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A constrained linear regression optimization algorithm for diaphragm motion tracking with cone beam CT projections

Jie Wei^a, Ming Chao^{b,*}

^aDepartment of Computer Science, City College of New York, New York, NY 10031, USA

^bDepartment of Radiation Oncology, Mount Sinai Medical Center, New York, NY 10029, USA

Abstract

Purpose: We presented a feasibility study to extract the diaphragm motion from the inferior contrast cone beam computed tomography (CBCT) projection images using a constrained linear regression optimization algorithm.

Methods: The shape of the diaphragm was fitted by a parabolic function which was initialized by five manually placed points on the diaphragm contour of a pre-selected projection. A constrained linear regression model by exploiting the spatial, algebraic, and temporal constraints of the diaphragm, approximated by a parabola, was employed to estimate the parameters. The algorithm was assessed by a fluoroscopic movie acquired at anterior-posterior (AP) fixed direction and kilovoltage CBCT projection image sets from four lung and two liver patients using the Varian 21iX Clinac. The automatic tracing by the proposed algorithm and manual tracking were compared in both space and frequency domains for the algorithm evaluations.

Results: The error between the results estimated by the proposed algorithm and those by manual tracking for the AP fluoroscopic movie was 0.54 mm with standard deviation (SD) of 0.45 mm. For the detected projections the average error was 0.79 mm with SD of 0.64 mm for all six enrolled patients and the maximum deviation was 2.5 mm. The mean sub-millimeter accuracy outcome exhibits the feasibility of the proposed constrained linear regression approach to track the diaphragm motion on rotational fluoroscopic images.

Conclusion: The new algorithm will provide a potential solution to rendering diaphragm motion and possibly aiding the tumor target tracking in radiation therapy of thoracic/abdominal cancer patients.

Keywords

Diaphragm motion; Cone beam CT projections; Radiation therapy; Tumor motion management

*Corresponding author. wei@cs.ccny.cuny.edu (J. Wei), ming.chao@mountsinai.org (M. Chao).

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1. Introduction

In highly conformal radiation therapy of thoracic or abdominal cancer, respiratory motion management is critical in precise delivery of radiation dose to the target region. A number of techniques have been proposed for better motion control, such as respiratory gating [1,2], incorporating motion into treatment volume [3,4]; breath holding [5-7], and tumor tracking [8-13]. Gating is widely chosen to treat lung cancer patients. It often employs a tumor surrogate such as an external marker or an abdominal belt to infer the tumor motion. The downside of this technique is that the correlation between the surrogate and the tumor target is unstable and can vary drastically depending on the patient's condition [1,2,14,15]. Additionally, it may suffer from the problem of phase shift as reported in a number of studies [14-19]. The internal target volume (ITV) strategy by incorporating motion as an internal margin is another common choice but it is subject to the obvious problem of over irradiation to healthy tissues [20]. Breath holding was proposed to immobilize the lung tumor almost two decades ago [5-7] although it is a more popular option to treat breast cancer aiming at reducing radiation dose to the heart [20]. The major problem is the patient's compliance, especially for lung cancer patients due to their compromised pulmonary conditions. Tumor tracking technique by implanting radiopaque fiducial markers or transponders near the tumor can directly provide information on tumor motion [11,12]. However, this involves an invasive procedure and may not be suitable for every patient owing to the potential risk of pneumothorax [21-23]. Given the practical issues of these methods, the non-invasive tumor tracking strategy appears particularly attractive in the motion management for lung cancer radiotherapy.

Tumor motion can be captured on fluoroscopic images acquired on either the anterior-posterior (AP) sequences or the rotational radiographic projection images for cone beam computed tomography (CBCT) acquired immediately prior to treatment, both with on-board X-ray imaging [19,24-27]. The bottleneck issue in tracing tumor motion on these images is the poor visibility of the tumor target because of the inherently inferior image contrast. For rotational projection images, depending on the view angles, complex anatomies such as vertebrate body and tissue could be overlaid on top of the tumor target, making the reliable target identification practically impossible. Even with sophisticated feature recognition techniques it is still hard to extract the tumor motion from the projection images or orthogonal X-rays, despite the relatively long computing time [28,29]. The detection of tumor motion is easier on AP image sequences than on rotational projection images. It is, however, unable to reveal the tumor's positional information in three dimensions.

A more practical method is to extract patient breathing motion based on prominent feature such as diaphragm or carina on projection images. The diaphragm has superior contrast to most lung tumors on the projection images, so it can be more reliably detected on these images. A robust method to extract the breathing motion from rotational projection images is through the procedure called the Amsterdam Shroud technique [10,30,31]. In this method the respiratory motion is extracted from the two-dimensional image formed by concatenating each projection that is summed into a column along the superior-inferior direction of the kV imager. However, the limitation of this method is that the breathing

motion pattern cannot be extracted until the entire scan is completed, making it impractical for real time tumor motion tracking.

