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RESEARCH ARTICLE

BENTHAM SCIENCE

CT-MRI Dual Information Registration for the Diagnosis of Liver Cancer: A Pilot Study Using Point-based Registration

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Abstract: ***Background***: Early diagnosis of liver cancer may increase life expectancy. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) play a vital role in diagnosing liver cancer. Together, both modalities offer significant individual and specific diagnosis data to physicians; however, they lack the integration of both types of information. To address this concern, a registration process has to be utilized for the purpose, as multimodal details are crucial in providing the physician with complete information.

Objective: The aim was to present a model of CT-MRI registration used to diagnose liver cancer, specifically for improving the quality of the liver images and provide all the required information for earlier detection of the tumors. This method should concurrently address the issues of imaging procedures for liver cancer to fasten the detection of the tumor from both modalities.

Methods: In this work, a registration scheme for fusing the CT and MRI liver images is studied. A feature point-based method with normalized cross-correlation has been utilized to aid in the diagnosis of liver cancer and provide multimodal information to physicians. Data on ten patients from an online database were obtained. For each dataset, three planar views from both modalities were interpolated and registered using feature point-based methods. The registration of algorithms was carried out by MATLAB (vR2019b, Mathworks, Natick, USA) on an Intel (R) Core (TM) i5-5200U CPU @ 2.20 GHz computer. The accuracy of the registered image is being validated qualitatively and quantitatively.

Results: The results show that an accurate registration is obtained with minimal distance errors by which CT and MRI were accurately registered based on the validation of the experts. The RMSE ranges from 0.02 to 1.01 for translation, which is equivalent in magnitude to approximately 0 to 5 pixels for CT and registered image resolution.

Conclusion: The CT-MRI registration scheme can provide complementary information on liver cancer to physicians, thus improving the diagnosis and treatment planning process.

Keywords: Computed tomography, magnetic resonance imaging, image registration, liver cancer, feature-based registration, RMSE.

1. INTRODUCTION

Liver cancer is the seventh most lethal cancer in the world [1]. In 2012, approximately 782,000 individuals were diagnosed with liver cancer, and 745,000 deaths associated with liver cancer were recorded worldwide [2]. Liver cancer is amongst the top five types of cancer in Malaysia and is prone to attack more Chinese men compared to women [3]. Like any other tumor, liver cancer begins with unhealthy growth rates of healthy cells, causing a tumor mass. Liver cancer is also prone to develop in those who have primary liver cancer, such as Hepatocellular Carcinoma (HCC) [4]. Approximately 80% of primary liver cancer is classified as HCC.

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are the main gold-standard imaging procedures for diagnosing liver diseases [5]. CT imaging provides detailed cross-sectional images of the liver [6]. CT imaging can offer information about tumors in the liver as well as the exact anatomical location of the tumor [7]. However, during the surgical procedure, the shape of the liver differs from that shown in preoperative CT images owing to the positioning of the patient for convenience during surgery. Therefore, it is quite challenging to match the accuracy of the images during an operation [8]. An MRI also offers a cross-sectional image of the liver with additional detailed information

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about blood vessels connecting to and surrounding the liver [9]. Conversely, due to low magnetic fields, MR images are less detailed than CTs in hard tissue areas.

Both CT and MRI are important for the diagnosis of liver disease [10]. However, each modality only provides unique individual information independently. A combination of information from both CT and MRI images can provide complete and detailed information on liver cancer to the physician [11]. To achieve complementary CT-MRI information, an image registration technique can be utilized. Although various image registration techniques have been previously proposed, a majority of the techniques utilize complicated high image processing techniques of intensity-based registration [12-14], which is time-consuming, costly, dependent on the image quality, and prone to registration error. It is also difficult to be implemented by physicians who are new to the file of image registration.

