MRI/TRUS data fusion in prostate cancer diagnostic and focal treatment.

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Abstract

Prostate cancer is the most common non-skin cancer in men and with a tendency to increase as the world population ages. Currently, there is no image modality that can both provide accurate needle navigation and be cost-effective, therefore limiting the ability to perform targeted biopsies and/or focal therapy. Thus, multi-modality registration of both MRI and TRUS images has been the most consensual solution. Following this line of research, in this work, a method combining semi-automatic segmentation followed by elastic registration is developed for the brachytherapy procedure. The semi-automatic segmentation is based on Active Shape Models (ASM), and the non rigid registration technique to pre-interventional MRI is based on Thin-Plate Splines interpolation. Using the developed tools for brachytherapy, a study is also performed for the biopsy procedure. This study quantifies the movement of the prostate gland during the biopsy procedure due to external loads from the contact of the tip of the ultrasound probe.

Keywords: Prostate cancer, Semi-automatic segmentation, Active Shape Models (ASM), MRI/TRUS image Registration, Thin-Plate Splines (TPS)

1 Introduction

PCa is the most common of all the non-skin cancers, representing 22.2% of all the cancer cases and being the third in number of deaths [1]. The probability of developing PCa increases with the age, being relatively rare below 40 (0.01%) and more common above 70 (12.48%), resulting in an overall probability of developing invasive PCa form birth to death of 15.90 % (approximately 1 in 6) [2]. As the population is ageing in more developed countries, it is likely that more and more persons may develop PCa and this value may increase.

Current diagnostic tools to obtain evidence of PCa include digital rectal exam (DRE), serum concentration of PSA and transrectal ultrasonography (TRUS). However, the definite diagnosis depends always on the histopathologic verification of adenocarcinoma in prostate biopsy cores or operative specimens [3]. The standard method is to perform TRUS-guided systematic biopsy. In this procedure a 2D US probe is equipped with a needle guide for transrectal (through the rectal wall) access to the prostate. The needle tra-
jectory is aligned with the TRUS image enabling the visualization of the needle trajectory and placement. Since some lesions are isoechoic, thus not visible in US images it is necessary to sample the prostate in a systematic randomized way.

Because the cores are sampled in a blinded way, without the aid of any visual references (in particular with respect to 3D space), it’s very difficult to know the correct position of the biopsy inside the gland. Therefore, it’s impossible to sample the exact same site in a later exam to investigate the development of a small cancer lesion over time and limiting the ability to adopt an active surveillance approach. Furthermore, with the current technique, it is possible to miss the cancer site since the exam performs a non-exhaustive systematic search for an invisible target. This results in a low detection rate of about 30 to 40% in traditional 12-core biopsies and even with saturation biopsies with 18-cores similar results have been obtained [4, 5].

Due to this limitation of US, in the last few years, interest has been increasing on the use of MRI in the diagnostic of PCa. Multiparametric MRI exams can provide information not only about the anatomy of the organ, as seen in regular T1 and T2-weighted images, but also about the physiology and chemistry of the organ, using modalities such as DWI, DCE and MRS [6]. A recent work trying to find histopathological correlation between multiparametric MRI findings, achieved a positive predictive value in the peripheral zone using all 4 MRI sequences of 98% and 97% in central zone [7].

Therefore, performing biopsies with the help of the MRI information is a good solution to overcome the problems of the US systems. The first MRI-guided solutions for prostate interventions started to be proposed in the beginning of this century using pure MRI solutions. In order to adapt the biopsy procedure for MR guidance, two magnetic compatible end-effectors for a transperineal approach were proposed by Hata et al. [8] and Susil et al. [9]. End-effectors for transrectal approaches were also proposed by Krieger et al. [10] and Beyersdorff et al. [11]. A fully actuated MRI compatible robot for transperineal access, called MrBot, was described in Stoianovici et al. [12] and Mozer et al. [13], where the physician does not directly control the robot but only defines the needle path and monitors its action.

