Medical Image Registration Using Evolutionary Computation:

An Experimental Survey

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Abstract–In the last few decades, image registration (IR) has been established as a very active research area in computer vision. Over the years, IR's applications cover a broad range of real-world problems including remote sensing, medical imaging, artificial vision, and computer-aided design. In particular, medical IR is a mature research field with theoretical support and two decades of practical experience.

Traditionally, medical IR has been tackled by iterative approaches considering numerical optimization methods which are likely to get stuck in local optima. Recently, a large number of medical IR methods based on the use of metaheuristics such as evolutionary algorithms have been proposed providing outstanding results. The success of the latter modern search methods is related to their ability to perform an effective and efficient global search in complex solution spaces like those tackled in the IR discipline.

In this contribution, we aim to develop an experimental survey of the most recognized feature-based medical IR methods considering evolutionary algorithms and other metaheuristics. To do so, the generic IR framework is first presented by providing a deep description of the involved components. Then, a large number of the latter proposals are reviewed. Finally, the most representative methods are benchmarked on two real-world medical scenarios considering two data sets of three-dimensional images with different modalities.

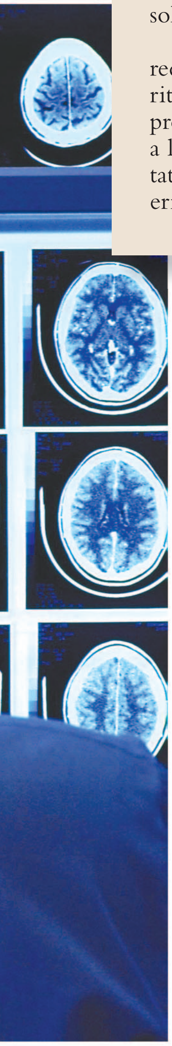
I. Introduction

There are many applications in digital image processing that require the proper alignment of different images. These problems arise from rather different domains. For example, in remote sensing it is important to put into correspondence the images acquired from different viewpoints in order to achieve a global cartography from partial views. Likewise, in medical imaging it is helpful to determine a proper matching between the images provided by different kinds of sensors that are capable of highlighting different characteristics of the human anatomy as bones, organs, or lesions.

Image registration (IR) [1] is an important research field in digital image processing. It is used to align two or more images acquired under different conditions: at different times, using different sensors, from different viewpoints, or a combination of some of the latter situations. In IR, the input and output images are available, but the specific transformation that produced the output image from the input one is usually unknown. IR aims to estimate the best geometric transformation leading to the best possible overlap thus transforming those independent images into a common one.

To clarify terminology, the input image is also called *scene* and it is the image that will be transformed to reach the geometry of a reference image called *model*. They both are related by the said transformation and the degree of resemblance between them is measured by a *Similarity metric*. The estimation of the transformation is usually tackled following an iterative *optimization procedure* in order to properly explore the search space of possible transformations. Two search approaches have been considered in the IR literature. On the one hand, we find the matching-based IR approach, where the optimization problem is intended to look for a set of correspondences from pairs of similar image features. From those correspondences, the registration transformation is typically derived using numerical methods. On the other hand, IR methods following the approach based on the transformation parameters directly explore the range of each parameter describing the transformation.

Medical IR is a mature research field with theoretical support and two decades of practical experience. A wide variety of applications have been proposed and there are excellent surveys that provide an up-to-date progress in the application of classical optimization techniques to the medical IR field [2]. Nevertheless, aspects such as presence of noise in images, image discretization, and orders of magnitude in the scale of the IR transformation parameters, among others, cause difficulties for the success of the optimization process applied by traditional IR methods, which are prone to be trapped in local minima. Recently, IR approaches based on *evolutionary computation (EC)* [3] and other *metaheuristics (MHs)* [4] have demonstrated to be a promising solution for facing these challenging drawbacks [5]–[13]. Although they are not free of the problem of local minima and there is generally no guarantee that they will reach the global optimum in polynomial time, they have largely demonstrated their capability to perform a robust search in complex and ill-defined problems such as IR [14] and image processing [15]. Thus, they are usually considered as global optimization approaches.



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In [16], the authors developed a comparative study on evolutionary IR methods for a different and specific application as 3D modeling. The aim of the current contribution is two-fold. On the one hand, we aim to review the state of the art of the IR methods that lay their foundations on EC and other MHs including, in our modest opinion, the most relevant works. On the other hand, we aim to develop an experimental study to test the capability of thirteen of the latter contributions to tackle different medical IR problems considering two image modalities. The performance of this family of methods will be compared with the outcomes achieved by two gradient-based methods, classically used in the medical IR field, thus leading to the global analysis of fifteen methods. To do so, two case studies tackling two real-world medical applications have been carried out. In both cases, we have considered a feature-based IR approach [1], [14] in which a preprocessing step, prior to the application of IR, is performed in order to extract a concise subset of salient features of the medical 3D images. The first image data set considered comes from the BrainWeb repository at McGill University [17]. The second one was kindly provided by the Brown Medical School of the Rhode-Island Hospital (USA) and it is composed of two different computed tomographies of human wrists from a real-world case study. In both cases, we will deal with complex scenarios by facing non-rigid IR problem instances considering similarity transformations, that constitute a rotation, a translation, and a uniform scaling. Thus, the conducted experiments will provide us with actual information about the degree of suitability of evolutionary and MH-based IR methods to solve IR problems in medical imaging.

The structure of this contribution is as follows. Section II describes the IR problem analyzing the principal components of a generic IR method. Next, Section III introduces a review of the state of the art in IR methods based on EC and other MHs. Section IV presents a broad experimentation with the two medical data sets considering thirteen of the reviewed IR methods and the two classical approaches. Finally, some conclusions are drawn in Section V.

II. Image Registration

There is not a universal design for a hypothetical IR method that could be applicable to all registration tasks, since various considerations on the particular application must be taken into account. Nevertheless, IR methods usually require the four following components (see Figure 1): two input **Images** (see Section II-A) named scene $I_s = \{\vec{p}_1, \vec{p}_2, \ldots, \vec{p}_n\}$ and model $I_m = \{\vec{p}\,'_1, \vec{p}\,'_2, \ldots, \vec{p}\,'_m\}$, with $\vec{p}_i$ and $\vec{p}\,'_j$ being image points; a **Registration transformation** f (see Section II-B), being a parametric function relating the two images; a **Similarity metric** F (see Section II-C), in order to measure a qualitative value of proximity or degree of fitting between the transformed scene image, noted $f'(I_s)$, and the model image; and an **Optimizer** which looks for the optimal transformation f inside the defined solution search space (see Section II-D). Next, we will describe each of the four IR components.

A. Nature of the Images

IR methods proposed in the literature have addressed problems involving 2D and 3D images. The former are commonly tackled in aerial and satellite applications, while the latter are present in more challenging real-world problems such as medical applications [1]. In those cases, different 3D image modalities are usually acquired as magnetic resonance images (MRIs) and computed tomographies (CTs) (see Figure 2).

According to the nature of the images the IR methods must deal with, they can be classified as *voxel*-based (or *intensity/surface*-based) and *feature*-based methods [1], [14]. While the former directly operate with the images raw data, the latter introduce a preprocessing step of the images (before the application of the IR method) in order to extract a reduced subset with the most relevant features. Since voxel-based methods can deal with a larger amount of data, they are often considered as *fine-tuning* registration processes. On the other hand, feature-based methods typically achieve a *coarser* approximation to the global solution due to the reduced set of characteristics they take into account. Thus, the latter approach is usually followed by a final refinement stage to achieve accurate IR results.

Most of the voxel-based approaches tackle the IR problem by looking for corresponding patterns in the scene and the model images. There is a need to delimit the region where the search is accomplished because of the large data sets under study. Therefore, voxel-based IR methods usually rely on a rectangular window that restricts the search of correspondences between scene and model images. That is an important drawback when the images are deformed by

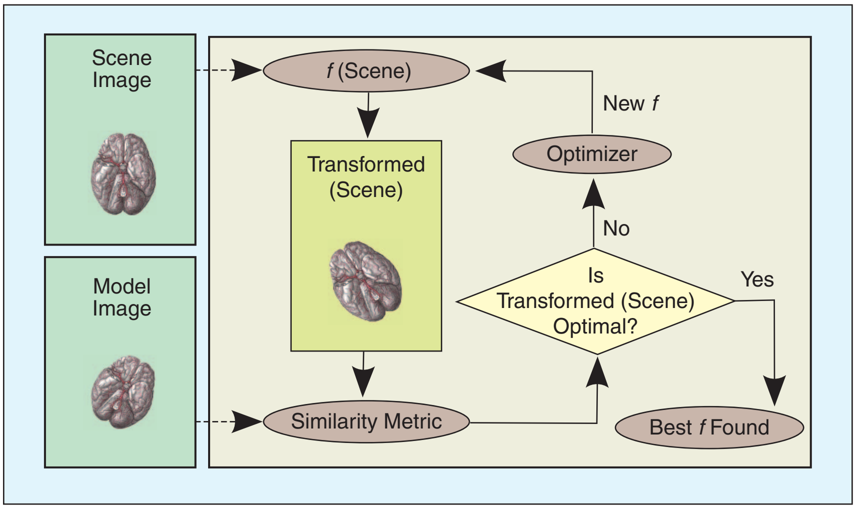

FIGURE 1 The IR optimization process.

complex transformations. Then, this type of window will not be able to cover the same parts of the transformed scene and model images. Moreover, if the window contains a smooth image region without any prominent detail, it will be likely incorrectly matched to other smooth image region in the model image by mistake. Nevertheless, the principal shortcoming of voxel-based methods appears when there are changes in the illumination conditions during the acquisition of the scene and the model images. In that case, the similarity metric offers unreliable measurements and it induces the optimization process to be trapped in local minima.

