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ONCOLOGY

Pilot study of rapid MR pancreas screening for patients with BRCA mutation

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Abstract

Purpose To develop and optimize a rapid magnetic resonance imaging (MRI) screening protocol for pancreatic cancer to be performed in conjunction with breast MRI screening in breast cancer susceptibility gene (BRCA)–positive individuals.

Methods An IRB-approved prospective study was conducted. The rapid screening pancreatic MR protocol was designed to be less than 10 min to be performed after a standard breast MRI protocol. Protocol consisted of coronal NT T2 SSFSE, axial NT T2 SSFSE and axial NT rFOV FOCUS DWI, and axial T1. Images were acquired with the patient in the same prone position of breast MRI using the built-in body coil. Image quality was qualitatively assessed by two radiologists with 12 and 13 years of MRI experience, respectively. The imaging protocol was modified until an endpoint of five consecutive patients with high-quality diagnostic images were achieved. Signal-to-noise ratio and contrast-to-noise ratio were assessed.

Results The rapid pancreas MR protocol was successfully completed in all patients. Diagnostic image quality was achieved for all patients. Excellent image quality was achieved for low *b* values; however, image quality at higher *b* values was more variable. In one patient, a pancreatic neuroendocrine tumor was found and the patient was treated surgically. In four patients, small pancreatic cystic lesions were detected. In one subject, a hepatic mass was identified and confirmed as adenoma by liver MRI.

Conclusion Rapid MR protocol for pancreatic cancer screening is feasible and has the potential to play a role in screening BRCA patients undergoing breast MRI.

Key Point

- *Develop and optimize a rapid magnetic resonance imaging (MRI) screening protocol for pancreatic cancer to be performed in conjunction with breast MRI screening in BRCA mutation positive individuals.*

Giuseppe Corrias and Mitchell C. Raeside contributed equally to this work.

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Keywords Early detection of cancer · Pancreatic neoplasm · Breast cancer · Magnetic resonance imaging · Screening

Abbreviations

ADC	Apparent diffusion coefficient
ANOVA	Analysis of variance
BRCA	Breast-related cancer antigens
CI	Confidence interval
CNR	Contrast-to-noise ratio
EUS	Endoscopic ultrasound
FNA	Fine needle biopsy
FOCUS DWI	Field-of-view optimized and constrained undistorted single-shot diffusion-weighted imaging
FSPGR	Fast spoiled gradient echo
ICC	Intra-class correlation coefficient
IPMN	Intraductal papillary mucinous neoplasms
MRCP	Magnetic resonance cholangiopancreatography
MRI	Magnetic resonance imaging
NEX	Number of excitations
NT	Navigator-triggered
PDAC	Pancreatic ductal adenocarcinoma
pNET	Pancreatic neuroendocrine tumor
RC	Repeatability coefficient
ROI	Regions-of-interest
SNR	Signal-to-noise ratio
SSFSE	Single-shot fast spin echo

Introduction

Both breast-related cancer antigens (BRCA1 and BRCA2) are associated with an increased risk of breast and ovarian cancer, pancreatic ductal adenocarcinoma (PDAC), prostate cancer, and melanoma [1]. While the overall lifetime risk for PDAC in people who are carriers of BRCA mutations has not been firmly established, it has been estimated to be approximately 1 to 5%, with a relative risk of 1.5–9.0 compared to the general population [2–4].

Population-based screening for pancreatic cancer has not been recommended [5] due to the low incidence of pancreatic cancer in the general population and because screening is either invasive or expensive. However, in selected populations at increased risk for pancreatic cancer, screening may be beneficial [6, 7].

BRCA-positive female patients undergo MRI screening for breast cancer, which is recommended annually between the ages of 25 and 75 [7, 8]. As these patients are already undergoing screening by MRI on a regular basis, there is a unique opportunity to incorporate non-invasive screening of other at-risk organ systems (e.g., pancreas, ovary) at the same MR session.

We propose a tailored protocol consisting of a limited number of sequences centered on the pancreas that could be performed for the purposes of rapid MRI screening, without moving the patient to the supine position or applying a dedicated body coil.

The main purpose of this study was thus to evaluate the feasibility of a novel pancreatic screening MR protocol without a dedicated body coil, in the prone position, to be performed after a contrast-enhanced breast MRI screening in BRCA-positive individuals. Other exploratory aims were to identify which *b* values could be used for diffusion-weighted imaging qualitative and quantitative image and to evaluate the inter-reader agreement of apparent diffusion coefficient (ADC) measurements of the pancreas.

