A multi-resolution strategy for a multi-objective deformable image registration framework that accommodates large anatomical differences

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ABSTRACT

Currently, two major challenges dominate the field of deformable image registration. The first challenge is related to the tuning of the developed methods to specific problems (i.e. how to best combine different objectives such as similarity measure and transformation effort). This is one of the reasons why, despite significant progress, clinical implementation of such techniques has proven to be difficult. The second challenge is to account for large anatomical differences (e.g. large deformations, (dis)appearing structures) that occurred between image acquisitions. In this paper, we study a framework based on multi-objective optimization to improve registration robustness and to simplify tuning for specific applications. Within this framework we specifically consider the use of an advanced model-based evolutionary algorithm for optimization and a dual-dynamic transformation model (i.e. two "non-fixed" grids: one for the source- and one for the target image) to accommodate for large anatomical differences. The framework computes and presents multiple outcomes that represent efficient trade-offs between the different objectives (a so-called Pareto front). In image processing it is common practice, for reasons of robustness and accuracy, to use a multi-resolution strategy. This is, however, only well-established for single-objective registration methods. Here we describe how such a strategy can be realized for our multi-objective approach and compare its results with a single-resolution strategy. For this study we selected the case of prone-supine breast MRI registration. Results show that the well-known advantages of a multi-resolution strategy are successfully transferred to our multi-objective approach, resulting in superior (i.e. Pareto-dominating) outcomes.

Keywords: Deformable registration, multi-objective optimization, evolutionary algorithms, multi-resolution strategy, large anatomical differences

1. INTRODUCTION

Numerous clinical applications could benefit from the use of deformable image registration methods. However, despite significant progress in the field of deformable image registration[1], there is still no widespread translation of these methods into the clinic. One of the main problems is that currently existing methods rely on many user-defined parameter settings (e.g. weights for the different objectives) and it is non-trivial how to find appropriate settings for a specific clinical application. Often the only person who is capable of performing this task is the researcher who developed and studied the method (i.e. the expert of the method) and this task is then performed by trial and error.[2]

For such reasons, we started studying deformable image registration from a multi-objective optimization perspective.[3,4] In multi-objective optimization, a collection of outcomes that represents efficient trade-offs between the different objectives (a so-called Pareto front) is computed, which allows for more insightful tuning for specific applications.

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Moreover, we combined our multi-objective approach with a dual-dynamic transformation model (i.e. two "non-fixed" grids: one for the source- and one for the target image) to tackle the hardest deformable image registration problems, including e.g. large deformations and anatomical changes.[5] In contrast with other work[6-11], the challenging problem of identifying (dis)appearing structures is considered 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. We illustrated that this provides an elegant and powerful approach that, when combined with proper optimization techniques, is capable of tackling different hard registration tasks, 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.[5]

So far[3-5], our multi-objective approach was based on a single-resolution strategy. In image registration, it is, however, common practice to use a coarse-to-fine (multi-resolution) strategy that first registers objects at a coarse resolution followed by matching fine structures at a finer resolution.[12,13] This substantially helps in preventing the optimization algorithm that drives registration from converging to a local optimum. Such multi-resolution strategies have so far however only been developed for and tested with single-objective registration methods. Here, we develop and study a multi-resolution strategy within our multi-objective deformable image registration framework.

2. MATERIALS AND METHODS

2.1 Multi-objective deformable image registration framework

Deformable image registration can be posed as an optimization problem where different objectives are of interest. Commonly, registration methods optimize a single function that represents a linearly weighted combination of two (or more) objectives (typically related to quality of fit and smoothness of deformation). However, the underlying optimization problem is actually multi-objective, i.e. find transformations that on the one hand maximize the similarity between the source and the target image and on the other hand minimize the amount of deformation.

