Ultrasonics 75 (2017) 174–184

Contents lists available at ScienceDirect

Ultrasonics

journal homepage: www.elsevier.com/locate/ultras

Spatial distribution of airway wall displacements during breathing and bronchoconstriction measured by ultrasound elastography using finite element image registration

Brian C. Harvey [a,*], Kenneth R. Lutchen [a], Paul E. Barbone [b]

[a] Biomedical Engineering, Boston University, 44 Cummington Mall, Boston, MA 02215, USA
[b] Mechanical Engineering, Boston University, 110 Cummington Mall, Boston, MA 02215, USA

ARTICLE INFO

Article history:
Received 26 May 2016
Received in revised form 10 September 2016
Accepted 28 November 2016
Available online 29 November 2016

Keywords:
Elastography
Finite element method
Image registration
Airway smooth muscle
Deep inspiration
Bronchodilation

ABSTRACT

With every breath, the airways within the lungs are strained. This periodic stretching is thought to play an important role in determining airway caliber in health and disease. Particularly, deep breaths can mitigate excessive airway narrowing in healthy subjects, but this beneficial effect is absent in asthmatics, perhaps due to an inability to stretch the airway smooth muscle (ASM) embedded within an airway wall. The heterogeneous composition throughout an airway wall likely modulates the strain felt by the ASM but the magnitude of ASM strain is difficult to measure directly. In this study, we optimized a finite element image registration method to measure the spatial distribution of displacements and strains throughout an airway wall during pressure inflation within the physiological breathing range before and after induced narrowing with acetylcholine (ACh). The method was shown to be repeatable, and displacements estimated from different image sequences of the same deformation agreed to within 5.3 μm (0.77%). We found the magnitude and spatial distribution of displacements were radially and longitudinally heterogeneous. The region in the middle layer of the airway experienced the largest radial strain due to a transmural pressure (Ptm) increase simulating tidal breathing and a deep inspiration (DI), while the region containing the ASM (i.e., closest to the lumen) strained least. During induced narrowing with ACh, we observed temporal longitudinal heterogeneity of the airway wall. After constriction, the displacements and strain are much smaller than the relaxed airway and the pattern of strains changed, suggesting the airway stiffened heterogeneously.

1. Introduction

The lungs and branching network of airways are periodically stretched with every breath. The luminal diameter of an airway, which determines the resistance to flow, is believed to be determined as a dynamic equilibrium of the forces which favor narrowing and those that oppose narrowing [1]. Bronchoconstriction, as occurred during an asthma attack, is a result of active force generated by airway smooth muscle (ASM) embedded with an airway wall in response to acetylcholine (ACh) released from parasympathetic nerves. The forces of tidal breathing and deep inspirations (DIs) may work to mitigate this airway narrowing in healthy subjects through straining of the ASM [2]. This beneficial effect of a DI is absent in asthmatics [3–6] and it has been hypothesized that this is because asthmatic are unable to sufficiently strain their ASM during a DI which is indicative of airway wall properties that are stiffer and that can potentiate more reactivity.

While most researchers have focused on the effect of stretching of strips of isolated ASM, the airway wall is a construct comprised of several different components which together create a nonlinear, heterogeneous, thick-walled cylinder. In contrast to the results from isolated ASM strip experiments, recent studies performed on healthy airway segments suggest that transmural pressures simulating tidal breathing and DIs are ineffective at preventing future airway narrowing and only moderately effective at reversing induced constriction [7–10]. The heterogeneous composition and mechanical properties throughout an airway wall likely modulate the strain felt by the ASM. Therefore, understanding the spatial distribution of displacements and strains throughout the thickness of an airway wall could lead to better understanding of airway narrowing by elucidating contributions of different tissue types to the mechanical behavior of the airway, and the role that breathing and DIs play in modulating airway narrowing.

* Corresponding author.
E-mail addresses: brian.c.harvey@gmail.com (B.C. Harvey), klutch@bu.edu (K.R. Lutchen), barbone@bu.edu (P.E. Barbone).

http://dx.doi.org/10.1016/j.ultras.2016.11.023
0041-624X/

Elastography is a technique to image tissue based on contrast in mechanical properties [11]. In quasistatic elastography, a tissue is imaged before and after a force is applied and the resulting images are compared to estimate tissue deformation. These deformations are then visualized directly (e.g., strain imaging) or used to infer the mechanical properties of the tissue via modulus reconstructions [11–13]. The technique has been applied in a variety of tissues using many different image modalities such as ultrasound [14], magnetic resonance [15], and optical coherence tomography [16]. In this study, ultrasound imaging was utilized due to its high axial resolution and phase information, high frame rate, and availability. Elastography has many different applications [17] such as detecting breast tumors [18] and predicting plaques vulnerable for rupture in atherosclerosis [19,20], but has never been used to study the spatial distribution of displacements throughout an airway wall.