In order to avoid many of the drawbacks related to voxel-based methods, the second IR approach is based on the extraction of prominent geometric primitives (*features*) from the images [1], [14]. The proper comparison of feature sets will be possible using a reliable feature detector that accomplishes the accurate extraction of invariant features. Those are features which are not affected by changes in the geometry of the images, radiometric conditions, and appearance of noise. There are many different kinds of features that can be considered, e.g., *region features*, *line features*, and *point features*. Among them, corners are widely used due to their invariance to the image geometry.

We have decided to follow the feature-based approach in the final experimental study developed in this contribution (Section IV). In particular, we consider features given by prominent image points, named crest-line points [18], extracted from 3D MRIs and CT images using local curvature information.

B. Registration Transformation

We can classify IR methods according to the registration transformation model used to relate both the scene and the model images. The first category of transformations includes *linear transformations*, which preserve the operations of vector addition and scalar multiplication, being a combination of translation, rotation, scaling, and shear components. Among the most common linear transformations in IR we found rigid, similarity, affine, projective, and curved. Linear transformations are global in nature, thus not being able to model local deformations. The second category of transformation includes *"elastic"* or *"non-rigid"* transformations which allow local warping of image features, thus allowing local deformations.

The transformation considered will depend on the application addressed and the nature of the images involved. In particular, we use similarity transformations for the two medical IR applications presented in Section IV. Such transformations have demonstrated their suitability in medical environments.

C. Similarity Metric

One of the most important components of any IR method is the similarity metric [19]. It is considered as a function F that measures the quality of the IR problem solution given by a registration transformation f. The final performance of any IR method will depend on the accurate estimation of F.

Each solution is evaluated by F as follows. First, f is usually applied to the scene image $\left(f(I_s)\right)$. Next, the fitting degree between the transformed scene and the model images, $\Psi(\cdot\,,\cdot)$, must be determined:

$$F(I_s, I_m, f) = \Psi(f(I_s), I_m). \tag{1}$$

There are different $\Psi(\cdot\,,\cdot)$ definitions depending on the dimensions and nature of the images:

- ❏ Voxel-based approaches: sum of squared differences, normalized cross-correlation (i.e., correlation coefficient or phase correlation), and mutual information [2].
- ❏ Feature-based approaches: metrics based on feature values and distance between corresponding geometric primitives [20], [21].

As the previous IR components, the F function is also affected by both image discretization and noise, causing worse estimations and favoring the IR method to get trapped in local minima.

The huge amount of data often required makes the problem-solving very complex and the IR procedure very time-consuming. Therefore, most of the IR contributions use some *spatial indexing* data structure in order to speed up the similarity metric computation. It aims to improve the efficiency of the considered optimization method; each time the closest point assignment computation between the transformed scene and model images must be computed. Such data structure is computed only once at the beginning of the IR method. Two main variants of spatial indexes can be found in the IR literature:

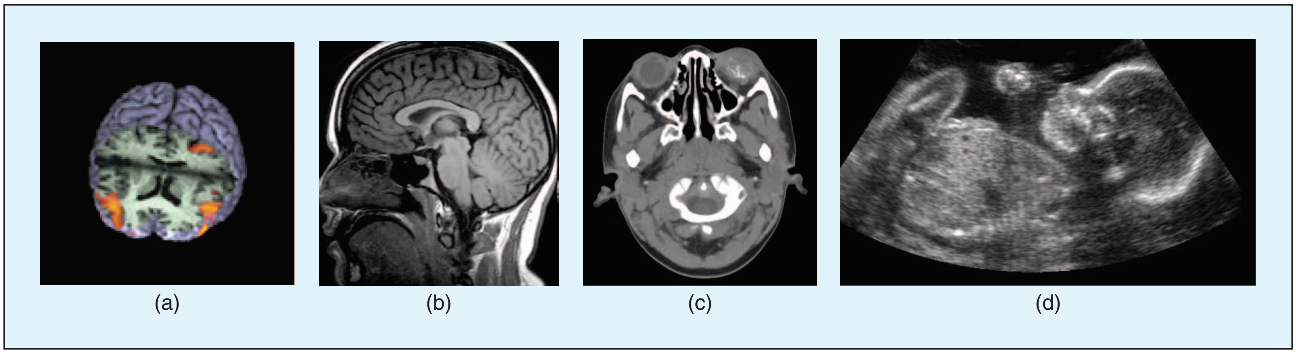

FIGURE 2 Different image modalities. From (a)–(d): functional MRI, MRI, CT, and ultrasound.

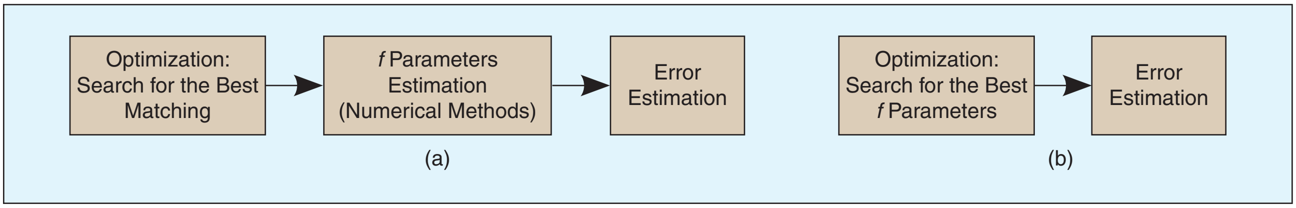

FIGURE 3 From (a) to (b), matching-based vs. transformation parameters-based IR approaches.

- *Kd-tree,* it is based on a generalization of bisection in one dimension to k dimensions. The first proposal applying *kd-trees* to the IR problem is to be found in [22].
- *Distance map,* every cell of this data structure usually stores the Euclidean distance to the closest point of the mapped image. Yamany et al. [6] considered a particular distance map, named *grid closest point* (GCP), which consists of two cubes splitting the 3D space.

D. Search Strategies

As said, the key idea of the IR process is focused on determining the unknown parametric *transformation* that relates two images by placing them in a common coordinate system, bringing corresponding points as close as possible. According to the search strategy component, we can distinguish two different IR approaches in the literature to determine that parametric transformation:

- *Matching*-based approach: it performs a search in the space of feature correspondences (typically, correspondences of image points). Once the matching of scene and model features is accomplished, the registration transformation is derived.
- *Transformation parameters*-based approach: a direct search in the space of the f parameters is done.

In both approaches, IR arises as a *non-linear optimization problem* that cannot be solved by a direct method (e.g. resolution of a simple system of linear equations) because of the uncertainty underlying the estimation of f. On the contrary, it must be tackled by means of an iterative procedure searching for the *optimal estimation* of f, following one of the said approaches. Classical numerical optimizers can be used. However they usually get trapped in a local minima solution.

1) Matching-Based Image Registration Approach

This search space exploration strategy needs to compute the two following steps. First, a typically big number of correspondences in both the scene and the model images must be established. IR approaches based on EC and other MHs have been proposed to tackle this complex first step (see Section III). Next, the transformation f is retrieved by numerical methods considering the matching determined in the previous step (see Figure 3, left). *Least squares* (LS) estimators are the most commonly used numerical methods [23] within this approach, due to their special and interesting properties, e.g., they only require means, variances and covariances.

Therefore, the complexity of both the matching step and the subsequent registration transformation estimation strongly depends on the method being considered. Likewise, an iterative process may be followed either for the estimation of the matching, or the registration, or both, until reaching convergence within a tolerance threshold of the concerned similarity metric. This is the case of the *Iterative Closest Point (ICP)* algorithm [24], well-known in computer aided design and medical imaging. ICP is an iterative gradient-based method based on the least squares estimation of the IR transformation from the computed matching between scene and model points considering the closest assignment rule. Notice that ICP is not guided by the similarity metric but by the computed matching, as the remaining matching-based IR methods. In this strategy, the function F (typically the Mean Square Error —MSE—) only plays the role of the stopping criterion. Moreover, the transformation estimator (numerical method) is dependent on the good outcomes of the matching step. Thus, the better the choice of the matching performed, the more precise the estimation of the transformation f. Consequently, the value of the similarity metric will be more accurate leading to a proper convergence.

The original ICP proposal has three main drawbacks: i) the algorithm is very dependent on the initial guess and it likely gets trapped in local optima solutions, which forces the user to manually assist the IR procedure in order to overcome these undesirable situations; ii) one of the two images (typically the scene one) should be contained in the other, e.g., in feature-based IR problems, the geometric primitives of one image should be a subset of those in its counterpart image; and ii) as previously mentioned, it can only handle normally distributed observations. Since that original proposal, many contributions have been presented extending and partially solving the latter shortcomings [22], [25], [26].

2) Transformation Parameters-Based Image Registration Approach

Opposite to the previous approach, the second one involves directly searching for the solution in the space of parameters of the transformation f (see Figure 3, right). In order to perform that search, the registration transformation f is parametrized and each solution to the IR problem is encoded as a vector composed by the values for the f parameters.

