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What is the best fruit juice to use as a negative oral contrast agent in magnetic resonance cholangiopancreatography?

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AIM: To identify, *in vitro*, the best fruit juice to use as oral contrast agent in magnetic resonance cholangiopancreatography (MRCP) and to test, *in vivo*, the best natural juice and the new parameters in MRCP sequences identified *in vitro*.

MATERIALS AND METHODS: The *in vitro* evaluations consisted of measuring the T2 values of a pure solution of manganese (Mn) and iron (Fe) at different concentrations, measuring the content of Mn and Fe in five commercial juices and their T2 relaxation times, and identifying the optimal juice dilution for suppressing the gastrointestinal fluid signal. The new parameters of MRCP sequences were tested *in vivo*.

RESULTS: Manganese alone strongly influenced the shortening of the T2 values (p=0.004). The T2 value with an echo time (TE) of ≥1,000 ms enabled sufficient intestinal fluid suppression in the case of high juice dilution. A flip angle of 90° maximised the differences between the high signal from static fluids, such as the bile and the fluid in the gastrointestinal tract, using fast imaging employing steady-state acquisition (FIESTA) sequences (p<0.001).

CONCLUSION: The shortening of the T2 relaxation time depended only on the Mn concentration. All the commercial juices had an Mn concentration sufficient to suppress the gastrointestinal fluid signal using long TE sequences. The oral ingestion of commercial juice before MRCP was enough to suppress the signal from the gastrointestinal fluids, regardless of its dilution after ingestion. When using FIESTA sequences, a flip angle of 90° allowed the best suppression of gastrointestinal fluid signals.

Introduction

Since its introduction in 1990,[1] magnetic resonance cholangiopancreatography (MRCP) has made great

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technical advances in providing images superior to those obtained with endoscopic retrograde cholangiopancreatography (ERCP), without the need of intravenous contrast media.[2] Furthermore, MRCP is a non-invasive imaging technique, less likely to cause patient discomfort or injury than ERCP, which is an invasive procedure having a complication rate of 3–9% and a mortality rate of 0.2–0.5%.[3,4] Therefore, MRCP is preferred as an initial non-invasive technique for evaluating the biliary tract if immediate therapy for a known problem is not the primary aim.[5]

Moreover, MRCP has a myriad of indications, such as the evaluation of the normal biliary anatomy and its variants, and congenital and acquired biliary pathologies.[6] It is performed with heavily T2-weighted (T2W) sequences, exploiting the fact that bile, like all static fluids, has long T2 relaxation times making the bile ducts hyperintense and well recognisable (white) from the decreased signal of the background tissues, such as solid organs and flowing blood.[2] In recent years, the fast imaging employing steady-state acquisition (FIESTA) sequence has also increasingly been used in magnetic resonance imaging (MRI) of the biliary tract.[7–9] In this sequence, similar to blood and gastrointestinal fluids, bile has increased signal intensity.[8,9] The FIESTA sequence has many advantages in biliary imaging compared to other MRI sequences: insensitivity to the dephasing effects of flowing bile, which can be misinterpreted as filling defects on fast spin echo (FSE) sequences; bright blood effects useful in diagnosing biliary pseudo-strictures due to vascular conditions on unenhanced MRCP studies, rapid acquisition times and high-resolution imaging.[7–9]

A recognised limit of MRCP is represented by the possible overlap of the static fluids in the pancreatobiliary system and those in the gastrointestinal tract (i.e., the stomach, duodenum, and proximal jejunum), which can obscure or simulate a disease.[10,11] To overcome this limit, several oral negative contrast agents have been produced in the past, containing paramagnetic substances, which shorten the T2 relaxation time, thus reducing the signal hyperintensity of the gastro-enteric fluids.[12] Nevertheless, these negative oral contrast agents have many limitations: they are relatively unpalatable, are too diluted in the gastrointestinal tract, or are too expensive.[12] In more recent years, natural fruit juices, of which the most popular are pineapple (PJ) and blueberry juices (BJ), have gained attention owing to their similar properties in suppressing the high T2 signal from the gastrointestinal tract liquids due to the high content of manganese (Mn) and iron (Fe), and to their higher palatability and low cost; however, the exact content of paramagnetic substances in the different juices available commercially and the correct juice dosage to suppress the T2 signal of gastro-enteric fluids have not been analysed and standardised to date.

