Registration of Cardiac SPECT/CT Data through Weighted Intensity Co-Occurrence Priors

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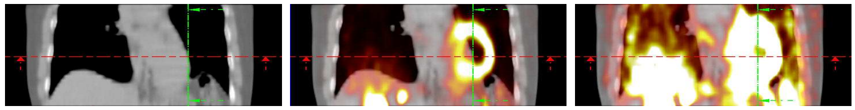
Abstract. The introduction of hybrid scanners has greatly increased the popularity of molecular imaging techniques. Many clinical applications benefit from combining complementary information based on the precise alignment of the two modalities. In case the alignment is inaccurate, then this crucial assumption often made for subsequent processing steps will be violated. However, this violation may not be apparent to the physician. In CT-based attenuation correction (AC) for cardiac SPECT/CT data, critical misalignments between SPECT and CT can lead to spurious perfusion defects. In this work, we focus on increasing the accuracy of rigid volume registration of cardiac SPECT/CT data by using prior knowledge. A new weighting scheme for an intensity co-occurrence prior is introduced to assure accurate and robust alignment in the local heart region. Experimental results demonstrate that the proposed method outperforms mutual information registration and shows robustness across a selection of learned distributions acquired from 15 different patients.

1 Introduction

The use of multi-modality imaging, especially PET/CT and SPECT/CT, in clinical practice has become more popular. Common hybrid scanners combine low resolution molecular images with anatomical context from high-resolution CT by placing both, e.g. SPECT and CT, scanners next to each other. This setup allows for a good registration between the two modalities when the imaged anatomical structures are undergoing no or little motion such as structures in the head. However, in the imaging of other body parts, critical misalignments, as shown in Fig.1, still occur significantly often due to breathing, patient motion, or motion caused by acquisition protocol restrictions [1]. An accurate registration between the two modalities is imperative to ensure the diagnostic confidence of physicians. It has been reported, for example, in the application of quantitative cardiac SPECT/CT analysis that spurious perfusion defect artifacts are introduced in the CT-based attenuation correction (AC) images of the SPECT acquisition due to misalignments. The misalignments falsify the uptake values that are utilized for diagnosis [2, 3]. Registration as preprocessing step



(a) CT (b) Window/Level 1 (c) Window/Level 2

Fig. 1. Three anterior views of a misaligned cardiac SPECT/CT data set, the CT (a), and the SPECT overlayed on CT with two different window level settings 1, (b) and (c). The figure visualizes the challenging multi-modal registration problem.

to CT-based AC SPECT cannot involve user interaction or correction. These demands may be somewhat addressed through a stringent acquisition protocol that, nevertheless, is both prone to errors and complicated to use in clinical practice. A better way of ensuring alignment is to utilize an automatic registration technique that is highly accurate and robust. In this paper, we propose a rigid registration method that is designed to address the above mentioned demands of cardiac SPECT/CT. The accuracy is achieved by incorporating weighted intensity co-occurrence priors about an accurate alignment of cardiac data. Using the joint probability distribution function (pdf) of previously registered image data as an intensity prior has been previously reported supporting for the accuracy of rigid as well as non-rigid multi-modal image registration by several research groups [4–9]. Hereby, an interesting energy minimization scheme of incorporating statistical priors was proposed as follows [7–9]:

$$E = \alpha\, E_{\mathrm{MI}} \;+\; (1-\alpha)\, E_{\mathrm{prior}}, \tag{1}$$

where E_{MI} is the MI energy and E_{prior} denotes a dissimilarity measure towards the prior information. The factor α controls the influence of the prior. Two aspects are essential for this application: The usage of a data-driven as well as a prior model-driven term to ensure robust and accurate alignment in general, and in particular the requirement of an accurate heart alignment. In the following, we are deriving a new registration method considering those aspects. The achieved accuracy of the proposed approach, that exploits prior information from cardiac SPECT/CT acquisitions, is compared to the accuracy of standard mutual information (MI) [10, 11] and a general learning-based approach [7]. This work extends previous works with the focus of applicability. Achieving higher accuracy and robustness than MI, the presented approach is not limited to the application of cardiac SPECT/CT imaging.

