The Pomegranate Theory: A Systematic Review on Decellularization Techniques for the Development of Tissue-Engineered Aortic Scaffolds

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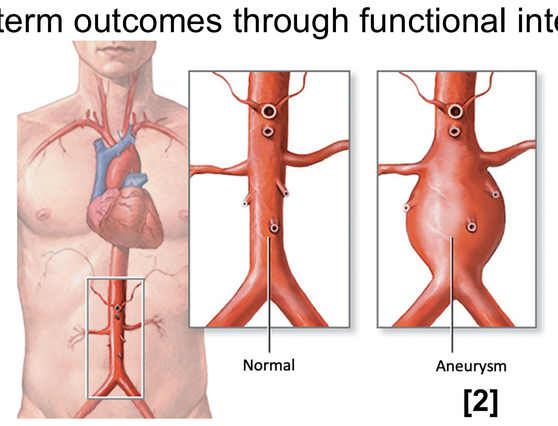
KING'S College LONDON

NATIONAL MEDTECH FOUNDATION

Farida AlWakeel[1], Rachel Duff[2], Valerie Fiamavle[3], Shakil Hussain[4], Danni-Leigh Harrison[5] , Rachel Clough[6] . [1]HealthTech Research Centre in Cardiovascular and Respiratory Medicine. King's College London, London (City of London) - United Kingdom, [2]HealthTech Research Centre in Cardiovascular and Respiratory Medicine. King's College London, London (City of London) - United Kingdom, [3]Queen's University Belfast, Belfast - United Kingdom, [4]City St. George's University of London, London (City of London) - United Kingdom, [5]Newcastle University, Newcastle upon Tyne - United Kingdom, [6]Biomedical Engineering and Imaging Sciences. King's College London, London (City of London) - United Kingdom

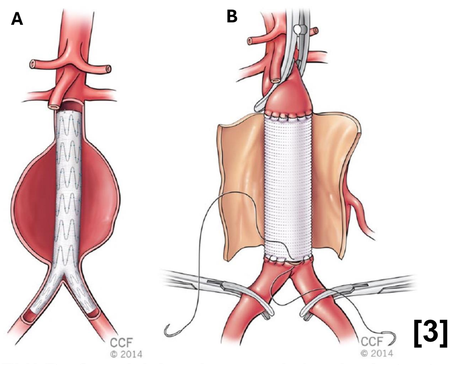
1: Abstract

Aortic aneurysms (AA) affect approximately 35 million individuals worldwide, accounting for 153,927 deaths in 2021 **[1]**. Endovascular aortic repair (EVAR), the gold standard treatment for ruptured and unruptured aneurysms, involves inserting a **synthetic stent graft** to reinforce weakened arterial walls and prevent rupture. Conventional metallic or polymeric graft materials may lead to biocompatibility complications like endoleaks, stent migration, and structural failure. Tissue-engineered **decellularized** aortic grafts offer a promising alternative, replicating native aortic architecture and improving long-term outcomes through functional integration with the host tissue.



[2]

Fig 1. Abdominal Aortic Aneurysm (AAA) diagram



[3]

Fig.2 A) EVAR of an AAA using an abdominal stent graft B) Open repair of an AAA

2: Purpose of the Study

To systematically evaluate chemical, enzymatic, and physical decellularization techniques, including the emerging use of sonication, to identify the most effective strategy for maintaining extracellular matrix (ECM) integrity, **biocompatibility**, and native **biomechanical properties** in tissue-engineered aortic grafts.

3: Methodology

Studies collected from databases/registers **n = 2542**

Embase (**n = 1060**)
Scopus (**n = 821**)
PubMed (**n = 652**)
IEEE Xplore (**n = 9**)

References removed **(n = 1251)**
Studies screened (**n = 1291**)
Studies excluded (**n = 1277**)
Studies sought for retrieval (**n = 63**)
Studies assessed for eligibility (**n = 63**)

31 Studies met the inclusion criteria

81.4% Porcine (**n = 26**)
45.2% In Tubular Form (**n = 14**)
19% In vivo Testing (**n = 6**)

Ovine (**n = 1**) / Goat (**n = 1**) / Bovine (**n = 1**) / Human (**n = 2**)

Studies including small animal tissue (diameter vessels <6mm) were excluded

Biomechanical Inclusion Criteria

1. Experimental original studies, healthy aortic tissue from large animal models
2. Reported at least one scaffold-relevant outcome, including;
   I. The removal of immunogenic cellular elements
   II. Preservation of biomechanical integrity

4: Results

Table 1: Tensile Strength Test

Study	Method	Tensile Strength	Units	Notes
Walawalkar et al. (2019)	Native Control	0.37	MPa	Untreated veins
Walawalkar et al. (2019)	Sodium Dodecyl Sulfate 1%	0.355	MPa	Slight reduction
Negishi et al. (2016-19)	Sodium Dodecyl Sulfate, Triton, High Hydrostatic Pressure	4.6 – 4.96	MPa	HHP highest tensile strength
Wang et al. (2015)	Fresh, GA-fixed, DCMC	1.11 – 1.91	MPa	GA-fixed increased tensile stress

Table 2: Burst Strength Analysis

Study	Method	Tensile Strength	Notes
Walawalkar et al. (2019)	Native control	4371 mmHg	Untreated veins
Walawalkar et al. (2019)	Sodium Dodecyl Sulfate 1%	2720 mmHg	SDS reduced burst strength
Walawalkar et al. (2019)	Sodium Dodecyl Sulfate + Recellularization	3175 – 3891 mmHg	Recellularization partially restored strength

5: The "Pomegranate Analogy": How Sonication Works?

