Résumé
Utilisation du jus d’ananas en tant qu’agent de contraste négatif en cholangiopancréatographie par résonance magnétique
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Objectifs. La qualité des examens de cholangiopancréatographie par résonance magnétique (CPRM) est fréquemment dégradée par le signal de contamination digestif. L’objectif de cette étude est d’évaluer les résultats obtenus par l’ingestion de jus d’ananas en tant qu’agent de contraste négatif en CPRM.

Matériels et méthodes. Nous avons comparé les résultats de la CPRM de 50 patients ayant ingéré du jus d’ananas et de 50 patients ayant ingéré un produit de contraste paramagnétique (ferumoxsil-Lumirem®). Les observateurs n’avaient pas la connaissance du produit de contraste ingéré. La qualité des examens a été évaluée en termes de suppression du signal au sein de l’estomac, du cadre duodénal et du grêle proximal et en termes de visualisation du canal pancréatique, des voies biliaires intra- et intrahépatiques et de la voie bilaire principale. Enfin, nous avons analysé l’intensité du signal de différents jus d’ananas disponibles sur le marché, en se servant de séquences pondérées en T1, de séquences pondérées en T2 et de séquences de CPRM. L’intensité du signal a été corrélée avec la concentration de manganèse mesurée par spectrométrie d’émission atomique. Finalement, les observateurs ont comparé les goûts des différents jus d’ananas et de ferumoxsil.

Résultats. Sur les séquences de CPRM, les résultats étaient équivalents en termes de suppression du signal de l’estomac, du cadre duodénal et du grêle proximal après ingestion de jus d’ananas ou de ferumoxsil. La visualisation du canal de Wirsung, des voies biliaires intra- et intrahépatiques et de la voie bilaire principale était équivalente après ingestion d’ananas ou de ferumoxsil. L’intensité du signal des différents jus d’ananas sur les séquences pondérées en T2 et sur les séquences de CPRM était bien corrélée avec la concentration de manganèse mesurée pour chacun des jus par spectrométrie. D’importantes variations de la concentration de manganèse ont été observées entre les différents jus d’ananas testés. La concentration de manganèse variait entre 3,65 et 27,24 mg/L. Les observateurs ont considéré que le jus d’ananas avait un laitoucbon « ou un laitouc très bon » goût alors que le ferumoxsil avait un laitouc mauvais » ou laitouc très mauvais » goût.

Conclusion. L’ingestion de jus d’ananas permet d’obtenir une diminution efficace du signal du tractus digestif en CPRM d’une façon comparable à celle qui est obtenue avec les produits de contraste paramagnétiques. Comme la concentration de manganèse est largement variable, la nature du produit de contraste ingéré peut être sélectionnée.

Mots-clés : Cholangiopancréatographie par résonance magnétique, Agents de contraste, IRM, voies biliaires, IRM, canaux pancréatiques, Manganèse, Spectrométrie d’émission atomique.

Abstract
Purpose. The quality of magnetic resonance cholangiopancreato-gra phy (MRCP) images is frequently degraded by signal from the gastrointestinal tract on heavily T2W images. The purpose of this study is to evaluate pineapple juice (PJ) as an oral negative contrast agent in MRCP.

Materials and Methods. Results from MRCP in 50 patients with PJ and 50 patients with paramagnetic contrast (ferumoxsil-Lumirem®) were compared. Reviewers were blinded to the type of contrast agent. Performance was assessed with regard to signal suppression in the stomach, duodenum and proximal small bowel and with regard to the visualization of the pancreatic duct and biliary ducts. In vitro, the signal characteristics of several commercially available brands of PJ were assessed using T1W, T2W and MRCP sequences. Signal intensity was correlated with the manganese concentration measured using atomic absorption spectrometry. Finally, the reviewers compared the taste of PJ and ferumoxsil.

Results. On MRCP sequences, results were similar with regards to signal suppression in the stomach, duodenum and proximal small bowel with PJ and ferumoxsil. Visualization of the pancreatic duct, intrahepatic bile ducts and CBD was similar with PJ and ferumoxsil. The signal intensity of commercially available brands of PJ on T2W and MRCP sequences correlated well with the measured manganese concentration on spectroscopy. Variations in manganese concentration were observed, with values ranging from 3.65 to 27.24 mg/L. The reviewers noted that PJ tasted “good” or “very good” and that ferumoxsil tasted “bad” or “very bad”.

