Deformable image registration by multi-objective optimization using a dual-dynamic transformation model to account for large anatomical differences

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ABSTRACT

Some of the hardest problems in deformable image registration are problems where large anatomical differences occur between image acquisitions (e.g. large deformations due to images acquired in prone and supine positions and (dis)appearing structures between image acquisitions due to surgery). In this work we developed and studied, within a previously introduced multi-objective optimization framework, a dual-dynamic transformation model to be able to tackle such hard problems. This model consists of two non-fixed grids: one for the source image and one for the target image. By not requiring a fixed, i.e. pre-determined, association of the grid with the source image, we can accommodate for both large deformations and (dis)appearing structures. To find the transformation that aligns the source with the target image we used an advanced, powerful model-based evolutionary algorithm that exploits features of a problem's structure in a principled manner via probabilistic modeling. The actual transformation is given by the association of coordinates with each point in the two grids. Linear interpolation inside a simplex was used to extend the correspondence (i.e. transformation) as found for the grid to the rest of the volume. As a proof of concept we performed tests on both artificial and real data with disappearing structures. Furthermore, the case of prone-supine image registration for 2D axial slices of breast MRI scans was evaluated. Results demonstrate strong potential of the proposed approach to account for large deformations and (dis)appearing structures in deformable image registration.

Keywords: Multi-objective optimization, evolutionary algorithms, deformable registration, large anatomical differences

1. INTRODUCTION

Existing deformable image registration methods (e.g. solely using biomechanical model-based or non-rigid intensity-based image registration methods) have limited success when large anatomical differences are involved. A hybrid method that was recently introduced proved to be more successful but reported registration accuracies were still not very good.[1] Further, so far, only a few studies addressed the issue of disappearing structures (e.g. due to tissue excision between image acquisitions).[2-7] Moreover, in these works the identification of the disappearing structures is considered a separate task, often as part of segmentation. Furthermore, when the focus is on intra-operative guidance, the assumption is used that disappeared tissue has been replaced by "air".[7] This will, however, not always be the case. For example in the case of breast-conserving surgery for breast cancer, the excision cavity is often closed for an improved cosmetic result. Post-surgery radiotherapy is subsequently planned on a CT scan acquired after surgery since this is most representative for the anatomy to be treated, making it, however, difficult to define the original tumor position (Figure 1). Radiotherapy planning could benefit extremely from deformable registration of pre- and post-operative imaging data.

We recently introduced the concept of multi-objective optimization for deformable image registration.[8] The rationale is that such an approach removes the need for a predetermined singular combination of objectives. By computing and presenting multiple outcomes that represent efficient trade-offs between the objectives (a so-called Pareto front) at once,

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Medical Imaging 2013: Image Processing, edited by Sebastien Ourselin, David R. Haynor,
Proc. of SPIE Vol. 8669, 866910 · © 2013 SPIE · CCC code: 1605-7422/13/$18
doi: 10.1117/12.2006783

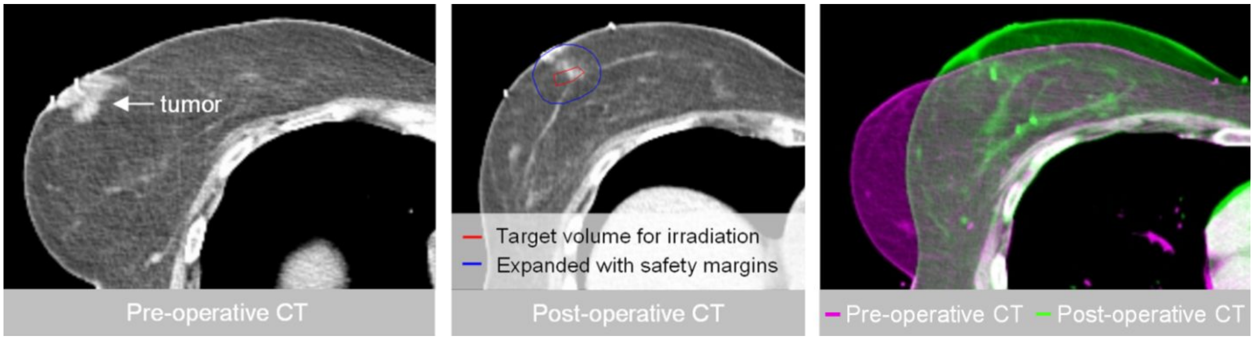

Figure 1. Left and middle: Pre- and post-operative breast CT scan example slices. Right: pre- and post-operative CT scan after rigid registration based on the ribs.

this approach allows for more insightful tuning of the manner in which to combine important objectives in deformable image registration such as transformation effort and similarity measure.