Materials and methods

IRB and HIPAA compliance

This prospective study was approved by the local Institutional Review Board (IRB) and was HIPAA compliant. Each recruited subject provided written informed consent for participation in the study. We included consecutive patients who were planning to undergo breast MR screening between August 2015 and October 2017 ($n = 40$). Funding could cover imaging up to 40 subjects.

Inclusion and exclusion criteria

Known BRCA-positive female patients scheduled to undergo routine screening breast MRI were invited to participate in this prospective study.

Inclusion criteria were as follows: known BRCA1 or BRCA2 mutation, age ≥ 25 years, female, and undergoing screening breast MRI with gadolinium contrast. Exclusion criteria were as follows: patients with known breast cancer, patients unable to complete their scheduled breast MRI, patients with prior pancreatic surgery or cancer, and patients with prior abdominal surgery with surgical clips in the stomach or liver.

Protocol design and image acquisition

The rapid screening protocol was designed to be completed in less than 10 min after the completion of the contrast-enhanced breast MRI examination. The images were acquired with the patient in the prone position, with the breast coil still in place, but using the built-in body coil of the MR scanner without placement of a dedicated phased array body coil (Fig. 1). No

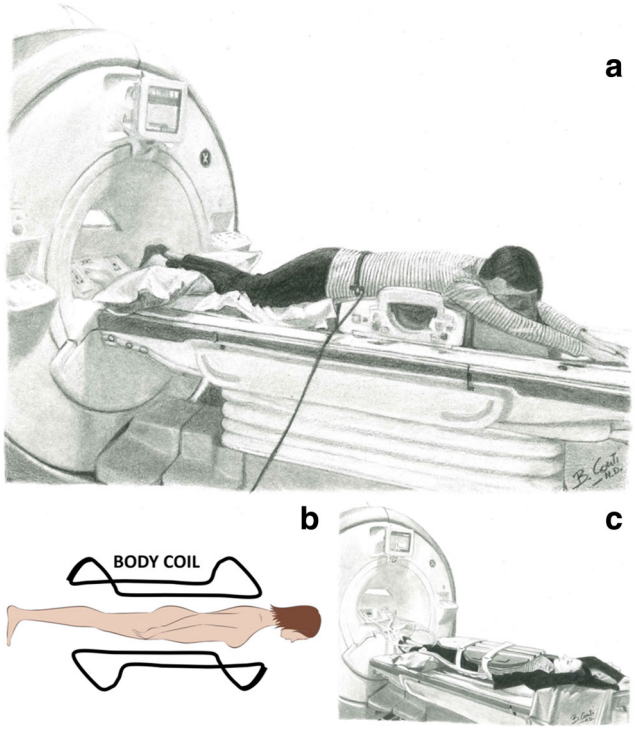

Fig. 1 **a** Positioning of patient for rapid pancreas MRI screening protocol at the conclusion of the breast MRI examination. **b** Demonstrating location of the built-in body coil within the bore of the magnet during the rapid pancreas MRI screening protocol rather than the surface coil. **c** Usual positioning of patient for magnetic resonance cholangiopancreatography (MRCP) demonstrating placement of surface coil

additional contrast material was administered. Gd-BOPTA (Multihance, Bracco Diagnostic, 0.1 mmol/kg) was administered during the breast MRI examination. All studies were performed on GE 3-T systems (MR750, GE Healthcare).

Sequences were performed as shown in Table 1, including coronal navigator-triggered (NT) T2 single-shot fast spin echo (SSFSE), axial NT T2 SSFSE, followed by axial T1 post-contrast fast spoiled gradient echo (FSPGR), and axial reduced NT FOV (rFOV) field-of-view optimized and constrained undistorted single-shot (FOCUS) DWI ($b = 0$, 20, 50, 80, 250, 500, and 800 s/mm^2). The FOCUS-specific parameters are shown on Supplemental Material Table 1. The variable number of excitations (NEX) was used for DWI (see Table 2). Multiple b values were acquired: $b = 0$ s/mm^2, three $b < 100$ s/mm^2 values, and three $b > 100$ s/mm^2 values; apparent diffusion coefficient (ADC, mm^2/s) was calculated with a monoexponential model using ReadyView software on Advantage Workstation VolumeShare 5 (GE Healthcare).

Image review: qualitative analysis

Image quality was qualitatively assessed by two experienced abdominal radiologists (LM and RKGD with respectively 12 and 13 years of experience in MRI) with a graded score system of 1–5: 1 = all diagnostic information present, 2 = most diagnostic information present, 3 = sufficient diagnostic information present, 4 = minimal diagnostic information present, and 5 = non-diagnostic (Supplemental Material Fig. 1). Following subject 1, parameters for axial T1 post-contrast and rFOV DWI were modified to improve image quality by varying NEX and voxel size. Sequence parameters were updated anytime a patient did not have a complete exam with diagnostic images (score of 1) for all sequences. The study endpoint chosen was an optimized protocol defined by diagnostic images (score of 1) achieved for five consecutive patients, based on scores given by at least one of the two readers. Images were also reviewed by one of the same diagnostic radiologists for detection of pancreatic lesions. In cases with a positive imaging finding, the subject was referred to a pancreaticobiliary surgeon for review and underwent a diagnostic MRCP.

