Optimization of breath-holding time for intrahepatic fat quantification using proton-magnetic resonance spectroscopy at 1.5-Tesla magnetic resonance imaging

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Abstract

Purpose We determined the minimum required breath-holding time (Modified ^1H -MRS) and conducted a backward study on patients who underwent intrahepatic fat quantification using the point resolved spectroscopy method. We investigated the correlation between dual echo-MRI (DE-MRI) and liver attenuation index (LAI) measurements and evaluated the validity of the analysis results to determine whether breath-holding time (BHT) could be reduced.

Methods In the MRS-fat fraction (MRS-FF) analysis, using only the reference datasets, the minimum required breath-holding time was set to 14 s. To evaluate the validity of the obtained MRS-FF, we compared the correlation using the dual echo-fat fraction (DE-FF) and LAI as a reference values, the correlation coefficient was investigated by obtaining the Spearman's rank correlation coefficient. Next, we compared the correlation in two subgroups of the abovementioned case groups: (1) those with a BHT of 23 s and (2) those with a BHT between 14 to 22 s.

Results The correlation coefficients between MRS-FF and DE-FF and MRS-FF and LAI were 0.841 ($p = 0.00$) and -0.726 ($p < 0.01$), respectively. Next, in the subgroup analysis, the correlation coefficients of MRS-FF and DE-FF and MRS-FF and LAI were 0.849 ($p = 0.00$) and -0.733 ($p = 0.00$), respectively, in group (1) and 0.886 ($p = 0.00$) and -0.761 ($p = 0.00$), respectively, in group (2).

Conclusion In the imaging using Modified ^1H -MRS, the present method suggested that the reduction in breath-holding time from 14 to 22 s did not affect the MRS-FF analysis results.

Introduction

Recent studies have shown that the incidence of non-virologic B and C liver cancers is increasing. In previous studies, the incidence of non-B and non-C hepatocellular carcinoma in Japan from 1991 to 2015 has shown an increasing trend, from 10% in 1991 to 24.1% in 2010 and 32.5% in 2015 [1,2]. Moreover, previous studies reported that there is a higher incidence of obesity and lifestyle diseases compared to viral hepatitis-associated hepatocellular carcinoma, but more than half of the patients are diagnosed in an advanced state [3]. Among them, there is an increased incidence of non-B and non-C hepatocellular carcinoma caused by non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis. Unlike virus-related hepatocellular carcinomas, for which the high-risk population and surveillance programs are well established, there are limited studies on the characteristics of these non-B- and non-C-type hepatocellular carcinomas. In the pathogenesis and progression of NAFLD, fat accumulation in the liver is the basis of pathogenesis, from which inflammation, fibrosis, and carcinogenesis progress [4,5]. Therefore, it is essential to detect the liver lipid deposition accurately and early by clinical examination. In Japan, the number of subjects with metabolic syndrome has been increasing, and data from medical and physical examinations have shown that 30% of the Japanese population have complications of fatty liver [6,7,8]. For the determination of intrahepatic fat, various imaging modalities, such as ultrasound and computed tomography (CT), have been developed, and magnetic resonance imaging (MRI) such as 3D

T1WI dual echo (DE) has the highest sensitivity and specificity. Particularly, MRS fat fraction (MRS-FF) measured by proton-magnetic resonance spectroscopy (^1H -MRS) correlates well with histopathological evaluation and can quantify the liver fat content, which is referred to as the “gold standard” alternative to histopathological evaluation [9,10,11]. A previous study by Rastogi et al. revealed the correlation coefficients between ^1H -MRS and CT (liver attenuation index [LAI]) and DE-MRI besides the correlation between ^1H -MRS and histopathological evaluation [12]. Recently, proton density fat fraction using the multipoint-Dixon method has been released commercially, but it can only be used with newer devices and is insufficiently versatile [13,14].

