

# Qualitative near-infrared vascular imaging system with tuned aperture computed tomography

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**Abstract.** We developed a novel system for imaging and qualitatively analyzing the surface vessels using near-infrared (NIR) radiation using tuned aperture computed tomography (TACT<sup>®</sup>). The system consisted of a NIR-sensitive CCD camera surrounded by sixty light emitting diodes (with wavelengths alternating between 700 or 810 nm). This system produced thin NIR tomograms, under 0.5 mm in slice thickness. The venous oxygenation index reflecting oxygen saturation levels calculated from NIR tomograms was more sensitive than that from the NIR images. This novel system makes it possible to noninvasively obtain NIR tomograms and accurately analyze changes in oxygen saturation. © 2011 Society of Photo-Optical Instrumentation Engineers (SPIE). [DOI: 10.1117/1.3595424]

**Keywords:** near infrared; tuned aperture computed tomography; near infrared tomogram; venous oxygenation index.

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## 1 Introduction

The regional vascular oxygenation level provides very important clinical information for the analysis of biological conditions. Vascular oxygenation levels need to be measured as an aid to monitor blood oxygen levels and saturation; therefore, noninvasive measurement methods under realistic biological conditions have been developed.<sup>1-5</sup> These are permitted by measurement method using near infrared (NIR). Systems described in the literature are based on a specific characteristic that NIR is absorbed by the hemoglobin in blood.<sup>6</sup> Additionally, development of noncontact sensing methods to define the location of the near surface veins holds considerable promise for aiding in obtaining blood samples from individuals whose veins are not evident from visual inspection.<sup>7</sup> Such capability would be especially useful for infants and those with elevated BMI values. Since NIR can transmit through thin regions such as through a finger, vascular images can be easily acquired<sup>8,9</sup> and monitoring blood oxygen saturation can be easily measured.<sup>10</sup> Although using a transmission method is limited to thin regions, this study developed a novel system for the noninvasive imaging of surface vessels in thick regions where NIR imaging is not always feasible. Additionally, NIR tomograms using tuned aperture computed tomography (TACT<sup>®</sup>) were obtained, as well as measurements of the regional vascular oxygenation levels.

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In this paper, we demonstrated the utility of this system and described its characteristics and potential future in clinical applications.

## 2 Materials and Methods

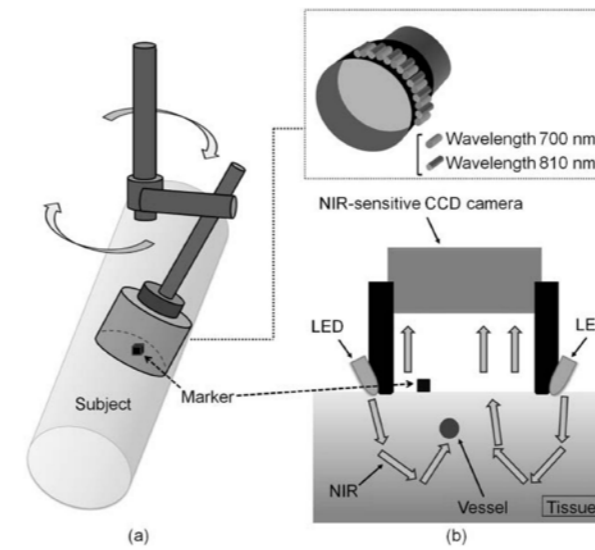
### 2.1 System

A NIR-sensitive charged-coupled device (CCD) camera (XC-EI50/50CE, Sony Corporation, Tokyo, Japan) was surrounded by sixty light emitting diodes (LED) (alternating wavelengths between 700 to 810 nm, VSF706C1 and LSF811C1, Optrans, Tokyo, Japan), that could only detect NIR from subcutaneous tissues (Fig. 1). The NIR was absorbed across surface vessels more than any other surrounding tissues.

### 2.2 Tuned Aperture Computed Tomography Theory

TACT is a reconstruction method that can be used to synthesize three-dimensional representation from multiple arbitrary prerecorded two-dimensional basis images (each acquired at a different angle) of an interesting region. The basic principles of the TACT algorithm are derived from the optical aperture theory and tomosynthesis.<sup>11,12</sup> The TACT stacks the basis images, inputs locations of fiducial markers for each basis image, and reconstructs a series of arbitrary multiplaner cross-sectional images. Stability for maintaining continuity in geometric is required for the generation of three-dimensional images, such as computed tomography, at the time of collection of images. However, TACT enables an arbitrary setup of projection directions,

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**Fig. 1** (a) Acquisition system and (b) schematic diagram for NIR imaging.

because the position of the fiducial markers is always available. Moreover, because image reconstruction often involves only shifting and adding two-dimensional images, the process is rapidly and efficiently managed by even the simplest image-processing computers. Iterative restoration is often utilized in TACT imaging in an attempt to improve detailed clarity.<sup>13,14</sup> The iterative restoration algorithm works for the deblurring of TACT slices to remove out-of-focus noise. TACT has been used in the clinical application of digital mammography<sup>15</sup> and

