A Statistical Approach for Estimating Brain Tumor Induced Deformation

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Abstract

A general statistical approach for predicting anatomical deformations is presented. Emphasis in this paper is on estimating deformations induced in the brain anatomy due to tumor growth. The presented approach utilizes the principal modes of co-variation between deformed (after tumor growth) and undeformed (before tumor growth) anatomy to estimate one given the other. In particular, with a statistical model constructed from a number of training samples, a patient’s brain anatomy prior to tumor growth is estimated based on the patient’s tumor-bearing images. This approach is suitable for use in registering a patient’s tumor-bearing images to an anatomical atlas for purposes of surgical, or radio-surgical planning. The proposed approach is tested on a data set of 40 axial 2D brain images of normal human subjects. A biomechanical model was used to simulate tumor growth in each image of the data set. Pairs of deformed and undeformed anatomy were generated by tracking locations of 94 landmark points. The quality of the estimates of the undeformed anatomy are evaluated using the leave-one-out method. Results indicate good estimation accuracy considering the relatively small sample size.

1. Introduction

Modeling and predicting deformation of body organs has gained increasing interest in recent years. These deformations can be caused by diverse factors such as breathing, changes in the patient positioning, surgical tools interaction with tissue, skull opening, natural bone growth after reconstructive surgery, or tumor growth. A statistical framework was recently proposed for estimating or predicting systematic anatomical deformations observed over a number of training cases [1]. This framework offers a speed advantage over biomechanical models, which therefore makes it more eligible for tracking real-time anatomical deformations. Moreover, the framework is capable of dealing with problems that are ill-posed in nature, and therefore not solvable using laws of mechanics unless simplifying assumptions are made. In the work presented here, the statistical framework of [1] is applied to one such problem, which is the estimation of a patient’s normal brain anatomy based on the same patient’s tumor-bearing brain images. The pre-tumor brain anatomy is estimated using a statistical model developed by sampling the joint distribution of the pre- and post-tumor anatomies. Training samples for purpose of statistical model construction are obtained using a biomechanical model for tumor growth.

Deformable registration of brain images to anatomical atlases has made possible the pooling of data from different individuals to a common stereotactic space. This enabled the construction of statistical atlases that are based on collective morphological, functional, and pathological information and therefore are capable of detecting correlations among these variables. Similar statistical atlases can be useful in planning neuro-surgical operations that deal with tumors by statistically linking functional, and structural neuroanatomy to variables such as tumor parameters, surgical approach and outcomes. Such statistical atlases can assist the surgeon in determining the optimal strategy to approach the tumor by assigning different importance levels to different functional units, different levels of tolerance in the volume of the unit that could be at risk, and different costs based on the tumor location and success rates for different ways to approach such tumor.

Adapting a statistical atlas of neuroanatomy to a patient’s images is, however, a challenging task, due to the complexity of the human anatomy and to the confounding effects of edema and severe deformations in the vicinity of the tumor. Since current anatomical atlases are based on images of normal human subjects (e.g. the Talairach atlas [2]), tumors are absent from these atlases, and this makes the matching problem more difficult. A possible approach to deal with this problem would be to utilize deformable registration techniques to match the atlas image to the patient’s tumor bearing image [3]. Such an approach is however, limited by the substantial dissimilarities between an atlas and a brain with tumor, by topological differences between the two, and by difficulties in developing a robust matching mechanism. An efficient model for predicting tumor-induced deformation in the brain tissue is therefore, an es-
sentential component of a system for registering tumor bearing images to an anatomical atlas.

Many anatomical deformations can be predicted to a large extent by statistical or biomechanical deformable models. The former require that the deformation of interest be observed in a number of cases, which are treated as training samples from which a statistical predictive model is built. The latter are based on knowledge of the biomechanical behavior of biological tissues.

