

学位論文 (博士)

Quantification of pancreas fat on dualenergy computed tomography: comparison with six-point Dixon magnetic resonance imaging.

(Dual energy CT による膵臓の脂肪定量化 : six-point Dixon MRI と比較検討)

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〔題名〕

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〔研究背景〕

内臓脂肪組織は、メタボリックシンドロームや心血管疾患の発症の危険因子として知られている。膵臓では膵脂肪沈着と2型糖尿病との関連が報告されており、膵内分泌機能の予後を推定するため、画像診断によって非侵襲的かつ正確に膵内脂肪量を定量化することは臨床的に有用と考えられる。しかしながら従来のCTでは膵内脂肪量を定量化することは困難であった。一方、MRIは組織脂肪含有量の定量化に優れており、特にsix-point Dixon法MRIなどのケミカルシフトイメージングやMRスペクトロスコピーは、肝臓や膵臓などを含む様々な臓器で組織脂肪定量の精度の高さが研究で明らかになっている。

Dual energy CT(以下DECT)は1種類の管電圧で撮影されるCTと異なり、2種類の管電圧を使用することで、一度の撮影で2種類のX線エネルギーのデータを取得することができる。DECTでは30%未満の肝脂肪量を評価できることが報告されており、膵内脂肪量の評価も有用と思われた。しかし、過去に膵脂肪量の定量化についてMRIとDECTを比較した報告はなかった。

この研究はDECTにより膵実質の脂肪含有率を測定し、six-point Dixon法MRIにおける脂肪定量画像で測定された脂肪含有率と比較することで、DECTによる膵脂肪定量化の実行可能性を検討することを目的とする。

〔要旨〕

方法：

2017年11月から2018年12月にかけて、当院でDECTを撮影した患者で、腹部MRI(fat fraction imaging)を撮影した28症例を対象とした。性別は男性18名、女性10名。年齢幅は49–84歳であり、平均年齢は69.4歳であった。基礎疾患は肝細胞癌12名、転移性肝腫瘍7名、胆管癌3名、胆嚢癌3名、膵臓疾患2名、総胆管結石1名。3cm以上の膵臓腫瘍1名、高度膵萎縮1名、膵臓腫瘍の外科的切除歴1名、また画質が不十分な患者3名は除外した(図1)。

DECTとMRIの撮影は30日以内に実施された。

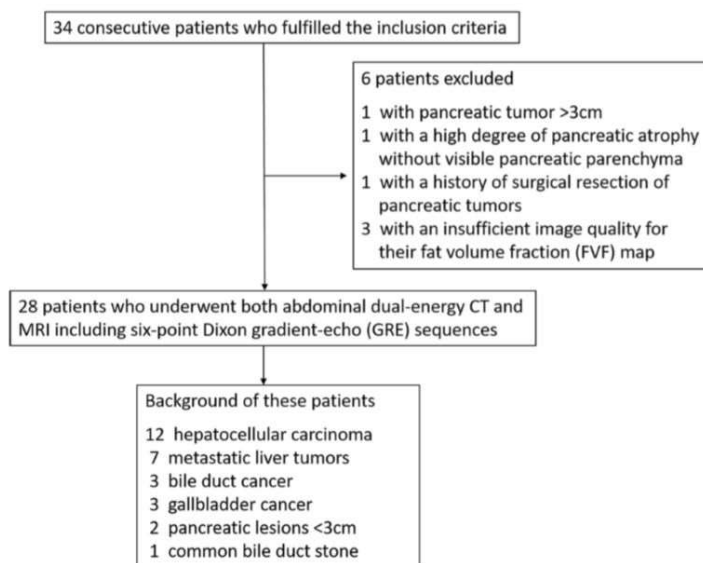
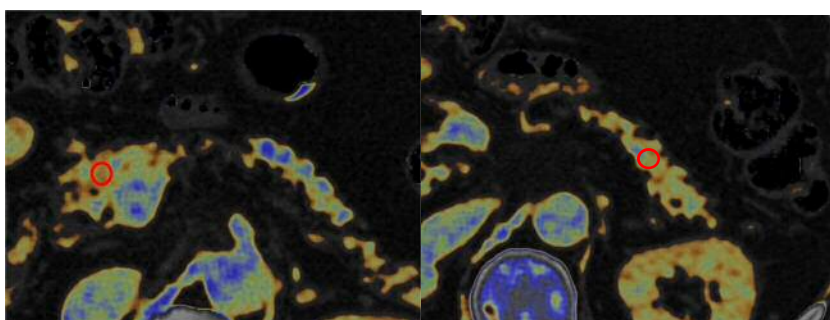


