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WFIRM scientists push bioprinting capability forward

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Wake Forest Institute for Regenerative Medicine (WFIRM) scientists are the first to report using bioprinting to print a tracheal tissue construct comprised of multiple different functional materials. They printed different designs of smooth muscle and cartilage regions in artificial tracheal substitutes showing similar mechanical properties to human tracheal tissue.

Previous attempts of tissue engineered tracheal constructs have presented many different limitations, mainly because they focused only on using regenerated cartilage tissue. The WFIRM tracheal constructs are novel in that they were bioprinted with separate cartilage and smooth muscle regions at the same time using a biodegradable polyester material and hydrogels containing human mesenchymal stem cells which can self renew and can become a variety of cell types. In this case, the stem cells differentiated into two different cell types—chondrocytes and smooth muscles cells—in different regions of the bioprinted tracheal constructs. The cartilage portion is stiff to provide mechanical support to avoid collapse while the smooth muscle is pliable and connects the ends of the cartilage rings, allowing sufficient flexibility for airway contraction.

"People have tried other materials, but the problem has been they were using just one material that is not strong enough to hold the airways open and does not provide the flexibility needed. Our bioprinting method provides a combination of flexibility and strength needed to mimic native tracheal tissue," said Sean Murphy, Ph.D., lead author and assistant professor of regenerative medicine at WFIRM.

The trachea is a hollow tube that is made of cartilage and smooth muscle tissue designed to allow a flexible airway that resists collapse. Tracheal stenosis is the abnormal narrowing and stiffening of the trachea, which can be caused due to prolonged intubation, inflammation and trauma or it can be a congenital abnormality. The primary treatments for the condition, which is rare but life threatening, are surgical interventions that have challenges and limitations.

For this study, published online in the journal *Biofabrication*, the research approach combines three tailored technologies: patient specific medical imaging, hydrogels designed to drive differentiation of stem cells, and polymeric scaffolding mimicking specific biomechanical properties.

Murphy said the approach was to incorporate softer hydrogels containing stem cells into the pores of the bioprinted tracheal structures. "We already knew we could differentiate these cells in 2-D into smooth muscle or cartilage, but the question of whether we could do that in bioprinted 3-D constructs remained," he said. "We added growth factors to help give them the extra push they needed."

"This early proof-of-concept study shows that we can streamline bioprinting capabilities and could someday provide the opportunity for regenerative medicine treatments for the replacement of damaged or diseased tracheal regions," said Anthony Atala, M.D., director of WFIRM and co-author of the paper. "Next steps in the research would be to evaluate long-term function to ensure appropriate tissue formation and strength retention."

More information: Dongxu Ke et al, Bioprinted trachea constructs with patient matched design, mechanical and biological properties, *Biofabrication* (2019). DOI: 10.1088/1758-5090/ab5354