2 Description of Method

In order to achieve the registration accuracy and robustness needed in CT-based AC for SPECT reconstruction, several open issues need to be resolved. How does the choice of α influence the registration result and how should it be selected for this application? Secondly, is the Kullback-Leibler (KL) divergence a sufficient distance measure for joint pdfs? And the most intriguing open question: how well does the proposed scheme (1) generalize over a large pool of patients? We address those questions by deriving a new registration method that employs weigthed co-occurrence priors.

2.1 Image Registration Using Prior Knowledge

The α-influence is studied by investigating the energy behaviour, Eq.(5), while manually translating a cardiac SPECT/CT data set away from ground truth alignment. See Fig. 2(a) for results of using different α values. We note that a smaller α, i.e. more prior influence, has a smoothing effect on the overall cost function. Hereby, $\alpha = 0.2$ is observed to be a good trade-off between data driven and prior term. Decreasing the influence of MI allows to smooth out its local optima while still keeping the feature of maximizing the mutual information that both images share.

In previous work [4, 6–8] the KL divergence is used to measure the dissimilarity of two distributions. In a discrete formulation, this can be written as:

$$E_{\text{prior}} = E_{\text{KL}}(p^{T_S}, p_{\text{prior}}) = \sum_{i,j} p^{T_S}(i,j) \log\left(\frac{p^{T_S}(i,j)}{p_{\text{prior}}(i,j)}\right), \tag{2}$$

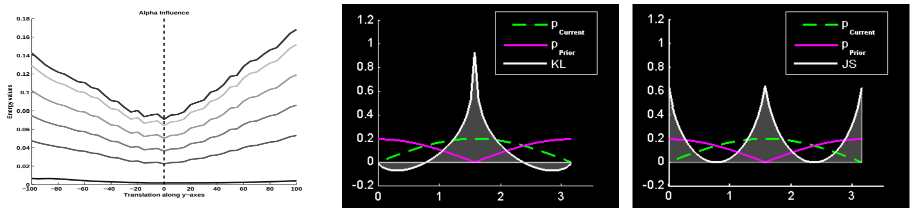
where p^{T_S} is a joint pdf of two volumes related to each other by transformation T_S, and p_{prior} is a joint pdf learned from two previously aligned volumes. Fig. 2(b) illustrates the drawbacks of KL's asymmetry using two artificial distributions. We can observe that equal dissimilarities between the distributions create differently signed contributions to KL dependent on the variables' order of comparison. A more appropriate statistical measure is provided by the Jensen-Shannon (JS) divergence. The definition for the prior energy becomes:

$$E_{\text{prior}} = E_{\text{JS}}(p^{T_S}, p_{\text{prior}}) = \frac{1}{2}\left(E_{\text{KL}}\left(p^{T_S}, \overline{p}\right) + E_{\text{KL}}\left(p_{\text{prior}}, \overline{p}\right)\right), \tag{3}$$

where $\overline{p} = \frac{p^{T_S} + p_{\text{prior}}}{2}$. Fig. 2(c) shows the properties of JS divergence. These properties are of importance when we want to emphasize organ specific contributions in the joint pdf.

Misalignments of the SPECT heart image into the lung region of CT attenuation map introduce artifacts that can lead to false diagnosis. Prior knowledge about the correct mapping within this area is important to ensure such a mapping in future registrations. A problem of the general approach in [7] is that information stored in the learned joint pdf is global and influenced by the size of the background in both volumes. Local alignments are driven by the global matching especially if the transformation model is also global. Thus, we propose a new formulation that utilizes local information stored in the learned joint pdf. The new prior energy is written as:

$$\begin{aligned} E_{\text{prior}} = \ & E_{\omega,\text{JS}}(p^{T_S},\ p_{\text{prior}}) = \omega \star E_{\text{JS}}(p^{T_S}, p_{\text{prior}}), \\ = \ & \tfrac{1}{2}\textstyle\sum_{\Omega} \omega(i,j) \left[p^{T_S}(i,j) \log\left(\frac{p^{T_S}(i,j)}{\overline{p}\,(i,j)}\right)\right. \\ & \left. + \, p_{\text{prior}}(i,j) \log\left(\frac{p_{\text{prior}}(i,j)}{\overline{p}\,(i,j)}\right)\right] \end{aligned} \tag{4}$$



