AN INTERVIEW WITH...

Gerard Goh, MD, FRANZCR, EBIR

Dr. Goh discusses many of his current research endeavors, including the SHIELD trial, DCB use in arteriovenous fistulas, IRE nonthermal tumor ablation, and more.

As the Australian Principal Investigator for the SHIELD trial, can you briefly explain the mechanisms by which SB-030 (Symic Biomedical) prevents inflammation and vascular injury due to percutaneous transluminal angioplasty? What stage is the trial in currently, and can you share any early results?

The SHIELD trial is a first-in-human, multicenter, blinded randomized controlled trial (RCT) examining the effects of using SB-030 versus saline after angioplasty of femoropopliteal atherosclerotic lesions. SB-030 acts to reduce acute extracellular-mediated inflammation and neointimal hyperplasia by binding to the extracellular matrix collagen that is exposed after angioplasty. SB-030 binds at a receptor site known for platelet-collagen interaction. When bound, the compound reduces the binding and activation of platelets, which decreases the inflammatory response (eg, cytokine release and white blood cell activation) and therefore results in less smooth muscle cell proliferation and a reduction of neointimal hyperplasia. This mechanism of action is different from paclitaxel, which reduces the smooth muscle cell proliferation due to its antiproliferative effects. SB-030 reduces the inflammatory pathway by physically blocking or coating the angioplasty-related vessel injury.

The trial is expected to complete enrollment in the first half of 2017, with results available in the second half of 2017. Preliminary results are encouraging and showing trends favoring SB-030 relative to the control group in terms of the target lesion revascularization (TLR) rate—an important safety and efficacy endpoint.

How have endovascular capabilities for vascular trauma improved in recent years? Where are improvements still needed most?

The improvement in endovascular treatment for vascular trauma has mainly been with the advances in diagnostic imaging and streamlining referral pathways to have a patient arrive to the angiography lab as soon as possible. Modern CT scanners are becoming quicker and more detailed in assessing vascular trauma, allowing high-resolution multiplanar reformats. When a patient is undergoing a CT scan for other bodily injuries, our CTA protocols for vascular trauma investigation add only a very short amount of additional scanning time. Our hospital has efficiently streamlined trauma and vascular trauma pathways to allow rapid assessment and decision making, which has translated to a significant reduction in the time to the angiography lab. We are currently assessing the logistics of REBOA (resuscitative endovascular balloon occlusion of the aorta) devices placed early in the emergency department.

The advancements in endovascular device technology haven't had as much impact as the imaging and referral pathways. Perhaps the most helpful improvement in device technology has been the development of lower-profile devices (eg, stent grafts), which are very helpful in hypoperfused, shut-down vascular systems.

Your center has worked in trials involving percutaneous creation of arteriovenous fistulas (AVFs). What do you see as the future for this method? What are the most significant hurdles it faces, and how do you think it will fare?

This is a very interesting space, and I think that this could be disruptive technology. Percutaneous AVF creation is still in the early days of early clinical trials, but the concept and technologies seem very promising. This technology has the capability to offer AVF creation in areas where skilled vascular or transplant surgery is not offered or to help reduce the waiting lists for patients requiring AVFs. We were involved as an investigator site for the NEAT trial for the everlinQ device (TVA Medical, Inc.), and the interim results were recently presented at VIVA 2016 and ASN 2016. The

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interim results of the single-arm study demonstrated that in a 60-patient cohort, there was a 98% technical success rate in creating fistulas, 91% of percutaneous fistulas were suitable for dialysis at 3 months, and safety endpoints were achieved.

Like all first-in-human and early safety and efficacy trials, there will be many things learned about the first generation of devices and the technique required to use the devices. The most significant hurdle percutaneous AVF creation technologies face, apart from conducting larger, more thorough clinical studies, is addressing the procedural learning curve and conducting education of physicians on how to use these devices. Because the technique is novel, there is a level of endovascular and ultrasound skills required.

You are performing some research into the use of drug-coated balloons (DCBs) in the treatment of hemodialysis AVFs. How is your research different from the current literature to date?

The use of DCBs in AVFs has gathered much interest over the last few years. The early data are composed of very small patient groups, and there is much work needed in this space. Most of the current trials evaluating DCBs in AVFs have focused on TLR and primary/assisted patency, which are important measures, but few have looked at dialysis outcomes. Our trial is an RCT examining the effects of DCBs versus angioplasty for the treatment of AVF stenoses. We are working very closely with our nephrologists, who are measuring a range of variables related to dialysis outcomes, which are metrics that we as endovascular proceduralists are often not familiar with. The other factor that makes our study different is that we are allowing participating centers to use almost any nonimplantable device leading up to DCB use. Almost all studies to date have excluded the use of scoring and cutting balloons. Cutting balloons in particular have been shown to have some superiority over high-pressure balloon angioplasty and standard angioplasty, so our study will reflect more "real-world" practice.