図1 フローチャート

DECTは dual-source CT scanner (SOMATOM FORCE; Siemens, Forchheim, Germany)、MRIは 3.0T MR システム (Magnetom Prisma; Siemens Healthcare, Erlangen, Germany) を使用して撮影した。すべての画像は、画像アーカイブ通信システム (PACS) ワークステーション (Shade Quest, Yokogawa Medical) 上で2人の放射線科医 (経験年数6年、30年) が評価を行った。

DECT で撮影した画像から fat map を作成し、膵頭部と体尾部各1か所に region of interest (ROI) を設定し計測した。ROI のサイズは円形 90–100mm<sup>2</sup> 程度、膵臓の形態に合わせて調整し、ROI の位置は画像上判別できる血管や主膵管を含まない位置を選択した (図2)。MRI で CT と同じ部位に ROI を設定し (図3)、計測。DECT で測定した CT-FVF (%) と Dixon MRI で測定した MR-FVF (%) の関係をスピアマン順位相関係数を用いて評価した。また MR-FVF (%) と単純 100kV CT で測定した CT 値 (HU) との相関をスピアマン順位相関係数で評価した。

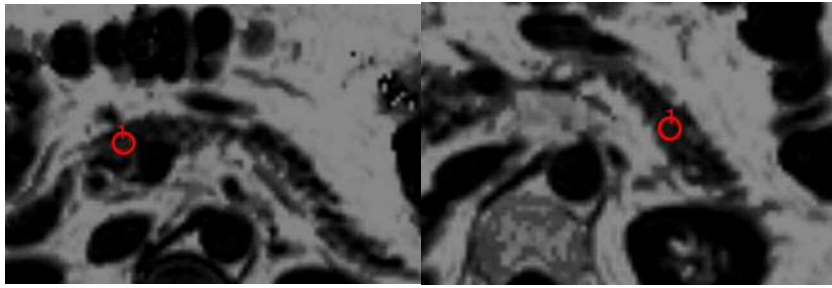


膵頭部

膵体尾部

図2 DECT 撮影画像から作成した fat map

膵頭部、体尾部に赤丸が示すように ROI を設定、CT-FVF を測定した。



膵頭部

膵体尾部

図3 MR-FVF maps

DECT の fat map と同じ場所に ROI を設定、MR-FVF 測定した。

結果：

DECT で測定した膵頭部脂肪含有率は 14.2% (範囲 0.1-81.2%)、膵体尾部は 9.4% (範囲 0-40.8%) だった。MRI で測定した膵頭部脂肪含有率は 12.2% (範囲 1.2-80.9%)、膵体尾部は 8.1% (範囲 0.3-43.7%) だった。DECT と MRI 測定された脂肪含有率の間には、それぞれ膵頭部  $\rho = 0.631$ ,  $P < 0.001$ 、膵体尾部  $\rho = 0.526$ ,  $P = 0.004$  の有意な正の相関関係を認めた(図4)。

膵臓脂肪変性に対する CT-FVF 値 (%) の診断能については、感度、特異度、曲線下面積 (AUC) は、それぞれ頭部で 0.53、0.90、0.76、体尾部で 1.00、0.33、0.66 であった。

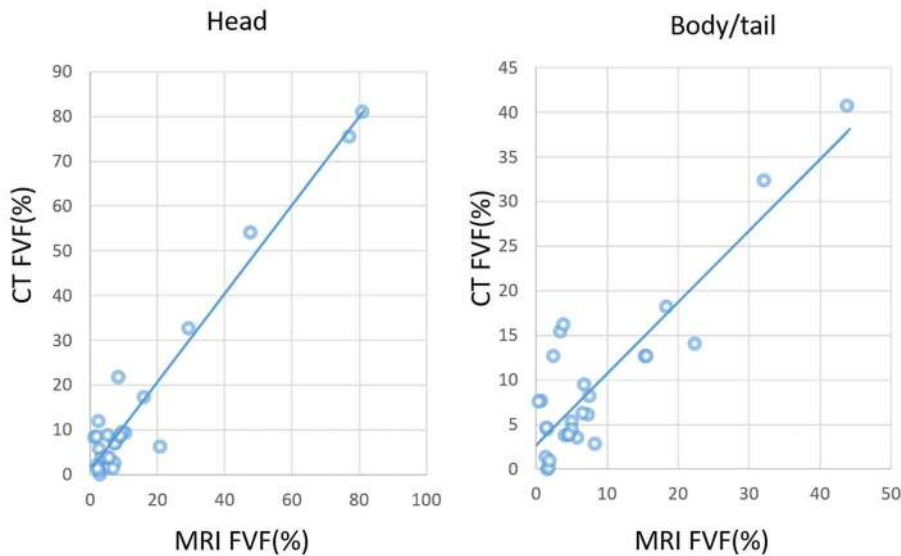


図4 CT-CTVF (%) と Dixon MRI で測定した MR-FVF (%)

