A novel Biomagnetic Instrumentation with four Magnetoresistive Sensors to Evaluate Gastric Motility

Fabiano C. Paixão, Rogério de Moraes, Murilo Stelzer, Luciana A. Corá, Madileine F. Américo, Uilian Andreis, Ricardo B. Oliveira, Oswaldo Baffa and José R. de A. Miranda.

Abstract — A novel instrumentation using anisotropic magnetoresistive (AMR) sensors associated with magnetic coils excitation was developed to evaluate gastrointestinal tract motility parameters. The susceptometer has four sensors that were used to measure the gastric activity contractions (GAC) in anaesthetized dogs, its performance was evaluated by manometry with good results.

I. INTRODUCTION

THE mechanical activity of the gastrointestinal (GI) tract can be studied by different techniques such as scintigraphy, eletogastrography [1]-[2] and manometry [3]-[5], but all of them present some inconvenience. An alternative to the conventional methods is to use biomagnetic methods to evaluate GAC [6]-[7], gastric emptying [8]-[11], orocaecal transit time [12]-[14], pharynx transit time and clearance [15], esophagus transit time [16], colon motility [17]-[22], measuring the decay of the remnant magnetization the meal mixing time [23]-[24] and disintegration of pharmaceutical dosages form with ferromagnetic material [25]-[31]. In these studies magnetic markers (MM) and magnetic tracer (MT) are used and the magnetic field produced by them measured at the torso surface. More recently, anisotropic magnetoresistive (AMR) sensors were used to monitor the gastrointestinal tract [32]-[33] using the magnetic pill. AMRs are more sensitive at low frequency and have a better specific spatial resolution than induction coils. However, up to now the association the AMR with AC magnetic excitation was not used to evaluate the gastrointestinal tract.

Manuscript received June 22, 2007. This work was supported in part by the Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP), Conselho Brasileiro de Desenvolvimento Científico e Tecnológico (CNPq) and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (Capes).

F. C. Paixão, Murilo Stelzer, R. de Moraes, L. A. Corá, U. Andreis and J. R. de A. Miranda are with the Departamento de Física e Biofísica, IBB – Universidade Estadual Paulista (UNESP), Distrito de Rubião Júnior, S/N, 18.618-000, Botucatu-SP, Brazil (phone: 55-14-3811-6254; fax: 55-14-38116346; e-mail: jmiranda@ibb.unesp.br).

O. Baffa are with the Departamento de Física e Matemática, FFCLRP-Univesidade de São Paulo, Av. Bandeirantes, 3900, 14040-901 Ribeirão Preto-SP, Brazil (phone: 55-16-3602-3642; fax: 55-16-3602-4887; e-mail: baffa@usp.br).

M. F. Américo and R. B. Oliveira, Departamento de Clínica Médica, FFCLRP-Univesidade de São Paulo, Av. Bandeirantes, 3900, 14040-901 Ribeirão Preto-SP, Brazil (phone: 55-16-3602-2457; fax: 55-16-3633-6695; e-mail: <u>rbdolive@fmrp.usp.br</u>).

This work presents a new biomagnetic instrumentation with four sensors for detection of magnetic fields produced by a MT associated with AC magnetic exaction coils. The idea is to combine the high sensitivity and spatial resolution of the AMR with the convenience of AC excitation. The system was used to evaluate GAC in anaesthetized dogs and the results were compared with those obtained by means of contemporary manometry.

II. MATERIAL AND METHODS

A. Instrumentation and operation

The instrumentation developed consisted of two coils and five AMR sensors. The coils are used to produce an AC magnetic field (10 kHz) and the sensors are used to measure this field and its changes due to the presence of ferromagnetic materials. Four sensors were used to detect magnetic field change and one sensor was used as reference signal. Figure 1 shows the sensors configuration. The sensors were positioned based on the radial symmetry of the magnetic field produced by the excitation coil. Thus, one AMR sensor was placed in the coil center and the others symmetrically, keeping a separation distance (radial) among them of 15.0 mm. This configuration tries to minimize the undesirable effects in the magnetic field non homogeneity produced by the coil. The excitation/detection pair is separated by a fixed distance or baseline of 100 mm.



The working principle is based on the fact that the pair (excitation/detection), located more distant from ferromagnetic material (ferrite) acts as reference and the other four sensors as measuring channels. In this system each detection AMR sensor had an instrumentation pre-amplifier for signal conditioning followed by a differential amplifier

arrangement using the same reference sensor, the differential amplifier also was made using instrumentation grade amplifiers. When there is no magnetic material near the system, the output signal is minimized. With the approximation of any magnetic mass, an unbalance occurs in the output signal and the variation of the magnetic field is measured as a voltage. This voltage can be measured, digitalized and acquired continuously with the use of four lock-in amplifier, an A/D board and a personal computer (PC). In this system each AMR sensor after pre- and differential amplification is connected in a lock-in amplifier. Figure 2 shows block diagram of this instrumentation.



