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Assessment of Regional Non-linear Tissue Deformation and Air Volume Change of Human Lungs via Image Registration

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Abstract

We evaluate the non-linear characteristics of the human lung via image registration-derived local variables based on volumetric multi-detector-row computed tomographic (MDCT) lung image data of six normal human subjects acquired at three inflation levels: 20% of vital capacity (VC), 60% VC and 80% VC. Local variables include Jacobian (ratio of volume change) and maximum shear strain for assessment of lung deformation, and air volume change for assessment of air distribution. First, the variables linearly interpolated from 20% and 80% VC images to reflect deformation from 20% to 60% VC are compared with those of direct registration of 20% and 60% VC images. The result shows that the linearly-interpolated variables agree qualitatively with those of registration ($P < 0.05$). Then, a quadratic (or linear) interpolation is introduced to link local variables to global air volumes of three images (or 20% and 80% VC images). A sinusoidal breathing waveform is assumed for assessing the time rate of change of these variables. The results show significant differences between two-image and three-image results ($P < 0.05$). The three-image results for the whole lung indicate that the peak of the maximum shear rate occurs at about 37% of the maximum volume difference between 20% and 80% VC, while the peaks for the Jacobian and flow rate occur at 50%. This is in agreement with accepted physiology whereby lung tissues deform more at lower lung volumes due to lower elasticity and greater compliance. Furthermore, the three-image results show that the upper and middle lobes, even in the recumbent, supine posture, reach full expansion earlier than the lower lobes.

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Conflicts of Interest Statement

There is no conflict of interest although E. A. Hoffman is a shareholder in VIDA diagnostics, which is commercializing lung image analysis software derived from the University of Iowa lung imaging group.

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Keywords

Lung mechanics; regional ventilation; Quantitative Computed Tomography; Image Registration

1. Introduction

The non-linear characteristics of the human lungs make quantitative assessment of lung deformation at intermediate inflation levels challenging. Previous studies showed that changes inside lungs, such as lung deformation, occur regionally (Olson & Rodarte, 1984). The ability to detect more sensitively regional changes of the lungs as a function of inflation level can potentially improve early detection of abnormalities in diseased lungs.

Several image-processing methods have been proposed to evaluate regional changes of the lungs (van Beek et al., 2004; Chon et al., 2007). One technique to assess lung expansion is deformable image registration (Christense et al., 2007; Reinhardt et al., 2008). Yin et al. (2009) developed a mass preserving non-rigid registration technique for pairs of lung images. Matching of two images yields the displacement field needed to calculate regional tissue deformation and air volume change. To evaluate lung expansion, parameters such as regional lung deformation and ventilation can be estimated. West & Matthews (1972) showed that lung may exhibit regionally anisotropic deformation, being independent from volume change. Consequently, some studies employed anisotropic deformation index in addition to volume change to provide some sensitive measures of regional lung deformation (Amelon et al., 2011; Choi et al., 2013). However, if only two lung volumetric images, typically one image at the end of normal expiration (functional residual capacity, FRC, or residual volume, RV) and the other at the end of a maximal inspiration (total lung capacity, TLC), are available, analysis and prediction of lung mechanical behaviors may not adequately account for non-linear behaviors of the lungs at intermediate inflation steps during normal breathing.

Recent advances in MDCT and four-dimensional CT allow one to interrogate regional changes in the lungs at multiple inflation levels and time points. Different studies used those images to consider different aspects of lung motion, such as dynamic airflow and tissue motion, to study the pulmonary function at different inflation levels (Dubsky et al., 2012; Guerrero et al., 2006; Lin et al., 2013; Reinhardt et al., 2008). Although dynamic images are more desirable than static images to study lung functions, static images provide higher spatial resolution images. Ding et al. (2009) performed CT experiments on four adult sheep to evaluate lung expansion for both static and dynamic images via image registration. They compared registration-derived volume changes to regional ventilation measured from Xenon-CT images, demonstrating good correlations between them for both dynamic and static images. However, only a few of studies investigated the non-linear behaviors of the lungs in comparison with linear counterparts using two images. Yin et al. (2010) proposed a method to simulate air flow in the human lung by registering two lung images for subject-specific regional ventilation, demonstrating more physiologically consistent lobar air distribution than the one image-based approach (Lin et al., 2007). Later, Yin et al. (2013) proposed a multiscale breathing lung model based on three MDCT lung images of one human subject. Unlike the two image-based approach with constant flow rates during

respiration, the three image-based algorithm can derive time-varying flow boundary conditions for computational fluid dynamics analysis of pulmonary airflow.