(a) Alpha Influence (b) Kullback-Leibler (c) Jensen-Shannon

Fig. 2. (a) Cost function influence of α values ranging from $\alpha = 0.6$ (top curve) to $\alpha = 0.1$ (bottom curve). (b) Plot of contributions (white curve) to KL divergence between two artificial distributions (green and magenta curve). The filled area denotes the KL value. (c) Plot of contributions to JS divergence. Distribution dissimilarities have positive, limited, and comparable contributions to JS.

where $\omega \in [0, 1]^{N \times N}$, and $\star$ denotes the element-wise multiplication in the discrete case. The term ω will be chosen such that it penalizes organ specific intensity matchings that are inconsistent with a learned distribution. Hence, this penalty term introduces, to some extent, spatial information to intensity-based registration. Organ specific appearances in the joint intensity distribution can be estimated by either a segmentation or a manual outline of the organ of interest, see Section 2.2 for details on the choice of ω. A crucial assumption of ω is that penalties need to be assigned comparably for differences between prior and joint pdf, see discussion KL vs. JS. This requires a symmetric and strictly positive similarity measure on distributions. The transformation between the two data sets is obtained by solving the following equation:

$$\hat{T} = \underset{T=\{T_S, T_I\}}{\arg\min} \left[\alpha \cdot E^*_{\mathrm{MI}}(p^T) + (1-\alpha) \cdot E_{\omega,\mathrm{JS}}(p^T, p^T_{\mathrm{prior}})\right] \tag{5}$$

where $E^*_{\mathrm{MI}} = -\,\beta\, E_{\mathrm{MI}}$, and $T = \{T_S, T_I\}$ is composed of a spatial rigid transformation T_S that aligns SPECT and CT volume and an intensity transformation T_I that warps p_{prior} to p^{T_S} to compensate for patient specific intensity variations. T_I is a 1-dimensional affine transformation between the prior SPECT intensities and the intensity range of the SPECT volume to be registered. We use the sum-squared-differences criterion for the matching. In our implementation, the two transformations are estimated sequentially but the framework above also allows for concurrent estimation.

2.2 Weighted Jensen-Shannon Divergence for Statistical Priors

The weighted Jensen-Shannon (WJS) divergence, defined in Eq. (4), is introduced to ensure an organ specific intensity co-occurrence. In order to derive a suitable ω for cardiac SPECT/CT registration, we segmented the heart in the SPECT volume using the method in [12]. The penalty area of ω, i.e. white area in Fig. 3(d), is then generated by studying the joint pdfs for different alignments

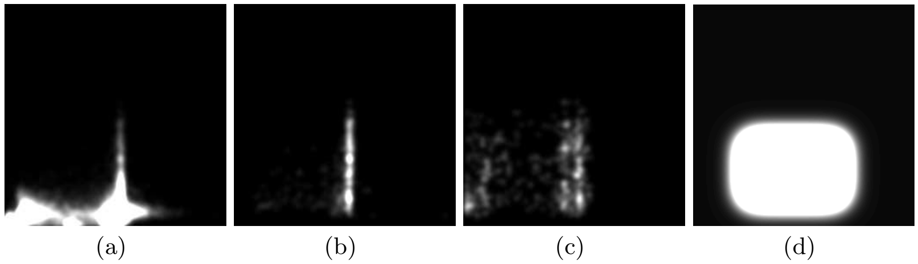


Fig. 3. Observed joint pdfs of cardiac SPECT/CT data. The distributions are displayed for (a) the full volume overlap, (b) the heart overlap, and (c) the heart overlap at misalignment. Image (d) presents the penalty term ω of Eq. (4) that is generated from the observations made in (b) and (c).

