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Method and Apparatus for Intra-esophageal Cough Detection

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Abstract— **Gastro-esophageal reflux disease (GERD) is a common cause of chronic cough. However, a low-cost diagnostic tool for linking GERD and cough in a cause and effect relationship is still lacking. In the present study, an intra-esophageal cough detection probe that comprises a miniature white-light interferometric fiber optic pressure sensor is proposed. This innovative catheter provides a custom encapsulation of the pressure sensor which specifically optimizes the sensitivity to pressure responses triggered by cough events. In vitro and in vivo testing results of the initial cough detection probe are presented. Experimental results demonstrated the feasibility of using the proposed catheter for identifying cough episodes. The presented work can be integrated with commercial reflux pH/impedance probes to facilitate simultaneous 24-hour ambulatory monitoring of cough and reflux events, with the ultimate goal of quantifying the temporal correlation between the two types of events.**

I. Introduction

THE latest comprehensive statistics provided by the National Institutes of Health suggest that gastroesophageal reflux (GER) and related symptoms affect approximately 20% of the US population, resulting in over 700,000 annual hospitalizations [1]. GER, characterized by the movement of gastric contents into the esophagus, occurs commonly in healthy individuals, where episodes are mostly asymptomatic. Gastroesophageal reflux disease (GERD) is a disorder resulting from GER events, characterized by the occurrence of problematic symptoms, such as heartburn, discomfort, and chest pain. This usually occurs when the refluxed material remains in contact with the distal esophageal mucosa for prolonged periods of time. Excessive exposure can lead to further consequences, such as esophagitis and esophageal ulceration.

GERD is commonly cited as a significant cause of chronic cough [2]-[5]: In multiple studies, GERD has been documented to be a cause of chronic persistent cough in 38-82% of patients [2]. Irwin *et al.* report that GER can cause cough either by aspiration of gastric contents, or by the stimulation of the distal esophagus due to repetitive or prolonged GER events [3]. It has also been documented that cough may precipitate reflux by stimulating transient lower esophageal sphincter (LES) relaxation [2]. To more effectively diagnose and treat GERD, it is important to quantify the temporal relationship between cough and reflux events [6]. Such real-time continuous correlation has yet to be achieved using a simple, low-cost, automated diagnostic tool.

To fully investigate cough patterns and their correlation with other events, it is important to perform 24-hour ambulatory studies, where the patients continue with their daily activities. Previous studies attempting to determine a temporal correlation between cough and reflux suffer from one of the following: (1) They use manual, patient dependent methods for identifying cough episodes, such as diaries and/or event markers [5], [7], [8]; (2) They do not offer a low-cost integrated solution which can easily be used for 24-ambulatory testing in conjunction with routine GERD testing [5]-[8]; and/or (3) They rely on time-consuming, manual analysis of manometric tracings [6].

More specifically, previous studies that relied on patient-triggered cough identification techniques were prone to user error, both with inaccuracies in indicating the timing of the cough, and with inconsistencies in recording the occurrence of a cough event [5], [7], [8]. The end result may be a misrepresentation or underestimation of cough episodes, as well as poor accuracy with regards to timing of the event.

The methodology was improved in a later study [6], which simultaneously detected both cough and reflux events via a double-intubation consisting of a combined pH/impedance catheter for detecting reflux and a 4-channel solid-state pressure catheter for identifying cough. The identification criterion for detecting cough was the occurrence of simultaneous, short duration, rapid pressure rises across all 4 manometric recording sites. While this study produced more reliable results, it introduced a factor of cost and complexity related to the need of a multi-channel solid-state catheter, which could be problematic for standard clinical use. Moreover, a dedicated cough-detecting sensor was not incorporated in the reported design.

In this paper, we report a pressure-sensing esophageal probe based on white-light interferometry, suitable for the detection of cough events. The single-channel probe could be integrated with existing reflux detection devices to facilitate simultaneous recording of both cough and reflux events, and therefore directly contribute to establishing a reliable temporal correlation between the two.

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II. METHODOLOGY

A. Catheter Design

The proposed esophageal catheter consists of a single white-light interferometric pressure sensor encapsulated in an innovative manner to be utilized as a cough indicator. The basis behind the proposed approach is to maximize the response to vessel pressure at the distal end of the catheter-encapsulated sensor, while minimizing the sensor's response to circumferential contact force, such as the squeezing pressure that occurs during esophageal peristalsis.

