Differentiation of Pancreatic lesions using Diffusion-Weighted MRI

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Abstract
The purpose of this study was to evaluate the role of diffusion-weighted imaging (DWI) in diagnosis of pancreatic lesions, to compare diagnostic accuracy of conventional MRI (MRI-c), DWI and diffusion coefficient (ADC) values of lesions.

Patient and methods: Thirty-six patients with pancreatic lesions (12 malignant and 24 benign) were included. MRI-c and DWI (b values 500 and 1000 s/mm²) were performed prospectively and consecutively in a 1.5-T system.

Results: The analysis was retrospectively performed. The sensitivity, specificity, accuracy, and positive and negative predictive values of DWI and MRI-c were 92%, 97%, 96%, 85%, 98% and 100%, 97%, 97%, 86%, 100%, respectively. Mean ADC values of malignant lesions were significantly lower than those of benign lesions. DWI has a similar accuracy to MRI-c in diagnosis of pancreas cancer.

Conclusion: Malignant tumors had lower ADC values than benign ones. DWI may be a routine sequence in oncologic settings and it provides much useful information about tumoral tissue.

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1. Introduction

Detection of pancreatic cancer at an early stage is not satisfactory by using ultrasonography, multidetector computed tomography (MDCT) and magnetic resonance imaging (MRI). New methods are required for early diagnosis (1,2). Diffusion-weighted imaging (DWI) is based upon the principles of Brownian motion of small molecules in a tissue (3,4). By using DWI, we can measure the apparent diffusion coefficient (ADC) in a given tissue. In malignant lesions, the larger volume cells and hypercellularity lead to restriction of the free movement of water particles. This results in a decrease in ADC and hyperintensity signals on DWI. In contrast, benign lesions have expanded extracellular space, with easier diffusion of water molecules. This is displayed as high ADC and hypointense signals on DWI (5–7). During recent years, DWI of diseases of the lower abdomen, e.g. prostate (8), urinary bladder (9), uterus (10) and rectum (11), has presented promising results. DWI of the upper abdomen has been a technical challenge due to respiration, bowel peristalsis, blood flow and long acquisition times. The implementation of ultrafast
imaging techniques, such as parallel imaging, has made DWI of the upper abdomen a feasible option. DWI has been found to be useful in differentiation of malignant from benign liver lesions (12,13). Apparent diffusion coefficient (ADC) values obtained from DWI have generally been shown to be lower in malignant than in benign tissue. Also, ADC values are lower in higher than lower grade tumors (14–16). At least nine studies have demonstrated significant lower ADC in pancreatic adenocarcinoma than in benign pancreas tissue (17–25). The purpose of this study was to evaluate the use of DWI in diagnosis of different pancreatic lesions and calculate the ADC values for these lesions.

2. Subjects and methods

The study was approved by the local ethics committee. During the period from October 2011 to August 2014, 36 patients referred to our department were examined in a prospective and consecutive manner by MRI examination with the use of our standard comprehensive upper abdomen protocol and additional DWI. Sixteen patients underwent pancreatic surgery or had diagnostic biopsy (10 men, 6 women, mean age 57 years with their ages ranged from 46 to 61). Twenty patients had a cross-sectional imaging follow-up (11 men, 9 women, mean age 49 years with their ages ranged from 37 to 58).

The final diagnoses of our cases were 12 malignant lesions and 24 benign lesions. Malignant lesions included 9 cases with adenocarcinoma (2 cases grade I, 4 cases grade II and 3 cases grade III) and 3 cases with neuroendocrinal tumors. Benign lesions included 8 cases with pseudocysts, 8 cases with mass forming pancreatitis, 5 cases with serous cystadenoma, 2 cases with mucinous cystadenoma and 1 case with lymphangioma. Four patients gave history of receiving chemotherapy as downstaging for treatment of pancreatic carcinoma.

2.1. MR protocol and parameters

– All patients were examined with a 1.5-T MR scanner (Achieva, Philips Medical Systems) using a phased-array body coil. All patients were examined initially with the routine MRI protocol for the upper abdomen that included unenhanced axial T1-weighted breath-hold spoiled gradient echo with and without fat suppression (TR/TE, 169/4.6; flip angle, 80°; number of excitations, 1), coronal and axial T2-weighted single-shot turbo spin-echo (700/80; number of excitations, 1; turbo spin-echo factor, 72), and axial T2-weighted single shot turbo spin-echo with fat suppression (700/80; number of excitations, 1; turbo spin-echo factor, 72) sequences.

