AN INTERVIEW WITH...

Andrew Holden, MBChB, FRANZCR, EBIR

Dr. Holden reflects on the legacy of paclitaxel and lessons learned from the controversy, research priorities for 2022, his philosophy for choosing which projects to accept, and more.

You are a prolific clinical researcher across a relatively wide range of vascular territories and disease states. How does your day-to-day practice break down in terms of which disease states/locations you treat most often?

I'm fortunate to be based in an academic tertiary hospital with most medical and surgical specialties available, servicing a population of around 1.8 million people. In particular, we have a busy vascular practice treating a big critical limb and claudicant population, venous disease, and a large endoluminal aortic program. We also provide hospital-based intervention for liver and renal transplant and dialysis services. Over a decade ago, my vascular surgical colleague Andrew Hill and I formed the Vascular Intervention Research Unit at Auckland Hospital, and we have been involved in well over 100 first- and early human trials, mainly but not exclusively involving vascular and renal dialysis patients.

One of the more frequent topics of your recent publications and presentations has been the use of drug-coated balloons (DCBs) in the lower extremities and dialysis access applications, with talks and papers focused not only on their safety and efficacy in a traditional sense but also the exploration of the safety concerns raised by Katsanos et al.[1] What do you envision the enduring legacy of paclitaxel will be, when all is said and done?

My first experience with paclitaxel-eluting devices began with the Zilver PTX drug-eluting stent (Cook Medical). We had early access to this technology and could immediately see a paradigm shift from the frequent, severe restenosis we saw with bare nitinol stents in peripheral arteries. Following this, we participated in many early paclitaxel-coated balloon trials that directly compared patency of these devices to plain angioplasty balloons. Not only did the vascular core laboratories confirm paclitaxel DCBs produced significantly less late lumen loss, but also, we saw this with our own eyes! Since then, we have routinely used paclitaxel-coated balloons and stents in almost all of our femoropopliteal arterial interventions, and patients have benefited from improved patency and lower reintervention rates. This is why we seriously evaluated the concerns raised by Katsanos and colleagues. Of course, we would have stopped using paclitaxel devices if we believed they caused increased mortality. Equally, we did not want our patients to unnecessarily endure increased morbidity and even mortality associated with higher rates of reintervention. In terms of a legacy, I believe paclitaxel will be a hard act to follow in femoropopliteal artery intervention, particularly for DCBs. The powerful antirestenotic effect as well as the ability of paclitaxel to enter and reside in the vessel wall provides a challenge for other DCBs to match in terms of durable patency.

Beyond the conclusions of papers and the black, white, and grey of the data, what have you learned from the past few years of paclitaxel research and controversy? What advice would you share regarding how to work through inherent biases, perhaps emotions at times, to produce scientifically sound research to further explore a finding that is counter to your prior work?

This is a great question. I admire Dr. Katsanos and his colleagues for having the conviction to alert the vascular interventional world of a potential safety concern with paclitaxel. I regret that many of the protagonists of paclitaxel causing mortality became entrenched in that position, and convictions hardened. Resolution of this issue ultimately required a huge collegial effort from clinicians, companies, and regulators, and I was humbled to be a small part of that. Important learnings have emerged from this controversy. We now appreciate that all of the pivotal vascular device trials were designed and powered for efficacy and not mortality. Although meta-analysis has been considered the most powerful tool to analyze these trials, we now understand that if there are inherent flaws in trial design, they will not necessarily be overcome by a meta-analysis. The issue of trial bias (particularly, treatment and ascertainment bias) is now well understood, as is the power of population-based research to assess endpoints like all-cause mortality. As a result, vascular device trial design has and will be modified and improved. We are now better placed to have a balanced, considered, and collegial pathway to

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resolve any future controversies that emerge in the vascular intervention space.

In a recent paper published in *Diagnostic and Interventional Radiology*, you and colleagues studied the impression of interventional radiology (IR) for female medical students, citing a lack of awareness about IR and misconceptions about radiation exposure as contributors to discouraging entry.[2] What do you think interventional radiologists can do to combat these barriers to entry for female students?

In many parts of the world, including here in New Zealand, medical students are not adequately exposed to the fantastic benefits of image-guided intervention provided by IR and other specialties. As a result, far fewer medical students and junior doctors consider IR as a career possibility. Specifically, for female medical students, there is also the misconception that IR will involve significant radiation exposure and potential safety concerns to the physician and her family. To address these issues, education is the key. Image-guided intervention and IR need a much higher profile in undergraduate medical training, and access to IR modules for junior doctors should also be provided. Education on the huge advances in radiation protection and safety is equally important. In these ways, IR can enjoy the benefits of greater diversity, particularly from more female participation in our specialty.

As Codirector of the Vascular Intervention Research Unit at Auckland Hospital, which has a number of concurrent clinical trials, how has your practice adjusted during the pandemic, both in research (eg, enrolling patients) and nontrial settings? Can you give us a preview of the unit's research priorities for 2022?

