Dental Implant With Contact Nano-Sensors for the Treatment of Xerostomia

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***Abstract*— Salivation is a biologically controlled process that self-regulates and has a crucial purpose in digestion, taste, hygiene and comfort in humans. However, this process can become disrupted, temporary or permanently, leading to a condition called xerostomia. Previous research regarding xerostomia successfully utilized electro-stimulation of the nerves in the oral cavity to treat the symptoms and manage the discomfort created by the condition. This paper describes a revolutionary way of treating xerostomia, by using a permanent micro-electronic implant which can measure and stimulate the salivary secretion in the oral cavity.**

Keywords—dental implant; embedded systems; low-power processing; bluetooth low-energy, salivary stimulation

I. INTRODUCTION

This paper will detail hardware and software requirements for an embedded device designed for the treatment and amelioration of xerostomia symptoms.

Salivation is a very important process that helps the body in digestion, hygiene, as well as taste and comfort. Compounds in the saliva begin the digestion process by starting to break down starch and fat [1]. Water soluble chemicals, like sugars and salts, are spread through the mouth until they reach the taste buds [3]. Saliva helps the act of chewing by lubricating the tongue and teeth and forms the bolus (the mass of food chewed and mixed with saliva), also having a key role in the act of swallowing as it lubricates the throat. Continuous salivation improves hygiene by maintaining a relatively stable level of acidity and reducing the number of bacteria. High levels of acidity are correlated with rapid tooth decay, cavities and halitosis. Salivary function varies based on physical aspects, such as time of day, and the act of chewing, and based on psychological aspects, such as stress, or thinking about food [4].

Xerostomia is a condition characterized by dryness of the mouth estimated to affect between one-fifth and one-third of the adult population, and can be triggered by numerous reasons: old age [5], medication (e.g. beta-blockers are known to cause a decrease of the salivary function) radiation exposure (patients with multiple neck and throat x-rays have been known to have the salivary functions permanently disrupted), Sjögren's syndrome, even cerebrovascular accidents.

Currently there exist some temporary solutions (e.g. drinking water often, or using artificial saliva [2] created in the medical/pharmaceutical industry), but there is currently no long-term solution. Research suggests that electrical stimulation of the buccal nerve and/or the lingual nerve can increase salivation and aid in reducing the discomfort and the medical problems associated with the condition [6] [7]. Our proposed intra-oral device will be able to offer long-term relief to patients, increasing their comfort and health and therefore their quality of life.

The device uses Bluetooth Low Energy for communication to a nearby Android device running our reference application. The application is designed to read the values measured by the sensors, and configure the device to produce different stimulation signals. The measurements are charted for immediate confirmation of stimulation and are also stored on the device for future data aggregation and analysis.

This paper will cover the following subjects:

- Sensor Electrical Specification
- Energy Requirements
- Physical Limitations
- Android Reference Implementation
- Stimulation Signal Parameters
- Prototype Design
- Clinical Trial

II. STATE OF THE ART

The concept of applying electrical stimulation to nerves in order to trigger a response in test subjects has been applied before and, with recent advances in micro-controller technology, can be controlled with a high degree of precision even from a small SOC (system-on-chip).

A. Electro-stimulation of nerves and signal parameters

Electro-stimulation of the nerves is a technique that can be used to trigger muscle contraction and reflexes. However, special care must be taken to trigger only the nerves that increase salivary production and not to bring any discomfort (pain, muscle twitches, etc.) while requiring a minimum amount of energy to be expended. Previous studies provided a window into previous signals used to stimulate nerves, so we could derive some insight regarding voltage and current limitations, stimulation duration, and other signal parameters.