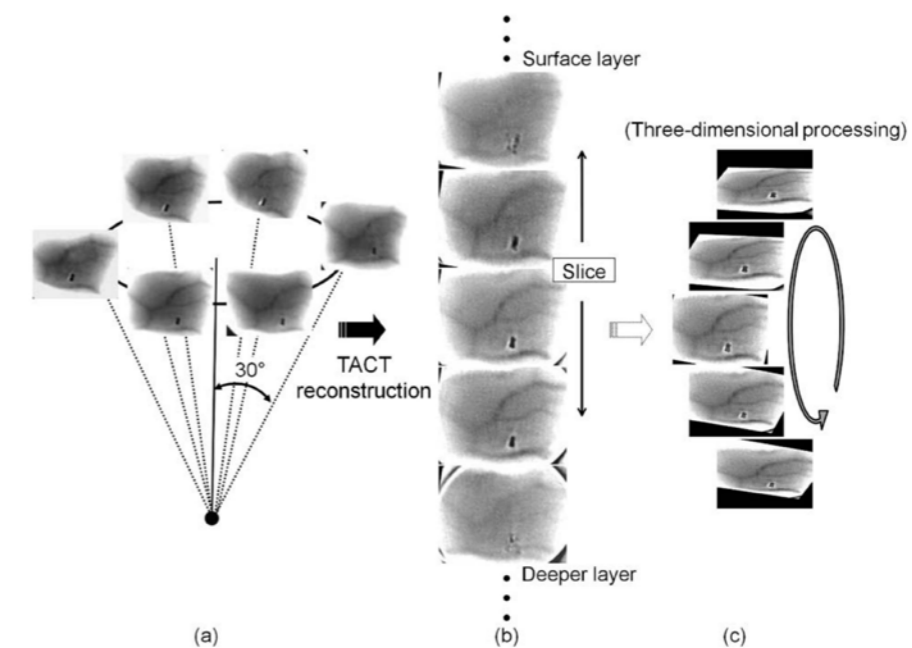
oral surgery using x-ray emitting devices,<sup>16</sup> whereas there has been no study, that we are aware of, that reconstructed NIR tomograms.

### 2.3 Tomograms

To increase the image contrast of the vessels and obtain three-dimensional information, we created tomograms calculated from NIR images (basis images) using the TACT program (TACT Workbench version 0.9.43). First, for the TACT series, a fiducial marker was used by attaching approximately 1 mm wire to the forearm skin within the field of view. Next, when considering the factors influencing the image accuracy of TACT,<sup>17-19</sup> six concentric NIR projections of surface vessels including the marker were obtained and reconstructed as tomograms (Fig. 2). The angular disparity was set at 30 deg during each projection. Reconstructed images were processed by using the proprietary iterative restoration algorithm three times (default setting).

### 2.4 Venous Oxygenation Index

Multiple NIR images (six projections in total) of surface vessels on the forearm were obtained before and after the loading test, that is, using a blood pressure cuff on the upper arm at each wavelength in accordance with the optical aperture theory<sup>11,12</sup> during the first second. We held the cuff pressure at more than 140 mmHg to occlude vessels. Then, tomograms were created using the TACT program and the venous oxygenation index (VOI) was calculated from the image signal intensities at each wavelength [Eq. (1)], which is an indicator of the oxygen



**Fig. 2** One example for TACT procedure. (a) NIR images (wavelengths: 810 nm) of surface vessels and projection geometry relationships between angular disparity and numbers of projections performed. (b) TACT slices reconstructed from (a). (c) Rotated three-dimensional data structures from (b).



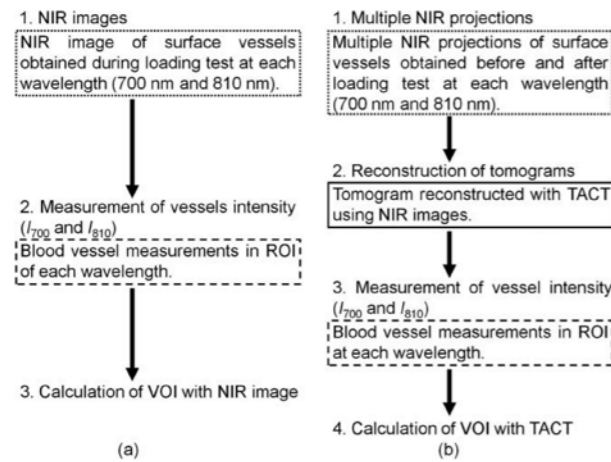


Fig. 3 VOI measurement procedures (a) without and (b) with tomograms.

saturation level,<sup>20</sup>

$$VOI = \frac{I_{700}}{I_{810}}, \quad (1)$$

where  $I_{700}$  and  $I_{810}$  are the signal intensities of the vessels for the 700 and 810 nm images, respectively. Figure 3 shows the measurement procedure for the calculation of VOI. Moreover, the VOI was compared to the oxygen saturation ( $SpO_2$ ) using a pulse oximeter. The study was performed in five healthy volunteers after informed consent was obtained from each human subject.