The objective of this paper is to examine non-linear characteristics of the human lung by matching MDCT volumetric lung images at three inflation levels. Local variables of lung deformation and air flow derived via image registration are then used to construct a quadratic relationship between local variables and global air volumes of the lung. The results are compared with the two-image based results in which local variables change linearly. We further quantify the differences of these local variables at intermediate inflation levels obtained by two-image linear interpolation and three-image quadratic interpolation, and discuss non-linear lung behaviors.

2. Method

2.1. MDCT image acquisition

The MDCT lung volumetric images for six normal human subjects were acquired in the supine position at three static inflation levels: 20% of vital capacity (VC), 60% VC and 80% VC. Variables corresponding to 20%, 60% and 80% VC are denoted with subscripts 1, 2 and 3, respectively. We used a Siemens Sensation 64-slice MDCT scanner (Forchheim, Germany) with 120 kV, 75 mAs, 0.75 mm slice thickness, 500 mm field of view. The University Institutional Review Board approved the scanning protocol. The software Apollo (VIDA Diagnostics, Coralville, Iowa) was used to segment the lungs and lobes of CT images.

2.2. Image Registration

If image intensity $I(\mathbf{x})$ in the Hounsfield unit (HU) is known at position $\mathbf{x}$, the air and tissue fractions are calculated as

$$\beta_{air}(\mathbf{x}) = \frac{HU_{tissue} - I(\mathbf{x})}{HU_{tissue} - HU_{air}} \quad \text{and} \quad \beta_{tissue}(\mathbf{x}) = \frac{I(\mathbf{x}) - HU_{air}}{HU_{tissue} - HU_{air}} \quad (1)$$

where the HUs of air and tissue are taken as $HU_{air} = -1000$ and $HU_{tissue} = 55$, respectively. In mapping two images, one image is chosen as the reference image and the other the floating image. The registration is to determine an optimal spatial transformation that matches the two images by minimizing a cost function E based on the local tissue difference between the corresponding regions (Yin et al., 2009).

$$E = \sum_{\mathbf{x} \in \Omega} [v_r(\mathbf{x})\beta_{tissue}^r(\mathbf{x}) - v_f(\mathbf{T}(\mathbf{x}))\beta_{tissue}^f(\mathbf{T}(\mathbf{x}))]^2 \quad (2)$$

where $\mathbf{T}(\mathbf{x})$ is the transformation function which maps a point at location $\mathbf{x}$ in the reference image to the corresponding point in the floating image. v_r and v_f are the volumes of the corresponding point in the reference and floating images, respectively. The subscripts (or superscripts) r and f denote the reference and floating images, respectively. In this study,

mappings are done for 20%–80% VC and 20%–60% VC pairs with 80% VC and 60% VC images as the reference images, respectively, and 20% VC is used as the floating image.

2.3. Variables definition

2.3.1. Deformation Indices—The transformation function obtained by image registration is used to construct variables for assessment of local volume change and anisotropic deformation. The deformation gradient tensor is defined below as the gradient of transformation function

$$\mathbf{F} = \nabla \mathbf{T} \quad (3)$$

The eigenvalues of $\mathbf{F}^T \mathbf{F}$, λ'_{pi} , at a given point, are associated with each local volume from 80% to 20% VC or 60% to 20% VC. Consequently, the principal strains of lung tissue deformation, λ_{pi} , from 20% to 80% VC or 20% to 60% VC are calculated as (Choi et al., 2013)

$$\lambda_{pi} = \frac{1}{\sqrt{\lambda'_{pi}}} \quad (4)$$

With principal strains, we can define two independent indices that measure lung deformation.

