EFFICIENCY OF THE LES IMPLANTABLE STIMULATOR IN ANIMAL TESTS

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Abstract. *Gastroesophageal reflux disease in recent years is gaining clinical and social significance. One of the new, promising treatment methods is the modulation of the tone of the lower esophageal sphincter using an implantable electrical stimulator. Author has developed and fabricated a prototype of a miniature electrostimulator, rechargeable wireless and with Bluetooth BLE control by Android smartphone. The effectiveness of the manufactured prototype was demonstrated during tests on laboratory animals (pigs).*

Key words: *GERD, midfield wireless implant powering, Bluetooth BLE.*

Introduction

Gastroesophageal reflux disease, the regurgitation of gastroduodenal contents into the esophagus, is a common chronic disease38. The strategic objectives of long-term treatment are prevention of erosive damage to the esophageal mucosa and its progression, as well prevention of severe complications, like Barrett's esophagus and adenocarcinoma23. One of the new, promising treatment methods is the modulation of the tone of the lower esophageal sphincter using an implantable electrical stimulator4. Because of its relatively large size, the pulse generator itself is implanted subcutaneously into the abdominal wall and connected to electrodes attached to the esophagus during the laparoscopic procedure. Wireless powered implantable stimulators could receive energy from an electric and / or magnetic field and may be significantly smaller sized, resulting improves quality, safety and ease of use1.

Object

The object of the clinical animal trials is an experimental prototype of a programmable micro-stimulator of the lower esophageal sphincter with wireless powering17. This prototype was manufactured within the framework of project No. 15.817.04.19A "Electrostimulation of the inferior esophageal sphincter with a wireless chargeable implantable micro-stimulator on patients with gastro-oesophageal reflux disease"5**Ошибка! Источник ссылки не найден.**67.

Scope

Evaluation of the clinical efficacy of various operating modes of the prototype during trials on laboratory animals.

Trials location

Trials were conducted on 15.10.2018 in *Centrul de chirurgie experimentală ”Pius Brânzeu”, P-ţa Eftimie Murgu Nr. 2, 300041 Timisoara, Romania*, equipped with a proper technical experimental base and trained personnel for surgical operations on laboratory animals.

Testing equipment and measuring instruments

Digital scope meter Siglent SHS810, tailor made test bench “Implant activity checker”, tailor made test bench “High resolution LES pressure manometry analyzer (HiLESPMA)”, PC (notebook).

Test conditions

Testing the clinical effectiveness of an implantable prototype was performed during surgery procedure with fixation of electrodes on the esophagus of a laboratory animal (pig), with subsequent registration of implant activity with test equipment. After implanting of the prototype, operational access was closed to test performance of wireless communication through animal tissues.

Prototype was programmed to perform 5 different modes of operation:

1. stimulation mode #1 (pulse width 220 μs, frequency 20 Hz, duration 10 sec)
2. stimulation mode #2 (pulse width 100 μs, frequency 10 Hz, duration 10 sec)
3. stimulation mode #3 (impulse width 300 μs, frequency 40 Hz, duration 10 sec)
4. stimulation mode #4 (pulse width 220 μs, frequency 20 Hz, duration 60 sec)
5. stimulation mode #5 (pulse width 375 ms, 6 imp / min, duration 60 sec)

Commands and telemetry data of the installed device (communication signal power, temperature, device version) was received via Bluetooth BLE radio communication using custom made mobile application installed on an Android-based smartphone (Samsung Galaxy J5).

Implant activity was registered with three different methods:

1. Comparative temperature measurements with esophageal probe vs internal prototype sensor;

2. Indirect electrical activity measurement with scope meter;
3. Modulation of esophageal sphincter pressure using Sengstaken-Blackmore catheter.

To evaluate the electrical activity and measure esophageal temperature was manufactured custom made catheter probe with 3 electrical leads and NTC thermocouple sensor, connected to test bench with digital thermometer and 3 leads test pins.

