

Elastic Registration of Multimodal Medical Images: A Survey

Karl Rohr

Image registration enables to integrate different images into one representation such that the complementary information can be accessed more easily and accurately. Multimodal images of the same person or of different persons generally differ by local geometric differences, and to map such images into one coordinate system nonrigid or elastic transformations are required. Fused image data can improve medical diagnosis, surgery planning and simulation as well as intraoperative navigation. This contribution reviews existing methods for elastic image registration and emphasizes landmark-based approaches.

1 Introduction

A fundamental problem in medical image analysis, which recently has well been recognized, is the problem of finding optimal *geometric transformations* between corresponding image data. This task is known as *image registration* (or image matching) and the aim is to compute spatial transformations, which map each point of an image onto its (physically) corresponding point of another image. Image registration allows for *image fusion*, i.e., to integrate images from different sensors (multimodal images) and from existing image databases (e.g., digital atlases) into one representation, i.e., one coordinate system, so that the complementary information in the images can be accessed more easily and accurately. The main challenge is that we have to deal with *multimodal* images, which generally represent different information, and this raises major difficulties in finding image correspondences. In addition, the spectrum of geometric differences between images is very broad, e.g., one has to cope with nonlinear image distortions, with images of different persons, and also with time-varying processes. Moreover, we generally need to register *multidimensional* images, e.g., 2D and 3D images.

As an example, we show in Fig.1 (left and middle) corresponding slices of 3D multimodal tomographic images of the human head. While the MR (Magnetic Resonance) image well represents soft tissue as well as a tumor visible as a white region in about the middle/right part, the CT (X-ray Computed Tomography) image mainly represents bone. The registration result is depicted in Fig. 1 on the right and represents the transformed MR image with overlaid edges extracted from the CT image. Based on this integrated representation it is now easier to

judge, for example, the position and extent of the tumor w.r.t. the bone and to plan a neurosurgical intervention or a radiotherapy more accurately. Besides MR and CT imaging, other relevant imaging modalities for registration tasks in medicine are, e.g., conventional X-ray, Ultrasound, PET (Positron Emission Tomography), SPECT (Single Photon Emission Computed Tomography), or fMRI (functional Magnetic Resonance Imaging).

Generally, images to be registered have to be aligned globally as well as locally. This means that the mapping has to comprise, for example, a global rigid transformation (translation, rotation) as well as a locally adaptive transformation which allows to cope with local geometric differences (cf. Fig. 2). The major class of locally adaptive nonrigid transformations in medical image analysis are *elastic transformations*. These transformations are based on models from elasticity theory. The clinical applications for elastic registration can be classified into diagnosis, surgery planning and simulation, intraoperative navigation as well as robot-assisted interventions. Application areas outside medicine are, e.g., morphometry, remote sensing, cartography, geographic information systems (GIS), geology, computer graphics (warping, morphing), and virtual reality (VR).

Note, that the definition of image registration as given at the beginning of this introduction is very general and actually subsumes a number of classical tasks in computer vision, e.g., motion analysis, stereo reconstruction, and structure-from-motion. There, typically 2D images of the *same* modality (monomodal images) are analyzed, and a central task is to determine image correspondences, i.e., also there a geometric transformation has to be computed in general. Principally, registration approaches can be distinguished into landmark-based and intensity-based schemes. *Landmark-based schemes* first extract

