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A review of localization systems for robotic endoscopic capsules

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A review of localization systems for robotic endoscopic capsules

Trung Duc Than, Gursel Alici, Hao Zhou, Weihua Li

***Abstract*—Obscure gastrointestinal bleeding (OGIB), Crohn disease, Celiac disease, small bower tumors, and other disorders that occur in the gastrointestinal (GI) tract have always been challenging to be diagnosed and treated due to the inevitable difficulty in accessing such a complex environment within the human body. With the invention of wireless capsule endoscope, the next generation of the traditional cabled endoscope, not only a dream has come true for the patients who have experienced a great discomfort and unpleasantness caused by the conventional endoscopic method, but also a new research field has been opened to develop a complete miniature robotic device that is swallowable and has full functions of diagnosis and treatment of the GI diseases. However, such an ideal device needs to be equipped with a highly accurate localization system to be able to exactly determine the location of lesions in the GI tract and provide essential feedback to an actuation mechanism controlling the device's movement. This paper presents a comprehensive overview of the localization systems for robotic endoscopic capsules, for which the motivation, challenges and possible solutions of the proposed localization methods are also discussed.**

***Index Terms*—localization, microrobots, tracking, wireless capsule endoscope.**

I. Introduction

ENDOSCOPY is a medical procedure used to examine and inspect the interior of a human body. In the 1960s when fiber optics were discovered [1], the flexible endoscope became a vital tool for diagnosing gastrointestinal (GI) diseases [2]. According to a study conducted in 2002, approximately 19 million people in the United States were estimated to be affected by disorders of the small intestine [3]. This statistic indicates that effective advancements in endoscopy technology are extremely worthy of investigation. The conventional techniques for examining the GI tract adopt a long flexible tube with a light and a miniature camera at the end. This equipment can be inserted through the mouth or the anus into the digestive tract. Owing to its rigidity and large diameter, it causes much pain and discomfort to whoever undergoes this procedure, especially when the endoscopists are not well skilled. This generally limits the willingness of patients to have their GI tract examined by the technique. Furthermore, the lack of capability to reach the entire small intestine [4], which is the longest part, is also a significant shortcoming of the current wired endoscope.

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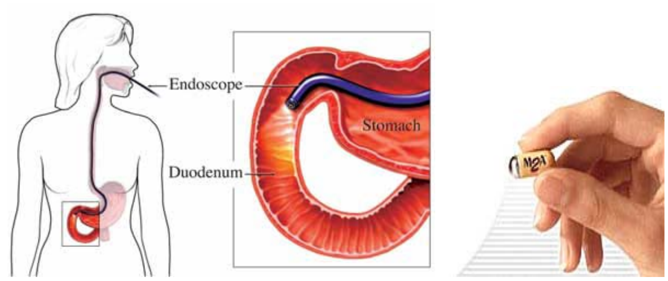
Wireless Capsule Endoscope (WCE), a significant step in the efforts of developing a more effective endoscopy technique, was invented to overcome the limitations. WCE is an ingestible pill-like device that contains a tiny camera and an illuminating system for capturing images and a transmission module for sending the images wirelessly to external receivers [5]. Being an innovative technique without cable connection, WCE offers a patient-friendly, non-invasive and painless investigation of not only the entire small intestine but also other GI parts [6-7]. Figure 1 shows the size of a commercial endoscopic capsule compared to the long shape of a traditional cabled endoscope. To date, it is reported that over 1,250,000 patients have benefited from WCE examinations all over the world [8].



(a) (b)

Fig. 1. (a) Conventional endoscopy (http://cjccorp.com).
(b) The first Given M2A capsule.

Since the introduction of the first wireless endoscopic capsule in 2000 by Given Imaging Ltd [9], this revolutionary approach has become an important field of research for engineers and physicians. Thanks to the potential benefits of capsule endoscopy, there have been a large number of innovative methods and modules proposed to improve the diagnostic and therapeutic capabilities of the swallowable capsules [10-11]. These innovations include: attempts at sufficiently accurate localization; active locomotion; enhanced power efficiency and data rate of wireless telemetry; quality improvements in endoscopic images; enabling intervention capabilities; and powering capsules wirelessly [12-13]. In favor of having a clear perception of one particular aspect among those perspectives, this paper will focus on reviewing past and ongoing research on localization systems for WCE.

Accurate knowledge of the position and orientation of the capsule when it moves along the GI tract is essential for endoscopists to identify where the endoscopic images are captured. The effect of drug administration, follow-up interventions and other therapeutic operations depend heavily on the accuracy of this spatial information [12]. Therefore, having a precise and reliable localization system plays an important role in enhancing the benefits of WCE. The methods for determining the capsule location which have been investigated so far are categorized into two groups: magnetic-field-strength based methods and electromagnetic-wave based methods. These will be discussed in Sections II and III of this paper, respectively. The overall aim is to highlight the advantages and disadvantages of the key localization methods reported before and to identify the fundamental and applied research issues in front of the current and future localization systems.

II. Localization Methods Based on Magnetic Field Strength

In the last decade, magnetic tracking methods for WCE localization systems have attracted the attention of researchers, as compared to other methods, for two main reasons. Firstly, static and low-frequency magnetic signals can pass through human tissue without any attenuation [14]. Secondly, magnetic tracking is a non line-of-sight method, in which the capsule does not need to be in the line of sight with magnetic sensors in order to be detected [15]. Consequently, the advantage of the negligible interaction between the magnetic field and the human body is not only exploited by those who are interested in localization systems, but also by those who focus on actuation systems. This is proved by a number of current efforts trying to design locomotion systems that can guide endoscopic capsules magnetically such as robotic magnetic steering [16-18], helical propulsion by a rotational magnetic field [19-22], magnetic levitation [23-24] and remote magnetic manipulation [25]. In addition to the medical purpose of locating diseases in the gastrointestinal tract, a localization system is also used to provide feedback for an actuation system [10]. Therefore, the actuation and localization systems must work together during a diagnostic procedure. However, one of the most challenging problems is the conflict between the two systems due to the interference of the two applied magnetic fields [26]. A few research groups have introduced methods that can avoid this conflict [16, 27], whereas others seem to ignore the influence of the magnetic actuation. Therefore, the tracking systems in this category are classified into two sub-groups, which are the magnetic localization for passive capsule endoscope and the magnetic localization for active actuation systems.

A. *Magnetic localization for passive capsule endoscope*

The two most important devices in a magnetic tracking system are a magnetic source and a sensor module. Depending upon how the magnetic source are created and whether the capsule acts as a field generator or a sensing module, the localization systems in this group are divided into three subsections.

