Registration of prone and supine CT colonography scans using correlation optimized warping and canonical correlation analysis

Shijun Wang,^{a)} Jianhua Yao, and Jiamin Liu

Imaging Biomarkers and Computer-Aided Diagnosis Laboratory, Radiology and Imaging Sciences, National Institutes of Health Clinical Center, Building 10, Room 1C368X, MSC 1182, Bethesda, Maryland 20892-1182

Nicholas Petrick

NIBIB/CDRH Laboratory for the Assessment of Medical Imaging Systems, Food and Drug Administration, 10903 New Hampshire Avenue, Silver Spring, Maryland 20993-0002

Robert L. Van Uitert and Senthil Periaswamy

iCAD Inc., 98 Spit Brook Road, Suite 100, Nashua, New Hampshire 03062

Ronald M. Summers^{b)}

Imaging Biomarkers and Computer-Aided Diagnosis Laboratory, Radiology and Imaging Sciences, National Institutes of Health Clinical Center, Building 10, Room 1C368X, MSC 1182, Bethesda, Maryland 20892-1182

(Received 6 August 2009; revised 5 October 2009; accepted for publication 12 October 2009; published 11 November 2009)

Purpose: In computed tomographic colonography (CTC), a patient will be scanned twice—Once supine and once prone—to improve the sensitivity for polyp detection. To assist radiologists in CTC reading, in this paper we propose an automated method for colon registration from supine and prone CTC scans.

Methods: We propose a new colon centerline registration method for prone and supine CTC scans using correlation optimized warping (COW) and canonical correlation analysis (CCA) based on the anatomical structure of the colon. Four anatomical salient points on the colon are first automatically distinguished. Then correlation optimized warping is applied to the segments defined by the anatomical landmarks to improve the global registration based on local correlation of segments. The COW method was modified by embedding canonical correlation analysis to allow multiple features along the colon centerline to be used in our implementation.

Results: We tested the COW algorithm on a CTC data set of 39 patients with 39 polyps (19 training and 20 test cases) to verify the effectiveness of the proposed COW registration method. Experimental results on the test set show that the COW method significantly reduces the average estimation error in a polyp location between supine and prone scans by 67.6%, from 46.27 ± 52.97 to $14.98 \text{ mm} \pm 11.41 \text{ mm}$, compared to the normalized distance along the colon centerline algorithm ($p < 0.01$).

Conclusions: The proposed COW algorithm is more accurate for the colon centerline registration compared to the normalized distance along the colon centerline method and the dynamic time warping method. Comparison results showed that the feature combination of z -coordinate and curvature achieved lowest registration error compared to the other feature combinations used by COW. The proposed method is tolerant to centerline errors because anatomical landmarks help prevent the propagation of errors across the entire colon centerline. [DOI: [10.1118/1.3259727](https://doi.org/10.1118/1.3259727)]

Key words: colon registration, correlation optimized warping, dynamic time warping, canonical correlation analysis, virtual colonoscopy

I. INTRODUCTION

Colon cancer is the second leading cause of cancer-related deaths in the United States, with 154 000 new cases and 52 000 deaths in 2007.¹ Computed tomographic colonography (CTC) allows relatively noninvasive detection of colorectal polyps and cancer screening.^{2,3} When CTC is performed in conjunction with computer aided detection (CAD) software, screening may become less time-consuming, and more potentially accurate for the radiologists.^{4–9} In CTC, a patient will be scanned twice—Once supine and once prone—to improve the sensitivity for polyp detection (Fig.

1). This increases CTC sensitivity by improving visualization of polyps that are located on one scan in uninterpretable collapsed or fluid-filled segments, and reducing false positives such as those due to residual stool, inadequate distention, and segmentation artifacts.^{10,11}

Because the colon moves between the prone and supine scans, colon registration is a challenging problem. One way to reduce the complexity of the problem is to register the centerlines of the prone and supine scans. To make full use of shape information of the colon for registration, Nain *et al.*¹² proposed a centerline registration algorithm based on

FIG. 1. Two typical three-dimensional colon CTC surface reconstructions of a 55 year old man (image generated using Viatronix CAD system). Left: Supine scan; right: Prone scan. Lines inside the segmented colon indicate centerlines. The Viatronix CAD system was only used for illustration of 3D colon surface. We used a hybrid segmentation proposed by Franaszek *et al.* (Ref. 17) for colon segmentation in the following experiments.

dynamic time warping (DTW) and colon distension along the centerline. They showed encouraging results for synchronized virtual colonoscopy. Nappi *et al.*¹³ proposed a region-based supine-prone correspondence method to reduce false positive CAD polyp candidates in CTC. Li *et al.*¹⁴ proposed a heuristic algorithm for the colon centerline registration by employing the coordinate information of the centerline. To assist radiologists in CTC reading, in this paper we propose an automated method for colon registration based on correlation optimized warping (COW) (Ref. 15) and canonical correlation analysis (CCA).¹⁶

II. EXISTING METHODS

In this section, we introduce the normalized distance along the colon centerline (NDACC) and DTW colon registration methods that can be found in the literature. These methods are described below and used as comparator methods in this study.

