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COMPUTER APPLICATIONS

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A comparative study on manual and automatic slice-to-volume registration of CT images

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Abstract In order to assess the clinical relevance of a slice-to-volume registration algorithm, this technique was compared to manual registration. Reformatted images obtained from a diagnostic CT examination of the lower abdomen were reviewed and manually registered by 41 individuals. The results were refined by the algorithm. Furthermore, a fully automatic registration of the single slices to the whole CT examination, without manual initialization, was also performed. The manual registration error for rotation and translation was found to be 2.7±2.8 ° and 4.0±2.5 mm. The automated registration algorithm significantly reduced the registration error to 1.6±2.6 ° and 1.3±1.6 mm ($p=0.01$). In 3 of 41 (7.3%) registration cases, the automated registration algorithm failed completely. On average, the time required for manual registration was 213±197 s; automatic registration took 82±15 s. Registration was also performed without any human interaction. The resulting registration error of the algorithm without manual pre-registration was found to be 2.9±2.9 ° and 1.1±0.2 mm. Here, a registration took 91±6 s, on average. Overall, the automated registration algorithm improved the accuracy of manual registration by 59% in rotation and 325% in translation. The absolute values are well within a clinically relevant range.

Keywords Slice-to-volume registration algorithm · Manual registration · Fluoro CT · Computed tomography

Introduction

Computed tomography (CT) is a widely used modality to guide percutaneous biopsy of lesions located within the liver and the lung [1]. Usually, a contrast-enhanced CT examination is obtained before the biopsy to localize a lesion by enhanced lesion-to-tissue contrast, to plan the best access to the target lesion for biopsy, and to determine the best table position for the subsequent biopsy. It is preferable to have both the skin entry point and the target lesion within the same imaging plane in order to follow the biopsy needle during the image-guided procedure and to avoid critical structures. This condition can be fulfilled by repeated image acquisition of 2D-CT slices using a technique called "fluoro CT" [1, 2]. With this technique, single transverse slices are obtained at a frame rate of 0.5–2 images/s at a specific table position. However, with this technique, only single slices of a target volume in a transverse orientation can be obtained; thus, both the skin entry point and the target lesion must be visible in the same transverse plane. This technique has been reported for biopsies of the lung [3], primarily, and the liver, but other applications, including biopsy retrieval of suspicious masses in the pelvis, have been reported as well [4–6].

In cases when the position of a target lesion and the skin entry point are located at a different table position, image guidance can only focus on either one of these points; thus, moving the CT table between both positions until the needle is located within the target might be necessary. To overcome this limitation, oblique, sometimes even double-oblique, reformatted imaging planes may provide a

reconstructed imaging plane that visualizes both the skin entry point and the target in one plane.

Another challenge is patient movement or movement of organs during breathing that may occur during the procedure; thus, the position of a certain target point assessed on the pre-interventional data set may no longer be at the same position on images obtained by CT fluoroscopy. In addition, the visibility of a target lesion can be hampered by the lack of lesion-specific contrast, once the applied contrast agent, injected during the first CT imaging set, has disappeared. To re-localize the target, CT fluoroscopy might be used extensively, or contrast injection might be repeated during needle guidance into the target. In addition to the risk of retrieving a false-negative biopsy sample, the radiation and contrast-agent dose for patients and staff might be increased in such cases.

The introduction of a 2D/3D registration method may improve the accuracy of CT-guided biopsies by combining high-resolution, pre-interventional, contrast-enhanced imaging (3D) data sets with the low-resolution (and often low-contrast-to-lesion) single-slice (2D) images obtained during the intervention using a fluoro CT mode. This so-called 2D/3D registration algorithm has already been introduced in the field of computer-aided, image-guided therapy [7, 8] and image-guided radiotherapy [9, 10]. In these cases, a digitally rendered radiograph (DRR) [11] is generated from CT data. Projection parameters are altered until an optimum match between the DRR and a projection-type X-ray image has been achieved.

