

# Landmark Constrained Non-parametric Image Registration with Isotropic Tolerances

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**Abstract.** The incorporation of additional user knowledge into a non-rigid registration process is a promising topic in modern registration schemes. The combination of intensity based registration and some interactively chosen landmark pairs is a major approach in this direction. There exist different possibilities to incorporate landmark pairs into a variational non-parametric registration framework. As the interactive localization of point landmarks is always prone to errors, a demand for precise landmark matching is bound to fail. Here, the treatment of the distances of corresponding landmarks as penalties within a constrained optimization problem offers the possibility to control the quality of the matching of each landmark pair individually. More precisely, we introduce inequality constraints, which allow for a sphere-like tolerance around each landmark. We illustrate the performance of this new approach for artificial 2D images as well as for the challenging registration of preoperative CT data to intra-operative 3D ultrasound data of the liver.

## 1 Introduction

Non-rigid image registration is one of the key problems in computer-assisted liver surgery. Based on a pre-operative CT volume, interventions are planned by means of segmenting tumors and vessels and defining resection volumes. During the intervention the surgeon is guided by 3D ultrasound (US), which captures the actual shape and position of the liver [1]. The aim of registration is to compensate for liver deformations, such that the pre-operative planning can be directly used to guide the surgeon. Registration challenges are the homogeneous structure of the liver and its elastic behavior. Therefore the use of variational methods appears to be inevitable. In [2] a method is described which is based on an intensity driven registration of CT and US-data equipped with additional anatomical landmark information. The use of landmarks within this approach is twofold. They not only provide a good initial deformation field [3] but their preservation throughout the whole registration process, nicely guides the scheme

to its final stage. However, the advantage of the approach - the simultaneous registration based on image gray values together with exact landmark matching - suffers from localization inaccuracies of the landmarks. These landmarks are set intra-operatively by the surgeon. Typical landmark positions are the junctions of the main vessels. However, due to the poor image quality, the location of these landmarks is inexact in general. Consequently, the assumption of exact landmarks appears to be not the correct modeling.

To avoid this drawback several other approaches are described in literature. The first one is an alternating optimization of a distance measure and a Gaussian elastic body spline (GEBS) based landmark registration with coupled displacement fields [4]. In this scheme anisotropic localization uncertainties of the landmarks are considered by a global penalty term. The second one is based on an additional penalty term [5, 6], that sums the local errors of the landmarks. This global error measure is added to the objective function and weighted by a corresponding parameter, so the landmark misfit is globally controlled. An individual landmark control is not possible. Secondly the penalty approach suffers from parameter tuning. Another approach is described in [7]. Here, a constrained optimization problem is invoked, which ensures small landmark errors without parameter tuning, but again only the global error is restricted.

Here we are presenting a new approach by considering individual landmark localization inaccuracies. For each landmark a tolerance estimating the localization error of the landmarks is defined. Similar to the CoLD-approach in [2], the new approach is formulated as a constraint optimization problem, this time however, with an inequality constraint for each individual landmark pair.

## 2 Methods

In the following we describe the above outlined new approach in more detail. Let  $R, T$  (US-) reference and (CT-) template volumes, with  $R, T : \mathbb{R}^d \rightarrow \mathbb{R}$ , continuous functions. Furthermore, let  $y : \mathbb{R}^d \rightarrow \mathbb{R}^d$  the deformation in question. The landmarks are given by  $r_j, t_j \in \mathbb{R}^d, j = 1, \dots, m$  and the corresponding tolerated error distance of the landmarks  $r_j, t_j$  by  $c_j \in \mathbb{R}$ . The key term within the optimization problem is given by

$$\mathcal{P}_j(y) = c_j^2 - \|y(r_j) - t_j\|^2.$$

Note that  $\mathcal{P}_j(y) \geq 0$  ensures that the squared difference of the deformed  $j^{\text{th}}$  pair of landmarks is less than  $c_j^2$ . Altogether we arrive at the following constraint optimization problem

$$\min_y \mathcal{J}(y) = \mathcal{D}(y) + \alpha \mathcal{S}(y) \quad \text{s.t.} \quad \mathcal{P}_j(y) \geq 0, \quad j = 1, \dots, m. \quad (1)$$

In contrast to [7] we do not summarize the differences of the landmarks, but handle each of them separately. As a consequence, we are able to guarantee an individual error for each pair of landmarks. The tolerance  $c_j$  may be interpreted as the radius of a sphere around the  $j^{\text{th}}$  landmark. A deformed landmark will be

accepted if it is located within this sphere, see Figure 1 (lower right). It should be noted, that the extension to anisotropic tolerance regions (e.g. an ellipsoid) [8] is straightforward. To keep the issues of interest clear, we only present the isotropic case, c.f. the tolerance region is a sphere.

The remaining terms of the functional  $\mathcal{J}(y)$  are the well known normalized gradient field (NGF) distance measure [9]

$$\mathcal{D}(y) = \frac{1}{2} \int_{\Omega} \left( 1 - \left( \frac{\langle \nabla T_y, \nabla R \rangle}{\|\nabla T_y\| \cdot \|\nabla R\|} \right)^2 \right) dx,$$

which is well suited for multimodal problems and the elastic regularizer [10]

$$\mathcal{S}(y) = \frac{1}{2} \int_{\Omega} \sum_{l=1}^3 \mu \|\nabla y_l\|^2 + (\mu + \lambda) \operatorname{div}^2 y \, dx.$$

Here  $\lambda, \mu \in \mathbb{R}^+$  are the so called Navier-Lamé constants, which control the elastic behavior of the deformation.