Table 1 Imaging protocol. The fast pancreas screening protocol is implemented at the end of a breast ceMRI. Images of the pancreas are acquired with patient in prone position, using the built-in body coils with the breast coil still in place. *T1w*, T1-weighted; *T2w*, T2-weighted; *SSFSE*, single-shot fast spin echo; *DWI*, diffusion-weighted imaging; *2D-EPI*, bidimensional, echo planar; *Gd-BOPTA*, gadobenate dimeglumine; *FRFSE*, fast recovery fast spin echo; *Fat-Sat*, fat suppressed; *BW*, body weight; *3D-FSPGR*, tridimensional, fast spoiled gradient echo; *FOCUS*, field-of-view optimized and constrained undistorted single-shot

	Breast ceMRI protocol		Fast Pancreas Screening Protocol
Scanner	GE Discovery MR 750, 3T (GE Healthcare, Milwaukee, WI)		
Patient position	Prone	NO CHANGES in patient position	Prone
Coil	Breast, phased-array	Breast coil still IN PLACE	Built-in Body Coils
Sequences	•Localizer: T2w SSFSE, three planes		•Localizer: T2w SSFSE, three planes
	•DWI: 2D-EPI, axial		•T2w: SSFSE, coronal and axial
	•T2w: FRFSE Fat-Sat, axial		•T1w: 3D-FSPGR, axial
	•T1w: 3D-FSPGR, axial, pre- and post-contrast		•DWI: 2D-EPI, FOCUS, axial
Contrast	Gd-BOPTA (MultiHance, Bracco Diagnostics, NJ); 0.1 mmol/kg BW		-

Table 2 MRI technical parameters, listed for subject 1 (initial) and subject 10 (final). After patient 13, parameters were not modified further. *T2-SSFSE*, T2w single-shot fast spin echo; *FOV*, field-of-view; *ST*, slice thickness; *TR*, repetition time; *TE*, echo time; *NEX*, number of excitations; *DWI*, diffusion-weighted imaging

Parameter	T2 SSFSE coronal		T2 SSFSE axial		T1 axial		DWI			
	Initial	Final	Initial	Final	Initial	Final			Initial	Final
TR (ms)	6375	3000	2025	3000	3.1	3.4			4444	4000
TE (ms)	97.8	98.6	99.6	102	1.4	1.6			75	75
NEX	0.54	0.63	0.55	0.63	0.7	0.69	*b*	0	8	8
								20	16	10
								50	8	8
								80	4	4
								250	4	6
								500	4	8
								800	16	16
Slice thickness (mm)	7	6	6	6	4	4			4	6
Slice spacing (mm)	7	6	6	6	2	2			5.5	6
Matrix	320 × 224	320 × 256	320 × 256	320 × 256	256 × 192	256 × 192			160 × 80	160 × 80
FOV (cm)	30	48	40	32	40	30			24	24

Image review: quantitative analysis

In all sequences, signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) were assessed quantitatively using an Advantage Workstation VolumeShare5 (GE Healthcare), with a Volume Viewer 10.3 software, module "Reformat" image. Circular regions-of-interest (ROI) with 5 mm diameter were placed manually by three radiologists (GC, MCR, and AA) in the pancreatic head, body, and tail, and the peripancreatic fat (Fig. 2). ROIs were propagated on all the series to improve reproducibility of measurements. Mean signal intensity (*S*) and standard deviation (SD) in each ROI were recorded. In those sequences where it was available (T2 SSFSE axial and T1 post-contrast axial), an ROI was placed in the background air for a direct assessment of image noise according to the following equations:

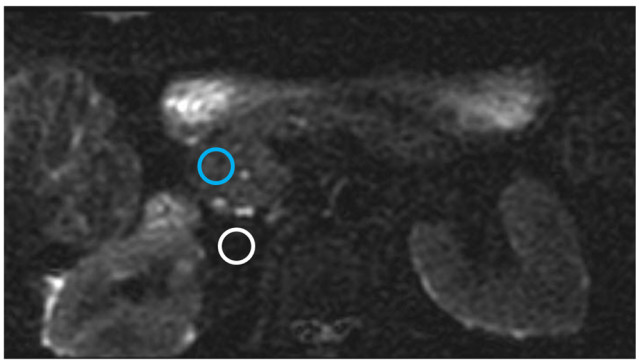

Fig. 2 ROI placement on DWI ($b = 50$ s/mm^2). Circular ROIs with 5 mm in diameter are placed respectively on pancreatic head (light blue, avoiding main duct) and on visceral fat (white) by 3 radiologists. Average signal intensity (SI) and standard deviation (SD) are recorded

$$\mathrm{SNR} = \frac{S_{\mathrm{pancreas}}}{SD_{\mathrm{air}}}$$

$$\mathrm{CNR} = \frac{S_{\mathrm{pancreas}} - S_{\mathrm{fat}}}{\mathrm{SD}_{\mathrm{air}}}$$

