Manual versus automatic image fusion of real-time ultrasonography and MR images: a prospective comparison of technical performance

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Aims and objectives

Ultrasonography (US) has been most commonly used imaging modality for guidance of percutaneous interventional procedures such as biopsy or local ablation therapy of focal hepatic lesions because of its well-known advantages including real-time guidance, no radiation hazard, easy accessibility, and low cost. However, small focal hepatic lesions are sometimes difficult to accurately localize with US because they often have poor conspicuity on US. This issue draws more attention since small focal hepatic lesions are more frequently detected with the use of state-of-the-art computed tomography (CT) and magnetic resonance (MR) imaging. It can be more challenging to perform precise US-guided interventional procedures for small focal hepatic lesions found in patients with liver cirrhosis when many cirrhosis-related nodules are present near a target lesion and hence, mistargeting can occur.

To overcome these limitations of US guidance, fusion imaging has been introduced and showed promising results. Fusion imaging combines real-time US images with pre-procedural CT or MR images and displays simultaneously both the real-time US image and the corresponding slice of CT or MR images as the angle and the position of US transducer change. Therefore, it can help operators conduct interventional procedures with high confidence and accuracy for target lesions of poor sonographic conspicuity with the real-time, multi-modality comparison capability.

However, fusion imaging techniques introduced by many vendors need several steps to complete image fusion process in a manual manner and thus the process may be cumbersome and time-consuming, especially for less-experienced operators. Although the registration time required for image fusion varies depending on the level of operators’ experience and the US machines, it was reported to take up to as long as 30 minutes. Therefore, the need of easier and faster image fusion of real-time US and pre-procedural CT or MR images in an automatic fashion has been raised to enhance the performance of fusion imaging technique. Although a few vendors have recently introduced automatic image fusion methods, there have been few literatures dealing with its performance including registration error and time required for image fusion. In this study, we developed new fusion imaging methods of real-time US and pre-procedural MR images, providing both manual and automatic methods. Since the newly developed manual and automatic image fusion methods are different from those of other vendors, their performances are unknown. The purpose of this prospective study is to compare registration error and time required for image fusion between the new manual and automatic methods.
Methods and materials

Patients and Enrollment Criteria

The study protocol was approved by the institutional review board of Samsung Medical Center, and all patients gave written informed consent before being enrolled. From June 2014 to September 2014, 20 patients who referred to our department for planning US of biopsy or radiofrequency ablation (RFA) of focal hepatic lesions were enrolled in our study. The inclusion criteria were as follows: a) patients referred for planning US of RFA for hepatocellular carcinoma (HCC) or for US-guided biopsy of focal hepatic lesions; b) patients with focal hepatic nodules with 1 - 3 cm in diameter detected at contrast-enhanced MRI with gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA); and c) patients with Child-Pugh score A. The diagnosis of HCC was based on the typical imaging features (arterial enhancement followed by portal or delayed washout) according to the American Association for the Study of Liver Disease (AASLD) guideline. 17

Exclusion criteria were as follows: a) patients expected to have poor sonographic window due to abundant omental fat (thickness more than 0.5 cm) or the colon surrounding the right liver, b) patients with previous history of right hemihepatectomy, c) aged less than 20 years old or more than 80 years old, or d) patients who denied to participate in our study.

When each examiner performed total ten cases, the study was terminated. The patient population included 19 men and 1 woman (mean age ± SD, 58.9 ± 11.8 years; age range, 34 -77 years). Eight patients were included for planning US of RFA and the remaining 12 patients were included for biopsy of focal hepatic lesion (metastasis from rectal cancer, n=3; metastasis from gastric cancer, n=2; metastasis from pancreatic neuroendocrine tumor, n=2; HCC, n=2, metastasis from lung cancer, n=1; eosinophilic abscess, n=1; and hepatic involvement of leukemia, n=1). Nine patients had liver cirrhosis due to hepatitis B viral infection and the other 11 patients had normal liver. All 20 patients had normal liver function (Child-Pugh A class). The diameter of the target lesions were 1.8 ± 0.6 cm (mean ± SD) and their locations were as follows: segment 5 (n=8), segment 8 (n=6), segment 6 (n=3), segment 7 (n=2), and segment 4 (n=1).

Operators

Two radiologists participated in this study to perform fusion imaging. One (A.Y.K) was a less-experienced radiologist in the first year of fellowship-training with about 50 cases
of US-guided biopsy but less than 20 cases of fusion imaging-guided procedures, at the starting point of our study. The other (M.W.L) was an expert radiologist with 10 years of experience in abdominal intervention (more than 1,500 cases of US-guided biopsy or RFA of focal hepatic lesions, including more than 500 cases under fusion imaging guidance). Each examiner performed more than 10 training sessions of both manual and automatic image fusion before enrolling patients in our study.

