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A Novel Cyber Physical System for 3-D Imaging of the Small Intestine *In Vivo*

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ABSTRACT Small intestine is the longest organ in the gastrointestinal tract where much of the digestion and the food absorption take place. Wireless video capsule endoscope (VCE) is the first device taking 2-D pictures from the lesions and the abnormalities in the entire length of the small intestine. Since precise localization and mapping inside the small intestine is a very challenging problem, we cannot measure the distance traveled by the VCE to associate lesions and abnormalities to locations inside the small intestine, and we cannot use the 2-D pictures to reconstruct the 3-D image of interior of the entire small intestine *in vivo*. This paper presents the architectural concept of a novel cyber physical system (CPS), which can utilize the 2-D pictures of the small intestine taken by the VCE to reconstruct the 3-D image of the small intestine *in vivo*. Hybrid localization and mapping techniques with millimetric accuracy for inside the small intestine is presented as an enabling technology to facilitate the reconstruction of 3-D images from the 2-D pictures. The proposed CPS architecture provides for large-scale virtual experimentations inside the human body without intruding the body with a sizable equipment using reasonable clinical experiments for validation. The 3-D imaging of the small intestine *in vivo* allows a lesion to be pinpointed for follow-up diagnosis and/or treatment and the abnormalities may be observed from different angles in 3-D images for more thorough examination.

INDEX TERMS Cyber-physical-system, video capsule endoscope, hybrid localization, body-SLAM, 3D reconstruction.

I. INTRODUCTION

Annually, over 3 million people in the US are hospitalized as a result of various GI diseases [1]. In recent years, inspired by the1966 science fiction movie the ''Fantastic Voyage'', a new wave of micro-robots (microbots) for discovery missions inside the human body have emerged in the health industry [2]–[5]. Wireless technologies, imaging techniques (live cameras, X-ray, and MRI) and magnetic field gradients can be used to assist in navigation, communication and control of these devices as they move along the human digestive tract or through the vascular tree. The wireless video capsule endoscope (VCE), which is the size of a large vitamin capsule and carries a video camera and an RF transmitter to transfer video information to the surface of the body, is perhaps one of the most popular precursors of these microbots, used for wireless gastrointestinal-tract (GI-tract) imaging. The first wireless VCE was developed by Given Imaging [5] and approved by the FDA in 2001. This device revived interest in the small intestine, which had been minimal because of difficulty in access. Since then, a variety of different VCE's have been developed to examine additional parts of the intestinal tract. It is now possible to capture high resolution images of the entire GI-tract in a noninvasive manner. These devices have one to four cameras, with frame rates varying from 2 to 38 frames per second, and they range in size from 26 to 31 mm in length and 11 mm in diameter. The images produced are of high resolution and enable the detection of intestinal bleeding and its source. VCEs have proven very useful in both diagnosing and in sequential follow-up of the therapeutic response to treatment of Crohn's disease [7]–[9]. In a typically eight hours long ''fantastic voyage'', the first generation VCEs that capture two 2D images per second,

produce a large data base of 57,500 images, approximately half of that from the small intestine, and use RF waveforms to carry the resulting 22 GB of information from inside to the surface of the human body to be stored for diagnostics of lesions and abnormalities inside the GI tract and in particular inside the small intestine where no other medical instrument can penetrate fully.

Ideally, RF signal transmitted from the microbot and the numerous pictures taken by the VCE should allow us to map the 3D path of movement of the microbot and use that to reconstruct the 3D image of the interior of the small intestine in vivo using 2D pictures taken by the VCE. However, the small intestine is a long twisted and convoluted organ with a length of 5-9 meters and a diameter of 2.5-3cm, occupying a relatively small area in the abdomen with dimension of around 20-30cm. Mapping its 3D path of movement accurately enough to reconstruct the 3D image of the small intestine requires very accurate millimetric localization precision inside the human body. This is a complex and extremely challenging problem because 1) the path of movement of the microbot inside the small intestine is very complex and unpredictable, 2) inside the human body is a complex non-homogeneous environment for RF propagation, and 3) repeatable experimentation inside the human body, needed for comparative performance evaluation of alternative algorithms, is formidable [10]–[12]. As a result, 15 years after the invention of the VCE [6] precision simultaneous localization and mapping science and engineering for the 3D path of movement for these microbots inside the small intestine is still in its infancy [13]–[15]. Without millimetric localization accuracy for the path of movement of a very long and small organ we cannot use the 2D pictures of the VCE to reconstruct the 3D image of the interior of small intestine. Consequently, we have ended up with a huge in vivo data base of 2D pictures from inside the small intestine collected from millions of patients but we have no clue of the actual shape and the 3D image of this vital organ in vivo.

In this paper we present a novel architectural concept for a Cyber Physical System (CPS) for simultaneous RF experimentation and 3D imaging inside the small intestine in vivo using 2D pictures taken by the VCE and RF signals carrying these pictures to the surface of the human body. To enable the 3D reconstruction, we present hybrid localization and mapping techniques inside the small intestine with millimetric precision using received RF signal in body mounted sensors and similarities among consecutive images from the VCE. The CPS architectural concept provides for a repeatable virtual experimentation inside the human body for design of optimal algorithms without introducing the human body with sizable equipment. The designed algorithm for path reconstruction is validated with limited clinical experimentations using a novel 3D X-Ray procedure. Since the VCE power budget is highly limited [56], [57], the proposed CPS allocate all computational load to the on-body units and off-body machines and there is no extra action required from the capsule pill. Such load allocation guarantees the adequacy of the power consumption and battery life of the VCE.

In the remainder of this paper we provide an overview of the CPS and explain how each element of the CPS can be constructed. Section two provides the elements and architecture of the CPS, section three explains how existing large data base of images and limited new clinical experiments with RF monitoring using body mounted sensors can be used for validation of algorithms, section four explain how we can model RF propagation inside the human body using existing software tools and how we can model motions of the VCE using consecutive images from the VCE, and section five explains the RF and visual emulation environment of the CPS. Section six is devoted to description of algorithms for simultaneous localization and mapping inside the human body (Body-SLAM) as well as algorithms for 3D reconstruction of the small intestine image using 2D picture from the VCE camera.

