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Wireless Insufflation of the Gastrointestinal Tract

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***Abstract*—Despite clear patient experience advantages, low specificity rates have thus far prevented swallowable capsule endoscopes from replacing traditional endoscopy for diagnosis of colon disease. One explanation for this is that capsule endoscopes lack the ability to provide insufflation, which traditional endoscopes use to distend the intestine for a clear view of the internal wall. To provide a means of insufflation from a wireless capsule platform, in this paper we use biocompatible effervescent chemical reactions to convert liquids and powders carried onboard a capsule into gas. We experimentally evaluate the quantity of gas needed to enhance capsule visualization and locomotion, and determine how much gas can be generated from a given volume of reactants. These experiments motivate the design of a wireless insufflation capsule, which is evaluated in *ex vivo* experiments. These experiments illustrate the feasibility of enhancing visualization and locomotion of endoscopic capsules through wireless insufflation.**

I. Introduction

EACH year 140,000 people in the United States are diagnosed with colorectal cancer, and approximately 50,000 people die from it [3]. Nearly all of these deaths are preventable through early diagnosis. The 5-year survival rate drops from 90% with early detection to 5% with late detection [4]. Standard colonoscopy is highly effective (above 95% sensitivity and specificity for detecting polyps larger than 10mm [5]), yet 22 million people neglect medically recommended screenings due to the indignity and discomfort of the procedure [6].

Swallowable capsules have the potential to be much better tolerated by patients [7]. Over the past few years they have become the tool of choice for diagnosis in the small intestine [8], and are widely used there. They have not yet made a similar impact in colorectal cancer screening because of their low specificity (as low as 64% for polyps of any size [9]).

One potential contributing factor to the high false negative rate of capsule endoscopes in the colon is that, unlike traditional colonoscopes, there is no means of insufflation to distend tissue and enable a clear view of the intestine surface (see Fig. 1). Poor visualization has been shown to be a potential cause for missed adenomas in traditional colonoscopies [12], and the low specificity rate of current capsules suggests that full visualization and examination of the colon are challenging for capsules. To provide insufflation, in this paper we propose the use of biocompatible effervescent chemical reactions as a means of generating large volumes of gas from small volumes of biocompatible weak acids and bases carried onboard the capsule. We note that in addition to enhanced visualization, a second potential benefit of this approach is to enhance locomotion (Fig. 1), which would be advantageous in nearly all of the many robotic locomotion methods that have been proposed for capsule endoscopes [13]–[15], particularly those actuated via magnetic fields [11], [16]–[18], and in other miniature surgical robots, such as the mobile robotic platform described in [19], [20]. In the sections that follow, we first experimentally examine how much gas must be generated to enhance visualization and capsule locomotion in the colon (Sec. II). We then propose effervescent reactions as a means to generate gas (Sec. III) and determine how much gas can be generated from various reactions (Sec. IV). We then describe the design of an insufflation capsule that makes use of these reactions, and provide ex vivo experimental results (Sec. V).

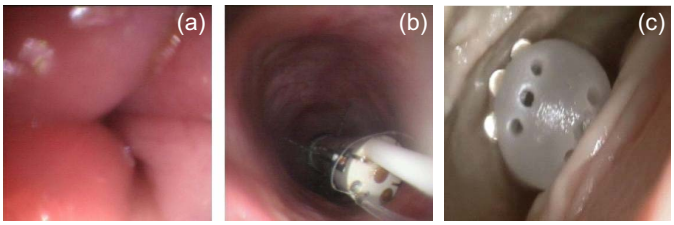

Fig. 1. (a) An image from a colonoscope of the colon prior to insufflation. (b) An image after insufflation illustrating the ability to view a larger portion of the intestinal surface. Also pictured is a capsule robot with legs [10]. (c) A magnetically-actuated capsule [11] whose motion is impeded by the collapsed intestinal folds.

II. Insufflation Experiments for Design Specifications

Toward determining the amount of insufflation a capsule endoscope must provide to enhance visualization and locomotion in the colon, we conducted the following two experiments.

A. Visualization Enhancement Experiment

An *ex vivo* experiment was conducted using a porcine large intestine 150cm long and 6cm in diameter, matching the dimensions of an average adult colon [21] (see Fig. 2). Nine colored markers serving as identifiable fiducials were

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A preliminary version of the results in Section II has been previously presented at conferences [1], [2].

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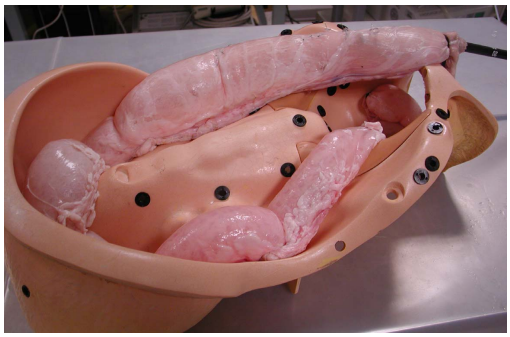

Fig. 2. The experimental setup for determining how much insufflation is required to improve visualization in the large intestine. *Ex vivo* porcine intestine was arranged in a phantom model to simulate the shape of the human colon within the abdomen.