Thus, the IR method generates possible vectors of parameter values, that is, candidate definitions of registration transformations. Unlike ICP-based strategies, the search space exploration is directly guided by the similarity metric F. Each solution vector is evaluated by such metric, thus clearly stating the IR task as a numerical optimization problem involving the search for the best f parameters that minimize F.

Notice that orders of magnitude in the scale of f parameters are crucial for IR methods dealing with this search space strategy. Unit changes in angle have much greater impact on an image than unit changes in translation. Indeed, when applying a rotation, the further a given point on the image from its center of mass (origin of rotation), the greater the displacement. Meanwhile, the distance between the transformed scene and the model images is kept constant in case of translations. This difference in the scale appears as elongated valleys in the parameter search space, causing difficulties for the traditional gradient-based local optimizers [7], [24]. Therefore, if the considered IR method is not robust tackling these scenarios, the theoretical convergence is not guaranteed and it will get trapped in local minima in most cases.

Together with the commonly used gradient-based optimizers [27], approaches based on EC and other MHs are the most extended optimization procedures for IR when this search space strategy is considered. That is shown by the large number of contributions proposed so far [5]–[13] (see Section III).

III. State of the Art of Image Registration Based on Evolutionary Computation and Other Metaheuristics

A. Evolutionary Computation and Metaheuristics

Approximate or *heuristic* optimization methods (also named MHs [4]) belonging to the field of EC use computational models of evolutionary processes for evolving populations of solutions as key elements in the design and implementation of computer-based problem-solving systems. EC approaches constitute a very interesting choice since they are able to achieve good quality outcomes when, for instance, global solutions of hard problems cannot be found with a reasonable amount of computational effort.

There is a variety of EC models that have been proposed and studied, which are referred as evolutionary algorithms (EAs) [3], [28]. Among them we refer to four well-defined EAs which have served as the basis for much of the activity in the field: genetic algorithms (GAs), evolution strategies (ES), genetic programming (GP), and evolutionary programming (EP). In particular, GAs are probably the most used EAs in the literature to face real-world optimization problems. Some other EAs have been proposed in the last few years improving the state of the art in this field by adopting more suitable optimization strategies: the CHC algorithm[1] and differential evolution (DE).

EAs are also considered a member of the set of MHs [4]. MHs are among the most prominent and successful techniques to solve a large amount of complex and computationally hard combinatorial and numerical optimization problems arising in human activities, such as economics (e.g., portfolio selection), industry (e.g., scheduling or logistics), or engineering (e.g., routing), among many others. MHs can be seen as general algorithmic frameworks that require relatively few modifications to be adapted to tackle a specific problem. They are a diverse family of optimization algorithms including methods as simulated annealing (SA), tabu search (TS), multi-start methods, iterated local search (ILS), variable neighborhood search (VNS), greedy randomized adaptive search procedures (GRASP), memetic algorithms (MAs), scatter search (SS), ant colony optimization (ACO), and particle swarm optimization (PSO).

Nowadays, MHs have become an interdisciplinary research area, intertwining disciplines such as computer science, operations research, engineering, etc. They have received enormous attention as witnessed by thousands of journals and conference papers, hundreds of authored and edited books published, and a large number of dedicated conference series.

B. Suitability of Evolutionary Computation and Metaheuristics in Image Registration

There are different strengths and limitations that have been stated either to justify or to avoid the use of these methods when tackling complex optimization problems like IR. Some advantages follow:

- ❏ Unlike classical gradient-based search methods, those based on EC and other MHs do not depend on the starting solution, thus are more robust approaches. Moreover, they provide specific strategies to scape from local optima. In particular, they can cope with multimodal functions to tackle IR [31].
- ❏ EC and MHs have been used in a wide variety of optimization tasks within IR including numerical optimization and combinatorial optimization problems, i.e. facing both the transformation parameters and the matching-based IR approaches, respectively.
- ❏ They are conceptually simple and easy to implement.
- ❏ They can handle arbitrary kinds of constraints and objectives easily. The latter can be considered weighted components of the fitness function. Thus, it is easier to adapt the optimization scheduler to the particular requirements of a wide range of possible objectives. They can also be integrated in a multi-objective scheme for solving the IR problem [13].
- ❏ Unlike other numerical IR techniques (e.g. gradient-based) that are only applicable for continuous functions or other constrained sets, their performance is independent of the solution representation.
- ❏ They offer a framework wherein including prior knowledge about the problem is easy. Thus, the search process is more appropriate, yielding a more efficient exploration of the space of possible solutions. For instance, a feature-based IR approach in [32]–[34] led to a better design of the objective functions to exploit information related to the geometry and the intensity of the images.
- ❏ They can also be easily combined with more traditional optimization techniques such as gradient-based methods [35]–[37]. The stochastic strategy is first applied and next the deterministic one is launched [37]. Another outstanding approach aims to exploit the benefits of both strategies by

[1]The CHC acronym stands for Cross generational elitist selection, Heterogeneous recombination, Cataclysmic mutation [29], [30].

their hybridization in the well-known memetic computation paradigm [38], [39]. Such scheme was successfully applied to the IR problem in [36]. Currently, this hybrid approach brings an outstanding performance due to the proper combination of the exploration and the exploitation capabilities of both stochastic and deterministic optimization schemes.

The most important shortcomings related to the use of EC and other MHs are shown as follows:

- Both stochastic optimization approaches need an initial tuning of control parameters following a manual expert-based procedure. In the last few years, advanced strategies are arising in order to provide new optimization algorithms with an adaptive behavior of control parameters [38].
- They are usually discarded when real-time requirements are needed. Typically, EC and MHs are time consuming. Parallel implementations have been proposed to face this pitfall [40].
- There is no formal proof that these approaches converge to the global optimum. However, results in IR and other problem domains are so good that those previously described hybrid approaches are usually considered to escape from local optima and try to reach the global optimum [36].
- The estimation of the appropriate stop criterion is not easy and it is closely related to the fair comparison of the different methods under study. Moreover, it is problem dependent. Either the CPU time or the number of function evaluations are typical criteria. The former should be preferred tackling methods with heterogeneous designs.

C. First Evolutionary Image Registration Methods

The first attempts to solve IR using EC approaches can be found in the early eighties. The size of data as well as the number of parameters that are looked for prevent an exhaustive search of the solutions. An approach based on a GA was proposed in 1984 for the 2D case and applied to angiographic images [41]. Later, in 1989, Mandava et al. [42] used a 64-bit structure to represent a possible solution when trying to find the eight parameters of a bilinear transformation through a binary GA. Brunnström and Stoddart [32] proposed a new method based on the manual prealignment of range images followed by an automatic IR process using a novel GA that searches for solutions following the matching-based approach. Tsang [43] used 48-bit chromosomes to encode three test points as a base for the estimation of the 2D affine registration function by means of a binary-coded GA. In the case of Yamany et al. [6] and Chalermwat et al. [8] proposals, the same binary coding is found when dealing with 3D and 2D rigid transformations, respectively. Yamany et al. enforced a range of $\pm 31°$ over the angles of rotation and ± 127 units in displacement by defining a 42-bit chromosome with eight bits for each translation parameter and six bits for each rotation angle. Meanwhile, Chalermwat et al. used twelve bits for the coding of the 2D rotation parameter to get a search scope of $\pm 20.48°$, therefore allowing the use of a precision factor for the discretization of the continuous rotation angle interval. Other ten bits stored each of the two translation parameters (± 512 pixels).

All the latter approaches showed several pitfalls from an EC perspective. On the one hand, they make use of the basic binary coding to solve inherently real coded problems, when it is well known that binary coding suffers from discretization flaws (as unreacheable problem solutions in the search space) and requires transformations to real values for each solution evaluation. Moreover, the kind of GA considered is usually based on the old-fashioned original proposal by Holland [44]. In this way, a selection strategy based on fitness-proportionate selection probability assignment and the stochastic sampling with replacement, as well as the classical one-point crossover and simple bit flipping mutation, are used. It is well known that such selection strategy causes a strong selective pressure, thus having a high risk of premature convergence of the algorithm. On the other hand, it has also been demonstrated that it is difficult for the single-point crossover to create useful descendants as it is excessively disruptive with respect to the building blocks.

D. State-of-the-Art Evolutionary Image Registration Methods

The old genetic framework described in the previous section is a clear pitfall affecting the latter group of proposals. Some outstanding IR methods that solve the latter drawbacks by using advanced EAs are as follow:

1) Rouet et al.'s GA-Based Proposal

In this contribution the authors face 3D MR-CT IR by means of a three step algorithm [5]. First, the transformation parameters-based approach is used and a rigid transformation is determined by a real-coded GA. Second, they use another matching-based GA trying to determine a global trilinear transformation. Last, they introduce a post-analysis of the output population of the previous step in order to achieve a fine tuning of the solution using a local optimization process. Despite the promising results they obtain, we still identify different weak points in their approach:

- Different studies have shown that a trade-off between population diversity and convergence to the solution is needed in order to get a good behavior of any EA (to avoid getting stuck in local minima) [36]. Although Rouet et al. used the principle of Latin squares to control the distribution of the population over the search space, there are other approaches that could perform this task better, for instance, niching techniques [28] as those used by Pascale et al. [31].
- The success of the second step of the algorithm depends on a precise definition of the curvature class of each point. Moreover, the use of simple operators (like uniform crossover) in a real-coded GA is not the best option in all cases, even if the aim is to improve the efficiency of the algorithm [45].

