Journal of Zhejiang University-SCIENCE B (Biomedicine & Biotechnology)
ISSN 1673-1581 (Print); ISSN 1862-1783 (Online)
www.zju.edu.cn/jzus; www.springerlink.com
E-mail: jzus@zju.edu.cn

An intelligent electronic capsule system for automated detection of gastrointestinal bleeding*

Hong-ying LIU[1], Gang WANG[1], Kang WEI[1], Xi-tian PI[†‡1,2], Lan ZHU[1], Xiao-lin ZHENG[1,2], Zhi-yu WEN[2]

([1]*Key Laboratory of Biorheological Science and Technology of Ministry of Education, College of Bioengineering, Chongqing University, Chongqing 400030, China*)

([2]*Key Laboratories for National Defense Science and Technology of Innovative Micro-Nano Devices and System Technology, Chongqing University, Chongqing 400030, China*)

[†]E-mail: pixitian@cqu.edu.cn

Received Feb. 9, 2010; Revision accepted Aug. 30, 2010; Crosschecked Nov. 11, 2010

Abstract: In clinical practice, examination of the hemorrhagic spot (HS) remains difficult. In this paper, we describe a remote controlled capsule (RCC) micro-system with an automated, color-based sensor to identify and localize the HS of the gastrointestinal (GI) tract. In vitro testing of the detecting sensor demonstrated that it was capable of discriminating mimetic intestinal fluid (MIF) with and without the hemoglobin (Hb) when the concentration of Hb in MIF was above 0.05 g/ml. Therefore, this RCC system is able to detect the relatively accurate location of the HS in the GI tract.

Key words: Smart capsule, Intestinal bleeding, Color sensor, Biomedical micro-electromechanical system (BioMEMS)
doi:10.1631/jzus.B1000047 **Document code:** A **CLC number:** TP7

1 Introduction

Although gastrointestinal (GI) bleeding is a common disease in the GI tract, severe GI bleeding may cause acute anaemia and hemorrhagic shock, and may even be life-threatening (Chou *et al*., 1989; Arora *et al*., 2002; Ko *et al*., 2009). For many treatments, it is often important to obtain an accurate location of the hemorrhagic spot (HS).

The physiological structure of the human GI tract is complicated, while the instruments used for detecting and locating the HS of the GI tract are diverse, mainly being enteroscopy, emission computerized tomography (ECT), angiography, and capsule endoscopy (Concha *et al*., 2007; Zuckerman *et al*., 2000; Singh and Alexander, 2009). Enteroscopy is most widely adopted, since its examining area can extend to 50–80 cm both from the proximal end of the jejunum and from the terminal ileum, which means that it can examine and locate most of the HS of the GI tract, except that of the small intestine. When enteroscopy is used during surgery, the diagnostic rate can be 58%–100%, and hemostatic surgery can be done directly with the aid of enteroscopy. However, detection with enteroscopy is invasive, technically challenging in some cases, and may cause bowel injury (Schmit *et al.*, 1996; Bezet *et al*., 2004; Chettiar *et al*., 2010). ECT, which is sensitive, safe, and non-invasive, is used in the detection of the HS of the small intestine with the shortcoming of failing to make qualitative diagnosis and locate the HS precisely (Olds *et al*., 2002; Hammond *et al.*, 2007; Datta *et al.*, 2008). The effect of angiography applied on the patients with low-level hemorrhage is not as good as that with active and massive hemorrhage (Keller and

‡ Corresponding author

* Project supported by the National Natural Science Foundation of China (Nos. 30700160 and 30970883), the Postdoctoral Science Foundation of China (Nos. 20070420718 and 200801225), Chongqing University Postgraduates' Science and Innovation Fund (No. 2008 01A1B0250284), and the Specialized Research Fund for the Doctoral Program of Higher Education (No. 20070611045), China

Rosch, 1981; Singer, 1995; Johnston *et al*., 2007).

