The Pharynx and Scar Tissue

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Abstract

Modeling of the pharynx will require understanding how it functions in respiration, swallowing, and vocalization. Endoscopy and videofluoroscopy along with manometric measures have provided much of the information on how the pharynx functions. With the advent of newer imaging systems including optical coherence and cone beam computed tomography, more imaging data is becoming available. Many patients develop swallowing disorders after treatment of cancers of the throat so that the mechanical properties of scar tissue will be important to incorporate into the model.

1. The Normal Pharynx

The pharynx is an elongated tube that extends from the base of the skull to the beginning of the esophagus and trachea serving as a gateway to two systems: the gastrointestinal tract, and the respiratory tract. The pharynx extends from the nasal cavity caudally to the vocal cords that lie over the trachea and adjacent to this area is a sphincter of striated muscle that maintains a closed upper portal to the esophagus. Three circular muscles, defined as the constrictors, wrap around the pharynx.[1] Three muscles compose the inner muscular layer of the pharynx and include the stylopharyngeus, the palatopharyngeus, and the salptngopharyngeus. The pharynx is a complex and highly controlled region of the head and neck as it must function in normal breathing, transporting food and liquids to the esophagus while not breathing, and rapidly changing shape to provide the resonance that alters the sounds used in speech and vocalization (Figure 1). The pharynx is unique as it has three major constrictor muscles, which can powerfully force food through the pharynx into the esophagus during a normal pharyngeal swallow, but also has its anterior wall on the ventral side of the body partially determined by the tongue that occupies both the oral cavity and part of the pharynx. The position of the tongue can be changed by multiple muscles but the one protruding muscle, the genioglossus, is the key to bringing the entire tongue, and its posterior surface forward to establish a more patent airway. Muscles connect the base of the tongue to the hyoid bone so that the position of the hyoid bone can alter the tongue base as well as the pharyngeal lumen.

The neural control of the pharynx depends on specific cranial motor nuclei with motoneurons from the Nucleus ambiguus that innervate the pharyngeal muscles. These cranial motoneurons can be coordinated into activity by interneurons, which link synaptically to provide an integrated and sequential signal to different motoneuron pools in the cranial motor nuclei. The brain stem of the central nervous system contains several of these interactive groups, often defined as central pattern pacemakers. The central respiratory pathway is complex and has interneurons which induce inspiration by controlling the primary muscle, the diaphragm, but also synaptically control pharyngeal muscles during one of the two phases of respiration, inspiration or expiration.[2] The central respiratory pathway can become a dominant synaptic drive on motoneurons innervating pharyngeal muscles when respiration becomes impaired, or impedance to airflow increases too much. The body senses alterations in respiration primarily by sampling blood gas levels for carbon dioxide, and, secondarily, for oxygen so the hypercapnic and hypoxic conditions can lead to greater CNS respiratory control of pharyngeal muscles.

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Eating and drinking require the pharynx to switch from its active respiratory role, and when food reaches regions of the pharynx, it triggers the most complex all-or-none reflex of the body, which includes the tongue and pharynx in a coordinated pattern for about 1 second, defined as pharyngeal swallowing. This pharyngeal swallow includes inhibiting respiration, elevating the soft palate to close the nasopharynx, and adducting the vocal cords to prevent food entering or being aspirated into the trachea and reaching the lung alveoli. Swallowing occurs over 1000 times in a 24 hour period and requires the pharyngeal constrictor muscles to contract in sequence while the pharynx is raised by other muscles to engulf the food bolus that is powerfully ejected into the pharynx by the tongue completing a complex response.

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Vocalization in humans and other animals requires other regions of the CNS to be involved and includes some central pattern generators in the brain stem, as well as descending input from the higher cortical regions involved with eliciting sounds and speech. Vocalization also requires rapid contraction of pharyngeal muscles in coordinated sequences to change the shape of the pharynx as air is expelled pass the vibrating vocal cords to work with the tongue and lips to articulate various speech sounds.

2. Imaging the Pharynx During Function

Much of the previous understanding of the pharynx has been from excellent dissections of cadavers who have implied much of the function of the muscles by evaluating the origin and insertions of the muscles.[1] The vector of force generated by the muscle can be implied by the direction of the muscle fibers, but electromyography provides direct recordings of muscle fiber recruitment as in pharyngeal swallowing.[3; 4] Studies with multiple intramuscular electrodes while obstructing the nasal cavity in the anesthetized rhesus monkey indicates that different regions of the pharyngeal constrictor muscles are recruited during respiration but varies as to which site is active in inspiration or expiration.[2]

Physiological studies have been able to visualize the pharynx during some functions using endoscopy, and manometric and impedance studies have been able to demonstrate the pressure changes in the pharynx during swallowing.[5; 6] One of the more recent approaches to visualize function of the pharynx has been with optical coherence tomography (OCT) which combines interferometry with low-coherence light to produce high-resolution imaging.[7] This imaging can be used to follow changes in the shape of the pharynx during breathing, as well as providing input on the epithelium, basement membrane, ducts, glands, blood vessels, invasive cancer, and mature scar tissue.