Can you tell us how the inferior vena cava (IVC) filter removal and patient tracking system was put in place at your center? How was it originally formed, and does it work? Do you see any areas for improvement?

Our IVC filter registry has been a project in constant evolution. We have learned what has worked and what hasn't and have adapted it to our individual hospital's environment. We had initially relied on the referring unit (ie, trauma or hematology) to arrange retrieval, and the retrieval rates were subsequently low. We then instituted multiple strategies on various levels of the patient care pathway, and the retrieval rates significantly improved. This involved educating patients on their filter, creating (and more importantly) maintaining an internal registry, reminding the referring unit verbally and writing in the patient's notes to arrange retrieval, just to mention a few of our methods. In my opinion, one of the most important and high-impact intervention steps is regular auditing. Regular audits allow us to capture where the retrievals are being missed and highlight where in the process things could be improved. This is time intensive but, in my opinion, has been one of the most important practices that has influenced our retrieval rates.

In your work, you have utilized robotic catheters for performing transarterial chemoembolization (TACE). What are the pros and cons of its use in this setting?

There is a subset of patients who have tortuous and unfavorable anatomy for catheter stability and placing a microcatheter into the liver to treat liver tumors, such as hepatocellular carcinoma. Some of these patients have undergone multiple unsuccessful attempts "by hand" when placing catheters into the liver segments to perform TACE. We were able to bring these patients back and offer them a second chance (and in some cases, a third or fourth chance) using the Magellan robotic technology (Hansen Medical, Inc.).

We've encountered a wide range of challenging anatomy, including tortuous aortas and iliac (hypogastric) arteries, as well as stenosed and early branching mesenteric vessels. The Magellan system allowed us to finely and precisely control the robotic catheter to enter the celiac axis and superior mesenteric artery. In addition, the system allows reasonably rigid catheter stability right to the tip of the robotic catheter, a feature that standard catheters don't have. The Magellan robot isn't suitable for all endovascular cases due to the relatively higher cost of disposables compared to conventional procedures.

Can you tell us about your research on irreversible electroporation (IRE) nonthermal tumor ablation for organ-confined prostate cancer treatment? How did this project come about, and what how do you view its trajectory?

Many men diagnosed with prostate cancer now have longer life expectancies with improved treatment options, but the relatively high rate of complications such as sexual dysfunction, incontinence, and rectal

injury can significantly affect a patient's quality of life. IRE potentially offers neural bundle-, ureter-, and capsule-sparing organ-confined treatment in a nonthermal manner, therefore reducing some of these complications.

There is a lack of clinically validated IRE treatment protocols for specific tissue and tumor types, and most IRE parameters were developed for ex vivo models. We designed a research project with the aim to first determine and characterize the IRE therapeutic dose response and safety profile necessary to enable effective and reliable IRE ablation treatment. The design is based on a conventional phase 1 to phase 2 safety and dose escalation regimen with postprostatectomy histologic assessment. This will be followed by a phase 3 standalone therapy efficacy study based on the findings from phases 1 and 2.

Our interim findings include a good safety profile and that prostatectomy can be safely achieved after IRE ablation. However, histologic findings indicate coagulative necrosis rather than an IRE effect at parameter settings used in ex vivo and animal models, so we are likely able to further fine-tune the parameters to optimize the electroporation while minimizing complications.

As someone who has practiced on multiple continents, what are some differences between your former practice in the United Kingdom versus your current practice in Australia, both in terms of the overall health care system and the day-to-day work?

I am fortunate to have worked in different health care systems and have been able to see the differences in them. Practice in the UK and Australia is quite similar in terms of the epidemiology of disease and high standards of patient care. The work within the endovascular space is very similar. There are some differences in the administrative side with the National Health Service having more "red tape" than the Australian health care system.

An interesting area is new technologies. In Australia and New Zealand, many first-in-human and preliminary safety and efficacy trials are often performed so we get a taste of new technologies, and based on our experiences, we have a chance to influence the direction of new technologies. However, when they are finally market released, new technologies tend to be released in Europe, then the United States, before the rest of the world, so sometimes we are waiting for devices to be available again in Australia for quite some time after we used them in the first-in-human studies! ■

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