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Rotationally resliced 3D prostate TRUS segmentation using convex optimization with shape priors

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Purpose: Efficient and accurate segmentations of 3D end-firing transrectal ultrasound (TRUS) images play an important role in planning of 3D TRUS guided prostate biopsy. However, poor image quality of the input 3D TRUS images, such as strong imaging artifacts and speckles, often makes it a challenging task to extract the prostate boundaries accurately and efficiently.

Methods: In this paper, the authors propose a novel convex optimization-based approach to delineate the prostate surface from a given 3D TRUS image, which reduces the original 3D segmentation problem to a sequence of simple 2D segmentation subproblems over the rotational reslices of the 3D TRUS volume. Essentially, the authors introduce a novel convex relaxation-based contour evolution approach to each 2D slicewise image segmentation with the joint optimization of shape information, where the learned 2D nonlinear statistical shape prior is incorporated to segment the initial slice, its result is propagated as a shape constraint to the segmentation of the following slices. In practice, the proposed segmentation algorithm is implemented on a GPU to achieve the high computational performance.

Results: Experimental results using 30 patient 3D TRUS images show that the proposed method can achieve a mean Dice similarity coefficient of 93.4% ± 2.2% in 20 s for one 3D image, outperforming the existing local-optimization-based methods, e.g., level-set and active-contour, in terms of accuracy and efficiency. In addition, inter- and intraobserver variability experiments show its good reproducibility.

Conclusions: A semiautomatic segmentation approach is proposed and evaluated to extract the prostate boundary from 3D TRUS images acquired by a 3D end-firing TRUS guided prostate biopsy system. Experimental results suggest that it may be suitable for the clinical use involving the image guided prostate biopsy procedures. © 2015 American Association of Physicists in Medicine.

Keywords: 3D TRUS prostate segmentation, convex optimization, nonlinear shape prior, kernel principle component analysis, rotational volume reslicing

1. INTRODUCTION

Prostate adenocarcinoma (PCa) is the most common noncutaneous malignancy in American men with over 200,000 new cases diagnosed each year.\textsuperscript{1,2} Definitive diagnosis of PCa currently requires a transrectal ultrasound (TRUS) guided biopsy, which involves sampling the prostate with approximately 12 cores.\textsuperscript{3} Recent development of biopsy systems, making use of fused 3D TRUS with MR images,\textsuperscript{4} has demonstrated increased positive yield and greater number of cores with higher Gleason grade.\textsuperscript{5,6} These techniques make use of 3D surface-based TRUS–MRI registration techniques, providing an alternative to MRI-based prostate biopsy\textsuperscript{7,8} to indirectly target biopsy needles toward regions of the prostate containing suspicious lesions identified with MR imaging.\textsuperscript{9} Considering the arduous and time consuming effort associated with manual 3D prostate segmentation, an accurate and efficient automated or semiautomated 3D TRUS prostate segmentation would be highly beneficial for registration of MR prostate images with 3D TRUS. However, the presence of US speckle, shadowing due to calcifications, missing edges or texture similarities between the inner and outer regions of the prostate\textsuperscript{10,11} make it challenging to implement such an automated or semiautomated segmentation. The objective of this study is to develop a segmentation approach that is accurate, efficient, and requires fewer interactions, which can be used in 3D endfiring TRUS guided prostate biopsy systems.\textsuperscript{12–14}

Although a complete review of medical image segmentation is beyond the scope of this paper, we briefly review some of the relevant works for prostate segmentation in 3D TRUS images. A detailed survey of prostate segmentation in other modalities can be found in Ghose et al.\textsuperscript{15} The existing
prostate segmentation methods from 2D/3D TRUS images can be broadly grouped into four different groups: contour and shape based methods, region-based methods, supervised and unsupervised classification methods, and hybrid methods, according to the information used to guide the segmentation. More specifically, prostate segmentation in 3D TRUS images can be categorized into two classes in line with segmentation procedures: direct 3D segmentation, and propagation approach based on 2D resliced slices. For the first class, the user initializes a 3D deformable surface in the 3D prostate image, which is then automatically refined by forces, such as image gradient and smoothness of the contour or surface. A classification technique, such as support vector machine (SVM), is also used to segment the prostate in 3D TRUS images. However, this classification based segmentation method depends on the training datasets and selected features, and its performance is also influenced by the poses of the US probe. Tsai et al. developed a method to segment 3D prostate MR images using a 3D PCA learned shape prior, but it is computationally expensive and cannot be parallelized on GPUs, making this approach not applicable with 3D TRUS images. Tsai et al. US probe. Tsai et al.

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Another limitation is that these two methods cannot be parallelized. In order to obtain high segmentation accuracy with high efficiency, we introduced a global optimization-based segmentation technique into this segmentation framework, which employed an inherent axial symmetry of the prostate as a shape prior for the prostate segmentation, combined with the continuity of neighboring contours. This method made use of a convex optimization approach in the propagation based segmentation framework, generating an efficient GPU-implemented solution to the investigated problem. The results in Qiu et al. demonstrated better performance in terms of accuracy and efficiency compared to Ding et al. and Qiu et al. However, this method relied on a careful initialization of the rotational axis and the first contour to guarantee axial symmetry, introducing observer variability.

In the current paper under review, our goal is to develop an automated segmentation algorithm for ultrasound images with minimum user interactions of initialization. Our approach makes use of a machine learning technique with our global optimization-based segmentation framework. Compared to the previous study, the major differences are as follows. (a) We used a statistical shape prior Kernel principle component analysis (KPCA) learned from presegmented prostate images, instead of a simple prior of prostate symmetry. The introduced shape prior includes the features of multiple presegmented prostate shapes in training datasets, which could reduce the dependence on the user initialization. (b) The introduction of the KPCA shape prior leads to a more complicated minimization function. A global optimization-based contour evolution algorithm was proposed to minimize this energy function. (c) Intensity histogram matching was applied as a data term.
instead of the negative likelihood of PDFs. (d) Local intensity distribution from a previous slice was used to drive the segmentation, which is more efficient in the presence of speckle and artifacts than global intensity distributions estimated only from a single slice.