Capsule endoscopy is a novel means used in the small intestine, and this form of endoscopy is increasingly adopted for its non-invasiveness, safety, and capability of picturing the entire GI tract. It has received increased attention since PillCam (Given Imaging Ltd., Israel) was issued, followed by Norika series (RF System Lab, Japan) and EndoCapsule series (Olympus Corporation, Japan) (Ogata *et al*., 2008; Iddan *et al*., 2000; Uehara and Hoshina, 2003; LePane *et al*., 2007; Kopáčová *et al.*, 2010). The capsule endoscopy OMOM (Jinshan Science & Technology Inc., Chongqing, China) has also had extensive application in clinical practice (Li *et al*., 2008; Liao *et al*., 2008). Researchers from Korea, Germany, Italy, and Belgium, respectively, have advanced our understanding of the advantages of capsule endoscopy (Lenaerts and Puers, 2007; Moglia *et al.*, 2007; Jansen *et al*., 2007). Nevertheless, capsule endoscopy also has some disadvantages. One study showed that there was a diagnostic rate of 92.3% when the hemorrhage was significant, compared to 44.2% when the hemorrhage was concealed (Gupta and Reddy, 2007). Another study demonstrated that capsule endoscopy could not accurately photograph some corners of the GI tract (Delvaux and Gay, 2006; Ersoy *et al*., 2006). In addition, capsule endoscopy, which transmits the images from the inside to the outside of the body, requires that the clinician should read a mass of images to judge the state of hemorrhage, and that the specific HS may not be located (Mishkin *et al.*, 2006). The idea of detecting the HS of the GI tract utilizing a hemoglobin (Hb)-based sensor was put forward by the researchers from Shanghai Jiao Tong University (Shi *et al.*, 2006).

A novel remote controlled capsule (RCC) microsystem with a non-invasive deglutible RCC and a color-based sensor that can identify the state of hemorrhage of the GI tract is described here. The combination of this system and a wearable magnetic locating and tracking system (WMLTS) achieves accurate localization of the HS of the GI tract.

2 Materials and methods

Combined with the WMLTS, this system consists of an RCC and a portable receiving alarm (PRA) (Fig. 1). After a patient's GI tract has been cleansed, the patient is required to swallow an RCC, which moves with GI peristalsis. Then a WMLTS is set on the waist of the patient. The RCC automatically detects and analyzes the state of hemorrhage every 5 s. When the RCC identifies that the GI tract is bleeding, the RCC will emit a radio frequency (RF) signal that will be received and saved by the PRA, from which alarm signals ensue. Then, the WMLTS will localize the HS. When the RCC identifies that the GI tract is not bleeding, no RF signal will be emitted in order to save the battery power. The WMLTS, successfully devised by our research team, is precise to the level of 1 cm (Wu *et al.*, 2008).

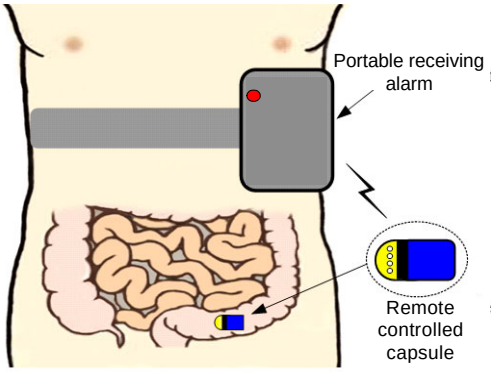

Fig. 1 Schematic diagram of the RCC for automatic detection of GI bleeding

2.1 Design of the RCC for automatic detection of GI bleeding

This RCC mainly consists of a power supply, power control module, localizer, micro-control chip, RF signal emission module, detecting sensor, and related peripheral circuit. The sectional view of this RCC is shown in Fig. 2. The shell of the RCC is made of biocompatible polycarbonate. To meet the requirements of energy consumption to accomplish one detection of the entire GI tract, the system is based on a low power design, and uses three high-energy button batteries, Sony SR9xx (diameter 9.5 mm, depth 2.09 mm), as the power supply. The power control module is composed of a normally open magnetic switch and the related circuit. The unused sealed RCC is to be set in a box with a permanent magnetic field which has a specific direction. Under the effect of the permanent magnetic field, the magnetic switch is off, and the button batteries are disconnected from the

circuit of all modules. When the RCC is taken out of the box, since the RCC is remote from the permanent magnetic field, the magnetic switch is on, the button batteries are then connected with the circuit of all modules, and the RCC starts to work.

