Received:
05 September 2017

Revised:
22 January 2018

Accepted:
23 January 2018

<https://doi.org/10.1259/bjr.20170671>

Cite this article as:
Chikui T, Yamashita Y, Kise Y, Saito T, Okamura K, Yoshiura K. Estimation of proton density fat fraction of the salivary gland. *Br J Radiol* 2018; **91**: 20170671.

FULL PAPER

Estimation of proton density fat fraction of the salivary gland

¹TORU CHIKUI, DDS, PhD, ²YASUO YAMASHITA, RT, PhD, ³YOSHITAKA KISE, DDS, PhD, ²TOMONORI SAITO, RT, ¹KAZUTOSHI OKAMURA, DDS, PhD and ¹KAZUNORI YOSHIURA, DDS, PhD

¹Department of Oral and Maxillofacial Radiology, Faculty of Dental Science, Kyushu University, Fukuoka, Japan

²Department of Medical Technology, Kyushu University Hospital, Fukuoka, Japan

³Department of Oral and Maxillofacial Radiology, School of Dentistry, Aichi Gakuin University, Nagoya, Japan

Address correspondence to: Dr Toru Chikui
E-mail: chikui@rad.dent.kyushu-u.ac.jp

Objective: Our first objective was to prove the validity of the six-point Dixon method for estimating the proton density fat fraction (PDFF) of the salivary gland. The second objective was to estimate the salivary gland PDFF using Dixon method to evaluate the pathological conditions.

Methods: At first, 12 volunteers underwent two types of sequences: single-voxel

magnetic resonance spectroscopy and the Dixon method and the PDFFs obtained by the two methods were compared. Next, a total of 67 individuals [normal, $n = 46$; Sjögren's syndrome (SS), $n = 11$; and IgG4-related dacryoadenitis and sialadenitis (IgG4-DS), $n = 4$, parotitis, $n = 6$] were enrolled to estimate the parotid gland (PG) and submandibular gland (SMG) PDFF using the Dixon method.

Results: This volunteer study demonstrated excellent correlation between two methods ($R^2 = 0.964$, slope

$= 1.05$). In the normal group, the PG-PDFF was correlated with the weight and body mass index (BMI) ($\rho = 0.38$, $p = 0.0085$; and $\rho = 0.63$, $p < 0.0001$). The SMG-PDFF was also correlated with the weight, BMI, and serum triglyceride ($\rho = 0.37$, $p = 0.0067$; $\rho = 0.42$, $p = 0.0022$; and $\rho = 0.35$, $p = 0.024$). The PG-PDFF of the SS group ($48.2 \pm 15.1\%$) was higher than that of any other groups; however, no significant difference was found due to the wide overlap. The SS group ($39.0 \pm 26.14\%$) also had significantly higher SMG-PDFF than the normal group ($8.9 \pm 5.4\%$), $p < 0.0001$ and IgG4-DS group ($3.8 \pm 2.3\%$), $p = 0.020$.

Conclusion: The Dixon method is a feasible method for estimating the PDFF and demonstrates fat accumulation in SMG in the SS group.

Advances in knowledge: The PDFF obtained by the Dixon method is helpful for understanding the salivary gland pathological condition.

INTRODUCTION

The clinical presentation of Sjögren's syndrome (SS) may vary considerably; however, slowly progressive dry mouth (xerostomia) and dryness of the eyes (keratoconjunctivitis sicca) are the most common symptoms. The fat deposition of the parotid gland (PG) has been considered characteristic in SS patients and useful for differentiating the patients from those with xerostomia by other lesions.^{1,2} Hyperlipidaemia is known to cause enlargement of the PG via extensive lipid infiltration, and the elevated levels of plasma triglyceride (TG) correlate with PG swelling.³ Although subjective and semi-quantitative analyses for the fat deposition in SS have been performed, few reports have performed a quantitative proton density fat fraction (PDFF) analysis.^{4,5} Furthermore, IgG4-related dacryoadenitis and sialadenitis (IgG4-DS) was recently recognized as an independent entity from SS because of its clinical and serological features. The salivary

function is either normal or improved with the administration of glucocorticoid in IgG4-DS; however, it is not affected by treatment in SS patients. Moreover, the marked elevation of the serum IgG level is found in IgG4-DS, but not in SS. Few reports are available at present regarding the imaging diagnosis of IgG4-DS.^{6,7}