One of the earliest white papers we located refers to a study that took place in 1986 regarding patients suffering from spinal injuries [8]. The study was attempting to provide patients with means to circumvent the spinal injury and achieve erection by stimulation of nerves. The paper describes the hardware configuration of the machine used in the clinical trials, and what ranges of signal parameters it can achieve. This study's highlights were the estimations of the required voltage and current tolerance of the human body. Using this information as a basis we can achieve nerve stimulation while not bringing any harm to the patients. The paper suggests that "frequencies between 20 Hz and 25 Hz proved to be most efficient" and a "limit for safe electrical stimulation of tissue" of "0.37mA/mm2". During the clinical trial we noticed that lower frequencies were just as good at stimulation, however, the final device retains the ability to have a configurable signal frequency, along with other configurable parameters.

Neuroelectrostimulation in treatment of hyposalivation and xerostomia in Sjögren's syndrome: a salivary pacemaker [9] aggregates data from multiple papers and clinical trials that all attempt to stimulate neurons in order to trigger salivary response. This paper suggests long stimulation times, with a minimum of 1 minute and a maximum of 10 minutes, multiple times through the day. The data is correlated with effectiveness of each treatment protocol. This paper also describes which nerves should be stimulated, namely the buccal and the lingual nerve.

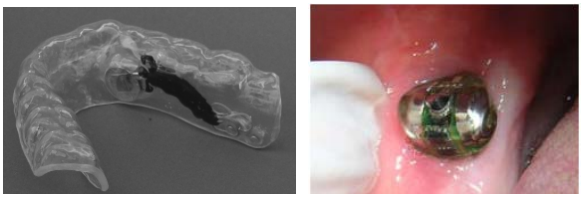

Fig. 1. Example of Saliwell device, detachable model(right) and implant(left)

B. *Saliwell devices*

The device is located on the right side in Fig. 1 and, as we can see through the transparent mold it contains a micro-controller, the stimulation electrodes and the battery that powers the device. Although not explicitly visible, the device also uses an IR sensor for receiving commands. Compared to our device, this device requires a large, inconvenient mold and due to the level of technology at that time, the micro-controller and the electrodes are quite large.

This device improves the design of Saliwell's GenNarino mold presented in Fig. 1 by greatly reducing the footprint to the size of a molar and permanently implanting it. The functionality is otherwise similar, without data collection and with IR communication, aspects that our solution improves upon.

C. *Our Improvements*

Our implementation's strengths compared to these current devices are the wireless communication and reduced footprint which enable us to seamlessly integrate within a person's life and will not inconvenience him/her in any way. Our solution is designed to be minimal, in both size and time required to adapt. Also, our solution allows for permanent monitoring of saliva production in order to allow for auto-triggering when the situation requires. Due to the fact we do not use a line of sight protocol, like infrared, and instead we use a wireless communication protocol, we do not need to inconvenience the user whenever we need to communicate with the device. In addition to the device presented at [7], our implementation is not limited by IR control, which is cumbersome to enable/disable, but instead uses wireless communication. This allows us to receive the data the device is monitoring, track progress across the day, and transmit alerts regarding the device state (for example, low battery levels will prompt the patient to schedule a consultation with the M.D. in order to change the batteries). Also, as we use Android phones for the device control, which are widely available, the costs for the development and distribution should be reduced. To increase security, there will be two versions of the control application, one for the medical professionals, which will have full access to all of the configuration options, and a limited functionality version for the end user, which the patient can use for notifications(e.g. low battery), real time tracking, device disable in case of an emergency, etc.

Fig. 2. Sensors' electrical description. The pH sensor(left) and the humidity sensor(right)

III. Implementation

This section describes the hardware requirements and our prototype's design. It is important to mention that as this device is meant for a dental implant, the real difficulty does not lie in merely designing the board and the sensor connections, but in creating a design that meets all requirements with a minimum physical footprint.

A. *Sensors' Electrical Specification*

One of the differentiating features of our implementation is the ability to monitor and report the humidity and acidity of the oral cavity. Monitoring the patient is done using two sensors that are specially calibrated for the conditions of the oral cavity. Both sensors can provide an analog reading that is correspondent to the pH level and the humidity level, respectively.