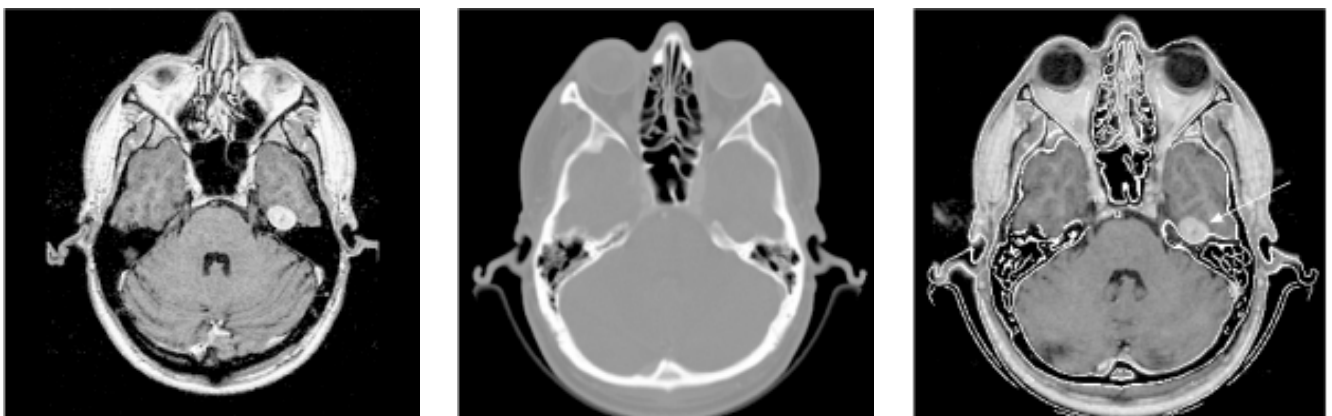


Fig. 1: MR (left) and CT image of the human head (middle), and registration result showing the transformed MR image and the overlaid edges of the CT image (right).

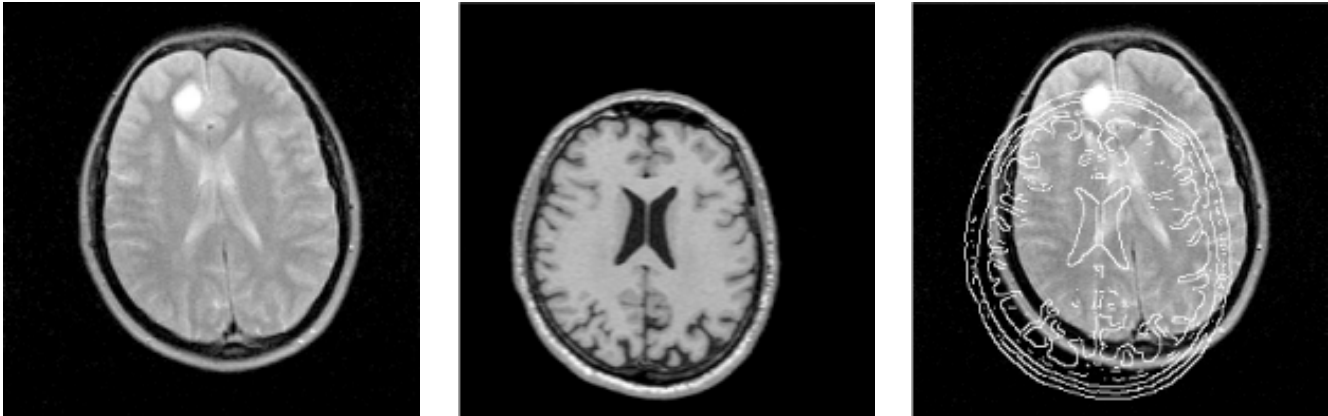


Fig. 2: Registration problem: Human brain MR images of different persons (left and middle), and overlay of the first image with edges of the second image (right).

landmarks (e.g., points, curves, surfaces) from the images and then compute a transformation based on these features. With *intensity-based schemes* the image intensities are directly exploited to compute the transformation.

In this contribution, we survey elastic registration methods for medical images with emphasis on landmark-based schemes. For other reviews concerning registration we refer to [7, 17, 40, 32, 57, 30]. In the following, we first introduce a general registration scheme and classify existing transformation models. Then, we describe landmark-based and intensity-based schemes for elastic registration. Finally, we mention recent work on biomechanical modelling of brain deformations aiming at integrating additional physical knowledge for registration tasks.

2 General Registration Scheme and Transformation Models

A general scheme of medical image registration is depicted in Fig. 3. Generally, the aim is to register multimodal images as well as digital atlases (e.g., [28, 34]) with each other.

One main question concerns the utilized image (or atlas) representation, i.e. the kind of used *image features*. Often, geometric features (e.g., points, curves, surfaces), denoted as landmarks, are used. Alternatively, one can directly exploit the image intensities.