II. OVERVIEW OF THE CPS FOR 3D VISUALIZATION OF INSIDE THE SMALL INTESTINE

One of the fundamental challenges for designing an embedded system in a microbot, such as a VCE, for operation inside the small intestine is a lack of access to the environment for physical experimentation. Additionally, a major challenge to designing sophisticated localization algorithms for the VCE is that there is no ground truth of the path of movement of the VCE inside the human body to use as a reference for performance evaluation of localization algorithms. There are also no validated models for the movement of the VCE or propagation of the RF signal from the VCE in order to compare the accuracy of different algorithms against one another in a realistic manner. The CPS presented in this paper overcomes these problems and precisely maps the path of movements of the VCE in real living humans so that we can reconstruct the 3D image of the entire small intestine. The CPS incorporates the design of an emulation environment for RF propagation and a series of images taken along a known path with models for VCE motion and RF propagation. The first iteration of algorithms is designed in this emulated environment. The models for motion and RF propagation as well as the algorithms are then tested on a few patients to provide a feedback for subsequent design iterations. The feedback process continuously adjusts the existing models, emulation environment and algorithms with clinical data until satisfactory results are achieved.

Figure 1 provides an architectural overview of the CPS. First, the speed of movement of the microbot is modeled using similarities between consecutive VCE images (**Figure 1, modeling VCE motion**) of patients with follow-up clinical "explorations" of locations of abnormalities inside the small intestine using an existing data base of VCE images (**Figure 1, visual data**). The abnormalities discovered by follow up CadScan and X-ray can be used as landmarks for distance traveled to validate speed-estimating algorithms using image processing techniques. The motion model is then imported to a hardware platform for

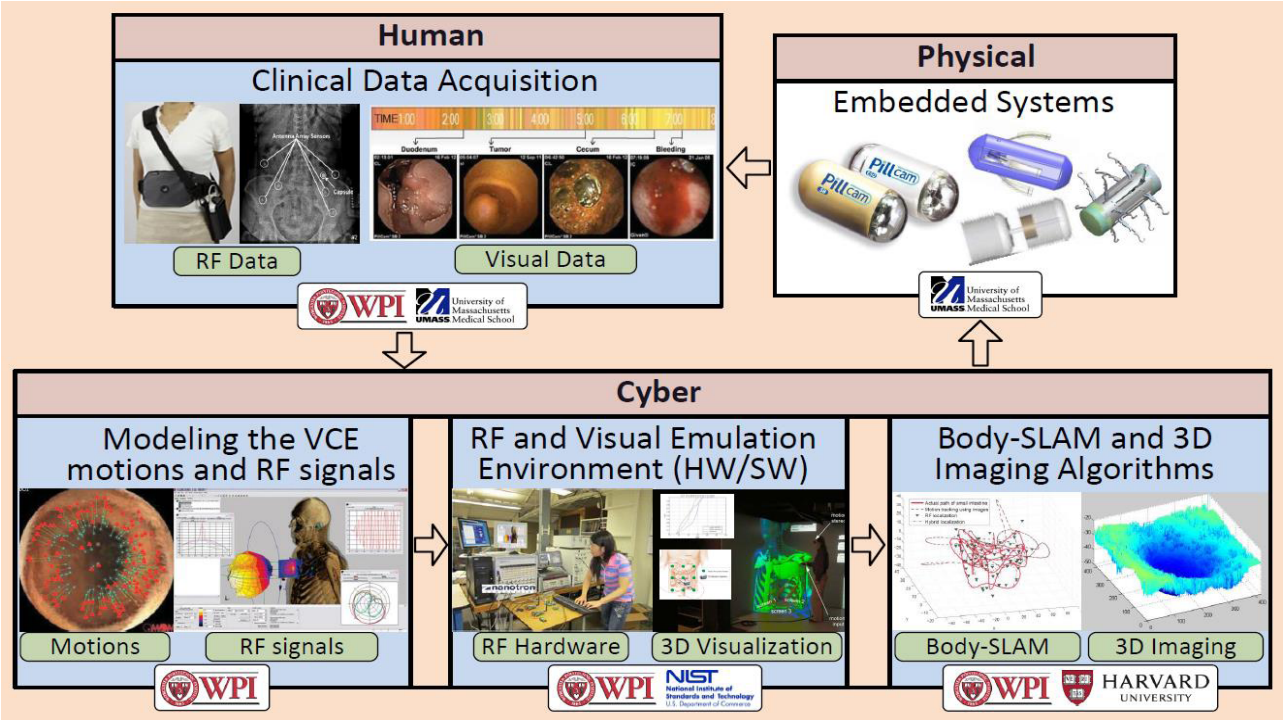

FIGURE 1. **Overview of the CPS for localization and distance traveled inside the small intestine.**

RF experimentation and a 3D visualization platform (**Figure 1, RF and Visual Environment**) to emulate a 3D shape of the small intestine allowing simultaneous emulation of the received wideband signal at body mounted sensors as well as the images observed by the VCE camera from any location of the known path of VCE movement. The heart of the hardware platform is a multi-port real-time RF channel emulator (e.g. PROPSIM C8) that is connected to the actual transmitter and receiver RF devices. This emulation environment is then used for modeling wideband radio propagation and designing the first iteration of the algorithm for Simultaneous Localization and Body-SLAM as well as 3D small intestine reconstruction algorithms which integrate the 2D images from the camera and the path of movement of the VCE (**Figure 1, Body-SLAM and 3D Imaging Algorithms**). The physical and the estimated location of the capsule along with the 3D images of the organs are imported to the virtual visualization platform. Using this segment of the CPS enable us to design and comparatively evaluate the performance of complex alternative algorithms in an emulated environment with known path of movement and 3D image of the small intestine as the ground truth. In this platform one can examine different alternatives for power efficient algorithms until the accuracy goal of a few centimeters in traveled length, needed by doctors for surgical operations, and a few mm in absolute 3D location estimate, needed for reconstruction of the 3D image, is achieved. Next stage is to examine these algorithms on human subjects to validate the accuracy and provide a feedback loop for next iteration of algorithm design.

The clinical study phase of the CPS begins by collecting synchronized visual and RF signals on limited human subjects (The clinical study phase of the CPS begins by collecting synchronized visual and RF signals on limited human subjects (**Figure 1, Clinical Data Acquisition**). This feedback loop allows the CPS to refine the RF model and the engineers to modify the algorithms until the precision requirements are also validated on the empirical data from real human. After completion of the design phase, the CPS can collect the 3D image of any patient for comparative studies of the shape of the small intestine or other educational and research applications. This is a scientific breakthrough in 3D imaging technology for the interior of small intestine using real 2D images of the microbot travelling inside the small intestine.). This feedback loop allows the CPS to refine the RF model and the engineers to modify the algorithms until the precision requirements are also validated on the empirical data from real human. After completion of the design phase, the CPS can collect the 3D image of any patient for comparative studies of the shape of the small intestine or other educational and research applications. This is a scientific breakthrough in 3D imaging technology for the interior of small intestine using real 2D images of the microbot travelling inside the small intestine.