The humidity sensor depicted in Fig. 2 acts like a resistor with a variable value, and will be connected to the microcontroller's ADC as part of a resistive divider. The value of the resistance from the humidity sensor can be easily extracted using the formula:

$$SensorValue = \frac{V_{CC}}{V_{ADC}} \times R1 - R1$$

By cross-checking the resistor value to the sensor datasheet we will be able to determine the humidity value.

The pH sensor acts like a DC voltage source and will output 50-350mV based on the current value of the salivary

pH. This is also connected to the microcontrollers ADC's, but this time there is no need for additional components. By cross-checking the voltage value to the sensor datasheet we will be able to determine the pH value.

B. Energy Requirements

The project requires a microcontroller with reduced power consumption that provides IO connectivity (digital and analog) and also provides some means of communication to the exterior.

NRF51822 is described by its producers, Nordic Semiconductor, as a Multiprotocol Bluetooth low energy System on Chip Processor. This microcontroller also presents another advantage for our design, as it comes in package variants with a footprint as small as 3.50 x 3.33 mm. The CPU of the microcontroller has a current consumption of 4.1mA, while the transceiver consumes 10.5mA with a transmit power of 0dBm.

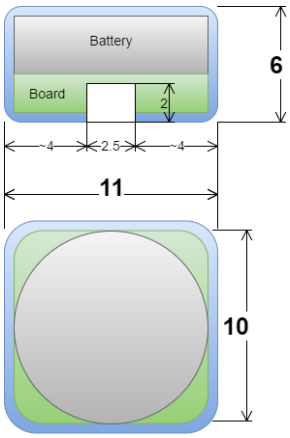

Fig. 3. Physical design dimensions and limitations

In order to reduce the amount of power consumed, and therefore energy consumed, as much as possible, the microcontroller will spend most of its time in a sleep state, where it draws only 600nA, and will schedule internal wakeups every couple of seconds, in order to read the values from the sensors. The values of the parameters measured by the sensors do not exhibit a fast variation without the intervention of the patient (for example: drinking liquids will greatly increase the humidity level, drinking carbonated drinks will substantially increase the acidity, etc.). This fact, coupled with the knowledge that we do not require precise measurements lead to a very long operational lifetime of the device. When the internal memory is full or on request the implant can begin transferring the data to an external collection device, which was implemented on an Android tablet. This episode is very energy consuming and we need to reduce the amount of time spent here in order to preserve our promise for a large battery life. We can achieve this by sending out the data in bursts, and refusing to send data on connections with poor signal.

We can compute an estimated average current consumption for the sensing task by considering that two parameters are continuously measured by the device every 2 seconds and relayed to the Android application ever so often. The parameter values are sampled using the internal ADC convertor which has a current consumption of 0.26mA. The duration of one conversion is 20µs. The two conversions will thus take 40µs (or 0.002% of the time) and consume 4.36mA. The BLE transmission speed is 1Mbps, and if we ignore the protocol overhead in relation to the useful data (more than one value is transmitted in one message) the two conversions will take 16µs (or 0.0008% of the time) to be transmitted and consume 14.6mA. The remaining 99.9972% of the time the device will be in sleep mode and consume 600nA. The estimated average consumption over a longer period of time for sensing will thus be ~800nA.

C. Physical Limitations

The most challenging aspect of designing this embedded device is how we can add all functionality in a heavily restricted physical space.

Current design iteration requires all components to be placed inside a toroid estimated at 6x13mm wide, with part of the center being consumed by a screw hole, as this is the standard size for tooth implants used by the dental industry. All of the components were selected so that they respect these size requirements. The battery is slightly smaller than 10x3mm, and the microcontroller form factor can go as low as 3.5x3.33 mm. Another requirement we have is that the Bluetooth Low Energy antenna does not get isolated in a Faraday cage, thus limiting our case materials to ceramic constructs, and the antenna position pointing away from the point of contact with the bone. We required a way to estimate the dimensions of the project.

The current design uses a CR927 or a CR1025 battery in the largest continuous section available and places the board in the toroidal space below it. Note that the board on which the microcontroller and associated electrical components reside has a hole in the center where the screw can be placed.

The high level hardware design is described in Fig. 4.

