A comparison of the accuracy of statistical models of prostate motion trained using data from biomechanical simulations

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1. Introduction

Statistical shape models (SSM) are widely used in medical image analysis to represent variability in organ shape. However, representing subject-specific soft-tissue motion using this technique is problematic for applications where imaging organ changes in an individual is not possible or impractical. One solution is to synthesise training data by using biomechanical modelling. However, for many clinical applications, generating a biomechanical model of the organ(s) of interest is a non-trivial task that requires a significant amount of user-interaction to segment an image and create a finite element mesh. In this study, we investigate the impact of reducing the effort required to generate SSMs and the accuracy with which such models can predict tissue displacements within the prostate gland due to transrectal ultrasound probe pressure. In this approach, the finite element mesh is based on a simplified geometric representation of the organs. For example, the pelvic bone is represented by planar surfaces, or the number of distinct tissue compartments is reduced. Such representations are much easier to generate from images than a geometrically accurate mesh. The difference in the median root-mean-square displacement error between different SSMs of prostate was <0.2 mm. We conclude that reducing the geometric complexity of the training model in this way made little difference to the absolute accuracy of SSMs to recover tissue displacements. The implication is that SSMs of organ motion based on simulated training data may be generated using simplified geometric representations, which are much more compatible with the time constraints of clinical workflows.
1. Introduction

1.1. Statistical shape modelling

Statistical shape models (SSMs) are widely used in medical image analysis to represent variability in organ shape and size (Heimann and Meinerz, 2009). In image segmentation and registration, for example, information on the statistical variation of the shape of an organ of interest provides useful prior knowledge that can lead to significant improvements in robustness, speed and accuracy by constraining the search space. For instance, in image segmentation, prior knowledge on the expected range of shapes of an anatomical structure to be segmented enables the segmentation to be constrained to only consider shapes within this range. This approach is particularly useful when segmenting noisy or artefact-corrupted images.

Similarly, when registering images of a deformable structure, it is often very useful to constrain the deformations considered by the registration algorithm by using prior knowledge of the way in which that structure deforms. In this way, non-physical deformations can be avoided and the speed and robustness of the registration algorithm improved. Again, this property is especially useful when large soft-tissue deformations and/or noisy image data are involved.

However, since imaging is the primary source of training data for constructing SSMs, building an SSM that represents subject-specific soft-tissue motion is often highly problematic for applications where the motion is caused by an instrument or other medical device during a surgical procedure or diagnostic investigation. In such cases, imaging organ motion prior to a procedure is often impossible or impractical due to technical difficulty, limited time, or expense. On the other hand, obtaining an SSM of organ motion prior to a procedure is often highly desirable to inform and constrain the (non-rigid) registration of pre- and intra-operative images so that the pre-operative images can be used directly for surgical guidance (Hawkes et al., 2005).

1.2. Finite element modelling

An alternative approach for generating computational models of organ motion is to employ biomechanical modelling techniques to compute soft-tissue deformations directly using a physics-based model (Carter et al., 2005; Hawkes et al., 2005). Finite element analysis (FEA) is a widely used biomechanical modelling method that provides a powerful, widely accessible, and highly flexible tool for predicting soft-tissue motion. In this method, structures of interest are represented as an FE mesh comprising many discrete volumetric elements, connected at node points. Elements are grouped into “compartments”, with each compartment corresponding to a different tissue type, and assigned material properties, which govern the way in which it deforms in response to external loadings.

Wittek et al. (2009) found that material properties were unimportant for modelling brain deformation. However, in their study, only homogeneous isotropic bodies and heterogeneous bodies where the ratios of stiffness and/or compressibility are held constant were considered. Furthermore, the brain tumour, defined as the region of interest, occupied only a small proportion of the model, so the expected effect on the deformation is small. When the assumption that tissue behaves as an incompressible material is not valid, and an organ comprises multiple tissue types, which each contribute substantially to the total volume, the accuracy of the tissue displacements predicted by FEA becomes highly dependent on the assignment of accurate values for the material properties which are known to vary widely between subjects and different tissue types (Chen et al., 2006; Hu et al., 2008a; Tanner et al., 2006). Setting physically realistic boundary conditions are also highly important.

Although it may be possible to reasonably estimate boundary conditions and material properties in some clinical applications, in general, these parameters are very difficult to measure in vivo and are subject to large inter-patient variability (which may be especially pronounced in pathological tissue). MR and ultrasound elastography, and related imaging methods, may in the future provide accurate estimates of tissue material properties in vivo, but these methods require significant further development before mechanical tissue properties can be accurately determined (Ma et al., 2010). One solution to the dependency on material properties and boundary conditions is to estimate forces within tissue and tissue material properties using an inverse problem approach (Alterovitz, 2006). However, this method requires that tissue displacements can also be determined throughout the volume of interest, for example by maximising an image similarity measure to non-rigidly register two images. This is relatively straightforward when the images are acquired using the same imaging modality, but can be very difficult when multiple modalities are involved (e.g. MR and ultrasound) due to a lack of corresponding image features. This model-based approach also requires the estimation of a large number of unknowns and can result in an ill-posed problem, which is challenging to solve in three dimensions.

