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● *Original Contribution*

IMAGE FUSION OF REAL-TIME ULTRASONOGRAPHY WITH COMPUTED TOMOGRAPHY: FACTORS AFFECTING THE REGISTRATION ERROR AND MOTION OF FOCAL HEPATIC LESIONS

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Abstract—Factors affecting the registration error (RE) and motion of focal hepatic lesions (FHLs) in image fusion of real-time ultrasonography (US) with computed tomography (CT) images were prospectively assessed by focusing on respiratory movement and FHL location. Real-time US and pre-acquired CT images at end-inspiration were fused with FHLs for 103 patients. Three-dimensional US data containing FHLs were obtained during end-inspiratory/expiratory phases. Multivariate analysis revealed that diaphragm motion ($p < 0.001$), chronic liver disease ($p = 0.02$) and the absolute difference in distance between the FHL and the central portal vein (CPV) during respiration ($p = 0.03$) were the independent factors that revealed the maximum effect on RE. In contrast, diaphragm motion ($p < 0.001$) and distance between the FHL and CPV at inspiration ($p = 0.036$) revealed the maximum effect on FHL motion. In conclusion, RE and FHL motion are affected by the degree of respiratory movement and the location of the FHL. Therefore, image fusion with CT images should be used with caution if the degree of respiratory motion is significant or if the FHL is located at the periphery of the liver. (E-mail: seolly1024@gmail.com) **© 2017 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Real-time ultrasonography, Computed tomography, Fusion imaging, Registration error, Liver, Respiration.**

INTRODUCTION

Interventional procedures for focal hepatic lesions (FHLs), including biopsy or radiofrequency ablation, can benefit from ultrasonography (US) and multimodality fusion imaging guidance. The advantages of US guidance include convenience, ease of accessibility and real-time guidance capability with flexible respiration control in patients during the procedure (Lencioni et al. 2005; Rhim et al. 2008). However, accurate localization of FHLs on US is often challenging when a FHL is not conspicuous on B-mode US. To overcome this limitation, fusion imaging of real-time US and pre-acquired computed tomography (CT) or magnetic resonance imaging (MRI) has been used. Fusion imaging enables operators to accurately localize challenging FHLs and provides a greater degree of confidence by multimodality comparison capability during the interventional procedures (Lee et al. 2013; Park et al. 2013).

Fusion CT/US imaging is, however, challenging and often suffers from misregistration when using current rigid registration methods. Image fusion can be facilitated when the respiratory cycle of the patient is similar to that of the CT images (Ewertsen et al. 2013). However, CT images of the abdomen are usually obtained during deep inspiration to evaluate the lung base covered in the CT scan. In contrast, a patient's normal respiration during the US-guided procedure is usually shallow and thus is quite different from the respiratory phase during a CT scan. Even when patients hold their breath after the operator's instruction, sustained breathholding for accurate image fusion may be difficult, especially in elderly patients. Consequently, the process of image fusion can be time consuming, and some degree of registration error is

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unavoidable depending on the patient's respiration, which may mislead doctors into an inaccurate diagnosis or treatment (Hakime et al. 2011; Wein et al. 2008). In addition, mistargeting after fusion imaging-guided percutaneous radiofrequency ablation of hepatocellular carcinomas was reported to be more obvious in the peripheral liver than in the central liver (Lim et al. 2014). This implies that hepatic displacement and deformation caused by the patient's breathing motion may differ with the location of the lesion, although this has not been definitively determined. A peripheral tumor location implies that large landmark anatomic structures that can be used to localize the tumor, such as a portal vein branch, are rarely available near the tumor on fusion imaging. This may also have affected treatment outcome in the previous study (Lim et al. 2014). Hence, more solid data on tumor location in relation to movement/deformation of the liver is needed. Identifying and quantifying the factors that affect FHL motion and registration error in the liver are important because sophisticated non-rigid registration technology, which helps us overcome current misregistration problems, can be developed with these data.

