Name Thomas Keast

E-mail Thomas.Keast@glasgow.ac.uk

Present employment Anaesthetic Clinical Research Fellow/St6 (University of Glasgow/ West of Scotland School of Anaesthesia)

Report for the Association of Cardiothoracic Anaesthesia and Critical Care on Clinical Observership to the Yale School of Medicine, New Haven, Connecticut, USA, from 03-07/10/22

I am working as an anaesthetic clinical research fellow with Professor Ben Shelley at the Golden Jubilee National Hospital, where we have commenced recruitment for the Incidence, Impact and Mechanisms of Perioperative Right VEntricular dysfunction (IMPRoVE) study.

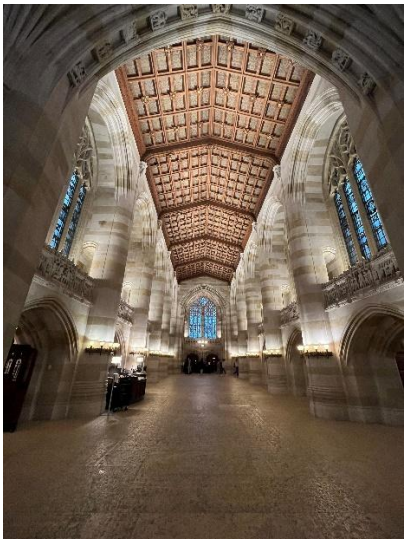
I will be focussing on a nested subgroup of participants, investigating the changes in haemodynamics within the pulmonary vasculature of patients following lung resection. Our working hypothesis is that increased indices of afterload contribute to right ventricular dysfunction (RVD) in this population. My study will involve taking 10 patients between days two to four post-operatively to the cardiac catheterisation laboratory for a right heart catheter, followed by same day cardiac MRI (CMR), thus combining two gold standard investigations of right heart function. This will yield a highly detailed assessment of the pulsatile components of RV afterload plus any changes in right ventricular performance in the immediate post-operative period. During the right heart study, we will sample blood from the coronary sinus and pulmonary arteries to assess the gradients of activated monocytes across the myocardium and pulmonary vascular bed. We will corroborate these findings with image correlates of myocardial inflammation on CMR potentially establishing inflammatory cause for postoperative RVD.

We are collaborating very closely with Professor Paul Heerdt from Yale School of Medicine. He is an anaesthesiologist by trade and has extensively investigated the changes in RV function caused by pulmonary hypertension and lung resection in both animal models and human patients. I was invited over to work with Prof Heerdt for a week last October along with my supervisor, Dr Adam Glass.

Yale university is situated in New Haven, Connecticut, a city about one hour's train ride north, along the coast, from New York City. Founded in 1810, it remains one of the most academically prestigious institutions in the USA. Its medical facilities are in multiple locations across the city, with the main teaching hospital in the centre. It has a capacity over 1500 beds with all major adult and paediatric specialities on site.

View of Yale New Haven York Street Campus from my hotel window

As well as its clinical facilities it has multiple onsite research divisions, one of which is the Division of Applied Haemodynamics where Prof Heerdt is director.



The vaulted ceiling of Yale's main library. A near identical building contains the main basketball court!

After a tour of the hospital and the wider university we sat down to work with Prof Heedt. Our initial discussions very quickly lead us to delve deep into his decades of research in this field interspersed with his experiences of working with industry (and more than a few nuggets of fringe animal physiology!). Prof Heerdt was particularly interested in the equipment I plan to use in the IMPRoVE study. Fluid filled catheters although relatively cheap and more familiar to clinicians produce lower fidelity waveforms than micromanometer tipped wires. Prof Heerdt has experience of both and we were able to troubleshoot in advance several potential issues with catheters I plan to use. Through his many contacts with industry Prof Heerdt has had access to many devices that have not made it through to clinical use. One of which is a fluid filled catheter tipped with four ultrasonic crystal arrays which detect a flow and diameter.