Many of the challenges we have encountered during the pandemic by the Vascular Intervention Research Unit here at Auckland Hospital have been faced elsewhere. Initially, patients scheduled for more elective interventions were deferred, which impacted recruitment to claudication and elective aneurysm repair trials. Clinical trials involving devices for more acute indications such as critical limb ischemia and dialysis access continued, largely undisturbed. Where possible, our research coordinators worked from home, although they were obviously required in the hospital for procedures and clinic visits.

One interesting development, by necessity, has been the evolution of remote support for first- and early human trials. Prior to the pandemic, almost all support for animal and bench studies as well as first-in-human procedures was provided in person by company and medical specialists traveling to our institution, which was a challenge given our location here in New Zealand! In association with a local audiovisual company, we are able to provide high-quality, real-time multicamera and audio support online, such as direct transmission of imaging data without degradation. The result is an experience very similar to having the specialists in the room—although I certainly miss the social contact! We have an exciting portfolio of trials planned for 2022: new DCBs, bioresorbable stents, and atherectomy and lithotripsy devices. In the aortic space, we continue to evaluate methods of aneurysm sac management, new complex endografts, and prophylactic small aneurysm management. Plenty more too!

You've had the opportunity to be at the forefront of many device investigations, including several that are now in interventionalists' everyday toolkit. What is your philosophy for selecting the devices (and companies) for which you will commit the time, energy, and resources to studying? How do you know when a project is optimal to accept and when to decline?

As you might expect, we are fortunate to be approached by a number of companies and investigators looking to include our unit in early human trials and postmarket registries. There are a number of important considerations: the originality of the device or procedure, whether it addresses an unmet clinical need, our ability to recruit sufficient patient numbers to the trial, and, most importantly, our capacity to manage the trial to the high level we always strive for. The "sweet spot" for our unit is an innovative and original early human device trial addressing an unmet need for a significant number of our patients. To date, we've been involved in a number of these trials, and the future looks promising!

Looking back on your term as President of the Asia Pacific Society of Cardiovascular and Interventional Radiology (APSCVIR), are there any particular projects or initiatives that you are proudest of?

I'm very proud to live in the Asia Pacific region, the largest global group of interventional radiologists, and to be Past-President of APSCVIR. One thing I'm particularly proud of is leading a review of guidelines for our annual scientific meeting, creating a fantastic and consistent educational opportunity at wonderful locations in our region. The next meeting in Kobe, Japan, in June 2022 will be no exception! The APSCVIR Outreach Program is a wonderful initiative of my colleague and friend Dr. Bien Soo Tan. This program brings an IR faculty to countries in our region that need our support, such as Myanmar, Mongolia, and Sri Lanka. During the pandemic, outreach sessions have been provided online, but we look forward to visiting our colleagues in person

in the near future. Finally, I'm grateful for the friendship and support APSCVIR has enjoyed with global partners such as the Cardiovascular and Interventional Radiological Society of Europe and the Society of Interventional Radiology.

You recently launched the podcast *Masters of Circulation* with vascular surgeons Prof. Ramon Varcoe and Dr. Peter Schneider. Can you tell us about the origin of this project and its goals?

This was a great idea of Ramon's, and I'm delighted to be working with Peter and Ramon on this project. The idea is to try and provide some key insights from thought leaders in vascular intervention that will be of interest and benefit to those involved in vascular care from all specialist backgrounds. We want to keep the conversations relaxed and wide ranging, and to date, I think we've achieved that, thanks in no small part to the energy and enthusiasm of our guests. The podcast format lends itself ideally to optimum utilization of time—perhaps, enjoying the conversation while driving or exercising—and is available on all podcast platforms.

How can congresses and news outlets better identify and work with rising voices from Oceania? And, similarly, what advice do you have for physicians who want to engage and share their research with audiences on other continents?

I do think congresses and news outlets are much more receptive to new ideas and rising voices than they were previously. A close connection with social media is particularly important because many physicians use these platforms to share important experiences and ideas. The fact that most international meetings are available in hybrid format with an excellent online component means these educational opportunities are accessible to many parts of the world, including Oceania. It also means that researchers can share their findings globally without necessarily requiring the challenges that travel currently provides. ■

1. Katsanos K, Spiliopoulos S, Kitrou P, et al. Risk of death following application of paclitaxel-coated balloons and stents in the femoropopliteal artery of the leg: a systematic review and meta-analysis of randomized controlled trials. J Am Heart Assoc. 2018;7:e011245. doi: 10.1161/JAHA.118.011245
2. Huasen B, Suwathep P, Khan A, et al. Female medical student impression of interventional radiology: what can we do to improve this? Diagn Interv Radiol. 2021;27:542-545. doi: 10.5152/dir.2021.20378

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