A modification of this technology is the slice-to-volume registration method [12, 13]. In this technique, a single slice, obtained by a cross-sectional imaging modality such as US, CT, or MRI, is iteratively compared to best match either the contour of the previously obtained 3D data set of an organ or to best match the "signal" (tissue pattern) of this organ.

To better match a single 2D slice to the 3D data set, six degrees of freedom in translation and rotation are altered iteratively until an optimum match between the reformatted slice and the slice obtained from interventional imaging has been achieved. The benefits of this procedure are twofold: first, the relative distance between the diagnostic pre-interventional CT examination and the actual imaging plane, including the exact spatial orientation of the patient in his/her current position on the CT table, is given, thus providing a roadmap to the optimum position for biopsy retrieval. Second, a reformatted 3D data set, containing the target lesion with optimum enhancement (while intravenous contrast agent was administered) can be visualized alongside the actual 2D slice obtained by the CT fluoroscopy used for needle guidance. As a result, improved lesion localization and reduced radiation exposure can be achieved.

Our goal was to investigate whether a registration algorithm could provide an alignment of a 2D slice to the 3D data set more reliably and faster than manual registration by an experienced radiologist. For this purpose, we compared the manual slice-to-volume registration capabilities of 41 individuals to the results with the automated algorithm and investigated the resulting accuracies and recorded time expenses. In addition, fully automatic registrations were also performed and compared to the results of the manual registration.

Materials and methods

Two- and three-dimensional registration: software and algorithms

A slice-to-volume registration is a method used to align a single 2D imaging slice, acquired during an interventional procedure to a 3D volume imaging dataset, acquired before the intervention [13]. To compare the 2D imaging slice with the 3D data set, a computer-generated slice is reformatted from the 3D volume data through iterative variation of spatial rotation and translation parameters by means of a so-called merit function assessing the similarity of imaging slices [7, 8, 12, 13]. A registration algorithm can be used to re-align the diagnostic 3D CT examination to show the same reformatted slice, including the better image quality and the additional information from contrast agents. Once an optimal match is achieved, the registration routine stops and the corresponding slice from the 3D dataset is considered to be aligned to the actual fluoro CT slice (associated with the geometry of an interventional imaging system). Figure 1 gives an overview of this process.

A number of 2D/3D registration algorithms and numerical optimization methods for slice-to-volume registration of CT and fluoro CT datasets were presented in [13]. In our study, cross-correlation was the merit function of choice for slice-to-volume registration. The optimization was performed by a local simplex algorithm [14]. The program was developed using C++ and the Qt-toolkit (Trolltech Inc., Norway) under SuSE Linux 10.1; part of its functionality was provided by the AVW toolkit (Biomedical Imaging Resource, Mayo Clinic, Rochester, MN) [15]. A screenshot of the custom-developed software can be found in Fig. 2. The software was installed on a conventional laptop (Toshiba Tecra T9100, 256 MB RAM, 1.6 GHz, standard LCD display with 1,024×768 pixel resolution). The user can upload a 3D CT examination and a single 2D reference image. The software allows manual alignment of the reformatting plane's location within six degrees of freedom that can be aligned manually. The overlay of the obtained reformatted slice and the reference slice is visualized as well. Once the user is satisfied with the manual pre-alignment, the algorithm is begun to optimize the already obtained manual match by further fine-tuning the rotation and translation parameters iteratively.