Fig. 2. Block diagram of AC biosusceptometer with four AMR sensors (ACB-AMR 4-channels).

B. Design circuit and components

The excitation coils were made with 220 turns of 26-AWG wire and 55.0 mm internal diameter. The coils are excited by a signal of 10 kHz (reference frequency) supplied by a lock-in amplifier.

The AMR HMC1001 (Honeywell Inc., USA) sensor, 1axis sensing, ± 2 gauss field range and 3.2 mV/V/gauss sensitivity was used in the system. The set/reset pulse was implemented to remove the sensor remnant magnetization.

The stage with instrumentation amplifier was used to preamplify and differentiate the signal of the two sensors, this configuration minimizes the noise in the output signal of the system. The circuits are excited by a \pm 5 V precision dual power supply.

A lock-in amplifier (Stanford Research Systems – SR830 DSP, USA) and three lock-in amplifiers (Stanford Research System – SR510, USA) were used to detect and measure output AC voltage signals of the differential system with AMR sensor. In this instrumentation, the signal measured by lock-in is referenced with the excitation.

The output signal of the instrumentation was digitalized by an A/D board (PCI-MIO-16XE-10, National Instruments Inc., USA) in 10 Hz sampled and acquired continually with a personal computer (PC).

C. In vitro study

For ACB-AMR 4-channels characterization a sensitivity matrix was made. This test determine the space resolution power of this new instrumentation. In this sensitivity test two MM were used. The first MM consists of a small amount ferrite powder (MnFe₂0₄; 80 $\leq \Phi \leq 125 \mu$ m) placed in cylinder (1.0 mm diameter and 3.00 mm height) and second MM used was obtained by direct compression from 1.0 g of ferrite powder mixed with 0.52 g of microcrystalline cellulose (Merck, Germany), the MM has cylindrical form weighing 1.52 g, 1.0 cm of diameter and density of 2.03 g/cm³.

The data of test were colleted by changing the position of MM on the matrix cells. For each cell the voltage value was taken and transformed into magnetic field. The matrix used has 17 rows and 15 columns, with 5.0 mm separation between rows and columns. The distance between the matrix and detectors sensor was 6.0 mm.

D. In vivo study

The study was performed at the Biomagnetism Laboratory, Department of Physics and Biophysics, Institute of Biosciences – Universidade Estadual Paulista (UNESP). The research protocol was approved by the UNESP Ethic Committee in Animal Research.

Six healthy female dogs weighing between 8.0 and 10.0 kg were used. The animals were anaesthetized with pentobarbital (30.0 mg/kg, Cristalia, Mexico) and placed in a supine position on a suited table. A gastric feeding tube with a balloon on its tip was introduced in the animal, 35.0 ml of MT (4.0 g ferrite homogenized in 60.0 ml yogurt - Danete®, Brasil) was introduced in balloon and 18.0 ml of water completed the feeding tube that was connected to pressure sensor (strain gauge type). This procedure allowed continuous recording of intragastric pressure. The ACB-AMR 4-channels were positioned on the animal abdomen at, the stomach projection region.

In order to analyze the performance of the new instrument in detecting GCA changes prostigmine® (0.04 μ g/kg, Neostigmine, Roche) and Buscopan® (2.2 mg/kg, *N*-butylscopolamine, Boehringer-Ingelheim) injection were used as GCA stimulator and inhibitor, respectively.

The manometry and ACB-AMR 4-channels signal were digitalized by an A/D board and acquired by LabView Inc. with 10 Hz sampling rate and stored in ASCII format, and were analyzed using programs written in MatLab afterwards (Mathworks Inc., USA). A bidirectional Butterworth filter between 20 and 150 mHz cutoff frequency and frequency analysis by Fast Fourier Transform (FFT) were performed.

The experimental protocol was 30 minutes-long divided in three 10 minutes periods: control, prostigmine® infusion and buscopan® infusion. The analyses of the widths were accomplished through the motility index (MI) and in the frequencies using the FFT, being taken the control period as reference.

III. RESULTS

The results of the in vitro tests were interpolated and are

shown in figure 3. The maximum point in the graphic (culminating points) shows the great sensitivity of each sensor. Through the graphs it is possible to confirm the good space resolution obtained by this instrumentation. In a circular area of 15.0 mm radius (4 sensors are arranged), the ACB-AMR 4-channels distinguished clearly the position of a point magnetic mass.