Conversely, ^1H -MRS using the single-shot-point resolved spectroscopy (PRESS) method is commonly used in a general clinical application. In ^1H -MRS for head tumors, water suppression is used because the water signal in the voxel disturbs specter analysis, but for liver fat quantification, the analysis of the specter peaks of water and lipid is necessary. However, because of the long scanning time, it is difficult to apply to patients who have difficulty in breath holding for a long time. Previous studies have not found the minimum required breath-holding time for the purpose of expanding the use of ^1H -MRS imaging to more patients. Therefore, we defined a minimum breath-holding time condition (Modified ^1H -MRS) and examined the correlation with DE-MRI and CT (LAI) results in patients who underwent intrahepatic fat determination using the PRESS method. The results of the analysis were validated to determine whether it is possible to reduce the breath-holding time.

Materials And Methods

Selection of Subjects

This retrospective study was approved by the Institutional Review Board No. 20R-399 of Tokai University Oiso Hospital. The study period was from August 1, 2015 to May 31, 2020. In this study, we used 3D T1WI DE-MRI and ^1H -MRS specter data of patients who underwent non-contrast liver MRI for intrahepatic fat quantification, and CT images of patients who underwent non-contrast CT for visceral fat quantification. Data were extracted from 58 patients who underwent ^1H -MRS scanning and CT scan on the same day. 3D T1WI DE-MRI and non-contrast CT provided axial images, and ^1H -MRS was performed with single-voxel acquisition. However, two patients with iron deposition in the liver and two aged <18 years were excluded from the extracted data. Therefore, the final number of patients was 54. The included patients did not receive any interventions before or after this study. The subjects in this dataset required liver MRI, ^1H -MRS, and abdominal CT at the discretion of their physicians, and the scans were performed by radiologists under optimal imaging conditions. When extracting patient data, we informed patients on the bulletin board and website that anonymized MRI, ^1H -MRS specter data, and CT images may be used in this study. Simultaneously, they were informed that they could opt out of this study. As a result, zero subjects disagreed to join the study.

Analysis Procedure

For DE-MRI and CT (LAI), region of interest (ROI) settings and value measurements were obtained using PACS viewer: ShadeQuest/ViewR version 1.22.85 (Yokogawa Medical Solutions Corporation, Tokyo, Japan).

The MRS-FF calculated from the MRS analysis was calculated using Eq. (1) using the ratio of area under the peak (AUP) at the specter peak of water to AUP at the specter peak of intrahepatic lipid [9-12].

$$\text{MRS-FF [\%]} = (\text{AUP}_{\text{Lipid}} / (\text{AUP}_{\text{Water}} + \text{AUP}_{\text{Lipid}})) \times 100 \quad \text{Eq. (1)}$$

In the comparison of MRI examinations, we used in-phase (IN) and opposed-phase (OP) images acquired by 3D T1WI DE-MRI, which had been scanned at the time of ¹H-MRS examination. In both images, ROIs were set at the same location as the voxel position set in the right lobe of the liver by MRS. The ROI was set at a location avoiding blood vessels and other structures with a size of 250–350 mm², and the dual echo-fat fraction (DE-FF) was calculated using Eq. 2 using the average signal intensity (SI) obtained from each ROI [12]:

$$\text{DE-FF [\%]} = ((\text{SI}_{\text{IN}} - \text{SI}_{\text{OP}}) / 2\text{SI}_{\text{IN}}) \times 100 \quad \text{Eq. (2)}$$

3D T1WI DE-MRI is the protocol that we always use for quantitative MRI of intrahepatic fat using ¹H-MRS in our hospital. Some previous studies, other than 3D T1WI DE-MRI as the MRI protocol to be compared with ¹H-MRS, evaluated fat deposition by the SI difference between fat saturation (FS) and non-FS images [15,16]. However, we did not scan fat-suppressed images in our routine protocol. Moreover, for intrahepatic fat quantification by 3D T1WI DE-MRI, d'Assignies et al. reported a correction for the T2* effect to exclude the effect of T2* shortening due to iron deposition in the liver. Besides, a study by Janakan Satkunasingham et al. validated the detection of hepatic fat in a clinical setting using the 3PD chemical shift sequence even in the presence of T2* shortening [17]. Nevertheless, 3D T1WI DE-MRI was used for comparison because the MRI system at our hospital does not allow correction for the T2* effect and use of 3PD chemical shift sequence.