**Image Fusion Technique**

**Equipment**

A RS80A US system (Samsung Medison, Seoul/Korea), capable of fusion imaging (S-Fusion, Samsung Medison, Seoul/Korea) was coupled with a magnetic field generator. Two electromagnetic position sensors were connected with a position sensing unit (three-dimensional guidance driveBAY tracker; Ascension Technology Corporation) and were attached on a convex-array CA1-7A transducer through a bracket (Fig. 1 on page 7).

**Manual Image Fusion**

Before image fusion, Digital Imaging Communications in Medicine data of up to 6 sequences of MR images were uploaded to the US machine. Among the 6 sequences, 20 minutes hepatobiliary phase was selected as a fused imaging sequence because the target lesion as well as landmark hepatic vessels, including the portal and hepatic veins, were relatively well visualized in this phase. After image fusion, the hepatobiliary phase image can be switched to other sequences of MR images.

Each consecutive patient who met the inclusion criteria assigned randomly to either the less-experienced or expert radiologist. During the study period, the order of image fusion method (manual method followed by automatic method or vice versa) was alternatively changed at each examination to minimize bias.

Manual image fusion consists of orientation lock and point lock. For the orientation lock, a radiologist usually places an US transducer in the sagittal plane to let the US system know the direction of US transducer relative to the patient's position. Although an US transducer can be placed on any location near a patient, usually it was placed on top of the solar plexus (junction between sternum and xiphoid process). Then, the radiologist performs the point lock a few times by marking corresponding anatomic landmarks (i.e., cysts, calcifications, vessel bifurcations or target lesion) within the liver between real-time US and MR images at the end expiratory phase of the patient's breathing. For the initial point lock, any plane of US scans can be used. That is, not only orthogonal axial, sagittal,
or coronal plane; but also oblique plane such as intercostal scan can be used for the initial point lock. On the other hand, corresponding MR images are always displayed in orthogonal axial, sagittal, or coronal plane. Therefore, if a target lesion is conspicuous enough to be easily detected with US image, the center of the target lesion can be marked at any US plane including oblique plane. When the target lesion cannot be easily localized on US image due to its small size or many other focal hepatic lesions, we usually use orthogonal axial, sagittal, or coronal plane at US since it is easier to correlate both real-time US and MR images in these planes. Among them, we prefer the coronal plane for the initial point lock where both inferior vena cava (IVC) and right hepatic vein are visualized well as anatomic landmarks and the vessel bifurcation site was used for the initial point lock. Then, additional point locks is performed to refine the registration near the target lesion by marking corresponding anatomic landmarks on the real-time US and fused MR images. This step can be repeated around the target lesion, up to maximum five times as much as it is needed and the last point lock should be performed at the center of the target lesion.

**Automatic Image Fusion**

It also requires aforementioned orientation lock. Unlike manual image fusion, orientation lock in the automatic method should be always performed on the top of the solar plexus. Then, intrahepatic IVC is marked on the uploaded hepatobiliary phase MR image to notify the system the location of the IVC. Hence, the automatic image fusion is named one-click registration. Then, the radiologists select a right intercostal space in which an US scan volume can cover both the liver dome and intrahepatic IVC. After positioning the transducer at the optimal intercostal space, a 3-dimensional (D) US volume is obtained by sweeping the liver of the patients in the end expiratory breath-holding state with an US transducer. Hence, this method is also called sweeping auto-registration. It takes about 10 seconds for the system to execute the calculation. After the initial registration is completed, initially fused real-time US image and MR image are displayed simultaneously on a split-screen display. Then, point locks are added to refine the registration using the aforementioned method.

During the study period, the automatic image fusion method was updated once from version 1.1 to version 1.2 to reflect the improvement in the diaphragm extraction from the 3D US volume. This updated version of automatic image fusion was applied in the latter cases of the study populations.

**Assessment of Registration Error and Time Required for Image Fusion**

After image fusion, the radiologists graded and recorded the quality of image fusion by comparing and correlating anatomic structures around a target lesion between a real-time...
US image and a fused MR image using a 4-point scale: 1, poor; 2, fair; 3, good; and 4, excellent. Grading of the quality of image fusion depended on the individual radiologist's judgment at the time of US examination.