Conclusion. Ingestion of PJ provides effective signal suppression in the GI tract on MRCP, similar to paramagnetic contrast agents. The manganese concentration is highly variable in commercially available PJ brands, a brand with high manganese concentration should be selected.

Key words: MRCP. Contrast agents. Biliary tract, MR. Pancreatic duct, MR. Manganese. Atomic absorption spectrometry.

The role of magnetic resonance cholangiopancreatography (MRCP) in the evaluation of the biliary tract and pancreatic ducts is now well established (1-5). The MR techniques used to image the biliary tract and pancreatic ducts are based on heavily T2W sequences to enhance signal from structures containing stationary fluid and provide anatomical representations of these structures. Signal from fluid in the stomach, duodenum and proximal small bowel may interfere with visualization of the biliary tract and pancreatic ducts. As such, MRCP is routinely performed in fasting patients and negative oral contrast agents are sometimes used. Most groups use paramagnetic oral contrast agents that reduce signal from gastric and bowel fluid by reducing the T2 relaxation time (6, 7).

Blueberry juice, characterized by a high manganese concentration, has also been used to reduce signal from gastric and bowel fluid (8-12). However, large quantities of blueberry juice are not readily available in routine clinical practice. In addition, ingestion of a large volume of blueberry juice often is difficult because of its bitterness. Pineapple juice (PJ), also characterized by a high manganese concentration, has been proposed as a negative oral contrast agent for MRCP (13-15).

The purpose of this article was to compare the efficacy of PJ as a negative oral contrast agent for MRCP to that of a paramagnetic contrast agent, compare the in vitro efficacy of different types of commercially available PJ, and compare the taste of these different contrast agents.

### Materials and Methods

**Magnetic resonance imaging**

MRCP examinations were performed on a 1.5T MR unit (Magnetom Symphony, Siemens, Erlangen, Germany) using the body coil and a six-element phased array coil. The imaging protocol included an axial breath-hold gradient-echo T1W (TR/TE: 174/4) sequence, an axial non-breath-hold non-fat-suppressed FSE T2W (HASTE – TR/TE msec: 1200/114; matrix 176x256; slice thickness 6 mm) sequence and a high-resolution 3D FSE sequence with very long TE (TR/TE: 1400/800). A restoration pulse less than 90 was applied at the end of the echo train to restore the residual transverse magnetization backup into the longitudinal direction. The matrix was 256x256, the slice thickness was 1 mm and the voxel size was 1x1x1 mm. Images were processed using a maximum intensity projection algorithm (MIP) to generate multiplanar reformatted anatomical representations. Free breathing acquisitions usually range from 3 to 6 minutes using the prospective acquisition and correction (PACE) feature. Patients were instructed to drink 400 ml of PJ (total manganese concentration: 18.73 mg/L) or 400 ml of ferumoxsil (Lumirem®) 15 minutes prior to scanning.

### In vivo evaluation

Three reviewers blinded to the type of oral contrast (ferumoxsil or PJ) evaluated the quality of signal suppression of gastric, duodenal and bowel fluid using a 5-point scale, from “very poor” to “very good” (table I). The observers then evaluated the quality of biliary tract and pancreatic duct visualization, also using a 5-point scale, from “very poor” to “very good” (table II).

### Table I

<p>| Quality of signal suppression (results shown in %). |
|-------------------------------|----------------|----------------|----------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>Stomach</th>
<th>Duodenum</th>
<th>Proximal bowel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very poor</td>
<td>Lumirem®</td>
<td>PJ</td>
<td>Lumirem®</td>
</tr>
<tr>
<td>Poor</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fair</td>
<td>6</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Good</td>
<td>30</td>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td>Very good</td>
<td>60</td>
<td>70</td>
<td>80</td>
</tr>
</tbody>
</table>