Still, MRI systems are a costly and sparse resource in most countries, and electromagnetic compatible instruments are also more expensive than traditional biopsy ones. To address this problem, several groups started to research MRI/TRUS registration methods, thus taking the advantages of the two modalities. On one hand, TRUS imaging doesn’t require a special magnetic compatible environment as MRI and can be used in any surgical room, and on the other hand it is a much cheaper modality and vastly available in current hospitals.

The first solutions using MR/TRUS image fusion for the prostate were published in 2007 by Xu et al. [14], Baumann et al. [15] and Andriole et al. [16]. The first two solutions proposed to acquire a US volume prior to the intervention to serve as anatomical reference, where real time US images would be superimposed using image-based registration. Xu acquired the 3D volume using a 2D TRUS probe with a magnetic tracking sensor to locate the acquired images in the world frame. In Baumann et al. [15] the implementation of the commercial Koelis Urostation was presented. With this system a US probe with an internal articulated, motorized transducer array was used allowing the acquisition of 3D images without moving the probe and a kinematic model for the probe movement was introduced to estimate the position of the probe in relation to the prostate. Andriole et al. [16] reviewed in his study the TargetScan™ system commercialized by Envisioneering Medical Technolo-
gies which uses a fixed TRUS probe, with an internal motorized side-fire array, therefore minimizing the deformation and displacement of the prostate during the procedure. The biopsy samples are then acquired using flexible biopsy needles and a motorized encoded stepper to place and track the needles. Makni et al. [17] used a different methodology, based on the elastic deformation of prostate models obtained from the segmentation of MRI and TRUS datasets using rigid alignment with Iterative Closest Point (ICP) and Thin-Plate Splines (TPS) as proposed by Chui and Rangarajan [18], which will be the technique implemented in this study.

Other authors have focused in systems using the transperineal approach, such as Ho et al. [19], were a robotic positioning system for transperineal needle insertion using TRUS guidance is presented. In Hadaschik et al. [20], the commercial system BiopSee® by MEDCOM is analysed. This product uses a brachytherapy like approach, acquiring the US volume in a way similar to Ho et al. [19].

2 Materials and Methods

2.1 Overview

In Figure 1.6, a schematic illustration summarizing the different steps performed during the registration procedure is shown. In this methodology, the MRI dataset acquired prior to the procedure is analysed and the prostate is segmented offline. Then, during the procedure, a set of US images is acquired and segmented with the help of a semi-automatic algorithm. Using the point clouds acquired in the segmentation phase, 3D models of the gland for each image modality are created using radial basis functions (RBF). Following, the models are aligned using rigid registration and an elastic deformation field is estimated using thin-plate splines (TPS). Notice that the framework developed was designed to be general enough to be extended to biopsy exams as well as other prostate applications.

![Figure 1: Schematic illustration showing the different steps of the proposed approach.](image)

2.2 Semi-automatic segmentation of TRUS images

The first step was the development of the TRUS segmentation used during the procedure, creating semi-automatic and supervised automatic algorithms that help the normal procedure and enable faster segmentation. Since US image segmentation is strongly influenced by the quality of the data and its artefacts, such as attenuation, speckle noise, shadows, and signal dropout, normal edge-detection algorithms tend to fail. In order to address this problem, a method involving prior knowledge of prostate shape had to be used. The implemented method is based in active shape models as the ones found in Hodge et al. [21] and Yan et al. [22], and required the implementation of statistical shape models (SSM) from the studied patients. The image is then searched in order to extract the contour by minimizing a given energy function.
2.2.1 Statistical shape model

The aim of SSM is to study the global shape of the prostate from a population and use statistical tools to acquire the mean shape and principal variation modes of the gland.

To create this model, a set of manually reconstructed prostate shapes are sampled in a systematic way so that each shape \( s \) is represented by \( M \) 3-D points as a vector like the one in equation 1 where each point represents the same prostate place in all the training patterns.

\[
s = \begin{bmatrix} x_1, x_2, ..., x_M; y_1, y_2, ..., y_M; z_1, z_2, ..., z_M \end{bmatrix}^T
\]

(1)

In this work, the points were acquired by sampling 10 prostate contours from the gland surface from base to apex at fixed intervals of 10% of the height of the prostate. Then 40 equally spaced points along the contour lines are collected in an anticlockwise direction.

