Automatic error correction using adaptive weighting for vessel-based deformable image registration

Jing Ren¹ · Mark Green¹ · Xishi Huang² · Anwar Abdalbari¹

Received: 31 May 2016/Revised: 4 November 2016/Accepted: 16 February 2017/Published online: 28 February 2017
© Korean Society of Medical and Biological Engineering and Springer 2017

Abstract In this paper, we extend our previous work on deformable image registration to inhomogeneous tissues. Inhomogeneous tissues include the tissues with embedded tumors, which is common in clinical applications. It is a very challenging task since the registration method that works for homogeneous tissues may not work well with inhomogeneous tissues. The maximum error normally occurs in the regions with tumors and often exceeds the acceptable error threshold. In this paper, we propose a new error correction method with adaptive weighting to reduce the maximum registration error. Our previous fast deformable registration method is used in the inner loop. We have also proposed a new evaluation metric average error of deformation field (AEDF) to evaluate the registration accuracy in regions between vessels and bifurcation points. We have validated the proposed method using liver MR images from human subjects. AEDF results show that the proposed method can greatly reduce the maximum registration errors when compared with the previous method with no adaptive weighting. The proposed method has the potential to be used in clinical applications to reduce registration errors in regions with tumors.

Keywords Deformable registration · Physics-based model · Image registration · Adaptive · Strain energy

1 Introduction

In order to guide therapeutic procedures and achieve more accurate diagnoses of diseases, it is often helpful to fuse together multiple images of soft tissues from different sources. To this end, the fast deformable registration of soft tissues finds many applications. Although image registration for mostly rigid structures such as the brain and bone is normally a manageable task, it is more difficult to align images of soft tissues when dealing with organ shifts and/or the deformation of soft tissues caused by patient motions such as respiration, heartbeats, and surgical manipulation. In our previous works, we have proposed a fast vessel-based registration [1] for deformable image registration for the liver organ. That work assumes the liver tissue is homogeneous. However this is not a valid assumption in many situations. For instance, the tissue with embedded tumor is in nature inhomogeneous since the hardness of the tumor is very different from the surrounding tissues. Since cancer is the leading cause of death in Canada and is responsible for 30% of all deaths [2], it is important to extend the image registration method to be able to deal with the tissues with embedded tumor(s) and inhomogeneous tissues in general.

Inhomogeneous tissues result in non-uniform error distribution over the region of interest (ROI) after deformable image registration [3, 4]. This important issue has not yet received enough attention. In a grand challenge for deformable lung image registration [5], twenty algorithms were presented and compared. The best deformable registration method [6] achieved an average landmark accuracy of 0.59 mm with an average registration time of 4.5 min. However, registration errors were as large as 15 mm in some local region. These studies demonstrate that non-uniform error distribution is a common problem and even

✉ Anwar Abdalbari
anwar.abdalbari@uoit.ca

¹ University of Ontario Institute of Technology, Oshawa, ON, Canada

² Istuary Innovation Group, 75 Tiverton Court, Markham, ON, Canada

the best deformable registration approach cannot achieve an acceptable accuracy of 2.5 mm in some region. In our previous study, we have proposed a fast vessel registration method that works well in most cases using the same weights for all the branch points or all the vessel centerlines [1]. However, we observe that the registration accuracy can remain much larger in the neighborhood of malicious tumors compared to that of the normal tissues. The variation of registration errors are mainly caused by inhomogeneous tissue properties of the tumor and the surrounding areas of the liver and complex force interaction with surrounding tissues.

In this paper, in order to address this issue, we take advantage of the fast computation of our method [1] and use it as a component in the inner loop to detect and correct registration errors by adjusting weights. We propose an adaptive weighting technique to address this important problem and reduce the maximum errors of the image registration to an acceptable level. Specifically, we automatically detect and correct the relatively large errors by dynamically adjusting weights of marks/centerlines with large errors so that we are able to achieve accurate registration for all the marks and centerlines of the liver. We have investigated the effectiveness of the proposed method for inhomogeneous tissues with non-uniform force distributions and tissues with a tumor. Our method can reduce the maximum errors and keep them within acceptable accuracy, it can also compensate errors caused by complex force interactions and complex boundary geometry. In other words, our method incorporates an evaluation feedback mechanism, during the registration process, such that we can dynamically update the registration energy function to improve the accuracy in all regions. The proposed method retains all the desired features of our previous fast deformable registration method and therefore can guarantee the global minimum optimization and physical consistency for the tissues with tumors.