III. CLINICAL DATA ACQUISITION

Since the ultimate performance of the proposed CPS largely depends on the quality of clinical data base, we start our discussion from the clinical data acquisition. In the initial

iteration of the CPS, clinical data acquisition uses a large data base of existing images to model the speed of movement of the microbot to be used in the emulated environment for the design of algorithms. Such data provides the simplest and most fundamental environment of the inside of small intestine. After that, in the following iterations, images with synchronized RF data will be acquired and applied to the system in order to further tune, evaluate and validate the algorithms.

Since the VCE was introduced to the market in 2001, several millions of them have been used on patients. This huge data base of pictures from inside the human body is waiting further processing and discovery. Specifically in our CPS, we employ the data base collected by Dr. Cave at the University of Massachusetts, which includes over 3000 patients from which 10-15% are annotated with follow up procedures. This database includes double tube experiments as well as a variety of capsules with different orientation and number of cameras.

For the existing data, it is necessary to associate the abnormality with its actual position, and four techniques can be used to validate the position within the abdominal cavity. (1) The VCE provides up to 55,000 images in jpeg format at 2 frames per second. These images are transmitted to a recording device in real time via an antenna attached to the patient's body. The resulting data are processed by proprietary software developed by manufacturers (e.g. Given Imaging Inc.) into a video which can be read by a trained observer at speeds ranging from single frame to full motion video speed. Since each image is associated with a timestamp, it is possible to identify the exact time when either a fixed point (landmark) such as the pylorus or ileocecal valve or an abnormality such as a tumor or site of bleeding is reached. In this way, the relationship of an abnormality can be related to the landmarks. However, this observation alone is inadequate for measurement of the distance because VCE movement is irregular within the G.I. tract. (2) Patients who are thought to have tumors on the basis of VCE usually undergo computed tomography (CT), which provides a 3D view of the entire small intestine and can localize the lesion anatomically. This technique can be enhanced by using orally and intravenously administered contrast agents to provide more accurate location for validating the motion estimation model. (3) The positional information measured from the previous steps can be further validated by deep enteroscopy. Deep enteroscopy is a new technique that employs two balloons or a spiral device [8] placed over a flexible endoscope which, when deployed in the small intestine, allows for pleating the small intestine on to the endoscope. Pleating effectively shortens the intestine, eliminates looping, and allows deeper penetration of the endoscope. It is usually possible to advance the scope up to 250 cm or more beyond the pylorus when it is inserted orally and up to 200 cm when inserted through the anus. As the scope reaches a point of interest, that point can be tattooed with India ink to facilitate localization at subsequent surgery or repeated VCE and to measure the distance from a fixed landmark such as the Ligament of Treitz [20 cm from the pylorus and readily seen at surgery but not by VCE] or ileocecal valve using a measuring tape to physically measure the location of a lesion with respect to the length of the small intestine. It is also possible to insert a metallic clip at the point of interest to enhance subsequent radiological detection. Such a clip attached to the mucosa eventually will drop off and be passed in the fecal stream. (4) Patients who have a VCE-detected lesion that requires surgery present the opportunity to physically measure its location with respect to fixed points in the small bowel during surgery. We can relate this measurement to the times of the VCE images using the algorithms and models described herein. Previously recorded images using each of these enhanced methods are available within the selected data set. Used alone, or in combination, they will permit the development of movement models and the validation of simulation, modeling and development of localization algorithms with enhanced use of radiofrequency tracking of small objects within the abdominal cavity.

Simultaneous acquisition of RF and visual data is more complex and it requires data acquisition hardware and multiple antennas mounted on the human body. There are only a few experiences with monitored RF signals at body mounted sensors that are reported in the literature. UMass Medical School have recently completed an IRB-approved pilot study with 30 volunteers designed to validate new software associated with a new video capsule (EC-10 from Olympus Corp, Tokyo, Japan) [12]. The software was designed to measure RF localization using TOA of the signal from the capsule in three dimensions. Validation was achieved by taking 5 sets of sequential abdominal images (AP and lateral) per patient at 15% of the standard dose required for routine abdominal digital radiographs. The capsule and 6 radio-opaque points on the antenna on the body surface were easily detected at the reduced dose (**Figure 1, RF Data**). Pairs of radiographs (AP and lateral view) were taken at 30 minute intervals after the capsule had passed the pylorus, as confirmed by the real time viewer on the data recorder. The time clock on the recorder and hence each digital image from the video capsule was synchronized to the time of each radiological image. The 3D (x,y,z) error as calculated for each of the 5 points was $\pm$ 2cm compared with that calculated by the software. This experiment demonstrated that clinical data acquisition for synchronized RF and visual data is feasible though it is very complex and expensive. The process involved human subjects; therefore, such experimentation has to be minimized. Our CPS follows the same procedure to validate the accuracy of our hybrid RF and visual Body-SLAM algorithm.

IV. MODELING THE VCE MOTION AND RF SIGNALS

The algorithms for Body-SLAM and reconstruction of a 3D image of the small intestine are designed based on the emulated visualization and RF propagation. These emulations rely on the accuracy of the models for motion and RF propagation (Figure 1). The emulation engine of the CPS (Figure 1; RF and Visual Emulation) begins with the motion