For the optimization of (1) we use the first-discretize-then-optimize-approach. That means, the objective function as well as the constraints are discretized first to achieve a finite optimization problem. In particular, the constraints are approximated by means of linear interpolation as described in [7].

We solve the finite optimization problem by a generalized Gauss-Newton-method [11, 12]. Applying a pre-registration based on thin plate splines (TPS) [10], we arrive at a starting point for the optimization procedure that fulfills the constraints. Due to the constraints, the resulting linear system, known as KKT-system, is indefinite. Therefore we use the iterative solution technique MinRes [13] for these systems. All algorithms are implemented in Matlab.

### 3 Experiments

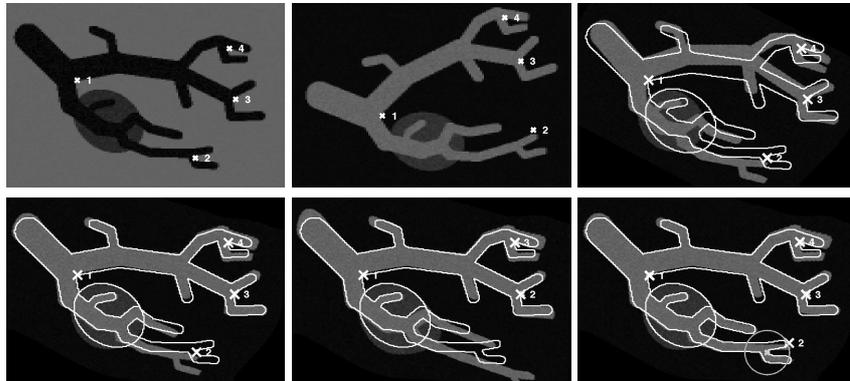
We demonstrate the applicability of the new method in two steps. First we start with artificial generated data. Afterwards we test it on real clinical data from liver surgery. In the upper left and middle images of Figure 1 we depict two dimensional reference and template test images. Also four pairs of corresponding landmarks are shown, where the second landmark is intentionally misplaced. The remaining images of Figure 1 demonstrate different registration results. To this end, the deformed template is overlaid by the boundaries of the reference, resulting in an easy visual validation. The upper right image shows the result of a TPS-based registration, while the lower left illustrates the solution of the CoLD-approach described in [2]. It should come as no surprise, that both methods suffer from the misplaced second landmark. Next we applied the CoLD-approach to the problem by completely ignoring the second landmark. Again the registration quality is poor which is apparent in the lower half of the image. Finally, we tested the new approach. For the second landmark we define a tolerance of  $c_2 = 1$ , (to compare, image domain is  $\Omega = (15, 10)$ ) drawn as a green circle (Fig. 1, lower

right). The overall result outperforms all other methods by generating a smooth and feasible deformation.

In a second step the algorithm was applied to real clinical data from a patient who underwent an oncological liver resection. The aim is to register pre-operative CT data to intra-operative 3D power Doppler ultrasound data. We defined eight landmarks interactively and intentionally moved one landmark by 2 mm. The contours of vessels from the registered CT data are shown after CoLD-registration with no tolerances (Fig. 2a) and with a tolerance of 2 mm at the moved landmark (Fig. 2b,c). Again, the new method shows a superior quality, even for this very challenging problem.

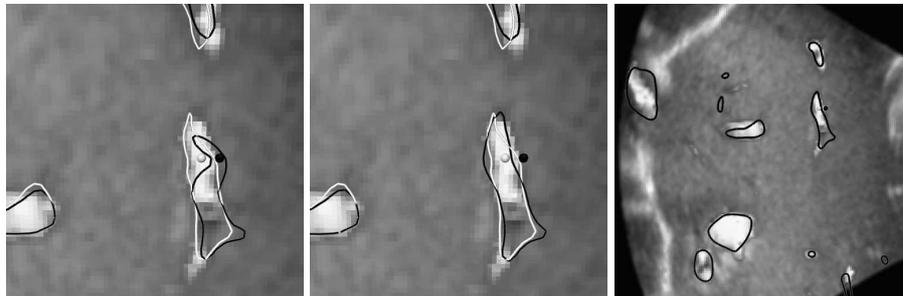
## 4 Discussion

We presented a non-rigid registration approach, which combines intensity-based registration with additional landmark constraints. The important contribution is the introduction of isotropic tolerances in order to be able to compensate for localization uncertainties of the landmarks. In clinical application these tolerances are set by the surgeon depending on the accuracy of the related landmark. We demonstrated the influence of an accidentally displaced landmark on the registration result and the satisfactory improvement by the new method. Furthermore, the outlined method exhibits success for real clinical data. In a forthcoming investigation we plan to evaluate the novel method for a large collection of clinical data sets.



**Fig. 1.** 2D example; *upper left*: reference; *upper mid*: template both with landmarks; *upper right*: TPS-based registration; *lower left*: CoLD-registration; *lower mid*: CoLD-registration without misplaced landmark; *lower right*: new approach; green: given landmark tolerance.

**Fig. 2.** One slice of real clinical 3D ultrasound data (B-mode + power Doppler) with isolines of registered CT data is shown; *left*: Registered with correct (white) and moved landmark (black) with no tolerances; *mid*: with 2 mm tolerance for the moved landmark (black); *right*: Overview of the whole slice with moved landmark with 2 mm tolerance.



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