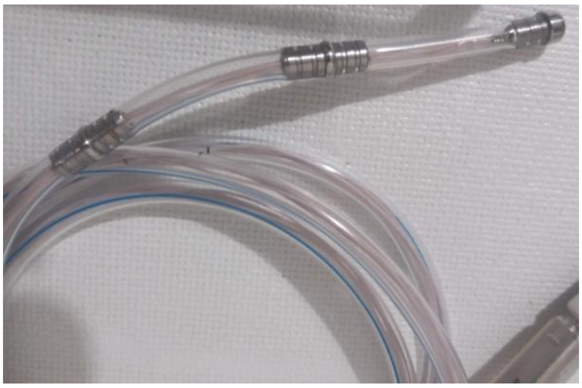

Fig. 1. Probe for evaluation of electrical activity and temperature.

During trials catheter probe was installed by its sensitive end in the esophagus of a laboratory animal in the projection of implanted prototype electrodes. At the other end, the probe connected to the "Implant activity checker" test bench with an oscilloscope connected to evaluate the output electrical activity of the prototype and to compare the probe temperature data with the temperature transmitted by the prototype, measured by high resolution digital temperature sensor.

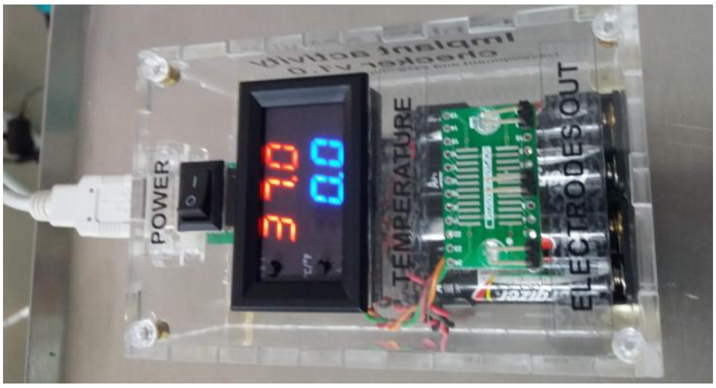

Fig. 2. "Implant activity checker" test bench with running temperature test.

During the tests, various operating modes of the prototype were sequentially launched from smartphone with simultaneous recording of electrical signals using an Siglent SHS810 oscilloscope.

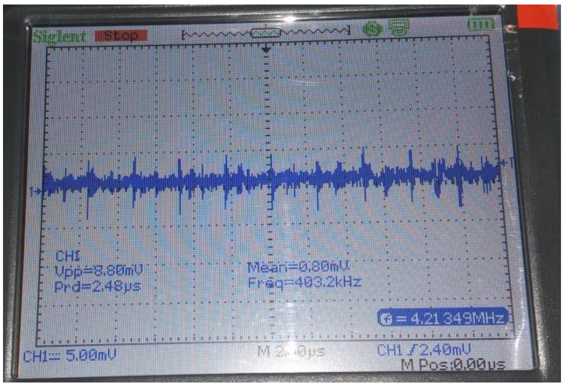

Fig. 3. "Implant activity checker" test bench with running electrical activity test.

To explore the effectiveness of modulating the tone of the lower esophageal sphincter (PS), a standard Sengstaken-Blackmore three-lumen esophageal obturating catheter was used, connected to the HiLESPMA (High Resolution LES Pressure Manometry Analyzer) custom test bench with data transfer to PC (laptop) with running Software (Honeywell SEK002 Sensor Evaluation Kit v4.0.0.5).

Fig. 4. “High Resolution LES Pressure Manometry Analyzer” test bench test.

Esophageal Sengstaken-Blackmore catheter was installed according to the standard technique with the location of the esophageal balloon in the projection of the lower esophageal sphincter.

The esophageal balloon of catheter was pre-inflated with a HiLESPMA’s microcompressor to a pressure about 50 mmHg by a dial gauge, after that were started electro stimulation of implanted prototype, resulting modulation of the lower esophageal sphincter (LES). Different pulse length, frequency and current values (2, 4 and 6 mA) were tried. LES tone changes were observed by moving of pressure dial gauge and registered with high resolution pressure sensor, connected to

PC with running data recording and analyzing software.