In the present study, we propose a point-based registration technique, which directly matches a selection of anatomical feature points, thus providing better accuracy and fast image registration results. Feature point selection and spatial alignment are two main issues that have been addressed in this study. This technique offers a novel way to display the liver in CT and MRI images for complementary information of liver cancer diagnosis. We demonstrated the applicability of this technique using three interpolated CT and MRI images of ten patients. The approach was validated qualitative and quantitatively. The method and feasibility study are presented in this report.

2. METHODOLOGY

2.1. Image Acquisition

Retrospective data of CT and MRI images were collected in this study. Note that this study received prior ethical consent from the Islamic Science University of Malaysia (USIM) Ethics Committee. Data on ten anonymous patients were collected retrospectively from an online database [15]. Each dataset contained both CT and MRI volumetric scans. The CT data were acquired using a 64-slice dual-source Somatom Definition CT scanner (Siemens Medical Solutions, Germany). They were of a matrix size 512 × 512. By contrast, the MRI data were acquired using a 1.5 Tesla (T) scanner 32-channel coil system (Avanto, Siemens Medical Systems, Erlangen, Germany). The MRI volumetric scans were of a matrix size 512 × 512. Table **1** indicates the demographics of the ten patients recruited.

2.2. Image Registration

In medical image processing, the most effective technique is known as image registration, and there are different issues on the perspective of registration and their application to exact medical imaging issues [16]. In image registration, a spatial transformation is defined between two images, which are the fixed (target) image and a moving (source) image. It is a compromised point-based registration mechanism with iterative-closest points embedded [17].

Table 1. Demographic of ten selected patients.

Patient	Age	Sex
1	68	Male
2	71	Male
3	54	Female
4	57	Female
5	65	Male
6	47	Female
7	63	Male
8	53	Male
9	46	Female
10	60	Male

There are three major steps in the image registration scheme proposed in this study, namely, CT and MRI pre-processing, and spatial registration. In the first and second steps, three major axis views of CT and MRI were interpolated. These views include coronal, axial and sagittal plane of the liver in CT and MRI images (Fig. **1**). These three views are interpolated from the volumetric data so that they matched each other during the spatial registration process.

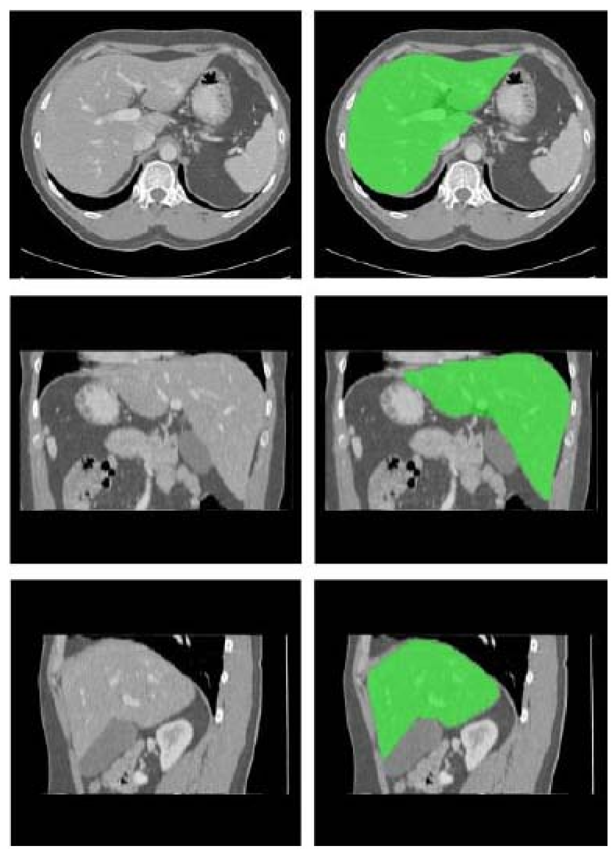

Fig. (1). Segmentation of the liver in three planar views including the axial, coronal, and sagittal planes [18]. The green areas in the right column images denote the liver area. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

During the third step, the various feature points on CT and MRI are selected. A rigid geometrical transformation is then applied to the CT images to spatially align them with the MRI images using a point-based registration algorithm. The overall proposed registration workflow of this study is shown in Fig. (**2**). Further information on the point-based registration process is provided in the following sections.