Image datasets

In our study, a CT dataset of the pelvis, in this case with a chondrosarcoma, was chosen because the pelvic anatomy provides a sufficiently high number of landmarks, simplifying the task of registration even for less experienced test personnel. The CT dataset was acquired using a multidetector CT (Philips Brilliance 64, Philips AG, Best, The Netherlands, field-of-view 370*370 mm, 512*512 pixel matrix, slice thickness 1.4 mm, 120 kV, and 236 mA). The data set was reconstructed so that each voxel had a diameter of 0.75×0.75×1.5 mm. This voxel size for this dataset was resampled using the Analyze AVW 8.1 software (Biomedical Imaging Resource, Mayo Clinic, Rochester, MN; [15]) to create cubic voxels of 1 mm^3. This was necessary to obtain an isotropic pixel size during the process of iterative oblique reformatting. The spatial transform determining the position of the reformatting plane was composed as $\mathbf{V} = \mathbf{T}\mathbf{R}_x\mathbf{R}_y\mathbf{R}_z$ with $\mathbf{V}$ being the full 4×4 volume transform matrix that gives the orientation and location of the reformatting plane, $\mathbf{R}_{...}$ being the rotation matrix for the indexed coordinate direction, and $\mathbf{T}$ being the translation matrix.

Three single slices were generated from this dataset by oblique reformatting with different orientations and positions of the imaging plane. The average "displacement" of these three single slices to be matched (Fig. 3) was 4.0 ±1.5° and 5.8±2.1 mm (geometric mean), relative to the axial, sagittal, and coronal orientations.

These slices were defined to be reference standard single slices, generated by the analysis software and manual user-dependent manipulation rather than acquired during CT intervention, running in a fluoro CT mode. Since interventional CT images are often acquired with the same machine using similar settings, this does not reduce the value of the study, from our point of view, but instead, allows for exact assessment of registration outcome. Decreased image quality, as is often encountered in clinical practice when using fluoro CT (such as additional noise), does not significantly interfere with the registration

