

Repair of large airway defects with bioprosthetic materials

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Tracheal resection is currently performed both for benign and malignant diseases and its reconstruction is usually obtained by using primary re-anastomosis (1). Most reports suggest 4 to 6cm of trachea or approximately 8 tracheal rings or 50% of the whole tracheal length in adults or 30% in children can be removed, performing pulmonary hilar release, suprahyoid release, and cervical neck flexion to decrease anastomotic tension (2-4). Longer segments of the trachea cannot be safely removed and since the first reports of tracheal surgery by Hermes Grillo in 1965, it still remains an unsolved problem (5).

In 1972 Neville and colleagues first reported a sort of synthetic tracheal replacement with a molded Silastic prosthesis, with no long-term effective results (6). Because no safe and effective airway prosthesis was available, many attempts to restore damaged tracheas by stents have been made (7,8), but with unfavourable outcomes due to the risk of erosion into mediastinal and cervical blood vessels and lethal bleeding (9,10). Transplantation of heterologous tissue may represent an effective alternative to airway prostheses, however needing long term immunosuppression (11). Orthotopic airway allotransplantation without the needing of immunomodulatory therapy could represent a viable option in case of benign tracheal disease but may be contraindicated in oncologic settings (12). Autologous tubular conduits from small bowel, oesophagus, skin and aorta have been widely proposed and may represent an effective option, in particular in emergency situation; however obstruction, pooling of bronchial secretions, infections and erosion into mediastinal structures still

remain a major issue (13,14).

After a personal preclinical experience of experimental tracheal transplantation using a cryopreserved aortic allograft (15), we reported a successful subtotal tracheal replacement by using a skin/omental graft for dehiscence after a resection for thyroid cancer (16). We reported on our experience with treating a tracheal anastomotic dehiscence that developed after an extended tracheal resection was performed for a thyroid tumor relapse. The technique used to repair the dehiscence a composite skin-omental-muscle graft allowed restoration of tracheal continuity and of a normal respiratory function, however needing an Ultraflex stent positioning by rigid bronchoscopy on postoperative day 7, for treating the beginning of stenosis of the graft (16).

With the advance of regenerative medicine, tissue engineering and stem cell technologies, tissue engineered tracheal grafts have been reported in more recent years, both in experimental and clinical settings (17-19); however, although highly publicized cases within the media to date, the attractive concept of bioengineered tracheal replacements has not yielded a definitive and reliable solution (20).

Our personal previous experience on experimental and clinical airway restoration by autologous mesenchymal stromal cells disclosed how stem cells can be used for treating small airway defects following post resectional bronchopleural fistula (21-23) but, to date, few although encouraging initial results have been reported for larger tissue defects (24); on this topic, the experience of Udelsman and coworkers remains one of the most intriguing,

reporting a retrospective series of 8 patients successfully undergoing repair of tracheal or bronchial defects with a bioprosthetic device, namely aortic homograft or acellular dermal matrix (25).

In conclusion, 40 years after the beginning of tracheal surgery, extended tracheal resection and reconstruction still remains an unsolved problem, as pre-recognized by his father Hermes Grillo, although regenerative medicine, tissue engineering, bioprosthetic materials development and new transplantation management techniques clearly showed the potential to overcome one of the last thoracic surgery boundaries.

