



Optimal target b-value on computed diffusion-weighted magnetic resonance imaging for visualization of pancreatic ductal adenocarcinoma and focal autoimmune pancreatitis

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Abstract

Purpose: To compare computed diffusion-weighted imaging (cDWI) feasibility with that of directly acquired DWI for visualizing pancreatic ductal adenocarcinoma (PDAC) and focal autoimmune pancreatitis (AIP).

Methods: From April 2012 to January 2017, 135 patients with PDAC ($n=111$) or focal AIP ($n=24$) were retrospectively enrolled. They underwent DWI with b-values of 0, 500, and 1000 s/mm². From DWI₀ and DWI₁₀₀₀, we generated cDWIs with targeted b-values of 1500, 2000, and 3000 s/mm². The lesions' signal intensities, image quality, signal-intensity ratio (SIR) of lesions and pancreatic parenchyma to spinal cord, and lesion-to-pancreatic parenchyma contrast ratio (CR) were compared among the five DWI protocols (DWI₅₀₀, DWI₁₀₀₀, cDWI₁₅₀₀, cDWI₂₀₀₀, and cDWI₃₀₀₀). SIR was analyzed by receiver operating characteristic (ROC) analyses.

Results: DWI₅₀₀, DWI₁₀₀₀, and cDWI₁₅₀₀ had higher image quality than cDWI₂₀₀₀ and cDWI₃₀₀₀ ($P < 0.001$). The incidence of clear hyperintense PDAC was highest on cDWI₂₀₀₀, followed by cDWI₁₅₀₀, and cDWI₃₀₀₀ ($P < 0.001$ – 0.002), while the incidence of clear hyperintense AIP was higher on DWI₁₀₀₀, cDWI₁₅₀₀, and cDWI₂₀₀₀ than on DWI₅₀₀ and cDWI₃₀₀₀ ($P = 0.001$ – 0.022). SIRs decreased whereas CRs increased as the b-value increased, for both PDAC and AIP. The area under the ROC curve (AUC) of SIR_{lesion} was significantly lower on cDWI₁₅₀₀ than on cDWI₂₀₀₀ and cDWI₃₀₀₀ ($P < 0.001$).

Conclusion: cDWI₁₅₀₀ or cDWI₂₀₀₀ generated from b-values of 0 and 1000 s/mm² were the most effective for visualizing PDAC and focal AIP; however, the SIR_{lesion} AUC was significantly lower on cDWI₁₅₀₀ than on cDWI₂₀₀₀ and cDWI₃₀₀₀.

Keywords: magnetic resonance imaging; computed diffusion-weighted imaging; pancreas; adenocarcinoma; autoimmune pancreatitis

Introduction

Pancreatic cancer is the seventh leading cause of global cancer deaths in industrialized countries [1] and the third leading cause of cancer-related deaths in the United States [2]. Pancreatic ductal adenocarcinoma (PDAC) is the most common type of pancreatic cancer, accounting for 90% of all pancreatic cancers [3]. Despite the advancement of diagnostic techniques, early diagnosis of PDAC is still challenging, and its incidence is estimated to continue to increase [4]. Autoimmune pancreatitis (AIP) is a rare autoimmune disorder that can cause similar symptoms to PDAC [5]. Diffuse enlargement of the pancreas (sausage-like) and low-attenuating rim-like capsule on contrast-enhanced computed tomography are well-known typical imaging findings of AIP [5]; however, 21.7–60.0% of AIP present as focal mass-forming pancreatitis [6-9]. Treatment options are completely different between AIP and PDAC; therefore, accurate differential diagnosis is required. Several reports have shown that magnetic resonance imaging (MRI) might be useful for distinguishing focal AIP from PDAC [6-12]; however, such differentiation remains challenging.

Diffusion-weighted imaging (DWI) has been used routinely in daily clinical practice owing to its excellent contrast resolution between lesions and the pancreatic parenchyma, without the use of contrast agents. Its usefulness in the detection and characterization of pancreatic diseases has been reported [13-15]. DWI with b-values of 800–1000 s/mm² is widely used; however, higher b-values can be useful for the detection and characterization of

PDAC [16] because diffusion-restricted tissues show relatively higher signal intensity (SI) than the normal pancreatic parenchyma with the increasing b-values. However, DWI with higher b-values has certain disadvantages, including the longer acquisition time and poorer image quality [16]. Computed DWI (cDWI) is a technique that can synthesize arbitrary target b-value DWI from a set of directly acquired b-value images by voxel-wise fitting [17]. cDWI can generate images with a higher diffusion effect than that achieved by clinical MRI units, as well as a higher signal-to-noise ratio in shorter acquisition time than with directly acquired DWI [17].

The usefulness of cDWI has been reported for several organs, such as the prostate [18], breast [19], liver [20], uterus [21], ovary [22], and middle ear [23]; however, only few reports are available on pancreatic cDWI [24, 25]. Moreover, several studies have reported the usefulness of DWI for AIP diagnosis [9-11], whereas the usefulness of cDWI in AIP has not been clarified. Thus, the purpose of this study was to assess the feasibility of cDWI in visualizing PDAC and focal AIP comparison with that of directly acquired DWI.

Materials and Methods

Patients

This single-center, retrospective, cross-sectional study was approved by the relevant institutional review board, who waived the requirement for obtaining written informed patient

consent due to the retrospective nature of the study. Patients with PDAC or AIP were consecutively enrolled between April 2012 and January 2017. The following inclusion criteria were used for PDAC: i) pathologically diagnosed by fine needle aspiration or resection, and ii) availability of 3.0-T MRI data within three months before fine needle aspiration or resection; for AIP, the criteria were: i) clinically diagnosed based on clinical diagnostic criteria in Japan (JPS2011) [26], ii) availability of 3.0-T MRI data before steroid therapy, and iii) focal type.

Of the 181 patients enrolled for the study, 46 patients were excluded (Fig. 1). The final study cohort consisted of 135 patients (mean age, 68.2 ± 10.2 [range, 40–88] years), including 111 patients with PDAC and 24 with AIP (Fig. 1).

DWI protocols

All MRI examinations were performed using a 3.0-T MR system (Discovery 750; GE Healthcare, Waukesha, WI, USA) with a 32-channel phased-array coil. The DWI data were acquired in the transverse plane by respiratory-triggered single-shot echo-planar imaging with water-selective excitation, using the respiratory triggering technique. Sections of 5 mm in thickness with no intersection gap were used to cover the pancreas. The following three b-values were used: 0, 500, and 1000 s/mm^2 , with three axes [x (RL), y (AP), and z (SI)] motion-probing gradient directions. The pulse sequence parameters were as follows:

repetition time, 3000–10000 ms (based on the respiratory interval); echo time, 70 ms; flip angle, 90°; field of view, 36 × 36 cm; matrix, 128 × 192; number of excitations, 8; sensitivity encoding acceleration factor, 2; and acquisition time, 150–180 s. Then, DW images with b-values of 0 and 1000 s/mm² were digitally transferred to dedicated post-processing software (SYNAPSE VINCENT; FUJIFILM Medical, Tokyo, Japan), and cDW images were generated with target b-values of 1500 (cDWI₁₅₀₀), 2000 s/mm² (cDWI₂₀₀₀), and 3000 s/mm² (cDWI₃₀₀₀) by fitting a mono-exponential model, to compare them with the directly acquired DW images with b-values of 500 (DWI₅₀₀) and 1000 s/mm² (DWI₁₀₀₀).

