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EXPERIMENTAL CHARACTERIZATION OF AN EIS-BASED METHOD FOR LOW-INVASIVE DIAGNOSIS OF PROSTHESIS OSSEOINTEGRATION

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Abstract: A digital measurement method for low-invasive clinical diagnosis of metallic prosthesis osseointegration was proposed. Electrical impedance spectroscopy is exploited to characterize the quality of the interface bone-prosthesis tissue. In this paper, *in vitro* and *in vivo* experimental results of the application of the proposed method to the evaluation of osseointegration of metallic implants used for percutaneous fixation are shown with a specific clinical case study in audiology. In particular, a cochlear implant BAHA ® from Cochlear ™ with direct bone conduction was used. *In vivo* measurements were performed on children with fixtures implanted respectively 7, 9, and 18 months before the test.

Keywords: Impedance Measurements; Electrochemical Impedance Spectroscopy; Biomedical Measurements, Biomedical Equipment.

1. INTRODUCTION

Metallic prostheses are implemented in bone as replacement of natural organs in different ways, directly (e.g. hip or tooth implants) or indirectly (e.g. cochlear implants) [1]-[2]. For all of them, the clinical success depends on the lack of mobility and the ability of the implant to uphold functional loading [5]. After some time the implant is positioned, an interface tissue (interface bone-prosthesis) grows [3]. Clinical success depends on the quality of this interface (Fig. 1) [3]-[5]. Theoretically, mechanical properties of the implant must be checked before its functional loading. This aspect is critical: the functionality of the organ replacement strictly depends on the quality of the deep contact between metal and bone, in absence of an interposing soft tissue layer, i.e. on the osseointegration [5]. Consequently, monitoring the osseointegration is a key factor to evaluate the success or the failure of the implant since the beginning.

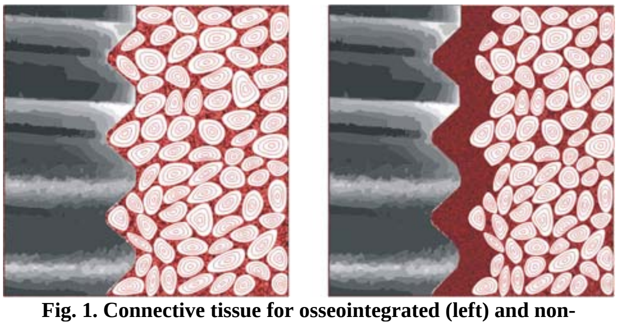

Fig. 1. Connective tissue for osseointegrated (left) and non-integrated (right) titanium prosthesis [5].

Clinical methods verify the stability of the implant, but give poor information about the hidden part of implant and the contact surface with living tissues. The most largely used instrumental method is the radiological. However, it is invasive and does not gives any characterization about new soft tissues in the first phase of osseointegration. In dentistry applications [6], the acoustical resonance frequency, obtained by beating the implant by means of a metal tool, is measured. However, this method is not well assessed yet.

Electrical Bioimpedance Analysis is one of the no–destructive, low-invasive, and most promising instrumental techniques for characterizing biological tissues [7]. Information about electrical characteristics of the analyzed tissue are gathered by injecting low-level sinusoidal currents in a given frequency bandwidth by external electrodes as usually done in Electrical Impedance Spectroscopy (EIS) [8]-[11]. In a previous work [13], the authors proposed a low-invasive measurement method based on EIS to analyze the interface between the bone and the metallic implant. Positive indications about the method effectiveness were gathered from experimental *in vitro* investigations on emulation of transcutaneous metallic implants.

In this paper, experimental results of the *in vivo* clinical validation of the proposed method are shown and compared to *in vitro* results. After a brief recall of the proposed method, a specific measurement setup for measuring electrical bioimpedance over a suitable frequency spectrum and a test procedure for gathering information about osseointegration of metallic audiology prosthesis are illustrated. Finally, *in vitro* and *in vivo* experimental results are compared and discussed.

2. BASIC IDEAS

In the following, the basic ideas underlying the proposed approach to osseointegration characterization are recalled [12]-[13].

