



# HHS Public Access

Author manuscript

*Laryngoscope*. Author manuscript; available in PMC 2018 October 01.

Published in final edited form as:

*Laryngoscope*. 2017 October ; 127(10): 2319–2320. doi:10.1002/lary.26670.

## Strategies for Advancing Laryngeal Tissue Engineering

**Susan L. Thibeault, PhD, CCC-SLP and Nathan V. Welham, PhD, CCC-SLP**

Division of Otolaryngology Head and Neck Surgery, Department of Surgery, University of Wisconsin-Madison, Madison, Wisconsin, U.S.A

Research in laryngeal tissue engineering was virtually nonexistent until the turn of the 21st century. Since that time, there has been rapid growth in the field, as demonstrated by a sharp increase in the number of publications describing the application of tissue engineering and regenerative medicine to the larynx. Despite progress, advances have been gradual, laborious, and limited by the need for greater fundamental characterization of the larynx, its many tissue subtypes, and its multiple specialized functions. It is difficult to develop effective regenerative strategies without these foundational biological insights, adequate models, cutting-edge techniques, and appropriate interdisciplinary teams. In laryngeal biology, these challenges are further complicated by a small number of investigators and limited research funding.

Given its potential to transform clinical care, and the fact that translational progress remains in the early stages, it is appropriate to assess strategic directions in laryngeal tissue engineering from the perspective of those who are actively pursuing basic and translational research worldwide. Although young, the field of laryngeal tissue engineering has progressed to the point where broad categories of research activity can be delineated and evaluated, facilitating the identification of remaining translational barriers. Toward this goal, we performed a tactical assessment of the state-of-the-field to guide researchers, clinicians, and other stakeholders—including funding agencies, policy makers, regulators, and companies in the private sector—by adopting a strategic assessment methodology, the Hoshin facilitation technique,<sup>1</sup> previously used to evaluate progress in the parent discipline of tissue engineering.<sup>2</sup>

Senior investigators in laryngeal and tracheal tissue engineering were asked to identify at least 10 critical steps needed to make the following statement a reality: “The field of laryngeal tissue engineering will exhibit broad clinical success by the year 2025.” A total of 149 raw ideas were categorized into 17 distinct concepts (see Supporting Information in the online version of this article); these numbers were comparable to those reported in 2007, when 24 editorial board members of the journal *Tissue Engineering* participated in a similar strategic planning exercise.<sup>2</sup> A number of concepts identified in our analysis—attention to

---

Send correspondence to Susan L. Thibeault, PhD, CCC-SLP, Department of Surgery, University of Wisconsin Madison, 5107 WIMR, 1111 Highland Avenue, Madison, WI 53705. thibeault@surgery.wisc.edu.

Susan L. Thibeault and Nathan V. Welham contributed equally to this work

Additional Supporting Information may be found in the online version of this article.

Editor’s Note: This Manuscript was accepted for publication April 10, 2017.

The authors have no other conflicts of interest to disclose.

regulatory issues, identification of best cell source, focus on parameters that improve cell/biomaterial performance, standardization of protocols and outcome measures, and improved understanding of basic biology and pathophysiology—correspond closely to those identified in the 2007 study, suggesting that many of the fundamental challenges seen in laryngeal tissue engineering reflect those facing the larger field, and that these challenges have persisted over the past decade.

We identified clear inter-relatedness between concepts. Such relationship strength is natural, given that much of what is required for translational success in (laryngeal) tissue engineering is sequential: a comprehensive understanding of the biology of the tissue engineering target, which informs development and refinement of the engineering approach, which informs preclinical testing, which informs regulatory strategy, which informs clinical testing, which informs decision making in the manufacturing and commercialization domains. Because of this, future progress in any concept area is likely to positively impact other areas; consequently, relationship strength may further improve as the field matures and stakeholders develop a wider perspective on overall translational strategy. The greatest progress to date was judged to be in the development of in vivo models, whereas the lowest progress was assigned to concepts associated with clinical translation and commercialization. These observations are reasonable given that laryngeal tissue engineering is an emerging subspecialty, and because the broader field of tissue engineering is itself just ~25 years old. Presumably, as foundational aspects of the field continue to be investigated and characterized, vertical progress can more easily be achieved.

Three concepts were identified to have the greatest potential for immediate impact upon the field: increased collaboration and sharing, attention to regulatory issues, and standardization of protocols and outcome measures. Efforts to improve collaboration and methodological consistency across research groups are tightly connected concepts that could allow more straightforward comparison of data generated by different groups, reduce redundancy and duplication of effort, and facilitate the scaling of ideas and implementation of ambitious projects. These potential advantages offer a stark contrast to the current state-of-the-field, where most advances have come from groups working in isolation, and where many assays and outcome measures (in both the preclinical and clinical sciences) are inconsistently applied. Improvement in these concept areas could be especially impactful given the small number of stakeholders and limited resources available to laryngeal tissue engineers.

As investigators working in the field, we have considered and navigated many of the abovementioned concepts. We agree that the need for additional foundational work in the basic biological sciences is acute; nevertheless, we are encouraged by an increasing appreciation among basic scientists for the larynx as a valuable model system in its own right, as well as greater representation of laryngeal biology in top-tier basic and translational science journals with broad multidisciplinary readerships. We have also experienced the positive benefits of collaboration and resource sharing firsthand. Given the scarcity and importance of primary human laryngeal tissues and cells, we established a practice of coordinating procurement and sharing fresh tissue between laboratories at our institution (allowing us to leverage this resource to support multiple projects in parallel), developed immortalized cell lines that are freely available to other investigators, and routinely deposit

our raw genomic, transcriptomic, and proteomic data in publicly accessible repositories. Our work has benefited enormously from strategic collaboration with partners from a variety of scientific fields: these partnerships both enhance the quality of scientific inquiry and accelerate progress.

Our survey-based Hoshin analysis highlights a series of research and development concepts that, due to their interrelatedness, relative influence, and lack of progress-to-date, have the greatest potential to drive laryngeal tissue engineering toward broad clinical success by 2025. Although these observations are not intended to provide a dogmatic blueprint for progress in laryngeal tissue engineering, they offer guidance to this emerging area of science that is receiving increasing focus worldwide but still faces substantial translational barriers. Also, as future progress is made, it is likely that the nature and importance of the abovementioned strategic concepts will change. For example, increased collaboration may yield progress in, and confer greater importance to, the definition of patient cohorts and standardization of outcome measures. It will therefore be worthwhile to evaluate progress and reassess strategic directions as scientific advances are made and the field further matures.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

This work was funded by the following grants from the National Institutes of Health, National Institute on Deafness and other Communication Disorders: R01 DC004428, R01 DC004336, R01 DC012773, R01 DC013508, R01 DC010777.

The authors have no other funding, financial relationships.

## BIBLIOGRAPHY

1. Tennant C, Roberts PA. Hoshin Kanri: a technique for strategic quality management. *Qual Assur.* 2000; 8:77–90. [PubMed: 11797824]
2. Johnson PC, Mikos AG, Fisher JP, Jansen JA. Strategic directions in tissue engineering. *Tissue Eng.* 2007; 13:2827–2837. [PubMed: 18052823]