



## RACP Foundation Research Awards

### FINAL REPORT

<b>Project / Program Title</b>	The Silent and Apparent Neurological Injury in Transcatheter Aortic Valve Implantation (SANITY) Study	
<b>Name</b>	Dr Jonathon Paul Fanning	
<b>Award Received</b>	2016 RACP Joseph Thornton Tweddle/NHF Health Profession Research Entry Scholarship	
<b>Report Date</b>	20 October 2017	
<b>Chief Investigator / Supervisor</b>	Dr Jonathon Paul Fanning / Prof John F. Fraser	
<b>Administering Institution</b>	The University of Queensland	
<b>Funding Period</b>	Start Date:	1 January 2016
	Finish Date:	31 December 2016

#### PROJECT SUMMARY

Severe Aortic Stenosis (AS) is the most common heart valve disease in the developed world affecting 3% of those greater than 75 years of age. Once symptoms develop the prognosis for these patients is very poor and 50% are dead within 2 years. Though aortic valve replacement (open heart surgery) is the gold-standard for treating this condition many of these patients are not fit enough to undergo the operation. Previously the management of such patients has been limited to medical management but the introduction of TAVI has offered an exciting alternative to a subgroup of such patients. Unfortunately though, the rates of stroke with TAVI have been double that of aortic valve replacement. In fact, stroke is but one of a number of neurological injuries associated with TAVI – other entities include or neurocognitive impairment and silent stroke, which has been reported in as many as 90% of patients.

Prior to this study neurological injury had undergone only limited investigation to date. This study investigated the cause and frequency of neurological injury amongst patients undergoing TAVI. Such knowledge has helped to characterize the injury and such improve understanding of:

1. Risk factors for the procedure
  - a. Select patients for the procedure to minimize harm, which is a fundamental ethical principal underlying all of medicine.
  - b. Inform patients of the risk of the procedure to permit a more educated decision
2. Improve the devices and techniques used during the procedure so as to minimize this occurrence and effects of neurological injury.
3. Optimise medical management before, during and after the aortic valve intervention to minimize the impact of this neurological injury.
4. Formed a platform for further investigation.

## PROJECT AIMS / OBJECTIVES

The SANITY study aimed to provide the most comprehensive characterization to date of neurological insult and injury - both clinically-apparent and silent - post TAVI. These encompass pre-existing patient factors, and both peri- and post-operative factors thought to influence neurological insults and injury sustained during aortic valve interventions.

## SIGNIFICANCE AND OUTCOMES

Objectively measured structural and functional neurological injuries remain a frequent occurrence, affecting the majority of intermediate-risk patients who undergo TAVI. New MRI-defined ischemic lesions were associated with reduced early cognitive function. These subtle injuries are of increasing significance for lower-risk patients who have both more time for neurological sequelae to manifest and alternate management options available to them compared with high-risk and inoperable patients. Thus, enthusiasm for extending TAVI into lower-risk patients must be tempered until the risk associated with subclinical injury is clarified and optimal neuroprotective strategies can be pursued.

Future research:

1. Using the above recruited patients analysis has been performed regarding the distribution of cerebral lesions and emboli.
2. MRI- modelling of cerebral emboli rheology.
3. Prothrombotic changes that occur as a result of TAVI and the effectiveness of antithrombotic regimes that are currently used.
4. Novel neuroprotective strategies that may reduce the impact of the intraoperative insult that occurs during the procedure.

## PUBLICATIONS / PRESENTATIONS

Peer-reviewed publications

Fanning JP, Walters DL, Wesley AJ, Anstey C, Huth S, Bellapart J, Collard C, Rapchuk IL, Natani S, Savage M, Fraser JF. Intraoperative cerebral perfusion disturbances during transcatheter aortic valve replacement. *Annals of Thoracic Surgery*. 2017;104:1564-1568.

Fanning JP, Wesley AJ, Walters DL, Eeles EM, Barnett AG, Clarke AJ, Platts DG, Wong AA, Strugnell WE, O'Sullivan C, Tronstad O, Fraser JF. Neurological injury in intermediate-risk transcatheter aortic valve implantation (TAVI). *Journal of the American Heart Association*. 2016;5:e004203.

Oral Presentations:

Fanning JP, Wesley AJ, Walters DL, Wong AA, Fraser JF. Topographical distribution of cerebral infarction associated with transcatheter aortic valve implantation. Asia Pacific Stroke Conference (APSC) 2016, Brisbane, AUSTRALIA.

Fanning JP, Wesley AJ, Walters DL, Clarke AB, Wong AA, Natani S, Fraser JF. Perioperative neurological injury in patients undergoing transcatheter aortic valve implantation (TAVI). Australian Society of Anaesthetists 2016 National Scientific Congress, Melbourne, Australia.

Fanning JP, Wesley AJ, Walters DL, Eeles EM, Barnett AG, Clarke AJ, Platts DG, Wong AA, Strugnell WE, O'Sullivan C, Tronstad O, Fraser JF. Neurological injury in intermediate-risk

transcatheter aortic valve implantation (TAVI). American Heart Association Scientific Sessions, New Orleans, LA, USA.

The following research distinctions were awarded during or as a result of the period research afforded by this scholarship:

The Prince Charles Hospital Graeme Nielson Award for Best Published Paper (2016)

Metro North Hospital and Health Services 'Rising Star' Research Excellence Award (2017)