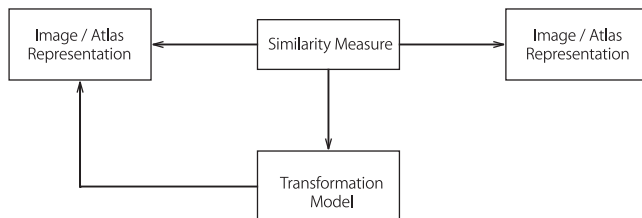


Fig. 3: General scheme for registration

Second, we have to specify the class of *transformations*. *Rigid* transformations can only correct for translational and rotational differences. Thus, generally *nonrigid* transformations are required. An example are *affine* transformations, which in addition to rigid mappings allow for scaling and shear (Fig. 4). Another class of nonrigid transformations are *elastic* transformations. These transformations are based on models from elasticity theory and describe *local deformations*. The central idea behind elastic registration is to consider images as continuous bodies and to model the geometric differences between

images such that they have been caused by an elastic deformation. This approach has been pioneered by Bajcsy et al. [2]. As an alternative, models from fluid mechanics have been proposed by Christensen et al. [9]. *Fluid models* are much more flexible, however, a problem is to constrain the mapping. Note, that the scheme in Fig. 3 also applies to transformations which describe projections of 3D images onto 2D images (3D-2D registration). Furthermore, the term registration also includes the finding of correspondences between image data and *non-image* data (e.g., the operation room or a surgical instrument).

Besides image features and transformation models a *similarity measure* is required to match the image/atlas representations with each other as well as to quantify the (remaining) registration error.

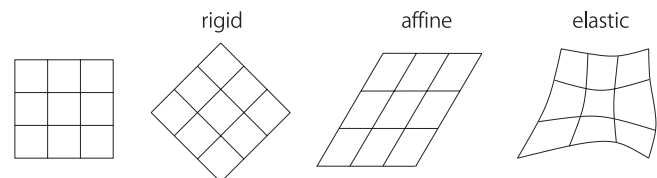


Fig. 4: Types of transformations

3 Landmark-based Elastic Registration

One principal approach to elastic registration of medical image data is based on corresponding landmarks, i.e. geometric image features. Such a *landmark-based* approach comprises three steps: (1) extraction of landmarks from the different datasets, (2) establishing the correspondence between the landmarks, and (3) computing the transformation between the datasets using the information from (1) and (2).

The different types of landmarks can be classified into points, curves (lines), surfaces, and volumes. Using curves (e.g., ridge or crest lines [51]) or surfaces (e.g., [53, 56, 13]) in comparison to point landmarks (e.g., [4, 18]) has the advantage that more information of the images is taken into account. However, a disadvantage is that the segmentation and the finding of correspondences is more difficult. One main advantage of using point landmarks is that the transformation often can be stated in analytic form. This leads to efficient computational schemes. 3D point landmarks may be either fiducial markers (e.g., points at a stereotactic frame, head screws, or skin markers) or anatomical point landmarks, which can be localized manually or by applying image operators (e.g., [41, 45]). Below, we focus on point-based elastic registration schemes.

3.1 Point-Based Registration Using Thin-Plate Splines

The most widely applied method for point-based elastic image registration is based on *thin-plate splines*. This approach has been introduced into medical image analysis by Bookstein [4]. Evans et al. [18] applied this scheme to 3D medical images. Previously, thin-plate splines have been used in computer vision for surface interpolation, i.e. mappings $\mathbf{u}: \mathbb{R}^2 \rightarrow \mathbb{R}^2$, given sparse scattered data (e.g., [6, 54]). In image registration we transform images onto each other, thus we deal with mappings $\mathbf{u}: \mathbb{R}^d \rightarrow \mathbb{R}^d$ where d denotes the image dimension. For related work in computer graphics on image warping and morphing, see [61, 1, 47].

Thin-plate splines are defined on the basis of an optimization problem. The functional to be minimized represents the bending energy of a thin-plate and thus has a physical interpretation. Although a thin plate is a rather crude model to describe local differences between images of the same or different persons, it serves as a flexible deformation model, and such a *physically-motivated* approach leads to more intuitive registration results. This is particularly important in clinical user-interaction scenarios. Another advantage of these splines is that the underlying mathematical theory is well understood ([15, 58]).

In nearly all work on point-based elastic registration an *interpolation* approach is applied (e.g., [4, 18]). This means that corresponding landmarks in the two images are forced to match exactly. The underlying (implicit) assumption is that the landmark positions are known exactly. This assumption, however, is unrealistic since landmark extraction is always prone to error, independent of whether landmarks are determined manually, semi-automatically, or automatically. To take into account landmark errors an *approximation* approach for thin-plate spline elastic registration has been proposed by Rohr et al. [43, 42, 44]. Using *approximating thin-plate splines* it is possible to include isotropic as well as anisotropic landmark errors as briefly described below.

