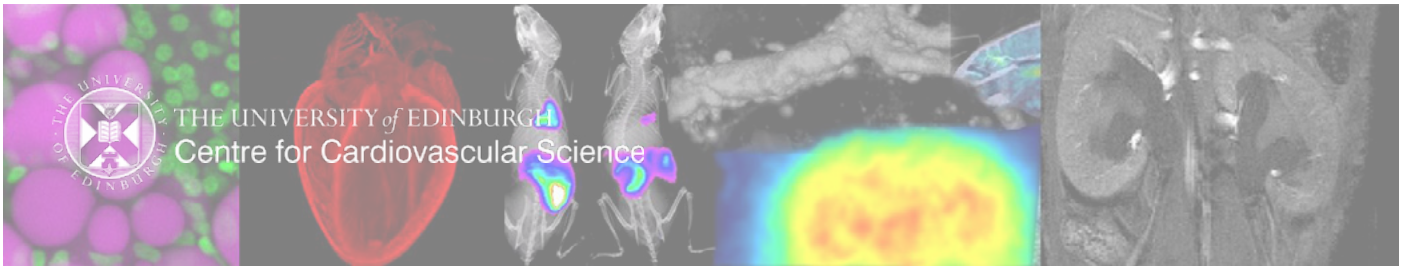
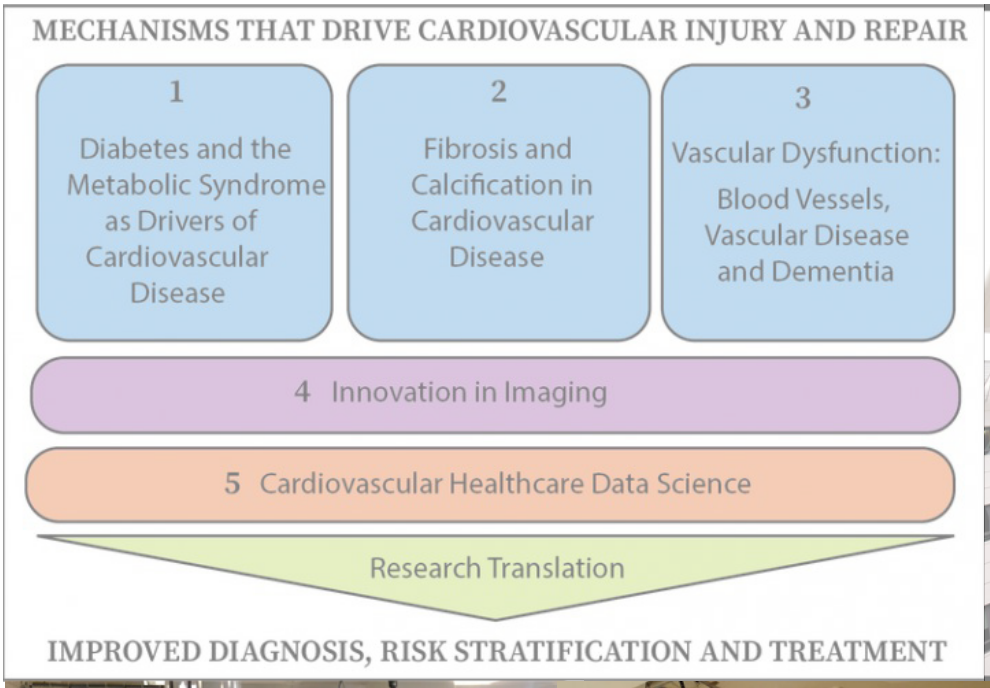
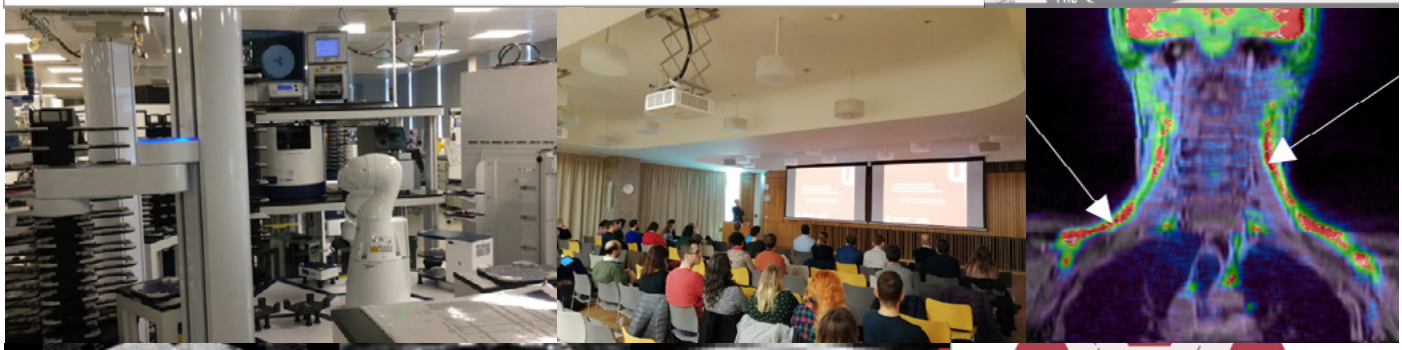
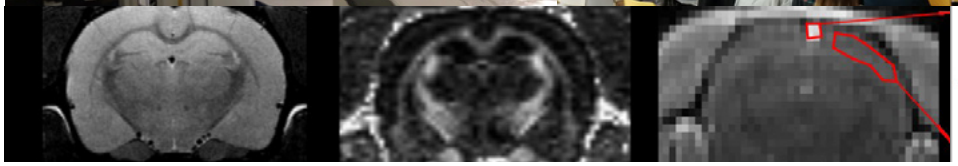