Jacobian, $J = v_r(\mathbf{x}) / v_f(\mathbf{T}(\mathbf{x}))$, is defined as the ratio of local lung volume at a given inflation level to the volume at 20% VC, measuring contraction or expansion relative to the 20% VC. That is, there is local expansion if $J > 1$ and local contraction if $J < 1$. The definition of Jacobian in terms of principal strains is

$$J = \lambda_{p1} \lambda_{p2} \lambda_{p3} \quad (5)$$

where subscripts $p1$, $p2$ and $p3$ denote three principal strains. Also, a body can deform while its volume is constant. For example, consider a cube whose lines are initially perpendicular to each other. A cube can be deformed into a parallelepiped volume by change in angle between any pair of orthogonal lines while remaining a constant volume. This change in angle, ψ , from 90° is a representation of shear strain, γ defined as

$$\gamma = \tan \psi \quad (6)$$

By sorting these eigenvalues as $\lambda_{p1} > \lambda_{p2} > \lambda_{p3}$, the maximum shear strain, γ_{max} , is given by (Fung, 1965)

$$\gamma_{max} = \frac{\lambda_{p1} - \lambda_{p3}}{2} \quad (7)$$

Similarly, Napadow et al. (2001) determined anisotropy index by subtraction of axial strains in a 2D plane. Since γ_{max} is proportional to maximum difference between principle strains, it can be considered as an anisotropy index in a 3D domain. Thus, isotropic deformation occurs when volume increases equivalently in all direction (e.g. $\lambda_{p1} > \lambda_{p2} > \lambda_{p3}$), which corresponds to γ_{max} . On the other hand, anisotropic deformation is associated with greater difference between principal strains, resulting in higher value of γ_{max} .

2.3.2. Air volume—For each registration, air volume at position $\mathbf{x}$ can be calculated at the two levels as

$$\begin{aligned} v_{air}^r(\mathbf{x}) &= v_r(\mathbf{x}) \beta_{air}^r(\mathbf{x}) \\ v_{air}^f(\mathbf{x}) &= v_f(\mathbf{T}(\mathbf{x})) \beta_{air}^f(\mathbf{T}(\mathbf{x})) \end{aligned} \quad (8)$$

where v_{air}^r and v_{air}^f are the air volumes at the reference image (60% or 80% VC) and floating image (20% VC), respectively. β_{air} is calculated by Eq. (1).

2.4. Interpolation method

For lung air volumes at three states 20% (V_1), 60% (V_2) and 80% VC (V_3), corresponding local variables f_1, f_2 and f_3 are used to approximate variable f as a quadratic function of the total lung air volume.

$$f(\mathbf{x}, V(t)) = a(\mathbf{x}) + b(\mathbf{x})V(t) + c(\mathbf{x})V(t)^2 \quad (9)$$

Since the images are scanned statically and the time information is not available, the global lung air volume change is assumed following a sinusoidal breathing waveform. The global lung air volume at a reference normalized time, t^* , with a time period of unity is taken as

$$V(t^*) = V_1 + \frac{\Delta V}{2}(1 - \cos(2\pi t^*)) \quad (10)$$

where V_1 and V_3 are roughly corresponding to FRC and TLC, respectively and $V = V_3 - V_1$. Thus, the reference times for the minimum volume (V_1) and the maximum volume (V_3) are 0 and 0.5, respectively, and the peak inspiratory flow rate corresponds to $t^* = 0.25$ (Yin et al., 2013). In the case of using linear interpolation based on two images (20% and 80% VC), the coefficient $c(\mathbf{x})$ in Eq. (9) is set to zero, whereas the waveform Eq. (10) remains the same.

By using air volume, Jacobian and maximum shear strain, respectively, as f in Eq. (9) measured at V_1, V_2 and V_3 , quadratic interpolation functions of these variables can be constructed as a function of global lung air volume. Then, the time rate of change of these variables can be calculated as

$$\frac{\partial f(\mathbf{x}, t)}{\partial t} = \frac{\partial f}{\partial V} \left[\frac{dV}{dt^*} \right] \frac{dt^*}{dt} = (b + 2cV) [\pi(\Delta V) \sin(2\pi t^*)] \frac{dt^*}{dt} \quad (11)$$

where $\frac{dt^*}{dt}$ is uniform and set to unity with $t^*=t$ hereafter.