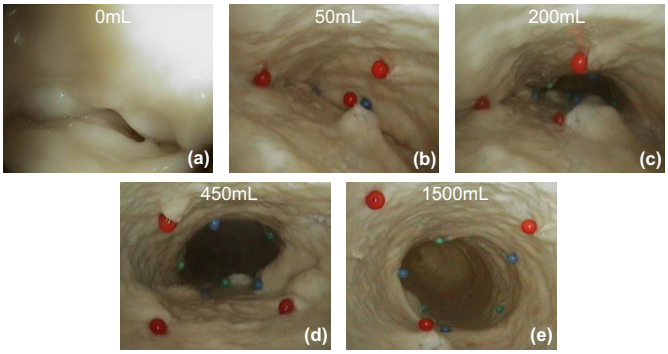

Fig. 3. Results of the colon inflation experiment pictured in Fig. 2. (a) The intestine in its deflated state with no markers visible. (b) With just 50mL of insufflation, 4 of the 9 markers became visible. (c) At 200mL, all 9 markers first came into the field of view. (d) The threshold above which all 9 markers were consistently visible was 450mL. (e) The intestine in its fully inflated state at 1500mL of insufflation.

attached in groups of three, with each marker evenly spaced from the others, at 3cm linear intervals along the intestine (see Fig. 3(e)). The deflated colon was then placed in a human anatomical model (Limbs & Things Ltd., Bristol, UK) as shown in Fig. 2 in a configuration approximating the curved path of the human colon and sealed at both ends.

A flexible endoscope (13803PKS, Karl Storz GmbH & Co., Germany), placed approximately 4cm from the markers, was used for visualization, simulating the view from a capsule-based camera. Using a controlled air compressor, the intestine was incrementally inflated through the single channel in the endoscope. The intestine was inflated by increasing the volume of air released in increments of 50mL from 0mL to 500mL. From 500mL to 1000mL, the increment was changed to 100mL since significant changes in the field of view were no longer observed. The maximum inflation applied was 1500mL. An in-line flow sensor (AWM3300V, Honeywell International, USA) was used to measure the inflation volume.

The number of markers visible at each increment is shown in Table I and Fig. 3. From this experiment, we observe that visualization is enhanced almost immediately, with as little as 50mL of insufflation needed to visualize just under half of the markers. With 200mL of insufflation, all 9 markers first became visible, and after 450mL of insufflation, all 9 markers were consistently visible. These results will be discussed further in Section IV-D, in the context of results obtained from gas generation experiments and insufflation capsule testing.

B. Locomotion Experiment

Insufflation also has the potential to enhance locomotion of capsules that are otherwise impeded by the folds of the deflated intestine. Even with active locomotion methods, such as magnetic guidance, capsules often have difficulty traveling through the entire lumen [11]. To assess the benefits of insufflation for locomotion, we performed a second experiment with a magnetically-actuated capsule, which has previously been validated in an endoscopic setting [11]. A 1.21T NdFeB N35 permanent magnet (Sintered NdFeB magnets, B and W Technology and Trade GmbH, Germany) having a diameter of 60mm, a length of 70mm, and a weight of 1.5kg, was attached to the end effector of a 6 degree of freedom Mitsubishi RV-3S serial manipulator (Mitsubishi Electric Corp., Japan). Three smaller internal magnets, (MTG Europe Magnet Technology Group, Germany), each having a diameter of 3mm, a length of 10mm, and a magnetic flux density of 1.21T, were placed inside of a pill-sized capsule (11mm diameter $\times$ 26mm long). The working distance between the internal and external magnets was 150mm.

The robotic arm was preprogrammed to follow a straight trajectory 300mm long, which approximates the length of the longest straight portion of the colon. The robot was programmed to stop its motion every 10mm, rotate around its roll axis by 10°, rotate around its yaw axis by 10°, and then continue forward motion at a velocity of 5mm/s. The rotational speed was between 5 and 10°/s. This behavior was performed in order to attempt to free the capsule from the collapsed lumen using a procedure similar to that which a surgeon might employ by hand with the magnet, or when teleoperating the robot for the same capsule locomotion purpose (see [11] for more details on magnetic locomotion). In this experiment, the capsule moved at approximately 5mm/s, the same velocity as the external magnet attached to the robot. We note that Ciuti et al. measured the average time it took surgeons to teleoperate a magnetic capsule over a 500mm collapsed colon to be almost 10min [11]. Assuming a total length of 1.5m as previously stated, this would suggest that the capsule could travel the entire length of the colon in less than 30min.

The magnetic capsule was placed inside fresh porcine large intestine (4cm diameter), and the intestine was sealed at both ends. A 50mL syringe connected to a tube whose outlet was located immediately behind the capsule was used to incrementally inflate the intestine in 25mL intervals from 0mL to 250mL. As shown in Fig. 4, this resulted in local inflation of the colon, such that the capsule could advance up until the far

TABLE I
THE NUMBER OF MARKERS VISIBLE AT SELECTED INFLATION VOLUMES. VISUALIZATION WAS ENHANCED AT 50mL AND ABOVE 450mL THE INTESTINE WAS FULLY INFLATED (ALL 9 MARKERS ALWAYS VISIBLE).