Qualitative image analysis

The directly acquired DW images (DWI₅₀₀ and DWI₁₀₀₀) and the cDW images (cDWI₁₅₀₀, cDWI₂₀₀₀, and cDWI₃₀₀₀) were reviewed by two independent radiologists (with 11 and 3 years of clinical experience in abdominal MRI) who were blinded to the clinical data aside from the information that the patients had PDAC or AIP based on other MRI sequences. For each dataset, the two radiologists evaluated the image quality using a 4-point visual score (4, excellent = the whole pancreas is clearly shown without artifacts; 3, good = minor degradation is present but suitable for the evaluation of the whole pancreas; 2, fair = only part of the pancreas is visible; 1, poor = the pancreas is barely visible) (Fig. 2a) and classified the SIs of the lesions, as follows: type 1, clearly demarcated hyperintensity relative to the

surrounding pancreas; type 2, hyperintensity, but with an unclear distal (tail sided) border because of hyperintense distal pancreatic parenchyma; and type 3, iso-intensity relative to the surrounding pancreas or no evidence of the lesions (invisible) [16, 24] (Fig. 2b).

Quantitative image analysis

The same radiologists who performed qualitative image analysis also conducted quantitative measurements for the following: (a) the signal-intensity ratio (SIR) of the lesions and proximal (head sided) or distal (tail sided) pancreatic parenchyma to spinal cord and (b) the contrast ratio (CR) of the lesions to the proximal or distal pancreatic parenchyma, using four manually-defined, circular or oval regions of interest (ROIs) (proximal and distal pancreatic parenchyma, lesions, and spinal cord) for each DW image. The ROIs were first placed on DWI₅₀₀, and then, the size, shape and location of the ROIs were kept constant for all images of each patient by applying a copy-and-paste function on the monitor. The ROIs were carefully placed to avoid pancreatic ducts, cystic lesions, vessels, peripancreatic fat or artifacts within the ROIs. If adequate areas were not available for measuring the proximal or distal pancreatic parenchyma due to the locations of the lesions, the sections were excluded from the evaluations. The SIR and CR were calculated using the following formulae [16,24], using the average SI for the calculations:

SIR of the proximal pancreatic parenchyma to the spinal cord ($SIR_{proximal}$) = SI of the proximal

pancreatic parenchyma/SI of the spinal cord

SIR of the distal pancreatic parenchyma to the spinal cord (SIR_{distal}) = SI of the distal

pancreatic parenchyma/SI of the spinal cord

SIR of the lesion to the spinal cord (SIR_{lesion}) = SI of the lesion/SI of the spinal cord

CR of the lesion to the proximal pancreatic parenchyma ($CR_{proximal}$) = (SI of the lesion – SI of the proximal pancreatic parenchyma)/(SI of the lesion + SI of the proximal pancreatic parenchyma)

CR of the lesion to the distal pancreatic parenchyma (CR_{distal}) = (SI of the lesion – SI of the distal pancreatic parenchyma)/(SI of the lesion + SI of the distal pancreatic parenchyma)

Statistical analyses

Patient demographic data, SIR, and CR were compared between PDAC and AIP by Wilcoxon test and χ^2 test. The size and location of the lesions were determined on MR images. Receiver operating characteristic (ROC) analyses were performed for SIRs and CRs that were significantly different between PDAC and AIP. The image quality was compared among the five DWI protocols by Friedman test, followed by Scheffe's paired comparison. The SI types of lesions were compared among the five DWI protocols by χ^2 test, followed by Wilcoxon signed-rank test. The SIRs and CRs were compared among the five DWI protocols by Friedman test. Cohen's kappa values (κ) or intraclass correlation coefficients (r) were

calculated to assess interobserver agreement. Agreement was considered excellent for κ or $r > 0.8$, good for $0.6 < \kappa$ or $r \leq 0.8$, moderate for $0.4 < \kappa$ or $r \leq 0.6$, fair for $0.2 < \kappa$ or $r \leq 0.4$, and poor for κ or $r \leq 0.2$. Coefficient of variation of SIRs and CRs were also calculated and compared between two readers by F test. Data from the first reader were used for the qualitative and quantitative analyses, while those from the second reader were used to calculate interobserver agreement.

All statistical analyses were performed using JMP software (version 14.2.0; SAS Institute Inc., Cary, NC, USA) and BellCurve for Excel (version 3.20; Social Survey Research Information Co., Ltd., Tokyo, Japan). P -values < 0.05 were considered statistically significant.

Results

Patients' characteristics

The patients' demographics and clinical characteristics are presented in Table 1. A significant difference was observed in the size of the lesions between PDAC and AIP ($P = 0.001$). Other factors including age, sex, body weight, and location of the lesions were not significantly different between groups ($P = 0.059$ – 0.817 ; Table 1).

Qualitative image analysis

The breakdown of image quality using the five DWI protocols is shown in Table 2 and Fig.

3a. There was a significant difference among the five DWI protocols ($P < 0.001$). In the paired comparison, no significant differences were observed between DWI₅₀₀ and DWI₁₀₀₀ ($P = 0.968$), DWI₅₀₀ and cDWI₁₅₀₀ ($P = 0.183$), and DWI₁₀₀₀ and cDWI₁₅₀₀ ($P = 0.548$). In all other combinations, DWI protocols with smaller b-values showed significantly higher median image quality than those with higher b-values (all $P < 0.001$).

The breakdown of SI types of lesions using the five DWI protocols is shown in Table 2 and Fig. 3b. In PDAC, there were significant differences among the five DWI protocols ($P < 0.001$). In the paired comparison, no significant difference was observed between cDWI₁₅₀₀ and cDWI₃₀₀₀ ($P = 0.627$). A higher incidence of type 1 lesions was found with cDWI₂₀₀₀ than with cDWI₃₀₀₀ ($P = 0.002$). In all other combinations, the incidence of type 1 lesions was significantly higher on DWI protocols with higher than with lower b-values ($P < 0.001$ – 0.002). In AIP, there were significant differences among the five DWI protocols ($P = 0.015$). In the paired comparison, the incidence of type 1 lesions was significantly lower with DWI₅₀₀ and cDWI₃₀₀₀ than with other protocols ($P = 0.003$ for DWI₅₀₀ vs DWI₁₀₀₀, $P = 0.001$ for DWI₅₀₀ vs cDWI₁₅₀₀ and for DWI₅₀₀ vs cDWI₂₀₀₀, and $P = 0.022$ for cDWI₃₀₀₀ vs cDWI₁₅₀₀ and for cDWI₃₀₀₀ vs cDWI₂₀₀₀). In all other combinations, no significant differences were observed ($P < 0.100$ – 0.328).

Quantitative image analysis

The mean size of ROIs was as follows: PDAC, $224.1 \pm 303.6 \text{ mm}^2$; AIP, $92.9 \pm 75.1 \text{ mm}^2$; proximal pancreatic parenchyma, $126.0 \pm 49.3 \text{ mm}^2$; distal pancreatic parenchyma, $133.3 \pm 70.7 \text{ mm}^2$; spinal cord, $28.3 \pm 5.8 \text{ mm}^2$.

The SIR and CR using the five DWI protocols are shown in Table 2 and Fig. 4.

There were significant differences in both ratios among the five DWI protocols ($P < 0.001$) for both PDAC and AIP. $\text{SIR}_{\text{proximal}}$, $\text{SIR}_{\text{lesion}}$, and $\text{SIR}_{\text{distal}}$ decreased, whereas $\text{CR}_{\text{proximal}}$ and $\text{CR}_{\text{distal}}$ increased, as the b-value increased (Fig. 4). Comparison of PDAC and AIP showed significantly higher $\text{SIR}_{\text{proximal}}$ and $\text{SIR}_{\text{lesion}}$ on all cDWIs, and significantly higher $\text{SIR}_{\text{distal}}$ on cDWI₂₀₀₀ and cDWI₃₀₀₀ in AIP than in PDAC ($P < 0.001$ – 0.031 ; Table 3). In contrast, there were no significant differences for $\text{CR}_{\text{proximal}}$ and $\text{CR}_{\text{distal}}$ on all DWI protocols between PDAC and AIP ($P = 0.194$ – 0.961 ; Table 3). The area under the ROC curve (AUC) of $\text{SIR}_{\text{lesion}}$ was significantly lower on cDWI₁₅₀₀ than on cDWI₂₀₀₀ and cDWI₃₀₀₀ ($P < 0.001$), whereas there was no significant difference in the AUC of $\text{SIR}_{\text{lesion}}$ between cDWI₂₀₀₀ and cDWI₃₀₀₀ ($P = 0.056$). Moreover, the AUC of $\text{SIR}_{\text{distal}}$ was significantly higher on cDWI₃₀₀₀ than on cDWI₂₀₀₀ ($P = 0.001$), while that of $\text{SIR}_{\text{proximal}}$ was not significantly different among cDWI₁₅₀₀, cDWI₂₀₀₀, and cDWI₃₀₀₀ ($P = 0.514$ – 1.000 ; Fig. 5).

