Batteryless implantable dual-sensor capsule for esophageal reflux monitoring

Hung Cao, PhD,1 Smitha Rao, PhD,2 Shou-jiang Tang, MD,3 Harry F. Tibbals, PhD,4 Stuart Spechler, MD,5 J.-C. Chiao, PhD1,5

Arlington, Dallas, Texas; Jackson, Mississippi, USA

Background: Chronic GERD affects approximately 15% of adults in the United States and is one of the most prevalent clinical conditions involving the GI tract. The commercial tools for monitoring GERD include multichannel intraluminal impedance (MII) probes and pH-sensing capsules. However, MII probes cause discomfort, which alters patients’ regular activities, whereas the pH-sensing capsule lacks the ability to detect weak or nonacid episodes, misses reflux episodes with similar pH values, and has a limited sampling rate and battery life.

Objective: To develop and test an implantable batteryless dual-sensor capsule that can be used to diagnose and monitor GERD.

Design: The implanted capsule is wirelessly powered by an external device. Simulated reflux episodes were created in 3 live porcine models. Impedance and pH data were continuously measured and recorded.

Intervention: The implant capsule was placed in the esophagus along with a commercial pH-sensing capsule for comparison.

Main Outcome Measurements: Precise impedance and pH readouts were obtained and compared with those from a commercial pH-sensing capsule.

Results: The wireless energy supplied by the external unit was strong enough to power the implant. The pH sensor accurately measured pH levels and the impedance sensor precisely located the reflux episodes.

Limitation: Simulated reflux events in a pig model.

Conclusion: Our wireless sensors are reliable in operation and provide accurate assessment of simulated reflux episodes. The entire device can potentially be used to diagnose and monitor GERD.
the device has several practical limitations. The battery-based operation limits the monitoring time to 48 hours; it has a maximum sampling frequency of every 6 seconds and a transmission every 12 seconds. This therefore limits the capability of long-term monitoring or recognizing fast/short episodes of reflux. Furthermore, the device is incapable of sensing weak or nonacid reflux episodes.9-12 Recently, we developed a miniature batteryless wireless dual-sensor capsule prototype for monitoring reflux episodes. The device can be endoscopically attached to the esophagus by a method similar to that used with Bravo. It can sense and transmit wirelessly both impedance and pH values with a much higher sampling rate. Our sensing system is called a batteryless endoluminal sensing telemeter (BEST) for its distinctive features in operation. In this study, we tested BEST in live porcine models to demonstrate its feasibility and robustness for diagnosing GERD.

MATERIALS AND METHODS

Animals

The experimental study protocol was approved by the University of Texas Southwestern Medical Center Institutional Animal Care and Use Committee. Experiments were conducted with 3 live female pigs in the animal laboratory at the Minimally Invasive Surgical Center, University of Texas Southwestern. The average weight of the pigs was 47.62 kg, and the average chest perimeter was 78.74 cm, measured at the level of the midsternum. The pigs were under general anesthesia during endoscopy. Electrocardiography was performed, with a regular heart rate of approximately 96 beats per minute. The oxygen saturation was obtained on the ear with readings of 96% to 99%, and blood pressure was measured noninvasively with readings of 66/24 mm Hg.

BEST capsule

Our BEST capsule prototype measures $0.4 \times 0.8 \times 3.8$ cm$^3$ and weighs 3 g (Fig. 1). It contains circuits to harvest electromagnetic energy sent from an external unit to operate 1 pH and 1 impedance sensor and to transduce signals back to the external unit. The impedance sensor is an interdigitated finger structure with thin gold film deposited on a 125-μm thick polyimide film. It has 10 pairs of fingers with a finger length of 2 mm, a finger width of 40 μm, and a separation gap of 60 μm (Fig. 1A). This specific structure forms a sensing capacitor with its value varying by different aqueous or solid materials presented on the surface. Our pH sensor, with different materials from the commercially available implantable or wired MII probe sensors, contains an iridium oxide working electrode and a silver/silver chloride reference electrode, both 1 × 1 mm$^2$ in size (Fig. 1B). Relaxation oscillators convert the impedance and pH values to frequencies that are loaded into the carrier signal back to the external reader. The implant was encapsulated with biocompatible polydimethylsiloxane to avoid electrical short-circuit issues. Sensors were calibrated before the animal experiments.

Power transfer and data communication through body tissue are implemented with low-power magnetic coupling between resonant circuits at 1.3 MHz (Fig. 2). This frequency was chosen to reduce the absorption by tissue, thus maximizing the power transfer efficiency as well as minimizing the side effects.5,6 The external transceiver weighed 70 g and was designed sufficiently small to be embedded in a belt to accommodate an antenna size of 12 × 12 cm$^2$. The pH and impedance data in encoded frequencies were recorded continuously to a digital memory card.

Experimental setup

A gastrostomy was created through the anterior gastric wall for gastric fluid drainage (Fig. 3). Our BEST and the Bravo pH capsules (Given Imaging, Yoqneam, Israel) were tied together and placed in the distal esophagus approximately 3 cm proximal to the gastroesophageal junction under endoscopic guidance (Fig. 4). A 16F nasogastric (NG) tube was inserted through the mouth and
larynx and into the midesophagus for flushing various solutions mimicking reflux episodes. The intraluminal location of the NG tube was confirmed by endoscopic visualization. The NG tube was secured externally to the skin by forceps. Test solutions with different pH values were flushed through by a syringe pump simulating the refluxes. A surgical tube with continuous suction was placed inside the stomach to remove excess solution. The location of the 2 devices and fluidic activities were monitored by direct endoscopic visualization continuously throughout the experiments. The external BEST reader unit was placed against the skin in the midsternum area. The Bravo reader was placed next to the pig at a distance of 3 cm. The distance between the external BEST reader and the implant was found to be approximately 8 cm as measured after the experiments.

