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Original contribution

Whole-tumor histogram analysis of non-Gaussian distribution DWI parameters to differentiation of pancreatic neuroendocrine tumors from pancreatic ductal adenocarcinomas☆

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ABSTRACT

Purpose: To evaluate the utility of volumetric histogram analysis of monoexponential and non-Gaussian distribution DWI models for discriminating pancreatic ductal adenocarcinoma (PDAC) and neuroendocrine tumor (pNET).

Materials and methods: A total of 340 patients were retrospectively reviewed. Finally, 62 patients with histopathological confirmed PDAC (n = 42) and pNET (n = 20) were enrolled in the study. All the patients accepted magnetic resonance imaging (MRI) at 3 T (including multi-b value DWI, 0–1000 s/mm^2). Isotropic apparent diffusion coefficient (ADC), true molecular diffusion (Dt), perfusion-related diffusion (Dp), perfusion fraction (f), distributed diffusion coefficient (DDC) and alpha (α) were obtained from different DWI models. Then, mean value, median value, 10th and 90th percentiles were obtained from histogram analysis of each DWI parameter.

Results: Histogram metrics derived from ADC, Dp, f and DDC were significantly lower in PDAC than pNET group ($P < 0.05$). In contrast, histogram metrics derived from α were observed significantly higher in the PDAC than pNET group ($P < 0.05$). No significant difference was found in Dt ($P \geq 0.05$) between PDAC and pNET patients. Among all parameters, f-median had the highest diagnostic performance (AUC 0.91, cutoff value 0.188, sensitivity 97.62%, specificity 80%).

Conclusions: f-Median derived from IVIM DWI model may be potentially more valuable parameter than ADC, Dp, DDC and α for discriminating PDAC and pNET. Histogram analysis based on the entire tumor was an emerging and valuable tool.

1. Introduction

Pancreatic ductal adenocarcinomas (PDAC) and neuroendocrine tumors (pNET) are the first and second common pancreatic tumor respectively [1,2]. However, the treatment strategy and prognosis are completely different. For pNET patients, more aggressive surgery approach may not significantly improve overall survival and lead to higher complications when compared with partial pancreatectomy [3]. For example, both the enucleation involving removal of just the tumor and the pancreaticoduodenectomy can be used to treat pNET. But the pancreaticoduodenectomy had significant morbidity [4], such as long-term gastrointestinal motility disorders and endocrine and exocrine insufficiency, while the enucleation can spare otherwise normal pancreatic parenchyma [5]. Given the fact that pNETs had a relatively well prognosis and higher resectability in comparison with PDACs, it would be a key component to differentiate pNETs from PDACs using preoperative imaging in clinical [6,7].

Dynamic MRI or CT is most frequently used to differentiate PDAC

Abbreviations: IVIM, Intravoxel incoherent motion; ADC, Apparent diffusion coefficient; Dt, True molecular diffusion; f, Perfusion fraction; Dp, Perfusion-related diffusion; DDC, Distributed diffusion coefficient; AUC, Area under the curve; pNET, Pancreatic neuroendocrine neoplasm; PDAC, Pancreatic ductal adenocarcinoma; ROC, Receiver operating characteristic; ROI, Region of interest

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and pNET in clinical practice. The characterized imaging appearance of PADC is hypovascular, as opposed to the often hypervascular appearance of pNET [8]. However, the atypical enhancement pattern of PDAC and pNET is not uncommon due to the differences in tumor differentiation and necrosis, leading to great difficulty in distinguishing them [9]. What's more, the toxicity of contrast agents is likely to pose a threat to patients with impaired renal function [10,11]. Hence DWI may be an alternative sequence to differentiate PDACs and pNETs for patients with renal insufficiency.

DWI is a relatively mature noninvasive imaging modality [12], which could display functional information without contrast media. An isotropic apparent diffusion coefficient (ADC) was calculated through monoexponential DWI model, which has been utilized to differentiate pancreatic tumors [13]. However, previous studies have demonstrated that the monoexponential model cannot really reflect the state of water molecules in the lesion [14]. Intravoxel incoherent motion (IVIM) and stretched exponential DWI models are based on non-Gaussian distribution theory. The IVIM model could separate the effects of microcirculation perfusion from the water molecules diffusion [15]. Previous study has indicated that IVIM parameters appear more accurate than ADC in identifying pancreas tumors [16]. The stretched exponential model, recently elucidated by Bennett et al. [17], could simultaneously quantify the diffusion of water molecules and voxel heterogeneity [18,19]. According to the investigation, the stretched exponential model has not been applied to identify pancreatic tumors.

Additionally, considering the heterogeneity of pancreatic cancer and neuroendocrine tumors, volumetric histogram analysis may superiorly reflect the heterogeneity. Previous studies have used ADC histogram analysis to differentiate pancreatic tumors [20]. However, there are limited researches that using the histogram of non-Gaussian distribution DWI models to differentiate pancreatic tumors.