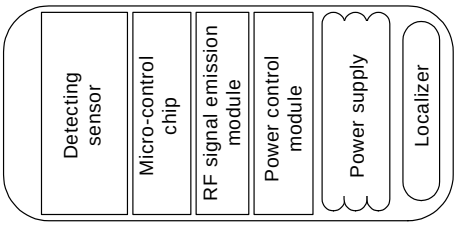

Fig. 2 Structure diagram of the RCC for the detection of GI bleeding

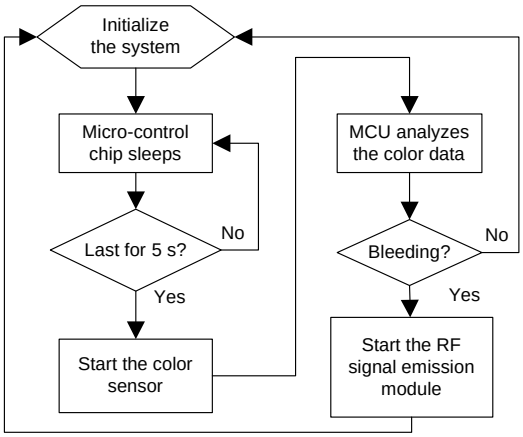

Fig. 3 Algorithm flow chart of the micro-control chip

The localizer is a columnar permanent magnet (diameter 9.5 mm, length 3.0 mm) placed in the RCC. The permanent magnetic field can be detected and analyzed to acquire its three-dimensional (3D) location by the sensor array made of Hall sensors, so as to determine the accurate 3D location of the RCC (Wu *et al.*, 2008).

The micro-control chip applies the chip PIC16F6xx, which is a micro-power consumption microcontroller unit (MCU). Once working, and the MCU enters a state of sleep after its initialization, and then every 5 s it automatically wakes up again and actuates the blood detecting sensor to accomplish one data acquisition. Then the detecting sensor transmits the color information to the micro-control chip, which analyzes the data to determine whether the HS exists. If it exists, the RF signal emission chip will be awakened to emit an RF signal out from the body; otherwise, the micro-control chip will enter the next period of sleep and wait for the next 5-s testing period, doing so repeatedly until the RCC is excreted. Fig. 3 is the algorithm flow chart of the micro-control chip.

The RF signal emission module uses the chip MICRF1xx, a low power consumption single chip Transmitter integrated circuit (IC), which is a true "data-in, antenna-out" monolithic device. All antenna tuning is accomplished automatically within the IC, which eliminates manual tuning and reduces production costs. The small outline package (SOP) and the printed circuit board (PCB) antenna contribute to the minimization of the volume of this module. This module receives the digital signal of the hemorrhage from the micro-control device and emits the same signal from the antenna after automatic tuning.

The blood detecting sensor, the hard core of the RCC, can detect the color feature of the blood. The columnar sensor (diameter 11.0 mm, length 9.5 mm) consists of an intestinal fluid smear device, color sensor, light emitting diode (LED) light source, and external circuit. Fig. 4 gives a structural diagram of the blood detecting sensor. Fig. 5 is a photograph of the blood detecting sensor.

The intestinal fluid smear device is composed of a transparent cover plate, intestinal fluid smear platform, and six drain holes (diameter 2.0 mm). The transparent cover plate is a circular thin section of polycarbonate (depth 0.2 mm) glued onto the inner surface of the shell. The intestinal fluid smear platform is a white opaque reflective truncated-cone made of polyethylene. The distance between the surfaces of the transparent cover plate and the intestinal fluid smear platform is 2.0 mm, which forms an intestinal fluid smear zone. The drain holes, uniformly distributed on one end of the shell of the RCC, serve as the access for the intestinal fluid to flow in and out. The diameter of the holes is determined by the viscidity of the intestinal fluid. In order to make the flow of the intestinal fluid smoother and guarantee the firmness of the RCC's structure, the diameter is designed 2.0 mm here.