Utilization of a permanent magnet enclosed inside a capsule

A stable and reliable source of magnetic field is essential for any real-time magnetic tracking system. A permanent magnet is such a source. Thanks to its capability of creating a steady magnetic field without batteries. The majority of the magnetic tracking systems generate magnetic field through integrating a permanent magnet inside the capsule. As magnetic flux intensities originating from the magnet vary their magnitudes and directions depending on the magnet's location and orientation, magnetic sensors are placed outside of a patient's body to measure these persistent magnetic signals. Based on a mathematical model of the small magnet, equations that represent the relationship between magnetic field strengths measured by the sensors and the position and orientation of the magnet can be established. In some cases, when the magnet is assumed to behave as a magnetic dipole, the magnetic flux intensity around the dipole source can be expressed by the following formula [28]

$$\vec{B} = B_x\vec{i} + B_y\vec{j} + B_z\vec{k} = \frac{\mu_0}{4\pi}\left(\frac{3(\vec{m}\cdot\vec{r})\vec{r}}{|\vec{r}|^5} - \frac{\vec{m}}{|\vec{r}|^3}\right) \quad (1)$$

where B_x, B_y, B_z are the three components of the magnetic flux intensity, is the magnetic dipole moment of the magnet, is the position vector of the magnet, and is the air magnetic permeability ($4\pi \times 10^{-7}$ J $A^{-2}m^{-1}$). From (1), it is possible to compute the localization parameters of the magnet, which are also referred to those of the capsule, by solving the inverse problem through an appropriate optimization algorithm.

One of the earliest systems that has employed such a technique for monitoring the gastrointestinal transit of a capsule is the tracking system presented by Weitschiles *et al*. [29-30]. The Magnetic Marker Monitoring (MMM) implemented in their method utilized a 37-channel, Superconducting Quantum Interference Device (SQUID) sensor system above a volunteer's abdomen. The position resolution was recorded as within a range of millimeters. However, it was reported that the monitoring procedure had to take place in a magnetically shielded room to reduce errors from environmental magnetic noise. Moreover, orientation data of the capsule, which is essential for locating pathological tissues and for capsule movement control loop [10], was not considered. Taking this into account, Schlageter *et al.* [31-32] introduced an approach using a 2D-array of sixteen Hall sensors to determine both position and orientation of a pill-size magnet coated with silicone. When the magnet with the volume of $0.2cm^3$ moved within the distance up to 20cm from the sensor plane, its position and orientation parameters were displayed in real-time at the rate of at least 20 times per second. Nevertheless, since the magnetic field strength decreases rapidly as the distance increases due to their inverse third power relationship, moving the magnet away from the sensor array leads to a significant drop in the system's accuracy. Therefore, enlarging the localization distance is one of the most desirable improvements for this method as the abdomen thickness of overweight subjects is usually larger than 20cm.

Adopting the idea of using a 2D magnetic sensor array, Chao *et al.* [14] solved this drawback by developing a 50cmx50cmx50cm cubic sensor array instead of only one sensor plane. This cubic sensor array is formed by two pairs of facing sensor planes, as seen in Figure 2. On each of the four sensor planes, they also installed sixteen magnetic sensors in a fixed uniform interval. The 3-axis magnetic sensor, Honeywell HMC1043 sensor, was used because of its high resolution and sensitivity to the Nd-Fe-B magnet. The system achieved an average position error of 1.8mm and orientation error of 1.6^{o} when the capsule, which enclosed a cylindrical magnet with the size of Φ5mm x L6.0mm, moved in the inner space of the sensor cube. In order to increase the system accuracy, different system developments had been investigated, such as the establishment of an innovative optimization algorithm which combines linear and nonlinear algorithms [33-36]; the implementation of efficient calibration procedures for the entire system [37-38]; and the evaluation of different sensor arrangement schemes in 3D space [39-40]. Although the accuracy and detecting volume of the system were improved noticeably, adding three sensor planes would quadruple the cost and complexity of the system.

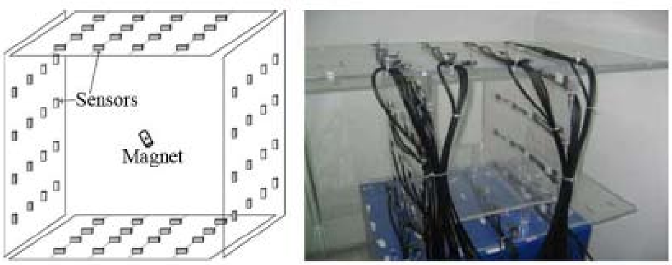


Fig. 2. A scheme of the cubic magnetic sensor array and its setup. [14].

In terms of cost, Aziz *et al.* [41] proposed a tracking system that employs only three 3-axis Honeywell sensors, HMC2003, placed orthogonally in 3D space and an extra sensor for cancelling environmental magnetic noise. However, due to system simplicity and insufficient measurement data, this technique could not provide a reasonable accuracy. An error of up to 3cm occurred when a Φ5mm x L6.0mm cylindrical magnet was tested in a volume of 10cm x 10cm x 10cm. In terms of portability and flexibility, on the other hand, Wu *et al.* [42] built a wearable magnetic locating and tracking system that allows patients to make basic movements with different postures during diagnostic procedures. They designed a wearable vest which has the coverage of about 40cm length x 25cm width x 40cm height and consists of six sensing modules at the front frame and the other four at the back frame, as shown in Figure 3. Each module is composed of six linear Hall-effect sensors A1321 which form 3 pairs of back-to-back sensors arranged perpendicularly to each other in 3D. With this mechanism, each pair is responsible for measuring one dimension of the magnetic field. In their design, the top two modules at the front were employed to eliminate the interference of earth magnetic field. Being placed far enough from the stomach region, they cannot detect any magnetic signals originating from a small (Φ5mm x L3.0mm) cylindrical magnet assembled inside the capsule. Therefore, by comparing the dynamic data measured by the two modules during the procedure with a set of quiescent data which was collected in different postures of the patient when the capsule was not swallowed, the current posture could be matched approximately in the quiescent data set. As such, an appropriate amount of earth magnetic field strength was subtracted from the dynamic data to accurately calculate the localization parameters of the capsule. Tracking errors were below 10% when they performed trial tests on volunteers. Since the localization algorithm is based on the mathematical model of a magnetic dipole, when the capsule is close to the sensing module, this model is no longer correct which results in a decrease in the system's accuracy [42].

