Personalized External Aortic Root Support in Aneurysm Disease

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In the last year CA has been reimbursed by the manufacturing company Exstent Limited for travelling expenses to proctor surgeons. Prior to that, as with the other authors TT and JRP, we have covered all our own expenses without the support of the company which was a self-funding start up.

Key points:

- The adoption of PEARS has increased to 30 centres 12 countries.
- By August 2022 there were 582 PEARS operations for aortic root aneurysms with one peri-operative death.
- There have been no aortic dissection in the supported ascending aorta.

Structured abstract <200 words [195]
Purpose of review:
To bring together and annotate publications about personalised external aortic root support reported in the 18 months preceding submission.

Recent findings:
The total number of PEARS operations is now approaching 700 in 30 centres in Australia, Belgium, Brazil, Czech Republic, Great Britain, Greece, Ireland, Malaysia, Netherlands, New Zealand, Poland and Slovakia. There are continued reports of stability of aortic dimensions and aortic valve function with the only exceptions known being where the surgeon has deviated from the intructions for use of the device. The median root diameter of Marfan patients having PEARS was 47 mm suggesting that the existing criterion of 50 mm is due for reconsideration. The peri-operative mortality in the first 200 patients was 0.5% and is currently estimated to be less than 0.3%. The first recipient remains alive and well after 18 years. The use of PEARS as an adjunct to the Ross operation to support the pulmonary autograft is being explored in several centres.

Summary:
The operation requires proctoring and adherence to a strict operative protocol and with those precautions excellent results are attained. The evidence and opinions provided in the cited publications indicate that PEARS is a proven and successful prophylactic operation for aortic root aneurysm.

Keywords: 3-5
Aortic root aneurysm; aortopathy; external support

Text <2000 1793 Words

Introduction:
The scope of this review is very precisely defined by its title. Personalised external aortic root support (PEARS) was first proposed at a meeting of the British Marfan Association in 2000 at St George's Hospital London by its inventor, Taliesin Golesworthy, a design engineer with inherited Marfan syndrome. The proposal was followed by careful analysis of the anatomy, possible materials, surgical feasibility, imaging requirements and manufacture. This included software development to enable computer assisted design (CAD) modelling and rapid prototyping, now commonly known as 3-D printing. The "first in man" operation was reported in The Lancet as a Research Letter in 2004.(1)

PEARS is "external" and acts as a "support" rather than as a replacement of the ascending aorta. It has two unique features which distinguish it from all other described techniques.

1. It is “personalised” in the sense that it is manufactured to replicate the patient’s own aorta with three dimensional spatial data obtained from digital imaging. This makes it quite distinct from the *ad hoc* intra-operative tailoring of graft material to support the ascending aorta. This may be with or without that is surgical excision of part of the aorta —aortoplasty — to reduce its circumference.(2-6)
2. The external support because incorporated to effectively form a neo-aorta. This is because instead of stiff low porosity vascular graft material, a soft pliant macroporous mesh with 0.7 mm pore size is used. Incorporation has been shown histologically in sheep implants and confirmed in man.(7, 8)

PEARS along with the David(9) and Florida sleeve(4, 5) are operations sparing of the aortic valve. It differs from them in that it requires preoperative manufacture of the implant. That effectively precludes its use in an emergency situation within the currently existing operative procedures in which “made-to-measure” is a key component. PEARS does not fit with *ad hoc* decision making. That is important in follow-up evaluation of clinical outcome because for other techniques the eventual decision of whether to conserve or replace the aortic valve can be made while the operation is in progress making “intention to treat” analysis undeliverable.

An important conceptual feature of PEARS is that the surgeon is provided with an engineered product and in the words of David Pye, furniture designer and academic, it replaces the “workmanship of risk” with the “workmanship of certainty”.(10) Skilled and experienced surgeons pride themselves in their ability to improvise and innovate as do artists and craftsmen but with that goes the possibility of error and bad judgement. The PEARS Instructions for Use(11) have only changed in two details since the first operation. With faster acquisition and lower radiation doses, computerised tomography (CT) can now be used instead of cardiac magnetic resonance imaging (cMRI). Rather than cutting a hole in the mesh for the coronary artery a star shape opening — or asterisk — is recommended, formed by three intersecting cuts each of the same length as the external diameter of the coronary artery as shown in Figure 3.(11, 12)