Although, many studies have aimed towards biomechanical modeling of the brain, only a few of those are concerned with the effects of tumor growth [4, 5, 6]. The mechanisms underlying the expansion of a tumor are very complex and are different for different kinds of tumors [6]. Under certain approximations, it can be demonstrated that it is possible to model soft tissue deformation by tumor growth, and to use this model for matching an atlas of the human brain to a patient’s images. In particular, a biomechanical model for tumor growth was used by Kyriacou et. al [4, 5] to register a patient’s tumor-bearing images to the Talairach atlas. In [5], a biomechanical model was used to grow a tumor in the atlas using an estimate of the patient’s tumor seed location and its size. Those estimates of the tumor parameters are obtained by using a regression procedure coupled with the biomechanical model of tumor growth operating on an estimate of the patient’s pre-tumor images. This estimate of the patient’s pre-tumor anatomy is obtained by running the same biomechanical model on the tumor-bearing images in the backward direction to shrink the tumor.

Since biomechanical models utilize knowledge about the physical properties of deformable organs, they are capable of accurately predicting deformations. However, biomechanical models have two major limitations. First, they require that boundary conditions and stress distribution in the initial configuration be known. This is rarely the case for deforming body organs, which renders such problems unsolvable without adopting simplifying assumptions. Second, they are computationally very demanding. The approach presented in [5] suffers from both limitations of biomechanical models. Particularly, lack of knowledge on initial stresses in the tumor-bearing anatomy makes the problem of reversing the effects of tumor growth ill-posed. Such residual stresses were assumed to be negligible in [5] which resulted in an “unrealistic” estimate of the patient’s brain anatomy prior to tumor growth. Statistical shape estimation methods or manual correction were suggested for adjusting this estimate. In addition to this, the use of the biomechanical model in every step of a regression procedure can consume prohibitively large computational resources, especially if a 3D finite-element model (FEM) is used.

An alternative approach for dealing with biomechanical deformations is based on statistical modeling utilizing a number of training samples for which the deformation is known [1, 7, 8]. Though applicable to various problems, the statistical framework of [1] is applied here to the problem of estimating normal brain anatomy prior to tumor growth based on tumor-bearing images. This statistical framework examines, not only the principal modes of variation of shape [9], or deformation [8], but also the principal modes of co-variation between shape and deformation. This property makes the statistical approach suited particularly well for the problem of estimating normal brain anatomy based on tumor deformed anatomy. During current neurosurgical planning practice, surgeons exploit symmetry of brain anatomy around the midsagittal plane to understand tumor induced deformations in the cerebral hemisphere from the contralateral side. Shape correlations between the brain hemispheres, such as symmetry, can effectively be captured by the modes of variation of shape of the statistical model, which are in turn correlated with the observed deformed shape. Therefore, anatomical information collected from a particular patient’s images can contribute to a more accurate estimate of how the patient’s anatomy could have been before tumor growth, compared to prediction based solely on statistical properties of the underlying deformation field [8], or the underlying shape characteristics. The statistical framework introduced in [1] also overcomes the limitations of the biomechanical approach presented in [5], particularly regarding the ill-posed nature of the problem, and the large computational requirements of FEM.

In Section 2, an approach for parameterizing the statistical properties of shape deformability due to tumor growth is presented. This approach involves the use of a biomechanical model for tumor growth to generate training samples which are composed of pairs of undeformed and deformed anatomy. The approach is applied to a data set composed of 40 2-D normal brain images. In Section 3, the leave-one-out method is used to test the accuracy of the estimation of the patient’s undeformed anatomy based on simulated tumor-bearing images. Estimation error in the undeformed configuration is computed and compared to the displacement induced by simulated tumor growth. An analysis of the sources of estimation error, as well as extensions to the current model are discussed in Section 4.

2. Methods

A general statistical model for parameterizing the statistical properties of shape deformability is presented in section 2.1. The model, which is based on Principal Component Analysis (PCA), enables the prediction of deformation based in part on the patient’s anatomy, and in part on a statistical model of shape deformability. Statistical sampling is used in conjunction with a biomechanical model to construct the statistical model. Methods for obtaining training samples for the purpose of statistical model building are de-
scribed in Section 2.2. The statistical model can serve as a statistical prior for estimating the anatomy of a tumor patient prior to the growth of the tumor. In Section 2.3, an approach for estimating a new patient’s undeformed anatomy based on the observed deformed anatomy for the same patient is presented. Next, the statistical approach for modeling and predicting deformations is specialized in Section 2.4 to the problem of estimating the anatomy of a patient’s brain prior to tumor growth. The biomechanical model used in conjunction with the statistical framework is detailed in Section 2.5.