REA3 BIMONTHLY NEWSLETTER

March 2021

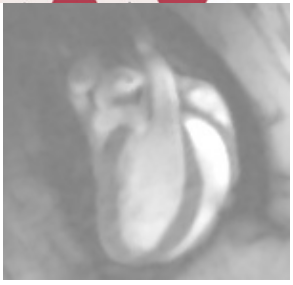


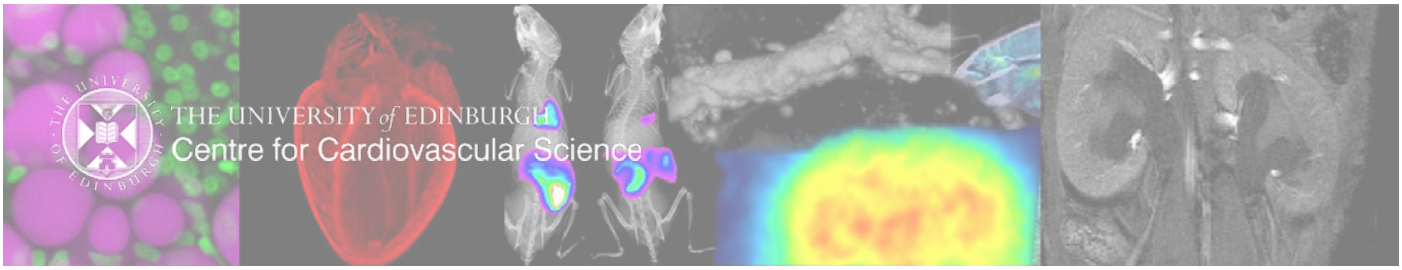




THE UNIVERSITY of EDINBURGH

BHF Research Excellence Award
University of Edinburgh

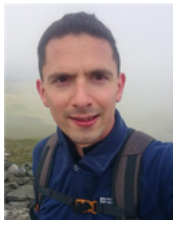




INTRODUCTION

Welcome to the latest edition of the REA3 Newsletter.

"Are we there yet?", is a familiar phrase heard from certain family and friends when we go on trips (not many, if any, this year and last) and applies in this current climate. We are *almost* there. Almost. Things are generally moving in the right direction with the roll out of the vaccination programme within the UK and beyond. It's still a bumpy road ahead but hopefully further advances will be made where forward planning can be more certain, especially concerning events, networking and in-person meet-ups.


Mr Samuel Debono

Our REA3 associates continue to be busy behind the scenes and are still working hard on delivering the objectives set out in the original funding from BHF. We are delighted to feature in this issue some further insight into vascular surgeon Mr Samuel Debono's project as part of his Clinical Fellowship funded by the REA3, **"Predicting endoleaks following Endovascular Aortic Aneurysm Repair using 18F-Sodium Fluoride: The PET-EVAR Study".** Samuel has also just been awarded funding from the BHF (Project Grant PG/21/10461, £293,581).


Dr Sphamandla Ntshangase

In November 2020, after delays caused by the pandemic, we welcomed Dr Sphamandla Ntshangase as a postdoctoral researcher who joined Professor Ruth Andrew's group in mass-spectometry. He has provided us with an overview of his background and also his current project testing the current hypothesis that the lipid composition of atherosclerotic plaques can be assessed by matrix-assisted laser desorption/ionisation mass spectrometry imaging (MALDI-MSI), generating spatial "phenotypes" of plaque composition relating to patient outcomes.