3. Biomechanical Models of the Pharynx

Concepts of how the pharynx functions have been studied particularly in swallowing and speech. Direct endoscopic observations combined with other imaging techniques have offered much information on how the pharynx changes shape. Videofluoroscopy is one of the most effective methods to evaluate swallowing as one can visualize a lateral view of a radiopaque bolus developing in the oral cavity, partially spilling into the pharynx and reaching certain regions of the pharynx that trigger the pharyngeal swallow.[8; 9] The pharyngeal swallow has been divided into multiple stages but a panel of experts has provided the latest viewpoint on what is pharyngeal swallowing.[10]

One of the alternative approaches to defining pharyngeal swallowing is to evaluate it as biomechanical model in which the actions are seen as having a purpose with each of the movements.[11] Such studies have used three-dimensional approaches to show volume dependent changes on the mechanical movements of the tongue, hyoid bone, thyroid cartilage, epiglottis, and upper esophageal sphincter. Whatever model is used for pharyngeal swallowing, it has to be validated by comparing it to known bolus volumes and viscosities swallows, as defined with videofluoroscopy. Increasing the volume of the bolus significantly alters the bolus transit time as has been tested with 1, 3, 5, and 10-ml thin liquids as well drinking the thin liquids from a cup. Additional measures include 3-ml of pudding-thick barium, and one quarter of a Lorna Doone cookie coated with barium pudding to have the patients chew before swallowing.[12; 13]

4. Potential Impairments of the Pharynx to Model

4.1 Motor Impairments

Damage or impairment to the neural control of pharyngeal muscles or to the muscles, themselves, can decrease the strength of pharyngeal wall contraction. The larynx needs to be closed properly during pharyngeal swallowing to prevent aspiration. Laryngeal closure begins with the true vocal folds and progresses to the laryngeal entrance and the epiglottis. The most important point of closure is where the false cords close and the arytenoids tilt forward to meet the epiglottic base as the larynx elevates. Damage or impairment leading to weakness of contraction or paralysis of the thyrohyoid muscle can impair the elevation of the larynx during swallowing (1.5 cm in females, 2 cm in males). Another example of the affect of motor impairment is with the lower part of the superior pharyngeal muscle, also defined as the glossopharyngeus muscle. Weakness in this region results in less movement of the tongue base posteriorly toward the posterior pharyngeal wall. This leads to a residue of food remaining in the valleculae after a swallow, which can lead to potential aspiration into the lungs on the next swallow. [14]

4.2 Head and Neck Cancer and Modeling

Treatment of head and neck cancer, which includes the pharynx, is continually trying to improve the life expectancy of the patient, and much research evaluates the use of surgery, chemotherapy, and radiation.[15; 16] The treatment can impair swallowing and eating in a high percentage of patients, and, often, leads to extensive scarring with deterioration in swallowing for years with as high as over 60% of treated head and neck cancer patients remaining with permanent swallowing problems.[17; 18; 19] Damage to tissue normally leads to the body repairing the site with fibrous tissue as seen with skin, mucosa, muscle and the heart, but not bone. The body repairs by laying down new collagen but with less local blood supply for support. [20]

Scar tissue has different mechanical characteristics than the tissue in which it is embedded.[21; 22; 23] The mechanical properties indicate the resistance of the tissue to deform and can be expressed in terms of force/unit width (N/mm; Figure 2). Skin is anisotropic which may be true for the mucosa in the pharynx. Studies usually use a dc motor to apply a known extension rate to make this measurement (i.e., 0.35mm/s with a load of 100gm) to generate load-extension curves. Grading of scars on human skin correlate well with the measured mechanical properties so that the higher scar value gives higher values of modulus of elasticity (E) and lower values of strain (e) inferring the scar is stiffer and less extensible. This is different from normal skin in which the load-extension curve displays an initial compliant phase in which a large extension is developed by a low load (< 100gm/cm width). Elastin determines this compliance phase, while collagen resists stretching at the higher loads. A scar with a high score stiffens quickly with even the smallest loads. Linear stiffness of skin and scar tissue differ at high loads (80% of failure rate). Normal skin shows similar linear stiffness in either the axial or transverse direction.[23] However, scar tissue demonstrates significantly higher linear stiffness in the axial direction than the transverse.