1.3. Combining statistical shape- and finite element modelling

In this paper, we adopt an alternative approach to soft-tissue modelling that combines statistical shape modelling and FEA to overcome the limitations of each of these techniques outlined above. Specifically, a statistical model of organ motion is built from...
simulated training data provided by FEA given varying boundary conditions that may be encountered in practice and values for tissue material properties randomly drawn from the known range of values quoted in the literature. This approach, originally proposed by Davatzikos et al. (2001), overcomes the practical problem of insufficient (image-based) training data, described above, and the problem of determining point-to-point correspondence between training shapes, since node-to-node correspondence is implicit between a deformed and an undeformed FE model. Generating SSMs using simulated training data also overcomes the problem of unknown material properties and application-specific boundary conditions, since uncertainty in these parameters is accounted for by the statistical nature of the model.

A further advantage of this approach is that by employing techniques such as principal component analysis (PCA), significant data reduction can be achieved, resulting in a low-dimensional model which is deformed by changing relatively few parameters. Such models are particularly well-suited to image registration since they can compute tissue displacements very rapidly and can be easily integrated into a numerical optimisation algorithm without adding significant computational burden. This is especially important for time-critical applications, such as intra-operative registration during image-guided surgical interventions. In summary, with the knowledge that, if our model deformation is constrained, such models can be registered to sparse data and compute displacements across an entire volume of interest. Again, these properties make these models well-suited to registration during image-guided interventions where a frequent challenge is to non-rigidly register diagnostic quality images to relatively poor-quality interventional images, which typically provide only sparse data on organ motion.

For clarity, and to distinguish SSMs generated using simulated training data from classical SSMs, we refer to such models as statistical motion models (SSMs). Building an SSM is very similar to building an SSM, but the training data reflects variability in the position and orientation of an organ, as well as its shape due to intra-subject tissue motion and deformation, rather than inter-subject variability in organ shape alone.

1.4. Previous work

We have demonstrated in our previous work how patient-specific SSMs of the prostate gland, trained using data from FE simulations, can be used to non-rigidly register MR images, acquired before an ultrasound-guided needle biopsy or ablative therapy procedure, to ultrasound images acquired during the procedure (Hu et al., 2009; Hu et al., 2008a,b). In this method, an FE model of the prostate gland, rectum, bladder and pelvic bone is created using anatomical information derived by (manually) segmenting a T2-weighted MR image. This FE model is then used to generate training data for an SMM by simulating prostate motion and deformation that may occur during a biopsy or therapy procedure.

This work was motivated by the growing clinical need for non-rigid registration technology that enables information on the location and extent of tumours (or suspected tumours), identified using MR imaging, to be used directly to target biopsy sampling and emerging minimally-invasive cancer therapies. These procedures are guided routinely by real-time transrectal ultrasound (TRUS) imaging, which provides important visual information on the location of biopsy needles and therapy delivery instruments with respect to the prostate gland, but tumours are poorly distinguished using TRUS and therefore this modality is of very limited use for accurate tumour targeting. Registering MR images — or deformable models of the prostate that contain pathological information — to TRUS images provides a low-cost and widely accessible alternative to performing these procedures within an MR scanner, as this an expensive as well as technically and logistically challenging option.

In (Hu et al., 2008a) and (Hu et al., 2008b), we show how an SMM of the prostate, trained using simulated data, can be registered to a 3D TRUS image of the deformed gland using a feature-based non-rigid registration scheme in which the surface of the prostate gland in the SSM is iteratively deformed to fit a set of target surface points identified in the TRUS image. Using the distance between image visible landmark points in the gland (such as the centres of small cysts and calcifications) to quantify the error in recovering tissue displacements within the gland, the mean $± SD$ error was $1.8 ± 0.7$ mm after registration compared with $5.0 ± 1.3$ mm before registration.

In (Hu et al., 2009) and (Hu et al., in press), we show how an SMM, trained using simulated data based on anatomical information derived an MR image, can be registered automatically to a 3D TRUS image using a novel surface-to-image registration algorithm. Once an SMM has been registered to a TRUS image, the transformation relating point co-ordinates in the original (undeformed) SMM and the target TRUS can be used to warp the MR image. Again, using the distance between corresponding landmark points visible in both the MR and TRUS images to determine the target registration error, and the latest implementation of our registration algorithm, the median (95th percentile) root-mean-square (RMS) error was reduced from 8.1 (15.0) to 2.4 (6.19) mm following registration (Hu et al., in press).