Gas (mL)	0	50	100	200	300	350	400	450	$\cdots$	1500
Markers	0	4	5	9	7	9	7	9	$\cdots$	9

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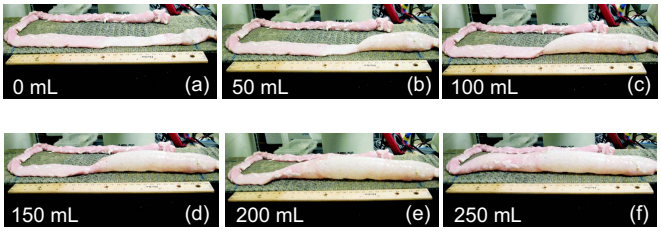

Fig. 4. The results of the locomotion experiment at different inflation increments. (a) The intestine in its deflated state, where no capsule motion was possible. (b) With just 50mL of insufflation, the capsule moved an average distance of 67mm. (c) At 100mL, the capsule moved an average distance of 150mm. (d) At 150mL, the capsule moved an average distance of 188mm. (e) At 200mL, the capsule moved an average distance of 243mm. (f) At 250mL, the capsule was able to move the entire length of the colon (300mm), with an average distance of 295mm.

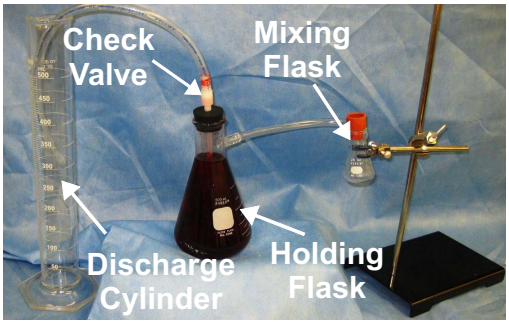

Fig. 5. Experimental setup for reacting known volumes of the base, the acid, and water to measure carbon dioxide production. The powdered acid and base were placed into the flask, and water was added through a syringe to start the reaction. The gas generated displaced water in the holding flask which was measured in a graduated cylinder.

border of the inflation "bubble." Three trials were performed at each inflation interval.

The distance (d) traveled by the capsule in this experiment was related to the amount of insufflation by $d = 1.16\ v_{\text{air}} + 13.64$, with $R^2 = 0.99$. This equation was calculated by plotting the amount of insufflation provided versus the distance traveled by the capsule, and then fitting a linear model to the data. We observe that locomotion enhancements occur almost immediately, with only 25mL of insufflation. At this point, the capsule was able to travel 37mm. With 250mL of insufflation, the capsule was able to travel the entire length of the desired trajectory. These results will be discussed further in Sec. IV-D in the context of gas generation experiments and the design of an insufflation capsule.

III. Proposed Solution: Effervescent Reactions

Given the potential benefits of insufflation and the need for an untethered air supply in a capsule endoscope, we now explore the potential of acid/base reactions in producing sufficient gaseous output to meet the visualization and locomotion requirements determined in Sec. II. In prior work, we explored the potential of using chemofluidic phase transition of Hydrogen Peroxide as a means for generating gas for insufflation [1]. Peroxide requires small liquid volumes to generate large gas volumes, but it is not biocompatible, and is a safety hazard if accidentally spilled on the intestine [22]. It also requires care to manage the heat generated by the reaction. Mild acid/base reactions, in contrast, create a relatively large amount of gas from basic ingredients that are safe to ingest.

Here, we explore four such candidate acid/base reactions, generated from all combinations of two bases, potassium bicarbonate ($KHCO_3$) and sodium bicarbonate ($NaHCO_3$), and two acids, acetic acid (CH_3CO_2H) and citric acid ($C_6H_8O_7$). These acids and bases were chosen because they are biocompatible and FDA approved at various concentrations, as are the byproducts of their reactions [23]. Tissue pathology studies will be required in the future to know if the specific concentrations of the acids and bases used in this study may be harmful to the large intestine if directly introduced, but we note that these acids and bases are not meant to come into contact with the intestine at any point, as the entire reaction takes place within the capsule. However, should the contents of the insufflation capsule escape, both potassium and sodium bicarbonate appear to be harmless, as they are found in foods, used in antacids, and do not cause skin irritation. Further, "the (body's) mechanisms for disposing bicarbonate intake in large amounts through excretion appear to be highly efficient" [23]. Citric acid is also found naturally in foods and does not cause skin irritation at the concentrations used in this study. Thus, we believe it will be safe even for direct large intestine contact. Acetic acid is the acid found in common vinegar (which is acetic acid diluted 20:1 with water). In this study we used undiluted acetic acid, which may cause skin irritation. Thus there is a reasonable chance of irritation to the intestine lining if it is spilled. Future in vivo experiments will be needed to support the above conjectures on the biocompatibility of these substances if they are directly introduced into the intestine through a catastrophic capsule malfunction. However, we note that the way the capsule is designed, only small ports are present. This limits the rate at which material can flow out of the capsule, even in an emergency condition, making it highly unlikely that the complete contents of the capsule would ever be directly introduced onto the intestine lining.

