Progress in Self-stabilizing Capsules for Imaging of the Large Intestine

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***Abstract* – This work reports on the progress and development advances in the design of self-stabilizing capsules for imaging the lower part of the gastro-intestinal tract, namely the large intestine (the colon). Macro-level design is reviewed, and the new miniaturized design and its components are described. Preliminary performance results are discussed.**

***Keywords* –** *Capsule endoscopy, Gastrointestinal tract, Imaging, Colon*

I. INTRODUCTION

A. Capsule-Based Imaging

Capsule-based imaging of gastrointestinal (GI) organs was introduced in 1997 [1]. Since then it has become the preferred imaging modality in the small intestine due to its non-invasiveness and its capability to deliver important wireless information via video imaging [2]-[3]. Usually it takes 8 to 24 hours for a video capsule endoscope (VCE) to traverse through the entire GI tract as a result of its passive movement. In view of the fact that the movement of these capsules is not controlled, missing diagnosis is likely and extensive observation of many interesting areas alongside the GI tract is difficult, if not impossible. The application of VCE is currently limited to small-lumen organs. In larger lumen organs, such as stomach or the colon, the capsules tend to tumble, which leads to incorrect recognition of a given organ segment by the capsule imaging system, thus rendering them unsuitable for use. Another problem that results from the tumbling of a capsule is that the perceived dimensions of a polyp or another lesion are widely influenced by the distance between the capsule and the lesion. An innovative method of imaging of the GI tract was proposed in [4]. This method can facilitate capsule-based imaging in the GI tract by enabling imaging of large-lumen organs without the effects of tumbling. The idea includes a capsule coating capable of dissolving in the colon, hence enabling a permeable, swellable container attached to the back of the imaging component to be exposed. The expandable container swells at exposure to colonic liquids and enables a stabilized structure with better imaging capabilities. The device is equipped with all components necessary for imaging and communication with the outside world, namely an imaging component, an illumination component, an RF transmitter, and batteries.

The macro-level design is described in Section 2. Sections 3 and 4 describe the test results, while Section 5 concludes the current work and outlines the remaining challenges.

II. MACRO-LEVEL DESIGN

The macro-level design consisted of an outer casing that targeted the colon, an inner capsule endoscope, coupled to an expandable stabilizing component comprising a liquid-permeable sac filled with dry superabsorbent polymer granules (Fig 1).

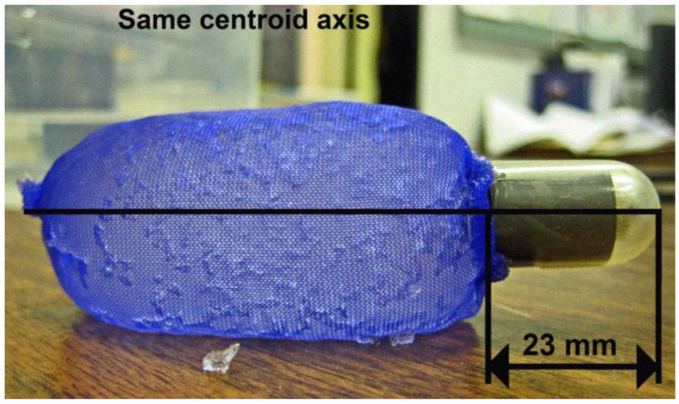

Fig. 1. Fully expanded self-stabilizing capsule endoscope

The outer casing was made of the colon targeting agent Eudragit (Evonik Industries - Pharma Polymers, Piscataway, New Jersey, USA), a coating resistant to gastric acid that dissolves only in the intestinal tract at a pH between 6.5 and 7 [5]. Thus, when the capsule reaches the colon, this outer shell breaks and allows the superabsorbent polymer granules placed within a knitted, permeable polyglycolic acid (PGA), mesh-like container attached to the end of the capsule to expand. Simultaneously, a moisture switch placed on the surface of the capsule activates the electronics inside the capsule, turning on the device. The expansion is completed relatively quickly, thus allowing quality imaging of the colon. The expanded container touches the walls of the colon and stabilizes the capsule precluding it from tumbling.

As a safety measure, once the expandable component has been activated it can be electronically separated from the capsule at any time using a specially designed wirelessly-controlled mechanism. The expandable component is attached very tightly to the capsule using PGA (USP 6-0) absorbable suture (Ethicon, Inc. in Somerville, NJ, USA). This separation safety mechanism comprises of a micro-heater which activates the heating of a filament in the presence of a magnetic field. The heating filament reaches a suitable local temperature to melt the PGA suture (≈220 ˚C) when a current passes through it, which separates the capsule away from the expandable material leaving open the PGA mesh while the temperature of the shell of the capsule does not change by more than 0.2 ˚C. The natural peristaltic movement of the colon completes the separation of the expandable component from the VCE. The

expandable component is biocompatible and is able to disintegrate in the GI tract after a certain period of time.