As a comparison to intrahepatic fat quantification by MRI and MRS, we used slice that included the liver and spleen of non-contrast CT images obtained for visceral fat quantification to calculate the LAI, which is the difference between the average Hounsfield units (HU) in the ROI placed in the liver and average HU in the ROI located in the spleen, using Eq. (3) [12]. ROIs for the liver and spleen were set in the same locations as in DE-MRI.

$$\text{LAI [HU]} = \text{HU}_{\text{ROI of liver}} - \text{HU}_{\text{ROI of spleen}} \quad \text{Eq. (3)}$$

According to a meta-analysis reported by Bohte et al., the mean HU of the spleen was used as an internal reference in all studies comparing ¹H-MRS and CT images for intrahepatic fat quantification.

In these study, intrahepatic fat quantification by CT images was measured using the attenuation value of the mean HU of the liver minus the mean HU of the spleen (LAI) or ratio of the mean HU of the liver to the

mean HU of the spleen (L/S) [18].

Subgroup Analysis

Next, as a subgroup analysis in the case groups of 2.2, we compared the correlation between MRS-FF and DE-FF and MRS-FF and LAI in two groups: group (1) with a breath-hold time (BHT) during imaging of 23 s and group (2) with a BHT between 14 and 22 s.

MRI Scanner and Parameters

The MRI system was a 1.5-Tesla MRI Signa HDxt software version.16 (GE Healthcare, Milwaukee, WI, USA), and an eight-channel body array coil (8 ch upper) was used for scanning. All ^1H -MRS analyses were performed using Sage software version 7.1 (GE Healthcare) as the MRS analysis software. For MRS analysis, two ^1H -MRS specter data obtained by reference datasets, 2TR were averaged and zero-dimensional correction and baseline correction, were applied to obtain the area under the specter peak of water and lipid. The scanning parameters for ^1H -MRS were as follows: pulse sequence, Probe-P; repetition time (TR), 1149.0 ms; echo time (TE), 27.0 ms; number of phase-cycles (NEX), 2.00; acquisition matrix, 1×1 ; average scans, 4.00; setting of voxels used for analysis, 1 voxel of $30\text{mm} \times 30\text{mm} \times 30\text{mm}$ was set in the right lobe of the liver, and scanning was performed with breath hold (by expiratory stop). In MRS imaging, proper acquisition techniques are required to collect spectra for fat fraction estimation. Besides the PRESS method used in this study, there were other methods using the stimulated echo acquisition mode (STEAM) method. Although this STEAM method could set a shorter TE than the PRESS method, it was known that the signal-to-noise ratio (SNR) of the STEAM method was about 1/2 lower than that of the PRESS method because of the signal acquisition by stimulated echo in the STEAM method [16]. Moreover, T2 bias should be considered when using the PRESS method for intrahepatic fat quantification. T2 bias was a common confounding factor for fat quantification methods, such as the PRESS method, which employs a refocusing pulse to generate echoes. Because the minimum echo time achievable with clinically available ^1H -MRS for intrahepatic fat determination was always greater than zero, some T2 relaxation occurs before echo sampling. As the T2 relaxation time of the intrahepatic water component was shorter than the T2 relaxation time of the intrahepatic fat component, there was relative enhancement in the signal from fat (i.e., longer T2 values) compared to the signal from water (i.e., shorter T2 values). To reduce the effect of this T2 bias, it was preferable to set the TE as short as possible. Therefore, compared with the STEAM method, which can select a shorter TE, the PRESS method underestimates the T2 value of intrahepatic fat and overestimates the fat fraction [25]. However, this study aimed to evaluate the MRS-FF using the minimum number of ^1H -MRS specter data required. Therefore, we used the PRESS method because the breath-holding time when using the STEAM method was far beyond the range of a single breath-holding and because we were concerned that the repeatability of the MRS-FF would be reduced due to the lower SNR when using the STEAM method on a universal 1.5-Tesla MRI.

