Feasibility of rigid and deformable liver registration for MRI-guided HDR brachytherapy

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Abstract

In interstitial HDR brachytherapy, liver cancer is treated by internal radiation, requiring percutaneous placement of applicators within the tumor guided by interventional MRI. A mapping of pre-planning information onto interventional data would reduce the radiologist’s cognitive load during the intervention. We performed a comprehensive investigation of available rigid and deformable volume-to-volume (V2V) and volume-to-slice (V2S) registration methods. Our objective was to find out if existing methods would be feasible for this clinical application and at which points there is need for further research. We compared about 400 combinations of transform, metric, and optimizer on 3D and 2D MRI sequences of eleven patients. The best rigid V2V-combination yielded Dice coefficients of 0.90±0.03 and 0.28±0.18 for liver and tumor, respectively. The best subsequent deformable V2V-registration improved results to 0.94±0.01 and 0.55±0.12. Regarding V2S-registration, no significant improvements were found for rigid, affine, and deformable registration over a purely scanner based initialization.

Keywords: HDR Brachytherapy, Liver Intervention, Magnetic Resonance Imaging, Image Registration

1 Problem

Percutaneous interstitial high-dose rate brachytherapy with ¹⁹²Iridium (∼¹⁹²Ir-HDR-BT) is a minimally-invasive cancer treatment based on internal radiation. The ¹⁹²Ir point source is placed inside surgically inoperable body tumors via flexible, bio-compatible plastic catheters (applicators) by means of an afterloading machine. Like radiofrequency or microwave ablation, ¹⁹²Ir-HDR-BT requires only short hospitalization periods [1]. Application areas of HDR-BT are prostate [2], breast [3], lung [4], or liver tumors [5]. The placement of applicators may be guided by ultrasound, X-ray computed tomography (CT-fluoroscopy), or by magnetic resonance imaging (MRI).

We focus on MRI-guided ¹⁹²Ir-HDR-BT of liver tumors, which involves three types of MR images: a 3D pre-planning image (3D pre-plan) and a number of interventional 3D and 2D images. The 3D pre-plan is used for virtual applicator placement and subsequent hybrid inverse planning optimization to maximize radiation exposure of the tumors and to minimize exposure of organs at risk and the healthy liver parenchyma. It is acquired one/a few days before treatment with the patient in supine position (see Fig. 1(a)). During the intervention 3D images are acquired at the beginning, in between, and after applicator placement (see Fig. 1(b) and 1(d)) while the applicator placement itself is guided by 2D images that are acquired in arbitrary slice orientation (see Fig. 1(c)). During intervention, the patient may be placed in decubital position to achieve safe access to the tumor and to ease the handling of the applicators within the scanner’s bore.

In order to reproduce the optimal applicator geometry determined during pre-planning, the interventionist has to mentally map the planned applicator trajectories from the 3D pre-plan to the interventional 3D and 2D images. This procedure is not only inaccurate but also cumbersome and time-consuming. Hence, a computer-assisted transfer of pre-planning information (e.g. optimized applicator trajectories) from the 3D pre-plan onto the interventional images would greatly support the interventionist and potentially increase the safety and efficiency of ¹⁹²Ir-HDR-BT. Such a transfer requires accurate and fast volume-to-volume (V2V) and volume-to-slice (V2S)-registration. The challenges of such registration tasks are, in particular, liver deformations due to different patient positioning or breathing and intensity inhomogeneities, image noise, low resolution, as well as a small field of view (FOV) due to the fast acquisition of the 2D interventional images with single loop surface coils, commonly used for interventions (see Fig. 1(c) or 4(a)). The registration time should not exceed two minutes, because applicator implantation is a time critical procedure.
Regarding V2V-registration, the few related works suitable for interventional liver data, are either limited to rigid registration [6], require CT data [7] [8] [9] [10], conclude with “unsatisfactory results” [11], or used complex strategies that alternate between bias field correction and deformable registration in a multi-resolution scheme [12]. Regarding V2S registration, related works are mainly focused on rigid registration of CT-fluoroscopic liver data [13] [14] [15] or on deformable registration of lung CT data [16] [17]. With regard to interventional MRI, V2S-registration was only applied for prostate tumors [18] or cardiac interventions [19], to the best of our knowledge.