A novel global optimization-based approach is proposed in this paper with an aim at reducing user interaction and improving the segmentation accuracy and efficiency of 3D rotationally resliced end-firing TRUS images used in prostate biopsy. Some preliminary results were presented in Qiu et al.\textsuperscript{36} The key contributions of this study are summarized as follows:

- KPCA (Refs. 37–41) as a nonlinear statistical shape prior is integrated into the framework of the rotationally resliced 3D prostate TRUS segmentation. This shape-driven learning technique allows for the simultaneous encoding of multiple types of shapes, and offers a convincing level of robustness with respect to noise, clutter, or partial occlusions. In this work, we incorporated this powerful statistical shape prior into a convex optimization-based segmentation algorithm. This technique requires user initializing of only one point inside the prostate to obtain an accurate segmentation for the first resliced image, instead of carefully selected 6–8 prostate boundary points required by the previous rotational-slice-based segmentation methods.\textsuperscript{16,34}
- The introduction of KPCA leads to a new energy minimization function, which includes an intensity distribution matching term, a nonlinear statistically shape term, and a regularization term. A convex optimization-based contour evolution method is proposed to minimize the defined energy minimization function, which is capable of propagating the evolution contour to its globally optimal position at each discrete time frame. It is potentially insensitive to the initial position of the contour and image noise. Moreover, the proposed algorithm can be parallelized and implemented on GPU to achieve short computational time.
- The segmented contour propagated from the previous slice is reused as a shape constraint to penalize the convex optimization method to segment the other resliced image frames. It makes use of the shape continuity between any two adjacent slices, decreasing the accumulated segmentation errors that occur in the propagation.
- Local intensity distributions are used to drive the segmentation, which are more efficient in the presence of speckle and artifacts than global intensity distributions estimated only from a single slice.

2. METHODS

2.A. Approach overview

The proposed rotationally resliced 3D prostate segmentation method is divided into four steps:

1. The 3D TRUS image of the prostate is first resliced into \( n \) slices about a rotational reslicing axis, which is in the middle of the 2D ultrasound image generated by the TRUS probe,\textsuperscript{15} so that they intersect approximately along the 3D scanning axis and have an equal angular spacing [Fig. 1(a)]. When the prostate is not in the middle of the TRUS image, the rotational axis needs to be selected manually.

2. Two points [in Fig. 1(a)] are manually chosen on the long axis of the prostate on the coronal view. The slice that contains these two points and is perpendicular to the coronal view is assumed to be the approximate transverse view of the prostate, and chosen as the initial slice. The approximate center of the prostate [in Fig. 1(b)] is chosen manually in the initial slice. A convex optimization method driven by histogram matching is then used to segment the prostate contour in this slice with a nonlinear statistical shape prior learned by KPCA, which is described in detail in Sec. 2.B.

3. The computed segmentation result is propagated in both a clockwise and counterclockwise [in Fig. 1(a)] directions for segmenting its two adjacent slices, where the segmentation result of the initial slice is used as both the propagation shape constraint and initial contour in the proposed convex optimization-based contour evolution scheme (described in

\begin{figure}
\centering
\begin{subfigure}[b]{0.45\textwidth}
\includegraphics[width=\textwidth]{fig1a.png}
\caption{(a) A coronal view of the 3D US image with the resliced planes delineated as the lines converging on the coronal axis. (b) The choice of the centroid of a prostate is shown on transverse plane. The rotational axis is shown as dotted line.}
\end{subfigure}
\end{figure}
2. B. Energy function for the segmentation of the first slice using kernel PCA as a shape prior

In this work, we denote \( u_i(x) = f, b \) (\( f, b \) denote the foreground and background pixels, respectively), as the indicator function of the estimated region \( \mathcal{R} \) such that

\[
    u_i(x) := \begin{cases} 
        1, & \text{where } x \text{ is inside } \mathcal{R} \\
        0, & \text{otherwise} \end{cases}, \quad i = f, b.
\] (1)

The indicator functions \( u_{f,b}(x) \in \{0,1\} \), for \( x \in \Omega \), are also called the labeling functions.

The indicator function \( u(x) \in \{0,1\} \) of the estimated prostate region for the first slice is minimized over the following energy function:

\[
    \min_{u(x) \in \{0,1\}} \alpha_1 E_{\text{matching}}(u) + \alpha_2 E_{\text{shape}}(u) + \alpha_3 \int_{\Omega} g(x)|\nabla u| dx, \quad (2)
\]

where \( E_{\text{matching}}(u) \) formulates the statistical intensity distribution matching energy inside and outside the prostate region (see Appendix A for details), the second term of Eq. (2) encodes KPCA shape information, and the last weighted total-variation function gives the boundary smoothness term, and \( \alpha_{1,2,3} > 0 \) are the positive penalty parameters. In this paper, the weight function \( g(x) \) in (2) is positive and is given by \( g(x) = \lambda_1 + \lambda_2 \exp(-\lambda_3 |\nabla I(x)|) \), \( \lambda_{1,2,3} \geq 0 \). Note that the values of \( g(x) \) fall within the range \( [\lambda_1, \lambda_1 + \lambda_2] \). \( \lambda_1 = 0.5 \), \( \lambda_2 = 0.8 \), and \( \lambda_3 = 30 \) were empirically chosen and fixed in our experiments.

