# A Cost Efficient Approach for Automatic Non-Rigid Registration of Medical Images

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**Abstract.** A common approach for non-rigid medical image registration is the hierarchical image subdivision-based strategy. In this approach, images are progressively subdivided, locally registered, and elastically interpolated. Although this approach seems to be among the fastest approaches for non-rigid registration, computation time is still a real challenge. This work deals with this problem and proposes a new hierarchical strategy. To reduce computational complexity, we propose to combine in the same framework the hierarchical image subdivision-based strategy with a Gaussian pyramid. The hierarchical subdivision method ensures that the registration process deals with small and large deformations, whereas the use of Gaussian pyramid decreases the computation time enormously. The proposed framework is preliminary validated in the context of monomodal registration by matching breast mammograms and MRI brain images with simulated deformations. Registration quality is evaluated by using image differences, mean square error, peak signal to noise ratio and correlation coefficient. Complexity study and experimental results show that the proposed approach reduces considerably the computation cost meanwhile maintaining comparable accuracy.

## 1 Introduction

Over the last years, advances in wide range of medical imaging modalities have led to an increased need for sophisticated registration techniques, allowing clinicians to advantageously gain the maximum amount of complementary information from various images. Indeed, image registration has widely opened up new medical imaging applications [5], such as serial MRI, perfusion imaging and image guided surgery and therapy (IGT). Thus, proper integration of complementary information from two or more images acquired from different scanners, at different viewpoints, from different subjects or at different time intervals is often desired. This process, called image registration or alignment, can be done manually. However, manual registration is boring and very time consuming. It is therefore desirable to establish fully automated registration. Its purpose is to find a geometrical transformation that relates the points of an image $I$ to their corresponding points of another image $\grave{I}$. During the past decades, many medical image

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registration algorithms have been developed, and several survey papers have been published [15, 10, 8]. These methods may be classified according to the used information, the similarity measure, the transformation model and the optimization process.

With respect to the first criterion, the proposed methods are classified as feature-based or area-based methods. The first group is based on the extraction of salient structures in the image, whereas the latter operates directly on the image intensities, without prior data reduction by the user or by a segmentation process. Since the final registration result of feature-based methods depends enormously on the segmentation step, its use is recommended only if the images contain enough distinctive and easily detectable objects [10]. Thus, as medical images do not contain enough details, area-based methods are rather employed. Nevertheless, the main drawback of these methods is the computation time.

The similarity criterion quantifies the similarity between the images to be aligned. Measures based on information theory, such mutual information (MI), are more suitable for multimodal registration and therefore they are often used in this case. Nevertheless, several problems have to be faced when using MI, particularly if it is applied to small-sized images, mainly computation coast and interpolation artefact [1]. Therefore, faster but reliable criteria are rather employed in the case of monomodal registation. In particular, the correlation coefficient (CC) is optimal when assuming a linear dependency between images intensities, which is a reasonable hypothesis in case of mono-modal registration [13].

The transformation model defines how one image can be deformed to match another image. The simplest examples are the rigid and the affine transformations. However, when the objects under investigation are highly non-rigidly deformed, a non-rigid transformation, capable to deal with more localized spatial changes, is always needed [4]. The most accurate non-rigid registration methods are based on physical models. However, those methods are computationally very expensive. Therefore, various simplifications have been proposed to approximate the underlying physical deformation [5]. One possible way to approach the related problems is to model the elastic transformation as an interpolation of multiple local rigid-body registrations. This approach involves subdivision of one or both the participating images, followed by independent registration of corresponding subimages. A smoothly global non-linear transformation is then generated from the local registration solutions using interpolation schemes [9]. Nevertheless, non-rigid transformations are always defined by a large number of parameters. Thus, searching for a such global registration transformation by using a similarity measure may result on an abundance of local minima and an increasing computational time. To overcome these problems, hierarchical matching strategies are always advised. Initial matches are often performed rapidly due to a reduction in input data quantity or the calculation of a simplified transformation. According to the reduction or the simplification done in the coarsest levels, hierarchical registration approaches can be classified as hierarchies of data or warp complexity [8]. Hierarchies of data complexity require parallel generation of a set of modified copies of the input images which contain decreasing levels of details. This will ideally create a hierarchy of images from the most global to the most intricate. Such hierarchies of decreasing data complexity are provided by scale spaces, where the image size is constant in all levels, or by pyramids, where image size is reduced in each successive level. In the latter case, the reduction in the amount of data to be processed in the coarse level images may speed up the computation of optimal parameters. This represents an additional advantage for pixel-based matching schemes. On the other hand, registration warps can be summarized either by coefficients of basis functions or by displacements of landmarks. At each level of the hierarchy, increasing the number of coefficients in the former and the number of landmarks in the latter, increases the complexity with which the warp can be described.

To be integrated in a computer-aided detection and diagnosis system, the non-rigid registration method must be fast and automated. Consequently, a convenient choice of the different components of the registration method may be as follows:

1. Used information: to be automated, the method must be area-based;
2. Similarity criterion: cross correlation can be used since we handle monomodal registration in our experiments;
3. Transformation model: as medical organs are elastic bodies, a robust elastic deformation model must be used. To decrease the computation cost, an appropriate choice may be the one based on image-subdivision;
4. Optimization process: to accelerate the registration algorithm, hierarchical matching strategies are very useful.

In this work, we propose a simple, but efficient, modification of the hierarchical image subdivision-based strategy for non-rigid registration [9], which decreases its computation cost. In fact, we combine in the same framework the hierarchical approach with a Gaussian pyramid. The hierarchical image subdivision method ensures that the registration process deals with small and large deformations, whereas the use of Gaussian pyramid accelerates the registration process enormously. The rest of this paper is organized as follows. The hierarchical subdivision strategy, the Gaussian pyramid and related works which tend to combine hierarchies of data and warp are discussed in the next section. The proposed framework and its validation are presented successively in sections 3 and 4. Conclusions and ideas for future works are summarized in section 5.

## 2 Hierarchical Registration

### 2.1 Hierarchical Image Subdivision

Likar and Pernus [9] have developed a hierarchical framework for automated non-rigid registration, with increasing warp complexity while increasing the number of landmarks in each level. The images to be registered are subdivided into four subimages, which are then locally and independently registered by a rigid transformation. This process is repeated until the regions are of a predetermined minimum size (Fig. 1). Thus, after completing $l$ stages, the image is divided into $4^l$ equal-sized pieces. For each subimage, a rotation angle and a translation value are determined. Elastic thin-plate splines technique [3] is then used to interpolate the centers of the registered sub-images. This hierarchical approach ensures that the registration process deals both with small and large deformations. Although this approach is faster than non-rigid algorithms based on physical models and it seems to be among the fastest elastic registration approaches [7], computation cost is the most challenging obstacle to widespread its incorporation into real time clinical applications.

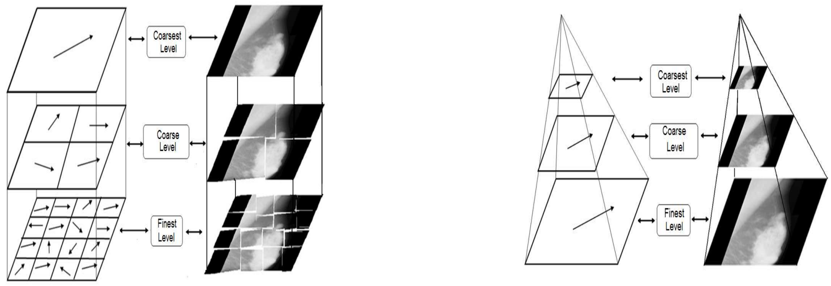


**Fig. 1.** The classical hierarchical image-based subdivision approach [9] and the Gaussian pyramidal approach for elastic image registration.

### 2.2 Gaussian Pyramid

Multiresolution is usually desirable in image registration, since it saves time and also improves the registration accuracy [11]. Gaussian pyramid is the most commonly used multiresolution representation for image registration [14]. It requires the parallel generation of a family of images from each of the original source and target images, where image size (resolution) is reduced in each successive level. Each level is formed by first applying Gaussian smoothing (on the original images) with increasing scale and then downsampling the previous level (smoothed images) (Fig. 1.). In addition to avoiding local minima traps, the Gaussian pyramid has the advantage of reducing computation time since the quantity of data is less in the lowest levels [8].

### 2.3 Combining Hierarchies of Data and Warp

In order to decrease computation cost of non-rigid registration, some works tend to combine hierarchies of data and warp complexity on the same framework. For example, Hellier et al. [5] proposed a hierarchical multiresolution and multigrid framework for non-rigid registration of MR images of the head. At each level of resolution, a multigrid minimization based on successive partitions of the initial volume is used. This method is based on transformations of higher complexity at initial subdivision levels with larger subvolumes and simpler modes at later levels having smaller subvolumes. Besides, Auer et al. [2] proposed an automatic non-rigid registration scheme for stained histological sections. They developed a hierarchical registration algorithm, by basically using a fast coarse rigid registration step, followed by a slower, but finer, non-rigid elastic registration. For the coarse registration, they used an image pyramid to speed up the algorithm. Although those methods combine hierarchy of data and warp, only either the data or the warp complexity increases at each level of the hierarchy.

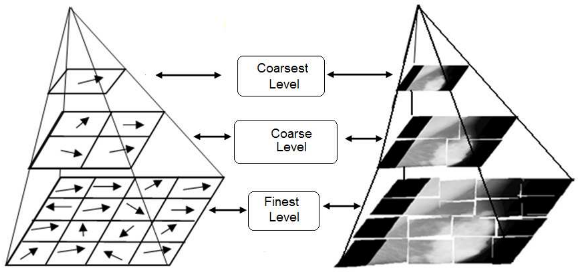


**Fig. 2.** The proposed hierarchical framework for non-rigid image registration.

## 3 Proposed Framework

The proposed method combines the hierarchical image subdivision-based approach and Gaussian image pyramid. Contrary to the aforementioned methods, the complexity of both data and warp increase at each level of the hierarchy (Fig. 2.).

Firstly, we construct Gaussian image pyramids for the reference and the target images. At each level of the pyramid, the images to be registered are subdivided into subimages of predetermined minimum size, which are then locally registered. In the coarsest level, as the image size is equal to the minimum size, only global rigid registration is required. In the second level, the images are subdivided into four subimages, which are then locally and independently registered by a rigid transformation. This process is repeated until the finest level in the pyramid is reached. As the algorithm progresses to finer resolutions, both the size of the image and the number of landmarks increase. In local rigid registration, we use CC (1) as a similarity measure since we handle monomodal registration. In addition, Powell's multidimensional scheme [6] is used as optimization method. Note that the levels' number is imposed by the predetermined minimum size of the smaller used subimage.

$$CC = \frac{\sum_i \sum_j (I(i,j) - \overline{I})(\grave{I}(i,j) - \overline{\grave{I}})}{\sqrt{(\sum_i \sum_j (I(i,j) - \overline{I})^2)(\sum_i \sum_j (\grave{I}(i,j) - \overline{\grave{I}})^2)}}. \tag{1}$$

Finally, thin-plate splines (TPS) is used to elastically interpolate the local transformations to obtain the final global smooth transformation. Indeed, TPS is a common tool for multi-dimensional interpolation problems and has useful smoothing properties. The use of this technique for elastic registration is pioneered by Bookstein [3]. The method has an elegant algebra expressing the approximation of a physical bending of a thin metal plate on point constraints. The smooth function $f(x, y)$, describing the plate, minimizes the following bending energy function:

$$I_f = \int \int_R^2 (\frac{\partial^2 f}{\partial x^2})^2 + 2(\frac{\partial^2 f}{\partial x \partial y})^2 + (\frac{\partial^2 f}{\partial y^2})^2 dx dy. \quad (2)$$

Suppose that we have two sets of $n$ corresponding centers $(x_i, y_i)$ and $(\grave{x}_i, \grave{y}_i)$ of the registered subimages, and let $f_x$ and $f_y$ two separate thin-plate spline functions which model the displacement of the subimages centers (landmarks) respectively in the $x$ and $y$ direction $((f_x(x_i, y_i), f_y(x_i, y_i)) = (\grave{x}_i, \grave{y}_i))$. The thin-plate spline interpolation functions which maps corresponding points can be written as:

$$f_x(x, y) = a_x + a_{xx}x + a_{xy}y + \sum_{i=1}^{n} w_{xi} U(|(x, y) - (x_i, y_i)|), \quad (3)$$

$$f_y(x, y) = a_y + a_{yx}x + a_{yy}y + \sum_{i=1}^{n} w_{yi} U(|(x, y) - (x_i, y_i)|). \quad (4)$$

where $U(r) = r^2 \log(r^2)$ is fundamental solution of the biharmonic equation ($\Delta^2 U = 0$) that satisfies the condition of bending energy minimization. The parameters $a_x$, $a_{xx}$, $a_{xy}$, $a_y$, $a_{yx}$ and $a_{yy}$ represent the linear affine transformation, while $w_{xi}$ and $w_{yi}$ represent the weights of the non-linear radial interpolation function $U$.

## 4 Validation

### 4.1 Computational Complexity

To illustrate the usefulness and the gain obtained in computation cost by our approach, we compare its computation complexity with the one of the classical hierarchical subdivision based scheme. In fact, the cpu time of a registration process is mainly consumed during the computation of the similarity measure. Therefore, our analysis of computational complexity will concentrate on the estimation of CC. According to the equation (1), the computation of the numerator in the CC formula requires $T^2$ multiplications when the subimages' size is $T \times T$ . In addition, to simplify the complexity computation, we assume that local rigid transformations are composed only of translations over $x$ and $y$ axis, and the allowable translation in each direction must not exceed the quarter of the image size. If an exhaustive search is used to find parameters of local transformations, then the complexity of computing CC in local registration is $\frac{T^2}{4}$. Thus, given two input $N \times N$ images $I$ (reference) and $\grave{I}$ (target) and let the number of levels is $l$ (the smallest subimage size is then $\frac{N}{2^{l-1}}$), in each level $j$ ($1 \leq j \leq l$) the number of subimages to be rigidly registered is $4^{j-1}$ for the proposed approach as well as for the classical one. However, the size of each subimage is $\frac{N}{2^{l-1}}$ (*resp.* $\frac{N}{2^{j-1}}$) in the case of our (*resp.* classical) solution. Thus, the cost of the level $j$ is $N^4.2^{(2j-4l)}$ (*resp.* $N^4.2^{(-2j)}$) in our (*resp.* the classical) case. Consequently, the total cost of the suggested scheme (5) and the one of the classical hierarchical scheme (6) are consecutively defined by:

$$\sum_{j=1}^{l} N^4.2^{(2j-4l)} = \frac{4.N^4}{3} 4^{-l} \quad (5)$$

$$\sum_{j=1}^{l} N^4.2^{(-2j)} = \frac{4.N^4}{3} (4^l - 1) \quad (6)$$

Besides, we compared the total cpu time for the two studied schemes while specifying the evolution of this time from a level of the hierarchy to the next one (Fig. 3). This was done for $512 \times 512$ MRI images with $l = 4$. Methods are implemented in Matlab, and the platform used is a Windows PC with Intel P-4 1.6 GHz processor and 1G RAM memory. While comparing the complexity cost as well as the total cpu time of the proposed solution with those of the classical subdivision-based scheme, it is clear that our method outperforms considerably the classical approach in terms of computation cost.