– Diffusion-weighted MR imaging was performed with single-shot spin-echo echo-planar imaging with a spectral pre-saturation attenuated inversion recovery (SPIAIR) fat-suppressed pulse sequence. Integrated parallel imaging techniques using generalized auto-calibrating, partially parallel acquisitions were used with twofold acceleration. The parameters were as follows: repetition time/echo time, 5000/80 ms; matrix, 156 × 192; bandwidth, 1446 Hz/ pixel; section thickness, 6 mm; gap, 1.8 mm; field of view, 300–400 mm; partial Fourier factor, 6/8; averages, 2; parallel imaging factor of 2; free breathing; and b values of 0, 500 and 1000 s/mm². Typical scanning time was less than 2 min. ADC maps were automatically generated on a voxel by voxel basis by using the software supplied with the MR unit. Apparent diffusion coefficient (ADC) maps were reconstructed from these images.

– Subsequently, 0.1 mmol/kg of gadopentetate dimeglumine (Magnevist, Bayer Schering) was administered. The patients underwent a multiphasic contrast-enhanced MRI protocol including arterial phase, pancreatic parenchymal phase, and portal venous phase imaging. The arterial phase images were initiated 25 s after the beginning of the injection of contrast material; pancreatic parenchymal phase images, 45–55 s after contrast injection; and portal venous phase images, 70–90 s after contrast injection.

2.2. Image analysis

(a) Detection of lesions was done by DWI. Then the DW images correspond with ADC maps for characterizing them as benign or malignant using b values of 500 and 1000 s/mm² (malignant lesions have high signal on DWI and low signal intensity on ADC map compared with the adjacent parenchyma). All results were recorded and the patients were classified as having benign, malignant or no lesions at all.

(b) The ADC of lesions was attained by drawing a region of interest (ROI) in the lesions. A free-hand (ROI) was traced along the edge of each lesion on the ADC map. Effort was made trying to avoid vessels, pancreatic and common bile ducts. In cases with localized pancreatic lesions, the ADC of remaining normal pancreatic parenchyma was also measured by placing a circular ROI proximal and distal to the mass.

(c) The results of the DWI were compared with those of the MRI examination protocol. The criteria favoring the diagnosis of an adenocarcinoma by contrast enhanced MRI (MRI-c) were as follows: 1- A relatively well demarcated lesion with decreased enhancement compared with parenchyma in the parenchymal phase; 2- A smoothly or beaded dilatation of the pancreatic duct with abrupt obstruction by a mass. Imaging findings indicating a mass forming pancreatitis were as follows: 1- Relatively poorly demarcated lesion; 2- The pancreatic duct has a normal or smoothly stenotic caliber inside the mass (duct penetrating sign). Results were recorded.

2.3. Statistical analysis

Sensitivity, specificity, accuracy, and positive and negative predictive values were calculated for DWI and MRI-c. Comparisons of data were performed by analysis of variance. Fisher exact test was used to control for multiplicity. Statistical comparison testing differences between two groups were made using the Student’s t-test. The within-group analysis was made by using the Student’s-t test for correlated means. In order to evaluate hypotheses of variables in contingency tables, the Chi-square test was used or, in the case of small expected frequencies, Fisher’s exact test. In addition to that, descriptive statistics and graphical methods were used to characterize the data. All analyses were carried out using the SAS system, and
the 5%, 1% and 0.1% levels of significance were considered. In the case of a statistically significant result the probability value \( p \) has been given.

### 3. Results

The final diagnosis of the 36 patients by histopathologic examination and follow-up was as follows: 12 patients had a malignant lesion and 24 patients had a benign lesion. By using DWI, eleven out of 12 malignant lesions were detected and correctly characterized with MRI-c. Out of the 24 benign lesions, 22 were correctly characterized with both DWI and MRI. Two false positive lesions were diagnosed by DWI, including two patients with pseudocysts (Fig. 1 and Table 1). There were two true negative lesions by MRI-c, including two patients with mass forming pancreatitis (Fig. 2). Furthermore, there was one false negative lesion by DWI. It was a case of adenocarcinoma in a patient with a past history of receiving chemotherapy. No false negative lesions with MRI-c. The accuracy was 91.6% for DWI and 94.4% for MRI-c (Table 2). The mean ADC value of the malignant lesions was significantly lower compared with benign lesions (Table 3). The ADC values of malignant and benign lesions are presented as a box plot and scatter plot in Fig. 4. From this diagram there was clear overlap with four benign lesions being in the range of malignant lesions. The difference between the ADC value of the lesion and the parenchyma was significantly lower in malignant lesions compared with benign \( p = 0.0003, 0.019 \) and \( 0.012 \) respectively; the latter presented in Table 3. The ratio between the ADC value of the lesion and the parenchyma was significantly lower in malignant lesions compared with benign lesions \( p = 0.0004, 0.029 \) and \( 0.019 \) respectively (Table 3).