In this study, we perform a comprehensive investigation of rigid and deformable registration approaches, which are freely available in ITK1. Our main objective is to find out if existing state-of-the-art registration methods are feasible for MRI-guided $^{192}\text{Ir}$-HDR-BT and if not, at which points there is still need for further research.

![Fig. 1: Different MR image types acquired prior to and during MRI-guided $^{192}\text{Ir}$-HDR-BT of liver tumors: (a) 3D pre-planning image; 3D interventional images before (b) and after (d) applicator placement; (c) 2D interventional image acquired in arbitrary slice orientation](image)

## 2 Material and Methods

ITK offers a variety of different transforms2, metrics3, and optimizers4, which results in a huge number of transform-metric-optimizer (TMO) combinations. First, we tested different TMO combinations for V2V-registration. Poorly performing TMOs were excluded successively during our experiments. Moreover, we tested different TMO combinations for V2S-registration, eliminating again successively poorly performing TMOs. Default settings were used in most cases for transform-, metric-, or optimizer-specific parameters.

The experiments were carried out on data of eleven patients with surgically inoperable liver tumors. The dataset of each patient comprises a pre-planning 3D spoiled turbo gradient echo sequence: Gd-EOB-DTPA3-enhanced T1-weighted High Resolution Isotropic Volume Excitation (eTHRIVE) sequence with spectrally adiabatic inversion recovery fat suppression and sensitivity encoding acceleration (Philips Intera 1.5T with TR = 4.0 - 4.1 and TE = 2.0) and one to three 3D interventional THRIVE images (Philips 1.0T Panorama HFO with TR = 3.8 - 4.6 and TE = 1.8 - 2.3). Both types of images were acquired with a voxel size of 0.98 x 0.98 x 3 mm and 1.19 x 1.19 x 2.5 mm, and a FOV of 315 x 315 x 240 mm and 285 x 285 x 210 mm, respectively. To simplify processing, we downsampled all images to yield isotropic voxels of 2.5 mm. Tumor targeting was facilitated with 2D T1w fast field echo (T1-FFE) images (TR = 10.4 and TE = 6.0), acquired in mutually orthogonal, arbitrary slice orientations with a frame rate of (1/6), resulting in about 550 image slices per patient with a resolution of about 1.1 x 1.1 x 8 mm and a FOV of 350 x 350 x 8 mm.

For validation of the registration, a radiologist with >5 years of experience in interventional MRI created groundtruth data comprising manual segmentations of the liver surface for both, 3D and 2D images as well as segmentations of the tumor tissue in the 3D images. To evaluate the TMO combinations, we assessed the segmentation volume overlap between registered images by means of the Dice coefficient (DC) for liver and tumor tissues. Furthermore, we estimated the average and worst-case surface-to-surface distance by Euclidean distance (ED) and Hausdorff distance (HD), respectively. All experiments are carried out on consumer hardware comprising an AMD FX™-6300 @ 3.5 GHz and 8GB RAM.

### 2.1 Volume-to-Volume Registration

V2V-registration was performed between the 3D pre-planning eTHRIVE images (moving) and the 3D interventional THRIVE images (fixed; acquired before and after applicator placement). After we initialized both