KPCA was introduced by Mika et al.,\(^{42}\) which is considered to be a nonlinear extension of the ordinary linear PCA, and is used for extracting nonlinear structures from a data set.\(^{39,43–46}\)

In the KPCA technique, a training data set \( \tau = \{ x_1, x_2, \ldots, x_N \} \) is mapped from an input space \( I \) into a high dimensional feature space \( F \) by a nonlinear function \( \Psi: I \rightarrow F \). The linear PCA is then applied in \( F \) to find the principal components corresponding to the largest variation in the mapped data set. The error in representing any of the elements of the training set by its projection onto the first \( l \) principal components is minimal in the least squares sense. The nonlinear map \( \Psi: I \rightarrow F \) is typically performed through the use of a Mercer kernel: \( k(\cdot, \cdot) \). Computing \( k(\cdot, \cdot) \) as a function of \( I \times I \) amounts to computing the inner scalar product in \( F : k(\chi_a, \chi_b) = \langle \Psi(\chi_a), \Psi(\chi_b) \rangle \), where \( \chi_a, \chi_b \in I \times I \). This distance \( d_F^2[\Psi(u), P^l(\Psi(u))] \) measures the discrepancy between a (mapped) element of \( I \) and the elements of the learned space, which can be minimized as an introduced shape energy functional in the contour evolution process. The definition of this prior energy is described as

\[
    E_{\text{shape}}(u) = d_F^2[\Psi(u), P^l(\Psi(u))]. \quad (3)
\]

The superscript \( F \) in \( E_{\text{shape}}(u) \) indicates that the shape information is denoted as a distance in the feature space. Minimizing \( E_{\text{shape}}(u) \) results in driving the test shape \( u \) toward the KPCA space. The details of calculating the distance \( d_F^2[\Psi(u), P^l(\Psi(u))] \) are given in Appendix B.

In order to take advantage of the KPCA technique with less dependency on the initial conditions, the shape energy for the exponential kernel is redefined as

\[
    E_{\text{shape}}(u) = -2\sigma^2 \log \left( \frac{2 - E_{\text{shape}}^F(u)}{2} \right). \quad (4)
\]

Typically, the object of interest in image \( I \) and the aligned training shapes do not have the same pose and differ by some transformation. This transformation needs to be recovered during the segmentation process in order to properly constrain the evolved contour. Even though nonlinear deformation is present in the prostate, a complete recovery of the transformation from a training image to a testing image is not necessary since the rigid transformation is only used to match the poses between two shapes. The subsequent segmentation procedure will refine the registered results toward a more...
accurate segmentation. In addition, much more computationally
cost caused by the nonlinear transformation limits it in this
application. Assuming that the object of interest in $I$ differs
from the registered elements of the training set by the trans-
formation $T[p]$ with parameters $p = [p_1, p_2, p_3, p_4] = [t_x, t_y, \theta, \rho]$, in
which $t_x$ and $t_y$ correspond to translation in the $x$- and $y$-
axis, $\theta$ is the rotation angle, and $\rho$ is the scale parameter. In
this application, the approximate center of the prostate in the
image is chosen by the user, giving a good estimation of $p_0$ of
$\rho$ so that the pose of the object of interest in $I$ approximately
matches the pose of one of the registered training shapes. The
recovery of the transformation $T[p]$ is applied to the image $I$
only, instead of transforming each element of the training set.
This approach is computationally efficient when dealing with
a large training set.39

The training set consisted of 25 2D prostate transverse
view images. The gray-level prostate images, as well as pro-
state shapes represented by binary images, were aligned us-
ing an appropriate registration scheme22 to remove differ-
ences between any two of them due to translation, rotation,
and scale. An average gray-level image and its corresponding
mean shape was then generated. Figure 3 shows some binary
maps after alignment corresponding to the diverse training
shapes. The mean shape was generated by thresholding the
average image of all training binary images by a value of 0.5,
which is shown as the first image in Fig. 3. The other images
in Fig. 3 show ten shape models from the training set after
alignment. All binary images in the training data were used for
the shape learning by KPCA. Note that the 25 images used for
training were from different patients, excluding from the testing
data set. The training images were manually selected from the
transverse view of the prostate, where the prostate had visually
the largest area.

2.C. Energy function for the propagation
segmentation using propagation shape constraint

We describe the method to penalize the difference between
the 2D segmentation contours of two adjacent slices to enforce
the rotational symmetry of the prostate along the scanning axis
of 3D end-firing TRUS, facilitating the segmentation for the
subsequent slice. Let $S_i$ and $S_{i+1}$ be the two adjacent slices,
$C^*$ be the computed segmentation contour of the slice $S_i$, and
$u'(x) \in \{0, 1\}$ the indicator function of $C^*$. The computation
result $C^*$ is propagated to the next slice $S_{i+1}$ to assist the
segmentation task over $S_{i+1}$ for which the indicator function
$u(x) \in \{0, 1\}$ of the estimated prostate region within $S_{i+1}$ is
optimized over the following energy function:

$$
\min_{u(x) \in \{0, 1\}} \omega_1 E_{\text{matching}}(u) + \omega_2 \int_{\Omega} |u - u'| dx
$$

$$
+ \omega_3 \int_{\Omega} g(x)|\nabla u(x)| dx,
$$

(5)

where $E_{\text{matching}}(u)$ formulates the statistical intensity distribu-
tion matching energy inside and outside the prostate region
(see Refs. 47 and 48 for details), the second weighted total-
variation term of (5) encodes and penalizes the symmetric differ-
ce of segmentations between the two neighbor slices $S_i$ and $S_{i+1}$.

2.D. Convex optimization-based contour evolution
for the minimization of energy functions

The conventional contour evolution methods, e.g., active
contour model26,49 and level set50 gradually propagate a con-
tour to the minimization of a certain energy function. The con-
tour may be trapped in a locally optimal position during each
time frame, by solving the associated time-explicit convection
partial differential equations (PDE).51 Moreover, the final
result relies heavily on the initial position of the contour,
and is also sensitive to image noise. In contrast, the global
optimization-based contour evolution approaches52,53 over-
come such challenges, and showed that a contour can be propa-
gated to its globally optimal position at each discrete time
frame. In this study, we make use of the convex relaxation-
based globally optimal approach proposed by Yuan et al.48,54,55
to evolve a contour to its globally optimal position at each
discrete time frame by solving a convex optimization prob-
lems.

