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## NON-RIGID REGISTRATION OF MEDICAL IMAGE DATA WITH INCOMPLETE INFORMATION <sup>1</sup>

O. Museyko\*, G. Leugering<sup>†</sup>, P. Hastreiter<sup>‡</sup>

\* *Institute of Medical Physics, University of Erlangen-Nuremberg, Germany*

*E-mail: museyko@gmx.de*

<sup>†</sup> *Chair of Applied Mathematics, University of Erlangen-Nuremberg, Germany*

<sup>‡</sup> *Department of Neurosurgery, Neurocenter, University of Erlangen-Nuremberg, Germany*

The problem of non-rigid registration of images, where certain parts are missing, is considered in the context of pre- and intraoperative or damaged data. A variational formulation of the problem is proposed such that a counterpart of the missing data can be restored in a template image along with a corresponding registration transformation between the images. The problem is a registrational variant of a free-discontinuity Mumford-Shah segmentation problem with the unknown discontinuity set representing the boundary of missing data; thus, no preliminary segmentation is needed to detect the missing information. An approximation of the free-discontinuity problem by an Ambrosio-Tortorelli-type approximation is used to compute the numerical solutions. Experiments with 2D examples demonstrate the efficiency of the proposed approach.

**Key words.** Non-rigid registration, incomplete information, Mumford-Shah segmentation, free-discontinuity problem.

### 1. Introduction

In medical imaging, registration is required for the alignment and fusion of image data obtained from the same or different sources. Typical imaging devices are computed tomography (CT), magnetic resonance tomography (MRT), and positron emission tomography (PET). They provide a great variety of anatomical and functional information and support diagnosis, therapy planning, and the analysis of diseases.

Besides rigid alignment of two datasets, there are many situations of practical importance where the underlying structures are deformed between successive scans. In these cases, the problem increases with the complexity of the required non-rigid transformation [1]. Another challenging problem of registration occurs if two images differ as a result of tissue removal or compression processes. Consequently, an unambiguous mapping between two datasets is missing and the registration is easily and severely deteriorated. Such effects are observed for instance if pre- and intraoperative images, histological dissections or atlas and image data

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are compared. Since there is no best choice in image registration, the variety of applications requires considering the specifics of each problem with its limitations and peculiarities [2].

For the assessment of deformations between pre- and intraoperative datasets, there are currently three strategies: (1) direct measurements within the physical space of the patient [3], (2) registration [4], and (3) simulation based on an underlying model [5].

Approaches suggested more recently cover different aspects related to a correct assessment of deformation phenomena. In [6], an approach was presented which measures brain variability on the registration of sulcal line sets which ensures a globally consistent deformation of the underlying space. For non-rigid matching, a method based on generalized surface flows was suggested using tailored deformation priors and multiresolution computations [7]. In order to solve registration problems for images having inhomogeneities, an approach for a combined homogenization and registration was presented [8]. In the field of atlas registration, manually labeled data at various degrees of "sharpness" and the joint registration-segmentation of a new brain with these atlases were applied [9]. Another approach uses a preoperatively computed atlas of model deformations to predict intraoperative brain shift [5]. New similarity measures were suggested which improve the registration of multimodal data [10, 11]. To overcome discontinuities in the displacement field and intensity variations in the data, an energy functional based on total variation regularization and a robust data term was used [12]. In order to improve non-rigid transformations, a computationally efficient non-parametric diffeomorphic image registration algorithm was suggested [13]. Another strategy applied segmentation to guide the registration process based on a complex physical model [14]. As a drawback, the method requires essential preprocessing of the data. In [15], a variant of image inpainting is constructed for the unknown displacement field (i.e. interpolation of the displacement within the missing part from its values in the neighborhood). This method seems to be highly suitable for the registration of incomplete images. However, explicit segmentation of the missing data is required. On the other hand, the accuracy of the interpolation is usually high only if the variation of the data involved in it is not too strong. Since the brain shift in pre- to intraoperative surgery is significant, the accuracy of this method in such situations requires verification. To our knowledge, there is no further contribution which allows for an efficient and robust treatment of missing correspondence after tissue removal or compression effects. Other related works are [16, 17, 18, 19, 20].