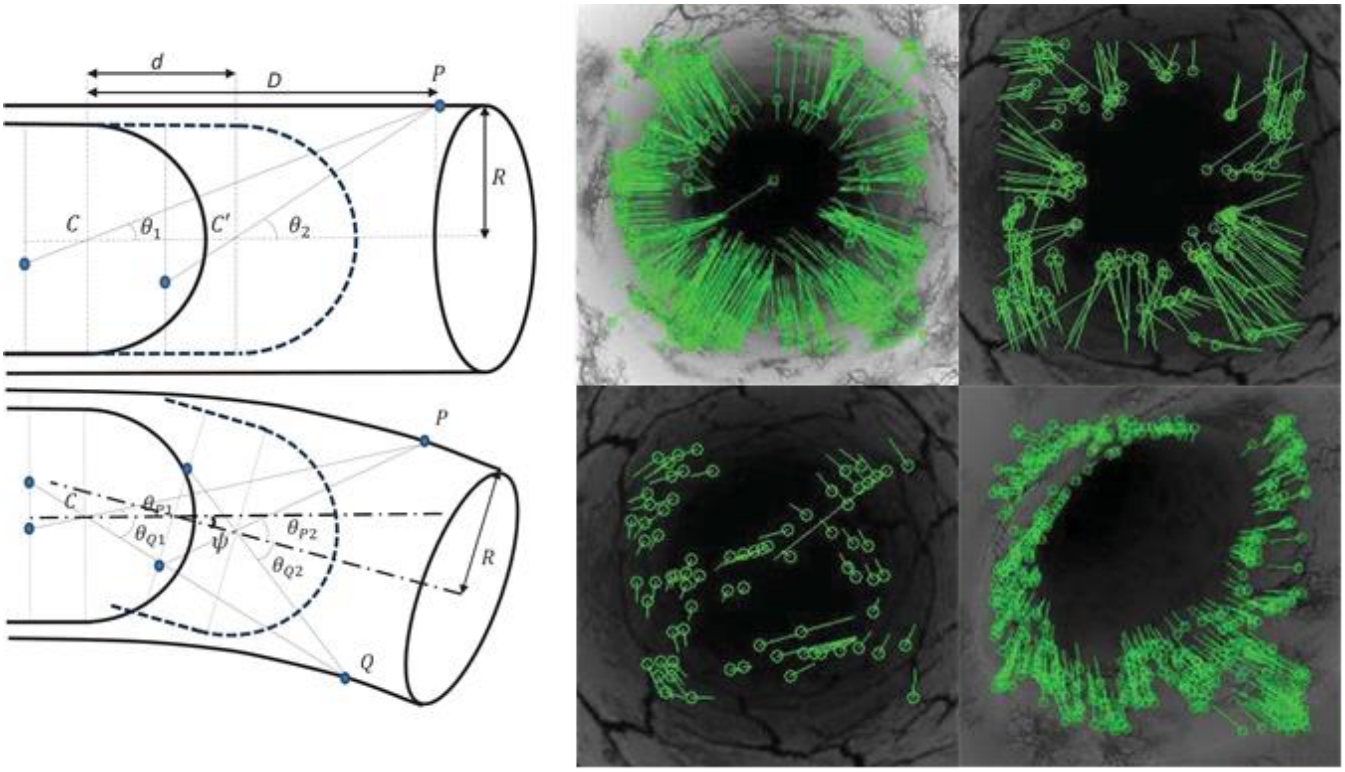

FIGURE 2. Feature extraction for estimating motion.

model of the microbot to specify its location on a given path of movement. From that location, the system emulates the images observed by the microbot's camera. The RF propagation models emulate features of the signals received from the microbot by the body mounted sensors. These models are exploited in the following emulation environment, which is then connected to development module for implementation of the algorithms.

A. MODELING THE MOTION SPEED OF THE MICROBOT

The speed of movement of microbot is highly complex. It is moved passively by peristalsis within a convoluted tube ranging in length from 5 to 9m. A typical microbot (e.g. VCE, Given Imaging, Yoqneam, Israel) is 11 × 26 mm and rigid, whereas the small intestine is soft, folded and distensible. Therefore, the capsule can move forward and backward, tumble and move toward or away from the body mounted sensors, presenting varying angles to the sensors. Despite these continuously changing positions, the mean transit time through the small intestine is remarkably consistent at about 4hr in the normal intestine [9].

To begin modeling this complex problem, we have used videos from patients who had received multimodal investigations to provide localization data that can be linked with RF measurements to validate location estimates in 3D [12]. A set of microbot's images of the small intestine from multiple patients can be used as the database on which to develop generalized statistical models for the movement of the capsule. As explained in the data acquisition section, we can use the pylorus (the beginning of the small-instine) as the landmark for distance and location measure in patients for whom the landmarks were localized using follow-up procedures to provide validated conclusive results. The patients should be selected to represent the maximum amount of diversity in the underlying anatomy and location of small intestine landmarks. We can primarily use video images obtained from the VCE augmented by information obtained from available CT scans, deep enteroscopy, and surgery in order to refine the models.

It is possible to extract visual features (**Figure 2**) on empirical data of the microbot images from the small intestine and use machine learning methods to: 1) model the speed of the microbot in individual patients as it travels through the small intestine; and 2) determine the differential angular movements of the microbot along the path of movement [14]. To model microbot speed, we began by modeling the movements with a bi-polar behavior consisting of moments of pause and motion with a constant speed [14]. Peristalsis is the major force that propels the capsule's transition. Peristalsis is a periodic contraction and relaxation of muscles that propagates in a wave down the intestinal tube. It propels the microbot capsule through the small intestine quickly but with variable velocity. During the breaks between waves of peristalsis, the capsule tends to stay still or move gradually with a small change in angle. Based on this observation, we modeled a bipolar speed movement for the speed of the VCE.

A Kernel-Support vector machine (K-SVM) classifier has been used in [16] to detect the two states (move, pause) of a capsule from a window of consecutive images that were reported by the microbot.

B. MODELING RF WAVEFORM TRANSMISSION INSIDE THE HUMAN BODY

A radio channel suffers from temporal, spatial and directional fading caused by human body motions and random variations of the multipath components carrying radio signals from one location to another. Inside the human body these multipath arrivals are caused by reflection and diffraction of the signal at the edges of the organs and the human body surface. In the literature for statistical measurement and modeling of the radio propagation, the wideband radio channel between a wireless transmitter and receiver is described by [17]:

$$h(d,t,\beta,\phi,\tau,\theta)=\sum_{i=1}^{L}\beta_i^d(t)e^{j\phi_i^d(t)}\delta[\tau-\tau_i^d(t)]\delta[\theta-\theta_i^d(t)] \tag{1}$$

where $h(d,t,\beta,\phi,\tau,\theta)$ is the overall channel impulse response at time t, between a transmitter and receiver that are at a distance d from one another; β_i^d, ϕ_i^d, τ_i^d, and θ_i^d are the amplitude, phase, delay, and angle of arrival of the i-th radio path, and L is the number of paths. Since the wireless microbot is travelling through the GI tract and the body-mounted sensors that are used as reference points for localization are always in small local motion caused by normal human functions such as breathing and walking, these paths and the channel impulse response are also functions of time and space.

In localization applications, either the received signal strength (RSS):

$$RSS(d,t)=\sum_{i=1}^{L}\left|\beta_i^d(t)\right|^2 \tag{2}$$

or time-of-arrival (TOA) of the first path can be used:

$$\tau_i^d(t)=c\times d \tag{3}$$

in which c is the speed of wave propagation which is the same as speed of light in free space.

