Unsupervised Deformable Image Registration with Fully Connected Generative Neural Network

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Abstract

In this paper, a new deformable image registration method based on a fully connected neural network is proposed. Even though a deformation field related to the point correspondence between fixed and moving images are high-dimensional in nature, we assume that these deformation fields form a low dimensional manifold. Thus, in our method, a neural network generates an embedding of the deformation field from a low dimensional vector. This low-dimensional manifold formulation avoids the intractatibility associated with the high dimensional search space that most other methods face during image registration. As a result, while most methods relies on explicit and hand crafted regularization of the deformation fields, our algorithm relies on implicitly regularizing the netweork parameters. The proposed method generates deformation fields from latent low dimensional space by minimizing a dissimilarity metric between a fixed image and a warped moving image. Our method removes the need for a large dataset to optimize the proposed network. The proposed method is quantitatively evaluated using images from the MICCAI ACDC challenge. The results demonstrate that the proposed method improves performance in comparison with a moving mesh registration algorithm and also it correlates well with independent manual segmentations by an expert.

1 Introduction

Medical image registration is essential for many clinical image processing tasks Sotiras et al. [2013]. The aim of image registration is to compute the mapping between fixed and moving images by minimizing an objective function that is based on a dissimilarity metric. Recently, promising methods using deep learning have been proposed to improve medical image registration de Vos et al. [2017], Krebs et al. [2017], Li and Fan [2017], Liao et al. [2017]. Deep learning methods such as convolutional stacked autoencoders have been used to extract features from a pair of images Wang et al. [2017]. On the contrary, some techniques used supervised deep learning to build prediction model of transformation matrix in order to obtain learning framework Krebs et al. [2017], Rohé et al.

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[2017], Sokooti et al. [2017], Yang et al. [2017]. These studies use convolutional neural network regressor to predict the spatial relation between fixed and moving images. Inspired by the recent works in reinforcement learning Krebs et al. [2017], Liao et al. [2017] applied an artificial agent which uses its own experience to learn and does not require explicitly designed similarity measures. They suggested a reformulation of image registration problem to optimize the deformation model parameters. The agent is trained in a supervised way and explores the space of deformations by choosing an action from a set of actions that update deformation model's parameters.

de Vos et al. [2017] proposed a deformable image registration (DIRNet) using CNNs. This method uses spatial transformer network (STN) Jaderberg et al. [2015] in order to generate a dense displacement field by using local deformation parameters that are estimated by a convNet. DIRNet estimates 2D control points and uses cubic B-splines to represent spatial transformations which register 2D images. Yoo et al. [2017] used bilinear interpolation instead of B-splines to obtain dense spatial transformations and estimated coarse-grained deformation fields at a low spatial resolution. The method can register 2D images by optimizing an image similarity metric derived from an autoencoder between fixed and transformed moving images. However, predicted coarse-grained spatial transformation which is obtained by these methods might fail to characterize small deformations Li and Fan [2017].

Inspired by fully convolutional networks (FCNs) Long et al. [2015] that facilitate voxel-to-voxel learning, Li and Fan [2017] has proposed a multi-resolution deformable image registration framework based on a deep self-supervised fully convolutional network. This method trains FCNs to estimate voxel-to-voxel spatial transformations to register images by maximizing image-wise similarity metric.

Training data is an important part of deep learning network-based image registration algorithms. There are a variety of strategies that have been proposed to build training data which include simulating synthetic deformation fields and applying them to a set of images to generate new images with known spatial transformations Sokooti et al. [2017]. However, these synthetic deformation fields may not be able to realistically capture the spatial correspondences between actual imagesLi and Fan [2017]. Krebs et al. [2017] proposed a ground truth generator that produces millions of synthetically deformed training samples based on a few real deformation estimations. However, the need for large datasets in the medical field with manual segmentation labels or known spatial transformations is still a major problem in deep learning based algorithms. Thus, we suggest a deep unsupervised network which is able to generate deformation fields independent of training data.

Unlike previous methods that take pairs of fixed and moving images as an input, in our network, inputs are latent, low dimensional vectors. In addition, our method is not trained with known registration transformations, but generates deformation fields and register images by direct optimization of image similarity metric between the fixed and deformed moving image. Furthermore, instead of representing spatial transformations by using B-spline, our method uses a bilinear interpolation to capture dense spatial transformations. To the best of the authors' knowledge, this is the first deep learning-based manifold embedding method for unsupervised deformable image registration. Thus, the main contributions of this work are: (1) proposing an unsupervised network and using low dimensional vectors as an input (2) generating spatial transformation fields by embedding.