### Table II

| Quality of visualization (results shown in %). |
|-----------------------------------------------|----------------|----------------|----------------|
|                                              | Pancreatic duct| Intrahepatic ducts | Suprapancreatic CBD | Intrapancreatic CBD |
|                                              | Lumirem®       | PJ             | Lumirem®       | PJ             |
| Very poor                                     | 2              | 0              | 0              | 0              |
| Poor                                          | 18             | 12             | 6              | 0              |
| Fair                                          | 18             | 6              | 18             | 8              |
| Good                                          | 16             | 20             | 20             | 14             |
| Very good                                     | 46             | 62             | 54             | 78             |

**In vitro evaluation**

Fifteen tubes containing samples from commercially available PJ (n=9), orange juice (n=2), grape juice (n=1), blueberry juice (n=1), water (n=1) and ferumoxsil (Lumirem®) (n=1) were imaged using the magnet previously described using gradient-echo T1W (TR: 174, TE: 4), HASTE T2W (TR: 1200, TE: 114) and RARE MRCP (TR: 4160, TE: 1100) sequences. The samples were then analyzed to determine the concentration of manganese. The samples were mineralized in the presence of heated concentrated nitric acid by microwave-assisted digestion.

Total manganese dose measurements were performed by atomic absorption spectrometry using induction plasma. The total manganese concentration for each sample was compared to the corresponding MR signal intensity.

### Taste evaluation

Ten observers then evaluated the taste of PJ and ferumoxsil. The observers were blinded to the nature of the proposed product for review and taste tests for both.
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products were not performed on the same dates. A 5-point scale was used: very bad, bad, drinkable, good, and very good.

Statistical analysis

All statistical comparisons either for quality of signal suppression, quality of biliary tract and pancreatic duct visualization or taste of different oral contrast preparations were performed with the chi-2 test for non-paired series using a p<0.05 for statistical significance.

Results

Signal suppression in the stomach, duodenum and proximal small bowel was “good” or “very good” in most cases with either PJ or ferumoxsil (table I). There was no significant difference regarding the efficacy of signal suppression between PJ and ferumoxsil. Visualization of the main pancreatic duct, intrahepatic bile ducts, suprapancreatic CBD and intrapancreatic CBD was considered “good” or “very good” in most cases (table II). There was no significant difference regarding the quality of visualization of the biliary tract or pancreatic duct.

The observers noted that signal from GI tract structures did not interfere with the visualization of the main pancreatic duct, intrahepatic bile ducts, suprapancreatic CBD and intrapancreatic CBD irrespective of PJ or ferumoxsil ingestion (fig. 1).

The difference between both agents was not significant. On gradient-echo T1W sequences, signal from the stomach after ferumoxsil ingestion was usually hypointense relative to spleen (fig. 2a) whereas signal from the stomach after PJ ingestion was always hyperintense relative to liver (fig. 3a).

On HASTE T2W sequences, signal from the stomach after ferumoxsil ingestion was usually hypointense relative to muscle (fig. 2b) whereas signal from the stomach after PJ ingestion was usually between that of liver and spleen or spleen and adipose tissue (fig. 3b).

Total manganese concentration was essentially zero for water and less than 1 mg/L for orange juice, grape juice and ferumoxsil. Total manganese concentration in blueberry juice was 41 mg/L.

Total manganese concentration for PJ was variable between brands (minimum 3.6 mg/L – maximum 27.2 mg/L) (table III). MR imaging of the different samples showed that the efficacy of signal suppression from GI structures on MRCP images was sufficient above a concentration of 15 mg/L (fig. 4). Signal suppression was insufficient for PJ brands with manganese concentrations of 3.6, 6.8 and 12 mg/L respectively.

The seven brands of PJ with manganese concentration above 10 mg/L were all made from concentrate and from different manufacturers. PJ juice in vivo had a manganese concentration of 18.7 mg/L. Both PJ brands with low total manganese concentrations (3.6 and 6.8 mg/L) were “pure squeezed” juices from standard or organic farming.

Fig. 1: 3D MRCP image (TR/TE 1400/800) after ingestion of PJ.

Fig. 2: Axial gradient-echo T1W image (TR/TE : 174/4) after ingestion of ferumoxsil (Lumirem®).

a Gastric signal is hypointense relative to muscle. On HASTE T2W image,

b Gastric signal is hypointense relative to muscle.

