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Development of a Patient Specific Artificial Tracheal Prosthesis: Design, Mechanical Behavior Analysis and Manufacturing

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Abstract — **There is a need to create patient specific organ replacements as there are differences in the anatomical dimensions among individuals. High failure rates in tracheal prosthesis are attributed to the lack of mechanical strength and flexibility, slow rate of growth of ciliated epithelium and leakage of interstitial fluid into the lumen. This paper proposes a methodology of design, simulations and fabrication of a patient specific artificial tracheal prosthesis for implantation to closely mimic the biomechanical properties of the natural trachea, and describes the prototype device and its materials. Results show that the patient-specific trachea prosthesis has mechanical properties approximate that of normal tracheal rings. The user centric tracheal prosthesis is demonstrated to be a promising candidate for tracheal replacement.**

I. Introduction

There is a need in the medical and healthcare industry to create patient specific organ replacement devices due to anatomical differences dimensions between individuals. Currently, the sole curative treatment for severe tracheal carcinoma is resection. However, resection length is limited to 6cm in adults and longer resections would require a viable tracheal replacement [1]. Although over the years, numerous types of trachea replacements have been studied and proposed [2, 3] they have a low success rate. High failure rates are attributed to the inability of the implanted prosthesis to regenerate ciliated epithelium in the lumen [4], failure due to inadequate and mismatched mechanical properties like flexibility and strength between the prosthesis and native tracheal tissues and leakage of interstitial fluid into the lumen.

Quick epitheliazation of the lumen in less than 8 weeks is paramount in preventing the formation of granulation tissues and ensuring the success of the implant. The migration of the ciliated epithelium originates from the native trachea at the anastomoses sites [5], therefore sufficient angiogenesis and vascularization is required throughout the prosthesis to support the epithelium growth. It has also been established by many studies that the prosthesis should consist of non-biodegradable components to provide permanent mechanical stability and biodegradable components like collagen to act as a temporary space filler for tissues in-growth [4, 6, 7].

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This paper proposes a methodology of design, simulations and fabrication of a patient specific artificial tracheal prosthesis for implantation that can closely mimic the biomechanical properties of the natural trachea. The design, materials and fabrication methodology of this prosthesis will be discussed in Section II. The finite element simulation study to analyze the stress behavior of the patient specific prosthesis will be discussed in Section III. Section IV will present and discuss the results obtained from the simulation study, followed by a conclusion in Section V.

II. Materials and Methods

In this section, the design, materials and manufacturing process of a patient specific tracheal prosthesis is presented. The prosthesis consists of multiple materials (Fig 1). Its constituents include a non-biodegradable Poly-di-methyl-siloxane (PDMS) skeletal structure that is surrounded by degradable Type I collagen sponge matrix that is loaded with vascular endothelial growth factor (VEGF) protein.

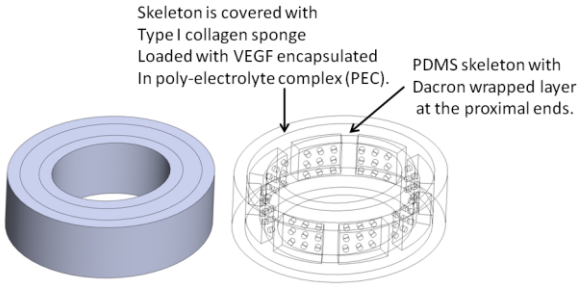


Figure 1: An isometric solid (left) and wireframe (right) view of the overall tracheal prosthesis.

A. Prosthesis Design

The design and dimensions of the PDMS scaffold is crucial as it is a permanent fixture that serves as a mechanical backbone to replace the excised cartilage rings. Its design should also consider the ease of manufacturability. It also should be porous to allow for tissue in-growth and angiogenesis. The final design of the tubular elliptical PDMS prosthesis can be found in Fig 2. Based on the collated 2D images of the patient, the geometry of the diseased portion to be excised is used to determine the dimensions of the prosthesis Fig 3. As the natural cartilage rings are almost elliptic in shape, the radius of the major and minor axis can be approximately measured from average of the inner and outer circumference of the D-shaped ring.

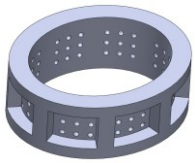


Figure 2: An isometric view of the non-degradable PDMS skeleton design.