II.A. Normalized distance along the centerline

A straightforward method for matching CTC scans is the NDACC method.¹⁸ The centerline distance is the distance from a point on the colon centerline to the starting point of the colon (cecum or rectum) measured along the centerline. Considering that the colon may have some shape deformation based on localized stretching or contracting, the NDACC method maps the centerline distance to $[0, 1]$ and uses normalized distance for matching prone and supine CTC scans. For example, if we use polyp location as a measure for the match evaluation, then the NDACC match error is defined as

$$\text{match error}_{\text{prone}} = \text{NDACC}_{\text{supine}} \times \text{Length}_{\text{prone}} - \text{NDACC}_{\text{prone}} \times \text{Length}_{\text{prone}},$$

$$\text{match error}_{\text{supine}} = \text{NDACC}_{\text{prone}} \times \text{Length}_{\text{supine}} - \text{NDACC}_{\text{supine}} \times \text{Length}_{\text{supine}},$$

where $\text{Length}_{\text{prone}}$ and $\text{Length}_{\text{supine}}$ are total lengths of colon (cecum through anorectal junction) measured in prone and supine CTC scans, respectively.

II.B. Dynamic time warping

DTW is a widely used time series matching algorithm.¹⁹ Given two one-dimensional time series which come from multiple measurements of a physical process or object under different conditions, DTW tries to find the maximum similarity between these two time series though nonlinear mapping. Let us assume that one time series is a target series T and the other a sample series P . DTW will map them to a common time axis $F\langle[T(k), P(k)]|k=1, 2, \dots, K\rangle$, where F is the mapping and K is the length of the common time axis.

Let us define $d[T(k), P(k)]$ as the cost or dissimilarity measure of a point pair, then the global optimization objective function can be expressed as

$$\arg \min D(F) = \frac{\sum_{k=1}^K w(k) d[T(k), P(k)]}{\sum_{k=1}^K w(k)},$$

where $w(k)$ is a weighted factor for each point on the common time axis and d is the Euclidian distance between two points along the two time series, respectively. If $w(k)=1$, $k=1, 2, \dots, K$, then DTW returns the solution with the shortest path length. Here we view matching problem as finding a path in the grid defined by axes T and P . The shortest path length is the one when we cross the grid from the upper left corner to the lower right corner. For two identical time series, the shortest path is the diagonal of the grid because the matching cost (similarities between point pair of T and P) is lowest for the diagonal path. Since for two similar time series, the shortest path will deviate from the diagonal of the grid, we call such deviation “warping.” In practice, we usually have certain limitations about the mapping F . For example, end points of the two time series are mapped to each other. We also have so called “local continuity constraints” of the form

$$0 \leq P(k+1) - P(k) \leq a$$

$$0 \leq T(k+1) - T(k) \leq b,$$

where a and b are integers which will limit the extent of warping of the two time series. But in real applications, it is hard to determine the two parameters. It may vary patient by patient. So in the DTW method proposed by Nain *et al.*,¹² they employed the distance along the colon centerline as a penalty item in the distance calculation. That means if two points along the colon centerlines of supine and prone scans have large difference regarding the centerline distance, then it will have less chance to be matched. In addition, since it is nonlinear mapping and considering that T and P may have different lengths, multiple points on one time series may be mapped to the same point on the other time series and vice versa.

III. CENTERLINE REGISTRATION ALGORITHM

Our method contains two major steps. The first step extracts the centerline of the colon and calculates features that describe the centerline (distension, z -coordinate, and curvature). We utilized different feature combinations for canonical correlation analysis in order to find the optimal combination. The second step formulates the colon registration problem as a multiple time series matching problem that uses COW and CCA in combination with *a priori* knowledge of the anatomical structure of the human colon.

III.A. Centerline calculation and feature extraction along the centerline

We employed a subvoxel precise centerline extraction method, which utilized information of the colon outer wall to determine the colon centerline.²⁰ Initially, segmentation of the colon is performed to obtain a subvoxel representation of the colon. The discrete segmentation is used as an initial surface for a narrow band level set segmentation to more accurately determine the location of the colon inner wall and smooth the boundary between the air and fluid-filled regions of the colon. From the level set segmentation, a subvoxel distance field is computed using the fast marching method. The centerline of a colon is then computed based on the distance field.

In order to calibrate the two centerlines from different scans, we need to find effective and reliable features along the centerline which can describe the shape and appearance of the colon. We utilized three features: Distension, z -coordinate, and curvature in this study. In the DTW method proposed by Nain *et al.*,¹² they used distension of the colon to calculate the distance between two scans. To compare with their method, the distension is measured as follows: First we compute progressive ring sets along the centerline. The ring sets are perpendicular to the centerline. The radius of the ring at a centerline point is used as the distension of the colon at that point. Besides distension, Li *et al.*¹⁴ found that z -coordinates along the centerlines of supine and prone scans have morphological similarity, which can also be used for registration. In addition, we also utilized curvature of the centerline for matching because it encodes some topology properties of the colon centerline. The curvature of a 3D curve is defined as the curvature of its osculating circle at each point. These topology properties include the twist of sigmoid colon, hepatic flexure, splenic flexure, etc.