### 2.5 System Characteristics

Correlation between the current supplied to the LED and the signal intensity of the NIR images was investigated, because signal intensity of a NIR image is relative value. When the current to the LED at each wavelength, respectively, was slowly increased to the maximum value, NIR images of LED light were obtained by CCD camera and the signal intensities of these images were measured.

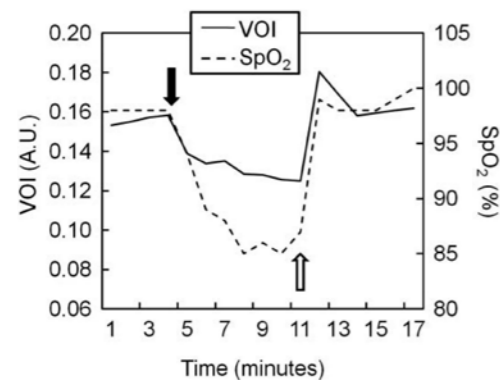


Fig. 4 Change in venous oxygenation index and  $SpO_2$  during the loading test. Black arrow shows cuff pressure on and white arrow shows cuff pressure off. Note that there was good agreement with VOI and  $SpO_2$ . A.U.: arbitrary unit.

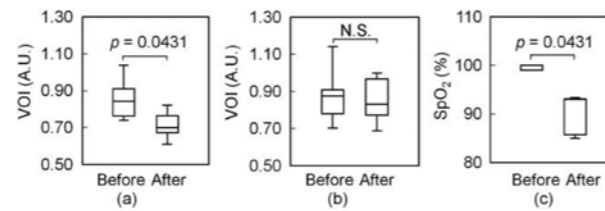


Fig. 5 Change in VOI (a) with and (b) without TACT, and (c) change in oxygen saturation ( $SpO_2$ ) measured by pulse oximeter before and after loading test. VOI with TACT and  $SpO_2$  after loading test were significantly greater than before. However, there was no significant difference in VOI without TACT ( $P$  value = 0.345). A.U.: arbitrary unit; N.S.: not significant.

In addition, we evaluated the effective slice-thickness of our system using a chart, which is a specially designed apparatus for the measurement of tomographic slice-thickness. This chart was placed at an angle  $11^\circ 32'$  relative to the tomographic plane. Six concentric projections of chart images were obtained and reconstructed as a tomogram using the TACT program. Slice-thickness property was visually evaluated by one of the authors.

### 2.6 Statistical Methods

The Wilcoxon signed-rank test was used to assess differences in VOI and  $SpO_2$  before and after a loading test. Multiple linear regression analysis was used to assess the relation between the current supplied to the LED and the signal intensity of the NIR images.

### 3 Results

Our system was capable of acquiring several projections for the tomograms within a few seconds in thick regions that cannot transmit [Fig. 2(a)] and easily reconstructs a tomogram using the TACT program [Fig. 2(b)].

VOI was good correlated with  $SpO_2$  in this system during the loading test using a blood pressure cuff (Fig. 4). Both VOI with TACT and  $SpO_2$  after the loading test were significantly lower than those before the loading test ( $P$  value = 0.0431,  $P$  value = 0.0431), but VOI without TACT showed no significant difference ( $P$  value = 0.345 (Fig. 5).

There was a high correlation between the signal intensity of NIR images and the current supplied to the LED at each wavelength in Fig. 6 ( $R^2 = 0.998$ ,  $P$  value < 0.001 in 700 nm,  $R^2 = 0.999$ ,  $P$  value < 0.001 in 810 nm). The effective slice-thickness of our system was 0.4 mm [Fig. 7(b)].

### 4 Discussion

A transmitted beam is generally used for NIR imaging,<sup>8,9</sup> but this system would obtain NIR images in thick regions that cannot transmit [Fig. 2(a)]. Some methods to obtain tomograms using NIR are reported,<sup>21,22</sup> but require lengthy imaging times, in the order of more than ten minutes, with the additional restraint of limited scan regions. We could obtain several projections for the tomograms within a few seconds and easily reconstruct a tomogram using TACT and even three-dimensional images [Figs. 2(b) and 2(c)]. TACT is usually used in an x-ray system

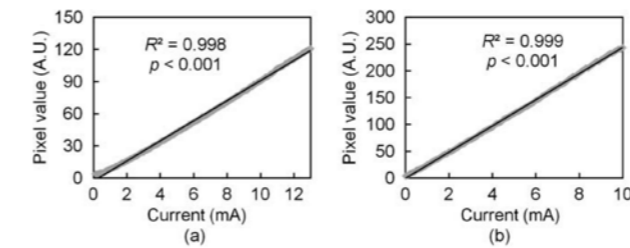


Fig. 6 Relationship between the signal intensity of NIR images and current (mA) in (a) 700 and (b) 810 nm LED. There was a high correlation between the signal intensity of NIR images and the current supplied to the LED at each wavelength. A.U.: arbitrary unit.