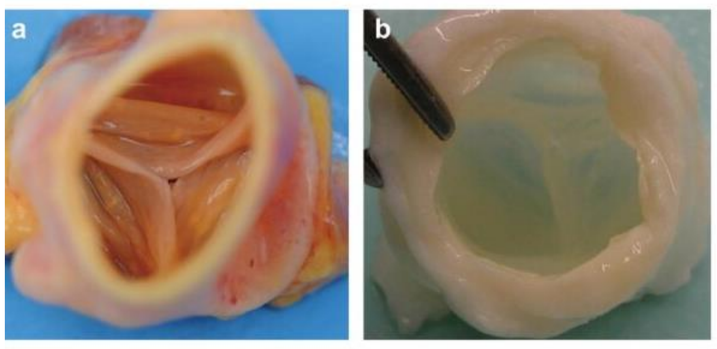


Fig 3. A) Human aortic-valve pre-decellularization B) Human aortic-valve post-decellularization [4]

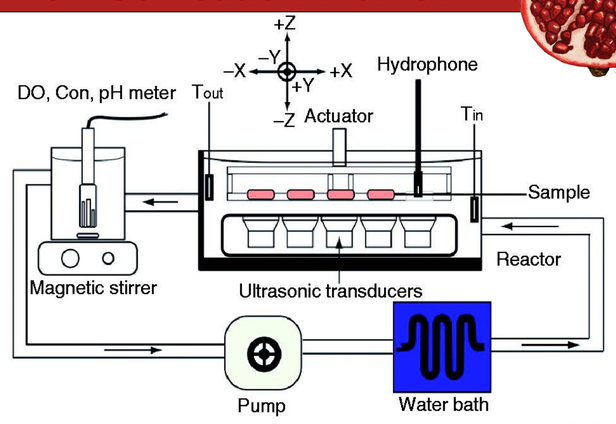


Fig 4. Sonication decellularization system diagram [5]

Imagine gently shaking a pomegranate, the seeds fall away while the inner structure remains intact. **Sonication decellularization** works in a similar way, using vibrational (ultrasound) waves to remove cellular material while preserving the ECM leaving behind a white, "ghost-like" scaffold. Like the pomegranate's core, the underlying structure is maintained, providing a strong foundation for biological grafts.

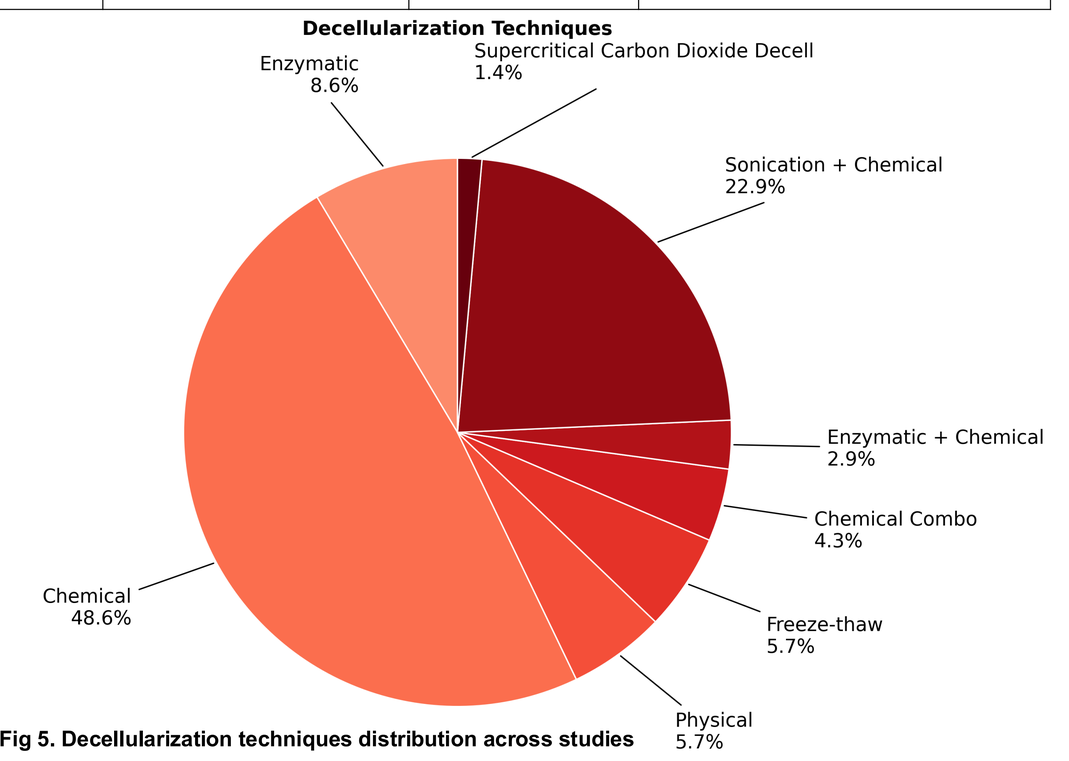


Fig 5. Decellularization techniques distribution across studies

6: Conclusion

No single protocol was identified as the universally optimal aortic tissue decellularization technique. However, our study found that multi-step detergent–enzymatic approaches incorporating sonication were most effective in removing cellular components while preserving ECM composition. Conversely, chemical-only decellularization reduced tissue elasticity, compromising mechanical properties. Further studies are needed to validate the potential of sonication-assisted decellularization in developing aortic grafts.

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7: References

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