Recently, several new imaging-based methods have been developed to measure the PDFF. In addition to compensation for the inhomogeneity of the static magnetic field, a six-point Dixon method allows for the correction for T_2^* decay in the tissue and consideration of a multipoint spectral model with several lipid components.^{8,9} Previous studies in the liver revealed a strong correlation between the PDFF obtained by the Dixon method and that by magnetic resonance spectroscopy (MRS), which is recognized as the gold standard for the estimation of PDFF.^{10–14}

To our knowledge, the PDFF of the salivary gland has not fully been estimated. Chang measured the PG-PDFF using T_1 and T_2 methods as well as a Dixon method and compared the findings. With both the T_1 and T_2 methods, the PDFF was estimated using the signal intensity of fat-saturated (FS) and non-FS images. The major drawback of these methods was the high sensitivity to B_1 and B_0 inhomogeneity.⁵ Recently, a report showed the validity of the estimation of the salivary gland PDFF using the Dixon method by comparison with the values obtained by MRS. However, the MRS values were fitted to a single main peak, and the multippeak components were not fully considered.¹⁵

The first aim of this study was to estimate the PDFF of the PGs in two different ways—mDIXON-Quant and MRS—and to prove the validity of mDIXON-Quant. The second aim was to estimate the PDFF in the PGs and submandibular glands (SMGs) using mDIXON-Quant under both normal and pathological conditions of the salivary gland.

METHODS AND MATERIALS

To satisfy the first aim, 12 healthy volunteers (mean age $\pm$ standard deviation: 36.8 ± 7.7 years, height: 166 ± 10 cm, weight: 66.5 ± 13.5 kg) were initially enrolled to test the validity of mDIXON-Quant for the estimation for PDFF of the PG. The institutional ethics review board approved this study (approval number 26080). We explained the purpose of the research and the contents of the experiments by verbal instruction and printed documentation. We then obtained informed consent from all of the volunteers. The inclusion criteria were that the volunteers not be addicted to alcohol use and have no history of salivary gland disease, no history of head and neck surgery or radiation therapy, and not have received chemotherapy. The subjects underwent two types of magnetic resonance imaging sequence to the measure PDFF in the PGs: single-voxel MRS (stimulated echo acquisition mode; STEAM) and mDIXON-Quant.

To satisfy the second aim, data were retrospectively collected from March 31 2014, to July 31 2016. At our hospital, mDIXON-Quant is used to obtain three-dimensional in-phase (non-FS) and water (FS) images for patients with suspicious lesions in the head and neck region ($n = 61$). We retrospectively analysed these data for the present study. The study plan was published on a website and the patients had right of refusal for inclusion in this study. The institutional ethics review board approved this study

(approval number 28–286). The inclusion criteria for the analysis were that the patients have no history of head and neck surgery or radiation therapy (three were excluded), not have received chemotherapy for systematic malignancy (one was excluded), and have no salivary gland tumour or cellulitis around the head and neck region (two were excluded). Two patients with suspicion with parotitis at the initial visit were excluded because the symptoms were slight and disappear until the MR examinations. Four patients with suspicion with SS were also excluded because the following examination did not meet the criteria of SS.

They underwent mDIXON-Quant sequence only, not MRS. Of the 49 patients enrolled, 11 were diagnosed with SS, 4 were diagnosed with IgG4-DS, and 6 were diagnosed with parotitis; the remaining 28 individuals who showed no salivary gland abnormalities were used as controls. We combined the 28 patients with no abnormalities of the salivary gland and the 18 volunteers into a normal group. The 12 volunteers were enrolled in the first study and 6 were enrolled in our previous preliminary study. Therefore, for the PG, we divided the patients into four groups (normal group $n = 46$, SS group $n = 11$, IgG4-DS group $n = 4$, and parotitis group $n = 6$). For the SMG, we divided patients into three groups (normal group $n = 52$, SS group $n = 11$, and IgG4-DS group $n = 4$).