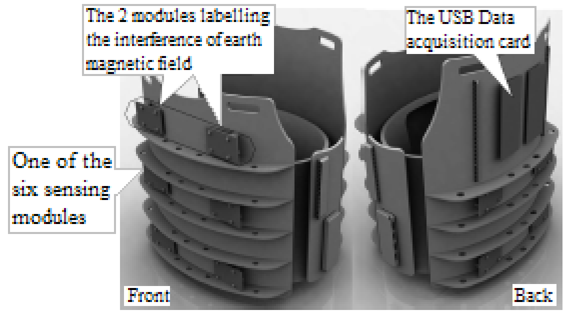


Fig. 3. Wearable sensing modules by Wu *et al*. [42].

Utilization of a secondary coil embedded in a capsule

Alternatively, the spatial information of the capsule can be obtained through utilizing a coil enclosed inside a capsule. The idea of tracking a receiving coil by a large 2-D array of transmitting coils was first proposed by Plotkin and Paperno [43-44]. It was then also exploited in the commercial Aurora tracking system [45]. In this technique, the field seen by the receiving coil is

$$\vec{B}_r = \vec{B}_t \cdot \vec{M} \qquad (2)$$

where is the magnetic moment of the receiving coil, is the magnetic flux intensity generated by the transmitting coil. Since can be expressed approximately by (1), computing the localization data in this case is similar to that of a permanent magnet. In other words, an optimization algorithm, such as Levenber-Marquardt, needs to be employed to solve the inverse problem for (2) once the electromotive force induced in the receiving coil has been measured.

Applying the idea to WCE, Nagaoka and Uchiyama [46] designed a single-axis coil made by 160 turns copper wire with the size of Φ6.5mm x L2.3mm to be inserted into a capsule. A magnetic field generator placed outside the body generated five alternating magnetic fields that operate in five different frequencies in order to calculate the coil's rotational position. The data of the electromotive force created by mutual induction was sent to the outer detector through transmitting 75 kHz signals from an integrated FM circuit. Owing to the fact that the magnetic field strength decreases proportional to the inverse third power of the distance between primary and secondary coils, the current flow in the primary coils was controlled automatically to keep the induced electromotive force at a constant range. To implement this function, a power amplifier was connected to the generator. The received data at the detector was not only used for computing the capsule's position but was also used for providing feedback signals continuously to the input of the power amplifier. Since the capsule is not able to move with a high speed in the GI tract, such feedback does not affect the tracking rate of the system [46]. Although it was reported that the system demonstrated an accuracy of 5mm when the capsule was up to 500mm far away from the generator, the experiment failed at several locations.

Utilization of a 3-axis magnetoresistive sensor mounted inside a capsule

Contrary to the methods in which a permanent magnet or a coil is embedded in the capsule, Guo *et al.* [47] developed another solution for the localization problem by sealing a HMC1023 3-axis magnetoresistive sensor inside a capsule to measure the intensity of the external magnetic field generated by three energized coils fixed on the patient's abdomen. The three coils are excited in turn by square waves with the same period of 0.03s. At the end of every cycle, there is a break period of 0.1s when the coils are not activated to estimate the earth's magnetic field magnitudes. The researchers then subtracted this value from the total magnetic field measured by the sensor at the capsule location to acquire the real data of the magnetic field generated by the coils. By means of a neural network algorithm, the three positional coordinates and three angles of the sensor which are also those of the capsule can be estimated. However, it is not a real-time tracking system as the calculation procedure was performed only after the completion of the experiments when all the data had been sent to a receiver by RF signals and stored in a flash memory. On the other hand, when the sensor is close to the coils (less than 50mm), the magnetic dipole assumption fails which causes a significant error in the experimental results. This situation becomes even worse if the coils' diameters are increased for enlarging the localization range [47]. Therefore, an improved localization model based on Biot-Savart Law was proposed to replace the magnetic dipole model [48]. The position and orientation errors reported vary from 6.25mm to 36.68mm and from 1.2^0 to 8.1^0 in the range of 0 to 0.4m. In addition to the effort of developing the system, this group also introduced an alternative method which employed eight energized coils excited by sinusoidal signals instead of square waves [49]. The experimental results after implementing an adaptive particle swarm optimization technique resulted in 14mm and 6.9^0 mean errors for position and orientation, respectively.

Discussion

Despite the mentioned advantages of magnetic tracking, the magnetic localization systems presented in Section II.A have some common drawbacks. To begin with, in order to apply the systems to medical clinics with the same accuracy as tested in laboratory experiments, all devices or equipments around them must be made of non-ferromagnetic materials. A small piece of a ferromagnetic bar unintentionally inserted into the detecting area could lead to a failure in locating the capsule with precision [50]. Secondly, due to the size constraint of the capsule to be swallowable, the limitation in tracking coverage for the systems based on permanent magnet tracking is also a significant disadvantage [51]. Last but most importantly, as previously stated, the question of how to remove the interference between magnetic localization and magnetic actuation is still to be answered. Making use of time division, i.e. activating and deactivating the operation of each system respectively and repeatedly, has been suggested [26], yet there are a few potential serious issues behind it. Owing to the hysteresis characteristics of magnetic field, the external magnetic field in the actuation mechanism is still available for a certain period of time after it has been turned off. As a result, a real-time localization would not be realized because the magnetic tracking system would have to wait until the external magnetic field has completely vanished to be put back into work again. Moreover, during the waiting period of the magnetic actuation, the capsule will likely move to a different position and orientation. In that case, the tracking system would not serve as a feedback system for the actuation system. Another solution for this problem, which involves taking advantage of high-frequency alternating magnetic field [52-53], will be discussed in detail in the next section.

B. Magnetic localization for active actuation systems

In the previous section, the mentioned localization methods were developed in the absence of actuation systems. In this section, magnetic localization systems that were designed to work effectively with their own magnetic actuation mechanisms will be evaluated.

