

Non-invasive transthoracic ultrasound therapy of calcified aortic stenosis: feasibility and safety

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Background, Motivation and Objective

Non-invasive therapy of calcified valve stenosis remains a major goal in cardiology. To date, no drug has demonstrated therapeutic efficacy on calcified valves. Valve replacement by surgery or minimally invasive techniques remains the only solutions available, despite the high risks and comorbidity. We recently proposed a novel non-invasive therapeutic approach based on the use of pulsed cavitation ultrasound (PCU) to soften the calcified valve tissues and improve the valvular function [1]. Our objective is to develop an extracorporeal clinical device guided by real-time echocardiography for the treatment of calcified aortic stenosis on human patients.

Statement of Contribution/Methods

A PCU system (Valvosoft, Cardiawave, Paris, France) was designed for transthoracic cardiac focusing. The system was composed of a high-power multi-element transducer with a bandwidth of [700kHz-1.25MHz] and driven by high-power electronics. Pulsed ultrasound emissions were delivered at a pulse repetition frequency (PRF) between 100 and 300Hz. Electronic steering was used to move the focus point at different depth [70-120mm]. Focal pressure was calibrated in a water tank using a hydrophone at low intensity (<10MPa). A 2D Echocardiographic probe at 2.5MHz was embedded in the center of the therapeutic transducer to guide and monitor the treatment. The device was evaluated in vitro on ex vivo samples including ribs and in vivo on the aortic valve of pigs (N=16).

Results/Discussion

A maximal amplitude of 70 MPa and -19 MPa respectively for positive and negative peak pressure was found at the focus by linear extrapolation of low intensity measurements. In vitro, the propagation through the ribs was found to induce an average loss of $59\% \pm 9\%$. In vivo experiments demonstrated that the device can accurately target the valve cusps. Cavitation activity was monitored in real-time by echocardiography embedded in the device. Feasibility and safety were demonstrated in all animals with no serious adverse event. Survival at 30 days was 100% and no significant histopathology damage was found. We demonstrated in vivo the feasibility and safety of transthoracic PCU targeting aortic valve. It is the first device, to our knowledge, for non-invasive calcified aortic stenosis therapy and. This novel ultrasound therapy could become a non-invasive therapeutic strategy in cardiology.

[1] Villemain O, Robin J, Bel A, Kwiecinski W, Bruneval P, Arnal B, Rémond M, Tanter M, Messas E, Pernot M. Pulsed Cavitation Ultrasound Softening: a new non-invasive therapeutic approach of calcified bioprosthetic valve stenosis. JACC Basic Transl Sci. 2017 Aug;2(4):372-383