When an electrical field is applied to a biological tissue, a resulting current passes through the tissue components at microscopic level. Consequently, on a macroscopic scale, complex electrical impedance can be used to define the electrical behaviour of the tissue. Therefore, the proposed approach was based on the following basic ideas [13]:

1. living biological tissues must be interested by low currents, thus, a low level of EIS stimulus guarantees a minimal invasivity to the proposed diagnostic approach;
2. an equivalent-circuit electrical model [14] of the electrochemical system constituted by the multi-layer set of biological tissues surrounding the prosthesis is built; with the aim of determining the behaviour of the connective tissue at the prosthesis interface and define osseointegration quality indexes EIS results can be analyzed by an equivalent electrical circuit model. Each model component represents a physical conduction process on the surface and inside of a tissue or a given set of biological tissues, including the bone-prosthesis interface and overlying tissues.

3. *IN VITRO* EXPERIMENTS

The proposed method was characterized and validated in laboratory through *in vitro* experiments on biological materials in order to verify its capability of measuring the osseointegration. In the following, (i) the *measurement setup*, and (ii) the *results* of *in vitro* experiments are described.

3.1. Measurement Setup

The interface tissue between prosthesis and bone was emulated by using a fresh cow long bone and two metal screws of 5 mm of diameter (Fig. 2), in order to emulate a percutaneous prosthesis (i.e., a prosthesis with a part outside the skin). Two twin screws in equal configuration were used in order to avoid problems of measurement electrodes and to enhance the measurement sensitivity. The measurement circuit was realized by linking the measurement points on the screw heads (Fig. 2) to a potentiostat Solartron Electrochemical Interface 1286 [15]. The 1286 was driven by a Frequency Response Analyzer Solartron SI 1250. Spectrum data were acquired in ASCII format via GPIB by a PC. Experiments were carried out in the frequency range (10 Hz, 65 kHz), in order to assess the electrode behaviour also in low-frequency range (< 100 Hz). The sample number, acquired within logarithmic frequency scale, was 200.

3.2. Results

For current densities lower than some mA/cm^2, the dielectric properties of simple biological tissues could be considered as linear [7]. However, the proposed approach consider non homogeneous materials (metallic implant and biological tissue), thus linearity and stability of the system were tested [13]. The limits of this local linearity were verified experimentally by applying different peak-to-peak values of the sine-wave stimulus (10, 50, and 100 mV) at a fixed level of dc polarization equal to 0.0 V to the abovementioned cow bone [13]. The results highlighted a satisfying response up to 100 mV. Hence, the following *in vitro* tests were carried out at 100 mV in order to increase the signal-to-noise ratio.

Variations on prosthesis-bone contact (i.e. on osseointegration level) were emulated by unscrewing and re-screwing the prosthesis consecutively. At the first screwing of the prosthesis, the best level of contact between bone and prosthesis is reached, by emulating the best osseointegration level. Then, the prosthesis was unscrewed and re-screwed for 3 consecutive times, in order to reduce the quality of the contact between bone and prosthesis progressively. The resulting Bode modulus diagram in the target frequency range (100 Hz, 1 kHz) [13] for the first screwing (1 in Fig. 3), and the successive 3 cycles of unscrewing/re-screwing (2, 3, and 4) are shown in Fig. 3. The diagram shows significant differences between the four different measurements. In particular, modulus impedance grows as increase the number of screws/unscrews. A direct relation between the wellness of the contact implant/bone and the impedance measured can be highlighted.

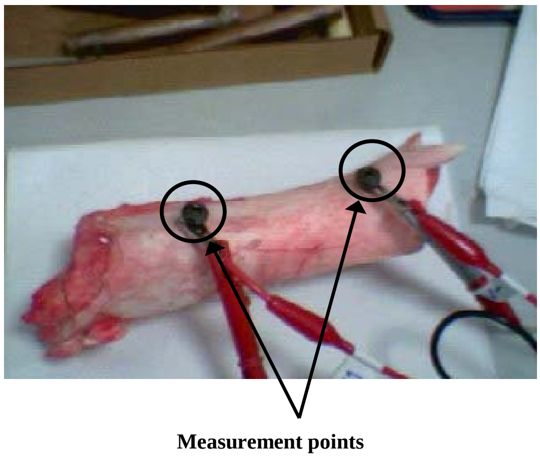

Fig. 2. Cow femur bone and measurement points that considers A+V+ and A-V- electrodes respectively.