Given the special geometric and the image contrast properties of the diaphragm, the commonly used method in detecting the diaphragm is the active contour algorithm [32-34]. The behavior of an active contour f is determined by the following commanding energy function:

$$E(f) = E_{ext}(f) + \lambda E_{int}(f), \quad (1)$$

where the *external energy term* $E_{ext}(f)$ is the data fitting term to penalize the difference of the evolving contour f from the given data; *internal energy term* $E_{int}(f)$ encodes the desired shape information of the curve, mostly a function of the similarity/continuity of the first or second order derivatives of f at adjacent locations. The shape weight parameter λ is employed to adjust the relative contributions of these two terms: if the smoothness of the curve is more desirable, a larger λ is assigned, and vice versa. The search for the optimal f is the minimization process of the total energy $E(f)$ through different optimization processes, such as gradient descent algorithm or level set optimization. In the presence of severe noises as on the CBCT projections, the variational framework dictated by Eq. (1) may not work well without proper constraints.

In view of the difficulty of the active curve approaches, we strive to attack this diaphragm motion tracking problem by exploiting the prior knowledge and the most desirable property of f with the parabolic curve, the global model we chose to approximate the shape of the diaphragm boundary, which provides a considerably stricter constraint for $E_{int}(f)$ and significantly reduces the search space of diaphragm boundary points. In consequence, we introduce a constrained linear regression technique facilitated by the spatial, algebraic, and temporal constraints in the geometry and dynamics of the diaphragm movements. Minimum manual intervention is needed to fit the diaphragm shape. The peak of the parabolic curve is calculated to serve as the estimated apex point of the moving diaphragm.

The goal of this work is to track respiratory motion of diaphragm based on a constrained linear regression optimization algorithm to facilitate the lung tumor motion tracking. The successful implementation of this technique will benefit lung cancer patients for their radiation treatment.

2. Materials and methods

2.1. Overview of the diaphragm tracking algorithm

The primary steps of the diaphragm motion tracking algorithm are summarized in the flow chart depicted in Fig. 1. Raw CBCT projections were acquired while the patients lay on the treatment couch prior to the radiation therapy treatment. The images were subsequently imported into an in-house software based on MATLAB (The MathWorks, Inc., Natick, MA). Initially the projections underwent a preprocessing step to enhance their inferior contrast using the procedure we introduced earlier, i.e., the intensity to attenuation conversion by normalizing each projection image intensity with the air intensity with a logarithmic

operation [31]. Meanwhile, the projection images were down-sampled by reducing the pixel number by a factor of two along both lateral and longitudinal directions while keeping the same spacing to reduce the required time and space computational complexity. The top boundary of the diaphragm is dome shaped and can be geometrically approximated by a parabolic function. The goal is to find the parabolic parameters for the diaphragm boundary on the CBCT projections. To avoid ineffective random searches for the parabolic objects on the images, initial points on a pre-selected projection are assigned. A clinical physicist interactively (by mouse clicks from a graphics user interface made available by an MATLAB script) selects an initial region of interest (ROI) where the diaphragm boundary is to be tracked and at least five diaphragm boundary points in the pre-selected projection F^1 , the initial parabola coefficients are then estimated. On the subsequent projections F^t , $t = 2, \dots, n$, the individual points on the diaphragm boundary are detected with a modified Canny edge detection procedure. The coordinates of the boundaries (x, y)'s together with the parabolic parameters are determined based on the proposed constrained linear regression algorithm including additional algebraic and motion band constraints. The ROI is also updated according to the estimated curve to ensure the diaphragm being tracked is enclosed. In the subsequent sections each step is described at great lengths.

2.2. Diaphragm boundary point detection

It is essential to search for a point on the diaphragm before the entire diaphragm shape can be established. Because of the high image contrast on the diaphragm layer between the thorax and abdomen, candidate points must be those with strong edge pixels. Among all edge detection methods, Canny edge detector [35] can usually deliver optimal results in general. However, for the purpose of diaphragm detection this otherwise powerful method reported too few edge pixels owing to the use of the *non-maximal suppression step*. We adopted a first-order morphological approach in search of the possible diaphragm boundary points as detailed below. For each pixel $I(x, y)$, the gradient is first computed:

$$\nabla I = \left(\frac{\partial I}{\partial x}, \frac{\partial I}{\partial y} \right)^T, \quad (2)$$

where $\cdot^T$ is the transpose operator. A thresholding step is next applied to label initial edge point candidates E :

$$E = \{(x, y): |\nabla I(x, y)|^2 \geq \delta_e\} \quad (3)$$

In this work, the threshold δ_e is adaptively evaluated by conducting *Ostu's method* over the gradient energy image $|\nabla I(x, y)|^2$.