As the rFOV DWI sequences did not include background air, for an estimation of noise in 18 patients, the DWI sequence was repeated during the same examination, allowing noise to be calculated as SD deviation using subtraction methods between the two DWI sequences (NEMA Standards Publication MS 1-2008 (R2014), Determination of Signal-to-Noise Ratio (SNR) in Diagnostic Magnetic Resonance Imaging). Since the screening protocol was modified after patient number 19 following an IRB-approved amendment to add sequences to screen for the presence of ovarian cancer, a single acquisition of rFOV DWI was subsequently acquired to save imaging time, allowing an SNR and CNR estimation in only 18 patients.

Quantitative analysis of ADC maps was performed by the same three radiologists with the placement of circular ROIs with 5 mm diameter; sampled regions included pancreatic head, body, tail, and respective peripancreatic/visceral fat on the same slice; average apparent diffusion coefficient (ADC, mm^2/s) was recorded.

Quantitative evaluation of cancer tissue signal was performed with placement of ROIs within the pancreatic mass.

Statistical analysis

Intra-class correlation coefficient (ICC) and repeatability coefficient (RC) were estimated to evaluate agreement between every pair of three readers on ADC values. The bias-corrected 95% confidence intervals (CI) for repeatability coefficients were estimated using nonparametric bootstrapping method

with 1000 replicates. The Bland-Altman plot on ADC value was plotted for every pair of readers. Image quality was evaluated by two readers and the agreement was assessed using weighted kappa statistic with squared weights. Analysis of variance (ANOVA) and Tukey's pairwise test were used to evaluate whether CNR value and SNR value were the highest under one *b* value, separately for *b* value < 100 and > 100.

A test with p value < 0.05 was considered statistically significant. No adjustment on multiple testing was applied considering hypothesis-generating purpose of the study. All statistical analyses were performed in software packages R version 3.3 (The R Foundation for Statistical Computing).

Results

Study population

Between August 2015 and October 2017, 40 subjects underwent rapid MRI pancreas screening in conjunction with their screening breast MRI. Mean age was 48 years (range 28–79 years). Twenty subjects were known BRCA1 carriers, 19 were BRCA2 carriers, and one was a carrier of both BRCA1 and BRCA2. Individual genetic mutations characteristics are detailed in Supplement Material Table 2.

Sequence protocol

The rapid pancreas MR protocol was successfully completed in all 40 patients. The mean of acquisition times for each sequence is listed in Table 3.

The screening protocol was considered optimized after patient 13 and parameters were not modified further as already shown in Table 2.

Imaging findings

In one subject, a suspicious lesion was found within the pancreatic head: a 42-year-old woman with BRCA 2 mutation had a 1.5-cm mass in the pancreatic head with slightly hyperintense signal on T2-weighted axial images and bright hyperintense signal on DWI axial images, *b* 50 s/mm^2 (Fig. 3). This patient was worked up with a pancreatic protocol CT of the abdomen, which confirmed the presence of a mass, and subsequently underwent endoscopic ultrasound (EUS) and a fine needle biopsy (FNA). The pathology (Fig. 4) results were consistent with a well-differentiated pancreatic neuroendocrine tumor (pNET). The patient was treated surgically with a pancreaticoduodenectomy and is being followed up at our institution. Imaging quality was scored as sufficient by the radiologists (score equal or below 3) for the patient with pancreatic cancer, for all sequences, with an excellent quality (score 1) for T2W axial images and T2W coronal images.

In four subjects, sub-centimeter pancreatic cystic lesions (from 0.5 to 0.8 cm) were detected (Fig. 5, Supplemental Material Figs. 2 and 3). These subjects were referred to a pancreaticobiliary surgeon for evaluation, and each subject underwent a subsequent diagnostic MRCP study, which confirmed the findings of the rapid screening MRI. Cystic lesions that were detected at screening were of similar size and appearance on the dedicated MRCP, and no additional lesions were identified on MRCP.

In one patient, a liver adenoma was incidentally detected. In one patient, the breast screening part of the MRI examination detected a breast cancer.