Finding optimal solutions, i.e. the optimal Pareto front of all non-dominated solutions, to high-dimensional multi-objective optimization problems is a non-trivial task. In practice, the goal is therefore often to find high-quality approximations of the optimal Pareto front. To find such high-quality approximations, we used a particular type of evolutionary algorithm, known as EDA (Estimation-of-Distribution Algorithm) which aims to exploit features of a problem's structure automatically in a principled manner via probabilistic modeling.[9-12] Moreover, we recently studied the use of a new variant of the EDA that we previously employed. This new variant has the advantage of converging faster while obtaining solutions of the same quality.[13] This allows us to use more fine-grained grids (that have more variables to be optimized) for the registration task, which is of importance for more complex registration tasks, especially when considering disappearing structures.

In this paper, we developed and studied, within the previously introduced multi-objective optimization framework, a dual-dynamic transformation model. We propose to consider the challenging problem of identifying (dis)appearing structures to be part of the overall optimization process, thereby letting the optimization algorithm decide and identify, using the dual-dynamic transformation model, which parts are most likely to have (dis)appeared, all at once during the registration process.

2. MATERIALS AND METHODS

2.1 Dual dynamic transformation model

Image registration is the process that determines the transformation that maps points in the source image to corresponding points in the target image. The transformation model, i.e. the representation of possible transformations is often based on a regular grid of points. The actual transformation then is given by the association of coordinates with each point in the grid. A means of interpolation is required to extend the so-established correspondence between grids to create the transformed source image. The number of real-valued parameters to be optimized equals the number of grid points (n_g) times the spatial dimensionality of the image (e.g., $n_g \times 2$ for a 2-dimensional image).

Instead of a fixed grid for the source image and a non-fixed grid for the target image, we will use two non-fixed irregular grids: one for the source image and one for the target image. No longer requiring a fixed, i.e. pre-determined, association of the grid with the source image provides the potential to correlate the grid in the source image better with underlying image structures. Moreover, both disappearing and appearing structures can be accommodated. Specifically, the location of each grid point in both target and source images can now be determined. To make a structure disappear, the grid points that in the source image delineate a structure that has disappeared can be placed on top of each other in the grid in the target image. Conversely, to make a structure appear, grid points that in the target image delineate a structure that has appeared can be placed on top of each other in the source grid. In this pilot study, however, we restrict ourselves to disappearing structures.

In this paper, linear interpolation inside a simplex after grid triangulation was used to extend the correspondence between grids (i.e. transformation) as found for the grid points to the rest of the volume to create the transformed source image. An advantage of this choice is that it can cope with non-convex grid elements.

2.2 Registration as an optimization problem

The task of deformable image registration, i.e. the process of aligning a source image with a target image, can be well posed as an optimization problem. For the task of image registration two issues are of prime interest. 1) Quality of fit: intensity similarity, i.e. the degree of similarity between intensity patterns in the target image and the transformed source image. 2) Smoothness of deformation: transformation effort, i.e., the amount of energy required to accomplish the transformation.

Our methodology can be combined with state-of-the-art similarity measures and deformation models. The main purpose of this study, however, was to observe the feasibility of using the dual-dynamic grid transformation model in order to tackle large deformations and (dis)appearing structures all at once. Therefore, in the following we provide rudimentary, but computationally useful models. We model similarity in intensity with a measure (to be minimized) that is defined as the sum of the squared differences in grey value between the target image and the transformed source image. The transformation effort is modeled by the use of Hooke's law.[14] The required energy to perform a transformation is computed on the basis of changes in the lengths of edges in the grid. For this purpose and to ensure that various shape changes result in an increase in required energy, all possible combinations between corner points, points halfway on a grid line, and combinations between corner points and points halfway on a gridline are considered (Figure 2). Now, if we denote the set of considered edges by E, we can define total energy $U_{total\text{-}deform}$ to be minimized as follows:

$$U_{deform}(e) = \frac{1}{2} l_e \left(\left\| e^{before} \right\| - \left\| e^{after} \right\| \right)^2 , \qquad U_{total-deform} = \sum_{e \in E} U_{deform}(e)$$

where l_e is an elasticity constant associated with the tissue that edge e crosses.