The 11 patients assigned to the SS group met the Japanese diagnostic criteria for SS (1999), which consist of four major areas: histopathology, an oral examination, an ocular examination, and a serological examination.¹⁶ IgG4-DS was serologically and histopathologically confirmed using the following diagnostic criteria: persistent symmetrical swelling involving >2 lacrimal and major salivary glands; an elevated serum level of IgG4 (>135 mg dl^{-1}); and infiltration of IgG4-positive plasma cells on immunostaining. Parotitis was clinically interpreted on the basis on such findings as swelling of the PGs, purulent discharge at the orifice of the salivary duct, and/or an increase in the blood amylase level. The subjects' characteristics based on the clinical data are shown in Table 1.

MRI unit

All MRI were performed using a clinical 3 T whole-body MRI system (Ingenia 3.0 T Release 5.3; Philips Healthcare, Best, Netherlands) with a head/neck coil. mDIXON-Quant sequence was acquired in both the volunteer study and clinical study, whereas

Table 1. Subjects characteristics based on clinical data

Group	Normal ($n = 46$)	SS($n = 11$)	IgG4-DS($n = 4$)	Parotitis ($n = 6$)
Age (year)	51.2 ± 19.6	66.4 ± 17.0	60.8 ± 14.9	55.0 ± 6.9
Height (cm)	163 ± 11	152 ± 9	157 ± 3	153 ± 4
Weight (kg)	60.2 ± 14.3	51.4 ± 13.0	57.8 ± 10.5	52.3 ± 7.3
BMI (kg m^{-2})	22.3 ± 3.8	22.2 ± 4.9	23.4 ± 4.2	22.8 ± 2.2
TC (mg dl^{-1})	204 ± 43	181 ± 41	194 ± 25	208 ± 15
TG (mg dl^{-1})	113 ± 69	126 ± 69	96 ± 34	118 ± 36

With the exception of the difference in height between the normal group and SS group ($p = 0.017$, Steel-Dwass test), no significant differences were found among the any of the parameters.

BMI, body mass index; TC, total cholesterol; TG, triglyceride.

MRS was performed only in the volunteer study. MRS was not performed in the clinical setting because the available time was limited.

Quantitative MRI mDIXON-Quant is a six-point three-dimensional gradient echo sequence, which is a commercial product. It was performed with the following parameters: repetition time (TR) = 10 ms, echo time (TE₁) = 1.3 ms, ΔTE = 1.0 ms, echo train length = 6, flip angle = 3°, water fat shift = minimum, and field of view = 230 × 230 mm. To avoid T₁ saturation, which reduces the water signal and increases the measured PDFF, a very low flip angle of only 3° was applied. With 75 consecutive axial images, the head and neck coverage was 15 cm, and the in-plane resolution of 1.47 mm was interpolated as 0.60 mm. Parallel acquisition was used with a SENSE factor of 2 in the anteroposterior direction, resulting in a scan duration of 4 min and 15 s.

¹H-MR spectroscopy and relaxometry

For the volunteer study, a series of five unsuppressed ¹H spectra with different TEs (TEs = 13–53 ms) was acquired via STEAM in PG tissue. MRS voxels were placed at both the left and right PGs; thus, 24 glands were included in this study. STEAM was performed with the following parameters: TR = 5000 ms, TE₁₋₅ = 13, 23, 33, 43, 53 ms, mixing time = 10 ms, 16 average per TE, samples = 1024, spectral Band width (Hz) = 2000, readout duration = 512 ms. To avoid T₁ saturation, a long TR of 5000 ms was applied, and multiple TEs were applied for extrapolation to zero TE. To reduce the effect of J coupling, we set the first TE and mixing time as low as possible.¹⁷ A scan duration of 7 min and 30 s for each voxel.

The MRS data (Philips SDAT/SPAR format) were transferred to a personal computer from the MRI operating console. Time-domain quantification was performed using the AMARES algorithm of the MRUI software package (<http://www.jmrui.eu/welcome-to-the-new-mrui-website/>). The main four fat peaks [5.3 ppm (–CH = CH–), 2.1 ppm (–CH₂–CH = CH–CH₂– or –CO–CH₂–CH₂–), 1.3 ppm (–(CH₂)_n–), and 0.9 ppm (–(CH₂)_n–CH₃)] and the water peak (4.7 ppm) were fitted with Gaussians. We excluded the 2.7 ppm (–CH = CH–CH₂–CH = CH–) and 4.2 ppm (–CH₂–O–CO–) peaks (Figure 1); the former is so small that it is generally not seen *in vivo*, and the latter could not be delineated due to the proximity of the water peak (4.7 ppm).^{8,10,17–19} The relaxation times T₂ of water and four individual TG components were determined with separate monoexponential fits of the respective spectral line integrals. PDFF (STEAM) was determined using the following equation:

PDFF (STEAM) (%) = $\Sigma Fi / (W + \Sigma Fi) \times 100$, where W is the area of the water peak and Fi is the area of each fat peak.