Imaging quality was scored as sufficient by the radiologists (score equal or below 3) for the patient with pancreatic cysts for all sequences, with an excellent quality (score 1) for T2W axial images and T2W coronal images.

Qualitative evaluation

Image quality was rated as 1 (all diagnostic information present) for most patients for the axial and coronal NT T2 SSFSE and axial NT T1 sequences (Supplemental Material Fig. 4). Excellent image quality was achieved in DWI for low *b* values, with a score of 1 for image quality in the pancreatic head and body for *b* values from 0 to 80 s/mm^2 in most subjects, and a score of 1 for image quality in the pancreatic tail for the same low *b* values for most subjects. DWI quality at higher *b* values (250, 500, and 800 s/mm^2) was more variable, with scores ranging between 1 and 5 (Supplemental Material Fig. 4). The results for this evaluation were grouped in two categories (score 1–3, sufficient image quality; score 4–5, insufficient image quality). Concordance with these two groups of scores was above 80% for almost all sequences analyzed except from high *b* value DWI (Supplemental Material Table 3).

Quantitative evaluation

SNR and CNR values for axial T2 SSFSE and axial T1 post-contrast sequences are reported in Supplemental Material Table 4, and SNR for the rFOV DWI sequence are reported in Supplemental Material Table 5. Adequate SNR and CNR

Table 3 Average time to complete the screening in 40 patients. DWI time can be further shortened as recommended in the text. *T1w*, T1-weighted; *T2w*, T2-weighted; *DWI*, diffusion-weighted imaging; *m:s*, minutes:seconds

Pancreas screening	
Sequence	Time (m:s)
T2w coronal	1:33
T2w axial	1:14
T1w axial	1:10
DWI	6:20
Total scan	10:17

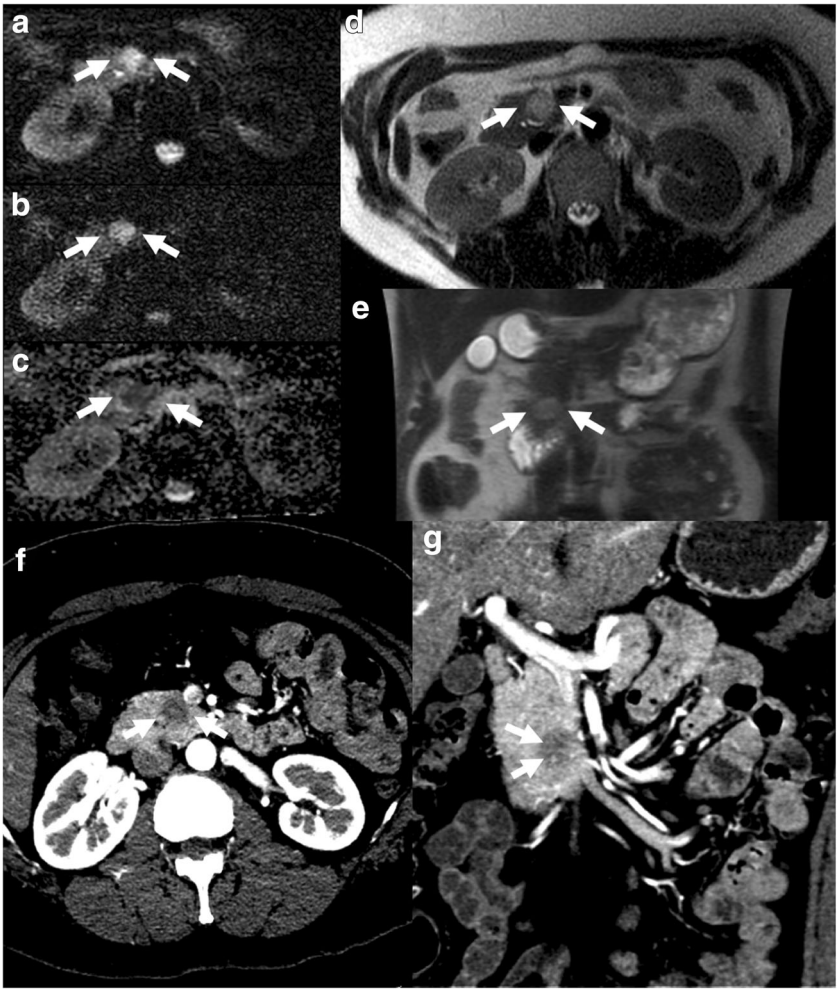

Fig. 3 Selected images from subject 37. Patient with a suspicious lesion of pancreatic head: women 42 years old, enrolled to this study. Evidence of mass of 1.5 cm in the pancreatic head demonstrated as brightly hyperintense on DWI axial images, $b = 50$ s/mm^2 ((**a**), white arrows) and intermediate (b) values, $b = 500$ s/mm^2 (**b**, white arrows). Low value in ADC map ((**c**), white arrows). The mass is seen as slightly hyperintense on T2-weighted axial images (**d**, white arrows), and in T2-weighted coronal images ((**e**), white arrows). A subsequent CT of the abdomen confirmed the presence of a mass within the pancreatic head (**f**, axial CT pancreatic phase; and (**g**) coronal CT, pancreatic phase)