The primary aim of this study was to identify the best fruit juice to use as an oral negative contrast agent for MRCP. Therefore, different fruit juices were analysed "*in vitro*", evaluating their paramagnetic substance content, their T2 relaxation times, their optimal concentration for nulling the gastrointestinal signal fluid, and their impact on the parameters of the MRCP sequences. The secondary aim of this study was an *in vivo* validation of the efficacy of the best natural juice and of the new parameters of the MRCP sequences identified by the *in vitro* examinations in improving the quality of the standard MRCP protocol.

Materials and methods

This study was approved by the local institutional review board and written informed consent was obtained from all the patients.

The MRI was performed using a 1.5T superconducting MRI unit (HDX-t Signa; General Electric, Milwaukee, WI, USA), with a maximum gradient strength of 33 mT/m for x–y–z, an effective value of 57 mT/m, a slew rate of 120 T/m/s, and an effective value 207 T/m/s, using a body transmit/receive coil, the HD eight-channel body full FOV array.

In vitro measurements

Eight pure chemical solutions were prepared in the laboratory, four having known concentrations of Mn (0.256, 0.640, 1.6, and 4 mg/dl starting from Sigma Aldrich manganese sulphate ($MnSO_4 \cdot H_2O$) and four with definite concentrations of Fe (0.128, 0.320, 0.8, and 2 mg/dl, respectively, starting from Sigma Aldrich iron chloride ($FeCl_3$) dissolved in 0.1 M nitric acid (HNO_3). Each solution was poured into a small numbered cylinder and the four cylinders containing the different concentrations of Mn (Fig 1a) and the four cylinders containing the different concentrations of Fe (Fig 1b) were inserted separately into two different phantoms filled with aqueous solutions containing paramagnetic salts (8 mM copper sulphate [$CuSO_4 \cdot 5H_2O$] plus 3.6 g/l sodium chloride [NaCl]). This solution corresponded to the standard "AAPM phantom refill", which has a known T2 value of 150 ms (as measured with a Stelar SpinMaster Spectrometer), and it was used as the standard of reference to evaluate the accuracy of the T2 value measurements in the MRI scanner.

Single shot fast-spin echo (SSFSE) T2W sequences were carried out with progressively increasing echo time (TE) values (60, 80, 100, 120, 140, and 160 ms) in order to calculate the T2 values of the single different chemical solutions of Mn and Fe.

The absolute T2 relaxation times and the relative signal intensities were then measured using the software Functool of the GE Advantage Windows Workstation (GE ADW 4.5 for MR 1.5T HDX-t SIGNA General Electric) by placing a region of interest (ROI) over each sample image to calculate the signal intensity (SI). The T2 relaxation time was defined as the time necessary to reduce the transverse magnetisation (the measured signal) by 63%. The software Functool is able to calculate the T2 value of the measured samples from the signal decay curve, obtained by placing a ROI on the images at different TE values. The T2 value of the reference solution (the standard "AAPM phantom refill") was also measured by placing an ROI within the fluid refill, which demonstrated a T2 value of 144±10 ms considered