2.1. Statistical model of shape deformability

Let the coordinates of a collection of point correspondences defining a shape be arranged in a vector \( \mathbf{s} \). In its simplest form, an associated vector, \( \mathbf{q} \), can be defined in terms of the coordinates of the deformed configuration of the same landmark points of \( \mathbf{s} \). Consider the vector \( \mathbf{x} \) of dimension \( N \), created by concatenating \( \mathbf{s} \) and \( \mathbf{q} \). Our assumption is that \( \mathbf{x} \) follows a multivariate Gaussian distribution, with density \( f(\mathbf{x}) \) that is parameterized by its mean

\[
\mu = \begin{bmatrix} \mu_s \\ \mu_q \end{bmatrix}
\]

and its covariance matrix

\[
\mathbf{C} = \begin{bmatrix} \mathbf{C}_{ss} & \mathbf{C}_{sq} \\ \mathbf{C}_{qs} & \mathbf{C}_{qq} \end{bmatrix}.
\]

The pdf \( f(\mathbf{x}) \), or equivalently \( \mu \) and \( \mathbf{C} \) that parameterize it, are estimated during the training stage based on a sufficient number of cases with corresponding pairs of \( \mathbf{s} \) and \( \mathbf{q} \). For purpose of model training, all vectors \( \mathbf{s} \) of the training samples are aligned in Procrustes space [10] to remove affine differences. Each vector \( \mathbf{q} \) was also aligned with it’s respective vector \( \mathbf{s} \). Two possibilities for obtaining training samples are discussed below in Section 2.2.

Let the eigenvectors of \( \mathbf{C} \) be denoted by

\[
\mathbf{v}_i = \begin{bmatrix} \mathbf{v}_{si} \\ -\mathbf{v}_{qi} \end{bmatrix}, \quad i = 1, \ldots, K - 1,
\]

where \( \mathbf{v}_{si} \) and \( \mathbf{v}_{qi} \) are the parts of \( \mathbf{v}_i \) corresponding to \( \mathbf{s} \) and \( \mathbf{q} \), respectively, and \( K \) is the number of training cases. The vector \( \mathbf{x} \) can be expressed in terms of the eigenvectors by:

\[
\mathbf{x} = \mu + \sum_{i=1}^{M} \alpha_i \mathbf{v}_i, \quad M \leq K - 1,
\]

from which it follows that

\[
\mathbf{s} = \mu_s + \sum_{i=1}^{M} \alpha_i \mathbf{v}_{si}, \quad (2)
\]

Equation (1) can be written in a more compact form as:

\[
\mathbf{x} = \mu + \mathbf{V} \mathbf{a},
\]

where

\[
\mathbf{a} = [\alpha_1, \ldots, \alpha_M]^T
\]

and \( \mathbf{V} \) is a matrix containing the \( M \) eigenvectors of \( \mathbf{C} \) that correspond to the \( M \) largest eigenvalues.

With the Gaussian assumption for \( f(\mathbf{x}) \), the pdf of the coefficient vector \( \mathbf{a} \) is given by

\[
g(\mathbf{a}) = c \exp \left\{ -\frac{1}{2} \sum_{i=1}^{M} \frac{\alpha_i^2}{\lambda_i} \right\},
\]

where \( \lambda_i \) denotes the \( i^{th} \) eigenvalue of \( \mathbf{C} \), and \( c \) is a normalization constant.

2.2. Training

In order to estimate the statistical parameters (mean and covariance matrix) of \( f(\mathbf{x}) \), a number of training samples for which the vector \( \mathbf{x} \) (i.e. both the deformed and undeformed anatomy) is known needs to be available. Training samples can be obtained in one of the following two ways: 1) If the undeformed and deformed configurations of a patient’s anatomy can be captured by tomographic imaging, for example, if intra-operative imaging is available, pre-operative and intra-operative images of a number of patients can be used to build a statistical model linking patient anatomy with its possible deformations. An example of such case is the prostate brachytherapy, where images are typically available for both the pre-operative supine position to the intra-operative lithotomy position. The extraction of point correspondences across different images has traditionally been performed manually or by using a deformable model based on training samples that are constructed manually [11]. Recently, an adaptive focus deformable shape model (AFDM) [12, 13] was proposed for automatic extraction of point correspondences across images.