Interobserver agreement and coefficient of variation

Interobserver agreement was excellent for the SI types of lesions on DWI₅₀₀, DWI₁₀₀₀,

cDWI₁₅₀₀, and cDWI₂₀₀₀ ($r = 0.817\text{--}0.848$) and for CR_{proximal} on DWI₅₀₀ ($\kappa = 0.814$) and was good for other protocols (r or $\kappa = 0.575\text{--}0.790$; Table 4). There was no significant difference in all the coefficient of variation of SIR and CR between two readers ($P = 0.106\text{--}0.995$; Table 5). Case examples are shown in Figs. 6 and 7.

Discussion

This retrospective study revealed that image quality was significantly higher with DWI₅₀₀, DWI₁₀₀₀, and cDWI₁₅₀₀ than with cDWI₂₀₀₀ and cDWI₃₀₀₀. The incidence of clear hyperintense (type 1) PDAC was the highest on cDWI₂₀₀₀, followed by cDWI₁₅₀₀ and cDWI₃₀₀₀. The incidence of clear hyperintense (type 1) AIP was significantly higher on DWI₁₀₀₀, cDWI₁₅₀₀, and cDWI₂₀₀₀ than on DWI₅₀₀ and cDWI₃₀₀₀. Interobserver agreement was good to excellent for all items. These results suggest that cDWI₁₅₀₀ or cDWI₂₀₀₀ are the most effective among the five DWI protocols, consistent with a previous report [24].

It is challenging to obtain directly acquired DW images at b-values of 1500 s/mm² for the pancreas because the image quality becomes worse and the acquisition time becomes longer as the b-value increases. cDWI can produce DW images without decreasing the signal and in a shorter acquisition time than with directly acquired DWI. Thus, cDWI₁₅₀₀ generated from DW images with b-values of 0 and 1000 s/mm² may be useful for pancreas imaging. Image contrast on DWI varies greatly with the b-value. At higher b-values, tissues with high

water molecule path lengths, such as the pancreatic parenchyma, tend to lose signal rapidly, while tissues with restricted water diffusion, including PDAC, yield relatively higher signals [27, 28]. This explains why the incidence of clear hyperintense (type 1) PDAC on cDW images with b-values ≥ 1500 s/mm² was higher than that on DWI₅₀₀ and DWI₁₀₀₀. Several reports have shown a lower apparent diffusion coefficient value for AIP than for PDAC with b-values 500–1000 s/mm² [9, 11, 12, 29], which might explain why the incidence of clear hyperintense (type 1) AIP on DWI₁₀₀₀ was equivalent to that on cDWI₁₅₀₀, and cDWI₂₀₀₀.

In our quantitative image analysis, all SIRs (SIR_{proximal}, SIR_{lesion}, and SIR_{distal}) decreased and all CRs (CR_{proximal} and CR_{distal}) increased as the b-value increased. The result of SI decrease can be explained by the fact that higher b-values yield lower signal-to-noise ratio [27, 28]. The result of CR_{distal} is consistent with that of a previous study, while the result of CR_{proximal} is not [24]. The authors reported no significant difference in PDAC to proximal pancreatic parenchymal CR among DWI₁₀₀₀, cDWI₁₅₀₀, and cDWI₂₀₀₀. This discrepancy may be caused by the different MRI scanners, scanning parameters, and post-processing software used. Further studies are needed to determine the optimal settings of cDWI for PDAC. When comparing PDCA and AIP, SIR_{proximal} and SIR_{lesion} on all cDWI protocols and SIR_{distal} on cDWI₂₀₀₀ and cDWI₃₀₀₀ were significantly higher in AIP than in PDAC. The results of SIR_{lesion} are consistent to those of previous reports showing lower apparent diffusion coefficient values in AIP than in PDAC when using b-values 500–1000 s/mm² [9, 11, 12, 29].

Increased cellularity due to dense infiltration of plasma cells and lymphocytes, chronic inflammatory changes with fibrosis, and edematous changes in AIP may be associated to the high signal intensity [5, 30]. It is not clear why $SIR_{proximal}$ and SIR_{distal} AIP were higher in AIP than in PDAC; however, the surrounding pancreatic parenchyma may also be infiltrated with plasma cells and lymphocytes, although this cannot be detected by imaging because of its autoimmune nature [31]. In this study, we found no significant differences in $CR_{proximal}$ and CR_{distal} on all DWI protocols between PDAC and AIP. Therefore, it may be difficult to distinguish AIP from PDAC by visual evaluation. The AUC of SIR_{lesion} on $cDWI_{1500}$ was significantly lower than that on $cDWI_{2000}$ and $cDWI_{3000}$, whereas there was no significant difference between the AUCs of SIR_{lesion} on $cDWI_{2000}$ and $cDWI_{3000}$. The AUC of SIR_{distal} on $cDWI_{3000}$ was significantly higher than that on $cDWI_{2000}$ ($P = 0.001$). These results indicate that $cDWI_{2000}$ and $cDWI_{3000}$ are better for quantitative analysis than $cDWI_{1500}$; however, lower image quality may be a problem in clinical practice. Validation studies are desired as a next step.

Our study has some limitations. First, AIP of various inflammatory activities was included in this study. The phase of inflammation can influence signal intensity on DWI because of differences in dense infiltration of plasma cells and lymphocytes or edematous changes. Second, significant differences in the size of lesions were observed between PDAC and AIP, possibly due to the retrospective study design. Degeneration or necrotic changes are

observed more frequently in larger lesions, especially in PDAC, which can also influence the signal intensity of DWI. Third, the retrospective nature and relatively small number of AIP cases in this study were also limitations. Further prospective studies with a larger sample size are necessary.

In summary, cDWI₁₅₀₀ or cDWI₂₀₀₀ generated from DW images obtained with b-values of 0 and 1000 s/mm² were found to be the most effective among the five tested DWI protocols (DWI₅₀₀, DWI₁₀₀₀, cDWI₁₅₀₀, cDWI₂₀₀₀, and cDWI₃₀₀₀) for visualizing PDAC and focal AIP; however, the AUC of SIR_{lesion} was significantly lower on cDWI₁₅₀₀ than on cDWI₂₀₀₀ and cDWI₃₀₀₀. Therefore, the combination of cDWI₁₅₀₀ and cDWI₂₀₀₀/cDWI₃₀₀₀ may be effective in diagnosing AIP.

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Figure legends

Fig. 1. Flowchart of patients' enrollment

Of the 181 patients enrolled for the study, 46 patients were excluded. The final study cohort consisted of 135 patients, including 111 patients with pancreatic ductal adenocarcinoma and 24 with autoimmune pancreatitis.