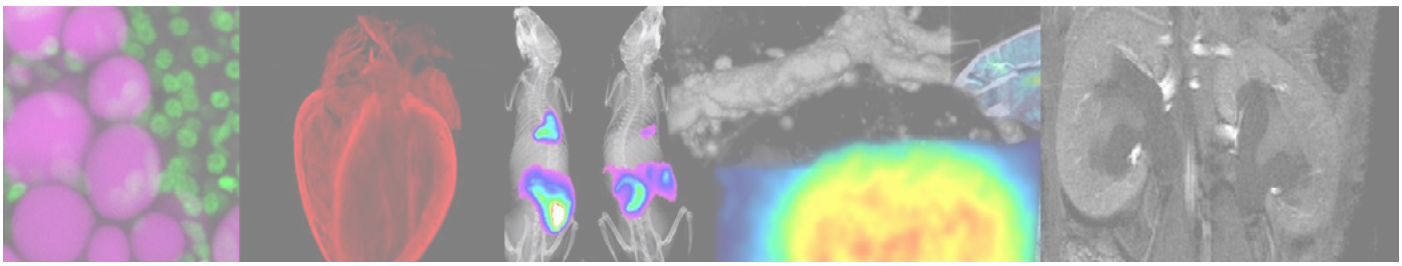

Professor Carmel Moran

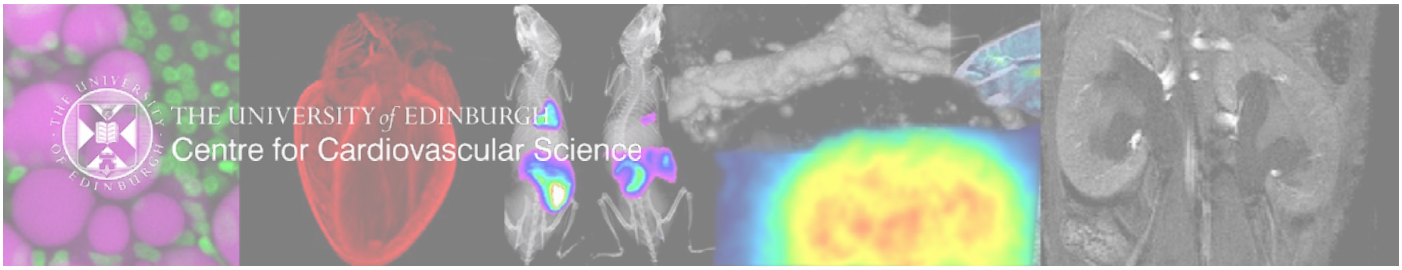
Finally, one of our REA3 Executive members, Professor Carmel Moran, has outlined her role within CVS, her own research, which is focussed on two main areas; 1. the development of ultrasonic contrast agents and novel contrast-specific imaging techniques and 2. the performance assessment of ultrasound imaging techniques, plus her contribution to encouraging transparency on the workings of REA3 from an equality and diversity perspective.

For the next edition, we are looking for any REA3-related contributors to get in touch with Gillian Joyce, to ensure we are highlighting all the great work and successes we are delivering: Gillian.Joyce@ed.ac.uk

As always we extend our thanks to everyone involved with REA3 and beyond and the commitment our researchers have shown during these difficult times.

Professor Andrew H Baker, Director REA3
Professor David Newby, Deputy Director REA3





Mr Samuel Debono - Clinical Research Fellow

Predicting endoleaks following Endovascular Aortic Aneurysm Repair using 18F-Sodium Fluoride: The PET-EVAR Study

I joined the Centre for Cardiovascular Science in August 2020 and I am extremely grateful to the British Heart Foundation Research Excellence Award programme which has been supporting me.

I am working with the cardiovascular imaging team led by Professor Newby and the focus of my research is to develop the use of Positron Emission Tomography using 18F-sodium fluoride in abdominal aortic aneurysms. 18F-Sodium fluoride detects cardiovascular microcalcification, and previous research has shown that high radiotracer uptake was associated with higher rates of aneurysm size increase and of requiring treatment or aortic rupture.