Recently, we started studying deformable image registration from a multi-objective optimization perspective, which removes the need to set a predetermined singular combination of objectives through trial and error.[3,4] Our framework results not in a single solution but in a Pareto front of solutions, which is a collection of solutions of efficient trade-offs between the objectives (i.e. solutions that are equally good (better in one objective, but worse in another)). Having an entire Pareto front provides far more insight into the interplay between objectives. Moreover, a multi-objective approach is inherently more powerful than a single-objective approach because potentially not all Pareto-optimal outcomes are explored when running existing single-objective registration techniques multiple times with different linear combinations of the weights for the objectives (i.e. if the Pareto front is concave).

2.1.1 Dual-dynamic transformation model

It is common practice to use a fixed grid for the source image and a non-fixed grid for the target image. We introduced the concept of using a dual-dynamic transformation model that uses two non-fixed grids: one for the source image and one for the target image.[5] This increases the flexibility of transformations substantially and in a manner that is especially required when tackling some of the hardest problems, in particular when large deformations and (dis)appearing structures are involved.

Previously, we used rectangular grids and employed grid triangulation to perform linear simplex interpolation when creating the transformed source image. This however results in artifacts when convex grid elements are mapped to concave elements. Therefore, we propose to use triangulated grids directly instead (see Figure 1).

2.1.2 Objectives

Our framework can be combined with arbitrary objectives (e.g. similarity- and deformation measures). The main purpose of the current work, however, is to develop and to study a multi-objective multi-resolution strategy. Therefore, we use rudimentary, but computationally useful measures. We define two objectives (both of which need to be minimized), one related to the quality of fit: intensity similarity; and one related to the smoothness of the deformation: transformation effort, i.e. the amount of energy required to accomplish the transformation. For intensity similarity we use the sum of the squared differences in grey value between the target- and the transformed source image. The transformation effort is

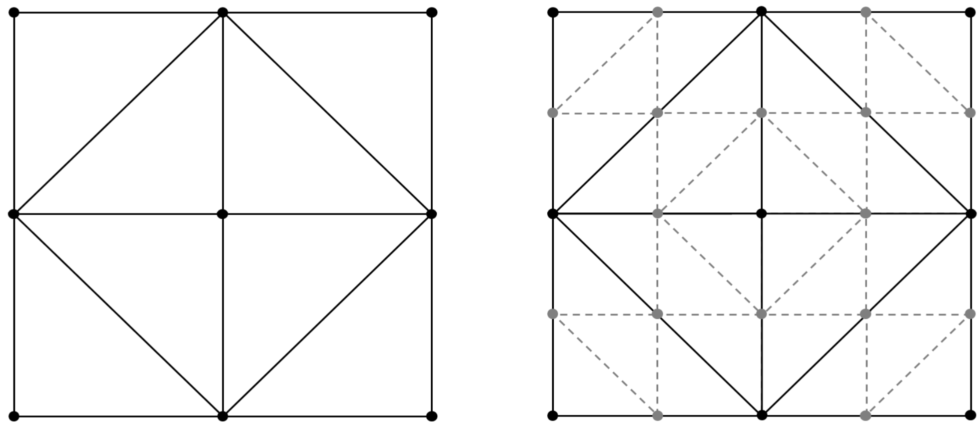

Figure 1. Left: Initial 3×3 grid of points used as a basis for the transformation model. Right: Second grid of points (5×5) used in the multi-resolution scheme. The light grey nodes and dotted edges illustrate the parts that are added to the initial 3×3 grid.

based on Hooke's law[14] using the changes in the lengths of the edges in the grid. Let the set of considered edges be denoted by E. The total energy can then be defined as follows:

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

2.1.3 Optimization algorithm

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. Population-based methods such as evolutionary algorithms (EAs) are among the state-of-the-art in solving multi-objective optimization problems.[15] To perform multi-objective optimization, we used a type of evolutionary algorithm (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.[16-19] The particular EDA that we employ is iMAMaLGaM-X+ (incremental Multi-objective Adapted Maximum Likelihood Gaussian Model miXture) in which the underlying probabilistic model is a Gaussian mixture distribution.[4] In related work, iMAMaLGaM-X+ was shown to have excellent performance, converging to high-quality approximations of the optimal Pareto front on well-known benchmark problems.[4]

In previous work where we first introduced our multi-objective approach to registration[3], 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 parameters 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[4]), the increase in convergence speed is substantial. Experimental results furthermore showed no loss in approximation quality. This improvement allows us to use more fine-grained grids (that have more parameters to be optimized) for the registration task, which is of importance for more complex registration tasks.