The fiber optic pressure sensor (FOP-MIV, FISO Technologies, Quebec, Canada) is based on white-light Fabry-Perot interferometry technology [9]. The sensor tip consists of a Fabry-Perot vacuum cavity terminated with a silicon diaphragm. Pressure applied to the sensor causes the diaphragm to flex, changing the cavity length, and consequently modulating the resonant frequency of the broadband light reflected back into the fiber. Unlike intensity-based modulation techniques, white light interferometry is relatively immune to fiber-bending losses and output fluctuations. The pressure sensor has dimensions of 550 µm by 375 µm. The fiber optic connecting the sensor to the external signal conditioner has an outer diameter of 175 µm. The following specifications have been provided by the manufacturer: relative pressure range of ±300 mmHg; precision of ±1 mmHg; accuracy of 1 mmHg; zero drift of ±1 mmHg/12 hours; zero thermal effect of ±0.5 mmHg/°C; frequency response of 30 kHz; and linearity and hysteresis of 1.5% full-scale output (FSO).

The white-light interferometric pressure sensor is potted at the distal end of the catheter with its sensitive diaphragm facing the catheter tip utilizing silicone adhesive (Fig. 1). The silicone adhesive (MED1-4013, NuSil Silicone Technologies, California, USA), which protects the sensor from dynamic mechanical shocks and acute forces while readily transmitting pressure, is suitable for medical devices implanted in the body for less than 29 days. At its proximal end, the pressure sensor is potted with a rigid epoxy (204-CTH, DYMAX Corporation, Connecticut, USA). The epoxy serves two purposes: (1) Prevents the sensor from moving within the catheter, which could manifest itself as a parasitic pressure response; and (2) Minimizes the detection of pressure from behind the sensor, such as contact forces applied to the catheter sides, resulting in negative pressure readings. The catheter end is sealed only with the silicone adhesive, so pressure can be readily transmitted via the catheter tip. The catheter section enclosing the sensor is more rigid, shielding the sensor from contact forces applied to the catheter sides. The rigidity at the tip prevents curling of the catheter tip inside the esophagus, resulting in erroneous pressure readings. A photograph of the catheter tip is shown in Fig. 2. The catheter material is tecothane medical grade aromatic polyurethane, and is used in commercially available esophageal intraluminal impedance catheters (Sandhill Scientific, CO, USA).

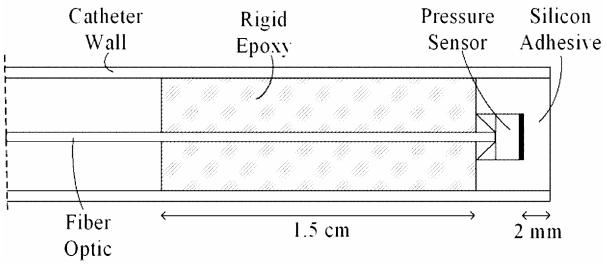

Fig. 1. Detailed diagram of catheter tip, showing encapsulation of fiber-optic pressure sensor.

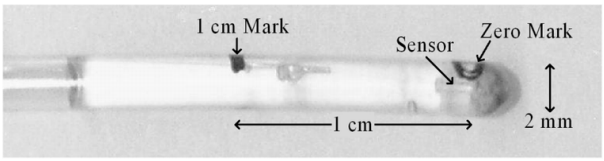

Fig. 2. Photograph of the distal end of the cough detection catheter.

B. Experimental Setup

The esophageal probe interfaces to an optical signal conditioner (PM-250, FISO Technologies, Quebec, Canada), which converts the optical signal to an analog output corresponding to the detected pressure. The signal conditioner performs a cross-correlation between the reflected spectrum with the known transmitted spectrum using an optical cross-correlator, or a Fizeau interferometer. The optical output of the Fizeau interferometer is read with a photodetector array, where the pixel location of maximum intensity corresponds with the cavity length, which in turn, is outputted as an analog signal corresponding to pressure. The white light interferometric interrogation technique is further described in [9]. The analog output is collected at 50 Hz using a data acquisition board (DAQ-AI-16XE-50 A/D, National Instruments, Austin, TX) and a custom-designed National Instruments LabWindows/CVI real-time software application. Block diagram of the system is shown in Fig. 3.

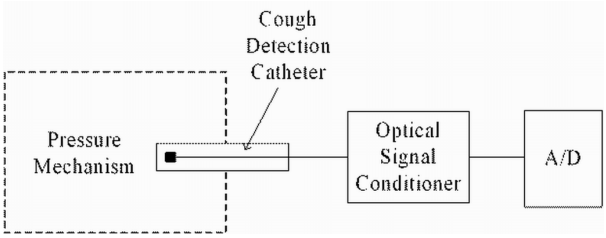

Fig. 3. Schematic diagram of experimental setup. The pressure mechanism is either a pressure chamber (for testing the sensor response to air pressure), or an apparatus for applying weight to the sensor (for testing the sensor response to contact force).