values were obtained using the built-in body coil, particularly for the T2 SSFSE and T1-weighted sequences and lower b values up to 250 s/mm^2. For the higher b values of 500 and 800 s/mm^2, the lower SNR obtained accounted for the subjectively lower image quality scores assigned.

To select a b value < 100 s/mm^2 and a b value > 100 s/mm^2 among multiple acquired b values, we compared every pair of CNR values with different b values using ANOVA analyses. The CNR was higher with b values of 0/20/50 compared to a b value of 80 among b values < 100 (Table 4), and CNR was also higher for b value of 250 than 500/800 among b values > 100, across the pancreatic head, body, and tail.

In the patient with a pancreatic head mass, CNR and SNR measurements of the pancreatic cancer had different values

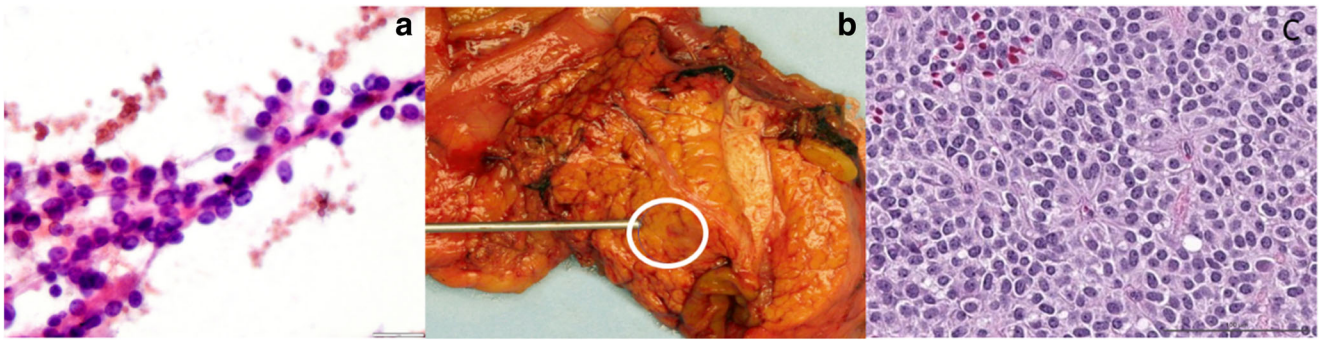

Fig. 4 **a** Endoscopic ultrasound (EUS)–guided fine needle biopsy (FNA) and Papanicolau stain (magnification × 100) demonstrate presence of neoplastic cells. **b** Gross pathology of pancreatic specimen after a Whipple procedure was performed. Tumor is seen within the head of pancreas (oval white marker). **c** H&E stain, magnification × 150, showing a well-differentiated pNET. The ki67 index was < 1%

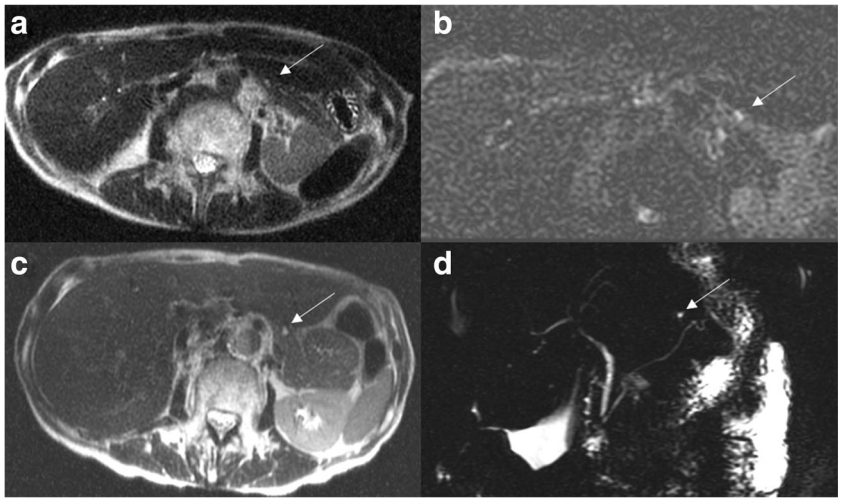

Fig. 5 Selected images from subject 3. Woman, 79 years old. Selected T2 SSFSE axial (**a**) and rFOV DWI, $b = 500$ s/mm^2 (**b**) images from rapid MR screening examination demonstrating pancreatic body cyst (white arrows), which was confirmed at diagnostic MRCP on (**c**) T2 SSFSE axial and (**d**) MRCP images

than average but there was an overlap with boxplots of normal pancreatic tissue measurements as shown in Supplemental Material Fig. 5.