Localization method based on high-frequency alternating magnetic field

In order to actuate the capsule magnetically, Olympus group [52] adopted the use of a spiral structure on the surface of a capsule in which they integrated a permanent magnet. Three pairs of coils were placed in three perpendicular axial directions to generate an external rotating magnetic field around the patient's body. Thanks to the spiral structure, rotating the capsule by applying this magnetic field on the magnet can propel it forward or backward. The frequency of the rotating magnetic field should not be higher than 10Hz because the capsule is not allowed to move too fast in the GI tract. Due to the fact that the low frequency (several Hz) rotating magnetic field does not influence the high frequency (from 1kHz to 1MHz) alternating magnetic field [52], the Olympus group employed the latter for addressing the problem of determining the position and posture of the capsule. For this localization purpose, exciting coils were built around the patient's body to produce the high frequency magnetic field. The operating frequency used in this system was chosen in the range of 1kHz to 1 MHz to avoid the absorption of the living tissue. A small coil was arranged inside and at one end of the capsule, forming a resonant circuit. Its direction is predetermined and set in the longitudinal direction of the capsule body. Based on the phenomenon of mutual induction, an induced magnetic field is also generated in the small coil. Hence, they built detecting coil arrays around the patient’s body to determine this induced magnetic field. The total magnetic field measured by the detecting coil arrays is [52]

$$\vec{B}_{total} = \vec{B}_{exciting} + \vec{B}_{resonant} \tag{3}$$

where is the magnetic field generated by the exciting coils, and is the magnetic field generated by the small coil. From (3), the strength of the magnetic field generated by the small coil can be calculated by subtracting the magnetic field generated by the exciting coils from the measurement magnetic field , Since is a function of the position and orientation of the small coil, it is possible to estimate localization information of the capsule. As reported in [54-55], this technique could achieve a detection accuracy of a sub-millimeter order when the resonant circuit, considered as a marker, was placed within the area of y=120mm from the detecting coil array. In this magnetic motion capture system, the detecting coil array, which is located 285mm far from the exciting coil, is composed of 25 pick-up coils positioned at 45mm intervals as shown in Figure 4. The marker has a size of 3mm in diameter and 10mm long with 250 turns. It was designed to work at a resonant frequency of 306 kHz.

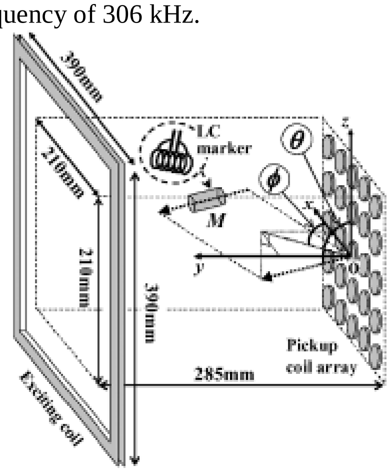


Fig. 4. The scheme of the motion sensing system by Hashi *et al*. [55]

To avoid the magnetic interference between the actuation and localization systems, a similar idea of using high frequency alternating magnetic field was also introduced by Graummann [53]. However, instead of using an integrated coil, a detector was inserted inside the capsule to measure this magnetic field. The measurement values were then sent to an exterior of the patient by a transmitter unit to calculate the localization data. Compared with the Olympus tracking system, this system consumes more power and takes more space of the capsule because it contains an additional microcontroller unit and a transmitting unit.

Localization method based on inertial sensing

Another way to move the capsule is via magnetic steering. Ciuti *et al.* [16] utilized a 6 degree-of-freedom robotic arm to carry a permanent magnet at the end-effector as shown in Figure 5. Four cylindrical magnets were mounted uniformly on the body of a capsule in order to create a magnetic link between the body and the external permanent magnet. By this design, the capsule can be dragged and steered effectively with the assistance of the magnetic interaction. The translation and rotation of the capsule are as desired only if the magnetic link is calibrated well, i.e., the internal magnets are aligned properly to the external magnetic field. Therefore, the capsule position, and its pitch and roll play an important role on the efficacy of this method.

For the localization function, a 3-axis accelerometer LIS331DL was inserted into the capsule. This inertial sensing not only provides the approximate location and orientation of the capsule in the digestive tract, but also provides feedback to the actuation system to preserve a reliable magnetic link between the external permanent magnet and the capsule. At first, a rough position estimate was obtained by magnetic scanning which involves moving the end-effector above the patient’s trunk to find the internal magnets. Before being detected, the capsule mostly stays still and thus the accelerometer output is almost zero. The internal magnets are then lifted towards the end-effector by magnetic attraction force as soon as they are close to each other. This sudden action is easily recognized since it results in an acceleration pulse on the output plots of the sensor. After successfully locating the capsule, pitch and roll data from the inertial sensor is used for orientation alignment of the two magnetic fields. The alignment is completed when any angular changes to the end-effector lead to an equivalent adjustment in the capsule. It is reported that the sensor could provide an orientation accuracy of 6^o. After the calibration procedure is completed, the position of the capsule can be estimated based on the position of the end-effector as long as the magnetic link is still maintained during the steering process.

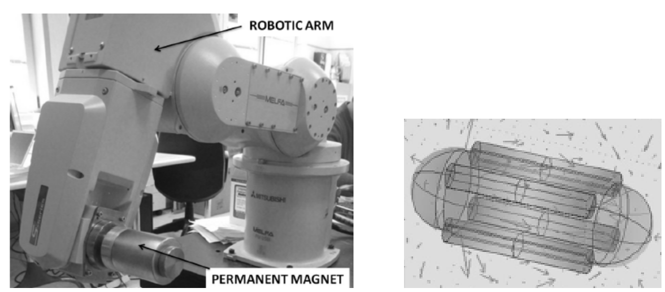
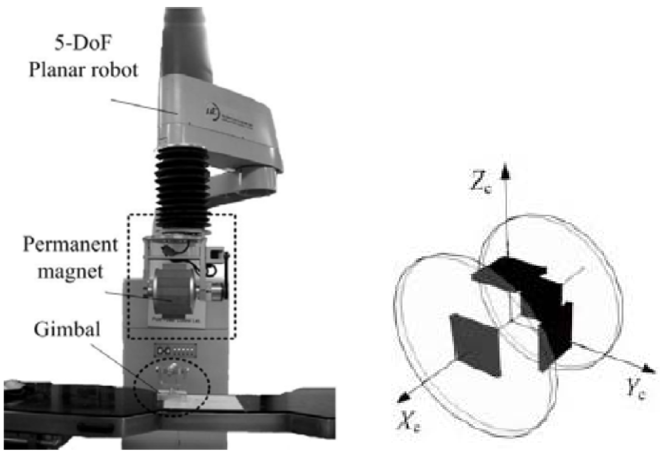


Fig. 5. A permanent magnet mounted at the end-effector of a 6 DOF robot and 4 cylindrical permanent magnets sealed on the capsule surface [16]

In this system, the conflict issue between actuation and localization does not exist. Instead, the actuation apparatus is also involved in locating the capsule. Nevertheless, it would be hard to make a compact capsular mechanism to be swallowable with the integration of an inertial sensing subsystem and four cylindrical magnets. Additionally, this localization technique only offers rough spatial information (an average error of 3cm) without data in a vertical direction. When the capsule stays in an unconstrained organ, it will be dragged first before being lifted which would cause errors in position estimation because in that case the end-effector may not be exactly above the internal magnets.