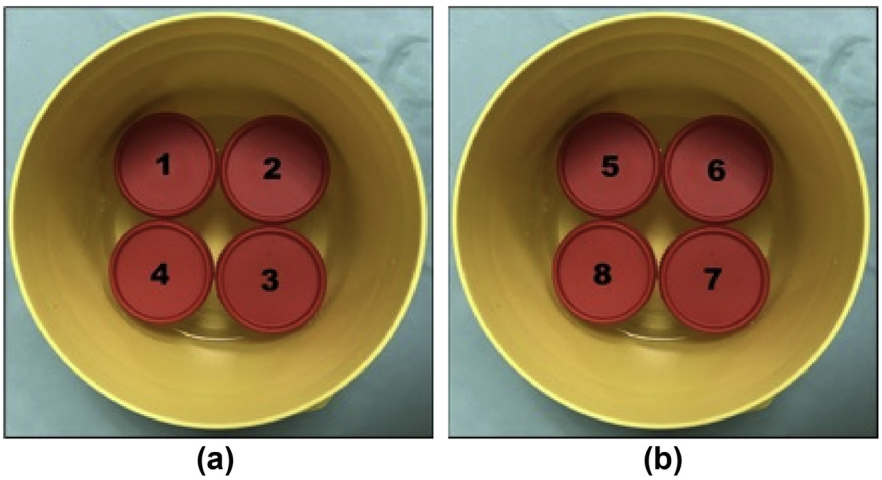

Figure 1 (a) Phantom containing four cylinders with different solutions of Mn (1=0.256, 2=0.640, 3=1.6, and 4=4 mg/dl). (b) Phantom containing four cylinders with different solutions of Fe (5=0.128, 6=0.320, 7=0.8, and 8=2 mg/dl).

compatible with the standard declared by the vendors, as measured by a spectrometer (150 ms). The T2 value measurements were repeated five times, in order to verify the reproducibility of the measurements carried out at different times and under different physical conditions.

In addition, five prepackaged commercial fruit beverages were compared as potential negative oral contrast agents: four PJs (n.1, n.2, n.3, n.4) and one BJ. The Mn and Fe concentrations were measured using atomic absorption spectrometry (Thermo iCE3300 FLAA using acetylene-air flame atomisation). Moreover, the Mn and Fe concentrations were evaluated using the same method described previously in five different batches of the same juice brand to test the constancy of the Mn and Fe content.

The T2 values of each fruit juice and the relationships of the Mn and Fe concentrations with the T2 relaxation times were measured.

As an additional step, in order to simulate the different possible dilution of the ingested juice with the gastrointestinal fluids, the variations of the T2 values of the juice which performed best were measured at five different degrees of water dilution.

The impact of the previous analysis on the SSFSE T2, on the thick or thin slab images, and also on the breath-hold 3D FIESTA sequences was assessed.

In vivo measurements

MRCP was performed in 15 healthy volunteers before and 15 minutes after the ingestion of 300 ml of PJ, identified as the best negative oral contrast agent in MRCP using the "*in vitro*" analysis (the MRCP protocol is detailed in Table 1). The images were assessed blindly by a radiologist using a standard grading technique based on contrast effect (degree of the signal suppression of gastrointestinal fluids). In particular, the radiologist analysed: (1) SSFSE T2, and thick and thin slab images of the same patient blinded to the fruit juice ingestion; (2) FIESTA sequences acquired in every patient blinded to the fruit juice ingestion and to the three different flip angle (FA) values (15°, 45°, and 90°) acquired pre- and post-ingestion of fruit juice. For each patient, the sequence providing both the highest signal intensity of the bile associated and the best gastrointestinal fluid suppression was recorded.

The quality of the three-dimensional (3D) FIESTA images, acquired post-ingestion of the fruit juice at the three different FA values, was graded using a four-point scale: Grade 1, excellent image quality (high signal intensity within the biliary lumen with optimal suppression of gastrointestinal fluid signal); Grade 2, good quality (good signal intensity within the biliary lumen with no excellent suppression of gastrointestinal fluid signal); Grade 3, moderate quality (low inhomogeneous signal intensity within the biliary lumen with very low suppression of gastrointestinal fluid signal), and Grade 4, non-diagnostic quality (no or minimal signal intensity within the biliary lumen, inadequate for analysis).

Statistical analysis

Quantitative variables were expressed as mean ± standard deviation (SD). Comparisons between groups were made using the chi-squared test or Fisher's exact test (two-tailed) for qualitative variables, while the Mann–Whitney test was performed for quantitative variables. The Kolmogorov–Smirnov test was used to test the uniform distribution of a variable. A p-value of <0.05 was considered statistically significant. All the analyses were conducted with SPSS 13.0 software (SPSS, Chicago, IL, USA) (see Table 1).

Results

In vitro measurements

The measurements of the absolute T2 values of the eight chemical solutions containing known concentrations of Mn and Fe are reported in Table 2. The Mn content strongly

Table 1
Standard protocol for magnetic resonance cholangiopancreatography examination.