Our formulation avoids any need for explicit regularization of the defromation field. In our case, the network architecture, the dimension of the latent vector and the L_2 norm of the network parameters implicitly regularize the image registration problem. Furthermore, our method can be applied to a sequence of images.

2 Method

The objective of the image registration task is to find the spatial transformation that aligns the image pairs: fixed image I and moving image J. It can be formulated as an optimization problem to maximize the similarity metric (or minimize a dissimilarity metric) between the fixed image and the transformed moving image. In a deformable image registration task, the spatial transformation is characterized by a dense deformation field f (or, $\{dx, dy\}$ in 2D) that encodes the displacement vector.

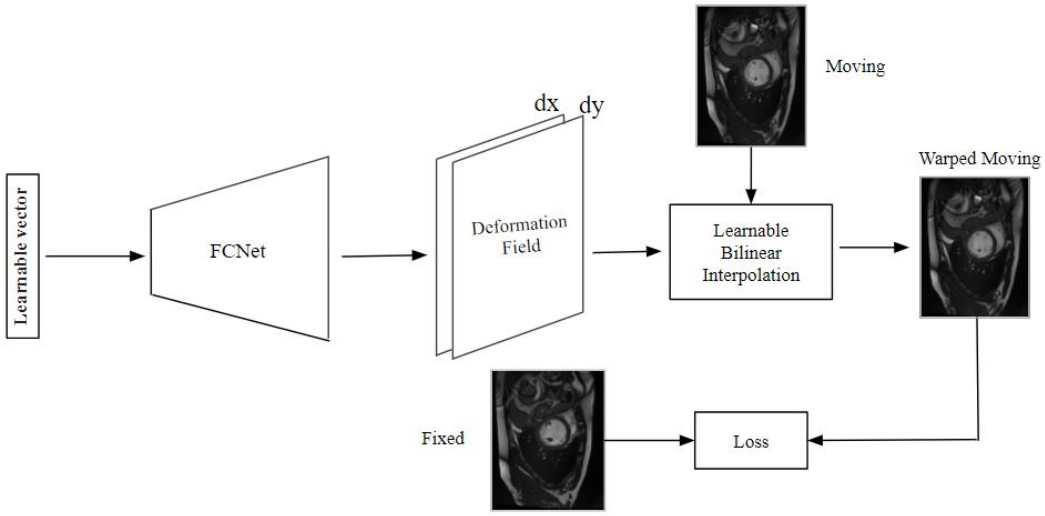

Figure 1: Schematic of the proposed image registration approach based on a fully connected network. The network uses one or more learnable vector which is initialized by a random vector as an input. The fully connected part generates 2-dimensional displacement vector field to warp a moving image to a fixed image. The network is unsupervised and optimizes the similarity metric using backpropagation.

2.1 Using fully connected network for optimizing an image dissimilarity metric

We propose a deep learning model using FCNet (fully connected network) to solve the optimization problem for image registration. As we use FCNet as a generator, we can directly obtain deformation fields at the same resolution of the images to be registered. In this method, for each image in a sequence of images, a low dimensional input vector (also known as latent vector) is defined. Then the FCNet applies 8 fully connected layers to generate a two dimensional deformation field $\{dx, dy\}$. The number of kernels (i.e., coefficient matrices) per layer can have an arbitrary size but the number of kernels of the output layer is determined by the dimensionality of the images (e.g. 2 kernels for 2D images that require 2D displacement). FCNet generates displacement field by minimizing a dissimilarity metric between fixed image and warping images using stochastic gradient descent Adam Kingma and Ba [2014]. The metric employed here is mean squared intensity difference between a fixed image and a deformed moving image for mono modality image registration. During the optimization, not only the network's parameters, but also input latent vectors are updated. The dense displacement vector fields generated by FCNet are employed to deform a moving image toward the fixed image. We applied bilinear deformation which has local support instead of cubic B-spline de Vos et al. [2017] or a thin-plate spline which has global support. The framework of our method is illustrated in Figure 1.