Compared with intensity-based image registration, feature-based image registration is normally less time-consuming and more robust. However, feature-based image registration requires the availability of corresponding features in both images. Since blood vessels are commonly clearly visible in different medical image modalities and are abundant in many organs, they can provide very useful features for driving image registration schemes. A general review of vessel-based image registration can be found in [7–9]. Since the centerlines of vessel segments can be treated as 3D curves, some general curve-matching techniques can also be used for image registration [10]. In this paper, we propose to segment blood vessels and use extracted vessels as the major landmarks for vessel-based image registration.

Some preliminary results of this method have been presented in [11]. In this paper, we will extend the method

in [11] and investigate how to achieve an optimal partition. Also, in this paper, we use FEM and MRI image sets of a volunteer to generate realistic synthetic image data and propose a new metric with the ground truth deformation field to evaluate the accuracy of the image registration in between the vessels and the bifurcation points. We will focus on investigating liver images in this paper, however, there are similar challenges when other abdominal organs are examined [5, 9, 12] and the above mentioned, proposed methods can be applied to these cases as well.

2 Adaptive weighting registration method

From our observations, the registration accuracy for different branch points and curves is different. Some have high accuracy while other have large errors. That is, the registration accuracy is not uniformly distributed. One possible reason is that the tissue properties are inhomogeneous. Sometimes, the maximum errors need to be kept under an acceptable level and there should be a tradeoff in registration accuracy among different regions. From the experiment data, the problem of non-uniform matching errors exist and need to be addressed. Here, we propose a new method to compensate the errors caused by inhomogeneous tissue properties.

The fast vessel registration method we have proposed in our previous work works well in most cases using the same weights for all the branch points or all the vessel centerlines. However, we observe that there are variations of matching accuracy for different branch points and centerlines. Some landmarks or centerlines have relatively large errors. To address this problem, in this study, we propose a novel methodology to automatically detect and correct the relative large errors by dynamically adjusting weights of marks/centerlines with large errors so that we are able to achieve accurate registration for all the marks and centerlines of the liver. We have demonstrated the effectiveness of our proposed method using realistic synthetic data and data from human subjects. We use fast vessel registration (FVR) to detect the registration errors. Therefore, based on the detected registration errors, we develop a novel correction methodology to compensate the registration errors locally with the help of the flexibility of our region-based NF transformation model.

In the following sections, we will discuss FVR and correction methods using dynamic weighting.

2.1 Fast vessel-based deformable registration

In this study, we apply multiple techniques to address the challenge of nonlinear registration of images with soft tissue deformation constrained by 3D curves, point marks

and strain energy. Our registration methodology is based on linear elastic solid mechanics and the minimum strain energy principle. We aim to minimize the following energy function:

$$J(p) = w_e E_e(T(x, p)) + w_c E_c(T(x, p)) + w_m E_m(T(x, p)) \quad (1)$$

where $T(x, p)$ is a deformable transformation and p the corresponding transformation parameters.

This energy function measures the quality of alignment between the fixed image and the transformed moving image. $E_e(T)$ is the strain energy produced by deformation of soft tissues. Minimization of strain energy yields physically consistent deformation. The curve energy term $E_c(T)$ penalizes the distance between pairs of 3D curves (i.e. blood vessel centerlines) extracted from the fixed and moving images, which ensures that the resulting optimal deformation should align internal vessel structures. The last term $E_m(T)$ penalizes the distance between corresponding point marks such as bifurcation points. Weights w_i are used to adjust the relative effects of each term.