After each shape has been sampled into a \( s_i \) vector, a principal component analysis (PCA) is performed on the training set by calculating the mean shape vector \( \overline{s} \) and the covariance matrix \( C \) according to equations 2 and 3 where \( N \) is the number of shapes in the training set.

\[
\overline{s} = \frac{1}{N} \sum_{i=1}^{N} s_i
\]

(2)

\[
C = \frac{1}{N-1} \sum_{i=1}^{N} (s_i - \overline{s}) \cdot (s_i - \overline{s})^T
\]

(3)

The eigenvectors and eigenvalues of \( C \) are then calculated in order to find the matrices \( U \) and \( D \) of the singular value decomposition of \( C \) (equation 4). The orthogonal column vectors of the matrix \( U \) correspond to the eigenshapes or the modes of shape variation while the diagonal matrix \( D \) stores corresponding eigenvalues which represent the magnitudes of the shape variations. These eigenshapes are then ordered according to the the percentage of the total variation they represent and a subset is chosen in order to preserve a minimum of 95% of the total.

\[
C = UDV^* \quad (4)
\]

Any new shape \( s \) can then be decomposed in terms of the eigenmodes using equation 5 and new shapes can be generated by varying the parameter vector \( b \) in equation 6.

\[
b = U^T(s - \overline{s}) \quad (5)
\]

\[
s = \overline{s} + Ub \quad (6)
\]

2.2.2 Energy minimization

At the beginning of the image search, the contour \( C \) is initialized with the mean shape obtained from the SSM. The search procedure is performed in order to minimize the term in equation 7 for each contour point \( p_i \). This is done via a local search around the point along the normal direction of the contour. A set of \( L_{\text{search}} \) pixels are chosen along the normal, both inside and outside of the curve, and the one that presents the lower energy is chosen to be the new point location.

\[
E(p_i) = E_{\text{image}}(p_i) + E_{\text{int}}(p_i) + E_{\text{shape}}(p_i) \quad (7)
\]

The above equation is composed by three terms, where \( E_{\text{image}}(p_i) \) is the one responsible for searching the prostate boundary features in the image and attract the contour point towards that boundary (equation 8); \( E_{\text{int}}(p_i) \) is the internal energy of the curve that introduces continuity and curvature constraints as defined in [23] (equation 9); finally \( E_{\text{shape}}(p_i) \) is related to the shape energy and measures the accordance between the contour points \( p_i \) and the prior shape obtained from SSM \( p'_i \) (equation 10).

\[
E_{\text{image}}(p_i) = 255 + \frac{1}{2m} g^T f \quad (8)
\]
where $g$ is a contrast filter of the form $[1, ... , 1, -1, ... , -1]$ with size $2m$ equal to the number of points in the normal vector profile and $f_i$, it contains the intensity of the pixels along the normal vector.

$$E_{int}(p_i) = \alpha(\|p_i - p_{i-1}\| + \|p_{i+1} - p_i\| - 2d) + \beta\|\langle p_i - p_{i-1}\rangle - \langle p_{i+1} - p_i\rangle\|$$

where the coefficients $\alpha$ and $\beta$ control the continuity and curvature respectively.

$$E_{shape}(p_i) = \gamma\|p_i - p_i'\|$$

where $\gamma$ is a weighting factor.

After the segmentation of each image in the set, the prior shape is updated based on previous segmentations and the SSM in order to improve initial contour for the next image.

### 2.3 3D modeling of the prostate

The segmented contours from both MRI and TRUS datasets were then interpolated in 3D using radial basis functions (RBF) to create implicit surfaces and three dimensional meshes. This step was performed using the method in [24] where biharmonic RBFs are used to compute a smooth implicit surface defined by the zeros of the function $s(x)$ in equation

$$s(x) = p(x) + \sum_{i=1}^{N} \lambda_i \|x - x_i\|,$$

where $p$ is a low degree polynomial, $\lambda_i$ are weight parameters and the biharmonic function $\| \cdot \|$ is the euclidean norm between a given point $x$ and the points $x_i$ that are the centers of the RBF.