Sequence	TE (ms)	TR (ms)	Bandwith (kHz)	Thickness (mm)	Matrix	Flip angle
FSEGR T1	In/out phase	110	61.25	4	256×224	80°
SS FSE T2	100	2000	41.67	4	256×224	90°
MRCP HR thick slab	1000	8000	41.67	40	416×320	90°
MRCP FR FSE T2 3D thin slab	1000	trigger	19.23	2	320×320	90°
MRCP FIESTA	Min full	auto	41.67	2	256×224	90°

SS FSE T2, single shot T2 weighted fast spin echo; FSEGR T1, fast spoiled gradient echo T1-weighted; MRCP, magnetic resonance cholangiopancreatography; HR, high resolution; 3D FIESTA, fast imaging employing steady-state acquisition; FR FSE T2, fast recovery fast spin echo T2 weighted; FAT SAT, fat saturation.

Table 2
Absolute T2 values on MRI single shot fast-spin echo T2-weighted sequence of the chemical solutions having known manganese (Mn) and iron (Fe) concentrations.

Mn pure solutions		Fe pure solutions	
Concentrations (mg/dl)	T2 (ms)	Concentrations (mg/dl)	T2 (ms)
0.256[a]	160±15	0.128	1140±50
0.640	135±12	0.320[a]	770±30
1.6	58±6	0.8	350±18
4	23±2	2	293 ±13

[a] p=0.004.

determined the reduction of the T2 relaxation time. Conversely, the Fe effect on shortening the T2 relaxation time was much lower than that of Mn (Fig 2). In chemically pure solutions at similar concentrations of Mn (0.256 mg/dl) and Fe (0.320 mg/dl), the shortening effect on the T2 relaxation time is much greater for the Mn than for the Fe (160±15 versus 770±30 ms; p=0.004).

Upon measuring the Mn and Fe content of the different commercially available juices (PJ and BJ) and the different brands of PJ, a wide variability in Mn concentrations (ranging from 1.16 to 2.38 mg/dl) was observed, coupled

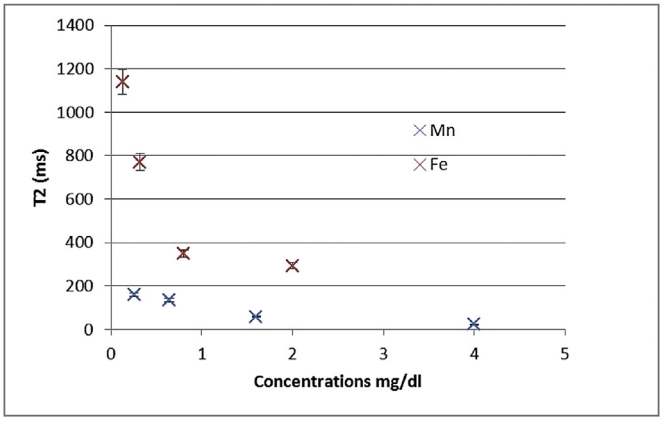

Figure 2 The scatter plot reports the absolute T2 values on MRI single-shot fast-spin echo T2-weighted sequence of the chemical solutions having known Mn and Fe concentrations.

with a more homogeneous but lower Fe content (from 0.118 to 0.150 mg/dl; Table 3). No significant differences in Mn and Fe concentrations were found among the five different batches of juice brands analysed (Electronic Supplementary Material Table S1). Moreover, analysing the effect of the five fruit juices on the T2 relaxation time, the T2 value was inversely proportional to the Mn concentrations (Table 3).

Comparing the effect on the T2 relaxation time of chemically pure Mn and Fe solutions with that of the fruit juices, similar Mn concentrations (1.6 mg/dl in the pure solution and 1.54 mg/dl in PJ n.3) obtained similar T2 values (58±6 and 68± 7 ms, respectively; Tables 2 and 3). The slight difference of 10 ms was mainly due to the counteraction of the Fe contained in the natural juices. In fact, in PJ n.3, the Fe concentration was 0.112 mg/dl, which had a very high T2 value (1140±50 ms) in the corresponding pure Fe solution (0.128 mg/dl); therefore, impairing the lowering effect of the Mn on the T2 image. Fortunately, in the natural juices the Fe absolute concentration was >10 times lower than that of the Mn, and this contrary effect was limited.