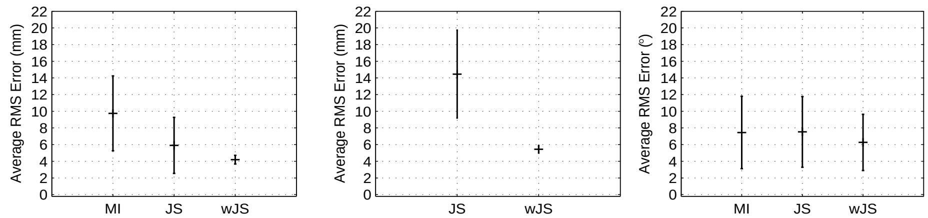
of the segmented heart with the CT, see Figs. 3(b) and 3(c). In Fig. 3, the coordinate system is defined as follows: The origin is located in the lower left corner of each image, the horizontal and vertical axis refer to CT and SPECT volume intensities, respectively. Several interesting aspects are observed:

1. The joint intensity mappings corresponding to a segmented object in both modalities occur in a limited region within the joint pdf space. This is true for all possible spatial alignments of the two volumes (Fig. 3(c)).
2. In order to ensure consistency with a learned distribution, the penalty term needs to cover all intensity pairs that the object may generate in the joint pdf. The reason is that a learned pdf not only states which intensities do match but also provides knowledge about which intensities do not match.
3. Evaluating a similarity measure on a subset of the joint pdfs eliminates unwanted influences from the unweighted learned distribution, e.g. background size dependency, global structure dependencies.

Using the defined ω, Fig. 3(d), we applied the proposed approach to a pool of cardiac SPECT/CT patients.

3 Experiments

We applied the proposed approach (WJS), MI, and a general learning-based method (JS), i.e. using eq. (3) in eq. (5), to 15 different cardiac SPECT/CT acquisitions. The data sets were acquired by a Siemens Symbia T6 scanner. The field-of-view (FOV) for SPECT data ($128 \times 128 \times 128$, $4.79 \times 4.79 \times 4.79$mm) includes the lungs, heart, and abdomen, whereas the FOV for CT data ($512 \times 512 \times 25$, $0.97 \times 0.97 \times 5$mm) includes only heart and lungs. All volumes have been manually aligned for a precise match of the heart region. From this ground truth, priors are generated and several validation studies are executed. A validation study is defined as follows: For all data sets, multiple registrations are done per data set with different initial transformations away from ground truth alignment. For each registration, the error is computed as the distance from the obtained



(a) Robustness Test (b) Prior Sensitivity Test (c) Robustness Test

Fig. 4. Comparison of error distributions for normalized MI, JS, and WJS over validation runs for translation (a) and (b), and rotation parameters(c). Using a mixture of prior and data driven model in combination with the newly weighted scheme, WJS, not only yields the best results but also generalizes well over multiple patients.

alignment to the ground truth alignment. Error mean and standard deviation of all registrations are then compared between the three methods.

Co-occurrence priors validation In order to validate how sensitiv the proposed approach is towards the chosen prior, 15 different priors were generated. We then performed two validation studies, i.e. multiple data/single prior and single data/multiple prior validation. In the first one, all patient data sets are registered using one randomly chosen prior, i.e. robustness test. In the second study, one data set is randomly chosen among all patients and registered multiple times using the available priors respectively, i.e. prior sensitivity test. Note that the learning-based approaches utilize only one prior. The results of the two studies are presented in Figs. 4(a) and 4(b).

The proposed approach is by definition not bound to any specific transformation model. Here, we apply a rigid transformation model. The initializations range from -60mm to $+60$mm in steps of 30mm in x-/z- or in y-/z- direction for translation and from $-30°$ to $+30°$ in steps of $5°$ around the z-axis for rotation. We evaluated translation and rotation initializations separately. The chosen α value for all experiments is fixed to 0.2 for WJS and to 0.75 for JS.

Correcting for intensity variations between patients and studies In Eq. (5), transformation T_I is also estimated during optimization. All 15 data sets showed minimal differences in the scaling parameter, i.e. it varied between 0.95 and 1.014, and no translational component was observed.