Voxels of interest (VOI) setting

In the first study, we matched the VOIs on the PDFF map obtained by the mDIXON-Quant method to those obtained with STEAM and compared the two PDFFs. We set the VOI for MRS based on water images acquired by the mDIXON-Quant sequence displaying multiplanar reformatted images along three orthogonal planes. The VOIs were matched using this

Figure 1. MR spectrum acquired from the PG. Stacked plot of TE series of STEAM-localized MR spectra (TR/TE₁₋₅ 5000/13, 23, 33, 43, 53 ms) from the VOI (a) and vertically zoomed first row (TE = 13 ms) to highlight the water and the TG components (b). The main four fat peaks [5.3 ppm (–CH = CH–), 2.1 ppm (–CH₂–CH = CH–CH₂– or –CO–CH₂–CH₂–), 1.3 ppm (–(CH₂)_n–), and 0.9 ppm (–(CH₂)_n–CH₃)] and the water peak (4.7 ppm) were identified. PG, parotid gland; TE, echo time; TR, repetition time; VOI, volume of interest.

information. We adjusted the rectangular VOI in order to exclude the retromandibular vein and reduce any contamination of the signal in the surrounding tissues. The volume of the VOI was $3.1 \pm 1.2 \text{ cm}^3$.

In the second study, we outlined the PGs and the SMGs in all slices and set them as VOIs. We drew the outline the PGs and the SMGs on both the right and left sides. The average of both sides was used for the PDFF, except for in the parotitis group. These procedures were performed using the Image J software program (National Institutes of Health, Bethesda, MD) by one radiologist with 22 years of experience.

Statistical analyses

In the volunteer study (24 PGs), the single regression analysis was used to compare the PDFFs obtained by the two methods. A Bland–Altman plot was also used for the comparison of the two methods.

In the clinical study of the normal group, the correlation between the PDFFs and subject parameters [age, height, weight, BMI, total cholesterol, and TG] in the normal group were evaluated using Spearman's rank correlation coefficient. The Steel–Dwass test was used to compare the PDFFs among each group. Furthermore, in the parotitis group, we performed a paired *t*-test between PG-PDF of the affected side and that of the unaffected side. *p*-value of less than 0.05 was considered statistically significant. The analyses were performed with the statistical software package JMP Pro v. 13.0.0 (SAS Institute, Cary, NC).

RESULTS

Volunteer study

STEAM with multiple TEs revealed that the T_2 values of the fat peaks (5.3: 36.2 ± 6.1 , 2.1: 56.2 ± 21.6 , 1.3: 66.7 ± 5.19 , and 0.9 ppm: 54.2 ± 7.3 ms) were higher than that of the water peak (25.7 ± 2.7 ms). The relative magnitudes of the 1.3, 2.1, 0.9, and 5.3 ppm peaks among all fat peaks were 61.8, 18.0, 11.9, and 8.3%, respectively. The ratio of the 1.3-ppm peak from the bulk methylene protons ($61.8 \pm 6.1\%$) was quite similar to that in the liver.¹⁰

We noted high correlation between the PDFF (mDIXON) and PDFF (STEAM) ($R^2 = 0.964$), using the following equation:

$$\text{PDFF (mDIXON)} = 1.05 \times \text{PDFF (STEAM)} - 2.07 \quad (\text{Figure 2a}).$$

The 95% confidence interval for the slope was 0.96 to 1.14. The 95% confidence interval for the intercept was -5.83 to 1.70 .

Figure 2b shows the associated Bland–Altman plot, where the dashed lines represent the 95% confidence interval. This was not significantly different from 0 [mean difference = -0.049 , SD = 2.84 , 95% confidence interval (-5.63 to 5.53), $p = 0.933$].