In our ^1H -MRS imaging using the PRESS method, a single ^1H -MRS specter data was detected using the spin echo signal obtained by 1TR (Fig 1). The total scanning time was determined by the total number of frames of the presaturation pulse, dummy sets, reference datasets, and datasets (Fig 2). Default ^1H -MRS imaging was performed in the following order: presaturation pulse, 10TR; dummy sets, 4TR; reference datasets, 2TR; datasets, 8TR; total scanning time (indicated value), 24TR (28 s). Conversely, the modified ^1H -MRS used in this study was acquired in the following order: dummy sets, 0TR; presaturation pulse, 10TR; reference datasets, 2TR; datasets, 8TR; and total scanning time (displayed value), 20TR (23 s). In the MRS-FF analysis using Sage as the analysis software, the minimum required BHT was defined as 12 TR (14 s), which was the sum of the presaturation pulse, 10 TR, and reference datasets, 2 TR.

The scanning parameters for the 3D T1WI DE-MRI used in this study were as follows: pulse sequence, 3D FSPGR; repetition time (TR), 6.7 ms; echo time (TE), 2.1 ms/4.5 ms; matrix, 256×160 (phase encode); slice thickness (scan), 4.0 mm (−2.0 mm); slice thickness (MPR), 7.0 mm; field of view, 360 mm×360 mm; number of averages, 1.00; received bandwidth, 62.5 kHz. Scan slab was set to cover the whole liver, and scanning was performed with breath hold (by expiratory stop).

CT Scanner and Parameters

In the acquisition of CT images for other comparisons, the 128-slice CT scanner SOMATOM Definition AS+ VA48A (Siemens Healthcare, Germany) was used. The imaging conditions (tube voltage, tube current) were appropriately determined by the radiologist. The optimal dose was determined depending on the patient's body size, and the image quality required for diagnosis was ensured in all patients (image noise within ± 10 HU).

Statistical Processing

The software used for statistical processing was EZR (64 bit, version 1.54) and Excel 2016 (Microsoft Corporation). A nonparametric test of correlation coefficients (Spearman's rank correlation coefficient) was performed to analyze the correlation coefficients between MRS-FF and DE-FF and between MRS-FF and LAI [19]. The comparison test between the samples of groups (1) and (2) was performed using unpaired t-test, and the significance test for the difference in correlation coefficient between the two groups was performed using Fisher r-to-z transformation [20].

Results

Subjects

In the subjects of this study, the mean age was 56.96 ± 13.46 years, the age range was 22–84 years, the mean body mass index (BMI) was 27.04 ± 3.51 (kg/cm²), and the male:female ratio was 28:26 (Table 1). If the cutoff value of MRS-FF for intrahepatic fat quantification was set at 6.25% from a previous study, intrahepatic fat deposition was observed in 22 patients and not 32 patients [17].

Comparison Between Fat Quantification Methods

The mean MRS-FF of the subjects was $13.01\% \pm 16.92\%$, the mean DE-FF was $13.07\% \pm 8.961\%$, and the mean LAI was -0.4886 ± 12.45 HU (Fig 3). The correlation coefficient between MRS-FF and DE-FF was 0.841 ($p = 0.00$), and the correlation coefficient between MRS-FF and LAI was -0.726 ($p < 0.01$) (Fig 4). The correlation coefficients between MRS-FF and both DE-FF and LAI in previous studies were 0.892 ($p = 0.00$) and -0.709 ($p < 0.01$) [12]. The difference between the correlation coefficients of Modified ^1H -MRS and those of previous studies was determined to be significant by Fisher r-to-z transformation ($p = 0.250$ [between MRS-FF and DE-FF], $p = 0.849$ [between MRS-FF and LAI]), and no significant difference was found in both cases.