Stepwise evaluation by the team evaluating PEARS confirmed that it held the aortic size over time and an undersized device could reduce the aortic size without crimping the wall or altering its morphology.(13) In a matched pair analysis it reduced operative time, it avoided or greatly reduced time of cardiopulmonary bypass and obviated the routine need for blood products.(14)

PEARS was used relatively early in our experience to safeguard a patient whose aorta had dilated during her first pregnancy.(15) We know of ten patients who have had PEARS with eleven subsequent successful pregnancies without evidence of further aortic dilatation. All are well. One of these patients had her (off-pump) PEARS surgery during her 2nd trimester.(18)

The use of a PEARS device to stabilise the neo-aorta in the Ross pulmonary autograft procedure has been proposed and was discussed in an Expert Review of Medical Devices(16) but it was not mentioned in an excellent review in Current Opinion in Cardiology 2022 which considered various method of supporting the pulmonary autograft after the Ross operation.(17) The omission is assumed to be because the

editors' instructions require references to published work in the previous 18 months. In an extension of the principle, PEARS supported pulmonary autografts for Ross operations, have been used in 69 patients.(18) At the time of writing the results are not yet published.

Review:

Literature searches for related publication in the 18 months up to the end of March 2022 discovered nine publications related to personalised aortic root support. For the purposes of the discussion we will summarise them under five headings.

Data on patient numbers, the case mix and outcomes

Because the device is only available from one manufacturer complete data are available as to how many operations have been done, at which centres, and the nature of the cases operated on.(18) On 17th January 2022 a total 570 patients have been treated, 392(69%) with various categories of congenitally determined aortic disease and the largest single pathological group — 274(48%) — are people with Marfan syndrome.

Patients from 1 to 317 who had operation at 25 surgical centres were the basis of a clinical report published in September 2020.(19) The most complete and detailed clinical reports was published by the originators and early adopters of PEARS. This includes the first 200 consecutive patients with follow-up of at least a year and a total 753 postoperative years.(20) There was one new type B dissection which was asymptomatic and discovered on imaging three years postoperatively. There were no device related aortic events. Of these 200 patients 48 had aortic valve regurgitation prior to their PEARS procedure, 42 grade 1/4 and 6 grade 2/4. Regurgitation was abolished in 30 and reduced or abolished in all but one of the grade 2 patients. Increasingly supports of 95% modelled size are used and there is a likelihood that this will further reduce residual aortic regurgitation.(20)

The report on the first 200 patients was accompanied by an Editorial which was unreserved in its recognition of the PEARS record:

> "The results published by Van Hoof and colleagues are nothing short of remarkable, considering some of the technical challenges of isolation of the coronary arteries and dissection to the level of the ventriculoaortic junction. This is especially true in the context of CPB use being limited in this series. If nothing else, this is an incredible display of surgical skill and technical evolution."(21)

Of course it follows that recognition of the level of surgical skill required to attaining such results also raised doubts about its general applicability. However its advantages in reducing the magnitude of surgery and potentially optimal and durable conservation of the aortic valve it can be used at an earlier stage in the progression of aortopathy and spare patients potentially years of anxiety and years of attempted medical treatment aimed at slowing the rate of progression.(22)

1.The technical challenge of the operation

Two papers are about the operative technique. One was from the authors of the 317 patient follow up study. Only a few of these patients were operated on by themselves

but the process of reviewing the results prompted a technical paper about PEARS — "how to implant it" — which should be required reading for any surgeons embarking on a PEARS programme.(12) The illustrations provided by Kenny et al are superb.(23) Figures 1, 2, 3

A third paper is very clearly about how not to do it.(24) There was an inadvertent "proof of concept" experiment. The surgeon had decided against completing the operation according to the manufacturer's intructions for use(23) and instead of dissecting the aorta down to the aorto-ventricular junction, he cut the personalised sleeve and discarded the portion intended to support the sub coronary root. The unsupported aorta progressively dilated in that segment and aortic valve regurgitation ensued. The cause was discovered at a rescue operation some years later and rectified.(24)

2.The relative merits of PEARS and an ad hoc wrap

It is interesting that Burke and Bavaria, praising the skill of the PEARS surgeons somewhat down played the benefits of this approach writing

