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Abstract. In-depth understanding of the diaphragm's anatomy and physiology has been of great interest to the medical community, as it is the most important muscle of the respiratory system. While noncontrast four-dimensional (4-D) computed tomography (CT) imaging provides an interesting opportunity for effective acquisition of anatomical and/or functional information from a single modality, segmenting the diaphragm in such images is very challenging not only because of the diaphragm's lack of image contrast with its surrounding organs but also because of respiration-induced motion artifacts in 4-D CT images. To account for such limitations, we present an automatic segmentation algorithm, which is based on *a priori* knowledge of diaphragm anatomy. The novelty of the algorithm lies in using the diaphragm's easy-to-segment contacting organs—including the lungs, heart, aorta, and ribcage—to guide the diaphragm's segmentation. Obtained results indicate that average mean distance to the closest point between diaphragms segmented using the proposed technique and corresponding manual segmentation is 2.55 ± 0.39 mm, which is favorable. An important feature of the proposed technique is that it is the first algorithm to delineate the entire diaphragm. Such delineation facilitates applications, where the diaphragm boundary conditions are required such as biomechanical modeling for in-depth understanding of the diaphragm physiology. © 2016 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: 10.1117/1.JMI.3.4.046004]

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1 Introduction

The diaphragm is a muscular and tendinous septum, which has two important roles of separating the thorax from the abdominal organs and serving as the primary muscle of respiration. Accurate delineation of the diaphragm in medical images is required in a number of biomedical and clinical applications. For instance, it is used in anatomical and functional assessment of the diaphragm.^{1–4} Segmentation of the diaphragm in medical images can also simplify segmentations of other abdominal organs, such as the liver.⁵

Mechanical modeling has recently emerged as an attractive approach for computer-assisted medical intervention. Examples of such applications, where the diaphragm geometry is required for modeling, include lung radiation therapy and liver intervention.^{6–10} Diaphragm segmentation is not straightforward as routinely acquired thoracic noncontrast computed tomography (CT) images have low contrast, such that the diaphragm image intensity distribution is similar to that of the surrounding organs, such as the heart, liver, and spleen.

While there is a plethora of segmentation algorithms in the literature, most algorithms fall into one of three approaches:

edge-based, region-based, and classification-based. None of these approaches or their combinations is suitable for diaphragm segmentation due to its small thickness, heterogeneity, and lack of contrast with surrounding organs. As such, most reported diaphragm segmentation methods in the literature use modeling with *a priori* knowledge of the diaphragm's anatomy to delineate its surface in noncontrast CT images.

One of the first diaphragm segmentation algorithms was proposed by Beichel et al.¹¹ and employed a three-dimensional (3-D) version of the active appearance model (AAM) proposed earlier by Cootes et al.¹² to segment the left and right domes of the diaphragm. Another algorithm was proposed by Zhou et al.,¹³ in which they modeled the diaphragm as a thin plate spline, which passes through the bottom surface of the lungs. A similar approach to that of Zhou et al.¹³ was proposed by Rangayyan et al.,¹⁴ in which they modeled the diaphragm domes as quadratic surfaces. The results obtained by this group are more accurate as they used active contours¹⁵ to pull the initial approximate diaphragm surface toward its actual surface in the image.

Recently, a method was proposed by Yalamanchili et al.,¹⁶ in which they modeled the diaphragm as a directed graph and solved the segmentation problem by determining the optimal

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surface in a volumetric graph. While applications such as biomechanical modeling require the entire diaphragm as well as accurate diaphragm boundary conditions, the only group that attempted to segment the entire diaphragm was Rangayyan et al.¹⁴ However, as Rangayyan et al.¹⁴ stated in their discussion, their algorithm overestimates the lumbar part of the diaphragm, and the details of diaphragm attachments to the ribcage and spine are missing in the final results.