2.1.1 Mark energy

Point marks are employed to anchor the deformation at some specific locations. We assume that there are N_m pairs of corresponding point marks (i.e. bifurcation points), (X_{fk}, X_{mk}) , $k = 1, 2, \dots, N_m$. Then we minimize the distance between corresponding point marks by adding the following term to the registration energy function,

$$E_m(p) = \sum_{i=1}^{N_m} \frac{1}{2} w_{BPi} \|T(X_{fk}) - X_{mk}\|^2 \quad (2)$$

2.1.2 Vessel energy

Vessel centerlines are able to provide reliable constraints for internal structures of soft organs during the image matching process. We aim to minimize the distance between pairs of corresponding vessel centerlines, which is formulated as the following minimization problem:

$$E_c(p) = \sum_{i=1}^{N_C} \sum_{k=1}^{N_{Ci}} \frac{1}{2} w_{ci} \|T(X_{fik}) - C_{mi}(t)\|^2 \quad (3)$$

where N_C is the total number of vessel centerlines, N_{Ci} the number of discrete points on the i -th centerline from the fixed image, X_{fik} ($i = 1, 2, \dots, N_C$, $k = 1, 2, \dots, N_{Ci}$) is the k -th discrete point on the i -th centerline from the fixed image, $C_{mi}(t)$ the continuous parametric B-Spline representation of the i -th vessel centerline from the moving image.

It can be proved that all the above three energy terms are quadratic functions of transformation parameters p [1].

The combination of the above energy terms provides different mechanisms to constrain the final registration solution to a physically consistent deformable match. In this study, we propose a novel fast analytical global solution to Problem (1) through specific design of different registration components.

The rationale of our proposed method is to formulate the deformable registration problem (1) as a quadratic optimization problem, that is, to derive the registration energy function (1) to a quadratic function of transformation parameters (p) by specific novel design of different components as follows:

$$J(p) = C_0 + C_1^T p + \frac{1}{2} p^T C_2 p \quad (4)$$

where C_1 is a N_p vector, C_2 a $N_p \times N_p$ matrix, and N_p the number of transformation parameters (p). Constants C_1 and C_2 are calculated based on given constraints of 3D curves, point marks and strain energy [13]. Thus we are able to obtain a closed-form optimal registration.

The optimal solution can be analytically obtained by solving the following system of linear equations,

$$\frac{\partial J(p)}{\partial p} = C_1 + C_2 p = 0 \quad (5)$$

The optimal solution is calculated by $p = -C_2^{-1} C_1$.

Furthermore, as it is well known, there is no local minimum in the quadratic optimization problem.

2.2 Region-based neuro-fuzzy (NF) transformation model

In this section, we propose a novel neuro-fuzzy transformation model that consists of N_R region-based sub-models. The advantage is that each region can have a different local model, which can be chosen according to deformation characteristics of the region, which can vary considerably. Many local deformation models such as B-Spline and free-form deformation have been developed [14, 15]. However, they generally require a large number of transformation parameters, which leads to large search space, making registration computationally intensive.

Neuro-fuzzy technique is a branch of artificial intelligence, which integrates artificial neural networks and fuzzy logic theory to take full advantage of both techniques. The main benefit of this approach is its ability to learn and adapt, good interpretability and easy integration of expert knowledge, that is, by using the fuzzy rules, the approach tries to simulate a person's line of thought in decision-making. We employ the neuro-fuzzy system [16] to seamlessly integrate region-based sub-models into a unified

transformation model. Our neuro-fuzzy system has the following N_R rules:

Fuzzy rule i : If point x is in region R_i ,
then $x' = T_i(x)$ (6)

where x is a 3D point in the fixed image space, x' the corresponding transformed point in the moving image space, $T_i(x)$ a local transformation model specifically tailored to Region i . In summary, the overall transformation $T(x)$ can be derived as [16],

$$x' = T(x) = \frac{\sum_{i=1}^{N_R} M_i(x) T_i(x)}{\sum_{i=1}^{N_R} M_i(x)} \quad (7)$$

where $M_i(x)$ is the membership function of a fuzzy set associated with region R_i .

In this study, membership functions are defined as 3D Gaussian functions.

$$M_i(x) = \exp \left\{ - \left[\frac{(x - c_{ix})^2}{2\sigma_x^2} + \frac{(y - c_{iy})^2}{2\sigma_y^2} + \frac{(z - c_{iz})^2}{2\sigma_z^2} \right] \right\} \quad (8)$$

where (c_{ix}, c_{iy}, c_{iz}) are the center of Region i , and parameters $(\sigma_{ix}, \sigma_{iy}, \sigma_{iz})$ are used to control the effective range of local model $T_i(x)$.