In this paper, we present a method for the non-rigid registration which is robust with respect to the presence of local damages of the image data. It is based on a new variational fully automatic model: it works without any prior segmentation or identification of landmarks. For a proof of concept, we conducted experiments with 2D image data. The achieved results demonstrate the value of this method for complex registration problems such as image data with poorly distinguishable lesions and with the brain shift phenomenon.

## 2. Methods: a free-discontinuity model

As we have mentioned, the presence of the missing part in the reference image invalidates the registration in its neighbourhood, since it has no correspondence in a template image to be matched with. Our idea then is to find what is that part of a template image which is missing in a reference by replacing the intensity of some piece of a template image by the intensity value of the missing part in a reference. If the image piece is detected correctly, then the registration energy for the modified template should be lower. Thus, a position and a shape of that piece in a template is another unknown of the registration problem.

We will build the new model on the basis of the following conventional registration problem:

$$J(u) = \frac{1}{2} \int_{\Omega} |I^T(x - u(x)) - I^R(x)|^2 dx + \frac{\beta}{2} a(u, u) \rightarrow \inf. \quad (2.1)$$

Here the template image  $I^T$  is registered to the reference  $I^R$  by the offset field  $u(x) = x - \varphi(x)$ ,  $u$  is an element of a space of admissible displacements  $W$ . The application dependent regularizing term  $a(\cdot, \cdot)$  penalizes the undesired properties of  $u$ . The criterion  $J$  is applicable for monomodal registration, that is for the images obtained on the same hardware so that the intensity of their pixels can be compared directly, as in the first term in  $J$ , the sum of squared differences (SSD).

We assume that the missing part in  $I^R$  has zero intensity. Then we could nullify the intensity of its counterpart  $E \subset \Omega$  in  $I^T$ , if it were known, by simply multiplying the template with the characteristic function  $c(x)$  of the complement set to  $E$ :

$$c(x) = \begin{cases} 0, & \text{if } x \in E, \\ 1, & \text{otherwise.} \end{cases}$$

This would make the conventional model (2.1) eligible for the registration of the modified template. The proposed model involves the relaxed intensity corrector  $c(x)$  for the template together with appropriate penalization terms:

$$J(u, c, \Gamma) = \frac{1}{2} \int_{\Omega} |cI^T(x - u) - I^R|^2 dx + \frac{\beta}{2} a(u, u) \\ + \frac{\alpha}{2} \int_{\Omega \setminus \Gamma} |\nabla c(x)|^2 dx + \gamma \mathcal{H}^{n-1}(\Gamma). \quad (2.2)$$

Let us consider the functional  $J$  term by term. The SSD part (first term) includes  $c(x)$  to introduce 'the missing part' into the template  $I^T$  so that its pixelwise comparison with the reference  $I^R$  becomes relevant. On the one hand, the optimal mask  $c$  is expected to be a characteristic-type function, that is having jumps. On the other hand, we don't want to restrict all admissible  $c$  to the class of characteristics functions, since it would make both the analysis and numerical treatment of (2.2) complicated. Thus, we relax the admissible masks  $c$ : they are assumed to be piecewise-smooth functions in  $\Omega$ , having 'jumps' on a discontinuity set  $\Gamma$  (a hypersurface in  $\Omega$ ). The third term in (2.2) penalizes the deviation of

the mask  $c$  from the constant value on each component of the set  $\Omega \setminus \Gamma$ , so that  $c$  tends to be a piecewise-constant function: the optimal  $c$  is expected to be close to the characteristic function of the complement to the recovered 'missing' set for the template, with the optimal  $\Gamma$  being its boundary. The last term, Hausdorff measure of co-dimension one of  $\Gamma$ , penalizes oscillations of this discontinuity set so that it doesn't grow too 'long'.

The problem of minimization of  $J(u, c, \Gamma)$  is the so-called free-discontinuity problem ([21, 22]). More precisely, it's a variant of the Mumford-Shah segmentation problem [23].