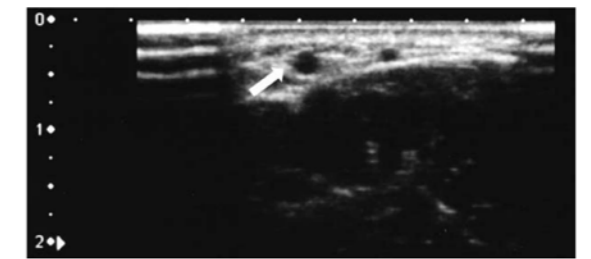


Fig. 8 Forearm surface vessels image by ultrasound. White arrow shows median antebrachial vein, which is 2.0 mm in diameter. Surface to vein distance is 5.0 mm.

(radiography is used as a basis image).<sup>11-19</sup> Although there has been no study that reconstructed NIR tomograms, the TACT reconstruction process in our system was a similar method to that in the x-ray system. Therefore, the number of projections needed to reconstruct the tomography, the accuracy of the method, and robustness of the method are not different between the x-ray system and our system.

VOI and  $SpO_2$  demonstrated good correlation in this system (Fig. 4). The result indicates that we can evaluate oxygen saturation of surface vessels. After the cuff pressure was released, the VOI temporarily tended to rise compared to before the loading test. It is assumed that the blood flow volume temporarily increased as the blood flow was interrupted by the load and was rapidly effused when the cuff pressure was released. Moreover, measurement sensitivity was improved when tomograms were used for the calculation of VOI (Fig. 5), because tomograms can only evaluate the blood signals. However, the NIR image signal without TACT overlapped with the surrounding thick tissue signal. Although, at least six NIR images were required to reconstruct the tomograms, all images were acquired within one second. Thereby, temporary resolution is satisfied with the loading test for evaluating the oxygenation change. We used a pulse oximeter as the gold standard to measure  $SpO_2$  and compared these findings with VOI, since it was desired to exclusively use noninvasive methods.

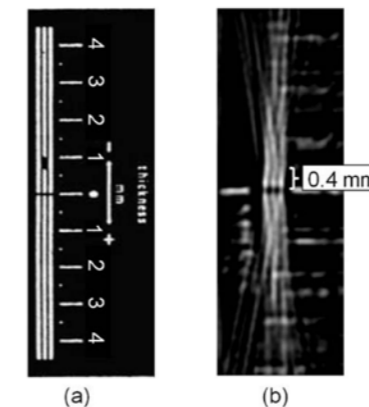


Fig. 7 (a) Picture of chart and (b) NIR image for assessing the slice thickness of NIR with TACT. Scale corresponding to the slice-thickness of the tomogram.

To analyze VOI, it is necessary that the relationship between NIR radiation and signal intensities of the images is linear, because signal intensity of an NIR image is relative value. In this study, there was a linear dependency between the current supplied to the LED and the image signal intensity (Fig. 6). Because it is already known that the relationship between the NIR signal intensity and current supplied to LED is linear,<sup>23,24</sup> linearity between NIR radiation and image signal intensities was verified by this study in the range where VOI was measured. Therefore, we can independently measure VOI of image signal intensity.

In tomosynthesis, slice-thickness is considered to be in relation to the angular disparity of the projection geometry, as in tomography. The effective slice-thickness of our system was 0.4 mm [Fig. 7(b)]. This was considered appropriate because forearm blood vessels used for the calculation of VOI were 2 mm in diameter (Fig. 8).

However, it must be noted that there are some variables in the measurement of VOI. First, the distance between the skin and CCD camera could have an impact on the acquired image data, because the focus of the lens mounted CCD camera of this system was matched to the surface vessels. Thus, NIR repeated scattering in air could be detected by the CCD camera, which might contribute to a decrease in image contrast. In the next series of studies, a grid will be attached, which is an optical fiber bundle, between the skin and CCD camera to decrease scattering effects. The different path lengths of the NIR transmitting subcutaneous tissue might cause different signal intensity attenuations. Therefore, an attenuation correction method by the analysis of skin tissues spatial fluorescence distribution by Monte Carlo simulation is required.<sup>25,26</sup> Additionally, to increase measurement precision of VOI, we need to establish a correction method of image inhomogeneous sensitivity at each wavelength.

We cannot show the advantage compared to the previous method on relevant NIR imaging, but it could enhance the proposed method, because, theoretically, the summation of images increases signal-to-noise ratio and image contrast of vessels compared with a single NIR image. Moreover, the ability to acquire three-dimensional spatial information would increase the diagnostically useful information available over that of a conventional two-dimensional display. Indeed, measurement sensitivity was improved when tomograms were used for the calculation of VOI. Of course, further clinically relevant investigations should be pursued in the future.



In future clinical works, we would like to apply our system to evaluate Reynaud's syndrome and torsion of the testis decreasing the regional vascular, tissue viability of skin grafts and bedsores, as well as skin inflammation due to breast radiation therapy.