2.3 Optimization algorithm

The underlying optimization problem in practice is multi-objective, i.e. find transformations that on the one hand maximize the similarity between source and target image (objective 1) and on the other hand minimize the amount of required energy (objective 2). In multi-objective optimization, the optimum is a set of solutions, called the optimal Pareto front, because many solutions may be equally good, e.g. solution a may be better in the first objective than solution b, but worse in the second objective. Therefore, a collection of outcomes (a so-called Pareto front) that represents efficient trade-offs between the objectives is computed and presented at once.

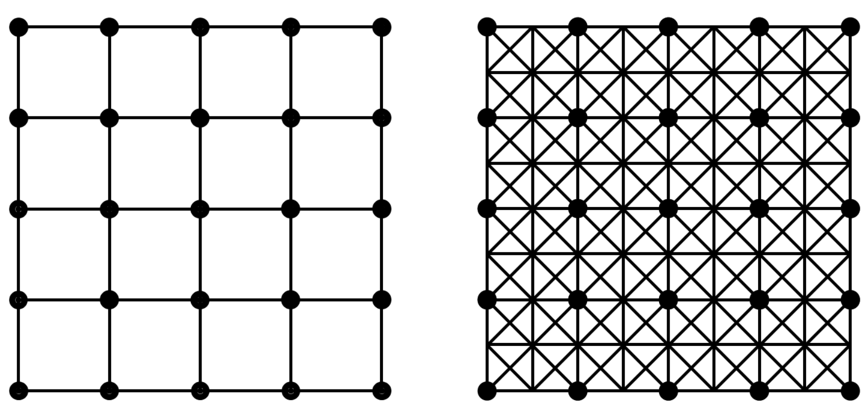

Figure 2. Left: Grid of points used as a basis for the transformation model. Right: Grid of points with all connections taken into account in the calculation of the required energy to accomplish the transformation.

By investigating deformable image registration from a multi-objective optimization perspective we remove the need to set a predetermined singular linear combination of objectives, which is commonly required and used in existing techniques for image registration. A multi-objective approach is inherently more powerful because potentially not all Pareto-optimal outcomes can be found when running existing single-objective registration techniques multiple times with different weights, depending on whether (parts of) the optimal Pareto front is convex or concave. Moreover, selecting a uniform spread of weight combinations may not necessarily result in a uniform spread of solutions along the Pareto front. To better understand the true possible outcomes of registration, it is therefore important to use a multi-objective approach. Then, after studying the possible outcomes, we can decide which outcomes are preferable for the application at hand.

Population-based methods such as evolutionary algorithms (EAs) are among the state-of-the-art in solving multi-objective optimization problems.[15] For optimization, we used a particular type of EA known as EDA (Estimation-of-Distribution Algorithm), that aims to exploit features of a problem's structure in a principled manner via probabilistic modeling.[9-11] This makes this type of EA typically more robust and capable of solving a large class of optimization problems reliably without using any problem-specific knowledge.

The specific EDA that we use, is known as iMAMaLGaM-X+ (incremental Multi-objective Adapted Maximum-Likelihood Gaussian Model miXture).[13] In previous work where we first introduced our multi-objective approach to registration[8], we considered the non-incremental version of this algorithm. MAMaLGaM-X uses a population of solutions, selects 35% of the best solutions according to a domination-rank ordering, estimates an l-dimensional normal mixture distribution (where l is the number of real-valued variables to be optimized) from these selected solutions and generates new solutions by sampling the estimated distribution. Using adaptive techniques that scale the covariance matrices of the normal distributions in the mixture according to improvements found during optimization, the risk of premature convergence is minimized. The + annotation, i.e. MAMaLGaM-X+, indicates a variant that is capable of obtaining an ever better spread of solutions by maintaining m additional components in the mixture distribution, one for each objective. Selection for these components is done completely independently on the basis of each respective individual objective, thereby specifically targeting convergence at the extreme regions of the Pareto front. Solutions from these specific clusters are furthermore also integrated into the selection procedure for the other components in the mixture distribution. In iMAMaLGaM-X+, incremental model learning is additionally used. This means that for every component in the mixture distribution the Gaussian model is updated using incremental updates, thereby strongly reducing the population size for each of the mixture components that is minimally required to ensure reliable convergence. Because the overall algorithm uses many mixture components (20 mixture components were previously suggested[13]), the increase in convergence speed is substantial. Experimental results furthermore showed no loss in approximation quality. For the application at hand, this improvement allows us to use more fine-grained grids (that have more variables to be optimized) for the registration task, which is of importance for more complex registration tasks, especially when considering disappearing structures.