Suppose $\{I_i\}_{i=1}^n$ is a sequence of images that we would like to register. We have a neural network with parameters θ that computes a deformation field $f_\theta(t_i) : R^d \rightarrow R^{2N}$, where N is the number of pixels and d is a number much smaller than N (in our work d is 25). We can call f_θ as an embedding function. Thus, for the ith image in the sequence, the neural network takes in a d-dimensional vector t_i and outputs a deformation field $f_\theta(t_i)$. We can warp a moving image I by this deformation field to get the warped image $I(f_\theta(t_i))$. Therefore, we can minimize the following cost function for registering image sequence $\{I_i\}_{i=1}^n$:

$$E_{data}(\theta, \{t_i\}_{i=1}^n) = \sum_i |I_i - I_{mov(i)}(f_\theta(t_i))| \tag{1}$$

The minimization is performed jointly over the parameters θ of the neural network and latent vectors $\{t_i\}_{i=1}^n$, where I_i is a fixed image and corresponding moving image is $I_{mov(i)}$.

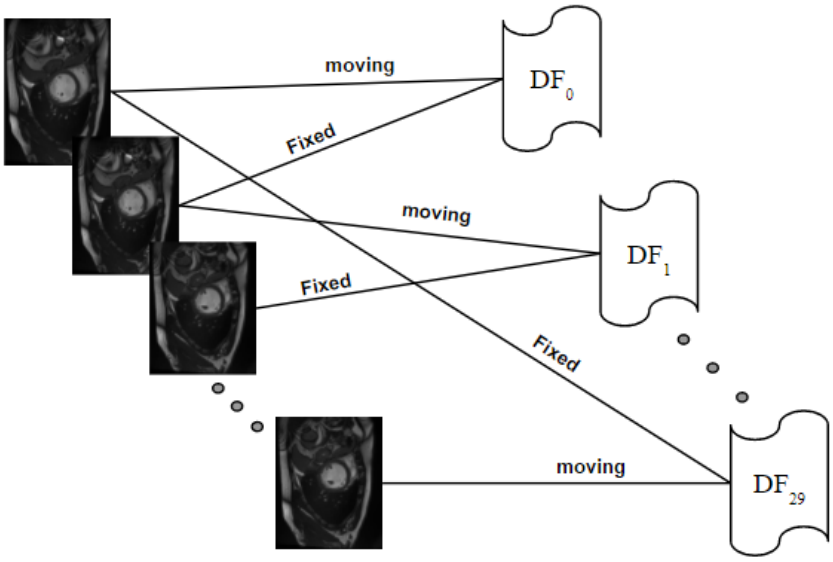

Figure 2: Selection of fixed and moving images in one sequence of the medical image. $DF_i(i = 0, 1, 2, ..., K)$ are deformation fields generated by the network for each pair of fixed and moving images.

2.2 Regularization

Image registration is inherently ill-posed so that the existence and the uniqueness of the solution is not guaranteed Myronenko [2010]. Thus, regularization is essential to avoid both physically implausible displacement fields and local minimum during optimization Vishnevskiy et al. [2017]. In general, estimating the N-dimensional displacement field between moving and fixed image with regularization term usually formulates as follow:

$$E(\theta, \{t_i\}_{i=1}^n) = E_{data}(\theta, \{t_i\}_{i=1}^n) + \lambda E_{reg}(\{dx_i, dy_i\}_{i=1}^n), \tag{2}$$

where dx_i, dy_i are deformation fields and $E_{reg}(.)$ is a regularizer on the deformation field, and λ is a parameter which controls the trade-off between the image dissimilarity measure and the regularization on the spatial transformation. As the most optimization methods based regularization image registration are typically computationally expensive and time-consuming, an alternative is to regularize network parameters θ. This regularization considers the mean of the sum of squares of the network weights (MSW):

$$MSW(\theta) = \frac{1}{N_w} \sum_{i=1}^{N_w} w_i^2, \tag{3}$$

where N_w represents the number of network weight parameters and w_i is an element of the parameter matrix in a vector expression W. The weights and biases of the network are assumed to be random variables and follow Gaussian distributions at the time of initialization. Finally, our optimization problem can be formulated as follows:

$$E(\theta, \{t_i\}_{i=1}^n) = E_{data}(\theta, \{t_i\}_{i=1}^n) + \lambda MSW(\theta), \tag{4}$$

The above optimization problem can be solved by backpropagation with stochastic gradient descent.

Our model is implemented using tensorflow. Adam optimization technique Kingma and Ba [2014] is used with learning rate 1×10^{-3} and batch size 10. The results were obtained with NVIDIA GTX 1080 Ti GPU, and 2000 iterations were adopted for the optimization.