Fig. 3: Axial gradient-echo T1W image (TR/TE : 174/4) after ingestion of ferumoxsil (Lumirem®).

a Gastric signal is hypointense relative to muscle. On HASTE T2W image,

b Gastric signal is hypointense relative to muscle.
Taste for PJ was considered “very good” or “good” in 80% of cases. Taste for ferumoxsil was considered “bad” or “very bad” in 80% of cases (p<0.05).

**Discussion**

MRCP has established itself as a preferred modality for morphological evaluation of the biliary tract and pancreatic duct (1-4). MRCP is based on heavily T2W sequences to enhance signal from stationary fluids. Signal from fluid in the stomach, duodenum and proximal small bowel may interfere with visualization of the biliary tract and pancreatic ducts. As a result, several investigators have looked at negative oral contrast agents to suppress signal from GI structures (6, 7).

The agent currently most frequently used is the paramagnetic contrast agent ferumoxsil (Lumirem®) consisting of a suspension of superparamagnetic iron oxide causing marked shortening in T2 relaxation time (6, 7). Other agents have been used, including blueberry juice characterized by a high manganese concentration (8-12).

We have demonstrated in this study that PJ was an attractive alternative with good suppression of signal from GI tract structures. Visualization of the main pancreatic duct, intrahepatic bile ducts, and CBD
was considered of “good” or “very good” quality in most cases with very little interference from bowel structures. Results with PJ and ferumoxsil were similar. Suppression of signal from GI structures was effective only on heavily T2W MRCP sequences. Signal suppression was not as effective on less heavily T2W sequences such as HASTE sequences.

We have also demonstrated in vitro that manganese concentration from different brands of commercially available PJ was variable, with two brands of “pure squeezed” PJ juice containing a manganese concentration too low to result in clinically useful signal suppression.

Finally, we have demonstrated that the taste of PJ was significantly better tolerated than the taste of ferumoxsil.

We are not aware of any complication related to the ingestion of a reasonable volume of PJ except for the associated sugar load whereas adverse reactions may occur with ferumoxsil, including oral paresthesia due to the concentration of high iron oxide, and gastrointestinal symptoms: diarrhea, abdominal cramps, bloating and flatulence.

In addition, even if the price of a bottle of Lumirem® is reasonable (15.31 euros), it remains markedly more expensive than a bottle of PJ billed at 0.20 euro in our institution’s kitchen.

Blueberry juice has been used as a negative oral contrast agent for MRCP (8-12). We have confirmed the high concentration of manganese in blueberry juice, higher than for PJ. However, this higher concentration is not an advantage by itself since a similar clinical effect can be achieved by using an agent with lower manganese concentration. It should be noted that given its very high manganese concentration, blueberry juice could be diluted to 1/4, which could make it more clinically usable and would also presumably reduce its bitter taste.

Some authors have proposed a mixture of PJ and Gadolinium to suppress GI signal (15). Reported results were good, but the mixing procedure is more complicated. Other authors have proposed the use of dilute Gadolinium as an oral contrast agent to reduce GI signal. Preliminary data from a patient population of 23 showed that this technique appeared effective and well tolerated (16). Our study presents several limitations. The administration of ferumoxsil and PJ was not randomized. We did not verify if all patients were fasting or had ingested the entire volume of negative contrast agent. This probably explains the rare cases of poor results, especially with ferumoxsil suggesting that some patients may not have ingested the entire volume of contrast.

Even though the reviewers were blinded to the type of negative oral contrast agent in any individual subject, they could suspect which agent was used by reviewing the signal intensity of gastric fluid on T1W images. Similarly, even though reviewers during the tasting phase were blinded to the nature of the ingested agent, they could easily deduce which contrast was under review based on evaluation of color and taste.

Finally, because of their high manganese concentration, PJ and blueberry juice are characterized by T1 relaxation time shortening causing fluids to appear hyperintense on T1W sequences. As a result, this type of contrast agent would be of limited value on MRCP acquisitions obtained following the intravenous administration of a contrast agent with short T1 and biliary excretion where T1W imaging would be required. The use of PJ or blueberry juice would increase signal from GI structures and interfere with the interpretation (17).

Conclusion

We believe that PJ is an attractive negative oral contrast agent for MRCP as long as the selected brand has a manganese concentration that is sufficient.

References