DECT と MRI 測定された脂肪含有率の間には膵頭部、膵体尾部で有意な正の相関関係を認めた。

単純 100kV CT で測定した膵頭部および体尾部の CT 値 (HU) の中央値は、それぞれ 29.5 (範囲-77.6~54.2) および 39.9 (範囲-4.4~144.8) であった。MR-FVF (%) と CT 値 (HU) との間には、膵頭、体尾部ともに有意な負の相関が認められた(頭部は  $\rho = -0.435$ ,  $P = 0.02$ 、体尾部は  $\rho = -0.403$ ,  $P = 0.033$ ) (図5)。

MR-FVF (%) と CT-FVF (%) の相関および MR-FVF (%) と CT 値の相関を比較したところ、MR-FVF (%)

と CT-FVF(%) の相関の p 値は、頭部 ( $P < 0.001$  vs  $P = 0.02$ ) と体尾部 ( $P = 0.004$  vs  $P = 0.033$ ) の両方で、MR-FVF(%) と CT 値の相関の p 値よりも良好であった。

膵臓脂肪変性に対する CT 値 (HU) の診断能については、感度は頭部で 0.32、特異度は 1.00、AUC は 0.68、胴体・尾部で 0.07、1.00、0.42 であった。

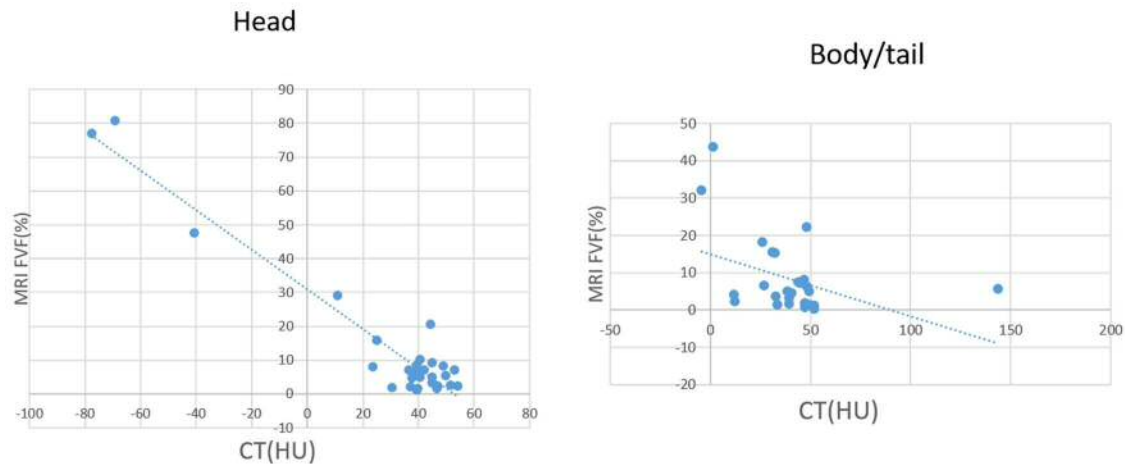


図 5 MR-FVF(%) と単純 100kV CT で測定した CT 値 (HU)

膵頭部および体尾部で MR-FVF(%) と CT 値 (HU) との間には有意な負の相関が認められた。

考察:

いくつかの研究では、 $\beta$  細胞機能障害とインスリン分泌障害の結果として、膵臓脂肪沈着が 2 型糖尿病の病態に関与している可能性があることが報告されている。膵臓脂肪沈着は耐糖能異常の非常に初期の段階からインスリン分泌の低下と共に始まっている可能性があることが示されている。

今回、脂肪定量において精度の高い手法として用いられる six-point Dixon 法 MRI と有意な正の相関を示したことにより、DECT での膵実質の脂肪定量化は可能と思われた。また CT-FVF(%) と単純 100kV CT で測定した CT 値 (HU) を比較すると、膵頭部と体尾部の両方で、MR-FVF(%) と CT-FVF(%) の相関は MR-FVF(%) と CT 値の相関よりも良好であった。これらの結果は、DECT で測定された CT-FVF(%) が、デュアルエネルギーモードのない従来の CT 画像から得られた CT 値よりも、より信頼性の高い膵臓脂肪変性の指標となる可能性を示唆している。DECT は MRI よりも撮影時間が短く、比較的簡単に撮影ができる。今後 DECT が広く利用できるようになれば、膵臓脂肪定量化において実用的で非侵襲的な画像診断方法となる可能性がある。

