

## *Euterpe Olerácea* (Açaí) as an alternative oral contrast agent in MRI of the gastrointestinal system: preliminary results

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### Abstract

Using contrast agents is a common practice in medical imaging protocols. Paramagnetic properties of certain compounds present in contrast agents can affect magnetic resonance imaging (MRI) signals. For abdominal applications, they are usually injected, but may also be administered orally. However, their use as a routine technique is limited, mainly due to the lack of appropriate oral contrast agents. We herein present the preliminary characterization and results for implementation of *Euterpe Olerácea* (popularly named *Açaí*) as a possible clinical oral contrast agent for MRI of the gastrointestinal tract. The pulp of *Açaí*, a fruit from the Amazon area, presented an increase in T<sub>1</sub>-weighted MRI signal, equivalent to that of gadolinium-diethyltri-amine pentaacetic acid, and a decrease in T<sub>2</sub>-weighted images. We looked for intrinsic properties that could be responsible for the T<sub>1</sub> signal enhancement and T<sub>2</sub> opacification. Atomic absorption spectra revealed the presence of Fe, Mn and Cu ions in *Açaí*. The presence of such ions contribute to the susceptibility value found of  $\chi = -4.83 \times 10^{-6}$ . This finding assents with the hypothesis that image contrast changes were due to the presence of paramagnetic material. The first measurements in vivo demonstrate a clear increase of contrast, in T<sub>1</sub>-weighted images, due to the presence of *Açaí*. Consistently, the opacification in a T<sub>2</sub>-weighted acquisition was evident, revealing a good contrast on bowel walls of gastric tissues. © 2004 Elsevier Inc. All rights reserved.

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### 1. Introduction

Magnetic resonance imaging (MRI) has become one of the main clinical imaging modalities in recent years. However, its implementation as an alternative approach for gastrointestinal (GI) tract imaging is relatively new and its routine use is still controversial. MRI is an expensive but risk-free procedure with high spatial resolution and high sensitivity for tissue contrast differences. Nonetheless, GI applications have been limited by several problems, such as peristalsis, respiratory, cardiac and pulsatile flow motion artifacts [1].

Recent advances in rapid imaging techniques and the implementation of torso-phased array coils, which allows high-quality breath-hold imaging with high spatial resolu-

tion, have extended the role of MRI in evaluating abdominal pelvic diseases and GI tract function and motility [2,3].

Nevertheless, the potential role of MRI in GI tract studies remains a matter of debate. As for computed tomography, the need for bowel opacification, by the use of oral contrast agents, is mandatory to differentiate between collapsed or fluid-filled bowel loops and intra-abdominal organs or pathologic lesions [3,4].

Although MRI contrast can be manipulated by different sequence design, the use of exogenous contrast agents is important in many clinical imaging procedures. They are used to increase the sensitivity to differentiate between normal and abnormal tissues. They are generally applied by means of an intravenous injection, allowing its distribution throughout the entire blood system [1–8].

On the other hand, contrast agents can be ingested as an oral solution. The evaluation of GI tract by means of MRI is closely related to availability of oral contrast agents [1,4].

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Table 1  
Chemical compositions of *Euterpe Olerácea*

| Components   | 100 g of pulp | 100 g of juice |
|--------------|---------------|----------------|
| Energy       | 247.0 Cal     | 182.4 Cal      |
| Water        | 45.9 g        | 60.4 g         |
| Proteins     | 3.8 g         | 2.1 g          |
| Lipids       | 12.2 g        | 6.0 g          |
| Carbohydrate | 36.6 g        | 30.0 g         |
| Calcium      | 118.0 mg      | 110.0 mg       |
| Phosphorus   | 58.0 mg       | 56.0 mg        |
| Iron         | 11.8 mg       | 9.3 mg         |
| Thiamine     | 0.36 mg       | 0.036 mg       |

Oral contrasts are close to ideal for MRI if they have good digestive acceptance, uniform distribution in the bowel lumen, unchanged contrast effect when diluted throughout the GI, no toxicity, no peristalsis stimulus and acceptable cost [1]. Although some of them are commercially available, they are still not used routinely in most clinical centers, due to possible side effects. Oral contrast agents are usually classified depending on if they increase (positive agents) or decrease (negative agents) the signal within the bowel [1].

Positive GI agents increase intraluminal signal either by a paramagnetic shortening of  $T_1$  of nearby tissues or by having intrinsically short  $T_1$  relaxation time [1,8,9]. Actually, many contrast solutions would be capable of increasing signal intensity (SI) typically based on heavy metal ions, as of gadolinium (III), manganese (II), manganese (III), iron (III) and copper (II) [10–13]. However, they have generally intrinsic side effects when used orally [1]. Ferric iron, for example, can provoke teeth-staining, gastric irritation, nausea, diarrhea and constipation. Mannitol may cause nausea, vomiting and diarrhea [1]. Gd-DTPA without Mannitol is

well-tolerated but usually fails in opacifying the entire bowel. It also needs to be buffered when used orally since this chelate is not very stable at low pH found in the stomach, what can alter the gastric function.