As in our framework a dual-dynamic transformation model is used, the coordinates in two grids need to be optimized. Therefore, the number of real-valued parameters to be optimized equals two times the number of grid points times the spatial dimensionality of the image.

2.2 Multi-resolution image registration

Deformable image registration methods commonly employ multi-resolution strategies where the result obtained using a lower resolution is used as the initial condition for the method at a higher resolution.[12,13] The main reason for such a strategy is to prevent the optimization algorithm from converging to local optima. Such multi-resolution strategies have been used so far only in combination with a single objective to be optimized whereas our work is inherently multi-objective, finding a complete Pareto front at once on the basis of a set of solutions rather than iteratively improving a single solution as is characteristic of most methods employed for single-objective optimization. Here, we introduce a multi-resolution strategy for the dual-dynamic transformation model that can be used in our multi-objective framework.

To establish a multi-resolution strategy, a method is required to refine the two grids associated with a solution so as to be able to continue computation at a finer grid resolution. Because we use a multi-objective optimization algorithm however, there are some extra challenges associated with this. A straightforward manner to refine a triangulation for instance would be to take a solution, define a new grid point in the center of each triangle and subsequently compute a completely new (Delauney) triangulation from the grid points (for both the source and target grids separately). This works adequately if a single solution needs to be refined. However, this is not the case in our multi-objective framework in which we have an entire Pareto front of solutions. This manner of refinement can then result in a correct refinement of a grid that is associated with a solution located on one end of the Pareto front, but if this new triangulation definition is used in solutions on the other end of the Pareto front in which grid points will have been displaced much, these grids then very likely violate certain constraints (no folding or crossing of edges). As a result, only a very small subset of solutions will be feasible in the next resolution phase, effectively removing the majority of the Pareto front and undoing much of the optimization effort spent so far. Therefore, a refinement method is required that refines all triangulations similarly without the need to redefine the triangulations (i.e. the underlying graph that connects the grid points). Although adding a point in the center and splitting up each triangle into 3 triangles (i.e. without completely re-computing a triangulation from the grid points) achieves this, this is not a preferable method because it results in flattened, elongated triangles and grid points with extreme degrees of connectivity. This prevents being able to capture, and eventually potentially dissolve, local structures nicely. We therefore instead add points on each edge of the grid to accomplish refinement. By doing so, each triangle is subdivided into 4 triangles in a manner that overcomes the aforementioned issues (see Figure 1).

A second aspect to consider is that after grid adaptation, the number of parameters is enlarged. Therefore, to ensure a good performance of the evolutionary optimization algorithm, also the number of solutions in the population needs to be enlarged. For this purpose, we employ a previously established guideline that dictates a population size of $10 \cdot \sqrt{l}$, where l denotes the number of parameters. In our case this corresponds approximately to doubling the number of solutions in the population. The solutions that are to this end additionally required are obtained by using copies of the refined solutions to which random noise was applied. This noise follows in all directions a normal distribution with a variance of 0.01 times the image resolution divided by the grid resolution.

2.3 Experiments

For our experiments we consider the case of prone-supine breast MRI registration. The MRI scans were acquired from a healthy volunteer. First, the two MRI scans were rigidly registered on the bony anatomy. Subsequently, one set of 2D slices was selected from the scans (Figure 2).

We performed tests with both a single-resolution strategy (SRS) and a multi-resolution strategy (MRS). With MRS, grid resolutions of 3×3, 5×5, 9×9, and 17×17 were considered, resulting in respectively 36, 100, 324, 1156 parameters to be optimized for which a budget of $1616 \cdot 10^4$ evaluations (respectively $36 \cdot 10^4$, $100 \cdot 10^4$, $324 \cdot 10^4$, and $1156 \cdot 10^4$ in a single run on the different resolutions) was allowed. For direct comparison of results from SRS with intermediate results from MRS, we also ran SRS for the four different resolution scales with respectively budgets of $36 \cdot 10^4$, $136 \cdot 10^4$, $460 \cdot 10^4$, and $1616 \cdot 10^4$ evaluations (which we refer to in the remainder as the low budget). Finally, we also ran SRS with the same number of evaluations used in total by MRS (which we refer to in the remainder as the high budget).