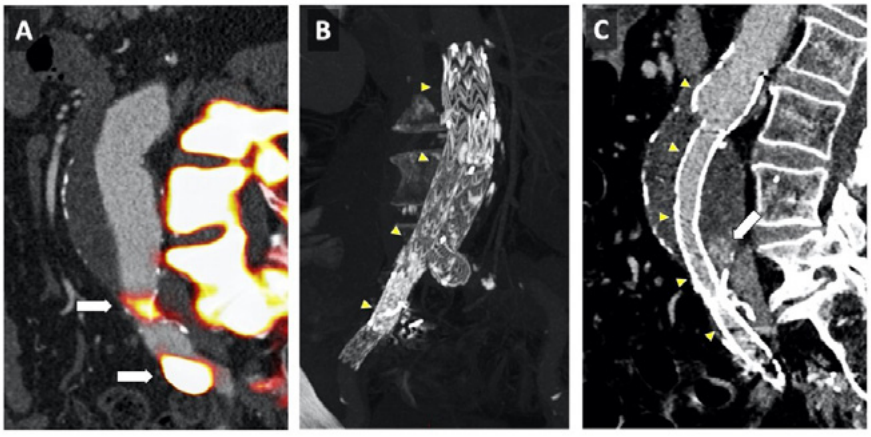
Traditional open surgical repair of an abdominal aortic aneurysm is associated with high perioperative morbidity and mortality and there has been a shift in treatment towards the minimally invasive Endovascular Aneurysm Repair (EVAR), which reduces these risks. When compared to open surgery, EVAR has a lower in-hospital mortality and aneurysm-related death within six months. With longer follow up however, aneurysm-related mortality and the risk of secondary intervention are higher after EVAR because the seal provided by the stent graft can be lost, this is called an endoleak.

There will be Scotland-wide identification and recruitment of patients into two studies:

Study 1 – a cross-sectional case control study comparing 18F-sodium fluoride uptake between patients who have developed endoleaks and those who have not.

Study 2 – a longitudinal cohort study to determine whether 18F-sodium fluoride uptake can predict endoleak development.

The panel of images below shows pilot data supporting the project:



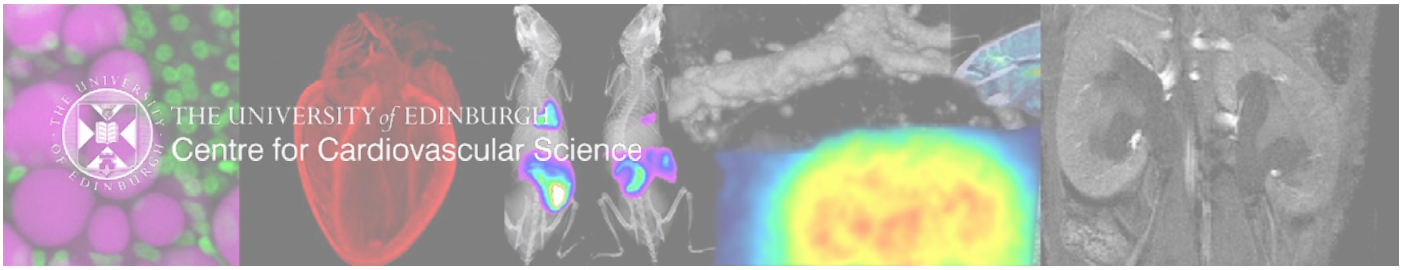
A - A pre-operative sagittal view of an abdominal aortic aneurysm with areas of high 18F-sodium fluoride uptake on PET-CT at the aortic bifurcation and right common iliac artery (white arrows).

B - The aneurysm subsequently treated with an EVAR stent graft.

C - Post-operative CT angiogram showing an area of contrast perfusion within the aneurysm sac consistent with an endoleak (white arrow).

In the last six months, we have defined the project protocol and obtained the necessary study approvals. We therefore hope to start patient recruitment this month.

If successful, this project would allow us as vascular surgeons to select patients for their aneurysm treatment: EVAR could be used in those with low or no risk of endoleak, and open repair reserved for those with a high risk of endoleaks.



Dr Sphamandla Ntshangase – Postdoctoral Researcher

I am from Jozini, a small town in South Africa near the Pongolapoort Dam (Lake Jozini), which is a popular Tiger fishing destination. I completed my PhD training at the University of KwaZulu-Natal in Durban, South Africa. There, I carried out a lot of mass spectrometry-based biomedical research, investigating how anti-retroviral drugs penetrate the central nervous system and study drugs that could protect patients from developing HIV-associated neurocognitive disorders. I am currently interested in mass spectrometry-based omics, a field that integrates different types of molecular information to help us understand patterns associated with any disease. I joined The University of Edinburgh, Centre for Cardiovascular Science (CVS) in November 2020 as a British Heart Foundation (BHF) REA3 postdoctoral researcher in Ruth Andrew's group. My decision to come here was largely inspired by my research interests, and being part of CVS is undoubtedly a great opportunity to apply my skills, broaden my knowledge and skill set as a researcher while also building a strong professional network. I had been waiting for this transition for a long time, and it was significantly delayed by the COVID-19 pandemic. While waiting for my visa application to be processed, I worked with a team of scientists from different disciplines doing PCR COVID-19 testing at UKZN-Global Health Innovations.

