

# Multi-objective optimization as a novel weight-tuning strategy for deformable image registration applied to pre-operative partial-breast radiotherapy

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## Introduction

Deformable image registration (DIR) has potential to enable novel approaches in radiotherapy (RT) such as dose accumulation, online adaptive planning, and response monitoring. Although DIR is predominantly formulated as a single-objective optimization problem, its inherent nature is multi-objective, i.e., there are multiple, conflicting objectives that need to be optimized simultaneously. A major challenge that limits its use in clinical practice, however, is the difficulty in choosing the optimal trade-off of these multiple objectives. Currently, primarily trial-and-error approaches are used to find weights to linearly combine multiple objectives into a single-objective function. Their success relies on a logical relation between the weights, objective values, and registration outcome, which is not well established. In this work, for the task of RT tumor response monitoring, we employ a multi-objective optimization approach that is not necessarily dependant on this logical relation and provides insightful tuning of weights even for hard registration cases.

## Materials & Methods

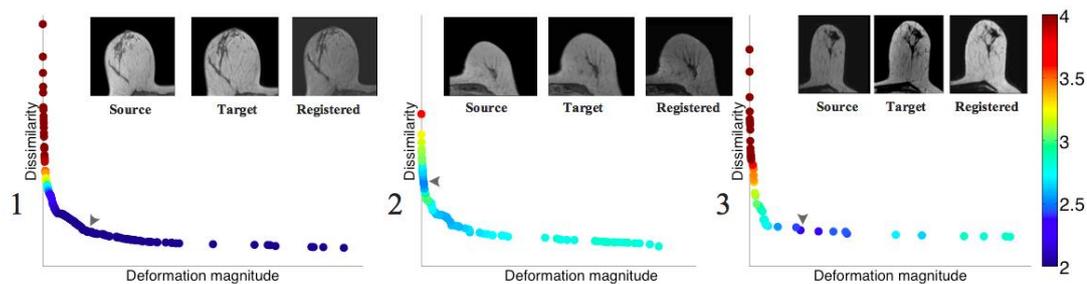
We consider DIR as a problem with two objectives (dissimilarity and deformation magnitude) to be minimized. In such problems, there is no unique optimal solution, but rather a set of solutions that represents the optimal trade-offs between the objectives, called the optimal Pareto front. Optimizing multiple linear combinations does not always yield solutions on the Pareto front, due to the local search nature of most single-objective optimization techniques used in DIR and their sensitivity to the shape of (parts of) the Pareto front (i.e., convex or concave). For this reason, we use a multi-objective evolutionary algorithm (EA) [1] to search for the best weights that correspond to linear combinations of objectives for which single-objective registration results in solutions that have high quality in the multi-objective sense and form a Pareto front. The particular EA used, estimates and samples a Gaussian mixture distribution from its population of candidate solutions and subsequently adapts its estimation in each generation based on the sampled solutions. Guideline settings were used with 20 clusters and 35% selection [1]. The single-objective registration method used here is elastix [2] with normalized correlation ratio as dissimilarity metric and bending energy penalty for deformation magnitude.

We tested this approach on 5 pairs of T1-weighted breast MR images, with a voxel size of 0.8x0.8x1.2 mm (acquired pre- and post-RT) of 5 breast cancer patients that underwent pre-operative partial-breast RT. Although there are no large global deformations, finding a perfect registration is sometimes still challenging due to radiation-induced changes present between image acquisitions (e.g., tumor shrinkage, edema). The registration accuracy was

calculated by the mean target registration error (TRE) in mm based on 8 expert-defined landmarks on each pair (i.e., 8 in each source image and 8 in each target image).

## Results

Pareto fronts with color-coded mean TRE distribution for cases 1, 2, and 3 are depicted below; results for cases 4 and 5 are similar to cases 1 and 3 in mean TRE distribution. Arrows indicate selected registration outcomes (lowest mean TRE). Mean TRE ranges per case are: case 1: 1.6-6.9; case 2: 2.5-3.8; case 3: 2.2-8.1; case 4: 2.8-6.5; case 5: 2.9-5.5 mm. The range of TRE values used in the color bar was chosen to best visualize the distribution of mean TRE values along the Pareto front. In cases 1, 3, 4 and 5, the mean TRE distribution is smooth along the Pareto front. Optimizing weights by trial and error is quite viable in these cases. For case 2, the mean TRE fluctuates more along the Pareto front because this case is harder with more detail in the images. Further, although in this case the mean TRE has limited range, overfitting with anatomically incorrect deformations still occurs (large values for deformation magnitude), making insightful weight tuning a necessity. Here, trial-and-error is far less intuitive, running the risk of being inefficient and not finding high-quality registration outcomes. This holds also for alternative approaches such as straightforward parameter sweeps; solutions found that way are often Pareto-dominated (worse in at least one objective) by solutions that form the Pareto front found with the EA.



## Discussion & Conclusions

The applied novel multi-objective weight optimization strategy for DIR removes the need to pre-determine a singular combination of objectives via trial-and-error and provides unique insight into the interaction between objectives of interest. This can be very valuable, especially for problems that are difficult to solve with single-objective techniques. Our approach facilitates insightful fine-tuning to specific clinical applications and can easily be extended to include more (weights for) objectives as well as other parameters.

## References

- [1] P.A.N. Bosman and T. Alderliesten, “Incremental Gaussian model-building in multi objective EDAs with an application to deformable image registration,” in *Proc. of the Genetic and Evolutionary Computation Conf. - GECCO '12*, 2012, pp. 241-248.
- [2] S. Klein *et al.*, “elastix: a toolbox for intensity-based medical image registration,” *IEEE Trans. Med. Imaging*, vol. 29, no. 1, pp. 196–205, 2010.

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