

# Total Laryngeal Transplant in the Setting of Active Laryngeal Malignancy



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## Abstract

Laryngeal transplant (LT) is a promising option to restore quality of life in patients with severe laryngeal dysfunction or a laryngectomy. These patients may be tracheostomy tube dependent or gastrostomy tube dependent and may lose their ability to verbally communicate. The loss of these important functions frequently results in social isolation and a severe decrease in quality of life. Laryngeal transplant has the potential to restore all of these important laryngeal functions. Herein, we report the first known documented LT performed in the setting of laryngeal chondrosarcoma.

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**O**n February 29, 2024, our team performed a total laryngeal transplant (LT) on a patient with active laryngeal chondrosarcoma. This was the third documented LT in the United States. Laryngeal transplant is an example of vascularized composite allograft transplantation, in which multiple tissue components are transplanted. These components can include the larynx, pharynx, esophagus, trachea, thyroid and parathyroid glands, neurovascular structures, and skin.

## HISTORICAL PERSPECTIVE

To date, only 3 case reports with detailed information about human total LT have been published, all from different institutions. The first human total LT was successfully performed in the United States in 1998.<sup>1</sup> The patient was a 40-year-old man in whom laryngeal stenosis developed after a motor vehicle accident. Postoperatively, he began speaking at 3 days, and his voice was considered normal after 36 months. He was able to swallow without aspirating 3 months after surgery. He kept his tracheotomy as a precaution. The larynx was explanted after 14.5 years because of chronic rejection.<sup>2</sup>

The second transplant was performed in the United States in 2010 for a 51-year-old woman with acquired laryngotracheal stenosis.<sup>3</sup> She was already receiving long-term immunosuppression for a kidney-pancreas transplant. She was able to speak at 14 days, and her voice was nearly normal at 18 months. At 11 months, she was able to eat a normal diet. She continues to be tracheostomy tube dependent.

A third LT was performed in Poland in 2015.<sup>4</sup> This patient was a 34-year-old man receiving immunosuppression for a kidney transplant. A T3N1 laryngeal squamous cell cancer developed, and he underwent a total laryngectomy with postoperative irradiation. Severe fistulas and infections developed after radiation therapy. He was disease free from laryngeal cancer for 6 years at the time of his LT and was considered cured. Initial voice production occurred at 14 days, and he was speaking normally at 2 years. He is eating without difficulty. He was the first LT patient to have his tracheostomy closed.

A review was recently published summarizing 11 transplant patients, which included the 3 discussed here.<sup>5</sup> Two additional transplants have been reported without details.<sup>6,7</sup>



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## CURRENT INDICATIONS AND CHALLENGES

The previous cases have demonstrated that human LT can be a viable option for select candidates and result in significant quality of life improvement. However, widespread use of LT has not been adopted for various reasons. The surgery is technically difficult and requires a collaborative team. Because of synkinetic reinnervation of the recurrent laryngeal nerves, vocal fold function is difficult to predict. The requisite lifelong immunosuppression and its associated risks deter many surgeons from performing LT. Current dogma prevents the use of immunosuppression in patients who have active cancer because of the concern of increasing recurrence or metastasis risk. This significantly limits the number of potential LT candidates because most patients who would benefit have laryngeal cancer. More research is needed to better understand the potential utility of LT and to expand the candidate pool. Until now, there has been no dedicated human clinical trial evaluating the safety and efficacy of LT.

## OUR PROGRAM

Our team at Mayo Clinic in Arizona has established the Larynx and Trachea Transplantation Program. The program includes both discovery science and a human clinical trial. The clinical program has been approved by the United Network for Organ Sharing. As a part of the program, we are conducting a clinical trial of multiple LTs to provide a consistent place dedicated to offering LT, better understanding its safety and efficacy, and expanding its utility. Furthermore, we are studying the ethics and patient expectations of LT to provide better informed consent. Our efforts have demonstrated feasibility and patient desire for LT. To date, more than 60 patients have been referred from outside providers, self-referred, or recruited within our hospital.