The T2 values of the five juices ranged from 86 to 51 ms. For the *in vivo* evaluations, PJ n. 4 was selected as the negative oral contrast agent that performed best in shortening T2 relaxation time (51±4 ms), due to its high Mn content (2.38 mg/dl; Table 3).

Before the *in vivo* evaluation, PJ n.4 was diluted with five different proportions of water (thus simulating the gastrointestinal fluid dilution of the juices) and the variations of the T2 value were measured using MRI. The results are shown in Table 4. Even in the case of the highest dilution simulating a large amount of gastrointestinal fluid (solution 5 = 20 ml of pineapple juice in 60 ml of water), the T2 value (140±10 ms) was still able to suppress the intestinal fluid signal in MRCP thick or thin slab acquisitions since the TE of these sequences (1,000 ms) was far longer than the T2 value of the most diluted juice solution; however, these T2 values were similar to the TE values of the morphologic SSFSE T2 sequence, usually acquired with a TE of 100 ms. Therefore, in this sequence, the signal intensity of the different juices could have varied from iso-intensity to mild hypointensity. To avoid this problem, the TE was increased from 100 to 150 ms in the *in vivo* evaluation.

The signal intensity variation of PJ n.4 at five known dilutions and of the reference chemical solution (AAPM phantom refill) at different FA values is shown in Table 5.

Table 3
Chemical analysis of the manganese (Mn) and iron (Fe) concentrations in the five commercially available juices and the corresponding T2 relaxation time.

Cylinder (n.)	Commercial juices (brand)	Mn (mg/dl)	Fe (mg/dl)	T2 value (ms)
1	Pineapple juice n.4	2.38	0.146	51±5
2	Pineapple juice n.2	1.98	0.150	59±6
3	Pineapple juice n.1	1.91	0.123	60±6
4	Pineapple juice n.3	1.54	0.112	68±7
5	Blueberry juice	1.16	0.118	86±9

Pineapple juice n.4 showed a significant best T2 value in respect to pineapple juice n.2 (p=0.025), n.1 (p=0.01), n.3 (p=0.005) and blueberry juice (p=0.004), respectively.

Table 4
Different *in vitro* dilutions of pineapple juice n. 4, simulating the *in vivo* dilution in the gastrointestinal tract, and the corresponding T2 values.

Dilution (n.)	Water/pineapple juice (ml)	Manganese (mg/dl)	T2 value (ms)
1	20/60	1.79	59±6
2	30/50	1.49	67±7
3	40/40	1.19	80±7
4	50/30	0.892	101±10
5	60/20	0.595	140±15

Table 5
Signal strengths (measured within the ROI) of the five dilutions of pineapple juice n. 4 and of the reference solution (a), as a function of the different values of flip angle (FA) in the 3D fast imaging employing steady-state acquisition sequence.

FA value	Solution 1	Solution 2	Solution 3	Solution 4	Solution 5	Reference solution
15°	1,990	1,880	1,462	1,603	2,054	2,003
30°	3,165	3,049	2,366	2,624	3,385	3,930
45°	3,411	3,334	2,595	2,898	3,815	5,444
60°	3,250	3,249	2,351	2,813	3,724	6,601
75°	2,896	2,950	2,280	2,553	3,390	7,308
90°	2,545	2,668	2,046	2,284	3,066	7,616

The signal intensity trend was similar for all the different fruit juice dilutions at the different FA values. In particular, the values were at a maximum for an FA between the 45–60° and were at a minimum for an FA of 15° and that between 75–90°. Unlike the PJ, the reference solution showed progressive signal growth with an increase in the FA value, having a minimum value for FA 15° and a maximum value for FA 90°. Therefore, an FA equal to 90° was proven to be the value at which the maximum signal intensity difference between the reference solution (simulating the high signal from static fluids, such as bile) and the juices (representing the fluid in the gastrointestinal tract) was obtained (Fig 3).