Given n corresponding point landmarks \mathbf{p}_i and $\mathbf{q}_i, i=1, \dots, n$, in two images of dimension d , the aim is to compute a transformation $\mathbf{u} = (u_1, \dots, u_d)$, which maps the two images as good as possible. In [42, 44], the transformation \mathbf{u} results as the solution of a well-defined functional:

$$J_\lambda(\mathbf{u}) = \frac{1}{n} \sum_{i=1}^n (\mathbf{q}_i - \mathbf{u}(\mathbf{p}_i))^T \Sigma_i^{-1} (\mathbf{q}_i - \mathbf{u}(\mathbf{p}_i)) + \lambda J_m^d(\mathbf{u}) \rightarrow \min. \quad (1)$$

This functional consists of two terms. The first term measures the distance between the two landmark sets and includes anisotropic landmark errors represented by the covariance matrices Σ_i (cf. Fig. 5). The second term $J_m^d(\mathbf{u})$ represents the bending energy of the transformation, i.e. its smoothness, and can be formulated rather generally as a function of the image dimension d and the order m of partial derivatives (see [58]). For the special case of $m = d = 2$ and for one component u_k of \mathbf{u} , the bending energy is

$$J_2^2(u_k) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} u_{k,xx}^2 + 2u_{k,xy}^2 + u_{k,yy}^2 dx dy \quad (2)$$

and consists of second order partial derivatives w.r.t. the space coordinates. The terms in (1) are weighted by a parameter λ , which determines the relative weight between closeness to the data (the landmark sets) and smoothness of the transformation. Interestingly, for the functional in (1) there exists a unique analytic solution, which can be stated as

$$\mathbf{u}_k(\mathbf{x}) = \sum_{v=1}^M a_{k,v} \phi_v(\mathbf{x}) + \sum_{i=1}^n w_{k,i} U(\mathbf{x}, \mathbf{p}_i), \quad k=1, \dots, d. \quad (3)$$

The solution consists of polynomials represented by ϕ_v and a superposition of certain radial basis functions $U(r), r = \|\mathbf{x} - \mathbf{p}\|$. For example, setting $m = 2$, for 2D images ($d = 2$) we have $U(r) = 1 / (8 \pi) r^2 \ln r$ and for 3D images ($d = 3$) we obtain $U(r) = -1 / (8 \pi) r$. An interesting property of this approximation approach is that interpolating thin-plate splines and optimal affine transformations result as limiting cases. Since we have an analytic solution, the searched transformation can be computed very efficiently by solving a relatively small linear system of equations. The required covariance matrices Σ_i can be estimated directly from the image data [42].

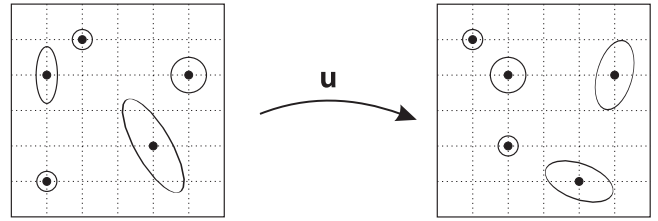


Fig. 5: Point landmarks and corresponding anisotropic errors as input data for landmark-based elastic registration.

Fig. 6 shows an application, where 2D MR brain images of different persons have been registered. Note, that the anatomy differs largely and that different imaging parameters have been used. In the images we have specified normal point landmarks (nr. 1-6 and 8) as well as arbitrary edge points (nr. 9-12), which are also denoted as quasi-landmarks since their positions are not uniquely defined. Quasi-landmarks are important since at the outer parts of the brain normal point landmarks are hard to define. In Fig. 6 on the bottom/left the registration result is shown when applying interpolating thin-plate splines ($\lambda = 0$). In this case, physically not corresponding points are forced to match exactly and thus an unrealistic deformation occurs. If we use only the normal landmarks and approximating thin-plate splines with isotropic errors (Fig. 6 bottom/middle), the registration result is quite good within the inner parts of the brain, but larger deviations occur at the outer parts. If, instead, we use all landmarks and apply approximating thin-plate splines with anisotropic errors, then we can significantly improve the registration accuracy (Fig. 6 bottom/right).

