Prosthetic reconstruction of the trachea: A historical perspective

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INTRODUCTION

Tracheal reconstruction has been widely researched over the last 50 years. There are numerous indications for tracheal reconstruction, most frequently post-intubation injuries, idiopathic stenosis, neoplasia and re-stenosis following surgery[1].

Following tracheal resection, primary reconstruction with direct anastomosis of the patient's own tracheobronchial tissue is generally accepted as the best...
option[2-7]. Anatomical studies suggest that up to half of the trachea can be resected in adults and directly anastomosed, without undue tension, by implementing mobilisation techniques such as suprathyroid release incisions and/or dissection of the hilum and pulmonary ligament[8]. This has been corroborated in large studies, with acceptable safety profiles and good long-term results, although the limits vary depending upon the patient’s age, body habitus, local anatomy, co-morbidities and previous treatments[1,9-12].

In patients with very extensive pathology, direct anastomosis following resection is not possible and as such, either stenting or replacement with a prosthesis remain the two principle options. This provides a significant subset of patients. For example, long-segment defects (greater than 50% of the trachea) constitute approximately half of tracheal stenosis cases, although more recently this has been innovatively and successfully managed via a slide tracheoplasty procedure[13,14]. A range of materials have been attempted and no ideal prosthesis has yet been developed. The ideal prosthesis is airtight, of adequate consistency to prevent collapse, well accepted by the host thus causing minimal inflammatory reaction, impervious to fibroblastic and bacterial invasion of the lumen and allows ingrowth of respiratory epithelium along the lumen[15,16].

In this review article we will provide a historical overview of tracheal reconstructive trends.

**EARLY WORK**

In the late 1890s and into the twentieth century, interest in tracheal reconstruction evolved[17-20]. Initially, as with many surgical specialities, a knowledge base was formed principally through isolated case reports. The focus at this time was autogenous replacements such as skin alone, or skin and fascial grafts[21,22]. Daniel et al.[23] heralded the advent of a more scientific approach with experimental animal studies. Throughout this period there was a transition from autogenous materials to solid prostheses such as tantalum, polyethylene, acrylic and steel tubes[24-27]. No ideal prosthesis was found and outcomes were variable. Indeed, often composite approaches were taken, usually in the form of a solid prosthesis with fascia lata grafts. The level of evidence remained low.

**1950s TO THE POROUS PROSTHESIS**

Following this initial interest and in vivo work (Table 1), Gebauer was amongst the first to develop porous prostheses to counteract some of the drawbacks of solid prostheses[28,29]. It was found that a porous prosthesis more closely approximates the function of tracheal cartilages as compared to a solid prosthesis[30]. However complications including strictures, granulation formation, chronic infection, pressure necrosis from the prosthesis and dislodgement remained problematic. Erosion of the brachiocephalic artery was also not infrequent. The porous structure was calculated to permit ingrowth of host connective tissue thus incorporating the prosthesis into the tracheal lumen; it was found that a minimal porosity of 40 to 60 μm is necessary for capillary ingrowth[31].

This culminated in a better understanding of an ideal prosthesis that the graft should be airtight, have adequate consistency, be well accepted by the host, cause minimal inflammatory reaction, be impervious to fibroblastic and bacterial invasion into the lumen but ideally allow ingrowth of respiratory epithelium along the lumen[15,31,35]. The decision of material to trial was often dependent upon industrial and commercial advances and availability, ranging from steel wire, tantalum, marlex, PTFE, dacron and teflon[29-36]. Combinations of materials were often employed. Towards the end of this period, as a result, prostatic reconstruction of the trachea was being performed in human patients[37,38]. The most promising outcomes were with silicone prostheses. The Neville group pioneered this approach and developed the Neville prosthesis, a silicone based mould under high compression available as straight or bifurcated tubes[15,16].

