka[4], Stefaan Vandenberghe[3], Adriana Alexandre S. Tavares[1,2]

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[2.] Edinburgh Preclinical Imaging (EPI), Edinburgh Imaging, University of Edinburgh, UK
[3.] Department of Electronics and Information Systems, MEDISIP, University of Ghent, Belgium
[4.] Department of Radiology, Imaging Research Laboratory, University of Washington, USA
[5.] Leeds Institute of Cardiovascular and Metabolic Medicine, Department of Biomedical Imaging Science, LIGHT Laboratories, University of Leeds, UK
[6.] Aberdeen Biomedical Imaging Centre, School of Medicine, Medical Sciences & Nutrition, University of Aberdeen, UK

**Abstract:**

Introduction: Preclinical Positron Emission Tomography/Computed Tomography (PET/CT) is a key non-invasive imaging tool for studying disease development/progression and for the development of novel radiotracers/pharmaceuticals. Despite this pivotal role, standardization of acquisition and reconstruction preclinical PET/CT protocols is essentially non-existent. This project addresses such lack of global standardized imaging protocols by evaluating biases across centres using default scanner protocols; followed by developing standardized protocols for optimization of PET/CT imaging.

Methods: Six different commercial preclinical PET/CT scanners in Europe and USA were enrolled. Eight different phantoms were used: CT air/water phantom (quantify Hounsfield (HU) bias in water/air), CT tissue-equivalent phantom (HU bias in different tissue-equivalent materials (TEM)), CT spatial resolution phantom, CT dose index phantoms (measure absorbed dose), PET image quality phantom (PET uniformity, recovery coefficients (RC) and spill-out-ratios (SOR)), PET rod phantom (PET resolution).

Results: Using default protocols: one scanner had HU values in water of 133±284HU. Another scanner outputted CT results as a linear grey scale instead of HU. TEM measured HU values are considered within expected ranges for lung, soft tissue and bone. However, one-way ANOVA established significant ($p$<0.0001) variation measured across scanners. CT spatial resolution, two scanners were unable to resolve 150µm lines. CT absorbed doses ranged from 11.5mGy to 268.2mGy. PET rod phantom, all but one scanner resolved 2.0, 1.5 and 1.2mm rods; none resolved 0.6, 0.8 and 1.0mm rods. One scanner failed PET uniformity limit of 15%. RCs were either overestimated or underestimated, maximum of 40% relative to expected activity.

Conclusion: Data revealed important quantification bias in preclinical PET/CT protocols, and variability in CT absorbed doses across sites using variable default protocols. This highlights the importance of preclinical PET/CT protocol standardization. Adhering to standardized protocols has the potential to improve reproducible and consistent imaging datasets, thus augmenting translational value of preclinical findings to the clinic.

## Abstract 7

**Title:** Non-invasive *in vivo* imaging of acute thrombosis; Development of a novel Factor XIIIa radiotracer

**Authors:** Jack Andrews[1], Christophe Portal[2], Tashfeen Walton[3], Patrick Hadoke[1], Carlos Alcaide Corral[1], Simon Wilson[4], Ian Wilson[2], Gillian MacNaught[3], Christophe Lucatelli[3], Marc Dweck[1,2], David Newby[1,2], Adriana Tavares[1]

**Affiliations:** [1.]Centre for Cardiovascular Science, University of Edinburgh, Chancellor's Building, Royal Infirmary of Edinburgh, 49 Little France Crescent, Edinburgh, EH16 4SB, UK
[2.] Edinburgh Molecular Imaging Ltd., 9 Little France Road, Edinburgh EH16 4UX, United Kingdom.
[3.] Clinical Research Imaging Centre, QMRI, Little France Crescent, Edinburgh, EH16 4SB, UK
[4.] Edinburgh Heart Centre, Royal Infirmary of Edinburgh, 51 Little France Crescent, Edinburgh EH16 4SB, UK

**Abstract:**

Objectives: To assess a novel optical and positron-emitting probe targeting Factor XIIIa (ENC2015) as biomarker of active thrombus formation.

Background: Cardiovascular thrombosis is responsible for one quarter of all deaths annually worldwide. Current imaging methods focus on anatomical identification of thrombus but cannot determine thrombus age or activity. Molecular imaging techniques hold promise for identifying and quantifying active thrombosis *in vivo*.

