学 術
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ノート

Volumetry of the Liver: Effect of measurement using fusion images

肝体積測定 ―融合画像を用いた測定の効果について―

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Key words: volumetry, liver, single-photon emission computed tomography (SPECT), computed tomography (CT), magnetic resonance imaging (MRI).

【Abstract】

Understanding liver function and volume as well as the positions of the blood vessels and organs before hepatectomy is important for preventing liver failure after surgery. Information regarding liver volume is acquired by SPECT, CT, and MRI, and a few studies have been published regarding the same. However, these studies are hampered by issues in the accuracy of measurements. The assessment of liver volume using SPECT/CT has been recently reported. However, not every hospital can perform this technique. Therefore, we analyzed MR images acquired during expiration in order to assess the liver volume using fusion images acquired by both SPECT and MRI.

First, we used a tailor-made phantom of the liver to measure the volume-changing image parameter in each modality. Then, we compared the images acquired using all three modalities. After obtaining the institutional review board approval and informed patient consent, we measured the liver volumes of 48 patients (mean age, 68 ± 10 years), using each of the modalities and compared them amongst each other. We assessed intra-observer reproducibility by performing the measurements twice.

The mean total liver volume measurements obtained using SPECT, CT, and MRI were not significantly different (1176.3 ± 330.3 cm^3, 1172.9 ± 341.7 cm^3, and 1187.6 ± 334.9 cm^3, respectively; p = 0.289). The mean residual liver volumes measured using SPECT, SPECT-CT fusion, SPECT-MRI fusion, CT, and MR images showed significant differences (511.8 ± 301.0 cm^3, 531.9 ± 266.7 cm^3, 551.9 ± 269.8 cm^3, 555.6 ± 259.0 cm^3, and 558.0 ± 243.3 cm^3, respectively; p < 0.05). The residual liver volumes measured using SPECT, SPECT-CT fusion, and SPECT-MRI fusion images showed good intra-observer positive correlations (ρ = 0.88, 0.91, and 0.97, respectively).

We conclude that the measurement of liver volume using fusion images acquired by SPECT and MRI shows good reproducibility.

【要 旨】

肝胆系の術前情報として重要となる体積測定に着目し，最も有効な結果が得られるモダリティー（SPECT・CT・MRI）を明確にするために調査を行った．まず，肝臓の模擬ファントムを作成し，各モダリティーで撮像条件を変化させて体積を測定し比較を行った．次に，倫理審査委員会の承認後，同意を得られた患者（48人）の画像を用いて，各モダリティーの画像から体積を測定し比較を行った．ファントムによる体積測定の結果は，ボクセルが小さいほど真値に近い結果が得られた．臨床では，SPECT画像とMRI画像とのフュージョンを併用することで，再現性良く体積測定できることが示唆された．

Introduction

Liver cancer is the fourth leading cause of death in Japan, after lung, stomach and colon cancer[1]. The incidences of lung, colon, and pancreatic cancer continue to increase, whereas that of liver cancer has decreased after peaking in the mid-2000s. There were about 33,000 cases of liver cancer in 2010[1]. The main methods of liver cancer treatment are surgery, percutaneous ethanol injection therapy, and transcatheter arterial embolization. Many patients with liver cancer experience complications such as chronic liver disease, hepatitis, cirrhosis, and fatty liver. Treatment selection takes into consideration liver function as well as the stage of cancer. It is important to understand liver function and volume as well as the locations of the organs and vessels before liver excision in order to prevent liver failure. Technetium-99m diethylenetriamine pentaacetic acid galactosyl human serum