結語:

本研究では、DECT は膵臓脂肪沈着の定量化に有用な検査法となり得ることが示された。早期の耐糖能異常の診断におけるこの技術の有用性を明らかにするためには、さらなる研究と検討が必要である。

## **Quantification of pancreas fat on dual energy computed tomography: Comparison with six-point Dixon magnetic resonance imaging**

### **Abstract**

**Objectives:** It is important to quantify the degree of fatty degeneration of the pancreas, given the reported relationship between pancreatic parenchymal fatty degeneration and pancreatic function disorder. However, it is difficult to make such a quantification using conventional computed tomography (CT). The present study evaluated the feasibility of pancreatic fat quantification by dual-energy CT (DECT) compared with T2\*-corrected six-point Dixon magnetic resonance imaging (MRI).

**Material and methods:** Twenty-five patients who underwent both DECT (100 and 150 kVp) and Dixon MRI were analyzed. The region of interest (ROI) was placed at the head and body/tail of the pancreas on fat volume fraction (FVF) maps generated using the multimaterial decomposition (MMD) algorithm on DECT. The FVF (%) of pancreatic parenchyma measured by DECT was compared with that measured on FVF maps calculated using Dixon MRI.

**Results:** The median FVF (%) values of the head and body/tail of the pancreas on DECT were 8.1% (range, 1.2% - 80.9%) and 9.4% (range, 0.3% - 43.7%), respectively. The median FVF (%) values of the head and body/tail of the pancreas on Dixon MRI were 12.2% (range, 0.1% - 81.2%) and 14.2% (range, 0% - 40.8%), respectively. FVF (%) measured by DECT showed a significant correlation with the FVF (%) measured by Dixon MRI in the head of the pancreas ( $r=0.894$ ,  $P<0.001$ ) as well as the body/tail of the pancreas ( $r=0.957$ ,  $P<0.001$ ).

**Conclusion:** DECT may be useful for quantifying the degree of fatty degeneration of the pancreas.

**Keywords:**

Dual Energy Scanned Projection Radiography; Pancreas; Fats

**Key points:**

There have been no reports comparing advanced MRI techniques with DECT for the quantification of pancreatic fatty degeneration.

FVF (%) of the pancreas measured by DECT showed significant correlation with FVF (%) measured by Dixon MRI.

DECT may have a potential to quantify the degree of fatty degeneration of the pancreas.

**Abbreviations:**

DECT Dual energy computed tomography

MRI Magnetic resonance imaging

ROI Region of interest

## **Introduction**

The accumulation of fat in the pancreas, known as pancreatic steatosis, is increasingly recognized as a cause of pancreatic dysfunction. For instance, pancreatic steatosis has been found to be associated with a decreased  $\beta$ -cell function and impaired insulin secretion, ultimately leading to diabetes [1-4]. Thus, it is important to quantify the degree of fatty degeneration of the pancreas reliably, noninvasively and conveniently by imaging modalities.

Magnetic resonance imaging (MRI) enables the non-invasive *in vivo* quantification of the tissue fat content [5,6]. The high accuracy of chemical shift-based MR techniques in particular, such as six-point Dixon and MR spectroscopy, for tissue fat quantification has been shown in various organs, including the liver and pancreas, in recent studies [7-10].

Although pancreatic steatosis can be visualized with computed tomography (CT), it has proven difficult to reliably quantify the tissue fat content in the pancreas using conventional CT [11,12]. However, with recent advances in dual-energy CT (DECT) technology, some studies have found that DECT with three-material decomposition was able to accurately quantify the liver fat content and could be performed on both contrast-enhanced and non-contrast-enhanced data sets [13-15]. Still, there have been no reports comparing advanced MRI techniques with DECT for the quantification of pancreatic fatty degeneration. The present study therefore evaluated the feasibility of pancreatic fat quantification by DECT in the comparison with T2\*-corrected six-point Dixon MRI.

## **Material and methods**

### **Study population**

This retrospective study was approved by the institutional review board, and the requirement for informed consent was waived. We searched our radiology and hospital information systems to identify patients who met the following inclusion criteria: (a) patients underwent both abdominal CT and MRI between November 2017 and December 2018; (b)



CT was performed in the dual-energy mode, and MRI included six-point Dixon gradient-echo (GRE) sequences; (c) DECT was performed within 30 days of MRI. Patients with a large pancreatic tumor (n=1), a high degree of pancreatic atrophy (n=1), history of surgical resection of pancreatic tumors (n=1) or an insufficient image quality for their fat volume fraction (FVF) map (n=3) were excluded.