On the other hand, (2.2) can be also viewed as a direct analog of the registration and homogenization model by Fischer and Modersitzki [8]:

$$J(u, c) = \frac{1}{2} \int_{\Omega} |cI^T(x - u) - I^R|^2 dx + \frac{\beta}{2} a(u, u) + \alpha E(c) \rightarrow \inf,$$

where  $c$  is a smooth function and the term  $E(c)$  penalizes the oscillation of  $c$ . That is,  $E(c)$  is either

$$\int_{\Omega} |\nabla c|^2 dx \quad (\text{for smooth intensity corrections})$$

or

$$\int_{\Omega} |\nabla c| dx \quad (\text{total variation of } c).$$

Although the penalization of the total variation is suitable for comparatively big corrections of intensity, it may be not sufficient, in general, for the functions  $c$  with 'jumps'. In this view, the problem (2.2) appears to be more suitable for the registration of incomplete images.

It can be shown that the problem (2.2), properly reformulated in terms of special functions of bounded variation (*SBV*, see [22, 21], e.g.), has a solution for every fixed  $u \in W$ .

## 2.1. Variational approximation of the free-discontinuity problem

The numerical computation of the solution to (2.2) is involved, since the energy functional is not differentiable in any reasonable norm, and moreover a numerical scheme should be aware of the (unknown) discontinuity set  $\Gamma$ .

Therefore, a number of approximations for free-discontinuity problems exist (and are actively explored), which are minimization problems for a differentiable functional defined usually on an appropriate Sobolev space. For the problem (2.2) we adopt the Ambrosio-Tortorelli-type approximation [22]. The idea behind this practical approach to a free-discontinuity problem is to approximate the discontinuity set  $\Gamma$  by a smooth function  $v(x)$  such that it is close to 0 on  $\Gamma$  and tends to 1 outside of it. Such a structure of  $v$  is energy-efficient: the energy functional of an approximation problem includes the (weighted) terms

$$\int_{\Omega} (v - 1)^2 dx \quad \text{and} \quad \int_{\Omega} v^2 |\nabla c|^2 dx,$$

the latter being an approximation for the term

$$\int_{\Omega \setminus \Gamma} |\nabla c|^2 dx$$

in the free-discontinuity problem. The approximation problem is set in the Sobolev space  $H^1(\Omega)$  for the mask  $c$ .

Thus, we define an approximation as a minimization problem for the functional

$$F_\varepsilon(u, c, v) = \begin{cases} \frac{1}{2} \int_{\Omega} |cI^T(x-u) - I^R|^2 dx + \frac{\beta}{2} a(u, u) \\ \quad + \frac{\alpha}{2} \int_{\Omega} (v^2(x) + k(\varepsilon)) |\nabla c(x)|^2 dx + \frac{\gamma^2}{2\varepsilon} \int_{\Omega} (v-1)^2 dx \\ \quad + \frac{\varepsilon}{2} \int_{\Omega} |\nabla v(x)|^2 dx, \text{ if } c, v \in H^1(\Omega), 0 \leq v(x) \leq 1, \\ +\infty, \quad \text{otherwise,} \end{cases} \quad (2.3)$$

where  $k(\varepsilon) > 0 \forall \varepsilon > 0$ ,  $k(\varepsilon) = o(\varepsilon)$ .

This problem approximates the original model (2.2) in the sense of convergence of the solutions  $(u_{\varepsilon_k}^0, c_{\varepsilon_k}^0)$  of the former to a solution  $(u^0, c^0)$  of the latter as  $\varepsilon \rightarrow 0+$  (under certain assumptions and in an appropriate functional space).

## 2.2. Numerical scheme

As the functional  $F_\varepsilon(u, c, v)$  defined by (2.3) is differentiable, we will use the necessary optimality conditions to compute the solution. Thus, taking the directional derivative of  $F_\varepsilon$  with respect to its arguments we obtain the following Euler-Lagrange system in  $\Omega$ :

$$\beta \mathcal{A}u + c(x)(c(x)I^T(x-u(x)) - I^R(x))\nabla I^T(x-u(x)) = 0, \quad (2.4)$$

$$-\alpha(v^2(x) + k(\varepsilon))\Delta c + (c(x)I^T(x-u(x)) - I^R(x))I^T(x-u(x)) = 0, \quad (2.5)$$

$$-\varepsilon\Delta v + \alpha|\nabla c(x)|^2 v(x) + \frac{\gamma^2}{\varepsilon}(v(x) - 1) = 0, \quad (2.6)$$

complemented with the natural Neumann boundary conditions:

$$\frac{\partial u^i}{\partial n} = \frac{\partial c}{\partial n} = \frac{\partial v}{\partial n} = 0 \text{ on } \partial\Omega, \quad i = 1, \dots, n. \quad (2.7)$$

Here, the linear operator  $\mathcal{A}$  is such that

$$\int_{\Omega} \mathcal{A}u \cdot w = a(u, w) \text{ for all } u, w \in W.$$

Note that some other boundary conditions on  $u$  may need to be applied depending on the choice of the space  $W$  and the bilinear form  $a(\cdot, \cdot)$ .