An important challenge, addressed in our previous work, is the compensation for prostate gland deformation that occurs between MR and TRUS imaging. To date, we have focused on TRUS probe pressure as the primary source of gland motion. Motion and deformation of the prostate gland are inevitable during TRUS imaging because good contact between the probe and rectal wall is essential to achieve acoustic coupling between the ultrasound transducer and prostate, which in turn is necessary for good quality TRUS images. From our experience of imaging during these procedures, greater probe pressure is required in some patients to optimise image quality. In some centres, the prostate is also deformed by an endorectal MR coil introduced during MR imaging, used to optimise image quality. All of the MR images used in this and our previous studies were obtained with a body coil, and therefore we assume that the prostate deformation between MR and TRUS imaging is dominated by TRUS probe pressure; as discussed in detail in Hu et al. (in press); gland shape changes due to bladder filling, stools in the rectum, and changes in patient position are assumed to be negligible.

We have developed a method for modelling motion due to TRUS probe pressure using FEA with an FE mesh of the prostate and surrounding organs derived from MR images of prostate cancer patients. This model is constructed by meshing the boundaries of the prostate gland, pelvis, rectum and bladder from a manually segmented MR image. Manual contouring of these structures was used to create a mesh with the highest geometric accuracy possible, but this method is both time-consuming and labour-intensive, and therefore impractical for a real-world clinical workflow. In the workflow proposed in our previous work, for each patient, a clinician systematically delineates the prostate gland (including the boundary between the peripheral zone and the central and transitional zones), rectum, bladder and pelvic bone on transverse slices of a T2-weighted 3D MR image prior to a surgical procedure. The resulting manually-drawn contours are then converted into a tetrahedral FE mesh automatically using special-purpose software. This mesh is used by FEA software developed in our research group (Taylor et al., 2008, 2009) to predict tissue displacements across a volumetric region enclosing the prostate given different combinations of material properties (assigned to each tissue compartment) and boundary conditions determined by the 3D position and orientation...
of the TRUS probe. By applying PCA to mesh node-point displacements corresponding to the resulting deformed meshes, an SMM for the prostate gland is built, represented as a deformable FE mesh. Following a simple initialisation step, the surface of the prostate in the SMM is then registered automatically to the gland surface as it appears in 3D TRUS images, acquired during a TRUS-guided procedure and the updated mesh node points of the deformed SMM are used to calculate the voxel displacements in the MR image. In this way, a diagnostic MR image containing information on the location and shape of tumours is warped to match the view depicted by TRUS images during the procedure, thus enabling tumour targeting.

In the workflow outlined above, the MR image segmentation process is not a time-critical task as in practice it can be performed anytime between MR image acquisition and a few hours of the surgical procedure. However, given the time and degree of user-interaction required to complete this step — a typical manual segmentation takes an experienced clinician 45 min to complete (Hu et al., in press) — it is highly desirable to reduce the amount of clinician time and effort required to generate the data required to build a patient-specific SMM. Therefore, methods for simplifying and speeding-up this process so that it fits within a practical clinical workflow are of major interest.

A number of semi- and fully-automatic algorithms for segmenting prostate MR images have been proposed (Betrouni et al., 2008; Cosio, 2008; Klein et al., 2008; Makni et al., 2009), but these tend to focus on the segmentation of the prostate gland rather than surrounding structures, which are required for accurate FE modelling of prostate motion. Accurate multi-organ segmentation, on the other hand, presents a significantly more complex task and manual segmentation remains the most accurate method available.

1.5. Contributions of this study

In this paper, we describe a previously uninvestigated alternative to automatic multi-organ image segmentation for reducing the burden of manual delineation and therefore making patient-specific SMM generation more clinically practical. Specifically, we investigate the use a geometrically simplified FE mesh, in which some anatomical structures are replaced by equivalent structures with a simplified geometry or omitted completely. This strategy is inspired by the observation that since a PCA-based SMM trained using a set of deformed FE meshes captures the statistical variation in mesh node displacements (assuming a normal probability distribution), adopting a geometrically simplified mesh may not affect the characteristic parameters of this distribution significantly. Therefore, the accuracy of the final SMM may not be compromised significantly by adopting a simplified mesh in the generation of training data.

The principal aim of this study was to investigate the impact of adopting a simpler and faster MR segmentation method by comparing the accuracy of MR-derived prostate SMMs built using different simplified FE mesh geometries with a reference model built from training data simulated using an FE mesh in which the geometry of the prostate, rectum, bladder and pelvic bone are all accurately defined.

In the following sections, we first describe the methodology used to define simplified FE meshes of the prostate and surrounding organs, generate SMMs using a non-linear FE solver and PCA, and quantify the accuracy of different SMMs based on simplified FE training models. Numerical results on the ability of the new SMMs to predict mesh node displacements within the prostate gland after non-rigid registration to unseen surface data are presented by comparing with node displacements computed directly by a non-linear FE solver using a geometrically accurate mesh of all of the organs. In this study, we focus on quantifying the performance of SMMs with respect to registration using simulated rather than in vivo data, which is considered in our previous work. Finally, we discuss the limitations of the study and its implications for model-based image registration in the prostate. The main contribution of this work is the development of a method that has the potential to substantially reduce the amount of clinician time and interaction required to generate patient-specific SMMs of the prostate for non-rigid image registration during minimally-invasive surgical procedures.