Ultimately, 28 patients met these criteria and formed the final study group (18 men, 10 women; age range, 49-84 years; mean age, 69.4 years). The clinical indication for MR examinations in these patients was the further evaluation of upper abdominal diseases (hepatocellular carcinoma=12, metastatic liver tumors=7, bile duct cancer=3, gallbladder cancer=3, small pancreatic lesions=2, common bile duct stone=1) suspected by ultrasound or blood examinations. Patients were required to fast for at least five hours before CT and MR examinations.

## **DECT**

DECT was performed with a dual-source CT scanner (SOMATOM FORCE; Siemens, Forchheim, Germany) equipped with 2 x-ray tubes (tube A, low kilovoltage; tube B, high kilovoltage) in dual-energy mode, and 2 corresponding detectors were installed with an angular offset of 95°. Craniocaudal CT was performed with a dual-energy protocol (detector collimation, 128 × 0.6 mm; pitch, 0.6; gantry rotation time, 0.5 second; matrix, 512 × 512). Tube voltages were set at 100 and 150 kVp (tubes A and B, respectively), using a 0.6-mm tin filter in tube B.

## **Six-point Dixon MRI**

MRI was conducted with a 3.0-T MR system (Magnetom Prisma; Siemens Healthcare, Erlangen, Germany) and an 18-channel body coil based on our routine abdominal protocol. Breath-hold T2\*-corrected six-point Dixon T1-weighted imaging was performed to obtain fat

fraction images using the following parameters: TR, 9 ms; TE, 1.12, 2.46, 3.69, 4.92, 6.15, 7.37 ms; flip angle, 4°; acquisition matrix, 111 × 160; parallel imaging factor, 2; slice thickness, 3.5 mm; field of view, 306 × 350 mm; and bandwidth, 1080 Hz/pixel. The FVF map was automatically calculated and reconstructed.

### **Image analyses**

All images were evaluated on a picture archiving and communication system (PACS) workstation (Shade Quest, Yokogawa Medical, Tokyo) by 2 radiologists (6 and 30 years' experience) in consensus, without access to the prospective reports or any clinical information. Regions of interest (ROIs) (size, 80-100 mm<sup>2</sup>) were placed at the head and body/tail of the pancreas on FVF maps generated using a dedicated dual-energy post-processing software program (Syngo via; Siemens Healthcare) with the multi-material decomposition (MMD) algorithm on DECT by the junior radiologist to measure the FVF (%) in the pancreas and then verified for accuracy by the senior radiologist.

Effort was made to draw the ROI circles as large as possible while avoiding the pancreatic duct, vessels and retroperitoneal fat. The FVF (%) of the pancreas was also measured on FVF maps obtained by six-point Dixon T1-weighted imaging at the same location as the FVF map of DECT (Figure 1). The FVF (%) of the pancreatic parenchyma measured by DECT was compared with that measured by Dixon MRI. In addition, CT attenuation values (HU) of the pancreas were also measured on unenhanced CT images at the same location as the FVF map of DECT and compared with the FVF (%) of the pancreas.

### **Statistical analyses**

The relationship between the FVF (%) measured by DECT and that measured by Dixon MRI was assessed using a Pearson's correlation coefficient analysis. The correlation between the FVF (%) measured by Dixon MRI and the CT attenuation value (HU) measured on

unenhanced 100-kV CT was also assessed using a Pearson's correlation coefficient analysis. A p-value <0.05 was considered to indicate a statistically significant difference. All statistical analyses were conducted using the SPSS software program (version 12 for Windows; SPSS, Chicago, IL, USA).

## **Results**

FVF maps of the pancreas were successfully obtained by both DECT and six-point Dixon MRI in all patients. The median FVF (%) values of the head and body/tail of the pancreas on DECT were 8.1% (range, 1.2%-80.9%) and 9.4% (range, 0.3%-43.7%), respectively. The median FVF (%) values of the head and body/tail of the pancreas on Dixon MRI were 12.2% (range, 0.1%-81.2%) and 14.2% (range, 0%-40.8%), respectively. The relationships between the FVF (%) measured by DECT and that measured by Dixon MRI are shown in Figure 2. The FVF (%) measured by DECT showed a significant correlation with that measured by Dixon MRI in the head of the pancreas ( $r=0.894$ ,  $P<0.001$ ) as well as the body/tail of the pancreas ( $r=0.957$ ,  $P<0.001$ ).