For the given contour $C^t$ at the current time $t$, its new
position $C^{t+1}$ at the next discrete time $t + 1$ can be achieved

![Fig. 3. Alignment results of ten prostates, showing as binary images. The first image is the mean shape.](image-url)
by solving the following optimization problem:

$$
\min_{c} \int_{c^+} e^t(x) \, dx + \int_{c^-} e^r(x) \, dx + \int_{\partial c} g(s) \, ds,
$$

(6)

where \( C^+ \) and \( C^- \) are the expansion and shrinkage regions with respect to \( C' \), and the functions \( e^t(x) \) and \( e^r(x) \) define the cost corresponding to the pixel \( x \) in \( C^+ \) and \( C^- \). In summary, the contour evolution during each time frame is performed with the minimum total cost with respect to region changes, i.e., expansion \( C^+ \) [the first term in (6)] and shrinkage \( C^- \) [the second term in (6)], and total region perimeter [the third term in (6)]. When the cost functions \( e^t(x) \) and \( e^r(x) \) are given by the distance between \( x \) and the boundary of \( C' \), the contour evolution given by (6) is equivalent to the well-known mean-curvature driven contour motion.\(^{56}\) Therefore, the typical contour evolution can be described by (6) with different configurations of \( e^t(x) \) and \( e^r(x) \).

In particular, the optimization problem (6) can be equivalently formulated as a spatially continuous min-cut problem

$$
\min_{u(x) \in \{0,1\}} (1-u,C_s) + (u,C_i) + \int_{\Omega} g(x)|\nabla u| \, dx,
$$

(7)

where \( u(x) \in \{0,1\} \) is the indicator function of the contour \( C \), and the two label assignment functions \( C_s \) and \( C_i \) are given by

$$
C_s = \begin{cases} 
  e^t(x), & \text{where } x \in C' \\
  0, & \text{otherwise}
\end{cases},
$$

(8)

$$
C_i = \begin{cases} 
  e^r(x), & \text{where } x \not\in C' \\
  0, & \text{otherwise}
\end{cases},
$$

(9)

where \( C_{s,i}(x) \) are cost functions for the object and background pixels, respectively, which are set up with respect to the current contour.\(^{48,57}\) For optimization with Kernel PCA as a shape prior, cost functions \( C_{s,i}(x) \) are assigned by the first two terms in Eq. (2), namely, \( \alpha_1 E_{\text{matching}}(u) + \alpha_2 E_{\text{shape}}(u) \); for optimization with propagation shape constraint, cost functions \( C_{s,i}(x) \) are assigned by the first two terms in Eq. (5), namely, \( \omega_1 E_{\text{matching}}(u) + \omega_2 \int_{\Omega} |u-u'| \, dx \).

To optimize the energy function (7) that are often highly nonlinear, we apply an efficient continuous max-flow algorithm\(^{54}\) by globally solving a dual continuous min-cut problem. Details about the continuous max-flow algorithm are given in Appendix C.

### 3. EXPERIMENTAL DESIGN AND IMPLEMENTATION

#### 3.A. Image acquisition

This study was approved by the Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) at the University of Western Ontario with a protocol title of Hybrid Imaging for Prostate Biopsy Guidance (REB #13958, approval date: March 6, 2013), and all subjects involved in this study provided written informed consent. All subjects were first imaged using multispectral MR technique in which suspicious tumors were identified. The US images were acquired with a rotational scanning 3D TRUS-guided prostate biopsy system,\(^{12}\) which made use of a commercially available end-firing TRUS transducer (Philips, Bothell, WA). The size of each 3D image was 448 × 448 × 350 voxels of size 0.19×0.19×0.19 mm\(^3\). Thirty patient images were tested in this paper. Each of them was resliced rotationally with a reslicing step angle of 6°, resulting in 30 2D slices.

#### 3.B. Initialization of the prior PDFs

Since global PDFs of the foreground and background estimated only from one slice might not be efficient to drive the segmentation of all the slices due to presence of speckle and artifacts, we used local PDFs derived by the mean shape in the first slice only for its segmentation. For the segmentation of each of the other resliced slices, the segmented contour propagated from the previous slice was substituted for the mean shape and was used to acquire the prior PDFs. In this study, we computed PDFs as negative log-likelihoods of foreground and background histograms, which were motivated by the underlying MAP–MRF formulation.\(^{58,59}\) For example, PDF\(_{f,b} = -\ln P(I|\Omega_{f,b}) \), where \( f, b \) mean the foreground and background, and \( P(I|\Omega_{f,b}) \) denotes the intensity distributions of the foreground or background pixels defined by the mean shape or propagated contour. The detailed procedure of computing prior PDFs is as follows. We first applied a registration scheme\(^{23}\) to generate a mean prostate binary shape and an average gray-level image using 25 2D prostate transverse view training images. The generated average gray-level image and mean shape were then registered to the first slice using the same registration technique. In order to obtain a more accurate and robust registration, we required the user to define an approximate center of the prostate to initialize the registration instead of an automatic affine registration, removing the difference between two images due to the translation. Specifically, the registered mean shape was overlapped on the initial slice by coinciding the center of gravity of the mean shape and the initial point chosen by the user. [The approximate prostate center point in Fig. 4(a).] As results of the registration, the deformations due to the scale and rotation were recovered, and the registered mean shape was used as the initial contour for the convex optimization. The intensities inside and outside the mean shape were used to calculate the prior PDFs for the foreground and background, respectively. Since the used affine registration was not able to recover nonlinear deformation, the mean shape was shrunk by 15 pixels [the inside contour in Fig. 4(a)] to model more accurate prior PDFs based on its signed distance functions (SDF). The intensities inside the shrunken mean shape were used to calculate the prior PDF for the foreground. The mean shape was also dilated by 15 pixels using its SDF, and the intensities outside the dilated mean shape [the outside contour in Fig. 4(a)] were used to compute the prior PDF for the background. For the segmentation of each of other resliced slices, the segmented contour propagated from the previous slice was substituted for the mean shape to calculate the prior PDFs.
3.C. Parameter settings

Five patient images excluded from the testing dataset were used to optimize the parameter values used in the segmentation algorithm. The parameter values were empirically chosen first, and then they were optimized sequentially by changing a single parameter at a time while holding other parameters fixed. For simplicity, only the DSC was used as the quantitative metric in this procedure. The optimized values of the parameters are shown in Table I, which were kept constant during the validation experiments.