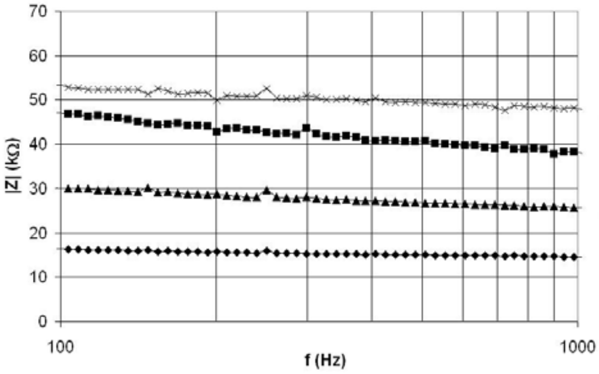

Fig. 3. Bode modulus spectra at varying contact prosthesis-bone (1 (◆) : first screwing, 2 (▲) , 3 (■) , 4 (X): after one, two, three unscrewing/re-screwing cycles).

4. *IN VIVO* EXPERIMENTAL RESULTS

In vivo tests were performed on percutaneous prostheses in order to approach the problem of clinical validation in a simpler way. As a matter of fact, although the osseointegration diagnostic of deep prosthesis can be of relevance, in this phase of the research, the measurement on this kind of prosthesis turns out to be difficult. For such implants, experiments have to be performed with electrodes positioned away of the metallic implant and passing through different layer of tissue, (muscle, fat, skin, etc.). This can play a role to be understood better through further physio-pathological considerations.

In the following, (i) the *measurement setup* and (ii) *preliminary results* of *in vivo* experiments are described.

4.1. Measurement setup

A cochlear implant BAHA ® from Cochlear ™ was selected. It is an osseointegrated bone conduction implant system utilizing direct bone conduction [16]. A small titanium implant (fixture) is placed in the skull (mastoid) bone behind the ear, where it bonds with the surrounding tissue through an osseointegration process. After a 3/6 months period, sound processor is attached, and the patient can ear a sound immediately upon fitting.

Two are the advantages of the choice of this implant. The fixture crosses the skin, thus electrode can be fixed to the metallic prosthesis directly, without introducing further tissue layers in the measurement circuit. The metallic part of the prosthesis enters three millimetres into the skull and is integrated in a homogeneous materials.

A suitable PC-based measurement system was developed (Figs.4-5). This allowed both custom hardware and software to be developed easily and the implemented application to be transferred in a dedicate instrument based on microcontrollers or DSP immediately [17]. Moreover, general patient data can be input via keyboard, as well as other monitored parameters eventually required for real-time computations.

The hardware is composed by (Fig.4): (i) a signal conditioning block, interfacing an analog-to-digital conversion board, plug in the laptop in order to acquire and convert analog signals of voltage and current; (ii) an on-board signal generator for stimulating the system under analysis; and (iii) cables and electrodes to apply electric signals on the implant.

The system is based on a battery-powered notebook PC for safety. The digitalization board is a PCMCI ADCard AI-16E-4 (National Instrument™, Austin, Texas) board. The equipment was qualified according to IEC 601 safety requirements. The software was designed in LabVIEW® environment (National Instrument™, Austin, Texas).

The measurement setup (Fig. 6) exploits three electrodes where the current injected through the electrode A+ and the voltage surveyed by the electrode V+ were superposed on the metallic implant. The fixture was connected through a pin clip to A+/V+ electrodes. Impedance was measured between V+ and V- electrodes and A- electrode were employed only to close de current circuit. A- and V- electrodes were connected to two self adhesive electrode (ABR type Silver/silver chloride disposable electrodes with adhesive and conductive gel for neurological application from Spes Medica mod. DENIL 15 x 20 mm), placed downwards along the neck about 6 cm. The distance between them was 1,5 cm. Before application of electrodes the skin was polished with alcohol.