2) He and Narayana's GA-Based Proposal

This IR method [7] is a slight improvement of the previously reviewed Yamany et al.'s approach [6]. It considers a real coding scheme that makes use of arithmetic crossover and uniform mutation operators within an elitist generational model including a restart mechanism. This evolutionary IR method deals with rigid transformations following a two-step technique. First, a coarse parameter estimation is tackled using a real-coded GA. Then, the obtained preliminary solution is refined by means of a local search procedure based on the dividing rectangle method. In the coarse resolution, the ranges of the parameters were set to: ± 20 voxels along x and y directions, and ± 40 voxels along z direction for the translation, and rotations of $\pm 10^\circ$ around x and y axes, and $\pm 20^\circ$ around z axis. However, the setting of the parameters range and the use of a simple rigid transformation may be a weak point when applying this method to some real-world environments.

3) Robertson and Fisher's GA-Based Proposal

As in [8], the GA-based IR method proposed by Robertson and Fisher [40] adopts a parallel computing approach in order to improve the efficiency of IR tasks dealing with range images. Specifically, a master node is dedicated to manage the evolution of the population of solutions (selection, mutation, crossover, etc.). Meanwhile, each slave node is fully dedicated to evaluating the solutions. Unlike in [8], this method is based on a real-coded representation of solutions corresponding to a rigid transformation given by six parameters. With regards to the specific design of the proposed GA-based IR method, the authors considered four and two different mutation and crossover operators, respectively. The main novelty of the method consists of providing a selection probability to each operator, and storing them in a normalized unit vector. The vector is updated according to the achievement of better solutions after the application of each operator. Tournament selection is also considered. Finally, it is not stated whether the evolutionary design ensures the crossover operator is applied at least once, which is a requirement to be accomplished by any GA [28].

4) Chow et al.'s GA-Based Proposal

The authors proposed in [9] the same generational and proportionate-fitness models for population reproduction than the method by He and Narayana [7]. However, Chow et al. introduced the use of a crossover operator that randomly selects the number of genes to be swapped. The value to be accumulated for a mutated gene is generated randomly within a constant range for the rotation genes and dynamically computed for the translation ones according to the fitness value of the chromosome. They also make use of a GA with more suitable components to the current EC framework such as a real coding scheme and a sophisticated restart mechanism (named "dynamic boundary"). In spite of these improvements, there are some drawbacks in terms of accuracy, due to the fact that the authors work with a smaller, randomly selected data set from scene images with a huge amount of data. Besides, although the algorithm aims to get a quick registration estimation with the latter procedure, the efficiency could be reduced since it needs to perform a sort operation for each evaluation of the fitness function. As many of the mentioned proposals, it also has the limitation of only considering a rigid transformation (translation and rotation). The restart scheme assumes that, prior to its application, the population will fall in a search space region that is near to the global optimum, which may not always be the case.

5) Silva et al.'s GA-Based Proposal

This contribution [46] addressed the pair-wise IR problem of range images acquired by 3D laser range scanners. Specifically, they used several range data sets obtained from the well-known SAMPL public-access database which were acquired with a Konica-Minolta Vivid 700© laser scanner (resource available at http://sampl.eng.ohio-state.edu). Each data set considers adjacent range images acquired every 20 rotation degrees of the turn table. The higher the degree of rotation, the lower the amount of overlapping existing between the images. The authors tackled the IR problem from the transformation parameters-based approach for rigid transformations. The proposed method is inspired in the steady-state evolutionary scheme of GAs (90% of the worst solutions are replaced instead of the entire population as done in generational schemes) [3], where tournament selection, uniform crossover and random selection mutation operators are considered. Moreover, a hill-climbing algorithm is added to the GA in order to achieve accurate results. In addition, the authors proposed a new similarity metric, named surface interpenetration measure (SIM), which reveals that more discriminating and accurate results can be obtained compared to those results achieved by metrics based on the Euclidean distances.

6) Lomonosov et al.'s GA-Based Proposal

Authors proposed a new method for the pair-wise IR problem of range images [12] facing three real-world noisy measured data sets provided by their REPLICA laser range scanner system and another two from the SAMPL public-access database. They considered the transformation parameters-based approach using rigid transformations. The main novelties of this contribution are the inclusion of a degree of overlapping parameter in the solution vector and the utilization of the trimmed squares metric as objective function to be minimized. They constitute a different schematic approach for the IR problem that offers correct coarse IR results at overlaps under 50%. A random sampling procedure is performed in order to speed up the performance of the method. According to the evolutionary design of their method, a generational GA performing search in the seven dimensional space formed by three translation parameters, three rotation parameters, and the newly added degree of overlapping parameter is considered. They used an integer coding representation of solutions which should be properly normalized onto the corresponding real-value range. Simple one-point crossover was employed and two mutation operators were introduced. Shift mutation alters one parameter randomly by a value not exceeding a 10% of the parameter range. Meanwhile, replacement mutation substitutes a parameter with a random value. Tournament and elitism were also employed.

7) Cordón et al.'s CHC-Based Proposal
This contribution used the sophisticated CHC EA [29], [30] that shows a very good intensification/diversification trade-off for the IR of MRIs [11]. Authors introduced two different variants of the method. First, they used binary-coded solutions and the HUX crossover [47], based on the original CHC structure. The second variant of the CHC-based IR method extends the latter structure to work in a real-coded fashion by considering a real to binary coding translation mechanism as well as using different specific real-coded genetic operators as the blend crossover operator (BLX- α). Authors considered similarity transformations, thus eight-dimensional real coded solutions are considered to encode the transformation (four parameters for rotation, three for translation, and one for uniform scaling). They proposed the following objective function in order to tackle these particular scenarios:

$$F(f, I_s, I_m) = \omega_1 \cdot \left(\frac{1}{1 + \sum_{i=1}^{N} \| (sR\vec{p}_i + \vec{t}) - \vec{p}_j{}' \|^2} \right) + \omega_2 \cdot \left(\frac{1}{1 + |\rho_c^s - \rho^m|} \right), \quad (2)$$

where I_s and I_m are the scene and model images; f is the transformation encoded in the evaluated solution; $\vec{p}_i$ is the ith 3D point from the scene and $\vec{p}_j{}'$ is its corresponding closest point in the model obtained with the GCP data structure (see Section II-C); ω_1 and ω_2 ($\omega_1 + \omega_2 = 1$) weigh the importance of each function term; ρ_c^s is the radius of the sphere wrapping up the scene image transformed with the current f; and ρ^m is the radius of the sphere wrapping up the model image. As the first term of F reveals, the modeled error corresponds to the MSE. Note that F maximizes up to 1.0 for a rarely perfect fit.

8) Winter et al.'s CMA-ES-Based Proposal
Authors presented a system for the IR of CT and intraoperative ultrasound images for pedicle screw insertion during spinal surgery [48]. They compared different optimization strategies: three gradient-based IR algorithms and the covariance matrix adaptation evolution strategy (CMA-ES) [49]. From the conducted experiments, large performance differences were observed between the optimization methods. Specifically, CMA-ES yielded the best results with regard to registration rate and precision. In fact, they mentioned that on a budget of ten thousand objective function evaluations, CMA-ES registered correctly in almost 100% of the tackled experiments. In addition, CMA-ES obtained outstanding results in recent contributions facing other IR problems [50].

9) De Falco et al.'s DE-Based Proposal
Authors proposed a new IR method based on the DE EA [51]. DE is a parallel direct search method that has proved to be a promising candidate to solve real-valued optimization problems [52], [53]. DE combines simple arithmetic operators with the classical crossover, mutation, and selection genetic operators within an easy to implement scheme. It shows the advantage of considering few control parameters, named mutation factor (F) and recombination rate (CR). The fundamental idea of DE is a new scheme for generating trial solutions by adding the weighted differenced vector between two population members to a third one. The proposed method is applied to two 2D IR problems: mosaicking and changes in time of satellite images. Registration is carried out from the transformation parameters-based approach searching for the most suitable affine transformation (given by eleven real-coded parameters) in terms of maximization of the MI similarity metric.

E. State-of-the-Art IR Methods Based on Metaheuristics
Instead of considering EC, there are some other IR methods based on other MHs. Some of the most important ones are described in this section.

1) Luck et al.'s ICP&SA-Based Proposal
In [54], the authors proposed the combination of the ICP algorithm with a SA technique [55] to face pair-wise IR problems of range images. Specifically, each two-step iteration of the method involves subsequently applying the ICP algorithm, optimizing the solution generated with the SA procedure, and starting again a new iteration. The resulting hybrid algorithm is robust in finding the correct registration and efficient in terms of the number of iterations. The system uses a robust error function to handle outlier points.

2) Wachowiak et al.'s TS-Based Proposal
In this contribution [56], the authors introduced an adapted TS [57] IR method to tackle 2D to 3D IR problems. Specifically, they adopted a transformation parameters-based approach and addressed medical IR problems considering 2D ultrasound scans (US) and 3D volumes of MRIs. They considered the maximum value of the overlap-invariant normalized MI [2] functional as Similarity metric. In their work, once the TS-based IR method has identified a promising area of problem solutions, the affine shaker algorithm [58] is applied to locate the best point in each subarea. The shape of the promising area is thus adapted to include areas of the search space that may have been missed during diversification. Finally, an intensified search is conducted around the most promising point using the Nelder-Mead simplex algorithm [59].