2. Materials and methods

2.1. MR image segmentation

MR images were segmented by manually delineating contours on transverse slices using a custom-made graphical user interface written in Matlab (Mathworks, Inc., MA). The outer surface of the prostate gland capsule was segmented and the gland divided into the inner portion of the gland, comprising the central and transitional zones, and the peripheral zone. The boundary of the peripheral zone is usually clearly visible in T2-weighted MR images. The pelvic bone, the rectum, and the bladder at the base of the prostate were also carefully segmented, as show in Fig. 1.

2.2. Finite element modelling

2.2.1. Mesh generation

Following segmentation, the prostate capsule surface contours were initially converted into a smoothed spherical harmonic representation, which were in turn converted into a triangulated surface mesh using a method described by Zacharopoulos (2005). Triangulated surface meshes were also generated for the pelvic bone, bladder, and rectum (see Fig. 2). All surface data were imported into the commercial FEA software package, ANSYS (ANSYS Europe Ltd., Oxfordshire, UK), and the solid modelling tools provided in this software used to construct an FE model comprising 35–60,000 tetrahedral elements.

Using the refinement tool available in ANSYS, the region around the rectum was re-meshed to obtain high element density in this region. This enabled the TRUS probe — or more precisely, the fluid-
filled sheath placed over the TRUS probe, approximated by a cylinder — to be modelled directly in each simulation without the need for re-meshing. The surrounding tissue was modelled as a block with same voxel dimensions as the field-of-view of the MR images. All the organs are assumed to be connected to the surrounding tissue. In the remainder of this paper, we refer to homogeneous tissue regions that are modelled using different material properties as compartments of the FE model. In the most complex mesh considered, distinct compartments were the two regions of the prostate gland, the rectal wall, the bladder, surrounding tissue, and the pelvic bone.

Finally, elements within all the tissue compartments of the FE model were labelled according to the corresponding tissue type. Different material properties could then be easily assigned to different structures. Modelling the geometry of the pelvic bone accurately provides a physically realistic rigid constraint on soft-tissue motion, which balances the driving force exerted by the movement of the TRUS probe.

For each patient, a geometrically accurate FE mesh including the prostate gland, rectum, bladder, and pelvic bone was used to build a control SMM (see Fig. 2). This SMM was generated by randomly assigning the boundary conditions and material properties for each tissue type and computing the subsequent deformation.

SMMs based on FE simulation data were also built by reducing the number of tissue compartments in the model (equivalent to assigning identical material properties to adjacent compartments in the control FE mesh) and/or simplifying the geometry of the pelvic bone. Both of these measures reduce the amount of prerequisite segmentation required to build an SMM from FE simulations.

2.2.2. Material properties

In the FE simulations, all soft-tissues were assumed to behave as isotropic, elastic materials described by a neo-Hookean model (Zienkiewicz and Taylor, 2000). Since the values of the material properties of each tissue type were assumed to be unknown, the Young’s modulus and Poisson’s ratio for each of the four soft-tissue compartments, corresponding to the peripheral and central prostate zone, the rectum, and surrounding tissue, were assigned randomly sampled values within the physiological ranges given in Table 1, assuming a uniform probability distribution. The usual condition of incompressibility (Poisson’s ratio, \( \nu = 0.5 \)) was not assumed because it can be argued that this is not appropriate for organs such as the prostate, rectum and bladder, which are compressible due to gain and loss of blood and other fluids, as well as the presence of cavities.

Material properties were assigned in two ways, depending on number of organs that needed to be segmented as follows:

MP1: In the first case, material properties were assigned independently to each of the 5 soft-tissue compartments (i.e., the rectal wall, the bladder, the two regions of the prostate gland, and the surrounding tissue (assumed to be homogeneous)).

MP2: In the second, simpler case, the prostate gland is treated as a single compartment.

2.2.3. Boundary conditions

Two types of boundary conditions were considered in this study: the rigid constraint imposed by the pelvic bone and displacement of the rectal wall—prostate interface determined by the 3D position and orientation of the TRUS probe. In one configuration of the simplified FE model investigated in this study, the pelvic bone was approximated by three boundary planes, as shown in Fig. 5. This choice of representation was motivated by the need for a clinically practical method for specifying bony constraints within the pelvis (Figs. 3 and 4).

The positions of these planes for an individual patient were determined by measuring two distances, \( d_x \) and \( d_y \), in the mid-gland transverse plane of the MR image, as shown in Fig. 6. Assuming that the prostate capsule has been segmented, \( d_z \) is the average of the two distances measured along the left—right axis from centre of mass of the prostate gland to the nearest intersections with the axis on the left and right sides of the pelvis. Distance \( d_x \) is the distance along the

![Table 1](https://example.com/table1.png)

Table 1: Summary of the boundary conditions and material properties used for the FEA simulations.

