Automatic Alignment of Pre- and Post-Interventional Liver CT Images for Assessment of Radiofrequency Ablation

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\section*{ABSTRACT}

Image-guided radiofrequency ablation (RFA) is becoming a standard procedure for minimally invasive tumor treatment in clinical practice. To verify the treatment success of the therapy, reliable post-interventional assessment of the ablation zone (coagulation) is essential. Typically, pre- and post-interventional CT images have to be aligned to compare the shape, size, and position of tumor and coagulation zone. In this work, we present an automatic workflow for masking liver tissue, enabling a rigid registration algorithm to perform at least as accurate as experienced medical experts. To minimize the effect of global liver deformations, the registration is computed in a local region of interest around the pre-interventional lesion and post-interventional coagulation necrosis. A registration mask excluding lesions and neighboring organs is calculated to prevent the registration algorithm from matching both lesion shapes instead of the surrounding liver anatomy. As an initial registration step, the centers of gravity from both lesions are aligned automatically. The subsequent rigid registration method is based on the Local Cross Correlation (LCC) similarity measure and Newton-type optimization. To assess the accuracy of our method, 41 RFA cases are registered and compared with the manually aligned cases from four medical experts. Furthermore, the registration results are compared with ground truth transformations based on averaged anatomical landmark pairs. In the evaluation, we show that our method allows to automatic alignment of the data sets with equal accuracy as medical experts, but requiring significantly less time consumption and variability.

\textbf{Keywords}: image-guided therapy, registration, intervention, radiofrequency ablation

1. \textbf{DESCRIPTION OF PURPOSE}

Percutaneous radiofrequency (RF) ablation is a minimally invasive, image-guided therapy for the treatment of primary and secondary liver tumors.\textsuperscript{1} Electric energy is locally induced via electrodes; the tumor cells are destroyed by a local resistive heating of the tissue. RF ablation therapy has become one of the most important methods if surgical resection is contraindicated. To assess the success of the treatment, pre- and post-interventional images are typically acquired to compare tumor and coagulation. Complete tumor destruction is assumed, if the tumor area is completely enclosed by the ablation zone, which is identified by a lack of contrast enhancement. The ablation failed if residual tumor tissue is detected outside the thermal necrosis. As a standard clinical assessment procedure (cf. Figure 1), pre- and post-interventional CT images are used to visually compare the shape, size, and position of tumor and coagulation.\textsuperscript{2}

To assist the clinicians with a fused visualization and a robust quantification, both areas must be segmented within the corresponding image data. Due to the varying acquisition times and accordingly different coordinate systems of the pre- and post-interventional images, a registration is required to allow a fused visualization and a quantification of possible residual areas. For that, we utilize an automatic rigid registration of the post-interventional template image onto the pre-interventional reference image in a local region of interest (ROI)

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around the tumor. Heizmann et al.\(^3\) describe in their study that a rigid alignment of the preoperative data can give satisfactory accuracy in a ROI in spite of inevitable deformation of the liver parenchyma. Thus, this procedure was considered sufficient for our purpose.

Weihusen et al.\(^4\) describe in their work a software tool which supports visual comparison of pre- and post-interventional RFA data sets. For the comparison, the data sets have to be aligned by the physician utilizing a manual rigid registration procedure.\(^5\) To ease the comparison, a color coding scheme within a 3D rendering is utilized.

In an early work, Carillo et al.\(^6\) utilize a manual and semiautomatic rigid registration method to align MR liver images acquired before and after RFA therapy. To assess the accuracy of the proposed methods, distances between iso-contours in selected regions of interests are measured in 2D and a registration error is estimated in 3D. The authors report a registration accuracy of approximately 3 mm, which is the typical voxel size of their data.

Niculescu et al.\(^7\) present a non-rigid registration of the liver for the assessment of the tumor response to RFA. A liver surface-based non-rigid method for tracking the tumor across pre- and post-interventional CT images is proposed. The volumetric deformations are modeled utilizing a linearly elastic finite element method. However, surface matching is in most cases not accurate enough when dealing with lesions in the center of the liver.