Of the two bases, potassium bicarbonate has higher solubility which would suggest a higher gas output, but is not suitable in patients with renal failure or cardiac disease [24]. For this reason, we also explore the sodium bicarbonate reaction, which is expected to have only slightly lower gaseous ouptut, but serves as a viable alternative in these specific cases. In all of these reactions, when the acid and base are mixed in the presence of water, carbon dioxide (CO_2), water, and a biocompatible citrate (for citric acid) or acetate (for acetic acid) are produced. The fact that CO_2 is released as the output gas (rather than air, oxygen, etc.) is particularly beneficial for insufflation in the colon, due to its rapid absorption by the mucosa, which has been shown to decrease patient discomfort in colonoscopy [25]. In both reactions, water is necessary to disassociate the ion pairs of the base and provide a medium for its protonation by the acid. For this reason, both water and the reactants are carried onboard the capsule, as discussed further in Sec. V.

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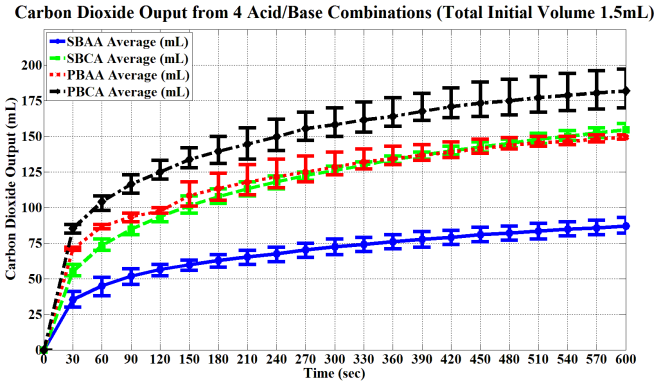

Fig. 6. The carbon dioxide generated by the four combinations of potassium bicarbonate (PB), sodium bicarbonate (SB), acetic acid (AA), and citric acid (CA). The average output is presented as a line, and the minimum and maximum values are presented with error bars. From this, we observe that the PB+CA reaction generated the most gaseous output.

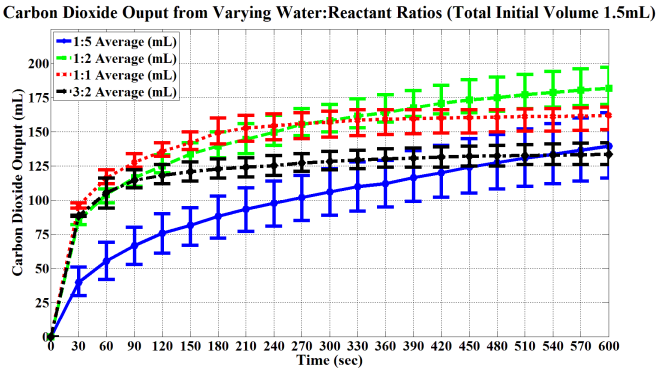

Fig. 7. The carbon dioxide generated by varying ratios of water to reactants for potassium bicarbonate and citric acid. The average output is presented as a line, and the maximum and minimum values are presented with error bars. From this, we observe that the 1:2 water:reactant ratio produced the most gaseous output.

IV. Acid Base Reaction Experiments

To determine the necessary volume of acid/base reactants needed to generate a given volume of gas, one may initially think that a simple computation using the chemical decomposition equation would suffice. While these computations provide a general range of reactant and product volumes, there are many factors that are not accounted for in such an ideal equation, including solubility, temperature, and heat of formulation, all of which impact the total volume of the products that are generated from the reaction. For this reason, we conducted a set of experiments to determine the optimal combination of reactants, the optimal water to reactants ratio, and the amount of CO_2 that can be generated from small initial volumes of solution, using the chemical decomposition equation to inform the starting volumes chosen. All experiments were conducted at the same temperature and pressure.

A. Acid Base Combination Experiment

We tested all four combinations of reactants (potassium bicarbonate, sodium bicarbonate, citric acid, and acetic acid), in order to determine which combination resulted in the most CO_2 output. The experimental setup, shown in Fig. 5, involved a mixing flask, a holding flask, and a discharge cylinder. The flasks were connected with rubber tubing and sealed with rubber stoppers. For each combination, one acid and one base were mixed together in the mixing flask, the flask was sealed, and water was added with a syringe. The CO_2 produced by the reaction was transferred to the holding flask, which held the water that was displaced through a plastic tube, a check valve, and into a graduated cylinder. The amount of water displaced corresponds to the gas produced by the reaction.

These experiments were performed with an initial volume of 1mL total of the two reactants and 0.5mL of water, for each of the four combinations of acids and bases. The reactants were mixed at stoichiometric ratios, according to the chemical equations of these reactions. We note that the total solution volume was 1.5mL, a volume that fits within the typical volume (2.5mL) of a commercial camera pill [26]. To ensure repeatability, three trials of each combination were performed. The amount of water output was recorded every 30 seconds for 15 minutes and averaged over the three samples for each combination. The results are shown in Fig. 6. Note that the figure shows only the first 10 minutes of data collection, as this was the point after which very little changes were observed. These results show that the citric acid solutions produce more CO_2 than the acetic acid solutions, which is consistent with predictions made from the chemical equations of each reaction. Overall, we found that the potassium bicarbonate and citric acid solution resulted in the largest output and fastest rate of reaction. Thus, we use this combination in subsequent experiments. We note, however, that the sodium bicarbonate and citric acid solution produced the second largest gaseous output, and is a good alternative for patients with preexisting renal and cardiac problems, as mentioned previously.