Abbreviations: FNA, fine needle aspiration; MRI, magnetic resonance imaging

Fig. 2. Example images of image quality grading and signal intensity types of lesions

(a) Image quality was assessed using a 4-point visual score (4, excellent = the whole pancreas is clearly shown without artifacts; 3, good = minor degradation is present but suitable for the evaluation of the whole pancreas; 2, fair = only part of the pancreas is visible; 1, poor = the pancreas is barely visible)

(b) Signal intensity types of lesions were classified as follows: type 1, clearly demarcated hyperintensity relative to the surrounding pancreas; type 2, hyperintensity, but with an unclear distal (tail sided) border of the lesions because of hyperintense distal pancreatic parenchyma; and type 3, iso-intensity relative to the surrounding pancreas or no evidence of the lesions (invisible).

Fig. 3. The breakdown of image quality and signal intensity types of lesions

(a) Image quality. There was a significant difference among the five diffusion-weighted imaging (DWI) protocols ($P < 0.001$).

(b) Signal intensity types of lesions. There was a significant difference among the five DWI protocols in both pancreatic ductal adenocarcinoma ($P < 0.001$) and autoimmune pancreatitis ($P = 0.015$).

Image quality was analyzed by Friedman test, and signal intensity types of lesions were analyzed by χ^2 test. Abbreviations: cDWI, computed diffusion-weight imaging

Fig. 4. Differences in signal intensity ratio and contrast ratio among the five diffusion-weighted imaging (DWI) protocols

$SIR_{proximal}$, SIR_{lesion} , and SIR_{distal} decreased, whereas $CR_{proximal}$ and CR_{distal} increased, as the b-value increased in both pancreatic ductal adenocarcinoma and autoimmune pancreatitis.

Abbreviations: cDWI, computed diffusion-weight imaging; $SIR_{proximal}$, signal intensity ratio of the proximal pancreatic parenchyma to the spinal cord; SIR_{lesion} , signal intensity ratio of the proximal pancreas to the lesion; SIR_{distal} , signal intensity ratio of the distal pancreatic parenchyma to the spinal cord; $CR_{proximal}$, contrast ratio of the lesion to the proximal pancreatic parenchyma; CR_{distal} , contrast ratio of the lesion to the distal pancreatic parenchyma.

Fig. 5. Receiver operating characteristic analysis of signal intensity ratio

The AUC of SIR_{lesion} was significantly lower on cDWI₁₅₀₀ than on cDWI₂₀₀₀ and cDWI₃₀₀₀ ($P < 0.001$); there was no significant difference between the AUCs of SIR_{lesion} on cDWI₂₀₀₀ and cDWI₃₀₀₀ ($P = 0.056$). The AUC of SIR_{distal} was significantly higher on cDWI₃₀₀₀ than on cDWI₂₀₀₀ ($P = 0.001$). The AUC of SIR_{proximal} was not significantly different among cDWI₁₅₀₀, cDWI₂₀₀₀, and cDWI₃₀₀₀ ($P = 0.514-1.000$).

The AUCs were compared by χ^2 test. Abbreviations: cDWI, computed diffusion-weight imaging; SIR_{proximal}, signal intensity ratio of the proximal pancreatic parenchyma to the spinal cord; SIR_{lesion}, signal intensity ratio of the proximal pancreas to the lesion; SIR_{distal}, signal intensity ratio of the distal pancreatic parenchyma to the spinal cord; AUC, area under the curve.

Fig. 6. Representative images of pancreatic ductal adenocarcinoma in a 78-year-old woman

Arterial phase of gadoxetate disodium-enhanced 3D fat-saturated T1-weighted imaging (repetition time/echo time, 3.44/1.43; flip angle, 12°) shows a hypointense lesion measuring 22 mm in diameter (arrow) in the pancreatic tail. On diffusion-weighted imaging (DWI) with a b-value of 500 s/mm² (DWI₅₀₀), the lesion (arrow) shows hyperintensity with an unclear distal border (type 2). On DWI with a b-value of 1000 s/mm² (DWI₁₀₀₀) and computed DWI with target b-value of 1500 (cDWI₁₅₀₀), 2000 (cDWI₂₀₀₀), and 3000 (cDWI₃₀₀₀) s/mm², the

lesion (arrow) shows clear hyperintensity relative to the distal pancreatic parenchyma (dotted arrow) (type 1); however, on cDWI₃₀₀₀, the distal pancreatic parenchyma is almost invisible.

Fig. 7. Representative images of autoimmune pancreatitis in a 48-year-old man

Unenhanced 3D fat-saturated T1-weighted imaging (repetition time/echo time, 4.34/1.43; flip angle, 15°) shows a vague hypointense lesion measuring 18 mm in diameter (arrow) in the pancreatic tail. On diffusion-weighted imaging (DWI) with a b-value of 500 (DWI₅₀₀) and 1000 (DWI₁₀₀₀) s/mm², and computed DWI with target b-value of 1500 (cDWI₁₅₀₀), 2000 (cDWI₂₀₀₀), and 3000 (cDWI₃₀₀₀) s/mm², the lesion (arrow) shows hyperintensity relative to the proximal (arrowhead) and distal pancreatic parenchyma (dotted arrow) (type 1); however, on DWI₅₀₀, the border between the lesion and the pancreatic parenchyma is somewhat unclear.

Table 1. Patient characteristics

	Pancreatic ductal adenocarcinoma	Autoimmune pancreatitis	<i>P</i> value
Number of patients	111	24	
Age (years)	68.9 ± 9.7	64.9 ± 11.9	0.182
Sex (men:women)	69:42	16:8	0.817
Body weight (kg)	55.3 ± 10.3	59.2 ± 10.1	0.059
Lesion location (head:body:tail)	56:21:34	11:8:5	0.266
Lesion size (mm)	22.4 ± 12.4	15.2 ± 7.0	0.001*

Continuous variables were analyzed by Wilcoxon test and are expressed as mean ± standard deviation. Categorical variables were analyzed by the χ^2 test and are expressed as ratios. * $P < 0.05$

Table 2. Results of qualitative and quantitative image analysis on each protocol

	DWI ₅₀₀	DWI ₁₀₀₀	cDWI ₁₅₀₀	cDWI ₂₀₀₀	cDWI ₃₀₀₀	<i>P</i> value
All patients (<i>n</i> = 135)						
Image quality (4:3:2:1)	118:16:1:0	108:26:1:0	90:40:5:0	49:61:23:2	4:42:73:16	< 0.001*
Pancreatic ductal adenocarcinoma (<i>n</i> = 111)						
SI types (type 1:2:3)	26:54:31	55:49:7	83:26:2	91:19:1	85:17:9	< 0.001*
SIR _{proximal}	0.37 ± 0.12	0.30 ± 0.11	0.22 ± 0.10	0.16 ± 0.09	0.09 ± 0.08	< 0.001*
SIR _{lesion}	0.67 ± 0.21	0.59 ± 0.20	0.48 ± 0.21	0.40 ± 0.22	0.27 ± 0.23	< 0.001*
SIR _{distal}	0.51 ± 0.22	0.42 ± 0.19	0.30 ± 0.18	0.22 ± 0.17	0.13 ± 0.14	< 0.001*
CR _{proximal}	0.29 ± 0.15	0.31 ± 0.15	0.36 ± 0.19	0.39 ± 0.23	0.45 ± 0.31	< 0.001*
CR _{distal}	0.14 ± 0.16	0.19 ± 0.16	0.26 ± 0.21	0.32 ± 0.26	0.41 ± 0.34	< 0.001*
Autoimmune pancreatitis (<i>n</i> = 24)						

SI types (type 1:2:3)	13:10:1	21:3:0	22:2:0	22:2:0	18:4:2	0.015*
SIR _{proximal}	0.40 ± 0.12	0.34 ± 0.10	0.27 ± 0.08	0.21 ± 0.08	0.13 ± 0.07	< 0.001*
SIR _{lesion}	0.66 ± 0.17	0.63 ± 0.15	0.56 ± 0.17	0.51 ± 0.18	0.41 ± 0.24	< 0.001*
SIR _{distal}	0.47 ± 0.19	0.43 ± 0.19	0.36 ± 0.20	0.31 ± 0.21	0.22 ± 0.21	< 0.001*
CR _{proximal}	0.25 ± 0.11	0.31 ± 0.13	0.36 ± 0.15	0.41 ± 0.19	0.48 ± 0.25	< 0.001*
CR _{distal}	0.18 ± 0.13	0.21 ± 0.13	0.24 ± 0.16	0.28 ± 0.32	0.34 ± 0.42	< 0.001*

Image quality was analyzed by Friedman test and is expressed in ratios. SI types of lesions were analyzed by χ^2 test and are expressed in ratios.