Since the characteristics of the RF channel changes rapidly with time and location, empirical statistical models of these characteristics are developed for different applications and environments. In traditional applications for wireless access and localization in urban and indoor areas, the characteristics of the received signal are physically measured in different times and in numerous locations. These physical measurements are then used to model the stochastic behavior of the characteristic parameters. Massive RF measurements inside the human body is impossible so researchers resort to emulation of the RF propagation using direct solutions of Maxwell's equations in typical human body fabric using Finite Difference Time Domain (FDTD) [2], [10], [11]. Models for RSS or path-loss inside the human body can be obtained [18]–[20], which provide a model for path-loss and shadow fading. For the calculation of TOA, since for a given location of a transmitter and a receiver on the surface of the body, radio wave propagates through different organs and since the speed of propagation in each organ is different, the exact speed of the RF waves cannot be accurately estimated. In practice if we use an average speed of propagation, it causes another source of error in distance measurement [21], [22]. Both existing models for the RSS and TOA do not provide the spatial correlation of the RSS in neighboring points. The spatial correlation properties are needed for modeling a sequence of RSS or TOA characteristics as the microbot moves along the path of small intestine. Another model needed for the localization inside the human body is the effect of the body's normal functions such as breathing, heartbeats and other motions [23]. Integration of these models into the channel models for radio propagation from inside to the surface of the human body, which is needed for our application requires additional research.

V. RF AND VISUAL EMULATION ENVIRONMENT

The RF and visualization emulation environment uses the results of modeling of the VCE movement from clinical data (section 4.1) and RF waveform transmission modeling (section 4.2) to design and integrate a hardware/software platform for emulation of RF propagation and images taken by the VCE along a 3D anatomic image of the small intestine (**Figure 1, HW/SW Emulation Environment**). Once we can emulate RF propagation inside the body, and we have a 3D visualization system showing inside of the small intestine as well as the location of the capsule. Therefore, we can ''virtually'' visualize VCE movement on its path in the small intestine and compare the accuracy of complex alternative algorithms. The feedback path to the emulation environment of the CPS comes from limited clinical measurements on human subjects with RF sensors and VCE camera (**Figure 1, Clinical Data Acquisition**) to be used for fine-tuning of the models and adjustment of complexity of algorithms. This way the CPS allows validated virtual experimentations inside the body without intruding the body with sizable equipment and with reasonable clinical experiments.

Once the model for VCE motion and empirical models for radio propagation from the VCE are established, we need to import an anatomic path of movements for the VCE inside the small intestine so that we can analyze the waveforms received on the body-mounted sensors and generate the images that the camera takes as the capsule moves through the small intestine. Based on the 3D anatomic model of the large and small intestines (**Figure 3a**), we can generate a 3D Computer Aided Design (CAD) digital model of the intestinal tract (**Figure 3b**). We can use this image to track the path of the capsule (**Figure 3c**). An important and challenging part of this process is determining the path. We can trace the center of the intestine volume, which is similar to a curled tube, in order to model VCE movement using 3D image

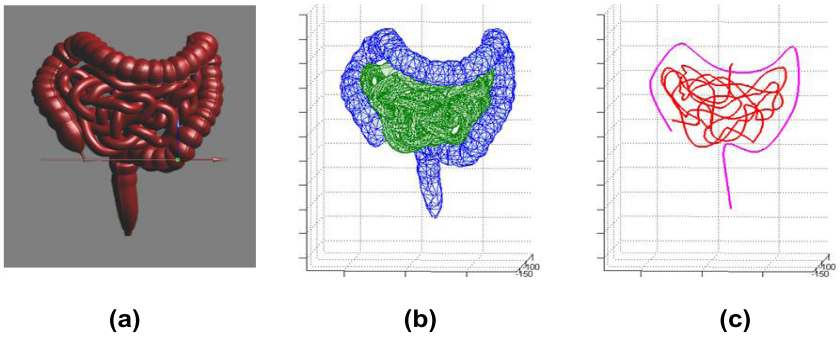

FIGURE 3. (a) The 3D model of the small and large intestine anatomy, (b) the 3D digittized CAD model and (c) the 3D model for the path of movement of the capsule.

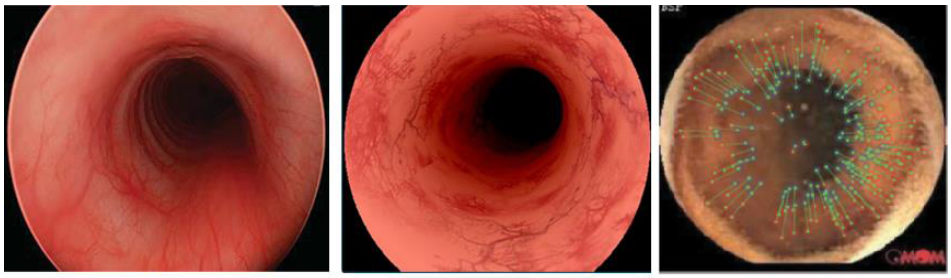

FIGURE 4. (a) a sample 2D image from the VCE (b) a 2D image taken from 3D reconstruction in the visualization testbed.

processing techniques. The large intestine has a very clear pattern that looks like a large hook, and so we apply the 3D skeletonization technique [24] to extract the path. Because the shape of the small intestine is much more complicated, we can develop an element sliding technique [24] to trace the path. Then, we can import the 3D digitized CAD model of the intestines (**Figure 3b**) into MATLAB and emulate a camera inside it to simulate the VCE images as the microbot travels along the small intestine.

In MATLAB we can add textures similar to the internal walls of the small intestine observed in the images sent from the VCE. (**Figure 4a**) shows a sample image from inside the small intestine of an eight-year-old child [25], (**Figure 4b**) shows an image from a camera inside the emulated small intestine [26]. This study demonstrates that we can simulate the images inside the intestines with reasonable textures. (**Figure 4c**) shows detected features of the images which are used for motion estimation algorithms described in (**Figure 2**) of section 4.1. The results can be visualized in a virtual platform, for example the one that exists at the NIST [19], [20], to visualize the movements of the capsule inside the small intestine.

To emulate the RF design environment to complement our visualization platform of the CPS, we can use a hardware channel simulation platform, for example PROPSIM C8 [27], [28]. The results of waveform transmission modeling can be used in RF channel emulation hardware. The channel emulator PROPSIM C8 can be used to emulate multiple RF channels representing the propagation environment between the microbot and multiple body mounted sensors. These channels will emulate the RF propagation environment between the VCE chipset development module and the sensor development modules.