3.2 Thin-Plate Spline Extensions and Other Spline-Based Approaches

Besides landmark errors, *additional attributes* can be incorporated in point-based elastic registration, e.g., the orientation of contours at landmarks or curvature information. This allows to further improve the registration accuracy without selecting additional landmarks [5, 33, 19, 44]. In [19, 44] a minimizing functional has been formulated which includes orientation attributes, while still an analytic solution can be stated. An important application is the preservation of the shape of rigid structures such as bone within otherwise elastic material. This is demonstrated by Fig. 7, where we have simulated the rotation of a rigid structure within otherwise elastic material. If we use point landmarks only (four landmarks at the corners of the rigid structure and four landmarks at the image corners), then the whole image is elastically deformed (Fig. 7 left). However, by

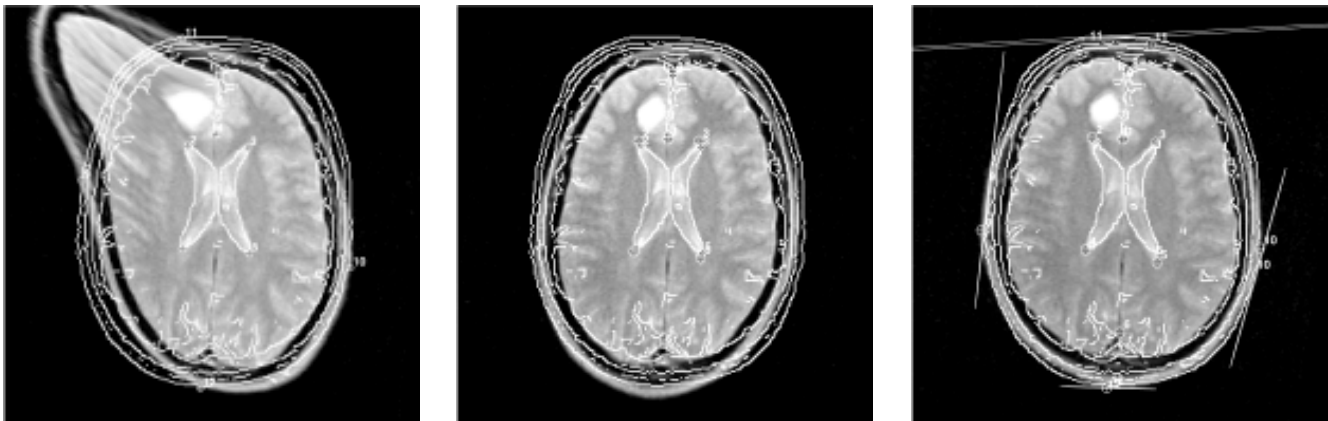
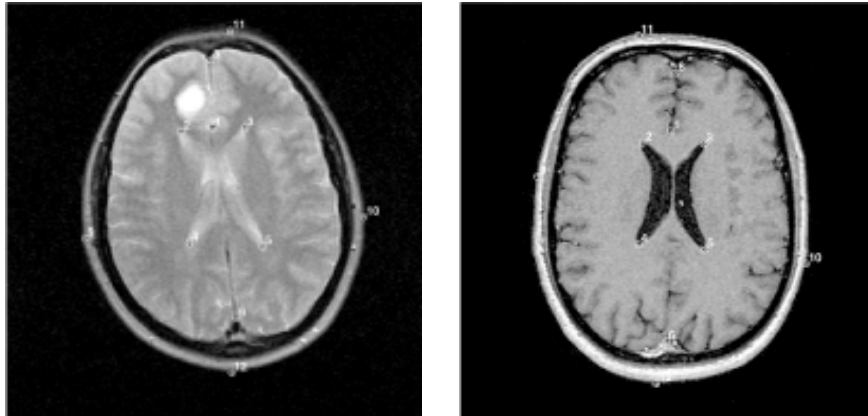


Fig. 6: 2D MR images of different persons with specified point landmarks (top) and registration result using thin-plate splines: interpolation (bottom/left), approximation with normal landmarks and isotropic errors (bottom/middle), and approximation with anisotropic errors (bottom/right).

incorporating two orientations at each corner of the rigid structure (which are aligned with the contours), we can well preserve the shape of the rigid object (Fig. 7 right). Note, that a full segmentation of the rigid structure as required in [31] is not necessary here.

