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# Estimation of the Young's moduli of fresh human oropharyngeal soft tissues using indentation testing

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ABSTRACT

Finite element (FE)-based biomechanical simulations of the upper airway are promising computational tools to study abnormal upper airway deformations under obstructive sleep apnea (OSA) conditions and to help guide minimally invasive surgical interventions in case of upper airway collapse. To this end, passive biomechanical properties of the upper airway tissues, especially oropharyngeal soft tissues, are indispensable. This research aimed at characterizing the linear elastic mechanical properties of the oropharyngeal soft tissues including palatine tonsil, soft palate, uvula, and tongue base. For this purpose, precise indentation experiments were conducted on freshly harvested human tissue samples accompanied by FE-based inversion schemes. To minimize the impact of the probable nonlinearities of the tested tissue samples, only the first quarter of the measured force-displacement data corresponding to the linear elastic regime was utilized in the FE-based inversion scheme to improve the accuracy of the tissue samples' Young's modulus calculations. Measured Young's moduli of the oropharyngeal soft tissues obtained in this study are presented. They include first estimates for palatine tonsil tissue samples while measured Young's moduli of other upper airway tissues were obtained for the first time using fresh human tissue samples.

## 1. Introduction

Obstructive sleep apnea (OSA) is a common clinical entity characterized by recurrent episodes of upper airway collapse that is associated with a number of negative health effects such as poor cognition, diminished memory recall and attentiveness, often leading to reduced professional efficiency (Quan et al., 2006; Ip et al., 2002; He et al., 1988). If left untreated, OSA may contribute to further complications such as hypertension, cardiovascular diseases, and metabolic dysfunctions (Punjabi, 2008). Abnormal upper airway anatomy is the prime etiology of the disease and multiple surgical techniques have been developed to treat OSA. Surgery should ideally target patient-specific areas of upper airway collapse, yet identifying these areas precisely is exceedingly difficult. For example, bedside clinical assessment is often challenging with high intra-patient and inter-rater variability (Rodriguez-Bruno et al., 2009; Golbin et al., 2016) while other sleep assessments such as drug-induced sleep endoscopy are costly from a healthcare resource standpoint (Golbin et al., 2016). Therefore, preoperative computer modeling may offer a potentially novel and cost-effective alternative to help guide therapeutic interventions.

Finite-element (FE) simulations and biomechanical modeling have been applied as powerful methods to simulate the biomechanics of the upper airway to elucidate which anatomical sites are predisposed to airway collapse, paving the way for optimal surgical intervention (Malhotra et al., 2002; Xu et al., 2009; Huang et al., 2005; Huang, 1995; Huang and Williams, 1999). In several FE studies, some oropharyngeal subsites are idealized as linear elastic materials. For such materials, the Young's modulus which characterizes the mechanical behavior of the material is required for modeling purposes. In particular estimates of the Young's moduli of critical subsites of the upper airway including the uvula, soft palate, base of tongue, and palatine tonsils are required (Malhotra et al., 2002; Xu et al., 2009; Huang et al., 2007).

Aside from FE modeling, independent Young's moduli estimates are also required for elastography, an image-based technique used to estimate mechanical properties such as the Young's modulus. Elastography is an emerging approach for cancer diagnosis and treatment

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monitoring. Shear wave elastography has been recently used in the area of oropharyngeal cancer for radiotherapy outcome assessment (Kałużny et al., 2014). Interpreting such elastography images requires comparison of the image data against a database of reliable Young's moduli values for various types of upper airway tissues, including normal and pathological cases.

The literature contains estimates of Young's modulus for some, but not all of the upper airway subsites. For instance, values have been estimated for the uvula and soft palate (Birch and Srodon, 2009; Sériès et al., 1999), but none have been published for the palatine tonsils or tongue base. The literature also contains other Young's modulus estimates based on methodologies and experimental setups that involve significant uncertainties (Malhotra et al., 2002; Payan et al., 1998). For example, some estimates use an optimization framework which involves a detailed FE model of the *entire* upper airway where the Young's modulus values in the model are manually adjusted until the closing pressure obtained from the FE model matches experimentally measured values (Malhotra et al., 2002). Other than uncertainties associated with the FE model, these values are estimated from highly variable palate closing pressures (Malhotra et al., 2002). Other groups obtained Young's modulus estimates for the uvula by testing *ex vivo* tissue specimens using uniaxial testing, which is known to involve fundamental issues due to strain and stress nonuniformity arising from specimen size or geometry (Sériès et al., 1999), while others obtained estimates from either cadaveric or animal histological specimens (Birch and Srodon, 2009). Reliable stiffness parameter estimates of fresh human upper airway tissues are lacking.