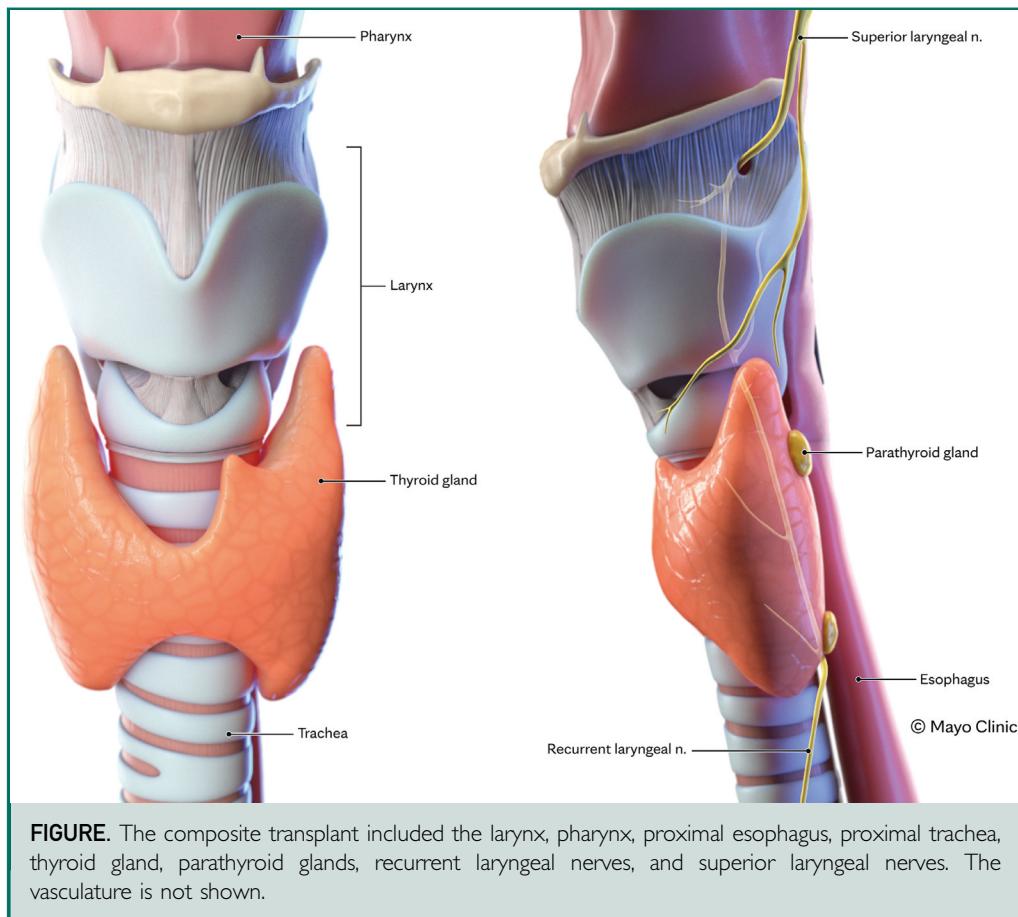
## OUR FIRST PATIENT

Our team performed a total LT on February 29, 2024. The patient is a 59-year-old man who had previous subtotal resections of a low-grade chondrosarcoma with various

attempts at complex reconstruction. Subtotal resection is a standard practice for low-grade chondrosarcoma, given the slow-growing nature and low risk for metastasis of this cancer. The multiple surgeries and reconstructive attempts resulted in a nonfunctional larynx. The patient was tracheostomy tube dependent because of severe stenosis. He had a severely strained voice that limited his ability to communicate. He was able to swallow with some difficulty. However, his ability to swallow without aspirating was thought to be secondary to his severe laryngeal stenosis preventing aspiration, not proper swallow function. Any attempts at opening the patient's laryngeal airway would likely have resulted in aspiration and loss of ability to swallow safely. The only remaining option to completely eradicate the laryngeal chondrosarcoma and to improve his ability to communicate was to perform a total laryngectomy. Any other option would not have had the same chance at cure and would have likely worsened any remaining laryngeal function.

The patient was already receiving immunosuppression from a previous kidney transplant. Therefore, there were no added long-term risks from immunosuppression. Because low-grade chondrosarcomas have a low likelihood of metastasizing, the patient and our team believed that the potential benefit of waiting for a transplant donor outweighed the risks. After the surgery, pathologic analysis of the removed diseased larynx did demonstrate an area of intermediate-grade chondrosarcoma. All surgical margins were negative.

During the surgery, the larynx, pharynx, proximal esophagus, proximal trachea, thyroid gland, and parathyroid glands were transplanted (Figure). We anticipate recovery of laryngeal functions to take a minimum of 1 year because of the slow recovery of nerve function and the time needed to train appropriate laryngeal mechanics. At this early stage, the patient is able to communicate with a voice quality estimated to be about 60% of normal, to swallow liquids and solids without limitation but not yet at



**FIGURE.** The composite transplant included the larynx, pharynx, proximal esophagus, proximal trachea, thyroid gland, parathyroid glands, recurrent laryngeal nerves, and superior laryngeal nerves. The vasculature is not shown.

a volume high enough to have his gastric feeding tube removed, to cap his tracheostomy tube intermittently, and he has regained sensation to the transplanted larynx. The patient is happy with his decision to have an LT and has no regrets.

### FUTURE OF LARYNGEAL TRANSPLANTATION

Although our transplantation in the setting of active cancer is another step toward expanding LT indications, more needs to be done before LT can be used to its full potential. In the opinion of our team, primary areas of focus should include better understanding ethical implications and patient expectations, optimizing proper vocal fold movement after transplantation, reducing/ removing the need for immunosuppression, and safely using LT for patients with more aggressive forms of laryngeal cancer.

Exciting work in these areas is being performed by our team and others.<sup>8-10</sup> Our team envisions a day in the near future when LT can be performed in active cancer patients with minimal immunosuppression and volitionally controlled vocal folds.

### POTENTIAL COMPETING INTERESTS

Girish Mour received consulting fees and honoraria from Evimed as course director and presenter for its continuing medical education program. Michael Hinni received royalties from Karl Storz for a laryngoscope design. The remaining authors have nothing to disclose.

### ACKNOWLEDGMENTS

We would like to acknowledge and thank our larynx transplant recipient for putting his trust in us, sharing our commitment to

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The patient described in this report provided written informed consent.

**Abbreviations and Acronyms:** LT, laryngeal transplant

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