In a recent work, Kim et al.\(^8\) evaluate a method for nonrigid registration of pre- and post-interventional CT data sets. 31 cases are evaluated to determine the effect on the safety margin assessment after RFA of the liver. The registration accuracy is validated by setting pairs of corresponding landmarks on the pre-interventional data sets and registered post-interventional data sets, and calculating the average distances. The authors report a mean difference of 1.3 mm and conclude that the registration method is an accurate and useful technique for assessing the safety margin after RFA. Because smoothness and volume preservation of the deformation is not reported, analyzing the results in terms of quantification is not possible.

Generally, the use of nonrigid registration is critical because the transformation after registration is difficult to understand, and a manual correction by the physician is not provided. Effect in size and shape can hardly be assessed reliable, hence, a robust quantification of the registered ablation zone and the lesion can only be achieved by rigid transformations. Due to these limitations, we utilize rigid transformations for the registration of pre- and post-interventional data sets. Based on segmentation masks of the pre-interventional lesion and the post-interventional thermo necrosis, a fully automatic workflow to align the data sets is proposed. In order to support the physician during assessment of the therapy success, the aligned lesion masks are utilized to facilitate advanced visualization and quantification techniques.\(^9\)

![Diagram](image.png)

**Figure 1.** The goal of radio frequency ablation is the destruction of all tumor cells. By evaluating the tumor coverage, the ablation result is verified in the assessment stage after the intervention.

### 2. METHODS

#### 2.1 Preprocessing

The initial preprocessing step is the segmentation of the tumor and coagulation areas. We use a semi-automatic, morphologically based region-growing algorithm\(^10\) that has proven to be robust and of good performance. For that, the user has to draw a stroke across the lesion, which is utilized for histogram analysis. Based on the drawn
stroke, the calculation of the segmentation mask is performed automatically. Because multiple segmentation masks can be created, corresponding lesions are connected by the user to unique tumor–coagulation pairs, which are assessed consecutively.

Subsequently, a region of interest (ROI) is defined from the segmentation masks’ centers of gravity (cf. Figure 2). The registration process is initialized by automatic position matching of the centers of gravity of both lesions. The resulting transformation is only applied in the ROI of both lesions to fulfill local rigidity constraints. Figure 3 illustrates the registration workflow.

![Registration Workflow](image)

Figure 2. Image (a) illustrates a pre-interventional tumor located in the vicinity of the inferior vena cava (IVC). A region of interest with uniform distance to the segmented tumor’s center of gravity is automatically defined. Analogously, in (b) the post-interventional coagulation is segmented and the corresponding region of interest calculated.

2.2 Manual Rigid Registration

For comparison of our method, we provide an intuitive manual registration workflow, which can be used without extensive training. The post-interventional template image is transformed by the user in order to match the anatomical features in the vicinity of the lesion of the pre-interventional reference image. To allow a fused visualization of both data sets, three fusion modes are available:

- An additive color scheme is used to allow a visually separation of the data sets. The reference image is colored in light blue and the template image in the complementary color, i.e. orange. We chose those colors for the reason that areas of different intensities stay colored and areas with similar intensities become grey.
- Also, both colors can be merged be linear interpolation of the color values. For that, a slider allows the user to linearly merge between pre-interventional reference image and post-interventional template image.
- In the last mode, both data sets are merged by linear interpolation, but instead of utilizing colored look-up tables, the original image intensities are displayed.

In addition to the 2D slice views, we also integrate a three-dimensional multi-volume rendering of both ROIs. In the volume rendering, we emphasize the liver vessels of both data sets utilizing an automatically determined appropriate transfer function and also apply the color schemes described above.

The manual registration of the data sets is performed in the orthogonal 2D slice views performing simple mouse interactions. The template image can be grabbed and translated in all three main directions. Furthermore, we integrate an image menu which is superimposed onto the image data and allows to translate the data set step by step using buttons for translation and also for image rotation. The image menu can be displayed at the current mouse pointer and defines the rotation center of the template data set. If the template image is interactively transformed by the user, the corresponding data set in the volume rendering is also immediately transformed, allowing for a fast exploration of the correlation of vascular structures. If the user is not satisfied with the registration result, the transformation may be reset to the initial matching of the centers of gravity.
As a pre-registration step, the regions of interests of both lesions are overlaid by matching the positions of the corresponding center of gravities. Subsequently, a rigid registration is performed to match the anatomical features around the lesions such as vessels. For the automatic registration algorithm, both lesions are masked out of the anatomical images.