Methods: Optical and positron emitting ENC2015 probes were assessed *ex vivo* using blood drawn directly from human volunteers and passed through perfusion chambers containing denuded porcine aorta as a model of deep arterial injury. Specificity and selectivity of ENC2015 has established with co-infusion of the Factor XIIIa inhibitor, iodoacetamide. $^{18}$F-ENC2015 biodistribution, kinetics, radiometabolism and ability to bind to an acutely thrombosed artery *in vivo* were characterised in rats.

Results: Both Cy5 and $^{18}$Fluorine labelled ENC2015 rapidly and selectively bound to both low and high shear thrombi with both thrombus fluorescence and PET activity significantly reduced in the presence of a factor XIIIa inhibitor. There was no metabolism of $^{18}$F-ENC2015 for over 8 hours when incubated *ex vivo* in whole human blood. *In vivo*, 42.0±0.5% of parent radiotracer remained in rat blood 60 min post-administration. Biodistribution studies demonstrated low uptake and rapid clearance from tissues with elimination via renal excretion. In an *in vivo* rat model of arterial thrombosis, $^{18}$F-ENC2015 uptake was markedly increased in the thrombosed carotid artery compared to the contralateral patent artery (mean standard uptake value ratio of 2.40 versus 0.74, $p<0.0001$).

Conclusion: ENC2015 rapidly and selectively binds to acute thrombus in both an *ex vivo* human translational model and an *in vivo* rodent model of arterial thrombosis. This tracer has major promise for the non-invasive identification of thrombus formation in cardiovascular disease.

## Abstract 8

**Title:** Alpha7 nicotinic acetylcholine receptor imaging with $^{18}$F-NS14490 in the context of angiogenesis

**Authors:** Mark G. MacAskill[1,3], Holly Stott[1], Nick Spath[1], Monika Dargyte[2], Algirdas Sackus[2], Johan Sandell[4], Christophe Lucatelli[3], Andrew H. Baker[1], David E. Newby[1], Patrick Hadoke[1], Dan Peters[5], Adriana A. S. Tavares[1,3]

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[2.] Chemistry Department, Kaunas University of Technology, Kaunas, Lithuania.
[3.] Edinburgh Imaging, University of Edinburgh, Edinburgh, UK.
[4.] Novandi Chemistry AB, Sodertalje, Sweden.
[5.] DanPET AB, Malmo, Sweden.

**Abstract:**

Angiogenesis plays a major role in a number of cardiovascular pathologies, including the development of vulnerable plaque and ventricular remodelling following myocardial infarction. Targeted imaging of angiogenesis can provide valuable insights to understand and modify cardiovascular disease outcomes. $^{18}$F-NS14490 is a selective alpha7 nicotinic acetylcholine receptor (α7) radiotracer which has been shown to have high uptake in vascular structures. As α7 is central to the angiogenic process, selective α7 radiotracers can be valuable as imaging biomarkers of the angiogenic process. This study aimed to investigate NS14490 binding in preclinical animal models of cardiovascular angiogenesis.

Saturation assays were performed with endothelial cell membranes to establish the binding affinity of $^{3}$H-N14490 to this cell type. A physiological (sponge implantation model) and pathological model of angiogenesis (myocardial infarction) was utilised to investigate the binding of $^{3}$H-NS14490 during this process using autoradiography.

Binding affinity of $^{3}$H-NS14490 to endothelial cell membranes was in the nanomolar range (55nM). Within the angiogenic sponge implantation model, specific binding of $^{3}$H-NS14490 significantly increased from 3.6± 0.2µCi/g at day 3 post-implantation to 4.9± 0.2µCi/g at day 7 (n=4, $p$<0.01), followed by a reduction in specific binding at day 14 and 21. This binding profile matches the onset of angiogenesis, but not peak blood vessel density (day 21) nor the infiltration of inflammatory cells such as neutrophils (day 3) or macrophages (day 21). Analysis of radiotracer binding in tissue from a rat myocardial infarction (MI) model indicate focal binding of $^{3}$H-NS14490 within infarct/peri-infarct areas.

This study suggests that NS14490 holds potential as a marker of the onset of angiogenesis through the upregulation of α7. Taken together with the uptake seen in our pathological model of angiogenesis, these results warrant further studies to validate $^{18}$F-NS14490 as a marker of angiogenesis in the cardiovascular field.

