Transoesophageal electrical bioimpedance measurements of the heart in humans

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Abstract.— **Previous studies have proved that post-transplant cardiac rejection is associated with changes in endomyocardial electrical impedance in humans.**

The aim of this study is to develop a safe transoesophageal system able to measure cardiac electrical impedance in transplanted patients and to evaluate the capability of this technique to detect heart graft rejection in humans in order to reduce the number of repetitive biopsies.

The impedance measurement is performed using a four wire configuration. We measured the impedance spectrum from 13 kHz to 1 MHz. The oesophageal ECG signal is used to evaluate the position of the catheter in the oesophagus with regard to the patient's heart.

So far measurements have been carried out on a group composed of 11 healthy volunteers (5 men) and 9 cardiac transplanted patients (7 men) with no histological signs of cardiac rejection.

Impedance spectrum measurements at different locations in the oesophagus showed a decrease of the impedance magnitude with the increase of the depth of the catheter in the oesophagus (about 1 ohm/cm). The phase value does not show significant changes when changing the catheter's position in the oesophagus.

There are gender differences in the magnitude but not in the phase angle of the transoesophageal cardiac electrical impedance. Transplanted patients with no graft rejection show impedance values similar to that of healthy volunteers, suggesting that the surgical intervention does not affect the impedance measures.

The oesophageal approach is safe and was considered for transplanted patients less annoying than the biopsy method. In consequence, if further results show a significant change of impedance in patients with cardiac rejection, a new less-invasive clinical method to detect graft rejection can be envisaged.

Keywords— **Heart transplant, Impedance Spectroscopy, Cardiac Rejection, Oesophageal.**

I. Introduction

According to the Spanish Instituto Nacional de Estadistica, in 2006 about 193,889 persons died in Spain for reasons related to heart problems.

Nowadays, people suffering an important heart failure or an advanced heart condition, which compromises severely the quality of life, can be considered candidates for a heart transplant. During 2007, in Spain were carried out about 2200 heart transplants in all the national territory.

However, this medical approach may have significant complications, like acute rejection of the donor heart. Therefore, the efficiency and the promptness in the detection of the heart rejection are of vital importance.

For this reason the transplanted patient has to follow periodical control in order to avert a possible heart rejection for life, and particularly during the first year when it is usual that the rejection could appear. So during the first year after the transplant each patient has scheduled about 13 biopsy sessions [4]. After the second year, in the absence of particular problems, controls are made every 3-6 months.

The gold standard to detect cardiac rejection is the biopsy of the endomyocardial tissue by means of an intracavitary catheter.

Previous studies in animals [2][3] have proved that cardiac graft rejection is associated with changes in the myocardial electrical impedance. Also, impedance measurements in the right heart cavities in human patients using a venous transcatheter method showed relevant differences of impedance in the graft rejection grade [4]. The presented system has been tested before in animal experiments in which a myocardial ischemia was produced by occluding a coronary artery [5].

The aim of this study is to develop a safe less-invasive transoesophageal system able to measure cardiac electrical impedance in transplanted patients and to evaluate the capability of this technique to detect heart graft rejection in humans to reduce the number of repetitive biopsies.

II. Methods

A. Measurement system

The designed bioimpedance spectroscopy system [1] (frequency range 13 kHz-1 MHz) consists of 2 boxes: 1) an optically isolated patient interface, including a two channel ECG board and a board to measure impedance, and 2) the control and signal processing box, which contains a sinusoidal signal generator, an A/D converter, the digital de-

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modulator and a rabbit board for control and communication with a PC via Ethernet (Fig. 1).

The impedance measurement is performed using a four wire technique. Current is injected between the distal electrode of the oesophageal probe and one standard electrode on the thorax in the 6^{th} intercostal space close to the sternum on the left side (at the position of the ECG lead V4). Voltage is measured between the proximal electrode of the probe and another standard electrode in the thorax on the right side of the sternum, close to V3 location (Fig. 2).

The study was approved by the ethical committee of the Hospital. Prior informed consent was signed by all participants.

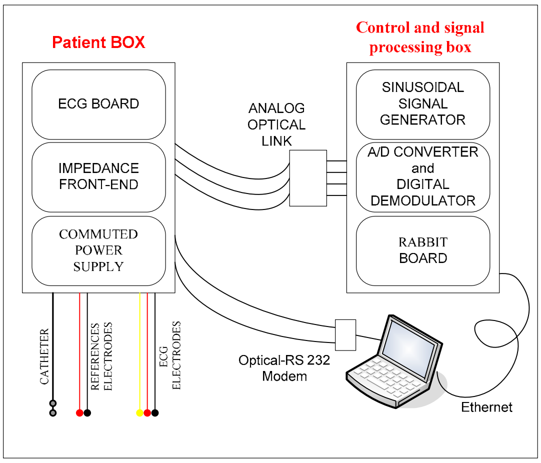

Fig. 1. Measurement system block diagram. The front-end is in contact with the patient, all other equipment is out of the patient area. Electrical isolation is based on 5 optical fibers.