> "Despite the PEARS procedure being a novel and potentially disruptive surgical technique to address aortic root dilation, the concept of aortic aneurysm 'wrapping' is not entirely new and has undergone several iterations in the past. The first report of aneurysm wrapping of the ascending aorta was published by Francis Robicsek in 1982."(3)

During the time frame of the search there was a publication reporting results for wrapping in the Robicsek style.(25) Aortic surgeons had not persisted with the method due to patterns of failure and indeed PEARS was predicted by some to be destined to fail in similar ways but the soft pliant porous nature of the device had not been appreciated. The paper was contradicted by Van Hoof of the Leuven group pointing to the evidence within the paper that ad-hoc wrapping with stiff low-porosity material designed for a quite different application remains unsatisfactory.(26)

3.The feasibility of a randomised controlled trial

The call for a controlled trial has been a recurrent theme in the progress of PEARS and was carefully considered at various points. A paper from Nienaber and colleagues carefully examined the issues.

> "A procedure probably most usefully applied early in the process of progressive dilation (such as PEARS) would be compared to an established operation intended for later in the dilation process, i.e., when reaching a critical threshold for replacement surgery (such as the David and Yacoub procedures). In other words, it would be comparing PEARS with apples, certainly not scientifically sound for randomization."(27)

5.PEARS as an adjunct to the Ross procedure

Although there are no published data on the Ross PEARS with 69 operations already done we can expect them.(18) The paper from the Leuven group is the product of a very fruitful collaboration and is an outstanding contribution on the concept.(28)

Conclusion:

It is 18 years since the first PEARS operation and numbers accrued very slowly during the first 10 years. The data are now being published and seem to be well received but the valve sparing root replacement is widely accepted and is being delivered at low risk. The continued collection and reporting of outcomes is going to be essential if PEARS is to be recognised as offering durable results at low risk.

One aspect that remains a concern for patients is the deliberate watch and wait for young patients for whom an operation is eventually going to be advised. The safer the operation the less justified is the wait and it is a more realistic balancing of benefits versus risk for early intervention which PEARS offers. What has been shown is that people ascribe quite different values to postponement to put off risk and earlier acceptance of risk to curtail the years of anxiety.(22) It is an area for collaborative work with patients and other advocated rather than a clinical guideline developed by clinician consensus.

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3. Conflicts of interest: none