III. PROPOSED SPECIFIC DESIGN

Presently, we have designed a 1:1 prototype of this self-stabilizing VCE. The complete block diagram of the proposed miniature self-stabilizing wireless endoscopic capsule prototype is shown on Figure 2.

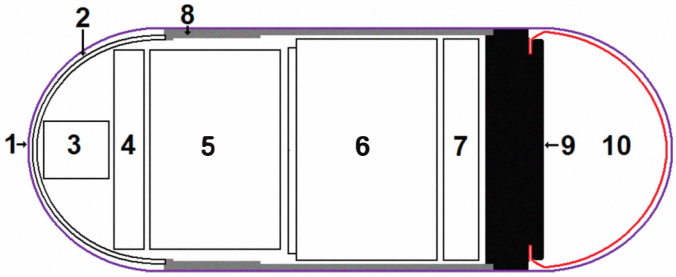

Fig. 2. Wireless Endoscopic Capsule Prototype. 1 – External capsule (outer casing), 2 – optical dome , 3 – longitudinally positioned CMOS color camera, 4 – Illumination system (LEDs), 5 – transmitter/antenna, 6 – battery, 7 – micro-heater, 8 – tapered cylinder, 9 – sealable lid, 10 – expandable component

This design consists of an outer casing, inner capsule, and expandable component. The inner capsule is comprised of a CMOS camera, RF transmitter, light emitting diodes (LEDs), magnetic switch and a micro-heater. After the expandable component has been activated it can be electronically detached from the capsule at the operator's command by magnetically enabling the fast-reacting micro-heater.

A. Outer Component

For the initial prototype model, the outer casing is a hard-shell gelatin capsule from Torpac, Inc. (Fairfield, NJ, USA) which dissolves very rapidly (2-4 minutes) in water. This capsule is sized for animal testing, and with the design limitations in mind, a capsule of size #13 (1/8 oz. 3.2 ml) was chosen. The gelatin capsule provides adequate space for the inner capsule containing the electronics and the expandable component. In the present prototype, the emphasis is on demonstrating stabilization and separation, and the testing assumes that the outer casing has reached the targeted organ. The colon targeting agent EUDRAGIT® FS 30 D [6] (Evonik Industries - Pharma Polymers, Piscataway, New Jersey, USA) was considered for the final application, but further study is required.

B. Inner Capsule

The inner capsule must protect the internal components from conditions inside the patient's body. It is composed of three parts, a tapered cylinder, an optical dome window, and a sealable cap. The shape of the capsule is specially designed to enable the increase in volume of the expandable material. The dimensions of the capsule were determined to allow it to fit inside the outer casing (Torpac #13 3.2 ml), and leave enough space for the 1.5 ml of expandable component required for the stabilization. Fig. 3 shows the designed inner capsule in comparison with the commercially available Pillcam™ Colon capsule (Given Imaging Ltd, Yoqnem, Israel).

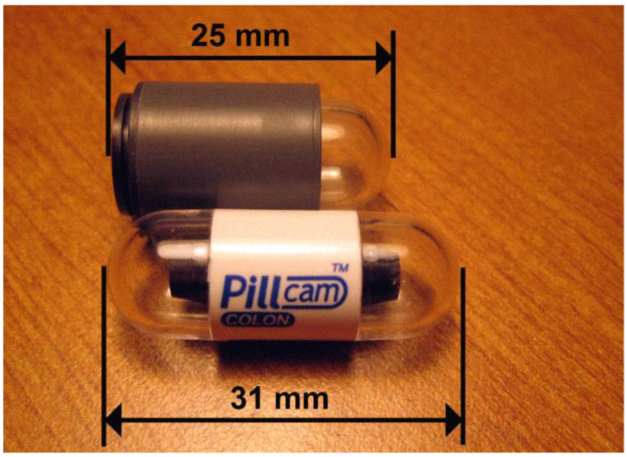

Fig. 3. 1:1 Prototype compared to a commercial capsule endoscope

C. Electronics Inside the Capsule

1) CMOS imager:

The proposed design has a CMOS imager which captures images of the colon walls and also suits the space constraint in the capsule. At the front of the camera is a short focal-length lens (0.77mm/f 3.0 <110°>) that is focused at the optical dome and a few centimeters beyond, so that the bowel laying against the optical dome would be in focus. This optical arrangement allows the tissue to be in focus even if it is in a close contact with the optical dome window, but also to remain in focus over a few centimeters if the lumen opens. This CMOS imager employs a wide-angle field of view which alone does not significantly improve miss rates, but permits more efficient examination of the large intestine. The selected image sensor for the prototype is the 1/18" Color CMOS camera MO-B802-105 (RF-LINKS, Toronto, Ontario, Canada). The camera operates at 3V, 18-19mA, its minimum required illumination is 2Lux at f1.2, and number of effective pixels is 320x240 (NTSC).

