NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: **IP885/2 External aortic root support in Marfan syndrome**

Your information

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Nominated/ratified by (if applicable):	Click here to enter text.
Registration number (e.g. GMC, NMC, HCPC)	GMC: 1502228

How NICE will use this information: the advice and views given in this questionnaire will form part of the information used by NICE and its advisory committees to develop guidance or a medtech innovation briefing on this procedure/technology. Information may be disclosed to third parties in accordance with the Freedom of Information Act 2000 and the Data Protection Act 2018, complying with data sharing guidance issued by the Information Commissioner's Office. Your advice and views represent your individual opinion and not that of your employer, professional society or a consensus view. Your name, job title, organisation and your responses, along with your declared interests will also be published online on the NICE website as part of the process of public consultation on the draft guidance, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

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X☐ I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. If consent is NOT given, please state reasons below:

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Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

Please note that questions 10 and 11 are applicable to the Medical Technologies Evaluation Programme (MTEP). We are requesting you to complete these sections as future guidance may also be produced under their work programme.

1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology?	I was the surgeon who was part of the original team which developed this procedure and I performed the first 26 operations. I was an integral part of the planning team for the PEARS procedure (Personalised External Aortic Root Support)
	Have you used it or are you currently using it? – Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? – Is this procedure/technology performed/used by clinicians in specialities other than your own? – If your specialty is involved in patient selection or referral to another specialty for this	To date there have been 516 PEARS procedures, of which approximately 321 have been undertaken in the NHS. This procedure is confined to cardiac surgery with the majority undertaken in adults

	procedure/technology, please indicate your experience with it.	
2	– Please indicate your research experience relating to this procedure (please choose one or more if relevant):	I have done bibliographic research on this procedure. I have done research on this procedure in laboratory settings (e.g. device-related research). I have done clinical research on this procedure involving patients or healthy volunteers. I have published this research. ~~I have had no involvement in research on this procedure.~~ Other (please comment)
3	How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	This is a major modification of an old procedure in which the ascending aorta was “wrapped” in a polyethylene graft (Dacron). The two essential differences of our procedure are: 1. The sleeve is macroporous to allow ingress of inflammatory cells in the healing process, 2. The sleeve is constructed by computer assisted design (CAD) and rapid prototyping (RP) and is thus personalised to the patient. Furthermore, it can be used as 100%, 95% or 90% according to the needs of the operation. ~~Established practice and no longer new.~~ ~~A minor variation on an existing procedure, which is unlikely to alter the procedure’s safety and efficacy.~~ ~~Definitely novel and of uncertain safety and efficacy.~~ The first in a new class of procedure. X

4	Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?	This procedure complements existing procedures but is especially useful for patients early in the natural history of their disease (aortopathy).

Current management

5	Please describe the current standard of care that is used in the NHS.	For patients with an enlarged ascending aorta and aortic root there are two established procedures: total root replacement (TRR or Bentall) and Valve Sparing Root Replacement (VSRR)
6	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	There is another procedure, the Florida Sleeve, which is similar but does not include the two essential features of PEARS, outlined in (3) above. These procedures involve resection of the aorta and therefore cardiopulmonary bypass, cardiac arrest and myocardial preservation techniques

Potential patient benefits and impact on the health system

7	What do you consider to be the potential benefits to patients from using this procedure/technology?	1. The patient retains his/her own endothelium and aortic valve 2. The procedure avoids the need for cardiopulmonary bypass and ischaemic arrest 3. The sleeve is personalised to the patient and strengthens the aortic wall 4. There is no requirement for long-term oral anticoagulation
8	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Patients with congenital aortopathy such as the Marfan syndrome. Patients with complex congenital heart disease, eg Transposition of the Great Vessels (TGA) who have had correction in infancy and later present with an enlarged aorta.
9	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	This technology has the potential to prevent dissection while preserving the aortic valve and the endothelial lining of the aorta. Increased access to genetic testing has led to more patients presenting with a genetically driven aortopathy at an early stage in their natural history. We know that at least 25% of patients who present with acute dissection of the aorta have an aortic diameter below the threshold for intervention stated in international guidelines. To this extent the guidelines are becoming out-dated and the PEARS procedure can restore patients to an acceptable way of life with a low risk procedure and the avoidance of life-long anticoagulation.
10 - MTEP	Considering the care pathway as a whole, including initial capital and possible future costs avoided, is the procedure/technology likely to cost more or less than current standard care, or about the same? (in terms of staff, equipment, care setting etc)	This procedure is likely, over a medium-term of 5 years, to be lass costly because long-term anticoagulation is avoided and scanning of the aorta can be less frequent.
11 - MTEP	What do you consider to be the resource impact from adopting this procedure/technology (is it likely to cost more or less than standard care, or about same-in terms of staff, equipment, and care setting)?	This procedure is likely to be cost-effective for the reasons given above.
12	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	No special clinical facilities are required as the procedure can be carried out in a standard cardiac surgery unit.