B. Solution Concentration Experiment

Having chosen potassium bicarbonate and citric acid as our preferred reactants, we performed a second experiment to determine the effect of the water to reactant ratio on the rate of the reaction and amount of CO_2 produced. To do this, we used the same experimental setup described above and shown in Fig. 5. While keeping the total volume of water and reactants fixed at 1.5mL, we studied four water:reactant (by volume) ratios: 1:5, 1:2, 1:1 and 3:2. Three trials were performed for each ratio. The amount of water displaced was recorded every 30 seconds for 15 minutes. The results are shown in Fig. 7.

From this experiment, we observe that a trade-off exists between the total amount of CO_2 produced and the rate at which it is produced, based on the intial volume of water. Too little water leads to longer gas generation times, which would likely be a disadvantage for capsule-based colonoscopy if this caused the procedure to take longer than an average colonoscopy (30-60 minutes). Too much water, on the other hand, leaves less space for the reactants, and thus, less CO_2 is produced. The 1:2 water to reactants ratio appears to be the best balance among the combinations tested, providing a quick rate of reaction and the most CO_2 produced.

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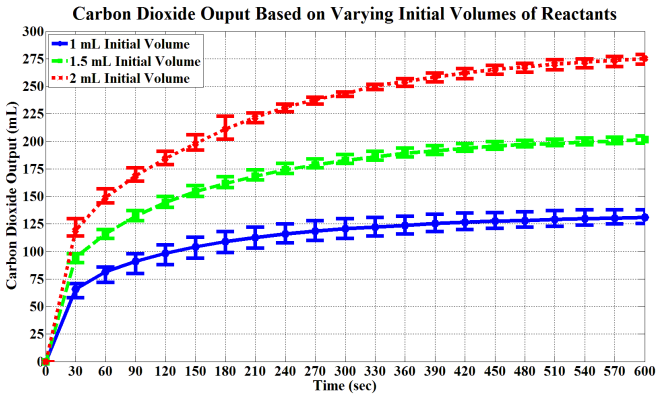

Fig. 8. The carbon dioxide produced by varying total initial volumes of reactants (potassium bicarbonate, citric acid, and water). The average output is presented as a line, and the maximum and minimum values are presented with error bars. From this, we observe that a larger initial volume produces a larger gaseous output, following a linear relationship.

C. Initial Volume Experiment

The final experiment explores how the CO_2 output depends on the total initial volume of reactants and water stored onboard the capsule. The experimental setup shown in Fig. 5 was used in this experiment. We investigated 3 initial volumes of solution, 1.0mL, 1.5mL, and 2.0mL, mixed at the optimal water to reactants ratio of 1:2 determined in the prior experiment. Three trials were performed at each initial volume. The amount of water displaced was recorded every 30 seconds for 15 minutes.

The results are shown in Fig. 8. One can see that the larger the initial volume, the larger the volume of gas produced. The average CO_2 output is also linearly related to the initial volume of solution ($v_{\text{gas}} = 150\ v_{\text{reactants}}$, $R^2 = 0.99$). This finding is consistent with the theoretical prediction of the relationship between CO_2 output and initial volume, which is derived from the chemical decomposition equation and is given by:

$$\frac{V_{CO_2}}{V_{tot}} = \left(\frac{M_{acid}}{\rho_{acid}} + 3\frac{M_{base}}{\rho_{base}}\right)R\frac{M_{CO_2}}{\rho_{CO_2}} = 147.17 \qquad (1)$$

where V_{CO_2} is the volume of CO_2, V_{tot} is the total initial volume of reactants, M is the molar mass, ρ is the density, and R is the molar ratio of base to acid. This linear trend was extrapolated to determine the initial volume of reactants needed to produce desired volumes of CO_2 with water carried onboard the capsule. Results are presented in Table II. In interpreting values on the table, note that the typical volume of a commercial camera pill is approximately 2.47mL, and that the volume of the Given Imaging, Inc. PillCam Colon is approximately 2.95mL.

D. Summary/Interpretation of Experimental Results

These experiments, viewed in light of those in Sec. II, illustrate the feasibility of generating sufficient levels of insufflation from a wireless capsule to enhance visualization and locomotion. As can be seen in Fig. 3, at just 50mL of inflation, visualization was significantly improved. The same level of insufflation freed the capsule for magnetic locomotion, enabling it to move 67mm. Fig. 8 shows that even 1mL of a 1:2 water to reactants ratio of potassium bicarbonate and citric acid can produce 50mL of CO_2 in less than one minute. One can extrapolate (see Table II) that even just 0.5mL of initial solution would result in more than 50mL of insufflation.

At 200mL of insufflation, the entire wall of the intestine is viewable (see Fig. 3(c)) and the capsule is able to magnetically locomote through more than 80% of the colon (see Sec. II-B). Our experiments suggest that a total initial volume of 1.34mL (including reactants and water) should be able to provide this amount of insufflation (see Table II). To reach the upper threshold of 450mL, beyond which we found no visualization benefit to further inflation, 3mL of initial solution volume would be required.