Clinical study (normal group)

The PG-PDF of the normal group was positively correlated with the weight and BMI ($\rho = 0.38$, $p = 0.0085$; and $\rho = 0.63$, $p < 0.0001$, respectively). Neither the height, total cholesterol, nor TG was correlated with the PG-PDF (Table 2). The SMG-PDF also correlated with the weight, BMI, and TG ($\rho = 0.37$, $p = 0.0067$; $\rho = 0.42$, $p = 0.0022$; and $\rho = 0.35$, $p = 0.024$, respectively) (Table 2).

Clinical study (comparison among diseases)

Figures 3–5 show the representative images of a patient with SS (Figure 3), with IgG4-DS (Figure 4) and parotitis (Figure 5).

Although the SS group values ($48.2 \pm 15.1\%$) were the highest among the categories, (normal Group $36.1 \pm 11.4\%$, IgG4-RD Group $36.0 \pm 21.8\%$, parotitis group [affected side] $30.1 \pm 18.5\%$), no significant difference was found (Figure 6). In the parotitis group, the PG-PDFs of the affected side ($30.1 \pm 18.5\%$) were lower than those of the unaffected side ($47.3 \pm 26.0\%$) (Figure 7). The mean difference was -17.2 and 95% confidential interval -5.9 to -28.6% ($p = 0.011$).

The SMG-PDF of the SS group was the highest of all groups, and a significant difference was found between the SS group ($39.0 \pm 26.1\%$) and both the normal group ($8.9 \pm 5.4\%$) ($p <$

Figure 2. Comparison between the PG-PDF obtained by mDIXON-Quant and by STEAM in 24 parotid glands of volunteers. Scatter plot displaying individual results and linear regression line (solid) (a). $\text{PDFF (mDIXON)} = 1.05 \times \text{PDFF (STEAM)} - 2.07$. The 95% confidence interval for the slope was 0.96 to 1.14. The 95% confidence interval for the intercept was -5.83 to 1.70 . The results of Bland–Altman plot, where the dashed lines represent the 95% confidence interval (b). This was not significantly different from 0 [mean difference = -0.049 , SD = 2.84 , 95% confidence interval (-5.63 to 5.53), $p = 0.933$]. PDFF, proton density fat fraction; PG, parotid gland; STEAM, stimulated echo acquisition mode.

Table 2. Correlation between the PDFFs and physiological parameters

	Parotid gland (<i>n</i> = 46)		Submandibular gland (<i>n</i> = 52)	
	Spearman rank-correlation coefficient	<i>p</i> -value	Spearman rank-correlation coefficient	<i>p</i> -value
Age	−0.003	0.98	0.21	0.131
Height	−0.07	0.62	0.15	0.282
Weight	0.38	0.0085	0.37	0.0067
BMI	0.63	<0.0001	0.42	0.0022
TC	0.017	0.923	0.052	0.74
TG	0.087	0.609	0.35	0.024

BMI, body mass index; PDFF, proton density fat fraction; TC, total cholesterol; TG, triglyceride.

0.0001) and the IgG4-DS group ($3.8 \pm 2.3\%$) ($p = 0.020$). As the SMG-PDFF of the normal group was small, the increased SMG-PDFF was characteristic of the SS group. In contrast, the IgG4-DS group did not show any marked increase in the PDFF compared to the normal group (Figure 8).

DISCUSSION

The six-point Dixon method is a sophisticated imaging-based quantification and provides useful data regarding both the PDFF and anatomy. Recently, Chang et al demonstrated that the PG-PDFF in healthy adults correlates positively with both age and BMI using a Dixon method.^{4,5} However, to our knowledge, the plausibility of applying a Dixon method to the salivary glands has not been fully proven.

On examining the STEAM sequences with multiTEs, we found that the T_2 values of the four fat peaks were much longer than that of the water peak.¹⁰ The T_2 values of both water and fat were quite similar to those previously reported in the liver. The relative magnitudes of the 1.3, 2.1, 0.9 and 5.3 ppm peaks among

all fat peaks were similar to those reported in the liver to some extent.¹⁰ The differences might be due to the fitting methods, the fat components (e.g. percentage of unsaturated fat) and effect of periodic J modulation.¹⁷

As with previous liver studies,^{10–14} a high correlation was observed between the PDFF (MRS) and PDFF (mDIXON) in the PGs, with a slope of 1.05. The reason why the slope is 1.05 might be because we assumed the four fat peaks to be the total fat signal in MRS.