Localization system based on measuring a rotational magnetic field generated by rotating an external permanent magnet

Similar to the idea of Olympus group, Kim *et al.* [27] also equipped an endoscopic capsule with a helical architecture and created an external rotational magnetic field to rotate two permanent magnets embedded inside the endoscopic device. Instead of utilizing six bulky coils around the patient's body, they rotated a big parallelepiped permanent magnet made by seven smaller rectangular magnets for generating a rotational magnetic field. This magnetic field generator was driven by an electrical motor mounted on a manipulator so that it could spin and its position could be changed during the control process of capsule movement as presented in Figure 6a.



(a) (b)

Fig. 6. (a) Rotating a permanent magnet for generating a rotational magnetic field. (b) A sensor module scheme inside a capsule [27].

One notable idea introduced in this system is that they exploited the external magnetic field which was generated to actuate the capsule for the aim of localization as well. When the external permanent magnet is spinning, the magnetic flux strength at the capsule location changes periodically. Its highest/lowest value occurs when the capsule lies on the XZ/XY plane. Therefore, by solving the magnetic flux density equations in these two special cases, the capsule position data can be determined by means of three Hall-effect magnetic sensors (A1391) set up orthogonally inside the capsule. An extra sensor was installed on the rotating axis at the opposite side of the first built sensor to remove the offset effect and thus improve the system precision. A scheme of this sensor module can be seen in Figure 6b. Once the capsule position had been determined, the rotation matrix which represents the angle changes of the capsule in three directions is acquired through comparing the three calculated orthogonal components and the three measured orthogonal components of the magnetic flux at this position. This system achieved the x,y,z position error ranges of (+2mm, +15mm), (-9mm, +12mm) and (-10mm, +3mm), respectively. The orientation error range was (-2^{o}, +13^{o}) in pitch direction and (-4^{o}, +11^{o}) in yaw direction.

Discussion

Beside the significant advantage of the Olympus's tracking method that can avoid the interference between magnetic localization and magnetic actuation, its potential flexibility to work with other actuation systems is also a noteworthy benefit. However, to achieve high accuracy and 5D tracking including 3D position, pitch and yaw, three pairs of facing exciting coils and three pairs of facing detecting coil arrays in three perpendicular axial directions need to be built around the patient's body [52]. Together with the three pairs of big facing coils to generate a rotating magnetic field for actuation purpose, they may make the entire system complex and bulky.

On the other hand, although the other two systems described above can achieve necessary localization information to some extent without being interfered with their own actuation systems, it is likely that they will not be able to deliver the same results when being applied to other actuation systems. In fact, it is still not certain that magnetic steering and rotating external permanent magnet based method are the most effective actuation methods [12]. Therefore, developing a more versatile and compact localization method is still needed.

III. LOCALIZATION METHODS BASED ON ELECTROMAGNETIC WAVES

To have an accurate knowledge of the location of an object placed within a narrow, thick and special medium such as the GI tract, the capsule needs to be in physical contact with different types of signals from the external world. In addition to the methods based on magnetic field strength that have been introduced, this section will focus on employing different waves in the electromagnetic spectrum for the aim of capsule tracking. The common advantage of these approaches is that they are not influenced by the magnetic field generated for the actuation purpose.

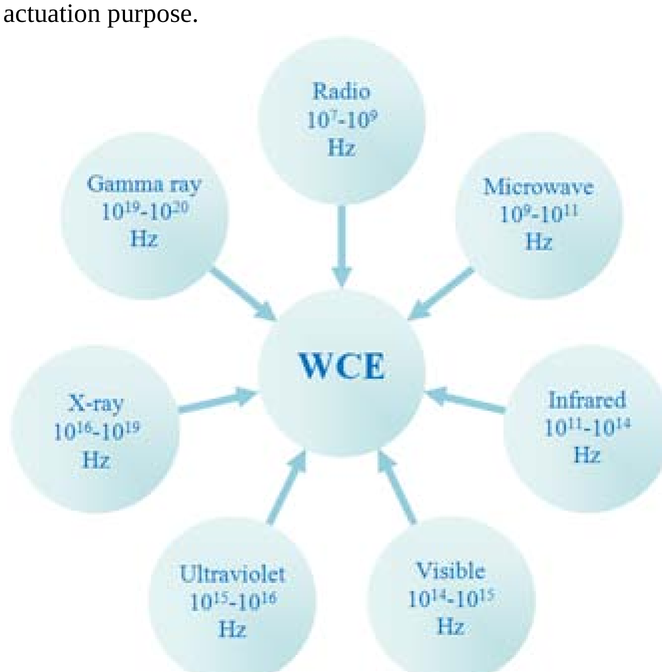


Fig. 7. Utilization of different electromagnetic waves for WCE localization

As shown in Figure 7, the different regions of the electromagnetic spectrum are radio, microwave, infrared, visible, ultraviolet, x-ray and gamma ray. However, only radio waves, visible waves, x-ray and gamma ray have been exploited for capsule tracking since microwaves, infrared waves and ultraviolet waves have very low penetrability through human tissue.

A. *Radio waves*

Radio frequency has been widely used for locating an object in both outdoor and indoor environments with the accuracy achieved up to hundreds of millimeters [56]. Nevertheless, applying radio frequency in the task of tracking an object when it moves inside a special environment, such as the GI tract, is a challenge. This is because high frequency signals suffer significant attenuation at different levels when they pass through different living tissues, whereas low frequency signals due to their long wavelengths are not able to deliver the desired precision of several millimeters [40]. The traditional techniques of localization using radio frequency include: received signal strength indicator (RSSI), angle of arrival (AOA), time of arrival (TOA), time difference of arrival (TDOA), and radio frequency identification (RFID). In this near field application, time based methods are unfeasible because radio waves travel with a very high speed ($3x10^8$m/s), thus an extremely strict time synchronization of less than 1ns is required in order to obtain the position resolution of 0.3m. Likewise, AOA are inapplicable in the digestive tract conditions due to its low reliability even in indoor environments [57-58]. Therefore, only RSSI and RFID have been investigated for the capsule localization.

Received signal strength indicator (RSSI)

The new generation of endoscope is called “wireless” capsule endoscope as it is equipped with a telemetry capability, which is one of the most important functions that make it an innovative technique compared to the previous generation. The transmitter built inside the capsule wirelessly sends endoscopic images, which are captured during its travel along the inner parts, to eight receivers placed uniformly on the exterior of the patient abdomen. Taking advantage of this integrated function, Fisher *et al.* [59-60] measured the strength of the received RF signals at the eight sensors in order to collect input data for the localization purpose. The tracking algorithm is based on the observation that the closer the receiver is to the transmitter, the stronger signal it catches. Approximately, two adjacent antennas will receive equal strength signals if the capsule is in between them. This localization technique, which has already been applied to the current commercial Given Imaging M2A capsule, is able to calculate the 2D position information with the accuracy of 3.77cm. One of the advantages of this method is that it does not need to add any more elements into the capsule. However, the above assumption is not always true due to noise and the complex radio wave absorption properties of human tissue [60]. The low accuracy achieved by this localization system can make it impossible to provide feedback for actuation systems.