3.D. Evaluation metrics

Our segmentation method was evaluated using the following metrics by comparing the algorithm segmentation result to manual segmentation, volume-based metrics: DSC and sensitivity (Se); and, distance-based metrics: the mean absolute surface distance (MAD) and maximum absolute surface distance (MAXD). The proposed method, which we symbolize as $M_{CG}$ method, was also compared to active contour based ($M_{AC}$ method) and level set based ($M_{LS}$ method) methods using the same rotationally resliced segmentation framework, in terms of the above metrics. The coefficient-of-variation (CV) of DSC ($CV = \frac{SD}{DSC} \times 100\%$) was used to evaluate the intra- and interobserver variability of our method, where $SD = \sqrt{\sum_{i=1}^{N} (SD_i/N)}$ and $DSC = \sum_{i=1}^{N} DSC_i/N$. $SD_i$ and $DSC_i$ for each 3D US image was computed using five repeated segmentations.

It should be noted that all manual segmentations were outlined by a technician and approved by a radiologist with more than ten years experience. The technician providing manual segmentations was excluded in the intra- and interobserver variability experiments. To avoid users from remembering a previous segmentation, five days were left between resegmenting the same case in the intraobserver variability test. Two trained graduate students and one trained postdoctoral fellow were involved in the interobserver variability test. The experimental results were considered significant when the probability of making a type I error was less than 5% ($p < 0.05$) in all statistical analyses.

Table I. Algorithm parameter values for the experiments.

<table>
<thead>
<tr>
<th>$\alpha_1$</th>
<th>$\alpha_2$</th>
<th>$\alpha_3$</th>
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3.E. Implementation details

The proposed convex max-flow algorithm was implemented using parallel computing architecture (CUDA, NVIDIA Corp., Santa Clara, CA) and the user interface in MATLAB (Natick, MA). The experiments were conducted on a Windows desktop with an Intel Core i7-2600 CPU (3.4 GHz) and a graphics card of NVIDIA GeForce 5800X. We also developed a CPU version of the proposed approach, which was compared to the CPU-implemented level set \(M_{LS}\) (Ref. 16) and active contour based \(M_{AC}\) (Ref. 34) methods using the same rotationally resliced segmentation framework. In addition, the \(M_{AC}\) method was implemented in C code, and both our CPU version and the \(M_{LS}\) method were implemented in MATLAB. More specifically, a 3D image was first resliced into 2D slices in the rotational manner in both the clockwise and counterclockwise directions. All the \(M_{AC}\), \(M_{LS}\), and \(M_{CO}\) methods were run on the same resliced images. Since the \(M_{AC}\) and \(M_{LS}\) methods need good initializations, five to eight points on the prostate boundary in the first slice were selected to fit a contour using cardinal spline interpolation,\(^{34}\) initializing the active contour model and level set function. In contrast, only an approximate center point was selected to initialize our proposed algorithm (the \(M_{CO}\) method). The segmented contours by the three methods were then propagated to the adjacent slice and reused as the initial contour for segmentation. This process was repeated until all slices were segmented.

4. EXPERIMENTAL RESULTS

4.A. Accuracy

One prostate surface (light color) segmented by the \(M_{CO}\) method is shown in Fig. 5, which is superimposed on the manual segmented surface (dark color). Visual inspection shows that the algorithm and manual segmented prostate surfaces agree well. The validation results in Table II show that the \(M_{CO}\) method can achieve a DSC of 93.4\(\pm\)2.2\% and a sensitivity of 92.6\(\pm\)2.8\% better than the \(M_{LS}\) method (92.8\(\pm\)2.8\% and 91.2\(\pm\)2.0\%) and the \(M_{AC}\) method (84.4\(\pm\)4.8\% and 85.7\(\pm\)5.5\%). MAD of 1.12\(\pm\)0.4 mm (5.9\(\pm\)2.1 voxels) and MAXD of 3.15\(\pm\)0.65 mm (16.6\(\pm\)3.4 voxels) of the \(M_{CO}\) method were comparable to the \(M_{LS}\) and \(M_{AC}\) methods. It is apparent from Table II that the proposed convex optimization method with the shape constraint can obtain the highest DSC with the least interaction. The active contour based method (\(M_{AC}\) method) resulted in the poorest performance with our used dataset. A single factor one-way ANOVA test (\(\alpha = 0.05\)) shows that there is a statistically significant difference (\(p < 0.004\)) in terms of DSC among the \(M_{CO}\), \(M_{CW}\), and \(M_{LS}\) methods. Two subsequent Tukey–Kramer tests (HSD = 3.49) indicate that the proposed algorithm \(M_{CO}\) improved the segmentation accuracy significantly regarding DSC compared to the \(M_{CW}\) (Tukey score = 3.6), but failed to demonstrate the statistically significant difference between
the $M_{CO}$ and $M_{LS}$ methods (Tukey score = 3.29). The $M_{LS}$ method can obtain a good segmentation accuracy due to the contribution of several external energy terms, such as anchor point, shape constraint, and statistical information in the local region. However, it requires greater computational time and interactions. We also report the results of the GPU implemented global optimization-based segmentation method with inherent axial symmetry prior ($M_{AS}$)\textsuperscript{35} in Table II. The $M_{AS}$ method generated slightly worse results compared to the proposed method in terms of DSC, MAD, and MAXD. However, it provided a faster solution to the investigated problem regardless of multiple-point initialization.

4.8. Reproducibility

To validate the variability introduced by the manual initialization (initial slice and initial points), 15 3D images were randomly selected for evaluating the reproducibility of the proposed method. Each image was segmented five times by the same observer for assessing intraobserver variability. A DSC of 93.0% ± 2.5% and a COV of 2.7% were found in this experiment. ANOVA analysis with a single factor failed to show that there is statistically significant difference between these five segmentations ($p = 0.95, F = 0.32$). These 15 images were also segmented three times by three untrained observers who were blinded to patient identity for assessing interobserver variability. The proposed method yielded a DSC of 93.5% ± 2.1%, 92.6% ± 3.1% and 92.3% ± 3.2%, and a COV of 2.3%, 3.3%, and 3.5%, respectively, compared to a COV of 7.5% of manual segmentations by different observers reported in Tutar et al.\textsuperscript{18} ANOVA analysis with a single factor failed to demonstrate a statistically significant difference between these three segmentations ($p = 0.53, F = 0.82$).