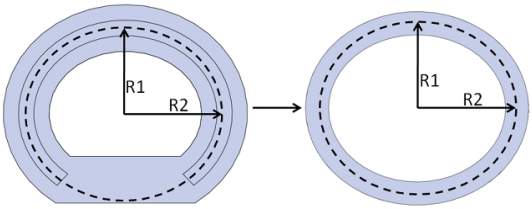


Figure 3: Radius of major and minor axis of the patient's native tracheal rings (left) used to determine the dimensions of the elliptical PDMS skeleton (right).

B. Materials

The material chosen for the non-degradable skeleton of the prosthesis is PDMS due to the similarity in mechanical properties to the native tracheal rings and its biocompatibility. The Young's Modulus and Poisson ratio of PDMS (*Sylgard*® 184 Silicone Elastomer) in 5:1 ratio has a value of 3.588MPa and 0.45 respectively [8, 9] which is closely matched to that of the cartilage rings which are 3.33MPa and 0.49 respectively [10]. Hence, it allows for a certain degree of bending and stretching while providing sufficient structural strength.

The degradable portion consists of a 2mm thick layer of Type I collagen sponge on both sides of the PDMS. Type I collagen been shown to promote the differentiation of tracheal ciliated epithelium [11], while serving as a temporary matrix for the in-growth of cells and blood vessels into the prosthesis. It also renders the device air tight when soaked in the patient's blood prior to implantation.

The collagen matrix is loaded with the protein VEGF before implantation to stimulate and accelerate the in-growth of blood vessels and cells into the prosthesis hence providing a suitable environment for the migration of ciliated epithelium from the distal ends. The VEGF may be encapsulated in Poly Electrolyte Complex (PEC) to prolong its lifespan in vivo. The collagen matrix will degrade gradually to make space for more tissue in-growth, until the entire PDMS scaffold is covered by the regenerated tracheal membrane tissues.

C. Fabrication Methodology

The design of the non-biodegradable PDMS scaffold has taken into account the mode of its fabrication via mold forming. A mold for the PDMS was designed (Fig 4) according to the final PDMS skeletal dimensions and fabricated by rapid prototype. The design of the mold is such that it is easily dismantled to facilitate easier removal of the cured PDMS. Sylgard 184^{TM} pre-polymer was combined with its curing agent in a 5:1 ratio and thoroughly mixed to achieve optimal strength. The mixture was then poured into the base mold and left in a vacuum oven for 20 minutes to remove any trapped bubbles which could affect the mechanical properties of the final product. The top cover of the mold was then assembled carefully into the base mold to avoid the formation of any new bubbles and left to cure in the oven (70^0C) for 8 hours to obtain the product (Fig 5).

A second mold made of aluminum was fabricated for the formation of the Type I collagen sponge matrix around the scaffold. The width of the hollow section of the mold was determined to ensure 2mm thickness of the collagen matrix on both sides of the skeleton. The cured PDMS scaffold was placed into the hollow region of the mold. Type I collagen (porcine) solution was dissolved in aqueous hydrochloric acid (pH 3) to give a final concentration of 1% by weight [4]. This was followed by homogenizing of the solution at 8000rpm for 15 minutes. The solution was then poured carefully into the mold cavity containing the scaffold and the entire mold was placed into a freeze drier at -80^{o}C. After which, the mold was placed into a vacuum oven at 140^{o}C for 12 hours for cross linking to occur. Upon completion, the artificial tracheal (Fig 5) was removed and sealed in an air tight plastic packaging for storage.

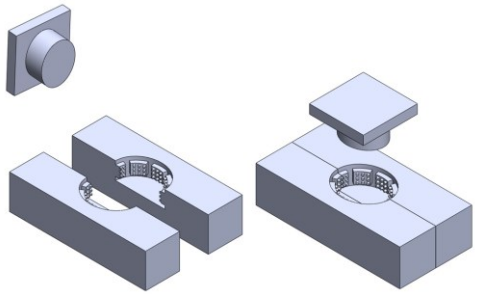


Figure 4: CAD model of the mold design for rapid prototyping. It consists of a separable base and a top to facilitated easy removal of the molded PDMS.

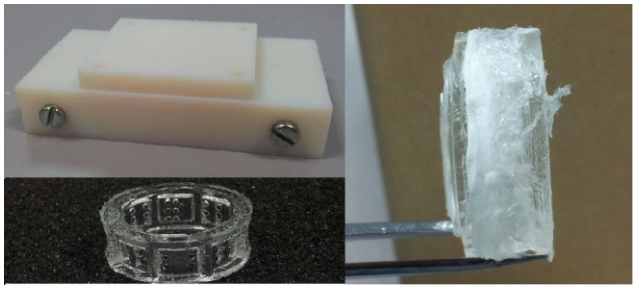


Figure 5: The three part mold held together by screws and nuts (top) and the molded porous PDMS skeleton after the curing process (bottom). Final collagen sponge coated PDMS product (right).