The entire human lung can be divided into left and right lungs. The left lung consists of two lobes [(left upper lobe, left lower lobe)=(LUL, LLL)], whereas the right lung consists of three lobes [(right upper lobe, right middle lobe, right lower lobe)=(RUL, RML, RLL)]. Thus, there are a total of five lobes and the left lung is usually smaller than the right lung. To find the rate in a region of interest R , we calculate

$$\sum_{\mathbf{x} \in R} \frac{\partial f(\mathbf{x}, t)}{\partial t} = \left(\sum_{\mathbf{x} \in R} \frac{\partial f}{\partial V} \right) \frac{dV}{dt} = \frac{\partial \sum_{\mathbf{x} \in R} f}{\partial V} \frac{dV}{dt} \quad (12)$$

With the assumption that the region R is the total lung and f is local air volume, $\sum_{\mathbf{x} \in R} f = V$, $\sum_{\mathbf{x} \in R} f(\mathbf{x}, t) / t = dV/dt$, indicating that the above method conserves the global lung air flow. The local variables of air volume, Jacobian and maximum shear strain are normalized by their respective medians at the 80% VC level, and are denoted by $airV^*$, j^* and γ_{max}^* respectively. Furthermore, the total air volume V in Eq. (10) is normalized as

$$V^* = \frac{(V - V_1)}{\Delta V} \quad (13)$$

Thus, $0 \leq V^* \leq 1$ and $V^* = (0, 0.5, 1)$ correspond to the beginning, peak and end of the inspiration $t^*=t=(0, 0.25, 0.5)$, respectively, in a sinusoidal waveform. In the following analysis, V^* is used in Eqs. (9) and (11) to account for inter-subject variations of lung size so that the average coefficients of a , b , and c based on all the subjects can be calculated. In the following presentation, data at different inflation levels are warped to the 80% VC domain for comparison.

3. Results

3.1. Assessment of two-image linearly interpolated intermediate state

If CT images are available only at 20% and 80% VC, variables at any intermediate state between them, e.g. 60% VC, can only be approximated using linear interpolation. Since the intermediate state at 60% VC is available in this study, we can derive, via registration, the variables in association with the volume change from 20% to 60% VC, and compare them with those linearly interpolated using the results from registering 20% and 80% VC images (see section 2.4, Eq. (9) with $c=0$). Fig. 1 (left column) shows the distributions of air volume, Jacobian and maximum shear strain obtained via direct registration of images at 20% and 60% VC, while Fig. 1 (right column) shows those obtained from linear interpolation between 20% and 80% VC. To quantify the differences between the two methods, the relative errors, the correlation factors using linear regression analysis and the paired student t-tests were performed for each subject (see Table 1). The sample size for

local variables in the whole lung as well as in each of the five lobes was large and ranged between 40,000 and 500,000. These data exhibit normal distributions. The t- tests are significant for all variables ($P < 0.05$) and the errors are greater in maximum shear strain than those found in Jacobian and air volume. Also, correlation factors ($r^2 < 0.85$) show that the variables at the intermediate state of 60 % VC calculated with linear interpolation only roughly agree with those by matching 20% and 60 % VC.

3.2. Three image-based, quadratic interpolation

With three images, the quadratic interpolation as described by Eq. (9) is employed to calculate variables at intermediate states. In all cases the lung air volume changes from 20% to 80% VC. The results are presented by lung and by lobe at multiple inflation levels (see V^* in Eq. (13)). Also the average rates of change of each variable with respect to V^* are displayed. Note that the rates of change based on linear interpolation between 20% and 80% VC are constant with respect to V^* .

3.2.1. Air volume—Fig. 2a shows the air volume distributions of a subject at $V^* = 0.01, 0.25, 0.50, 0.75$ and 0.99 in a sagittal section at which the dorsal surface and the ventral surface are on the right and left, respectively, and the diaphragm is at the bottom. Air volume at $V^* = 0.01$, closest to the 20% VC, has the minimum value in all regions and increases to the maximum value at $V^* = 0.99$, closest to 80% VC, which is almost uniform in all regions. The result shows that the ventral section reaches the maximum capacity for air first and then, the dorsal regions are filled with air. Fig. 2b shows the average lobar distributions of air volume based on all the subjects at various inflation levels. At the initial states, the upper and middle lobes have greater values than the lower lobes, but with increasing V^* , the difference of the air volumes between them is diminished and they reach to almost the same level and become uniform at the final stage. The averages of the coefficients in Eq. (9) for all the subjects are tabulated in Table 2 for the whole lung and for each lobe. In addition, to compare the air volumes calculated with two-image linear interpolation and three-image quadratic interpolation, paired student t-tests were done in the whole lung and in each lobe, indicating that they are different ($P < 0.05$).

