Apparent diffusion coefficient measurements of the pancreas, pancreas carcinoma, and mass-forming focal pancreatitis

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Abstract
Background: Mass-forming focal pancreatitis (FP) may mimic pancreatic cancer (PC) on magnetic resonance (MR) imaging, and the preoperative differential diagnosis is often difficult. Recently, the usefulness of diffusion-weighted imaging (DWI) in the diagnosis of pancreatic cancer has been reported in several studies.

Purpose: To investigate if apparent diffusion coefficient (ADC) measurements based on diffusion-weighted echo-planar imaging (DW-EPI) may distinguish between normal pancreas parenchyma, mass-forming focal pancreatitis, and pancreas carcinoma.

Material and Methods: MRI was performed on 64 patients: 24 with pancreas carcinoma (PC), 20 with mass-forming focal pancreatitis (FP), three patients with other focal pancreatic disease as well as 17 controls without any known pancreatic disease. Diffusion-weighted sequence with ADC maps and T2-weighted sequence for anatomical information was performed. Apparent diffusion coefficient (ADC) maps were automatically created and analyzed using a dedicated user interface. In the group with pancreas disease the abnormal parenchyma was detected by using T1- and T2-weighted images and the region of interest (ROI) was transferred exactly to the ADC map and the coefficients were registered. In the control group the ROI was set to the head of the pancreas followed by a similar registration of the ADCs.

Results: ADC values for mass-forming FP and PC differed significantly from ADC values for normal pancreas parenchyma ($P = 0.001$/$P = 0.002$). Mean ADC values for mass-forming FP were $0.69 \pm 0.18 \times 10^{-3}$ mm$^2$/s. ADC values for PC were $0.78 \pm 0.11 \times 10^{-3}$ mm$^2$/s, compared to ADC values of $0.17 \pm 0.06 \times 10^{-3}$ mm$^2$/s in the control group. However there was no significant difference in ADCs between PC and mass-forming FP ($P = 0.15$).

Conclusion: ADC measurements clearly differentiated between normal pancreatic tissue and abnormal pancreas parenchyma (PC and mass-forming FP). However there is an overlap in values of PC and mass-forming FP, with the consequent problem of their correct identification.

Keywords: MRI, diffusion-weighted imaging, apparent diffusion coefficient, abdominal imaging, pancreas

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been applied to the abdomen (2–5). The results suggest that ADC measurements can be useful in the evaluation of diffuse liver (6) and renal diseases (7, 8) as well as for characterizing focal hepatic (4, 9), pancreatic (10–15), and renal (16) lesions. The purpose of our study was to evaluate DWI findings and measure the difference between ADC values of normal pancreas parenchyma, mass-forming focal pancreatitis (FP) and pancreas carcinoma (PC). We chose these pathologic conditions, as differentiation between them can be difficult. As there is a wide range of reported ADC values (10, 17, 18) for PC and mass-forming FP we had to establish our own reference values. Our aim was to test whether there is a significant difference in ADCs for normal pancreas and abnormal pancreas parenchyma (PC and mass-forming FP), as well as to test whether or not it is possible to differentiate between PC and mass-forming FP by using ADC measurements. This would allow us to establish a non-invasive imaging of pancreatic lesions protocol in the clinical routine to differentiate between PC and mass-forming FP.

Material and Methods

Patients

In this prospective study 64 subjects were included. Informed consent was obtained from all participants. The PC group was composed of 24 patients (12 women and 12 men; age range 38–81 years, mean age 64 years) with histological proof of ductal adenocarcinoma (PC) through Whipple procedure. Twenty patients (7 women and 13 men; age range 15–74 years, mean age 52 years) were included in the mass-forming FP group. Sixteen of these patients underwent surgery because malignancy could not be ruled out by either imaging or fine-needle aspiration. In four patients mass-forming FP was diagnosed without histopathologic proof, based on repeated imaging (MRI or dynamic computed tomography) and clinical follow-up (13–25 months) after the initial presentation. Seventeen subjects without any pancreatic disease (5 women and 12 men; age range 12–78 years, mean age 45 years) were included as control group and had normal MRI/MRCP findings.

All patients underwent the same imaging protocol for the diffusion-weighted imaging, and were scanned within 14 days prior to the surgery. Histological findings were determined from the records of our Department of Pathology. We had to exclude three patients from our study due to the following conditions: serous cyst adenoma (1), adenocarcinoma of unknown primary localization (1), and diffuse disease of intestine (measurement not possible) (1).