<table>
<thead>
<tr>
<th>Description</th>
<th>Parameter(s)</th>
<th>Range</th>
<th>Reference value(s)</th>
<th>DOF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probe initial position</td>
<td>( T_{0x}, T_{0y}, T_{0z} )</td>
<td>([\text{local co-ordinates}^{**}] )</td>
<td>( T_0 )</td>
<td>3</td>
</tr>
<tr>
<td>Probe initial orientation</td>
<td>( \phi_{0x}, \phi_{0y}, \phi_{0z} )</td>
<td>([-10, 10])</td>
<td>Local co-ordinates</td>
<td>3</td>
</tr>
<tr>
<td>Probe end position</td>
<td>( T_{1x}, T_{1y}, T_{1z} )</td>
<td>([\text{local co-ordinates}] )</td>
<td>( T_1 )</td>
<td>3</td>
</tr>
<tr>
<td>Young's modulus</td>
<td>( E_1, E_2, E_3, E_4^{***} )</td>
<td>([10, 200]) kPa</td>
<td>( E )</td>
<td>4</td>
</tr>
<tr>
<td>Poisson ratio</td>
<td>( \nu_{1x}, \nu_{1y}, \nu_{1z} )</td>
<td>([0.30, 0.49])</td>
<td>( \nu )</td>
<td>3</td>
</tr>
</tbody>
</table>

*\( R_0 \) denotes the radius of the TRUS probe used in guidance. ** Local co-ordinates are defined by rotating MR co-ordinates by 15° in sagittal plane and using mid-point of anus as the origin. *** The subscripts 1—4 correspond to the prostate central zone, peripheral zone, the rectal wall, and the surrounding tissue, respectively. DOF — Degrees of freedom.

Fig. 2. Illustration of surface meshes of gland (red), bladder (yellow), rectum (green) and pelvis (grey).

Fig. 3. Illustration of TRUS probe (blue cylindrical structure) position relative to the prostate gland and the pelvis.

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anterior–posterior axis from the prostate centre of mass to the nearest point on the posterior side of the pubis. In this study, these distances were computed automatically from the segmented contours of the pelvic bone, but, importantly, both can be easily measured without segmenting pelvis. The displacement at each mesh node of the pelvic bone, or, alternatively, the surrogate planes, was fixed to zero for all simulations (Fig. 6).

In the experiments described below, three different pelvic boundary conditions, referred to as BC1, BC2, and BC3, were used. These are defined as follows:

BC1: An anatomically realistic, patient-specific pelvic bone. This requires complete segmentation of the bone in an MR image.

BC2: Three planes placed according to the patient-specific measurements, as described above. This requires only simple measurements from an MR image.

BC3: Three planes placed at fixed positions determined by the average linear measurements calculated for the remaining 6 patients in the test dataset. Setting this boundary condition only requires segmentation of the prostate capsule to compute the centre of mass of the gland.

As the driving force for the prostate motion, the size and 3D motion of the TRUS probe were specified in terms of the diameter of the water-filled sheath surrounding the probe, and the motion with respect to a local 3D co-ordinate system, defined with respect to an initial reference position (see Hu et al., in press for further details).

### 2.2.4. Simulation of soft-tissue motion

Biomechanical simulations of TRUS-probe-induced prostate motion were performed to provide training data for the SMMs. The ranges of the assigned boundary conditions and material properties for the control FE model (BC1 and MP1, respectively) are summarised in Table 1.

To investigate the effect of using simplified FE models to generate the training data, different configurations of the boundary conditions, BC1, BC2, or BC3, and material properties (MP1 and MP2) were compared, resulting in a total of 6 different SMMs for each patient.

Five hundred training datasets were generated for each of the 6 configurations in Table 2. For each FE simulation, the material properties and boundary conditions were assigned using values randomly sampled from the ranges given in Table 1, assuming a uniform probability distribution. Mesh node displacements were computed using a fast, non-linear FE solver, implemented to enable parallel computations using a graphics processing unit (GPU) (Taylor et al., 2008).

A recently developed four-node formulation...
was adopted to overcome the volumetric locking problem (Bonet and Burton, 1998; Joldes et al., 2009). Using this method, the time taken to complete 500 simulations was approximately 140 min.

To assess the impact of FE mesh density on the node displacements computed by the FE solver, a much denser mesh with approximately 150,000 elements was built. One hundred FE simulations were performed using the random configurations above. The mean difference in nodal displacements was 0.02 mm with 95% of these smaller than 0.65 mm in all of the x-, y-, and z-components. Therefore, we conclude that the original density of the model used in this study is adequate to accurately describe prostate gland motion.