3) Wachowiak et al.'s PSO-Based Proposal
The authors contributed with a broad study of the performance of PSO algorithms [60], [61] for solving the IR problem in biomedical applications [62]. In particular, they consider registering single slices (2D images) of 3D volumes to whole 3D volumes of medical images. In contrast to usual EAs which exploit the competitive characteristics of biological evolution (e.g., survival of the fittest), PSO exploits cooperative and social aspects, such as fish schooling, birds flocking, and insects

swarming. However, both EAs and PSO approaches are considered population-based schemes. In particular, PSO algorithms start with a random population (swarm) of individuals (particles) which iteratively change their search space location by performing movements based on a velocity vector. The authors addressed the IR problem from the transformation parameters-based approach, considering a rigid transformation and the MI similarity metric as the objective function to be maximized. The variant called *PSO7* is the one achieving the best performance. It refers to a basic PSO with the following formulation for the velocity vector update:

$$\begin{aligned} \nu_i(t) = \chi[\nu_i(t-1) + \varphi_1\mu_1(p_i - x_i(t-1)) \\ + \varphi_2\mu_2(g - x_i(t-1))] \end{aligned} \quad (3)$$

being the optimization parameters $\kappa = 1.0$, $\varphi_1 = 2.1$, $\varphi_2 = 1.3$, and the constriction coefficient $\chi = 0.7298$.

However, the performance of the method is dependent on the initial orientation of the images to be registered that should be provided by the user.

4) Cordón and Damas' ILS-Based Proposal

In [33], the authors used the ILS MH [4] for tackling the IR problem from the matching-based approach, making use of image-specific information to guide the search and proposing a new representation of solutions based on the use of a permutation. Hence, a combinatorial optimization problem is tackled. It exploits problem dependent information by taking into account the curvature information extracted from synthetic and MR images. The main novelty of this feature-based IR method is that the heuristic values of the features are used to guide the matching. In particular, it exploits the information relative to local curvature characterizing the set of crest-lines points [18] extracted as relevant features of the scene and model images. Thus, the authors propose an advanced coding scheme where a given point matching is represented as a permutation. Besides, they define a function $m_{\text{error}}(\cdot)$evaluating the accuracy of the matching stored in a given solution, π, by using the said curvature values:

$$m_{\text{error}}(\pi) = \Delta k_1 + \Delta k_2, \;\; \Delta k_j = \sum_{i=1}^{r} (k_j^i - k_j^{\pi_i})^2, \;\; j = \{1, 2\}. \quad (4)$$

Δk_1 and Δk_2 measure the error associated to the matching of scene and model points with different values for the first and second principal curvatures, respectively.

Meanwhile, the objective function of this IR method will include both information regarding the usual IR measure $g(\pi)$(MSE of the registration transformation resulting from the point matching encoded in π) and the previous criterion as follows: $F(\pi) = w_1 \cdot g(\pi) + w_2 \cdot m_{\text{error}}(\pi)$, where w_1, w_2 are weighting coefficients defining the relative importance of each term. Specifically, similarity transformations were considered, where a rotation, a translation and uniform scaling is numerically derived from the point-matching coded in the solution.

5) Cordón et al.'s SS-Based Proposal

The main idea behind SS [63] is a systematic combination between solutions (instead of a randomized one like that usually done in GAs) taken from a considerably reduced and evolved pool of solutions named Reference Set (between five and ten times lower than usual GA population sizes). The fact that the mechanisms within SS are not restricted to a single uniform design allowed the authors the exploration and design of strategic possibilities that demonstrated to be effective tackling point-matching IR problems [34]. Furthermore, new designs for three of the five SS components – the generator of diverse solutions, the improvement, and the combination methods – were proposed to develop a method outperforming the state-of-the-art point matching approaches. In particular, the authors adopted the same feature-based approach and the same representation of solutions based on permutations previously proposed in [33] (see Subsection III-E4). Similarity transformations present in 3D MRIs of human brains and 3D CTs of human wrists were also considered in this work. In particular, they succeeded at dealing with significant transformations between the two registered images, one of the ICP's pitfalls (see Section II-D).

6) Santamaría et al.'s SS-Based Proposal

After their successful IR approach tackling 3D synthetic and MR images [10], the authors provided several extensions of their SS-based method to tackle a real-world application focused on the 3D reconstruction of forensic objects from range images [36], [64]. In both contributions, the transformation parameters-based approach dealing with rigid transformations was used. In this case, they adopted a similarity metric based on the median square error with the aim of tackling data sets of range images with a significantly low overlapping between adjacent images (acquired considering 40 degrees of rotation of the turn table). The GCP data structure is used in order to speed up the computation of the closest point rule (see Section II-C). The authors specifically performed a broad study about the performance capabilities of different memetic-based IR methods based on SS [36]. MAs are the result of the conjunction of the global search capabilities of EAs and the local search behavior of other *low-cost* heuristic procedures [39], [65]. Besides, MAs have been successfully applied to other image analysis tasks [66]. In [36], the authors considered three existing EC-based IR methods as the baseline algorithm: SS [10], CHC [11], and DE-based [51] IR methods. For each of the previous three techniques, they considered the use of several local search algorithms (XLS [67], Solis&Wets [68], and Powell [69]) as improvement method. Two different criteria (deterministic and probabilistic) were taken for the application of the local search, and different search intensity levels were tested. Thus, eighteen different variants were developed for each of the three EAs, fifty seven different memetic IR method designs overall. The obtained experimental results in the 3D reconstruction of different human skull models, supported by a complementary non-parametric statistical test, revealed that the SS variant that

TABLE 1 Detailed description of the BrainWeb image data set generated by the on-line SBD system (http://mouldy.bic.mni.mcgill.ca/brainweb/).

BW IMAGE	ANATOMICAL MODEL	MODALITY	SLICE THICKNESS (MM)	LEVEL OF NOISE	PROTOCOL	RF (%)
BW1	NORMAL	T1	3	0	ICBM	20
BW2	MILD MS	T1	3	1	AI	20
BW3	MILD MS	T1	3	5	AI	20

made use of the deterministic local search application criterion and the XLS local search algorithm offered the best performance among all the developed memetic-based IR methods. It also outperformed the authors' previous methods based on the CHC [11] and SS algorithms [10], [64].

7) Queirolo et al.'s SA-Based Proposal

In [70], the authors proposed a new IR method based on SA and the SIM as similarity metric to face 3D face recognition problems. One of the main goals of the proposed method was to overcome the run time limitation of their previous GA-based contribution [46] tackling pair-wise IR problems using range images (see Section III-D5). However, they performed an experiment to verify whether the recognition rate could be improved if the time constraint is avoided and it was shown that the SA-based IR method achieved the best results when using a larger number of iterations. Nevertheless, they showed the potential of the SIM as similarity score for 3D face recognition.

IV. Experimental Study

A. Medical Image Data Sets

We use a first data set from the BrainWeb public repository[2] of the McConnell Brain Imaging Centre [17]. The BrainWeb repository is a Simulated Brain Database (SBD) providing synthetic MRI data computationally generated. Such MRIs have been extensively used by the neuroimaging community to evaluate the performance of different methods [62], [71]–[73]. In particular, Wachowiak et al. [62] generated a T1 MRI volume of a normal brain with the BrainWeb system in order to register single 2D-slices with respect to the whole 3D volume. The SBD provides MRI data based on two anatomical models: normal and multiple sclerosis (MS). Full 3D data volumes have been simulated for both models using three sequences (T1-, T2-, or proton-density- (PD) weighted) and a variety of slice thickness, noise levels, and levels of intensity non-uniformity (RF). Table 1 describes the particular settings considered to generate every BrainWeb image of our study (named BW1, BW2, and BW3).

The second data set (kindly provided by the Rhode-Island Hospital in the United States) corresponds to real-world CT data of two human wrists from a volunteer with no history of wrist injury or chronic disease that might affect the wrists [74]. Both wrists (named *Wrist(1)* and *Wrist(2)*) were imaged simultaneously with a GE HiSpeed Advantage CT scanner (GE Medical, Milwaukee, WI). Contiguous, 1.0 mm, transverse slices of the entire carpus were acquired at a resolution between 0.2 and 0.4 mm. The functional neutral wrist position was imaged while the subject was comfortably grasping a rubber bicycle handle in neutral supination-pronation.

We extracted the isosurface and select crest-lines points with relevant curvature information from the original images using a 3D crest-line edge detector [18]. The resulting data sets comprise around five hundred points (see Figure 4). Table 2 details the nature of every medical image of each data set.

[2]Available at http://www2.bic.mni.mcgill.ca

B. Experimental Design

We considered the following thirteen methods reviewed in Section III:

- Evolutionary-based IR methods: Yamany-GA_{Binary} [6] (EV1); He-*GA* [7] (EV2); Chow-*GA* [9] (EV3); Silva-*GA* [46] (EV4); Lomonosov-*GA* [12] (EV5); Cordón-CHC_{Binary} [47] (EV6); Cordón-*CHC* [11] (EV7); and DeFalco-*DE* [51] (EV8).
- Metaheuristic-based IR methods: Luck-*ICP&SA* [54] (MH1); Wachowiak-*PSO* [62] (MH2); Cordón-*ILS* [33] (MH3); Cordón-*SS* [34] (MH4); and Santamaría-*SS* [36] (MH5).