Next, the *image opening* operator, one of most popularly used morphological operators in image processing [36-38], is applied to filter out isolated edge points in E according to Eq. (3): only those edge points in E that belong to a connected component with significantly large size s , are deemed plausible edge point set P for diaphragm boundaries:

$$P = \{(x, y): (x, y) \in E \text{ and } |C(x, y)| > s\} \quad (4)$$

where $C(x,y)$ is the connected component. Each site in a component is 8-connected according to Eq. (3), and its size $|C(x,y)|$ is the number of site. The rationale behind Eq. (4) is: this morphological operator is based on the observation that diaphragm boundary points, with considerably large gradient energies, are mostly connected edge points, thus any relatively isolated edge pixels should be discarded as false positives. A parameter learning procedure [38] should be incurred to render our algorithm effective. This procedure is offline thus computational intensity is not an issue. A *grid search* with the ranges for s to be in the range [10, 100], is conducted with the available image data.

The final points $F(x, y)$ are those points in P of maximal ordinate y for each column (constant x) inside the special narrow band $B(\mathbf{v}^{t-1})$ determined by the parabola $\mathbf{v}^{t-1}$ at the preceding time instant $t - 1$ (see Eq. (17) of Section 2.4 below for technical details):

$$F = \{(x, y): (x, y) \in B(\mathbf{v}^{t-1}) \cap \operatorname{argmax}_{(x,y)}(x_c, y) \in P \text{ for } \forall x_c \in P_x\}, \quad (5)$$

where $\operatorname{argmax}_{(x,y)}$ is the operator to find the parameters x and y that maximize the following function, P_x is the set of all possible x values in the set P . As shown in Eq. (5), a step similar to but different from Canny edge detector's non-maxima suppression is conducted: instead of finding the points whose gradients are of the largest magnitudes along the gradient orientation, the most likely diaphragm points should be the ones having the highest ordinates, thus the use of *argmax* operator in Eq. (5). From Eqs. (2)-(5), it can be concluded that our approach to detecting diaphragm boundary points is closely related to Canny edge detector: except that we did not use the *non-maximal suppression* and *double threshold* step. In their place, to more reliably and closely reflect the special nature of diaphragm boundary points, we used image opening, Eq. (4), and highest point option.

2.3. Geometric shape of diaphragm boundaries: the parabola

Mathematically, the diaphragm boundary can be approximated by a parabola defined by the following formula:

$$y = a * x^2 + b * x + c, \quad (6)$$

where (x,y) are the horizontal and vertical coordinates of the points on the diaphragm; for ease of algebraic manipulation and mathematical presentation, after formulating the following data vector for x :

$$\mathbf{x} = [x^2, x, 1]^T, \quad (7)$$

Eq. (6) can be rewritten in the following equation:

$$y = \mathbf{x}^T \mathbf{v}, \quad (8)$$

Eq. (8) is the inner product of the parabola coefficient vector $\mathbf{v} = [a, b, c]^T$ and the data vector $\mathbf{x}$. Given data points (x_i, y_i) , $i = 1, \dots, n$, yielding the corresponding $(\mathbf{v}_i, y_i)$, by stacking all $\mathbf{v}_i$'s and y_i 's together:

$$X = [\mathbf{x}_1, \dots, \mathbf{x}_n]^T, \mathbf{y} = [y_1, \dots, y_n]^T, \quad (9)$$

where X is an $n \times 3$ matrix, while $\mathbf{y}$ is an n -dimensional vector. Based on the representation by Eq. (9), the system of n equations according to Eq. (8) is expressed in the following succinct form:

$$\mathbf{y} = X\mathbf{v}, \quad (10)$$

for $n \geq 4$, Eq. (10) is an actual over-determined system of linear equations, the coefficient vector $\mathbf{v}$ can be estimated by a linear regression procedure that minimizes the discrepancy between $\mathbf{y}$ and $X\mathbf{v}$:

$$\mathbf{v} = \operatorname{argmin}_{\mathbf{v}} \|\mathbf{y} - X\mathbf{v}\|, \quad (11)$$

The square error, namely, the inner product $(\mathbf{y} - X\mathbf{v})^T(\mathbf{y} - X\mathbf{v})$, is often chosen as the error norm $\|\cdot\|$, thus yielding the following vector $\mathbf{v}$:

$$\mathbf{v} = X^+ \mathbf{y}, \quad (12)$$

As illustrated in Fig. 2, using an in-house MATLAB script facilitating user inputs and visualization, a clinical physicist used mouse clicks to interactively choose five points on each side of the diaphragm, depicted as blue crosses. The parabola coefficient vectors $\mathbf{v}$'s for the diaphragm boundary are then estimated by the script based on Eq. (12). The parabola parameters for the diaphragm shown in Fig. 2 are $[a, b, c] = [0.005, -0.949, 404.041]^T$ and $[0.007, -6.695, 1921.597]^T$ for the left and right sides, respectively. Based on the estimates, all the diaphragm boundary points can be evaluated according to Eq. (6) or Eq. (7), which are plotted in Fig. 2 as two red lines. Visual inspection indicates that these two parabolas traced the diaphragm boundary desirably.