2.3. Statistical motion modelling

2.3.1. Dimensionality reduction

For each of the FE training simulations, the FE mesh nodes displacements within the prostate gland are assembled to produce a displacement vector \( \mathbf{d} = [d_1, d_2, d_3, d_4, d_5, \ldots, d_N] \), where \( N \) is the total number of prostate nodes in the model. \( d_1, d_2, d_3 \) is the displacement vector that specifies the displacement of the \( n \)th node with co-ordinates \( (x_n, y_n, z_n) \) in the initial (undeformed) mesh, derived from the MR image. These data provide the training data for building an SMM. Using PCA, a deformed FE model, represented by the node co-ordinate vector \( \mathbf{x}_{\text{def}} = [x_1, y_1, z_1, \ldots, x_N, y_N, z_N] \), can be approximated by:

\[
\mathbf{x}_{\text{def}} = \mathbf{x}_0 + \mathbf{d} + \sum_{i=1}^{L=M} b_i \mathbf{e}_i = \mathbf{x}_0 + \mathbf{d} + \mathbf{P} \mathbf{b}
\]  

(1)

where \( \mathbf{x}_0 \) is a 3N vector contains the node co-ordinates of the initial model; \( \mathbf{d} \) is the mean node displacement vector; \( \mathbf{e}_i \) is the \( i \)th eigenvector of the covariance matrix formed from the set of training displacement vectors; \( b_i \) is a scalar weight; \( M \) is the number of simulations performed; \( \mathbf{P} = [b_1, b_2, \ldots, b_L] \) is a weight vector; and \( \mathbf{P} \) is an \( LN \) by \( L \) matrix whose columns contain eigenvectors ordered so that the corresponding eigenvalue \( \lambda_i \) decreases in magnitude as \( i \) increases. Each of the terms in the summation in (1) corresponds to a so-called principal component, which explains a decreasing proportion of the variance in the training data. Given a sufficiently large training dataset, \( L \) is usually much smaller than both \( 3N \) and \( M \), and the training data is projected into a lower dimensional space without compromising the variance in the mesh node displacement captured by the SMM.

2.3.2. Model fitting

As explained in Section 1, in image registration, the SMM described by (1) has the role of constraining the registration transformation that relates the SMM and the deformed prostate, represented by new image data (TRUS images in this case). The vector \( \mathbf{b} \) can be thought of as containing the parameters of the SMM that are optimised to finding the vector \( \mathbf{b} \) which minimizes a fitness function that quantifies how well the SMM fits the target data represented by the node co-ordinate vector \( \mathbf{x}_{\text{target}} \). Three different forms of \( \mathbf{x}_{\text{target}} \) were considered, each of which requires a different method for finding \( \mathbf{b} \), as follows: In a simplest case, \( \mathbf{x}_{\text{def}} \) takes the same form as the training data, i.e. a vector containing of co-ordinates of all the FE mesh nodes within the prostate gland. Fitting the SMM – equivalent to solving for \( \mathbf{b} \) in (1), given \( \mathbf{x}_{\text{def}} = \mathbf{x}_{\text{target}} \) – then becomes a linear least squares problem with the following solution:

\[
\mathbf{b} = (\mathbf{P}^{T}\mathbf{P})^{-1}\mathbf{P}^{T}(\mathbf{x}_{\text{target}} - \mathbf{x}_0 - \mathbf{d})
\]  

(2)

where \( \mathbf{d}_{\text{target}} = \mathbf{x}_{\text{target}} - \mathbf{x}_0 \) is a vector that represents the displacements of the target data relative to the reference model. In the present application, the very different appearance of MR and TRUS images results in a lack of common features being present within the prostate. This means that establishing the relative displacements of corresponding voxels across the gland is very challenging. However, it is possible to measure the location of the gland surface (capsule). For this reason, we also consider the second case where the observed data comprises only surface nodes, denoted by \( \mathbf{x}_{\text{target}} \). The length of the vector \( \mathbf{x}_{\text{target}} \) is 3S where \( S \) is the number of surface nodes. In this case, \( \mathbf{b} \) can still be found via a linear least squares solution if \( S > L \). When this condition is satisfied, the parameter vector of the fitted SMM is given by:

\[
\mathbf{b} = (\mathbf{P}_S^{T}\mathbf{P}_S)^{-1}\mathbf{P}_S^{T}(\mathbf{d}_{\text{target}} - \mathbf{d}_S)
\]  

(3)

where the matrix \( \mathbf{P} \) in (2) is replaced by the \( 3S \) by \( L \) matrix \( \mathbf{P}_S \), and the vectors \( \mathbf{d}_{\text{target}} \) and \( \mathbf{d} \) are replaced by the measured and mean surface displacement vectors, \( \mathbf{d}_{\text{target}} \) and \( \mathbf{d}_S \), respectively.

In the more general case where the correspondence between points on the SMM and target surfaces is unknown, the problem of finding \( \mathbf{b} \) can be posed as a non-linear numerical optimisation problem in which the Euclidean distance between the SMM and observed surface points are minimized, i.e.

\[
\mathbf{b} = \arg\min_{\mathbf{b}} \left( \| \mathbf{D}(\mathbf{b}, \mathbf{x}_{\text{target}}) \| \right)
\]  

(4)

where \( \mathbf{D} \) is a vector function that returns the distances between the surface of the prostate in the instantiation of the SMM, given the parameter vector \( \mathbf{b} \), and the target surface points.