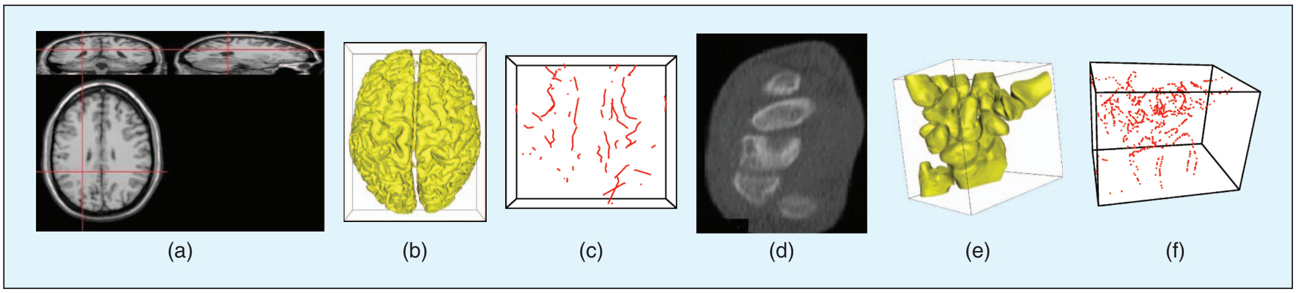

FIGURE 4 From (a)–(f): the original medical image, the corresponding extracted isosurface, and the crest-lines extracted from the isosurface. Images from the BrainWeb and Wrist data sets, respectively.

TABLE 2 Detailed description of the medical image data sets.

DATA SET	LESION	NOISE	CREST-LINE POINTS	DATA SET	LESION	NOISE	CREST-LINE POINTS
BW(1)	–	–	583	WRIST(1)	–	–	575
BW(2)	YES	1%	348	WRIST(2)	–	–	412
BW(3)	YES	5%	284				

Moreover, our study includes two classical gradient-based IR methods frequently studied. Foremost, we considered a more recent version of the original ICP algorithm by Liu [25] Liu-*ICP* (LICP) which tries to overcome the drawbacks of the first ICP proposal [24]. Then, we included a method based on Powell's contribution [69] (PW) which is one of the standard baseline algorithms in IR [27].

The justification to selecting those methods based on EC and other MHs is two-fold. Firstly they can be considered as good representatives of the wide spectrum of techniques that lay their foundations on those two disciplines. Secondly we have taken the search strategy approach adopted into account (see Section II-D) in order to select outstanding methods following both a matching-based approach (MH1, MH3, MH4, and LICP) and a transformation parameters-based approach (EV1 to EV8, MH2, MH5, and PW). These fifteen IR methods have been implemented in C++ and compiled with GNU/g++. We used a computer with an Intel Pentium IV 2.6 MHz processor and 2GB RAM.

We considered the parameter values originally proposed by the authors in every contribution (see Table 3). Nevertheless, we have adapted the majority of the methods by using the same objective function in order to carry out a fair comparison. First, according to the geometric transformations relating the medical images we considered, Eq. 2 was taken as the objective function. Moreover, we utilized the GCP data structure (see Section II-C) to speed up the closest point computation for every method in both IR applications. The only exceptions to the latter are Cordón-*ILS* and Cordón-*SS* IR methods because their specific objective function designs are strongly interrelated to the structure of the optimization algorithms. Thus, we maintained their original objective functions.

A feature-based IR approach [1, 14] has been considered for both medical applications. It aims to reduce the huge amount of data of the original images in order to speed up and guide the optimization procedure. Feature extraction is considered as a preprocessing step, prior to the application of the IR method. It is based on the selection of a small subset of truly representative characteristics of the images to be registered. We used a 3D crest lines algorithm [18] to obtain feature points from both medical image domains considered: MRIs and CTs. These preprocessed images are the ones that will be used by every IR method to estimate the registration transformation. Once the IR method has finished, the raw images are considered to measure the quality of the final results.

We designed several IR problem instances, taking into account similarity transformations (rotation, translation, and uniform scaling) for medical applications, thus coping with the specific characteristics of this application domain. For each problem instance tackled by the fifteen IR methods, thirty different runs are performed. Each run considers a different similarity transformation. In order to perform a fair comparison among the methods included in this study, we considered CPU time as the stop criterion. In our opinions, that is the best choice because we aim to compare the performance of methods with heterogeneous designs. After a preliminary study, we noticed that twenty seconds was a suitable stop criterion to allow all the algorithms to converge properly.

The way a particular run is performed is as follows: a random (similarity) transformation is applied to the ground-truth image and then the IR method estimates the unknown inverse transformation. Thus, ground-truth registration is available for both medical applications. In particular, similarity

TABLE 3 Parameter settings. Methods with "*" were manually tuned due to the lack of information in their description.

EVOLUTIONARY-BASED METHODS			METAHEURISTIC-BASED METHODS		
METHOD	*PARAMETERS*		*METHOD*	*PARAMETERS*	
EV1*	*POPULATION = 100	BIT-LENGTH / GENE = 15	MH1*	ICP #ITERS = 40	SA #ITERS = 20
	CROSSOVER = 0.6	MUTATION = 0.1		SA MAX. TRIALS = 40	SA $\mu = 0.3$
EV2	POPULATION = 41	CROSSOVER = 0.9		SA $\phi = 0.3$	SA TOLERANCE = 0.1
	MUTATION = 0.1		MH2	SWARM SIZE = 35	$\kappa = 1.0$
EV3	POPULATION = 500	CROSSOVER = 0.583		$(\varphi_1, \varphi_2) = (2.1, 1.3)$	$\chi = 0.7298$
	MUTATION = 0.1666		MH3	$(\omega_1, \omega_2) = (0.1, 0.9)$	PERTURBATION = 50%
EV4	POPULATION = 100	CROSSOVER = 0.9		TIME = 5% (INNER LOOP) + 95% (OUTER LOOP)	
	MUTATION = 0.02		MH4	$(\omega_1, \omega_2) = (0.5, 0.5)$	PSIZE = 80
EV5	POPULATION = 500	CROSSOVER = 0.9		$(b_1, b_2) = (7, 3)$	LS #ITERS = 80
	MUTATION = 0.5		MH5	PSIZE = 100	$(b_1, b_2) = (8, 0)$
EV6	POPULATION = 100	BIT-LENGTH / GENE = 15		BLX-$\alpha = 0.3$	XLS #ITERS = 100
EV7	POPULATION = 100	BLX-$\alpha = 0.3$			
EV8	POPULATION = 30	(CR, F) = (0.5, 0.7)			

TABLE 4 Medical IR results. Each entry corresponds to the minimum (top), mean (bottom), and standard deviation (in parentheses) MSE values obtained from the thirty different runs. The best minimum and mean MSE values are in bold.

CODE	IR METHOD	BW(1)-BW(2)	BW(1)-BW(3)	BW(2)-BW(3)	WRISTS	AVERAGE
			IR Methods Based on Classical Methods			
		796.1	796.1	791.6	199.9	646.0
PW	POWELL [69]	4085.6	4085.6	3788.8	1476.5	3359.1
		(±2089.4)	(±2089.4)	(±1892.4)	(±747.3)	(±1093.7)
		0.279	0.046	0.042	0.002	0.092
LICP	LIU-*ICP* [25]	2788	3009	2929	25	2187
		(±2364)	(±2279)	(±2094)	(±22)	(±1251)
			Evolutionary-Based IR Methods			
		0.010	0.017	0.017	0.009	0.013
EV1	YAMANY-GA_{Binary} [6]	1678	2517	1868	13	1519
		(±2876)	(±3463)	(±2931)	(±21)	(±923)
		0.466	1	0.342	0.021	0.457
EV2	HE-*GA* [7]	1214	718	2014	2	987
		(±2794)	(±2182)	(±3158)	(±6)	(±732)
		19	19	18	5	15
EV3	CHOW-*GA* [9]	4261	3604	2398	38	2575
		(±3417)	(±3351)	(±2667)	(±16)	(±1610)
		0.030	0.009	0.013	0.004	0.014
EV4	SILVA-*GA* [46]	2209	2647	1751	12	1654
		(±2920)	(±3571)	(±2507)	(±22)	(±999)
		1	0.516	1	0.168	0.671
EV5	LOMONOSOV-*GA* [12]	838	830	179	21	467
		(±2422)	(±2426)	(±857)	(±23)	(±371)
		0.021	0.012	0.024	0.007	0.016
EV6	CORDÓN-CHC_{Binary} [47]	1935	2352	1397	13	1424
		(±3056)	(±3123)	(±2072)	(±22)	(±882)
		0.001	0.007	0.008	0.002	0.005
EV7	CORDÓN-*CHC* [11]	1124	1910	1865	3	1225
		(±2338)	(±3283)	(±2998)	(±12)	(±771)
		0.001	0.006	0.024	**0.001**	0.008
EV8	DEFALCO-*DE* [51]	132	0.013	**0.026**	**0.003**	33
		(±708)	(±0.002)	(±0.001)	(±0.001)	(±57)
			Metaheuristic-Based IR Methods			
		0.001	**0.004**	**0.004**	**0.001**	**0.003**
MH1	LUCK-*ICP&SA* [54]	2863	2579	2463	25	1982
		(±2549)	(±2276)	(±2162)	(±22)	(±1139)
		0.018	0.160	0.347	0.008	0.133
MH2	WACHOWIAK-*PSO* [62]	681	1060	645	27	603
		(±1817)	(±2496)	(±1908)	(±18)	(±370)
		2	20	41	0.335	15
MH3	CORDÓN-*ILS* [33]	3687	3868	3688	32	2818
		(±2627)	(±3183)	(±2518)	(±19)	(±1610)
		0.200	17	34	0.089	13
MH4	CORDÓN-*SS* [34]	577	743	1133	11	616
		(±1715)	(±1596)	(±1785)	(±18)	(±403)
		0.001	0.005	0.021	**0.001**	0.007
MH5	SANTAMARÍA-*SS* [36]	**0.003**	**0.011**	0.028	0.004	**0.012**
		(±0.001)	(±0.003)	(±0.004)	(±0.001)	(±0.010)