The purpose of this study was to assess the factors affecting the registration error and the motion of FHLs in image fusion of real-time US and pre-acquired CT images by focusing on respiratory movement and the location of FHLs.

METHODS

Study population

This prospective study was conducted at two tertiary hospitals (Chung-Ang University Hospital and Samsung Medical Center) and was approved by their respective institutional review boards. Informed consent was obtained from all patients before enrollment. From May 2015 to December 2015, 105 patients who were referred to our department for US examination of the liver were screened. The patients presented with at least one FHL, as seen on multiphase contrast-enhanced CT (either abdomen–pelvis CT or liver dynamic CT) images. Among them, 13 patients were excluded for the following reasons: refusal to participate (n = 2), poor cooperation (n = 3), FHL location in a sonographically blind area (*i.e.,* the anterior subphrenic area of the right liver [n = 3]) or FHLs that were invisible or poorly conspicuous on B-mode US (n = 5). The remaining 92 patients with 103 FHLs constituted our study population. Eleven of these patients had two FHLs. Diagnosis of the FHLs was based on either pathologic confirmation by percutaneous biopsy in 21 patients (hepatocellular carcinoma [n = 5], cholangiocarcinoma [n = 3], metastasis [n = 11], melanoma [n = 1] and focal nodular hyperplasia [n = 1]) or typical imaging findings with clinical information in 71 patients. The baseline characteristics of the 92 patients are summarized in Table 1.

Ultrasonography with fusion imaging

Two radiologists (T.W.K. and H.J.P.) with 5 and 6 y of experience in fusion imaging, respectively, participated in the study. Before enrolling the patients, the radiologists performed more than 30 cases of automatic image fusion (Positioning auto-registration, S-Fusion, Samsung Medison, Seoul, Korea) using an US system (RS80 A, Samsung Medison) to familiarize themselves with the US system and to control the patients' breathing motion appropriately. This US system does not support built-in image correction algorithms. The image fusion system consisted of an electromagnetic sensor attached to the ultrasound probe and tracker system that reads the position of the sensor. The auto-registration method extracted the position of the solar plexus (the junction between the sternum and xiphoid process) from the CT by using sternum segmentation and registered it with US transducer location while the US transducer was aligned with the top of the solar plexus of the patient. Before image fusion, CT images were carefully reviewed to determine what contrast phase gave the clearest FHL images. Portal-venous phase images were most commonly used as the reference data set because the target lesions and the hepatic vessels were identified clearly in this phase (83 FHLs). However, when the FHL was not clearly identified with this phase, we used arterial or 3-min delayed phase images (for 8 and 12

Table 1. Baseline characteristics of the 92 patients with 103 focal hepatic lesions

Characteristic	Value
Age (y)	63.6 ± 11.5 (23–80)*
Sex: male/female	59/33
Weight (kg)	63.0 ± 10.3 (44.2–90)*
Body mass index (kg/m^2)	23.9 ± 3.2 (17.5–32.1)*
Chronic liver disease: yes/no	34/58
Etiology of chronic liver disease	
HBV/HCV/alcohol/idiopathic	24/5/2/3
Liver cirrhosis: yes/no	32/60
Previous laparotomy history: yes/no	9/83
Type of FHL	103
Benign	52
Cyst/abscess/calcification/ hemangioma/DN/FNH	36/4/6/3/2/1
Malignancy	51
HCC/CC/metastases/melanoma	21/3/26/1
FHL size (cm)	
Mean ± standard deviation	1.7 ± 1.2
Range	0.5–7.5
FHL location, segment 1/2/3/4/5/6/7/8	3/10/16/18/12/19/10/15

CC = cholangiocarcinoma; DN = dysplastic nodule; FHL = focal hepatic lesion; FNH = focal nodular hyperplasia; HBV = hepatitis B virus; HCV = hepatitis C virus; HCC = hepatocellular carcinoma.
* Mean ± standard deviation (range).