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albumin (^{99m}Tc-GSA) scintigraphy and X-ray computed tomography (CT) can provide this information[2)–6)]. At our hospital, liver function is measured using ^{99m}Tc-GSA scintigraphy prior to hepatectomy. Liver volume is measured using single-photon emission computed tomography (SPECT), which provides an indication of reserve capacity after hepatectomy. In many cases, liver volume is evaluated using CT and magnetic resonance imaging (MRI)[7)–11)]. Measurement of liver volume using SPECT images provides inadequate information about the vessels and lacks accuracy[12)]. In comparison, CT provides excellent accuracy of measurements. The volume of the liver, however, is not a reflection of liver function[13)]. The evaluation of liver function from MR images was recently attempted using gadoxetic sodium (Gd-EOB-DTPA). However, it does not become instead of SPECT yet[14), 15)]. In addition, liver volume measurements acquired using CT and MRI tend to be greater than the actual liver volume[16)]. It is necessary to evaluate the information and confirm the accuracy of liver volume measurements using each modality prior to hepatectomy. Accuracy has been a problem when SPECT and CT, CT and MRI were used to measure liver volume[16)–19)]. The fusion of SPECT and CT images in order to improve the accuracy of liver volume measurements was reported by a study. The accuracy of image fusion poses a problem because CT images are usually obtained during inspiration, while SPECT images are acquired during free breathing. Recently, SPECT/CT has been used in a study as a method to compensate for these deficiencies[20)]. However, not every hospital has the facilities for SPECT/CT imaging. The purpose of this study was to evaluate liver volumes using a custom-made phantom as well as clinical images acquired using three modalities — SPECT, CT, and MRI.

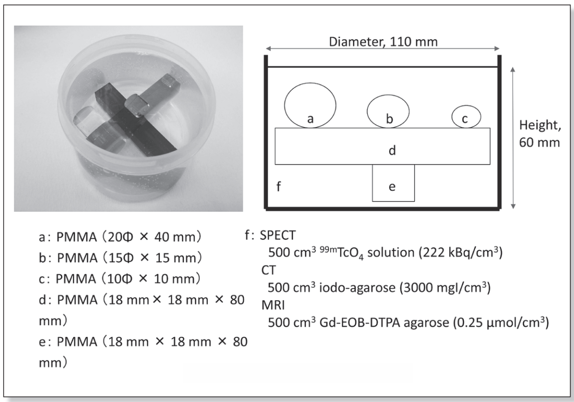

Figure 1 Tailor-made liver phantom.

Materials and methods

Experimental Setup

Each imaging modality was evaluated using a custom-made phantom. The phantom was composed of polymethyl methacrylate (PMMA) in a 500 cm^3 solution of contrast agent (Figure 1).

Patients

The study included 48 patients (male, 31; female, 17) with or without an injured liver, who underwent hepatectomy at the Showa University Hospital between March 2012 and August 2013. The mean (SD) age of the patients at the time of surgery was 68 ± 10 years (range, 35–83 years). The participants underwent SPECT, CT, and MRI examinations within 2 weeks prior to hepatectomy. Finally, patients undergoing right (n = 34) or left (n = 14) lobe hepatectomy were included, and those undergoing partial hepatectomy were excluded. Patient consent was obtained after approval by the institutional review board of the hospital.

Imaging Acquisition

The studies were performed using a SPECT system (Symbia S; Siemens Healthcare, Erlangen, Germany) with low-energy high-resolution collimators, a CT scanner (SOMATOM Definition AS+; Siemens