In addition to the efforts of developing a tracking system for WCE using RSSI, Arshak and Adepoju [58] adopted an empirical signal propagation model, which has been widely used in RF localization. This model describes the mathematical relationship between RSSI value and distance from the transmitter to the receiver [61]

$$RSSI(d) = P_T - PL(d_0) - 10n\log_{10}\frac{d}{d_0} + X_\sigma \tag{4}$$

where d is the distance between transmitter and receiver, P_T is the transmit power, $PL(d_0)$ is the path loss for a reference distance d_0, n is the path loss exponent, X_σ is a Gaussian random variable. From (4), the distances between the capsule and each of the sensors could be estimated with the aid of RSSI measurement data. Trilateration method was employed to calculate the capsule location once the distances from the transmitter to the receivers had been determined. It is reported that an average error of approximately 25% of the tracking distance, which is still low, was observed. Instead of using a signal propagation model, Shah *et al.* [62] presented an algorithm based on a lookup table for position estimation. Offline measurement was carried out first, in which at each position of the capsule, both the corresponding signal strength measured by each of the sensors and 2D position data were recorded into the table. During the experiment, online data was compared with the data stored in the lookup table to find the closest match and thus to select the most appropriate position.

A propagation attenuation model plays a vital role in the RSSI technique. The empirical model mentioned above is not accurate enough for the complex environment of the GI tract. In order to reduce the position error of this localization method, it is necessary to develop a more appropriate attenuation model when RF signal travels in the internal parts of a human body. Lujia *et al.* [63-64] took into account not only the distance dependence of the signal strength, but also the influence of the antenna orientation factor and tissue absorption to build a compensated attenuation model. However, the accuracy of this model has not yet been tested in WCE tracking. On the other hand, Yi *et al.* [65] compared the impact of different organs and sensor-arrays topology on the position error in localization systems based on the RSSI technique. It is reported that when there is only one 4x4 sensor array, the location errors are up to 52mm, 65mm, and 110mm in the small intestine, in the stomach and in the large intestine, respectively. However, when two 4x4 sensor arrays are available, these maximum location errors are decreased to 40mm in the small intestine, 42mm in the stomach and 55mm in the large intestine.

Radio frequency identification (RFID)

Beside the RSSI technique, RFID is also investigated in radio frequency based localization systems for WCE [66-68]. A cubic antenna array is built surrounding a patient’s body to track a RFID tag integrated inside a capsule. At first, the tracking algorithm was based on the assumption that the tag is only detected by the closet antennas [66]. Hence, after all the antennas in the cubic array have polled the tag, only the IDs of the antennas that have detected the tag are collected for a position estimate. Through computing the collected data using the center of gravity principle, the position of the tag which refers to that of the capsule can be determined. However, due to the inaccuracy of the center of gravity principle, this tracking algorithm produced large errors. Therefore, a better method for location estimation was then presented to replace the previous one. In this method [67-68], the tag consists of a bidirectional antenna that can transmit RF signals in two opposite directions. After receiving a wake-up signal from the RFID reader, the tag, which is powered by its own battery, sends a reply signal to the cubic array. Thanks to the bidirectional characteristic of the radiation pattern, some antennas in two opposite faces of the cubic array receive the reply signal. These antennas form two traces on two opposite faces. The shape and the position of the traces with respect to the edges of two opposite faces are dependent on the position and orientation of the tag. Since the antenna radiation pattern is predetermined as shown in Figure 8, the position of the tag can be estimated through matching the results created by a virtual model with the measured results. This matching algorithm based on shrinking the searching ranges is completed once the virtual results match the measured ones approximately. Although it is reported that the system achieved the errors of 0.5cm in x and y directions and 2cm in z direction via computer simulation, this method does not seem practical to apply. This is because the frequency is limited below the UHF band for the RF signals to pass through the human body. But, in this band, it is impossible to generate directional radiation by a compact antenna with the size of less than 1cm in length. Another significant drawback of this system is that when the longitudinal axis of the tag's antenna is in the same direction with the main axis of the patient, the radiation pattern does not intersect with the cubic array, and thus the matching algorithm will not be able to determine the position of the capsule. To solve this problem, at least one more tag in a perpendicular direction with the first tag may need to be inserted into the capsule.

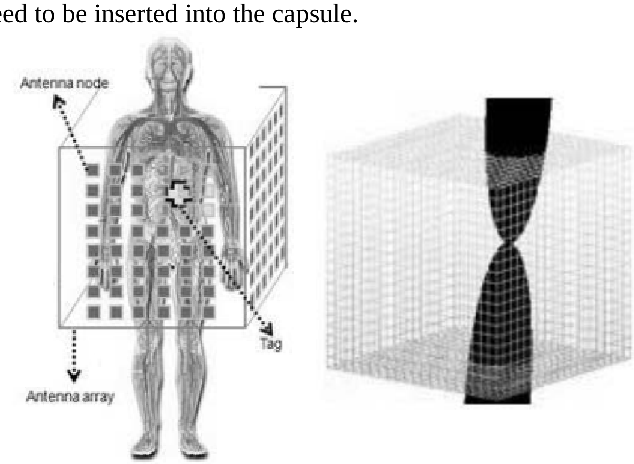


Fig. 8. A cubic antenna array and radiation pattern of RF signals transmitted by a RFID tag [67].