III.B. Correlation optimized warping algorithm

The COW algorithm was proposed by Nielsen *et al.*¹⁵ to align chromatographic profiles for chemometric data analysis. Given two time series to be aligned, we designate one as the target series T and the other the sample series P . The sample series P has $L_P + 1$ elements and total length L_P (for equally spaced time series data and sampling resolution of 1). If we segment the whole series P into segments of uniform length m , then the number of sections N is given by $N = L_P/m$. (With N , we can segment the target series T into N

pieces at the same time, so both P and T have N sections.) Each segment will be stretched or compressed using linear interpolation in order to generate aligned time series A . The border points of segments are referred to as nodes and the position of the starting point of section i in the target series T is defined as x_i . Note that x_i is also the starting point of segment i in aligned time series A after warping. For each segment, a slack variable t (an integer) is introduced. The slack variable t determines the warping magnitudes of each segment by adjusting the border nodes of each segment. The actual warping of section i is called u_i (which is limited by the slack variable t). If there is a large difference between the length of time series T and P , then warpings are limited to fall in the interval $(\Delta - t; \Delta + t)$, where Δ is the difference of section length between T and P (L_T is the length of target series): $\Delta = (L_T/N) - m$.

To show how good the warping is for each section, we utilize the correlation coefficient ρ between the two corresponding segments of series T and A as the measure of alignment quality $f(I)$: $f(I) = \rho(I_T, I_A)$, where I denotes the I th segment. Segment alignment quality $f(I)$, which is also called the benefit function, defines the local alignment quality for each section. Our goal is to find the global optimal alignment between the entire series P and T . In order to achieve this, we must find an optimal combination of warpings of all segments as determined by the node positions in the aligned series A . The optimization problem can be formulated as follows:

$$\text{Given } x_0 = 0 < x_1 < \cdots < x_{N-1} < x_N = L_T,$$

$$u_i \in [\Delta - t, \Delta + t]; i = 0, \cdots, N-1, \text{ and } x_{i+1} = x_i + m + u_i; i = 0, \cdots, N-1, \text{ the optimal warping}$$

$\bar{x} = \arg \max_{\bar{x}} (\sum_{i=0}^{N-1} f[x_i : x_{i+1}])$, where $[x_i : x_{i+1}]$ denotes the section defined by border points x_i and x_{i+1} .

The optimization problem shown above is a combinatorial optimization problem and can be solved by dynamic programming. More specifically, the algorithm is based on a matrix F whose size is $(N+1) \times (L_T+1)$ and contents are the benefit function values. All the elements in F are initialized as minus infinite, except $F(N+1, L_T+1)$, which equals zero and indicates that the last points of T and P are aligned. During the backward optimization process, each element in F is replaced by the accumulative benefit function $F_{i,x} = \max(F_{i+1, x+m+u_i} + f([x; x+m+u_i]))$, $i = 1, \cdots, N-1$. The global optimization value can be achieved at $F_{0,0} = \max(\sum_{i=0}^{N-1} f([x_i; x_{i+1}]))$.

III.C. Canonical correlation analysis

The original COW algorithm can only align two one-dimensional time series. That means we can use only one feature of the centerline for alignment. However the centerline can be characterized by multiple different features. These features may have some complementary effects and combining them together may lead to better alignment. For example, the z -coordinate feature can only characterize the height of the centerline but adding centerline shape informa-

tion from its curvature may improve registration. To make full use of the features extracted along the colon centerline, we embed canonical correlation analysis,¹⁶ which is a way of computing cross-covariance matrices for two groups of random variables with the correlation-based COW algorithm for extending the algorithm to multiple time series. Assume that we have two groups of variables $X \in R^p$ and $Y \in R^q$ with zero mean. Each group of variables has n observations of samples. CCA considers a new coordinate for X by choosing a mapping W_x (canonical factor) and projecting X onto this new direction $X \rightarrow \langle W_x, X \rangle$. The same is done for Y by choosing a mapping W_y . The projections $x = W_x^T X$ and $y = W_y^T Y$ are called as canonical variables. The optimization objective function of CCA is $\rho = E[xy] / \sqrt{E[x^2]E[y^2]} = E[W_x^T X Y^T W_y] / \sqrt{E[W_x^T X X^T W_x]E[W_y^T Y Y^T W_y]}$, where E is the expectation.