### 2.3 Automatic Rigid Registration

Similarly to the manual registration, the preprocessing steps presented in Section 2.1 are also utilized for automatic registration. The input images for the algorithm are transformed by the initial position matching of the centers of gravity of both lesions and clipped by a ROI of both lesions’ vicinities to fulfill local rigidity constraints.

To prevent the registration algorithm from matching both lesion shapes instead of the surrounding anatomy, we specify a registration mask. For that, the pre-interventional lesion mask is dilated utilizing a morphological operation and subsequently inverted. Thus, the registration algorithm uses only a subset of the pre-interventional image ROI for similarity calculation.

For further exclusion of anatomical structures such as ribs or neighboring organs from the similarity calculation, a rough liver segmentation is computed automatically. With no need to delineate exact liver boundaries, this coarse segmentation is based on the observation that liver tissue mainly contributes to the upper parts of the image’s histogram. Image points with gray values between the last peak in the histogram ($v_1$) and the 95%-quantile ($v_2$) are amplified by multiplication with a Gaussian function with expectation value $\mu = \frac{v_1 + v_2}{2}$ and standard deviation $\sigma = \frac{v_1 - v_2}{2}$. By subsequent thresholding and morphological closing, a mask can be obtained that excludes bones and other abdominal organs. Using this kind of mask, the registration is significantly faster and more robust.

To compute the complete transformation, we utilize an automatic registration algorithm based on the Levenberg-Marquardt optimization scheme\textsuperscript{13} using the Local Cross Correlation (LCC) similarity measure.\textsuperscript{14} For a complete overview of the used registration framework, we refer the reader to the work of B"ohler et al.\textsuperscript{15}

### 2.4 Estimation of the Ground Truth Registration

To assess the accuracy of the rigid registration, we present a rigid landmark matching method. For that, a physician has to define at least 3 landmarks around the lesion in the reference data set by clicking into the 2D viewer. Subsequently, the corresponding landmarks in the template image have also to be determined. Because manual determination of landmarks is inaccurate, further landmarks are specified by additional medical experts. For that, the reference landmarks of the initial landmark set are shown, and each medical expert has to specify the corresponding landmarks in the post-interventional template data set.

Consequently, we have multiple corresponding post-interventional landmarks for each registration case and pre-interventional landmark. To increase the robustness of the landmark match, we eliminate outliers and calculate the median landmark from the remaining landmarks. For that, the center of gravity of all landmarks, matched to a single anatomical feature is calculated. Further, the median distance of all landmarks to the center is computed. A landmark is specified as an outlier, if its distance to the center of gravity is larger than 1.6 times the median distance. Subsequently, all outliers are eliminated, and a new center of gravity is
calculated from the remaining landmarks. Thus, the new center of gravity is the stable template landmark of a pre-interventional reference landmark set. Figure 4 illustrates the elimination of an outlier and the calculation of the resulting average landmark. Figure 5 shows a 3D rendering of the tumor and surrounding vessels. The five sets of landmarks are placed by the experts onto features of the vessels, whereas each landmark is represented by different colored spheres. The larger white spheres represent the averaged landmarks after outlier elimination.

3. RESULTS

To evaluate our automatic registration method, we align 41 pre-interventional lesions with the corresponding post-interventional coagulations that have been recorded before and after the RFA therapy, respectively (cf. Figure 6). For statistical analysis, the elapsed computation time and the transformation matrix are stored for every case. To assess the computation time and the accuracy of the resulting transformations, the optimal registration is calculated, and all data sets are registered by four medical experts manually.

In a first step, we calculate the optimal registration for all data sets. For that, five experienced medical experts specified 4-5 landmark pairs, from which robust landmarks are calculated, as described in Section 2.4. We measured the average distance to the center of gravity per landmark set. The median of all averaged distances is 2.71 mm, the minimum 0.73 mm, and the maximum 33.57 mm. Finally, the optimal registration of the landmarks is calculated using an Iterative Closest Point (ICP) algorithm leading to a mean Euclidean distance of 2.29 mm and a median Euclidean distance of 2.16 mm. We denote the resulting distance after ICP landmark matching as the system error of the rigid registration, which is related to the general variation of landmark positioning by humans and the remaining non-linear transformation fraction of the deformation. The small value of the system error supports the validity of our rigid approach for rigid image data alignment.