Another technique for localization of a RFID tag mounted in a capsule is based on phase difference. In a system with one transmitter and several receivers, the RF waveforms at the i^{th} receiver can be illustrated by the following equations [69]

$$\begin{aligned} I_i(t) &= A_i \cos(2\pi(f_r - f_c)t + \phi_i) + \sigma_i n_{i1} \\ Q_i(t) &= A_i \sin(2\pi(f_r - f_c)t + \phi_i) + \sigma_i n_{i2} \end{aligned} \tag{5}$$

where I(t) and Q(t) are the inphase and quadrature components of the signal; A, f_r, f_c, ϕ, σ, n denote the received signal magnitude, the frequency at the receivers, the carrier frequency, the phase difference between the carrier at the tag and the carrier at the receiver, the noise level, and Gaussian noise, respectively. By presenting experimental results, Hekimian-Williams *et al.* [69] showed that although exact phase value of a single signal received at an antenna cannot be used to calculate the distance that the signal has travelled, the phase difference between signals within the same burst arrived at different antennas can be employed for location estimation. Although this group demonstrated the smooth change of the phase difference when the tag was moved to different position, the localization algorithm to determine the tag location with the aid of phase difference measurement was not presented [70]. Taking this into account, Wille *et al.* [70] developed a RFID navigation system using the phase difference to track medical instruments such as needles or catheters. Support Vector Regression (SVR), a machine learning algorithm, was applied to estimate the position of the RFID tag by employing the phase difference data collected at different RFID receivers. Three different experiments based on different shapes of the datasets were performed to test the accuracy of the position estimation. At first, the tag was moved in four linear paths between four pairs of antennas. In these tests, mean accuracies reported were between 0.8mm and 2.9mm. In the second experiment, a mean accuracy of 1.7mm was achieved when they took measurements on a box dataset consisting of an area of 10mm x 10mm in y-z plane around each point of a linear path. Finally, for the experiment on a cubic dataset with the volume of 3cm x 3cm x 3cm, a mean accuracy of 1.6mm was recorded. Although the experimental results indicate the feasibility of the phase difference method for accurate localization of RFID tags, there are still a lot of improvements needed before applying this method to capsule tracking. The reason is that two important factors that could affect the accuracy of the localization method were ignored during the experiments. One of these factors is the orientation of the tag which was kept constant in all of the tests. The second factor is that the significant influence of human tissues on the RF signals was not considered [70].

B. *Visible waves*

In spite of the fact that visible waves cannot penetrate human body, it has still been exploited for the aim of capsule localization through computer vision. Inside the WCE, white light emitting diodes (LED) illumination sources are used in conjunction with a miniature camera for capturing endoscopic images during its travel along the GI tract. By means of processing the captured images coming from the capsule, the region of the GI tract in which it is located can be determined [71-72]. In order to classify images into appropriate regions, Neural Networks (NN), Vector Quantization (VQ) and combination of VQ with Principal Component Analysis (PCA) were tested. These classification methods, which used Homogeneous Texture descriptor and a MPEG-7 visual content descriptor, were able to distinguish between the upper and lower parts of a GI tract and between different regions in the upper part, such as esophagus, cardia, corpus of the stomach, pylorus, and duodenal cap. Although NN method produced slightly more accurate results than VQ and VQ+PCA, the latter sped up the computation significantly. Another effort using computer vision for classifying different organs of the GI tract in a WCE video is via event boundary detection algorithm [73]. Events such as when the capsule enters the next organ or intestinal bleedings can be detected by color change pattern analysis. It is reported that the precision of 51% was achieved after performing experiments with ten WCE videos. However, these localization methods provide only basic information of which region the capsule is located in, which is not sufficient. Therefore, the localization information can only be considered as reference information for the endoscopists.

Aiming to a different target, Li *et al.* [74] presented a localization method based on computer vision to determine a roll angle, i.e. the rotation angle along the longitudinal axis of the capsule. As previously described, the tracking systems using magnetic sensor arrays can obtain only 5D localization parameters with the absence of roll angle information because the magnetic field created by a cylindrical magnet does not change when the capsule spins along its main axis. Thus, 6D localization data of the WCE could be achieved with the aid of this method. Based on the similarity between two consecutive endoscopic images, the rotation parameters of the capsule can be estimated through a combination of several algorithms such as Lucas-Kanade optical flow, 8-point algorithm, and quaternion algorithm. These algorithms were used for tracking correspondent feature points, selecting feature points, and rotation decomposition, respectively [74]. When the roll angle varied within the range of less than 30^o, the maximum angle error of 1.775^o was recorded, but a significant error occurred when the angle change was larger than 30^o. Accordingly, one of the most important weaknesses of this method is that a large variation in two successive images results in a failure in determining the rotation angle data. Moreover, it is likely that the capsule will be rotated or dragged rapidly in WCE systems which are furnished with active actuation, e.g. the system using spiral structure on the capsule body, while the image capturing rate is usually low at 2-4 Hz. Therefore, this method may not be able to operate effectively in the presence of active actuation systems.

C. *X-ray*

Beside the application of medical imaging, X-rays can also be exploited to track an object, e.g. an endoscopic capsule, placed inside the digestive tract. Fluoroscopy, which is a type of imaging technique based on X-ray radiation used to display continuous x-ray images on a monitor in real-time, was integrated in a magnetic steering system to provide images that show the location of the capsule to the maneuvers [17]. However, this method can only supply visual information of the capsule location via radiation images, while it is impossible to obtain actual parameters of its position and orientation to serve as feedback data for actuation systems. Aiming to solve this issue, Kuth *et al.* [75] proposed a method which takes advantage of both x-ray imaging and image processing for automatically determining position and orientation of the WCE. The solution was based on the fact that when the distance between an x-ray source and a radiation detector plane is kept unchanged, every change in the position and orientation of an object within the coverage of the x-ray beam will lead to a corresponding alteration in its shadow, i.e. its projection on the detector. Therefore, by means of image processing, the position and orientation data of the capsule can be calculated depending on the shape of the shadow on the radiation images if the capsule geometry is already known. In extreme cases such as when the longitudinal axis of the capsule is perpendicular to the detector, another x-ray source fixed at an angle to the first one could be turned on to enhance the system's accuracy. The automatically obtained value is then sent to a navigation device to alternate the external magnetic field which is generated for the purpose of capsule actuation. The x-ray image recording rate is controlled according to the speed of the capsule being actuated. Steps in the iterative algorithm for back calculating the position and orientation of the capsule from its shadow on the x-ray images is explained in detail in [76].