In this series of 62 patients, outcomes were reported to be good and the use of silicone was explicated by its resilience, non-reactivity, smooth inner surface and ability to be readily moulded[15,39]. This, therefore, fulfilled all the criteria for an ideal graft except for ciliated epithelium traversing the inner surface. Suture line granulomas remained problematic and were treated endoscopically[15,16,37]. This connective tissue ingrowth initially serves to fix and integrate the porous prostheses but this continued proliferation leads to scar tissue, obstruction and stenosis alongside with resultant chronic infection[31].

At this time, progress was also being made in surgical techniques, led by Grillo’s team in Boston. Anatomic studies indicated that up to half the trachea in adults can be resected and closed primarily with an end to end anastomosis[40]. The same group has validated this with resulting large case series with low morbidity and mortality[14,9-11,13,31]. Slide tracheoplasty and other mobilisation techniques including suprahyoid release incisions, dissection of the hilum and pulmonary ligament have all been successfully used to achieve primary closure. Undoubtedly this remains the gold standard management of tracheal resection. However, it is not always possible and is dependent upon the patient’s age, body habitus, local anatomy, extent of disease, co-morbidities and previous treatments such as radiotherapy[3,4,9-11,13,31].

These studies therefore established that primary repair remains the method of choice and should be employed wherever possible. In addition, it was concluded that an entirely satisfactory tracheal graft will never be available[31,39]. The silicone airway is at least as satisfactory as any prosthesis yet fashioned for tracheal replacement and any alternative must be wholly dependable with minimal morbidity and mortality[31]. This remains the...
### Table 1  Tracheal reconstruction methodology over time