4.4. Computational time

The mean run time of the segmentation algorithm was determined from five repeated segmentation for each 3D TRUS image. The results in Table II show that our proposed methods require the shortest time. The mean segmentation time for all tested images was 14.3 ± 2.5 s, which is less than 85 ± 3.5 s of the $M_{LS}$ method and 50 ± 3.0 s of the $M_{AC}$ method. The total segmentation time was about 20 s for a given prostate 3D TRUS image including 5 ± 2 s for initialization. The developed CPU version required ≈35 s for the continuous max-flow computation, leading to a total segmentation time of ≈40 s with nonoptimized CPU-implemented MATLAB code.

5. DISCUSSION AND CONCLUSION

Prostate segmentation from 3D TRUS images is a critical step in planning prostate interventional procedures, such as 3D end-firing TRUS guided prostate biopsy with MR image fusion. The proposed method was only applied on 3D TRUS images with a complete prostate after the 3D acquisition was performed. This is ensured by first adjusting the ultrasound depth setting after general exploration of the prostate using 2D TRUS imaging. The algorithm can be used for general prostate segmentation from 3D TRUS images, and is not limited to the rotational acquisition system mentioned in Sec. 3.A, but can be potentially extended to any other 3D TRUS prostate images. Compared with the segmentation methods based on 3D deformable models,"17,19,20,61 slice-based 3D segmentation methods are faster, and therefore, appropriate for clinical applications requiring short segmentation times. However, these methods suffer from accumulated segmentation errors, especially during the later stage of the propagation. Furthermore, typical slice-based prostate segmentation methods\textsuperscript{33,34} used an active contour model to obtain prostate contours, which may be trapped in local minima and are highly sensitive to initial condition. The main goal of this study was to develop and evaluate a semiautomatic segmentation algorithm to delineate the prostate boundary with fewer interaction of 3D end-firing TRUS images and reduce accumulation of segmentation errors.

The proposed method incorporated a global optimization method driven by histogram matching into a rotational-slice-based segmentation framework. The use of image information alone often leads to poor segmentation of the prostate in TRUS images. The introduction of shape priors in the contour evolution process has been shown to be an effective way to address this issue, leading to more robust segmentation. KPCA, as an unsupervised nonlinear learning technique, was included in our global optimization method to segment the prostate in the first slice. This technique, borrowed from the level set framework,\textsuperscript{39} combines image information
and shape knowledge in a consistent fashion, and keeps both of them in a meaningful balance. It allows us to use fewer interactions to obtain a good segmentation result, addressing the issue that DDM or level set is sensitive to the initial condition. Reasonable segmentation performances highlighted the accuracy of the proposed approach. In order to address the accumulated errors caused by the propagation, another additional propagation shape prior was defined to constrain the evolution of the binary image so as to reduce the shrinking or expanding of adjacent contours during the propagation. This technique encodes and penalizes the symmetric difference of segmentations between any two neighboring slices, leading to consistent segmented prostate contours.

The validation results in Table II show that the proposed method is capable of segmenting these images accurately with a mean DSC of 93.4%. Specifically, the proposed method generated a comparably low standard deviation of 2.2%, which is lower than the values reported in most of the literature, demonstrating good consistency and robustness. The reproducibility experiments in Sec. 4.B show that the proposed method yielded low inter- and intraobserver variability, suggesting that it is independent of observers. In the following, we discuss the algorithm in terms of accuracy on the first slice, accumulated error and sensitivity to the resliced step angle.

5.A. Comparison with previous methods

We compared our proposed approach with the prostate segmentation algorithms using 3D TRUS images, which used similar evaluation metrics and provided best segmentation accuracy in a review paper. The mean DSC of 93.4% and Se of 92.6% obtained by our method are comparable to a volume overlap of 83.5% obtained by Tutar et al. and 86.4% obtained by Garnier et al. and a volume overlap error of 6.63% obtained by Mahdavi et al. The mean MAD of 1.12 mm obtained by our method is less than 1.26 mm obtained by Tutar et al. The mean MAXD of 3.15 mm obtained by our method is less than 4.06 mm obtained by Tutar et al. and 4.06 mm obtained by Garnier et al. In addition, the computational time of 14.3 s of our method, excluding initialization time, is less than 1–4 min obtained by Tutar et al., 14 s with 1–3 min modification obtained by Mahdavi et al., and 26 s obtained by Garnier et al. Thus, the proposed method shows the advantages of both accuracy and efficiency.

5.B. Accuracy on the first slice

The accuracy of the choice of the first slice was analyzed to evaluate the nonlinear shape prior introduced by KPCA. Figure 6 shows three segmentation examples of the prostate transverse view using an active contour model, level set, convex optimization with and without KPCA, using the same initialization described in Sec. 3.B. The first column in Fig. 6 shows three initial images with their initial shapes determined by users. The active contour method did not obtain an accurate prostate boundary in this experiment since it was usually trapped in a local minima due to the weak edge information and an inaccurate initial shape [see Fig. 6(b)]. Two other region-based methods, such as level set and convex optimization with histogram matching, can segment the prostate well when the prostate image has high signal-to-noise ratio and strong edges [see the first row in Figs. 6(c) and 6(d)]. However, they failed to give a favorable result.
Accuracy comparison in slice 1 to slice 15, showing the sensitivity of the propagation-based methods to the accumulation errors. The 3D image was resliced to 30 slices by $6^\circ$. (a) DSC, (b) Se, (c) MAD, and (d) MAXD.

when dealing with inhomogeneous images with weak contrast and low signal-to-noise ratio [see the second and third rows in Figs. 6(c) and 6(d)]. In contrast, the convex optimization method with KPCA functioned better in images with a low signal-to-noise ratio and a weak or incomplete object contour due to the contribution of the learned nonlinear statistical shape prior, as shown in Fig. 6(e). Figure 7(a) shows that the proposed approach can obtain a mean DSC of 93.6% for the first slice, which is comparable to 94.5% of the M$_{LS}$ method initialized by 4–8 points. It can be seen that the proposed approach for segmenting the first slice is capable of taking the advantage of the KPCA technique, resulting in less dependence on initial conditions while preserving the accuracy and efficiency of the convex optimization method with histogram matching.