Fig. 3a shows the average total lung air flow rate calculated with Eq. (12). As expected, air flow rate has its peak at the middle with $V^* = 0.5$. Since the global variable in Eq. (9) is the total air volume, two image-based (linear interpolation between 20% and 80% VC) and three image-based (quadratic interpolation between 20%, 60% and 80% VC) methods give the same result for the flow rate of the whole lung. However, the local flow rates in three image-based method are different from those of two image-based method in which the rates are constant. For example, Figs. 3b and 3c show the lobar flow rates in the respective left and right lungs. The flow rates in the lower lobes are greater than those of the upper and the middle lobes, and reach their maxima later at $V^* \cong 0.054$ and 0.56 for LLL and RLL, respectively, than the peak of the total lung flow rate. On the other hand, the peaks of the middle and upper lobes occur earlier at $V^* \cong 0.039, 0.46$, and 0.44 for RML, RUL and LUL, respectively.

3.2.2. Jacobian—Fig. 4a shows the distributions of Jacobian at four different volumes of $V^* = 0.25, 0.5, 0.75, 1$. Jacobian at volume close to 20% VC is almost unity and is not shown. The dorsal surface and the bottom close to the diaphragm have most expansion as the volume increases. Furthermore, Fig. 4b shows that the largest and smallest Jacobian values occur in the lower lobes and the upper lobes, respectively. The averages of the coefficients in Eq. (9) for Jacobian based on all six subjects are given in Table 3. To compare two and three image-based results, paired student t-tests were performed, showing that the Jacobian calculated by linear and quadratic interpolations are different ($P < 0.05$).

3.2.3 Maximum shear strain—Fig. 5a shows the distributions of maximum shear strain γ_{max}^* at different inflation levels. Maximum shear strain is mainly found at the bottom of the ventral surface. With increasing V^* , the increase of γ_{max}^* starts from the bottom of the ventral surface, and then spreads to the upper regions. Fig. 5b shows that the lobar changes of average γ_{max}^* at various inflation levels. The results show that high γ_{max}^* is located in the lower and middle lobes of LLL and RML, whereas low γ_{max}^* is found in the upper lobes of LUL and RUL at all inflation levels. The average interpolation coefficients for γ_{max}^* are listed in Table 4. Paired student t-tests were performed to compare γ_{max}^* calculated by two image-based and three image-based methods. The result shows $P < 0.05$, indicating that they are different. Also, a comparison between γ_{max}^* and the anisotropic deformation index (ADI)

defined as $\sqrt{\left(\frac{\lambda_{p1}-\lambda_{p2}}{\lambda_{p2}}\right)^2 + \left(\frac{\lambda_{p2}-\lambda_{p3}}{\lambda_{p3}}\right)^2}$ by Amelon et al. (2011) shows a strong correlation coefficient of $r^2 > 0.88$.

Fig. 6a exhibits the average rates of γ_{max}^* in the total lung as a function of V^* calculated with two-image linear interpolation and three-image quadratic interpolation. With quadratic interpolation, average rates of γ_{max}^* reaches the peak at $V^* = 0.37$, which is earlier than those of air volume and Jacobian at $V^* = 0.5$. Figs. 6b and 6c further show the averages of γ_{max}^* in the left and the right lungs, respectively. The peaks of the rates in the lower and middle lobes occur earlier (at $V^* \cong 0.032, 0.34, 0.31$ for LLL, RLL and RML, respectively) than those of the upper lobes (at $V^* \cong 0.039$ and 0.44 for LUL and RUL, respectively).

4. Discussion

In this study, we examined non-linear behaviors of lung deformation and air volume change by applying image registration to CT images acquired at three static inflation levels. Specifically the change of local volume and anisotropy in lung deformation were measured by two independent indices: Jacobian and maximum shear strain. These indices were calculated using the eigenvalues obtained from the registration-derived transformation function (Eqs. (5) and (7)). Moreover, to investigate air volume change in the lung, we calculated air volume by Eq. (8). With two images, regional variables are assumed to change linearly. With three images, nonlinear behaviors of the lung in terms of the above variables can be investigated by employing quadratic interpolation.