Subjects of the Subgroup Analysis

The subgroup analysis showed that there were 39 patients in group (1) with a BHT of 23 s and 15 patients in group (2) with a BHT between 14 and 22 s. The mean age of group (1) was 55 ± 12.18 years, mean BMI was 27.24 ± 3.83 (kg/cm^2), and the male:female ratio was 20:19. The mean age of group (2) was 62.07 ± 15.63 years, the mean BMI was 26.55 ± 2.55 (kg/cm^2), and the male:female ratio was 8:7 (Table 2). If the cutoff value of MRS-FF for intrahepatic fat quantification was set at 6.25% from previous studies, intrahepatic fat deposition was found in 16 cases in group (1) and not 23 cases and 6 cases in group (2) and not 9 cases [17].

Comparison Between Fat Quantification Methods by Subgroup Analysis

A comparison test for MRS-FF, DE-FF, and LAI between the subgroups of groups (1) and (2) was performed ($p = 0.93$, $p = 0.86$, and $p = 0.63$, respectively), and there was no significant difference in all (Fig 5). In the subgroup analysis, the correlation coefficient between MRS-FF and DE-FF in group (1) was 0.849 ($p = 0.00$), and that between MRS-FF and LAI was -0.733 ($p = 0.00$), while, for group (2), the correlation coefficients were 0.886 ($p = 0.00$) and -0.761 ($p = 0.00$), respectively. The difference between the correlation coefficients of groups (1) and (2) was significant by Fisher r-to-z transformation ($p = 0.653$ [between MRS-FF and DE-FF], $p = 0.849$ [between MRS-FF and LAI]), and no significant difference was found in both groups (Figs. 6 and 7).

Discussion

The correlation coefficients between MRS-FF, DE-FF, and LAI in the previous study and that in the Modified ^1H -MRS were determined by Fisher r-to-z transformation. There was no significant difference between the correlation coefficients of the two methods ($p = 0.250$ and $p = 0.849$, respectively). Therefore, the reliability of MRS-FF by modified ^1H -MRS imaging was verified. In this method, the dummy sets were set to 0TR, but the recommended default by the vendor is 4TR. In ^1H -MRS as head tumors, the dummy sets are the parameters used to suppress the signal of surrounded and inherent water and stabilize the signal detection of metabolite with a small SI of approximately 15 mM [21]. Because there is little SI difference

between various metabolites, measurement errors can easily occur if the acquired signal is unstable [22]. Conversely, water and lipid, which are the targets of this study, detected specter data with signal intensities as high as 35 M compared to metabolites. Moreover, the scanning parameters used in this study were short TR (1149.0 ms) because breath holding should be performed during scanning. This causes the longitudinal magnetization of the water to not sufficiently recover, and the AUP of the water becomes smaller with each successive frame. Therefore, increasing the number of dummy sets may overestimate the MRS-FF because the AUP of water detected by the reference datasets becomes smaller [23,24]. These results suggest that there was no difference between our results and those of previous studies even if the dummy sets are set to 0TR in this study.

The reason for the nonsignificant difference in the results of the subgroup analysis was the use of Sage version 7.1 (GE Healthcare) as the analysis software, which can calculate MRS-FF by extracting only the reference datasets: 2TR. The modified ^1H -MRS used in this study consisted of the following parameters: presaturation pulse, 10TR; reference datasets, 2TR; and datasets, 8TR. The presaturation pulse of 10TR saturated the signal, and it was a parameter that is performed internally by the application so that it surrounds the setting voxel of ^1H -MRS and could not be set to a value $< 10\text{TR}$. This presaturation pulse was necessary to suppress the influx of water components from outside the setting voxel of ^1H -MRS [21]. Therefore, to use the AUP of water and AUP of lipid for the calculation of MRS-FF, the data of the unsuppressed signal of water was an essential parameter. In the PRESS method, two ^1H -MRS data with specter peaks of water and fat were obtained in this reference datasets: 2TR. In contrast, datasets of 8TR obtains data of suppressed water signal for metabolites, which is unnecessary for intrahepatic fat quantification. From these findings, only the reference datasets that obtain the data of the unsuppressed water signal were used to calculate the MRS-FF, while the datasets that obtain the data of the suppressed water signal were not needed. Therefore, even if breath holding was canceled during the acquisition of datasets during the imaging time, it was suggested that there was no significant difference in the results of the MRS-FF analysis.