2) In certain applications, such as estimating deformation due to brain tumor growth, there is a major limitation which prevents the aforementioned approach from being practical. It is very unlikely that a large enough number of patients can be found that have been scanned both before and after the tumor growth. In order to overcome this limitation, a large number of training samples can be generated via statistical sampling, in conjunction with a biomechanical model. With the assumption that tumor growth can be approximated as a pure biomechanical process, and starting with MRI scans of normal subjects, pairs of pre- and post-tumor brain anatomy can be generated using a biomechanical tumor growth model. This approach to obtaining training samples is the one adopted in this paper.
2.3. Predicting $s$

The procedure described above effectively determines, not only the main modes of variation of $s$ and $q$, but also the main modes of co-variation between $s$ and $q$. Therefore, if $s$ is to be estimated from $q$, the statistical knowledge captured from the training samples can be used as a statistical prior. The patient’s post-tumor growth anatomy can be obtained from a tomographic image data set such as that obtained during standard diagnostic MRI scans of the head.

Let the patient’s deformed anatomy be represented by the vector $q_o$. Since $q_o$ is known, it can be expressed in terms of the eigenvectors and the coefficients vector, $a$, as in (3). Typically, if an orthonormal basis is available, the coefficients of expansion are found by projection on that basis. However, $\{v_i\}$ form an orthogonal basis for the entire vector $x$, not for the truncated vector $q$. Therefore, projection on $\{v_i\}$ is not possible. Projection on $\{v_{qi}\}$, the truncated eigenvectors, will not provide the correct coefficients vector either, since $\{v_{qi}\}$ do not necessarily constitute an orthogonal basis. Therefore, in order to find the vector $a$ which represents an expansion of $q_o$ in terms of $\{v_{qi}\}$, an optimization problem is formulated in which $a$ is sought so that it yields a shape that fits $q_o$ and that has high likelihood, the latter being expressed by $g(a)$ as in (5).

Specifically, for a given $q_o$, the vector $a$ is found such that it minimizes the following objective function:

$$
\mathcal{E}(a) = ||q - q_o||^2 + w \frac{1}{g(a)}
$$

where $w$ is a relative weighting factor. The first term in (6) seeks vectors that get as close as possible to the patient’s observed deformed anatomy, $q_o$, whereas the second term favors shape representations as in (3) that are likely, according to what has been observed in the training samples. The solution is found using the Levenberg-Marquardt [14] nonlinear optimization scheme.

Let $\hat{a}$ be the vector minimizing $\mathcal{E}(a)$, and let it be expressed as:

$$
\hat{a} = [\hat{a}_1, ..., \hat{a}_M]^T
$$

Therefore, the estimate of $s_o$ is given by

$$
\hat{s}_o = \mu_s + \sum_{i=1}^{M} \hat{a}_i v_{si}.
$$

2.4. Statistical Model Specialization to Brain Tumor Growth

The pdf $f(x)$ cannot, in general, take the parametrically tractable form a Gaussian distribution, for the tumor growth problem. For example, samples of $x$ generated by separate simulations of tumors growing in opposite sides of the brain cannot be a result of sampling from a unimodal distribution such as a Gaussian distribution. The pdf $f(x)$ may however be parameterized as a Gaussian distribution only for a given tumor location and growth factor, in which case it reflects normal variation of anatomy, as well as relationships between the undeformed anatomy and the deformed anatomy, for that particular size and location of the tumor.

Let $t$ be a vector holding the coordinates of a seed representing the initial location of the tumor, or the center of mass of a small region corresponding to the initial shape of the tumor. Also, let $g$ be a scalar quantity representing the amount of expansion of the tumor, which can be directly calculated from the size of the tumor. Accordingly, the joint pdf can be rewritten as $f(s, q; t, g)$, or equivalently, $f(x; t, g)$, where the semi-column, reflects the fact that $f(.)$ is family of probability density functions parameterized by $t$ and $g$.