In this work, a Matlab implementation of the standard Levenberg–Marquardt algorithm was used to solve (4). \( \mathbf{D} \) was computed by calculating the distance between the each target node point and the nearest point in a densely sampled pointset that represents the SMM prostate surface. To avoid over-fitting of the model to target data, resulting in highly implausible deformations, \( \mathbf{b} \) was constrained during the optimisation so that \(-3\sqrt{\lambda_i} \leq b_i \leq 3\sqrt{\lambda_i}\). This ensured that the values of the weights in \( \mathbf{b} \) lie within 3 standard deviations of the mean value determined by the training data. Imposing this constraint can be especially useful when the target data is subject to noise or contains outliers.

2.4. Performance measures

Three different quantitative performance measures were computed for the SMMs, described below. These were used as a basis for comparison between different SMMs.

2.4.1. Generalisation ability

The generalisation ability of a model measures its ability to describe unseen data (Styner et al., 2003). This is arguably the most important performance measure since it relates closely to the most common intended application of SMMs, i.e. capturing organ motion to provide prior information for registering to unseen data. The generalisation...
ability can be defined as the average error between a statistical shape model and unseen data (Styner et al., 2003). A similar measure has also been derived in shape feature space (Jeong et al., 2008).

Here, we adopt a measure defined as the root-mean-square RMS Euclidean distance between the node positions within the prostate gland of an instantiated SMM and the corresponding node positions of a ground truth deformed model. For the purposes of this investigation, the fully-specified FE model (MP1; BC2) was used to provide the ground truth tissue motion, assuming that this mostly closely approximates the real tissue motion. When the RMS distance is computed on all nodes inside and on the surface of the prostate gland, this measure becomes analogous to the target registration error (TRE), which is a widely adopted measure for evaluating the accuracy of image registration algorithms (Fitzpatrick et al., 1998).

The following leave-one-out scheme, illustrated in Fig. 7, was adopted to avoid bias in the generalisation ability: firstly, one of the 500 training samples was selected at random. The SMM was then built using the remaining 499 samples and the boundary conditions and material properties used to generate the selected SMM used to generate the ground truth dataset, based on an FE simulation using the most geometrically accurate mesh for that particular patient. In this way, the 6 simplified models could be compared directly in terms of RMS distance error.

In addition, for each of 6 patients, a clinician identified a region of interest (ROI) on the MR images in which biopsy-verified cancer was present. The absolute distance errors of these tumour ROIs were also computed using the same leave-one-out scheme as described above.

2.4.2. Model compactness

An important aspect of PCA-based SMMs is dimensionality reduction. Model compactness, defined as

$$C(L) = \frac{\sum_{i=1}^{M} \lambda_i}{\sum_{j=1}^{M} \lambda_j}$$  \hspace{1cm} (5)$$

where $\lambda_i$ is the $i$th eigenvalue of the covariance matrix of the training data, was used as a measure of this property. This measure represents the relative cumulative variance described by an SMM.

2.4.3. Model specificity

Model specificity is another useful measure, which indicates the degree to which deformations of an SMM are constrained. This is significant because it is desirable for the model to be robust to corrupted data, for instance due to image artefacts or noise. Furthermore, the model should be able to predict missing data.

We adopted the framework proposed by Styner et al. (2003) to quantify model specificity using Monte Carlo simulations. For each SMM, 500 instances were generated by setting each parameters, $b_i$, to a randomly selected value drawn from a zero-mean multivariate normal distribution with standard deviation $\lambda_i$. The model specificity was computed as follows: First, for each instantiated SMM, the RMS distance between the nodes of this model and the corresponding nodes of each of the simulated FE meshes in the training dataset was computed. The specificity was then defined as the smallest RMS distance, which may be interpreted as a measure of how closely the SMM approximates the geometrically closest sample in the training dataset. The absolute distances for the tumour ROIs were also computed as an error measure for specificities.

2.5. Data acquisition and processing

T2-weighted MR images were acquired on 7 patients. Multiple organs were manually segmented as described in Section 2.1. These
segmentations were used to generate the 6 different FE element model configurations and 500 FE simulations performed for each model to provide training data for 6 SMMs. Each training sample was generated after randomly assigning material properties and boundary conditions.

All 3000 FE simulations were performed using a C++ implementation of a non-linear finite element solver (Taylor et al., 2008) on a desktop PC with a 2.33 GHz Intel® Core™ dual CPU processor, 3 GB of RAM, and a 256 MB NVIDIA® GeForce™ 8600 GT GPU installed. Each simulation took on average 16 s to compute the deformation of an FE model containing on average 45,000 elements.