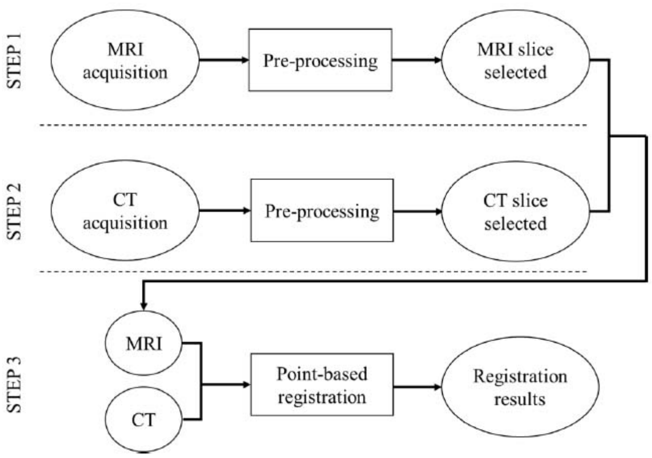

Fig. (2). Overall registration workflow.

2.3. Point-based Registration

The registration scheme proposed in this study utilizes a rigid 2-D to 2-D direct feature-based registration technique, employing a normalized cross-correlation to apply a spatial registration between the CT and MRI images [19]. During the registration process, various liver anatomical points were selected. Approximately 20 points were selected in each of the CT and MRI images, covering almost all prominent features of the liver. Next, a normalized cross-correlation was utilized on all individual control points of the CT images and around the matching control points of the MRI images. The correlation between the values at each individual pixel in the region was measured and the highest correlation value position was then located. This highest correlation value position is the optimal position of the control point. The linear spatial transformation is applied to the CT to be registered to the MRI images. If the registration is unsuccessful, the process is repeated by selecting new feature points on the images. The normalized correlation for the two-time series is defined in Eq. (**1**).

$$\varphi'_{xy}(t) = \frac{\varphi_{xy}(t)}{\sqrt{\varphi_{xx}(0)\varphi_{yy}(0)}} \tag{1}$$

The normalized quantity φ'_{xy} (t) is limited to a range between -1 and 1. As MATLAB does not have zero or negative indexes, the cross-correlation sample with zero lag is the central element in the output vector. Alternatively, using the conv command (phi$_{xy}$ = conv (y, x (end: -1:1))), without padding zeroes, is the way to make a cross-correlation. It ranges from -1 to 1. A φ'_{xy} (t) = 1 value indicates that the two-time series have the same shape at t alignment, but the amplitude is different, whereas φ'_{xy} (t) = -1 symbolizes that the two-time series have the same shape except for the opposite signs. A value of φ'_{xy} (t) = 0 shows that they have no relation at all.

The linear spatial transformation is applied on CT to be registered to the MRI images. A rigid feature-based registration scheme was applied with mutual information in a similitude scale and patterns as the underlying optimizer to achieve the spatial registration of each CT and MRI image of liver cancer. The frame of the MRI image was chosen as a reference. I Its detailed images of a soft tissue are produced in particular in blood vessels around the liver. For each dataset, three planar views consisting of coronal, axial and sagittal from CT and MRI were interpolated and registered. The registration was successful when all the images of CT and MRI merged precisely with each other. If registration was not successful as the registered image did not merge correctly, the process was redone again by selecting new feature points on the images. The overall point-based registration process is shown in Fig. (**3**). The proposed registration algorithm was applied using the R2016a version of MATLAB (Math Works, Natick, USA) on a computer with an Intel(R) CPU B815 @ 1.65 GHz.