The median CT attenuation values (HU) of the head and body/tail of the pancreas measured on unenhanced 100-kV CT were 29.5 (range, -77.6-54.2) and 39.9 (range, -4.4-144.8), respectively. Figure 3 shows the comparison between the FVF (%) measured by Dixon MRI and the CT attenuation value (HU) measured on unenhanced 100-kV CT. There was a good correlation between the FVF (%) measured by Dixon MRI and the CT attenuation value measured on unenhanced CT in the head of the pancreas ( $r=-0.960$ ,  $P<0.001$ ), while the FVF (%) measured by Dixon MRI showed a weak correlation with the CT attenuation value in the body/tail of the pancreas ( $r=-0.416$ ,  $P=0.028$ ).

## **Discussion**

Visceral adipose tissue is a known risk factor for the development of metabolic syndrome and cardiovascular diseases [1,2]. In the pancreas, several studies have shown that increased intrapancreatic fat is associated with type 2 diabetes [3,4] and with the exacerbation of acute pancreatitis because of its lipotoxicity [16]. Therefore, the noninvasive quantification of pancreatic fat is clinically important.

The present study showed that there was a significant positive correlation between the FVF (%) measured by DECT and that measured by Dixon MRI in the pancreas. This indicates that FVF measurement on DECT is useful for the quantification of pancreatic steatosis, since six-point Dixon MRI has been used as a highly accurate technique for quantifying fat content of abdominal organs. Notably, FVF measurement using DECT is an advanced technique that can only be applied using the latest CT systems. However, given that CT can be performed conveniently with a short acquisition time and has a higher potential throughput and better cost-effectiveness than MRI, DECT may be an extremely practical, noninvasive imaging modality for the quantification of pancreatic fat when it becomes widely available in clinical practice.

Some studies have suggested that pancreatic fat deposition might play a role in the pathogenesis of type 2 diabetes as a result of beta cell dysfunction and impaired insulin secretion [3,4,17]. In addition, pancreatic steatosis might begin with a decline in insulin secretion from the very early stage of glucose intolerance [18]. Therefore, the quantification of the severity of pancreatic steatosis by DECT will be important for the surveillance of impaired glucose tolerance, although the mechanism by which pancreatic steatosis might induce decreased insulin secretion in the early stage of the disease is not clearly understood. Further clinical studies in patients with pancreatic endocrine dysfunction as well as surveillance of impaired glucose tolerance will be necessary in order to validate the present results derived from the DECT quantification of pancreatic fat.

Several imaging modalities have been developed to assess pancreatic steatosis. Ultrasonography (US) is simple but is of limited value in the evaluation of the entire pancreas due to the location of the pancreas behind the stomach or colon [19]. In addition, US provides only a qualitative assessment of pancreatic steatosis [20]. Conventional single-energy CT has also been used to assess pancreatic steatosis. However, CT attenuation measurements are semiquantitative, with the pancreatic fat concentration merely inferred [21], and these assessments can be affected by other components in the pancreas, such as manganese [22], which can mask changes in CT attenuation induced by fatty infiltration [23].

A recent study showed that pancreatic fat measurements on unenhanced CT images and in histologic specimens obtained from pancreatectomy were significantly correlated [24]. On comparing the FVF (%) measured by Dixon MRI and the CT attenuation value (HU) measured on unenhanced 100-kV CT in this study, the FVF in the head of the pancreas correlated well with the CT attenuation value, while the FVF in the body/tail of the pancreas showed only a weak correlation with the CT attenuation value. In our study, the degree of pancreatic steatosis was relatively severe in the body/tail compared with the head of the pancreas. These results suggest that the FVF might be a more reliable indicator of pancreatic steatosis than the CT attenuation values derived from conventional CT images without a dual-energy mode.

Several limitations associated with the present study warrant mention. First, a selection bias may have been unavoidable due to the retrospective nature of this study. In addition, our study enrolled a relatively small number of patients with various pathological diagnoses, which may have been a confounding factor. Second, there was no histological correlation in the degree of pancreatic steatosis. However, several MR studies have shown the effectiveness of the Dixon MR technique for the quantification of the tissue fat content [25,26]. Third, the size of the subgroup with moderate-to-severe pancreatic steatosis (FVF  $\geq$ 20%) was small. The validity of our results should be investigated in a larger cohort group involving moderate-to-

severe fat infiltration of the pancreas. Fourth, regarding the ROI measurements, it would have been better to measure the FVF of the head, body and tail of the pancreas separately (three ROIs) for a more precise evaluation. However, ROI measurement from the pancreatic tail was often difficult because of age-related atrophic changes or hypoplasia.