In this paper, a fully automatic algorithm is presented for segmentation of the entire diaphragm. This algorithm is a substantially refined and more accurate version of the algorithm we presented recently.¹⁷ In the previous algorithm, the feasibility of full diaphragm segmentation was demonstrated by applying a conceptual version of the proposed algorithm on one case. In this study, the enhanced algorithm was applied to nine diaphragm cases and statistics of Hausdorff distance, mean distance to the closest point (MDCP), average symmetric absolute surface distance (ASASD), and symmetric RMS surface distance (SRMSSD) are presented. The main idea of the proposed method is that although the diaphragm is not clearly visible in noncontrast CT images, it has contact surfaces with its surrounding structures, which can be segmented reasonably accurately in these images. As such, the entire diaphragm can be segmented by finding its contact surfaces with the surrounding structures followed by applying a B-spline approximation method to connect them.

Section 2 provides necessary information about the human diaphragm anatomy, which was directly used in the algorithm.

Section 3 describes the segmentation method, whereas Sec. 4 presents segmentation results obtained in this study. Section 5 summarizes the findings, strengths, and limitations of the proposed algorithm, and finally, conclusions are presented in Sec. 6.

2 Diaphragm Anatomy

Given that the proposed segmentation algorithm relies on anatomical information of the diaphragm and its surrounding structures, this section describes relevant anatomical features of the human diaphragm. The diaphragm is a dome-shaped sheath that separates the thorax from the abdomen by serving as the floor of the former and roof of the latter. Figure 1(a) is an inferior view of the diaphragm with its attachments to the surrounding structures. As shown in this figure, the periphery of the diaphragm consists of muscular fibers, which originate from the posterior surface of the xiphoid process, sixth to twelfth ribs, the costal cartilage, and the lumbar vertebra. The central portion of the diaphragm, which is attached to the pericardium, is tendinous. The diaphragm has several openings, one of which is located at its posterior part to allow the descending aorta to pass from the thoracic through the abdominal cavities.¹⁸ In fact, the diaphragm is attached to the lumbar vertebrae by means of two diaphragm pillars that wrap around the aorta, as shown in Fig. 1(a). Figure 1(b) illustrates an axial CT image acquired from a lung cancer patient. In this image, the aorta and diaphragm's pillars are shown with arrow heads. Figure 1(c) illustrates a coronal view of the diaphragm, where the diaphragm domes are seen in contact with the bottom surface of the lungs while the diaphragm's central

Fig. 1 (a) A schematic view of the human diaphragm, where surrounding structures (e.g., ribs and aorta) are shown, (b) an axial CT image showing the aorta and diaphragm pillars, (c) a schematic view of the human diaphragm, and (d) a coronal CT image showing the relative positions of the thoracic organs and abdominal organs.

tendon is attached to the pericardium. This figure also illustrates the circumference of the diaphragm originating from the ribs, while its lateral sides are located adjacent to the sixth to twelfth ribs. The relative positions of the lungs, heart, and lower seven ribs with respect to the diaphragm are depicted in Fig. 1(d), where a coronal slice of a human chest CT scan is shown.

It is notable that the relative position of the diaphragm to its surrounding structures does not change significantly during respiration. As such, it is expected that unlike with the AAM approach,¹¹ the shape variations of the diaphragm during respiration do not affect the accuracy of this proposed algorithm, rendering it suitable for segmenting the diaphragm in all phases of respiration to assess its function.

3 Methods

3.1 Data Acquisition

The 3-D CT images used in this study correspond to the end exhalation phase of four-dimensional (4-D) CT datasets acquired from the thorax and abdomen of nine cancer patients. The patients were scanned using a 16-slice Philips Brilliance Big Bore CT scanner (Philips Medical Systems, Cleveland, United States) operating in helical mode. The scanning parameters are 120 kVp and 400 mAs/slice for tube potential and current, respectively. The pitch of the couch depends on the patient's breathing period and it was set to ~ 0.1 . The intraslice pixel size of the data varied from 0.98 to 1.29 mm while slice thickness was 3 mm. The 4-D CT images were sorted into 10 respiratory phases using the real-time position managementTM system. In this study, efforts were made to include patients with various anatomies and disease stages to investigate the robustness of the algorithm. For example, some patients had lung and abdominal tumors located close to the diaphragm while some others had severe lung diseases, such as advanced chronic obstructive pulmonary disease (COPD). The next section describes the segmentation algorithm in detail.