If we define $C_{xx} \in R^{p \times p}$ and $C_{yy} \in R^{q \times q}$ as the within-group covariance matrices of X and Y , respectively, and $C_{xy} \in R^{p \times q}$ as the between-group covariance matrix, then the objective function can be written as $\rho = W_x^T C_{xy} W_y / \sqrt{W_x^T C_{xx} W_x W_y^T C_{yy} W_y}$. It can be shown that the stationary points W^* of ρ (i.e., the points satisfying $\nabla \rho(W^*) = 0$) can be obtained by singular value decomposition (SVD) of the matrix $T = C_{xx}^{-1/2} C_{xy} C_{yy}^{-1/2} \in R^{p \times q}$. Let $T = UDV^T$ be a SVD of T where U is a $p \times p$ unitary matrix, D is a $p \times q$ matrix with nonnegative real numbers on the diagonal (these numbers are eigenvalues of $T^T T$), and V denotes the conjugate transpose of V , a $q \times q$ unitary matrix. Then the i th canonical factor pair is $W_x^i = C_{xx}^{-1/2} u_i$ and $W_y^i = C_{yy}^{-1/2} v_i$, where u_i and v_i are the i th columns of U and V , respectively. The corresponding canonical correlations are the eigenvalues (diagonal entries of D).

III.D. Border points localization based on anatomical structure of the colon

In the COW algorithm introduced above, the time series are divided into segments of uniform length. In other words, the border points or nodes along the time series are determined arbitrarily. However, the colon has a known anatomical structure that allows us to set constraints on the nodes. For example, two flexures (splenic and hepatic) and two junctions (rectum-sigmoid and sigmoid-descending) play important roles in the segmentation of the colon.²¹ These four anatomical landmarks can serve as border points or nodes (Fig. 2). In particular, the shapes of the splenic and hepatic flexures tend to be preserved between the supine and prone scans and are therefore more reliable landmarks. So in this study we did not adopt the original implementation of COW with uniform segments. Instead, we used the four anatomical landmarks as border points which lead to colon centerline segments with different length. In Fig. 2, we show CT slices which contain detections of landmarks. We mapped these detections to the colon centerline based on the minimum Euclidean distance between a detection's centroid and centerline points. By utilizing these anatomical landmarks, we

FIG. 2. Four landmarks of a patient (prone scan). We show CT slices which contain the automatically detected landmarks. The landmarks are marked by circles.

can define more natural segments of the colon automatically and apply the COW method to the segments between the anatomical landmarks.

IV. CTC DATA SET AND EVALUATION METHODS

IV.A. CTC data set

Our institution's OHSR declared this project to be exempted from IRB review. Our data set consisted of CTC examinations of 39 patients collected from three medical centers. We split patients into training and test sets which contained 19 and 20 patients, respectively. Each patient was scanned in the supine and prone positions. Each scan was done during a single breath-hold using a four-channel or eight-channel CT scanner. CT scanning parameters included 1.25–2.5 mm section collimation, 15 mm/s table speed, 1 mm reconstruction interval, 100 mAs, and 120 kVp. Each patient had one or more polyps. We randomly selected one polyp from each patient for comparison of matching error of different registration methods. These 39 polyps measured 6–25 mm in size. The polyps were confirmed by both tradi-

TABLE I. Registration errors of NDACC, DTW (using distension feature), and COW (using z -coordinate and curvature features) on the training set (units are millimeters). Z= z -coordinate feature, C=curvature feature, and D=distension feature.

Error/methods	NDACC	DTW D	COW Z+C
Mean	29.06	35.16	11.02
Std	22.64	26.93	10.43
95% CI	[18.15 39.98]	[22.18 48.13]	[6.00 16.05]

TABLE II. p -values of the Wilcoxon signed-rank test (pairwise comparison) of NDACC, DTW, and COW on the training set.

	NDACC	DTW D	COW Z+C
NDACC	1		
DTW D	0.3525	1	
COW Z+C	0.0003	0.0013	1

tional optical colonoscopy and virtual colonoscopy. The histologic diagnoses of these polyps were either hyperplastic or adenomatous.

IV.B. Evaluation of centerline registration

To evaluate the registration quality, we calculated the warping error along the centerline. It is difficult to define registration ground-truth along the entire colon because the movement of the colon between scans introduces both local stretching and compression. In this paper, we use a point evaluation strategy (the polyp position) to evaluate the calibration quality. We have the ground-truth information of the colonic polyps, which were confirmed by optical colonoscopy and radiologists. A polyp's position along the centerline can be computed by finding the minimum distance between the polyp's position on the colonic wall and the points along the centerline. After the warping, we map the polyp's supine centerline position to the prone centerline and use the difference of the centerline distances between prone point and estimated supine point on the prone centerline as the warping error. The centerline distance is defined as the distance of a point on the centerline to the centerline starting position at the rectum measured along the centerline. To evaluate the effectiveness of the proposed COW method, we compared it to the NDACC method¹⁸ and to the DTW method. We utilized distension information for matching prone and supine CTC scans as proposed by Ref. 12 in the DTW implementation. To compare the performance of different methods on the CTC data set, we used the Wilcoxon signed-rank test.

