

## **Pancreatic intraductal papillary mucinous neoplasm: inter-reader agreement for standardised evaluation according to Fukuoka guidelines**

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## Aims and objectives

The detection rate of Pancreatic cystic neoplasms (PCNs) as incidental finding has shown a continuous increase in the last decade, in particular in the elderly population. However, this is to be accounted more to the extensive use of cross-sectional imaging than to an effective increase of incidence in the general population [1]. Among the cystic lesions of the pancreas, intraductal papillary mucinous neoplasia (IPMN) is one of the most frequent [2]. IPMNs are characterized by intraductal proliferation of neoplastic mucinous cells with consequent cystic dilation of the pancreatic ducts and formation of macroscopic masses [2]. IPMN are classified in main duct type (MD-IPMN), branch duct type (BD-IPMN), and mixed type (MD + BD) taking into account the involved duct ( [Fig. 1](#) on page 3 ) [3].

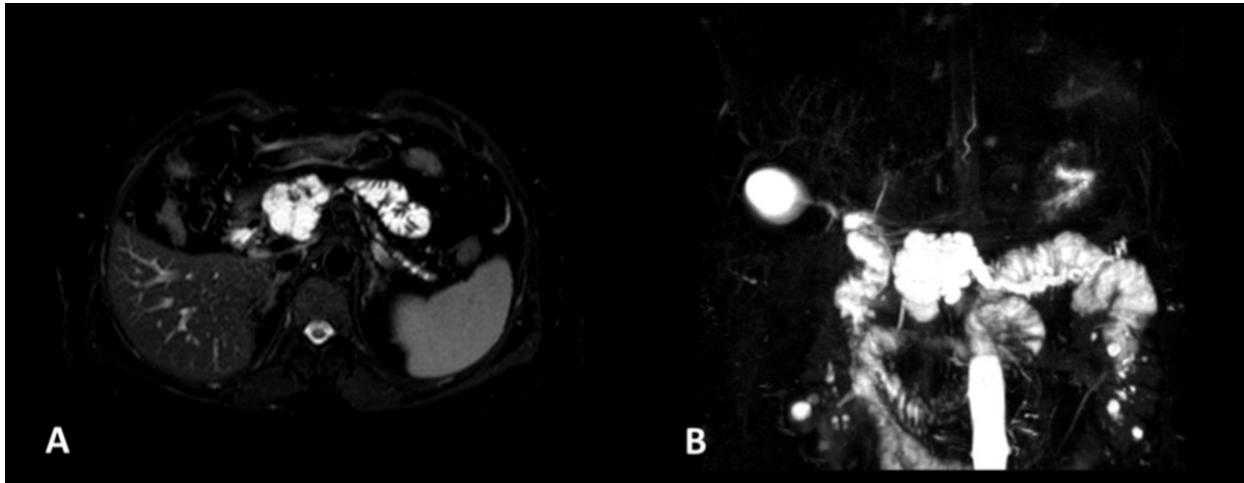
IPMNs have a well-known potential of malignant transformation and are associated with an increased risk of pancreatic ductal adenocarcinoma (PDAC) in different sites within the gland [2, 3]. The probability of malignant transformation is relatively low (1.4% - 6.9% per year), and increases in elderly people [4-7]. The variability in malignant transformation requires an accurate stratification of at-risk patients, but the management of these patients is still under debate [8,9].

Several guidelines have been developed for stratification and management of patients with IPMN: the more widespread are the International Association of Pancreatology 2012 Guidelines v2017 (the Fukuoka Guidelines) [3], European Study Group on Cystic Tumors of the Pancreas 2013 Guidelines v2018 [10] and the American Gastroenterological Association (AGA) 2015 Guidelines [11]. All these guidelines have common key features and are widely validated. In particular, the Fukuoka Guidelines define the "worrisome features" (WF) and "high-risk stigmata" (HRS) to be assessed in CT or MRI studies for adequate stratification and management of patients with IPMN [3,12]. As an example, the presence of a WF is an indication for endoscopic US (EUS) evaluation and fine needle aspiration (FNA) while the presence of HRS is an indication for surgical resection [3,11].

Good reproducibility and inter-reader agreement (IRA) provide by standardized evaluation of imaging findings is desirable in terms of stratification, clinical management, and outcomes. Fukuoka and AGA guidelines demonstrated similar levels of accuracy in the detection of malignant transformation [13]. However, the Fukuoka Guidelines propose CT or MR as first-line evaluation, while other guidelines delegate this role to EUS; therefore, Fukuoka guidelines may have the theoretical potential of good reproducibility.

The aim of this study is to retrospectively evaluate IRA of observers with different experience for pancreatic IPMN by using the Fukuoka guidelines.

**Images for this section:**



**Fig. 1:** Mixed-type IPMN. A, T2W SPAIR axial image. B, 3D MR cholangiopancreatography (MRCP), Maximum Intensity Projection (MIP), coronal.

