Clinical Feasibility of *Açai (Euterpe olerácea)* Pulp as an Oral Contrast Agent for Magnetic Resonance Cholangiopancreatography

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Background: We evaluate the effectiveness of the Amazonian fruit pulp from *Euterpe olerácea* (popularly named *Açaí*) as a negative oral contrast agent applied to clinical routine. The use of such contrasts is particularly important in magnetic resonance cholangiopancreatography (MRCP) to reduce overlapping.

Materials and Methods: We administered *Açaí* pulp to 5 nonsymptomatic subjects and 35 patients submitted to unspecific abdominal MR imaging, intending to set up optimal protocol. In 8 MRCP examinations, contrast and image effects were assessed and graded blindly by 2 independent radiologists. Quantitative analysis was performed by Wilcoxon test as to verify the potential of the *Açaí* to eliminate overlap signal over the pancreaticobiliary tract. Adverse effects and subject tolerance were also addressed.

Results: The *Açaí* pulp elicited a local brightness decrease in T2-weighted images. The depiction of gallbladder, common bile duct, ampulla of Vater, and pancreatic duct was markedly improved after *Açaı* ingestion because of the suppression of the overlapping from bowel loops and gastric content ($P < 0.01$). All patients considered *Açaı* palatable, and no side effect was registered.

Conclusions: The *Açaí* pulp can be used routinely in MRCP studies as a natural, safe, and inexpensive negative oral contrast agent with high efficacy and patient acceptance.

Key Words: MRI, MR cholangiopancreatography, oral contrast agent, *Euterpe olerácea*, *Açaí*

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Magnetic resonance cholangiopancreatography (MRCP) has become one of the most powerful techniques to image the biliary and pancreatic ducts.[1,2] This technique is based on heavy T2-weighted image sequences.[3] These sequences are usually applied in coronal and coronal oblique, once they display the pancreaticobiliary anatomy similar to the endoscopic retrograde colangio pancreatography (ERCP), which is the most familiar to surgeons and clinicians and which was used as criterion standard to validate the MRCP.[4–11]

Although many MR centers do not use oral contrast for MRCP examinations, it is well known that its use can greatly improve the visualization of both biliary tree and pancreatic ducts, facilitating the evaluation of distal ducts and ampulla.[12–14] Other indications for the use of oral contrast are MR imaging (MRI) evaluation of the stomach and small bowel,[15–17] gastric motility, and the gastroenteric and enteric transit studies.[18] The properties of each one of these, as relaxation properties, composition, and pH, will determine its most useful indication. For instance, MRCP oral contrast agent must have low signal intensity (SI) on T2-weighted images.

Many types of oral contrast agents for MR studies have been developed. As a rule, the ideal agent must have good digestive acceptance, good accommodation in the gastrointestinal (GI) tract, produce a homogeneous signal, unchanged signal while it is diluted through the GI tract, nontoxicity, absence of collateral effect, minimum peristaltic stimulation, and an accessible price.[19]

Intending to null the signals proceeding from the bowel handles in MRCP, Chan et al[20] have shown the possibility to use gadopentetate dimeglumine as a negative oral contrast agent for MR of the GI tract in MRCP. Similarly, Galvão et al[21] also demonstrated the effect of conventional contrasts agents based on solution-type superparamagnetic iron oxides (SPIOs) for MRCP applications. Many other investigators reported on the use of the SPIOs in the GI tract as oral contrast agents. Unfortunately, SPIO is unpalatable and may cause adverse reactions.[21]

In the search for palatable and safe contrast agents, several natural substances have been tried.[22–24] A recent alternative is the fruit pulp of the *Euterpe olerácea*, known as *Açaí*, a palm from the Amazonic region. It is widely available, commercialized in the form of integral pulps, juices, or wines, and shown to be a powerful negative contrast in T2-weighted images.[25] Therefore, the present study aims to evaluate the clinical feasibility of *E. olerácea* as a negative oral contrast agent. After a preliminary study in 35 patients with unspecific abdominal illnesses, MRCP figured out as the optimal protocol for *Açai* clinical application. We focused the analysis on its capacity to reduce overlapping signals during MRCP and to enhance the depiction of pancreaticobiliary structures.

MATERIALS AND METHODS

Oral Contrast Preparation

The commercially available *Açaí* pulp was obtained from frozen samples. There was no special preparation once the pulp was offered after being defrosted and mixed to all patients. The standardized ingested volume was 200 mL per individual after 12 hours of fasting. To standardize the study protocol, 5 nonsymptomatic subjects were tested, and the final protocol was applied to 35 patients with nonspecific symptoms. Ten axial slices centered at the stomach region were acquired under 2 distinct experimental conditions: first in the fasting state (baseline) and then after the ingestion of *Açaí*.