On one side of the transparent cover plate are the color sensor and white light LED, both fabricated onto the PCB. The color sensor adopted here is the TCS230D (TAOS Inc., USA) programmable RGB color light-to-frequency converter with a digital

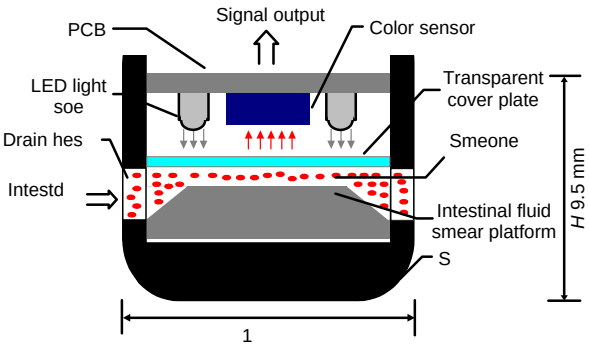

Fig. 4 Structure diagram of the blood detecting sensor

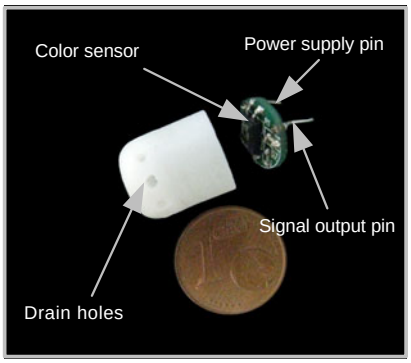

Fig. 5 Photograph of the blood detecting sensor

compatible interface. The TCS230D can convert the components of the primary colors (red, green, blue) of the color light into periodic voltage signals and output them, because the components are related to the voltage frequencies. The LED serves as the source of white light. The white light penetrates through the transparent cover plate and irradiates onto the intestinal fluid. Then the reflected color light can be acquired by the color sensor.

The sealed RCC for automatic detection of GI bleeding is a cylinder (diameter 11.0 mm, length 26.0 mm). A photograph of this RCC is shown in Fig. 6. When the RCC is in the GI tract, the intestinal fluid, under the effect of gravity and GI peristalsis, flows into the smear zone via the drain holes of the RCC's shell. The detecting sensor works every 5 s under the control of the micro-control chip. During the working period, the LED irradiates consistently for 1 s. Under the irradiation, the color sensor accomplishes one data acquisition and transmits the data to the MCU. Since the blood contains the Hb, a great difference exists between the intestinal fluid with Hb and the one without. In accordance with the difference, the MCU determines whether a sign of the HS exists, thereby determining whether the RCC is in the region of the HS.

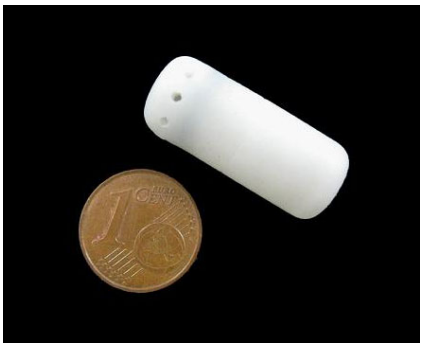

Fig. 6 Photograph of the RCC for the detection of GI bleeding

2.2 Design of the PRA

The PRA is comprised of a power supply (two AA batteries), RF signal receiving module, alarm module, and related circuit. The receiving module adopts the chip MICRF0xx, which is a single chip ASK/OOK (ON-OFF Keyed) Receiver IC for remote wireless applications. The combination with the emitting chip MICRF1xx forms the RF signal emitting-and-receiving system. Composed of a buzzer and LED, the alarm module is fabricated to the output pin of the RF signal receiving module. Once the RF signal receiving module receives the RF signal sent by the RCC, its output pin actuates the alarm module to emit the sound and light alarm, warning the patient that the symptom of hemorrhage is found. Fig. 7 is a photograph of the PRA.