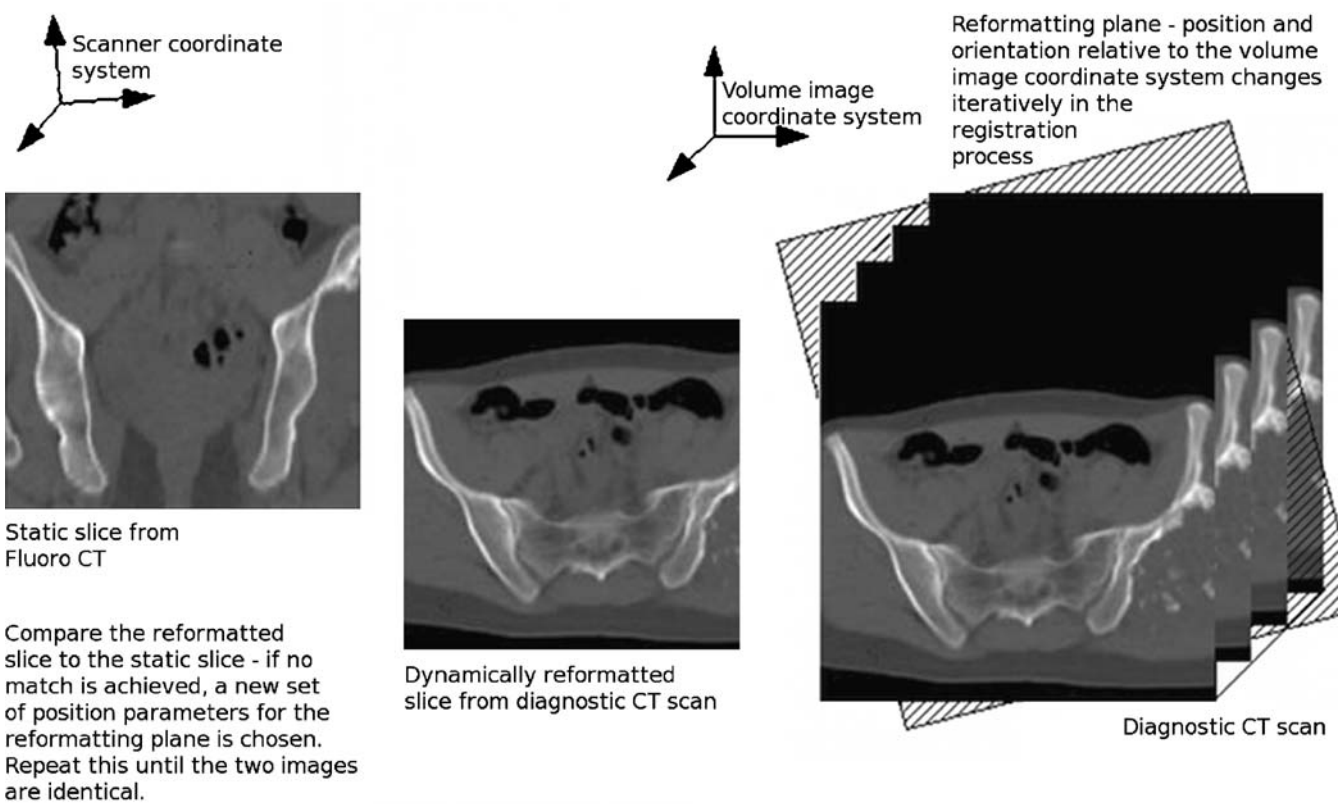

Fig. 1 Schematic overview of a 2D/3D slice-to-volume registration. The orientation and location of the reformatting plane for retrieving reformatted single slices from a pre-interventional, contrast-enhanced 3D volume data set are varied until an optimum match to the static fluoro CT slice is achieved. All six degrees of freedom in motion (three rotations and three translations) are used in this iterative process. Location of the fluoro CT slice relative to the contrast-enhanced diagnostic 3D CT is, therefore, known immediately, and details visible due to contrast enhancement can be visualized on the interventional CT examination. For illustration purposes, the left single slice represents a coronal slice, which is a large exaggeration compared to the displacements encountered in clinical practice