3.2 Diaphragm Segmentation Algorithm

A step-by-step approach is employed in the proposed algorithm to segment the entire diaphragm. Figure 2 illustrates an overview of the segmentation process. As shown in this figure, the segmentation procedure begins by segmenting the diaphragm's surrounding organs. This is followed by segmenting each organ's contact surface with the diaphragm. Finally, the entire diaphragm's surface is obtained by assembling the delineated contact surfaces using multilevel B-spline approximation method.

3.2.1 Image denoising

Before beginning the segmentation process, all CT images used in this study were first filtered by a curvature flow filter, which was proposed by Malladi and Sethian.¹⁹ The advantage of using this filter over other denoising filters is that the boundaries remain sharp and do not become blurred. In fact, the smoothing occurs only within a region, which is very important in the context of the proposed segmentation method. The main idea of this image denoising method follows the level sets concept of viewing the pixel values as topographic maps. The very small contours in the image, which correspond to spikes of noise, can be removed by letting each contour undergo motion by a curvature obtained from solving the following anisotropic diffusion equation:

$$I_t = F(\kappa)|\nabla I|, \quad (1)$$

where I is the image, κ is the curvature, and F is the speed function.

3.2.2 Segmentation of the ribcage and lungs

As described in Sec. 2, the circumference of the diaphragm runs along the sixth rib through to the twelfth rib as well as the costal

Fig. 2 Block diagram of the proposed segmentation method.

cartilage. As such, the entire ribcage has to be segmented to find its contact surfaces with the diaphragm. For this purpose, after removing noise from the CT images, the rib cage was roughly segmented by thresholding the image for values greater than 120 HU to capture the entire bones and cartilage in the image. This threshold value was obtained from careful assessment of the image histograms of all nine cases to find a threshold value for separating other soft tissues from the bone and coastal cartilage. Next, connected component analysis was used to choose the largest component of the resulting image, which corresponds to the rib cage. In order to segment the lungs, the CT images were thresholded at values between -950 and -300 HU. It is noteworthy that although the average density of lung tissue is about -700 HU and is never denser than -500 HU, we used a broader density range obtained from the image histograms to include the fibrotic tissue. Next, the lungs were found by searching for the largest connected component of the image, which is located inside the ribcage. The result includes the left and right lungs as well as the bronchial tree. Since the separation of the left and right lungs is necessary for the proposed diaphragm segmentation algorithm, the bronchial tree must be segmented and then subtracted from the output obtained in the previous stage. Several algorithms have been proposed for bronchial tree segmentation. Most of these algorithms use an extended version of the region growing segmentation method to delineate the pulmonary airways.²⁰⁻²⁴ In the proposed algorithm, the main aim of bronchial tree segmentation is to separate the left and right lungs while fine details of the bronchial tree are not necessary for diaphragm segmentation. As such, the original region growing algorithm was used to segment the bronchial tree. In order to initialize the region growing algorithm, the seed point was detected automatically by searching the CT axial slices one by one, starting from the first axial slice. Figure 3(a) illustrates the intersection of an arbitrary axial slice of the CT image with the trachea being segmented. As shown in Fig. 3(b), the oval area of the trachea is usually present in the CT axial slices located above the lung apex. Accordingly, the initial seed point for the region growing algorithm was detected by exploring the area of intersection to find a voxel with CT number smaller than -950 HU. The -950 HU was used instead of the air CT number, -1000 HU, to account for partial volume averaging. After separation of the bronchial tree and lungs, if the left and right lungs remain connected even following bronchial tree removal, dynamic programming can be used to separate the lungs from each other.²⁵ However, in all the

cases used in this study, the left and right lungs were successfully separated after bronchial tree removal.