2) Video Transmitter:

There are several critical requirements for the transmitter in the capsule endoscope, including size, power consumption and data rate. The hardware needs to be robust in order to withstand the knocks and bumps of normal human body movement. The transmitter layout complements the other electronic components, making the most out of the small space inside the inner capsule. In order to transmit the diagnostic real-time high-resolution image data at high speed and because of the effect of human body tissue on antenna propagation characteristics, the transmission frequency may slightly shift during operation [7]. Thus, a wide-bandwidth, higher transmission frequency needs to be employed along with a tunable receiver. With CMOS technology, the output frequency typically increases as the physical size diminishes. Among the industrial, scientific, and medical (ISM) frequencies, 1.9 GHz is frequently used for transmission, and

the smallest transmitters that are commercially available operate in this range. The selected transmitter DX-5A (RF-LINKS, Toronto, Ontario, Canada) operates at 1980MHz (channel frequency), draws 8mA from a 3V source, and its power output is less than 1mW. This transmitter is ultra small (4.8x5.5x1.2mm), ultra low weight (0.1g), tunable in gain and is capable of transmitting an NTSC signal. The frequency stability of this RF transmitter is ± 250 KHz. It has hardwired antenna. The capsule travels passively in the GI tract, and therefore is randomly oriented. Thus, the direction of transmission radiation is uncontrolled, and to detect the transmitted signal independently of the transmitter position, the antenna is required to emit an omni-directional radiation pattern [8]-[9].

3) External Video Receiver:

The external receiver records images received from the in-vivo sensing device into its digital memory, and simultaneously processes and displays images on a PC display, while the sensing device is inside the patient's body. This small receiver can monitor the 1900-2100 MHz video bandwidth and the frequency is controlled in 0.25 MHz steps, which is entirely sufficient for stable real time recording and display of the results. In addition, the receiver has built-in a special Automatic Frequency Tuning (AFT) control function for best stability.

4) Illumination System:

The challenge in developing an illumination system for a capsule endoscope is obtaining a uniform illumination [10] on the observed object. Four white flat-top, wide-angle, surface-mount LEDs were utilized to minimize the space volume and the current draw, while still providing adequate illumination to cover a 170-degrees range. The Nichia NSSW156T LEDs (NICHIA Corporation, Tokyo, Japan) were selected based on their luminous intensity, viewing angle, and dimensions (3.0x1.4x0.8mm). The experimental luminous intensity of a single LED is above 130 mcd at a forward current of 1mA. This provides sufficient illumination for the CMOS imager to clearly view an image in the large intestine when the four white LEDs are circumferentially positioned at the camera side end of the capsule. To be effective, the illumination needs to provide an adequate amount of uniform light and to come from the correct angle, so as to avoid shadow effects.

5) Power Supply:

Since there are only certain types of batteries commercially available that can fit in the limited space of the capsule, the power supply needs to be designed very efficiently. The CR 1/3N battery (Duracell Canada Inc, Mississauga, Ontario, Canada) provides enough continuous current to allow for reliable operation of all electronics inside the capsule. The operational voltage, continuous discharge current, and small dimensions were deciding factors when selecting the power supply. Another important parameter to consider was the internal resistance since the battery must provide enough continuous discharge current of 30mA for the electronics and 400 msec/80mA pulses to trigger the micro-heater simultaneously. The lower the internal resistance, the less restriction the battery encounters in delivering the needed power spikes. Using a DC load test the internal resistance was measured to be in range of 250 mOhms.

