

Development of a Tissue Engineered Trachea

J. Enmark¹, E. Clark², J. Johnson¹, N. Hibino², T. Shinoka², C. Breuer²

¹Nanofiber Solutions, Columbus, OH; ²Nationwide Children's Hospital, Columbus, OH



Background

Currently, for large tracheal defects and injuries, patients are primarily limited to cadaverous allografts, requiring them to meet donor recipient requirements as well as follow an immunosuppressant schedule for the remainder of their life. According to the United Network of Organ Sharing (UNOS) the general market for tracheal transplants and tracheal repair and replacement surgeries account for approximately 4,000 cases annually in the U.S. While many minor tracheal defects can be treated by resection of the damaged tissue and sewing together the remaining tissue back together, this method is limited to one-half the original tracheal length in adults.

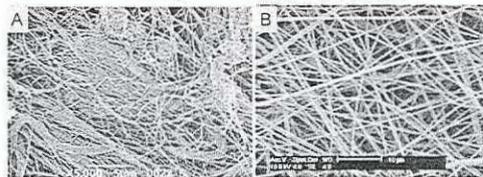
Objectives

- Demonstrate *in vivo* efficiency of intraoperatively seeded tracheal implants.
- Determine if the mechanical strength of the tracheal implant developed *in vivo* matches that of the native trachea.
- Validate that the use of a closed system, disposable seeding chamber allows uniform cell seeding throughout the scaffold thickness.

Methods

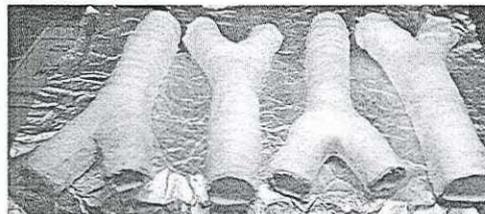
Trachea scaffolds are made via electrospinning a proprietary blend of polyethylene terephthalate (PET) and polyurethane (PU). In collaboration with Dr. Christopher Breuer at Nationwide Children's Hospital, scaffolds are seeded with the patient's own stem cells via a closed, disposable seeding chamber that efficiently separates MNC's from bone marrow. *In vivo* clinical trials are to be conducted using sheep as transplant hosts; surgeries are to be performed at Nationwide Children's Hospital in Columbus, OH.

Scaffold Analysis



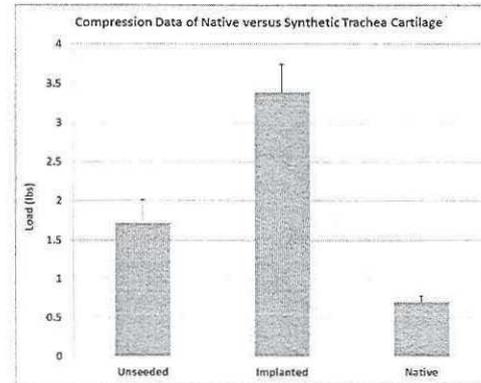
Electrospun nanofibers (B) closely mimic the nanostructure of decellularized human tracheal tissue (A).

The nanofiber scaffolds created are highly porous, replicating natural decellularized human extracellular matrix, and has mechanical properties which mimics that of human trachea.



Nanofiber trachea scaffolds manufactured at Nanofiber Solutions.

Results



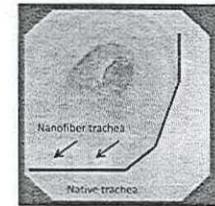
The first round of *in vivo* tests have been performed; one sheep had native trachea tissue excised and replaced with a nanofiber trachea scaffold. The sheep was able to successfully breathe on its own without any assistance. Shortly after, the sheep was euthanized, and the trachea scaffold was extracted for mechanical testing for $t=0$.

Early results yielded positive results; compression data gathered from mechanical testing performed on an unseeded scaffold, an implanted scaffold, and native trachea tissue indicate that the compressive strength of the nanofiber scaffold is significantly higher than that of the native tissue.

Initial cell absorbance measurements yielded a seeding efficacy of 1.56% after an incubation period of 2 hours in the novel vacuum seeding approach.

Discussion

Using this technology, an "off-the-shelf" scaffold can be readily available for patients unable to wait long periods of time for trachea repair, such as those who have obtained severe trachea damage due to trauma. Shorter incubation times also would greatly reduce chances of infection in the patient. The trachea scaffolds manufactured by Nanofiber Solutions have been used successfully in four human surgeries to date; it is also the first nanofiber synthetic trachea in the world to be successfully implanted into a human.



Bronchoscopy of patient implanted with Nanofiber trachea scaffold three days after surgery demonstrating the dramatic similarity between epithelial airway cell coverage and vascularization of the native tissue and the synthetic trachea. The arrows point to the sutures.

Future Work

In vivo tests of $t=14$ days and $t=60$ days are scheduled to take place in early March. Criteria for success will be determined by endoscopic and histological evaluation to observe whether formation of a continuous ciliated epithelium on the lumen of the implant and cartilage at the edges of the scaffold. Furthermore, compression data will be collected on these implanted scaffolds; successful scaffolds will yield compression strengths of no less than 90% of the as-manufactured values.

References

1. Johnson, J., *Project Description, Trachea Grant Proposal*, NSF, Submitted 2013.
2. United Network for Organ Sharing, *National Data Report, Organ Procurement and Transplantation Network, Lung Datasource*, 2012.