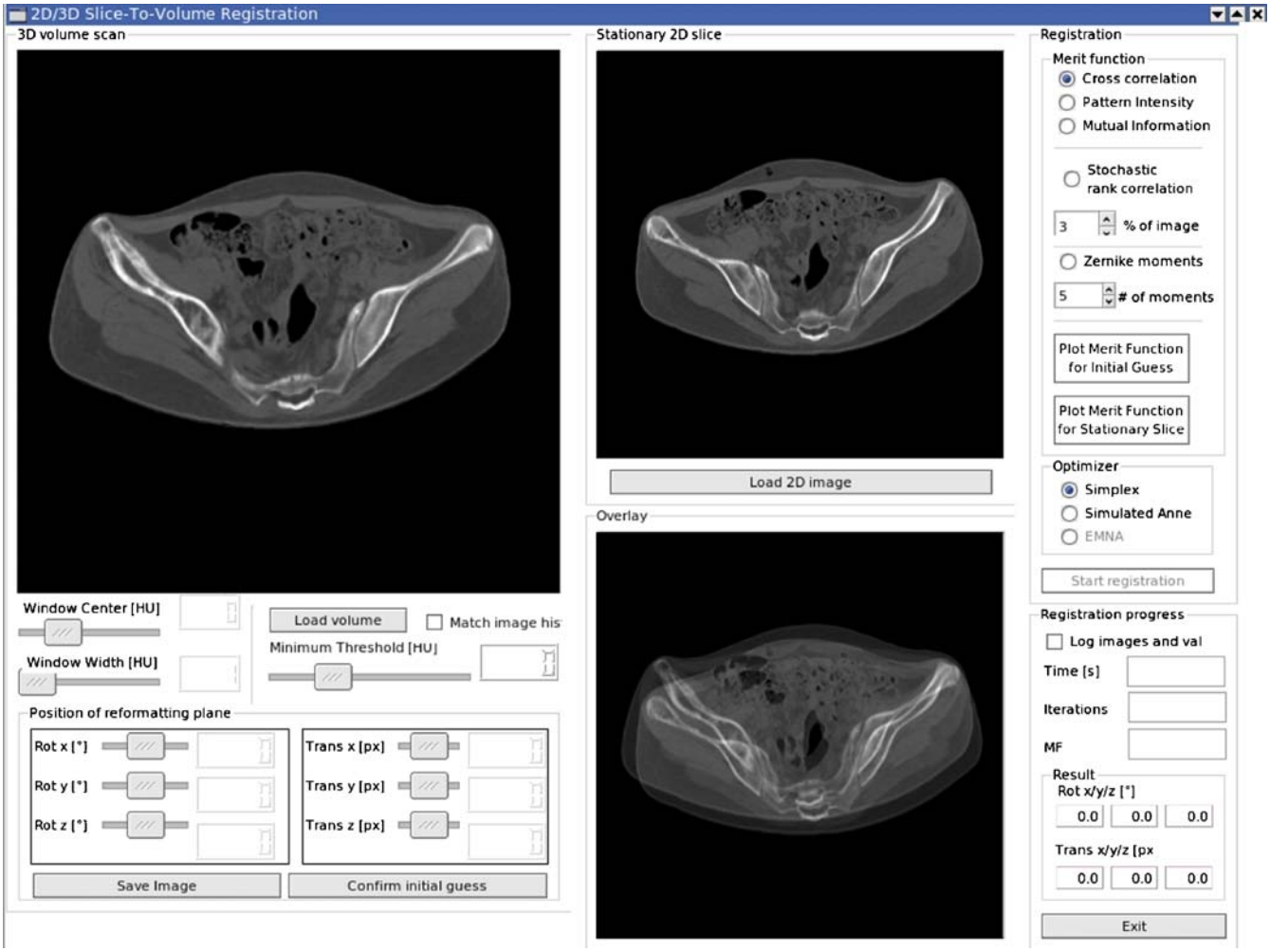

Fig. 2 The graphical user interface for the slice-to-volume registration algorithm as presented to the test personnel. The actual guess for the single slice, reformatted from pre-interventional CT and matching the fluoro CT slice, is found in the left frame. The user can manually control all six degrees of freedom in rigid motion of the reformatting plane by moving the slider elements below the frame. The upper right frame shows the static fluoro CT slice to be matched. An overlay of the two slices, giving an immediate impression of the registration quality, can be found in the lower right frame; this resulting image allows for assessment of image overlay quality. After manually choosing an initial registration, the algorithm will be started for further refinement. The algorithm's result is displayed in the overlay image after convergence of the algorithm. This illustration shows a typical initial setup as presented to the test personnel—both rotation and translation parameters were displaced by an amount of several millimeters and degrees

process, as additional measures, such as low-pass filtering, are common prior to registration.

Test personnel, evaluation, and deviation modeling

Forty-one individuals from two medical centers, all with a medical background, were asked to manually register the three reference standard single slices to the 3D dataset. Among these individuals were 12 board-certified radiologists, 11 interns, 8 technicians, and 10 students. Therefore, four categories of test personnel were formed and evaluated separately. The difference between the reference standard registration parameters (Φ_{xg}, Φ_{yg}, and Φ_{zg} for angular orientation, and t_{xg}, t_{yg}, and t_{zg} for translation of the reformatting plane) and the parameters $\Phi_{\ldots}$ and $t_{\ldots}$, as given by the test personnel or the algorithm, was computed as the arithmetic mean, $\Delta\Phi = 1/3 * \left(\left|\left(\Phi_x - \Phi_{xg}\right)\right| + \left|\left(\Phi_y - \Phi_{yg}\right)\right| + \left|\left(\Phi_z - \Phi_{zg}\right)\right|\right)$ for orientations and the geometric mean $\Delta t = \left(\left(t_x - t_{xg}\right)^2 + \left(t_y - t_{yg}\right)^2 + \left(t_z - t_{zg}\right)^2\right)^{1/2}$ for translation. A t-test for paired variables comparing average values, $\Delta\Phi$ and Δt, as determined by the test personnel and the algorithm, was performed using SPSS 15 (SPSS Inc., Chicago, IL). In addition to the results for the registration, the time required for registration and a