### 4. Discussion

In our study, The DWI showed 91.6% sensitivity and specificity in differentiating benign from malignant pancreatic lesions, which were less than those in the study of Ichikawa

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**Table 1** True +ve, true −ve, false +ve and false −ve of DWI and MRI-c for pancreatic lesions.

<table>
<thead>
<tr>
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<th>True +ve</th>
<th>True −ve</th>
<th>False +ve</th>
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<tr>
<td>DWI</td>
<td>11</td>
<td>22</td>
<td>2</td>
<td>1</td>
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<tr>
<td>MRI-c</td>
<td>12</td>
<td>22</td>
<td>2</td>
<td>–</td>
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<td>DWI + MRI-c</td>
<td>12</td>
<td>24</td>
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*a Contrast enhanced MRI.

**Fig. 1** A 55-year-old male patient with histopathologically proven pancreatic adenocarcinoma. The lesion showed low signal intensity (arrow) at T1WI (a) and isointense signals (arrow) to the pancreas at T2WI (b). It displays high signal intensity in DW images (arrow) with \( b \) values of 1000 (c) compared with the adjacent parenchyma and low signal intensity on corresponding ADC map, and the ADC value measured at the tumor area is \( 1.032 \times 10^{-3} \text{ mm}^2/\text{s} \) (d).
Fig. 2  A 49-year-old female patient with pancreatic pseudocyst contains areas of hemorrhage. The lesion showed low signal intensity at T1WI with hyperintense signals at anterior part (a) and hypointense signals to the pancreas at T2WI (b). It displays high signal intensity restricted diffusion with low signals at anterior part in DW images (c) and slightly high signal intensity on corresponding ADC map 2.51(d).

Fig. 3  A 67-year-old male patient with mass-forming focal pancreatitis of the pancreatic head. T2-weighted MRI with fat suppression (a) shows an ill defined hyperintense pancreatic head mass (arrow) (b) Diffusion weighted images show a slightly hyperintense pancreatic head mass (arrow) with ADC values on the ADC maps, the ADC value measured at the tumor area is \(0.91 \times 10^{-3}\) mm\(^2\)/s (c).
et al. (11) (96.2% and 98.6% respectively). Furthermore, our results showed that, DWI of pancreas cancer has an accuracy of 91.6%, which was comparable to that of MRI-c (94.4%). In our study, MRI-c showed higher sensitivity than DWI. The sensitivity and specificity of MRI-c were 100% and 91.6% respectively. The mean ADC values of malignant lesions were significantly lower compared with benign lesions. There was a considerable overlap as four benign lesions had ADC values in the range of malignant lesions. Qualitative DWI seems to be more accurate than the quantitative analysis and can be used as an accurate method for detection of pancreas cancer. In positive cases, another imaging modality as MRI-c or MDCT will be needed for staging. By using DWI, pancreatic cancer can be excluded with a high percentage as the NPV was equal to 95.6%. Both the examination and the reading time are shorter for DWI compared with MRI-c. There were two false positive lesions by DWI in our study. There were two cases with complicated pseudocyst as they displayed restricted diffusion (Fig. 2). A previous study by Nicolaos et al., stated that pseudocysts can show some grade of restriction in diffusion (26). Restricted diffusion is thought to be due to high viscosity of its content (27). There was one false negative lesion with DWI. It was adenocarcinoma in a patient with past history of receiving chemotherapy. The three other cases of pancreatic adenocarcinoma with past history of receiving chemotherapy showed positive findings for malignancy on DWI. The false negative result may represent a good response to treatment. However, larger studies are needed to assess whether DWI can be used to evaluate response after chemotherapy. DWI correctly characterized the two cases with mass forming pancreatitis that were falsely characterized as malignant lesions on MRI-c. Takeuchi et al. (15), showed that the inflammatory pseudotumors did not show high signal intensity on DW images. The choice of b values in the application of DWI in the upper abdomen is a compromise. Low b values lead to contamination of other forms of intravoxel incoherent motion such as perfusion in the capillary bed, which results in increased ADC values (28). At high b values a decrease in signal-to-noise ratio (SNR) is seen and long acquisition times are required. As a compromise a b value of 500 s/mm² was chosen. Recently, it has been reported that higher b values, such as 1000 s/mm², have high sensitivity and specificity for malignant abdominal tumors (29) and in the detection of pancreatic adenocarcinoma (13–15). The DWI might be cost effective in screening for pancreatic malignancy. Also DWI can be used for investigating patients for whom contrast-enhanced CT or MRI studies are contraindicated. In conclusion, DWI and MRI-c have nearly equal accuracies for the detection of pancreas cancer. In positive findings for malignancy with DWI, MRI-c examination is probably needed for further characterization and staging.

Conflict of interest

There is no conflict of interest to declare.

References