The waveform observed by the sensors can be processed for detection of features of the signal pertinent to localization (RSS, TOA and DOA). These features of the signal will be used by RF localization algorithms in the next section to determine the estimated 3D location of the capsule. The location estimate will be reported to the visualization system and mapped on the virtual map of interior of the small intestine, along with the actual location provided by the movement model. Different sensor network topologies can be simulated by this testbed and used for real-time comparative performance analysis of alternative algorithms to achieve the desirable localization accuracies. Using the emulation environment of our CPS will allow comparative performance evaluation necessary for design and analysis for optimal solutions to the problem.

VI. BODY SLAM AND 3D IMAGING ALGORITHMS

The algorithm design unit of the CPS (Figure 1; Body-SLAM and 3D Imaging) takes advantage of the emulated environment and the path to design the optimum Body-SLAM algorithm for a given emulated environment. Initially, this

environment is an anatomic path and emulated pictures and it changes as we go along to the actual estimated path from a live human and reconstruction of the real interior of the small intestine of a live subject based on the images taken by the VCE and the RF data that is collected from sample human subjects. There are two sets of algorithms, (1) The Body-SLAM for simultaneous localization and mapping of the 3D path of the microbot using motion estimates from the images and 3D RF localization. (2) Algorithms for reconstructing the 3D image of the small intestine from 2D images from the microbot's camera.

A. DESIGN OF BODY-SLAM FOR HYBRID RF AND VISUAL LOCALIZATION

The theoretical accuracy of 3D RF localization inside stomach and intestines to demonstrate the feasibility of designing new algorithms for precise RF localization inside the small intestine is available in the literature. The theoretical Cramer-Rao Lower Bound (CRLB) of the variance of the estimation error for RSS-based localization inside these organs using path-loss models reported by NIST [18]–[20] is available at [21] and [22]. A novel model for the accuracy of the TOA-based localization affected by the non-homogeneous fabric of human tissues and the CRLB of the accuracy of TOA based localization using this model is also available at [21] and [22]. These works provide the theoretical bounds on the achievable 3D accuracy of RSS and TOA-based localization of the VCE as a function of number of body-mounted sensors in different organs. These results reveal that with eight sensors, we can attain accuracies of around 12 cm in 90% of locations for RSS-based localization, while TOA-based localization provides accuracies on the order of 2 cm. More importantly, TOA-based localization shows much less sensitivity to the increase in number of sensors that makes this approach more accurate, scalable and practical. These precisions can be improved by designing algorithms, which take advantage of hybrid localization to refine the multipath profiles. Most recent research work on CRLB for hybrid VCE localization shows that an overall accuracy of 1-2 mm in 3D and a few centimeters in estimated traveled length would be enabled by implementation of the combination of image based VCE tracking and TOA based RF localization [29]. (**Figure 5**) plots the hybrid localization accuracy against the VCE video frame counts. Given 10% of step estimation error and 10o of direction estimation error, the hybrid VCE localization only suffers from sub-millimeter level of in accuracy. The performance bound shows the feasibility of Body-SLAM algorithm and further research in this area is needed to determine different alternatives for implementation of the Body-SLAM to attain very precise localization needed for 3D reconstruction of the interior of the small intestine.

1) DESIGNING RELIABLE ALGORITHMS FOR RF LOCALIZATION

Desinging RF localization in non-homogeneous environments, such as human body, is at its infancy because channel

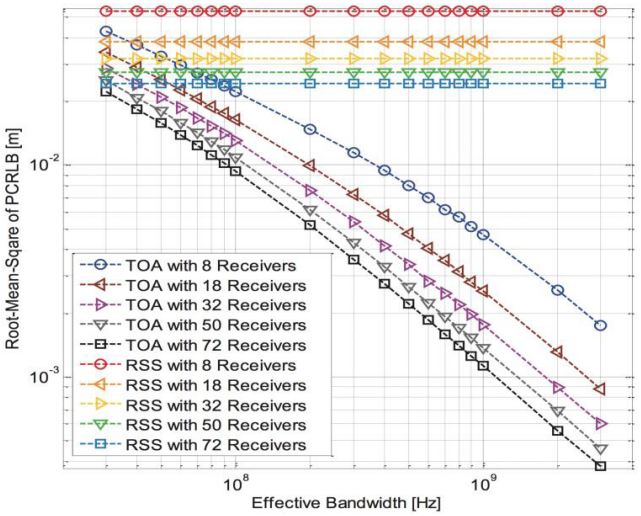

FIGURE 5. Pilot research on the theoretical performance bound for Body-SLAM algorithm with TOA ranging.

modeling for localization inside the human body is at its infancy. As previously explained, channel models are required to characterize spatial and temporal variation of the signal as a microbot moves along the intestine paths. With a reliable model for RF propagation one can work to find an algorithm for RF localization inside the human body that can achieve a 3D (x,y,z) accuracy of approximately a few centimeter. One candidate for reliable RF localization is Super-resolution algorithms to refine TOA signal bandwidth and achieve accurate estimate of direct path between transmitter and receiver. In severe indoor multipath environment, super-resolution algorithms have shown to be effective and they have the potential to resolve the multipath components in a bandwidth limited situation through advanced spectrum estimation techniques [30]. Since the FCC's MedRadio band [31], currently used in capsule endoscopy devices, only spans 5 MHz, super-resolution can be a proper approach to improve the localization accuracy for microbot application when TOA based estimates are employed. One needs to examine the effectiveness of super-resolution algorithms in resolving multipath arrivals caused by signal deflections on the boundaries of different organs to reduce the bandwidth requirements for achieving sufficient accuracy and precision to localize a microbot moving along the intestines.

Another candidate approach could be cooperative localization algorithms using relative location of reference points and multiple microbots inside the intestines. Cooperative algorithms are widely used for localization in challenging environments such as indoor areas [32], [33]. These algorithms use the relative location of a number of reference points with a few targets with fuzzy location estimates and use the relative location of targets with each other to determine an optimum location for all targets. Since endoscopy using multiple capsules has been examined for clinical purposes [9], this is an important class of algorithms to use for performance evaluation inside the human body. Preliminary results

for bounds on the performance of cooperative localization algorithms for RSS-based and TOA based localization [22] for the VCE are very promising. Further research is needed to modify these algorithms for cooperative localization to be applied to the microbot localization inside the intestines. One needs to administer different numbers of microbots in different time intervals and measure the improvement in the accuracy of localization. The outcome of this research is a robust RF localization algorithm that, when used on each set of waveforms for a given location of the microbot along the path, the algorithm can estimate the 3D (x,y,z) location of the capsule with approximately 1 cm of accuracy from its simulated location.