V. EXPERIMENTAL RESULTS

V.A. Comparisons of NDACC, DTW, and COW on the CTC data set

Table I shows the estimation error of polyp position along the centerline for the three methods on the training set. NDACC, DTW, and COW achieved the lowest estimation error on two, four, and 13 polyps, respectively. The statistical

TABLE III. Registration errors of NDACC, DTW (using distension feature), and COW (using z -coordinate and curvature features) on the test set (units are millimeters). Z= z -coordinate feature, C=curvature feature, and D=distension feature.

Error/methods	NDACC	DTW D	COW Z+C
Mean	46.27	75.51	14.98
Std	52.97	122.84	11.41
95% CI	[21.48 71.06]	[18.02 133.00]	[9.63 20.32]

TABLE IV. p -values of the Wilcoxon signed-rank test (pairwise comparison) of NDACC, DTW, and COW on the test set.

	NDACC	DTW D	COW Z+C
NDACC	1		
DTW D	0.1054	1	
COW Z+C	0.0056	0.0002	1

analysis from Table II shows that COW improves supine-prone registration significantly compared to NDACC and DTW with DTW and NDACC showing no significant difference at significance level 0.05. Comparisons of the three methods on the test set are shown in Tables III and IV. NDACC, DTW, and COW achieved the lowest estimation error on seven, one, and 12 polyps, respectively. On the test set COW again showed significant improvement compared to the other two methods. Using COW, the estimation error of polyp location could be reduced by 67.6% compared to NDACC. The test set was more challenging than the training set for NDACC and DTW, which achieved far worse matching errors compared to those on the training set. In contrast, COW showed greater consistency on the two data sets suggesting that this new method may be more robust than the other methods we evaluated in this study.

V.B. The effects of different features and their combinations for colon centerline registration

One may ask that, since we have three features available to describe characteristics of the colon along the centerline, how would the performance of DTW and COW differ if we utilize different features or feature combinations. To answer these questions, we first tested DTW methods with different features: z -coordinate, curvature, and distention. In Table V, we listed matching errors of polyp locations when different features were utilized in the DTW algorithm on the training set. Table V shows that by utilizing z -coordinate features, DTW achieves significantly better registration effect compared to that of DTW using the distension feature or curvature feature alone based on the Wilcoxon signed-rank test (see Table VI). Our results suggest that the z -coordinate feature may be a more powerful single feature than distension or curvature for colon CTC scan registration. Note DTW using distension did achieve the lowest registration error on five polyps indicating that distension does work well for some subset of cases. However, we do expect the distension feature to be less consistent compared to the z -coordinate for

TABLE V. Registration errors of the DTW algorithm utilizing different centerline features on the test set (units are millimeters). Z= z -coordinate feature, C=curvature feature, and D=distension feature.

Error/methods	DTW Z	DTW C	DTW D
Mean	28.85	82.91	75.51
Std	32.11	119.56	122.84
95% CI	[13.82 43.88]	[26.95 138.87]	[18.02 133.00]

TABLE VI. *p*-values of the Wilcoxon signed-rank test (pairwise comparison) of the DTW algorithm when different features were utilized on the test set.

	DTW Z	DTW C	DTW D
DTW Z	1		
DTW C	0.0017	1	
DTW D	0.0401	0.8986	1

all colon sections because of the variation in distension caused by the movement of gas inside the colon between the two scan acquisitions. We also found that the curvature feature and the distension feature show no significant difference for the colon centerline registration. Because of the movement of colon between supine and prone scans, the curvature of the colon centerline, especially the transverse colon (please see Fig. 1), will change a lot, which makes it a weak feature for registration.

We also tested the COW method with CCA using different feature combinations. In Table VII, we listed all four possible combinations of the three features. COW using *z*-coordinate and curvature feature combination achieved the best performance of the four combinations. The Wilcoxon signed-rank tests in Table VIII show that feature combination Z+C is significantly better than feature combination D+C at significance level 0.1. It is not surprising that it is a little bit worse if we utilize all three features because the distension feature may introduce noise for canonical correlation analysis on some patients. In addition, we show results of COW with *z*-coordinate feature only in Tables VII and VIII. We can find that by introducing the curvature information, COW Z+C achieved lower matching error of colonic polyp and smaller standard deviation compared to COW Z, which shows that it is more accurate and consistent. In this study we only considered three features of the colon centerline. But the proposed registration framework can be applied to other centerline features. In future studies, if we can discover new features and more efficient feature combinations compared to the feature combination of *z*-coordinate and curvature, we may see more accurate registration results.

V.C. Correlation analysis for the COW method

In order to verify that the COW method leads to higher correlation between prone and supine centerlines, we show the first pair of canonical variables from prone and supine centerlines of a patient with/without our matching method in Fig. 3. This figure shows that after centerline COW registration, the two canonical variables are better aligned than be-

fore registration. The figure also shows similar shapes for the canonical variables after alignment. An example of this is seen with the removal of the spikes in the prone canonical variables [see Fig. 3(a)] with COW. These noise spikes are related to curvatures from the prone scan. They are removed in Fig. 3(b) because CCA finds a direction which contains more common characteristics of the two scans after alignment.

