# Matching CT and Ultrasound data of the Liver by Landmark constrained Image Registration

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# 1 Abstract

In navigated liver surgery the key challenge is the registration of pre-operative planing and intra-operative navigation data. Due to the patients individual anatomy the planning is based on segmented, pre-operative CT scans whereas ultrasound captures the actual intra-operative situation. In this paper we derive a novel method based on variational image registration methods and additional given anatomic landmarks. For the first time we embed the landmark information as inequality hard constraints and thereby allowing for inaccurately placed landmarks. The yielding optimization problem allows to ensure the accuracy of the landmark fit by simultaneous intensity based image registration. Following the *discretize-then-optimize* approach the overall problem is solved by a generalized Gauss-Newton-method. The upcoming linear system is attacked by the MinRes solver. We demonstrate the applicability of the new approach for clinical data which lead to convincing results.

**Keywords:** nonlinear image registration, landmark registration, guided liver surgery, constrained optimization, discretize-then-optimize

## 2 Introduction

Liver tumors belong to the five most common malignancies in the western world. Here, surgical resection is the main curative treatment. The success of the resection depends on two opposing strategies. On one hand, large enough safety margins have to be achieved in order to arrive at a R0-resection and to ensure a long-term benefit for the patient. On the other hand and for the same reason, the remaining functional liver volume has to be maximized. To obtain an optimal balance between resection and preservation, 3D computer tomography data is used to capture the individual anatomy of the liver and to build up 3D models of the patient's vascular system before the surgery.<sup>1,2</sup> Based on this imagery, an individual resection plan is worked out to guide the surgeon during the intervention, where the actual location and status of the liver is captured via an intra-operative ultrasound device. To locate the ultrasound probe and also other surgical instruments a tracking device is attached allowing precise measurements of their position. Typically two different ultrasound techniques are used: For the standard 2D technique the volume is computed from the captured slices<sup>3</sup> whereas in the 3D scanner case the volume is automatically determined by motor-driven probe shifting.<sup>4,5</sup>

However, the challenging task is to adapt the planning data to the intra-operative situs, which is deformed by liver movement, bedding, and patient's breathing (see Figure 1). Consequently, a sophisticated registration problem has to be solved.<sup>6</sup> To compensate for the non-rigid liver deformation and to mimic the elastic behavior of the liver, an elastic potential based variational registration approach has been chosen. The comparison of CT and intra-operative ultrasound yields a multimodal problem, so special distance measures like normalized gradient<sup>7</sup> or mutual information<sup>8</sup> have to be applied. As it is typical for non-linear approaches, the success of such a method depends on good starting guesses. Here, the idea is to incorporate user knowledge into the registration process. In liver surgery the concept of landmark based registration turned out to be highly efficient.<sup>9,10</sup> Here, pairs of corresponding points are to be detected in both volumes and the initial deformation has to match these points. Typically positions of these landmarks are junctions of the liver vessels as shown in Figure 1. They may be detected with great precision in the pre-operative planning data but the intra-operative placement by the surgeon suffers from the inaccuracy of the ultrasound device, so an exact matching would overrate the landmark information. In Figure 1 an additional problem of the given multimodal registration problem is shown. One can see, that the CT data (see Figure 1 (a)) contains more vessel information than the US data (see Figure 1 (b)). Hence a pure landmark based approach is bound to fail which leaves us with the need for a combined intensity and landmark based approach, allowing for tolerance in the landmark precision.



Figure 1. Figure (a) shows a single slice of CT data combined with the vessel model generated by the CT data. Figure (b) shows the vessel model with one single slice of US data. The corresponding landmarks are enumerated accordingly.

Only few work on the topic of US-CT registration is published. Starting with rudimental rigid registration techniques only based on image information<sup>11</sup> a second step was the extension to non-rigid deformations.<sup>12</sup> To take landmark information into account, first pure landmark registration was described (especially for the case of US-MRI registration).<sup>13</sup> Typically thin-plate-spline (TPS)<sup>14</sup> based algorithms were used to derive a deformation. A first step towards the combination of landmark information and image data was given in,<sup>15</sup> where the authors present a method that allows an exact fitting of landmarks combined by a simultaneous minimization of an energy function (so called variational formulation). In the SPIE article of Papenberg et al.<sup>9</sup> the variational setting was refined by an additional term, which penalizes the deviation is controlled by a weighting parameter. Its actual choice is a tricky problem, but nevertheless may greatly influence the outcome of the registration process. By applying constrained optimization methods in<sup>16</sup> the authors get rid of the weighting parameter. The presented algorithm ensures that the global landmark error is less than a given threshold. Using special spline based models Wörz et al<sup>17</sup> described an alternative way to combine both landmark and image information.