Since the number of boundary points that can be identified is likely larger than three in most projections, the regression operation as defined in Eq. (11) can thus effectively identify the diaphragm boundary for each projection. With the linear regression based method, Eq. (12), a clinical physicist only need to click on clearly evident diaphragm boundary points. The unique peak of the diaphragm, a proxy of the apex of the diaphragm, is readily available from the estimated parabola coefficient vector $\mathbf{v}$.

2.4. Constraints of the dynamic movements of a diaphragm

2.4.1. Temporal redundancy—Owing to the short time interval (< 0.1 s) between adjacent projections, the diaphragm's shape and position cannot experience drastic changes, namely, for the same diaphragm boundary, its shape D_t at time t should be in a location similar to D_{t-1} at preceding time $t - 1$. This feature is referred to as the *temporal redundancy*, which is the enabling technique behind the successful industry standards in video compression: H.264, MPEG-1, -2 and -4 [39], so it should provide a valuable constraint on solving Eq. (1). This technique yields a motion compensation approach:

instead of encoding each individual video frame (in CBCT cases, frame is often named as projection) F , for each small region $F_{i,j}^t$, referred to as a macro-block, indexed by its upper left corner located at coordinate (i, j) , in F , search for the matching region $F_{i',j'}^{t-1}$ in frame F^{t-1} at time instant $t - 1$ around adjacent spatial locations minimizing a certain error norm, e.g., L_2 measure, namely,

$$(i', j') = \underset{i1=[i-k, i+k], j1=[j-k, j+k]}{\operatorname{argmin}} \|F_{i1, j1}^{t-1} - F_{i,j}^t\| \quad (13)$$

Due to temporal redundancies, a region similar to $F_{i,j}^t$ is likely to present in a location adjacent to that of $F_{i,j}^t$, which is defined as the square of size $2k + 1$ centered at $F_{i,j}^t$, the location difference between the matching region $F_{i',j'}^{t-1}$ in F^{t-1} and $F_{i,j}^t$ is referred to as the *motion vector* $\mathbf{m}$, defined below:

$$\mathbf{m} = (i - i', j - j')^T, \quad (14)$$

according to Eq. (13) the magnitude of either component of $\mathbf{m}$ is at most k , based on the *prior belief* that the regions in F^{t-1} can only move at most k pixels. As done in most video processing literature [38], k is taken to be 3.

Based on the motion vector $\mathbf{m}$, one can encode the region difference $\delta_{i,j} = F_{i,j}^t - F_{i',j'}^{t-1}$ to represent $F_{i,j}^t$: due to temporal redundancy and the minimization procedure dictated by Eq. (13), this region difference $\delta_{i,j}$ is mostly of extremely small magnitude thus achieving data compression.

As illustrated in Fig. 3, two adjacent projections F^1 and F^2 , similar to the ones illustrated in Fig. 2, with parabolic diaphragm boundaries estimated by Eq. (12), are overlapped to emphasize the similarity and difference between these two projections. While the parabolic coefficients for the left diaphragm are similar, $\mathbf{v}_L^1 = [0.005 - 1.025 \ 407.006]^T$, $\mathbf{v}_L^2 = [0.005 - 1.071 \ 408.523]^T$: in Fig. 3 the corresponding two parabolas, the magenta and green ones, are essentially indistinguishable. The ones for the right diaphragm are discernibly different: $\mathbf{v}_R^1 = [0.007 - 6.795 \ 1934.866]^T$, and $\mathbf{v}_R^2 = [0.007 - 6.082 \ 1759.323]^T$, but still of relatively small magnitudes: with relative difference ratio at 0.0, 0.1, and 0.09, respectively. As delineated by Fig. 3: For a known diaphragm parabola $\mathbf{v}^{t-1}$ estimated in projection F^{t-1} , the corresponding diaphragm parabola $\mathbf{v}^t$, as a 3-D vector, should be present in the nearby location dictated by a 3-D threshold vector $\delta_{\mathbf{v}}$, all three components of which are of small magnitude. This is formulated in the following inequality as our first constrain due to temporal redundancy:

$$\mathbf{v}^{t-1} - \delta_{\mathbf{v}} \leq \mathbf{v}^t \leq \mathbf{v}^{t-1} + \delta_{\mathbf{v}}, \quad (15)$$

In our work, $\delta_{\mathbf{v}}$ is set at $0.1 * |\mathbf{v}^{t-1}|$, a 3-D constraint where the different scales innate to the three parameters are accounted for.