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1 “The Insight Segmentation and Registration Toolkit”, www.itk.org
3 https://itk.org/Doxygen/html/group__ITKOptimizers.html
4 https://itk.org/Doxygen/html/group__ITKOptimizers.html
5 Gd-EOB-DTPA is a hepatocyte-specific contrast agent excreted partially via the bile, which produces strong signal enhancement in healthy liver parenchyma in T1-weighted (T1w) hepatobiliary phase images (~20 min. post injection) while signal is absent in focal liver lesions.
images according to their geometrical center, a rigid registration was used to model the differences in patient positioning between the images. Artifacts caused by implanted applicators were negligible for the rigid registration, because they affected only small portions of the interventional data. Bias field artifacts were only imposed on parts of the interventional data and thus did not impede rigid registration either. More problematic was the extensively varying signal-to-noise ratio (SNR) in the interventional images (e.g. see Fig. 3(a)) possibly causing errors if the registration process is not initialized close to the anticipated transformation. To cope with this issue, we employed a pyramidal multi-resolution registration scheme. Starting with the initial registration on a rather coarse image resolution, we refined the transformation subsequently on images of increasing resolution until full resolution was reached (downsampling factors: 1/6, 1/4, 1/2). This multi-resolution scheme proved to be stable with respect to varying noise levels, because noise cancels out on coarser resolutions, providing good initializations for registration refinement at higher resolutions.

After rigid registration, affine and deformable registrations were applied subsequently to cope with local liver deformations. For reasons of computation time, deformable registration methods could only be applied to a single, coarser resolution. In this regard, different initial downsampling factors were investigated (1/6, 1/4, 1/2) to find the best tradeoff between registration quality and computation time. Finally, about 300 different TMOs were examined for rigid, affine, and deformable V2V-registration.

### 2.2 Volume-to-Slice Registration

V2S-registration was performed between the 3D interventional THRIVE images (moving) and the 2D interventional FFE images (fixed). Since these images have slightly different intensity characteristics, we used a square root filter to normalize intensities and to deal with intensity peaks. After pre-processing, the 2D images were initialized according to their DICOM scanner coordinates providing a good starting point for further registration. Liver deformation and tumor displacement in the 2D images were mainly caused by different states of breathing during image acquisition. Hence, we examined if available rigid, affine, or deformable registration approaches would be able to compensate these deformations. Finally, about 90 different TMOs were evaluated, whereby most of the deformable registration methods were not applicable to V2S-registration.

### 3 Results

For the sake of focus, only the best TMO combinations for V2V- and V2S-registration will be discussed.

#### 3.1 Volume-to-Volume Registration

**Rigid Registration** With regards to quality and computation time, best rigid registration TMO results were achieved employing a 3D Euler transform in combination with normalized cross correlation (NCC) and gradient descent (see Tab. 1). Although Mutual information (MI) as well as NCC metrics achieved similar mean DC, ED, and HD values of 0.90, 3.32 mm, and 17.34 mm for the liver and 0.28, 4.31 mm, and 10.99 mm for the tumor tissue, standard deviation DC values of NCC (±0.03) were smaller than those of MI (±0.05). Thus, NCC was chosen for the best TMO combination (used in Tab. 1), performing within 4.4 s on average. Exemplary results of the rigid registration can be seen in Figure 2(b), whereby the initial alignment of both images is shown in Figure 2(a). Since affine registration did not perform significantly better than rigid registration, it was neglected as initialization for the deformable registration.

**Deformable Registration** Based on the best performing rigid TMO combination (3D Euler – NCC – gradient descent), various deformable registration methods were applied to improve the tumor alignment. Most deformable