Fig. 7 Photograph of the PRA

2.3 In vitro study of the detecting sensor

In vitro experiments were carried out to verify the detecting effect of this sensor. The solutions to be detected were made of bovine Hb (Sigma H2625, Worthington Corporation, USA) and phosphate

buffer (CellChip Biotechnology Co., Ltd., Beijing, China). The Hb concentration of normal human blood ranges from 0.11–0.15 g/ml, but it will be diluted by the intestinal fluid when the GI tract is bleeding. Therefore, the concentrations of bovine Hb compounded here were 0, 0.01, 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.10, 0.12, 0.14, and 0.16 g/ml. The color of these 13 groups of solutions reddened gradually from achromaticity to as red as blood as the Hb concentration increased.

The sealed detecting sensor was placed vertically, and the end with drain holes on it was immerged in the solution to be detected which flowed into the smear zone and automatically formed a smear of mixture. The power supply pin of the detecting sensor was connected to a 4.5 V direct current (DC) power supply (CA17303D, Ketai Electronic Instrument Co., Ltd., Jiangsu, China), and the signal output pin was connected to a digital storage oscilloscope (UT2025B, UNI-T Inc., China). When the power supply and the digital storage oscilloscope were switched on, the LED in the detecting sensor emitted white light, which penetrated through the transparent cover plate and irradiated on solution to be detected. Afterwards, the reflected color light penetrated through the transparent cover plate and irradiated on the photosensitive surface of the color sensor. Then the signal output pin of this color sensor output respectively the periodic voltage signals related to the components of the primary colors (red (R), green (G), and blue (B)) of the color light. After the power supply was switched off and the detecting sensor was removed, the intestinal fluid zone was washed by distilled water and air-dried, so as to avert the impact on the next detection, which was caused by the residual solution. The other two solutions of this group were detected in the same way. Then, the average periods of the pulse signals of the components of the primary colors (T_{R_1}, T_{G_1}, and T_{B_1}) were calculated. Other groups were detected in the above-mentioned way. The results are shown in Table 1.

Table 1 Concentrations of the bovine Hb and the average periods of the pulse signals of the components of the primary colors in in-vivo experiments

Group *a*	Concentration of bovine Hb (g/ml)	Period of pulse signal		
		T_{R_a} (μs)	T_{G_a} (μs)	T_{B_a} (μs)
1	0	120	120	200
2	0.01	120	130	230
3	0.02	120	130	230
4	0.03	120	135	247
5	0.04	120	140	250
6	0.05	120	145	260
7	0.06	120	150	259
8	0.07	120	150	259
9	0.08	120	150	264
10	0.10	125	155	268
11	0.12	125	160	270
12	0.14	125	160	270
13	0.16	130	160	280

T_{R_1}: period of the pulse signal of the red color; T_{G_1}: period of the pulse signal of the green color; T_{B_1}: period of the pulse signal of the blue color. T_{R_a}, T_{G_a}, and T_{B_a} are the respective periods of the components of the primary colors of the solutions after white balance adjustment of Group *a* (*a*=2,3,…,13)

3 Results and discussion

When the detecting sensor is applied the first time, the white balance adjustment is the key to accuracy. Since the concentration of the bovine Hb in Group 1 was 0 g/ml, the white balance adjustment was based on the data of Group 1. As shown in Table 1, in Group 1, T_{R_1} and T_{G_1} were 120 μs, and T_{B_1} was 200 μs. D is a constant. T_{R_a}, T_{G_a}, and T_{B_a} are the respective periods from Groups 2 to 13. R_a, G_a, and B_a (a=2,3,…,13) represent the components of the primary colors of the solutions after white balance adjustment, respectively. Then the calculation is based on Eqs. (1) to (3) as follows:

$$R_a = D \times T_{R_1} / T_{R_a}, \quad a = 2,3,...,13; \tag{1}$$

$$G_a = D \times T_{G_1} / T_{G_a}, \quad a = 2,3,...,13; \tag{2}$$

$$B_a = D \times T_{B_1} / T_{B_a}, \quad a = 2,3,...,13. \tag{3}$$

The color of these 13 groups of solutions reddened gradually from achromaticity to as red as blood as the Hb concentration increased. In order to show the change of the solution color, R_a was chosen to be the reference standard. L_a is a curve of the change of the color, and M_a is another one. The calculation is given by Eqs. (4) and (5), and the curves are shown in Fig. 8.