2) DESIGNING THE BODY-SLAM

It is well established that the data fusion of multiple independent location estimates can enhance localization performance to the maximum [24]. At the same time, two typical estimates of microbot location can be achieved including (1) dynamic measurement of microbot velocity and heading angles (see section 4.1), which can be used to track microbot but suffers from the drifting effect due to the accumulation of tracking error; (2) absolute RF based localization in (previous section), which suffers from the randomly fading nature of in-body RF channel. Once we combine the knowledge of microbot location from above mentioned independent sources, the disadvantage of each approach can be compensated by each other and microbot localization performance can be optimized from the perspective of non-linear filtering, and therefore, achieve ultimate microbot localization accuracy needed for reconstruction of the path of movement of the microbot.

The Body-SLAM algorithm integrates the RF localization algorithm discussed in previous section for the 3D (x,y,z) localization and motion estimation results from section 4.1. One can use Bayesian Updates [35]–[38], Kalman [15], [39] and particle filters for this integration to obtain the location and reconstruct the path of movement simultaneously. These algorithms leverage the drifting effect in VCE movement path estimation using velocity model with the 3D location estimates and vice versa. The results of applying these filters are very promising since these methods show the potential to smooth the localization path while reducing the 3D (x,y,z) error by up to an order of magnitude [15]. In the localization literature, these classes of algorithms are known as SLAM algorithms [34]. In our application, since we are using the algorithm for inside the human body, it is named as Body-SLAM algorithm [13]–[15]. With an order of magnitude improvement on the results of RF localization inside the human body, one should be able to reach accuracies within a few millimeter which allow a reasonable accuracy for reconstruction of the 3D path of movement of the VCE inside the small intestine. In the CPS validation and visualization of this performance is performed by comparing clinical data and emulated images. If the performance of Body-SLAM algorithms does not meet the benchmark, one may need to combine these algorithms with the inertial measurement techniques using micro gyroscopes, accelerometers and manometers to further improve the performance. A number of these techniques which have been examined for indoor geolocation and indoor robotics applications have also been tested for VCE localization [40]–[44].

3) CLINICAL VALIDATION OF THE BODY-SLAM ACCURACY

Our co-authors at UMass Medical School have recently completed an IRB-approved pilot study with 30 volunteers designed to validate new software associated with a new video capsule (EC-10 from Olympus Corp, Tokyo, Japan) [12]. The software was designed to measure RF localization using TOA of the signal from the capsule in three dimensions. Validation was achieved by taking 5 sets of sequential abdominal images (AP and lateral) per patient at 15% of the standard dose required for routine abdominal digital radiographs. The capsule and 6 radio-opaque points on the antenna on the body surface were easily detected at the reduced dose (Figure 1, RF Data). Pairs of radiographs (AP and lateral view) were taken at 30 minute intervals after the capsule had passed the pylorus, as confirmed by the real time viewer on the data recorder. The time clock on the recorder and hence each digital image from the video capsule was synchronized to the time of each radiological image. The 3D(x,y,z) error as calculated for each of the 5 points was $\pm$ 2cm compared with that calculated by the software. The CPS follows the same methodology to validate the accuracy of the hybrid RF and visual Body-SLAM algorithms used to reconstruct the 3D path of movement of the microbot inside the small intestine. Ultimately, the accuracy of this path is a guide to the measurement of true distance of a pathological lesion, detected by images, from a fixed point, the pylorus. The clinical data in the CPS provides a guide for refining models for motion and RF propagation as well as details of emulated visual platform used for design of algorithms. This set up allows for massive experimentation in a repeatable environment for algorithms design and limited experimentation on human subjects.

B. RECONSTRUCTION OF THE SMALL INTESTINE

In this section, we explain how one can design algorithms to utilize the robust in-body localization result from Body-SLAM algorithm and propose a systematic approach to construct the 3D representation of interior of small intestine environment. This algorithm synthesizes the VCE image stream to create discrete 3D surface model of small intestine wall and then exploit the predicted VCE movement path to reconstruct the 3D representation that can be used for anatomical visualization of interior of the human body by clinicians. Existing endoscopic based human organ 3D reconstructions require either the multi-view image sequences [45], [46] or the precise prior knowledge of camera movement path and organ shape [14], [15], [47]. Pilot researches on laryngoscope [48] show that it is possible to reconstruct the 3D representation of human airway with images manually taken from multiple views. Similar researches on cystoscopy [49]

