A Dynamic Model of Average Lung Deformation Using Capacity-Based Reparameterization and Shape Averaging of Lung MR Images

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Abstract. We present methods for extracting an average representation of respiratory dynamics from free-breathing lung MR images. Due to individual variations in respiration and the difficulties of real-time pulmonary imaging, time of image acquisition bears little physiologic meaning. Thus, we reparameterize each individual's expiratory image sequence with respect to normalized lung capacity (area, as a substitute for volume), where 1 represents maximal capacity and 0 minimal capacity, as measured by semi-automated image segmentation. This process, combined with intra-subject pairwise non-rigid registration, is used to interpolate intermediate images in the normalized capacity interval $[0, 1]$. Images from separate individuals with the same normalized capacity are taken to be at corresponding points during expiration. We then construct an average representation of pulmonary dynamics from capacity-matched image sequences. This methodology is illustrated using two coronal 2-D datasets from healthy individuals.

1 Introduction

The lung is a highly elastic organ composed of fibers connecting the large airways, intricate vasculature and pulmonary interstitium. A healthy lung is normally highly compliant, deforming easily during respiration, [1]. Pathological processes that affect the lung typically alter the normal mechanical properties of lung tissue, and manifest as observable changes in lung morphology and function. The ability to quantify differences in pulmonary deformation would be useful in early detection of disease, evaluation of treatment efficacy and improved assessment of disease staging and prognosis. Magnetic resonance (MR) imaging and other structural imaging modalities can be used to capture *in vivo* deformation of the lung between sequential images by harnessing the power of non-rigid registration algorithms, [2,3].

In prior studies, we have employed a variational registration algorithm with a linear elastic prior to quantify lung motion captured in serial image sequences, by registering sequential pairs of images I and J and examining the resulting displacement fields, [4]. We impose the linear elastic behavior of the image via a finite element mesh constructed over the domain of I . We have also applied this

Fig. 1. (a) Evolution of pulmonary cross-sectional areas over imaging time in two healthy individuals. The decrement in area between each image pair is non-uniform throughout expiration. The large circles indicate the lung areas within the images interpolated via reparameterization. (b) At a fixed point in time, the extent of respiratory deformation will vary between individuals; this motivates our efforts toward establishing temporal correspondence.

technique to quantify the differences in pulmonary deformation between normal mice and transgenic mice with sickle cell disease, [5]. In related work, the original registration algorithm has been modified to yield the diffeomorphic fluid deformation framework which is assumed in this paper, [6]. The diffeomorphic component requires that the solution to the registration be continuous, differentiable and invertible. When combined with the fluid framework and approached from the Eulerian perspective, the total deformation between fixed image I and moving image J is considered to be a composition of incremental transformations, each of which is diffeomorphic.

One of the challenges in comparing the respiratory dynamics of two individuals is in achieving temporal correspondence between physiologically similar points of the respiratory cycle. Dynamic modeling as well as inter-subject matching are ongoing areas of research in cardiac imaging as well. Solutions have been proposed that include extending the B-spline framework used to perform pairwise registrations to simultaneous spatio-temporal image matching, as well as applying translation and scaling in the temporal domain as a precursor to non-rigid registration in the spatial domain, [7,8].

The images used in these experiments are acquired at a constant time interval while the volunteers breathe slowly and deeply, consciously controlling their respiration. Hence, even though the images are evenly spaced in time, the deformation of the lung is non-uniformly sampled during image acquisition (figure 1a). Consequently, the motion that occurs between one pair of images is not equivalent to the motion within the subsequent image pair. In order to be able to make accurate comparisons between individuals, it is necessary to correlate points during their respiratory cycles. Furthermore, we expect that at any fixed time during respiration, cross-sectional areas will differ between healthy subjects due to natural individual variations in respiratory deformation (figure 1b).

Fig. 2. Capacity-based reparameterization of the expiratory image sequences is performed as shown above. The desired intermediate image is acquired via linear search along the pre-computed deformation field between the two adjacent images.

