

### **C61. In Vivo Spontaneous Tissue Regeneration Of Allogeneic Decellularized Aortic Valves**

Laura Iop<sup>1</sup>; Alessandro Gandaglia<sup>1</sup>; Antonella Bonetti<sup>2</sup>; Maurizio Marchini<sup>2</sup>; Michele Spina<sup>1</sup>; Cristina Basso<sup>1</sup>; Gaetano Thiene<sup>1</sup>; Gino Gerosa<sup>1</sup>

<sup>1</sup>University of Padua, Padua, Italy; <sup>2</sup>University of Udine, Udine, Italy

**OBJECTIVES:** To assess the in vivo functional regenerative capabilities of decellularized heart valve scaffolds in an allogeneic porcine model.

**METHODS:** Porcine allogeneic decellularized aortic roots were implanted in pulmonary position in minipigs (n=8). Valve function was echocardiographically evaluated at different specific times during follow-up until animal sacrifice at 6 (n=4) and 12 (n=4) months. The explanted roots underwent tissue analysis and cell characterization.

**RESULTS:** Ultrasonographic studies revealed good valve function with progressive growth. Inflammatory cell infiltration was observed nearby neovascularized medial regions, remaining limited over time. Endothelial lining was clearly evident on cusps and aorta lumen. At 6 months, intima and leaflets were completely repopulated by myointimal-like cells and myofibroblasts respectively, while adventitia showed at 12 months a new vascular network with neo vasa vasorum. Cell number and differentiation towards a smooth muscle phenotype was increasingly attained in medial layer after 1 year. Engrafted cells displayed ultrastructurally intercellular junctions and good secreting activity: besides new collagen synthesis, elastogenesis aspects were detectable with formation and fusion of new microfibrils in mature elastic fibers. Neoinnervation of aortic wall was documented. Markers of stem lineages were detectable in media, adventitia and leaflets: tissue derived-primary cultures displayed in vitro a cell pattern suggestive of mesenchymal stem cells of bone marrow origin.

**CONCLUSIONS:** These excellent results, obtained from one year-follow up of allogeneic cell-free valve scaffolds implanted in pulmonary position, confirm the capability of the in vivo tissue guided regeneration approach to create a living and functional heart valve substitute.