Denoting

$$M_{ni}(x) = M_i(x) / \sum_{i=1}^{N_R} M_i(x) \quad (9)$$

we rewrite the overall transformation as

$$T(x) = \sum_{i=1}^{N_R} M_{ni}(x) T_i(x) \quad (10)$$

By selecting an appropriate membership function for each region, transition of the transformation model from one region to another can be gradual or sharp, which provides great flexibility to achieve desirable smooth transitions between the sub-models. Furthermore, with the help of flexibility to select an appropriate membership function associated with each region, we can easily choose proper local membership function to limit the effective range of a global transformation model to the desired region in our neuro-fuzzy model. Therefore, we can take full advantage of good generalization of global models and representation capability of local deformation of local models. To represent complex deformation in one region, we have the flexibility to either select a more complicated model or place more dense local models. All the local models are not necessarily distributed uniformly, so our model can

significantly reduce the total number of transformation parameters.

In general, the overall transformation model $T(x)$ is nonlinear with respect to spatial position x and transformation parameters. However, if local models $T_i(x)$ are linear with respect to transformation parameters, transformation $T(x)$ is also linear with respect to transformation parameters after membership functions are determined. This leads to a closed-form optimal solution with the combination of other components.

2.3 Adaptive weighting method

In order to address the issues of large registration errors in some regions in fast vessel registration method, we propose a novel methods for dynamic weighting of the objective function (1). In other words, dynamic weighting aims to find the optimal weighting in $J(p)$ in the sense that the registration errors (TRE/ACD) are minimized by selecting appropriate weights for each landmark and each vessel centerline. Figure 1 shows the schematic diagram for the dynamic weighting registration methods.

2.3.1 Weight adjusting of branch points

At each iteration, after we perform fast vessel registration, we compute the TRE for all the branch points. Then we sort the TRE errors in descending order, and increase the weights of top $M_{BP}\%$ of branch points with largest registration errors. The weights of selected branch points are adjusted by the following formula:

$$w_{BPi}(k+1) = w_{BPi}(k) + \Delta w_{BPi} \quad (11)$$

$$\Delta w_{BPi} = s_{wBP} \frac{e_i - e_{Th}}{e_{\max} - e_{Th}} \quad (12)$$

where

- $w_{BPi}(k)$ is the weights at current iteration k ,
- Δw_{BPi} the increased weight for the i -th branch point at the next iteration $k+1$,
- s_{wBP} the maximum increase of weights for each iteration,
- e_i the error associated with branch point i at current iteration k ,
- e_{Th} the error threshold, if the error $e_i > e_{Th}$, the weight of mark i will be increased, otherwise, the weight does not change,
- $e_{\max}$ the maximum error of all the branch points at iteration k .

Similarly, the same procedure is applied in weight adaptation of curves.

Fig. 1 Schematic diagram for the dynamic weighting registration approach

2.3.2 Weight adjusting of vessel curves

After we perform fast vessel registration, we first compute the average curve distance (ACD) between the corresponding centerlines. Then we sort the ACD errors in descending order, and increase the weights of top $M_C\%$ of curves with largest registration errors. The weights of selected curves are adjusted by the following formula:

$$w_{Ci}(k+1) = w_{Ci}(k) + \Delta w_{Ci} \quad (13)$$

$$\Delta w_{Ci} = s_{wC} \frac{e_{Ci} - e_{CTh}}{e_{Cmax} - e_{CTh}} \quad (14)$$

where

- $w_{Ci}(k)$ is the weight of curve i at current iteration k ,
- Δw_{Ci} the increased weight for the i -th curve at the next iteration $k+1$,
- s_{wC} the maximum increase of curve weights for each iteration,
- e_{Ci} the error associated with curve i at current iteration k ,
- e_{CTh} the error threshold, if the error $e_{Ci} > e_{CTh}$, the weight of curve i will be increased, otherwise, the weight does not change,
- e_{Cmax} the maximum error of the curves at iteration k .