This study has three limitations. First, we did not perform a correlation study with histopathological evaluation by liver biopsy. The reason for the first limitation was that this was a retrospective study and liver biopsy was not performed in all included patients. Moreover, the gastroenterologists at our hospital understood that MRS-FF analysis by ^1H -MRS was a gold standard alternative to histopathological evaluation and chose to use this method because it is noninvasive for patients. Second, the study was performed only with the GE 1.5-Tesla MRI and not with other vendors or magnetic field strengths. The reason for second limitation was that the only MRI system owned by our hospital was a general-purpose GE 1.5-Tesla MR scanner. Third, only single-voxel analysis was used in this study, not multivoxel analysis. This was because the time required for multivoxel ^1H -MRS imaging was far beyond the range of a single breath holding and thus would lead to a respiratory-induced motion artifact. Therefore, it was not addressed in this study, which aims to evaluate it with the minimum number of ^1H -MRS specter data and minimum BHT required [16]. Our results showed that the minimum required BHT was shorter than that of the conventional method (displayed value) using ^1H -MRS for intrahepatic fat determination by the PRESS

method, which is generally recognized as time-consuming. Our results suggest that this method can be extended to patients who have difficulty in performing longer breath hold. The expanded scope of the ^1H -MRS is expected to be used for liver screening to detect fat deposition in the liver at an early stage by clinical examination in more hospitals that have MRI systems. However, training of the technologist is essential because the examination can be completed in a shorter time than the number of times displayed as the scanning time.

Conclusion

The correlation coefficients between MRS-FF and DE-FF and between MRS-FF and LAI were strongly correlated using Modified ^1H -MRS and Sage (for ^1H -MRS analysis application). These results were not significantly different from the correlation coefficients of previous studies, suggesting that shortening the BHT requirement from 14 to 22 s compared with 23 s did not affect the ^1H -MRS analysis results.

Abbreviations

NAFLD: non-alcoholic fatty liver disease

DE: dual echo

LAI: liver attenuation index

^1H -MRS: proton-magnetic resonance spectroscopy

MRS-FF: MRS fat fraction

PRESS: point resolved spectroscopy

ROI: region of interest

AUP: area under the peak

IN: in-phase

OP: opposed-phase

DE-FF: dual echo-fat fraction

SI: signal intensity

FS: fat saturation

HU: Hounsfield units

BHT: breath-hold time

TR: repetition time

TE: echo time

STEAM: stimulated echo acquisition mode

SNR: signal-to-noise ratio

Declarations

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Conflicts of interest/Competing interests:

All other authors have no conflicts of interest.

Availability of data and material:

Data available on request due to privacy/ethical restrictions.

Code availability:

'Not applicable'

Ethics approval

This retrospective study was approved by the Institutional Review Board of Tokai University Oiso Hospital (IRB number: No. 20R-399).

Consent to participate

Informed consent was waived from all patients by the IRB.

Consent for publication

Informed consent was waived from all patients by the IRB.

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Tables

Table 1. Subject features

Age		
	Average (years)	56.96 ± 13.46
	Range (years)	22–84
Sex		
		(n = 54)
	Male	28
	Female	26
BMI		
	Average (kg/cm ²)	27.04 ± 3.51
	Range (kg/cm ²)	21.64–35.43
MRS-FF		
	Average (%)	13.01 ± 16.92
	Range (%)	0.3249–62.87
DE-FF		
	Average (%)	13.07 ± 8.961
	Range (%)	0.4793–37.66
LAI		
	Average (HU)	–0.4886 ± 12.45
	Range (HU)	–40.4–22.5

