Francesca di Marco, MD, PhD
Gino Gerosa, MD
Department of Cardiological
Thoracic and Vascular Sciences
Division of Cardiac Surgery
Padua University Medical School
Padua, Italy

References

1. Vincentelli A, Wautot F, Juthier F, Fouquet O, Corseaux D, Marechaux S, et al. In vivo autologous recellularization of a tissue-engineered heart valve: are bone marrow mesenchymal stem cells the best candidates? *J Thorac Cardiovasc Surg.* 2007;134:424-32.
2. Menasche P, Hagege AA, Scorsin M, Pouzet B, Desnos M, Duboc D. Myoblast transplantation for heart failure. *Lancet.* 2001;357:279-80.
3. Bertipaglia B, Ortolani F, Petrelli L, Gerosa G, Spina M, Pauletto P, et al. Cell characterization of porcine aortic valve and decellularized leaflets repopulated with aortic valve interstitial cells: the VESALIO Project (Vitalitate Exornatum Succedaneum Aorticum Labore Ingenioso Obtenibitur). *Ann Thorac Surg.* 2003;75:1274-82.

doi:10.1016/j.jtcvs.2007.10.075

Reply to the Editor:

We thank Drs Di Marco and Gerosa for considering that injection of mesenchymal stem cells (MSCs) in decellularized scaffolds before in vivo implantation represents an innovative concept in the valvular field, and we completely agree that this concept requires a careful validation. However, they expressed some concern about our conclusion that bone marrow-derived mononuclear cell injection induced a structural deterioration of the scaffold and that MSCs induced a protective effect.

We believe that the observation of a deleterious effect of bone marrow-derived mononuclear cells is an interesting point because these cells had never been tested in the field of valve tissue engineering, whereas they are currently used in clinical assays in the field of myocardial failure. Also, we agree that endothelialization and scaffold recolonization are 2 distinct processes that do not always take place together. However, Bertipaglia and colleagues¹ have demonstrated that 2 weeks after in vitro interstitial cell seeding into decellularized leaflets, grafted cells were found penetrating the decellularized scaffold and expressed various immunologic differentiation patterns, such as fibroblasts, myofibroblasts, smooth muscle cells, and

also endothelial cells. Similarly, we observed a significant recolonization after injection of MSCs, and moreover, as stated in our article, pulmonary leaflets exhibited a typical organization in 3 layers (ie, fibrosa, spongiosa, and ventricularis) in each animal of the MSC group.²

Finally, several lines of evidence indicate that in vivo recellularization of valve scaffolds is no longer a “nonvalidated route.” In a previous work we demonstrated evidence of spontaneous recellularization of a decellularized valve.³ Such results were emphasized by Dohmen and coworkers⁴ comparing in vitro seeded and nonseeded valves implanted in sheep. After 6 months, valves from both groups exhibited full recolonization of the leaflets, with comparable hemodynamic behavior and valve remodeling.

We recognize that further studies are needed to compare spontaneous recolonization of an appropriated scaffold and the effects of in situ injection of autologous cells. Also, we have to investigate how injected autologous MSCs improve in situ recolonization by myofibroblasts and endothelial cells or improve host cell migration. However, the challenge seems now to understand and to favor in vivo, rather than in vitro, valve scaffold recolonization.

André Vincentelli, MD, PhD^{a,b}

Francis Juthier, MD^{a,b}

Brigitte Jude, MD, PhD^{a,b}

Centre Hospitalier Régional^a

Universitaire de Lille

Pôle de Chirurgie Cardiovasculaire

Institut d'Hématologie Transfusion

Lille, F-59037 France;

Université de Lille 2^b

EA 2693

Faculté de Médecine

Lille, F-59045 France

References

1. Bertipaglia B, Ortolani F, Petrelli L, Gerosa G, Spina M, Pauletto P, et al. Cell characterization of porcine aortic valve and decellularized leaflets repopulated with aortic valve interstitial cells: the VESALIO Project (Vitalitate Exornatum Succedaneum Aorticum Labore Ingenioso Obtenibitur). *Ann Thorac Surg.* 2003;75:1274-82.
2. Vincentelli A, Wautot F, Juthier F, Fouquet O, Corseaux D, Marechaux S, et al. In vivo autologous recellularization of a tissue-engineered heart valve: are bone marrow mesenchymal stem cells the best candidates? *J Thorac Cardiovasc Surg.* 2007;134:424-32.
3. Juthier F, Vincentelli A, Gaudric J, Corseaux D, Fouquet O, Calet C, et al. Decellularized heart

valve as a scaffold for in vivo recellularization: deleterious effects of granulocyte colony-stimulating factor. *J Thorac Cardiovasc Surg.* 2006;131:843-52.

4. Dohmen PM, da Costa F, Yoshi S, Lopes SV, da Souza FP, Vilani R, et al. Histological evaluation of tissue-engineered heart valves implanted in the juvenile sheep model: is there a need for in-vitro seeding? *J Heart Valve Dis.* 2006;15:823-9.

doi:10.1016/j.jtcvs.2007.12.030

Percutaneous aortic valve replacement with the CoreValve bioprosthesis

To the Editor:

We read with interest the recent article by Marcheix and colleagues¹ in the *Journal* dealing with percutaneous aortic valve implantation. They reported their experience using the second generation (21F) of the CoreValve prosthesis (CoreValve, Inc, Paris, France) in 10 consecutive high-risk surgical patients (median logistic EuroSCORE of 32%). The prosthesis was successfully delivered in all cases, with a doubling of the aortic valve area (from 0.57 ± 0.19 to 1.2 ± 0.35 cm²) and a significant decrease in transvalvular gradient.

We would like to comment on these results and also ask for some clarifications regarding their data:

Prosthesis sizing is an important issue. On one hand, undersizing may be responsible for valve migration (owing to poor anchoring), perivalvular leak, or patient-prosthesis mismatch. On the other hand, oversizing may theoretically lead to coronary obstruction or favor atrioventricular block. There is actually only one available size of the CoreValve prosthesis, with a 21-mm bioprosthesis implanted within the stent frame. This valve is at the present time indicated when the aortic annulus diameter ranges from 20 to 27 mm.² Although the authors did not report the annulus size in their group of patients, we do not understand how proper sizing could be achieved with a single-sized bioprosthesis.

Aortic bicuspidy is observed in half of cases of severe aortic stenosis.³ In our experience, misdeployment of a valved stent is likely to occur within a bicuspid aortic valve,^{4,5} which may alter its long-term durability. Did the authors face a case with a bicuspid aortic valve or have they systematically preoperatively screened the patients and excluded for the endovascular procedure those with a bicuspid aortic valve?