The ECG measurement system has two channels: surface and oesophageal.

The surface channel has conventional features: band pass frequency response with cut-off frequencies of 0.05 Hz and 100 Hz and gain of 1000. We measured Lead I with electrodes in the depression corresponding to the Mohrenheim fossa and the reference electrode placed near the navel. The oesophageal ECG channel has several differences. The signal is obtained between the electrode at the tip of the catheter and a surface electrode. The gain can be programmed to 10, 100 or 1000. Cut-off frequencies are 0.5 Hz or 0.05 Hz (selectable) for the high pass filter and 100 Hz for the low pass filter [1].

In particular, the oeasophageal ECG channel will be used to evaluate the position of the catheter in the oesophagus with regard to the patient's heart.

B. Measurement protocol

The measurement population is divided into 2 categories: healthy control volunteers and transplanted patients.

The protocol for the first category began with an anthropometric measurement and is followed by a standard precordial ECG recording to evaluate the possible presence of cardiac alterations in healthy volunteers. Thereafter the transoesophagic impedance measurement was undertaken.

Transplanted patients are measured the same day that they have an endocardial control biopsy.

As a control method to evaluate the adequate skin-electrode contact impedance of measuring electrodes, we perform a 2 wire measurement of both electrodes located on the 6^{th} intercostal space. This information could be used also in the future to compensate errors due to electrode impedances.

The catheter is introduced through the nostril with the patient seated on a stretcher with the headrest placed at an angle of 80º. In order to facilitate the introduction of the catheter in the oesophagus and to prevent it for entering in the trachea the patient ingests a little amount of water.

The oesophagic ECG signal is acquired and evaluated during the introduction of the catheter since the distal electrode is placed near the heart in the oesophagus. Previous studies have shown that this position is reached when the internal ECG signal shows a waveform with a r/s=1 corresponding to a biphasic P wave. Next step is to make 5 measurements at 5 different locations in the oesophagus corresponding to ±2 cm and ±4 cm referred to the first position. The measurement at each frequency takes time enough (about 15 s) to average some respiratory cycles. We repeated the measurement at five different frequencies (13 kHz, 30 kHz, 100 kHz, 300 kHz and 1 MHz).

Fig. 2. Oesophageal probe and surface electrode positions.

According to the protocol, the same day of the measurement we have to:

- Obtain the informed consent
- Record the patient's clinical data
- Annotate the position of the catheter during the 5 measurements
- Ask the patient an evaluation of the degree of nuisance of the oesophageal measurement compared to the biopsy method.

When the biopsy result shows a rejection degree higher than 2, another measurement is carried out to evaluate the impedance changes.

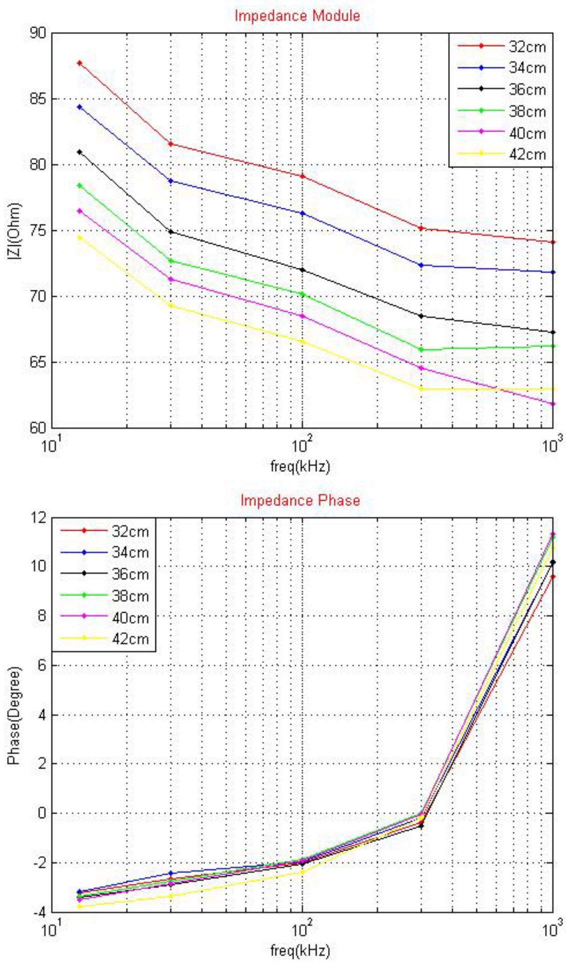

Fig. 3. Magnitude and Phase Angle spectrum of impedance vs.Catheter's depth in the oesophagus for a representative patient. Measurement frequencies: 13, 30, 100, 300, 1000 kHz.

