3D Printed Scaffolds for Tracheal Tissue Engineering Using Novel Polymers

Anna Johnston[1,2,3], James O'Connor[3,4], Viviane Chiaradia[3,5], Andreas Heise[3,5], Karen Redmond[4], Sally-Ann Cryan[1,2,3]

[1]School of Pharmacy and Biomolecular Sciences, RCSI, Dublin, Ireland [2]Tissue Engineering Research Group, RCSI, Dublin, Ireland [3]CÚRAM, Research Ireland Centre for Medical Devices, University of Galway, Ireland, [4]Mater Misericordiae University Hospital Dublin, [5]Department of Chemistry, RCSI, Dublin, Ireland

INTRODUCTION

There are several ways to develop airway trauma including congenital abnormalities, traumatic injury and tumours. While small airway trauma can be surgically repaired relatively easily, major trauma remains difficult to treat. The main treatment options currently available are transplants and prosthetic devices, both of which are often associated with poor outcomes including stenosis, migration and infections. Therefore, there is a clinical need for better tissue engineered tracheal scaffolds.

There has been limited work on these implantable scaffolds to date, and more advanced materials, biofabrication methods and pre-clinical models are required for tissue-engineered airway repair. 3D printing is widely used for scaffold fabrication, but commonly used polymers such as polycaprolactone (PCL) exhibit low bioactivity and slow degradation, limiting their suitability for tissue-engineering applications.

We are developing a 3D printed tubular scaffold using PCL as well as investigating novel polymer (P_1) that has demonstrated higher bioactivity than PCL *in vitro*. The scaffolds consist of a 3D printed polymer tubular backbone (with an inner diameter of 12mm and an outer diameter of 16mm) combined with collagen and hyaluronic acid (Co-HyA). The scaffolds can be combined with spatially selective cell seeding to produce implantable scaffolds with an epithelial layer on the inner lumen[1].

To asses the potential of these scaffolds we have carried out early pre-clinical testing in a 20kg porcine *ex-vivo* lung perfusion (EVLP) model[2].

METHODS

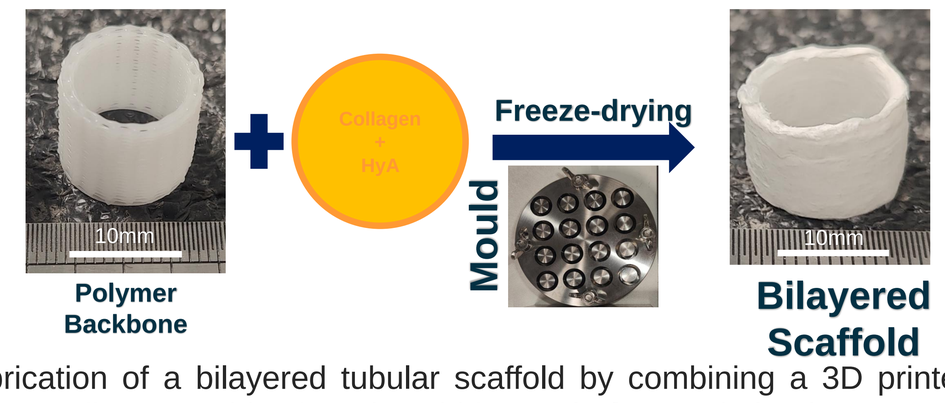


Figure 1 Fabrication of a bilayered tubular scaffold by combining a 3D printed polymer (PCL) backbone with a collagen and hyaluronic acid layer via freeze-drying in a custom stainless steed mould.

A previously developed fabrication protocol (**Figure 1**) consisted of combining a 3D printed PCL backbone with Co-HyA acid via freeze drying in a custom stainless steel mould, with an additional Co-HyA film on the inner lumen to produce a bilayered scaffold.