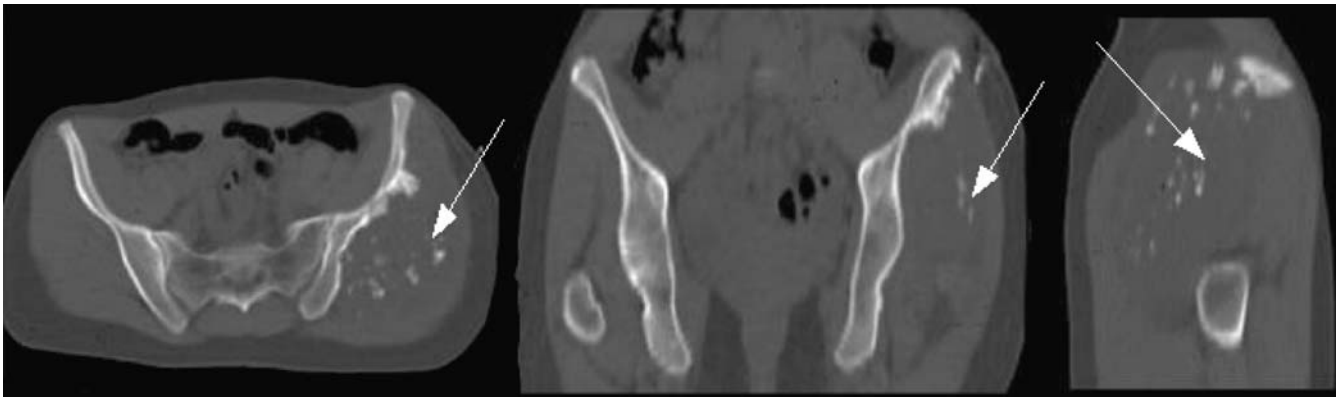

Fig. 3 Reference slices presented to the test personnel. The volume data were taken from a clinical dataset of a patient suffering from a chondrosarcoma of the pelvis (white arrow). The test personnel had to adjust the registration parameters manually until an optimum match was found between the single reference standard slices with known orientation and the slices reformatted from the CT examination by the software. Average initial displacement prior to manual registration was relative to the orthogonal slices for each rotational degree of freedom (4.0±1.5 ° and 5.8±2.1 mm for the geometric mean of translation)

visual assessment of registration quality were recorded. The score for registration quality ranged from 5 (optimum match, no visible misregistration) to 1 (obvious mismatch).

The potential impact of registration errors on biopsy target localization (also referred to as target registration error [16]) was assessed using a simplified geometric model. We assumed that the coordinate system, describing the linear motion of the interventional device, could be shifted to the insertion point and that the average angulation error, $\Delta\Phi$, is applied in one coordinate axis. For a lesion located at depth ***d***, the displacement of the biopsy needle caused by the error in angulation is given as ***d****tan($\Delta\Phi$) (mm). Adding the additional error in translation Δt, the total deviation of the instrument tip is given as $\Delta x = \boldsymbol{d}*\tan(\Delta\Phi)+\Delta t$ [mm]. Applying the Gaussian law of error propagation, one can also model the impact of the standard deviations, $\sigma_{\Delta\Phi}$ and $\sigma_{\Delta t}$, as $\sigma_{\Delta x} = \left((d/\cos^2(\Delta\Phi))^2\sigma^2_{\Delta\Phi} + \sigma^2_{\Delta t}\right)^{1/2}$. The values of Δx and $\sigma_{\Delta x}$ were modeled for the varying results of the registration efforts for lesion depths ***d***, ranging from 25 to 300 mm, which should cover all possible target locations within the torso.

Results

Table 1 provides a summary of all results. Total error in orientation, with regard to rotation and translation, was found to be 2.7±2.8 ° and 4.0±2.5 mm, respectively, for all manual registrations, whereas the registration algorithm improved the registration results to 1.6±2.6 ° and 1.3±1.6 mm, respectively. All personnel groups performed similarly, with the senior radiologists and the students showing the smallest variance. For radiologists it took 2 min, on average, to complete registration, whereas the students needed 5 min or more.