Another variety of contrast agents is based on natural sources such as milk, water, blueberry and tea [14–19], which have the advantage of not presenting alterations in the GI system and being palatable.

We herein present a preliminary characterization and implementation of *Euterpe Olerácea*, usually called *Açaí*, as a new alternative oral contrast agent for GI tract evaluation. *Açaí* is a fruit typically found at the north region of Brazil. It is widely available, usually commercialized as pulp, juice and wine. It is considered an energy food with great caloric value, and its composition is shown in Table 1.

## 2. Methods

The amount chemical components (iron, manganese and copper) of the commercial pulp of *Açaí* were confirmed by means of atomic-absorption (AA) spectroscopy with a Varian, AA-175 series atomic absorption spectrophotometer.

In order to have insight into how these paramagnetic ions may influence the magnetic properties of *Açaí*, volumetric magnetic susceptibility was determined using a susceptometer based on a chemical balance [20,21], shown in Fig. 1.

A whole body MRI scanner (Siemens, Magnetom Vision, 1.5 T) was used for phantom and in vivo measurements. First, a phantom consisting of five samples was prepared to evaluate and compare the performance of different contrast under specific image sequences. The samples were: (a) 25 mL of ferrous sulfate in 110 mL of  $H_2O$ , (b) a composite of

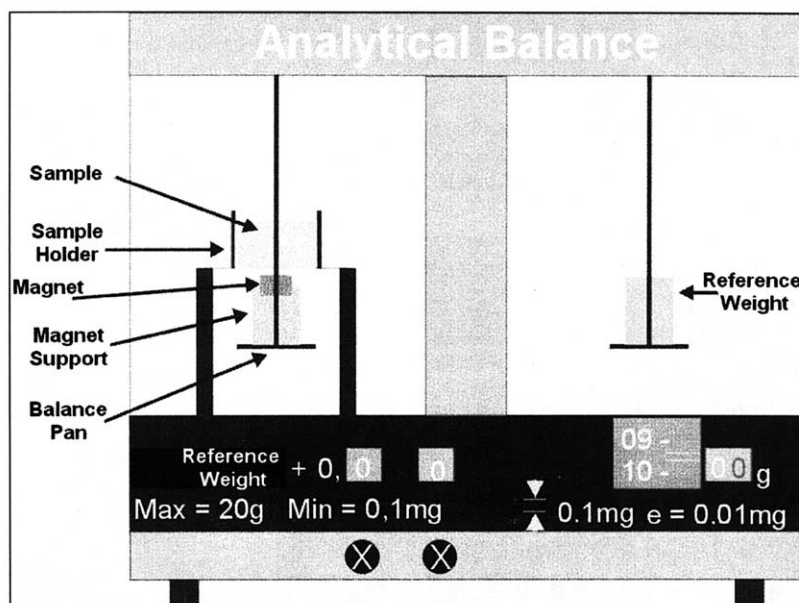


Fig. 1. Schematic description of the setup used for the *Açaí* susceptibility measurements.

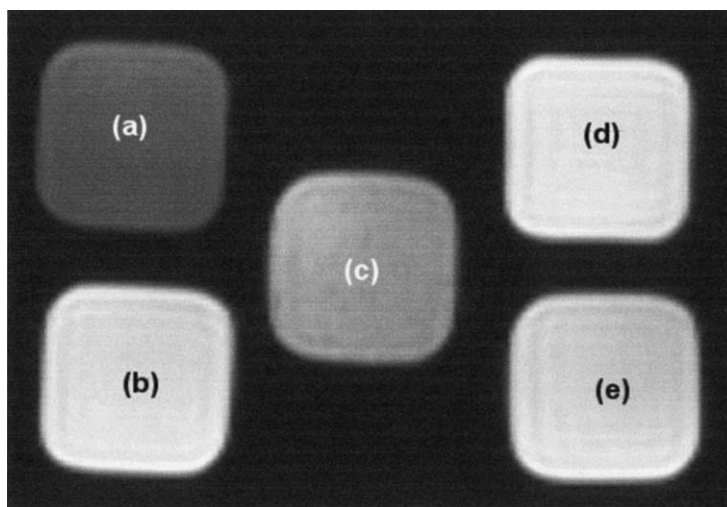


Fig. 2.  $T_1$ -weighted image with fat-saturation pulse, of a phantom consisted of: (a) ferrous sulphate solution, (b) solution of Mn, Cu and Fe; (c) water; (d) Gd-DTPA and (e) *Açaí*.