SIR and CR were analyzed by Friedman test and are expressed as means ± standard deviation. * $P < 0.05$

Abbreviations: SI, signal intensity; SIR_{proximal}, signal intensity ratio of the proximal pancreatic parenchyma to the spinal cord; SIR_{lesion}, signal intensity ratio of the proximal pancreas to the lesion; SIR_{distal}, signal intensity ratio of the distal pancreatic parenchyma to the spinal cord; CR_{proximal}, contrast ratio of the lesion to the proximal pancreatic parenchyma; CR_{distal}, contrast ratio of the lesion to the distal pancreatic parenchyma.

Table 3. Differences in signal intensity ratio and contrast ratio between pancreatic ductal adenocarcinoma and autoimmune pancreatitis

	Pancreatic ductal adenocarcinoma ($n = 111$)	Autoimmune pancreatitis ($n = 24$)	P value
<hr/>			
SIR _{proximal}			
DWI ₅₀₀	0.37 ± 0.12	0.40 ± 0.12	0.181
DWI ₁₀₀₀	0.30 ± 0.11	0.34 ± 0.10	0.176
cDWI ₁₅₀₀	0.22 ± 0.10	0.27 ± 0.08	0.009*
cDWI ₂₀₀₀	0.16 ± 0.09	0.21 ± 0.08	0.003*
cDWI ₃₀₀₀	0.09 ± 0.07	0.13 ± 0.07	0.002*
<hr/>			
SIR _{lesion}			
DWI ₅₀₀	0.67 ± 0.21	0.66 ± 0.17	0.895
DWI ₁₀₀₀	0.59 ± 0.20	0.63 ± 0.15	0.190
cDWI ₁₅₀₀	0.48 ± 0.21	0.56 ± 0.17	0.031*
cDWI ₂₀₀₀	0.40 ± 0.22	0.51 ± 0.18	0.004*
cDWI ₃₀₀₀	0.27 ± 0.23	0.41 ± 0.24	0.001*
<hr/>			
SIR _{distal}			
DWI ₅₀₀	0.51 ± 0.22	0.47 ± 0.19	0.366
DWI ₁₀₀₀	0.42 ± 0.19	0.43 ± 0.19	0.649

cDWI ₁₅₀₀	0.30 ± 0.18	0.36 ± 0.20	0.069
cDWI ₂₀₀₀	0.22 ± 0.17	0.31 ± 0.21	0.007*
cDWI ₃₀₀₀	0.13 ± 0.14	0.22 ± 0.21	<0.001*
<hr/>			
CR _{proximal}			
DWI ₅₀₀	0.29 ± 0.13	0.25 ± 0.11	0.308
DWI ₁₀₀₀	0.32 ± 0.15	0.31 ± 0.13	0.961
cDWI ₁₅₀₀	0.36 ± 0.19	0.36 ± 0.15	0.922
cDWI ₂₀₀₀	0.39 ± 0.23	0.41 ± 0.19	0.801
cDWI ₃₀₀₀	0.45 ± 0.31	0.48 ± 0.25	0.760
<hr/>			
CR _{distal}			
DWI ₅₀₀	0.14 ± 0.16	0.18 ± 0.13	0.205
DWI ₁₀₀₀	0.19 ± 0.16	0.21 ± 0.13	0.428
cDWI ₁₅₀₀	0.26 ± 0.21	0.24 ± 0.16	0.777
cDWI ₂₀₀₀	0.32 ± 0.26	0.28 ± 0.20	0.413
cDWI ₃₀₀₀	0.42 ± 0.34	0.34 ± 0.27	0.194

Data were analyzed by Wilcoxon test and are expressed as mean ± standard deviation. * $P <$

0.05

Abbreviations: SIR_{proximal}, signal intensity ratio of the proximal pancreatic parenchyma to the spinal cord; SIR_{lesion}, signal intensity ratio of the proximal pancreas to the lesion; SIR_{distal},

signal intensity ratio of the distal pancreatic parenchyma to the spinal cord; CR_{proximal} , contrast ratio of the lesion to the proximal pancreatic parenchyma; CR_{distal} , contrast ratio of the lesion to the distal pancreatic parenchyma.

Table 4: Interobserver agreement between two radiologists

	DWI ₅₀₀	DWI ₁₀₀₀	cDWI ₁₅₀₀	cDWI ₂₀₀₀	cDWI ₃₀₀₀
Image quality	0.685 (0.535–0.835)	0.702 (0.563–0.842)	0.734 (0.641–0.826)	0.747 (0.648–0.846)	0.670 (0.582–0.758)
SI types of lesions	0.822 (0.737–0.907)	0.848 (0.764–0.933)	0.818 (0.706–0.931)	0.817 (0.690–0.945)	0.740 (0.616–0.864)
SIR _{proximal}	0.732 (0.643–0.802)	0.732 (0.643–0.801)	0.689 (0.589–0.768)	0.654 (0.546–0.741)	0.609 (0.490–0.705)
SIR _{lesion}	0.790 (0.696–0.858)	0.751 (0.635–0.835)	0.718 (0.589–0.811)	0.685 (0.538–0.793)	0.647 (0.495–0.761)
SIR _{distal}	0.699 (0.588–0.785)	0.673 (0.554–0.765)	0.653 (0.528–0.749)	0.616 (0.482–0.721)	0.575 (0.432–0.690)
CR _{proximal}	0.814 (0.729–0.874)	0.782 (0.670–0.859)	0.774 (0.660–0.854)	0.759 (0.638–0.843)	0.718 (0.581–0.815)
CR _{distal}	0.776 (0.687–0.842)	0.763 (0.670–0.833)	0.742 (0.642–0.817)	0.713 (0.605–0.795)	0.679 (0.561–0.770)

Cohen's kappa values for image quality and signal intensity types of lesions and intraclass correlation coefficients for SIR_{proximal}, SIR_{lesion},

SIR_{distal}, CR_{proximal}, and CR_{distal} are presented with the 95% confidence interval in parentheses.

Abbreviations: SI, signal intensity; SIR_{proximal}, signal intensity ratio of the proximal pancreatic parenchyma to the spinal cord; SIR_{lesion}, signal

intensity ratio of the proximal pancreas to the lesion; SIR_{distal} , signal intensity ratio of the distal pancreatic parenchyma to the spinal cord;

CR_{proximal} , contrast ratio of the lesion to the proximal pancreatic parenchyma; CR_{distal} , contrast ratio of the lesion to the distal pancreatic parenchyma

Table 5: Coefficient of variation between two radiologists

	DWI ₅₀₀			DWI ₁₀₀₀			cDWI ₁₅₀₀			cDWI ₂₀₀₀			cDWI ₃₀₀₀		
	R1	R2	<i>P</i>	R1	R2	<i>P</i>	R1	R2	<i>P</i>	R1	R2	<i>P</i>	R1	R2	<i>P</i>
SIR _{proximal}	0.290	0.270	0.955	0.328	0.297	0.528	0.404	0.370	0.209	0.534	0.431	0.465	0.818	0.543	0.374
SIR _{lesion}	0.302	0.260	0.413	0.329	0.300	0.803	0.411	0.402	0.288	0.515	0.472	0.461	0.710	0.610	0.646
SIR _{distal}	0.435	0.383	0.828	0.466	0.383	0.254	0.615	0.548	0.969	0.797	0.685	0.656	1.192	0.913	0.939
CR _{proximal}	0.449	0.417	0.466	0.490	0.632	0.106	0.523	0.797	0.116	0.589	0.899	0.254	0.674	1.092	0.136
CR _{distal}	0.996	0.755	0.492	0.776	0.674	0.836	0.759	0.648	0.800	0.783	0.731	0.830	0.814	0.715	0.995

Data were analyzed by F test.

