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Tumor localization using radio-frequency identification clip marker: experimental results of an ex vivo porcine model

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Abstract

Purpose With the widespread use of minimally invasive surgery, tumor detection is becoming more difficult. We present the experimental results of a radio-frequency identification (RFID) lesion detection system in an ex vivo porcine model.

Methods The efficacy and feasibility of a newly developed RFID lesion detection system were examined. It was applied to the stomach and colon of pigs weighing 40 kg. The RFID clip was attached to the upper and lower mucosal sides of the stomach. Colon specimens with thin and thick walls were used. The clipped sites were marked on the serosa by a pin. The longest distance from the pin the RFID tag could be detected was measured 25 times in each direction.

Results In the upper gastric wall, the RFID tag detection distance was 4.5 ± 0.9 mm, 5.6 ± 0.7 mm, 12.5 ± 0.7 mm, and 5.3 ± 0.5 mm in the four directions, respectively (right, left, upper, and lower). In the antrum, the RFID tag detection distance was 5.8 ± 0.7 mm, 6.9 ± 0.5 mm, 5.6 ± 0.5 mm, and 3.7 ± 0.5 mm in the four directions. In the thin colon, the RFID tag detection distance was 6.3 ± 0.5 mm, 5.0 ± 0.5 mm, 9.7 ± 0.7 mm, and 6.4 ± 0.4 mm in the four directions. In the thick colon, the RFID tag detection distance was 3.5 ± 0.8 mm, 6.6 ± 0.5 mm, 8.4 ± 0.6 mm, and 9.8 ± 0.5 mm in the four directions. The area of detection was smallest for the antrum (83.7 mm^2) and similar for the other sites (150.6, 154.7 and 157.7 mm^2 for the upper body, thin colon, and thick colon, respectively).

Conclusions The distance at which the RFID tag was detected was usually within 10 mm. These results indicate the feasibility of the clinical application of the add-on clip and RFID tag as a marker for identifying the location of various gastrointestinal tumors.

Keywords Gastrointestinal tumor · Lesion detection · Radio-frequency identification · Endoscopic clip

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With the development of surgical instruments and improvements in surgical skills, laparoscopic surgeries have evolved for 2 decades. In this flow, interest in the quality of life and the results of several studies have changed the recent trend of gastrointestinal surgery from open to laparoscopic [1–3]. Laparoscopic surgery has some advantages related to postoperative courses, such as less pain, rapid recovery, and good cosmetic outcomes compared with conventional open surgery [4, 5]. However, identifying the exact location of a lesion remains a problem because the surgeon cannot palpate the lesion by hand during surgery [6]. Especially in cases of early cancer or benign tumors showing endophytic growth, it can be difficult to decide the appropriate resection margin because the lesion is not present on the serosal surface of the intestine [7].

In gastrectomy, intraoperative endoscopy or abdominal radiographs have been introduced for lesion confirmation;

however, there is no widely accepted method in the clinical field because of the complexity of the procedure or the difficulty of cooperation with other departments. Although the tattooing technique was introduced in colectomy, the additional preoperative colonoscopy results in patient discomfort and economic problems. Moreover, this approach is not effective for lesion identification due to the rapid washout of the dye use for tattooing during the diagnostic colonoscopy [8–10]. Because of these problems, there have long been unmet needs for new medical technologies for gastroenterological lesion identification. The authors have paid attention to radio-frequency identification (RFID) technology and designed a lesion identification system including an RFID detector and tag attached to a metal clip that can be applied to the intestinal mucosa. The efficacy and usefulness of this system in tumor localization were evaluated through ex vivo experiments using porcine stomachs and colons.

Methods

Pilot study

A pilot study was conducted before this study to verify the applicability of RFID using a passive-type RFID card, which embedded small RFID tag. The study was designed as an ex vivo test using the stomach and colon of a 40 kg pig (Fig. 1A, B). The RFID card (Fig. 1C) was placed under the intestine, and its location was indicated by a pin. A coil-shaped antenna was used, and its internal diameter was 9 mm (Fig. 1D). RFID module was presented in Fig. 1E. Then, the longest distance was measured and recorded that the tag could be detected (Fig. 1F, G). The distance was measured at the five following sites: the gastric cardia, the anterior wall, the greater curvature, the lesser curvature, and the antrum. In addition, the colon was investigated in two thin sections and one thick section. The thickness was also measured at each site of the stomach and colon to analyze the correlation between the thickness and the detection range (Fig. 1F).