3 Registration accuracy measure: AEDF

3.1 Image preprocessing and feature extraction

3.1.1 Image preprocessing

In the raw MR images, blood vessels are black. Negated images (inverse of image intensity) were used to highlight blood vessels, which are required by the further image processing algorithms. A vessel enhancement filter was employed to enhance liver vessel structures, which was followed by a threshold filter to remove background noise and small vessels. These preprocessed images were then used for centerline extraction of blood vessels (Fig. 2).

3.1.2 Centerline extraction

First, a level set based segmentation method was used to segment blood vessels with the VMTKEasyLevel-SetSegmentation module in 3D Slicer [17, 18]. After source seed points and target points were specified, centerlines were then extracted using the Slicer VMTK centerline extraction module [17, 18] (Fig. 3).

3.1.3 Accurate localization of bifurcation points

After vessel centerlines were extracted, bifurcation points were calculated as the intersections of the centerlines using custom software. However, these bifurcation points are sometimes sensitive to small changes/errors in centerline extraction. In order to accurately and robustly localize consistent homologous bifurcation points across different MR images, a bifurcation correction algorithm is applied on the calculated intersection points. The corrected new bifurcation point is a weighted sum of four reference points in the region of bifurcation, which are calculated considering both the two centerlines and their radii (Fig. 4).

Fig. 2 **a** Input MR image, **b** after applying the enhancement algorithms

3.2 Evaluation metric: average error of deformation field (AEDF)

In general, registration accuracy is evaluated by calculating the misalignment of natural landmarks in two images after registration. Registration accuracy can be best evaluated by using ground truth deformations in ROI. In clinical practice, however, acquiring ground truth data is the most challenging task for in vivo human subjects if not impossible. Natural anatomical landmarks such as branch points of vessels are not enough dense and uniformly distributed to assess the entire regions of interest. Measures from edges and surfaces are also limited due to the ambiguity in one and two dimensions respectively. The AEDF is a promising metric to provide more complete information to assess the registration performance.

In order to assess the quality of the proposed registration in the regions which are not covered by the branch points and centerlines, i.e. the regions where natural landmarks are not available. We propose to compute the average errors between the ground truth deformation field and the deformation field derived from the registration. The ground truth deformation field is generated using FEM based on the branch points of the fixed and moving images.

Fig. 3 Centerlines extraction

The average residual registration error e_R for the resulting transformation is calculated as follows.

$$e_R = \frac{1}{N} \sum_{i=1}^N \|T(x_i) - T_{GS}(x_i)\| \quad (15)$$

where N is the number of points (i.e. image voxels) in the region of interest that are used to compute the registration error, and $\|T(x_i) - T_{GS}(x_i)\|$ is the distance between the corresponding points in moving deformed space, which are mapped by the registration transformation and gold standard deformation field from the same point x_i in fixed image space.

In order to calculate the above registration accuracy measure, we need to extract vessel centerlines, localize

Fig. 4 Bifurcation point's detection with a bifurcation correction algorithm is applied on the calculated intersection points

bifurcation points of blood vessels. In this study, the 3D Slicer and VMTK modules were used to achieve these extraction tasks.

3.3 Gold standard deformation field

It is very challenging to quantitatively evaluate the registration accuracy of deformable registration techniques in clinical practice due to limited marks and complex deformation patterns. In order to accurately assess the accuracy, the real entire deformation field is required, which is not available for real human subjects in clinical environments. In this study, we create and use realistic synthetic data with the known ground truth to thoroughly evaluate our proposed registration method. In particular, we use a biomechanically based finite element method (FEM) to create gold standard deformation fields in order to more completely evaluate the overall performance of our proposed non-rigid registration method. The registration accuracy can be assessed in a more complete way with the help of the complete and dense deformation fields in deep internal regions.

The procedure to create synthetic data is as follows. First, two MR images of the same subject are acquired at the different conditions. Then the homologous landmarks (branch points) are accurately identified in both images and their correspondences are also established. Next, a finite element method (FEM) is employed to find the deformation field that matches the landmarks in the fixed image to those in the moving image. The derived deformation field is thus a realistic deformation field. Then the deformation field is used to transform the fixed image to moving image

space, which is called the synthetic moving image. Therefore, the fixed image and synthetic image are used to evaluate the registration methods with the known ground truth of the deformation field (Fig. 5). This allows more accurate and more reliable evaluation of deformation registration techniques (See Fig. 5 for the procedure flowchart).