III. SIMULATION

This section provides a methodology for the evaluation of the designed tracheal prosthesis in a simulated patient specific tracheal environment. A related work was done by Palomar, *et al.* [12] in utilizing a computer simulation to predict the mechanical consequences of implanting a tracheal stent in 3D constructed patient trachea. This paper however simulates the daily tracheal motions of bending and stretching on the implanted prosthesis which have been

embedded in the space previously occupied by the diseased cartilage rings.

A 3D patient specific tracheal model was created using volume images captured from the patient's trachea via clinical devices such as CT in the axial direction. These captured images were processed and reconstructed in computer aided design (CAD). The tracheal model constructed for the purpose of this simulation is 58mm long and has 10 cartilage rings, each of 4mm thickness with a spacing of 2mm between rings. The trachea consists primarily of 2 different tissues, namely the membranous tissues and the cartilage rings, each with their own different biomechanical properties and behaviors.Although recent research has utilized the elastic Neo Hookean model for tracheal cartilage behavior and Holzapfel strain energy of two orthogonal families of collagen fibers for the membranous tissue [10], these models were invalid for a 3D solid tracheal model undergoing motions due to their inherent assumptions of incompressibility. The adopted model in this paper assumes the mechanical properties of the cartilage ring to be homogenous [10] and linearly elastic for strains of up to 10% with minimal residual strains [13]. For the model of the mucosa membrane, literature research [14] has shown that the membrane behaves differently in the longitudinal and transverse directions, hence the membrane was modeled as an orthogonal behavioral material with different properties in all three principle axis according to values from [14]. The values used are as follows:

Trachea cartilaginous rings		
E = 3.33MPa	υ = 0.4	
Mucosa membrane		
E_{xx}(longitudinal)=0.36MPa	G_{xy}=0.124MPa	υ_{xy}=0.45
E_{yy}(transverse)=0.3MPa	G_{xz}=0.124MPa	υ_{xz}=0.375
E_{zz}(radial)=0.3MPa	G_{yz}=0.124MPa	υ_{yz}=0.375

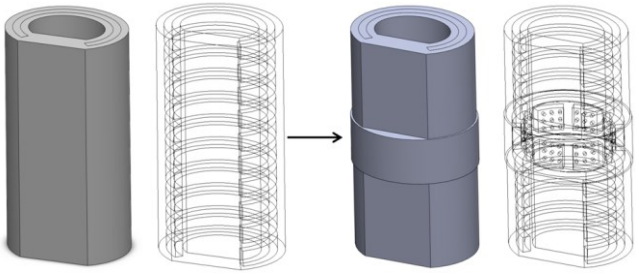


Figure 6: The 3D natural tracheal model with 10 rings (left) and augmented tracheal model with 5th and 6th rings replaced with the prosthesis (right).

Using Solidworks™ assembly module, the 5th and 6th cartilage rings from the tracheal model were removed and replaced with the designed scaffold (Fig 6). For comparison purposes, circular shaped and elliptical shaped prostheses were designed. The assembly was then subjected to stretching and bending motions in COMSOL™ Multi-physics to study the stress concentrations in the different regions during daily motions of the trachea (Fig 7) and results are presented in Section IV. Longitudinal stretching by 10% strain (due to swallowing) and sideways bending in the Y and Z directions (due to head movements) were simulated on both natural and augmented tracheal models to study the stress effect of the prosthesis on surrounding membrane and cartilage rings. Maximum stress concentration values were taken from the surrounding membrane and from the closest cartilage ring.

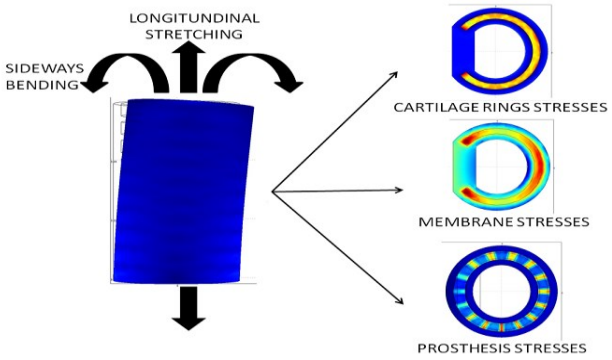
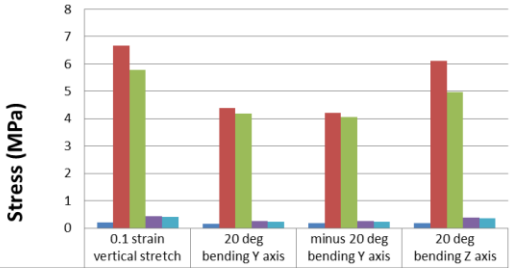


Figure 7: Longitudinal stretching and sideways bending of the model in COMSOL™ Multi-physics to study the resultant stress concentrations in the cartilage rings, membrane and prosthesis.