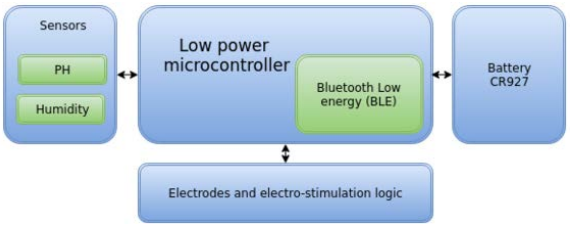

Fig. 4. Electrical Design

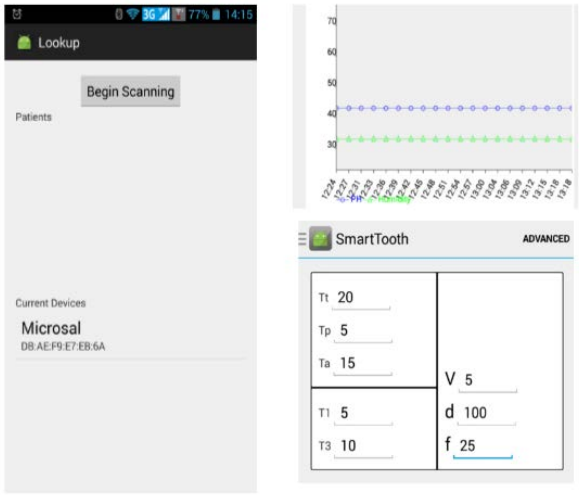

Fig. 5. Application screenshots

D. Android reference Implementation

The Android reference implementation is designed to have 2 operating modes: the patient mode, where the patient can track results collected from the sensors (pH, humidity, battery), and the medical specialist mode, where a MD can modify the parameters of the waveform used in electro-stimulation. Because the latter requires both general medical knowledge and experience in the domain, and to limit accidents it is not available for the patient.

In the patient mode, the app allows only real-time data collection and displaying, in order to determine the stimulation is having an objective effect, other than the subjective comfort the patient might be experiencing.

In the medical specialist mode, the app allows connecting to multiple devices, for each device viewing real-time measurements and allowing access to the configuration of specific waveform parameters for each patient.

The Android reference implementation was designed to be handled by medical professional only and is designed to have full control of the device. The application scans for nearby devices and, if they respect the MicroSal specification (regarding name, MAC address, and services and characteristics provided), will add them to the graphical interface. From there, the user can either start reading the measurements from the sensors or modify parameters of the stimulation signal (Fig. 5).

E. Stimulation Signal Parameters

As described the state of the art section, the stimulation should continue through the day, in the form of pulses We have designed our initial prototype to take this matter into consideration. Our test device is designed and programmed to emulate a signal composed of multiple groups of pulses. The parameters for the stimulation signal are detailed below, in order of their respective importance, and each with its limitations:

- V. Voltage, measured from cathode to anode or from anode to cathode
- TT. The length (in ms) of the total duration of the stimulation signal. TT must be a multiple of TA + TP, and controls the number of pulse/pause cycles.
- TP. The length (in ms) of the pause front between a group of pulses (TA). Must be a multiple of 30 ms.
- TA. The length (in ms) of the group of pulses. TA must be a multiple of sum(T1-T4), and controls the number of positive/negative stimulation. A correct configuration will have TA a multiple of 32, with TA different from 0.