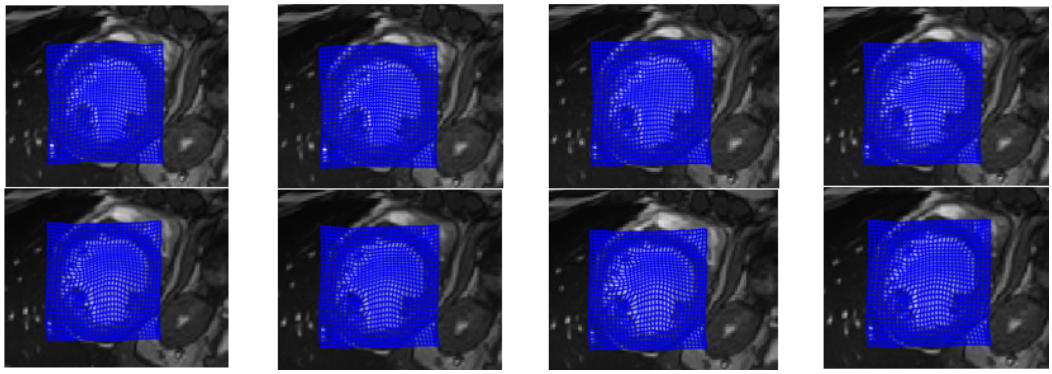

Figure 3: Representative examples of the displacement field obtained by the proposed method

3 Experimental Evaluation and Comparisons

We applied the method to 100 short axis cardiac cine MR sequences of 10 patients (30000 images). We compared the accuracy of the proposed method with a moving mesh correspondence algorithm presented in Punithakumar et al. [2017, 2013] by using the same datasets.

3.1 Data

The proposed method is evaluated with clinical Magnetic Resonance Imaging (MRI) images from MICCAI Automated Cardiac Diagnosis Challenge (ACDC) dataset ACDC [2017]. The ACDC 2017 dataset contains 100 exams (all from different patients) that each exam has a sequence with 25-30 frames. Cine MR images were acquired in breath hold with a retrospective or prospective gating and with a steady-state free precession (SSFP) sequence in short axis orientation. A series of short axis slices cover the Left Ventricle (LV) from the base to the apex, with a thickness of 5 to 8 mm and with an interslice gap of 5 mm. The spatial resolution goes from 0.83 to 1.75 mm2/pixel. For more details on the dataset, please refer to the ACDC website ACDC [2017].

3.2 Evaluation measures

3.2.1 Dice metric

For the geometrical metrics, we use Dice Metric (DM) which usually is used to measure the similarity (overlap) between two surfaces. DM is defined as the ratio of the intersection by the sum of the two regions.

$$D(M,N) = \frac{2(M \bigcap N)}{M+N} \tag{5}$$

Where M is correspondence to the area or volume enclosed by the automatic counters and N is the manual counter. The DM varies from 0 (total mismatch) to 1 (perfect match).

3.2.2 Reliability

We evaluate the reliability of our method by using a reliability function (the complementary cumulative distribution function (ccdf)) of the obtained Dice metrics Ayed et al. [2009].

$$R(d) = P(DM > d) \tag{6}$$

This equation means that for each d $\in$ [0,1], $R(d)$ is (number of images segmented with DM higher than d)/(total number of images). $R(d)$ measures how reliable the algorithm in yielding accuracy d.

3.3 Quantitative Evaluation

The proposed method is evaluated on 100 short axis cardiac cine MR sequences, a total of 30000 images. In each sequence I_i is selected as a moving image and I_{i+1} is selected as a fixed image