In conclusion, DECT has potential utility for quantifying the degree of fatty degeneration of the pancreas. Further studies will be required in order to determine the usefulness of this technique for the early detection of impaired insulin secretion to prevent the development of diabetes.

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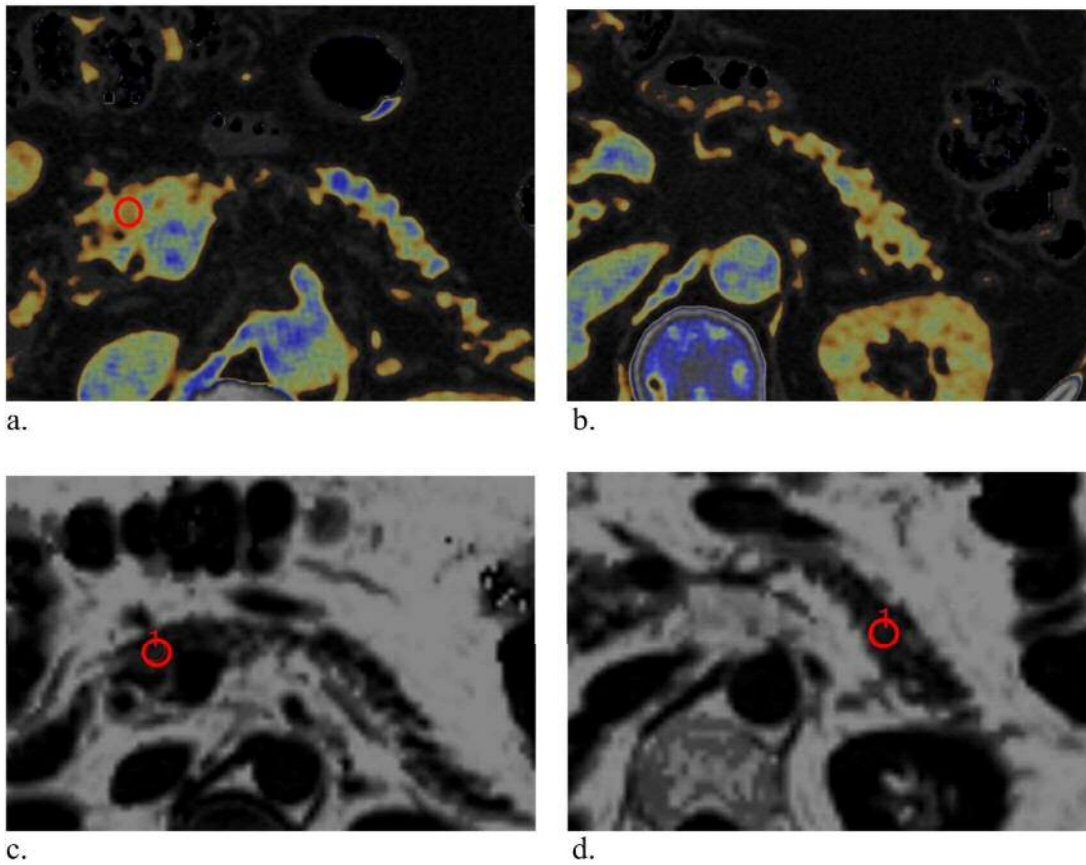
## Figure legends

**Figure 1.** Measurement of fat volume fraction (FVF) (%).

a) and b) FVF maps generated from DECT. c) and d) FVF maps obtained by six-point Dixon T1-weighted imaging. Red circles in the head and the body/tail of the pancreas represent ROIs placed for the measurement of FVF (%). ROIs were initially placed on the FVF maps of DECT, and then were placed on the FVF maps of Dixon MRI at the same location as the FVF map of DECT.