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Footnote

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References

1. Fabre D, Singhal S, De Montpreville V, et al. Composite cervical skin and cartilage flap provides a novel large airway substitute after long-segment tracheal resection. *J Thorac Cardiovasc Surg* 2009;138:32-9.
2. Galetta D, Spaggiari L. Tracheal reconstruction for a long tracheal resection. *Ann Thorac Surg* 2006;82:1953; author reply 1953-4.
3. Fabre D, Fadel E, Mussot S, et al. Autologous tracheal replacement for cancer. *Chin Clin Oncol* 2015;4:46.
4. Fabre D, Kolb F, Fadel E, et al. Autologous tracheal replacement: from research to clinical practice. *Presse Med* 2013;42:e334-41.
5. Grillo HC. Circumferential resection and reconstruction of the mediastinal and cervical trachea. *Ann Surg* 1965;162:374-88.
6. Neville WE, Hamouda F, Andersen J, et al. Replacement of the intrathoracic trachea and both stem bronchi with a molded Silastic prosthesis. *J Thorac Cardiovasc Surg* 1972;63:569-76.
7. Lenot B, Macchiarini P, Dulmet E, et al. Tracheal allograft replacement. An unsuccessful method. *Eur J Cardiothorac Surg* 1993;7:648-52.
8. Villegas-Cabello O, Vázquez-Juárez JL, Gutiérrez-Pérez FM, et al. Staged replacement of the canine trachea with ringed polyethylene terephthalate grafts. *Thorac Cardiovasc Surg* 1994;42:302-5.
9. Graziano JL, Spinazzola A, Neville WE. Prosthetic replacement of the tracheal carina. *Ann Thorac Surg* 1967;4:1-11.
10. Sekine T, Nakamura T, Ueda H, et al. Replacement of the tracheobronchial bifurcation by a newly developed Y-shaped artificial trachea. *ASAIO J* 1999;45:131-4.
11. Macedo A, Fadel E, Mazmanian GM, et al. Heterotopic en bloc tracheobronchial transplantation with direct revascularization in pigs. *J Thorac Cardiovasc Surg* 2004;127:1593-601.
12. Delaere P, Vranckx J, Verleden G, et al. Tracheal allotransplantation after withdrawal of immunosuppressive therapy. *N Engl J Med* 2010;362:138-45.
13. Davidson MB, Mustafa K, Girdwood RW. Tracheal replacement with an aortic homograft. *Ann Thorac Surg* 2009;88:1006-8.
14. Wurtz A, Porte H, Conti M, et al. Surgical technique and results of tracheal and carinal replacement with aortic allografts for salivary gland-type carcinoma. *J Thorac Cardiovasc Surg* 2010;140:387-393.e2.
15. Carbognani P, Spaggiari L, Solli P, et al. Experimental tracheal transplantation using a cryopreserved aortic allograft. *Eur Surg Res* 1999;31:210-5.
16. Spaggiari L, Calabrese LS, D'Aiuto M, et al. Successful subtotal tracheal replacement (using a skin/omental graft) for dehiscence after a resection for thyroid cancer. *J Thorac Cardiovasc Surg* 2005;129:1455-6.
17. Batioglu-Karaaltin A, Karaaltin MV, Ovali E, et al. In vivo tissue-engineered allogenic trachea transplantation in rabbits: a preliminary report. *Stem Cell Rev* 2015;11:347-56.
18. Macchiarini P, Jungebluth P, Go T, et al. Clinical transplantation of a tissue-engineered airway. *Lancet* 2008;372:2023-30.
19. Elliott MJ, De Coppi P, Speggiorin S, et al. Stem-cell-based, tissue engineered tracheal replacement in a child: a 2-year follow-up study. *Lancet* 2012;380:994-1000.
20. Sjöqvist S, Jungebluth P, Lim ML, et al. Editorial Expression of Concern: Experimental orthotopic transplantation of a tissue-engineered oesophagus in rats. *Nat Commun* 2016;7:13310.
21. Petrella F, Toffalorio F, Brizzola S, et al. Stem cell transplantation effectively occludes bronchopleural fistula in an animal model. *Ann Thorac Surg* 2014;97:480-3.
22. Petrella F, Spaggiari L, Acocella F, et al. Airway fistula closure after stem-cell infusion. *N Engl J Med*

- 2015;372:96-7.
23. Petrella F, Rizzo S, Borri A, et al. Current Perspectives in Mesenchymal Stromal Cell Therapies for Airway Tissue Defects. *Stem Cells Int* 2015;2015:746392.
 24. Aho JM, Dietz AB, Radel DJ, et al. Closure of a Recurrent Bronchopleural Fistula Using a Matrix Seeded With Patient-Derived Mesenchymal Stem Cells. *Stem Cells Transl Med* 2016;5:1375-9.
 25. Udelsman BV, Eaton J, Muniappan A, et al. Repair of large airway defects with bioprosthetic materials. *J Thorac Cardiovasc Surg* 2016;152:1388-97.

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