IV. Results and Discussion

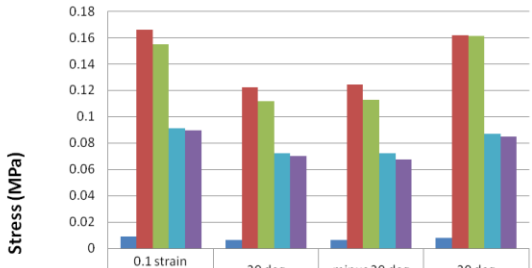
Stress Results for Different Implants in Tracheal Motion Simulation



	0.1 strain vertical stretch	20 deg bending Y axis	minus 20 deg bending Y axis	20 deg bending Z axis
Natural Cartilage Ring	0.2	0.166	0.168	0.167
316L Stainless Steel Implant	6.67	4.38	4.215	6.112
316L User Centric Stainless Steel Implant	5.773	4.186	4.066	4.97
PDMS 3mm thick	0.442	0.2615	0.256	0.372
PDMS User Centric Implant	0.401	0.24	0.24	0.349

Figure 8: Table of values of the effect of different prosthesis on the maximum stress concentration of the prosthesis under different conditions.

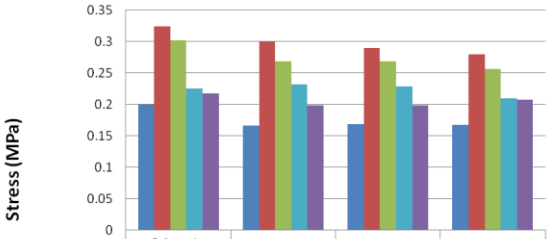
Membrane Stress Results for Different Implants in Tracheal Motion Simulation



	0.1 strain vertical stretch	20 deg bending Y axis	minus 20 deg bending Y axis	20 deg bending Z axis
Natural	0.00922	0.006578	0.006641	0.008
316L Stainless Steel Implant	0.1661	0.1222	0.1245	0.162
316L User Centric Stainless Steel Implant	0.1551	0.1117	0.1128	0.1614
PDMS 3mm thick	0.09131	0.07248	0.07242	0.08701
PDMS User Centric Implant	0.0894	0.07013	0.06767	0.085

Figure 9: Table of values of the effect of different prosthesis on the maximum stress concentration of the membrane under different conditions.

Cartilage Rings Stress Results for Different Implants in Tracheal Motion Simulation



	0.1 strain vertical stretch	20 deg bending Y axis	minus 20 deg bending Y axis	20 deg bending Z axis
Natural	0.2	0.166	0.168	0.167
316L Stainless Steel Implant	0.3241	0.2991	0.2892	0.2799
316L User Centric Stainless Steel Implant	0.3012	0.2682	0.2686	0.2562
PDMS 3mm thick	0.2246	0.2314	0.228	0.2099
PDMS User Centric Implant	0.2169	0.1988	0.199	0.2077

Figure 10: Table of values of the effect of different prosthesis on the maximum stress concentration of cartilage rings under different conditions.

The maximum stress values in the three respective regions were collated and presented in Figure 8, 9 and 10. From the results, a significant reduction in stress concentration of the implant and between the surrounding tissues was observed when PDMS was used instead of 316L Stainless Steel, which is a popular implant material in tubular organs. Therefore, PDMS was confirmed to be the material of choice for the skeleton due to closer similarities in stress concentration values to the native tracheal rings and membrane. Furthermore, the data also pointed out a reduction in stress concentrations when user centric elliptical dimensions were used rather than a circular geometrical shape for both 316L Stainless Steel and PDMS material. This simulation study shows that prosthesis that are subjected to dynamic motions in the body should be designed as closely as possible in terms of shape and dimensions to the native tissue being replaced, as it better mimics the natural biomechanical properties. Possible applications of this designing process could be in other tubular organs like blood vessels, intestines and the esophagus.