Comparison of air volumes obtained by directly matching 20% and 60 %VC images and by linearly interpolating between 20% and 80% VC (Table 1 and Fig. 1) showed that the linear interpolation reveals non-uniform regional air volume, but is not sensitive enough to detect local non-linear features with $r^2 < 0.85$, RMS error > 12% and $P < 0.05$. Subsequently, a three image-based method was applied to examine the changes of air volume at multiple inflation levels. Because of body posture and diaphragm motion, dorsal surface and lower lobes can inflate more so that air is distributed uniformly at the 80% VC stage in the whole lung (Fig. 2). These results are consistent with the observed physiology of ventilation in subjects with supine position (Milic-Emili et al., 1966; Reinhardt et al., 2008)

As for Jacobian, both two and three image-based method showed that the Jacobian has the largest values in the lower lobes and also in the dorsal surfaces (Figs. 1 and 4), which are consistent with the diaphragm motion and in good agreement with the principle that volume changes more in the regions close to the diaphragm (Amelon et al., 2011). However, unlike the flow rates obtained by two-image linear interpolation whose peaks occur at the middle of $V^* = 0.5$, the three-image results (see Fig. 3) showed that the peaks of the flow rate in the upper and the middle lobes occur earlier than those of the lower lobes. These observations agree with the fact that some regions in these lobes reach their maximum capacity for air before the 80% VC level (Fig. 1a).

In this study, the index of maximum shear strain was adopted to represent anisotropic deformation. Since there was a good correlation between the maximum shear strain and the ADI index proposed by Amelon et al. (2011) with $r^2 > 0.88$, it is concluded that maximum shear strain can be used to measure the degree of anisotropic deformation. As for maximum shear strain, Table 1 and Fig. 1c showed that the two-image linear interpolation approach yields more error in predicting local non-linear tissue deformation in terms of shear strain (or ADI) than air volume and Jacobian. The three-image results showed that maximum shear strain has the highest value in the inferior region due to large deformation in association with the diaphragm motion. With two image linear interpolation, the rates of all local variables with respect to V^* are constant and the peaks of both the flow and the maximum shear strain rates occur at $V^* = 0.5$, being the same as the peak of the sinusoidal waveform (Figs. 3a and 6a). However, three image-based results showed that shear strain rate peaks at $V^* \cong 0.37$, which is earlier than the peak of the flow rate (Fig. 6a). This earlier peak was also observed in the results of ADI.

From the perspective of lung mechanics, the current result is consistent with the notion that under quasi-static conditions the elasticity at low lung volume is lower, especially in dependent lung regions, than at high lung volumes. Thus, lung tissue deforms more at low lung volumes, as has been shown by Hoffman et al using early volumetric CT methodologies (Hoffman, 1985, Hoffman & Ritman, 1985, Hoffman et. al, 1986). That is, shear strain represents tissue deformation and tissue deforms more at low lung volumes, thus the peak of shear rate occurs earlier than the peak inspiration. In addition, the lower lobes have higher shear strains and airflow rates than the upper lobes. Therefore, the three image-based variables, as expected, provide more sensitive measures of non-linear lung mechanics both in time and space. This is important when seeking to understand regional interactions associated with lung pathophysiology, particularly when evaluating the lung for mechanical

changes associated with early pathological processes. A critical pathway that bridges lung mechanics and biology is through the mechanosensing capability of bronchial epithelial cells (Fredberg et al., 2006). Sensitive measures of local lung structural and functional variables can allow one to study local alterations of mechanical forces that may lead to inflammation.

In all cases, we constructed the interpolation function as a function of total air volume and then we applied the sinusoidal waveform independently to calculate the rates (Eq. (10)). For other waveforms, the time rate of change of variables can be assessed by merely re-calculating $[dV/dt^*]$ in Eq. (11). Also, the calculated interpolation coefficients (Tables 2–4) allow one to estimate the average of each variable in the total lung and each lobe at arbitrary inflation levels. This is important to improve simulation of pulmonary gas flow as described in Yin et al. (2010, 2013). In conclusion, we showed that three image-based method is able to capture some nonlinear behaviors of the lung that are missing in the two-image based analysis.

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Fig. 1.

Comparison between normalized variables obtained by image registration between 20% and 60 %VC and linear interpolation at 60% VC between 20% and 80% VC: (a) Air volume (b) Jacobian (c) Maximum shear strain

Fig. 2.