To quantify the performance of the encapsulated fiber optic pressure sensor and to determine its suitability for in vivo testing in the esophagus, a series of in vitro tests was performed over multiple days covering the physiological

pressure and temperature ranges of the intended application. The performance of the cough detection probe was examined when subjected to vessel pressure and contact force. The sensor was evaluated for accuracy, linearity, hysteresis, zero drift, thermal effect, and effect of fiber bending. Three separate trials were performed for each test to determine repeatability, which was defined as the ability to reproduce a given measurement under the same reference pressure and external conditions.

As is defined in [10], [11], the criteria utilized for evaluating the sensor non-linearity, hysteresis, accuracy, drift, thermal effect, and sensitivity were as follows: (1) Accuracy is the difference between the measured pressure and the reference pressure; (2) Nonlinearity is the maximum deviation of a measured data point from the corresponding point in a least-squares straight line approximation; (3) Hysteresis is the maximum deviation between two measurements for the same reference pressure, with one measurement taken as the pressure is being increased, and one taken as the pressure is being decreased; (4) Zero drift is the change in sensor output with zero pressure applied at a constant temperature over a specified period of time; (5) Zero thermal effect is the change in sensor output as the temperature varies at zero pressure; and (6) Sensitivity is the ratio between change in measured pressure over a change in applied pressure.

To test the response of the packaged sensor to air pressure, the distal end of the catheter was placed in a pressure chamber, consisting of a calibration tube with a rubber stopper at one end. The rubber stopper had an adjustable opening. The catheter tip was inserted into the pressure chamber through the hole in the rubber stopper so that the pressure sensor lay inside the pressure chamber. The hole was tightened to provide an air-tight seal around the catheter. A second hole in the stopper accepting a sphygmometer/air pump was employed, so that air could be pumped into the chamber, while the pressure of the chamber was simultaneously monitored. As the pressure was varied in the calibration tube, the response of the sensor was monitored. To test the response of the packaged sensor to contact force, various amounts of weight were applied to the catheter while observing the sensor output. Contact pressure was applied both in radial and axial directions.

Zero thermal effect was evaluated by monitoring the pressure response as the catheter was submerged in water, with measurements taken as the water temperature varied between 23°C and 37°C. Zero drift was evaluated by zeroing the sensor at a reference pressure, and monitoring the sensor output for a period of 60 minutes. The effect of fiber bending was assessed by monitoring the sensor output while subjecting the catheter to bending at an approximate angle of 120 degrees and a radius of 10 cm under constant pressure.

Preliminary in vivo human testing was performed to obtain the sensor response to pressure dynamics in the esophagus, including cough episodes. In vivo testing was performed at the research facilities of Sandhill Scientific (Colorado, USA). The catheter was passed trans-orally into the esophagus of a healthy volunteer. Sensor response was monitored as the patient initiated various events, including talking, heavy breathing, bending at the waist, sitting, standing, head rotation, laughing, belching, swallowing, and coughing. The events were repeated in random order, and event occurrence was indicated on the pressure recordings. Three independent trials were performed.

III. Results

A. *In Vitro Studies*

In vitro experimental results indicated low nonlinearity, hysteresis, zero drift and thermal effect. Negligible sensitivity to fiber bending was also demonstrated. The low standard deviation for all parameters indicates good repeatability. The results are summarized in Table I.

TABLE I
CATHETER-ENCAPSULATED SENSOR PERFORMANCE

	Mean	Standard Deviation
Nonlinearity (% FSO)	0.52	0.14
Hysteresis (% FSO)	4.53	0.33
Zero Drift (mmHg/min)	0.08	0.03
Zero Thermal Effect (mmHg/°C)	2.20	0.49
Fiber Bending Error (% FSO)	0.05	0.02
Accuracy (% FSO)	2.58	1.77
Sensitivity to Vessel Pressure (mmHg/mmHg)	1.00	0.01
Sensitivity to Circumferential Force (mmHg/mmHg)	0.17	0.09

An accuracy error of 2.58% FSO was reported for air pressure measurements. This can be observed in Fig. 4 which depicts a close correlation between the reference pressure and the measured pressure as the pressure is first increased to 300 mmHg, and then decreased back to zero. In agreement with the design intention, the sensitivity of the catheter to air