ADC maps inter-reader agreement

The obtained ADC values for three readers are summarized in Supplemental Material Table 6a. The agreement on ADC values was calculated between the three readers in the first 18 patients which had a double rFOV DWI acquisition which allowed calculation of SNR. The agreement between the three readers on ADC values was good in particular for the head of the pancreas (Supplemental Material Table 6b, Supplemental Material Fig. 6).

Table 4 Differences of estimated mean CNR between *b* values. Significant differences were found between 80 and all the other values among *b* values < 100 and between 250 and all the other values among *b* values > 100. *CNR*, contrast-to-noise ratio; *CI*, confidence interval

b values	CNR difference	Lower 95% CI	Upper 95% CI	*p* value
Among *b* values < 100				
20-0	− 0.20	− 1.47	1.08	0.979
50-0	− 0.69	− 1.97	0.59	0.507
80-0	− 2.64	− 3.92	− 1.36	< 0.001
50-20	− 0.49	− 1.77	0.79	0.755
80-20	− 2.44	− 3.72	− 1.17	< 0.001
80-50	− 1.95	− 3.23	− 0.67	0.001
Among *b* values > 100				
500-250	− 0.74	− 1.46	− 0.02	0.044
800-250	− 0.89	− 1.62	− 0.16	0.012
800-500	− 0.15	− 0.88	0.58	0.877

Discussion

This study demonstrates that rapid pancreas MRI screening using the built-in body coil on a 3-T magnet can be performed under than 10 min, yielding diagnostic image quality for the pancreas. Combined with breast MRI screening, this study offers a rapid, non-invasive, and potentially inexpensive screening tool of the pancreas for BRCA patients.

A BRCA mutation is a germline mutation in either of the two tumor suppressor genes BRCA1 and BRCA2. Mutations have been associated with increased risk of developing breast and ovarian cancer, but recently, Friedenson has shown how any kind of invasive cancer, including pancreatic cancer, prostate cancer, and colon cancer, can be related to harmful mutations in BRCA genes [9]. A BRCA1 mutation increases lifetime risk of developing pancreatic cancer approximately by a factor of two or three; a BRCA2 mutation by a factor of three to five. About 1 to 5% of people with pancreatic cancer have a BRCA mutation [9]. Like other cancers associated with BRCA mutations, pancreatic cancer associated with BRCA mutations tends to appear a decade earlier than cases not associated with mutations. Given the earlier age at which PDAC and its precursors may develop in BRCA-positive patients, this may justify implementing the screening tool in a population of young patients, such the one in our study.

PDAC with germinal BRCA mutation has more favorable outcome than non-hereditary PDAC, and a better response when treated with platinum-based agents in stages 3 and 4 [10] compared to advanced-stage PDAC arising in a general population as proven by a metanalysis by Golan et al [4, 11]. Implementing a screening program in this population might help diagnosing cancers in an earlier stage opening a scenario for further studies investigating whether an earlier diagnosis might influence response to treatment in this particular population.

At the present time, there are no proven screening or surveillance methodologies (either image or blood-based) for the early detection of PDAC even in higher risk populations. Most of the screening studies that used MRI for PDAC screening used MRCP to aid the diagnostic process [12–17] (Supplemental Material Table 7). MRCP has been suggested as a safe and effective initial screening modality [15]. Our protocol was specifically intended to perform without a dedicated body coil, whereas, due to a long echo time, MRCP sequences might not have enough signal-to-noise ratio if performed with the built-in coil [18].

In our study, the MR pancreas screening protocol included the following: coronal NT T2 SSFSE, which was used to localize the pancreas and plan the FOV of the other axial sequences, axial NT T2 SSFSE and axial NT rFOV FOCUS DWI for lesion detection, and axial T1 for detection of enhancement [13, 19–28].