Here I work with an incredible team that has helped me settle so quickly, and I am very grateful for their support, particularly considering that I joined during these challenging times. My current role is to embed mass spectrometry (MS)-led lipidomics in CVS by leading novel pilot projects to add innovation to subsequent funding bids and you'll find me in the MS Core lab, working closely (not socially!) with Shazia Khan. As an early career researcher, I am honoured to be the recipient of the **"Dr Diran and Elizabeth Kay Research Award 2021."** This award will provide the assistance I need to meet my research objectives. In my project, I will validate an approach to demonstrate the value of MS imaging in the translational understanding of atherosclerotic plaque structure and stability. Atherosclerosis is a common cause of cardiovascular disease; it begins early in life and can progress silently for years before producing life-threatening symptoms. Studying molecular changes of plaques is key to understanding risk factors associated with disease progression. It is well established that lipids play key roles in the development of atherosclerotic plaques. The lipid composition of atherosclerotic plaques has been studied extensively. However, we lack spatial information within vulnerable and stable plaques.

In my current project, I will test the hypothesis that the lipid composition of atherosclerotic plaques can be assessed by matrix-assisted laser desorption/ionisation mass spectrometry imaging (MALDI-MSI), generating spatial "phenotypes" of plaque composition relating to patient outcomes. My aim is to study translational models of atherosclerotic plaques, establishing similarities and differences, ultimately validating an MSI method to map lipids in plaques in model organisms and humans spatially. I will be working closely with Paddy Hadoke, Dave Newby, and Jakub Kaczinski.

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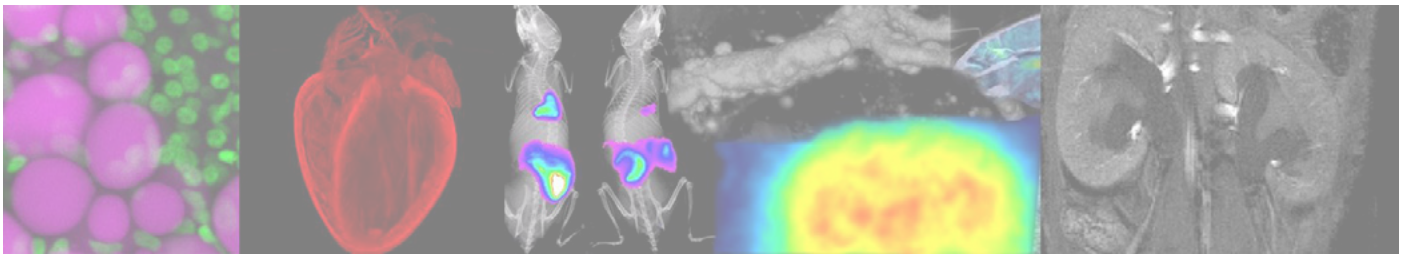
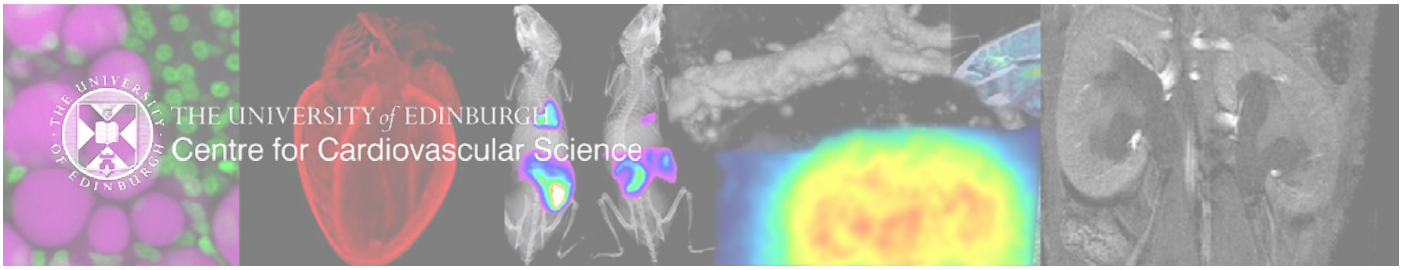




Dr Sphamandla Ntshangase – Postdoctoral Researcher

Since my arrival, I've been working on developing a MALDI-MSI method in human and rabbit atherosclerotic plaques, and the preliminary images in Figure 1 show how this method can profile lipids spatially. I am currently optimising this MSI method to boost signals, enable imaging with greater spatial resolution, and develop the image analysis workflow.