In this work, we apply a novel capacity-based reparameterization to resample dynamic sequences of 2-D free-breathing lung MR images with the goal of achieving correspondence between individuals’ respiratory cycles. Normalizing the lung capacity with respect to its maximum value at end-inspiration yields a “physiologic” time axis whose value is 1 at end-inspiration and zero at end-expiration. These two time points are selected manually by an expert user. The image sequence is then registered in time to find deformation fields (generally small) between an individual’s lung state at time t_i and time t_{i+1} , with areas A_i and A_{i+1} , respectively. An interpolation method using these deformation fields and segmentations of both lungs is applied to estimate images which represent the lungs at desired area, A , where $A_i \leq A \leq A_{i+1}$. A dynamic average lung representation of the expiratory segment of breathing is then constructed by assuming inter-subject correspondence of images with identical relative areas, $\{A_0, \dots, A_i, \dots, A_1\}$, and computing the shape (or deformation) and intensity average between each area-coincident set of images.

2 Methods

We apply our method to two sequences of free-breathing coronal images collected from individuals with no known pulmonary disease (FIESTA, GE Signa, TR=3.22ms, TE=1.45ms, slice thickness=15mm, FOV=35cm, matrix=256x256). Volunteers were instructed to breathe as slowly and deeply as possible while images were continuously acquired every 1.4 seconds. In each dataset, approximately twenty-two images were acquired over one full breath (expiration followed by inspiration). Lung deformation was not smoothly sampled, since each individual was free to breathe at a comfortable pace. End-inspiration and end-expiration were determined by finding the maximal and minimal cross-sectional areas, respectively, of both lungs during the respiratory cycle. In these preliminary experiments, we focus on the expiratory phase of respiration alone.

In order to estimate the cross-sectional area of the lungs in each image, we stack the images into a volume and segment the lungs and vasculature using

Fig. 3. Construction of dynamic atlases of lung deformation from sequences of images would proceed as shown above. Please refer to the text for further details.

ITK-SNAP, an open-source implementation of semi-automated level set segmentation, [9]. The segmentations are manually refined, smoothed with a median filter of radius 1, and post-processed using morphological closing (dilation followed by erosion) with a 6x6x6 structuring element. The resulting segmentations include the pulmonary parenchyma and most of the branches of the pulmonary vascular tree; however, some of the largest blood vessels remain as holes within the segmentation.

We first perform pairwise registration between consecutive images in each sequence of N images using the fluid registration discussed previously. The resulting set of deformation fields, $\{\mathbf{U}_1, \dots, \mathbf{U}_{N-1}\}$ reveals the change in capacity between each image pair through the jacobian of the field, $\mathcal{J} = \int |\mathbf{D}\mathbf{U}_i| d\mathbf{x}$, with Ω the domain of the lung segmentation. By construction, $A_{i+1} = \int_{\Omega} |\mathbf{D}\mathbf{U}_i| d\mathbf{x}$. The non-uniform sampling of the imaging sequences (caused, in part, by each individual's voluntary modulation of respiration and illustrated in figure 1a) is also measured.

In order to appropriately compare the two sequences, we normalize the trend of capacities (i.e, cross-sectional areas) observed during expiration such that capacity has value 1 at end-inspiration and 0 at end-expiration. Within each sequence, intermediate images are reconstructed by solving the following minimization between consecutive images,

$$E(\gamma) = \frac{1}{2} \left(\int_{\Omega} |\mathbf{D}(\gamma \mathbf{U}_i)| d\mathbf{x} - A \right)^2, \quad (1)$$

with $A_i \leq A \leq A_{i+1}$ and γ a scalar in $[0, 1]$. Linear scaling is used here because the deformation between images i and $i + 1$ is small, justifying a local linear approximation. We use normalized capacity values $A = \{0.25, 0.5, 0.75\}$

Fig. 4. The shape and intensity averaging evaluation process is illustrated above. Images taken at $t_1 = 1$ and $t_2 = 2$ from a single-subject image sequence are shape and intensity averaged. A third image, taken at time t , with $t_1 < t < t_2$ and with approximately equal deformation energy to each of its neighbors, is used as an estimate of ground truth to evaluate the quality of the mean image. The symmetric averaging method in [10] is used to estimate the mean shapes (shown in the bottom row on the left side of the equation), which are then intensity averaged to yield the image on the right side of the equation. The intensity difference between this average image and the image at time t was less than the difference with the images at t_1 and t_2 . Similar results have been found with a set of slices from brain images.

to generate new sequences of five images each that represent the configuration of the pulmonary anatomy at particular values of the cross-sectional area. Note that each of the values between 1 and 0 represents a physiologic time during the expiratory phase, at which the lungs of all individuals have achieved the same reduction in capacity with respect to end-inspiration. Hence, we are now able to directly compare and match the images at these physiologic time points.