2.4 Proof of principle experiments

To test whether the proposed approach is able to tackle large deformations in deformable image registration we selected 2D slices from MRI scans acquired from a healthy volunteer. One from an MRI scan acquired with the volunteer in prone orientation and one from an MRI scan acquired with the volunteer in supine orientation. Prior to selection of the 2D slices, the 3D MRI scans were rigidly registered on the bony anatomy. The prone image served as the source image and the supine image as the target image.

To demonstrate the ability of taking into account disappearing structures, we created an artificial 2D example. Additionally, pre-operatively and post-operatively acquired computed tomography (CT) scans from a patient suffering from breast cancer were used for this purpose. Similar to the MRI example 2D slices were selected from the CT scans after rigid registration of the scans on the bony anatomy.

For all examples, first two 9×9 grids, corresponding to 324 parameters for the optimization algorithm, were defined and used in our multi-objective optimization framework. The outcomes were studied and for two selected trade-offs between the objectives we ran a single-objective variant of the optimization algorithm with a higher resolution of the grid (17×17 points for each grid) for illustration purposes. Here a multi-scale initialization method was used, whereby the outcome of a coarser grid was iteratively used to create a finer grid that served as a basis for initialization: from 3×3 to 5×5 to 9×9 to 17×17. The cost function for the single-objective optimization algorithm is a linear combination of the objectives. These weight factors can easily be determined from the Pareto fronts by finding a straight line tangent to the convex Pareto front (note that where the Pareto front is concave, this is impossible). Furthermore, in this pilot study, we did not further distinguish between different tissue types and therefore used only one flexibility value.

3. RESULTS

It is important to note that because for this proof of principle 2D slices were used that only comprises part of a 3D data set a perfect registration is often not obtainable without extreme, anatomically incorrect, deformations. The illustrated test cases should therefore be seen only as proof of concepts that illustrate the capacity of the proposed approach.

From the results in Figure 3, we first note that desirable behavior is observed in the sense that the large deformations required for prone-supine matching are found, in just one run of the algorithm. Moreover, in both the artificial and the real-world CT breast example the approach is capable of removing parts that have disappeared, again in just one run.

The CT breast example illustrates that the homogeneity in grey values in breast tissue makes it difficult to determine whether a part of the tissue has been removed or has been largely deformed. Although the tumor is successfully removed by the approach, the change in shape of the breast is mainly achieved by deforming the breast instead of correctly identifying that a larger piece of tissue surrounding the tumor has been operatively removed. The observed manner of deformation is a direct result of the optimization algorithm exploiting the modeling of tissue deformation in the objective function. Therefore, it is important to realize that this does not diminish the usefulness of the combination of the dual-dynamic grid model and the powerful optimization framework. It does indicate, however, that in future work an improved modeling of deformation is required to ensure the desired manner of deformation is achieved.

Overall, although these examples are still preliminary, it illustrates plausible and desirable behavior of the proposed methodology. In future work, we will include the possibility to adaptively subdivide the grid, use local optimization of subdivisions to speed-up the overall process, and extend it to 3D volumes.

4. DISCUSSION AND CONCLUSIONS

In this work we developed and studied, within a previously introduced multi-objective optimization framework[8,13], a dual-dynamic transformation model to be able to tackle the hardest problems in deformable image registration, i.e. problems where large anatomical differences occur between image acquisitions. In this proof of principle we illustrate that the proposed model is an elegant and powerful approach that, when combined with proper optimization techniques, is capable of tackling different hard registration problems, e.g. in which large deformations occur due to images acquired in prone and supine positions and in which structures between image acquisitions disappeared due to surgery.

Currently, these hard image registration problems can still not be solved satisfactorily using existing registration approaches. In the few publications [2-7] that address (dis)appearing structures, these structures need to be explicitly identified which is often considered as a separate (segmentation) task, which is not required in the approach presented here.

A major strength of our methodology is that the objectives can be easily reformulated as required. It can therefore be combined with state-of-the-art similarity measures and deformation models. Our methodology can be used to obtain an improved understanding of the interaction between the obtained registration outcome and one or more regularization terms and objectives for typical medical image registration problems, allowing improved tuning of existing algorithms to specific problems. Moreover, the preliminary results presented in this paper indicate that the presented methodology is also highly likely capable of paving the road to an elegant solution to some of the hardest deformable image registration problems.