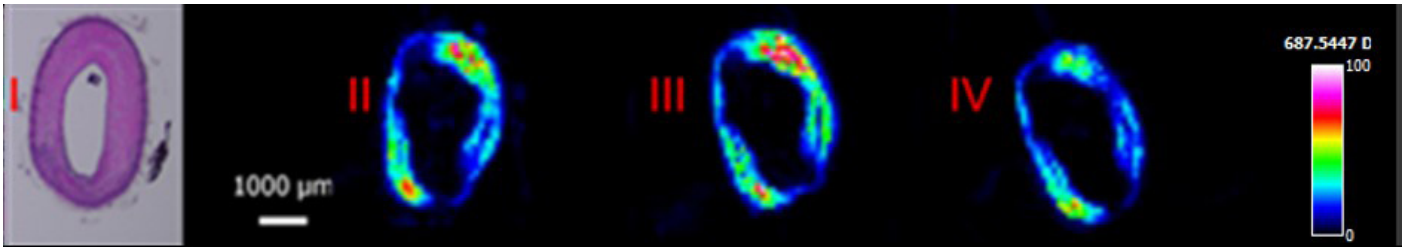
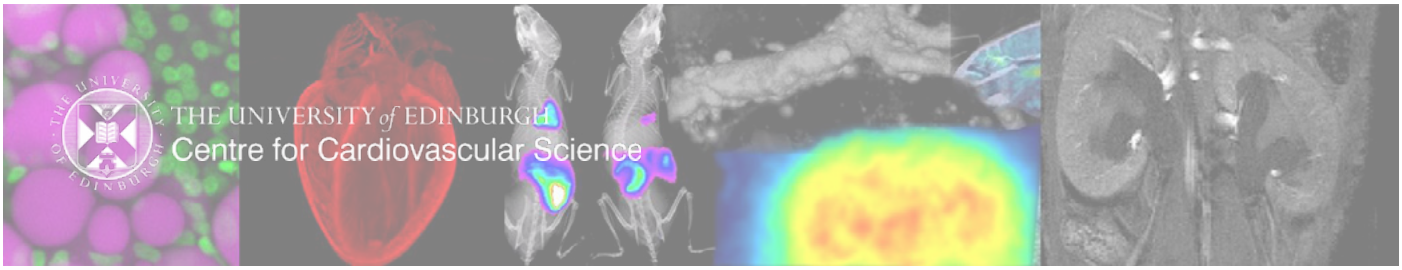


Figure 1. *(I) Rabbit aortic histology, (II-IV) m/z 687.5447 Sphingomyelin (d18:1/16:0), [M-CH3]- ion images generated by MALDI-MSI.*

This project will allow me to achieve my personal career goals of establishing MSI as an innovative research approach in cardiovascular science. This is timely with the advent of technologies such as I-Knife allowing biopsies with real-time omics fingerprints, currently revolutionising surgical oncology. The project will enable understanding of plaque subtypes and place CVS researchers in a prime position to study at-risk characteristics using accessible biomaterials, e.g. carefully characterised animal models and patients. My collaborative team is ideally placed to expedite such studies with my input. If you have further ideas for collaborative projects, please do not hesitate to contact me. I very much enjoy being in Edinburgh, and I'm looking forward to joining the gym, exploring the city more, and meeting everyone at the CVS in person, once the restrictions are lifted.

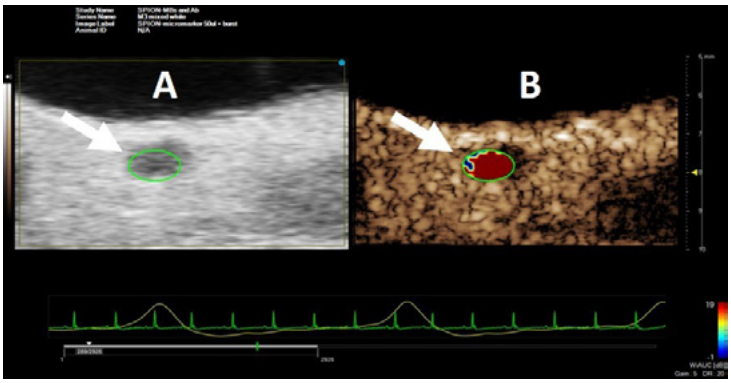


Professor Carmel Moran, Chair of Translational Ultrasound, Director of Preclinical Ultrasound Imaging Facility, CVS

As an ultrasound physicist within CVS, my research is focussed on developing new techniques for ultrasound diagnosis and therapy. I joined CVS in 2012, when the academic department of medical physics was dissolved. Prior to this in 2008, with CVS colleagues I had established the preclinical ultrasound imaging facility with a Wellcome Trust multi-user equipment grant and extended the facility in 2019 with further Wellcome Trust funding. To date, over 60 research projects have been supported and over 5K animals have been scanned of which approximately 70% have been CVS projects primarily assessing cardiac function in neonate, juvenile and adult rodents. I continue to provide scientific input into the many research projects the facility supports.