Given the volumes of commercial capsules such as the PillCam SB (Given Imaging, Inc.) and MAARS capsule [26], it is reasonable to expect a single capsule to be easily able to generate sufficient insufflation to enhance visualization and locomotion. If one wishes to inflate the entire intestine (e.g. at the 450mL level, or greater), more than one insufflation capsule will be required. This is not problematic, however, since it is reasonable to ask a patient to swallow several pills in sequence.

We note that these benchtop experiments may not capture the effects of pressure applied to the intestine by surrounding tissue. These effects, however, appear to be small, as "the abdomen behaves as a hydraulic system with a normal intra-abdominal pressure of about 5–7 mmHg" [27]. This pressure would reduce the volumes of gas delivered by the capsule by less than 1% assuming an ideal gas at constant temperature. This should be noted in interpreting the results in these experiments and the prototype experiments in Section V-A, as they apply to *in vivo* conditions.

V. Insufflation Capsule Prototype

Using the results from the above experiments, we now describe the design of a swallowable capsule that carries water plus reactants onboard. Our capsule prototype (Figs. 9 and 10) consists of a cylindrical capsule measuring 12mm in diameter $\times$ 32mm long with rounded end caps. These dimensions provide an internal volume matching the PillCam Colon, given the 1mm wall thicknesses we selected to ease assembly. The

TABLE II
Volume of Reactants Required for Various Insufflation Levels, Extrapolated from Experiments in Section IV-C.

CO_2 (mL)	Reactants + Water (mL)
50	0.33
100	0.67
150	1.00
200	1.34
250	1.67
300	2.00
350	2.34
400	2.67
450	3.00
1500	10.02

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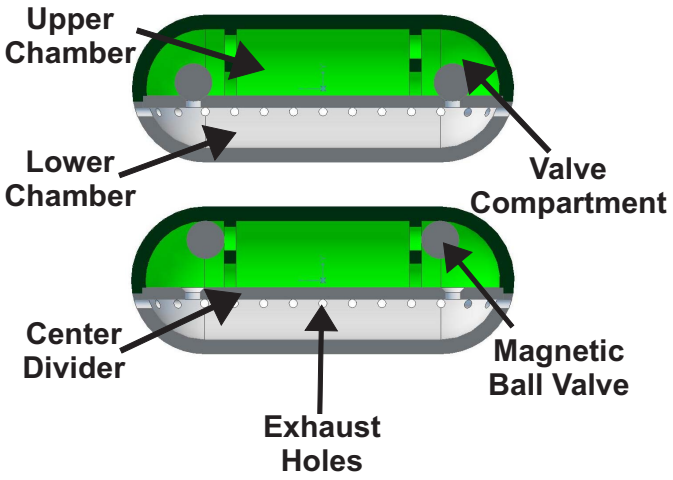

Fig. 9. Cross-section views of the capsule in its closed (top) and opened (bottom) state.

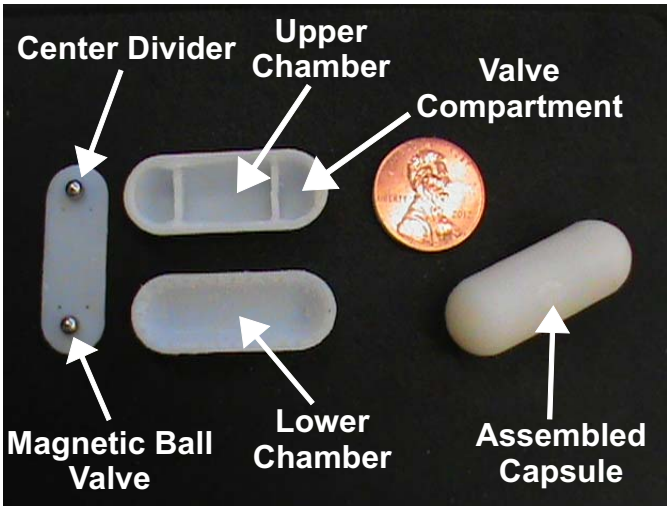

Fig. 10. The capsule prototype and its components. The upper chamber is designed to hold the acid solution, while the lower chamber holds the powdered base. In the presence of an external magnetic field, the two magnetic ball valves move toward the top of the upper chamber, and the citric acid solution mixes with the potassium bicarbonate. The CO_2 produced is vented through small perforated holes just under the midline of the capsule.

capsule was made using a 3D Printer (Objet 30 Pro, Objet Geometries Inc., MA), with polypropylene-like material.

The capsule has two chambers, with a 1mm thick center divider that separates the upper and lower chambers. The upper chamber has a volume of 1.0mL, and the lower chamber has a volume of 0.64mL. The capsule has 28 exhast ports, each 0.7mm in diameter, along the upper edge of the lower chamber, to vent CO_2 into the intestine. Two magnetic ball valves located on the center divider at each end of the capsule provide a flow gate for mixing the reactants contained in the two chambers.