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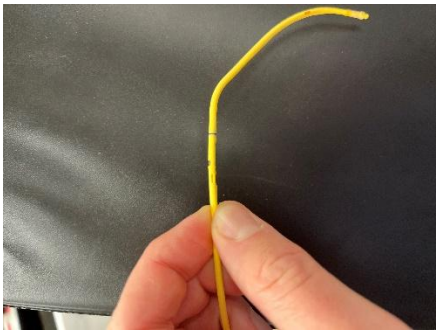
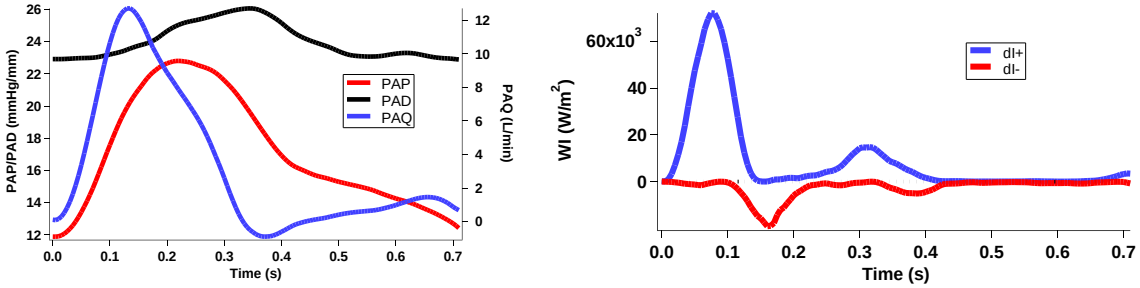


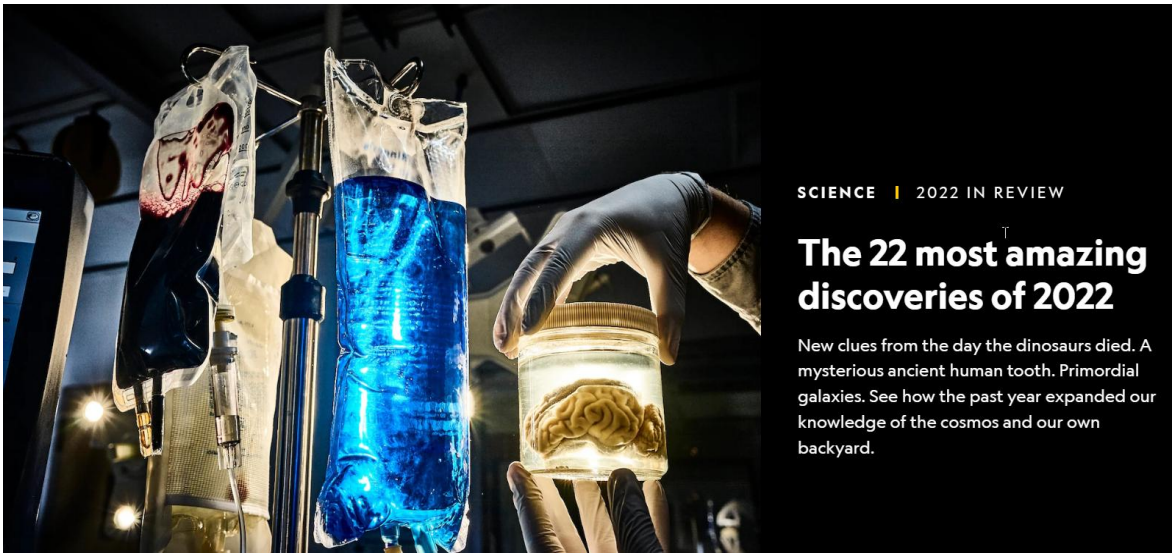
Cardiometric flocath tipped with pressure, flow and diameter sensors

He was able to share with me data he had taken from a pig lung resection model using this catheter. I began the process of conducting wave intensity analysis (WIA) using this data. WIA gives a global assessment wave reflection within blood vessels.