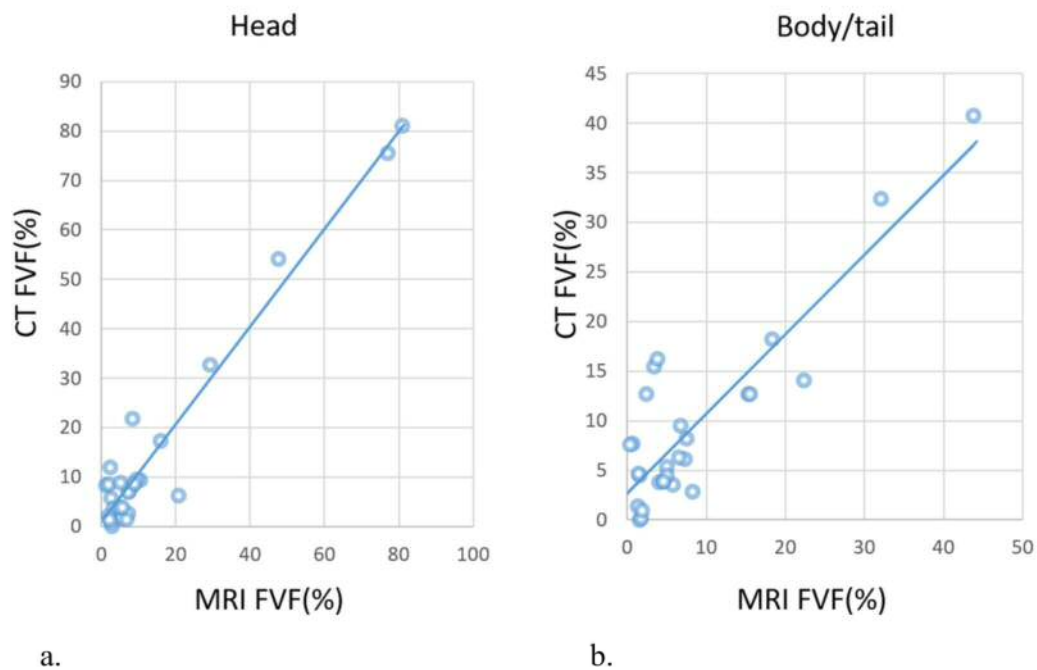
**Figure 2.** a) and b) The relationship between FVF (%) measured by DECT and FVF (%) measured by Dixon MRI in the head (a) and the body/tail (b) of the pancreas. FVF (%) measured by DECT showed significant correlation with FVF (%) measured by Dixon MRI in both head ( $r=0.969$ ,  $P<0.001$ ) and body/tail ( $r=0.877$ ,  $P<0.001$ ) of the pancreas.

**Figure 3.** a) and b) The relationship between FVF (%) measured by Dixon MRI and CT attenuation value (HU) measured on unenhanced 100kV CT in the head (a) and the body/tail (b) of the pancreas. CT attenuation value measured on unenhanced CT in the head of the pancreas showed good correlation with FVF (%) measured by Dixon MRI ( $r=-0.956$ ,  $P<0.001$ ) while it showed weak correlation with FVF (%) measured by Dixon MRI in the body/tail ( $r=-0.416$ ,  $P<0.05$ ).

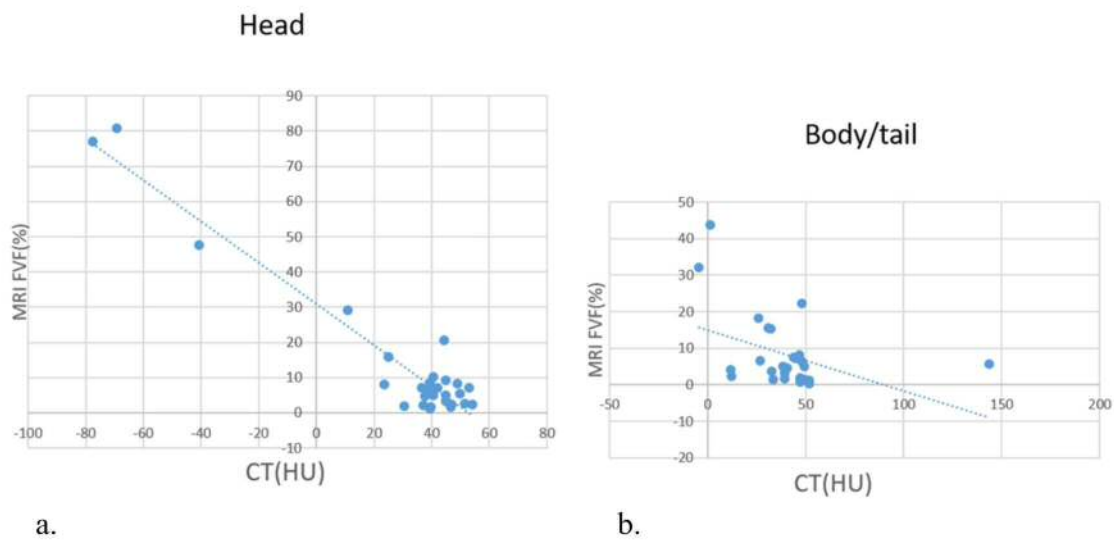


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