<table>
<thead>
<tr>
<th>V2V</th>
<th>Average Runtime [s]</th>
<th>DC</th>
<th>ED [mm]</th>
<th>HD [mm]</th>
<th>DC</th>
<th>ED [mm]</th>
<th>HD [mm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>-</td>
<td>0.44 ± 0.21</td>
<td>20.9 ± 8.6</td>
<td>58.7 ± 23.2</td>
<td>0.01 ± 0.05</td>
<td>40.2 ± 20.3</td>
<td>51.7 ± 22.2</td>
</tr>
<tr>
<td>Bounds</td>
<td>-</td>
<td>0.90 ± 0.02</td>
<td>-</td>
<td>-</td>
<td>0.41 ± 0.23</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Rigid</td>
<td>4.4</td>
<td>0.90 ± 0.03</td>
<td>3.3 ± 0.8</td>
<td>17.3 ± 4.6</td>
<td>0.28 ± 0.18</td>
<td>4.3 ± 1.7</td>
<td>11.0 ± 3.6</td>
</tr>
<tr>
<td>Affine</td>
<td>10.6</td>
<td>0.91 ± 0.03</td>
<td>3.0 ± 0.9</td>
<td>17.1 ± 5.9</td>
<td>0.36 ± 0.22</td>
<td>3.9 ± 3.1</td>
<td>9.3 ± 4.4</td>
</tr>
<tr>
<td>DispField  (1/3)</td>
<td>26.4</td>
<td>0.94 ± 0.01</td>
<td>1.9 ± 0.4</td>
<td>15.1 ± 4.0</td>
<td>0.55 ± 0.12</td>
<td>2.2 ± 0.8</td>
<td>7.2 ± 2.8</td>
</tr>
<tr>
<td>DispField  (1/2)</td>
<td>144.3</td>
<td>0.95 ± 0.01</td>
<td>1.6 ± 0.4</td>
<td>16.0 ± 5.3</td>
<td>0.61 ± 0.13</td>
<td>1.8 ± 0.6</td>
<td>6.1 ± 2.0</td>
</tr>
</tbody>
</table>

Tab. 1: Final results of our best TMO combinations for V2V-registration. For DispField, the initial downsampling factor is given in brackets. The upper limits for rigid registration and volume preserving deformable registration of segmentation masks are indicated in the row “bounds”. 
methods were computationally expensive and thus inappropriate for a time critical clinical application. For B-Spline transforms, limited-memory Broyden-Fletcher-Goldfarb-Shanno (LM-BFGS) optimizers worked in a reasonably short amount of time. Best deformable B-Spline registration results were achieved using an initial down-sampling factor of 1/4 and a mesh grid size of 3x3x3 in combination with LM-BFGS and ANTs6. With this TMO combination, a liver DC of 0.92 and a tumor tissue ED of 3.6 ± 1.2 mm could be achieved in about 56 s on average. Finite element based registrations failed in nearly all of our experiments by producing arbitrary deformations. In this context, we evaluated a huge number of different parameter sets without success. Overall the best TMO combinations involve a displacement field transform (DispField) – which performs a Gaussian smoothing of the displacement field after adding the update array – in combination with ANTs metric and gradient descent optimizer. With respect to this TMO, several initial downsampling factors were tested to find the optimal tradeoff between registration quality and computation time. Best results could be achieved using factors of 1/3 and 1/2, which results in liver DC values of about 0.94 and 0.95, tumor tissue EDs of 2.2 ± 0.8 mm and 1.8 ± 0.6 mm, and computation times of 26 s and 144 s on average, respectively (see Tab. 1). Rigid and deformable registration results are shown in Figure 2.

3.2 Volume-to-Slice Registration

Rigid Registration Table 2 shows briefly summarized the results of our best performing TMOs for V2S-registration. For rigid and affine registration, several TMO combinations perform equally well, i.e. a 3D Euler, a 3D versor, and a quaternion-based transform in combination with MI or ANTs and LM-BFGS or gradient descent. All registrations yielded comparable DC, ED, or HD values and could not improve the initial values (see Tab. 2). In a few cases, rigid registration was able to improve the initialization overlap (see Fig. 3) but we did not find substantial improvement in the majority of cases, because of a huge number of failed registrations.

Deformable Registration With regards to deformable V2S-registration, most of the methods (e.g. FEM, DispField) are not applicable without extensive code modifications. B-Spline based transforms proved to be the most suitable for our problem. In this context, the ANTs metric in combination with LM-BGFS performed best, however the final liver DC and ED values indicated that the improvement of the initialization was not pronounced (see Tab. 2).