Abbreviations: R1, reader 1; R2, reader 2; *P*, *P* value; SIR_{proximal}, signal intensity ratio of the proximal pancreatic parenchyma to the spinal cord;

SIR_{lesion}, signal intensity ratio of the proximal pancreas to the lesion; SIR_{distal}, signal intensity ratio of the distal pancreatic parenchyma to the spinal

cord; CR_{proximal}, contrast ratio of the lesion to the proximal pancreatic parenchyma; CR_{distal}, contrast ratio of the lesion to the distal pancreatic

parenchyma.

Figure 1

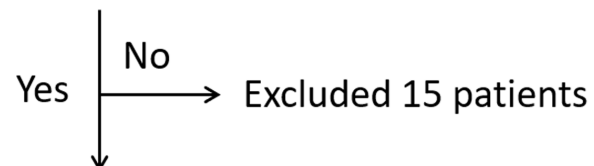
Reviewed database of pathology including following conditions

- Between April 2012 and January 2017
- Pathologically diagnosed pancreatic ductal adenocarcinoma by FNA or resection



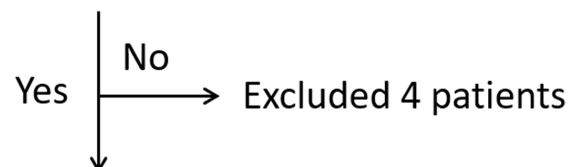
130 patients with pancreatic ductal adenocarcinoma

With MRI data within 3 months before FNA or resection?



115 patients

With 3.0-T MRI?



111 patients

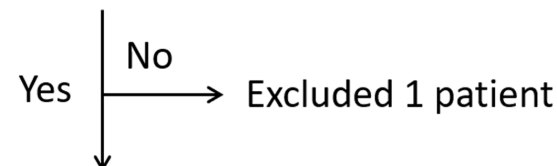
Reviewed database of MRI and medical records including following conditions

- Between April 2012 and January 2017
- Clinically diagnosed autoimmune pancreatitis



51 patients with autoimmune pancreatitis

With 3.0-T MRI?



50 patients

Focal type?



24 patients

135 patients



Figure 2

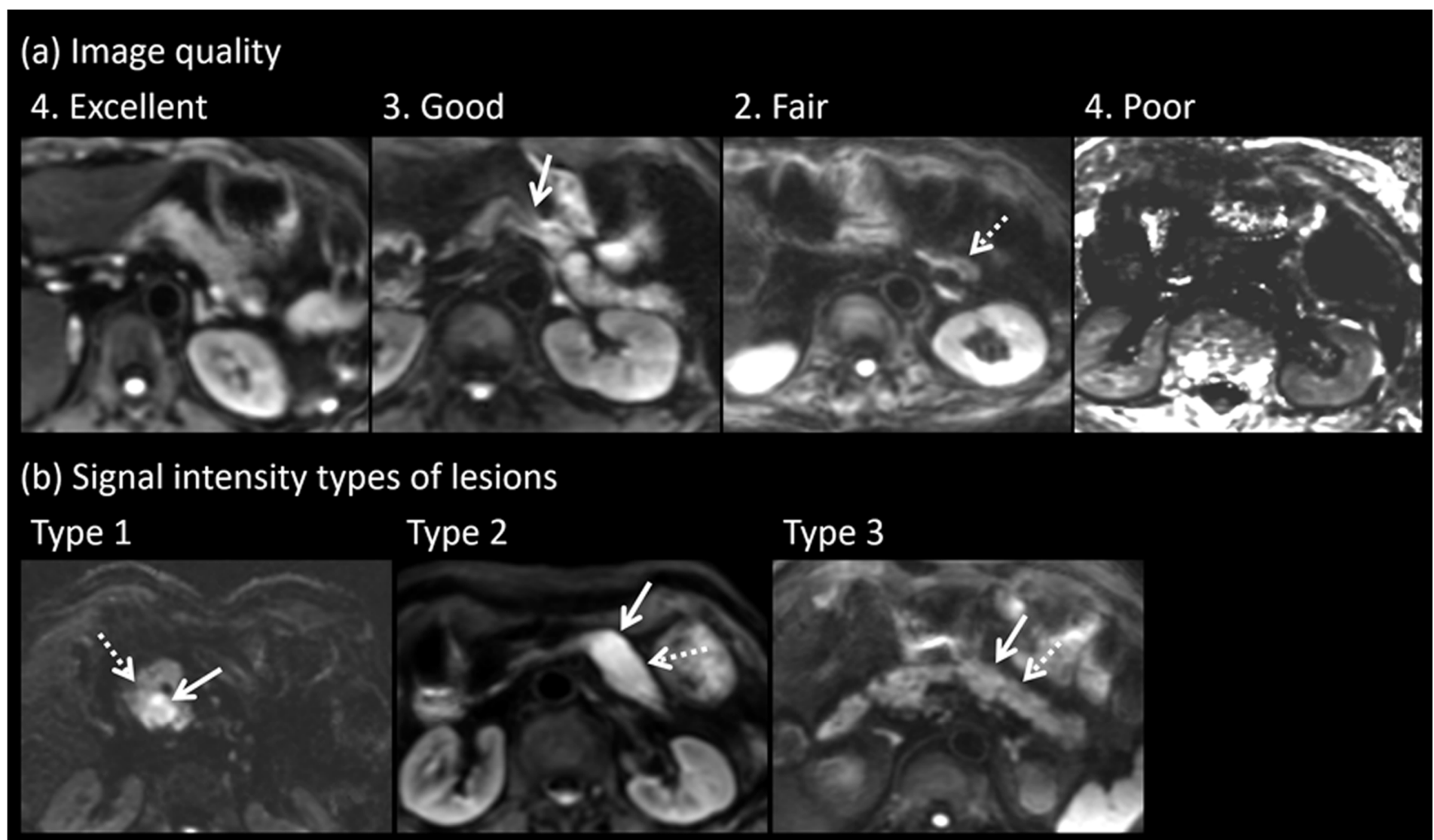
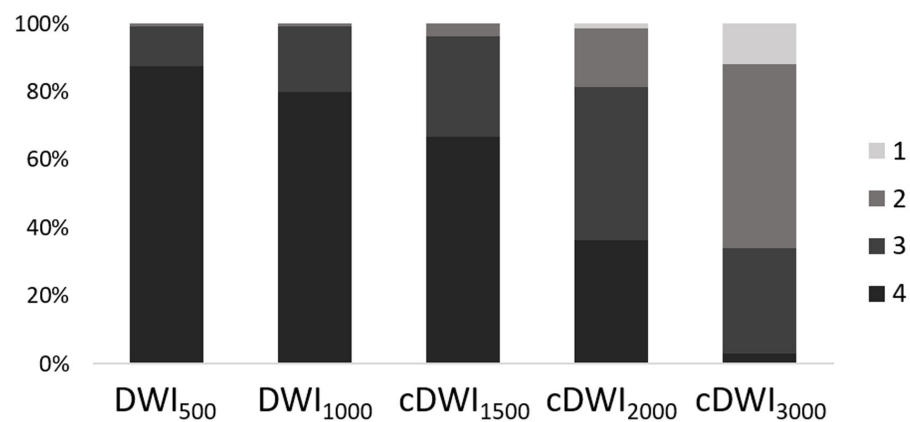
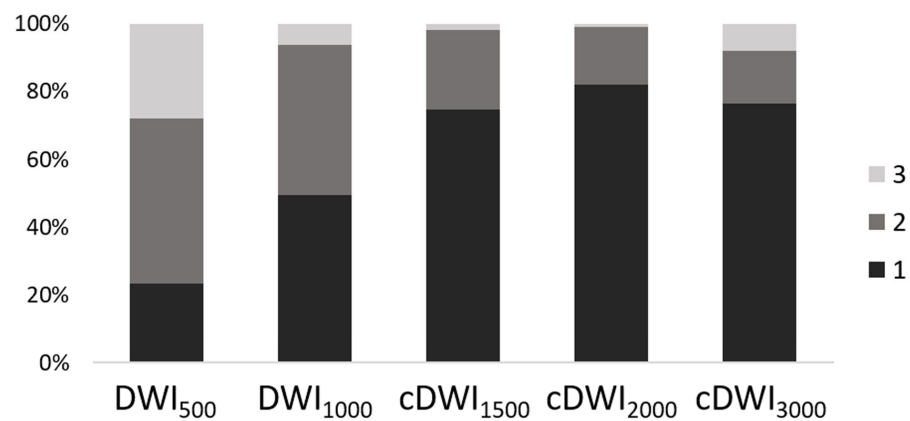