In vivo validation

There were statistically significant improvements in contrast image quality between pre- and post-ingestion of PJ n.4. In all patients, when standard HR MRCP thick or thin slab sequences were acquired, the maximum degree of signal suppression of the gastrointestinal fluid was found after PJ ingestion as compared to the images obtained prior to PJ ingestion.

The morphological SSFSE T2 sequences, acquired with a TE of 150 ms after PJ ingestion, were considered to be of good quality, according to the degree of intestinal fluid signal suppression.

The 3D FIESTA images were judged to be of excellent quality (Grade 1) in 14/15 images (93.3%) with the highest FA value (90°), to be of good quality (Grade 2) in 1/15 (6.7%) with the highest FA value (90°) and in 9/15 (60%) with the intermediate FA value (45°) and to be of moderate quality (Grade 3) in 6/15 (40%) with the intermediate FA value (45°) and in 13/15 (86.7%) with the lowest FA value (15°). Two out of 15 (13.3%) of the 3D FIESTA images acquired with the lowest FA value (15°) were judged to be of non-diagnostic quality (Grade 4; Table 6). On the contrary, the majority of patients without ingestion of PJ n.4 showed 3D FIESTA images of non-diagnostic quality ($p<0.001$) regardless the FA values (Table 6). Moreover, after ingestion of PJ n.4, the 3D FIESTA sequence with the highest FA value (90°) had the greatest signal intensity of the pancreatobiliary fluid coupled with the best degree of gastrointestinal fluid signal suppression ($p<0.001$; Table 6). No significant changes in gallbladder distension between pre and post- fruit juice ingestion were observed.

Discussion

Several studies have shown the utility of negative oral contrast agents before MRCP in providing non-superimposed visualisation of the bile and pancreatic ducts, thus improving image quality.[10,11,13–22] As an alternative to artificial contrast media, natural negative contrast agents, such as fruit juices, were introduced[12,23–30]; however, in these juices, the optimal Mn or Fe concentrations and their related T2 values (needed to suppress static fluid signal from the gastrointestinal tract) still have to be clarified, and previous studies have reported conflicting results.

The wide variability of Mn concentration, depending on juice concentration, has previously been reported in the products on the market (from 0.365 to 2.724 mg/dl).[24] Coppens *et al.*[23] showed that the Mn concentration in commercial PJ ranges from 0.93 to 1.25 mg/dl, which is adequate to suppress the gastrointestinal fluid signal. Other studies using homemade PJ found a two to three times higher concentration of Mn (2.76 mg/dl).[12] The amount of Mn ions may also vary according to the soil where the pineapple was cultivated and the way the juice was prepared. The present study, evaluating the Mn and Fe concentrations in five different brands of commercially available juices in Italy, confirmed a manifest variability in the Mn concentration among the five different juices (from 1.16 to 2.38 mg/dl) but a more constant Fe concentration among them (from 0.112 to 0.150 mg/dl), 10–20 times lower than that of Mn. The Mn and Fe concentrations in these five juices were almost constant among different production lots of the brands evaluated. Therefore, once the most palatable and economically convenient fruit juice has been identified as an oral negative contrast agent, it is possible to use the same juice brand without unexpected differences in the concentration of paramagnetic substances among batches. A wide variability in Mn and Fe concentrations exist in fruit juices from year to year, from different batches and different countries; however, according to the present results, any fruit juice is sufficient to suppress the signal from gastrointestinal fluids using long TE sequences in MRCP because the Mn concentration required for this purpose is minimal.