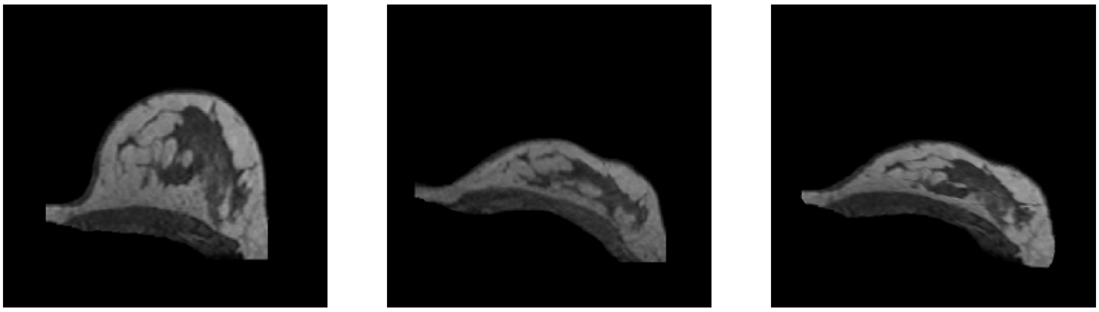

Figure 2. Axial slices from breast MRI scans acquired from a healthy volunteer. Left: prone acquisition (source). Middle: supine acquisition (target). Right: transformed source image associated with the solution indicated with a × symbol in the right lower graph in Figure 3.

