

# Laryngeal transplantation: is it a thing?

BY MARTIN BIRCHALL

Few organs could be said to be more complex than the larynx when it comes to transplantation. Martin Birchall looks at past challenges, current issues and future prospects.

I am not clear exactly why I chose to spend a life researching ways of replacing laryngeal functions. Maybe it was because I devoured science fiction as a kid. Anyway, I ended up investigating the most complex ways imaginable to reconstruct what is arguably the most complex solid organ in the body: transplantation, tissue engineering and, presently, soft robotics. Transplantation was my first shot, though, and once ethical issues were at least discussed openly, this approach seemed to make sense, at least in the 1990s. A decade's research later, I was invited to join a team for the world's second documented laryngeal transplant, at UC Davis, California (the first was at the Cleveland Clinic Ohio in 1998). Our recipient has done well and is still speaking with her replacement larynx 14 years later, though age, immunosuppression and prior illnesses, including a previous kidney transplant, have taken some toll.

Now, however, there have been a total of 16 documented laryngeal transplants to my knowledge: six in Poland, five in Colombia, three in the United States and one each in China and France, two of these (France and the Mayo Clinic, USA) in the last year. Indications varied from severe trauma to active laryngeal malignancy (three patients: two squamous cancer and one lymphoma). We recently published collected data on the first 11, with transplantations performed between 1998 and 2022, of which eight had reasonable follow-up data at the time of data collection.

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Successful laryngeal transplantation has been a dream for laryngologists and head and neck surgeons since the 1950s. Sixteen documented transplants have been performed since 1998, with steady improvement in surgical technique and aftercare.

After a minimum of 24 months (median 73) follow-up, three patients had died (27%) and there were two graft explants in survivors, one total and one partial, due to chronic rejection. In the remaining cases, voice was functional in 62.5%, and 50% had entirely oronasal breathing at the time of reporting. Swallowing was initially restricted in all, but only one patient was gastrostomy-dependent by six months, and all had normal or near-normal swallowing by the end of year two following transplantation. Functional (voice, swallowing, airway) recovery plateaued between 12 and 24 months (See Table). Since then, another patient has died (abdominal problems) and one more has had their larynx explanted after six years due to chronic rejection.

So, what do these 16 transplants spread over a quarter of a century tell us? Well first, it's not an easy undertaking. You need a really rare candidate, ideally one who is already on immunosuppression as our Californian recipient was, with a sufficiently troubled existence and no clear conventional path to a better life. They need to be fit enough for eight to 20 hours of surgery. The surgical teams (one retrieval, one implantation) need high levels of skill and training and their institutions or states (as in the French patient) need to foot the

bills (over \$1 million). This is not a checklist that most laryngectomees or persons with severely compromised laryngeal function, nor their managing medical teams, would easily pass.

Secondly, the outcomes are very varied. Some can go stoma-free, but usually with breathy voices and likely borderline aspiration as one cord is fixed in abduction, the method favoured in Poland. However, most retain a tracheostomy. It takes a year to relearn swallowing and a few remain gastrostomy dependent for some or all their nutrition. Even non-selective reinnervation should provide adducted cords with reasonable bulk and tone, so an excellent voice is possible, with a little modulation if the superior laryngeal nerves are also repaired. We await with great interest the motor outcomes of the French patient, the first to undergo bilateral highly selective laryngeal reinnervation. It is also difficult to know what all the recipients themselves truly think of all this, as no detailed qualitative or psychological studies have been performed to date. However, when the very first recipient had the graft explanted a decade later, he is documented as saying he would happily undergo the same thing again.