MR protocol

Diffusion-weighted sequence with ADC maps as well as the routine pancreatic MR imaging protocol for anatomical information were performed using a Magnetom Avanto 1.5 T scanner (Siemens Medical Solutions, Erlangen, Germany) and a commercially available cp body phased array coil. Diffusion-weighted images were acquired using a single-shot echo-planar imaging pulse sequence in expiration breath-hold. The following parameters were used for the axial DW-EPI sequence: matrix size of 144 × 192, a field-of-view of 375 × 500 (pixel size 2.6 × 2.6 mm), and a section thickness of 2.6 mm. The b factors used were 50 and 500 s/mm². In addition the routine pancreatic MR imaging protocol for the patient group consisted of TRUE-FISP imaging sequences, non-contrast T1-weighted fat-suppressed and dynamic gadolinium-enhanced gradient-echo imaging as well as magnetic resonance cholangiopancreatography (MRCP) and angiography (MRA). The ADC maps were automatically created and analyzed using a dedicated user interface (Leonardo, Siemens Medical Solutions, Erlangen, Germany). The pancreas lesions were detected using the T1- and T2-weighted images and the according coefficients were registered (Figs. 1 and 2). In the control group the ROI was set to the head of the pancreas gland followed by a similar registration of the ADCs. In the diseased population ROIs ranged from 70 to 879 mm².
mean 354 mm²), whereas in the control group a fixed ROI of 100 mm² was used.

**Image analysis**

Consensus reading was performed by two experienced radiologists (15 years and 6 years of experience). ADCs were calculated on a workstation with dedicated software. Signal intensities on ADC maps were measured by using an operator-defined region of interest (ROI). ADCs were calculated for normal pancreas and focal lesions of the pancreas. The ROIs for the pancreas were circular. Pancreas vessels, the pancreatic duct and the common bile duct were left out of the ROI. At the time of ROI placement, the operator was aware of the location of the lesions and could refer to routine MR images and to the histopathological diagnosis. We examined patients with PC, mass-forming FP, and without pancreatic disease. In three patients with mass-forming FP and pancreatic pseudo cysts the ROI was placed outside these cystic lesions. ADC values of the control group were used to establish the normal values. The ROI within each lesion was circular and placed on the largest possible area, including necrotic parts. Mean ADCs of the two lesion types and mean values of healthy pancreatic tissue were compared.

**Statistical analysis**

The non-parametric Mann-Whitney U test was used to determine whether there was a significant difference between ADC values for normal pancreas, PC, and mass-forming FP. The degree of inter-observer agreement in ADC value measurements was evaluated using the inter-class correlation (ICC) coefficient. An ICC value of less than 0.40 indicates poor reproducibility, ICC values between 0.40 to 0.75 indicate a fair to good reproducibility, and an ICC value of greater than 0.75 shows excellent reproducibility. All values were expressed as mean ± SD, and a P value of <0.05 was considered statistically significant. All statistical analysis was performed using SPSS for Windows, version 15.0 (SPSS Inc., Chicago, IL, USA).

**Results**

ADC measurements for all 24 PCs as well as the 20 mass-forming FP showed lower ADC values compared to normal pancreas parenchyma. The maximum tumor diameter of PC ranged from 1.7 to 6.1 cm (mean 3.8 cm), the corresponding values for the mass-forming FP where 2.2 to 5 cm (mean 3.4 cm).

The corresponding ADC values ($\times 10^{-3}$ mm²/s) were as follows: pancreatic carcinoma ($n = 24$), $0.78 \pm 0.11$. Mass-forming FP ($n = 20$), $0.69 \pm 0.18$, and normal pancreas in healthy volunteers ($n = 17$), $0.17 \pm 0.06$ (Table 1, Fig. 3).

ADC values of the pancreatic carcinoma proved to be significantly higher compared with those of the normal pancreatic tissue in healthy volunteers (Table 2). The Mann-Whitney U test demonstrated a statistically significant difference ($P < 0.001$). ADC values of the mass-forming FP also proved to be significantly higher compared with those of the normal pancreatic tissue. The Mann-Whitney U test demonstrated a statistically significant difference compared with those of the normal pancreatic tissue albeit at a lower significance level ($P < 0.002$). There was no significant difference in ADCs between PC and mass-forming FP ($P = 0.15$). The inter-observer agreement for ADC measurements was analyzed using the ICC method. A ‘fair to good agreement’ was obtained for the average ADC value of mass-forming FP (ICC = 0.623). ‘Excellent’ inter-observer agreement was observed for the ADC values of PC and the control group (ICC = 0.768 and ICC = 0.823).