## 5 Conclusion

This novel imaging system makes it possible to noninvasively obtain NIR tomograms containing three-dimensional information that can then be used to accurately analyze changes in oxygen saturation levels. There are several clinical applications for which this system will be best utilized, such as to increase treatment efficacy or to detect early symptoms of the adverse effects of radiation on the sensitive tissues of the skin. Further clinical studies are required to refine the system for everyday clinical usage.

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## [Original Article]

### Simultaneous $R_2^*$ and Liver Fat-fraction Measurement Using Modulus and Real Multiple Gradient-echo with Low-field MRI

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**Abstract :** We evaluated the  $R_2^*$  (iron content) and fat-fraction of liver tissue simultaneously using the modulus and real multiple gradient-echo (MRM-GRE) sequence at low-field MRI. Using a 0.4-Tesla open MRI, modulus images of 4 gradient-echoes (typically 8.9, 17.8, 26.7, and 35.6 ms) were obtained by MRM-GRE. The real part of the first echo image was also reconstructed to differentiate below and above the 50 percent fat-fraction.  $R_2^*$  and the fat-fraction were obtained from the parameters of a theoretically fitted formula for each echo signal.  $R_2^*$  and fat-fraction were measured with MRM-GRE from phantom data, liver of healthy volunteers ( $n=12$ ) and from patients with fatty liver ( $n=3$ ). The phantom MRI-derived fat-fraction was in good agreement with the actual value, with  $R_2^*$  showing a strongly positive correlation to actual iron content. MRI-derived fat-fraction in fatty liver was higher than that in the volunteer. However, no significant difference in  $R_2^*$  was found between fatty liver and volunteers. These results show that MRM-GRE enables a method to differentiate causes of signal reduction whether due to an increasing  $R_2^*$  or increasing fat-fraction. MRM-GRE enables a simple and accurate assessment of fat and iron content at low-fields.

**Key words :** magnetic resonance imaging (MRI),  $R_2^*$ , fat-fraction, gradient echo (GRE), liver

## 1. Introduction

Reports on the role of imaging in the assessment of liver disease continue to gain in clinical importance [1]. The most frequently used modalities for liver imaging are ultrasonography, computed tomography and magnetic resonance imaging (MRI). Of these three techniques, MRI is a clinically powerful technique that is well recognized for its ability to depict and characterize disease of the liver [2]. MRI has been proposed for non-invasive detection and quantification of liver status [3]. Two useful methods,  $R_2^*$  and fat-fraction analysis, have been reported for evaluating liver status using MRI [4–12].  $R_2^*$  analysis was found useful in evaluating liver iron concentrations such as in increasing iron contents (e.g. hemochromatosis or hemosiderosis) [4–5]. Fat-fraction analysis was often useful in the evaluation of liver tissue [8–12]. We reported on a useful fat-fraction analysis method based on the Dixon method, that is, the modulus and real multiple gradient-echo (MRM-GRE) method [13–15]. Using MRM-GRE,  $R_2^*$  and fat-fraction are simultaneously obtained. Moreover, this method can distinguish above and below the 50% fat-fraction. The  $T_2^*$ -iterative decomposition of water/fat using echo asymmetry and least-squares estimation (IDEAL) [16] is also especially useful for assessment when there is co-occurrence of hepatic steatosis and iron deposition (e.g. non-alcoholic hepatitis) [17–19]. However, these methods have been used with high-field MRI systems, but more than 15% of MRI systems in the world are low-field. Therefore, to expand the method to lower field strength, we evaluated liver tissue metabolism with a low-field MRI system. In this paper, we describe its characteristics, and demonstrate the utility of MRM-GRE.

## 2. Methods and Materials

### 2.1 $R_2^*$ and fat-fraction analysis

First, four multiple echo modulus images, including first opposed-phase and in-phase images, were acquired using multiple echo GRE sequence. A real image was also obtained at the first opposed-phase echo to differentiate above and below 50% fat-fraction. Next, signal intensities from each obtained echo images were measured and fitted with a theoretical equation (Marquardt-Levenberg algorithm) [20]. The signal from a voxel containing water and fat can be written as [21]:

$$I_t = \{ |I_{w0}|^2 + |I_{f0}|^2 + 2|I_{w0}||I_{f0}|\cos\Delta\omega t \}^{1/2} \exp(-t/T_2^*) \quad (1)$$

where  $I_t$  is total signal intensity,  $I_{w0}$  and  $I_{f0}$  are initial water and fat signal intensities,  $\Delta\omega$  is the frequency difference between water and fat. In equation (1),  $T_2^*$  of water and fat are combined. In addition, since equation (1) contains the  $T_2^*$  decay term and the phase difference term between water and fat, the initial signal intensities of water and fat obtained by fitting are without the influence of  $T_2^*$  decay and phase cycling [21]. Finally,  $R_2^*$  ( $=1/T_2^*$ ) were directly obtained from the parameters of a formula theoretically fitted with each echo signal, and the fat-fraction was calculated by substituting the initial signal intensities into equation (2).

$$\text{Fat-fraction}(\%) = 100 I_{f0} / (I_{w0} + I_{f0}) \quad (2)$$

Then, using the real image obtained in the first opposed-phase echo, fat-fractions of below and above 50% were determined by the signs of signal intensities from this real



component. A real positive component implied the signal intensities of water were larger than those of fat; therefore, the fat-fraction was determined as below 50%. Likewise, when the real component was negative, signified the signal intensities of water were smaller than those of fat; therefore, the fat-fraction was determined as above 50%.