Another main direction towards generalization of point-based elastic registration is to include *more general types of landmarks*, in particular, curves or surfaces (e.g., [10, 21]). Related to these spline-based approaches are curve- or surface-based schemes for elastic image registration, e.g., [53, 51, 13, 38]. There the underlying elasticity equations are solved numerically, e.g., by applying finite differences (FD) or the finite element method (FEM), which is computationally more expensive (see also the survey of deformable models in [35]). For work combining elasticity models with statistical deformation models based on training examples, see [11].

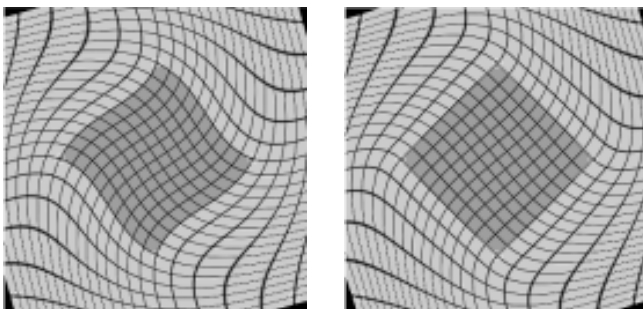


Fig. 7: 2D synthetic images simulating the rotation of a rigid structure within otherwise elastic material: Registration results with interpolating thin-plate splines using only point landmarks (left) and incorporation of orientations at landmarks (right).

Thin-plate spline based image registration has also been combined with intensity information (mutual information) [36]. In [46] thin-plate splines have been applied for the analysis of spatio-temporal medical images (cardiac images). Alternative splines based on analytic solutions of the Navier equation (elastic body splines) have been proposed in [14]. For splines based on a functional involving the linear elasticity operator, see [10]. Splines with compact support (Wendland functions), which are particularly suited to increase the local influence in elastic registration, have recently been proposed in [20] (see also [45] in this issue).

4 Intensity-Based Elastic Registration

Intensity-based approaches for elastic registration of medical images directly exploit the image intensities (e.g., [2, 23, 9, 49, 55]). The main advantage of these schemes is that an explicit segmentation of the images is not required. Disadvantages are the generally much higher computation time and the larger dependence on image modality and imaging parameters. Pioneering work on intensity-based elastic registration has been done by Bajcsy et al. [2]. This work is based on the Navier equation in elasticity theory and describes the deformation of homogeneous 3D bodies under applied forces. Assuming small deformations, which is the case of *linear elasticity theory*, we have for the (elastostatic) equilibrium

$$\mu \Delta \mathbf{u} + (\lambda + \mu) \nabla (\nabla \cdot \mathbf{u}) = \mathbf{f}, \quad (4)$$

where $\mathbf{u} = (u_1, u_2, u_3)$ is the displacement vector field, Δ the Laplacian operator, ∇ the Nabla operator, $\nabla \cdot \mathbf{u}$ the divergence of \mathbf{u} , and $\mathbf{f} = (f_1, f_2, f_3)$ the vector of force density. The Lamé

constants $\lambda, \mu > 0$ describe material properties. Prior to elastic registration, in [2] a global affine transformation is determined in a preprocessing step.

Intensity-based approaches to elastic registration are closely related to *optic flow estimation* algorithms in computer vision, where typically monomodal 2D video images are analyzed (e.g., [52, 55, 59]). Since the intensities are directly used to compute a similarity measure between images, often by computing the sum of the squared differences, these approaches generally depend rather strongly on the image modality and the chosen imaging parameters. A current trend to reduce this dependence is to use some kind of entropy measure, e.g. mutual information, for intensity-based elastic registration (e.g., [22, 36]). Previously, entropy measures have successfully been applied for rigid registration (see the evaluation study of West et al. [60]). *Hybrid* approaches, which combine landmark-based and intensity-based schemes, have been suggested in [23, 36, 10, 12].

Most approaches to elastic registration assume small deformations. To cope with *large deformations* a fluid model has been proposed in [9]. An incremental elastic approach, which is landmark-based, has been introduced in [37]. Criteria to distinguish between small and large deformations have been suggested in [3, 37].