3.2.3 Heart segmentation

As part of this study, we developed a fast and robust method for heart segmentation, which is described in this section. Given that the heart is located between the lungs in coronal slices, it can be located using the segmented lungs. After locating the subimage which contains the heart, it is thresholded for values smaller than 35 HU to segment the heart's surrounding tissue. This threshold value corresponds to the maximum of the subimage histogram, which is ~35 HU for all nine cases. The resulting thresholded subimage, which is shown in Fig. 4(a), is a binary image in which the heart appears like a cavity. In the next step, zero voxels in each of the resulting coronal binary images are labeled as "contained" or "uncontained" voxels. A "contained" voxel is a voxel, which is bounded by at least four nonzero voxels; otherwise, it is labeled as "uncontained." It is noteworthy that using the aforementioned criteria for labeling the voxels, a voxel which is labeled as "contained" is not necessarily inside the heart. The result of this labeling step is shown in Fig. 4(b), where the "contained" voxels are shown in blue while the "uncontained" voxels remain black. Finally, the heart is segmented by finding the largest connected component of the "contained" voxels in order to eliminate "contained" voxels outside the heart. The resulting surface is then smoothed by morphological image closing. The connected components of the "contained" voxels are shown with different colors in Fig. 4(c), whereas the segmented heart is shown in Fig. 4(d). The heart boundary obtained through the proposed segmentation algorithm may not always be smooth. Nevertheless, the diaphragm segmentation algorithm remains effective as the segmented heart is used indirectly to segment the heart's contact surface with the diaphragm.

3.2.4 Delineation of descending aorta

According to Figs. 1(a) and 1(b), the diaphragm is attached to the lumbar spine by means of two tendinous pillars, which wrap around the aorta. In order to segment this part of the diaphragm, the descending aorta was segmented and used to find the position of the diaphragm's lumbar part. The aorta segmentation has been tackled by many groups, such as Behrens et al.²⁶ and Avila-Montes et al.,²⁷ who used Hough transform for this purpose. Since segmentation of the entire aorta is not necessary in this

Fig. 3 (a) The intersection area between the first axial slice of the 3-D CT volume and the trachea being segmented by image thresholding used to find the initial seed point for bronchial tree segmentation. (b) The box depicts the trachea (oval area), which is usually present in the first axial slice of the CT image.

Fig. 4 (a) A coronal subimage containing the heart, which was thresholded for values smaller than 35 HU, (b) The zero voxels in the thresholded binary subimage are labeled as "contained" (blue) and "uncontained" (black) voxels, (c) the color labeled connected components of the "contained" voxels, and (d) segmented heart overlaid on the CT image.

context, the position of the lumbar spine, which is the spine portion below the lungs, was used to find the approximate location of the descending aorta. For this purpose, a volume around the spine which, according to the human anatomy includes the aorta, was extracted from the CT image. Next, Hough transform was used to find the aorta in each axial slice of the extracted volume.

3.2.5 Segmenting the diaphragm contact surfaces with adjacent anatomical structures

In order to segment the diaphragm's contact surfaces with its adjacent structures, first, all the segmented anatomical structures were dilated with a structuring element of size 1. Segmentation of the contact surfaces between these structures and the diaphragm is described in the following subsections.

Lung. As shown in Fig. 1(c), the diaphragm is in contact with the bottom surface of the lungs. As such, the diaphragm domes were segmented by developing an algorithm, which uses the coronal slices of the CT image to find the arc shaped curves at the bottom surface of the lungs in each slice. For each lung, the algorithm begins with reading the coordinates of the voxels from one end of the lung's bottom surface. Based on the shape of the lung's bottom surface in the coronal slices, the algorithm first finds five consecutive voxels, which have ascending height by marching toward the other end of the bottom surface. Once found, they are stored as the first diaphragm voxels in that coronal slice. Finding more such voxels is continued as long as the arc's peak is not reached. Once the height of a specific voxel starts to decline, the criteria for choosing a voxel as the diaphragm's voxel changes to having descending

Fig. 5 The diaphragm's contact surfaces with both lungs obtained from applying an arc detection algorithm on the most inferior voxels of both lungs.

height. The application of this algorithm to the lung's most inferior voxels is illustrated in Fig. 5.

Heart. In order to find the heart–diaphragm contact surface, a narrow box around the bottom part of the heart was considered and Canny edge detection method was used to segment the diaphragm edges in this area. The size of the box is adjusted automatically for each coronal slice by first finding the most left, right, and inferior voxels of the heart in the coronal slice. The co-ordinates of the box vertices are (L+10, B–5), (L+10, B+5), (R–10, B+5), and (R–10, B–5), where L is the most left, R is the most right, and B is the most inferior voxel in each coronal slice. The box co-ordinates and Canny filter parameters were obtained empirically by testing all nine cases and averaging between them. The canny filter parameters were set to: lower threshold = 8, upper threshold = 10, and variance = 10. After applying Canny edge detection to the area within the box, only the closest detected edge to the heart is selected as the diaphragm's contact surface with the heart. The result is shown in Figs. 6(a) and 6(b).

