and Masetti \(^1\) deserve credit for the results number of patients studied, Kouchoukos in these situations. Omy will facilitate the distal anastomosis be considered before deciding on a brain assessment of the cerebral circulation as well as careful selection of cases should always be considered before deciding on a brain protection strategy.

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References


Bioengineered airway tissue

To the Editor:
In the brief communication “First Human Transplantation of a Bioengineered Airway Tissue,” Macchiarini and associates \(^1\) point out that tracheal replacement by tissue engineering seems to hold potential. Question is to be raised whether this report actually does provide “definitive evidence that a tissue engineered patch...can functionally...fill all requirements for an airway patch.”

The patch was applied to a defect 1.5 \(\times\) 1.5 cm after breakdown of anastomosis after carinal pneumonectomy. Omentum was applied over the patch; this was further buttressed, and the space was filled with a subcapsular muscle flap. To further obliterate the space, complementary thoracoplasty was performed. The leak healed, and ciliated respiratory epithelium was eventually found to cover the repaired defect.

Closure of a defect such as this with an omental flap, especially with further use of a muscle flap plus thoracoplasty to obliterate residual space, would in most cases suffice to seal the defect successfully. Epithelium undoubtedly migrates from the respiratory epithelium of the surrounding trachea and bronchi to cover the scar that forms over the mesenchymally repaired defect. Epithelization occurs over vascularized autogenous flaps used over smaller defects in trachea and bronchi. Whether the graft actually survived or the tissue ultimately seen was partly or entirely scar that would form over the mesenchymal bed of omentum is not demonstrated.

One must also question placement of a free graft of any tissue over an area that is still contaminated, even if not grossly infected, by the bacteria that necessarily are present in such a situation, despite all cleanup treatment before repair. More to the point, however, is the fact that defects of this sort have long been closed by vascularized pedicled autogenous tissues (omentum, pericardium, intercostal muscle, and other muscle flaps). Addition of an engineered tissue graft seems superfluous.

The potential of bioengineering to produce tracheal replacement segments in the future is a goal worthy of continued research attention nonetheless.

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Reply to the Editor:
It is a distinct privilege to have attracted the interest of Hermes Grillo, and frankly speaking, his comments were expected. In his letter to the Editor, Dr Grillo questions clinical and experimental issues that I am delighted to address.

It is certainly correct that the airway defect could have been closed without the interposition of the engineered airway tissue. However, we all know that (1) it is technically demanding and risky to free (by further devascularizing it) a leaky postradiation (70 Gy) carinal anastomosis, and that (2) an intrathoracic transposed omentum buttressed over an airway defect is almost never immediately tight, and this jeopardizes the spillage of omentum produced fluid into the unique lung and induces a motion- (and foreign body-) temporary cough.

However, and with great respect, we disagree that the addition of an engineered airway tissue was superfluous. From a clinical viewpoint, a repeatedly thoracotomy- and previously irradiated (70 Gy) operative field is unlikely to guarantee engrafting (eg, intercostals muscle) or allow harvesting (pericardium) of autogenous tissues. Hence, the closure of the defect with the tissue-engineered graft ensured a tight interface permitting a physiologic secretion transport without having all the complications related to the indirect closure through autogenous tissues. Having experienced the scenario with and without \(^1\) this new tool, I must admit my pleasure in having an extremely powerful and valid clinical alternative.

From an experimental viewpoint, our disagreement is even more important because the lessons learned from this clinical application are very important. Because of the concise nature of the chosen article
format, we did not report in detail the molecular biologic fate of the patch. However, we did observe ciliar activity as soon as day 3 after implantation, a time frame that is shorter than that reported by other investigators studying autologous pericardial patch tracheoplasty. The objection that one would expect a partial or even entire fibrous scar formation at the patch implantation site is countered with the in vitro observation that the engineered patch underwent a profound tissue remodeling process resulting in a fibromuscular tissue formed by 80% muscle cells and 20% fibroblasts. Because this composition cannot be explained by simple cicatrization, one may suppose that the engineered patch itself and not the transposed omentum was the mesenchymal support of the entire architecture. The late protein, biochemical, and human genetic findings of the engineered airway tissue are currently under review elsewhere and therefore cannot be elucidated here in detail.

I hope that our ongoing experimental tracheal research will at some point overcome some of the clinical barriers of this beautiful organ. I am very grateful to Dr Grillo for his open and very pertinent scientific difference of opinion.

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Reference