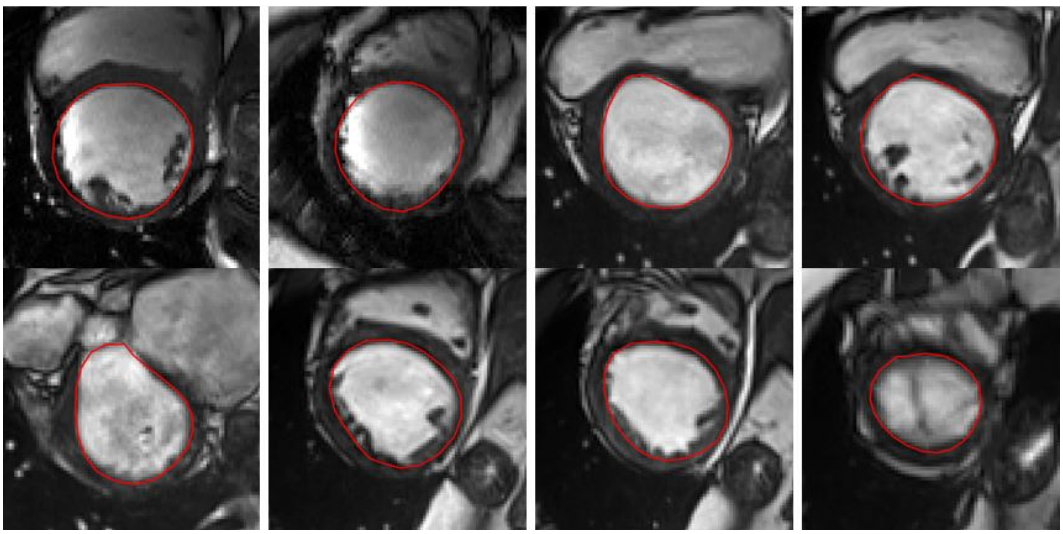

Figure 4: Sample of the boundary results with the proposed FCNet.

Figure 2. Our suggestion approach yielded a DM equal to 0.89 ± 0.03 for all the data analyzed (DM is expressed as mean $\pm$ standard deviation). Table 1 DM statistics for the proposed method and moving mesh correspondence method Punithakumar et al. [2017]. Using the same data, the method in Punithakumar et al. [2017] yielded a DM equal to 0.85 ± 0.03. Figure6 (a) depicts the DM for a representative sample of the analyzed images. Table 1 reports the accuracies for FCNet in comparison with moving mesh correspondence method and it shows that our suggestion approach led to a significant improvement in average the accuracy. In addition, Table 1 reports the reliability of the proposed method and Punithakumar et al. [2017] in different accuracy levels $(d = 0.80, d = 0.85, d = 0.90)$ and plot R as a function of d in Figure6 (b). Our algorithm led to a higher reliability curve and improvement in reliabilities.

3.4 Visual Assessment

By using a grid mesh, we show the displacement fields obtained by FCNet Figure 3. The comparison of the result of FCNet and moving mesh correspondence method Punithakumar et al. [2017] are given in Figure 5. In Figure 3, we give a representative sample of borders obtained by our method. The FCNet approach yielded more accurate results than moving mesh correspondence method in a number of image sequences.

4 Discussion and Conclusion

In this paper, we proposed a deformable image registration algorithm based on the deep fully connected network to generate spatial transformations. Our network predicted deformation field at the same resolution of fixed and moving images. The image registration optimizes spatial transformation with deep supervision network through feedforward and backpropagation computation. The experimental results show that our method obtained promising performance to register a sequence of cardiac MRI images.

Most deep learning based image registration methods learn spatial transformations from training data with known deformation fields Sokooti et al. [2017], Yang et al. [2017], Krebs et al. [2017], Yoo et al. [2017]. On the other hand, other methods estimate spatial transformations by using the pairs of images (fixed and moving images) de Vos et al. [2017], Li and Fan [2017]. Unlike of these methods, our algorithm directly generates spatial transformations by maximizing a similarity metric between fixed and deformed images based on low dimensional learnable vector initialized by random vector, independent from moving and fixed image.

In conclusion, the results have demonstrated that unsupervised deep learning models built upon generative fully connected networks could achieve satisfying performance for deformable medical