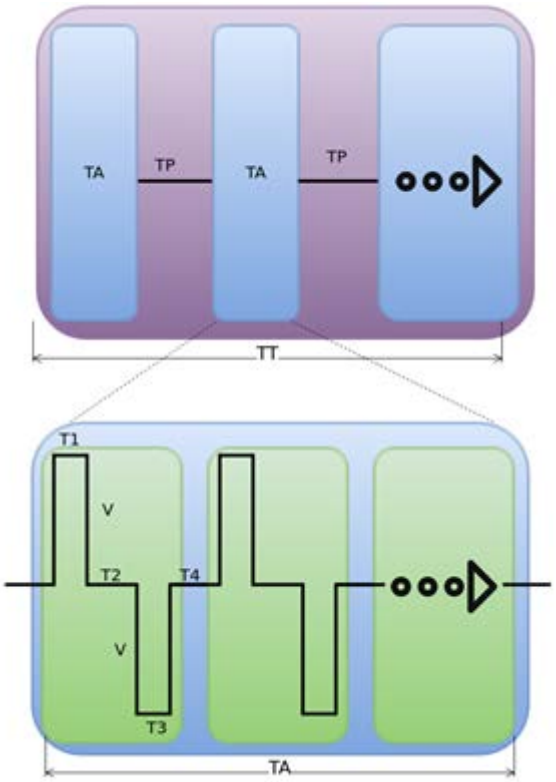

Fig. 6. Signal descripton

- T1. The length (in ms) of the positive front. Must be a multiple of 32ms. A correct configuration will not use this parameter with a value equal to 0.
- T2. The length (in ms) of the pause after the positive front. Must be a multiple of 32 ms, but can be 0.
- T3. The length (in ms) of the negative front. Must be a multiple of 32 ms, but can be 0. If T3 is equal to 0, the device will only stimulate in one direction
- T4. The length (in ms) of the pause after the negative front. Must be a multiple of 32ms. If T3 is equal to 0, T4 should also be equal to 0, otherwise it should be different than 0.

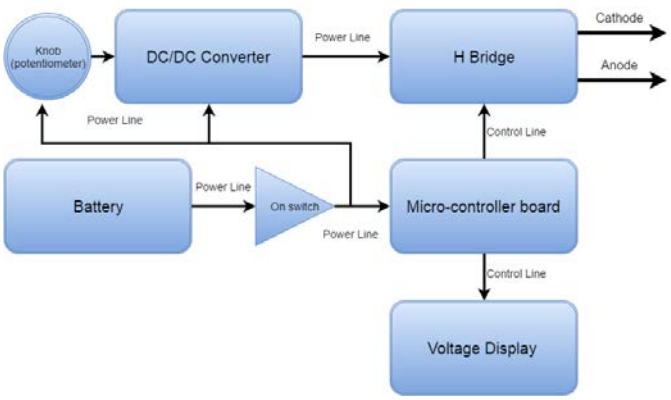

Fig. 7. Electrical Design of the prototype

Due to the large number of parameters, and the fact that we wanted to test variable voltage (including "negative" voltage), the prototype design schematic is considerably more complex than the final version. Due to the strict space and power consumption requirements, designing a board that could generate all these signal parameters would have proven to be a difficult task. Fortunately, after testing (detailed in Section 5.2), we have determined that only some of the parameters are required. The others remain available for future tests, but will, of course, be removed from the final prototype.

F. Prototype Design

Before the final, minimized version of the device could be built, we first needed to determine the stimulation signal parameters that will always produce a salivary reaction.

Therefore, an experimental device was built, that allows setting all stimulation signal parameters, along with the ability to set the voltage of the signal. Although the final device will have a fixed voltage, we wanted to be thorough and investigate all possible variations (Fig. 8).

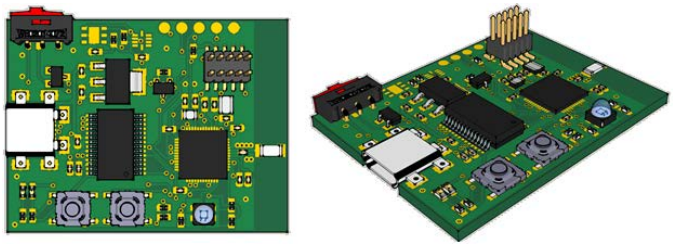

Fig. 8. Test device circuit board. This macro-prototype device was used for determining the optimum simulation waveforms, interfacing sensors and testing Bluetooth communication.