Ribs, lumbar spine, and descending aorta. After segmentation of the ribcage and descending aorta, we used the same concept described in Sec. 3.2.3 for heart segmentation to

Fig. 6 (a) A subimage (within the shown box) containing the heart's contact surface with the diaphragm and (b) the segmented heart's contact surface with the diaphragm obtained from applying the Canny edge detection algorithm on the selected subimage.

segment the contact surfaces between the diaphragm and these organs. For that purpose, we first used morphological image closing to combine the ribcage and aorta, as shown in Fig. 7(a). Next, the image voxels were labeled as “contained” and “uncontained” similar to what was done for the heart segmentation, thereby allowing the boundary between the “contained” voxels and closed ribcage, shown in Fig. 7(a), to be found. Finally, the inferior part of the obtained boundary, which is located below the lungs, was found and selected as the contact surface between the ribcage, aorta, and diaphragm. The result is shown in Fig. 7(b).

3.2.6 Multilevel B-spline

For interpolation between the diaphragm fragments obtained to approximate its entire surface, the B-spline approximation technique was used. However, it is known that a trade-off exists between the surface smoothness and segmentation accuracy. As such, the multilevel B-spline approximation method proposed by Lee et al.²⁸ was used for approximating the diaphragmatic surface in order to circumvent the aforementioned trade-off. The multilevel B-spline technique is based on the B-spline method of function fitting/approximation to a set of scattered data represented by $P = \{(x_c, y_c, z_c)\}$. The function $z \cong f(x, y)$, which approximates P can be formulated as a uniform bicubic B-spline function, which is defined by a control lattice Φ overlaid on a two-dimensional (2-D) plane as follows:

$$f(x, y) = \sum_{k=0}^3 \sum_{l=0}^3 B_k(s) B_l(t) \phi_{(i+k)(j+l)}, \quad (2)$$

where $i = \lfloor x \rfloor - 1$, $j = \lfloor y \rfloor - 1$, $s = x - \lfloor x \rfloor$, $t = y - \lfloor y \rfloor$, and B_k and B_l are uniform cubic B-spline functions. As such, function f can be derived by solving for ϕ_{ij} that best approximates the data in P . These control points can be determined by using a least squares-based approach, leading to

$$\phi_{kl} = \frac{B_k(s) B_l(t) z_c}{\sum_{a=0}^3 \sum_{b=0}^3 (B_a(s)^2 B_b(t)^2)}. \quad (3)$$

The multilevel B-spline approximation is a hierarchical version of B-spline approximation technique. In this method, a hierarchy of control point lattices, $\Phi_0, \Phi_1, \dots, \Phi_h$ are used to find the approximation function f , where 0 and h correspond

to the coarsest and finest lattices, respectively. The approximation process begins with applying the B-spline approximation technique on the coarsest grid to find the general shape of the object, which is further refined in following steps. The function f_0 obtained from the first step leaves a deviation of $\Delta^1 Z_c = z_c - f_0(x_c, y_c)$ for each point (x_c, y_c, z_c) in P . In the following step, the finer grid Φ_1 is used to find the function f_1 , which approximates the deviation $\Delta^1 Z_c$. As such, $f_0 + f_1$ results in a smaller deviation for each point. Repeating this algorithm results in a more accurate approximation of P .

The accuracy of the output depends on the size of the finest mesh or the largest level used in the multilevel B-spline approximation method. In this study, the diaphragm portions segmented in the previous steps were interpolated using B-spline interpolation method with initial grid size of 4 and level 6, leading to favorable segmentation results.

The final step in this diaphragm segmentation algorithm is to obtain the end points of diaphragm's attachments to the spine. It is known that the diaphragm's pillars are attached to the third lumbar vertebra.¹⁸ As such, an algorithm was developed to find the location of the third vertebra in the CT image by finding the location of the transverse processes of the third vertebra. For this purpose, first, the start point of the right twelfth rib, where it is attached to the spine, was found. Hence, a narrow volume with 40 mm × 60 mm cross-section located below and at the right side of this point was inspected from top to bottom to find the third connected component. The location of the third lumbar vertebra was used to determine the circumference of the diaphragm close to the spine.