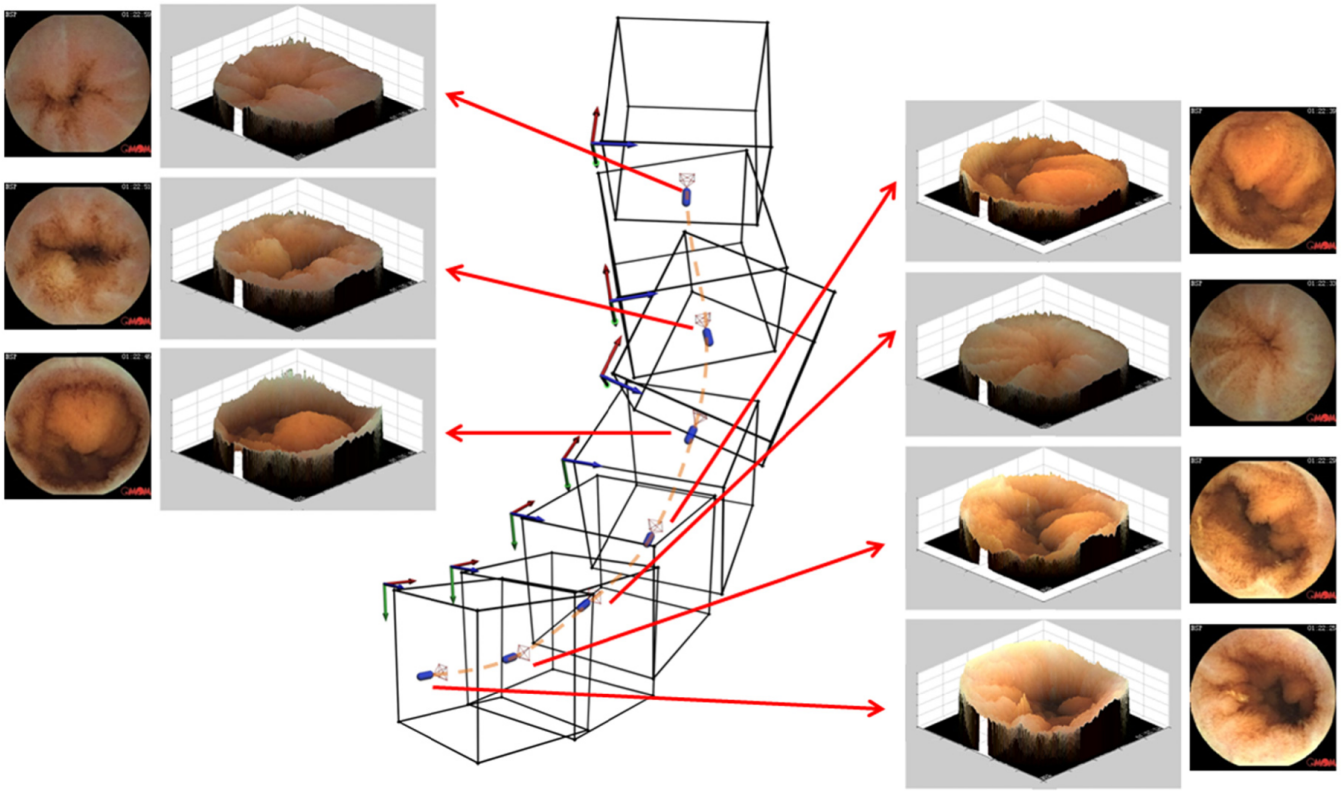

FIGURE 6. Discrete 3D surface model for individual VCE images along the movement path from Body-SLAM algorithm.

also illustrate that geometric constraints on the organ shape can benefit the reconstruction of human bladder. When trying to reconstruct the interior of small intestine, none of those two requirements can be completely satisfied. On the one hand, only monocular image can be obtained during the ''voyage'' of VCE since it passively goes through the small intestine and no manual actuation can be applied to the capsule. On the other hand, the estimated VCE movement path from Body-SLAM algorithm still suffers uncertainty. It is also worth mentioning that both cystoscopy and laryngoscopy based approaches work on relatively static and rigid scene while VCE based 3D reconstruction deals with dynamic and non-rigid scene caused by intestinal movement, which makes the problem extraordinarily complex and challenging demanding additional fundamental research.

1) PHOTO SYNTHESIS BASED 3D RECONSTRUCTION OF SMALL INTESTINE

Similar to most of the existing endoscopic based human organ 3D reconstructions, one can begin from single image Shape-from-Shading (SfS) [50], [51] algorithm to obtain individual depth map as the discrete 3D surface model (**Figure 6**). The discrete 3D surface model for each individual VCE image only contains relative depth information, which has an unknown offset from the reference plane. To calculate the offset, one can use a partial stereo monocular calibration approach using the camera location information from Body-SLAM algorithm. The partial stereo approach runs on the overlapped portion of two consecutive VCE images. To find the overlapped portion, Canny Edge Detection [52] (CED) with noise filtering can be applied to VCE images to get prominent and salient features and Coherent Point Drift [53] (CPD) algorithm may be used for non-rigid point matching. With a properly calculated offset, calibrated 3D surface model is obtained, which can be directly used in 3D reconstruction. Finally, using the estimated VCE movement path from the Body-SLAM algorithm, one may implement volumetric based dynamic registration and update algorithm to fuse the calibrated individual 3D surface models into a continuous and complete 3D representation of interior small intestine.

2) MODELING THE EFFECTS OF STEREO CAMERAS OF VCE

VCE design is experiencing the revolution from monocular camera to stereo camera in the pursuit of superior sharpness and resolution. Such revolution can also significantly simplify the aforementioned 3D reconstruction approach. VCE capsule with stereo cameras are already in the market, for example Given Imaging ''Colon2'' with two cameras on both ends of the capsule pill [54]; RF System Lab ''Norika3'' with 45o aligned rotatable camera [55]; or the latest RF System Lab ''Sayaka'' with stereo camera sets located in the middle of capsule pill, facing the intestine wall directly [56]. This revolution sets up challenges on understanding the

characteristics of stereo camera systems. The CPS for 3D representation of interior of small intestine is able to provide us a virtual environment to emulate the VCE behavior under various image processing related conditions including camera sampling rate, camera numbers, camera heading direction and camera locations on the capsule pill. One may begin the CPS operation with monocular camera, isolate each factor and establish statistical analysis on the localization error of alternative algorithms for the Body-SLAM. Then one may continue the investigation on 3D reconstruction with multiple stereo cameras until we reach satisfactory reconstruction accuracy. The analysis on stereo cameras can also guide the future direction of VCE capsule design and implementation.

VII. CONCLUSION

3D visualization of the small intestine in vivo using pictures taken from interior of this organ is a revolutionary technology for medical imaging, research and education in GI-tract. VCE's take clear pictures of small intestine at rates of at least two pictures per second, but precision of current localization techniques inside the human body cannot provide millimeteric accuracies needed for reconstruction of the 3D images from the 2D pictures. Precise localization in vivo inside the small intestine is difficult because we do not have any idea of the shape of the organ that governs the path of movement of the VCE, we have no model for the motions of the VCE inside the small intestine, we have no validated model for RF propagation inside the human body, and we cannot perform massive visual and RF experimentation inside the human body. We presented a novel concept for a CPS that can solve this challenging problem. The CPS models the motions inside the small intestine using sequence of images taken by the VCE and models RF propagation inside the human body using FDTD. Using these models, an anatomic path of movement for the VCE, and massive visual and RF experimentation, the CPS designs algorithms with 1-2 mm precision and applies them on limited human bodies with clinical experimentation to create their path of movement in vivo. The result of the clinical visual and RF experimentation is then used to refine models for motion and RF propagation to tune the algorithms until it reaches precision required for 3D reconstruction of the small intestine in vivo.

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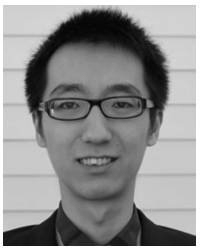

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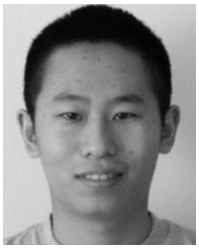

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