(0.22 Fe; 0.08 Mn; 0.024 Cu)g in 250 mL of  $H_2O$ , (c) water, (d) Gd-DTPA and (e) *Açaí*.

A body array coil was used to generate  $T_1$ -weighted images [repetition time (TR)/echo time (TE) = 177.8/4.1 ms; field-of-view (FOV) = 350 mm,  $256 \times 256$ , 6-mm slice thickness] and  $T_2$ -weighted images (TR/TE = 4400/64 ms, FOV = 350 mm,  $256 \times 256$ , 6-mm slice thickness) at a standard spin echo (SE) sequence. Also, a fat-saturation sequence (TR/TE = 160.0/2.3 ms, FOV = 350 mm,  $256 \times 256$ , 6-mm slice thickness) was obtained to evaluate whether or not contrast alteration could be due to fat present in the *Açaí* pulp.

For in vivo measurements, the same sequences were applied to five non-symptomatic subjects, with 12 h of fasting. Ten axial slices centered at the stomach region were acquired, under three distinct experimental conditions: first in the fasting state with an empty stomach (baseline), followed by the ingestion of water and finally by the ingestion of *Açaí*.

### 3. Results

In order to test for the magnetic characteristics of *Açaí*, its AA spectra and magnetic susceptibility were obtained. The susceptibility measurements showed that *Açaí* has  $\chi = -4.85 \times 10^{-6}$ . AA measurements were used to quantify iron, manganese and copper present in *Açaí* pulp. The content was found to be Fe = 8.9 mg/dL, Mn = 4.3 mg/dL and Cu = 1.2 mg/dL. Moreover, the amount of water in the commercial pulp was about 60%.

Figure 2 presents a  $T_1$ -weighted image, with a fat-saturation pulse, comparing the phantom containing: (a) 25 mL of ferrous sulfate in 110 mL of  $H_2O$ , (b) a composite of (0.22 Fe; 0.08 Mn; 0.024 Cu)g in 250 mL of  $H_2O$ , (c) water, (d) Gd-DTPA and (e) *Açaí*.

The positive effect of the *Açaí* (Fig. 2e) is comparable to either Gd-DTPA (Fig. 2d) or artificial composite (Fig. 2b). These first observations suggested that *Açaí* has a paramagnetic behavior.

Images from the stomach of a healthy fasting volunteer are presented in Fig. 3, where  $T_1$ - and  $T_2$ -weighted images were obtained. Figures 3a and 3d present an empty stomach. As it is observed, the low contrast signal in the stomach region is due to air, in  $T_1$  (Fig. 3a) and high contrast in  $T_2$  (Fig. 3d). Subsequently, the subject ingested 200 mL of water, and another  $T_1$ - $T_2$  sequence was acquired. Figure 3b show a  $T_1$ -weighted image. The expansion of the gastric volume is clearly observed and two phases can be identified on the images: a small dark region corresponding to air and a larger area of slight contrast increase corresponding to water. The high contrast of water in the  $T_2$  sequence (Fig. 3e) was also observed. Finally, 200 mL of the *Açaí* pulp was ingested by the subject and the last series of MR images were obtained. Figure 3c shows one  $T_1$ -weighted image under this condition. The increase of contrast due to the presence of *Açaí* is conspicuous. Three well-defined regions can be identified: air, water and *Açaí*. Also, the  $T_2$  sequence presents a low contrast due to the present of *Açaí* (Fig. 3f).

### 4. Discussion and conclusions

Heavy ions have intrinsic paramagnetic properties. These molecules are generally at a randomized magnetic structure within the forming substance. However, if these substances are present in an external magnetic field, just like paramagnetic contrast agents in MRI, there will cause an increase in the local magnetic field experienced by the tissue. Therefore, it will decrease  $T_1$  and  $T_2$ , affecting SI and, consequently, the contrast in MRI [8].