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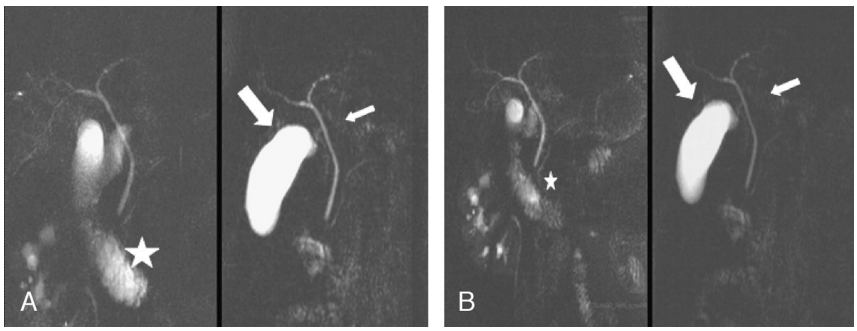

FIGURE 1. T2-weighted images from 2 patients (A) and (B) during fasting (left) and after oral administration of *Acai* (right). Overlap is eliminated (star), which allows gallbladder and biliary ducts (large and small arrows) to be more visible because of the presence of *Açaí*.

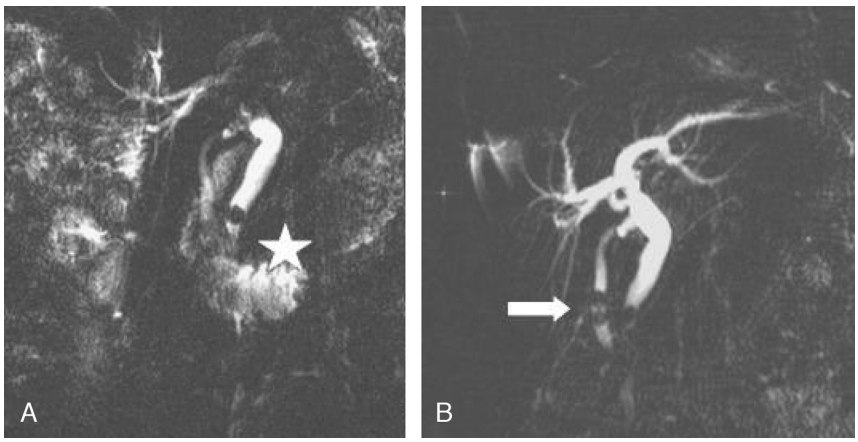

FIGURE 2. Coronal T2-weighted images before (A) and after (B) *Açaí* ingestion. The signal from the duodenal loop and stomach allows overlap to be eliminated (star), which contributes to a complete diagnostic evaluation of gallstones (arrow) present in the biliary tract.

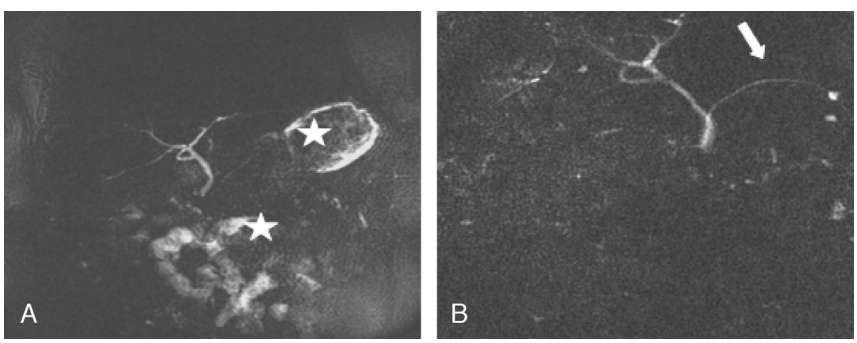

FIGURE 3. T2-weighted images in coronal plane before (A) and after (B) *Açaí* ingestion. The signal from *Açaí* decreased overlapping from bowel loops and stomach (stars). It allows a complete observation of pancreatic duct (arrow).