## Abstract 9

**Title:** Evaluation of external dose rate measurements in a PET-CT Department

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**Abstract:**

Introduction: As PET Technologists we are trained from the very beginning on the main principles of radiation protection. The purpose of these measurements was to evaluate if closing a door of the bay where a patient is resting after receiving a radioactive injection would lead to different exposure rates for the staff involved in the care of such patients.

Methods: Exposure rates were obtained after the radiopharmaceutical administration.

The measurements were obtained for seven subjects who had received a radioactive injection of an amyloid tracer. Measurements were obtained at 1 meter distance, with a Mini 900 Ratemeter, at three different time points: the first time point was immediately after administration, the second was just before voiding and the third was after voiding.

Results: Six participants received a radioactive injection of $^{18}$F-Florbetaben. The mean dose administered was 282.4 MBq, the median dose administered was 289.1 MBq and the standard deviation is 19.11.

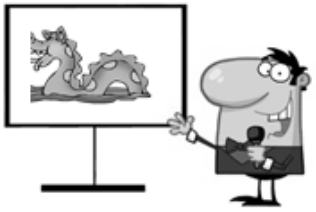
An additional participant received a radioactive dose of $^{18}$F-Florbetapir. The dose administered was 351.4MBq. Participants 2, 4, 5 and 7 received the highest administered doses. Participants 1, 3 and 6 received lower administered doses which is reflected in the dose rate measurement obtained after the injection.

Discussion: In order to test whether a difference is present, the t-test assuming unequal variances was used and the significance level was set to $\alpha$=0.05. For the measurements obtained immediately after the injection, a $p$=0.34 was obtained. For the measurements obtained before voiding, $p$=0.52 was obtained. For the measurements obtained after voiding, $p$=0.32 was obtained.

Conclusion: In all three scenarios, the $p$-value was higher than $\alpha$=0.05 and the results do not demonstrate a statistically significant difference between having the door open or closed, during the uptake time.

# Introducing the "PiW Delegate Engagement Prize"

1



Meet the poster presenter or sponsor delegate

2

Examine the poster

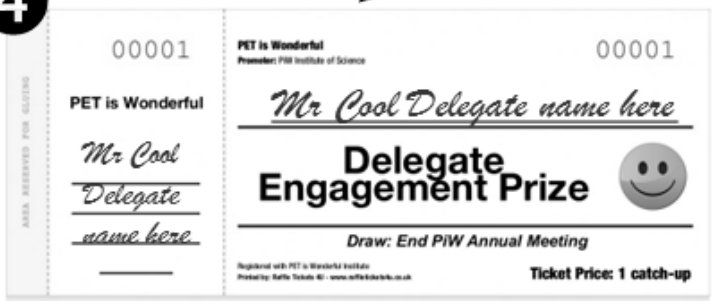
***AND/OR***

Ask questions and network

3

Feel happy with scientific discussions and networking exercise

4




Standard – 10 working days despatch

5


Get your "Delegate Engagement Prize" raffle to enter in the competition and place it in the voting box


***More raffles = higher chance to WIN!***

THE UNIVERSITY of EDINBURGH

**PET is Wonderful**
**Annual Scientific Meeting 2018**

29th October 2018

South Hall Complex, Edinburgh

# FEEDBACK FORM

| **Scientific content & research overview** | Not useful ☹ | | | | Very useful ☺ |
|---|---|---|---|---|---|
| | | | | | |
| ***Invited talks*** | | | | | |
| ***Keynote speakers*** | | | | | |
| ***Poster presentations*** | | | | | |

| Comments |
|---|
| |

| | Not good ☹ | | | | Excellent ☺ |
|---|---|---|---|---|---|
| **Catering (quality & quantity)** | | | | | |
| Comments | | | | | |

| **Future Meetings** | | | | | |
|---|---|---|---|---|---|
| ***Format*** | Disagree ☹ | | Unsure | | Agree ☺ |
| Include proffered talks | | | | | |
| Keep invited talks | | | | | |
| Increase number posters | | | | | |
| Increase networking time | | | | | |
| Add 1-to-1 meetings | | | | | |
| Other comments | | | | | |

# Save the date!

**Next "PET is Wonderful" Annual Meeting:**

# 29th October 2019

Abstract submission deadline: 29th June 2019

***Details to be circulated in due course.***
***Stay tuned!***