Within CVS, my own research is focussed on two main areas – (1) the development of ultrasonic contrast agents and novel contrast-specific imaging techniques (2) the performance assessment of ultrasound imaging techniques. Key research projects in which I am currently involved are outlined below:

- With funding from CRUK and Bowel and Cancer Research and collaborators in IGMM and Universities of Strathclyde and Lund, we are currently developing high resolution ultrasound imaging techniques (magneto-motive ultrasound imaging) for the detection of SPION-loaded ultrasonic contrast agents within sentinel lymph nodes in cancer mouse models.



A: B-mode ultrasound imaging and B: Contrast-specific imaging mode ultrasound images of inguinal mouse lymph node with colour enhancement indicating cumulative accumulation of contrast

- Based on previous work conducted within CVS with Megan Holmes and with collaborators in University of La Sapeinza, Rome we are investigating the use of nano- and microbubbles combined with focussed ultrasound to temporarily open the blood brain barrier in mouse models

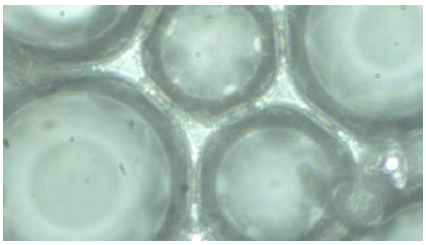


Figure showing contrast microbubbles under a microscope

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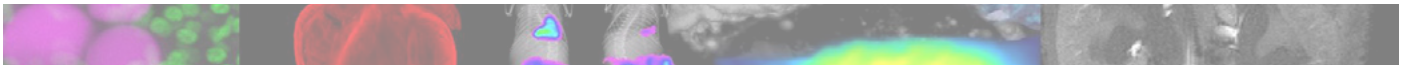
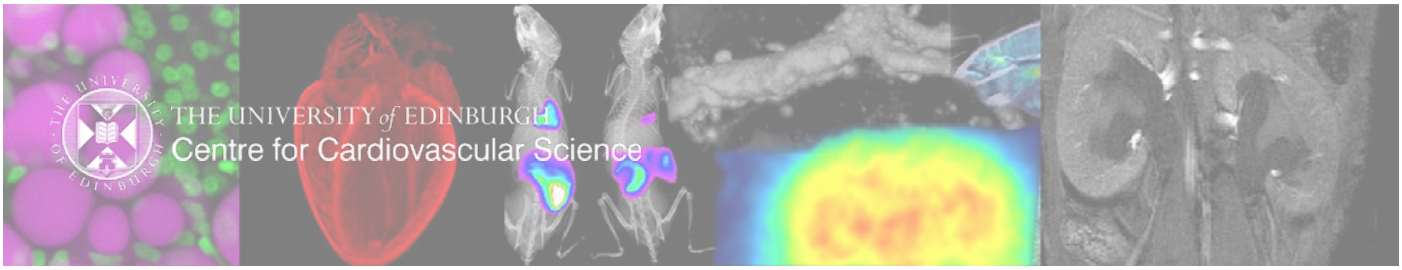




Professor Carmel Moran, Chair of Translational Ultrasound, Director of Preclinical Ultrasound Imaging Facility, CCVS

- With an innovation grant from Institute of Physics and Engineering in Medicine and colleagues in NHS Medical Physics in Edinburgh, Leicester and in Guys and St Thomas's hospital, we are developing ultrasound test objects for the measurement of performance of ultrasound scanners.

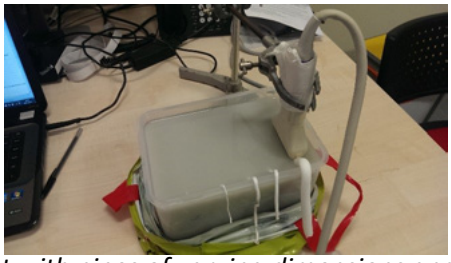


Figure showing ultrasound test object with pipes of varying dimensions and elastic modulus being scanned.

- With a ScotPEN public engagement grant, and in collaboration with NHS Medical physics and physics teachers in local high schools, we are developing echogenic test objects embedded with agar mice of varying sizes. These test objects will be scanned with handheld ultrasound scanners to encourage discussion of animal research but also of resolution and imaging techniques.