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Healthcare, Erlangen, Germany), and a similar 3.0 Tesla MRI system (MAGNETOM Trio A Tim; Siemens Healthcare, Erlangen, Germany) with a body-matrix coil as well as a spine-matrix coil consisting of 12 coil elements. In the phantom study, the parameters for SPECT image acquisition included the following: each set of projection data was obtained in 64 projections (5.6°/step, 20 s/step), and the energy window was 20% width at photo-peak; for each image, the acquisition time was assumed to be constant, and the voxel size was changed (matrix, 64 × 256) as shown in Table 1. The reconstruction parameters used after data collection were as follows: reconstruction method, filtered back projection; filter, Butterworth; cutoff, 0.15 cycles per pixel; attenuation correction, none; scatter correction, none. For volumetric imaging with CT, the acquisition parameters were as follows: tube voltage, 120 kV; tube current, 200 mA; collimation, 0.6 × 64 mm; pitch factor, 1.0; and rotation time, 0.5 s. The field of view (FOV) and slice thickness values for each image are shown in Table 2. For MRI volumetric imaging, we used the Volumetric Interpolated Breath-hold Examination (VIBE) with 3D-GRE-T1WI sequence. The parameters included the following: repetition time, 3.8 ms; echo time, 1.5 ms; flip angle, 10°; matrix size, 512 × 512; bandwidth, 444 Hz/pixel. The FOV and slice thickness values for each image are shown in Table 3. For image acquisition of the clinical cases, SPECT was performed with a voxel size of 9.6 mm, with free breathing during scanning. The spatial resolution for CT was 0.68 mm × 0.68 mm × 0.75 mm, and the images were acquired while holding inspiration. The spatial resolution for MRI was 1.46 mm × 1.09 mm × 3.5 mm, and the images were acquired while holding expiration. The patients were administrated total bolus intravenous injections of 185 MBq ^{99m}Tc-GSA at scintigraphy, 600 mg/kg iodinated contrast medium at CT, and 0.10 mmol/kg Gd-EOB-DTPA at MRI.

Image Analysis

In the phantom study, the phantom volumes measured using each modality were compared. In the clinical cases, the liver volumes were measured using each modality and evaluated; both whole and partial liver volumes were measured. The SPECT images were acquired 20 min after ^{99m}Tc-GSA scintigraphy, CT images during the portal phase, and MR images during the hepatobiliary phase of Gd-EOB-DTPA imaging. The volumes were measured using the standard semi-automatic extraction function of the 3D application AZE Place Raijin, version 3.1 (AZE, Ltd Tokyo, Japan). In the horizontal view, a part of the solution was extracted by enclosing the border of the solution resembling liver tissue in the direction of the body axis, creating the mask shown in Figure 2, using the radial basis function (RBF) interpolation function. In the SPECT images, the cutoff value of the count was set using the threshold value change

Table 1　Volume of tailor-made liver phantom with SPECT.

Voxel size (mm)								
0.8	0.9	1	2	3	3.9	4.8	6.6	9.6
299.9	460.2	481.7	553.1	548.6	548.7	548.3	561.3	673.0

(cm^3)

Table 2　Volume of tailor-made liver phantom with CT.

Pixel size (mm)	Slice thickness (mm)				
	1	2	3	4	5
0.6	499.4	533.1	562.6	594.3	626.5
0.7	505.8	538.9	567.6	599.0	630.5
0.8	511.6	543.3	571.7	602.9	634.3
0.9	516.5	547.3	575.2	606.4	637.8
1.0	523.1	552.6	579.2	609.7	641.2

(cm^3)

Table 3　Volume of tailor-made liver phantom with MRI.

Pixel size (mm)	Slice thickness (mm)				
	1	2	3	4	5
0.6	502.1	535.3	570.8	603.0	640.6
0.7	506.6	538.3	573.6	605.8	643.1
0.8	511.3	541.7	575.6	608.3	645.5
0.9	516.1	545.5	579.5	610.4	648.9
1.0	519.6	550.5	583.2	614.1	652.2

(cm^3)

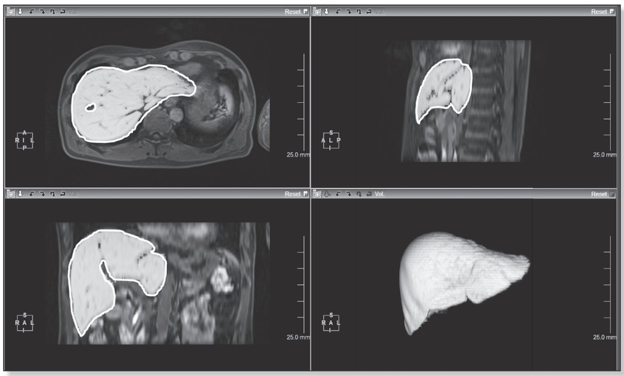

Figure 2 Liver extraction using Virtual Place. Areas within the white enclosure show masked images.