**Table 1**  Mean ADC values for normal pancreatic tissue, pancreatic carcinoma, and mass-forming focal pancreatitis

<table>
<thead>
<tr>
<th>Pancreatic disease</th>
<th>n</th>
<th>ADC values $\pm$ S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>17</td>
<td>$0.17 \pm 0.06$</td>
</tr>
<tr>
<td>Pancreatic carcinoma</td>
<td>24</td>
<td>$0.78 \pm 0.11$</td>
</tr>
<tr>
<td>Mass-forming FP</td>
<td>20</td>
<td>$0.69 \pm 0.18$</td>
</tr>
</tbody>
</table>

*Data are mean ($\times 10^{-3}$ mm²/s) ± standard deviation

ADC = apparent diffusion coefficient; FP = focal pancreatitis
been reported by several studies (4, 8, 19). The usefulness of DWI with a single-
weighted MR imaging with apparent diffusion coefficient (ADC) measurements. The
may lead to a difficult preoperative differential diagnosis. Usually morphologic
changes of chronic pancreatitis result in a shrunken and atrophic pancreas, but occasionally it may present as a
mass-forming FP and thus may mimic a PC (12). This
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Discussion
Pancreatic cancer is the third most common malignancy of
the gastrointestinal tract; the incidence rate is estimated at
about 10 new cases per 100,000 people per year. The main
task in diagnostic imaging of the pancreas is the detection
and differentiation of pancreatic lesions into malignant
and benign (e.g. inflammatory) entities as well as to assess
resectability of pancreatic cancer. Usually morphologic
changes of chronic pancreatitis result in a shrunken and
atrophic pancreas, but occasionally it may present as a
mass-forming FP and thus may mimic a PC (12). This
may lead to a difficult preoperative differential diagnosis. Recent technical innovations have introduced diffusion-weighted MR imaging with apparent diffusion coefficient (ADC) measurements. The usefulness of DWI with a single-shot spin-echo echo-planar sequence (EPI) for the evaluation of neoplastic diseases in the abdominal region has been reported by several studies (4, 8, 19).

However, measured abdominal ADC values depend on
the exact selection of b values, in addition ADC values
also depend on the field strength of the scanner (20).
There is a consistent decrease of ADC values with increased
diffusion weighting as well as with increased field strength.
This might partially explain the variations of ADC values
increased ADC values (14). Yoshikawa et al. found signifi-
cantly increased ADC values for PC compared to ADC
values for healthy pancreas parenchyma (18). Similarly,
we found increased ADC values for PC and mass-forming
FP compared to the pancreatic gland in the control group.
This might be due to the large lesions sizes (PC and mass-
forming FP) in our study compared to previous studies, as
these larger lesions are more commonly associated with
necrosis and inflammation. ADC values for the mass-
forming FP also proved to be significantly higher compared
with those of the normal pancreatic tissue. However, there
was a significant overlap in ADC values for PC and mass-
forming FP, with the consequent problem of their correct
differentiation. Chronic pancreatitis can also contain areas
of fibrosis and focal inflammatory reactions (12), which
might explain the difficulty to differentiate these severe
pancreatic lesions.

This study has some limitations, such as that the average
age of the patients was significantly higher than that of our
healthy controls. This might have independently influenced
the measured ADC, however, the age range for the two
patient groups was comparable. Second, the patient and
control group were relatively small. Thus a statistically
significant difference in ADC values might be established
in a larger sample. An additional limitation is that we
only analyzed the quantitative information of ADC maps,
leaving aside the qualitative information of the obtained
DWI images (24). Thus, we only evaluated the value of
ADC in differentiating PC, mass-forming FP, and normal
pancreas from each other. The additional information of
the original images with different b values has not been
used and the value of DWI in the detection and differen-
tiation has not been analyzed. Furthermore, we did not
evaluate ADC values of adjacent pancreas parenchyma
surrounding the lesion, which could have also yielded
extra information. Finally, the ROIs to acquire ADC values
covered the whole lesion including central necrosis. These
larger ROIs were used, to make the method feasible in the
daily clinical routine; however this might have biased the
measurement of ADCs in the patient group.

In conclusion, we could not demonstrate that using ADC
measurements of focal pancreatic lesions is a viable

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sample sizes</th>
<th>Mann-Whitney U</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal pancreas vs. pancreatic carcinoma</td>
<td>n = 17, n = 24</td>
<td>13.5, &lt;0.001*</td>
<td></td>
</tr>
<tr>
<td>Normal pancreas vs. mass-forming FP</td>
<td>n = 17, n = 20</td>
<td>69.5, 0.002*</td>
<td></td>
</tr>
<tr>
<td>Pancreatic carcinoma vs. mass-forming FP</td>
<td>n = 24, n = 20</td>
<td>179.0, 0.15</td>
<td></td>
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</tbody>
</table>

*P < 0.01
FP = focal pancreatitis

![Fig. 3 Box plots of ADC values for normal pancreatic tissue, pancreatic carcinoma, and mass-forming focal pancreatitis](image-url)
approach to differentiate between PC and mass-forming FP. However, a differentiation of healthy pancreatic tissue from PC and mass-forming FP was possible. Given the limited accuracy of routine MRI (T1- and T2-weighted images) for the differentiation of tumors, further studies are necessary to investigate whether DWI can improve the accuracy of MR imaging. Furthermore it remains to be seen if ADCs can be used as an imaging response criteria for therapy monitoring (5) and follow-up of palliative chemotherapy in patients with metastatic or locally advanced inoperable pancreatic cancer.

Conflict of interest: None.

REFERENCES