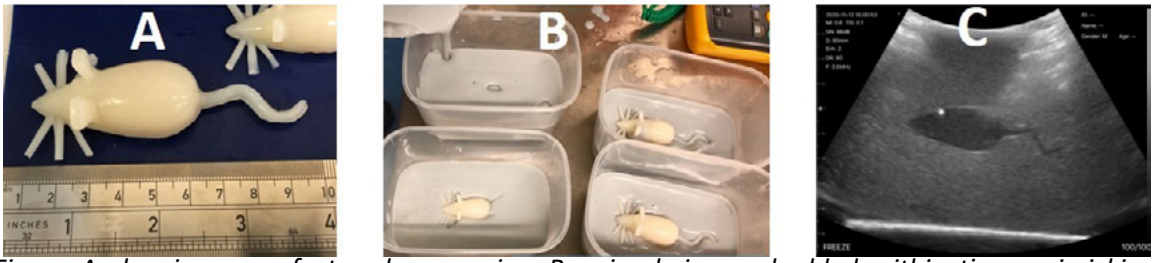
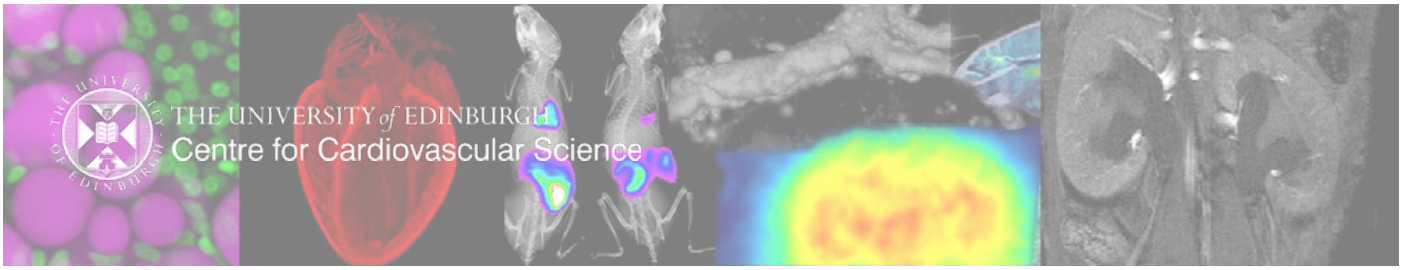


Figure A showing manufactured agar mice, B. mice being embedded within tissue mimicking material and C. ultrasound scan of one of the agar mice within the test-object.

Finally, another significant part of my role over the past 6 years has been as a member of the Athena SWAN (AS) self-assessment team for Edinburgh Clinical Medical School (ECMS) and latterly as a co-convenor of this team. The results of our recent AS submission to Advance HE will be announced in April this year -https://www.ed.ac.uk/medicine-vet-medicine/edinburgh-medical-school/athena-swan .

I was invited to join the REA3 Executive to encourage transparency on the workings of the REA3 activity from an equality and diversity perspective. The experience gained from AS has been helpful as it aims to identify key stages in STEMM academic careers where inequalities are more likely to occur and to put in place structures to support academics as they move through these stages. In the previous newsletter a gender analysis on applications and success rates of REA3 pump priming awards was reported. Appreciating that sex is only one of the nine protected characteristics, we will aim to collect more detailed information in upcoming pump-priming rounds to ensure equality and diversity is maintained across all protected characteristics within the REA3.

I hope this has given you an insight into the research I am undertaking within CVS. Of course, this research is not done in a vacuum and in particular I would like to acknowledge Adrian Thomson who undertakes the highly-skilled preclinical ultrasound scanning and of course the many CVS colleagues, collaborators, MPhys and PhD students who contribute to these research projects.



BHF GLASGOW UNIVERSITY CENTRE OF EXCELLENCE IN VASCULAR SCIENCE AND MEDICINE - VIRTUAL SYMPOSIUM

The first BHF CoRE Glasgow Virtual Symposium - "Hot Topics in Cardiovascular Research" takes place on 26th April 2021, from 13:00 - 16:30 (BST) and is hosted by Professor Rhian Touyz, Director of the BHF Centre of Research Excellence, based at the Institute of Cardiovascular and Medical Sciences at the University of Glasgow.

This symposium brings together national and international experts in cardiovascular research focusing on priority topics in the Glasgow BHF Centre of Research Excellence (CoRE). In addition our BHF CoRE-funded fellows will provide updates and highlights of their exciting research projects. Topics to be covered include Cardio-oncology, Heart Failure, Sex and Gender and Covid19.

Further information can be found on their website:

https://www.gla.ac.uk/researchinstitutes/icams/bhfcoeglasgow/events/virtualsymposium2021/

FINALLY.....

The education system was starting to fail in the Joyce household.

Gillian Joyce has been celebrating the return to school with copius amounts of.....tea: