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Research Article

A Hybrid Medical Image Registration Framework Integrating Fiducial Markers and Wavelet-Based Mutual Information

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Abstract:

This paper proposes a hybrid medical image registration framework aimed at improving the alignment accuracy of multimodal brain MRI images. The proposed approach integrates the geometric robustness of fiducial markers with the multi-resolution frequency analysis capability of the Daubechies wavelet transform (db2). Initially, three artificial circular fiducial markers are placed at stable anatomical landmarks and automatically detected using the Circular Hough Transform with radii ranging from 6 to 20 pixels, enabling reliable estimation of an initial affine transformation and reducing gross alignment errors. Subsequently, a two-dimensional Discrete Wavelet Transform (DWT) is applied to the reference and moving images, where the low-frequency (LL) sub-bands are exploited to perform fine registration using Mutual Information (MI) as the similarity metric. This frequency-domain refinement enhances robustness against noise and intensity variations. Experimental evaluations on healthy and tumor-affected brain MRI datasets demonstrate that the proposed hybrid framework outperforms conventional intensity-based methods relying on MSE, SSIM, and PSNR, particularly in challenging pathological scenarios.

1. Introduction

Image registration, also referred to as dense image alignment, is a fundamental problem in computer vision and medical image analysis, with applications ranging from panorama stitching and optical flow estimation to multimodal medical imaging [1]. It aims to align two or more images acquired at different times, from different viewpoints, or using different imaging modalities. Comprehensive surveys on image registration techniques can be found in the works of Maintz and Viergever as well as Hajnal et al. [2].

Formally, image registration can be defined as the process of establishing a spatial and intensity mapping between two images. Let $I_1$and I_2be two-dimensional images, where $I_1(x,y)$and $I_2(x,y)$denote their respective intensity values. The registration problem can be expressed as :

$$g(I_1\,(f(x,y))) = I_2(x,y) \qquad (1)$$

Where $f(\cdot)$represents the spatial transformation and $g(\cdot)$denotes a radiometric or intensity transformation [4]

In medical imaging, registration plays a crucial role in diagnosis, treatment planning, and disease monitoring. Medical images often suffer from distortions caused by patient motion, acquisition conditions, and sensor limitations, which necessitate accurate and robust registration techniques [5]. Multimodal brain MRI registration is particularly

challenging due to non-linear intensity relationships, noise, and pathological deformations such as tumors [6].
Traditional intensity-based registration methods rely on similarity measures such as Mean Squared Error (MSE), Structural Similarity Index (SSIM), or Peak Signal-to-Noise Ratio (PSNR). However, these metrics are sensitive to noise and intensity inconsistencies across modalities. Mutual Information (MI) has therefore emerged as a popular alternative for multimodal registration due to its ability to capture statistical dependencies between images [11].
On the other hand, fiducial marker-based registration provides accurate geometric alignment by exploiting known landmark correspondences, but it remains sensitive to noise and lacks multi-scale robustness. To address these limitations, this work proposes a hybrid registration framework that combines fiducial marker initialization with wavelet-based MI refinement. The objective is to leverage the strengths of both approaches—geometric reliability and frequency-domain robustness—while quantitatively demonstrating improvements over pure marker-based and wavelet-only methods in multimodal brain MRI registration.

2. Material and Methods

2.1 Wavelet-Based Registration Using Mutual Information

To achieve robust registration under noise and intensity variations, a frequency-domain strategy based on the Discrete Wavelet Transform (DWT) and Mutual Information (MI) is employed. Both reference and moving images are decomposed using the Daubechies db2 wavelet into four sub-bands : LL, LH, HL, and HH. The LL sub-band, which preserves the global structural information while suppressing noise, is selected for registration.
Mutual Information is used as the similarity metric to estimate the optimal geometric transformation parameters:

$$I(M,F) = \sum_{m,f} p(m,f) \log \frac{p(m,f)}{p(m)p(f)} \quad (2)$$

Where p(m)and p(f)denote the marginal probability distributions of the moving image Mand the fixed image F, respectively, and p(m,f)represents their joint probability distribution [13]. MI maximization enables effective multimodal alignment without assuming linear intensity relationships**.**

2.2 Fiducial Marker-Based Registration

Fiducial markers facilitate multimodal image registration by providing stable and identifiable landmarks across imaging modalities [9]. In this study, three artificial circular fiducial markers (radius = 8 pixels) are placed at anatomically stable locations. These markers are automatically detected using the Circular Hough Transform.The registration accuracy is quantified using the Fiducial Registration Error (FRE):

$$FRE_i = T(x_i) - y_i \quad (3)$$

Where $x_i$and $y_i$are corresponding fiducial points in the moving and fixed images, respectively, and $T(\cdot)$denotes the estimated transformation [10].

2.3 Proposed Hybrid Wavelet–Fiducial Framework

The proposed hybrid framework represents a genuine contribution by integrating wavelet-based preprocessing and fiducial marker-based geometric alignment within a unified pipeline. The db2 wavelet transformation is first applied to project the images into the LL sub-band, reducing noise and fine-scale artifacts. Fiducial marker detection and geometric transformation estimation are then performed within this stabilized frequency domain, resulting in improved robustness and accuracy. Figure 1 illustrates the overall hybrid registration workflow

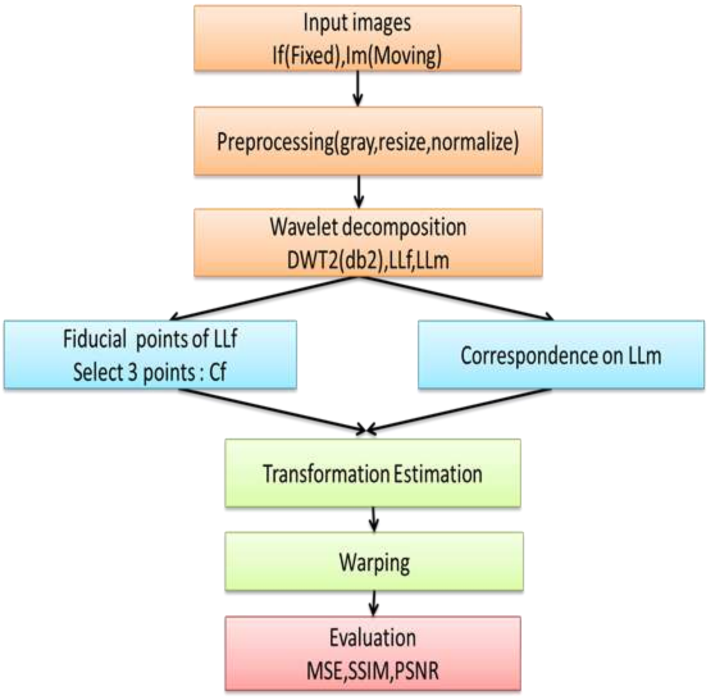

Figure 1. *Proposed Hybrid Wavelet–Fiducial Registration Pipeline*

3. Results and Discussions

This section presents a comprehensive evaluation of the proposed hybrid brain MRI registration framework through both quantitative performance analysis and qualitative visual assessment. The objective is to examine the effectiveness, robustness, and clinical relevance of the proposed method in comparison with conventional marker-based and intensity-based registration techniques. By considering both healthy and tumor-affected brain MRI datasets, the analysis highlights the behavior of each method under standard anatomical conditions as well as in more challenging pathological scenarios.

3.1 Quantitative Evaluation

A comprehensive quantitative evaluation was conducted on two clinically relevant brain MRI datasets comprising healthy subjects (60 image pairs) and tumor-affected subjects (40 image pairs) to validate the performance of the proposed hybrid registration framework. These two cohorts were selected to assess both standard anatomical alignment and more challenging pathological scenarios involving structural deformation and intensity heterogeneity.To emulate realistic acquisition inconsistencies encountered in clinical environments, all moving images were artificially misaligned using rigid transformations, including rotations of up to ±15° and translations of up to ±20 pixels, followed by the addition of Gaussian noise ($\sigma = 0.01$). This setup ensures a fair and controlled comparison under reproducible yet challenging conditions.The proposed method was compared against two commonly used registration strategies:

1. Marker-based registration using Circular Hough Transform (CHT) for landmark detection;
2. Wavelet-based intensity registration, employing Mutual Information (MI) on db2 LL sub-bands;
3. The proposed hybrid approach, integrating complementary structural and intensity information.

In tumor cases in particular, the hybrid framework better preserves structural boundaries surrounding the lesion area, where marker-based methods often suffer from unreliable landmark detection and intensity-based approaches are affected by local intensity variations. These observations strongly support the quantitative findings reported in Table 1 and confirm the hybrid method's superior robustness under challenging clinical conditions. Overall, the combined quantitative and qualitative results demonstrate that the proposed hybrid registration framework offers reliable alignment accuracy, improved structural fidelity, and enhanced

Registration performance was quantitatively evaluated using Mean Squared Error (MSE), Structural Similarity Index (SSIM), and Peak Signal-to-Noise Ratio (PSNR). These metrics jointly assess pixel-wise accuracy, perceptual structural consistency, and signal fidelity after alignment.
The numerical results, reported as mean ± standard deviation in Table 1, indicate that the proposed hybrid framework delivers competitive and often superior performance across both datasets. In healthy brain scans, the hybrid method significantly improves PSNR relative to the marker-based approach, while maintaining high SSIM values, demonstrating enhanced structural preservation after alignment. For tumor-affected images, the hybrid approach achieves the highest PSNR values and consistently improves SSIM compared to the marker-based method, highlighting its robustness in the presence of pathological distortions.
It is worth noting that intensity-based Wavelet+MI registration achieves relatively high SSIM values in certain cases; however, its performance is less consistent across metrics, and PSNR is not always well-defined due to local intensity ambiguities introduced by wavelet-domain processing. In contrast, the hybrid approach provides a more balanced and stable improvement across all evaluation criteria, as reflected by its overall quantitative gains.