$$L_a = \frac{G_a}{R_a} = \frac{D \times T_{G_1} / T_{G_a}}{D \times T_{R_1} / T_{R_a}} = \frac{T_{G_1} \times T_{R_a}}{T_{R_1} \times T_{G_a}},\ a = 2,3,...,13; \quad (4)$$

$$M_a = \frac{B_a}{R_a} = \frac{D \times T_{B_1} / T_{B_a}}{D \times T_{R_1} / T_{R_a}} = \frac{T_{B_1} \times T_{R_a}}{T_{R_1} \times T_{B_a}},\ a = 2,3,...,13. \quad (5)$$

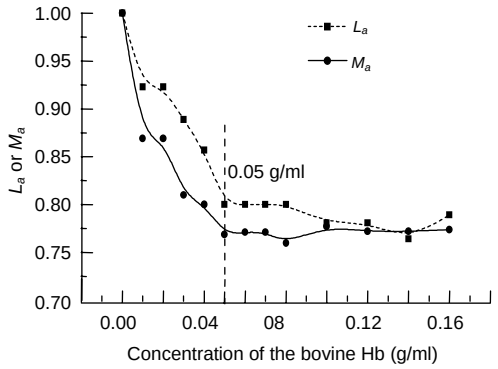

Fig. 8 RGB frequency ratio curves of different concentrations of the bovine Hb solutions

As Fig. 8 shows, when the concentration of the bovine Hb was 0 g/ml, both L_1 and M_1 equaled 1, indicating that no bovine Hb was in the target solution. This solution was deemed pure white. L_a and M_a decreased as the concentration increased. L_a and M_a kept fluctuating between 0.75 and 0.80, but never higher than 0.80, as the concentration of the bovine Hb stayed above 0.05 g/ml. Since the concentration of the Hb in human blood is much higher than 0.05 g/ml, we can consider that the symptom of hemorrhage exists when both L_a and M_a belong to (0.75, 0.80].

The RCC system advanced here is able to detect the relatively accurate location of the HS in the GI tract. Combined with the WMLTS, the detection of this system can be precise to the level of 1 cm. The system is non-invasive, operates in real-time and conveniently, and provides no blind spots for the entire GI tract. It can shorten the detection time to find the HS compared with other means. The combination with the RCC for site-specific drug delivery in human GI tract may enhance the efficacy of medication in the GI tract. For instance, this system can be applied to deliver hemostatic drugs to the HS of the GI tract. In the further research, we will focus on improvements in accuracy, integration, and micromation.

References

Arora, N.K., Ganguly, S., Mathur, P., Ahuja, A., Patwari, A., 2002. Upper gastrointestinal bleeding: etiology and management. *Indian J. Pediatr*., **69**(2):155-168. [doi:10.1007/BF02859378]

Bezet, A., Cuillerier, E., Landi, B., Marteau, P., Cellier, C., 2004. Clinical impact of push enteroscopy in patients with gastrointestinal bleeding of unknown origin. *Clin. Gastroenterol. Hepatol*., **2**:921-927. [doi:10.1016/S1542-3565(04)00397-0]

Chettiar, R., Selby, W.S., Kaffes, A.J., 2010. Antegrade double balloon enteroscopy for continued obscure gastrointestinal bleeding following push enteroscopy: is there a role? *Dig. Dis. Sci*., **55**(5):1381-1384. [doi:10.1007/s10620-009-0892-3]