The registration algorithm, without manual initialization, achieved an average error in orientation of 2.9±2.9 ° and

Table 1 Results of the registration study for the four groups of test personnel (columns 2 –5), for the manual registration result improved by the software (column 6), and for the result of the software without manual initialization (column 7)

	Radiologists	Interns	Technicians	Students	Total	Algorithm	Algorithm stand-alone
No. of registrations	12	11	8	10	41	41	41
$\Delta\Phi$ (°)	2.7±2.2	2.7±3.2	3.0±3.0	2.4±2.4	2.7±2.7	1.6±2.6	2.9±2.9
Δt (mm)	4.3±2.5	4.2±2.7	3.7±2.6	3.4±2.2	4.0±2.5	1.3±1.6	1.1±0.2
T (s)	132±78	216±157	168±93	344±311	213±197	83±15	91±7
Quality	4 (3.75–4)	4 (3–4)	3 (3–3)	4 (3–4)	4 (3–4)	4 (3–5)	4 (3–5)
Success (%)	100	100	100	100	100	93.7	100

Values for registration error in angulation ($\Delta\Phi$) and time required (T) are given as an arithmetic average; error in translation (Δt) was computed as a geometric mean. For these three values, the standard deviation was also computed. The quality of registration was assessed using a score between 5 (optimum registration) and 1 (obvious mismatch). The median of this score is given, together with the first and third quartile, in parentheses. Finally, cases where registration was unsuccessful (for instance, due to preliminary program abortion because of exceeding the timeframe) were also recorded

1.1±0.2 mm for rotation and translation. Errors were found to be in a similar range for all three coordinate axes; rotation error for the test personnel was 3.2±4.2 ° for the axial slice, 1.5±1.5 ° for the coronal slice, and 3.8±2.6 ° for the sagittal slice. The corresponding errors in translation were found to be 5.5±3.2 mm (axial), 3.3±2.4 mm (coronal), and 3.1±1.3 mm (sagittal). Applying the algorithm to the manual results gave rotational errors of 0.7±1.1 ° and 2.6±4.2 mm (axial), 0.1±0.3 ° and 1.2±0.2 mm (coronal), and 3.4±2.2 ° and 1.0±0.4 mm (sagittal). The fully automatic registration error was fairly isotropic. Time required was 213±197 s for manual registration and 83±15 s for automatic registration following manual registration. The paired t-test showed highly significant (α=0.01) differences in average registration error for both angulation and translation error. Without the manual initialization step, the registration algorithm required 91±6 s.

As far as the visual quality assessment is concerned, the test personnel scored the result of their efforts with a median of 4 (first quartile: 3, third quartile: 4). The reference standard slices were not shown to the test personnel; therefore, this score was blinded. The result of the registration, as improved by the algorithm, was also scored with a median of 4, but the quartiles (first quartile: 3, third quartile: 5) indicate that the registration result was apparently improved. Registration success in general was categorized as a sufficient overlay of the single reference standard slice and the slice reformatted using the result of the algorithm. However, in three cases, the algorithm failed to converge and did not produce a meaningful registration; thus, the success rate is only 93.7%. Compared to the average initial displacement (4.0±1.5° and 5.8±2.1 mm), all groups were able to achieve an improved alignment.

The results of the estimated impact on target localization error can be found in Table 2. For example, the estimated error, Δx, for a lesion depth of 150 mm is 11.1±7.5 mm for the manual 2D/3D registration, 5.5±7.0 mm for the manual registration improved by the algorithm, and 8.7±7.6 mm for the registration performed by the algorithm alone.