5.C. Comparison on accumulated errors

The segmentation accuracy for each slice obtained from the three different methods (M$_{CO}$, M$_{LS}$, and M$_{AC}$ methods) was quantitatively evaluated to address the accumulated segmentation errors. For simplicity, the comparison was conducted using slice 1 to slice 15 only, which corresponded to slices resliced in clockwise direction. Figure 7 shows the accuracy comparison result of the three segmentation methods on these slices. At the beginning of the propagation (slice 1), the values of DSC, Se, MAD, and MAXD appear similar for the three methods. With the progress of the propagation, DSC [Fig. 7(a)] and Se [Fig. 7(b)] slightly decrease for the M$_{CO}$ and M$_{LS}$ methods, but they decline noticeably for the M$_{AC}$ method; MAD [Fig. 7(c)] and MAXD [Fig. 7(d)] tend to increase slightly for the M$_{CO}$ and M$_{LS}$ methods while increasing greatly for the M$_{AC}$ method. In addition, the M$_{CO}$ method works better than the M$_{LS}$ method with respect to MAD and MAXD at the later stage of propagation (slice 10 to slice 15). As a result, both the M$_{CO}$ and M$_{LS}$ methods can result in good segmentation accuracy due to the introduction of the propagation constraint, superior to the M$_{AC}$ method. Furthermore, the M$_{CO}$ method performs slightly better on accuracy than the M$_{LS}$ method, but more efficiently since it requires fewer initialization points and computational time.

5.D. Sensitivity test of the resliced step angle

The resliced step angle plays an important role influencing the accuracy and efficiency for the slice-by-slice based segmentation methods. Figure 8 shows the results of DSC and computational time of our method with different resliced step angles. The resliced step angles of $12^\circ$, $6^\circ$, $3^\circ$, $1.5^\circ$, and $1^\circ$ give rise to the resliced number of slices of 15, 30, 60, 120, and 180, respectively. The result in Fig. 8 shows that the DSC increases from $88.2 \pm 4.4$ to $93.5 \pm 2.1$ when the resliced step angle decreases from $12^\circ$ to $6^\circ$. The DSC of our method does not show obvious increase with the decreasing resliced step angle.
angle from 6° to 1° [Fig. 8(a)]. In contrast, the computational time increases gradually from 7.9±2.1 s to 94.1±3.5 s [Fig. 8(a)]. The resliced step angles of 6° and 3° are the optimum trade-off between efficiency and accuracy in our application.

5.E. Limitation and future work

The main disadvantage of propagation-based segmentation methods is that sequentially segmenting 2D slices often carry segmentation errors appearing in one slice to the segmentation of the following slices, thus causing an accumulated segmentation error in all subsequent segmentations. Even though a propagation shape constraint has been applied, there are still some accumulated errors occurring during the segmentation, especially in the later phase of the propagation. One potential solution to decrease the accumulated errors is to include the information of a following slice, since the propagation follows in one direction, and the segmentation result of any slice does not help to refine the segmentation of its preceding slices. Moreover, the KPCA learning technique is only used for the first slice. The learned shape information imposed on more slices would improve the segmentation accuracy. In addition, an accurate and efficient automatic segmentation approach that does not require user initialization would be of great benefit.

In conclusion, the proposed approach makes use of the approximate rotational symmetry of prostate shapes and reduces the original 3D segmentation problem to a sequence of simple 2D segmentation subproblems by means of rotationally reslicing the 3D TRUS image. Based on convex relaxation technique, it provides a fully time-implicit scheme to move the contour to its globally optimal position at each discrete time, which allows a large evolving time step-size to accelerate convergence. The algorithm was also implemented with CUDA and evaluated with 30 3D patient images obtained during a 3D end-firing TRUS guided prostate biopsy procedure. The quantitative validation results using different metrics (DSC, Se, MAD, MAXD) showed that it is capable of delineating the prostate surface accurately, efficiently, and robustly with a low intra- and interobserver variability. The proposed method exhibits the advantages of both accuracy and efficiency in comparison to the local optimization-based methods such as level set- and DDM-based methods. Its performance results suggest that it may be suitable for the clinical use involving the image guided prostate biopsy procedures.

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APPENDIX A: INTENSITY HISTOGRAM MATCHING

Let \( I(x) \in \mathbb{Z} \) be a given prostate 3D TRUS image, where \( \mathbb{Z} \) is the set of image intensity values. Using the definitions of Eq. (1), we can estimate the PDF \( p_i(u, z) \), where \( z \in \mathbb{Z} \) and \( i = f, b \), for the estimated region \( \mathcal{R} \) by the Parzen method, such that

\[
p_i(u, z) = \frac{\int_{\mathcal{R}} K(z - I(x)) u \, dx}{\int_{\mathcal{R}} u \, dx}, \quad i = f, b,
\]

where \( K(\cdot) \) is the Gaussian kernel function such that \( K(x) = (1/\sqrt{2\pi\sigma^2})\exp(-x^2/2\sigma^2) \).

We define \( q_i(z) \), as the intensity PDF model of the region \( \mathcal{R} \), where \( i = f, b \) and \( z \in \mathbb{Z} \). We then make use of the statistical divergence, e.g., Bhattacharyya\(^{47}\) or symmetric Kullback–Leibler distance,\(^{63}\) to measure the distance between the estimated PDFs \( p_i(u, z) \), \( i = f, b \), for the two estimated regions and their corresponding PDF models \( q_i(z) \). In this work, the Bhattacharyya distance\(^{47}\) is used for intensity PDF matching

\[
E_{\text{matching}}(u) = -\sum_{i=f,b} \sum_{z \in \mathbb{Z}} \sqrt{p_i(u, z) q_i(z)}.
\]
APPENDIX B: CALCULATION OF KERNEL PCA PRIOR

The centered kernel matrix \( \tilde{K} \) corresponding to the training data set \( r \) is defined as
\[
\tilde{K} = \left( \Psi(\chi_i) - \overline{\Psi} \right) \left( \Psi(\chi_j) - \overline{\Psi} \right) = \Psi(\chi_i) \cdot \Psi(\chi_j), \quad i \in \{1, N\}.
\]
(B1)

with \( \overline{\Psi} = \frac{1}{N} \sum_{i=1}^{N} \Psi(\chi_i), \) \( \overline{\Psi} = \Psi(\chi_i) - (\overline{\Psi}) \) being the centered map corresponding to \( \chi_i \) and \( \tilde{k}(\cdot, \cdot) \) denoting the centered kernel function. \( \tilde{K} \) can be decomposed as \( \tilde{K} = \Sigma \Sigma^T \), where \( \Sigma = [\epsilon_1, \ldots, \epsilon_N] \) is a diagonal matrix containing the eigenvalues of \( \tilde{K} \). \( \Sigma \) is an orthonormal matrix.