III. RESULTS

So far measurements have been carried out on a group composed of 11 healthy volunteers (5 men) and 9 cardiac transplanted patients (7 men). The endomyocardial biopsies taken in all transplanted patients the same day showed no histological signs of rejection.

To show the effect of the catheter position on the measured impedance, we reproduce in figure 3 the results of a representative patient. In all the cases, there is a decrease of the impedance magnitude with the increase of the depth at what the catheter is inserted (about -1 ohm/cm). Whereas, the phase value does not change significantly with the change of the catheter's position. The positive phase angle measured at 1 MHz is unrealistic and is due to measurement errors related to input impedances and skin-electrode impedances.

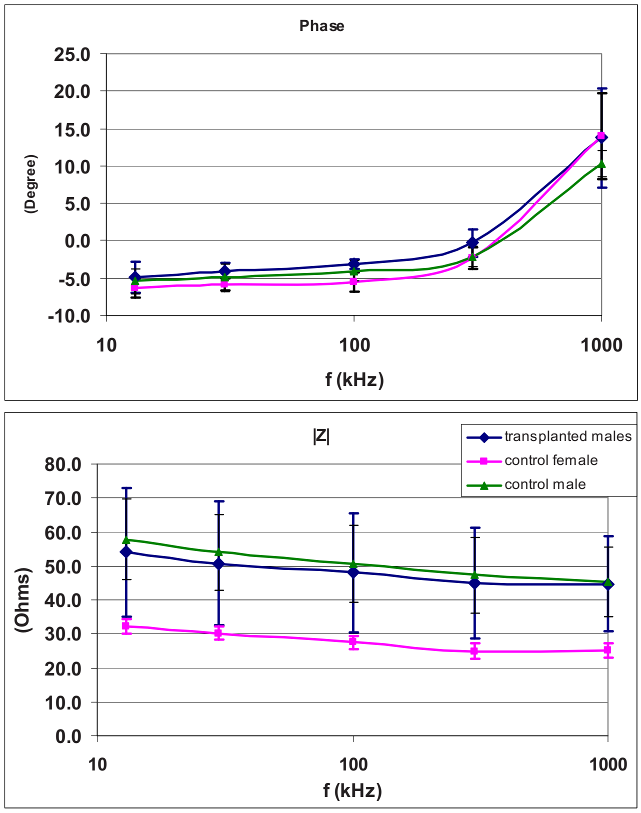

Fig. 4. Mean value and standard deviation of bioimpedance module and phase angle for transplanted and healthy volunteers.

Figure 4 shows the mean and standard deviation of impedance measurements for control volunteers (men and women) and transplanted pacients (we show only men because we only have two transplanted women). For each patient and volunteer, we selected the impedance measurement corresponding with the biggest biphasic P wave detected in the esophageal ECG, as described in the methods section. At all frequencies we observed a significant difference between genders in the impedance magnitude but not in the phase angle. For instance, at 30 kHz, the amplitude of transcardiac module impedance in volunteers was lower in women (30.1 ± 2.0 Ohm vs 54.0 ± 11.3 Ohm at 30 kHz, p=0.008) but the phase angle was comparable among both genders (-5.9 ± 0.8º vs –4.9 ± 1.8º, p=0.331). Transcardiac impedance in transplanted male patients was comparable to controls (magnitude: 50.8 ± 18.1 Ohm vs 54.0 ± 11.3 Ohm at 30 kHz, p=0.71; and phase angle: -4.0 ± 1.0º vs –4.9 ± 1.8º, p=0.33). The questionnaire made to the volunteers revealed that the test was painless, and considered it less annoying than biopsy and free of complications.

IV. CONCLUSIONS

There is a decrease of impedance magnitude with the increase of the depth at what the catheter is inserted in the oesophagus of about -1 ohm/cm, but the phase angle does not change significantly with the catheter position.

If we select the measurement with the catheter closer to the atrium (maximum biphasic P wave), there are gender differences in the magnitude but not in the phase angle of the transoesophageal cardiac electrical impedance. Transplanted patients with no graft rejection depict similar impedance values than healthy volunteers, suggesting that the surgical intervention does not affect the impedance measures.

The oesophageal approach is safe and was considered for transplanted patients less annoying than the biopsy method. In consequence, if further results show a significant change of impedance in patients with cardiac rejection, a new less-invasive clinical method to detect graft rejection can be envisaged.

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