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IMAGES IN INTERVENTION

Transapical Aortic Implantation of Autologous Marrow Stromal Cell-Based Tissue-Engineered Heart Valves

First Experiences in the Systemic Circulation

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Within 1 procedure, tissue-engineered, living heart valves (TEHVs), fabricated from biodegradable scaffolds seeded with autologous bone marrow–derived mononuclear cells (Fig. 1A), were integrated into self-expanding nitinol stents (20 mm × 30 mm) and transapically delivered into the descending aorta (n = 2) (distal to the brachiocephalic trunk) and the brachiocephalic trunk (n = 1) of sheep (Fig. 1A). Native valve incompetence was created by applying the Hufnagel procedure (1) before implantation (Fig. 1A). After successful deployment (Figs. 1B and 1C), valve function and optimal positioning were confirmed using fluoroscopy (Fig. 1B, Online Video 1), computed tomography (CT) (Figs. 1D and 1E, Online Video 2), and echocardiography (Figs. 1F to 1M, Online Videos 3A, 3B, and 3C). The crimping time of the TEHVs was 15 ± 2 min. The overall duration of the procedure, from the preparation of cells to the successful delivery, was 2 h. Post-mortem analysis displayed fully intact TEHVs and, in particular, well-defined leaflets showing coaptation. There were no signs of leaflet rupture, microstructure damage, or thrombus formation detectable.

So far, successful TEHV implantations have only been reported for low-pressure systems such as in the pulmonary position (2), and clinical trials have been initiated. This is the first report demonstrating the feasibility of the minimally invasive, catheter-assisted implantation of TEHV into the systemic circulation with adequate valvular functionality in an acute study based on an easily accessible, clinically relevant cell source (3) and minimally invasive techniques for both cell harvest and delivery (2) within 1 procedure. Such autologous and living heart valves may hold potential to overcome the limitations of the currently used bioprosthetic valves inherently prone to calcification and progressive dysfunctional degeneration. This may broaden the future clinical application of transcatheter valves beyond elderly high-risk patients.

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APPENDIX

For supplementary videos, please see the online version of this article.

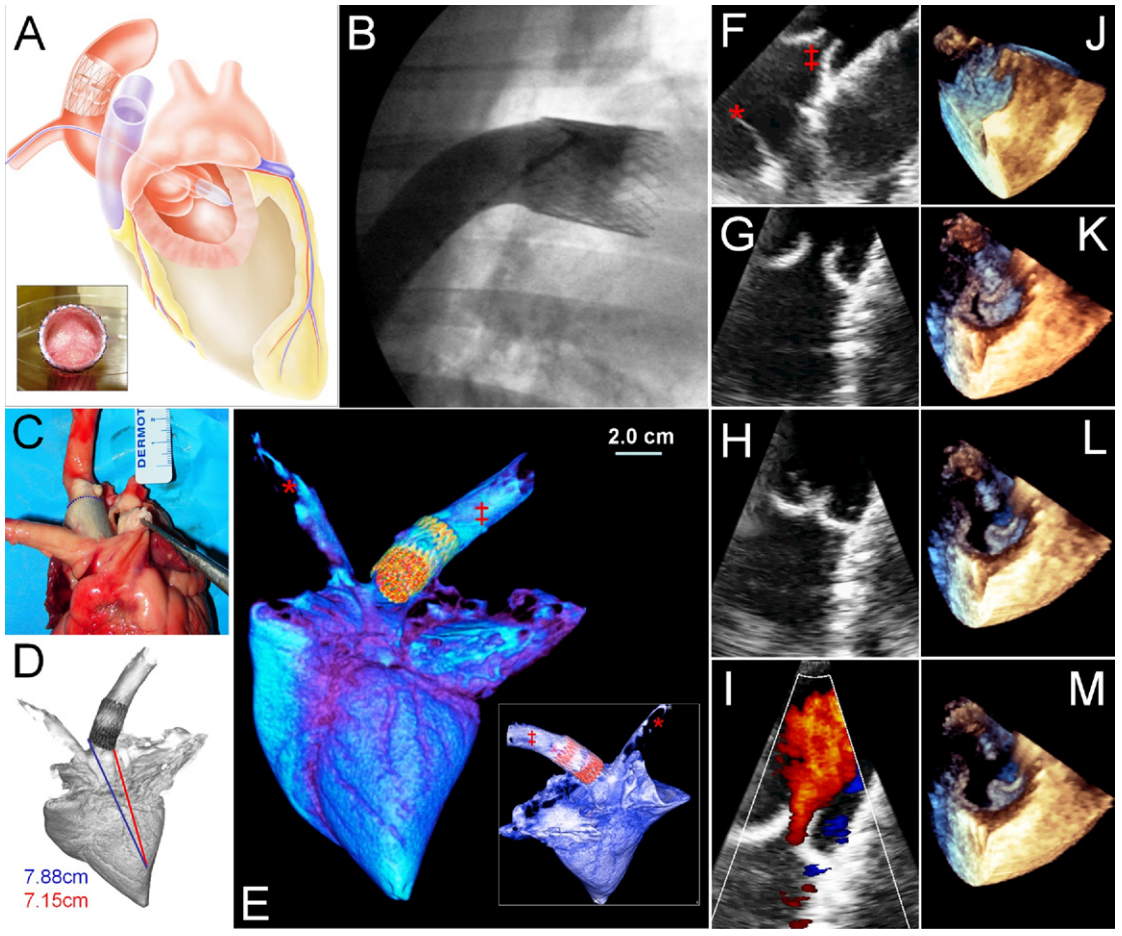

Figure 1. Tissue-Engineered Heart Valves

(A) Tissue-engineered heart valves (TEHVs) **(inset)** were transapically delivered into the descending aorta (distal to the brachiocephalic trunk) and into the brachiocephalic trunk of adult sheep after creating native valve insufficiency by applying the Hufnagel procedure. **(B)** Contrast angiography displayed optimal positioning and normal function of the TEHV. **(C)** Post-mortem analysis confirmed positioning in the descending aorta distal to the brachiocephalic trunk. **(D and E)** Three-dimensional (3D) computed tomography reconstruction of the adult sheep heart (**D** and **E** showing anterior view, **inset** showing posterior view) with the self-expanding nitinol stent positioned in the descending aorta (‡) distal to the brachiocephalic trunk **(*)**. (**F to M**) Transesophageal echocardiography (TEE) in the 2-dimensional (2D); **(G and H)**, 2D color **(I)**, and 3D **(J to M)** modes displayed the TEHV in the descending aorta **(‡)** above the native valve **(*)**. In particular, the TEE analysis showed well-defined leaflets showing sufficient coaptation. There were no signs of pressure damage, leaflet rupture, or thrombus formation detectable. Also See Online Videos 1, 2, 3A, 3B, and 3C.