

## EDITORIAL COMMENT

# Unbreak My Heart (Valve)

## Can Ultrasound Be Used for the Treatment of a Degenerated Surgical Bioprosthesis?\*



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**S**urgical aortic valve replacement increasingly uses bioprosthetic implants rather than mechanical valves. Because of this and the expanding indications for transcatheter heart valve therapies, the majority of patients undergoing an aortic valve replacement procedure will receive a pericardial tissue valve (1). Owing to this considerable shift toward bioprosthesis implantation, it is expected that patients will increasingly present with degenerated bioprostheses over time. Structural valve deterioration can result in leaflet degeneration and failure, as evidenced by valve stenosis, regurgitation, or a combination of both (2). Treatment of such patients remains a clinical challenge. Although reoperation is considered the standard of care, these patients are frequently elderly and repeat cardiac surgery is associated with a significant risk of morbidity and mortality. Transcatheter valve-in-valve implantation has emerged as a promising alternative treatment option for patients at high surgical risk; however, it comes with its own complications and limitations (3). Therefore, repair of a structurally degenerated bioprosthetic valve would be an intriguing causative therapy approach.

For more than 3 decades, other therapeutic strategies have been investigated to “unbreak” calcified native or bioprosthetic valves. One promising approach was ultrasound-based but remained limited

at that time, because it still needed open heart surgery with cardiopulmonary bypass (4,5). Nevertheless, this limitation must be revisited again with the recent improvement of technologies and concepts of pulsed cavitation focused ultrasound (PCU). PCU or histotripsy is a noninvasive, cavitation-based technique that focuses very short, high-pressure ultrasound pulses in tissues to generate a dense, energetic, and lesion-producing bubble cloud. Although histotripsy can be used to produce sharp lesions, recent studies have suggested that cavitation activity can also soften biological tissues.

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In this issue of *JACC: Basic to Translational Science*, Villemain et al. (6) demonstrated the in vitro efficacy of PCU on human explanted calcified bioprosthetic aortic valves mounted on an artificial heart pump, and they quantified the improvement of the valvular function by elastography. With PCU for approximately 1 h, the investigators showed a reduction in both the mean and maximum gradient of more than 50%.

In a second step, the investigators demonstrated the in vivo feasibility and efficacy by implanting explanted human calcified aortic bioprostheses in the mitral position of an ovine beating heart model. Valvular function was assessed by echocardiography, catheter-based hemodynamic measurement, and elastography, and again, gradients across the aortic bioprosthetic valves implanted in the mitral position were reduced by 50% on average after a mean PCU duration of 1 h.

Although the sheep study had some limitations, for example one-half of the animals did not survive the hemodynamic deterioration caused by the degenerated, severely stenosed, human bioprostheses, the investigators can be congratulated for presenting a

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promising approach for percutaneous transthoracic treatment of degenerated bioprosthetic heart valves without the need for re sternotomy or transcatheter valve-in-valve implantation. Interestingly, the investigators found no modification of the calcium pattern in the degenerated leaflets or reduction of the calcium volume but observed multiple micro-fragmentations within the calcification after PCU. Therefore, the investigators hypothesized that this “leaflet softening” might have led to an overall change in biomechanical properties with improvement of leaflet motion and simultaneous reduction of transvalvular gradients.

With further technical improvement such as the addition of a multielement transducer to steer the focal spot electronically in real time, the investigators hope to increase the accuracy of this therapy and avoid off-target cavitation. However, the clinical risks such as the possibility of cerebral debris embolization need to be further evaluated in future studies. Although the nonchanged calcium volume per leaflet in computed tomography imaging is an argument against a major risk of cerebral embolization, this should be evaluated in magnetic resonance imaging studies.

The major limitation of this report by Villemain et al. (6), and therefore the whole therapeutic approach, is

that the persistence of the tissue-softening effect on degenerated prostheses was not evaluated, because all animals were sacrificed directly after the procedure. Surgical decalcification often leaves a fibrillar structure that tends rapidly to accumulate calcium. Even normal-appearing tissue from diseased valves has a higher potential for calcification than normal valvular tissue does. From other therapeutic approaches we have unfortunately learned that the therapeutic effect after the procedure may not be sustainable. For example, because of the high restenosis rates, balloon aortic valvuloplasty nowadays only plays a minor role as a palliative treatment choice or bridging therapy to transcatheter aortic valve replacement. Another issue is that we do not know how PCU would affect degenerated bioprostheses properly implanted in the aortic position and whether the results would be the same.

Taken together, we are looking forward to learn more about this promising approach in future studies and hope this could be the beginning of a new way to “unbreak” a heart valve (prosthesis)!

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## REFERENCES

1. Holmes DR Jr., Mack MJ, Kaul S, et al. 2012 ACCF/AATS/SCAI/STS expert consensus document on transcatheter aortic valve replacement. *J Am Coll Cardiol* 2012;59:1200-54.
2. Foroutan F, Guyatt GH, O'Brien K, et al. Prognosis after surgical replacement with a bioprosthetic aortic valve in patients with severe symptomatic aortic stenosis: systematic review of observational studies. *BMJ* 2016;354:i5065-9.
3. Dvir D, Webb JG, Bleiziffer S, et al., for the Valve-in-Valve International Data Registry Investigators. Transcatheter aortic valve implantation in failed bioprosthetic surgical valves. *JAMA* 2014;312:162-70.
4. Worley SJ, King RM, Edwards WD, Holmes DR Jr. Electrohydraulic shock wave decalcification of stenotic aortic valves: postmortem and intraoperative studies. *J Am Coll Cardiol* 1988;12:458-62.
5. Freeman WK, Schaff HV, Orszulak TA, Tajik AJ. Ultrasonic aortic valve decalcification: serial Doppler echocardiographic follow-up. *J Am Coll Cardiol* 1990;16:623-30.
6. Villemain O, Robin J, Bel A, et al. Pulsed cavitation ultrasound softening: a new noninvasive therapeutic approach for calcified bioprosthetic valve stenosis. *J Am Coll Cardiol Basic Trans Science* 2017;2:372-83.

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