2.4.2. Algebraic constraint of the temporal redundancy—By Eq. (6), the three components of $\mathbf{v}^t$ are of different nature, thus the three values in the threshold vector $\delta_{\mathbf{v}}$ differ correspondingly. Ineq. (15) essentially dictates that instead of performing the *brute-force* linear regression procedure, as dictated by Eq. (11), to make the call of possible parabolic coefficient $\mathbf{v}^t$, which is highly sensitive to both random and system noise, the temporal redundancy constraint Ineq. (15) should be inserted. Just like the iterative decompression step in the video case [40], this procedure can iterate as a causal process in the same manner: Combining Eq. (11) Ineq. (15), the optimization procedure to estimate the parabolic coefficient vector is mathematically formulated as the following problem:

$$\mathbf{v} = \operatorname{argmin}_{\mathbf{v}} \|\mathbf{y} - X\mathbf{v}\|, s.t. \mathbf{l} \leq \mathbf{v} \leq \mathbf{u}, \quad (16)$$

Comparing Ineq. (15) and Eq. (16), the unknown $\mathbf{v}$ is constrained by the lower bound $\mathbf{l}$ ($= \mathbf{v}^{t-1} - \delta_{\mathbf{v}}$) and upper bound $\mathbf{u}$ ($= \mathbf{v}^{t-1} + \delta_{\mathbf{v}}$), whose values are known prior to the optimization procedure searching for $\mathbf{v}^t$. Eq. (17) is an actual constrained linear regression, which is available in most numerical computing package, e.g., **lsqlin** function in the optimization toolbox of MATLAB. The search space of $\mathbf{v}$ is thus reduced from unconstrained free 3D space $\mathbf{R}^3$ to a significantly smaller region bounded by $\mathbf{l}$ and $\mathbf{u}$ that can be effectively resolved.

2.4.3. Band constraint of the temporal redundancy—The temporal redundancy of diaphragm motion captured by Ineq. (15) is only the algebraic part. Since the diaphragm often moves at the breathing rate, ~15 breaths/minute, the candidate diaphragm points (x, y) used by the optimization procedure dictated by Eq. (16) should also be limited accordingly: in projection F^t , with known diaphragm parabola $\mathbf{v}^{t-1}$ in F^{t-1} , any candidate point (x, y) that is too far away from the locations the parabola can possibly reach should be discarded. Using the vector notation $\mathbf{x}$ for co-ordinate x, cf. Eq. (9), the necessary condition for any point (x, y) to be included in the constrained linear regression optimization procedure Eq. (16) should in addition satisfy the following condition:

$$B(\mathbf{v}^{t-1}): |y - \mathbf{x}^T \mathbf{v}^{t-1}| \leq b, \quad (17)$$

where b is a constant acting as a threshold. Similar to the parameter s in Eq. (4), a *grid search* with the ranges for b of [5,20] is conducted with the available image data. Upon empirical studies, b with a value of 10 yielded desirable results. More details about parameter training can be found in the Discussions section. Eqs. (16) and (17) essentially indicates that the candidate parabola for the diaphragm in the next projection F^t can only occur within the band $B(\mathbf{v}^{t-1})$ of width $2*b$ swept by the known parabola defined by $\mathbf{v}^{t-1}$ in the preceding projection F^{t-1} , which yields the narrow band constraint as summarized in Eq. (5) of Section 2.2.

2.5. Case studies and algorithm evaluation

CBCT projection image sets from four lung and two liver patients, together with a sequence of AP fluoroscopic images acquired at 15 frames per second, were retrospectively enrolled in the study to assess the performance of the algorithm developed in previous sections. All

CBCT projections were acquired with the On-board Imager on the Varian iX Clinac System Linear Accelerator (Varian Medical Systems, Palo Alto, CA). The imager has a geometric dimension of 40×30 cm with 1024×768 pixels in transverse and longitudinal directions correspondingly, measured by the resolution 0.39×0.39 mm² and the pixel pitch is 139 μ m². The imaging system has a source-to-axis distance (SAD) of 100 cm, and a source-to-imager distance (SID) of 150 cm. All image sets have 640–645 projections, acquired by a full circle of 360 degrees using a half fan CBCT acquisition mode in one minute, so the angle gap is around 0.55 degree. In the following, we adopt the projection number rather than the gantry angle to represent each view. The AP fluoroscopic movie was downloaded from a website (www.WAPWON.com) with patient information anonymized. In these series images we describe each image as a frame.

Objective assessment of the algorithm is infeasible because there is no ground truth for the diaphragm shape and location. Therefore, assisted by an in-house MATLAB code snippet enabling user inputs, visualization and data storage, a manual identification of the diaphragm apex point for all frames used in this study by a clinical physicist is conducted to provide plausible proxies of ground truth, and the automatic tracing based on the proposed algorithm and that by a clinical physicist is compared to evaluate the performance.

The computation was carried out on a normal workstation, Dell Precision T7610 with Intel Xeon CPU E5-2630 v2 @ 2.60 GHz, 32 GB RAM. For higher resolution CBCT cases, we only need a more powerful workstation with higher CPU speed and RAM size. For this work, all computing is performed in CPU since this is adequate for us to showcase the proof of concepts. If graphics processing unit (GPU) computing is employed, the processing time can be reduced furthermore so that real time tracking could be achieved.