Figure titles and legends

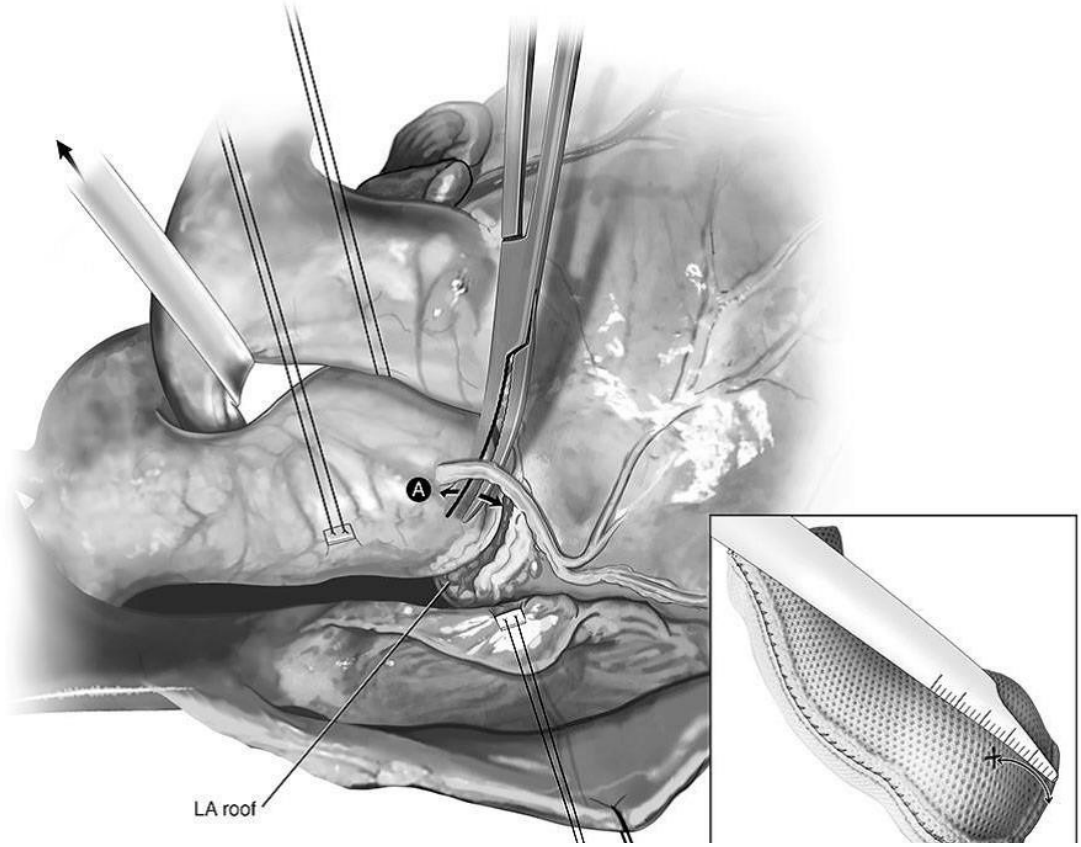

Figure 1. A right-angled forceps is introduced below the right coronary artery and a plane is created between it and the aneurysm. [A] This plane is deepened using a combination of blunt and sharp dissection the level of the ventriculo-aortic junction below the convexity of the right coronary sinus. The PEARS former is helpful in determining completeness dissection. (Illustration from Kenny et al)(23)

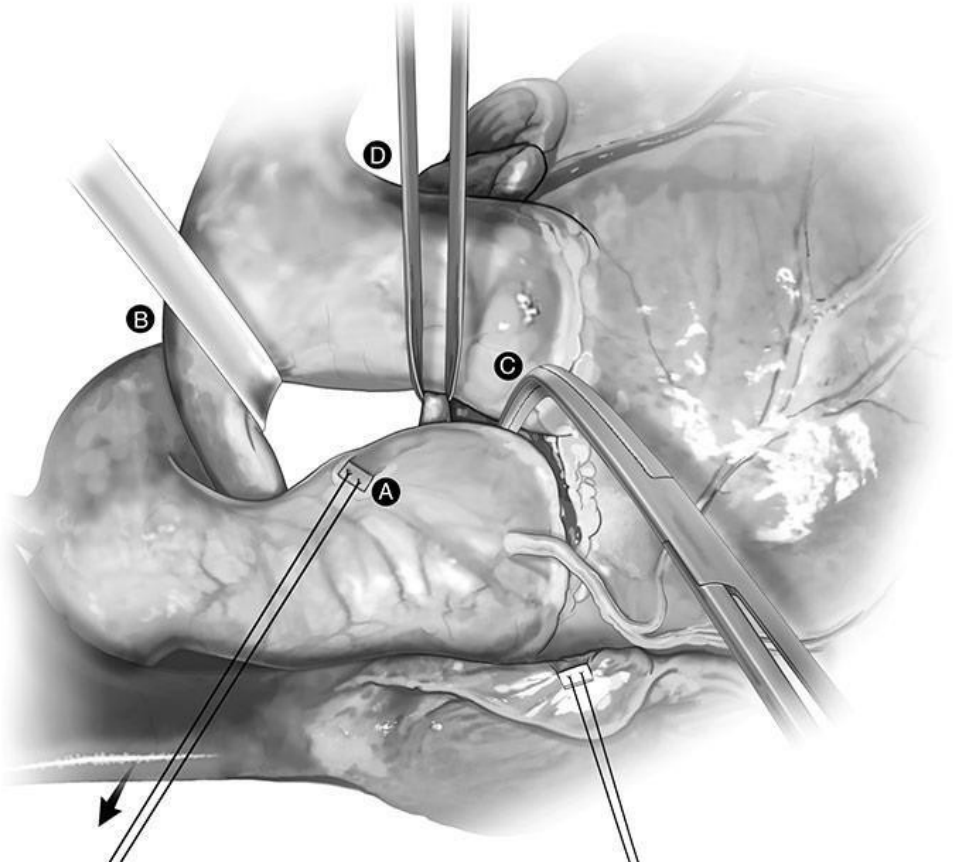

Figure 2. [A] The aorta is retracted cranially to the right using a retraction suture. [B] The pulmonary artery is retracted cranially and to the left with a malleable retractor. [C] The plane between the root of the pulmonary artery and the left coronary sinus is dissected using the same blunt and sharp combination until the left coronary artery comes into view. A right angled forceps is then used to gently dissect the tissue between the coronary artery and the aortic wall. [D] Once space is created between the left main coronary artery. (Illustration from Kenny et al)(23)