transformations are randomly generated following a uniform probability distribution as follows: each of the three rotation axis parameters will be in the range $[-1, 1]$; the rotation angle will range in $[0°, 360°]$; the three translation parameters in $[-40\text{ mm}, 40\text{ mm}]$; and the uniform scaling ranges in $[0.5, 2.0]$. The quality of the final IR result is evaluated using the image estimated by the IR method and its counterpart ground-truth (both images in their original/raw versions, i.e. previous to the application of the feature extraction) as follows:

$$\text{MSE} = \frac{\sum_{i=1}^{r} \| f(\vec{x}_i) - \vec{x}'_i \|^2}{r}, \tag{5}$$

where $f(\vec{x}_i)$ refers to the scene image's *ith* point transformed by the estimated similarity transformation f, r is the scene image size, and $\vec{x}'_i$ is the latter $\vec{x}_i$ scene point considering in its ground-truth coordinates. It is clear that this procedure cannot be used in situations where ground-truth is not available. It is only a mean to accomplish an accurate evaluation of the performance of the IR methods considered.

C. Results

Our results correspond to a number of medical IR problem instances for the 3D medical images presented in Table 2. The four IR scenarios we consider are: BW(1)-BW(2),

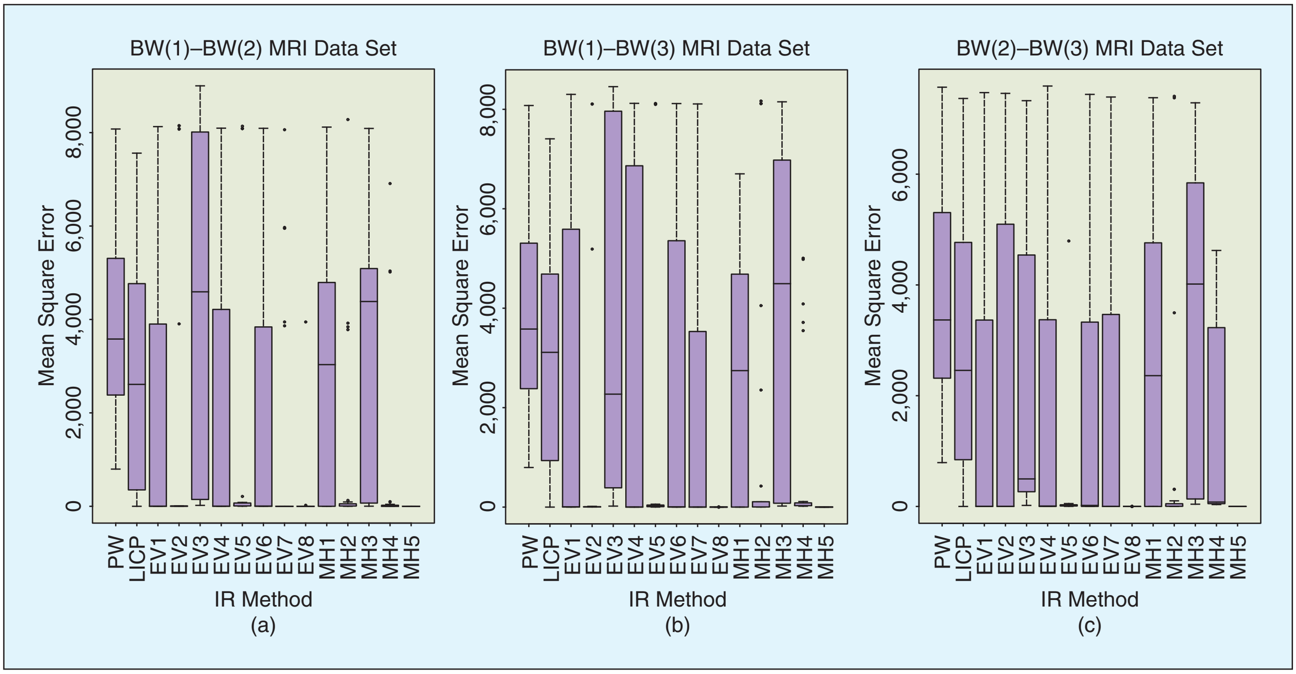

FIGURE 5 Box-plots (a)–(c) highlighting the MSE distribution during the 30 runs of all the IR methods tackling the BrainWeb data set.

BW(1)-BW(3), BW(2)-BW(3), and Wrist(1)-Wrist(2), each one considering a randomly generated similarity transformation in every of the thirty runs performed. Thus one hundred and twenty different IR problem instances are addressed by every IR method.

Since we are performing thirty runs per IR problem and method, we can analyze the distribution of the registration error during the said runs. Table 4 shows statistical results computed from the MSE (Eq. 5) of the fifteen IR methods included in our study. Every entry of the table refers to the minimum, mean, and standard deviation (in brackets) MSE values in the thirty runs. The best minimum and mean MSE values in each IR problem are highlighted using bold font. The code included in the first column of the table will be used to refer to every method from now on. The last column averages the mean MSE values along the four considered IR scenarios. The unit length of the data in this table is in squared millimeters.

Figures 5 and 6 include four box-plots derived from the MSE values of the thirty different runs[3]. Every box-plot includes 15 boxes corresponding to each IR method considered. In each box, the minimum and maximum MSE values are the lowest and highest lines, the upper and lower ends of the box are the upper and lower quartiles, and a thick line within the box shows the median. In data with no dispersion, all the quartiles are grouped together and the box turns into a single line. Circles represent outliers.

The right chart of Figure 6 shows the ranking of the IR methods regarding to the average performance tackling the *BW*() and *Wrist*() medical data sets (see the last column of Table 4).

D. Discussion

We first aim to compare the averaged performance of the methods in Table 4 (column 7). According to minimum MSE values, the four most accurate methods are: Luck-*ICP*&*SA* (MH1), Cordón-CHC (EV7), Santamaría-SS (MH5), and DeFalco-DE (EV8). Their minimum MSE values range [0.003, 0.008]. While the latter three methods follow the transformation parameters-based IR approach, Luck-*ICP*&*SA* (MH1) is a hybrid method combining both the matching and the transformation parameters approaches.

We also aim to analyze the robustness of the methods in the IR problems considered. Beyond the minimal result that one method could achieve in one of the thirty different runs, we will summarize the behavior of every method in those runs analyzing mean and median MSE in Table 4 and Figure 5, respectively. For the mean MSE values in Table 4 (columns 3–7), we note the following facts:

- The poor performance obtained by the Powell's method (PW) demonstrates the low effectiveness of general-purpose gradient based methods without a good initial starting point for the search.
- Liu-ICP (LICP) is another gradient based method. It outperforms Powell's method in all the problems because LICP is specifically designed to tackle IR. Nevertheless, the high mean MSE values obtained by LICP reflect it is still trapped in local optima.
- Nine of the thirteen methods based on EC and other MHs outperform LICP in the four scenarios. Only the mean

[3]The error of the Wrists CT data set (box-plot of Figure 6, left) is in logarithmic scaling to ease the comparison of the methods' performance.