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# Methods and materials

## Patient Selection

Inclusion criteria: patients with EUS or pathological diagnosis of IPMN who underwent an MRI examination between July 2015 and December 2017 at Department of Radiology of University Hospital of Ancona, Italy. Exclusion criteria: lack of MRI examination, contraindication to contrast media administration and lack of EUS, pathological and clinical data.

## MRI technique

MRI studies were performed with a 1.5-T scanner (GE Signa HdXt, Milwaukee, WI) and an eight-channel phased-array body coil.

The examination protocol included axial and coronal fast spin-echo (FSE) T2-weighted sequences, axial T1-weighted gradient echo (GRE) in- and opposite-phase, diffusion-weighted imaging (DWI,  $b=0, 800 \text{ s/mm}^2$ ), and 3D MR cholangiopancreatography (MRCP) with heavily T2-weighted fast recovery FSE. A multiphase post-contrast study was performed with a 3D fast spoiled GRE sequence (LAVA) and administration of Gd-DOTA, 0.1 mmol/Kg (Dotarem, Guerbet, France) at 2 ml/s followed by a saline flush. Pre-contrast, arterial, venous, and delayed phase were obtained.

## Image Analysis

Three radiologists with different experience, reader A (30 years), reader B (10 years), and reader C (1 year), retrospectively reviewed in blind all the MRI.

MRI studies were evaluated as per Fukuoka guidelines v2017, the presence of Worrisome Features (WF) and High-Risk Stigmata (HRS) was assessed [3].

WF included: pancreatitis (pancreatic edema); cyst  $\geq 3\text{cm}$ ; cystic mural thickening or enhancement; not-enhancing mural nodule  $< 5 \text{ mm}$ ; main pancreatic duct (MPD) diameter between 5 and 9 mm; abrupt change in the MPD diameter with pancreatic atrophy; lymphadenopathy (short axis  $> 10 \text{ mm}$ ).

HRS included: obstructive jaundice (choledochal diameter  $\geq 8 \text{ mm}$ ); enhancing mural nodules or solid component; MPD  $\geq 10 \text{ mm}$ .

## Statistical Analysis

Quantitative variables were expressed as dichotomous following the thresholds in the previous paragraph. The IRA was calculated with Intraclass Correlation Coefficient (ICC) and 95% confidence interval (95%CI).

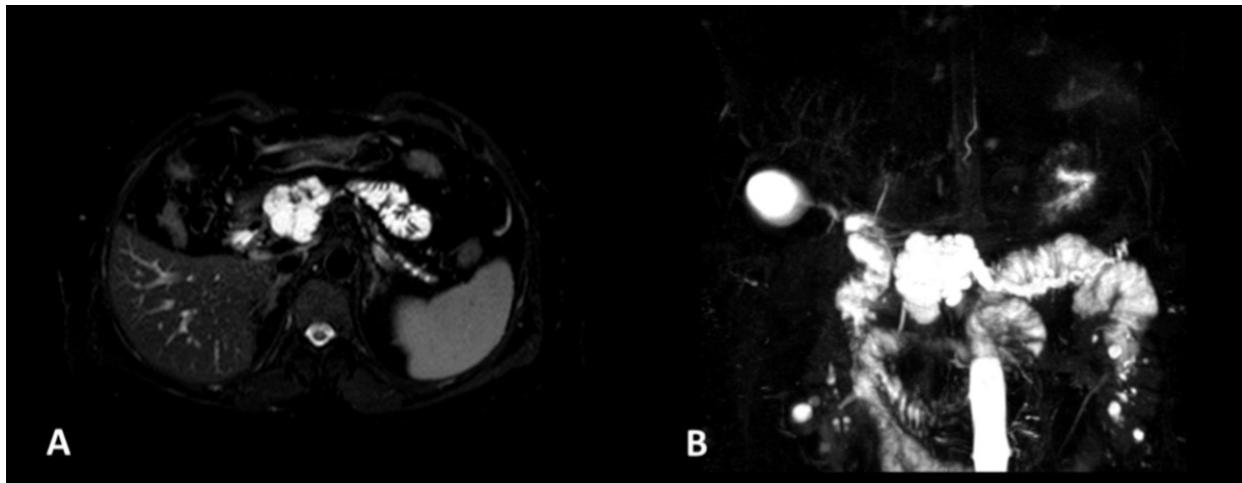
## Results

A total of 33 patients were included (13 male, 21 female) with mean age 67 (range 43-82 y.o.) with an average of 2.1 of cystic lesions >5mm per patient and an average of cystic diameter of 15.2 mm.

[Table 1](#) on page 7 shows demographics and evaluation of WF and HRS by reader A.

Figure 2 shows IRA between the three readers for the WF and HRS with ICC values included between 0.623 and 0.905. No significant differences between ICC were detected due to 95%CI overlap ( [Fig. 2](#) on page 8 ).

Images for this section:



**Fig. 1:** Mixed-type IPMN. A, T2W SPAIR axial image. B, 3D MR cholangiopancreatography (MRCP), Maximum Intensity Projection (MIP), coronal.