## 2.2 In Vitro Phantom Study

### 2.2.1 Phantoms

Fat-Water (iron) phantoms consisting of bottles (approximately 200 mL) filled with equal volumes of distilled water and triglyceride (lard) were used to test the MRM-GRE method quantitatively. Aliquots of superparamagnetic iron oxide (SPIO) (Feridex, Bayer healthcare) were added to the vials to shorten  $T_2^*$  values in varying iron concentrations (0.05, 0.2, 0.4, 0.6, and 0.8 mM). In this scene, water and lard were separated in two layers, because of differences of specific gravities between water and lard. To vary the fat-fraction by using partial volume effect, the slice level which was oriented parallel to water-lard boundary was moved up and down. Additionally, to evaluate the state of emulsion, mayonnaises of 38.3% and 79.2% fat-fraction were measured.

### 2.2.2 Phantom Imaging

Imaging was performed with a 0.4-T open MRI system (APERTO Eterna; Hitachi Medical Corporation, Japan). For imaging, phantoms were individually fixed in an acrylic container filled with deionized water to avoid susceptibility artifacts caused by air around the phantoms. The phantoms were positioned centrally in a QD Head coil. After performing three plane localizing sequences, MRM-GRE scan was performed. Imaging parameters included 150 ms repetition time (TR), 4.4, 8.9, 13.3, and 17.8 ms echo time (TE), 40 mm section thickness to minimize the effect of imperfect slice profiles, single section acquired, 256 mm field of view (FOV), 256 × 256 matrix, ± 100 kHz bandwidth (BW) for reducing water-fat shift, ten number of signal averages to improve the signal-to-noise ratio, rephasing gradient off, and low flip angle (12°) was used to minimize  $T_1$  effects [22-23].

Fat-fraction using MRM-GRE was compared to fat-fraction using Double-GRE Dixon method. Fat-fraction using Double-GRE Dixon method was obtained using equation (3, 4 and 5).

$$I_m = I_w + I_f, \quad (3)$$

$$I_{opp} = I_w - I_f, \quad (4)$$

$$\text{Fat-fraction (\%)} = 100(I_m - I_{opp}) / 2 I_m, \quad (5)$$

where,  $I_m$  and  $I_{opp}$  are in-phase and opposed-phase signal intensities, and  $I_w$  and  $I_f$  are water and fat signal intensities. Imaging parameters used were the same scan parameters as in MRM-GRE scans except for TE, i.e., 8.9 and 17.8 ms TE.

## 2.3 In Vivo Human Study

### 2.3.1 Subjects

This study was approved by the institutional review board of Kanazawa University and informed consent was obtained from each participant. Twelve healthy volunteers [mean age, 23.2; standard deviation (SD), 2.7 years; range 21-29; twelve men] and three patients diagnosed with fatty liver [mean age, 34.3; SD, 12.7 years; range 26-49; three men] were included

in the study. The diagnosis of fatty liver was established as hyper-echogenicity of liver relative to kidney on ultrasound scanning. We measured the fat-fraction at the right lobe of the liver.

### 2.3.2 Human Imaging and MR Spectroscopy

Imaging was performed with a 0.4-T open MRI system with a QD Flexible Body coil. Each participant was placed in the supine position. MRM-GRE scan of the liver was performed in the axial plane using the scan parameters modified from those for phantom scans (150 ms TR, 8.9, 17.8, 25.6, and 35.6 ms TE, 10 mm section thickness, 11 mm interval, three sections acquired, 340 × 272 mm rectangular FOV, 240 × 102 matrix, ± 30 kHz BW, one number of signal averages, 17 seconds scan times) to adjust scan times within a single breath-hold period.

In typical clinical cases, single voxel breath-hold MR Spectroscopy (MRS) data was acquired to provide a reference standard from two patients with fatty liver [mean age, 38.5; SD, 16.3 years; range 26-49]. MRS was performed with a 3.0-T MRI (Signal HDx, GE Healthcare, Waukesha, WI) using phased array TORSO coil. Spectra were acquired using point-resolved spectroscopy without water suppression. A 3.0 × 3.0 × 3.0 cm<sup>3</sup> MRS voxel was placed in the same attempted location for MRM-GRE scan while avoiding large vessels, but without references to MRS including the following: 1500 ms TR, one number of signal averages.  $T_2$  corrections were performed during postprocessing, 25, 45, 65, 85, 135, 185, 235, and 285 ms TE were acquired, within single 15 s breath hold. MRS spectra were postprocessed using spectroscopy analysis from General Electric (SAGE) to integrate the area under the water peak (4.7 ppm) and total area under the fat peaks (1.3 ppm), to obtain MRS fat-fraction.