Here, we present a novel and flexible approach, which enables the user to prescribe the allowed misfit of the landmarks. Of course a measure for the landmark accuracy has to be chosen by the user. Therefor an upper bound for the overall landmark error is an intuitive key figure. In contrast the penalty based approach parameter weights the influence of the landmark error to the unknown energy. Furthermore, the new approach does not demand for any additional parameter.

#### 3 Methods

In this contribution, we present a new approach for the registration of a given ultrasound volume  $\mathcal{R}$  with a CT volume  $\mathcal{T}$  subject to pairs of corresponding landmarks  $(t_j, r_j)$ . Let  $\mathcal{R}, \mathcal{T} : \Omega \subset \mathbb{R}^3 \to \mathbb{R}$  and  $t_j, r_j \in \mathbb{R}^3$  with  $j = 1, \ldots, \nu$ , where  $\nu$  denotes the number of corresponding landmarks. The problem may be formulated in a variational setting as follows. Find a transformation  $y : \mathbb{R}^3 \to \mathbb{R}^3$ , which solves the following constrained optimization problem

$$\min_{y} \mathcal{J}(y) = \mathcal{D}(y) + \alpha \mathcal{S}(y)$$
  
subject to  $\mathcal{P}(y) \ge 0$ ,

with a regularizing parameter  $\alpha \in \mathbb{R}^+$ . Here,  $\mathcal{D}$  measures the distance between the two volumes. We employ the NGF (normalized gradient field) measure for multimodal image data.<sup>7</sup> It focusses on the alignment of edges in the data and is given by

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

where  $T_y$  is deformed template T using y and  $\nabla T_y$  resp.  $\nabla R$  are the image gradients. The two image gradients are compared using the inner product denoted by  $\langle \cdot, \cdot \rangle$ .

To measure the smoothness of the displacement field  $y = (y_1, y_2, y_3)$  and to mimic the deformation of the liver, we choose the elastic regularizer<sup>6</sup>

$$\mathcal{S}(y) = \frac{1}{2} \int_{\Omega} \sum_{\ell=1}^{3} \mu \left\| \nabla y_{\ell} \right\|^{2} + (\mu + \lambda) \operatorname{div}^{2} y \, \mathrm{d}x.$$

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

The landmark misfit is measured by the constraint function  $\mathcal{P}(y)$ , which computes the overall accurateness of the given pairs  $(r_j, t_j)$  with respect to the actual displacement field

$$\mathcal{P}(y) = c - \sum_{j} \|y(r_{j}) - t_{j}\|^{2}, \qquad (1)$$

with a landmark tolerance constant  $c \in \mathbb{R}^+$ . The actual choice of the constant c is intuitive because it simply describes an upper bound for the overall landmark error. A straight forward choice could depend on a single landmark tolerance multiplied by the number of landmarks. This formulation becomes greater than zero when all landmarks fit correctly or when the summation of their errors is less than c. Of course an individual handling of each landmark distance can be realized by introducing additional weights for each landmark. Although those weights do not complicate the later optimization problem, here we solely deal the homogeneous case.

In contrast to the method described in the last year's SPIE paper, $^9$  where the constraints were added as weighted penalizer

$$\min_{y} \mathcal{J}(y) = \mathcal{D}(y) + \beta \mathcal{P}(y)$$

and thus still leading to an unconstrained optimization problem, we now have to deal with a constrained optimization problem. It is solved by employing a generalized Gauss-Newton-method,<sup>18,19</sup> which may be seen as a specific sequential quadratic programming (SQP) method. It is tuned towards the minimization of least-squares-problems, which is what we want.

An advantage of the above described formulation of the constraint function (1) is that the landmarkinformation are resolution independent, see Papenberg et al.<sup>9</sup> We are going to use this property while applying a multilevel-strategy<sup>20</sup> to solve the registration problem. To apply a multi-level strategy means to attack the problem by first solving it on a low resolution level. Then we use the obtained solution as initial guess on the next finer level and so on, until the highest resolution level is reached. One benefit of this method is the fact that most of the registration work is done on the broad resolutions, which means less iteration steps and faster convergence on the higher, more time consuming resolutions. Another benefit is the avoidance of local minima, due to good initial guesses.