The threat of allograft rejection casts a long shadow over the whole field of

	Preoperative			Postoperative								
	Airway Patency	Voice	Swallowing	Airway patency at 6 months	Voice Quality at 6 months	Swallowing function at 6 months	Airway patency at 12 months	Voice Quality at 12 months	Swallowing function at 12 months	Airway patency at 24 months	Voice Quality at 24 months	Swallowing function at 24 months
Patient 1	Absent	Absent	Restrictive	Excellent	Good	Total oral intake	Excellent	Good	Total oral intake	Excellent	Excellent	Total oral intake
Patient 2	Absent	Absent	Total oral intake	Excellent	Satisfactory	Restrictive	Excellent	Good	Restrictive	Excellent	Good	Total oral intake
Patient 3	Absent	Satisfactory	Restrictive	Good	Poor	PEG	Absent	Poor	Partially oral	Good	Poor	Partially oral
Patient 4	Absent	Poor	Restrictive	Absent	Poor	Partially oral	Absent	Poor	Restrictive	Good	Satisfactory	Total oral intake
Patient 5	Absent	Absent	Partially oral	Good	Satisfactory	Restrictive	Satisfactory	Satisfactory	Partially oral	Good	Satisfactory	Restrictive
Patient 6	Absent	Absent	PEG									
Patient 7	Absent	Absent	Restrictive	Satisfactory	Excellent	Restrictive	Satisfactory	Excellent	Partially oral	Good	Excellent	Restrictive
Patient 8	Absent	Absent	PEG	Good	Satisfactory	Restrictive	Good	Satisfactory	Restrictive	Good	Satisfactory	Restrictive
Patient 9	Absent	Absent	PEG	Absent	Satisfactory	Total oral intake	Absent	Good	Total oral intake	Absent	Absent	Total oral intake
Patient 10	Absent	Absent	Total oral intake									
Patient 11	Absent	Absent	PEG	Absent	Absent	Restrictive						

Table documenting outcomes for 11 laryngeal transplants reported between 1998 and 2022. Red = function absent, orange = function poor, light green = qualified success, strong green = normal / near normal. Table also shows where data collection was censored due to limit of observation at time of reporting or death of recipient. The table shows a gradual transition from absent function to good function over a 24-month observation period, but a 'patchy' outcome overall, making it difficult to accurately predict functional results.

transplantation, not least the area of composite allografting (face, limb, larynx). To my knowledge (a caveat necessary without a global registry), the reported rate of chronic rejection for laryngeal transplants is 3/16 (19%), though this will certainly rise with longer follow-up and more transplants. However, there is no data on what acute or chronic rejection of a larynx looks like, either clinically, serologically or histologically. We can only extrapolate from the experience of other solid organ transplants and, once again, a global registry would be invaluable to gradually fill in the missing pieces of this story. The Ohio graft developed oedema and reduced phonation, whilst the Polish patient develop dysphagia. One

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potential way forward is to adopt a sentinel skin transplant, as performed in some of the Polish series. Skin is especially susceptible to rejection, so adding a revascularised patch of skin in continuity with or separate from (e.g. forearm) the larynx might give early warning of rejection and provide easily accessible biopsy material. Management of rejection post-diagnosis also requires research and standardisation.

Where do we go from here? There seems to be continuing global appetite for taking the procedure on from time to time for exceptional patients and there is some evidence of benefit, albeit highly inconsistent. If laryngeal transplantation were ever to become more common, however, I think a number of things really need to happen. First, we need improved technologies to permit functional vocal fold movements. Secondly, teams must be early adopters of advances in immunomodulation, including consideration of genetically humanised donor animals. Finally, it is critical that we establish international guidelines and standards and start a global registry with universally agreed outcome measures, including functional and psychological.

**References**

1. Candelo E, Belafsky PC, Corrales M, et al. The Global Experience of Laryngeal Transplantation: Series of Eleven Patients in Three Continents. *Laryngoscope* 2024;**134**:4313–20.
2. Strome M, Stein J, Esclamado R, et al. Laryngeal transplantation and 40-month follow-up. *N Engl J Med* 2001;**344**(22):1676–9.
3. Farwell DG, Birchall MA, Luu QC, et al. Laryngotracheal transplantation: technical modifications and functional outcomes. *Laryngoscope* 2013;**123**(10):2502–8.

4. Céruse P, Albert S, Baujat B, et al. 2023: First laryngeal transplantation in France by the "ECLAT" group! *Eur Ann Otorhinolaryngol Head Neck Dis* 2024;**141**(1):1–2.
5. Hames MV. Mayo Clinic marks medical milestone with world's first known successful total larynx transplant performed in a patient with an active cancer as part of a clinical trial. <https://newsnetwork.mayoclinic.org/discussion/mayo-clinic-marks-medical-milestone-with-worlds-first-known-successful-total-larynx-transplant-performed-in-a-patient-with-an-active-cancer-as-part-of-a-clinical-trial/>. 2024.

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