5 Biomechanical Modelling of Brain Deformations

A recent trend in medical image registration is to model biomechanical properties of anatomical structures more precisely. A central topic in developing such *physically-based* approaches is to deal with *nonhomogeneous* tissue properties. In the case of the human head one principally has to distinguish between rigid (e.g., bone), elastic (e.g., brain tissue), and fluid parts (e.g., the ventricular system). Besides surgical simulation and training, an important application for *biomechanical models* is the prediction of brain deformations for intraoperative navigation tasks. Image-guided surgical navigation in most cases relies on preoperatively acquired image data (e.g., MR images). During an intervention, however, generally brain deformations occur. For example, when opening the skull and the dura mater, liquor flows off which generally leads to a *brain shift* (see Fig. 8 as well as [8, 27]). Anatomy changes also result from surgical interventions such as the (incremental) resection of a tumor. To continue accurate navigation it is then necessary to correct the preoperative image by registering it with the current anatomical situation, e.g., based on intraoperative measurements from a portable CT scanner or from an Ultrasound device.

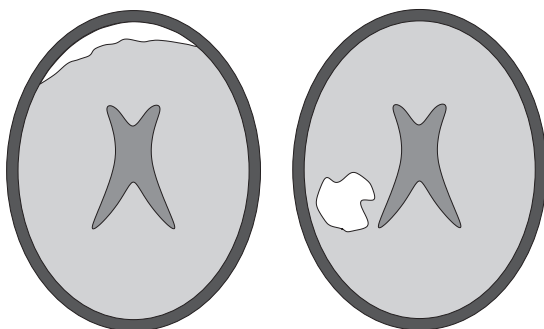


Fig. 8: Brain shift (left) and tumor resection (right).

The first approaches introduced for intraoperative image correction have been based on a mass-spring model [8] and a combination of different energy terms [16]. In both models, however, real physical material parameters have not been included. Approaches dealing with nonhomogeneous tissues based on elasticity theory which incorporate real physical material parameters and apply the finite element method (FEM), have been proposed in [29, 24] (see also [45] in this issue). In other work, homogeneous material is assumed or deformations are restricted by imposing certain boundary conditions (e.g., [50, 37, 39]). Brain models for simulation purposes but not for registration have been described, e.g., in [48, 26]. An approach, where different physical models (an elastic and fluid model) have been coupled, has recently been proposed in [25].

6 Conclusion

As can be learned from the literature, the work on elastic and nonrigid registration has increased tremendously in recent years. While here we mainly considered images of the human head, elastic registration is also important for other organs, e.g., human liver, breast, and heart. A problem with elastic registration is that currently it is not possible to judge which approaches perform better than others. A systematic evaluation study as in the case of rigid registration [60] has not yet been performed. However, one has to note, that performance characterization of elastic schemes is also very difficult. On the one hand, a prerequisite would be the quantification of typical deformations of anatomical structures as well as the provision of 'ground truth'. On the other hand, one should note, that elastic registration of multimodality images is still a relatively young research field, and the current focus is on exploring principal models and approaches. Actually, the task of elastic registration is rather difficult, and the mathematical level for understanding existing work or developing new approaches is generally rather high. Nevertheless, theoretical soundness is important to guarantee required properties and to end up with algorithms of predictable performance.

Important topics for further research are, for example, the integration of more physics in form of biomechanical models, the combination of physical and statistical deformation models, the combination of landmark-based and intensity-based schemes, the treatment of large deformations, the integration of uncertainties and error information, the investigation of similarity measures between images, as well as the development of efficient computational schemes. In comparison to traditional monomodal 2D image analysis, a clear challenge is the analysis of multimodal 3D or even higher-dimensional image data.

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¹ <http://kogs-www.informatik.uni-hamburg.de/PROJECTS/Imagine/Imagine.html>

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Contact

Dr. Karl Rohr
 Universität Hamburg,
 Fachbereich Informatik, AB Kognitive Systeme
 Vogt-Kölln-Str.30,
 D-22527 Hamburg,
 Germany
 rohr@informatik.uni-hamburg.de



Karl Rohr studied Electrical Engineering at the University of Karlsruhe and received his Ph.D. degree (1994) as well as his Habilitation degree (1999) in Computer Science from the University of Hamburg. Since 1994 he is project leader of the IMAGINE project at the Computer Science Department of the University of Hamburg. Dr. Rohr was awarded a DAGM prize in 1990 and received the Springer Best Paper Award KI-95. His research areas are computer vision and medical image analysis.

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