## 3. Results

### 3.1 In Vitro Phantom Study

$R_2^*$  value of the phantom showed a strongly positive correlation with the actual iron content ( $R^2=0.998$  and  $P$  value < 0.001 in 0% fat-fraction,  $R^2=0.981$  and  $P$  value < 0.001 in 10% fat-fraction,  $R^2=0.989$  and  $P$  value < 0.001 in 30% fat-fraction; multiple linear regression analysis) (Fig.1).

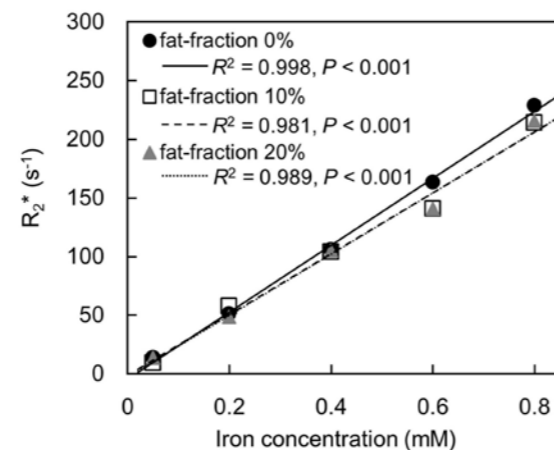


Fig.1 Relationship between phantom  $R_2^*$  and iron concentration. A strong positive correlation exists between  $R_2^*$  and iron concentration.

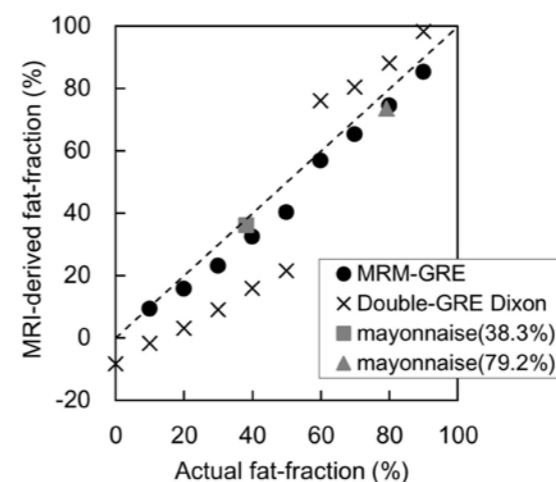


Fig.2 Relationship between phantom MRI-derived and actual fat-fraction. Double-GRE Dixon method yielded overestimations under conditions of high fat content and underestimations in low fat-fractions, whereas MRI-derived fat-fraction using  $T_2^*$  decay correction with MRM-GRE signals corresponded with the actual fat-fraction. Dashed line represents unity.

Fat-fractions using MRM-GRE with phantoms and mayonnaises were in good agreement with the actual value; however, fat-fraction using Double-GRE Dixon with phantom was either underestimated (< 50%) or overestimated (> 50%) (Fig.2).

### 3.2 In Vivo Human Study

Fig.3 illustrates the influence of fat-fraction on iron concentration of the liver. There was no significant correlation between  $R_2^*$  and fat content of the liver ( $R^2=0.040$  and  $P$  value=0.531; multiple linear regression analysis) (Fig.3). The fat-fractions using Double-GRE Dixon were quite smaller than those with MRM-GRE (Fig.4(a)), and the fat-fractions using MRM-GRE in fatty liver were in good agreed with those using 3.0-T MRS (Fig.4(b)).

in low-field conditions. The  $T_2^*$ -IDEAL [16] is also especially useful in the assessment when there is co-occurrence of hepatic steatosis and iron deposition (e.g. non-alcoholic hepatitis), but this method is not necessarily implemented in standard MR imagers. Therefore, we evaluated  $R_2^*$  and fat-fraction analysis of the liver using MRM-GRE at low-field MRI system.

The phantom study demonstrated a strong positive correlation between  $R_2^*$  and iron concentration (Fig.1). This result implies that the assessment of liver iron concentration could be directly obtained from the  $R_2^*$  value. As shown in the methods section 2.1, we could correct for  $T_2^*$  decay and phase cycling using MRM-GRE, as we obtained the initial water and fat signal fitted by equation (1), which contains the  $T_2^*$  decay term and the phase difference term between water and fat. Therefore, MRI-derived fat-fractions using MRM-GRE method were in good agreement with the actual fat-fractions. In addition, MRI-derived fat-fractions of mayonnaises corresponded with the actual fat-fraction. This also confirms that MRM-GRE method can be as effective in emulsions. On the other hand, the fat-fractions using Double-GRE Dixon method were affected by both  $T_2^*$  decay and phase cycling. The fat-fractions using Double-GRE Dixon were either underestimated (< 50%) or