Different studies[27,30] have carried out *in vitro* testing of the concentration of metal ion content (Fe, Mn, and copper) in fruit juices; however, the authors did not distinguish

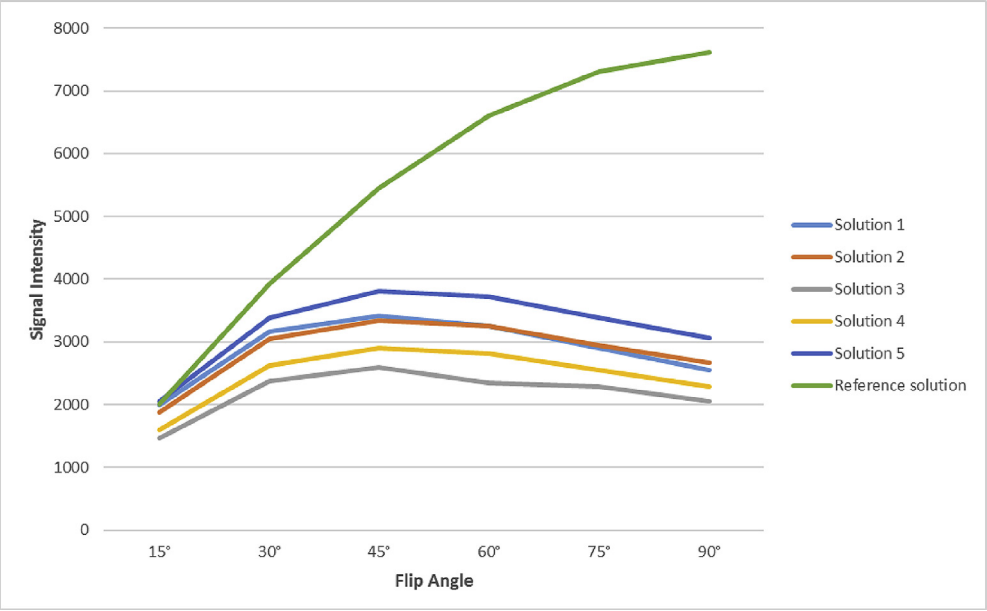

Figure 3 The line graph shows the signal strengths of the five dilutions of pineapple juice n. 4 and of the reference solution at different FA values in the 3D FIESTA sequence.

Table 6
The 3D fast imaging employing steady-state acquisition (FIESTA) images judgment pre and post fruit juice ingestion at three different flip angles (FA).

3D FIESTA images scale	FA values (after ingestion of PJ n.4, n=15)			FA values (control patients n=15)		
	90°	45°	15°	90°	45°	15°
Grade 1	14 (93.3%)	0	0	0	0	0
Grade 2	1 (6.7%)	9 (60%)	0	0	0	0
Grade 3	0	6 (40%)	13 (86.7%)	4 (26.7%)	2 (13.3%)	1 (6.7%)
Grade 4	0	0	2 (13.3%)	11 (73.3%)	13 (86.7%)	14 (93.3%)

which metal ion was more relevant in obtaining T2 shortening. The present study investigated the cut-off value of the Mn or Fe concentrations needed to shorten the high T2 value of the gastrointestinal fluid. To answer this question, the T2 values of pure chemical solutions of Mn and Fe were measured in different dilutions of five commercially available juices.

In pure chemical solutions, the influence of Fe is irrelevant in shortening T2 values and the only ion strongly relevant in this action was Mn; the same trend has also been confirmed in natural juices with similar Mn and Fe concentrations. In the five commercial beverages analysed, which contain Mn and Fe concurrently unlike the pure solutions, the Fe content did not influence the T2 values, which varied from 86 to 51 ms dependent only on the Mn content. At similar Mn concentrations, the PJ showed a T2 value (68±7 ms) very similar to the pure Mn solution (58±6 ms); this slight difference was mainly due to the interaction of the Fe paramagnetic properties, which counteract the T2 shortening of Mn. Therefore, the present results confirmed the first data from Coppens *et al.*,[23] which reported that Mn was the substance responsible for the signal suppression.

In the present study, the efficacy of the best fruit juice to use as a negative oral contrast agent when diluted in saline was tested *in vitro*, thus simulating *in vivo* juice dilution in the gastrointestinal tract fluid. Karantanas *et al.*[27] carried out an *in vivo* quantitative analysis of T1 and T2 shortening, testing a dilution of these juices in 50 ml of distilled water; none of the T2W sequences showed detectable signal loss of the gastric or intestinal contents, using T2W sequences with a very short TE (75 ms). The dilution of the juice probably reduced the net effect of the Mn on T2 shortening. Conversely, it is well known that the use of long TE (>1,000 ms) in the selected sequences enhances the T2 shortening effects. Using an "*in vitro*" examination, even in the presence of extremely diluted Mn ions in the gastrointestinal tract (PJ/water ratio of 20:60, 25%), the T2 value was 140±10 ms, which was still effective when heavily T2W sequences (TE 1,000 ms) were used.