3. Results

3.1. Anterior-posterior fluoroscopic image sequence

The proposed technique was first applied to the AP fluoroscopic image sequence. In these images the thoracic cavity including the diaphragm is in the field of view (FOV) while the under- and overlapping anatomy to the region is minimal, especially to the diaphragm. The diaphragm is clearly dome shaped in the sequence. Thus, this dataset can be utilized to evaluate the algorithm with high precision. As illustrated in the top row of Fig. 4, on frames #100, #200, and #300 the detected contour of the diaphragm is drawn as a red line. Fig. 5 demonstrates the diaphragm apex, or the *peak* position of the parabola function, of the motion trajectory (left) and the corresponding frequency spectrum (right). The blue curve corresponds to the results automatically estimated by the proposed algorithm, whereas the orange curve signifies the manual ones, which are overlaid for better visualization. The mean absolute difference between these two curves is 0.54 mm with the standard deviation (SD) 0.45 mm.

3.2. CBCT projection images

Different from the AP fluoroscopic movie where the dome shaped diaphragm is clearly visible on every frame, the CBCT projections have different diaphragm shapes at different

gantry angles. At some projections it could be completely absent owing to the half fan acquisition mode like in patient #3. Most importantly, noises coming from varied anatomies such as muscle and bone overlay on the diaphragm further aggravate the visibility. Therefore, the parabola model is unable to fit the diaphragm at every gantry angle, esp. from lateral sides even with the strong constraints. Indeed even clinicians cannot visually identify the diaphragm location in these angles. When the lung diaphragm is visible, mostly when CBCT projections are away from the two lateral sides where the gantry angles are 90 degree or 270 degree, the proposed algorithm can trace the diaphragm reliably. The third row of Fig. 4 shows the diaphragm boundary detection (red line) for one of the lung cancer patients (pat #1). Three representative projections #80, #100, and #120 are displayed. Fig. 6 depicts the overlaid diaphragm peak motion trajectories for four lung cancer patients. Note that for illustration purpose, in Fig. 6 we only show the projections where successful tracking is continuously extracted without any failure. The detection failure happens on projections when gantry rotates to the lateral side. The percentage of successful tracking on projections is listed in Table 1 for all enrolled patients.

The top two rows of Fig. 6 are from the same patient (#1) scanned at different time; the next two rows are from another same patient (#2), similarly scanned at different time. The last two are from different patients (#3 and #4). For patient #1 there are two rotational periods that clearly correspond to the respiratory motion of diaphragms as reported in Table 1. The top and second rows show the projections 40–180 and 350–450, respectively. Owing to the above-mentioned reasons, reliable diaphragm could not be always identified by the algorithm over all the projections, so only those where the diaphragm could be continuously detected are included in this figure. Similarly for patient #2 the consecutive projections being successfully detected are shown in the third row projections 40–190 and the fourth row projections 150–250. For patients #3 only on 100 continuous projections the diaphragm boundary could be reliably detected without failure due to the fact that the tumor is located in upper lung region thus in most projections the diaphragm falls beyond the FOV. Patient #4's diaphragm is in the middle of the FOV, but the noises on this image set prevent the algorithm from detecting the diaphragm boundary without interruption. The average errors range from 0.47 mm (from patient #2) to 1.07 mm (from patient #1) while the standard deviations follow the same pattern spanning from 0.36 mm to 0.94 mm as tabulated in Table 1. The average error and standard deviation are 0.79 mm and 0.66 mm, respectively. In the frequency domain, the agreement between the calculation and the manual detection is observed.

The diaphragm detection for one of the liver patients is demonstrated in the second row of Fig. 4 on projections #10, #35, and #70. Fig. 7 depicts the diaphragm apex motion trajectories for two liver cancer patients. Similar to the lung cases, only the continuous views where diaphragms were successfully detected are shown. The left is from patient #5 and the right from patient #6. For example, projections 400–500 and projections 1 – 201 are desirable for patient #5 and #6 without failure, respectively. The overall percentages of the successful detections on all projections are 96 and 85 for these two patients, respectively, where failures are almost all in the lateral scanning region. The average errors are 0.73 mm and 0.87 mm, respectively; while the SDs are very close, ~0.6 mm as listed in Table 1. The average error and the standard deviation are comparable to those of the lung cancer patients.

When initializing the search with the points on the diaphragm boundary, a small rectangle with the diaphragm around the center is chosen as the region of interest (ROI) to reduce the computational load thus making the entire algorithm almost in real-time: for an ROI of size 100×300 , the processing time taken by one iteration of the constrained optimization is consistently less than 0.1 s, hence 10 Hz CBCT capturing frequency can be processed in real time. The MVCBCT study [34] reported the computation time on a 2.66 GHz CPU was 30 s, leaving a big room for improvement, should real time diaphragm motion tracking be the goal.