The test device diagram is summarized in Fig. 7. It runs on two simple AA batteries, which power all of the electronics. The on/off switch was added in order to preserve battery life between tests. Voltage configuration is done "manually", by turning a potentiometer. This controls the Voltage Amplifier and the whole system also feeds the micro-controller board sensors which detect the voltage and display it across the LCD. The final signal waveform is controlled by the means of an H-bridge, a device that allows a controller to send voltage across the anode/cathode pair both in a positive front and a negative front. This design was required by our testing protocol while we tried to discover which signal best suited our needs to allow stimulation and be extremely power efficient.

The results from building the functional prototype are summarized in the next section. They validated the viability of the design and allowed us to proceed to the next step, of miniaturizing the components and integrating them into a single printed circuit board, which can fit inside the implant case, as detailed in Fig. 9.

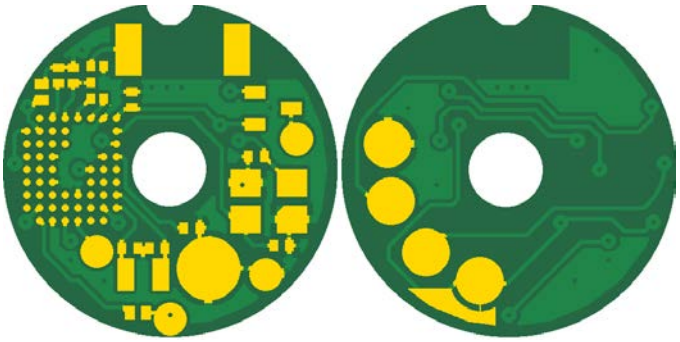

Fig. 9. Printed circuit board design (top-bottom) of the final electronic module for the dental implant.

G. Clinical Trial

After finishing the implementation of the test device, we had a controlled clinical study on a patient suffering from xerostomia. We will present and interpret the results in this section.

TABLE I. EXPERIMENTAL DATA

	Pulse length	**Frequency**	**Voltage**	**Voltage swing**
1	4 ms	0.1 Hz	3.25 V	positive
2	4 ms	1 Hz	3 V	positive
3	10 ms	1 Hz	3 V	positive
4	10 ms	2 Hz	3 V	positive
5	4 ms	4 Hz	3 V	positive
6	4 ms	8 Hz	3 V	positive
7	10 ms	8 Hz	3.25 V	positive
8	10 ms	8 Hz	5 V	positive
9	10 ms	8 Hz	5 V	positive & negative

The experimental results are detailed in Table 1. Each experiment lasted one minute, and the 9th experiment, the one that had both the positive and negative voltage swing had on both the positive and the negative front the same parameters(10ms positive and 10ms negative pulse length and +5V and -5V). The electrodes were placed on each side of the gums, behind the wisdom tooth, in an attempt to stimulate the buccal nerve and the lingual nerve, as in [7]. The stimulation was successful (subjective, with the medical professional as a judge) in almost all cases, other than the first one. Preliminary data suggests that any of the configuration tested with a frequency higher or equal to 1Hz is enough to trigger salivary response. This is of great help in the iterative design of the prototypes, because we now know, with experimental data to

back up our claim, that there is no need for the advanced H-bridge design with a voltage buck converter. Therefore we can use a simpler hardware design, thus reducing the risks and the challenge of the miniaturization and debugging process.

IV. Conclusions

In this paper we have presented the high level design of an innovative implantable device for the treatment of patients with xerostomia. We have detailed the inner workings of our prototype and presented results from our clinical trial. We believe our device has better ease of use and longer battery life as strong advantages over previous devices and previous research

Preliminary clinical trials were encouraging, confirming many of our device decisions while also helping us to find new ways to improve and simplify our device. Stimulation produced increased salivary flow compared to the lack of stimulation. We also noticed that the effects did not linger, as soon the stimulation stopped, the salivary response stopped as well. This confirmed our decision of using the device as a dental implant with immediate control from nearby Bluetooth devices and the need of using sensors to detect and limit salivary stimulation. Clinical trials also helped us determine a simplified but effective waveform of the simulation signal that enabled us to achieve our goal of extended battery life.

V. Acknowledgements

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