The polynomial coefficients and the weight parameters $\lambda_i$ are then calculated so that $s(x) = 0$ for every $x$ that belongs to the surface, and is an approximate value of the distance between $x$ and the surface, for points offsurface.

### 2.4 Registration

For the registration process, a feature-based non-rigid registration method was used based on Chui and Rangarajan [18] and Makni et al. [17]. At first, a rigid registration is performed using an iterative closest point (ICP) algorithm, then an elastic deformation is estimated using TPS.

#### 2.4.1 Rigid Registration

Given the implicit surface $S$ from the RBF reconstruction obtained from the MRI images and a set of 3-D points obtained from the US implicit surface $P = \{ p_1, ..., p_N \} p_i \in \mathbb{R}^3$, the objective is to find the transformation $T : p_i \rightarrow p_i'$, composed by translations and rotations along the three coordinate axis, that minimizes the mean distance from the set $P$ to $S$ given by

$$E(P, T) = \sum_{i=1}^{N} d(T(p_i), S)$$

where $d(p_i', S)$ is the distance from the $i$th point of the set to the surface and $p_i'$ is the transformed point according to equation [13]. This distance was obtained by evaluating the interpolant function that implicitly defines the MRI surface $s_{MRI}(x)$ at the point $p_i'$.

$$p_i' = T(p_i) = R p_i + t$$

with $R \in \mathbb{R}^{3 \times 3}$ representing the rotation matrix and $t \in \mathbb{R}^3$ the translation vector.

The algorithm presented here is a form of a gradient descent method that searches the best solution through minimizing the cost function around the neighbourhood of certain predefined parameters, in this case the 6 degrees of freedom that define the transformation. In order to provide a good initial guess, the search was initialized by calculating the center of mass of the two point clouds and center them in the MRI reference system. The minimization was
then performed by alternating the search according to translation and rotation. In each iteration of the minimization processes, the algorithm calculates the cost function resultant from varying each one of the components of the transformation, \( t_x, t_y \) and \( t_z \) for the translation and angles \( (\phi, \theta, \psi) \) for the rotation, by a given step \( \eta \) and chooses the one with smaller cost. Since it is a coarse-to-fine approach, the step \( \eta \) decreases in each iteration in order to enable a smoother fit.

2.4.2 Elastic Deformation

The principle of TPS is to compute a non-rigid mapping between two corresponding points datasets \( X = \{x_1, \ldots, x_N\} \) and \( Y = \{y_1, \ldots, y_N\} \). In this case, these sets will be chosen to be the US points after the rigid transformation and the MRI points, respectively, organized in a way such that each point \( x_i \) in the US cloud represents the same prostate location of the point \( y_i \) in the MRI prostate. Since after the rigid transformation the two cloud points are supposed to be very close to each other, the correspondences were taken so that each point \( x_i \) in US would correspond to the nearest point in the MRI surface \( y_i \). Therefore, one is looking for a function \( f \) that minimizes the cost function

\[
E = \sum_{i=1}^{N} \| x_i - f(y_i) \|^2 \tag{14}
\]

The function \( f(y_i) \) used to minimize this cost function is the TPS model which takes the form

\[
f = Y.A + \Phi.W \tag{15}
\]

and is composed by two terms. \( A \) is a \((4 \times 4)\) matrix that represents the affine transformation and \( W \) is a \((N \times 4)\) matrix that describes the warping transformation. The matrices \( X \) and \( Y \) must be padded with a column with ones to be the form \( Y_1 = \{1, x_{ix}, y_{iy}, y_{iz}\} \) in order to be multiplied by the affine matrix \( A \). As regards \( \Phi \) it is a \((N \times N)\) radial function matrix similar to the one in RBFs and is given by

\[
\Phi_{i,j} = \| y_i - y_j \| \quad i, j = 1, \ldots, N \tag{16}
\]

This function is minimized according to [15] by using a QR factorization of the points matrix \( Y \) of the form

\[
Y = [Q_1Q_2] \begin{bmatrix} R_1 \\ 0 \end{bmatrix} \tag{17}
\]

where \( Q_1 \) and \( Q_2 \) are \((N \times 4)\) and \((N \times N-4)\) respectively orthonormal matrices and \( R_1 \) is upper triangular.