Experimentally induced scars have been studied in the rat palate. Strips of the scar tissue were removed to measure tensile strength as well as to obtain electron micrograph scans within 30 days after the operation. The EM scans showed that thick fiber bundles converged from the edge to the center of the wound. The mechanical properties of the tissue changed significantly in tensile strength, strain at failure as well as with the tangent modulus.[24]

A hypertrophic scar is actually a fibroproliferative disorder of the skin with increased collagen and other extracellular matrix proteins compared to normal tissue due to an imbalance between synthesis and degradation. Transforming growth factor Beta1 (TGF-B1) is a cytokine that modulates growth and differentiation of fibroblasts and is considered the key cytokine leading to excessive scar formation.[25] Much of the present studies in scar tissue are examining chemical pathways in which the imbalance in synthesis and degradation is corrected or modified to decrease the collagen tissue.

5. Rehabilitation and Modeling

Techniques to rehabilitate and improve swallowing often involve altering the mechanical position of the tongue and hyoid bone to enhance a weak pharyngeal swallow. Several exercise regiments are being used to improve poor pharyngeal swallowing. The exercises can improve swallowing, and take 2 weeks to 2 months to have an effect.[14] Resistance exercises used in which the tongue resists the pressure of a tongue blade or the Iowa Oral Pressure balloon does improve tongue strength and coordination, and this immediately improves swallowing.[26] There are three exercises to improve pulling the tongue base back and include having the patient repeatedly practice pulling the tongue back and holding with some effort for 1 second; or gargling and holding the tongue in the most posterior position for 1 second; or yawning and holding the tongue in the most posterior position.

5.1 Intraluminal Pressure and Esophageal Muscle Contractile Properties as Related to Modeling for the Pharynx

The mechanics of the swallowing process as assessed by manometry and videofluoroscopy can be used to suggest how muscles are contracting and developing forces. Models of esophageal wall muscle mechanics during bolus transport have been developed for circular and longitudinal muscles.[27; 28] Other models exist to provide a perspective of how mechanical forces are used to propel a bolus of food.[29; 30] Much of the present modeling of the pharynx will need to understand both the normal mechanics of swallowing and the affect of scar tissue that alters this mechanical action..

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Figures

Figure 1: Examples of three dimensional images obtained from a Hitachi MercuRay cone beam computed tomography scan. A: Segmentation of the mandible and airway of one human subject. B: Three dimensional image of one subject in which the software (CB Works 3.0, V Works, Seoul, Korea) allows color depiction of different CT units showing the skeleltal, facial, and airway strutures. C: Another three dimensional image using different colors to depict the different tissues and demonstrating the relationship of the airway to the mandible. D: A second type of scan in which the recording system does not move and depicts movement, which in this case is the swallowing of some barium liquid.

Figure 2: Hypothetical concepts of mechanical properties of pharyngeal mucosa with and without scar tissue: A: Stiffness with Modulus of elasticity (N/mm), and Extensibility (Strain percent) at a given load. B: Force-displacement for a tensile failure test