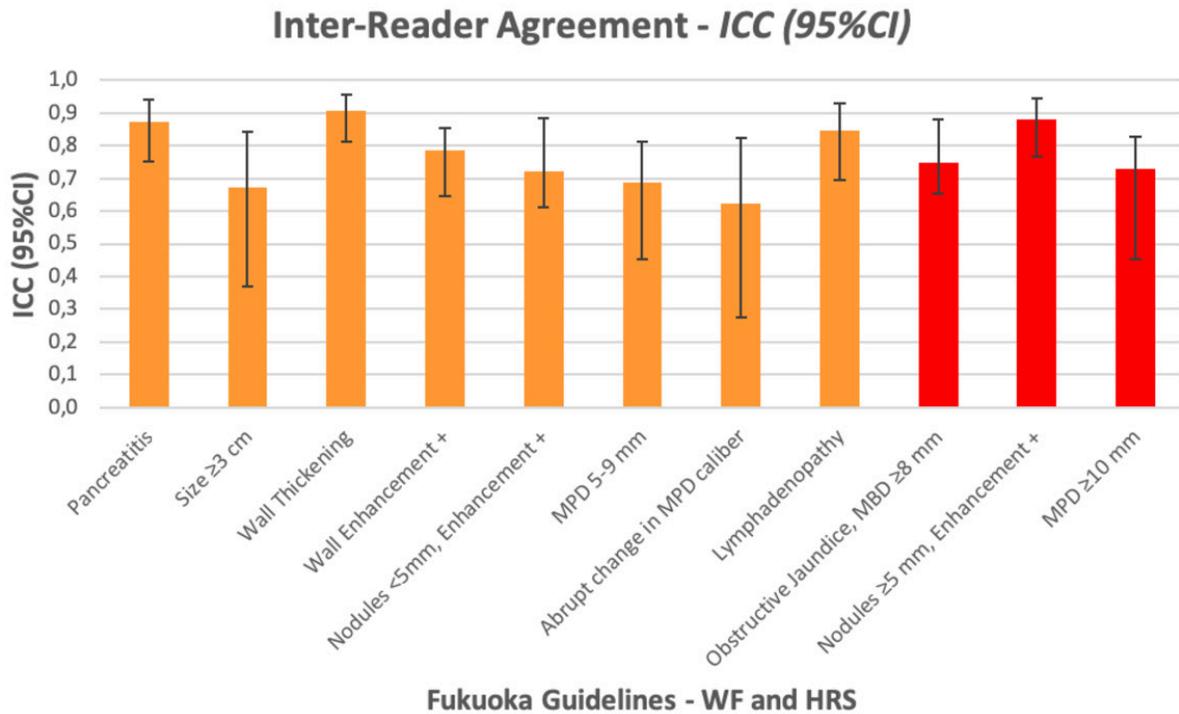
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Table 1. Demographics and images analysis			
Parameters		N	
<b>Demographics</b>	<b>Patients (M/F)</b>	<b>33 (13M / 21F)</b>	
	<b>Age (years). Mean (range)</b>	<b>67 (43 - 82)</b>	
<b>Fukuoka MRI findings: Reader A</b>	<b>Worrisome Features</b>	<b>Pancreatitis; N (%)</b>	<b>1 (3%)</b>
		<b>Cyst of <math>\geq 3</math> cm; N (%)</b>	<b>18 (37%)</b>
		<b>Thickened of cyst walls; N (%)</b>	<b>16 (48%)</b>
		<b>Enhancement cyst walls; N (%)</b>	<b>10 (30%)</b>
		<b>Mural nodule &lt;5mm, Enhancement+; N (%)</b>	<b>4 (12%)</b>
		<b>MPD (5-9 mm); N (%)</b>	<b>10 (30%)</b>
		<b>abrupt change in MPD caliber; N (%)</b>	<b>11 (33%)</b>
		<b>Lymphadenopathy; N (%)</b>	<b>3 (9%)</b>
	<b>High-Risk Stigmata</b>	<b>Dilatation of MBD <math>\geq 8</math> mm; N (%)</b>	<b>3 (9%)</b>
		<b>Mural nodules <math>\geq 5</math>mm, Enhancement+; N (%)</b>	<b>3 (9%)</b>
<b>Dilatation of the MPD <math>\geq 10</math> mm; N (%)</b>		<b>8 (24%)</b>	

**Table 1:** Demographics and image analysis. Table shows the demographics and evaluation of imaging findings defined by Fukuoka Guidelines, performed by reader A (30

years of experience). MPD: main pancreatic duct; MBD: main biliary duct; Enhancement +: positive enhancement.

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**Fig. 2:** Inter-reader agreement. The figure shows the intraclass correlation coefficients (ICC, reader A vs B vs C) and 95% confidence intervals (95% CI, error bars) for Worrisome Features (WF, Orange) and High-risk Stigmata (HRS, Red). Enhancement +: positive enhancement. MPD: Main Pancreatic Duct. MBD: Main Biliary Duct.

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## Conclusion

The Fukuoka Guidelines for IPMN allowed for a reproducible evaluation of WF and HRS with moderate to good IRA in readers with different experience.

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