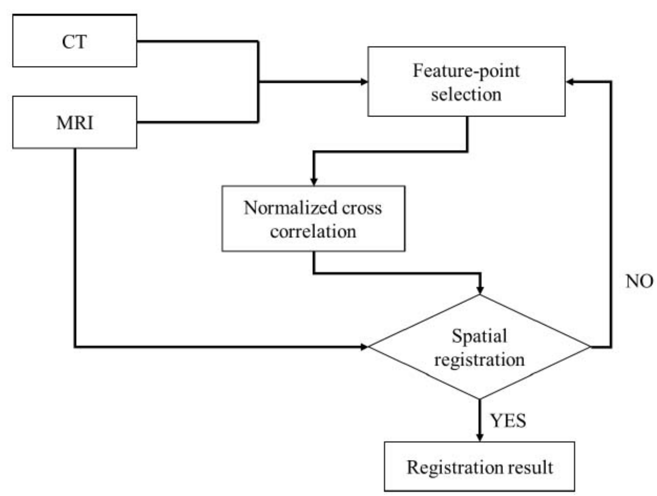

Fig. (3). Point-based registration pipeline.

2.4. Validation of Registration Accuracy

Overall CT-MRI registration by the suggested technique was validated qualitatively and quantitatively. For qualitatively, CT-MRI registration method was assessed and validated by two experts, each having more than 7 years of experience in the field. The qualities of the registered images were validated by scoring them from 1 to 4 (Table **2**). A score of 1 denoted an “excellent” image quality and was given if the image had excellent visibility with clear differentiation of the liver’s anatomical details relevant for the diagnosis of liver cancer. A score of 2 denoted a “good” image quality and was given if the image showed good visibility with related anatomical details of the liver for cancer diagnosis.

Table 2. Registration accuracy score metric.

Score	Denote
1	Excellent image quality
2	Good image quality
3	Poor but still diagnostic
4	Poor image quality

A score of 3 denoted a "poor but still diagnostically useful". This score indicated that the image has poorly anatomical details of the liver. The MRI image seems to be slightly deviated from the planned liver plane, as shown in the CT. Finally, a score of 4 denoted a "Poor" image quality. The image shows a non-diagnostic image quality and makes delineation of the liver structures impossible. The MRI image plane is totally shifted away from the plane of the CT image. Cohen's κ statistic expressed in Eq. (**2**) was used to define the interobserver agreement for the image quality [20].

$$k = \frac{p_o - p_e}{1 - p_e} \quad \textbf{(2)}$$

Where p_o is the corresponding experimental agreement among raters, andp_e is the hypothetical possibility of chance agreement.

The Root Means Square Error (RMSE) was calculated to contrast each transformation parameter between the CT and the registered images to perform a quantitative analysis of the transform parameter. It is defined as some average or sum (or integral) of a square of the error between two images. This measure is defined in Eq. (**3**).

$$RMSE = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(\| T_{m_i} - T_{a_i} \|)^2} \quad \textbf{(3)}$$

Where T_m is transformation (translation) parameter acquired by the standard expert registration and corresponds to the proposed algorithm with the resulting transformation parameter. The RMSE helps to combine the magnitudes of the errors in forecasts for various times into a single predictive power measure. A higher RMSE indicated that the reference and the moving image vary more significantly. This liver measurement is considered a fair indicator of the clinical intention to register both CT and MRI images to determine the registration accuracy of the proposed procedure.

3. RESULTS AND DISCUSSION

Registration results on two patient datasets are shown in Fig. (**4**). Columns 1, 2, and 3 are the three image planes of the CT and MRI images. By contrast, rows 1, 2, and 3 denote the MRI, CT, and registration results for each patient dataset, respectively.