3. Results

3.1. Model compactness

At total of 42 SMMs were generated for 7 patients using 6 different FE model using the geometric simplifications summarised in Table 2. Fig. 8 shows the median and 95% confidence interval of the compactness, C, computed for different values of L (from 1 to 30). As can be seen from Fig. 8, increasing the number of modes of variation of the SMM, increases cumulative relative variance of the model, compared with the training data, and the compactness converges to a value close to one for L > 9. It was found that 99.5% of total tissue motion variance was captured for all of these models if L = 12. This number was adopted when computing the generalisation ability and specificity presented below.

3.2. Generalisation ability

The generalisation ability, computed for each SMM using the three model fitting methods described in Section 2.3.2, are plotted in Fig. 9. There was found to be a small difference between the accuracy of SMMs built using simplified FE models (SMM 2–6) and the SMM based on the fully-specified FE model (SMM 1) in terms of generalisation ability, with the latter SMM yielding the highest accuracy. Similar results were obtained when only surfaces were used to register the models. By comparing the results shown in Fig. 9, very little difference was found between using the surface node points and all internal gland node points when point correspondence was known. The errors were slightly larger for the more realistic case when only a surface is used for registration and point correspondence between the SMM and target surface is unknown.

Of the SMMs based on simplified FE models, SMM 4 was consistently found to be the most accurate. Since this model was based on an FE mesh comprising an anatomically realistic representation of the pelvic bone, this result suggests that the SMM is sensitive to the geometry of the pelvis. However, the difference in the median error between using an SMM based on an FE model with simplified pelvic boundary conditions and SMMs based on an FE model which reflects the true anatomy of the pelvic bone was small – between 0.1 and 0.2 mm. We believe that this level of error is acceptable given the magnitude of errors (1–3 mm) found in our previous studies on MR-to-TRUS registration of the prostate (Hu et al., in press, 2009).

Further inspection of Fig. 9 reveals very little difference between the accuracy of the different SMMs that were based on FE models with planar pelvic boundary conditions (SMMs 2, 3, 5 and 6). This result suggests that simply using the average positions from measurements made on a group of patients may be sufficient for the purposes of SMM generation. This insight naturally leads to an MR segmentation protocol in which only the prostate capsule would need to be segmented.

3.3. Model specificity

The model specificities are shown in Fig. 10. Compared with the generalisation ability, there was found to be a much smaller difference between the SMMs based on simplified FE models and the reference SMM.

4. Discussion

Combining biomechanical modelling and statistical shape modelling techniques to predict soft-tissue motion overcomes the problem of needing to specify accurate values for tissue material properties and application-specific boundary conditions by taking into account variations in these properties. Such techniques are particularly useful for time-critical applications, such as image-guided surgery, since SMMs are linear models with far fewer parameters than the underlying biomechanical model and therefore can be instantiated very rapidly.

However, the sensitivity of SMMs based on biomechanical simulations to the complexity of the biomechanical model is an important issue that has received very little attention in the literature. Conventional logic suggests that as accurate a biomechanical model as possible is required for training an SMM, but often there is significant burden in creating such a model, particularly if a new model needs to be built for each new patient, as in this study. Since automatic, multi-organ segmentation tools are not widely available, this burden may have a significant impact on the clinical workflow required to use motion modelling techniques in clinical applications.

However, since uncertainty is inherently taken into account by the statistical modelling, it can be argued that the accuracy of the underlying biomechanical model is of relatively little importance compared to its ability to capture the typical variation in organ motion. Based on an analysis of the SMM generalisation ability and specificity, the results of this study support this hypothesis and suggest that it is possible to simplify the FE model used to generate training data considerably without a significant impact on the accuracy of the associated SMM.
Specificity and generalisation ability are both important as one often finds that a model performs well according to one measure, but the other reveals inadequacies. In practice, both of them should be taken into account and a significant error in either of them should be regarded as a significant indication of a difference between the candidate SMMs.

The FE model used to determine ground truth tissue displacements in this study has the advantage that node correspondence is not required.

Fig. 9. Generalisation abilities for all the models across 7 patients, shown as the median RMS error (RMSE) and 95% confidence interval for three different model fitting methods specified in Section 2.4.1.

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Therefore, modelling and registration errors can be clearly distinguished. One limitation of this approach is that the accuracy of the FE model in representing true tissue motion is unknown, although the predictive accuracy achieved in our previous research using 3D TRUS images, acquired before and after deforming the prostate, and an SMM based on an FE model with very similar geometry (Hu et al., 2008a,b) indicates that this model is a reasonable approximation of TRUS-probe-induced motion of the prostate gland. In an experiment that uses serial 3D TRUS imaging, however, the prostate motion that takes place between MR and TRUS imaging cannot be simulated adequately since the prostate cannot be imaged without a transrectal probe in place. In addition, because TRUS has a limited field-of-view, a comprehensive FE model of the organs surrounding the prostate cannot be constructed from TRUS images. Subsequently, in future work we propose to simulate TRUS-probe-induced motion within an MR scanner, and use MR imaging to quantify real tissue displacements within the gland (for example, using corresponding landmarks).

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**References**