The ball magnets (3.2mm in diameter) are seated in cone-shaped holes (4mm in diameter on the top of the center divider and 2mm in diameter on the bottom), and are held in place with a ferromagnetic ring attached to the opposite side of the center divider. Each ball magnet is confined in a small compartment on the top chamber, to enable each of them to be repeatedly opened and closed in the presence of an external magnetic field without colliding with one another. This enables throttled control of liquid flow, which can be used to prevent the reactants from mixing too quickly and generating large pressure spikes which may cause the ejection of some non-reacted contents through the exhaust ports. In the presence of an external magnetic field, the ball magnets first spin to align their field with the external field, and are then separated from the ferromagnetic ring to open the valve hole, as shown in Fig. 9. Since the magnets are spherical and can spin to the appropriate orientation, the capsule does not have to be in a particular orientation for the valves to open. While the flow of the acid solution does rely on gravity (and thus, pill orientation with the top chamber up and the bottom chamber down is preferential), the pill can work if it is laying on its side or when it is oriented with one of the ends vertical. Due to the capsule's center of mass being located in the bottom chamber, the capsule tends to roll on its side, preventing it from being oriented directly upside down. Should it become oriented upside down, any slight perturbation (such as that introduced from the external magnetic field) reorients it to a more desireable configuration. When the external magnetic field is removed, the ball magnets are attracted back to the ferromagnetic rings, and the valves are closed, as shown in Fig. 9.

A. *Insufflation Capsule Experiments*

Two sets of experiments were conducted to evaluate insufflation capsule performance: a first experiment on the benchtop at room temperature, and a second experiment in *ex vivo* intestine in a water bath heated to body temperature. The first experiment used the experimental setup of Sec. IV, which is shown in Fig. 5. The capsule was filled with 0.78g (0.36mL) of potassium bicarbonate powder and 0.9mL of liquid citric acid solution in the lower and upper chambers, respectively. The citric acid solution was made by dilution with water to the concentration required to obtain a water to reactants ratio of 1:2. The capsule was then placed into the dry, sealed mixing flask. An external magnetic field was used to activate the capsule, and CO_2 production was recorded at 1 minute intervals. After 5 minutes, at which point the reaction appeared to be approaching a steady state, 3mL of water were injected into the flask to mimic the moist environment of the colon. CO_2 output recording was then continued at the same frequency for an additional 10 minutes. Three trials of this experiment were performed at room temperature, and the final CO_2 output both before and after the addition of water is

TABLE III
TOTAL CO_2 PRODUCTION IN ROOM TEMPERATURE BENCHTOP EXPERIMENTS WITH THE PROTOTYPE INSUFFLATION CAPSULE BEFORE AND AFTER THE ADDITION OF 3ML OF WATER.

Trial	CO_2 Before H_2O (mL)	CO_2 After H_2O (mL)
1	91	167
2	88	156
3	102	168
Mean	94	164

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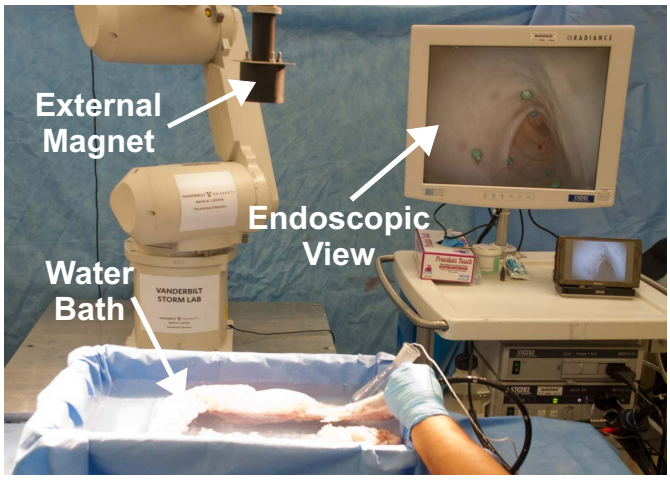

Fig. 11. Experimental setup for *ex vivo* insufflation capsule experiments, consisting of a heated water bath, an endoscope, and an external magnet attached to a robotic arm.

shown in Table III.

The second experiment consisted of two ex vivo trials using a heated bath, a fiber-optic endoscope, an image acquisition system, and an external magnetic field source for actuating the capsule, as shown in Fig. 11. In order to replicate both the temperature and pressure of a human colon, a porcine large intestine 5.5cm in diameter was immersed in a bath of water at body temperature (37°C) and constrained with suture to an acrylic sheet with holes in it, to maintain its position underwater in a configuration representative of a human colon. Note that the intestine was sealed, and no water from the bath was able to flow into the intestine. A pattern of 9 markers was arranged along the intestine, as previously done for the visualization experiment in Sec. II-A.

The capsule was then placed inside the intestine, 10cm past the group of markers furthest from the endoscope, and a robot arm with an attached external magnet was used to activate the capsule. A second, thin piece of acrylic was placed on top of the heated bath in order to limit the displacement caused by the magnetic attraction between the external permanent magnet and the magnets onboard the capsule, much like the skin and adipose tissue of a human would do. The endoscope was placed on the opposite side of the marker rings from the capsule and was used to observe the level of insufflation provided by the capsule.