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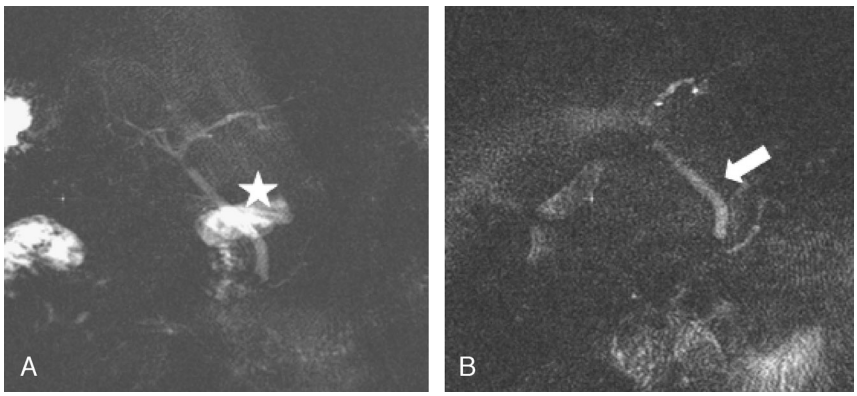

FIGURE 4. T2-weighted images from another patient in coronal plane before (A) and after (B) *Açaí* ingestion. The signal caused by the presence of *Açaí* eliminates overlap from the duodenal loop (star) on the CBD. It allows a complete observation of that (arrow) after *Açaí* ingestion.

Patients

After the standard protocol definition, 8 patients (4 women, 4 men; aged 28-73 years; mean age, 53.3 ± 17.2 years) were selected. They represented a group of consecutive patients who underwent MRCP. The clinical indication for the MRCP study was jaundice and an ultrasound suggesting extrahepatic cholestasis.

Institutional review board was obtained for this study, and all patients have agreed and signed the informed consent form. After the examination, all patients answered an acceptance evaluation for the oral contrast ingestion.

MR Imaging

Magnetic resonance imaging was performed with a 1.5-T system (Magnetom Vision; Siemens Medical Systems, Erlangen, Germany). A phased-array body coil was used, and the MRCP sequences were obtained before and after oral contrast ingestion. The following selected T2-weighted–based sequences were repeated: Turbo Spin Echo (TR/TE, 2800/1100 milliseconds; FOV, 150 mm, 240 × 256; thickness, 4 mm) and Half-Fourier Acquisition Single-Shot Turbo Spin-Echo (TR/TE, 11.8/95 milliseconds; FOV, 350 mm, 240 × 256; thickness, 4 mm).

Qualitative Analysis

All MRI examinations were retrospectively and independently reviewed by 2 radiologists experienced in abdominal MRI, and the prospective MR interpretation was withheld from the reviewing radiologists.

Both MR data sets, before and after ingestion of oral contrast, were evaluated in conjunction with each reviewer regarding image quality and how they classify the change after the ingestion of the oral contrast. The reviewers assessed all studies

TABLE 1. Qualitative Image Analysis Results by Reviewer Regarding Each Structure Studied From All Patients

		CBD		Cystic Duct		Ampulla of Vater		Pancreatic Duct		Stomach		Duodenum	
Patient	Oral Contrast Phase	R1	R2	R1	R2	R1	R2	R1	R2	R1	R2	R1	R2
1	Pre	3	3	1	1	2	2	2	2	2	2	3	3
	Post	4	4	2	2	2	2	3	2	1	1	2	2
2	Pre	3	3	3	3	2	3	2	2	3	3	3	3
	Post	4	4	2	2	3	3	4	4	2	2	2	2
3	Pre	3	3	2	3	3	3	2	2	3	3	3	3
	Post	3	4	4	4	3	3	4	4	2	2	2	2
4	Pre	3	3	3	3	3	2	3	3	3	2	3	3
	Post	3	3	3	3	3	3	4	4	2	1	2	3
5	Pre	3	3	0	0	3	3	2	2	3	3	3	3
	Post	4	3	0	0	2	2	2	2	2	2	2	2
6	Pre	4	4	3	3	3	3	2	2	3	3	3	3
	Post	4	4	3	3	3	3	3	3	2	2	2	2
7	Pre	3	3	0	0	3	3	3	3	3	3	3	3
	Post	3	3	0	0	1	1	4	4	2	2	2	2
8	Pre	3	3	0	0	3	3	2	2	2	2	3	3
	Post	3	3	0	0	3	3	3	3	1	1	2	2

0, not visualized; 1, poor image quality; 2, fair image quality; 3, good image quality; 4, excellent image quality.
R1 indicates reviewer 1; R2, reviewer 2.

