TRANSCATHETER DEBRIDEMENT DEVICE TDD REDUCES CALCIUM DEPOSITS FROM HUMAN CALCIFIC AORTIC VALVE LEAFLETS

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Abstract

The Transcatheter Debridement Device or TDD is a system for reducing and removing calcium deposits on aortic leaflets, in stenotic valves.

The aim of the treatment made with the TDD is to restore, in whole or in part, the pliability of the valve leaflets, in order to improve the flow and mitigate aortic valve stenosis.

The TDD device is based on the use of ultrasound impulsive waves and is designed to debulk calcium deposits present in the leaflet's matrix.

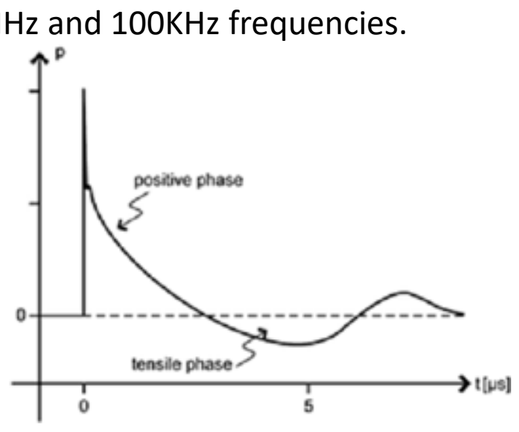
Introduction

Similar to lithotripsy, ultrasounds, properly modulated in intensity, frequency and waveform, can be used to produce fractures and structural changes in calcium deposits.
The combination of two ultrasonic fields, generated by opposed piezoelectric transducers at different frequencies, (1,2,3), allows to amplify the disruptive effects on dystrophic calcifications.
Low intensity energy avoids any dangerous temperature increase while maintaining efficacy without damaging vital tissues.
The total duration of the treatment is 30 minutes or less.

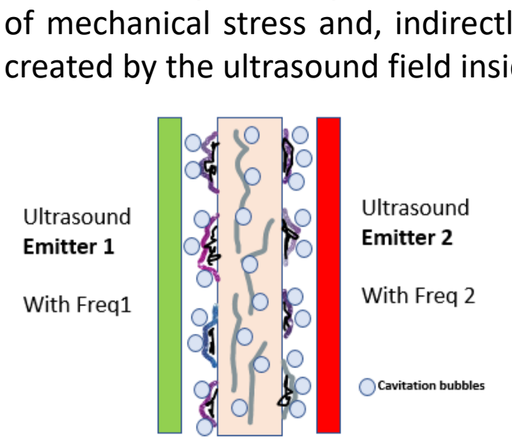
Methods and Materials

The **Transcatheter Debridement Device** includes a set of small piezoelectric transducers able to generate local low intensities ultrasound shockwaves, at 3MHz and 100KHz frequencies.

The shockwave is a short-duration positive pulse, followed by a negative pressure pulse.



The acoustic pressure pulse acts directly on the calcium as a force of mechanical stress and, indirectly, by some cavitation bubbles, created by the ultrasound field inside the biological tissue.

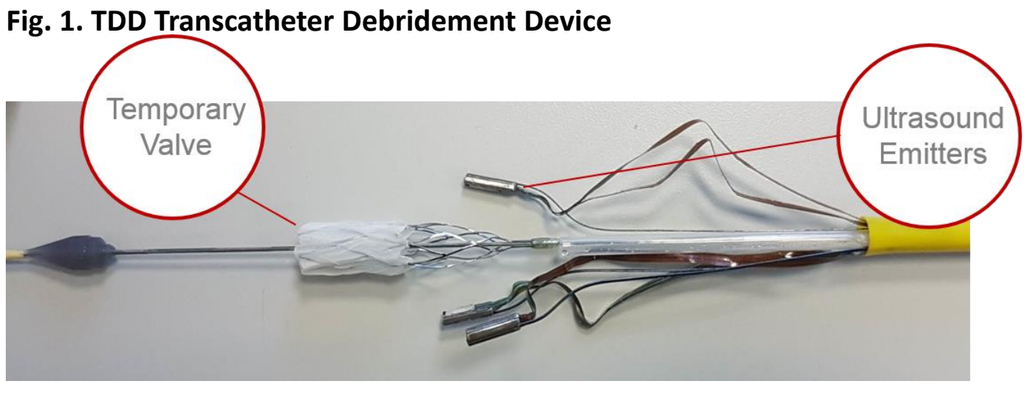


The rapid expansion followed by rapid collapse or implosion of these bubbles, causes fragmentation of the calcified structures.

Calcific valve cusps excised from patients undergoing surgical aortic valve replacement were analyzed with micro CT scan, pre and post treatment with TDD, to observe the effects on calcium deposits.

Histological analysis was performed to evaluate the integrity and structural coherence of the healthy aortic valve tissue after ultrasound treatment and to assess the effect on the calcium nodules .

Fig. 1. TDD Transcatheter Debridement Device



Results

Numerous tests of treatment made on explanted calcific leaflets, have allowed to demonstrate the efficacy of this technique.

In particular a stimulation from opposite directions of the ultrasonic field generators, maximize the reduction of the deposited calcium, as evidenced by the tomographic scans* of 39 leaflets pre and post treatment with the TDD.

Moreover, histological analyses** of 9 calcific leaflets have confirmed the integrity and structural coherence of the healthy aortic valve tissue, after the exposure to the ultrasonic field.