In the first trial, an insufflation capsule with the same payload as in the benchtop experiments was placed in the colon. The robot was then used to bring the external magnet 10cm above the colon to activate the capsule, opening the valves. To verify that the valves could open and close as desired, the external magnet was repeatedly moved away from the setup and back to the activation position, and it was visually observed that insufflation started and stopped as desired. As shown in Fig. 12, the capsule successfully inflated a section of the colon surrounding it, measuring 3.18cm in diameter $\times$ 14.0cm in length. We observed that distention of the intestine to its full diameter (5.5cm) was not required to enhance visualization, which is consistent with results obtained

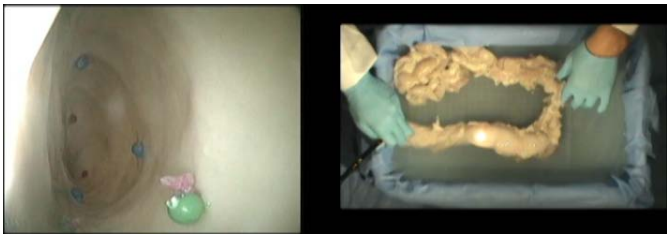

Fig. 12. Endoscopic view (left) and external view (right) demonstrating the level of insufflation provided by a single internal reaction capsule approximately four minutes after activation, at which point 6 of the 9 markers were visible.

in our visualization experiment (Section II-A). The images in Fig. 12 were taken approximately four minutes after the capsule was activated. Based on the dimensions of the inflated colon, we calculated the volume of CO_2 produced to be approximately 110mL, which is comparable to the insufflation observed prior to adding the additional 3mL of water to the glass flask in the benchtop experiments described earlier. With this insufflation level, 6 markers were clearly visible. We also note that there was very little foam, a byproduct of the reaction, generated by this capsule in the intestine (presumably due to the fact that the gas generated is forced through the orifaces), and what little foam was produced did not hamper the ability to view the intestinal lining, as shown in Fig. 12.

To test the ability of multiple insufflation capsules to work in cooperation to inflate the intestine, we conducted a second experiment in which three capsules were used simultaneously in the *ex vivo* colon. The same protocol was used as in the single capsule experiment above. In this case, the three capsules were close enough in proximity that they were all activated when the external magnetic field was introduced, but were not magnetically joined together when activated. One could also envision, however, moving the external magnet across larger distances if the capsules were further apart, which would cause the capsules to open one after the other. After one minute, 6 of the 9 markers could be viewed with the appropriate endoscope angle. Fig. 13 shows an endoscope image obtained four minutes after the initial activation, at which time 8 of the 9 markers were visible. We note that with slight endoscope manipulation, all 9 markers could be seen, though there was no single image in which we could see all 9 simultaneously. The length of intestine inflated was approximately 33cm, with a diameter of 3.8cm, leading to an estimated total CO_2 output of 375mL.

While the quantities of gas generated in both single and multiple capsule experiments are sufficient to enhance visualization and locomotion in light of the results in Section II, they are lower (approximately 75-90mL less) than benchtop reaction studies in Sec. IV would suggest. This might be explained by the possibility of potassium bicarbonate powder being ejected through the exhaust holes before being reacted with the citric acid solution. In this case, our total reactant volume would be lower, which would result in lower CO_2 output. Though we tried to ensure that all of the contents of both chambers were mixed by opening the valves multiple times, it is also possible that the citric acid solution com-

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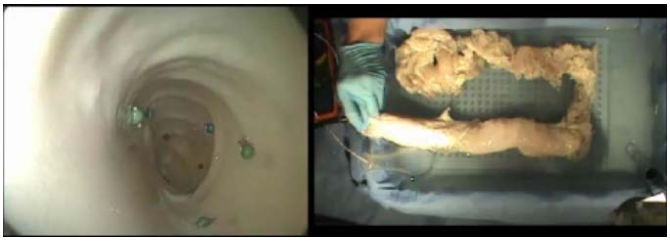

Fig. 13. Endoscopic view (left) and external view (right) demonstrating the level of insufflation provided by three internal reaction capsules approximately four minutes after the initial activation. At this point, 8 of the 9 markers were visible on the intestinal wall.

partment was not completely emptied into the lower chamber housing the potassium bicarbonate. This would also result in a lower volume of reactants, and would lower our expected CO_2 output. In comparing the capsule experiments alone, we observe that the capsules produced approximately 20mL more in the *ex vivo* tests compared with the benchtop tests. This is likely due to the increase from room temperature to body temperature since the reaction is endothermic.

VI. Conclusion

The experiments and prototype presented in this paper indicate that it is possible to carry a sufficient volume of reactants and water onboard a capsule to provide wireless insufflation useful for enhancing visualization and locomotion in the colon. Future studies will be needed to determine whether this can reduce the false negative rates of wireless capsule endoscopes in colon inspection and provide a screening method that will encourage more people to obtain recommended colon cancer screenings. Future studies will also be needed to determine if such insufflation can act as an adjunct to assist robotic capsules of various designs [13]–[15], [28], but this seems likely, given that robotic capsules are typically tested with endoscope-delivered insufflation assistance. One can easily envision how an insufflation capsule such as ours could be used as part of a multi-capsule platform where one or more capsules provide insufflation, while other capsules are used to acquire images, provide diagnostic functions, or deploy therapeutic intervention. With the ability to improve visualization and locomotion, it is likely that wireless insufflation capsules will enhance the diagnostic capabilities of capsule endoscopes and propel robotic capsules into an expanding variety of clinical applications.

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