Trials results. The test results are shown in table 1.

Table 1.

Parameters	Compliance criteria	Tests results
Electrical activity	Registration of pulses with a width corresponding to the width of the mode of stimulation pulses	successful registration of electrical pulses of a given width and amplitude
LES tonus modulation	Increasing the LES tone over background fluctuations	* LES tone clearly increased depending on the mode of stimulation
Telemetry	Establishing communication with the module, obtaining telemetry data (signal power, temperature, stimulation current, etc.)	Successful establishment of communication with the prototype - signal power up to -81 dB. Acquisition of stimulation current data (2, 4 or 6 mA), temperature values (difference with probe temperature ± 0.5 ° C)

* see photo of the modulation of the LES below.

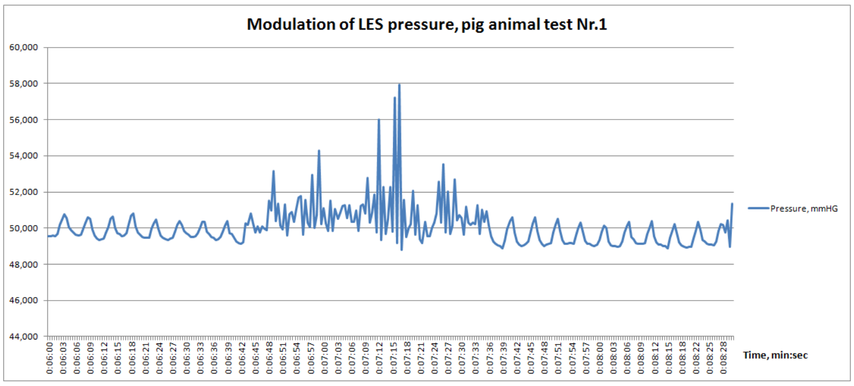

Fig. 4. LES pressure modulation during work of prototype.

During the modulation of the LES tone test, a positive increase up to +8.78 mmHG was recorded above the background fluctuations caused by respiration.

At the same time, the normal pressure of the lower esophageal sphincter in a healthy person is about 20 mmHG, while pathological - less than 10 mmHG.

It should be noted that the most pronounced results were obtained for 6 mA stimulation current. Receiving similar effect from weaker currents like 1-2 mA should require modification of the type of electrode contact with muscle tissue from a single point to a diffuse contact (for example, circular or multi-point).

To estimate the bioimpedance, the output pulse of working mode #5 was recorded with a direct connection of the oscilloscope to the implanted electrodes. A pulse amplitude of 1.6 volts was recorded, which, at programmed pulse current of 6 milliamps, is equivalent to electrodes bioimpedance of 266.7 Ohms.

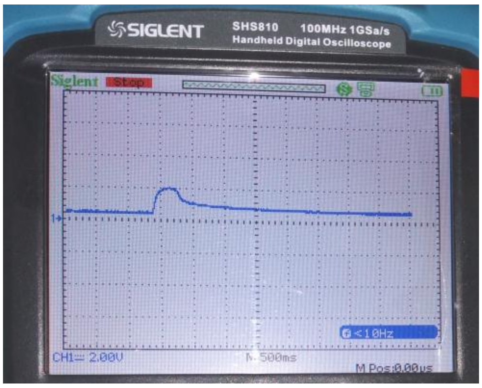

Fig. 5. Recorded electrical activity of prototype, working mode #5.

Conclusion

The manufactured prototype successfully demonstrated the possibility of modulating the tone of the lower esophageal sphincter. The most effective was the operation mode #5 with a stimulation current of 6 mA. Additional modification of the Bluetooth transceiver antenna is necessary to compensate shielding effect of biological tissues. For a more detailed estimation of the effectiveness of various LES electrostimulation modes, additional studies are required.

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