After image fusion, the radiologists were also asked to obtain 3D volume data by sweeping the liver containing the target lesion. For the registration error assessment, the 3D US volume data should be aligned to MR data through the previously saved registration information in image fusion. In both modality, we selected a pair of corresponding points in the target lesion and then 3D Euclidean distance was automatically calculated between the two selected points in an in-house software (Accuracy Measurement Tool; version 1.0) (Fig. 2 on page 7). Total three pairs of corresponding points were used to calculate the average value of registration error.

Time required for image fusion was automatically recorded in the US machine and was calculated using an in-house software (Elapse Time Calculation Tool; version 1.0) (Fig. 3 on page 8). It was defined as the sum of the elapse time during orientation lock and the time interval between starting registration and the last point lock.

**Statistical Analysis**

The quality of image fusion, the number of point lock, registration error of image fusion, and time required for image fusion were compared between manual and automatic image fusion according to the level of operator's experience using the Wilcoxon signed-rank test. These variables were also compared between the two radiologists using Mann-Whitney U test. Time required for initial image fusion immediately after sweeping the liver in the automatic method was compared between the two radiologists using Mann-Whitney U test. P values less than 0.05 were considered to indicate a statistically significant difference.

Since automatic image fusion was updated once during the study period, we also compared registration error of initial image fusion immediately after sweeping the liver with an US transducer between version 1.1 and version 1.2 using two-way ANOVA.
Fig. 1: Equipment for fusion imaging (S-Fusion, Samsung Medison, Seoul/ Korea). The RS80A ultrasound system (left), the CA1-7A transducer with two position sensors attached in a bracket (right upper), and the three-dimensional guidance driveBAY tracker (right lower).

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**Fig. 2:** Accuracy Measurement Tool (version 1.0). The upper images are MR slices from three different directions: axial, sagittal, and coronal images, respectively. The lower images are transformed US slice aligning to MR DICOM volume image. Two modalities are showing the similar anatomical structure, because it was saved after fusion image.

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Fig. 3: Time required for image fusion was calculated using a self-produced software (Elapse Time Calculation Tool; version 1.0). Left side is the time needed for manual image fusion and right side for automatic image fusion.

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Results

Registration Error of Image Fusion

Manual image fusion was successful for all 20 patients whereas automatic image fusion performed by the less-experienced radiologist was failed for one case due to improper feature extraction by the system. The details of image fusion between manual and automatic methods are summarized in Table 1. The quality of image fusion was not different between manual (Fig. 4 on page 13) and automatic methods (Fig. 5 on page 13) in both the expert and less-experienced radiologists ($p = 1.000$ and $p = 0.317$, respectively). The number of point lock required for image fusion was not also different between manual and automatic methods in both radiologists ($p = 0.435$ and $p = 0.096$, respectively). In terms of registration error after image fusion, it was not different between the two methods in both radiologists ($p = 0.575$, $p = 0.515$, respectively).

<table>
<thead>
<tr>
<th></th>
<th>Manual method</th>
<th>Automatic method</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expert Quality of image fusion</td>
<td>4 (3-4)</td>
<td>4 (3-4)</td>
<td>1.000</td>
</tr>
<tr>
<td>Expert Number of point lock</td>
<td>2.0 (1 - 4)</td>
<td>2.0 (1 - 3)</td>
<td>0.435</td>
</tr>
<tr>
<td>Expert Registration error (mm)</td>
<td>3.18 (1.00 - 6.74)</td>
<td>3.68 (1.83 - 5.17)</td>
<td>0.575</td>
</tr>
<tr>
<td>Expert Time required for image fusion (seconds)</td>
<td>66.5 (50 - 145)</td>
<td>83.0 (46 - 101)</td>
<td>0.720</td>
</tr>
<tr>
<td>Less-experienced radiologist Quality of image fusion</td>
<td>4 (2-4)</td>
<td>4 (2-4)</td>
<td>0.317</td>
</tr>
<tr>
<td>Less-experienced radiologist Number of point lock</td>
<td>2.0 (1 - 3)</td>
<td>2.0 (1 - 5)</td>
<td>0.096</td>
</tr>
<tr>
<td>Less-experienced radiologist Registration error (mm)</td>
<td>4.92 (3.29 - 22.03)</td>
<td>6.40 (2.08 - 21.19)</td>
<td>0.515</td>
</tr>
<tr>
<td>Less-experienced radiologist Time required for image fusion</td>
<td>109.0 (51 - 245)</td>
<td>163.0 (83 - 303)</td>
<td>0.038</td>
</tr>
</tbody>
</table>
Table 1: Comparison between manual and automatic image fusion according to the radiologists.

Data are median value and data in parentheses indicate range.