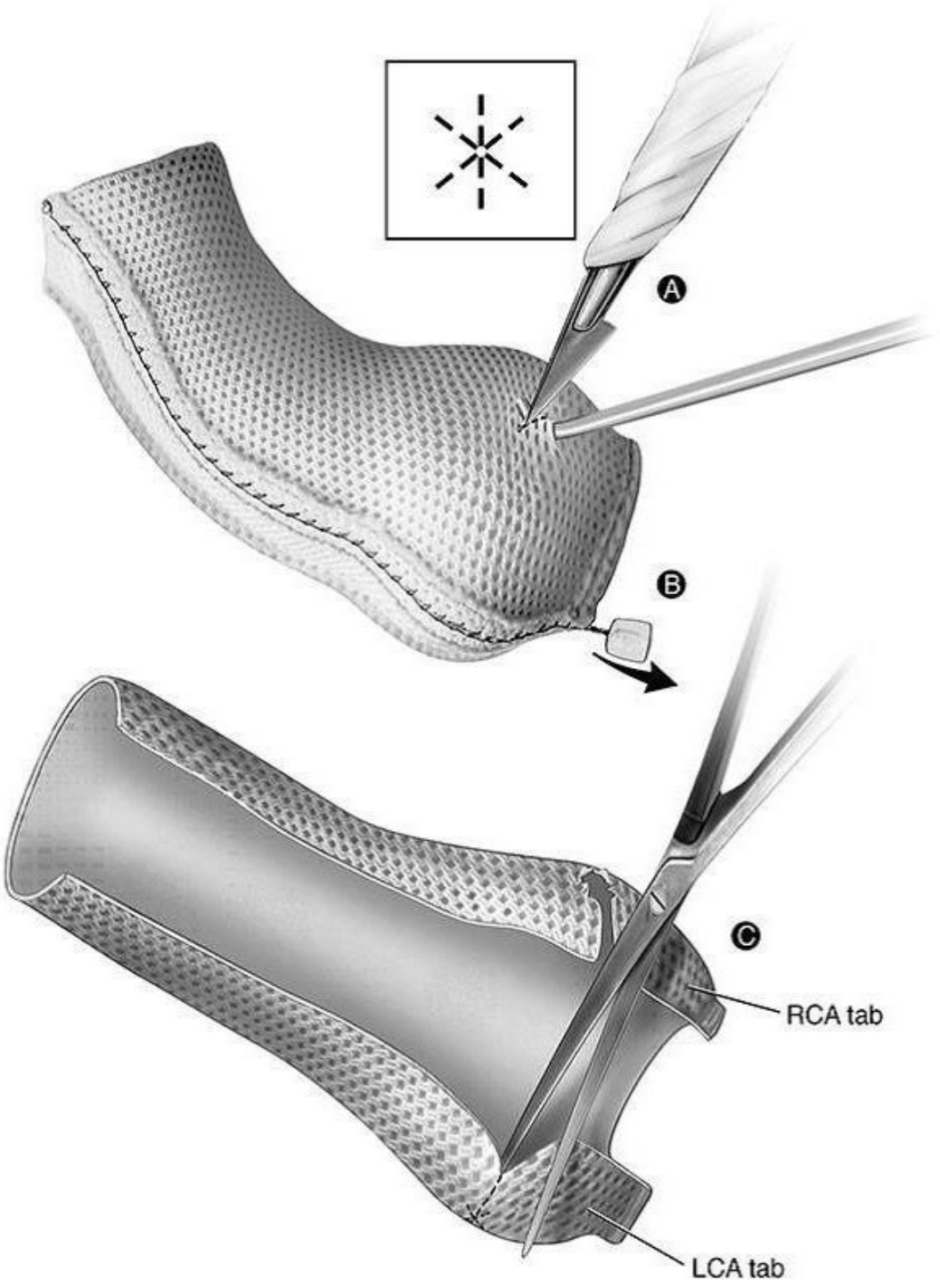

Figure 3. [A] Making the asterisk shaped incisions for the exit of the coronary arteries. [B] The chain stitch is released to open out the device. [C] Radial incisions are made to the openings for the coronary arteries thus fashioning the tabs to pass beneath the arteries. (Illustration from Kenny et al)(23)

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12. Nemec P, Kolarik M, Fila P. Personalized external aortic root support - how to implant it. Acta Chir Belg. 2022;122(1):70-3.