| Year | First author | Category¹ | Material | Study type (number) |
|------|--------------|-----------|----------|---------------------|
| 1898 | Bruns[27]    | Autogenous| Prosthesis unknown | Human |
| 1911 | Hohmeier[18] | Autogenous| Fascia lata | Animal |
| 1912 | Levin[9]     | Autogenous| Fascia | Human (1) |
| 1927 | Fairchild[28] | Autogenous| Skin | Human (1) |
| 1935 | Lejeune[31]  | Autogenous| Split thickness skin graft | Human (2) |
| 1945 | Crafoord[30] | Autogenous| Cutaneous and costal cartilage | Human (1) |
| 1946 | Belsey[29]   | Solid prosthesis| Steel with fascia lata | Human (1) |
| 1948 | Claggett[32] | Solid prosthesis| Polyethylene | Human (1) |
| 1948 | Daniel[33]   | Solid prosthesis| Fascia, Metal Tube | Animal |
| 1948 | Longmire[34] | Solid prosthesis| Acrylic tube | Human (1) |
| 1949 | Roh[27]      | Solid prosthesis| Tantalum with fascia lata | Human (4) |
| 1950 | Kerzin       | Autogenous| Pericardium and bronchus | Human (1) |
| 1950 | Jarvis       | Solid prosthesis| Stainless Steel | Human (1) |
| 1950 | Gebauer[29]  | Porous prosthesis| Wire-enforced dermal graft | Human (11) |
| 1951 | Bache[34]    | Porous prosthesis| Stainless steel wire mesh | Animal |
| 1952 | Cotton[35]   | Solid prosthesis| Stainless steel tube | Human (2) |
| 1953 | Edgerton     | Solid prosthesis| Split grafts with foam rubber | Human (12) |
| 1953 | Pressman[33] | Autogenous| Decalcified bone | Animal |
| 1955 | Morfit       | Solid prosthesis| Polyethylene | Animal |
| 1962 | Beall[36]    | Solid prosthesis| Polyethylene | Animal |
| 1964 | Aletras      | Solid prosthesis| Teflon frame with pericardium | Animal |
| 1967 | Graziano[30] | Porous prosthesis| Silicon with dacron | Animal |
| 1968 | Pearson[36]  | Porous prosthesis| Marlex (Polyethylene) | Animal |
| 1973 | Monk         | Autogenous| Dermal grafts | Human (6) |
| 1973 | Demos        | Porous prosthesis| Silcone | Animal |
| 1974 | Montgomery[38] | Porous prosthesis| Silcone t tube | Human (94) |
| 1974 | Pearson      | Porous prosthesis| Marlex (Polyethylene) | Human (6) |
| 1976 | Neville[39]  | Porous prosthesis| Silcone | Human (26) |
| 1977 | Lindholm     | Autogenous| Bone/periosteum/muscle | Human (2) |
| 1982 | Neville[39]  | Porous prosthesis| Neville prosthesis (silicon with dacron rings) | Human (54) |
| 1982 | Westaby      | Porous prosthesis| Bifurcated silicone stent | Human (1) |
| 1985 | Toomes[42]   | Porous prosthesis| Neville prosthesis (silicon with dacron rings) | Human (9) |
| 1986 | Scheree[43]  | Tissue engineering| Bioprosthesis | Animal |
| 1989 | Har-El       | Autogenous| Alloplast implanted muscle flap | Animal |
| 1990 | Neville[39]  | Porous prosthesis| Silcone tubes | Human (62) |
| 1990 | Cull         | Porous prosthesis| PTFE | Animal |
| 1990 | Jorge        | Porous prosthesis| PTFE | Animal |
| 1990 | Kato[44]     | Autogenous| Oesophagus and Silcone T tube | Animal |
| 1990 | Letang[45]   | Tissue engineering| Jejunum and Silcone T tube | Animal |
| 1990 | Varela       | Porous prosthesis| Stainless steel wire mesh | Human (5) |
| 1992 | East[46]     | Autogenous| Composite fascia, septum | Human (1) |
| 1994 | Okumura[48]  | Porous prosthesis| Collagen and Marlex mesh | Animal |
| 1996 | Sharpe       | Porous prosthesis| Marlex and pericardium | Human (1) |
| 1996 | Eliot[49]    | Homograft | Homograft | Human (5) |
| 1997 | Kiriyama[50] | Homograft | Oesophageal autograft | Animal |
| 1997 | Teramachi[51] | Porous prosthesis| Marlex with collagen | Animal |
| 2000 | Sekine[50]   | Porous prosthesis| Marlex | Animal |
| 2003 | Pfitzmann[52] | Porous prosthesis| Oesophagus | Human (1) |
| 2004 | Kim[53]      | Porous prosthesis| Skin and polypropylene mesh | Animal |
| 2005 | Martinod[54] | Homograft | Allogenic aorta | Animal |
| 2005 | Shi[55]      | Porous prosthesis| Polypropylene mesh with polyurethane/collagen | Animal |
| 2006 | Jaillard[56] | Homograft | Allograft aorta | Animal |
| 2008 | Sato[57]     | Porous prosthesis| Polypropylene mesh with collagen | Animal |
| 2008 | Macchiarini[58] | Homograft | Stem cell seeded homograft | Human |
| 2009 | Nakamura[59] | Porous prosthesis| Polypropylene with additional collagen, stem cells | Animal |
| 2010 | Makris[60]   | Homograft | Allograft aorta | Animal |
| 2010 | Sato[57]     | Tissue engineering| Bioprosthesis | Animal |
| 2010 | Tsukada[61]  | Tissue engineering| Bioprosthesis | Animal |
| 2011 | Autogen [60] | Tissue engineering| Radial forearm flap with PTFE or polyethylene | Human (7) |
| 2012 | Jungebluth[62] | Tissue engineering| Stem cell bioartificial scaffold | Human (1) |
| 2012 | Elliott[62]  | Tissue engineering| Stem cell bioartificial scaffold | Human (1) |
| 2012 | Gray[63]     | Tissue engineering| Stem cell bioartificial scaffold | Animal |
| 2012 | Tani[64]     | Tissue engineering| Collagen scaffold with PFG | Animal |
| 2012 | Wurtz[71]    | Homograft | Allograft aorta with fascial graft and external cartilage | Animal |
| 2014 | Chang[65]    | Tissue engineering| Stem cell bioartificial (3D Printed) scaffold | Animal |
| 2016 | Delaere[66]  | Allotransplant | Vascularised allograft | Human |

¹A number of these are composite strategies. PTFE: Polytetrafluoroethylene; FGF: Fibroblast growth factor.
case today.