4. Discussions

The respiratory motion of diaphragm was previously investigated with the AP fluoroscopic image sequence [19,32] and megavoltage (MV) CBCT projection images using the active contour models [34,41]. In these former studies, an energy function similar to Eq. (1) was optimized to search for the optimal diaphragm contour using a dynamic programming procedure. The contour search was accomplished with high accuracy without strict constraints. This was possible because of the following two factors: (1) the strong intensity gradient of the diaphragm border; and most importantly (2) the negligible interference of objects of similar shape nearby. In the latter study, the authors tried to extract the motion from megavoltage CBCT rotational projection images. More sophisticated techniques were necessary owing to the more severe noise in the vicinity of the diaphragm boundary. Active contour model alone was insufficient to derive the motion reliably. They chose the dynamic Hough transform to search for the boundary with approximation and subsequently refine the boundary contour with the active contour model. The projection images in their study were acquired with full fan mode which means that the diaphragm structure was in all views. In this work, one of the major reasons why we have only partial arc motion trajectories from the 360° scan is that the projection images did not always have diaphragm in all views due to the half fan acquisition mode as illustrated in patient #3. Both studies required human initialization process as we did. This step is necessary in that it will avoid the random search of the parabolic objections in the images. In the MVCBCT study, they even manually initialized the detection on two full inhale and two full exhale projections while we only placed initial points on one projection. The average root-mean-square error was found to be less than < 1.5 mm along the superior-inferior direction in their study. A better accuracy (< 1 mm) was achieved in our results, which is clinically acceptable.

Strong correlation has been established between the diaphragm motion and the lung tumor [19,32,34,41]. As demonstrated in these studies, the correlation factor could be over 0.95 (1.0 represents perfect correlation) and the average error of 0.8 mm. While the correlation is evident, caution on the phase shift needs to be taken into account [14-18]. This encouraging data motivated us to develop an efficient and effective approach to derive the respiratory motion based on the geometry and dynamic characteristics of the diaphragm.

In this work two parameters need to be fixed: one is the component size threshold s in Eq. (4); the other is the band length b in Eq. (17). A parameter learning procedure [38] should be incurred to render our algorithm effective. This procedure is offline thus computational intensity is not an issue. A *grid search* with the ranges for s and b are [10, 100] and [5,20],

respectively, is conducted with the image data based on ten patients. The training data set is more than those reported here as many of them are only portion of a full scan which, although incomplete to be presented as results, are valuable to be employed for parameter learning, where higher statistical significance can be ensure with more training data. The values of s and b with the optimal performance, the lowest mean errors between the automatically detected traces and the manual results (as a proxy of ground truths), is opted as the chosen values. After this procedure, the values chosen for s and b are 50 and 10, respectively. Indeed, the choices of these two parameters are not critical, slightly different values, such as $s = 45$ or 55 and $b = 8$ or 12 , will only yield slightly worse results.

The constrained linear regression technique was chosen with practical reasons. We have tried many well-established segmentation and tracking approaches such as snakes, level sets and gradient vector flow methods [42], without much success: no matter how many high quality initial points or even line segments were provided as the initial guess within this framework, due to the integration and rotating actions of the CBCT scan process, even in the angles close to the anterior and posterior projections that can be reliably handled by our proposed method, these active curves are quickly (persistently < 10 projections) disturbed by system noises and missed the diaphragm boundaries altogether. This is the primary reason for the algorithm failure. In this sense, we need prior knowledge about the geometric shape of the diaphragm boundary and more efficient constraints so that the identification and tracking of the diaphragm boundaries in the noisy cone beam projections could be accomplished.

The advantage of choosing the parabolic shape for the diaphragm boundary considerably reduced the search space of the most desirable curve f . A reasonably valuable estimate can be attained if more than three points along the authentic diaphragm boundary are available. However, to accomplish scalable diaphragm identification and tracking, except the initial human intervention to bootstrap the identification procedure, means should be found to let the computer find these points automatically without any additional help from human operators by using dynamic information learning in regions/durations with high confidence.¹ This adaptive learning based approach is viable since our current method can estimate diaphragm motion for more than 80% of the entire duration persistently, some as high as 96% (cf. last column of Table 1). Given that in human lungs or livers, many nondiaphragm organs are in the shape similar to a parabola, e.g., human heart, ribs, lung contours, the parabolic shape of diaphragm is not adequately outstanding to detect diaphragm boundary. A Hough transform based method [34], a widely used voting strategy to find shapes defined by a small number of parameters, such as lines, circles or ellipse by a voting strategy in the (possibly hierarchical) discrete parameter space grid, is ineffective to seek out parabolic shapes as diaphragm boundary. In this work, the algebraic simplification of the diaphragm, i.e., the parabola function, together with temporal redundancies, give rise to an effective constrained linear regression methodology to trace out diaphragm movements with encouraging performances.

¹Bayesian filtering approach is under active study in an effort to exploit curves estimated in reliable regions/time to bootstrap curve estimation in unreliable regions/time.