Given the results of the regression analysis and the Bland–Altman plot, we considered the PDFF (mDIXON) to be plausible and mDIXON-Quant, a feasible method for estimating the PDFF in the PGs in a clinical setting.

The clinical study revealed that the weight and BMI correlated significantly with the PG-PDFF, as shown in previous reports.⁵ In contrast to the report by Chang, we did not find any correlation between the PG-PDFF and age,⁵ likely because the age was

Figure 3. Representative images of a 62-year-old female patient with SS. Water (a), fat (b), and colour-coded FF map (c) in the right SMG. The FF in the right SMG is 76.3%. FF, fat fraction; SMG, submandibular gland; SS, Sjögren's syndrome.

Figure 4. Representative images of a 50-year-old female patient with IgG4-DS. Water (a), fat (b), and colour-coded FF map (c) in the right SMG. The FF in the right SMG is 1.1%. FF, fat fraction; SMG, submandibular gland.

negatively correlated to weight and BMI in our study ($\rho = -0.36$, $p = 0.014$ and $\rho = -0.32$, $p = 0.030$ respectively). Although the SMG-PDFF was smaller than the PG-PDFF, the fact that the SMG-PDFF was also correlated with weight and BMI was something of a surprise.

Bloch et al examined the salivary glands of cadavers and showed that extensive fat infiltration occurred in the salivary glands of subjects with SS, where minimal to moderate lymphocyte infiltration was present.²⁰ Takagi demonstrated that the fat area in the PGs interpreted based on the signal intensity of T_1 weighted images increased in proportion to the sialographic grade, and a large fat area was characteristic of the SS group and useful for

Figure 5. Representative images of a 58-year-old female patient with parotitis. The PDFF of the affected side (left) was 15.6%, and that of the unaffected side (right) was 28.5%. PDFF, proton density fat fraction.

differentiating these patients from those with xerostomia by other reasons.² Our findings were compatible with those from these previous reports. However, the PG-PDFF was correlated with the weight and BMI; therefore, the distribution of the SS group and the other groups showed considerable overlap. On the other hand, the SMG-PDFF was quite small; thus, advanced fat deposition in the SMGs was a characteristic of the SS group. Therefore, further research will be needed to confirm whether or not FF is useful for the differential diagnosis of patients with SS and those with sicca symptoms not meeting the criteria for SS.

Few reports have been published regarding the imaging diagnosis of IgG4-DS.^{6,7} Shimizu demonstrated that, on sonography, multiple hypoechoic areas and hyperechoic lines were characteristic of SS, and that reticular and nodal patterns were predominantly detected in IgG4-DS cases.^{6,21} However, this imaging

Figure 6. Comparison of PG-PDFFs among the disease categories. The PG-PDFF of the SS group was the highest among the four groups; however, no significant differences were found between any pairs. PG, parotid gland; PDFF, proton density fat fraction; SS, Sjögren's syndrome.

Figure 8. Comparison of SMG-PDFFs among the disease categories. The SMG-PDFF of the SS group was also the highest, and a significant difference was found in the values between SS group and both the normal group ($p < 0.001$) and the IgG4-DS group ($p = 0.020$). PDFF, proton density fat fraction; SMG, submandibular gland; SS, Sjögren's syndrome.

interpretation can be difficult for radiologists unfamiliar with sonography of the salivary glands. In this respect, the PDFF will surely be helpful for differentiating between the two diseases.

Although no significant difference was found between PG-PDFF of the parotitis group and that of the other groups, the decreased FF in the affected side compared to the unaffected side was thought to be due to oedema, which increased the water content.