The column vectors \( \epsilon_i = [\epsilon_{i1}, \ldots, \epsilon_{iN}] \) are the eigenvectors corresponding to the eigenvalues \( \gamma_i s \). It can easily be shown that \( \tilde{K} = HKH \), where \( H = I - \frac{1}{N} \mathbf{1} \mathbf{1}^T, \mathbf{1} = [1, \ldots, 1] \) is an \( N \times 1 \) vector. The subspace of the feature space \( F \) spanned by the first \( l \) eigenvectors of the covariance matrix \( C \) of the elements of the training set mapped by \( \Psi \) is referred to as the KPCA space.\(^{42}\)

The exponential kernel is used as the nonlinear kernel function \( k(\cdot, \cdot) \) in this paper and is given by
\[
k_{\text{exp}}(U_i, U_j) = e^{-\frac{||U_i - U_j||^2}{2\sigma^2}}, \tag{B2}
\]
where \( \sigma^2 \) is a shape variance parameter estimated from the training dataset and \( ||U_i - U_j||^2 \) is the squared \( L_2 \)-distance between two binary images \( U_i \) and \( U_j \). The subscript \( \psi \) stands for the nonlinear mapping corresponding to the exponential kernel; this mapping also depends on the choice of \( \sigma \).

Let \( \chi \) be any element of the input space \( I \). The projection of \( \chi \) on the KPCA space is denoted by \( P^\psi(\chi) \) (\( l \) refers to the first \( l \) eigenvectors of \( C \) used to build the KPCA space). The squared distance \( d_F^2 \) between a test point \( \chi \) mapped by \( \Psi \) and its projection on the KPCA space is given by
\[
d_F^2[\Psi(\chi), P^\psi(\chi)] = ||\Psi(\chi) - P^\psi(\chi)||^2 = k(\chi, \chi) - 2(P^\psi(\chi))^T(P^\psi(\chi)) + (P^\psi(\chi))^T \cdot P^\psi(\chi). \tag{B3}
\]
This distance measures the discrepancy between a (mapped) element of \( I \) and the elements of the learned space. It can be expressed only in terms of kernels as
\[
d_F^2[\Psi(\chi), P^\psi(\chi)] = k(\chi, \chi) + \frac{1}{N} \mathbf{1}^T \mathbf{1} - \frac{2}{N} \mathbf{1}^T k + \mathbf{k}^T M \tilde{k} + \tilde{k}^T M \tilde{k}, \tag{B4}
\]
where \( \mathbf{k} = [k(\chi, \chi_1), k(\chi, \chi_2), \ldots, k(\chi, \chi_N)]^T \), \( \tilde{k} = H(k - \frac{1}{N} \mathbf{1}) \), and \( M = \frac{1}{N} \sum_{i=1}^{N} \epsilon_i \epsilon_i^T \). It will be minimized as an introduced shape energy functional in the contour evolution process.

APPENDIX C: CONVEX RELAXATION AND CONTINUOUS MAX-FLOW APPROACH

To optimize the energy function (7) which is highly nonlinear, we introduce an efficient continuous max-flow algorithm\(^{54}\) by globally solving the following continuous min-cut problem:
\[
\min_{u(x) \in [0,1]} \left\{ (1-u(C_r)) + \langle u, C_r \rangle + \int_{\Omega} g(x) |\nabla u| \, dx \right\}, \tag{C1}
\]
where the binary constraints \( u(x) \in \{0,1\} \) are substituted instead of its convex relaxation \( u(x) \in [0,1] \). The continuous min-cut problem implies that the new contour \( C^{t+1} \) at the next time step \( t + 1 \) is globally optimal, so that the given contour is propagated to its globally optimal position during the current time frame. In addition, the new contour position at each evolution step is computed in a fully time-implicit manner, which allows a large time step and a parallelized algorithm, substantially speeding up contour propagation. In this study, we use a continuous max-flow configuration similar to the one proposed in Yuan et al.\(^{54}\) Let \( p_r(x) \) and \( p_s(x) \) be source and sink flows to and from pixel \( x \) to the source and sink terminals. The spatial flow \( p(x) \) exists around the neighborhood of pixel \( x \). Then, the continuous max-flow model that maximizes the flow can be formulated as follows:
\[
\max_{p_s, p_t, p} \int_{\Omega} p(x) \, dx \tag{C2}
\]
subject to the flow capacity constraints
\[
\begin{align*}
p_s(x) & \leq C_s(x), \quad \forall x \in \Omega, \\
p_t(x) & \leq C_t(x), \quad \forall x \in \Omega, \\
|p(x)| & \leq g(x), \quad \forall x \in \Omega.
\end{align*} \tag{C3}
\]
and the flow conservation condition
\[
\text{div}(p(x) - p_s(x) + p_t(x)) = 0, \quad \forall x \in \Omega. \tag{C4}
\]
In Yuan et al.,\(^{54}\) it was proven that the continuous max-flow model (C2) is equivalent to the convex relaxation problem (7). The continuous max-flow model (C2) is then formulated and solved using the classical augmented Lagrangian method,\(^{64}\) where the readers are referred to Refs. 48 and 54 for more details.

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\(^{1}\)American Cancer Society, American Cancer Society: Cancer facts and figures (American Cancer Society, 2010); see http://www.cancer.org/.