4 Experimental results

4.1 Image acquisition method

All of the images used in this study were acquired from one human volunteer. High-quality MR images were acquired in the axial plane using a 1.5 T GE scanner (GE Medical Systems, Milwaukee, WI). Image acquisition was performed using the LAVA gradient echo sequence with $TR = 3.79$ ms, $TE = 1.72$ ms, a flip angle of 12° , an image matrix size of 256×256 , in-plane pixel size of $1.3 \text{ mm} \times 1.3 \text{ mm}$ and slice thickness of 1.5 mm . Each pair of image sets was acquired with a breath-hold at the end of inhalation and exhalation respectively.

Fig. 5 Flowchart of using AEDF

4.2 Average error of deformation field (AEDF) in ROI

Figure 6a shows a liver with vessels and an embedded tumor. Figure 6b shows the registration results of using both the previous method and the proposed adaptive weight adjusting method. Through the visual inspection, the results in Fig. 6b clearly show that the matching errors in the neighborhood of the tumor are large using the registration method without adaptive weighting, and reduced after using the adaptive weighting. In this study, we use one pair of images from one subject to compute AEDF. The average AEDF error of the deformation field in the neighbor of the tumor is 1.45 ± 0.51 mm for the previous method, and 1.03 ± 0.39 mm for our new proposed method. The registration time of the proposed method is within 5 s on PC with Intel Core i7-2600 CPU at 3.4 GHz and 8 GB RAM. In a recent related study on registration of liver MRI images [19], Noorda et al. reported their registration accuracy of vessel alignment is 3 mm and the registration time is 45 s for 2D MRI to 2D MRI registration.

Fig. 6 **a** Surface (red), tumor (yellow), vessels (red lines) of the liver; **b** vessels after registration, red lines: ground truth vessels, yellow lines: without adaptive weighting, green lines: with adaptive weighting using the proposed method. (Color figure online)

5 Discussion

Our technique can ensure the maximum TRE is within the acceptable accuracy tolerance which the user has prescribed. The current results have shown that we can achieve this goal under the condition that there are enough degrees of freedom (DOFs) in our region-based NF transformation model.

FEM method has its advantages and disadvantages. In theory, there is no any other registration methods that can do better than the FEM method if the FEM assumptions are satisfied, since in ideal environment, FEM provides the ground truth deformation based on the solid elastic theory. However, there are some limitations in applications of FEM in clinical practice. First, the long processing time of FEM limits clinical applications of FEM techniques such as intra-operative image guided procedures. Secondly, the FEM technique requires the accurate measurements of tissue properties and complex boundary conditions of complex patient-specific complex geometric models (e.g. surfaces of ROI) and/or complex interactive forces with surrounding tissues or complex internal forces within ROI

such as the lungs. The accurate measurements of tissue properties and boundary conditions are very challenging for in vivo patients in clinical settings if not impossible. The proposed registration techniques can outperform the FEM method in the cases that the assumptions of FEM cannot hold, for example, accurate elastic properties and complex boundary conditions are not available in most clinical applications.

6 Conclusion and future work

Deformable registration of inhomogeneous tissues proves to be a very challenging task. However, tissues with malicious tumors are often inhomogeneous in nature and are common in clinical applications. In our previous work, we proposed a fast deformable registration method based on physics-based registration. The higher hardness of these tumors makes them react to physics-based registration techniques differently compared to other normal soft tissues. This non-uniform property of the soft tissues often results in relatively large registration errors in some regions such as the regions with tumors. In this paper, based on our previous work on deformable registration, we proposed a novel method to solve the problem caused by tissue inhomogeneity. We dynamically adjust the weights of each region and thereby reduce the relatively large registration errors in the neighborhood of the tumors. We have demonstrated that the dynamic weighting is better than the registration without weighting adaptation. We have also proposed a FEM based evaluation metric to thoroughly evaluate the registration accuracy in between the curves and branch points. The proposed technique has the potential to significantly improve the registration capability and the quality of clinical diagnosis and treatment planning. This method is validated using the liver MRI images. However, the generality of this method allows it to be adapted to more general tissues or organs with modest modification. In the future, we plan to extend the proposed method to other organs and/or different imaging modalities.