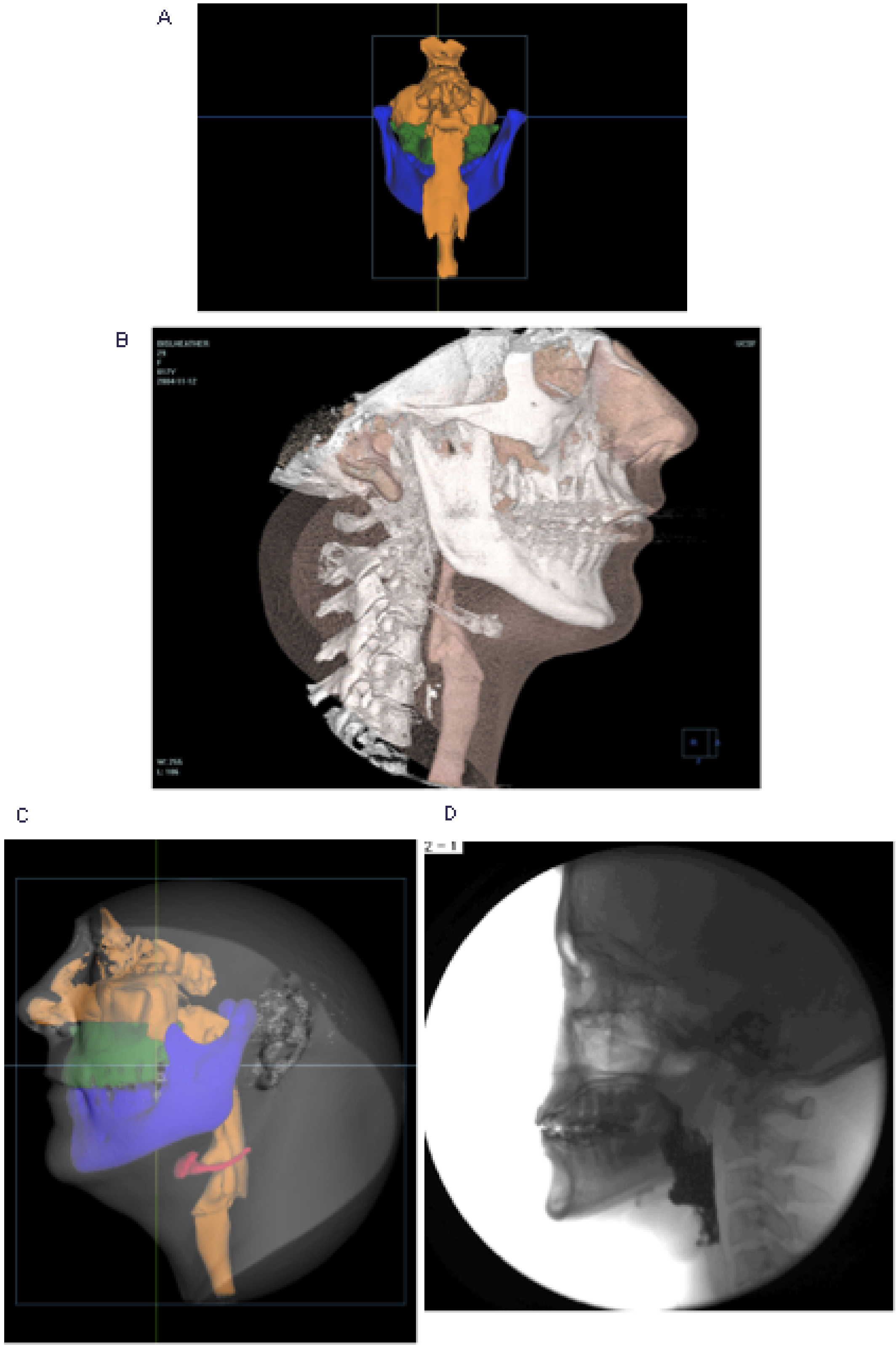

Figure 1

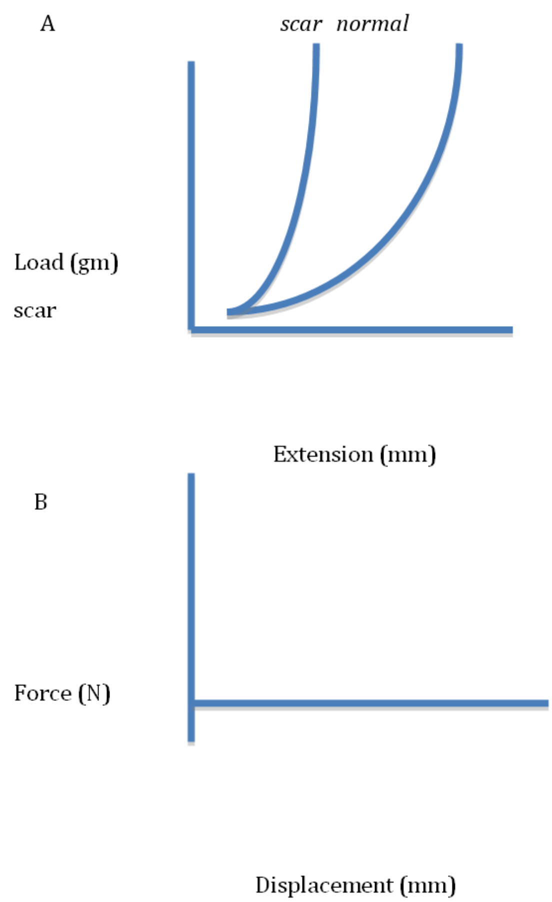
A
scar
normal
Load (gm)
scar
Extension (mm)
B
Force (N)
Displacement (mm)

Figure 2