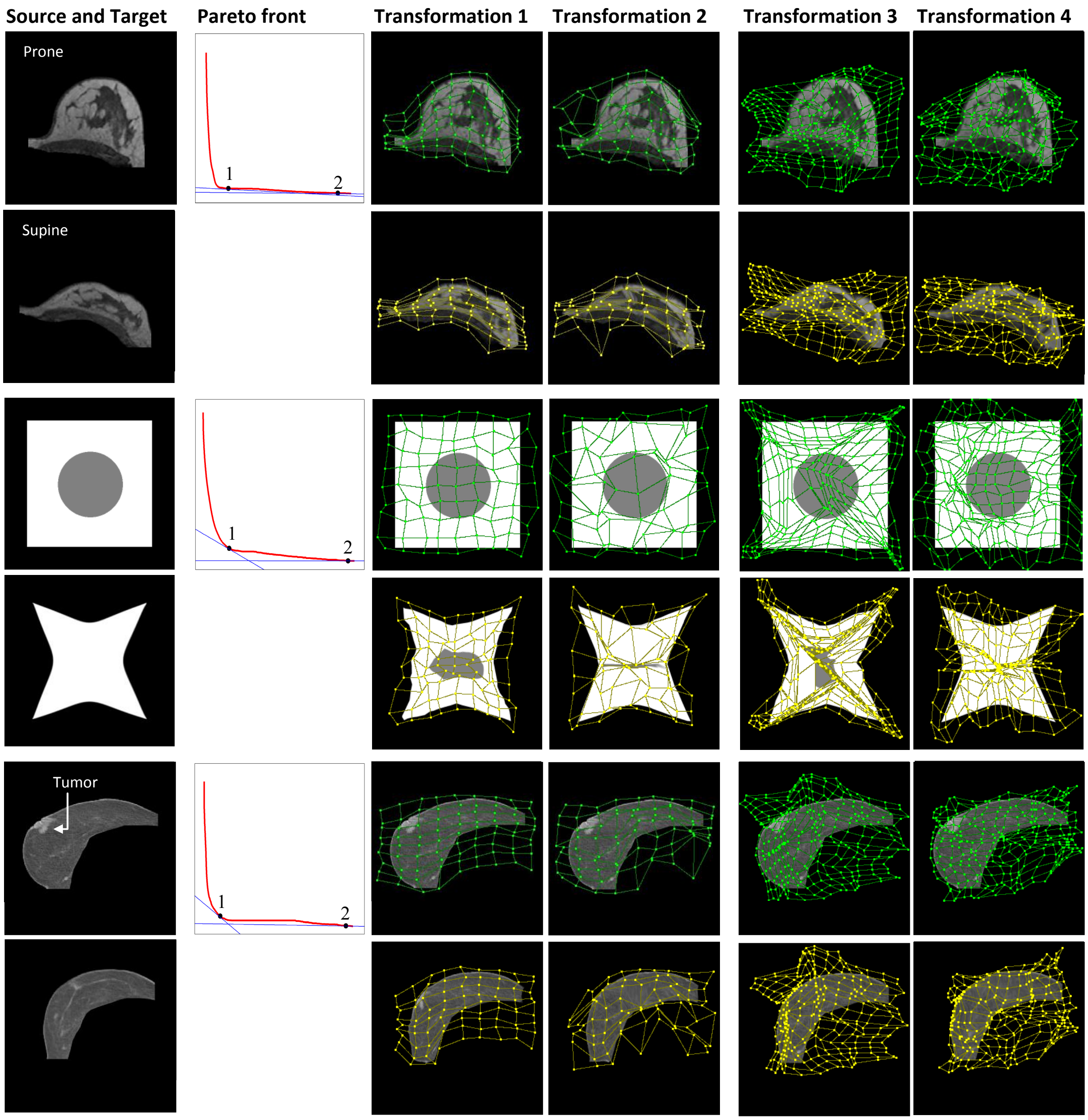

Figure 3. From top to bottom: prone and supine breast MRI, artificial example with a disappearing structure, breast CT data pre and post surgical removal of a tumor. From left to right: source and target image, Pareto front with the locations of the selected solutions indicated (horizontal axis: transformation effort; vertical axis: similarity measure; scales omitted because actual values are irrelevant), Transformation 1 and 2: two solutions selected from Pareto front, Transformation 3 and 4: associated single-objective results. For each transformation the grid associated with the source image (green) and the grid associated with the target image (yellow) are shown as an overlay on the source and transformed source image, respectively.

ACKNOWLEDGEMENTS

Financial support of this work was provided by the Dutch Cancer Society (Grant No. KWF 2008-4024).

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