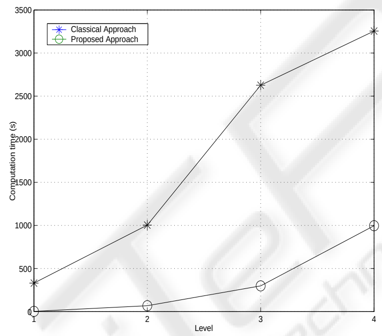


**Fig. 3.** Evolution of the cpu time relatively to the hierarchy level.

### 4.2 Registration Accuracy

In order to validate the registration accuracy of the proposed framework, simulated deformation are randomly introduced to breast mammograms (from the MIAS digital mammogram database [12]) and to MRI brain images. Since we handle images of the same modality, image-subtraction comparison can be used to visually assess the quality of the registration process (Fig. 4, Fig. 5). Besides, to quantitatively assess the quality of the registration, we compute the correlation coefficient (CC) (1), the mean square error (MSE) (7) and the peak signal to noise ratio (PSNR) (8). In Tab.1 (*resp.* Tab.2) we illustrate the CC, MSE and PSNR errors for the pre-registration, the affine registration, the classical hierarchical subdivision approach and the proposed framework recorded with mammogram (*resp.* MRI brain) images. The above obtained results indicate that both the classical hierarchical subdivision approach and the proposed framework perform better than affine registration. Moreover, we can deduce that the classical and the proposed approaches produce almost similar results in terms of CC, MSE and PSNR. This proves the effectiveness of the proposed framework, since it accelerates the registration process without significant loss of the registration quality. Note that affine registration removes most of the global differences from the studied images, whereas non-rigid registration performs mainly local improvements.

$$MSE = \frac{1}{NM}\sum_{i}^{M}\sum_{j}^{N}[I(i,j) - \grave{I}(i,j)]^2. \quad (7)$$

$$PSNR = 10.log\frac{255^2}{MSE}. \quad (8)$$

**Table 1.** CC, MSE and PSNR registration errors for mammograms.

| | CC | MSE | PSNR |
|---|---|---|---|
| Pre-registration | 0.79 | 2729 | 31.70 |
| Affine registration | 0.951 | 661 | 45.87 |
| Classical approach | 0.953 | 636 | 46.27 |
| Proposed approach | 0.953 | 635 | 46.28 |

**Table 2.** CC, MSE and PSNR registration errors for brain MRI.

| | CC | MSE | PSNR |
|---|---|---|---|
| Pre-registration | 0.64 | 3423 | 29.44 |
| Affine registration | 0.89 | 1116 | 40.64 |
| Classical approach | 0.916 | 847 | 43.39 |
| Proposed approach | 0.911 | 897 | 42.82 |

## 5 Conclusions

Although the hierarchical image subdivision-based procedure seems to be among the fastest non-rigid registration methods, its computation cost is a real challenge to be integrated in real-time clinical routines. To reduce the computational complexity, we have proposed a simple and elegant method which combine in the same framework the hierarchical method with a Gaussian pyramid. Indeed, a Gaussian pyramid is first defined for each of the reference and the target images. Then, at each level of the pyramid, the images to be registered are subdivided into four quarters, which are then locally and independently registered using a rigid transformation based on CC score and Powell optimization technique. Then, relatively to each subimage, a landmark is defined as its center. Lastly, given the set of corresponding landmarks, the TPS interpolator is used to estimate the correspondence function between the two studied images. Experimental results show the effectiveness of our method for non-rigid registration of medical images. One of the benefits of the proposed approach is its ability to run automatically, avoiding the reliance on accurate segmentation or control-point extraction. Another benefit is the reduction in computation complexity. Indeed, when compared to classical approach, our solution decreases considerably computation cost without meaningful loss