Regional normalized air volume at different levels: (a) Air volume distribution for a certain subject (b) Bar graph showing lobar air volume values. The average and standard deviation show the median of a group of six subjects.

Fig. 3. Normalized flow rates: (a) the whole lung: comparison between linear and quadratic forms. The lines represent the average and standard deviation of the median flow rate of six subjects. (b) left lobes (c) right lobes.

Fig. 4. Regional normalized Jacobian at different levels: (a) Jacobian distribution for a certain subject (b) Bar graph showing lobar Jacobian values. The average and standard deviation show the median of a group of six subjects.

Fig. 5. Regional normalized maximum shear strain at different levels: (a) Shear strain distribution for a certain subject (b) Bar graph showing lobar shear strain values. The average and standard deviation show the median of a group of six subjects.

Fig. 6. Normalized maximum shear rates: (a) the whole lung: comparison between linear and quadratic forms. The lines represent the average and standard deviation of the median flow rate of six subjects. (b) left lobes (c) right lobes.

Table 1

Comparison of two-image based and image registration methods for the air volume, Jacobian and maximum shear strain in the total lung and each lobe.

<i>airV*</i>	RMS error%	r (correlation factor)	P (t test)
Total lung	11.27	0.82	< 0.05
LLL	12.39	0.81	< 0.05
LUL	11.19	0.77	< 0.05
RLL	11.35	0.85	<0.05
RML	11.49	0.82	<0.05
RUL	9.41	0.86	<0.05
<i>J*</i>	RMS error %	r (correlation factor)	P (t test)
Total lung	7.34	0.86	< 0.05
LLL	9.26	0.82	< 0.05
LUL	8.55	0.77	< 0.05
RLL	8.33	0.86	< 0.05
RML	9.43	0.81	< 0.05
RUL	6.85	0.84	< 0.05
γ_{max}^*	RMS error%	r (correlation factor)	P (t test)
Total lung	28.34	0.78	< 0.05
LLL	27.07	0.78	< 0.05
LUL	27.54	0.73	< 0.05
RLL	32.21	0.77	< 0.05
RML	31.66	0.79	< 0.05
RUL	23.16	0.81	< 0.05

Table 2

Means ($\pm$ SE) of a, b and c coefficients in Eq. (9) for the air volume of the total lung and each lobe.

<i>airV</i> *	a	b	c
	Mean ($\pm$ SE)	Mean ($\pm$ SE)	Mean ($\pm$ SE)
Whole	0.0129 (0.001)	0.4317 (0.010)	0.5433 (0.009)
LLL	0.0459 (0.004)	0.4623 (0.009)	0.4695 (0.017)
LUL	-0.0413 (0.006)	0.4398 (0.021)	0.5873 (0.015)
RLL	0.0766 (0.001)	0.4105 (0.004)	0.4908 (0.002)
RML	-0.0519 (0.001)	0.4051 (0.028)	0.6511 (0.022)
RUL	-0.0220 (0.005)	0.4180 (0.003)	0.5941 (0.007)

Table 3

Means ($\pm$ SE) of a, b and c coefficients in Eq. (9) for the Jacobian of the total lung and each lobe.

J^*	a	b	c
	Mean ($\pm$ SE)	Mean ($\pm$ SE)	
Whole	-0.0193 (0.001)	0.4038 (0.008)	1
LLL	0.0059 (0.008)	0.4698 (0.021)	1
LUL	-0.0465 (0.005)	0.3793 (0.016)	1
RLL	0.0056 (0.007)	0.4371 (0.006)	1
RML	-0.0652 (0.005)	0.3375 (0.018)	1
RUL	-0.0307 (0.001)	0.3526 (0.008)	1

Table 4

Means ($\pm$ SE) of a, b and c coefficients in Eq. (9) for the maximum shear strain of the total lung and each lobe.

γ_{max}^*	A	b	c
	Mean ($\pm$ SE)	Mean ($\pm$ SE)	
Whole	-0.4969 (0.028)	1.4131 (0.034)	0
LLL	-0.5988 (0.021)	1.7023 (0.071)	0
LUL	-0.3487 (0.011)	1.2054 (0.028)	0
RLL	-0.6491 (0.097)	1.5609 (0.117)	0
RML	-0.6792 (0.017)	1.7938 (0.051)	0
RUL	-0.3739 (0.049)	1.1602 (0.045)	0