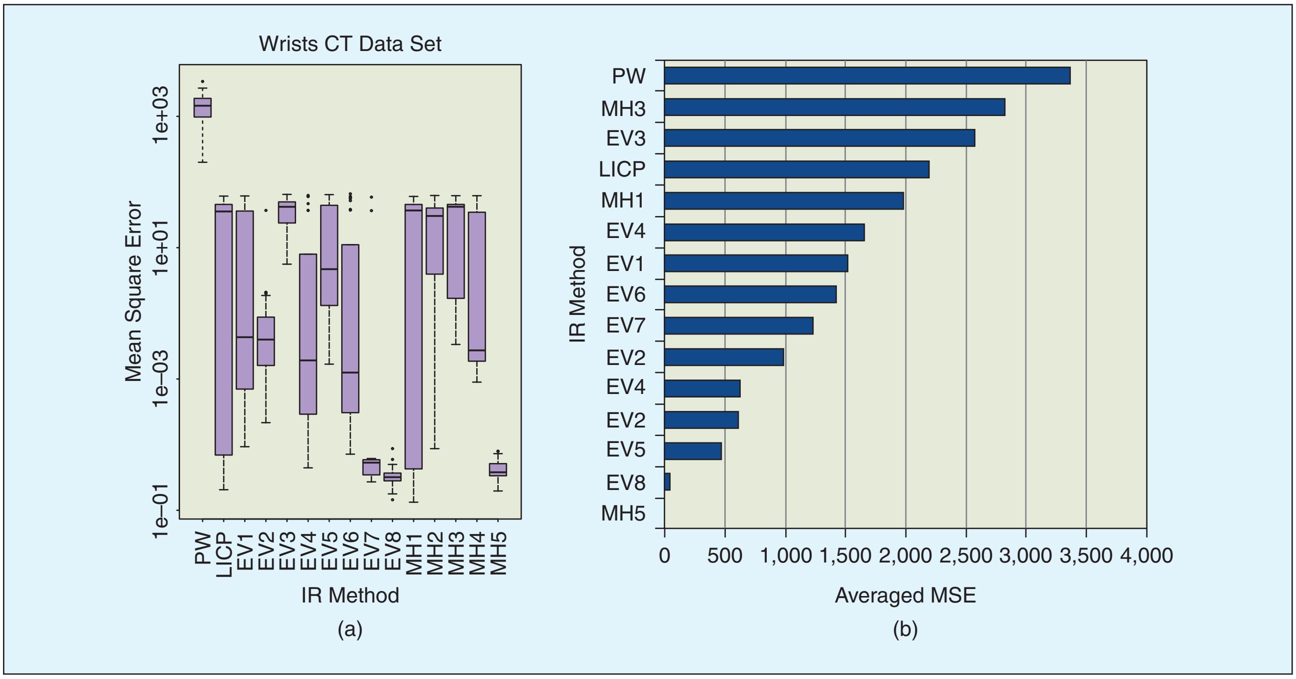

FIGURE 6 (a) Box-plots highlighting the MSE distribution during the 30 runs of all the IR methods tackling the Wrists data set. (b) Ranking of IR methods by averaging the MSE reported by every IR method in all the medical problems studied.

MSE values by Cordón-ILS (MH3) are worse than those by LICP in all the problems.

- DeFalco-DE (EV8) and Santamaría-SS (MH5) achieve the best performance in all the considered medical IR problems. Both methods follow the transformation parameters-based IR approach.

This behavior is corroborated in the box-plots of Figure 5 and 6 reflecting the MSE distribution along the thirty runs. According to the median MSE values, we can assert that:

- PW always reports the worst median MSE values.
- LICP outperforms PW in all the IR problems.
- Nine of the thirteen methods based on EC and other MHs outperform LICP in the four problems. Only the median MSE values by Cordón-ILS (MH3) are worse than those by LICP in all the problems.

In addition to the analysis of the median values, the box-plots also show that there are two methods providing outstanding results in terms of performance and robustness, i.e. very low error value and error dispersion in all the runs for all the problems. They are DeFalco-DE (EV8) and Santamaría-SS (MH5). Both methods show a very similar behavior.

Among the thirteen evolutionary and MH-based IR methods in the right chart of Figure 6, only two of them (Cordón-ILS and Chow-GA) obtain a lower overall performance than the baseline gradient-based IR methods, LICP and Powell (PW). While the bad behavior of Cordón-ILS is due to the lack of time to converge to a better solution, as this method is significantly slower than the remainder, the bad performance of Chow-GA is related to the restart strategy proposed by the authors, named *dynamic boundary*. Boundary constraints of range space progressively reduce the solution space of the last generation before convergence. Restart is applied after a predefined number of generations without improvement of the population. That is a weak assumption if the search space is either complex or wide. Then the EA usually falls into local minima. It is thus a more appropriate fine-tuning IR method to refine the results achieved by a more robust procedure.

Note that, the majority of the transformation parameters-based IR methods achieve the best average performance, being the most robust techniques. Among them, real-coded methods obtain the best results nearly followed by the integer-coded Lomonosov-GA (EV5). The difference in performance with respect to the binary-coded approaches Yamany-GA$_{\text{Binary}}$ (EV1) and Cordón-CHC$_{\text{Binary}}$ (EV6) is rather important.

Besides, the high reliability of Cordón-SS (MH4) matching-based approach is remarkable. In fact, it is the fifth method in the ranking. Surprisingly, Chow-GA (EV3) is the real-coded transformation parameters-based IR method with the lowest quality results in its category, even worse than some methods based on the point matching approach as Luck-*ICP/&SA* (MH1) and Liu-ICP (LICP). As said, the bad performance of Chow-GA is related to the restart strategy proposed by the authors.

Finally, Figure 7 graphically complements the latter analysis on the methods robustness. Unlike the high variability between the best and the worst solutions shown by the best gradient-based method (LICP), the outstanding stability of the most robust method (MH5) along the thirty runs is remarkable.

V. Conclusion

The large number of contributions related to IR shows the high relevance this topic has reached in the computer vision

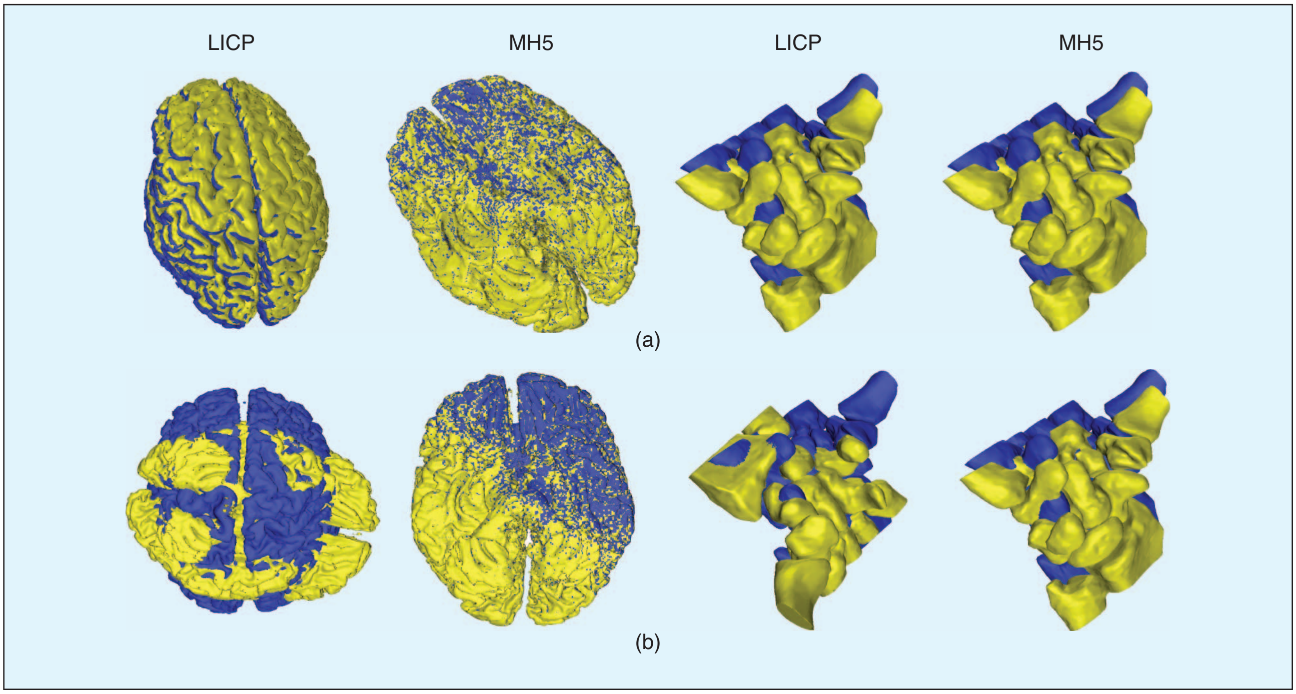

FIGURE 7 From left to right: every column presents the best (a) and the worst (b) solution along the thirty runs achieved by the best gradient-based method (Liu-*ICP:* LICP) and the best evolutionary and metaheuristic method (Santamaria- *SS*: MH5) tackling both the BW(1)–BW(2) and Wrists IR problem scenarios, respectively.

area. Recently, the adoption of optimization techniques coming from both the EC and MH communities have become a promising solution due to their behavior as global optimization techniques. They own a capability to perform robust search in complex and ill-defined spaces in order to overcome the drawbacks of the traditional IR algorithms, with the ICP algorithm as the main exponent.

Unlike traditional methods, IR methods based on EC and other MHs have demonstrated their good behavior handling this ill-conditioned problem in the last few years. The main difficulty to be tackled is to find a reliable/robust manner to escape from locally optimal registration solutions. None of the previous works reviewing the IR state-of-the-art ([1, 75]) addresses those IR contributions adopting an EA or any other MH in their optimization components in depth. With the aim of bridging this gap, in this work we have introduced an experimental survey of the most relevant IR methods of the said optimization approaches.

In order to establish a better comprehension of this family of methods, a broad experimentation using two case studies tackling a realistic and a real-world medical imaging application have been carried out. In particular, we adopted a feature-based IR approach and we considered a similarity transformation in order to better face the specific characteristics of both applications. Medical image data sets were carefully chosen to tackle different challenging IR problem instances according to different criteria, e.g. frequency of use, presence of noise and anatomic lesions, and different modalities, among others. From the results obtained we highlighted the high performance and accurate results offered by several of the reviewed IR methods against those achieved by the traditional ones, as the Powell's method and the ICP algorithm. In particular, those IR methods based on EC and other MHs that consider the transformation parameters-based IR approach provided the most robust and globally accurate results.

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