A strict relationship between the absolute T2 value of the paramagnetic ions and the sequence used during MRCP has previously been reported.[28,29] Papanikolaou *et al.*[28] demonstrated that efficient gastrointestinal signal suppression was achieved with only a 1.9 mg/dl Mn concentration using long TE sequences (1,000–1,300 ms) to carry out the heavily T2W sequences. In the present study, all T2 values of the five different fruit juices tested, including BJ with a very low Mn concentration (1.16 mg/dl), were equally effective in obtaining a dark signal of the gastrointestinal fluids when long TE sequence, such as MRCP thick or thin slab sequences (TE=1,000 ms), were used. Unlike Papanikolaou *et al.*[28] the present study tested juices even with lower Mn concentrations.

Using T2 sequences with a short TE of 70 ms, Hiraishi *et al.*[29] found that blueberry juice with an Mn concentration

of 3 mg/dl was optimal for acting as a negative contrast agent. In the present study, testing commercial fruit juices with a far lower Mn content (maximum Mn concentration of 2.38 mg/dl) produced a similar result by performing the morphological SSFSE T2 sequences using a TE >150 ms.

In recent years, FIESTA has been an emerging new sequence, which is also useful in evaluating the biliary tract.[7–9] No previous studies have assessed the signal reduction of the intestinal fluid by natural beverages when using FIESTA sequences. The present results demonstrated that an FA of 90° in FIESTA sequences achieves the maximum difference in T2 signal intensity between the static fluids, such as bile (which appears hyperintense) and the juice mixed with gastrointestinal fluids (which appears hypointense).

As a final step of the study, the results were tested *in vivo* on 15 healthy volunteers. In 2004, Riordan *et al.*[12] first proved *in vivo* that an oral dose of 400 ml of PJ administered 15 minutes before MRCP improved the visualisation of the pancreatic and extrahepatic bile ducts, using T2 sequences with a TE of 800 ms. The present study demonstrated *in vivo* that a lower oral dose (300 ml) of PJ administered 15 minutes before MRCP improved the quality of the thick or thin slab sequences (TE=1,000 ms). Moreover, the present study confirmed the superiority of the FIESTA sequences, acquired *in vivo* with an FA of 90°, in suppressing the gastrointestinal tract fluid as compared with those acquired with lower FA values.

The present study has some limitations. First, eventual absorption of Mn into the circulation was not evaluated; however, there are no reports of toxicity or contraindications to juices in the literature.[29] Furthermore, the goals of the present study were the *in vitro* evaluations. Second, only healthy patients were analysed so it is not known if there could be reflux of the fruit juice into the common bile duct in patients with sphincterotomy of the ampulla of Vater. Previous experience with using of oral negative suspension, such as Ferumoxsil Suspension, indicated no problems in evaluating the biliary tree due to reflux into the common bile duct. Therefore, it was assumed that there are no problems in the use of fruit juice also in this subgroup of treated patients. Third, MRCP examinations were performed on a GE MRI unit using FIESTA sequences, but signal suppression of the intestinal fluids obtained after fruit juice ingestion can also be visualised using MRI machines from other manufacturers and via other sequences similar to FIESTA.

In conclusion, the Fe content does not influence the shortening of the T2 relaxation time, which, conversely, is strictly dependent on the Mn concentration in both artificial and commercial juices. The minimum concentration of pure Mn necessary to suppress the gastrointestinal signal is approximately 1 mg/dl and all commercially available juices, despite their wide variability of Mn content, can reach this concentration, provided that long TE sequences are used. When a FIESTA sequence is employed, an FA of 90° is recommended. The oral assumption of 300 ml of commercial PJ before MRCP is enough to suppress the signal of the intestinal fluids, regardless of gastric dilution after ingestion.

Conflict of interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.crad.2018.11.005.

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