Validation results Figures 4(a) and 4(b) show the mean registration error for the robustness and prior sensitivity validation results w.r.t. translation parameters. Figure 4(c) displays the mean angular registration errors for the robustness test. It can be observed that both JS and WJS are more accurate on average than MI, and WJS additionally shows a small standard deviation. The proposed approach, WJS, outperforms MI and the general learning-based method, JS, with a mean translation error of 4.19 ± 0.5mm. Note that the error is smaller than a SPECT voxel. Normalized MI and JS show a mean error of more than 2 [9.74 ± 4.49mm] and more than 1 [5.9 ± 3.36mm] voxel(s), respectively. We further noticed that optimization of MI is attracted to local optima and that the

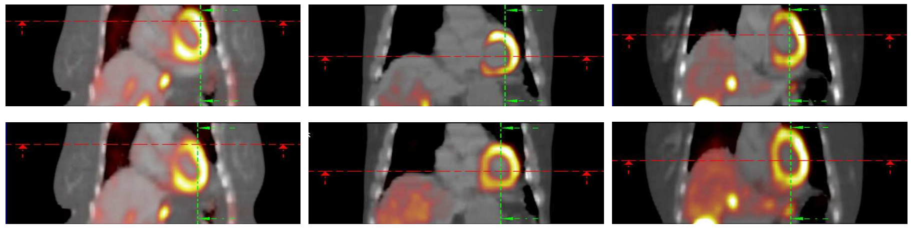


Fig. 5. Registration results for 3 out of 15 patients. The top row shows the MI result and the bottom row denotes the WJS results. The images illustrate the deviations from the optimum for MI registration and high accuracy achieved by WJS approach.

global optimum for MI deviates from the correct alignment if bright artifacts occur in CT data.[1] The learning-based methods do not get disturbed in those data sets. The rotation results also confirm the superiority of WJS over MI, see Fig. 4(c). The generally high observed mean angular error for WJS (6.2°), JS (7.5°) and for MI (7.4°) is probably due to the little structural information apparent in SPECT. The angular error is an accumulation of errors in all three axis. In addition, Fig. 6 shows a clinical scenario for registration where the scanned data is strongly mis-aligned. We were only able to register this data set using weighted intensity co-occurence priors.

The preliminary studies show that the proposed approach fullfills the clinical demands for registration accuracy of maximum 1 voxel mis-alignment in CT-based AC for cardiac SPECT, as mentioned in [2, 3], and suggest the feasibility to use the approach for automated registration in hybrid scanners.

4 Discussion and Conclusion

We have presented a robust registration approach for the application of CT-based AC of cardiac SPECT data. The achieved registration error of the proposed method (4.2 ± 0.5mm) is significantly lower than for MI (9.7 ± 4.49mm) and for a general learning-based method (5.9 ± 3.36mm). Clinical accuracy requirements are met for this application. The proposed approach can be easily extended to other applications where high accuracy in an organ specific region-of-interest is sought. Future work include validating this approach on a larger number of data sets and applying it to other modalities and applications.

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[1] The observation was made while investigating those data sets where the registration validation studies resulted in high errors.

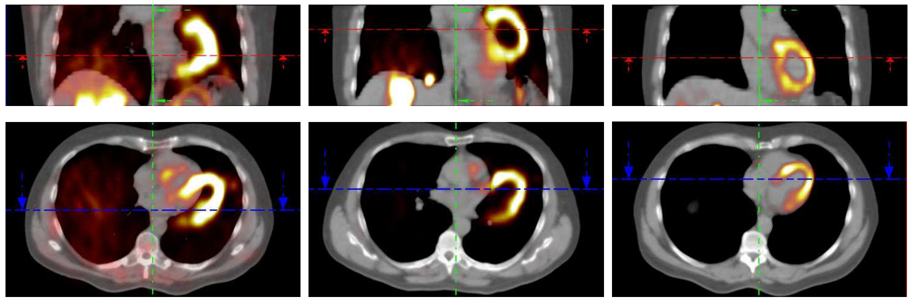

Fig. 6. Registration of a misaligned cardiac SPECT/CT scan. Two views are shown for misalignment after acquisition (left column), MI registration result (middle column), and weighted JS result using prior knowledge from a different scan(right column). The images show that the crucial alignment is only achieved by our proposed method.

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