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TABLE 2. Results of Correlation and Agreement Obtained Between the 2 Reviewers' Classifications for Image Quality of All Structures Evaluated

Structure Evaluated	Correlation			Agreement
	rs	CI	*P*	κ
CBD	0.71	0.3145–0.8947	<0.01	0.86
Cystic duct	0.97	0.9320–0.9925	<0.0001	0.73
Ampulla of Vater	0.75	0.3911–0.9109	<0.001	0.77
Pancreatic duct	0.94	0.8370–0.9813	<0.0001	0.93
Stomach	0.88	0.6856–0.9610	<0.0001	0.83
Duodenum	0.88	0.6775–0.9599	<0.0001	0.88

CI indicates confidence interval; κ, weighted κ coefficient; *rs*, Spearman correlation coefficient.

based on the predetermined structures, and their final scores were recorded. These structures were the common bile duct (CBD), cystic duct, ampulla of Vater, pancreatic duct, stomach, and duodenum.

For the quality assessment, each image was evaluated regarding resolution, sharpness, and clarity. The image quality of each structure was evaluated by rating its conspicuity and contrast using a subjective grading from 1 to 4, referring to *poor*, *fair*, *good*, and *excellent*, respectively, adding 0 when the structure was not visualized in that slice.[26,27]

Oral contrast effects for the visualization of each structure was judged based on 3 possibilities: (1) worse (when a prior score was higher than after contrast ingestion), (2) equivalent (no score changes), and (3) better (when a prior score was lower than after contrast ingestion). The reviewers were also asked to classify what was the impact of the oral contrast on the diagnosis for each case, rating as positive, negative, or indifferent.

Correlations between reviewers' classifications were analyzed using the Spearman coefficient. Agreement between the 2 reviewers was assessed using weighted κ statistic with associated 95% confidence intervals. The level of agreement was defined by κ values as follows: less than 0, no agreement; 0 to 0.40, poor agreement; 0.41 to 0.75, good agreement; and 0.76 to 1.0, excellent agreement. After independent MRI evaluation, the frequency of findings was determined by the reviewers in a consensus reading.

Quantitative Analysis

For quantitative analysis, data were selected from image regions of interest (ROIs), with the same area and the same number of pixels, before and after the administration of the contrast media. All ROIs were selected over the blurring signal, which emerges from the bowel loops close to the pancreaticobiliary structures, of interest on MRCP. The mean values of signal intensity and standard deviation were obtained in each ROI using the software ImageJ®. Furthermore, to evaluate the statistical significance of the signal overlapping reduction from the bowel loops or stomach portions, because of *Açaí*, a nonparametric Wilcoxon signed rank test was applied to the ROI data.

RESULTS

Qualitative Analysis

Ultrasound and clinical evaluation provided final diagnoses of choledocholithiasis in 7 of 8 patients and malignancy in 1 of 8 patients (cholangiocarcinoma), all of them being confirmed by surgery and/or ERCP. All patients reported good acceptance of the *Açaí* pulp, and there were no side effects related to its ingestion.

Generally, the presence of *Açaí* solution inside the stomach and bowel loops reduces the overlapping signal on MRCP images, as what can be observed in Figures 1–4. The T2-weighted MRCP of the pancreatic and biliary ducts, before and after the administration of the *Açaí*, are presented. In Figure 1A, before the ingestion of the *Açaí*, only a small portion of the gallbladder could be observed because of overlapping of the intestinal handle. However, after the *Açaí* ingestion, both the gallbladder (Fig. 1B) and CBD (Fig. 1B) could be observed in much greater detail. Another example is presented in Figure 2A, where a clear overlapping of the intestinal handle signals is observed. A region where the diagnosis could have been ambiguous is shown (Fig. 2A), which is clarified after the ingestion of *Açaí* (Fig. 2B).

Besides the content of the bowel handles, the gastric juice also presents intense signals in the MRCP examinations (Fig. 3A). Such overlap can also be eliminated with the use of a negative oral contrast agent. In Figure 3B, the ingestion of *Açaí* eliminates the overlapping signal and, thus, allows the complete observation of the pancreatic duct. The duodenal loop is particularly problematic for MRCP evaluation when fluid-filled, which can be prevented with the use of *Açaí* (Fig. 4).

The individual reviewer's evaluations, for each studied structure, are presented in Table 1. There was a good agreement between reviewers regarding the imaging quality classification for all structures as shown in Table 2. The agreement between the 2 reviewers was excellent for all structures evaluated, except the cystic duct, which was considered in good concordance (Table 2).