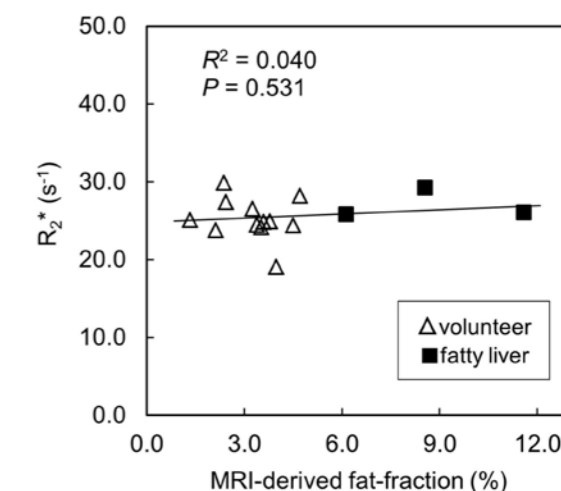


Fig.3 Relationship between human  $R_2^*$  and MRI-derived fat-fraction. There was no significant correlation between  $R_2^*$  and fat content of the liver.

## 4. Discussion

Utility of  $R_2^*$  and fat-fraction analysis have been reported for evaluating the condition of liver using high-field MRI system [4-12]; however, these methods were not established

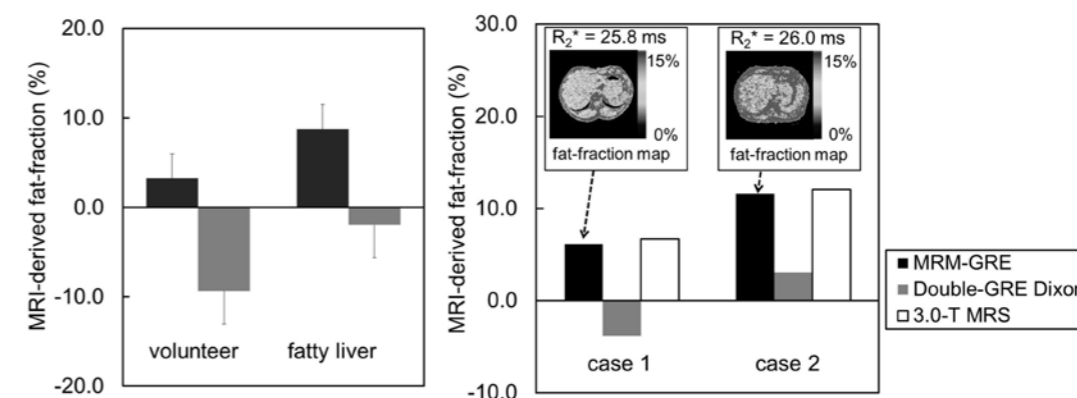


Fig.4 (a) Comparison of MRM-GRE and Double-GRE Dixon with human imaging. The fat-fractions using Double-GRE Dixon were smaller than those with MRM-GRE. (b) Typical cases with fatty liver comparison among MRM-GRE, Double-GRE Dixon, and 3.0-T MRS. MRI-derived fat-fraction using MRM-GRE in fatty liver agreed with those using 3.0-T MRS.



overestimated (> 50%), because of  $T_2^*$  decay and phase cycling (Fig.2).

The human studies showed no significant correlation between  $R_2^*$  and fat content of the liver (Fig.3). This result implies that assessment of iron concentration of the liver is unaffected by differences in fat content. The fat-fractions using Double-GRE Dixon were quite smaller than those with MRM-GRE due to  $T_2^*$  decay and phase cycling (Fig.4(a)). Additionally, the fat-fractions using MRM-GRE in typical cases with fatty liver were in good agreement with those using 3.0-T MRS (Fig.4(b)). MRM-GRE at low magnetic field strengths could be an effective clinical tool as a consequence of these results.

Fat suppression techniques are commonly used in MR imaging and are required in many clinical situations. However, since chemical-shift between water and fat is relatively small in low static field, frequency-selective fat suppression [24-25] or binominal pulse techniques [26] have difficulty in suppressing fat signals. The MRM-GRE method makes it possible to simply obtain the water and fat signal. MRM-GRE method can also measure  $T_2^*$  relaxation time. Accordingly, MRM-GRE method is an effective water-fat separation (i.e. fat-suppression) and  $T_2^*$  decay correction technique at low static magnetic field strength.

## 5. Conclusion

It was possible to simultaneously acquire measurements of  $R_2^*$  and fat-fraction using MRM-GRE at low-field MRI. A linear dependency between  $R_2^*$  and iron concentration, and MRI-derived fat-fraction using MRM-GRE method was in good agreement with actual values. MRM-GRE method makes it possible to simply and accurately assess iron and fat contents with low-field MRI. The ability to obtain both values at the same time allows one to optimize the advantages of each and obtain more information regarding liver metabolism at low static magnetic field strength.

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