Table 2 The effects of the average 2D/3D registration error on target localization for target depths between 50 and 300 mm, given together with estimated standard deviations

	Modeled error of registration method (mm)		
Lesion depth (mm)	Manual registration	Manual registration and registration algorithm	Registration algorithm stand-alone
50	6.4±3.4	2.7±2.8	3.6±2.5
100	8.7±5.3	4.1±4.8	6.2±5.1
150	11.1±7.5	5.5±7.0	8.7±7.6
200	13.4±9.8	6.9±9.2	11.2±10.2
250	15.8±12.1	8.3±11.5	13.8±12.7
300	18.1±14.4	9.7±13.7	16.3±15.2

These values are modeled using the simplified geometric approach given in the Methods section. The impact of registration error on target localization inside the body can be estimated from these data

Discussion

Image fusion has generated considerable interest in both medical image processing and radiological research. While a large number of studies have been published about the accuracy of various registration algorithms, little is known about the efficacy of automated image registration results compared to manual methods. In the case of slice-to-volume registration, comparing efficiency is of special interest since the registration application presented here is closely connected to clinical practice in interventional radiology, particularly if the orientation of a biopsy needle is considered an especially difficult task of mental image matching. It is also noteworthy that orientation on slice images is a common task for radiologists, as opposed to alignment of, for instance, multimodal 3D volume data, such as MR and PET. In these experiments, we have, however, not provided additional artificial landmarks such as markers; manual registration was therefore carried out based on image content only.

Our results indicate that a statistically significant improvement in alignment is achieved by applying an automated registration algorithm. The results in translational accuracy are also in accordance with the results reported by other groups [12], where a registration error below 2 mm was reported. In the initial presentation of the registration method used in this study [13], an evaluation on ideal and clinical image data, including Gaussian noise, artifacts, and different windowing parameters, resulted in an average translation error of approximately 1.0 mm; the angulation error in this study was slightly larger, but also within the range of errors measured in [13], where the average angulation error ranged from 0.5°–1.7°. In this study, we found the average angulation error when improving the initial guess of the test personnel to be 1.6°. Without this pre-alignment, average angulation error was 2.9°. It has, however, to be stated that registration algorithm outcome is mainly governed by image properties, such as FOV, resolution, and image content. Slight variations in results from roundoff errors are therefore not surprising and have to be accepted within a certain range. For this reason, it is also clear that even the registration algorithm produces results that are stricken with a residual error as evident from Table 1. This is also confirmed by the visual assessment of registration quality. While the median of registration quality remained the same after optimization by the algorithm, the third quartile became better, and results indicate that at least 25% of all registrations were considered excellent (scoring 5 of a possible 5); for the manual registration, the third quartile was found to be good (scoring 4 of a possible 5).

Time requirements, as detailed in Table 1, are critical; while the computer outperforms test personnel, the effects of learning how to handle the registration program might change these results. On the other hand, the algorithm had to be run on a small laptop since the test personnel were distributed in different locations at different hospitals; the almost-continuous improvement in computer performance will most likely compensate for this, and alternative implementations that utilize the computing power of the graphics processor card are also feasible. The fact that a non-optimal display was used for the evaluation is also a product of the mobility required for this type of study. Furthermore, it should also be stated that the limited size of the laptop monitor may affect the performance of the manual registration. However, the slices under comparison were presented at their original resolution.

Clinical studies on therapeutic outcomes in interventional radiology, also considering dosimetric issues for both patients and staff, will be required to determine the usefulness of this technique for interventional radiology. A dose reduction for fluoro CT imaging, however, appears to be a reasonable goal. The median patient radiation dose reported in the literature was within a range of 43 mGy [2] to 29.5 mGy [3], and the average whole body dose for the radiologist was reported to be 0.025 mGy [17].

Although we have shown that a registration algorithm outperforms a human, we cannot answer the question whether this improvement would have an impact on patient outcome. The results of lesion localization modeling do, however, indicate that a measurable difference is to be expected.

Based on these considerations, we conclude that slice-to-volume registration should have a tangible impact on localization of deep-seated lesions because it allows for visualization of low-contrast lesions during fluoro CT and should significantly improve accuracy while reducing the number of slices acquired, thus also reducing the radiation dose for patients and staff.

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