V. Conclusion

The proposed patient specific elliptical design of the PDMS skeletal prosthesis for tracheal replacement has been shown to be able to closely mimic the biomechanical properties of the natural tissue. The proposed fabrication methodology and mold design also allows for quick and simple production of the tracheal prosthesis of various sizes. In-vitro and in-vivo testing of the device will be done to assess its effectiveness to regenerate the epithelium. This methodology of the creation and assessment of prosthesis is also applicable in other tubular organ replacement applications.

References

[1] P. Macchiarini, P. Jungebluth, T. Go, M. A. Asnaghi, L. E. Rees, T. A. Cogan, A. Dodson, J. Martorell, S. Bellini, P. P. Parnigotto, S. C. Dickinson, A. P. Hollander, S. Mantero, M. T. Conconi, and M. A. Birchall, "Clinical transplantation of a tissue-engineered airway," *The Lancet,* vol. 372, pp. 2023-2030.

[2] A. E. Doss, S. S. Dunn, K. A. Kucera, L. A. Clemson, and J. B. Zwischenberger, "Tracheal Replacements: Part 2," *ASAIO Journal,* vol. 53, pp. 631-639 10.1097/MAT.0b013e318145ba13, 2007.

[3] K. A. Kucera, A. E. Doss, S. S. Dunn, L. A. Clemson, and J. B. Zwischenberger, "Tracheal Replacements: Part 1," *ASAIO Journal,* vol. 53, pp. 497-505 10.1097/MAT.0b013e3180616b5d, 2007.

[4] M. Yamashita, S.-i. Kanemaru, S. Hirano, A. Magrufov, H. Tamaki, Y. Tamura, M. Kishimoto, K. Omori, T. Nakamura, and J. Ito, "Tracheal Regeneration After Partial Resection: A Tissue Engineering Approach," *The Laryngoscope,* vol. 117, pp. 497-502, 2007.

[5] H. Tsukada, S. Matsuda, H. Inoue, Y. Ikada, and H. Osada, "Comparison of bioabsorbable materials for use in artificial tracheal grafts," *Interactive CardioVascular and Thoracic Surgery,* vol. 8, pp. 225-229, February 1, 2009 2009.

[6] H. Shi, Z. Xu, X. Qin, X. Zhao, and D. Lu, "Experimental Study of Replacing Circumferential Tracheal Defects With New Prosthesis," *The Annals of Thoracic Surgery,* vol. 79, pp. 672-676, 2005.

[7] T. Nakamura, T. Sato, M. Araki, S. Ichihara, A. Nakada, M. Yoshitani, S.-i. Itoi, M. Yamashita, S.-i. Kanemaru, K. Omori, Y. Hori, K. Endo, Y. Inada, and K. Hayakawa, "In situ tissue engineering for tracheal reconstruction using a luminar remodeling type of artificial trachea," *The Journal of Thoracic and Cardiovascular Surgery,* vol. 138, pp. 811-819, 2009.

[8] A. Mata, A. Fleischman, and S. Roy, "Characterization of Polydimethylsiloxane (PDMS) Properties for Biomedical Micro/Nanosystems," *Biomedical Microdevices,* vol. 7, pp. 281-293, 2005.

[9] F. Schneider, J. Draheim, R. Kamberger, and U. Wallrabe, "Process and material properties of polydimethylsiloxane (PDMS) for Optical MEMS," *Sensors and Actuators A: Physical,* vol. 151, pp. 95-99, 2009.

[10] O. Trabelsi, A. P. del Palomar, J. L. López-villalobos, A. Ginel, and M. Doblaré, "Experimental characterization and constitutive modeling of the mechanical behavior of the human trachea," *Medical Engineering & Physics,* vol. 32, pp. 76-82, 2010.

[11] E. A. Davenport and P. Nettesheim, "Type I Collagen Gel Modulates Extracellular Matrix Synthesis and Deposition by Tracheal Epithelial Cells," *Experimental Cell Research,* vol. 223, pp. 155-162, 1996.

[12] A. Pérez del Palomar, O. Trabelsi, A. Mena, J. L. López-Villalobos, A. Ginel, and M. Doblaré, "Patient-specific models of human trachea to predict mechanical consequences of endoprosthesis implantation," *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences,* vol. 368, pp. 2881-2896, June 28, 2010 2010.

[13] J. K. Rains, J. L. Bert, C. R. Roberts, and P. D. Pare, "Mechanical properties of human tracheal cartilage," *Journal of Applied Physiology,* vol. 72, pp. 219-225, January 1, 1992 1992.

[14] P. A. Sarma, R. M. Pidaparti, and R. A. Meiss, "Anisotropic properties of tracheal smooth muscle tissue," *Journal of Biomedical Materials Research Part A,* vol. 65A, pp. 1-8, 2003.