The system of equations (2.4)-(2.7) is essentially non-linear. To avoid the complexity of dealing with the large system of coupled non-linear equations we

adopt the alternating scheme (cf. [24]), i.e., each of the equations (2.4)-(2.6) is solved successively independent of the others, which forms a one cycle of the iterative process.

The equations (2.5) and (2.6), when considered independently, are linear elliptic equations and can be solved with a help of a number of available effective software solvers. As for the equation (2.4), it is by itself an Euler-Lagrange equation for the problem (2.1) with the template image  $cI^T$  ( $c$  is fixed). Therefore, a number of well-known approaches for the numerical solution of the image registration problem of type (2.1) are applicable (see [1]).

### 3. Results

We have implemented a 2D version of the described numerical scheme using Matlab 7.5. All tests were conducted using a standard PC equipped with Pentium 4 (3 GHz). The applied test data consisted of 2D  $256 \times 256$  pixel images. The runtime of the classical registration without masking (which is solving the equation (2.4) alone with  $c \equiv 1$ ) was about 2 minutes. Using the proposed new model, the registration with a mask (i.e. solving the system (2.4)-(2.7)) lasts about 2-4 times longer than the classical registration. For the experiments, the following parameter values were found to be reasonable:

$$\alpha = 10^{-3}, \quad k = \varepsilon = 10^{-6}, \quad \gamma^2 \in [10^{-5}; 10^{-6}], \quad \beta \in [10^{-3}; 10^{-6}].$$

For the evaluation of our approach, let us first consider a synthetic registration example: in Figure 1, the template image was obtained from the reference by an artificially generated non-rigid transformation. Additionally, some part of the reference image was erased to imitate a 'missing region', such as a resected tumor. The results of the registration with the conventional model (2.1) and the new registration model with masking (2.3) are shown. The curvature approximating term was used to regularize the offset field  $u$ , i.e.,

$$\mathcal{A}u = \Delta^2 u.$$

It is clearly visible that the direct approach leads to a misregistration. It maps the 'hole' in the reference onto the unrelated area in the template with low intensity values, resulting in a disproportional stretch. On the other hand, the registration with a mask allows getting a good guess for the position of the removed part in the template image.

Our second example is more realistic and deals with the registration of intra- and preoperative MR brain images, extracted from the rigidly aligned volumes. The characteristic brain shift which occurs during surgery is easily seen in the reference image. In Figure 2, one can see that the mask-hardened registration model properly guesses the main direction of the deformation around the tumor, so that the brain tissue surrounding it shifts inside the free area after extraction.