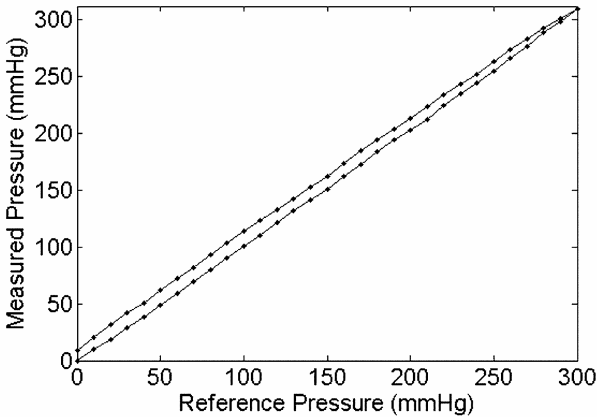

Fig. 4. Comparison of the pressure measured by the cough detection catheter against the reference air pressure. The pressure is increased to a maximum of 300 mmHg and then decreased. The sensor provided an accurate, linear response with low hysteresis.

pressure is 1.00 mmHg/mmHg, whereas a significantly lower sensitivity of 0.17 mmHg/mmHg was obtained for contact force applied to the catheter sides, indicating a low sensitivity to circumferential forces, such as that experienced during esophageal peristalsis.

B. *In Vivo Studies*

Fig. 5 shows a sample pressure recording from one healthy volunteer. Preliminary studies revealed a distinct response to cough events, with a much smaller response to other respiratory and gastrointestinal events, such as swallowing, belching, and heavy breathing.

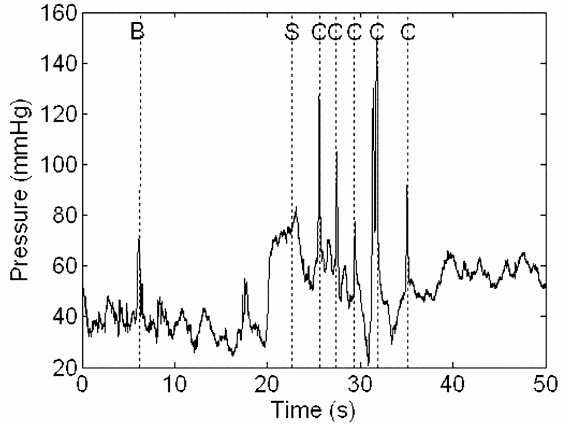

Fig. 5. In vivo pressure recording from a healthy volunteer. Individual initiated a series of gastrointestinal and respiratory events while pressure was continuously monitored. The cough detection sensor was most responsive to cough events. C indicates a cough event, B indicates a belch event, and S indicates a swallow.

IV. DISCUSSION

This study demonstrates that the proposed cough detection catheter accurately measures pressure applied to the catheter tip. Results showed an accuracy of 2.58% FSO, with 0.52% FSO nonlinearity, 4.53% FSO hysteresis, zero thermal effect of 2.20 mmHg/℃, and zero drift of 0.08 mmHg/min. Fiber bending error was negligible. Low standard deviations between trials indicated high repeatability. Also revealed was a low sensitivity to pressure applied to the catheter sides, which in combination with the high sensitivity obtained for pressure applied to the catheter tip, suggest suitability of the proposed catheter for intra-esophageal cough detection. Initial in vivo studies favor this hypothesis, demonstrating a more distinctive, reliable response to cough events than to any other gastrointestinal or respiratory events.

While the proposed cough detection catheter shows strong performance results, most measured parameters are slightly lower than the specifications supplied by the sensor manufacturer. These slight variations can be attributed to the presence of several small air bubbles within the silicone adhesive, which could introduce a damping effect. A second generation of the cough detection catheter is currently being professionally fabricated. Improvements over the initial prototype include the elimination of air bubbles in the silicone, and use of a more rigid epoxy (208-CTH, DYMAX Corporation, Connecticut, USA) to further reduce sensitivity to circumferential force. Upon its completion, detailed and extensive in vitro and in vivo studies will be undertaken.

The presented catheter-based cough detector, which relies on a Fabry-Perot white-light interferometric pressure sensor, allows for integration with a commercial pH/impedance probe [12]-[14] to potentially achieve a diagnostic tool for simultaneously evaluating GERD and chronic cough. The resulting integrated solution would overcome the inaccuracies of user input-based cough indicators [5], [7], [8], and would present a lower-cost, simpler solution than cough detection based on multi-channel solid-state manometry analysis [6].

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