4.2. Preliminary Results

In preliminary *in vivo* measurements, two young children participated to the experiments: (i) M.M. (one implant), male, seven-years old, implant BAHA, depth three mm, implanted seven months before the test; and (ii) D.D. (two implants), female, ten-years old, implant BAHA, depth three mm, implanted nine and eighteen months before the test respectively. From a clinical point

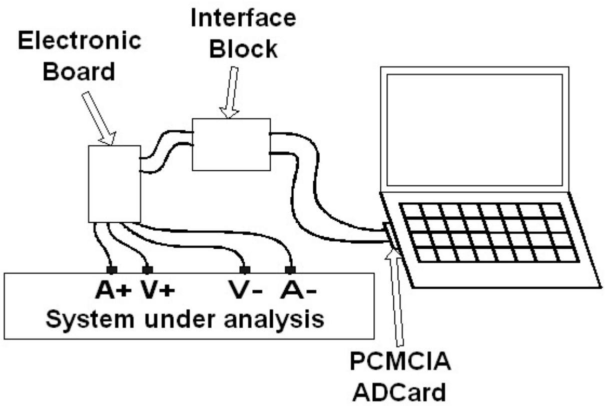

Fig. 4. Block diagram for the measurement setup.

Fig. 5. PC-based device for in vivo measurements.

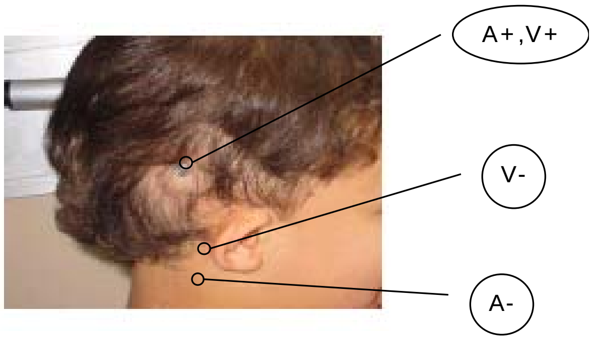

Fig. 6. Three-electrodes placement on a young patient seven years old. Layout of BAHA implant corresponding to the A+/V+ electrodes.

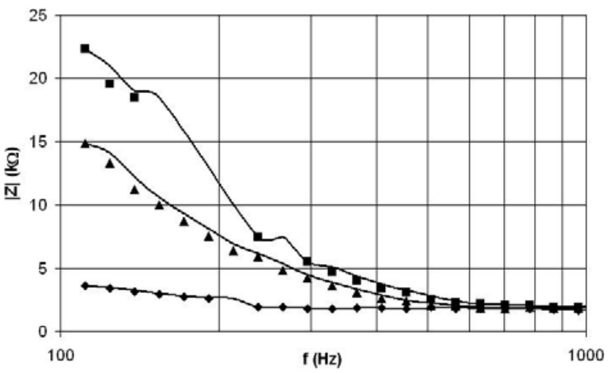

Fig. 7. Comparison of three amplitude spectra of EIS for different in vivo implant:
18 month ■ - 9 month ▲ - 7 month ◆

of view, the patients implants were diagnosed by traditional techniques as working in a perfect way: at prosthesis fixtures electronic parts were applied and patients were able to ear correctly.

Significant information can be gathered from the analysis of the module Bode plots for the considered implants (Fig. 7). Such as for *in vitro* measurements, Bode modulus diagrams show significant differences in impedances for different osseointegration degrees. In particular, the most recent implant shows the lowest impedance modulus. In fact, as time goes by, good implant integration shows a high contact surface and a relative higher impedance measured.

Analogues conclusions were highlighted for *in vitro* tests on cow femur bone, thus *in vivo* preliminary measurements confirm previous *in vitro* results.

6. CONCLUSIONS

An EIS-based approach to the diagnosis of prosthesis osseointegration was tested *in vivo*. The *in vivo* experiments on different osseointegration levels confirm clearly the difference in contact between prosthesis and bone for the prosthesis site enlargement due to successive unscrewing/re-screwing experimented *in vitro*.

In vivo experimental results pointed out positive indications for the full method implementation, by highlighting its capability of detecting the presence of a satisfying connective tissue. As matter of fact, EIS measurement shows a significant trend in the modulus of measured impedance.

However, *in vivo* measurements have to be fit by a suitable model in order to relate electrochemical phenomena to osseointegration quality. Thus, the final goal of describing living systems by ideal electrical circuits is still a difficult problem to be investigated deeply in further research.

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