The SNR and subjective image quality decreased at higher *b* values in the DWI sequence, as expected. The use of multiple *b* values in this study was not intended for intravoxel incoherent motion (IVIM) analysis, but rather to investigate different potential combinations of *b* values to be incorporated into a future screening protocol. In this experimental protocol, more *b* values (7 in total) and NEX were used than would be expected to be used in the final protocol when it is implemented in the clinical setting. In the screening setting, where detection of a lesion for subsequent diagnostic workup is more important than the accurate initial characterization of the lesion, the use of fewer and relatively lower *b* values with higher associated SNR may be sufficient. As this protocol is considered for clinical practice, the number of *b* values could be decreased to 3. This would further reduce the acquisition time or potentially allow for an increased NEX and further improvement in image quality. Based on our findings, we suggest the following *b* values (s/mm^2): $b = 0$, a low *b* value such as $b = 20$–50 (which would suppress signal from moving fluid and vessels), and a moderately high *b* value such as $b = 250$ for lesion detection.

ADC values obtained were slightly lower than, but comparable with and within the ranges provided by literature data (Supplemental Material Table 8), even if images were acquired with the patient in a prone position with the built-in body coils [28, 29]. The inter-reader agreement was limited (intra-class correlation coefficient from 0.562 to 0.875).

Although this study was not designed to assess the incidence of pancreatic lesions or to evaluate the effectiveness of pancreatic screening itself, the rate of observed positive findings in 5 of 40 subjects with BRCA1 and BRCA2 mutations is within the range of expected pancreatic lesions in this population [1].

Our study led to the findings of two cancers in total, a breast cancer recognized from the routine breast MRI examination and a pancreatic cancer found from our investigational screening protocol (Supplemental Material Table 2), both of which were surgically treated.

The patient with pancreatic cancer, an asymptomatic .42-year-old woman, had a pancreatic head mass which was surgically removed with a Whipple procedure. Pathology confirmed the diagnosis of low-grade pNET (WHO 2010 grade 1), with a mitotic rate of 2 per 50, an estimated proliferative index (Ki67) of 0.2% in tumor cells. None of the 22 analyzed lymph nodes were found to be positive for metastasis. The final staging of the tumor was pT1, pN0, M0.

It is not clear whether an association between BRCA mutations and pNET exists, so our finding was probably only a chance occurrence, but nonetheless it provides further evidence that this protocol may identify early pancreatic cancers in an at-risk population.

The other significant findings were pancreatic cystic lesions on T2-weighted SSFSE that were probably branch-duct intraductal papillary mucinous neoplasms (IPMN). Previous studies investigating screening for pancreatic cancer have demonstrated that small cysts, mostly branch-duct IPMN, are the most commonly detected abnormality [1, 30, 31]. IPMN should be considered part of the phenotype of familial pancreatic cancer [30]. Additional MRCP workup of these patients confirmed the findings of the rapid screening study and did not reveal any additional lesion. Interestingly, all these pancreatic lesions, both benign and malignant, were all found in patients with deleterious mutations of the BRCA genes (Supplemental Material Table 2). While preliminary, the concordant results of our rapid screening protocol with the follow-up MRCP are promising.

In this research protocol, the whole pancreas screening examination was performed at the completion of the clinical breast screening MRI. However, in the actual clinical setting, we would also perform a pre-contrast T1 axial sequence during the breast MRI component of the examination prior to the administration of IV contrast. This would further improve evaluation of the pancreas, which is well seen on pre-contrast T1 sequences. To facilitate more formal testing and evaluation of rapid MR screening of the pancreas, the final recommended protocol is outlined in Table 5. The final protocol with only three *b* values for DWI and with a pre-contrast axial T1 would further shorten our protocol total acquisition time which would last about 7 min.

Limitations of this study include the small number of patients included in a prospective pilot study. Each individual

Table 5 Proposed protocol for rapid MR screening of the pancreas in clinical practice. *T1w*, T1-weighted; *T2w*, T2-weighted; *SSFSE*, single-shot fast spin echo; *DWI*, diffusion-weighted imaging; *rFOV*, reduced field-of-view

Recommended sequences
T2w SSFSE coronal
T2w SSFSE axial
3D T1w pre- and post-contrast
rFOV DWI ($b = 0$, 20/50 and 250 s/mm^2)

patient with "negative" rapid screening MRI protocols did not undergo a formal diagnostic MRCP or other workup (e.g., endoscopic ultrasound) to confirm the absence of pancreatic lesions. Thus, the sensitivity of our screening protocol compared to a traditional MRCP sequence is unknown, and so is its accuracy, due to a lack of pathological correlation. Furthermore, also imaging quality has not been compared with a standard of reference, such as MRC with dedicated body coil. Finally, SNR and CNR of DWI were estimated only in 18 patients.

Conclusion

A rapid MR protocol for pancreatic cancer screening for BRCA patients in the prone position and use of the built-in body coil is feasible with diagnostic quality images for the detection of focal abnormalities within the pancreas.

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Compliance with ethical standards

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Informed consent Only if the study is on human subjects:

Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- prospective
- observational
- performed at one institution

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