The reviewers agreed that there was an improvement in the visualization of the pancreatic duct in 87.5% of the patients after the ingestion of the oral contrast, whereas the visualization of the CBD, cystic duct, and duodenal papilla also improved in 50%, 25%, and 25%, respectively. They also agreed that the visualization of stomach and duodenum was worsened in all cases after the ingestion of oral contrast, which also happened for the visualization of the duodenal papilla in 25% of cases and for the cystic duct in 12.5% of cases. There was no difference

TABLE 3. Consensus Reviewers' Evaluation of the Effects of the Ingestion of Oral Contrast Comparing Before and After Oral Contrast Use for Each Structure Evaluated

	CBD	Cystic Duct	Ampulla of Vater	Pancreatic Duct	Stomach	Duodenum
Worse	0/8 (0)	1/8 (12.5)	2/8 (25)	0/8 (0)	8/8 (100)	8/8 (100)
Equivalent	4/8 (50)	5/8 (62.5)	4/8 (50)	1/8 (12.5)	0/8 (0)	0/8 (0)
Better	4/8 (50)	2/8 (25)	2/8 (25)	7/8 (87.5)	0/8 (0)	0/8 (0)

Values are expressed as no. (%).

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before and after the ingestion of oral contrast use for the visualization of the cystic duct in 62.5% of cases, of the duodenal papilla and CBD in 50% of cases, and of the pancreatic duct in 12.5% of cases (Table 3).

Quantitative Analysis

The Wilcoxon nonparametric analysis showed a statistical significant difference between SI before and after *Açaí* administration ($P < 0.01$), demonstrating that there was a significant reduction of overlapping signals from the content of adjacent tissues over pancreaticobiliary tract structures, which confirm the previous qualitative image analysis.

DISCUSSION

The MRCP has gradually replaced diagnostic ERCP to investigate biliopancreatic disease,[28,29] mainly because of its noninvasiveness and reliable depiction of biliary and pancreatic ductal anatomy. Nonetheless, the presence of GI fluid, bright in MRCP sequences, may preclude proper visualization of ductal anatomy, demanding the use of oral contrast agents.[19]

This study demonstrates that the oral administration of *Açai* pulp before MRCP examinations provides an effective reduction ($P < 0.01$) of the overlap between bright signal from GI content and those from different small ducts. Therefore, its use may improve MRCP diagnosis of different biliopancreatic pathologies.[28] Indeed, this effect was reliably observed in 8 successive patients who underwent MRCP in our service. It is important to point out that this study used a clinical MRCP protocol, which reinforces the feasibility of *Açaí* implementation in the clinical routine.

Açaí acted as a negative contrast agent reducing the local brightness of T2-weighted images, possibly caused by the presence of a reasonable amount of paramagnetic ions, such as Mn and Fe.[22–25] Some features of *Açaí* pulp turn it into an excellent oral contrast,[19] such as good digestive acceptance, uniform distribution in the lumen, no side effects, good taste, and likely nontoxicity at this level of intake as it is commonly ingested as a food. Furthermore, in Brazil, the cost of a dose of *Açaí* pulp, for an MRCP examination, is about 23 times cheaper than that of a conventional contrast agent. Moreover, its commercialization is viable, as it is already being exported to the United States and Europe as an energetic food.

Although the use of *Açaí* pulp suppressed overlapping over all biliopancreatic ductal structures, the pancreatic duct visualization was the most benefited (7/8 cases; Table 3). This may reflect the anteroposterior anatomical relationship between stomach and pancreas, considering that gastric content is the main barrier to visualize the pancreatic duct on MRCP (Fig. 3). Moreover, *Açaí* pulp has improved depiction in 50% of CBD studies, which can be fundamental in selected cases, mainly in those with minimal disease involving its retroduodenal portion.[30]

Although the diagnosis in this study was focused at the investigation of jaundice caused by choledocholithiasis (7/8) and cholangiocarcinoma (1/8), it is our belief that other abdominal clinical problems, such as chronic pancreatitis and small bowel disease, will also benefit from this contrast.

Moreover, recently, new technological MR advances permitted an increase of its spatial and temporal resolutions, allowing the implementation of functional imaging.[31–33] For instance, functional imaging of the exocrine glandular pancreas has been conducted using intravenous injection of secretin, which allows the inspection of how much pancreatic juice is delivered into the duodenum.[28,34–39] For such applications, the use of a negative oral contrast is mandatory. Therefore, it is reasonable to speculate that the use of *Açaí* pulp is suitable for secretin-MRCP examinations because it improves signal from pancreatic duct by suppressing the high-intensity fluid content in the duodenal loop.

In conclusion, we demonstrated the clinical feasibility and efficiency of *Açaí* pulp as an alternative oral contrast for MRCP examinations, as it significantly improves the visualization of the pancreatic duct as compared with MRCP without oral contrast.

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