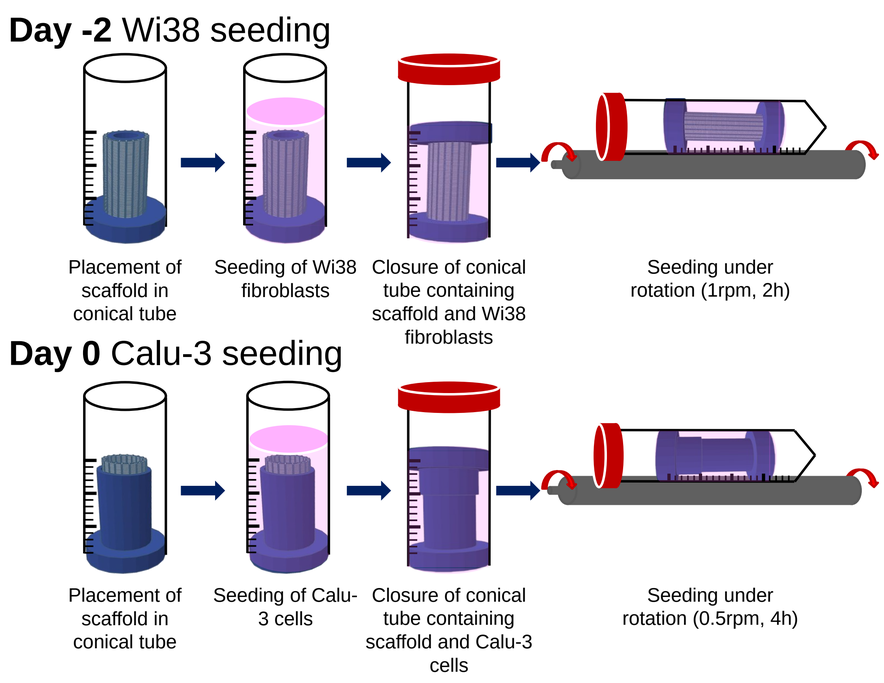


Figure 2 3D printed accessories were used to achieve spatially selective seeding of Wi38 fibroblast onto the outer layer and Calu-3 epithelial cells onto the inner layer of the scaffold

Fabrication was scaled up to produce scaffolds with an inner diameter of 12mm and an outer diameter of 16mm, in order to add the scaffolds to the EVLP model.

3D printed accessories were used to achieve spatially selective seeding of Wi38 fibroblasts onto the outer layer and Calu-3 epithelial cells onto the inner layer of the bilayered scaffolds (**Figure 2**)**.** This resulted in an epithelial-like layer in the inner lumen of the tubular scaffold.

RESULTS

Scaled-up scaffolds were successfully fabricated and implanted into a porcine EVLP model (**Figure 3**). After 24 hours of perfusion, blood gas and air leak measurements compared to intact controls showed no major air leaks or changes in gas composition, indicating preserved airway function (**Figure 4**)**.** The scaffolds were mechanically robust and tolerated surgical handling and *ex-vivo* implantation. Scale-up of the spatially selective cell seeding is ongoing, and preliminary results have shown that P_1 supports higher Wi38 and Calu-3 activity than PCL.



Figure 3 20kg porcine EVLP model with cartilaginous tracheas replaced with tubular PCL Co-HyA scaffold.

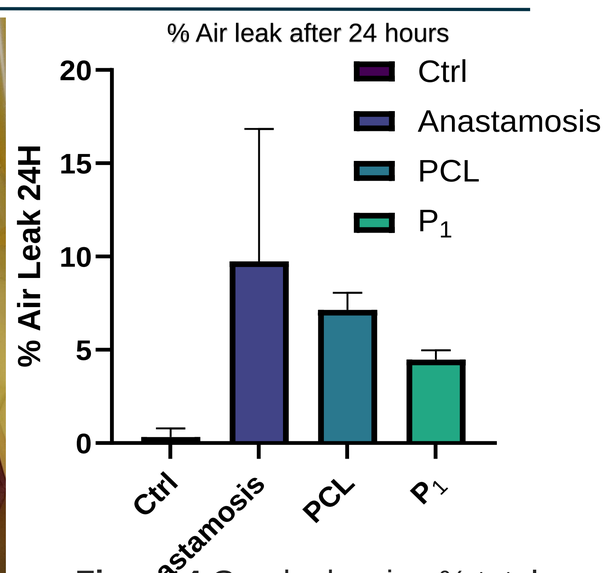


Figure 4 Graph showing % total air leak from the EVLP system after 24 hours with either no defect (control) or with the cartilaginous portion of the trachea replaced with PCL or P_1 (n=2).

CONCLUSIONS

This work demonstrates the feasibility of scaling 3D printed tubular tracheal scaffolds to clinically relevant dimensions and evaluating them in an EVLP model. Early findings support further investigation of P1 as a promising alternative to PCL and establish a reproducible workflow integrating 3D printing, composite biomaterials and spatially selective cell seeding.

ACKNOWLEDGEMENTS

Funding for this research was provided by Research Ireland and the European Regional Development Fund (Grant Number 13/RC/2073 & 13/RC/2073_P2)

REFERENCES

1 Soriano (*et al.*), ACS Biomaterials Science & Engineering 11(9): 5293-5305, 2025.
2 Prasad (*et al.*) Transplantation 105(5): 979-85, 2021
3 Soriano (*et al.*) European Respiratory Review 30 (162), 2021