As noted, the Young's modulus can be measured using a direct method such as uniaxial testing (Miller and Chinzei, 1997). This method generally requires significantly large specimens with regular geometry to ensure strain and stress uniformity throughout the tissue specimen volume which is necessary to achieve reliable Young's modulus estimates. However, surgical specimens derived from oropharyngeal procedures yield only small samples which cannot be cut into a regular shape for testing, thus precluding the possibility of using this method. However, indentation techniques developed previously (Krouskop et al., 1998; Samani et al., 2003; Samani and Plewes, 2007), can be utilized for a more accurate measurement of the Young's modulus. This technique is suitable for testing small tissue specimens acquired from surgery and is much less sensitive to the specimen's shape. As a result, the purpose of our study was to estimate the Young's modulus of four tissue types found within the upper airway: the uvula, soft palate, palatine tonsils, and base of tongue. Moreover, we endeavored to undertake this by using indentation methods on fresh human surgical specimens.

## 2. Methods

### 2.1. Specimen preparation

The tissue samples in this study were obtained from 13 patients who underwent OSA surgery. They consisted of 14 palatine tonsils, 5 soft palates, 5 uvula, and 3 tongue base specimens. Research ethics approval for the study was acquired from Western University Research Ethics Board and the participants provided informed consent in accordance with the terms of approval. For all patients involved in this study, the OSA surgery included tissue excision in all of the four upper airway subsites of palatine tonsils, soft palate, uvula and base of tongue. Small representative samples of the excised tissues were cut and placed into containers containing a solution of physiologic saline. The tissue specimens were at least 7.5 mm in diameter to gain accurate measurement using an indenter with a 1.5 mm diameter. This satisfies the condition of having a specimen-to-indenter diameter ratio of 5 which is necessary for having negligible displacement and strain in the specimens' lateral surfaces. The specimens were transported from the operating room to the mechanical testing laboratory immediately to undergo indentation testing. To obtain relatively uniform thickness, each sample was shaved off carefully using a sharp scalpel. Fig. 1 shows a palatine tonsil tissue specimen acquired from an OSA patient.

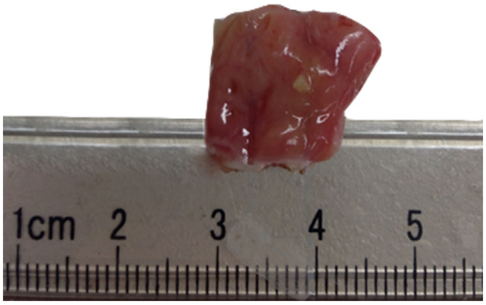

**Fig. 1.** A freshly excised palatine tonsil specimen photographed immediately before the indentation procedure.

### 2.2. Tissue indentation apparatus

In this study, a tissue indentation technique was used as the method of choice for measuring the stiffness of small tissue samples with complex geometry and boundary conditions. Unlike uniaxial testing, this technique does not assume uniform strain and stress conditions and, as long as the specimen-to-indenter diameter is larger than 5, it is insensitive to the specimen geometry. Another advantage of this technique is that, compared to uniaxial testing, it requires only a very small preload value to establish full contact between the indenter and specimen surface. This technique involves indenting the tissue using a plane ended or spherical indenter and acquiring resulting indentation force–displacement data followed by determining the tissue's stiffness parameters by processing these data (Samani et al., 2003; Samani and Plewes, 2007). Fig. 2 shows a schematic of the indentation system used in this study for acquiring tissue indentation force–displacement data. The system consists of four main components: tissue actuation and indentation displacement measurement, force measurement sensor (load cell), motion controller box, and a computer. The tissue actuation component is comprised of a cylindrical indenter attached to a servo motor (Model: LAL-30, SMAC, Carlsbad, CA, USA) with a motion range of 25 mm, resolution of 0.5 µm, and accuracy of 1 µm. The force measurement component consists of a load cell sensor (Model: LCL-113, Omega, Quebec, Canada) with 113 g full range capacity and 0.01 g sensitivity. The motion controller (6K2 motor controller, Parker Hannifin Corporation, Rohnert Park, CA, USA) is comprised of custom-made circuit boards which control the actuator's motion based on a user-defined computer program involving the user-defined motion profile and feedback from the load cell and servomotor. The computer

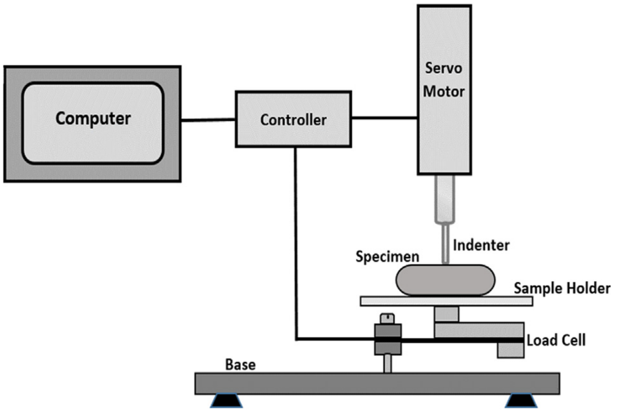

**Fig. 2.** Schematic of the indentation system used for acquiring tissue indentation force-displacement data.