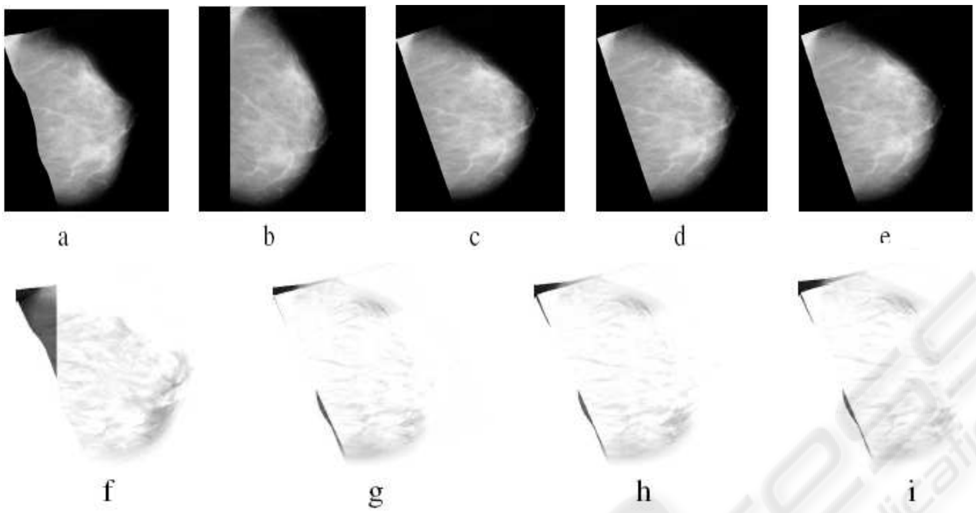


**Fig. 4.** Hierarchical registration results of mdb050 mammogram with simulated deformations: a) Target mammogram. b) Reference mammogram. c) Affine registered image. Non-rigid registered image using: d) Classical hierarchical non-rigid registration, e) Proposed method. f) Pre-registration difference image. Post-registration difference image using: g) Affine registration, h) Classical hierarchical non-rigid registration, i) Proposed method.

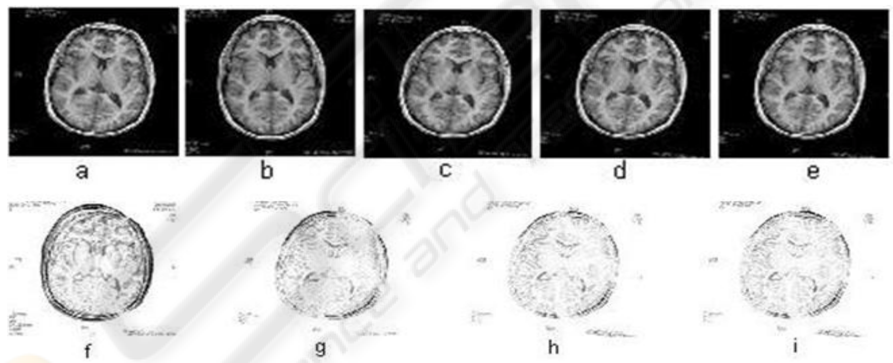


**Fig. 5.** Hierarchical registration results of brain MRI with simulated deformations: a) Target image. b) Reference image. c) Affine registered image. Non-rigid registered image using: d) Classical hierarchical non-rigid registration, e) Proposed method. f) Pre-registration difference image. Post-registration difference image using: g) Affine registration, h) Classical hierarchical non-rigid registration, i) Proposed method.

of the registration accuracy. Actually, we are working on the application of the suggested approach for bilateral mammogram registration in the context of breast tumors diagnosis. Besides, since the proposed method deals with intensity based registration, it is of great interest to extend this approach to multimodal registration. Therefore, our future work will focus in the adaption of the proposed framework to mutual information based registration. Finally, as the partitioning scheme ignores the information, notably edges information, which lies exactly on the partition, it seems interesting that each subimage can overlaps with its adjacent subimages.

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