*Açaí*, just like most organic and inorganic compounds,

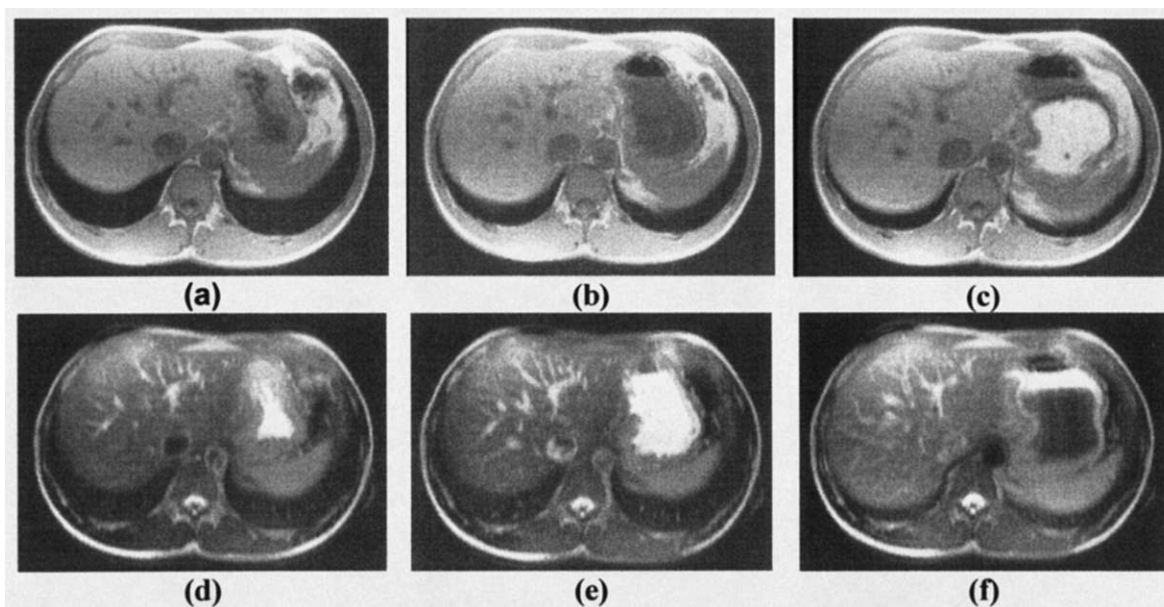


Fig. 3. T<sub>1</sub> and T<sub>2</sub>-weighted images in a coronal plane. T<sub>1</sub> images are on the top line, while T<sub>2</sub> are on the bottom. (a) T<sub>1</sub> image of an empty stomach. (b) T<sub>1</sub> of the same volunteer with air and 200 mL of water. (c) T<sub>1</sub> image with air, 200 mL of water and 200 mL of Açai. (d) T<sub>2</sub> image of an empty stomach. (e) T<sub>2</sub> image of air and 200 mL of water. (f) T<sub>2</sub> image of air, 200 mL of water and 200 mL of Açai.

has a net diamagnetic behavior, especially because it is constituted by about 60% of water. Pure water has its magnetic susceptibility equal to  $\chi = -9.90 \times 10^{-3}$ . Nevertheless, increasing paramagnetic elements in a water solution will increase its susceptibility [8]. Therefore, the presence of paramagnetic metal ions in the Açai compound gave rise to its final magnetic susceptibility value. As a result, it is reasonable to think that the observed changes in image contrast due to the presence of Açai are mainly because of paramagnetic ions found in the substance.

This kind of contrast agent affects relaxation and so does it for T<sub>1</sub> and T<sub>2</sub> simultaneously because of the dual and coupled nature of relaxation mechanisms. Actually, increasing the concentration of paramagnetic substances will probably increase SI for T<sub>1</sub>-weighted images. On the other hand, a concentration enhancement will probably decrease SI for T<sub>2</sub>-weighted images [8,20].

The magnetic signal in MR images had a positive characteristic in T<sub>1</sub>-weighted (Fig. 3c) and negative appearance in T<sub>2</sub>-weighted (Fig. 3f), indicating that relaxations rates  $1/T_1$  and  $1/T_2$  are affected by the presence of this natural contrast agent. Fortunately, the presence of Açai does not cause a saturation of image contrast, which would happen if one applies pure GD-DTPA, due to its high paramagnetic behavior [22].

The contribution of the agent concentration in MRI images was previously discussed on a preliminary study of natural contrast agents [20]. The increase in signal intensity was due mainly to the manganese-rich substance. Although it would be reasonable to think that the same mechanism would hold for Açai, the relation between concentration and SI still needs more experimental tests.

The contrast enhancement due to Açai in T<sub>1</sub>-weighted images is evident (Fig. 3c), producing a better definition of the gastric lumen. Thus, these results open a wide perspective for Açai as an alternative oral contrast agent that can be employed for imaging the intestinal lumen, functional evaluation of dyspepsia, in addition to the applications of the gastrointestinal motility [23].

We saw better signal homogeneity in stomach and the bowel walls present increased contrast with the pulp on image (Fig. 3c).

Açai has a great advantage over artificial oral contrast agents currently used in clinical applications. It is a natural pleasant food and, we expect, devoid of side effects or adverse reactions. Its commercialization is easy and economic in the Brazilian market and it is exported to the United States and Europe.

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