Table 2. Features of subject in subgroup analysis

		(1) BHT = 23 s	(2) $14 \leq \text{BHT} < 23 \text{ s}$
Age			
	Average (years)	55 ± 12.18	62.07 ± 15.63
	Range (years)	22–69	22–84
Sex		(n = 39)	(n = 15)
	Male	20	8
	Female	19	7
BMI			
	Average (kg/cm^2)	27.24 ± 3.83	26.55 ± 2.55
	Range (kg/cm^2)	21.64–35.43	22.70–31.22
MRS-FF			
	Average (%)	12.21 ± 16.22	12.63 ± 15.51
	Range (%)	0.3717–62.87	0.3249–38.19
DE-FF			
	Average (%)	12.77 ± 9.027	13.07 ± 6.726
	Range (%)	0.4793–37.66	4.975–25.04
LAI			
	Average (HU)	-1.058 ± 13.38	0.7173 ± 11.43
	Range (HU)	-40.4–22.5	-26.3–13.60

Figures

Figure 1

Pulse sequence diagram of 1H-MRS using PRESS technique. Figure 1 is a pulse sequence diagram of 1TR of 1H-MRS imaging using the PRESS method. After one excitation pulse and two refocusing pulses are applied, a spin echo is generated, and MRS specter data are acquired.

Figure 2

Overview of total scan time with the PRESS technique by combining any frames (presaturation, dummy sets, reference datasets, and datasets). Figure 2 shows the concept for calculating the total scan time of 1H-MRS using the PRESS method. One TR is one frame in the PRESS method, which is a single-shot method, and one specter data are acquired. Presaturation, dummy sets, reference datasets, and datasets are scanned in this order. The sum of these is the total scanning time.

Figure 3

Distribution of each measurement results (MRS-FF, DE-FF, and LAI). Figure 3 shows the distribution of the measured MRS-FF, DE-FF, and LAI results for all subjects in the graph. The graph shows the maximum, minimum, and median values in a box plot.

Figure 4

Correlation between MRS-FF and DE-FF (left) and MRS-FF and LAI (right). Figure 4 shows the horizontal axis of MRS-FF [%] and vertical axis of DE-FF [%] (left) and LAI [HU] (right), showing the strong correlation between them. MRS-FF and DE-FF had a positive correlation with a correlation coefficient of 0.841 ($p = 0.00$). MRS-FF and LAI had a negative correlation with a correlation coefficient of -0.726 ($p < 0.01$).

Figure 5

Comparison of distribution in each measurement results (MRS-FF, DE-FF, and LAI) in the subgroup analysis (comparison by “BHT = 23 s” or “ $14 \leq \text{BHT} < 23$ ”). Figure 5 shows the results of comparing the distribution of MRS-FF, DE-FF, and LAI by subgroup analysis. The horizontal axis of all graphs shows the category of the subgroup, with group (1) BHT = 23 s on the left and group (2) BHT = 14–22 s on the right. The left is MRS-FF [%] on the vertical axis and shows that there was no significant difference in the distribution between subgroups ($p = 0.93$). The center is DE-FF [%] on the vertical axis, and there was no significant difference in the distribution between subgroups ($p = 0.89$). The right is LAI [HU] on the vertical axis, and there was no significant difference in the distribution between subgroups ($p = 0.63$).

Figure 6

Correlation between MRS-FF and DE-FF from group (2) is not significantly different from group (1). Figure 6 shows the horizontal axis of MRS-FF [%] and vertical axis of DE-FF [%], showing the strong correlation between them. The left shows the result of subgroup (1) BHT = 23 s, and the correlation coefficient was 0.849 ($p = 0.00$). The right shows the results of subgroup (2) BHT = 14–22 s, and the correlation coefficient was 0.886 ($p = 0.00$). The results of Fisher r-to-z transformation on both correlation coefficients showed that there was no significant difference between the subgroups ($p = 0.653$).

Figure 7

Correlation between MRS-FF and LAI from group (2) is not significantly different from group (1). Figure 7 shows the horizontal axis of MRS-FF [%] and vertical axis of LAI [HU], showing the strong correlation between them. The left shows the result of subgroup (1) BHT = 23 s, and the correlation coefficient was -0.733 ($p = 0.00$). The right shows the results of subgroup (2) BHT = 14–22 s, and the correlation coefficient was -0.761 ($p = 0.00$). The results of Fisher r-to-z transformation on both correlation coefficients showed that there was no significant difference between the subgroups, $p = 0.849$.