D. Expandable Component

The expandable material should be able to deform under pressure but regain its original shape when the pressure is removed. The expanded implement should also maintain its consistency and not change state under the influence of water or colonic fluids. The overall expansion time should be very short (<1min). The materials that had the desired properties were categorized according to the preferred mechanism of expansion, osmosis (release of potential energy). Osmosis has proven to be effective in several medical applications such as stents that help relieve pathological obstruction of tubular structures in vascular, urologic and GI systems, as well as in self-expanding prostheses [11]. The availability of stent structures that can resist the peristaltic motion in the colon without them moving is indicative that osmosis is the preferred mechanism for the proposed apparatus [12]. The material used in this design are salt granules of hydrophyllic, non-toxic, crosslinked polyacrylate polymer (Favor PAC, Evonik Industries, Essen, Germany). These granules can absorb several hundred times their weight in water, but cannot dissolve because of their three-dimensional polymeric network structure. The use of this super-absorbent polymer as an expandable material for this device can be justified by its ability to: be biocompatible; swell extensively; swell in a relatively short period of time; exert a reasonable swelling pressure on the walls of the lumen; and withstand the pressure in the colon by remaining attached to the imaging component while keeping its consistency. Thus, the expandable portion consists of two components, the Favor PAC granules and a custom-made, knitted PGA-based mesh. The Favor PAC granules within this previously collapsed permeable PGA mesh expand upon contact with fluids, serving as their container. The faster the expansion, the faster the imaging capsule would be stabilized in the colon, allowing quality imaging of the organ as soon as the capsule enters the cecum. The pressure exerted upon expansion on the walls of the colon should not be harmful. The colon wall of the human body can bear ≈7.71 pound-force/square inch [13].

IV. LABORATORY TESTING

Laboratory testing included comparing the image quality between the stabilized and unstabilized capsules.

Methodology: A transparent acrylic tube with a 4.5 cm diameter, and 90 cm length, was sealed at one end, filled with water/oil (approximately 1.5 l), and the capsule was let to fall down its entire length. Agitation of the cylinder was delivered manually, with a displacement of 12 cm from the centre of the tube, at a frequency of approximately one back and forth oscillation per second. A scaled paper grid was placed on the floor below the center of the acrylic tube for the purpose of

amplitude control while agitation of the tube was performed. The stabilized capsule was dropped down the tube while agitating it, with the intention of recording as lengthy trials as possible. This was repeated with the unstabilized capsule, using both water and canola oil as the medium in the tube to reduce the speed at which the capsule fell, and to enable more consistent video comparison. The improvement of video stabilization was quantified using optical flow evaluation provided by the software package Syntheyes Camera Tracker (Andersson Technologies LLC, Malvern, PA, USA). Optical tracking is used to monitor spatial and temporal changes in an object during a video sequence, including its presence, position, size, shape, etc. This is accomplished by solving the temporal correspondence problem, which essentially boils down to matching the target region in successive frames of a sequence of images taken at closely-spaced time intervals [14].

Type of data collected: Estimated average pixel tracker motion trajectory (optical flow), maximum tracker rate of change for subsequent images, average radius movement of the capsule endoscope relative to the centroid of the tube, average number of tumbles for stabilized and unstabilized capsule endoscopes.

Observations: There were 10 video footages for both the stabilized and the unstabilized cases. The centroid of the cylinder was chosen as a tracking object. This is simply because if the center of the capsule where the camera is located (viewing angle 110°) is aligned within the center of this tube, it is impossible to miss any important areas as the capsule sweeps along the walls of the cylinder.

The average optical flow trajectory for the stabilized capsule was measured to be 900.42±36.02 pixels whereas for the unstabilized one it was in the range of 3214.58±48.20 pixels. This shows a major difference in average optical flow trajectories and proves the stabilization concept. Additionally, the stabilized capsule did not lose visual contact with the centroid of the cylinder during the transit.

The maximum tracker rate of change for subsequent images was measured to be 71.32±28.70 pixels/second for the stabilized case while the unstabilized has shown 351.02±64.09 pixels/second. It can be clearly seen that the average pixel movement for subsequent frames of a chosen tracked object acquired for the stabilized capsule was much smaller than for the unstabilized one. The stabilized capsule showed significantly greater average improvement in the optical flow tracking of its recorded video, versus the unstabilized capsule.

The average radius movement of the designed capsule endoscope relative to the centroid of the cylinder was 69.72±24.26 pixels for the stabilized capsule and 90.54±42.71 pixels for the unstabilized capsule. This shows that on the average, the centroid of the cylinder moved away much less from the center of the camera for the stabilized capsule.

At no time in this testing the stabilized capsule tumbled within the acrylic tube. The simple reason for this was that both the combined length of the capsule and the stabilization mechanism exceeded the diameter of the tube. Because the connection between the two was rigid, the completed assembly was unable to deform, and tumbling within the acrylic tube became a geometric impossibility. Results from this test evidently demonstrated the effectiveness of the stabilization mechanism.

V. CONCLUSION

Progress in the design and implementation of self-stabilizing capsules for colon imaging was reported. Challenges were discussed, and improvement in the optical flow tracking of our new stabilized capsule design, compared to an unstabilized one was shown. The proposed device can be used in the screening of large-lumen organs and has the ability to greatly improve GI diagnostics. Animal testing of the proposed approach are ongoing.

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