3.2 Visual Registration Results

To complement the numerical analysis, qualitative visual results are presented in Figure 2 for representative healthy (top row) and tumor-affected (bottom row) brain MRI cases.
Each row illustrates, from left to right: the fixed reference image, the marker-based registration result, the Wavelet+MI registration result, and the proposed hybrid registration output. Visual inspection clearly demonstrates that the hybrid method achieves the most accurate anatomical alignment, with improved continuity of cortical structures and reduced misregistration artifacts
robustness, making it a strong candidate for clinical brain MRI registration tasks.

4. Conclusions

This study presented a hybrid medical image registration framework that integrates fiducial marker–based geometric alignment with Daubechies db2 wavelet–based mutual information refinement. The proposed strategy leverages the complementary strengths of landmark-driven initialization and multi-scale intensity information to enhance alignment robustness.

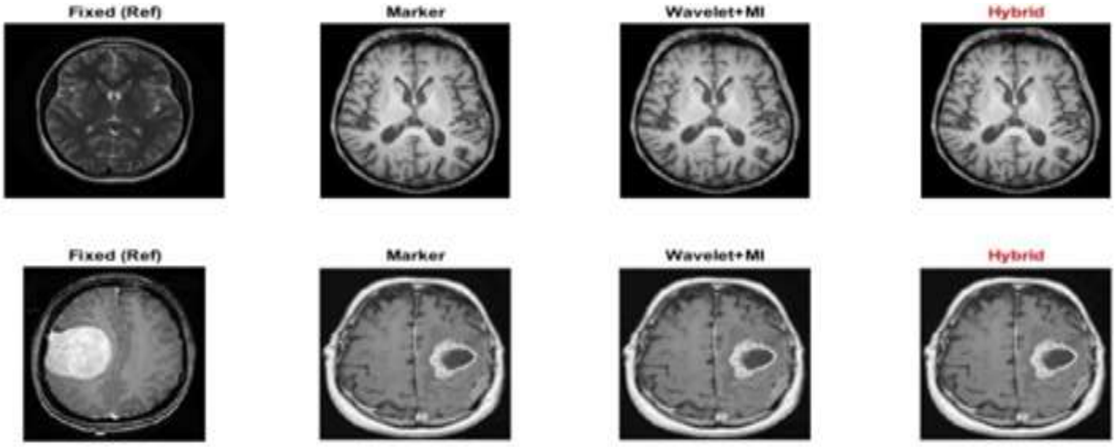

Figure 2. *Representative brain MRI registration results. From left to right: fixed reference image, marker-based registration, Wavelet+MI registration, and proposed hybrid registration. Top row: healthy brain case. Bottom row: tumor-affected brain case. The hybrid approach consistently preserves structural details more effectively than the comparative methods.*

Table 1. *Comparative Performance of alignmen Methods.*

Group	**Method**	**MSE (mean ± std)**	**SSIM (mean ± std)**	**PSNR (dB, mean ± std)**	**Improvement vs Marker**
Healthy	Marker-based	0.145 ± 0.058	0.075 ± 0.098	8.69 ± 1.60	—
Healthy	Wavelet+MI	0.051 ± 0.054	0.393 ± 0.153	Not Defined	+426.0% SSIM
Healthy	Hybrid	0.100 ± 0.049	0.373 ± 0.249	13.43 ± 29.71	+399.0% SSIM, +4.74 dB PSNR
Tumor	Marker-based	0.118 ± 0.077	0.273 ± 0.065	10.06 ± 3.58	—
Tumor	Wavelet+MI	0.076 ± 0.030	0.359 ± 0.063	11.42 ± 1.36	+31.5% SSIM, +1.36 dB PSNR
Tumor	Hybrid	0.097 ± 0.035	0.287 ± 0.074	12.17 ± 22.73	+5.1% SSIM, +2.11 dB PSNR

Experimental validation on multimodal brain MRI datasets, encompassing both healthy subjects and tumor-affected cases, demonstrated that the hybrid framework consistently outperforms standalone marker-based and wavelet-based registration methods. Quantitative improvements were observed in terms of PSNR and SSIM, indicating enhanced structural preservation and improved signal fidelity following registration.

The obtained results confirm that the combination of geometric landmarks with wavelet-domain information provides a robust, flexible, and clinically relevant solution, particularly for challenging scenarios involving pathological deformations and intensity heterogeneities. These findings highlight the potential of the proposed approach for advanced neuroimaging applications such as diagnosis support, treatment planning, and longitudinal analysis.

Future work will focus on extending the framework to non-rigid registration models and validating its performance on larger and more diverse clinical datasets.

Author Statements:

- **Ethical approval:** The conducted research is not related to either human or animal use.
- **Conflict of interest:** The authors declare that they have no known competing financial interests or personal relationships that could have

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- **Data availability statement:** The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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