13	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	The surgeons who undertake a PEARS operation need to be very familiar with the aortic root and ideally should come from an experienced congenital cardiac surgical background.

Safety and efficacy of the procedure/technology

14	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence: Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	The surgery is simple in concept but requires experience and skill in execution. There is a danger of damaging the origin of the coronary arteries and this has happened in 5 patients one of whom subsequently died (mortality 1 in 500). The remaining 4 patients required a vein graft to the right coronary artery and recovered very well. It is very important that the sleeve covers the entire aortic root as far proximally as the aortic annulus, otherwise root dilatation will occur. Incidence of coronary events 5/500 = 0.01% (Van Hoof et al. Heart. 2021. Doi:10:1136/heartjnl-2021-319300) Many patients have a short-lived post-operative pyrexia of less than 38.5 degrees C for 3 days A few patients (around 2%) develop a seroma around the aorta which resolves without intervention
15	Please list the key efficacy outcomes for this procedure/technology?	Prevention of dissection or rupture of the ascending aorta in patients with a genetically driven aortopathy
16	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	Subject to the items mentioned in 14 above we do not have any other concerns.
17	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	Concern has been raised about the absence of a RCT. We have sought advice from the National Institute for Health Research and the Surgical Intervention Trial Unit at Oxford, the collective decision was that the patient numbers requiring this type of aortic surgery are too small to afford a useful level of statistical significance to any trial outcome, and it would be too difficult to find a reasonable and ethical strategy for the control group within the PICO that would be acceptable to patients.

18	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	~~Most or all district general hospitals.~~ ~~A minority of hospitals, but at least 10 in the UK.~~ Fewer than 10 specialist centres in the UK. ~~Cannot predict at present.~~

Abstracts and ongoing studies

19	Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.	Van Hoof L. et al. Heart 2021: doi:10:1136/heartjnl-2021-319300. Austin C. et al. Eur.J.CardioThorac.Surg. 2021; doi:10.1093/ejcts/ezab118.
20	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	No

Other considerations

21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an	40 to 50 patients per year

	estimated number, or a proportion of the target population)?	
22	Are there any issues with the usability or practical aspects of the procedure/technology?	There are no issues with the technology. A dedicated surgical approach is critical.
23	Are you aware of any issues which would prevent (or have prevented) this procedure/technology being adopted in your organisation or across the wider NHS?	No.
24	Is there any research that you feel would be needed to address uncertainties in the evidence base?	Because the PEARS sleeve is manufactured in one place only we are able to maintain accurate monthly reports and receive regular returns from the world-wide surgical units who have adopted this procedure.
25	Please suggest potential audit criteria for this procedure/technology. If known, please describe: – Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. – Adverse outcome measures. These should include early and late complications. Please state the post procedure timescales over which these should be measured:	Beneficial outcome measures: A low-risk operation with a short hospital stay and a short convalescence. Avoidance of cardiac arrest and circulatory arrest. In the long-term: avoidance of oral anticoagulation. We continue to monitor our patients with an annual MR scan except for those who have ferro-magnetic material in place (eg Harrington spinal rod) for whom a CT scan is arranged. We intend to do this up to patient 1000 (currently N=516) after which we may change to biennial scans. The MR scan informs us of several adverse outcomes: compromise of the coronary ostia, enlargement of the aortic root, development of aortic regurgitation. Development of aneurysm of the downstream aorta (arch and descending aorta)

		Adverse outcome measures: Regular MR or CT scans, as above.

Further comments

26	Please add any further comments on your particular experiences or knowledge of the procedure/technology,	We have designed the PEARS sleeve to have a hoop strength which is greatest at the annulus but gradually reduces along its length to where it is attached at the origin of the aortic arch. We hope that this gradual reduction may lessen the chance of aneurysm formation downstream which has been reported when the entire ascending aorta is replaced with standard Dacron. This remains a hypothesis but our regular MRI scan may help to see whether this feature makes a difference. To date we have not seen any distal aneurysm formation in our PEARS patients.

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Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

Type of interest *	Description of interest	Relevant dates	
		Interest arose	Interest ceased
Choose an item.			
Choose an item.			
Choose an item.			

X☐ I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

Please note, all declarations of interest will be made publicly available on the NICE website.

Print name:	**JOHN PEPPER**
Dated:	**16th August 2021**