In order for a particular value of $t$ and $g$ to be comparable across individuals, inter-individual variability in overall size of the brain must be accounted for. Accordingly, it is assumed that $t$ and $g$ represent the tumor position and growth factor, respectively, in canonical space. To eliminate pose and size differences among subjects, the landmark points extracted from the 2-D slices were normalized spatially via Procrustes fit [10]. The tumor is inserted in each case at the same location in Procrustes space and is grown with the same approximate growth factor. Thus, the generated pairs of deformed and undeformed anatomy represent a sampling of $f(.)$ for fixed values of $t$ and $g$.

Figure 1. An example axial 2D brain slice with superimposed landmark points identified by small white crosses.
Biomechanical Model for Tumor Growth

Biomechanical simulations of tumor growth were carried out using Abaqus CAE [15] environment. The outer boundary of the FEM was generated by a cubic spline that is defined in terms of 30 landmark points that lie on the outer boundary of the brain and the falx. Ventricular boundaries form the innermost boundary in the FE mesh. Landmark points around the ventricles were used to define a closed hollow cubic spline with zero internal pressure. Since the ventricles are cavities filled with fluid, they were allowed to move freely in the biomechanical model. Due to the increase in size of the tumor during simulations, opposite surfaces of the ventricles come in contact with each other under stress. To avoid self-intersections of the FEM elements, the ventricles were therefore defined as a self-contacting surface. This also allows contact pressure to be transmitted to the side of the brain opposite to that where the tumor was placed if contact occurs.

The tumor was also modeled by a hollow closed spline with a constant hydrostatic pressure inside to induce tumor growth-like effect. The same value of the hydrostatic pressure was used in all the cases to simulate the same approximate tumor growth factor. FE meshes with plane-strain quadratic triangular elements were automatically generated within Abaqus CAE. An example FE mesh is shown in Figure 2 for the same case of Figure 1. For good FE solution accuracy, the mesh density was chosen to be high around the tumor area, where a high stress gradient is to be expected. The anatomy of the brain is such that deformation of the brain tissue is constrained by the dura, the falx, and the skull, which are relatively much stiffer than brain tissue. A no-displacement boundary condition was therefore imposed on the outer boundary of the FEM.

Depending on the area of application, researchers concerned with the mechanics of brain tissue have used different material constitutive relationships. The brain tissue behavior has been modeled as linear elastic, non-linear elastic, visco-elastic, and poro-elastic. Our concern is to model the displacement of structures surrounding the tumor caused by its growth, which can be described as a quasi-static process. Studies that have investigated the quasi-static behavior of the brain include [16, 5]. Adopting a similar constitutive relationship to the ones used in those studies, a homogeneous, almost incompressible, Mooney-Rivlin material model was assumed here. The constitutive equation for this material is:

\[ w = C_{10}(I_1 - 3) + C_{01}(I_2 - 3) + \frac{1}{D_1}(J - 1)^2, \]

where \( I_1 = \lambda_1 \lambda_2 \lambda_3 \), and \( I_2 = \lambda_1^{-2} + \lambda_2^{-2} + \lambda_3^{-2} \). Here, \( C_{10}, C_{01}, D_1 \) are material parameters, \( \lambda_i \) are principal stretches, \( J \) is the volume ratio, and \( w \) is the strain energy density [15]. Values of the elastic parameters for brain tissue reported in the literature vary enormously. In the work presented here, \( C_{10} = 1200\text{Pa}, C_{01} = 0 \), and \( D_1 = 0.0001\text{Pa}^{-1} \) (an initial poisson’s ratio of 0.49) was assumed for brain tissue. The values of the constants for the Mooney-Rivlin material are consistent with the range of elastic properties for brain tissue reported in the literature.

3. Results

Landmark points that were manually placed on the input non-tumor-bearing images, were tracked following the deformation of the FEM. Since the outer boundary of the model remained fixed in the biomechanical simulations of tumor growth, the 30 landmark points on the outer boundary were excluded from the vectors \( s \) and \( q \), and therefore...
Figure 3. The percentage variance explained by the retained eigenvectors relative to the total variance in the set of 40 training samples is plotted versus the number of retained eigenvectors.