The proposed algorithm was implemented using ITK. The desktop used in this study was a core i7 Intel, 2 GHz. Parallel programming and multithreading was not used at this stage.

4 Results

4.1 Qualitative Assessment

In order to validate the algorithm, all the images were manually segmented by an experienced radiologist. Figures 8–10 illustrate the results obtained for three patients. The top row of each figure shows the automatically delineated (blue) sections of the diaphragm overlaid on their manually delineated counterparts (white). Figures 8(a) and 8(b), 9(a) and 9(b), and 10(a) and 10(b) illustrate automatically delineated coronal sections of

Fig. 7 (a) Segmented ribcage and aorta after performing morphological image closing overlaid on the CT image and (b) axial section of the contact surface between the diaphragm, ribs, spine, and aorta.

Fig. 8 The results obtained for subject #1. The first row depicts automatically delineated (blue) sections of the diaphragm overlaid on their manually delineated counterpart (white). (a) and (b) Coronal and (c) an axial view. The second row depicts 3-D construction of the diaphragm surface. (d) Front, (e) back, and (f) top views.

Fig. 9 The results obtained for subject #2. The first row depicts automatically delineated (blue) sections of the diaphragm overlaid on their manually delineated counterpart (white). (a) and (b) Coronal and (c) an axial view. The second row depicts 3-D construction of the diaphragm surface. (d) Front, (e) back, and (f) top views.

the diaphragm overlaid on their manually delineated counterparts, while Figs. 8(c), 9(c), and 10(c) depict the same results for an axial slice of the diaphragm. The results were evaluated by comparing the automatically segmented contours with those segmented manually and independently by the radiologist. In general, there is a very good agreement between the automatic and manually segmented contours. The strong agreement exists close to the lungs, ribcage, and aorta. As it is expected, the errors mainly occur close to the heart and coastal cartilage due to the difficulties in segmentation of these organs. However, only a small portion of the diaphragm is in contact with the heart and coastal cartilage. As such, the overall accuracy is not affected by these errors.

In Figs. 8–10, the bottom row of each figure illustrates different views of the 3-D surface of the patient's diaphragm constructed using the automatic segmentation technique. The Model Maker module in 3-D slicer was used to visualize the 3-D surfaces. The model maker module is a pipeline of algorithms that start from the segmented image, creates a binary label map from the segmented image, generates a marching cubes model, and runs triangle reduction and triangle smoothing algorithms.

4.2 Quantitative Assessment

To assess the proposed technique's accuracy, results of the automatic segmentation of the nine patients were compared to their

Fig. 10 The results obtained for subject #3. The first row depicts automatically delineated (blue) sections of the diaphragm overlaid on their manually delineated counterpart (white). (a) and (b) Coronal and (c) an axial view. The second row depicts 3-D construction of the diaphragm surface. (d) Front, (e) back, and (f) top views.

manually segmented counterparts. For this comparison, four different measures were used: the Hausdorff distance, MDCP, ASASD, and SRMSSD. Results obtained from this comparison are summarized in Table 1. The Hausdorff distance measure was calculated for the entire diaphragm surface and for its superior portion. The superior portion surface is the portion of the diaphragm that is in contact with the inferior surfaces of the lungs. The latter Hausdorff distance was calculated in order to facilitate comparison with the diaphragm automatic segmentation techniques, which segment only the diaphragm’s upper surface. The table shows that the average MDCP is 2.55 mm, the average ASASD is 2.06 mm, the average SRMSSD is 3.51 mm, and

finally, the average Hausdorff distance for the entire diaphragm and upper surfaces are 23.42 and 18.72 mm, respectively.

5 Discussion

A fully automatic anatomy-based algorithm was proposed for segmentation of the entire diaphragm in noncontrast CT images, which are the most common images used in the clinic. The challenges associated with the diaphragm segmentation, such as its similar tissue density distribution to its surrounding organs, are dealt with by using *a priori* anatomical knowledge about the human diaphragm. By relying more on the diaphragm’s anatomy and less on its appearance in CT images, the proposed

Table 1 Results summarizing the comparison between the automatic and manual segmentation of the diaphragm of nine patients using the mean distance to the closest point (MDCP), Hausdorff distance, ASASD, and SRMSSD.