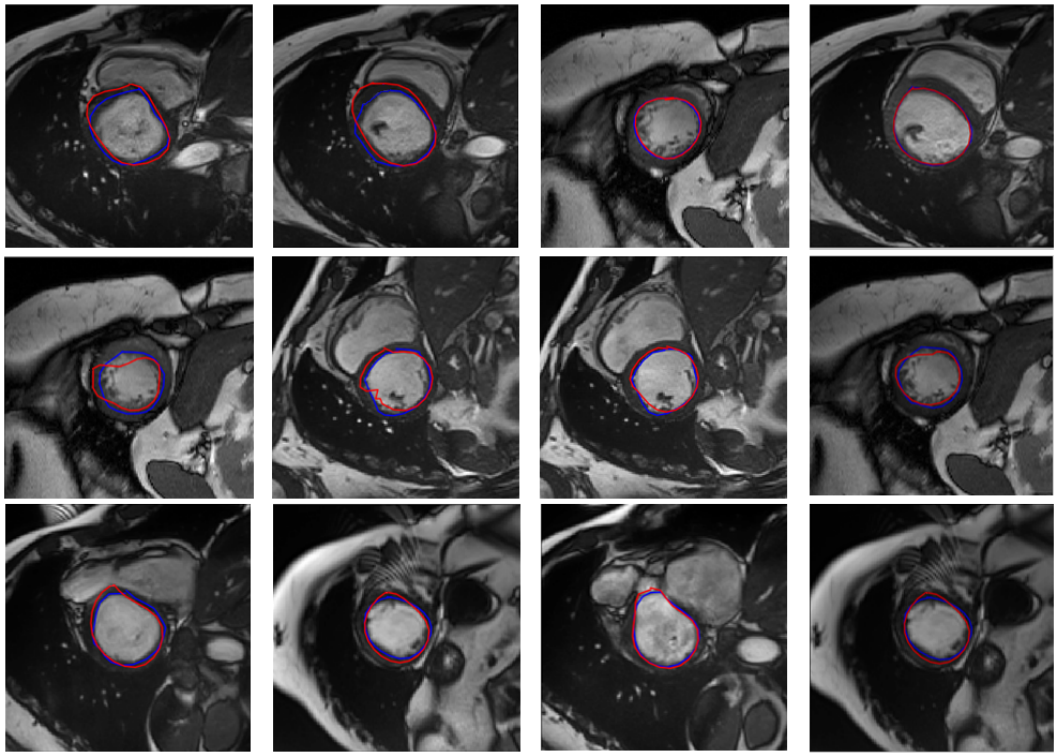

Figure 5: Representative examples of obtained borders of the LV with FCNet (blue) and moving mesh correspondence Punithakumar et al. [2017] (red) methods where FCNet provided significantly more accurate results than Punithakumar et al. [2017].

Table 1: The mean, standard deviation of Dice score and Reliability function $(R(d) = P(DM > d))$. The higher the DM and R, the better the performance.

	Dice	$R(0.80)$	$R(0.85)$	$R(0.90)$
Punithakumar et al. [2017]	0.85 ± 0.03	0.95	0.66	0.06
our method	0.89 ± 0.03	1	0.91	0.44

image registration. This study shows that the proposed approach improves the performance over recent state-of-the-art image registration with respect to accuracy.

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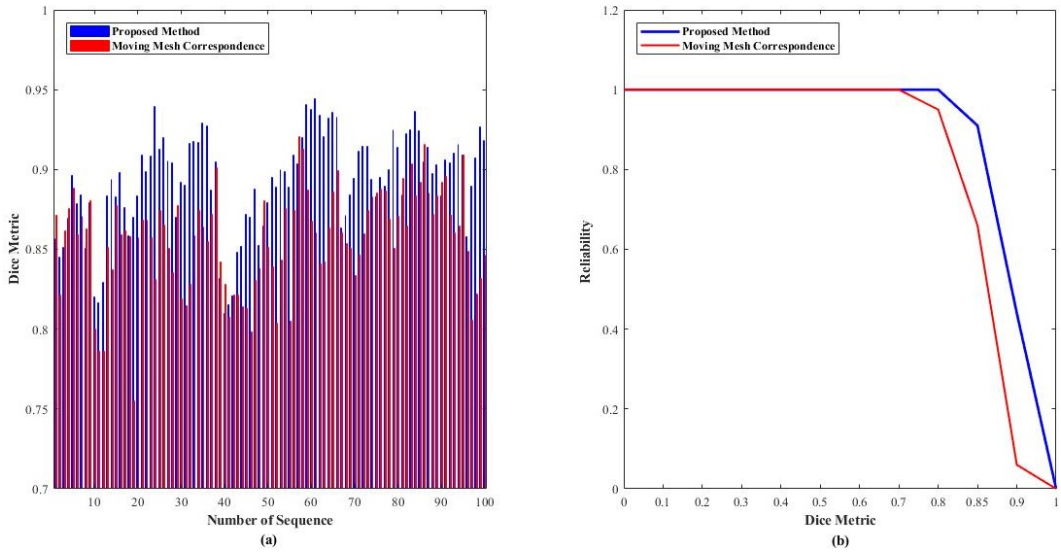

Figure 6: Comparison between proposed method and Punithakumar et al. [2017] for 100 sequences (30000 images). (a) Dice metric (DM) for the proposed method and Punithakumar et al. [2017]. (b) Reliability ($R(d) = Pr(DM > d)$) for the proposed method and Punithakumar et al. [2017]. The proposed method led to a higher reliability curve.

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