<table>
<thead>
<tr>
<th>V2S</th>
<th>Initial</th>
<th>Rigid</th>
<th>Affine</th>
<th>B-Spline</th>
<th>DispField</th>
<th>FEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Runtime [s]</td>
<td>~ 1</td>
<td>~ 1</td>
<td>~ 1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>DC</td>
<td>0.91 ± 0.04</td>
<td>0.92 ± 0.05</td>
<td>0.91 ± 0.04</td>
<td>0.92 ± 0.03</td>
<td>Failure</td>
<td></td>
</tr>
<tr>
<td>ED [mm]</td>
<td>3.9 ± 1.5</td>
<td>3.5 ± 1.6</td>
<td>3.8 ± 1.6</td>
<td>3.5 ± 1.4</td>
<td>Failure</td>
<td></td>
</tr>
</tbody>
</table>

6 An NCC approach using a small neighborhood for each voxel to compute metric values between two images [19].
4 Discussion

With regards to rigid V2V-registration the tested TMO combinations yielded results which compared well to the upper bounds of the maximum achievable result quality (see Tab. 1). The differences of the tested combinations were rather small, e.g., the average liver DCs differed by 0.02, while it was 0.48 initially. Therefore, we conclude that the tested TMOs are sufficiently close to the optimal transformation and that significant improvement of the performance cannot be gained without additional degrees of freedom from deformation. In this context, we observed that an additional affine transform did not improve the registration quality but increased computation times due to more degrees of freedom during optimization.

The relatively low tumor DCs need to be interpreted with caution: small misalignments together with likewise small ground truth imperfections may result in large differences in DCs solely because of the small tumor sizes in our data (1.71±1.61 ml on average). Furthermore, an upper bound value of 0.81 ± 0.14 for the volume preserving deformable registration of the tumor segmentations indicates that manual segmentation of small tumors in different MR images is a challenging task, even for an expert radiologist.

For deformable V2V-registration, the best TMO combination (DispField+ANTS+gradient descent) achieved promising results in terms of liver registration quality. ANTs probably performs better than other metrics because it computes metric values locally, which compensates for intensity inhomogeneities in the interventional images. Although our results are promising, final DC, ED, and HD tumor values indicate that there is still room for improvement in deformable registration. Even our best TMO combinations for deformable V2V-registration have limitations in exceptional cases with extensive noise in the interventional 3D images (see Fig. 4(a)). In such cases, additional shape information would be needed for accurate registration. Moreover, deformable registration could be improved by using a multi-resolution approach, however, time constraints should be kept in mind.

The best tradeoff between registration accuracy and computation time can be achieved with an initial downsampling factor of 1/3. The combined rigid and deformable registration performs within 30.8 s on average (4.4 s for rigid and 26.4 s for deformable registration), which meets the previously defined requirements for a clinical application.

In terms of V2S-registration, we conclude that the evaluated TMO combinations did not significantly improve the registration accuracy compared to an initialization using the scanner coordinates of 2D interventional image slices. Furthermore, the results were not accurate or robust enough for a clinical setting. The high standard deviations indicate that there are many cases, where rigid or deformable registration methods worsen the results of initialization and cannot compensate the liver deformations caused by breathing. Reasons for these findings could be: lack of information in the 2D images, extensive intensity inhomogeneities, or strong noise in the 3D interventional images (see Fig. 4(a)).

5 Conclusion

Our comprehensive feasibility study of rigid and deformable V2V- and V2S-registration of the liver for MRI-guided 192Ir-HDR-BT shows that rigid V2V-registration of the liver works well for clinical data in terms of registration quality and computation time, i.e., by using a 3D Euler transform in combination with NCC and gradient descent. Our best deformable V2V-registration approach – a Gaussian displacement field transform combined with ANTs and gradient descent – achieves high accuracy with respect to the liver volume overlap and Euclidean distances between liver surfaces. However, tumor overlap accuracy could potentially be improved by further research in this area.

With regard to V2S-registration, we conclude that registration fails with current state-of-the-art registration methods and needs to be improved. Future work could include a kind of adaptive breathing compensation registration framework. Namely, a registration, which is continuously performed and once both images (interventional 3D image and 2D image slices) have identical states during breathing cycle, provides a feedback to the interventionist.
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References