Subject	MDCP for entire diaphragm surface (mm)	Hausdorff distance for entire diaphragm surface (mm)	Hausdorff distance for diaphragm’s superior surface (mm)	ASASD (mm)	SRMSSD (mm)
P # 1	3.01	23.98	18.03	2.51	4.19
P # 2	2.27	22.12	20.10	1.99	3.26
P # 3	2.73	24.07	19.01	1.88	3.08
P # 4	2.01	24.27	14.33	1.78	3.02
P # 5	2.88	22.44	21.21	2.33	3.98
P # 6	3.03	24.11	20.61	2.40	3.95
P # 7	2.52	23.90	19.92	2.12	3.80
P # 8	2.04	23.01	17.00	1.64	3.01
P # 9	2.43	22.86	18.23	1.93	3.30
Mean ± STD	2.55 ± 0.39	23.42 ± 0.81	18.72 ± 2.13	2.06 ± 0.30	3.51 ± 0.47
Range	[2.01, 3.03]	[22.12, 24.27]	[14.33, 21.21]	[1.64, 2.51]	[3.01,4.19]

algorithm is robust to noise-level and image contrast. An example of anatomical information utilized in the algorithm pertains to the fact that a large portion of the diaphragm is in contact with the lungs and ribcage. The lungs and ribcage have sufficient contrast with their surrounding regions in CT images, rendering their segmentation less sensitive to noise level. Besides segmenting the entire diaphragm and using the most accessible clinical images, the proposed algorithm has two important features: (1) it is fast, as it typically takes ~ 28 min using a core i7 desktop to segment a full diaphragm while manual segmentation by an expert took 5 h on average, and (2) the algorithm is easy to implement and can be used by nonexperts to segment the diaphragm for various applications, including biomechanical modeling or function analysis. The proposed technique has a limitation pertaining to segmentation of the sternal part of the diaphragm, where the diaphragm is in contact with the costal cartilage and the heart. The reason is that segmentation of the costal cartilage and heart is challenging due to their similar tissue density distribution to the surrounding anatomical structures. We developed a reasonably accurate segmentation technique for the heart segmentation. However, the accuracy of segmentation in that region is lower. Another limitation pertains to a small group of subjects, who have anatomical abnormalities. To address these limitations, more rigorous algorithms should be used in the first step for segmenting the diaphragm's surrounding organs, which may increase the computation time. Concerning the first limitation, since only a small portion of the diaphragm is in contact with the heart and costal cartilage, accuracy in these regions does not affect the overall accuracy significantly. As for the second limitation, the step-by-step nature of the proposed algorithm allows to replace the initial segmentation steps with more rigorous algorithms. However, as it increases the computation time and the algorithm's complexity while only a small group of subjects may benefit from that, developing a separate algorithm for such subjects is justified.

The proposed algorithm might have a limitation regarding any kind of disease, which affects the diaphragm's anatomy or the anatomy of its surrounding organs. In our dataset, there are cases, where the anatomy of ribcage or aorta has been altered but the results are still accurate as the diaphragm's anatomy has changed in a similar way. We believe that as long as the diaphragm is still in contact with its surrounding organs and those organs can be segmented with the proposed segmentation methods, the proposed algorithm can be used to segment the diaphragm effectively.

The quantitative results are listed in Table 1. There are four other groups, who have conducted studies on diaphragm segmentation. While the four methods proposed by those groups are suitable for the applications they were designed for, none of them meets the segmentation requirements for applications, which involve the diaphragm's mechanical boundary conditions (e.g., biomechanical modeling of the diaphragm). The algorithm proposed by Beichel et al.¹¹ has two limitations. First, it was designed for segmenting the diaphragm's dome surface only and not the entire diaphragm. Second, their algorithm is based on AAMs, which means that it is sensitive to diaphragm shape variations during breathing. The test dataset they used for validating their algorithm consists of six original and two computer-generated datasets. Signed error between all voxels of the reference surface (ground truth) and the closest voxels of the model dome surface was used to assess the segmentation accuracy. They reported an

average signed error of -0.16 ± 2.95 mm for their complete dataset. To facilitate comparison with this work, we calculated the average signed error of our dataset, which led to a value of 0.18 ± 0.08 mm that compares well with the value of -0.16 ± 2.95 mm. It is noteworthy that our results correspond to the full diaphragm scenario while their results pertain to the diaphragm's upper surface only.