Chou, Y.H., Hsu, S.C., WANG, C.Y., Chen, C.L., How, S.W., 1989. Ischemic colitis as a cause of massive lower gastrointestinal bleeding and peritonitis. *Dis. Colon Rectum*, **32**(12):1065-1070. [doi:10.1007/BF02553883]

Concha, R., Amaro, R., Barkin, J.S., 2007. Obscure gastrointestinal bleeding-diagnostic and therapeutic approach. *J. Clin. Gastroenterol*., **41**(3):242-251. [doi:10.1097/01.mcg.0000225616.79223.75]

Datta, I., Ball, C.G., Parr, Z., Mew, D., 2008. The use of a gamma probe and radioactive technetium to identify obscure gastrointestinal bleeding. *Am. J. Surg.*, **196**(5):e53-e55. [doi:10.1016/j.amjsurg.2008.01.027]

Delvaux, M., Gay, G., 2006. Capsule endoscopy in 2005: facts and perspectives. *Best Prac. Res. Clin. Gastroenterol*., **20**(1):23-39. [doi:10.1016/j.bpg.2005.08.002]

Ersoy, O., Sivri, B., Arslan, S., Batman, F., Bayraktar, Y., 2006. How much helpful is the capsule endoscopy for the diagnosis of small bowel lesions? *World J. Gastroenterol*., **12**(24):3906-3910.

Gupta, R., Reddy, D.N., 2007. Capsule endoscopy: current status in obscure gastrointestinal bleeding. *World J. Gastroenterol*., **13**(34):4551-4553.

Hammond, K.L., Beck, D.E., Hicks, T.C., Timmcke, A.E., Whitlow, C.W., Margolin, D.A., 2007. Implications of negative technetium 99m-labeled red blood cell scintigraphy in patients presenting with lower gastrointestinal bleeding. *Am. J. Surg*., **193**(3):404-408. [doi:10.1016/j.amjsurg.2006.12.006]

Iddan, G., Meron, G., Glukhovsky, A., Swain, P., 2000. Wireless capsule endoscopy: the discomfort of internal gastrointestinal examination may soon be a thing of the past. *Nature*, **405**(6785):417. [doi:10.1038/35013140]

Jansen, D., Fawaz, N., Bau, D., Marc Durrenberger, M., 2007. A small high performance microprocessor core sirius for embedded low power designs, demonstrated in a medical mass application of an electronic Pill (EPill®). *IFIP*, **231**: 363-372. [doi:10.1007/978-0-387-72258-0_31]

Johnston, C., Tuite, D., Pritchard, R., Reynolds, J., Mceniff, N., Ryan, J.M., 2007. Use of provocative angiography to localize site in recurrent gastrointestinal bleeding. *Cardiovasc. Intervent. Radiol*., **30**(5):1042-1046. [doi:10.1007/s00270-007-9107-5]

Keller, F.S., Rosch, J., 1981. Value of angiography in diagnosis and therapy of acute upper gastrointestinal hemorrhage. *Dig. Dis. Sci.*, **26**(s7):78-89. [doi:10.1007/BF01

300813]

Ko, K.H., Tsai, S.H., Yu, C.Y., Huang, G.S., Liu, C.H., Chang, W.C., 2009. Unusual complication of superior mesenteric artery syndrome: spontaneous upper gastrointestinal bleeding with hypovolemic shock. *J. Chin. Med. Assoc*., **72**(1):45-47. [doi:10.1016/S1726-4901(09)70020-6]

Kopáčová, M., Tachecí, L., Květina, J., Bureš, J., Kuneš, M., Špeda, S., Tyčová, V., Svoboda, Z., Rejchrt, S., 2010. Wireless video capsule enteroscopy in preclinical studies: methodical design of its applicability in experimental pigs. *Dig. Dis. Sci*., **55**(3):626-630. [doi:10.1007/s10620-009-0779-3]

Lenaerts, B., Puers, R., 2007. An inductive power link for a wireless endoscope. *Biosens. Bioelectron*., **22**(7):1390-1395. [doi:10.1016/j.bios.2006.06.015]