**

This paper revisits the technical details of how exactly to perform the operation. It provides technical tips which the authors have learned the hard way and if studied carefully, and the advice heeded, should hasten the learning experience.(19)

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19. Nemec P, Pepper J, Fila P. Personalized external aortic root support. Interact Cardiovasc

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This study published in September 2020 summarise the nature of all 317 PEARS operations from the first in April 200 to March 2020 in 25 centres in 9 countries. Marfan syndrome was the indication in 57%. There was one perioperative death (0.3%) 19 had lived more than 10 years since operation. There are interesting reflective comments on how PEARS technical details and appropriate follow up and surgeon considering adopting this surgery would gain valuable insights. The noted a randomized trial would be hard to realize.(16)

20. Van Hoof L, Rega F, Golesworthy T, Verbrugghe P, Austin C, Takkenberg JJM, et al. Personalised external aortic root support for elective treatment of aortic root dilation in 200 patients. Heart. 2021;107(22):1790-5.
**
This reports the first 200 consecutive intention to treat PEARS operations. The median age was 33 years. For 147 Marfan patients the median aortic diameter was 47 mm indicating that cardiac terms were implementing this a truly prophylactic operation the majority having a root aneurysm below the 50 mm.(17)

21. Burke CR, Bavaria J. The personalized external aortic root support procedure: interesting niche or ready for prime time? Heart. 2021;107(22):1768-9.
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This editorial gives a carefully considered commentary on PEARS praising the results achieved in the first 200 but sceptical of the general applicability. (18)

22. Treasure T, King A, Hidalgo LL, Golesworthy T, Pepper J, Takkenberg JJ. Developing a shared decision support framework for aortic root surgery in Marfan syndrome. Heart. 2018;104(6):480-6.

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**
A comprehensive account of PEARS including a description of the key principles of patient selection, surgical steps and postoperative care and detailed figures describing the implantation of a PEARS device with complementary video clips.

24. Austin C, Thompson P, Fittipaldi M, Treasure T. The consequences of incomplete covering of the critical part of the aortic root in Personalized External Aortic Root Support. Eur J Cardiothorac Surg. 2021;59(5):1095.

**
This is a case report where the surgeon departed from the "Instructions for Use" of a personalised device, cutting off discarding the part of the mesh sleeve intended for aorta between the coronary arteries and the aorto-coronary junction, leaving the root uncovered. As a result the aortic sinuses continued to enlarge and the aortic valve became incompetent. This was "an inadvertent 'double-blind' trial of a sham operation" since neither the patient or colleagues following up the patient were informed.(20)

25. Kim HH, Lee S, Lee SH, Youn YN, Yoo KJ, Joo HC. The long-term fate of ascending aorta aneurysm after wrapping versus replacement. J Thorac Cardiovasc Surg. 2021.

26. Van Hoof L, Rega F, Treasure T, Pepper J. What's in a wrap? J Thorac Cardiovasc Surg. 2021.
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This correspondence challenges a somewhat atavistic report suggesting equivalence of a Robicseck style "wrapping" and root replacement.(21, 22)

27. Nienaber C, Ernst S, Yuan X. PEARS procedure and the difficulty to provide evidence for its benefits. European Heart Journal. 2020;41:4086-8.

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This essay published in November 2020 went into more detail about whether a controlled trial would be appropriate. It merits reading. The authors examine the essential requirements for randomisation that at a point in time there are two treatments similarly applicable and conclude that "the fundamental basis for an RCT is just not present."(25)

28. Van Hoof L, Verbrugghe P, Jones E, Humphey J, Janssens S, Famaey N, et al. Understanding the pulmonary autograft remodeling after the Ross procedure: stick to the facts. Frontiers in Cardiovascular Medicine. 2022;9(February).

**

An outstanding analysis of “mechanobiology of the Ross Procedure”. This comes from a team at the University of Leuven which brings together bioengineers, biologists and surgeons who have explored in depth the challenge of the use of the pulmonary autograft in the aortic root and paves the way for its practical implementation.(26)