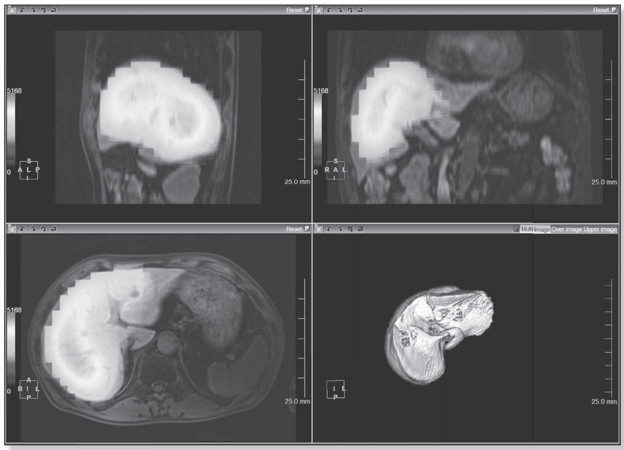

Figure 3 Liver Fusion by Virtual Place; The images were acquired by SPECT and MRI.

function to remove the background count. The cutoff value was assumed to be 35% of the maximum count value[21]. With CT and MRI, the liver volumes were measured using the semi-automatic extractor function, after the main blood vessels (portal and vein), intrahepatic bile ducts, and a part of the mass were excised at the workstation. Partial liver volumes of right and left lobes were measured separately, and the volume on the residual side was evaluated. The base that separated the right and left lobes was assumed to be the Cantlie line. Liver volumes were also measured using the fusion images of SPECT with CT and MRI. As shown in Figure 3, the fusion images were manually fitted using the workstation application.

The partial liver volumes were again measured a month later using SPECT, CT, and MRI, and the intra-observer reproducibility was evaluated.

Statistical Analysis

The Friedman test was used to determine the significance of the differences between the SPECT, CT, and MRI measurements. Spearman's rank correlation coefficient and Passing–Bablok regression analysis[22] were used to evaluate the whole liver volumes measured using each modality, based on the best result of the phantom study. Intra-observer reproducibility was evaluated using Spearman's rank correlation coefficient, Bland–Altman analysis, and Passing–Bablok regression analysis. All of the statistical analyses were performed using MedCalc, version 13.1 (MedCalc Software, Mariakerke, Belgium).

Results

Phantom study

The liver volume parameters measured using SPECT, CT, and MRI are shown in Tables 1, 2, and 3. The volumes obtained using SPECT showed a tendency to be underestimated with decreasing voxel size, resulting in values lower than the true value at a voxel size of 0.8 mm. Moreover, as the voxel size increased, the volumes also increased, resulting in an approximately 10% error compared to the true value. The CT and MRI measurements approached the true values when the slice thickness was thin and the pixel size small, and were closest when the slice thickness and pixel size were 0.6 mm and 1 mm, respectively. The volumes were overestimated by CT and MRI when the pixel size and slice thickness were increased.

Clinical study

There were no significant differences in the mean whole liver volumes measured

Table 4 Liver volume in clinical cases.