V.D. Optimization of the anatomical landmarks

In the colon registration method proposed, anatomical landmarks play an important role in dividing the colon centerline into segments. These anatomical landmarks are relatively stable between prone and supine scans compared to the movement of other parts of the colon. Such stability improves the registration of prone and supine scans. However, these landmarks may not be detected correctly in all patients. In such situations, COW embedded with CCA provides an effective way to optimize the locations of the landmarks. To show the effectiveness of landmark optimization, we compared the proposed registration method to that without landmark optimization. In landmark registration without optimization, one first segments the colon centerline using the anatomical landmarks and then matches the segments using linear interpolation based on the distance along the colon centerline segment. Experiments on the training set show that the average matching error of the landmark registration method is $34.31 \text{ mm} \pm 36.98 \text{ mm}$ [95% C.I. (16.49 mm 52.13 mm)]. The Wilcoxon signed-rank test shows that it is significantly lower performance than the COW method ($p < 0.01$) and validates the use of landmark optimization in our COW implementation.

V.E. Tolerance to colon centerline errors

Colon centerline extraction is a key component in all three methods: NDACC, DTW, and COW. A bad centerline may introduce significant error during the matching process of colon CTC. Examples of incorrect centerlines include over extension of the centerline into the small intestine or rectal tube.¹⁸ When this is the case, all the features extracted from the centerline will be affected which can introduce significant bias. In Fig. 4 we show an example of overextension of the colon centerline into the small intestine. In our experiments, we correct this error by removing the extra centerline manually. For NDACC, the matching error was reduced from 170.61 to 56.29 mm after the correction. Contrary to the result of NDACC, the proposed method still achieved a low

TABLE VII. Registration errors of the COW method utilizing different centerline feature combinations on the test set (units are millimeters). Z=*z*-coordinate feature, C=curvature feature, and D=distension feature.

Error/methods	COW Z+C	COW Z+D	COW D+C	COW Z+C+D	COW Z
Mean	14.98	18.65	23.76	19.27	17.10
Std	11.41	13.68	24.29	11.41	14.98
95% CI	[9.63 20.32]	[12.25 25.05]	[12.39 35.13]	[13.93 24.61]	[11.84 22.35]

FIG. 3. (a) The first pair of canonical variables from prone and supine centerlines of a patient before registration. (b) The first pair of canonical variables from prone and supine centerlines of a patient after applying our COW registration method.

matching error of 10.05 mm on this problematic case without correction. The matching error of COW on this polyp is 0 mm after correction. After further examination, we found that the polyp of this patient is located in the transverse colon. Since our method is based on linear interpolation between colon segments, which are defined by the four anatomical landmarks, it has certain tolerance of centerline error if the centerline errors occur in other colon segments.

We identified four patients with such centerline problems and COW worked well on these cases without centerline correction. We list matching errors of NDACC, DTW, and COW on the four cases with/without centerline correction in Table IX. It can be seen that COW was affected less compared to the other two methods on these problematic cases, which shows that it has certain tolerance to the colon centerline error.

TABLE VIII. *p*-values of the Wilcoxon signed-rank test (pairwise comparison) of the COW method when different features were utilized on the test set.

	COW Z+C	COW Z+D	COW D+C	COW Z+C+D	COW Z
COW Z+C	1				
COW Z+D	0.3289	1			
COW D+C	0.0569	0.5217	1		
COW Z+C+D	0.3300	0.9265	0.5706	1	
COW Z	0.1754	0.4951	0.3683	0.8124	1

FIG. 4. Three-dimensional colon CTC surface reconstructions of a patient. Left: Prone scan; right: Supine scan. Lines inside the segmented colon indicate centerlines. The centerline extraction algorithm incorrectly included a small intestine segment (arrow) leading to incorrect colon centerline.

VI. DISCUSSION

In this paper, we proposed an automated method for colon registration. Four anatomical salient points on the colon were first automatically identified as landmarks along the central path of the colon. Correlation optimized warping was then applied to the segments defined by the anatomical landmarks to improve global registration using local correlation between segments. The original COW algorithm only aligns one-dimensional time series. To make full use of the features extracted along the centerline, we extended this algorithm to handle two-dimensional time series by embedding canonical correlation analysis to compute cross-covariance matrices for two groups of random variables. We tested the algorithm on a CTC data set of 39 patients with 39 polyps that were confirmed by optical colonoscopy. Experimental results on the test set show that our method reduced polyp location estimation error between supine and prone scans by 67.6% compared to NDACC ($p < 0.01$). Experimental results show that the z -coordinate was more powerful than curvature and distension for the colon registration. For COW, the combination of z -coordinate and curvature achieved the lowest match error compared to all other feature combinations we evaluated. The proposed method is tolerant to centerline errors because anatomical landmarks help prevent the propagation of errors across the entire colon centerline.