Figure 3

(a) Image quality



(b) Signal intensity types of lesions
Pancreatic ductal adenocarcinoma



Autoimmune pancreatitis

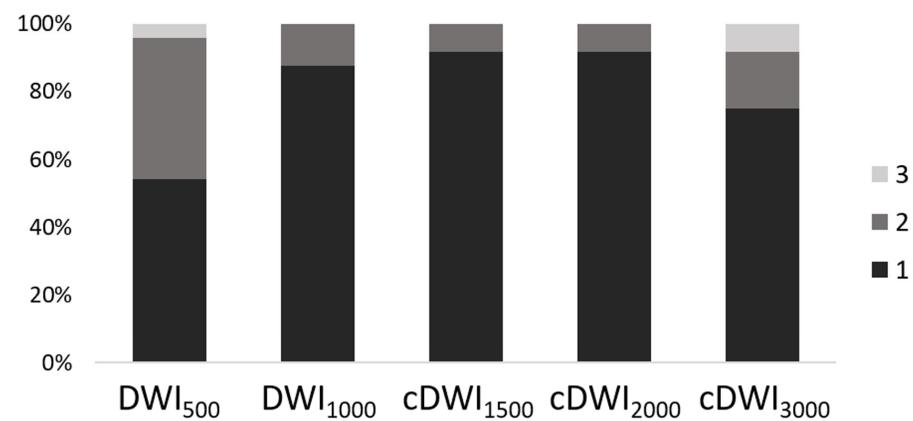
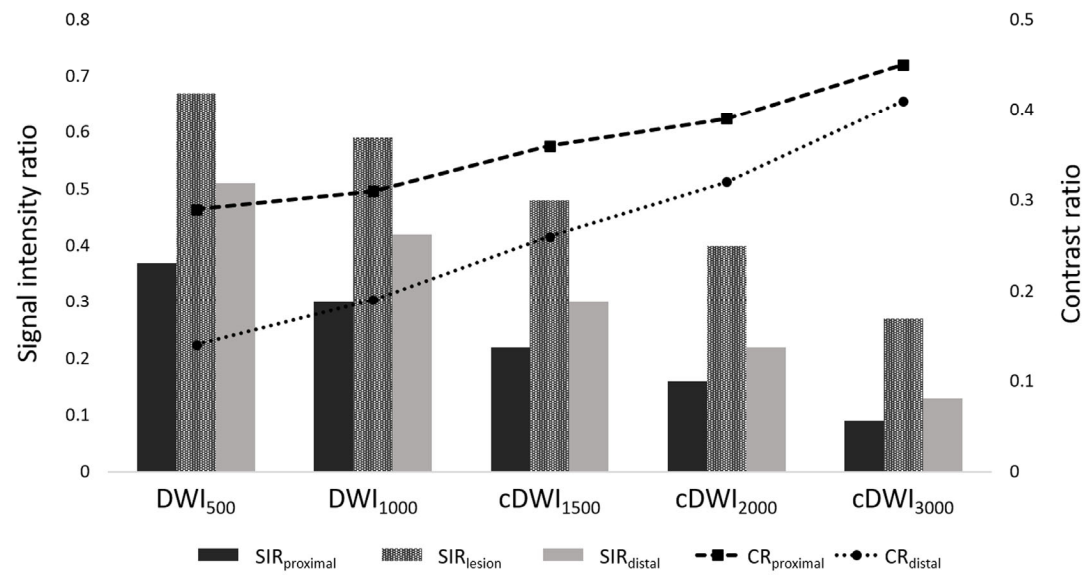


Figure 4

Pancreatic ductal adenocarcinoma



Autoimmune pancreatitis

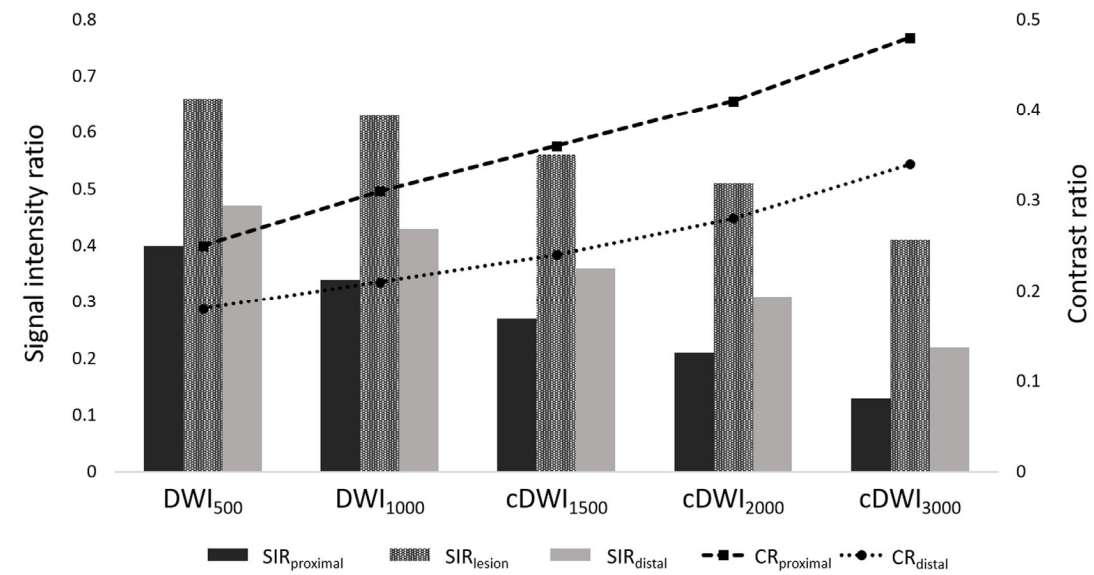
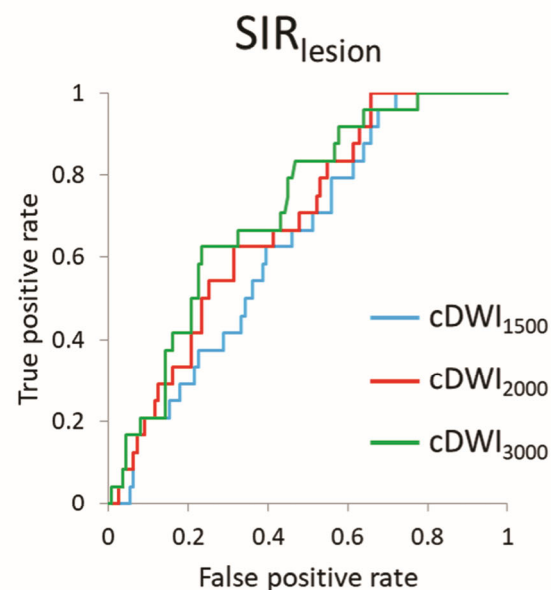
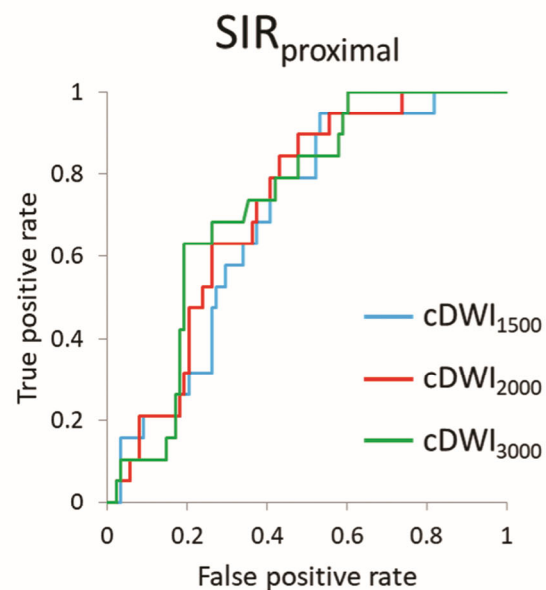