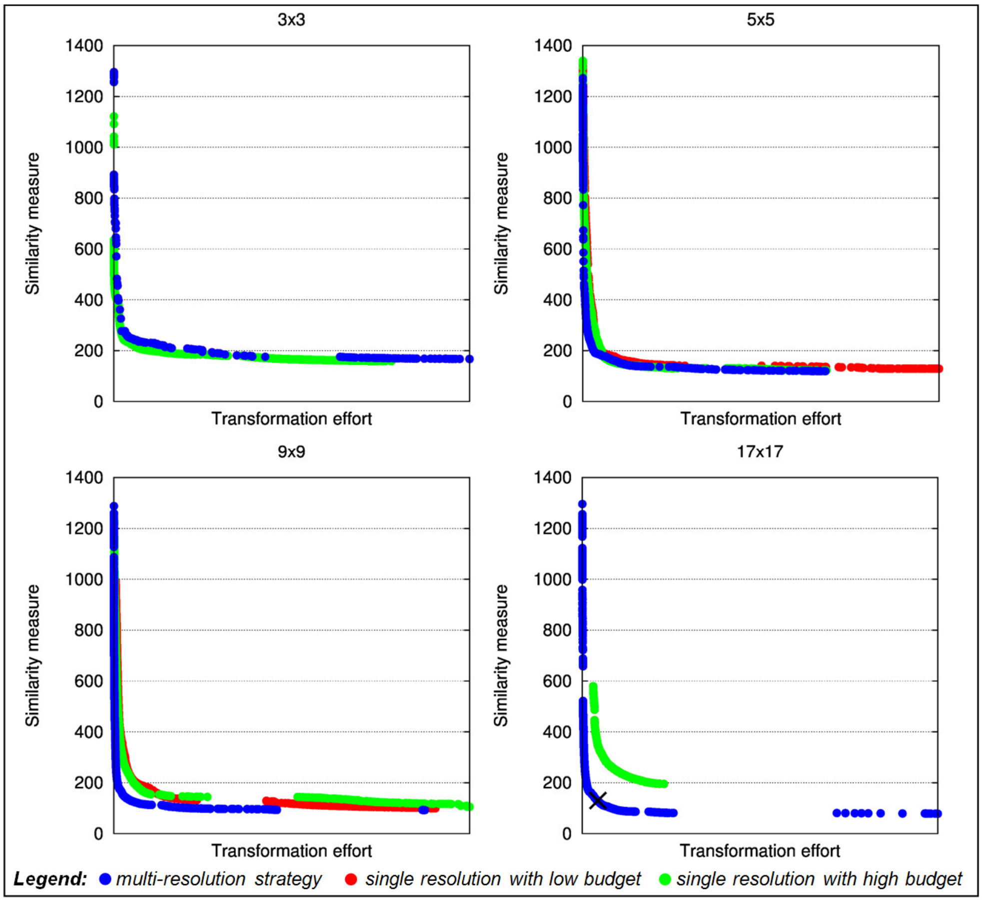

Figure 3. Pareto fronts resulting from a multi-resolution strategy and from single-resolution strategies with different evaluation budgets and grid resolutions. Note: given the budgets as outlined in the paper, in the 3×3 graph red results coincide with blue results and in the 17×17 graph red results coincide with green results (no separate batches of 10 runs were performed for these particular cases because parameter settings were identical).

3. RESULTS

It is important to note that because 2D slices were used that only comprise part of a 3D data set a perfect registration is often not obtainable without extreme, anatomically incorrect, deformations. The illustrated test case should therefore be seen only as an example illustrating the effect of the use of MRS compared to SRS.

Figure 3 shows Pareto fronts computed over 10 independent runs of the EA. A scale is omitted on the x-axis because graphs pertaining to different resolutions are not directly comparable with respect to the transformation effort objective due to the different number of edges that is taken into account. A transformation pertaining to a solution obtained with MRS is given in Figure 2 and indicated with a × symbol in Figure 3.

The results show that the proposed multi-resolution strategy is effective. For sufficiently fine-grained grids (i.e. already at 9×9 and definitely at 17×17) the multi-resolution strategy is able to obtain far better Pareto fronts than are obtainable with a single-resolution strategy, even if the optimization algorithm is run longer.

It should be noted that the EA is stochastic and the optimization problem is high-dimensional and rugged with many local optima. Therefore the outcomes of individual runs are not necessarily identical. This also explains why in the graph for the 9×9 grid resolution the low-budget results are in a part of the objective space better than the high-budget results. A higher budget alone does not necessarily help the algorithm escape local optima. Moreover, local optima may already be found quite early on and the algorithm may spend the rest of its budget covering that local Pareto front with many points. Hence, a multi-resolution strategy is vital to obtain superior results.

4. DISCUSSION AND CONCLUSIONS

Commercially available deformable image registration software often solely offers one method with fixed settings to be used for all clinical applications. However, one solution to all deformable image registration problems does not exist. Moreover, it is a challenge to tune developed methods to specific problems (i.e. how to best combine different objectives such as similarity measure and transformation effort). To overcome this issue we introduced a multi-objective framework for deformable image registration.[3,4] A major strength of our framework 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 framework 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.

In this work we developed and studied, within our multi-objective framework, a multi-resolution strategy for deformable image registration and compared its results with a single-resolution strategy. Although multi-resolution strategies have been established before for other registration methods, these are not targeted at the use of multi-objective optimization, making this a novel contribution. In this study, we successfully illustrated that with the proposed multi-resolution strategy our framework is capable of producing substantially improved Pareto fronts. This will allow even more accurate and insightful tuning of deformable image registration techniques for problems that demand the use of high-resolution grids (i.e. the hardest deformable image registration problems).

The results in this paper show complete, unzoomed Pareto fronts. These fronts therefore clearly also contain less interesting parts (i.e. solutions with near-zero transformation effort). Although it is theoretically interesting to see the size and shape of the Pareto fronts, these are practically less relevant. Therefore, in future work we shall include adaptive steering mechanisms in the framework to automatically focus more on areas of interest. Furthermore, we shall extend the work to 3D volumes. With the multi-resolution strategy as established here we have a solid foundation to further study also the complex but important registration problems in which structures / tissues (dis)appear between image acquisitions for which we already know, based on our previous results[5], that our framework is a promising approach.

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