Our registration method matches the colon centerlines point by point using centerline features. Nappi *et al.*¹³ proposed a region-based supine-prone matching method without

centerline extraction. In this method, a colon is initially separated into several pieces. Then a directional breadth-first region-growing is applied to the colonic lumen of each segment. They record the Euclidean 3D distance traversed from the starting point and call it lumen distance. The final registration is based on the lumen distance. The advantage of their method is that it does not rely on the colon centerline. So it will not be affected by the centerline extraction error. Like our method, they also utilized anatomical landmarks to segment the colon at the initial registration stage. The difference in the two methods is that we simplify the problem of colon matching to centerline matching and the method of Nappi *et al.*¹³ matches colon segments using distance derived from region-growing process in 3D space. One important issue of the region-based supine-prone matching method is that it requires the colon to be fully distended between two consecutive landmarks. But as we know for some patients, the colon may have significant deformation between prone and supine scans. For example, the distension of the colon may change because of the movement of gas bubble between supine and prone scans. Such change in the distension of the colon may have significant influence on the region-growing processes in prone and supine scans and result inaccurate matching of the colon lumen. In extreme situations, when some parts of the colon are missing in one scan because of collapse of the colon or segmentation issues, the region-growing based method may fail to find correct matching. On the contrary, our COW method can still be effective by estimating centerline of the missing colon part.

Li *et al.*¹⁴ proposed a colon centerline matching method based on the z -coordinate feature. The key idea of their method was to find local extreme points along the colon centerline and match these points using a heuristic algorithm. The local extreme points are local minimum or maximum points of the centerline feature. They reported similar matching error (12.66 mm) as ours on a data set with 24 patients, which is consistent with our finding that z -coordinate is more powerful for the colon matching than the other distension and curvature centerline features we evaluated in this study. A potential drawback of the method of Li¹⁴ is that when faced with a complicated colon that includes many local extreme points or the colon has significant shape deformation in supine and prone scans, it tends to give erroneous matching result. In addition, their method did not utilize the anatomical information of the human colon and treated the colon as a whole. Such matching strategy makes it more and more

TABLE IX. Matching errors of NDACC, DTW, and COW on four patients with/without manual colon centerline correction (units are millimeters). Z= z -coordinate feature, C=curvature feature, and D=distension feature.

No./methods	NDACC		DTW D		COW Z+C	
	without	with	without	with	without	with
Patient 1	170.61	56.29	208.61	71.09	10.05	0
Patient 2	155.24	14.63	410.66	43.04	14.29	10.64
Patient 3	172.22	33.27	427.08	40.67	5.62	12.41
Patient 4	138.87	28.84	115.50	29.01	80.93	45.76

complex as the colon becomes longer and more complicated regarding to the shape. On the contrary, our method utilized the four anatomical landmarks and matched the colon segment by segment under the constraint of global alignment quality. Such “divide and conquer” strategy can reduce the complexity of the matching problem and was proved to be effective.

As we showed in the previous section, the method proposed by Nain *et al.*¹² using DTW and distension feature of the colon had bigger registration error compared to that of the proposed COW method. The key problem of their method is that the distension feature of the colon is not a reliable feature. It depends on some random factors such as shape deformation and gas bubble movement between supine and prone scans. It also does not utilize the anatomical structure of the colon and can only handle one-dimensional time series. The advantage of the method of Nain¹² is that it is relatively simple and faster compared to our method.

The COW method we have proposed is a general registration method that can be integrated into any computer aided diagnosis (CAD) or CTC analysis system. It has many potential applications including

1. Synchronization of supine and prone colon fly-through of computed tomographic colonography
2. Estimation of polyp candidate location in the other view once radiologist finds a suspicious polyp in one view
3. False positive reduction before the final classification stage of a CAD system

In conclusion, in this paper we propose a new and effective colon centerline registration method for prone and supine CTC scans using COW and CCA based on the anatomical structure of the colon.

ACKNOWLEDGMENTS

This research was supported by the Intramural Research Programs of the NIH Clinical Center and the U.S. Food and Drug Administration (NP). We thank Dr. Perry Pickhardt, Dr. J. Richard Choi, and Dr. William Schindler for providing CT colonography data.

^{a)}Electronic mail: wangshi@cc.nih.gov

^{b)}Author to whom correspondence should be addressed. Electronic mail: rms@nih.gov; Telephone: (301) 402-5486 and (301) 435-0055; Fax: (301) 451-5721; URL: http://www.cc.nih.gov/about/SeniorStaff/ronald_summers.html.

¹A. Jemal, R. Siegel, E. Ward, Y. P. Hao, J. Q. Xu, T. Murray, and M. J. Thun, “Cancer statistics, 2008,” *Ca-Cancer J. Clin.* **58**, 71–96 (2008).

²P. J. Pickhardt, J. R. Choi, I. Hwang, J. A. Butler, M. L. Puckett, H. A. Hildebrandt, R. K. Wong, P. A. Nugent, P. A. Mysliwiec, and W. R. Schindler, “Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults,” *N. Engl. J. Med.* **349**, 2191–200 (2003).