The estimation of the parameters $\mu$ and $\Sigma$ (and therefore, the eigenvectors of $\Sigma$) of the pdf $f(x; t, g)$ requires a sufficient number of training samples for any fixed value of $t$ and $g$. If an insufficient number of training samples is used, the resulting eigenvectors of the covariance matrix will not, in general, span the space of vectors representing all possible deformed and undeformed anatomies. If this is the case, they will however, only span the subspace in which the training samples reside. Since the test vector is not among the training cases, it will not, in general, lie in the space spanned by the eigenvectors $\{v_i\}$.

The number of eigenvectors needed to span the space of all possible vectors $x$ is equal to the dimension (complexity) of that space, which cannot be larger than the number of dimensions of the input vectors, but it can be smaller, depending on how the admissible vectors $x$ are oriented in that space. PCA is very popular for dimensionality reduction when the dimensionality of the space is smaller than the number of training vectors [17]. An implicit assumption in PCA is that the smallest $N - M$ elements of the diagonalized covariance matrix are negligible. Hence, the choice of $M$ is such that the eigenvectors corresponding to the $M$ largest values of the diagonalized covariance matrix explain most of the variability encountered in the training samples.

The percentage variance explained by $M$ retained eigenvectors relative to the total variance of all $K-1$ eigenvectors is given by

$$\text{%var} = 100 \times \frac{\sum_{i=1}^{M} \lambda_i}{\sum_{i=1}^{K-1} \lambda_i}$$}

In Figure 3, the percentage variance is plotted versus the number of retained eigenvectors for the available data set. From the figure it can be deduced that the number of samples used for training is approaching the required number of samples needed to explain the shapes and deformations of concern. More than 99% of the variability in the training samples can be explained by the first 35 eigenvectors. In subsequent work however, all the eigenvectors were retained in order to evaluate the validity of estimation methodology.

The reconstruction error can be defined as the error between the original test vector and the best possible (least mean-squared error) reconstruction of that vector in the space spanned by the retained eigenvectors. The estimation error $\hat{e}_a$ between $\hat{s}$ and the actual vector $s_o$ is therefore composed of two components, the reconstruction error, which is simply attributed to the relatively small number of samples and inaccuracies in manually selecting correspondences, and an error that is inherent in the estimation process, which is due to the fact that the undeformed anatomy cannot be entirely predicted by the deformed one.

Since the goal of this work is to estimate the undeformed configuration of the test sample, we computed the reconstruction error of the undeformed part of the test vector only (rather than the reconstruction error of the whole vector $x_o$, which can be easily computed by projection of $x_o$ on space spanned by the eigenvectors). Let the best mean-square-error representation of the vector $s_o$, in the space spanned by the eigenvectors
by \( \{ \mathbf{V}_s \} \), be referred to as \( \tilde{s}_o \). The reconstruction error of the vector \( s_o \) can therefore be defined by

\[
\mathbf{e}_s = \tilde{s}_o - s_o .
\]

The vector \( \tilde{s}_o \), is that which minimizes the square magnitude of the reconstruction error, \( ||\mathbf{e}_s||^2 = ||\tilde{s}_o - s_o||^2 \), while assuming the form \( \tilde{s}_o = \mu_a + \mathbf{V}_a \tilde{a} \). Therefore, The coefficients vector \( \tilde{a} \) can be computed as

\[
\tilde{a} = \arg \min \mathcal{F}(a),
\]

where \( \mathcal{F}(a) = ||\mu_a + \mathbf{V}_a \tilde{a} - s_o||^2 \), which is easily obtained by solving a matrix pseudo-inverse problem. The estimation error can therefore be written as

\[
\hat{e}_s = \hat{e}_z + \mathbf{e}_z .
\]

The error \( \hat{e}_z \) lies in the space spanned by \( \{ \mathbf{v}_a \} \) and therefore, is orthogonal to the reconstruction error.