To start the whole process and to avoid local minima, we first compute an affine-linear registration based solely on the landmark information. Based on this initial solution the described multilevel-approach is started to gain solutions on every level. Where subsequently, the variational problem is attacked by the socalled *discretize-then-optimize* approach. That is, we discretize the functional  $\mathcal{J}$  followed by an optimization strategy. To generate a search direction, a linear system of equations has to be solved. The underlying Karush-Kuhn-Tucker-system (KKT-system) is indefinite. To cope with large indefinite systems and also the memory and time requirements we use the well-known MinRes-procedure.<sup>21</sup> An Armijo line search is used for computing the step length of each step with respect to an augmented Lagrangian, which penalizes steps leaving the feasible region.<sup>22</sup> The algorithm terminates when it fulfills the termination criteria described in Gill, Murray, Wright.<sup>23</sup> The method is summarized in Algorithm 1.

Algorithm 1 Landmark Constrained Image Registration
<b>Input:</b> $\mathcal{R}, \mathcal{T}$ (reference and template volumes)
$t_j, r_j$ (corresponding landmarks for $\mathcal{R}$ and $\mathcal{T}$ )
$\lambda, \mu, \alpha$ (parameter for registration process)
c (tolerance for misfit of landmarks)
calculate $y^0$ via affine-linear registration based on landmark information
for $k = low$ resolution to full resolution do
calculate $\mathcal{R}^k, \mathcal{T}^k, t^k_i, r^k_i$
repeat
$ ext{calculate } \mathcal{J}(y),   abla \mathcal{J}(y),   abla^2 \mathcal{J}(y),  \mathcal{P}(y),   abla \mathcal{P}(y)$
calculate search direction $s$ using MinRes on KKT-system
calculate step size $t$ by Armijo line search
update $y \leftarrow y + ts$
<b>until</b> optimality condition in level $k$
end for

**Output:** displacement field  $y^{\text{opt}}$ 

#### 4 Results

To demonstrate the effectiveness of the new registration method we use data from a clinical intervention. The planning-data was acquired by a abdominal CT using an contrast agent to enhance the vascular system. Delayed scans allow the illustration of portal and hepatic veins. During the surgery a Voluson 730 ultrasound machine (GE Healthcare) was used to capture the actual liver position. In Figure 1, a visualization of the pre-operative CT data (a) and a visualization of intra-operative 3D ultrasound data (b) is seen. Eight pairs of landmarks were hand chosen by the surgeon. We tested the algorithm for various cases. Here, we report on three cases which give a representative picture of the new method. The data was recorded during three different surgical interventions at the Charitè - Universitätsmedizin Berlin. We chose  $\alpha = 0.1$ ,  $\lambda = 0$ ,  $\mu = 1$  and the tolerance for the landmarks' misfit was selected to be c = 0.01. The results were computed on a grid with  $32^3$  grid points and have been interpolated to the actual data resolution. The algorithm is implemented

using MATLAB 7.7 and is not yet optimized for runtime. The averaged overall computation time on a 2 GHz Intel Core 2 duo was 94.3 sec.



Figure 2. Slices from three different ultrasound volumes (line by line) with white edges of the vessels out of the 3D planning data. First column ((a), (d), (g)) after rigid pre-registration, second column ((b), (e), (h)) after thin plate spline registration, third column ((c), (f), (i)) result of the new inequality constrained approach.

In Figure 2 we show the data of all cases. To visualize the results we pick a slice out of the volumetric

data and overlay the reference image (US) by highlighted image edges of the template (CT). To evaluate our hybrid algorithm based on landmarks and intensity values we compare its results to a pure state of the art landmark-based approach. To this end we choose a thin plate spline registration.<sup>24</sup> Corresponding slices of both algorithms are presented. The tests were performed on different data sets. For each case three images are shown line by line: after a rigid pre-registration (see (a), (d), (g)), a thin plate spline based registration (see (b), (e), (h)) and the results of our new approach (see (c), (f), (i)). It is apparent that the vessels in the center are much better aligned by the new approach than by the thin plate spline-approach.

Although the solution varies with the choice of c we picked the parameter c in such a way that the constraints become active in each test case. However, in our future work we will present experiments describing the influence of this parameter.

## 5 Conclusion

We present a novel semi-automatic procedure for the registration of pre-operative CT data with intraoperative ultrasound data. The new approach takes into account, that some of the hand selected landmarks might have spatial inaccuracies. Due to its clever formulation as a constrained optimization problem, there is no need for a somewhat non intuitive parameter tuning, as for example in penalty-term based approaches. Nevertheless the overall scheme nicely converges, even though the landmark information is not perfect. This underscores the value of the more realistic modeling of the registration procedure within a real surgery.

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