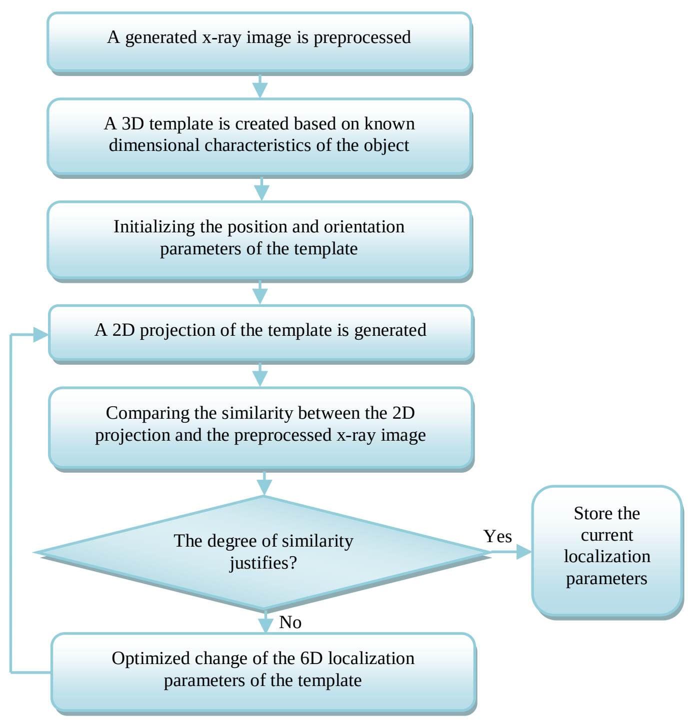


Fig. 9. Steps to calculate position and orientation parameters of an object from its shadow on an x-ray image

The algorithm shown in Figure 9 is mainly based on comparing repeatedly the shape of the actual shadow with that of the virtual projection created by projecting a 3D template which has the same constructional features with the capsule on

Table 1 A comparison of the key methods presented in this study. "-" indicates that the information is unknown. The accuracy may be "High" (position error < 2mm), "Moderate" (position error is from 2mm to 20mm), or "Low" (position error > 20mm).

	Localization methods	Take extra space of the capsule	Consume extra power of the capsule	Accuracy	Interference with magnetic actuation	Real-time	Adverse health effects
Magnetic localization (passive WCE)	Permanent magnet [14,42]	Yes	No	High	Yes	Yes	No
	Secondary coil [46]	Yes	Yes	Moderate	Yes	-	No
	Magnetoresistive sensor [47-49]	Yes	Yes	Moderate	Yes	No	No
Magnetic localization (active WCE)	HF alternating magnetic field [54,55]	Yes	No	High	No	Yes	-
	Inertial sensing [16]	Yes	Yes	Low	No	-	No
	Rotating external permanent magnet [27]	Yes	Yes	Moderate	No	-	No
Electromagnetic waves	Radio frequency [59,60]	No	No	Low	No	No	No
	Visible waves [71,73]	No	No	Low	No	-	No
	X-ray [75]	No	No	-	No	Yes	Yes
	Gamma ray [77,78]	Yes	No	-	No	Yes	Yes
Others	MRI [79,81]	Yes	Yes	High	-	Yes	Little
	Ultrasound [85,86]	Yes	Yes	-	No	Yes	Little

an equivalent virtual detector plane. The optimization loop is halted once the degree of similarity is in an acceptable range, and then the set of six rotation and transformation parameters of the template is adopted to be those of the capsule. Although this method is promising to deliver highly accurate results, the most significant disadvantage of the system is the potential hazard for the patient in the case of high x-ray usage. Regarding this problem, one notable point of the above system is that the internal components of the capsule are usually metallic or radiation-opaque, hence it is possible to show reasonable quality x-ray images with extremely low radiation dose[75]. Furthermore, using a hybrid system which combines the x-ray method with one of the other 3D localization methods has been suggested to reduce the radiation burden on the patient's body [17].

D. *Gamma ray*

Although a gamma ray has not been employed in the localization approaches for WCE, it was exploited in gamma-scintigraphy technique to visualize the position of an Enterion capsule, a drug-delivery type capsule, in real-time [77]. The capsule that is loaded with gamma-emitting radioisotopes can be detected by scintillation cameras. Since gamma rays are absorbed partly by human tissues when it travels from the radioactive agent to the camera, both dorsal and ventral images are taken to enhance the tracking accuracy [78]. However, similar to the x-ray based localization system, this method can be harmful to the patients.

IV. OTHER LOCALIZATION METHODS

Beside the above localization systems, magnetic resonance imaging (MRI), a diagnostic imaging technique used widely in medical clinics, could also be employed for localization [79-81]. Dumoulin *et al.* [79] proposed a method for tracking interventional devices such as catheters, biopsy needles in real-time using MRI. In this method, the spatial position of an interventional device was determined by incorporating one or more miniature RF coils into the device to sense special MRI pulse sequences. Adopting this tracking method, Krieger *et al.* [81] demonstrated that six degree-of-freedom (6-DOF) position and orientation of a biopsy needle which carries three micro-tracking coils could be computed with the tracking speed, mean positional error and rotational error of 20Hz, 0.2mm and 0.3^0, respectively. However, the need for custom-programmed pulse sequences which are different from the standard pulse sequences of commercial MRI scanners would be a disadvantage of this method [82-83].

Ultrasound, another diagnostic imaging technique, is also a potential method for localization in soft tissue. The position information can be estimated by means of two different approaches. The first approach is based on measuring the time of flight (ToF) between ultrasonic pulses transmitted from an external source and the echoes reflected by the capsule [84]. In this approach, the accurate knowledge of the speed of sound in human soft tissue plays an important role in the tracking accuracy. Moreover, the capsule must always lie in the scanning plane to be sensed [85]. This drawback can be overcome by the second approach, in which an ultrasound transducer is embedded inside the capsule, and external receivers are located around the patient's abdomen to detect the emitted ultrasonic signals [85-86]. Since the ultrasonic signals only need to travel through the media once, this approach offers twice deeper penetration than the first approach. Although the fact that bone and gas shield ultrasonic signals [87], the localization method based on ultrasound is promising in providing high speed, safety and low cost [88].

V. CONCLUSION

As reported in the literature, it is anticipated that the next generation of WCE, which is an active WCE with the capability of moving automatically in the digestive tract under an external control, will be introduced to the medical field in the near future [89-90]. Such an active system requires a sufficiently accurate localization system, since the visual feedback via endoscopic images is not enough for an active control of the capsule movement. Moreover, the localization system is already indispensable in current medical procedures using passive WCE to determine the location of lesions and the distance that the capsule has travelled.

Although many localization methods have been proposed as reviewed in this study, none of them could offer a complete solution to address the challenging capsule localization problem. To date, a commercial WCE can only provide rough 2D position information. Table 1 illustrates a comparison of different methods presented in this paper. As shown in the table, the approaches which have potential to obtain high accuracy position and orientation data are either influenced by the magnetic field to be used for actuation or be complex and still at the proof-of-principle stage.

A future WCE is expected to have fully robotic capabilities such that it will be able to accomplish both diagnosis and disease treatment. In order to achieve such an autonomous WCE, building a complete localization system, which is acceptably accurate in real-time, minimally invasive, able to work with different actuation mechanisms and easily implementable, is greatly desirable. This has posed a serious challenge for engineers and physicians who are keen on developing active WCEs. Possible solutions include designing novel approaches, improving the proposed methods or even developing hybrid strategies to exploit a combined advantage of different techniques.

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