* Wilcoxon signed-rank test was used.

Regarding automatic image fusion, version 1.1 was used for the former 12 patients (n = 5 for the expert and n = 7 for less-experienced radiologist, respectively) and version 1.2 for the latter 8 patients (n = 5 for the expert and n = 3 for the less-experienced radiologist, respectively). The registration error of initial image fusion immediately after sweeping the liver with an US transducer was smaller in version 1.2 (median, 16.63 mm; range, 5.38 - 26.62) than in version 1.1 (median, 25 mm; range, 3.13 - 76.94 mm). However, it did not reach statistical significance (p = 0.242).

Time Required for Image Fusion

Time required for manual image fusion tended to be shorter than time required for automatic image fusion in both the expert and less-experienced radiologist. Although it was not significantly different in the expert radiologist, it showed difference in the less-experienced radiologist (p = 0.720 and p = 0.038, respectively). However, in terms of automatic image fusion, time required for initial image fusion immediately after sweeping the liver was not different between the expert and the less-experienced radiologist (median, 40 seconds; range, 32 - 55 seconds vs. median, 46 seconds; range, 24 - 73 seconds; p = 0.093).

Comparison between the Expert and Less-Experienced Radiologist

Table 2 shows the comparison of image fusion between the expert and less-experienced radiologist. The quality of image fusion was not different between the expert and less experienced radiologist in both manual (p = 0.726) and automatic method (p = 0.764). The number of point lock required for image fusion was also not statistically different between the two radiologists in both manual (p = 0.776) and automatic method (p = 0.156). However, the registration error of image fusion was significantly smaller in the expert than in the less-experienced radiologist in both manual (p = 0.013) and automatic
method \( p = 0.014 \). The time required for image fusion was significantly shorter in the expert than in the less-experienced radiologist in both manual \( p = 0.034 \) and automatic method \( p = 0.001 \).

<table>
<thead>
<tr>
<th>Method for image fusion</th>
<th>Expert</th>
<th>Less-experienced radiologist</th>
<th>( P-value^* )</th>
</tr>
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<tbody>
<tr>
<td>Quality of image fusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manual method</td>
<td>4 (3-4)</td>
<td>4 (2-4)</td>
<td>0.726</td>
</tr>
<tr>
<td>Automatic method</td>
<td>4 (3-4)</td>
<td>4 (2-4)</td>
<td>0.764</td>
</tr>
<tr>
<td>Number of point lock</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manual method</td>
<td>2.0 (1 - 4)</td>
<td>2.0 (1 - 3)</td>
<td>0.776</td>
</tr>
<tr>
<td>Automatic method</td>
<td>2.0 (1 - 3)</td>
<td>2.0 (1 - 5)</td>
<td>0.156</td>
</tr>
<tr>
<td>Registration error (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>Automatic method</td>
<td>3.68 (1.83 - 5.17)</td>
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<td>0.014</td>
</tr>
<tr>
<td>Time required for image fusion (seconds)</td>
<td>Manual method</td>
<td>66.5 (50 - 145)</td>
<td>109.0 (51 - 245)</td>
</tr>
<tr>
<td>Automatic method</td>
<td>83.0 (46 - 101)</td>
<td>163.0 (83 -303)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* Mann-Whitney U test was used.
**Fig. 4:** Fusion imaging of real-time US and pre-procedural MR image in a patient with a 3 cm sized hepatocellular carcinoma (HCC). Fused US (left) and MR (right) image after manual image fusion by a less-experienced radiologist. The number of point lock was one at the center of the HCC (arrow) and the time needed for image fusion was 51 seconds. The mean registration error after three measurements was 4.53 mm.

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**Fig. 5:** Fusion imaging of real-time US and pre-procedural MR image in a patient with a 3 cm sized hepatocellular carcinoma (HCC). Fused US (left) and MR (right) image after automatic image fusion by a less-experienced radiologist. The number of point lock was one at the center of the tumor (arrow) and the time needed for image fusion was 83 seconds. The mean registration error after three measurements was 4.31 mm.

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Conclusion

Since image fusion between real-time US and pre-procedural CT or MR images can be difficult for less-experienced operators, automatic image fusion has been developed by some US vendors in recent years. Although automatic image fusion between real-time US and pre-procedural CT images has been introduced,\textsuperscript{18} it should also work with pre-procedural MR images. This is because MR images generally have been preferred as a reference data set over CT images for fusion imaging since MR images provide higher contrast than CT images between the liver and the target lesions as well as intrahepatic vasculatures.\textsuperscript{5,19} Moreover, unlike CT images in which CT scanning is usually performed in the end-inspiratory phase of patients, MR images are usually acquired during the end-expiratory phase of patients. Therefore, the respiration status of MR images is closer to that of US images that are acquired when patients breathe shallowly. Therefore, the registration error of fusion caused by patients' breathing motion is theoretically less in MR images than in CT images. When these factors are taken into consideration, fusion imaging between real-time US and pre-procedural MR images that is easy to use and accurate is needed for interventional procedures.