- ³C. D. Johnson, “Accuracy of CT colonography for detection of large adenomas and cancers,” *N. Engl. J. Med.* **359**, 1207–1217 (2008).
- ⁴H. Yoshida and J. Nappi, “Three-dimensional computer-aided diagnosis scheme for detection of colonic polyps,” *IEEE Trans. Med. Imaging* **20**, 1261–1274 (2001).
- ⁵D. S. Paik, C. F. Beaulieu, G. D. Rubin, B. Acar, R. B. Jeffrey, J. Yee, J. Dey, and S. Napel, “Surface normal overlap: A computer-aided detection algorithm, with application to colonic polyps and lung nodules in helical CT,” *IEEE Trans. Med. Imaging* **23**, 661–675 (2004).
- ⁶Z. Wang, Z. Liang, L. Li, X. Li, B. Li, J. Anderson, and D. Harrington, “Reduction of false positives by internal features for polyp detection in CT-based virtual colonoscopy,” *Med. Phys.* **32**, 3602–16 (2005).
- ⁷J. Nappi and H. Yoshida, “Feature-guided analysis for reduction of false positives in CAD of polyps for computed tomographic colonography,” *Med. Phys.* **30**, 1592–1601 (2003).
- ⁸K. Suzuki, H. Yoshida, J. Nappi, S. G. Armato, and A. H. Dachman, “Mixture of expert 3D massive-training ANNs for reduction of multiple types of false positives in CAD for detection of polyps in CT colonography,” *Med. Phys.* **35**, 694–703 (2008).
- ⁹J. Li, R. Van Uitert, J. H. Yao, N. Petrick, M. Franaszek, A. Huang, and R. M. Summers, “Wavelet method for CT colonography computer-aided polyp detection,” *Med. Phys.* **35**, 3527–3538 (2008).
- ¹⁰S. C. Chen, D. S. Lu, J. R. Hecht, and B. M. Kadell, “CT colonography: Value of scanning in both the supine and prone positions,” *AJR, Am. J. Roentgenol.* **172**, 595–599 (1999).
- ¹¹J. Yee, N. N. Kumar, R. K. Hung, G. A. Akerkar, P. R. G. Kumar, and S. D. Wall, “Comparison of supine and prone scanning separately and in combination at CT colonography,” *Radiology* **226**, 653–661 (2003).
- ¹²D. Nain, S. Haker, W. G. E. Cosman, W. Wells, H. Ji, R. Kikinis, and C. Westin, “Intra-patient prone to supine colon registration for synchronized virtual colonoscopy,” *Proceedings of the Medical Image Computing and Computer-Assisted Intervention*, 2002.
- ¹³J. Nappi, A. Okamura, H. Frimmel, A. Dachman, and H. Yoshida, “Region-based supine-prone correspondence for the reduction of false-positive CAD polyp candidates in CT colonography,” *Acad. Radiol.* **12**, 695–707 (2005).
- ¹⁴P. Li, S. Napel, B. Acar, D. S. Paik, R. B. Jeffrey, and C. F. Beaulieu, “Registration of central paths and colonic polyps between supine and prone scans in computed tomography colonography: Pilot study,” *Med. Phys.* **31**, 2912–2923 (2004).
- ¹⁵N. P. V. Nielsen, J. M. Carstensen, and J. Smedsgaard, “Aligning of single and multiple wavelength chromatographic profiles for chemometric data analysis using correlation optimised warping,” *J. Chromatogr. A* **805**, 17–35 (1998).
- ¹⁶D. R. Hardoon, S. Szedmak, and J. Shawe-Taylor, “Canonical correlation analysis: An overview with application to learning methods,” *Neural Comput.* **16**, 2639–2664 (2004).
- ¹⁷M. Franaszek, R. M. Summers, P. J. Pickhardt, and J. R. Choi, “Hybrid segmentation of colon filled with air and opacified fluid for CT colonography,” *IEEE Trans. Med. Imaging* **25**, 358–68 (2006).
- ¹⁸R. M. Summers, J. A. Swift, A. J. Dwyer, J. R. Choi, and P. H. Pickhardt, “Normalized distance along the colon centerline: A method for correlating polyp location on CT colonography and optical colonoscopy,” *AJR, Am. J. Roentgenol.* **193**, 1296–1304 (2009).
- ¹⁹D. Berndt and J. Clifford, “Using dynamic time warping to find patterns in time series,” *Proceedings of the AAAI-94 Workshop on Knowledge Discovery in Databases*, Seattle, WA, 1994 (unpublished).
- ²⁰R. L. Van Uitert and R. M. Summers, “Automatic correction of level set based subvoxel precise centerlines for virtual colonoscopy using the colon outer wall,” *IEEE Trans. Med. Imaging* **26**, 1069–1078 (2007).
- ²¹P. J. Glynn and R. M. Summers, “Automated labeling of anatomic segments of the colon in CT colonography,” *Proceedings of the SPIE Medical Imaging*, 2009 (unpublished).