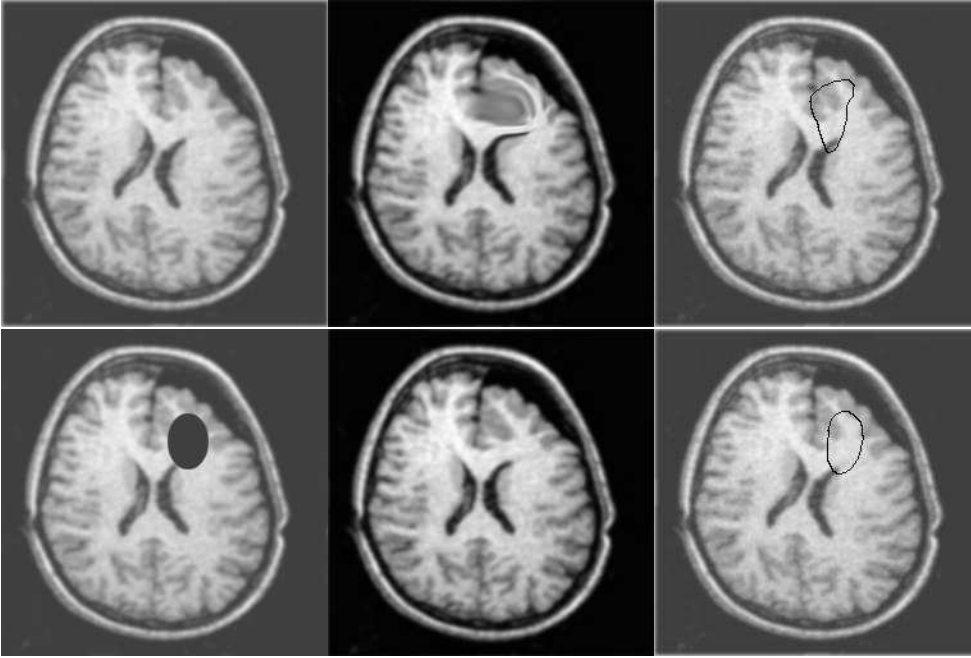


Fig. 1. Model example of registration with the reference image having a 'hole'. From left to right, row by row: a) Template image. b) Template image registered without masking. c) Correspondent restored position of a 'hole' in the template. d) Reference image. e) Template image registered with masking. f) Correspondent restored position of a 'hole' in the template.

#### 4. Discussion

The proposed method has shown to be promising for the registration of incomplete images. What seems to be the most attractive feature of this free-discontinuity model, is its automatism: any manual preprocessing of the images such as segmentation of the damaged part is avoided. On the other hand, a manual control is still possible, if needed, by providing an initial guess for the mask.

The presented 2D examples serve as a proof of concept. However, one has to note that it is generally not possible to recover the true offset of the tissue on a single pair of 2D slices extracted from 3D data (cf. Figure 2). Usually, the brain shift occurs in all three dimensions. Besides, the SSD registration criterion is in general not the right choice for MRI, since the contrast of images varies from scan to scan. Nevertheless, the SSD criterion is robust enough to show the potential of our method.

In the future, the following ideas and problems will be addressed. First, the method will be extended to the multi-modal registration by a corresponding modification of the mutual information functional. Second, the problem (2.3) used for the approximation of free-discontinuity registration problem (2.2) has additional variables, and quite a few parameters to be tuned. This, together with the additional variable  $c$  as compared to the 'pure' model (2.1), increases the complexity of the problem and may lead to increased computation times. One way to improve the situation is to adopt another smooth approximation for the free-discontinuity problem; some recent non-local approximations (see [21], for

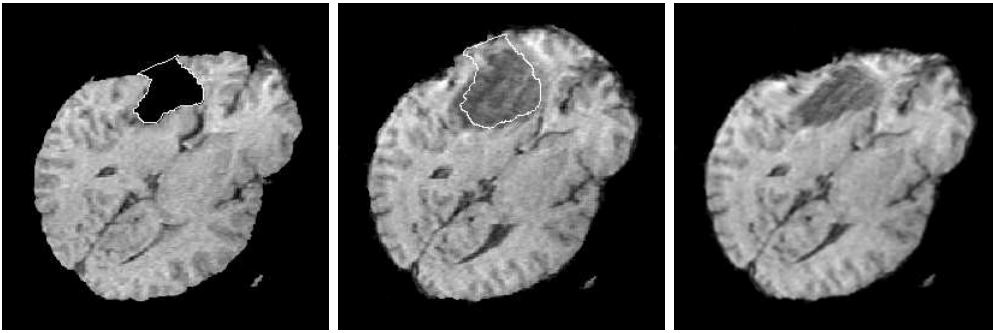


Fig. 2. Example of registration of the preoperative brain image (with tumor) to the intraoperative image (resected tumor, significant brain shift). From left to right: (a) reference (intraoperative image) with the shape of extracted tissue; (b) original template (preoperative image) with the restored shape of extracted tissue (image of the shape shown in the reference image under the registration transformation); (c) template image registered with masking.

instance) seem to be very promising. Finally, the other obvious way to increase the performance is to apply some more elaborate numerical scheme for the problem (2.4)-(2.7). The multigrid technique may be the method of choice here.

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