

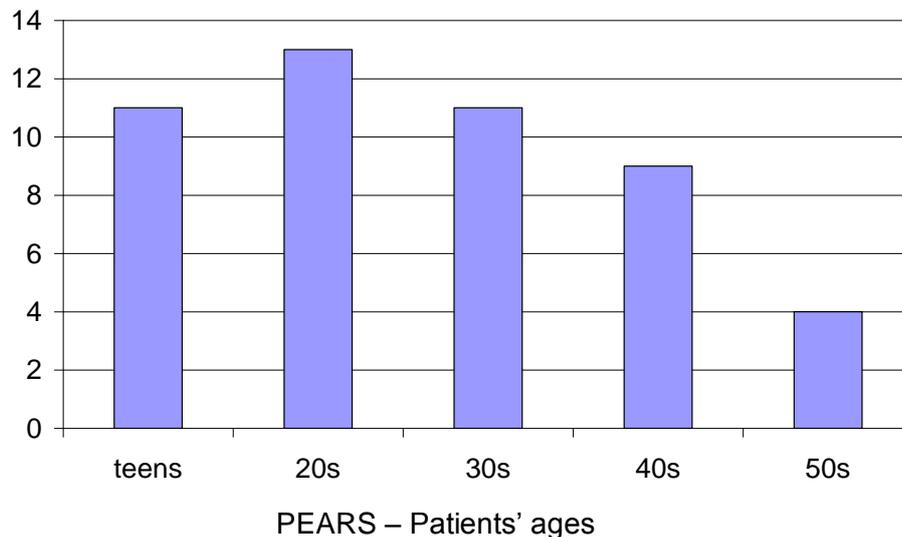
ExoVasc[®] Personalised External Aortic Root Support (PEARS)

Project Status – January 2015

1. Patient Numbers & Demographics

As of January 30, 2015 we have treated 48 patients with aortic dilation using the ExoVasc PEARS implant:

- 29 males + 19 females
- A collective total of 208 post Operative Patient Years
- Patient 1 @ 128 months
- 20 patients @ > 5 years post-op



2. Disease types treated

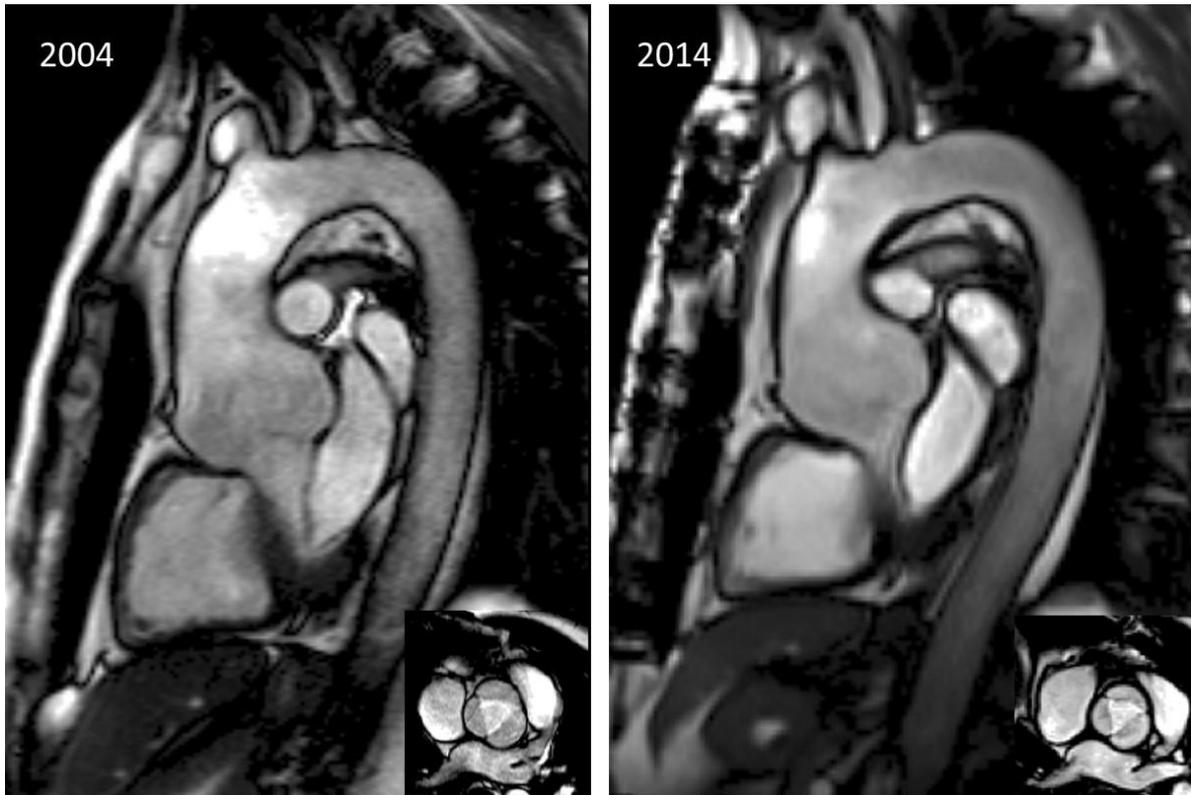
PEARS surgery has been applied to aortic dilation associated with:

- Marfan syndrome - 39
- Bicuspid Aortic Valve disease - 4
- Transposition of the great arteries repaired by a switch operation as an infant -1
- Loeys-Dietz syndrome - 1
- Tetralogy of Fallot -1

- Unspecified - 2

3. Control of Aortic Dilation

Patients have been invited to have annual cardiac MRI. Patient 1 was recently MR scanned 10.5 years post op:



Patient 1: April 2004 (3 weeks pre-op) and November 2014 (10.5 years post-op)

This demonstrates stability of the aortic dimensions and morphology within the PEARs implant over a significant time period.

Two young female patients who have received a PEARs implant have subsequently had successful pregnancies and given birth without evidence of further aortic dilatation.

4. Patency of coronary arteries through the PEARs implant

Patient 1 had exercise induced angina in 2011 (7 years post PEARs surgery). A routine coronary angiogram carried out at the time showed smooth coronary lumens and widely patent coronary orifices where the coronary arteries pass through the soft, pliant textile of the PEARs implant.

(see: <http://www.exstent.com/images/contentpage/downloads/icvts.ivs237.full.pdf>)

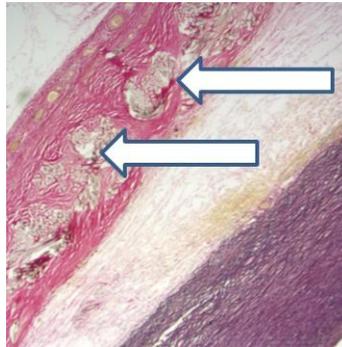
Patient 16 (Marfan syndrome + BAV) died of a non-aorta related event some 4.5 years after PEARs surgery. As part of a post mortem examination, his aorta was examined. The coronary orifices and proximal coronary arteries were patent and appeared normal.

(see:

<http://www.exstent.com/images/contentpage/downloads/Pepper%20Goddard%20RM%20TT%20ejcts%202014.pdf>)

5. Incorporation of the PEARS implant

Further histological inspection of patient 16's aorta also showed complete incorporation of the implant into the adventitia, including neovascularisation.

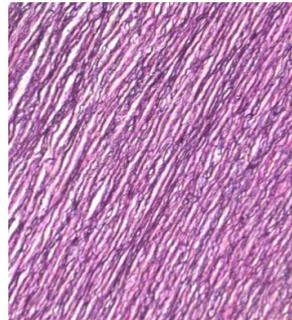


Neovascularisation (small yellow circles, top left of image) in the outer layers of the adventitia. The implanted textile (arrowed) is fully incorporated. (Note that the media has separated from the adventitia during sample preparation)

6. Repair of Media within the PEARS implant

Not only does the ExoVasc[®] PEARS implant become incorporated into the adventitia, but the media within the implant recovers. While it remains fibrillin deficient, the media assumes a normal histological appearance. This is entirely consistent with the tensile loading having been removed from the media and handled by the implant. The following images are taken from the recent paper by John Pepper and Martin Goddard:

<http://www.exstent.com/images/contentpage/downloads/Pepper%20Goddard%20RM%20T%20ejcts%202014.pdf>



Recovered media within PEARS implant showing "normal" histology

7. Surgical mortality

Of 49 patients intended for PEARS surgery, 1 died peri-operatively. The patient had a severe pectus which compromised access to the aorta. During the dissection of the aorta in preparation for this procedure, the left main coronary stem was nicked. Despite being swiftly put onto bypass (and later ECMO), the patient recovered slowly (72 hours) and then suffered an intra-cranial bleed from which he did not recover. The PEARS was not implanted in this patient.

8. Operation time

Surgical operation times for the PEARS procedure have been shown at around 2 hours. This contrasts well with TRR and VSRR where patients might expect to be anaesthetised for anything from 3 to 6 hours.

This relatively shorter time in the operating room must have a beneficial impact on overall procedure costs as well as patient experience & recovery.

9. Cardio Pulmonary Bypass

PEARS surgery is routinely carried out on a beating heart without CardioPulmonary Bypass (CPB). In a small number of specific cases, for example, where anomalous coronary morphology or adhesions exist, CPB has been used.

Apart from the reduction in procedure costs this represents, patient experience & recovery are both improved.

10. Reference publications:

Copies of all of the clinical papers on PEARS can be found at:

<https://exstent.sharefile.com/d/s84b2bb9d79a4037b>

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January 2015