Using these capacity-coincident images, we are able to build a dynamic average lung model. First, the shape average of each set of capacity-coincident images is computed. This inter-subject average is determined by performing a simultaneous, symmetric registration of the two images, and traversing the gradient of the similarity at a constant step length, [10]. This produces a new sequence of

five images representing the average respiratory deformation of the two individuals. The intensities of these symmetrically registered images are then averaged to give a least squares best representation of the database of anatomy at each of the five normalized capacity points $\{\mathcal{A}_i\}$.

The methodology for representing the average lung deformation relies on the composition of deformation fields, as shown in figure 3. The goal is to represent all deformation patterns with respect to the set of average configurations, $\{\mathcal{A}_i\}$, constructed from deformation- and intensity-averaging of the datasets for each capacity A_i . We only perform intra-subject registrations in time and inter-subject registrations at a given fixed normalized capacity. No registrations create a diagonal connection such as the one in figure 3. To illustrate, we denote the existing intra-subject transformation between a subject at end-inspiration, I_0^1 , and its subsequent anatomy with capacity A_1 , as $\mathbf{U}_0^1$. The same transformation from capacities A_0 to A_1 in a second subject, I_0^2 , is $\mathbf{U}_0^2$. Then, the average end-inspiratory anatomy estimated from these two subjects would be $\mathcal{A}_0$, where transformations $\mathcal{U}_0^1$ and $\mathcal{U}_0^2$ map each subject, respectively, to $\mathcal{A}_0$. Each $\mathbf{U}_0^k$ is represented in the domain of $\mathcal{A}_0$ by composing $\mathcal{U}_0^{k-1}$ onto $\mathbf{U}_0^k$. In this domain, these fields (if small enough) may be averaged.

3 Results

The pairwise registrations between each sequence computed at the beginning of this paper quantify the non-uniform sampling of respiratory deformation that motivates this work. However, in each sequence, there is an image which is equidistant from its adjacent neighbors, where the distance is defined by deformation, [10]. We choose to reconstruct these images as validation of the shape averaging method (figure 4).

Figure 5 illustrates the results of the capacity reparameterization of both sequences. The newly interpolated images at equally spaced area fractions between end-inspiration and end-expiration are shown. Recall that these images do not represent physiologic conditions in each volunteer at the same point of elapsed time after end-inspiration, since each individual breathes at his or her own pace. Instead, the interpolated images represent a physiologic correspondence between the two individuals. The amount of time and respiratory deformation required to arrive at this anatomic configuration in each individual is different; however, they are proportionately at the same point in their respective breathing cycles. Achieving this correspondence enables us to make further quantitative comparisons between the two individuals with respect to deformation patterns and regional pulmonary strains. Furthermore, we can now construct the average lung deformation sequence using these correlated sequences. Despite the large intensity variations in the data associated with vascular and fluid-containing structures entering the imaging plane, we are still able to compute reasonable averages between the images, and produce a smooth representation of average lung deformation during expiration.

Fig. 5. Interpolated images are produced at specific physiologic times via area reparameterization in each individual, and the average lung deformation sequence can be computed via shape averaging of the area-coincident images.

4 Discussion and Future Work

We presented a method for reparameterizing images taken in time according to some physiologic function, in this case, lung capacity. In these experiments, we use cross-sectional area; in the three-dimensional case, we would naturally use lung volume. Given this reparameterization, we are able to bring images into correspondence with respect to this known physiologic reference. We can now confidently create an average model which will serve as the basis for further studies of normal and abnormal variations in lung deformation. Furthermore, we can use these techniques to perform inter-subject comparisons of deformation patterns and regional strains within the lung, by composing the incremental deformation fields required to arrive at the coincident anatomic configurations, and then making quantitative assessments of these total deformations. This technique is equally applicable if the data is acquired using breath-holding instead of free-breathing. The flexibility of the method is especially useful in volumetric MR studies, where the time necessary to image the whole chest exceeds the normal duration of a single breath (4-5 seconds).

We chose to focus on the expiratory phase of breathing in this paper to better illustrate the concepts presented. However, our approach can be extended to include the entire respiratory cycle, as well as to include more than two individuals in the mean deformation model. Furthermore, the quantitative information produced by our approach stimulates a number of interesting questions about respiratory deformation. In the future, we would like to explore the symmetry of the inspiratory and expiratory phases of respiration, and the disruption of any inherent symmetry as a result of disease. Additionally, we intend to investigate other physiological bases for reparameterization (e.g. deformation), extend this analysis to more than two individuals, and further explore the creation of 3-D dynamic atlases of the lung.

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