1990s ONWARDS

Further avenues of research have evolved in the last few decades. This has focussed on homografts, various composite strategies (including further work on porous prostheses) and latterly, tissue engineering\[1,5,9,10,12,14,40-67\]. Scherer et al\[67\] were first to experiment with bioprostheses by transplanting tracheas from various animals as autografts, allografts and xenografts. Rejection seemed to be avoided\[31,67\]. This preceded a plethora of animal studies, particularly transplantation studies, and in the last few years, attempts to translate this to patients\[80,41,43,44,49,50,54,56,61\]. Recently, research has focused on tracheal stem cell regeneration. Despite initial positive results, the outcomes have been generally poor and as such should be used with caution\[62\]. Pedicled flaps may serve to implant and maintain the stem cell generated trachea prior to reconstruction\[46\]. A recent pilot study has used three-dimensional printing of an artificial tracheal graft\[46\]. In addition, there has been some focus on the use of intestinal (either jejunal or oesophageal) tubes to replace the trachea\[66\]. This autogenous tissue can be categorised into free grafts with and without foreign material support (e.g., the composite wire and fascia or dermal grafts); vascularised tissue flaps (e.g., pedicled intercostal muscle) and autogenous tube construction (e.g., oesophagus)\[31\]. Autologous tracheal replacement using radial forearm fasciocutaneous free flap has also demonstrated positive outcomes\[58\].

Further homografts include pericardium and aorta\[50,54,56\]. Patch repair of the trachea using pericardial allografts\[69\] and xenografts\[70\] have been shown to have good outcomes\[71\]. More recently, aortic homografts used as a bioprosthetic device for patch repair have also shown favourable results\[72,73\]. Circumferential replacement of the trachea using aortic homografts has shown poorer results, in both animal\[74\] and human\[75\] models. Wurtz demonstrated that silicone-stented aortic allografts have no cartilage regeneration, probably due to ischaemia prior to neoangiogenesis\[76\]. This led to proposals of a composite, fascial flap-wrapped allogeneic aortic graft with external cartilage ring support\[77\]. Again, no reconstruction has been as successful as direct anastomosis, or even silicone prostheses alone.

CONTROVERSIES AND FUTURE DEVELOPMENTS

The intriguing yet unsolved surgical dilemma of tracheal replacement remains a challenge to clinicians. Currently, work from the Leuven group (Delaere et al\[80\]) has shown promising results with the judicious use of allotransplants. Surgical ingenuity will lead to novel approaches to these problems\[80\]. However, it is important to note that these techniques should not create more problems than they solve and patients are to be treated as an individual with a duty of care attached to that. As a corollary to this, it is worth highlighting that where a series of animal experiments are successful, application of these procedures to humans almost inevitably presents greater issues and a higher failure rate\[3\]. Work on tracheal regeneration using stem-cell implanted scaffolds\[44,48,79\] which has been the centre of recent controversy, showed questionable data and ultimately poor results.

CONCLUSION

Direct revascularisation of the trachea is unsuitable due to its lack of an intrinsic blood supply. Its anatomical features (proximity to major vessels, segmental blood supply) and the presence of a variety of different tissue types (respiratory epithelium, cartilage, blood vessels) make reconstruction difficult. Recent attempts with tissue-engineered transplants have all failed due to this reason\[80\]. Tracheal reconstruction is optimal when primary anastomosis is possible with undue tension. Patients requiring reconstruction should be managed in a multidisciplinary team at a high volume tertiary referral centre to optimise treatment. Tracheal replacement can be divided into prosthesis, homograft and autogenous tissue reconstruction, or a combinatorial methodology. None have proven ideal conduits as tracheal replacements. The most convincing evidence has historically been silicone based prostheses, and more recently revascularised tracheal homografts and allotransplants. Stenting of the trachea has shown poor results. In emergent situations, endobronchial debulking and laser is preferable over stenting as this may prevent primary surgery.

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