Several limitations associated with the present study warrant mention. First, we did not evaluate the validity of the estimation of the SMG-PDFF by comparing the PDFF (MRS) and PDFF (mDIXON). The longer acquisition time for MRS may cause the contamination of the signals from the surrounding adipose tissue in the SMGs, which are susceptible to jaw movement. However, the relative intensities of the lipid peaks should be almost the same in salivary glands; thus, we were of the opinion that this did not matter. Second, abnormalities might not have been completely eliminated in the 28 cases interpreted as being without abnormality in the salivary gland, as this interpretation was based on the medical sheet, health history, and the imaging findings, including MRI. However, the PG-PDFF and SMG-PDFF of this group was 36.4 ± 9.9 and $9.5 \pm 5.4\%$, values that are very similar to those of the volunteers (35.5 ± 13.7 and $8.1 \pm 5.5\%$, respectively). Therefore, the effect might have been trivial. Third, the population in this study was relatively small. While a high PDFF was characteristic of the SS group, whether or not these findings yield greater diagnostic power over conventional images is uncertain. Although no significant differences were found in the mean PDFF between the SS group and other

Figure 7. Comparison of PG-PDFFs between the affected side and the unaffected side in the parotitis group. The affected side had significantly lower PG-PDFF than the unaffected side ($p = 0.011$). PG, parotid gland; PDFF, proton density fat fraction.

groups, we intend to perform more sophisticated analyses, like a histogram analysis, in a larger population. Furthermore, we only examined four IgG4-DS patients. Therefore, further studies with a large population will be needed to verify our findings.

In conclusion, our study revealed high correlation between the PDFF on the multipeak fat model obtained by STEAM and the PDFF obtained by mDIXON-Quant. Clinically, mDIXON-Quant revealed marked fat deposition of the salivary glands in SS patients compared with other subjects. In particular, the SMG-PDFF was quite small in the normal group, and the observed increased SMG-PDFF was specific for the SS group.

ACKNOWLEDGEMENT

The authors acknowledge the technical support of Mr. Atsushi Takemura at Philips Electronics Japan.

FUNDING

This work was supported by a MEXT (The Ministry of Education, Culture, Sports, Science and Technology) Grant-in-Aid for Scientific Research (C) 15K11073.

REFERENCES

- Izumi M, Eguchi K, Nakamura H, Nagataki S, Nakamura T. Premature fat deposition in the salivary glands associated with sjögren syndrome: MR and CT evidence. *AJNR Am J Neuroradiol* 1997; **18**: 951–8.
- Takagi Y, Sumi M, Sumi T, Ichikawa Y, Nakamura T. MR microscopy of the parotid glands in patients with sjögren's syndrome:

- quantitative MR diagnostic criteria. *AJNR Am J Neuroradiol* 2005; **26**: 1207–14.
3. Izumi M, Hida A, Takagi Y, Kawabe Y, Eguchi K, Nakamura T. MR imaging of the salivary glands in sicca syndrome: comparison of lipid profiles and imaging in patients with hyperlipidemia and patients with sjögren's syndrome. *AJR Am J Roentgenol* 2000; **175**: 829–34.
 4. Chang HC, Juan CJ, Chiu HC, Liu YJ, Cheng CC, Chiu SC, et al. Parotid fat contents in healthy subjects evaluated with iterative decomposition with echo asymmetry and least squares fat-water separation. *Radiology* 2013; **267**: 918–23. doi: <https://doi.org/10.1148/radiol.12112599>
 5. Chang HC, Juan CJ, Chiu HC, Cheng CC, Chiu SC, Liu YJ, et al. Effects of gender, age, and body mass index on fat contents and apparent diffusion coefficients in healthy parotid glands: an MRI evaluation. *Eur Radiol* 2014; **24**: 2069–76. doi: <https://doi.org/10.1007/s00330-014-3265-z>
 6. Shimizu M, Okamura K, Kise Y, Takeshita Y, Furuhashi H, Weerawanich W, et al. Effectiveness of imaging modalities for screening IgG4-related dacryoadenitis and sialadenitis (Mikulicz's disease) and for differentiating it from sjögren's syndrome (SS), with an emphasis on sonography. *Arthritis Res Ther* 2015; **17**: 223. doi: <https://doi.org/10.1186/s13075-015-0751-x>
 7. Fujita A, Sakai O, Chapman MN, Sugimoto H. IgG4-related disease of the head and neck: CT and MR imaging manifestations. *Radiographics* 2012; **32**: 1945–58. doi: <https://doi.org/10.1148/rg.327125032>
 8. Reeder SB, Cruite I, Hamilton G, Sirlin CB. Quantitative assessment of liver fat with magnetic resonance imaging and spectroscopy. *J Magn Reson Imaging* 2011; **34**: 729–49. doi: <https://doi.org/10.1002/jmri.22580>
 9. Hu HH, Kan HE. Quantitative proton MR techniques for measuring fat. *NMR Biomed* 2013; **26**: 1609–29. doi: <https://doi.org/10.1002/nbm.3025>
 10. Kukuk GM, Hittatiya K, Sprinkart AM, Eggers H, Gieseke J, Block W, et al. Comparison between modified Dixon MRI techniques, MR spectroscopic relaxometry, and different histologic quantification methods in the assessment of hepatic steatosis. *Eur Radiol* 2015; **25**: 2869–79. doi: <https://doi.org/10.1007/s00330-015-3703-6>
 11. Irwan R, Edens MA, Sijens PE. Assessment of the variations in fat content in normal liver using a fast MR imaging method in comparison with results obtained by spectroscopic imaging. *Eur Radiol* 2008; **18**: 806–13. doi: <https://doi.org/10.1007/s00330-007-0801-0>
 12. Meisamy S, Hines CD, Hamilton G, Sirlin CB, McKenzie CA, Yu H, et al. Quantification of hepatic steatosis with T1-independent, T2-corrected MR imaging with spectral modeling of fat: blinded comparison with MR spectroscopy. *Radiology* 2011; **258**: 767–75. doi: <https://doi.org/10.1148/radiol.10100708>
 13. Rehm JL, Wolfram PM, Hernando D, Eickhoff JC, Allen DB, Reeder SB. Proton density fat-fraction is an accurate biomarker of hepatic steatosis in adolescent girls and young women. *Eur Radiol* 2015; **25**: 2921–30. doi: <https://doi.org/10.1007/s00330-015-3724-1>
 14. Krishan S, Jain D, Bathina Y, Kale A, Saraf N, Saigal S, et al. Non-invasive quantification of hepatic steatosis in living, related liver donors using dual-echo Dixon imaging and single-voxel proton spectroscopy. *Clin Radiol* 2016; **71**: 58–63. doi: <https://doi.org/10.1016/j.crad.2015.10.002>
 15. Kise Y, Chikui T, Yamashita Y, Kobayashi K, Yoshiura K. Clinical usefulness of the mDIXON quant the method for estimation of the salivary gland fat fraction: comparison with MR spectroscopy. *Br J Radiol* 2017; **90**: 20160704. doi: <https://doi.org/10.1259/bjr.20160704>
 16. Fujibayashi T, Sugai S, Miyasaka N, Hayashi Y, Tsubota K. Revised Japanese criteria for sjögren's syndrome (1999): availability and validity. *Mod Rheumatol* 2004; **14**: 425–34. doi: <https://doi.org/10.3109/s10165-004-0338-x>
 17. Hamilton G, Middleton MS, Bydder M, Yokoo T, Schwimmer JB, Kono Y, et al. Effect of PRESS and STEAM sequences on magnetic resonance spectroscopic liver fat quantification. *J Magn Reson Imaging* 2009; **30**: 145–52. doi: <https://doi.org/10.1002/jmri.21809>
 18. Hamilton G, Yokoo T, Bydder M, Cruite I, Schroeder ME, Sirlin CB, et al. In vivo characterization of the liver fat ¹H MR spectrum. *NMR Biomed* 2011; **24**: 784–90. doi: <https://doi.org/10.1002/nbm.1622>
 19. Szczepaniak LS, Nurenberg P, Leonard D, Browning JD, Reingold JS, Grundy S, et al. Magnetic resonance spectroscopy to measure hepatic triglyceride content: prevalence of hepatic steatosis in the general population. *Am J Physiol Endocrinol Metab* 2005; **288**: E462–8E468. doi: <https://doi.org/10.1152/ajpendo.00064.2004>
 20. Bloch KJ, Buchanan WW, Wohl MJ, Bunim JJ. sjögren's syndrome. A clinical, pathological, and serological study of sixty-two cases. *Medicine* 1965; **44**: 187–231.
 21. Shimizu M, Okamura K, Yoshiura K, Ohyama Y, Nakamura S, Kinukawa N. Sonographic diagnostic criteria for screening sjögren's syndrome. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006; **102**: 85–93. doi: <https://doi.org/10.1016/j.tripleo.2005.09.012>