Fig. 3. ACB-AMR 4-channels sensibility: a) Smallest magnetic marker; b) Tablet magnetic marker.

In the *in vivo* test of GCA was recorded by four sensors of ACB-AMR in all animals. The GCA intensity was identified by both measurements. Figure 4 shows an ACB-AMR and pressure signal with their FFT, where a frequency around 75 mHz is observed. This behavior was observed in all animals.



Fig. 4a. GCA measure sample measurement by ACB-AMR and respective FFT. The arrows indicate the drugs infusion instants.



Fig. 4b. GCA measure sample by Manometry and respecitive FFT. The arrows indicate the drugs infusion instants.

The MI was calculated in all experiments. The mean value of four AMR sensors was calculated and the result was compared to manometry. Figure 5a and 5b shows these results.

Present results demonstrate that the new biomagnetic instrumentation is capable to recording the GCA and to characterize the signal in frequency terms. It was still possible to observed and analyze the increase and decrease on GCA, caused by prostigmine® and buscopan® action.



Fig. 5. a) ACB-AMR 4-channels signals mean of MI; b) Manometry signals mean of MI.

Table I shows the GCA frequency results in the control period. The results are show in contractions per minute (CPM).

TABLE I GASTRIC MOTOR ACTIVITY FREQUENCY	
Instrumentation	Mean (CPM) ± SD
ACB-AMR 4-channels Manometry	$\begin{array}{c} 4.67 \pm 0.39 \\ 4.75 \pm 0.36 \end{array}$

Compared to manometry the ACB-AMR results indicated a great similarity of frequency of GCA signals and any statistical difference in GCA frequency value measurements.

The gain of spatial resolution can be compared to other biomagnetic instrumentations. The results presented by Corá *et. al.* [31] was obtained with 30.0 mm diameter sensor and in this work the system developed has four sensors in a same area. Thus, the AMR sensor implementation has better spatial resolution than conventional AC biosusceptometry.

IV. CONCLUSIONS

The results shows that ACB-AMR 4-channels is a valid alternative method as compared to the standard methods. It is this non-invasive, non-expensive, ionizing radiation free and has a better spatial resolution than conventional AC biosusceptometry [31]. In conclusion, ACB-AMR has potential application in the fields of gastroenterology motility, pharmacology, pharmaceutical and medical clinical practice.

ACKNOWLEDGMENT

The authors are grateful for the technical support for Júlio Cézar Martin Ribeiro and Antônio Carlos de Barros Tardivo.

REFERENCES

- J. D. Z. Chen, R. D. Richards and R. W. Mccallum, "Identification of gastric contractions from the cutaneous electrogastrogram", *Am. J. Gastroenterol.*, vol. 89, pp.79-85, 1986.
- [2] M. P. Mintchev and K. L. Bowes, "Comparative quantification of gastric electrical activity and electrogastrograms", *Med. Biol. Eng. Comput.*, vol. 36, pp.96-100, 1998.
- [3] F. Azpiroz and J. R. Malagelada, "Pressure activity patterns in the canine proximal stomach: response to distension", *Am. J. Physiol.*, vol. 247, pp.G265-272, 1984.
- [4] F. Azpiroz and J. R. Malagelada, "Intestinal control of gastric tonic", *Am. J. Physiol.*, vol. 249, pp.G501-509, 1985a.
- [5] F. Azpiroz and J. R. Malagelada, "Physiological variations in canine gastric tone measured by an electronic barostat", *Am. J. Physiol.*, pp.G229-237, 1985b.
- [6] R. Moraes, "Measurement of gastric contraction activity in dogs by means of AC biosusceptometry", *Physiol. Meas.*, vol. 24, pp.337-345, 2003.
- [7] E. Stathopoulos, "Magnetic pill tracking: a novel non-invasive tool for investigation of human digestive motility", *Neurogastroenterol. Motil.*, vol. 17, pp.148-154, 2005.
- [8] E. H. Frei, "Measurements of the emptying of the stomach with a magnetic tracer", *IEEE Trans. Magn.* vol. 6, pp.348-349, 1970.