The final solution for the least squares minimization of equation 14 for \( A \) and \( W \) is

\[
\hat{W} = Q_2(Q_2^T\Phi Q_2 + \lambda(N-4))^{-1}Q_2^TX \tag{18}
\]

\[
\hat{A} = R_1^{-1}(Q_1^TX - Q_1^T\Phi \hat{W}) \tag{19}
\]

3 Experiments and Results

3.1 Data

The data presented in this study was acquired in two different procedures: prostate brachytherapy and prostate biopsy.

3.1.1 Brachytherapy

In the brachytherapy procedure both MRI and TRUS dataset have been acquired. The MRI images were acquired prior to the procedure using a Philips Intera at 1.5 Tesla without endorectal coil. T2 images with a 3.6 mm spacing between slices and a size of 336 \times 336 with each pixel corresponding to 0.6579 mm were used to build the prostate model.

As for the set of US images, they were acquired using a Pro Focus 2202 US system with a transrectal biplanar transducer, both commercialized by B-K Medical. A set of axial slices was collected at the
beginning of the intervention with the help of a stepper with two degrees of freedom. The images were collected with a spacing of 5 mm between slices and a size of $512 \times 444$ with each pixel corresponding to 0.155 $mm$.

3.1.2 Biopsy

The images acquired during the biopsy exam were collected using a Mindray M5 US system and an end-fire transducer. The position of the probe was monitored using a Polaris Spectra® optical tracking system commercialized by NDI.

3.2 Evaluation method

In order to evaluate the performance of both the automatic segmentation procedure and the registration algorithm, two error metrics were used. The first is the mean absolute distance (MAD), as given by the equation

$$MAD = \frac{1}{N} \sum_{i=1}^{N} ||p_i - p'_i||$$

(20)

In the segmentation results, $p_i$ is the $i$th contour point obtained from the segmented line and $p'_i$ is the respective point from the ground truth contour. As in the registration section, $p_i$ is the $i$th point of the US cloud and $p'_i$ is the closest point in the MRI surface to that point.

The second metric used was the dice similarity coefficient (DSC) defined by equation

$$DSC = \frac{2|A_s \cap A_g|}{|A_s| + |A_g|}$$

(21)

Once more, the parameters $A_s$ and $A_g$, have different meaning in the two sections. In the segmentation, $A_s$ is the area inside the segmented contour and $A_g$ is the area enclosed by the ground truth contour. As for the registration, the DSC is calculated with volumes instead as in equation

$$DSC = \frac{2|V_{MRI} \cap V_{US}|}{|V_{MRI}| + |V_{US}|}$$

(22)

where $V_{MRI}$ is the volume contained by the MRI implicit surface and $V_{US}$ the volume enclosed by the US transformed surface.

3.3 Results

3.3.1 Segmentation

The results obtained using the semi-automatic segmentation algorithm without manual editing are shown in table 1.

<table>
<thead>
<tr>
<th>Region</th>
<th>MAD ± Std</th>
<th>DSC ± Std</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>2.07 ± 0.36</td>
<td>0.88 ± 0.03</td>
</tr>
<tr>
<td>Base</td>
<td>2.74 ± 0.90</td>
<td>0.79 ± 0.13</td>
</tr>
<tr>
<td>Midgland</td>
<td>1.63 ± 0.36</td>
<td>0.94 ± 0.01</td>
</tr>
<tr>
<td>Apex</td>
<td>2.31 ± 0.83</td>
<td>0.84 ± 0.06</td>
</tr>
</tbody>
</table>

As expected, the performance of the automatic segmentation is best at midgland, where the gland usually presents well defined boundaries, with a DSC of 95%, which means that almost all the segmented area overlaps with the ground truth. The MAD is also better than was for the total gland with a value around 1.6 $mm$. Nevertheless, the results at apex and base are rather poor, with mean distances of 2.3 and 2.7 respectively. As for the overall gland a MAD of 2 $mm$ to the ground truth and a DSC of near 90% were obtained, similar to the first two methods proposed in a similar study found in [22].
3.3.2 Registration

Figure 2: Fusion images obtained for two different patients after elastic registration.