Many different approaches have been developed to estimate tissue motion from ultrasound image sequences. Among the most common is block matching using normalized cross-correlation [11]. In this approach, the motion within each block of pixels is assumed to be uniform. While the block matching method is computationally inexpensive and easy to implement, it performs poorly at estimating displacements in regions of highly heterogeneous deformation or large strains [21,22], it has recognized biases when estimating sub-sample displacements [23,24], and incorporating prior information through regularization in a systematic way is cumbersome. In this study we utilized a finite element based image registration approach similar to the deformable grid methods [25–28]. These methods easily accommodate arbitrary geometries, allow for large local strain within an element, and accommodate prior information through regularization in a natural way. They have the drawback that they are comparatively computationally costly, which for the present application was not a concern.

In this study, we optimized our finite element image registration method to measure the spatial distribution of displacements and strains throughout an airway wall during pressure inflation within the physiological breathing range, as well as monitor tissue motions during induced narrowing. To measure large deformation over the entire physiological range of transmural pressure (Ptm), we incrementally match images captured over small changes in Ptm. We estimate the strain distributions throughout the airway walls which are used to gain insight into the relative moduli of the different airway wall components. We found the displacements and strain during inflation to be longitudinally and radially heterogeneous. The region in the middle layer of the airway experienced the largest radial strain due to a Ptm increase simulating tidal breathing and a DI, while the region containing the ASM (i.e., closest to the lumen) strained least. During induced narrowing with ACh (10^{-3} mol/L), we observed temporal longitudinal heterogeneity of the airway wall. Equal pressure increments lead to much smaller strain and displacements in the constricting airway than in the relaxed airway. The spatial patterns of displacements and strains also changed, suggesting the components of the airway stiffened heterogeneously.

2. Material and methods

2.1. Intact airway system

An intact airway (main stem bronchus, generations 4–10, 35 mm long) was dissected from a fresh bovine lung (Research 87, Boylston, MA) and side branches were ligated to form a leak-free airway. Cannulas were inserted into each end and the airway was mounted inside a tissue bath with heated (37 °C, 5% CO_2) Krebs solutions (Sigma, St. Louis, MO). The entire setup was secured to a floating optical table (Newport I-2000/S-2000) to isolate the system from building vibrations and increase displacement SNR. The airway was stretched to 120% of its resting length to mimic airway lengthening during breathing and its length was held fixed throughout the experiment [29]. The pressure inside the airway was controlled by modulating the height of fluid in a pressure column in series with the airway [30]. Following 60 min in the heated bath, tissue viability was confirmed with electric field stimulation (EFS) as previously described [8,30,31].

2.2. Ultrasound data acquisition

Ultrasound radio frequency (RF) data were collected and digitized to 16-bits at 40 MHz using an ultrasound system (SonixTablet, Ultrasonix Medical Corporation, Richmond, BC, Canada). A 128 element linear array transducer (L40-8/12, 12 mm width) was partially submerged in the tissue bath and mounted less than 7 mm above the outer edge of the airway and positioned parallel to the long axis of the airway segment (Fig. 1). The imaging plane of the transducer cuts through the middle of the airway along its length and the region was more than two diameters away from the proximal and distal cannulas to minimize end effects. This transducer orientation allowed for the dominant displacement component to be aligned with the direction of ultrasound propagation. The field of view in the ultrasound axial direction (hereafter the "axial" direction) and ultrasound lateral direction (hereafter the "lateral" direction) was 22 mm and 12 mm, respectively, and the axial and lateral pixel sizes were 18.7 μm and 46.9 μm, respectively. The resolution in the axial direction was approximately 103 μm. The transducer had a center frequency of 15 MHz and −6 dB bandwidth from 10.5 to 19.5 MHz. The RF data were upsampled by a factor of two using the fast Fourier transform interpolation method in order to improve the discrete integration of the image during processing.

In order to measure the displacement distributions throughout an airway wall, we collected ultrasound RF image data as the airway Ptm was incremented throughout the entire physiological range (i.e., −10 to 25 cmH_2O). Data were collected in increments of 0.5 cmH_2O, except in the range of Ptm where airways are most compliant (i.e., −5 to 10 cmH_2O), where data were collected in increments of 0.2 cmH_2O. The airway was held for approximately 5 s at each Ptm before data were captured. Two full cycles were recorded to verify measurement repeatability. Before data collection, the Ptm was slowly cycled between −10 and 25 cmH_2O at a constant rate of 1 cmH_2O to normalize for volume history. We repeated this process after the airway was constricted with an ASM agonist (ACh, 10^{-3} mol/L) in order to assess the changes that occur in displacement distributions of the airway walls due to ASM activation.

To induce airway narrowing akin to what occurs during an asthma attack, the airway was exposed to cumulative doses of ACh (10^{-5}, 10^{-4}, and 10^{-3} mol/L) and allowed to narrow against a constant Ptm of 5 cmH_2O for 10 min at each dose. During the constriction, ultrasound data were collected at a frame rate of 1.5 Hz in order to visualize narrowing dynamics.

During tidal breathing, Ptm fluctuate between approximately 5 cmH_2O at end-expiration and 10 cmH_2O at end-inspiration. During DIs, which people naturally take every 6 min [32], Ptm increases to approximately 25 cmH_2O.

2.3. Displacement estimation

2.3.1. Edge detection and mesh generation

An automated segmentation algorithm developed in MATLAB (MathWorks, Natick, MA, USA) was used to determine the location