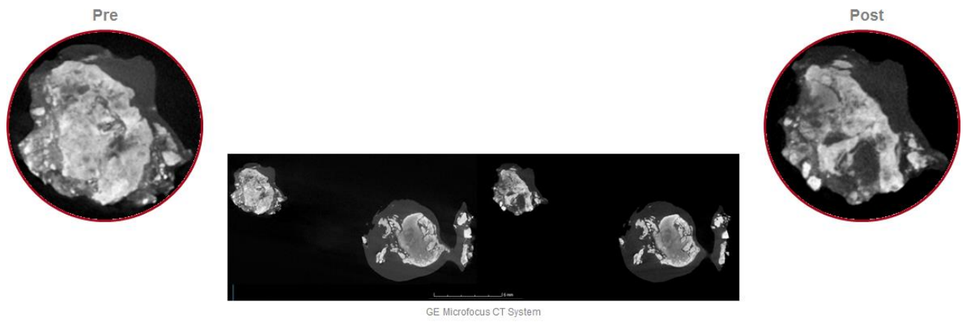


Fig. 2. CT evidences of calcium debridement

Processing the tomographic data an average percentage reduction of the residual calcium surface of **%ΔSm = -10,73%** and volume of **%ΔVm=-13,87%** were found.

The picture labelled as "post" shows the reduction of calcification of the leaflet, if compared to "pre" treatment.

The post-treatment histological analysis confirms the effects of the cavitation microbubbles, capable of breaking down calcification (Fig. 3).

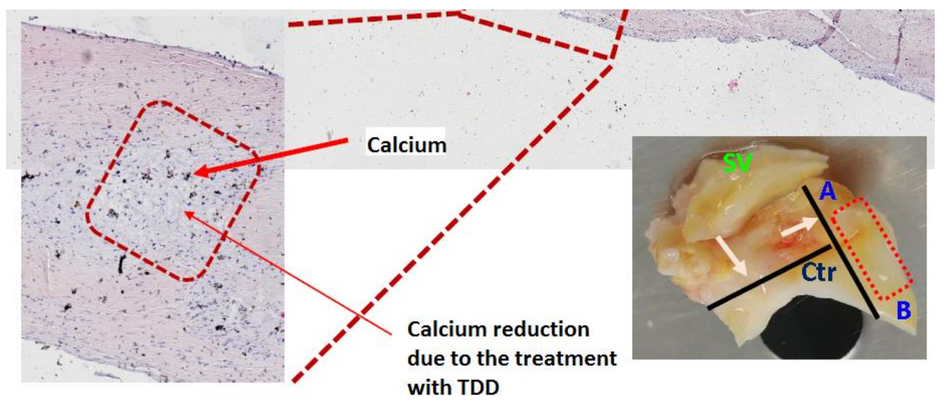


Fig. 3. Histological analyzes of the leaflets after the treatment

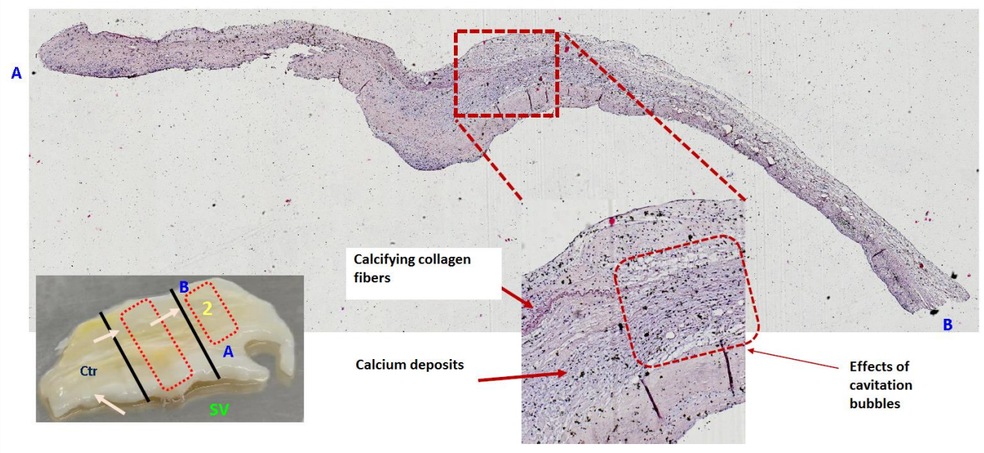


Fig. 4. Histological analyzes of the leaflets after the treatment

Von Kossa staining shows residual calcifications spots, with evidence of some "holes" (Fig. 4) created by the microbubble implosions without macroscopic damage to the collagen structures.

Conclusions

The use of a combination of ultrasound frequencies maximizes the disruptive effects on calcifications of human aortic valve leaflets.

On calcified aortic valve leaflets, removed from surgical patients, baseline and post-treatment microtomographic scans demonstrate the fragmentation and reduction of calcifications, while histological analyses confirm the cellular and matrix integrity of the aortic valve leaflets' treated with TDD.

References

*CT scans have been performed at the Labormet2 laboratory in Turin (Italy)
**Histological tests have been performed by the Tissue Engineering Research Unit at the "Centro Cardiologico Monzino" in Milan (Italy)
[1] Lernetti G. et al. "Enhancement of high-frequency acoustic cavitation effect by a low-frequency stimulation", Ultrason. Sonochem, vol. 4, no. 3, pp. 263-268, 1997
[2] Feng et al. "Enhancement of ultrasonic cavitation yeld by multi-frequency sonication", Ultrason. Sonochem vol 9, no. 5, pp. 231-236, 2002
[3] Lu et al. «Single-transducer dual-frequency ultrasound generation to enhance acoustic cavitation», Ultrason. Sonochem, vol 16, no. 3, pp. 431-438, 2009