To the best of our knowledge, this is the first comparison study to date between manual and automatic image fusion of real-time US and pre-procedural MR images. In this study, we presented a new manual image fusion method that consists of orientation lock and point lock. After orientation lock-placing an US transducer in the sagittal plane to let the US system know the direction of US transducer relative to the patient's direction-the operator was able to fuse the real-time US and MR images by just marking the corresponding internal structure within the liver on both images. Thanks to orientation lock, the initial point lock could be performed using any US plane including oblique planes such as intercostal scan. Therefore, we did not have to spend time to find the same plane between real-time US and MR images for the initial point lock. Even with mismatched image planes of real-time US and MR images, the orientation lock has an effect of correcting the mismatch between real-time US and MR images. Therefore, this kind of workflow would have resulted in time-saving image fusion in our study even in the less experienced radiologist (median, 109.0 seconds; range, 51 - 245 seconds). Although it is not easy to compare our results with previous investigations directly due to differences in patient population, patients' breathing status at the time of CT/MR scanning (inspiration vs. expiration), and reference data set used (CT vs. MR images), our manual method seems to be the fastest compared to other methods reported in the previous studies where the image fusion time ranged from 3.7 to 30 minutes.\textsuperscript{5,9,15}

In this study, we also introduced a new automatic image fusion between real-time US and pre-procedural MR images by sweeping the liver with an US transducer and the
Automatic image fusion was feasible in 95% (19/20, hit rate: 95%) of patients. Although it tended to take longer time than manual image fusion, the automatic image fusion was completed within acceptable time even with the less experienced radiologist (median, 163.0 seconds; range, 83 - 303 seconds). Given that some operators rarely perform US-guided interventional procedures and would be not familiar with fusion imaging, our automatic image fusion is likely to help these operators or beginners. In our study, the registration error of initial image fusion immediately after sweeping the liver was 25 mm (range, 3.13 - 76.94) in version 1.1 and 16.63 mm (range, 5.38 - 26.62) in version 1.2, respectively and thus, acceptable image fusion could be achieved by performing several point locks. If a patient has good sonographic window for the right liver, our automatic image fusion would help operators who are not familiar with manual image fusion. However, it should be pointed out that automatic image fusion using the sweeping manner may not always yield desirable results as demonstrated in our study. Given that the patients with poor sonographic window for the liver were excluded in our study, the hit rate using this kind of sweeping manner might have been overestimated in our study. Moreover, like manual image fusion, automatic image fusion also required additional point locks between real-time US image and its corresponding MR image after initial image fusion to refine the initial registration. This process may be cumbersome, especially for less-experienced radiologist, which explains why the less-experienced radiologist took longer than the expert to conduct image fusion with automatic method while the time required for initial image fusion and the number of point lock needed after sweeping the liver was not different between the two radiologists. Hence, more robust automatic image fusion that is easy to use and does not affected by sonographic window is needed.

In terms of the time required for image fusion, it was not statistically different between manual and automatic image fusion in the expert radiologist. However, it took shorter in the manual method than in the automatic method in the less-experienced radiologist ($p = 0.038$). It can be explained by the following reasons. First, through training sessions with more than 10 cases, the radiologist may have already been familiar with manual image fusion of this system. In addition, the less-experienced radiologist may be on a steep learning curve in a short time during the study period, since our study was performed within a relatively short study period.

In terms of registration error of image fusion, it was not significantly different between manual and automatic method in both the less-experienced and expert radiologist. The median value of registration error was 6.40 mm (range, 2.08 - 21.19 mm) in the less-experienced radiologist with automatic method. Although it is difficult to directly compare the results of our study with those of previous investigations, our results seems to be better than previous studies where its mean value ranged from 8.1 mm to 19.1 mm. Since we used MR images, not CT images as a reference data set and 3D volume data was obtained at the end-expiratory phase, not at the end-inspiratory phase of patients, the registration error seems to be not high.
In conclusion, the registration error was not different between the manual and automatic methods in both the expert and less-experienced radiologists. The manual image fusion took shorter time than the automatic image fusion for the less-experienced radiologist while it was not significantly different for the expert radiologist.
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