Unlike Beichel et al.,¹¹ the algorithms proposed by Zhou et al.¹³ and Yalamanchili et al.¹⁶ are not sensitive to diaphragm shape variations. Both algorithms use the lung's bottom surface to find the diaphragm's upper surface. The first algorithm takes advantage of the thin plate spline interpolation, whereas the second algorithm uses a graph-based method to approximate the diaphragm's upper surface from the lung's bottom surface. While both algorithms work well for diaphragm's upper surface segmentation, again they are not suitable for applications, where the entire diaphragm including its inferior boundaries is required (e.g., diaphragm biomechanical modeling application). Yalamanchili et al.¹⁶ applied their algorithm on seven patients and reported an average Hausdorff distance of 18.339 ± 3.655 mm, which is comparable with the Hausdorff distance we have obtained for the superior portion of our segmentation, 18.72 ± 2.13 mm. Zhou et al.¹³ performed a step-by-step validation scheme. In the first step, they used a threshold value to divide the results to two groups of "good" and "poor." In the second step, the average absolute shortest Euclidean distance was used to assess the results for 30 subjects, who were labeled as "good" in the first step. They reported an average error of 2.97 voxels (1.8 mm) for the 30 patients they selected from the "good" group. We believe that direct comparison between our results and the results reported by Zhou et al.¹³ is not possible because they removed the poor results from their study. Although we did not exclude the poor results from our dataset, the mean ASASD of our results is 2.06 mm, which compares well with 1.8 mm, considering that we segmented the entire diaphragm and not just its superior surface.

The results presented by Rangayyan et al.¹⁴ are closer to what is required for diaphragm biomechanical modeling. However, as Rangayyan et al.¹⁴ state in their discussion, their algorithm overestimates the lumbar part of the diaphragm, where it is close to the spine. This overestimation results in a different diaphragm shape compared to its real shape, which can affect the accuracy of a respective diaphragm's biomechanical model. In addition, the results obtained by our group are more accurate than those reported by Rangayyan et al.¹⁴ (MDCP = 2.55 mm versus MDCP = 5.85 mm). It is noteworthy that their segmentation goal is different from our segmentation goal and what they have achieved satisfies their goal, which is abdominal tumor segmentation. However, their results are not satisfactory for diaphragm biomechanical modeling.

6 Conclusion

Segmentation with sufficient morphological details obtainable from the proposed segmentation technique is a prerequisite for many biomedical applications. The major application of the entire diaphragm segmentation is to develop accurate computational biomechanical models of the diaphragm. Accurately segmented diaphragm can be easily turned into a computational finite-element mesh, while its outline can be used to delineate necessary boundary conditions of the model. In addition, the diaphragm computational models can be used in various applications ranging from in-depth understanding of the diaphragm's

physiology and developing effective diagnostic techniques of relevant respiratory diseases to computer assisted clinical procedures, such as lung cancer radiotherapy and liver intervention. In-depth understanding of the diaphragm's physiology can be achieved by biomechanical modeling of the diaphragm to quantify its contraction forces and assess their variation throughout respiration cycle under normal and pathological conditions. Lung cancer radiotherapy can also benefit greatly from accurate biomechanical modeling of the diaphragm as a major driver of lung tumor motion during respiration cycle. In this case, the model can be integrated with the lung's biomechanical model to facilitate accurate prediction of the tumor motion, paving the way for computer-assisted motion compensation in the radiotherapy procedure. In addition, considering that the diaphragm is an important landmark separating the thorax from the abdomen, segmenting its surface can simplify localization and segmentation of the other abdominal and thorax organs, such as the liver.

The results obtained in this study indicate that the proposed algorithm is capable of accurate delineation of the entire diaphragm, paving the way for accurate biomechanical modeling of the diaphragm necessary for many clinical applications.

Disclosures

No conflicts of interest, financial or otherwise, are declared by the authors.

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