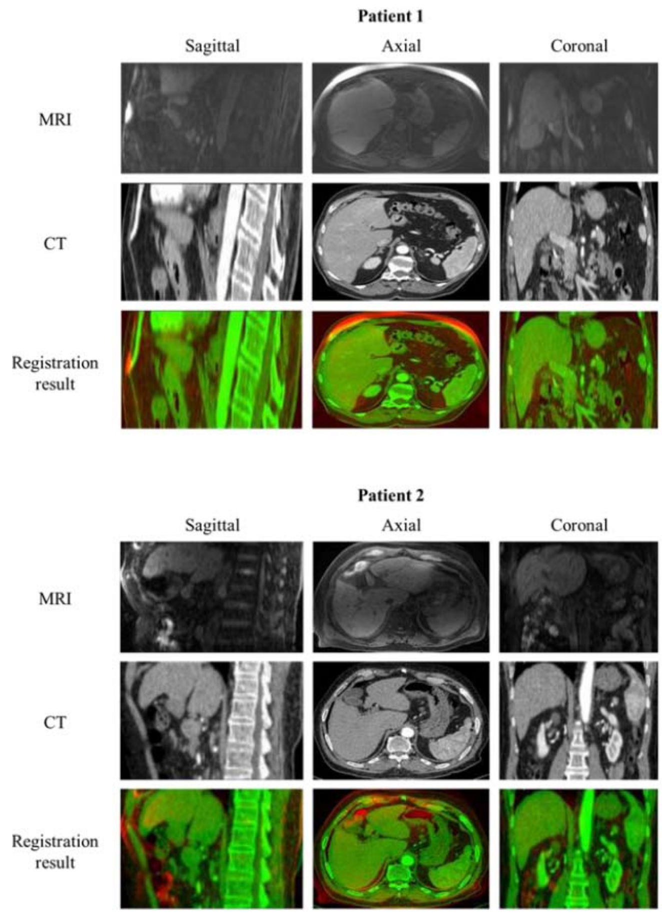

Fig. (4). Registration results on two patients using the proposed point-based registration method. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

A good interobserver agreement (κ = 0.81) was achieved through the qualitative assessment of the two experts as shown in Table **3**, who rated 30 of the registration results of the data on the ten patients. Thirty-four images were rated as score 1 (excellent), representing 56.7% of the total registration results. Twenty-six were rated as score 2 (good), representing 43.3% of the total registration results. Neither expert rated any of the registration results as score 3 (poor but still diagnostic) or score 4 (poor and non-diagnostic).

Table 3. Data from two experts using Cohen's kappa statistics.

-	Observer 1					
	Score	**1**	**2**	**3**	**4**	**Total**
Observer 2	**1**	14	3	0	0	17
	2	0	13	0	0	13
	3	0	0	0	0	0
	4	0	0	0	0	0
	Total	14	16	0	0	30

Number of observed agreements: 27 (90.0% of the observations).
Number of agreements expected by chance: 14.9 (49.6% of the observations).
Kappa= 0.81 Standard Error (SE) of kappa = 0.106.

For the transformation (translation) parameter, the Root Mean Square Error (RMSE) is computed to perform a quantitative transformation analysis. A quantitative error in the transformation parameters is tabulated in Table **4**. The RMSE ranges from 0.02 to 1.01 for translation, which is equivalent in magnitude to approximately 0 to 5 pixels for CT and registered image resolution.

Table 4. RMSE of the transformation parameter between CT and registered image.

Patient	Translation (mm)	
	Δtx	Δty
1	0.14	0.04
2	0.71	0.95
3	0.87	1.01
4	0.02	0.28
5	0.12	0.07
6	0.06	0.53
7	0.54	0.05
8	0.11	0.92
9	0.04	0.37
10	0.61	0.49

Δtx and Δty refer to RMSE for the translation.

The transformation parameters between CT images and registered images show small deviation (RMSE ≤ 1.01mm deviation) in translation. A higher RMSE shows a greater difference between the reference and moving image. It concluded that the lower the RMSE, the better the image produced for feature point-based registration.