Segment	SPECT (Non-fusion)	SPECT (Fusion with CT)	SPECT (Fusion with MRI)	CT	MRI	p-value*
Total	1176.3 ± 330.3 (1127.5)	–	–	1172.9 ± 341.7 (1080.0)	1187.6 ± 334.9 (1100.0)	0.289
Right lobe	813.7 ± 246.1 (845.0)	723.8 ± 227.1 (727.0)	731.5 ± 229.8 (758.0)	698.4 ± 249.3 (701.5)	706.3 ± 231.6 (716.5)	< 0.05
Left lobe	362.6 ± 213.2 (287.0)	452.5 ± 261.8 (405.5)	444.8 ± 237.2 (381.5)	474.5 ± 218.3 (418.0)	481.3 ± 213.6 (428.5)	< 0.05
Resection lobe	664.5 ± 327.8 (690.0)	664.4 ± 283.1 (678.5)	624.4 ± 274.8 (687.0)	617.3 ± 257.2 (657.5)	629.7 ± 251.6 (631.5)	0.073
Residual lobe	511.8 ± 301.0 (409.0)	531.9 ± 266.7 (501.0)	551.9 ± 269.8 (502.5)	555.6 ± 259.0 (487.5)	558.0 ± 243.3 (498.5)	< 0.05

(cm^3)

Values are represented as Mean ± SD (Median); SD: standard deviation.
*Friedman test.

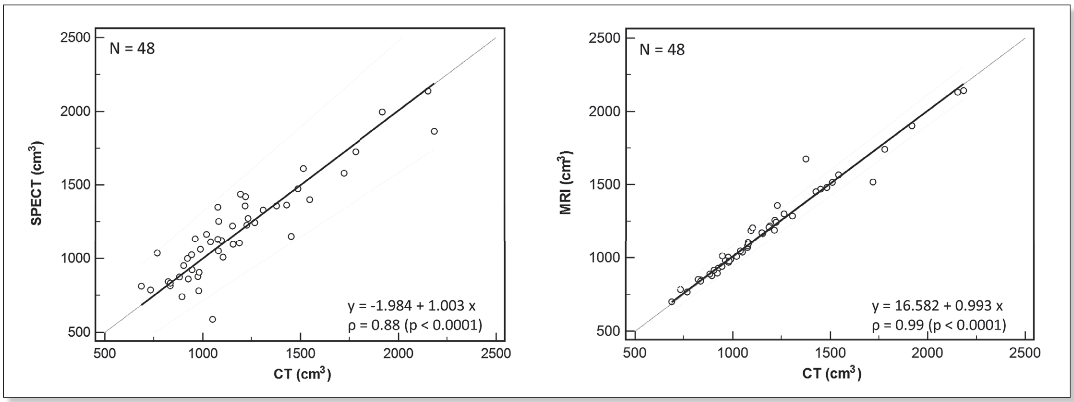

Figure 4 Passing-Bablok regression analysis of total liver volume.

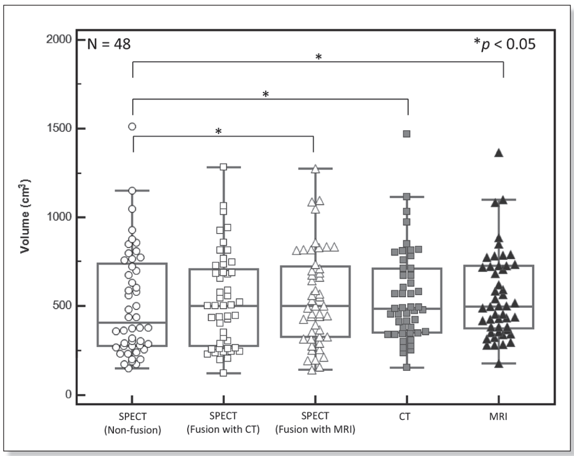

Figure 5 Box plot of residual liver volume in clinical cases.

using SPECT, CT, and MRI (1176.3 ± 330.3 cm^3, 1172.9 ± 341.7 cm^3, and 1187.6 ± 334.9 cm^3, respectively; p = 0.289) (Table 4). The SPECT and MRI measurements were positively correlated to the CT measurements (ρ = 0.88 and 0.99), as demonstrated by the Passing–Bablok regression plots in Figure 4. The mean residual liver volume measurements acquired using SPECT, SPECT-CT fusion, SPECT-MRI fusion, CT, and MRI showed significant differences (511.8 ± 301.0 cm^3, 531.9 ± 266.7 cm^3, 551.9 ± 269.8 cm^3, 555.6 ± 259.0 cm^3, and 558.0 ± 243.3 cm^3, respectively; p < 0.05; Table 4 and Figure 5).