A typical result of an analysis which seeks to show changes in wave intensity (a means of assessing pulsatile afterload) in the main pulmonary artery between sham and post-lung resection pigs. PAP= pulmonary artery pressure, PAD= pulmonary artery diameter, PAQ= pulmonary artery flow, dI+, dI- = forwards and backwards wave intensity

Prof Heerdt took us on a tour of the wider department, and we were able to visit the world-renowned animal imaging laboratory. I had hoped to witness some animal experiments however, during the week of my observership, the main lab was taken over by photographers from the National Geographic. They were working on a piece which celebrated the work conducted by colleagues of Prof Heerdt in the Clinical Neuroscience Research Department.



Photograph taken from a mocked-up experiment within the animal laboratories in Yale. Taken from 'Scientists are trying to resurrect nearly dead organs- here's why' from https://www.nationalgeographic.com/science/article/most-amazing-discoveries-2022

Another of Professor Heerdt's interests is the use of invasive CPET testing in undifferentiated breathlessness (Heerdt, Shelley, and Singh 2022). I was able to witness three of these tests being undertaken. Patients would have a radial arterial line inserted, and Swan floated in the cathlab before walking to an upright cycle ergometer. They were then attached to a standard metabolic cart. Baseline PFTs were taken, ramp protocol was established and then the patients were exercised to VO_2max with systemic and pulmonary gases and pulmonary capillary wedge pressures taken every minute. This labour-intensive process involved three respiratory physiologists, three nurses, two clinical doctors and two research doctors. In addition to witnessing such a comprehensive clinical investigation, I was also able to see Labchart® equipment being used to capture invasive haemodynamic data. We have now purchased this for the IMPRoVE study and it was fantastic to see it 'in-action' being used by experienced operators.

Prof Heerdt also organised for us to spend a day in theatre where I had the opportunity to witness a major open vascular case, a left thoraco-laparotomy for an extended oesophago-gastrectomy and the insertion of an Impella device for a patient with decompensated dilated cardiomyopathy. I found observing management of these complex cases, with subtle differences to the UK practice I'm familiar, to be a deeply enriching clinical experience. On my last day I attended the wider Anaesthesiology department morbidity and mortality meeting before Adam, and I finished our observership by giving a presentation to Yale Cardiovascular Research Centre about our work.

An example of Labchart read-out of a simulated RVP waveform and a derived calculation of RVEF.

Demonstrator Impella 5.5

Adam and I were treated so well by the wider staff at Yale New Haven Hospital. People unfailingly went out of their way to ensure we got the most out of our week whilst expressing a real interest in our lives as doctors back home (one resident was even enquiring about coming to work for the NHS!).

Aside from all the hard work I had a wonderful time with Adam and Paul. We ate like kings every day (the 'Stinky Bomb' sub from a cart outside the hospital's main door will live long in my memory). Paul showed me around his hometown and wider Connecticut with its famous trees beginning to show their fall colours and I finally got to understand American football.



The Sally's Potato Pizza- a New Haven delicacy, Yale vs Dartmouth Football derby and a striped bass out of the Husatomic River.

In summary during this clinical observership I was able to:

1) Have multiple in-person meetings with world renowned experts pulmonary vascular haemodynamics. The feedback I received will strengthen my research.
2) Witnessed the use of the software and instruments I plan to use in my own project.
3) Tour the Yale Cardiovascular Research Centre and see their famous animal imaging facilities.
4) Witness clinical sessions including invasive CPET for the assessment of undifferentiated breathlessness, cases of thoracic, vascular, and cardiac surgery and attend the local anaesthetic M+M meeting.
5) Present my proposed project to an audience of academics from the Yale Cardiovascular Research Centre.

The experience gained from this observership will be invaluable for me for my research. I am incredibly grateful to the ACTACC for their generous support.

Finally, I would just like to thank the following people for helping me make the most of my observership:

Prof Paul Heerdt.
Dr Wanda Popescu and the wider team of anaesthesiologists at Yale School of Medicine.
Dr Adam Glass.
Prof Ben Shelley.

Yours faithfully,

Dr Thomas Keast
Anaesthetic Clinical Research Fellow/St6
University of Glasgow/ NHS Golden Jubilee

Heerdt, P. M., B. Shelley, and I. Singh. 2022. 'Impaired systemic oxygen extraction long after mild COVID-19: potential perioperative implications', *Br J Anaesth*, 128: e246-e49.