In Fig. 8, both the robustness and failure of the algorithm are illustrated. In the first row, for patient 5, while the significant noise exists such as ribs overlapping with the diaphragm, relatively acceptable diaphragm contour is detectable. On the other hand, as depicted in the second row, it is a typical case when the proposed tracking method began to fail. While successful tracking prior to projection # 180 for patient 1 as shown on the second panel, when the patient's rib starts to make its presence, the strong edge pixels due to rib are indistinguishable since neither the algebraic nor the spatial constraints can disqualify them, thus in projection #182, the left end of the estimated curve is dragged significantly to the left; and for the same reason, in projection #185, this interference is even more severe. In these two cases the resultant curves are still roughly acceptable and highly relevant to the diaphragm—the peaks of both estimated curves, although unable to track the authentic diaphragm tightly, remain to be of similar value (along the SI direction) of the apex of diaphragm. The situation is getting worse in the sequel: in projection #187, in addition to the left ribs, the strong edge pixel caused by lung tissues on the right part is present, whence the right part of the estimated curve is considerably away from the diaphragm. This is deemed as tracking failure. The curves estimated afterwards are entirely off the target, as illustrated in the rightmost projection #189. Based on the current tracking algorithm, the gradual tracking failure due to internal systematic interference such as entering ribs illustrated in Fig. 8 is inevitable, especially when the scanning angle is on the lateral sides. From our studies, the diaphragm contour can be tracked for around 90% of the views: Although the diaphragm cannot be tracked for the entire duration due to rampant noise and occlusion, esp. the left and right lungs switch sides, the rightly tracked portion is adequate to reliably estimate and predict diaphragm motion due to the innate regularity of the actual diaphragm motion. As shown in Fig. 7, if the periodic motion of the diaphragm boundaries can be tracked for more than two cycles, the periodic movement of the diaphragm can be closely extrapolated in other possibly missed region, combined with our previous work using global shape constraint [30]. Of course, ideally means should be found to not miss the diaphragm at all during the tracking process to render a more robust and reliable diaphragm motion tracking, new insights, predictive methodology and constraints are still needed to address this issue.

5. Conclusion

By taking advantage of the geometrical and dynamic properties of the diaphragm motion in CBCT projection images, its respiratory motion can be reliably traced by the constrained linear regression model using a parabola function. On the AP fluoroscopic movie sequence the diaphragm motion was reliably tracked. For rotational CBCT projections, the diaphragm contour can be detected and tracked reliably on around 90% of the views, with an average error of 0.79 mm compared to manual detections. With this sub-millimeter detection accuracy the tracking algorithm provides a practical tool to quantify the respiratory motion of the thoracic diaphragm in fluoroscopic images and rotational cone beam projection images. Additionally, the respiratory motion of the diaphragm obtained from this work can serve as the valuable guide for us to further trace the motion of lung tumors, which is being actively investigated.

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Fig. 1.
Flow chart of the proposed diaphragm motion tracking algorithm.

Fig. 2.
The top boundaries of diaphragms can be closely approximated by parabolas (the two red line). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Fig. 3. The similarities of parabolic diaphragm boundaries between two adjacent projections: magenta (projection F^{-1}) vs. green shapes (projection F^t). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Fig. 4. Illustration of tracking results for fluoroscopic image sequence (top row), a liver case (middle row) and a lung case (bottom row). Column 1: original frames; Columns 2–4: three sample tracking images. Red lines: the estimated parabolas tracking the shape of diaphragm boundaries. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Fig. 5.

The overlaid motion trajectories for the respiratory motion of the diaphragm peaks (blue) provided by the proposed algorithm overlaid with the manual detection of the diaphragm apexes (orange) on the anterior-posterior fluoroscopic image sequence. The position is zero-mean according to the algorithm detected peaks. The point-wise differences between the estimated values and the ground truth are plotted as the black curve. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Fig. 6.

The zero-mean respiratory motion trajectory, unit: mm, of the diaphragm peaks (blue) overlaid with those identified by manual detection (orange) on the CBCT projection images from four lung cancer patients. The top two rows are scanned from the same patient (#1) at different time. The next two rows are scanned from another patient (#2) at different time. The last two are from different patients (#3 on the left and #4 on the right). The point-wise differences between the estimated values and the ground truth are plotted as the black curve. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Fig. 7.

The motion trajectories of diaphragm apex points generated by automatically detected respiratory motion of the diaphragm peaks (blue) overlaid with those by manual detection (orange) on the CBCT projection images from two liver cancer patients. The left and right plot are from patient #5 and the patient #6, respectively. The point-wise differences between the estimated values and the ground truth are plotted as the black curve. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Fig. 8. Illustration of how the tracking method resists (top row) and fails (bottom row) in the presence of interfering structures.

Table 1

Summary of diaphragm contour detection for six patients enrolled in this study. Included in the table are successful projection range without failure (third column), mean error (fourth column) and standard deviation (fifth column). The last column shows the successful tracking percentage of projections relative to all projections.

Patient No.	Disease Type	Projection Range	Mean Error (mm)	Standard Deviation (mm)	Tracking percentage (%)
1	Lung	40–180	1.07	0.94	87
1	Lung	350–450	0.89	0.69	–
2	Lung	40–190	0.83	0.75	89
2	Lung	150–250	0.47	0.36	–
3	Lung	400–500	0.80	0.72	92
4	Lung	340–440	0.65	0.48	81
5	Liver	400–500	0.73	0.60	96
6	Liver	1–201	0.87	0.61	85