Intra-observer reproducibility

The liver volumes (measured twice) are shown in Table 5. The residual liver volumes measured using SPECT, SPECT-CT fusion, and SPECT-MRI fusion showed positive intra-observer correlations (ρ = 0.88, 0.91, and 0.97, respectively); the mean differences were -13.7 ± 124.0 cm^3, -38.3 ± 92.3 cm^3, and -4.6 ± 73.5 cm^3, respectively (see Bland–Altman and regression plots in Figure 6).

Discussion

In the phantom study, the volumetric measurements acquired using SPECT were underestimated when the voxel size was 1 mm or less, with a deficiency of count for

Table 5 Intra-observer reproducibility of liver volume in clinical cases.

A1

Modality	Segment	Time 1	Time 2	Mean difference(SD_2)	ρ
SPECT	Right lobe	813.7 ± 246.1 (845.0)	752.3 ± 253.4 (790.5)	61.4 (108.3)	0.92*
(Non fusion)	Left lobe	362.6 ± 213.2 (287.0)	424.0 ± 246.7 (359.5)	−61.4 (108.3)	0.87*
	Resection lobe	664.5 ± 327.8 (690.0)	650.8 ± 304.5 (688.5)	13.7 (124.0)	0.92*
	Residual lobe	511.8 ± 301.0 (409.0)	525.5 ± 281.7 (452.0)	−13.7 (124.0)	0.88*
SPECT	Right lobe	723.8 ± 227.1 (727.0)	684.5 ± 240.0 (725.0)	39.3 (91.9)	0.92*
(Fusion with CT)	Left lobe	452.5 ± 261.8 (405.5)	491.8 ± 241.2 (456.5)	−39.3 (91.9)	0.87*
	Resection lobe	664.4 ± 283.1 (678.5)	606.1 ± 265.8 (618.0)	38.3 (92.3)	0.93*
	Residual lobe	531.9 ± 266.7 (501.0)	570.2 ± 251.8 (527.5)	−38.3 (92.3)	0.91*
SPECT	Right lobe	731.5 ± 229.8 (758.0)	700.6 ± 230.6 (705.5)	30.8 (66.8)	0.92*
(Fusion with MRI)	Left lobe	444.8 ± 237.2 (381.5)	475.6 ± 241.8 (461.0)	−30.8 (66.8)	0.95*
	Resection lobe	624.4 ± 274.8 (687.0)	619.8 ± 259.2 (634.5)	4.6 (73.5)	0.95*
	Residual lobe	551.9 ± 269.8 (502.5)	556.5 ± 261.2 (532.5)	−4.6 (73.5)	0.97*
CT	Right lobe	698.4 ± 249.3 (701.5)	715.5 ± 261.2 (532.5)	−17.1 (59.7)	0.97*
	Left lobe	474.5 ± 218.3 (418.0)	457.3 ± 218.9 (418.0)	17.1 (59.7)	0.95*
	Resection lobe	617.3 ± 257.2 (657.5)	630.9 ± 257.4 (637.5)	−13.6 (60.9)	0.96*
	Residual lobe	555.6 ± 259.0 (487.5)	542.0 ± 253.5 (457.0)	13.6 (60.9)	0.96*
MRI	Right lobe	706.3 ± 231.6 (716.5)	721.5 ± 230.4 (745.0)	−15.2 (36.3)	0.98*
	Left lobe	481.3 ± 213.6 (428.5)	466.1 ± 212.7 (426.5)	15.2 (36.3)	0.97*
	Resection lobe	629.7 ± 251.6 (631.5)	633.3 ± 258.0 (639.5)	−3.6 (39.2)	0.98*
	Residual lobe	558.0 ± 243.3 (498.5)	554.4 ± 248.8 (473.0)	3.6 (39.2)	0.98*

(cm^3)

Value are Mean±SD1 (Median), SD1: standard deviation, SD2: standard deviation of mean difference.
*p < 0.0001.
A1: Values are represented as Mean ± SD1 (Median); SD1: standard deviation; SD2: standard deviation of mean difference.

