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Tensile modulus mismatch may contribute to graft failure.

Tracheal replacement scaffolds implanted in compassionate use cases have supraphysiologic mechanical properties. Mechanical incompatibility has been implicated as a mechanism of graft failure. Radial testing does not adequately replicate the forces exerted on the trachea in vivo. We have created an ex vivo model that recapitulates physiologically relevant force applications, which will be used to determine the mechanical properties of a tissue engineered trachea (TETG)-human trachea composite.

Methods

Scaffolds (3.5 cm length / 2 cm outer diameter) were electrospun from a blend of 80% polyethylene terephthalate 20% polyurethane with 3D printed polycarbonate rings. Fiducial markers were placed along the scaffold and trachea at 5 points (Figure 1). Tracheas and trachea scaffolds were tested separately in medial-lateral (ML) and anterior-posterior (AP) compression (p<0.05) of 25% of their total diameters using a servohydraulic materials test frame [588 Bionix, MTS Corp., Eden Prairie, MN (MTS)] (Figure 2). TETG-human trachea* composites were then tensile tested to failure using the MTS (Figure 1). TEMA motion and Microsoft excel software were used to analyze stretch burden using the coordinates of fiducials and the MTS (Figure 1). TEMA motion software showed that the anastomotic region experienced 41% of the total strain of the construct (data not shown).

Results

The max load to 25% radial compression was 2.12±0.23 N for human trachea and 32.8±30.8 N for TETGs for the ML direction, and 5.03±1.40 N for human trachea and 104.4±13.07 KPa (average±SD), at the anastomosis in all specimens (Figure 4). An ANOVA showed that the variance in tensile testing was different than the variances from radial compressive testing (p<0.05).

Analysis of marker movement using TEMA motion software showed that the anastomotic region experienced 41% of the total strain of the construct (data not shown). An ANOVA showed that the variance in tensile testing was different than the variances from radial compressive testing (p<0.05).

Discussion

Stenosis is the leading cause of failure in tissue engineered tracheas. Stenosis results in increased wall shear stress and decreased flow velocity across tissue engineered tracheas, which is correlated with increased presence of respiratory distress symptoms. Stenosis may be managed via bronchoscopic dilation and stenting. One of the mechanisms of stenosis may be mechanical incompatibility. This study was conducted to define the mechanical properties of a scaffold–trachea construct to inform efforts to improve scaffold integration.

There was significantly higher variance in the tensile properties of the scaffold–trachea composites compared to the compressive properties of human tracheas. Motion analysis determined that the fiducial markers on the graft moved less than the markers on the trachea. Thus, tensile modulus mismatch may contribute to graft failure, leading to stenosis and delayed epithelialization. It is necessary to continue to explore the viability in tensile properties of the human tracheas as it relates to implantation of tissue-engineered constructs and to focus on the mechanics at the anastomosis. Furthermore, the substantial variance in human trachea properties could signify the need for patient-based scaffold design.

I am looking to expand this study to investigate how scaffold mechanical properties affect stenosis in airway reconstructive procedures.