**Experimental procedures**

Several solutions including acid with pH values of 2, 3, and 5; alkaline with a pH value of 11; saltwater; tap water with a pH value of 7; orange juice with and without pulp, labeled as OJ(P) and OJ(W), respectively, with a pH of approximately 4; and deionized water were used as refluxants to test the system performance. Tap water was flushed between test solutions to clean the residues in the esophagus.

In clinical situations, several reflux episodes may occur within a short period of time, which may indicate severe symptoms, especially during sleep. The Bravo device samples the pH value every 6 seconds and could miss some of the reflux events. In the first experiment, to evaluate the quick response feature for sensing impedance and the consequent advantage of a high sampling rate from batteryless operation, the performance of short-episode detection was examined. Simulated episodes with durations of 5 seconds were created by using a pH 3 solution. In the second experiment, each of the aforementioned test solutions was flushed in sequential order, and data were recorded continuously. The same experiments were repeated with 3 pigs, and 5 sets of data were obtained.

**RESULTS**

Figure 5A shows the results with simulated short refluxes by using the pH 3 solution. The baseline frequencies in our dual sensors were obtained during 12 seconds...
at 10.55 kHz and 25.34 kHz for the impedance and pH sensors, respectively. At the 13th, 23rd, and 35th second time points, the pH 3 liquid passed through the esophagus at the device location. Our device responded to every simulated reflux episode immediately with modulated frequencies at 13.94 kHz and 29.05 kHz for impedance and pH sensors, respectively. The frequencies returned to the baseline after each episode, clearly indicating the reflux occurrence. For comparison, the Bravo pH sensor remained at the same reading with a pH value of 3.1 during the whole test period from the 13th to the 45th second. This was expected because the reflux episode time was shorter than the sampling rate. The frequency variations in 3 different episodes were within ±0.1 kHz, which were insignificant compared with the frequency shifts caused by the reflux episodes.

The recorded modulated frequencies from our pH sensor were converted in real time by the software in the reader with the calibration to pH values. Figure 5B shows the comparison of our pH data with those recorded by Bravo for different refluxants. The pH sensor readings had good agreement with pH value differences less than ±0.4 in most of the cases. However, our pH sensor could indicate the alkaline solution with a pH value of 10.8, whereas the Bravo pH sensor indicated out of range.

Figures 5C and 5D show the statistical performance of our system from 5 experiments with 3 pigs. For the pH sensor, we obtained less than 0.33 in standard variations of pH for all solutions except tap water, which has a pH value variation of 0.48. For the impedance sensor, we obtained standard deviations of less than 0.16 kHz among all the tested liquids, except for tap water with standard deviations of 0.37 kHz. The reason for tap water having larger standard deviations was because the tap water was used to clean the residues between acid/alkaline episodes in the esophagus and the residues altered the ion concentrations and pH value of the liquid passing through the electrodes.

DISCUSSION

The dual-sensor system using our impedance and pH sensors can detect both acid and nonacid refluxes continuously in real time. Because the impedance sensor responds to the change in ion concentration immediately (Fig. 5A), it is able to provide the precise numbers and timing of the reflux episodes while the pH sensor detects the pH nature of the refluxant. Nevertheless, only impedance sensing will fail to detect pH levels because a pH 2 solution and saltwater pH 7 may give similar impedance responses (Fig. 5C). The recognition of reflux flow directions is an important issue, and it can be achieved by implementing 2 impedance sensors placed at each end of the device so that a time delay in sensor signals provides the direction of the material passing.

The experiments with data shown in Figure 5A demonstrate the improved capability of our device over that of the Bravo pH meter in detecting short-episode refluxes. This feature ensures almost complete capture of any reflux episodes. Based on a more robust sensing principle, our pH sensor can detect a wider pH range compared with the Bravo sensor. This clearly can be seen in Figure 5B. In most cases, the refluxes are acidic, but nonacid ones do occur and play an important role.13 Covering a wider sensing range of pH values will not only provide additional advantages but also enable a tool to diagnose non-erosive reflux disease.

The batteryless operation feature allows our device to work much longer compared with other devices including the Bravo. It also prevents toxic leakage issues associated with battery-based systems. Even though some experts advocate that a monitoring duration of 48 hours is enough for GERD patients, longer testing time will likely provide a more accurate diagnosis and also help to assess drug efficacy. Human studies are needed to validate our dual-sensor capsule and wireless system. Future devices may incorporate an attachment method similar or equivalent to that used by the Bravo, which was approved by the U.S. Food and Drug Administration.

In conclusion, the BEST dual-sensor capsule prototype is capable and reliable for detecting various reflux episodes. Compared with the commercial pH-sensing capsule, the BEST sensor was shown to be capable of identifying more reflux episodes and pH values. The compact
size allows endoscopic implantation. The batteryless wire-
less powering operation and wireless data transduction
allow higher sampling rates and comfortable long-term
monitoring of GERD and evaluation of drug efficacy. The
future device will likely have more than 2 sensors so that
it can distinguish refluxes and swallowed bolus and detect
accurately the pH nature of the refluxant.

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