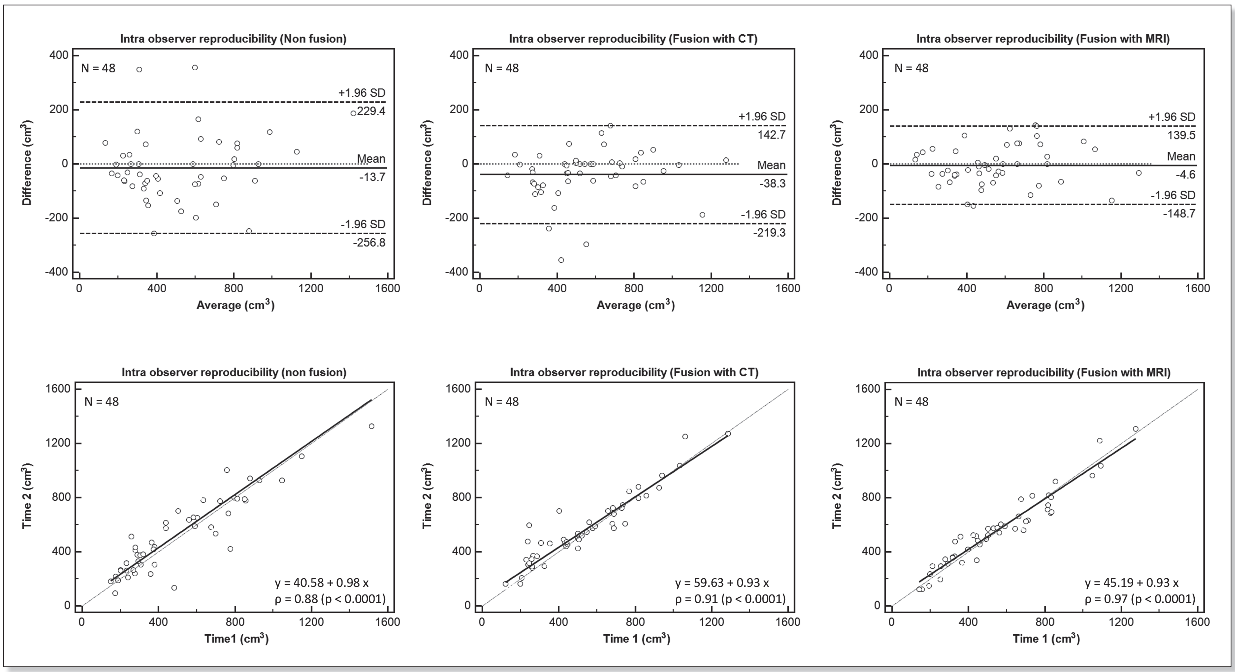

Figure 6 Intra-observer reproducibility of residual liver volume: Bland-Altman plot (above) and Passing-Bablok regression (below); SD = Standard deviation.