Figure 5



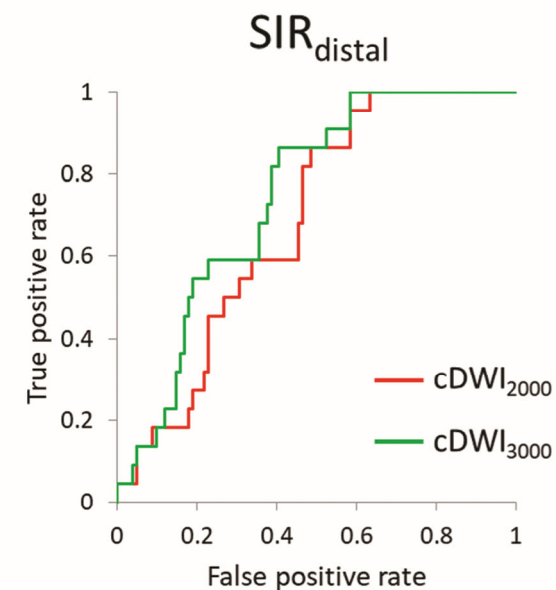
AUC	
cDWI ₁₅₀₀	0.641 (0.534–0.749)
cDWI ₂₀₀₀	0.687 (0.583–0.791)
cDWI ₃₀₀₀	0.720 (0.618–0.821)

Comparison of AUC	<i>P</i> value
cDWI ₁₅₀₀ vs. cDWI ₂₀₀₀	< 0.001*
cDWI ₁₅₀₀ vs. cDWI ₃₀₀₀	< 0.001*
cDWI ₂₀₀₀ vs. cDWI ₃₀₀₀	0.056



AUC	
cDWI ₁₅₀₀	0.691 (0.578–0.805)
cDWI ₂₀₀₀	0.719 (0.612–0.826)
cDWI ₃₀₀₀	0.720 (0.624–0.835)

Comparison of AUC	<i>P</i> value
cDWI ₁₅₀₀ vs. cDWI ₂₀₀₀	0.514
cDWI ₁₅₀₀ vs. cDWI ₃₀₀₀	0.982
cDWI ₂₀₀₀ vs. cDWI ₃₀₀₀	1.000



AUC	
cDWI ₂₀₀₀	0.684 (0.581–0.786)
cDWI ₃₀₀₀	0.743 (0.648–0.838)

Comparison of AUC	<i>P</i> value
cDWI ₂₀₀₀ vs. cDWI ₃₀₀₀	0.004*

Figure 6

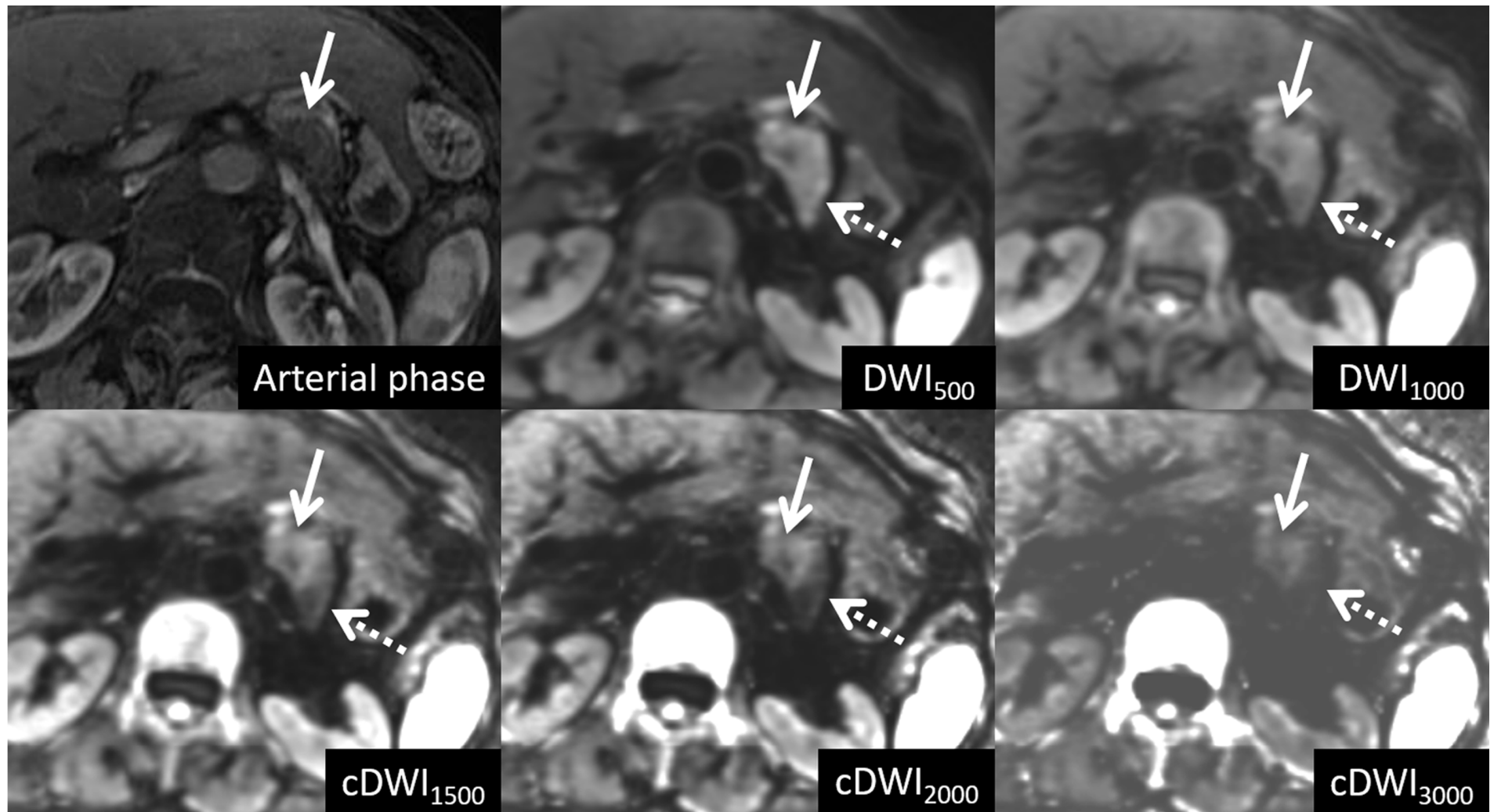


Figure 7