LePane, C.A., Barkin, J.S., Parra, J., Simon, T., 2007. Ulcerative jejunoileitis: a complication of celiac sprue simulating Crohn's disease diagnosed with capsule endoscopy (PillCam). *Dig. Dis. Sci*., **52**(3):698-701. [doi:10.1007/s10620-006-9556-8]

Li, C.Y., Zhang, B.L., Chen, C.X., Li, Y.M., 2008. OMOM capsule endoscopy in diagnosis of small bowel disease. *J. Zhejiang Univ.-Sci. B*, **9**(11):857-862. [doi:10.1631/jzus.B0820034]

Liao, Z., Li, F., Li, Z.S., 2008. Clinical application of OMOM capsule endoscopy in China: a review with 1068 cases. *Gastrointest. Endosc*., **67**(5):AB265. [doi:10.1016/j.gie.2008.03.726]

Mishkin, D.S., Chuttani, R., Croffie, J., Disario, J., Liu, J., Shah, R., Somogyi, L., Tierney, W., Song, L.M.W.K., Petersen, B.T., 2006. ASGE technology status evaluation report: wireless capsule endoscopy. *Gastrointest. Endosc*., **63**(4):539-545. [doi:10.1016/j.gie.2006.01.014]

Moglia, A., Menciassi, A., Schurr, M.O., Dario, P., 2007. Wireless capsule endoscopy: from diagnostic devices to multipurpose robotic systems. *Biomed. Microdevices*, **9**(2):235-243. [doi:10.1007/s10544-006-9025-3]

Ogata, H., Kumai, K., Imaeda, H., Aiura, K., Hisamatsu, T., Okamoto, S., Iwao, Y., Sugino, Y., Kitajima, M., Hibi, T., 2008. Clinical impact of a newly developed capsule endoscope: usefulness of a real-time image viewer for gastric transit abnormality. *J. Gastroenterol.*, **43**(3):186-192. [doi:10.1007/s00535-007-2140-y]

Olds, G.D., Sivak, M.V., Wong, R.C.K., 2002. The clinical utility of technetium 99m-labeled bleeding scans in the evaluation of acute lower GI hemorrhage. *Am. J. Gastroenterol*., **97**:s121. [doi:10.1016/S0002-9270(02)04838-4]

Schmit, A., Gay, F., Adler, M., Cremer, M., Gossun, A.V., 1996. Diagnostic efficacy of push-enteroscopy and long-term follow-up of patients with small bowel angiodysplasias. *Dig. Dis. Sci*., **41**(12):2348-2352. [doi:10.1007/BF02100126]

Shi, J., Yan, G.Z., Fang, J., 2006. Non-invasive method for detecting and locating the hemorrhagic focus of digestive tract. *Beijing Biomed. Eng*., **25**(5):545-547 (in Chinese).

Singer, A.A., 1995. Value of CT in localizing site of gastrointestinal hemorrhage following negative angiography. *Abdom. Imaging*, **20**(1):31-32. [doi:10.1007/BF00199640]

Singh, V., Alexander, J., 2009. The evaluation and management of obscure and occult gastrointestinal bleeding. *Abdom. Imaging*, **34**(3):311-319. [doi:10.1007/s00261-008-9423-5]

Uehara, A., Hoshina, K., 2003. Capsule endoscope NORIKA system. *Minim. Invasive Ther. Allied Technol.*, **12**(5):227-234. [doi:10.1080/13645700310014933]

Wu, X.D., Hou, W.S., Peng, C.L., Zhen, X.L., Fang, X., He, J., 2008. Wearable magnetic locating and tracking system for MEMS medical capsule. *Sens. Actuators A*, **141**(2):432-439. [doi:10.1016/j.sna.2007.10.051]

Zuckerman, G.R., Prakash, C., Askin, M.P., Lewis, B.S., 2000. AGA technical review on the evaluation and management of occult and obscure gastrointestinal bleeding. *Gastroenterology*, **118**(1):201-221. [doi:10.1016/S0016-5085(00)70430-6]