each voxel. It was, therefore, assumed that a voxel size of 1 mm or more was necessary for volumetric measurement using SPECT. When the voxel size increased, the volumes were overestimated. The resolution ability at the PMMA-solution border changed as the voxel size increased, and the actual solution volume measured was greater than its true value, possibly because of the partial volume effect[23), 24)]. It is necessary to extend the acquisition time in order to achieve SPECT images with quality similar to that of CT or MR images. However, this requires deviation from a realistic examination time. Additionally, it is assumed that the spatial resolution of SPECT is lower than that of CT and MRI. Therefore, we concluded that the volumes were overestimated in the clinical cases. In the CT and MR images, the volumes were overestimated at greater pixel size and slice thickness values. This is similar to the phenomenon observed in SPECT, where the volume varies greatly with slice thickness. We believe that the influence of the partial volume effect caused this variation, because the resolution ability at the PMMA-solution border decreased as the voxel size increased, and the actual solution volume was greater than its true value[23), 24)]. The volume variable was influenced by pixel size and slice thickness. However, the effect of pixel size on the volume is lower than that of slice thickness. Therefore, we concluded that the change in slice thickness greatly affected liver volumetry in the clinical cases. Finally, we believed that CT could measure liver volume with greater accuracy than the other two modalities. However, no statistically significant differences were not found between the whole-liver volume measurements acquired using SPECT, CT, and MRI in clinical cases. It is possible that portions of the vessels and bile duct volumes were included in the CT image measurements. It is necessary to recognize this error in liver volumetry. Moreover, owing to the influence of the partial volume effect, a greater liver volume reduction might have occurred in the clinical study compared to the phantom study.

The patients underwent examinations with SPECT, CT, and MRI within a 2-week period. The doubling speed of an indistinct boundary tumor is 106.8 ± 20.9 days[25)], and, therefore, we assumed that the tumor size would not change in 2 weeks.

Statistically significant differences were found in the partial volume measurements between the three modalities. The inaccuracy of the volume measurements by SPECT might have influenced results. In addition, anatomical information is scarce for accurate SPECT image evaluation. Therefore, the accuracy of measurement was improved by using a combination of SPECT with CT or MRI. The combination of CT and MRI data did not demonstrate any significant differences in the residual liver volumes. The mean difference of the SPECT volumetric measurements combined with the MR images was less than that of their combination with the CT images. We believe that the accuracy of the fusion measurements was influenced by the differences in the breath pattern during image acquisition between CT (inspiration) and MRI (expiration). We also believe that the image locations obtained by image acquisition during expiration are closer to those obtained during free breath than to those obtained during inspiration.

Study limitations

The cutoff value used in the present study was assumed to be 35% of the maximum count value at scintigraphy, based on a previous study[21)]. However, the reconstruction parameters used in this study might have been different from those in the previous study. The previous study performed assessments with attenuation correction, whereas, in the present study, attenuation correction was not performed. Therefore, the hepatic volumes measured using SPECT in the present study might have been overestimated.

Additionally, SPECT examinations of the clinical cases did not include the evaluation of some of the parameters (e.g., voxel size changes from 2.0 mm to 4.8 mm) because such high resolution imaging is not practical in clinical studies. We believe that, had the images been obtained at a higher resolutions, the SPECT-based volumetric measurements might have been more accurate. Additionally, image reconstruction in this study was performed only using filtered back projection; we have not evaluated different reconstruction methods for SPECT since there was no need to consider using a different method in this study.

Conclusion

The combination of SPECT and MR images for the measurement of liver volume could improve the reproducibility of the measurements.

Acknowledgments

The authors thank the other investigators, educators, staff, and patients involved in this study for their valuable contributions.

図の説明

Figure 1 自作肝臓ファントム
Figure 2 肝臓の抽出
Figure 3 SPECT画像とMRI画像のフュージョン
Figure 4 CTを基準とした全肝体積の回帰分析
Figure 5 臨床における残存側肝体積の箱ひげ図
Figure 6 残存肝体積の測定者内再現性
上段：Bland-Altman plot
下段：Passing-Bablok regression

表の説明

Table 1 ファントムの体積（SPECT）
Table 2 ファントムの体積（CT）
Table 3 ファントムの体積（MRI）
Table 4 臨床における肝体積
Table 5 臨床における肝体積測定の測定者内再現性

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