In a second step, the 41 data sets are registered manually by four medical experts, independently. Again, the processed time and the transformation matrix are stored for every data set. To compare the result of the automatic registration method with the optimal rigid registration and the manual registration, the averaged template landmarks are transformed with the stored registration matrices. After the transformation, the average Euclidean distance from the transformed template landmark set to the reference landmark set is measured for every case.
Figure 6. Screenshot (a) shows case 27 after matching of the centers of gravity. Both lesions are aligned but the surrounding vasculature is mismatched (11 mm). After automatic registration in the region of interest around the lesions (b), the vasculature is matched resulting in a pre-post landmark distance of 4 mm.

For all medical experts, a mean distance of 5.46 mm and a median distance of 4.60 mm is measured. The mean distance after automatic registration is 6.24 mm and the median distance is 3.95 mm. The mean distance of the automatic method is higher than all the averaged distance of all experts, but nevertheless slightly smaller than the worst medical expert’s mean accuracy. The median distance of our method is lower than the median of all medical experts but roughly 2 mm less accurate than the optimal landmark registration. However, the measured distances indicate that our method is at least accurate as the registration of the medical experts. Regarding the minimal distance of the optimal landmark registration, the automatic registration is 28% less accurate than the system error, and the averaged group of medical experts almost 50% less accurate. In 27% of the cases, the automatic method is more accurate than the manual registration performed by the best medical expert, in 24% the automatic method is less accurate as the experts, and in 49% the method is in the distribution of the medical experts accuracy (in 29% the distance is lower than the median, in 20% higher). Figure 7 illustrates the average distance of all registered data sets.

Figure 7. The box plot illustrates the average distance of all registered data sets. From left to tight, the distance from the initial position matching, medical expert 1 - 4, the automatic method, and the optimal registration after ICP matching of the landmarks.

Furthermore, we compare the time consumption of the presented registration methods. The mean processing time of all medical experts for all cases is 333 seconds and the median time is 283 seconds. We also measure the computation time for the automatic algorithm, including the calculation of the proposed registration mask. Note that the processing time for data loading and the preprocessing steps (lesion segmentation and ROI calculation) is not included in the measurement of both methods. The mean calculation time of the automatic registration
algorithm is 45 seconds and the median is 32 seconds. Thus, the automatic registration method is significantly faster than the medical experts, resulting in a mean $7 \times$ speedup and a median $8.8 \times$ speedup, respectively. With increasing computing performance of the hardware and constant processing time of the medical experts, an even higher speedup can be expected in the future.

Additional observations are, that without our masking method, the landmark distance after automatic alignment is significantly greater (mean 8.79, median 6.7 mm). Furthermore, the outliers of our automatic method (cases: 8,15,16,17,19,20,33,35,39; cf. Figure 8) all have lesions that are peripherally located (close to the liver’s capsule). The worse registration matches are related to of inadequate registration masks, which lead the algorithm to also calculate the similarity of extra-hepatic neighboring organs and try to align them. As we have discovered the cause of this, we will investigate how the mask calculation can be improved to reach a higher robustness, even for peripheral lesions. Nevertheless, we believe that users are easily able to detect those failed registration results and may correct the alignment manually.

**Figure 8.** Box plot of all 41 cases. The boxes illustrate the landmark distances of the manually registered data sets. The dots show the distance per case after ICP matching of the landmarks and the triangles the distance of the automatic registration method.

### 4. CONCLUSIONS

In this work we describe a method to perform an automatic rigid alignment of pre- and post-interventional CT image data for the assessment of radio frequency ablation and compare it with the manual expert registration. In an evaluation of 41 data sets with four medical experts, we measure the time effort and the accuracy of our automatic method and compare it with the result of the medical experts as well as the minimal distance after landmark matching.

Our automatic method reaches an accuracy in the range of the medical experts’ registration transformation with significantly less time. Although the variance of the resulting distance after automatic registration is higher than the measured distance from the medical experts, we show that the average distance is slightly smaller. Thus, we believe that the automatic rigid registration is a useful tool to fuse pre- and post-interventional data
sets in a local region of interest to allow assessment of the RFA therapy success. We recommend a combination of both automatic and manual approaches, where the physician is able to manually adjust the transformation after automatic registration to achieve the optimal result.

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