The root-mean-square value of the error vectors \( \hat{e}_s \) and \( \hat{e}_z \) were computed and averaged over the whole set of test vectors using the leave-one-out method. To investigate how the errors change with the number of training samples, the error measures were computed for different number of training samples varying between 10 and 40. The average root-mean-square reconstruction and estimation errors are plotted in Figure 4. The rms reconstruction error falls steadily with the increase in the number of training samples used. The same trend is exhibited by the estimation error, which is always greater than the reconstruction error. The difference between the rms values of the estimation and reconstruction errors is due to the component \( \hat{e}_z \) which is due to the inability to predict the vector \( s_o \) based on \( q_o \).

The estimates of the post-tumor and pre-tumor landmark locations for the case in Figure 1 compared to their true values are shown in Figure 5 and Figure 6 respectively. The average rms error in this case for the estimation of the pre-tumor landmark locations was 0.68mm, while the maximum error was 1.49mm, with corresponding average rms and maximum reconstruction errors of 0.66mm and 1.4mm respectively. Using all available 40 samples, the average rms estimation error for prediction of the undeformed anatomy was 1.01mm, while the corresponding reconstruction error was 0.96mm. Thus, on average, the rms reconstruction error constituted 95% of the rms estimation error. Over all the 40 samples, the maximum error in the estimation of the location of the landmarks was 2.8mm (50% of the deformation at that landmark). However, the reconstruction error was 2.63mm (94% of the estimation error) at that point, which means that the best representation of that vector in the space spanned by the training samples would only produce an error that is about 6% smaller in magnitude than the error obtained using the tested statistical method. Clearly, more samples need to be generated for a better estimation.

4. Discussion

A methodological statistical approach for predicting or estimating deformations was presented and applied to the problem of estimating brain undeformed anatomy based on images of tumor-bearing deformed anatomy. An ear-
lier attempt to approach this problem using a biomechanical model resulted in unrealistic estimates of brain undeformed anatomy due to the use of oversimplifying assumptions that are necessary to solve such an ill-posed problem. The presented statistical approach, which requires a training data set of deformed and undeformed shapes corresponding to systematic deformations, does not require direct knowledge of boundary conditions or stresses in the tumor-bearing images. Such knowledge regarding the mechanics of the problem is implicitly specified within the training data set, provided that the deformation observed is systematic across all cases. Although the statistical approach is not capable of producing a continuous displacement field, it offers a speed advantage over biomechanical models. Since there is no theoretical limitation on the number of landmark points to be used in the statistical model, a dense map of landmark points can be used to cover all structures of interest for neurosurgical planning purposes. A continuous deformation field, if desired, can still be obtained by using a biomechanical model as an interpolant between the points estimated by the statistical model.

The presented statistical approach was tested on 2D images of simulated brain tumor growth. Results indicate that the majority of the error in the estimation of a patient’s anatomy prior to tumor growth is caused by the reconstruction error. Such error results from the inability of representing the test case as a linear combination of the eigenvectors of the covariance matrix \( \mathbf{C} \). Therefore, the reconstruction error can be attributed to either the absence of a similar shape (or deformation) from the training data set, or to inaccuracies in selecting point correspondences. An automatic landmark selection and identification algorithm such as AFDM [12] can remedy the second problem to some extent, and, at the same time, can act as the necessary tool for extending the current work to the 3D domain. The inability to represent the test vector as a linear combination of the eigenvectors of \( \mathbf{C} \) means that the space of possible deformations and shapes is inherently non-linear, or that the training vectors are not sufficient to represent that space.

In the initial work presented here, it is assumed that the tumor location and size are fixed for the training cases, and are known for the input deformed anatomy. An extension to this work involves the generation of training samples, spanning ranges of possible values of \( t \) and \( g_i \) in conjunction with a non linear model such as non-linear PCA or a mixture of probabilistic PCA (MPPCA) [18]. Specifically, with MPPCA, each component of the mixture can correspond to certain tumor parameters. Thus, during fitting a patient’s deformed anatomy to the components of the mixture, the component which best fits the deformed anatomy will readily yield the tumor parameters (i.e tumor seed and location). Such mixture of linear models, or a completely non-linear model can also more effectively capture non-linear behavior caused by large deformations and non-linear material constitutive relationships. Investigation of such models is underway. On-going work is also focused on the implementation of the approach in 3D, and on the application of this method in several other clinical problems.

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