References

- Huang X, Ren J, Abdalbari A, Green M. Vessel-based fast deformable registration with minimal strain energy. *Biomed Eng Lett.* 2016;6(1):47–55.
- Canadian Cancer Society. <http://www.cancer.ca/en/cancer-information/cancer-101/cancer-statistics-at-a-glance/?region=on>. Retrieved on 3 Aug 2014.
- Ljungberg M, Strand SE. Attenuation and scatter correction in SPECT for sources in a nonhomogeneous object: a Monte Carlo study. *J Nucl Med.* 1991;32(6):1278–84.
- Trivedi A, Basu S, Mitra K. Temporal analysis of reflected optical signals for short pulse laser interaction with nonhomogeneous tissue phantoms. *J Quant Spectrosc Radiat Transf.* 2005;93(1–3):337–48.
- Murphy K, van Ginneken B, Reinhardt JM, Kabus S, Ding K, Deng X, Cao K, Du K, Christensen GE, Garcia V, Vercateren T, Ayache N, Commowick O, Malandain G, Glocker B, Paragios N, Navab N, Gorbunova V, Sporring J, de Bruijne M, Han X, Heinrich MP, Schnabel JA, Jenkinson M, Lorenz C, Modat M, McClelland JR, Ourselin S, Muenzing SE, Viergever MA, De Nigris D, Collins DL, Arbel T, Peroni M, Li R, Sharp GC, Schmidt-Richberg A, Ehrhardt J, Werner R, Smeets D, Loeckx D, Song G, Tustison N, Avants B, Gee JC, Staring M, Klein S, Stoel BC, Urschler M, Werlberger M, Vandemeulebroucke J, Rit S, Sarrut D, Pluim JP. Evaluation of registration methods on thoracic CT: the EMPIRE10 challenge. *IEEE Trans Med Imaging.* 2011;30:1901–20.
- Han X. Feature-constrained nonlinear registration of lung CT images. *Med Image Anal Clin Grand Chall.* 2010;63–72.
- Sotiras A, Davatzikos C, Paragios N. Deformable medical image registration: a survey. *IEEE Trans Med Imaging.* 2013;32(7):1153–9.
- Zitova B, Flusser J. Image registration methods: a survey. *Image Vis Comput.* 2003;21:977–1000.
- Hill D, Batchelor P, Holden M, Hawkes D. Medical image registration. *Phys Med Biol.* 2001;46(3):R1–45.
- Xia M, Liu B. Image registration by super curves. *IEEE Trans Image Process.* 2004;13(5):720–32.
- Ren J. Adaptive deformable image registration of in-homogeneous tissues. *SPIE Med Imagin.* 2015.
- Baumhauer M, Feuerstein M, Meinzer HP, Rassweiler J. Navigation in endoscopic soft tissue surgery: perspectives and limitations. *J Endourol.* 2008;22(4):751–66.
- Huang X, Bari A, Zaheer S, Looi T, Ren J, Drake J. 3D curve constrained deformable registration using a neuro-fuzzy transformation model. *Conf Proc IEEE Eng Med Biol Soc (EMBC2012).* 2012;5294–7.
- Holden M. A review of geometric transformations for nonrigid body registration. *IEEE Trans Med Imaging.* 2008;27(1):111–28.
- Rueckert D, Sonoda LI, Hayes C, Hill DL, Leach MO, Hawkes DJ. nonrigid registration using free-form deformations: application to breast MR images. *IEEE Trans Med Imaging.* 1999;18(8):712–21.
- Huang Xishi, Ho Danny, Ren Jing, Capretz Luiz F. A soft computing framework for software effort estimation. *Soft Comput.* 2006;10(2):170–7.
- 3D Slicer. <https://www.slicer.org/>.
- VMTK. <http://www.vmtk.org/>.
- Noorda YH, Bartels LW, Viergever MA, Pluim JP. Subject-specific four-dimensional liver motion modeling based on registration of dynamic MRI. *J Med Imaging.* 2016;3(1):015002.