By analysing the results presented in Figure 3, one may verify that after aligning the center of mass for the initial guess of the registration one can already induce a good match between the two modalities, with a MAD of 0.51 mm and a DSC of 90.8%. These values are then slightly improved with the rigid registration until a MAD of 0.47 mm and a DSC of 91.5%. At this point the difference between the two surfaces is mainly due to different deformation states and no further iterations can improve this value. The elastic deformation step is then applied, resulting in a reduction of the MAD errors to approximately half and increasing the DSC to 96.7%, a value very close to the perfect match. Figure 2 shows the resulting fused images after elastic registration for two different patients.

3.4 Biopsy

In the first column of the table 2, one may analyse the effect of injecting the 6 cm\(^3\) of anaesthetic between the rectum wall and the gland. Comparing this volume to the mean size of the prostate that according to [25] is between 24 cm\(^3\) at age of 50-54 years and 38 cm\(^3\) above 75 years, one may conclude that it is very significant. As seen in the table, this injection results in a mean displacement of approximately 4 mm.

Table 2: Displacement of the prostate in mm relative to the initial position during the biopsy exam, in three different moments of the biopsy exam: after the anaesthesia (\(t_1\)), at the middle of the procedures (\(t_2\)) and after all the biopsy cores being collected (\(t_3\)). Mean value was calculated without the patient 3 and 6 as the values are discrepant from the others.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Displacement in mm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(t_1)</td>
</tr>
<tr>
<td>1</td>
<td>1.79</td>
</tr>
<tr>
<td>2</td>
<td>2.35</td>
</tr>
<tr>
<td>3</td>
<td>11.99</td>
</tr>
<tr>
<td>4</td>
<td>1.74</td>
</tr>
<tr>
<td>5</td>
<td>7.89</td>
</tr>
<tr>
<td>6</td>
<td>24.05</td>
</tr>
<tr>
<td>7</td>
<td>5.37</td>
</tr>
<tr>
<td>8</td>
<td>4.42</td>
</tr>
<tr>
<td>Mean</td>
<td>3.93</td>
</tr>
</tbody>
</table>

Figure 3: Evolution of the MAD a) and DSC b) mean values along the different steps of the registration process.

Figure 4: Images showing the results of different biopsy exams. In brown is the prostate model based on the images acquired at the beginning of the procedure. The red points represent segmentation of images acquired at the time of each biopsy core acquisition. The biopsy cores location are also displayed in the image.
The biopsies were then collected resulting in a mean displacement of approximately 12 mm after collecting the first half of the cores and 18 mm at the end of the procedure.

4 Conclusion

The improvements of the brachytherapy procedure proposed in this work were twofold. The first improvement was the implementation of a semi-automatic prostate segmentation, contributing to a faster execution of the procedure while still keeping the medical team hands-on. The results obtained in full automatic operation were very successful, with the possibility of being improved by manual editing in the end. This enables the clinician to have full supervision, taking advantage of their medical expertise.

The second improvement was the registration of pre-operative MRI images into the US data that once finished enables the overlay on the TRUS images the location of the lesions obtained from the MRI, thus allowing the visualization of their relative position to the radioactive seeds.

Finally, this study has quantified the movement of the prostate during the biopsy procedure, verifying a big displacement of the gland throughout the exam, therefore limiting the ability to extend the proposed method to the biopsy. Future work would benefit from 3D transducers to acquire the prostate volume automatically. Another major improvement to the biopsy procedure would be the implementation of a robotic system to better control the exerted force and achieve higher targeting ability.

References