Therefore, the purpose of this paper is to evaluate the diagnostic performance of different DWI mathematical models for differentiating PDAC and pNET, by using the whole-tumor histogram analysis.

2. Materials and methods

2.1. Patients

This study has obtained the permission from the local institutional review board and informed consent was waived. After a review of radiology database for the period of June 2012 to July 2017, we identified 340 patients, who were suspected of pancreatic tumor and underwent MR examinations Including DW imaging. According to the following exclusion criteria, 278 patients were excluded from this study: (a) patients who have accepted treatment before surgery; (b) no pathological results or pathologically confirmed other pancreatic tumors; (c) without multiple b values DWI examination; (d) inadequate image quality. Finally, 62 patients including 42 PDACs and 20 pNETs were enrolled. A flowchart of the study population was presented in Fig. 1.

2.2. MRI technique

MR examinations were performed with patients in a supine position, using a 32-channel torso array coil at 3.0-T system (Discovery MR750; GE Healthcare, Milwaukee, WI). The routine abdominal protocols were carried out, including: (a) coronal SSFSE sequence (repetition time/echo time [TR/TE], 2195.7/6.8 ms; matrix, 256 × 256; FOV: 36–44 cm; slice thickness, 5 mm; slice number, 18); (b) axial T1-weighted image (repetition time/echo time [TR/TE], 5 ms/2.5 ms; matrix, 256 × 256; FOV: 36–44 cm; slice thickness, 3 mm; intersection gap, 0 mm); (c) axial respiratory-triggered T2-weighted image (repetition time/echo time [TR/TE], 7500/84 ms; matrix, 256 × 256; FOV:36–44 cm; slice thickness, 4 mm; intersection gap, 1 mm), and finally (d) multiple b values DWI image. For patients who need to take dynamic contrast enhanced (DCE) - MRI examination, the DWI was obtained before the injection of contrast agents. Among the patients included in this study, 23 patients underwent contrast enhanced examination (PDAC = 15, pNET = 8), and 39 patients did not (PDAC = 27, pNET = 12).

The DWI (matrix, 256 × 192; FOV: 36–44 cm; slice thickness, 4 mm; slice number, 17; intersection gap, 1 mm; bandwidth 250 KHz/pix; acquisition time, 4–5 min; acceleration factor 3) was performed in the cross-section by using respiratory-triggered single-shot echo-planar sequence, and b values (including 0, 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000 s/mm^2) were used in patients.

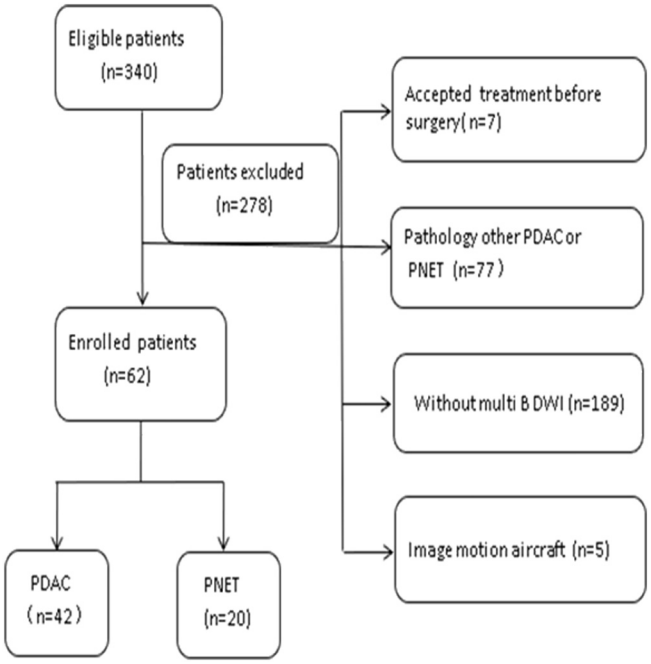

Fig. 1. Flowchart of the study population.

Table 1
Characteristics of patients with PDAC and pNET.

	PDAC	pNET	*P*
Number of patients	42	20	
Age, year	55(41–75)	48(39–65)	0.055
Sex			0.150
Man	17	12	
Woman	25	8	
Tumor size, cm	3.15(1.8–4.8)	2.91(2.1–4.55)	0.221
Location			0.897
Head	28	13	
Body or tail	14	7	

Data in parentheses are ranges.
PDAC = pancreatic ductal adenocarcinomas, pNET = pancreatic neuroendocrine tumors.

2.3. Image analysis

DICOM data of DWI was transferred from the picture archive and communication system (PACS) into a computer and processed with open source software Fire voxel (https://files.nyu.edu/hr18/public/projects.html). Two radiologists (6 and 14 years of imaging experience in abdominal MRI), unknowing the histopathologic results, reviewed all the MR images respectively. They manually drew the region of interest (ROI) along the edge of the lesion at each section referencing the axial T2-weighted image, while excluding areas of obvious cystic or necrosis. The ROI of each layer was fused automatically to obtain the whole tumor voxel information. Volumetric ADC map was constructed by