- [9] Y. Benmair, "Study of gastric emptying using a ferromagnetic tracer", *Gastroenterology*, vol. 73, pp.1041-1045, 1977.
- [10] J. R. Miranda, "An AC Biosusceptometer to Study Gastric Emptying", *Med. Phys.*, vol. 19, pp.445-448, 1992.
- [11] M. Forsman, "Gastric emptying of solids measured by means of magnetised iron oxide powder", *Med Biol Eng Comput*, vol. 36, pp.2-6, 1998.
- [12] O. Baffa, "Analysis and Development of a Simple AC Biosusceptometer for Orocaecal Transit Time Measurements", *Med.* & *Biol. Eng.* & *Comput.*, vol. 33, pp.353-357, 1995.
- [13] R. B. Oliveira, "Evaluation of a Biomagnetic Technique for Measurement of Orocaecal Transit Time", *Eur. J. Gastroent. & Hepatol.*, vol. 8, pp.491-496, 1996.
- [14] M. Basili, "Measurement of segmental transit time in man" *Digestive Disease Sciences*, vol. 37, pp.1537-1543, 1992.
- [15] C. A. Miquelin, "Pharyngeal Clearance and Pharyngeal Transit Time Determined by a Biomagnetic Method in Normal Humans", *Dysphagia*, vol. 16 (4), pp.308-312 FAL 200M.
- [16] N. A. Daghastanli, "Oesophageal Transit Time Evaluated by a Biomagnetic Technique", *Physiol. Meas.*, vol. 19, pp.413-420, 1998.
- [17] J. R. A. Miranda, "A novel biomagnetic method to study gastric antral contractions", *Phys. Med Biol.*, vol. 42, pp.1791-1799, 1997.
- [18] A.Ferreira, "Study of the magnetic content movement present, in the large intestine" J. Magn. Mag. Mat., vol. 283 (1), pp.16-21, Nov 2004.
- [19] M. Forsman, L. Hultin and H. Abrahamsson "Measurements of Gastrointestinal Transit Using Fluxgate Magnetometers", in *Biomagnetism: Fundamental Research and Clinical Applications*, L. Decke, C. Baumgartner, G. Stroink and S.J. Williamson, Eds. Amsterdam: Elsevier, pp.739-742, 1993.
- [20] W. Weitschies, "Magnetic markers as a noninvasive tool to monitor gastrointestinal transit", *IEEE Trans. on Biomed. Eng.* vol. 41, pp.192-195, 1994.
- [21] W. Weitschies, "Magnetic markers monitoring of esophageal, gastric and duodenal transit time of non-disintegrating capsules", *Pharmazie*, vol. 54, pp.426-430,1999.
- [22] T. Cordova-Fraga, "Spatiotemporal evaluation of human colon motility using three-axis fluxgates and magnetic markers", *Med. & Biol. Eng. & Comput.*, vol. 43(6), pp.712-715, Nov 2005.
- [23] A. A. O. Carneiro, O. Baffa and R. B. Oliveira, "Study of Stomach Motility Using Magnetic Tracers", *Phys. Med Biol.*, vol. 44, pp.1691-1697, 1999.
- [24] M. Forsman, "Intragastric movement assessment by measuring magnetic field decay of magnetised tracer particles in a solid meal", *Med Biol Eng Comput*, vol. 38, pp.169-174, 2000.
- [25] M. Moreira, L.O. Murta Jr. and O. Baffa. "Imaging Ferromagnetic Tracers With an AC Biosusceptometer", *Rev. Sci. Instrum.*, vol. 71, pp.2532-2538, 2000.
- [26] F. G. Romeiro, "A novel biomagnetic approach to study caecocolonic motility in human", *Neurogastroenterol. Motil.*, vol. 18 (12), pp.1078-1083, Dec 2006.
- [27] L. A. Corá, "Enteric coated magnetic HPMC capsules evaluated in human gastrointestinal tract by AC biosusceptometry", *Pharm. Res.*, vol. 23 (8), pp.1809-1816, Aug 2006.
- [28] L. A. Corá, "Gastrointestinal transit and disintegration of enteric coated magnetic tablets assessed by ac biosusceptometry", *Eur. J. Pharm. Sci.*, vol. 27 (1), pp.1-8, Jan 2006
- [29] L. A. Corá, "Magnetic images of the disintegration process of tablets in the human stomach by ac biosusceptometry", *Phys. Med Biol.*, vol. 50 (23), pp.5523-5534, Dec 2005.
- [30] L. A. Corá, "AC biosusceptometry in the study of drug delivery" Adv. Drug. Deliv. Rev., vol. 57 (8), pp.1223-1241, Jun 2005.
- [31] L. A. Corá, "Desintegration of magnetic tablets in human stomach evaluated by alternate current biosusceptometry", *Eur. J. Pharm. Biopharm.*, vol. 56, pp.413-420, 2003.
- [32] W. Andrä, "A novel method for real-time marker monitoring in the gastrointestinal tract", *Phys. Med. Biol*, vol. 45, pp.3081-3093, 2000.
- [33] R. Guignet, "Magnet Tracking: a new tool for in vivo studies of the rat gastrointestinal motility", *Neurogastroenterol. Motil.*, vol. 18, pp.472-478, 2006.