Image registration is an important procedure for diagnosing patients with liver cancer [21], and MRI and CT images provide unique information in such diagnoses. CT images can provide primary information on the presence and locality of the tumor; they can also detect multifocal liver involvement. MRI images provide additional detailed images of the liver and quantify the types of tumors. Through a CT-MRI registration, complementary information in the diagnosis of liver diseases is achieved. In this study, a feature-point-based registration was conducted to align MRI and CT images. The MRI image acts as a reference image because it produces a clearer image of soft tissue as compared to a CT image. The qualitative assessment by two experts in medical imagery revealed that the proposed registration scheme is capable of aligning the images, thus aiding physicians with complete information for the diagnosis of liver cancer.

At present, retrospective data have been utilized to test the registration algorithm. Nevertheless, the validation results have shown promising accuracy of the proposed technique for application in feature point-based registration for liver disease. Furthermore, the registered CT-MRI images show highly complementary information for physicians. The data implemented in MATLAB software, which consists of the iterative-closest point increases the looping speed, thus shortening the registration time.

Moreover, the feature point-based registration method was evaluated by two techniques. Firstly, two experts in anatomy assessed the appearance of the liver in registered MRI and CT images. Both images must be merged accurately to contribute valuable images and references for physicians to fasten the diagnosis of liver cancer. Cohen κ statistics were used to represent the inter-observer adjustment for the image quality. Besides, the registered images of CT and MRI showed good agreement with each other in terms of insignificant visible representation. Cohen κ statistics show good inter-observer agreement for the overall quality of registered CT-MRI images in each of the ten patients. Next, the RMSE transformation parameter for translation of quantitative analysis was found minimal. It ranged between 0.02 and 1.01, which can be concluded that the lower the RMSE, the better the image produced.

In addition, the proposed method requires a prior understanding of the anatomy and orientation of the liver to achieve accurate registration results. Thus, a physician with excellent knowledge of anatomy can select the matching feature of the liver during registration, thus improving the overall registration time for practical clinical application. The method suggested in this study provides fast registration results compared to the previous methods that iteratively depend on the intensity and quality of images [22].

Although the current study presents a pilot proof of concept on a point-based registration of CT-MRI images of the liver, more datasets should be acquired to test this algorithm in the future. In addition, only 20 feature points were selected. We believe that additional selected points can provide a higher level of accuracy of the registration results yet they will consume more of the registration time. Furthermore, a quantitative analysis should also be conducted, including a Dice Similarity Coefficient (DSC) test and a Hausdorff Distance (HD) test [23] to provide an accurate level of accuracy on the suggested methods.

CONCLUSION

This was a pilot study on a proposed proof of concept utilizing a feature point-based registration method. Instead of relying on the intensity or quality of the images, we directly selected the feature points to be matched on both images, thus improving the overall registration time suitable for clinical practice. The outcomes on the dataset of ten patients showed a favorable validation of the proposed image registration scheme for application to a liver disease diagnosis. Cohen's kappa statistics and the root mean square error verified the quality of images obtained by this technique. The recommended registration structure could be implemented in the examination and image supervision procedure for CT and MRI images for liver cancer. Results on ten patients designated the promising efficiency of the suggested technique to be applied for the diagnosis of liver diseases. However, the limitation of the current study included a lack of data and a limited selection of feature points. Finally, additional datasets, more selection feature points, and more quantitative analysis are recommended for investigation in a future study.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study has been ethically approved by the Faculty of Science and Technology, Islamic Science University of Malaysia (USIM) for supporting the current study [approval number: NMRR-20-1963-56187].

HUMAN AND ANIMAL RIGHTS

Not applicable.

CONSENT FOR PUBLICATION

We further certify that proper citations to the previously reported work have been given and no data/tables/figures have been quoted verbatim from other publications without giving due acknowledgment and without the permission of the author.

STANDARDS OF REPORTING

STROBE guidelines were followed for the study.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

FUNDING

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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