Composition of RFID lesion detection system

The RFID lesion detection system used in this study consisted of the following components: (1) a cylindrical RFID tag (Width: 12.25 mm, Diameter: 1.93 mm, 125 kHz frequency, SparkFun, SEN-09416); (2) a metal clip; (3) a stick-shaped tag detector with antenna (for 10-mm laparoscopy trocar port); (4) an MCU (Micro Control Unit, ATmega 168, Atmel Co.); (5) a wireless communication module (802.11b protocol); and (6) an RFID detect circuit (EM4100) using universal asynchronous receiver/transmitter (UART) communication. MCU and RFID circuit can communicate each

other by UART protocol. If MCU receives a signal from RFID circuit, MCU copies the signal and sends it to wireless module. The wireless module converts it to UDP (User Datagram Protocol) message and then sends it to user's PC. The communication interval time between the module and user's PC is less than 1 ms average so the delay time does not affect the user's area detection and appropriate for real-time application. A schematic illustration of this system is presented in Fig. 2. In this study, an RFID add-on clip was prepared by modifying a conventional metal clip; a plastic ring was then used to tighten the clip's jaw and fix the clip to the gastric mucosa. RFID tag was inserted into the plastic ring and attached to the clip (Fig. 3A–C). This RFID add-on clip grabbed the gastric wall inside and it works the same way as the conventional endoscopic hemoclip. Generally, RFID tags can be classified into either active or passive types. A passive-type cylindrical RFID tag was used which has no internal battery. Because of the shorter detection range, which is advantageous for lesion identification, a low-frequency (125–134 kHz) RFID tag with a detection distance range of 1–10 cm was used. A capacitive-type detector was designed in a stick shape for utilization in laparoscopic surgery, and the antenna and reader were embedded in the handle (Fig. 3D). The detection algorithm program is compiled by C++ programming language and shows RFID's ID number and when it is detected. And it has a feature to make a beep sound and record the ID and detection time in the computer when a tag was identified with a graphic user interface.

Ex vivo experimental protocol

The stomach and colon from a 40-kg pig were used in the pilot study. An RFID tag was applied to the upper and lower gastric mucosa via the add-on clip, and each site was marked using a pin on the serosal surface of the intestines to confirm the exact location of the clip. Based on this pin, we tried to recognize the RFID tag 25 times for each site in four directions (up, down, left, right) and recorded the detection distance. Two colon specimens were used, one 8 mm (thick colon) and one 3 mm (thin colon) in thickness, and an RFID tag was applied to each colon specimen. As in the case of the stomach, the detection range of the RFID tag was recorded 25 times in four directions (upper, lower, left, right) for the thick and thin colon specimens.

Statistical analysis

All continuous variables were assessed by Student's t-test and are expressed as the mean ± standard deviation. Logistic regression analysis was used for analyzing the correlation between intestinal thickness and detection distance in the pilot study. Each value is presented on a four-direction scale

Fig. 1 Porcine viscera and RFID device used for the pilot test. **A** Stomach. It has a shape and structure similar to that of a human. a: Cardia, b: body, c: antrum, d: greater curvature, e: lesser curvature. **B** Colon. a: Thin area, b: thick area (with fat tissue). **C** Card-shaped tag (passive type, 125 kHz). **D** Antenna, approximately 9 mm in diameter. **E** Overview of the RFID module. a: Antenna, b: reader, c: controller. **F** The porcine stomach was incised along the greater curvature, and the tag was inserted into the gastric cavity. The RFID tag was localized by a pin. *RFID* radio-frequency identification. **G** Measurement of the detection range. The distance from the edge of the transceiver field to the passive tag was measured at the site where the first signal was detected. **H** The thickness of each site was measured. The antrum was 6 mm thick
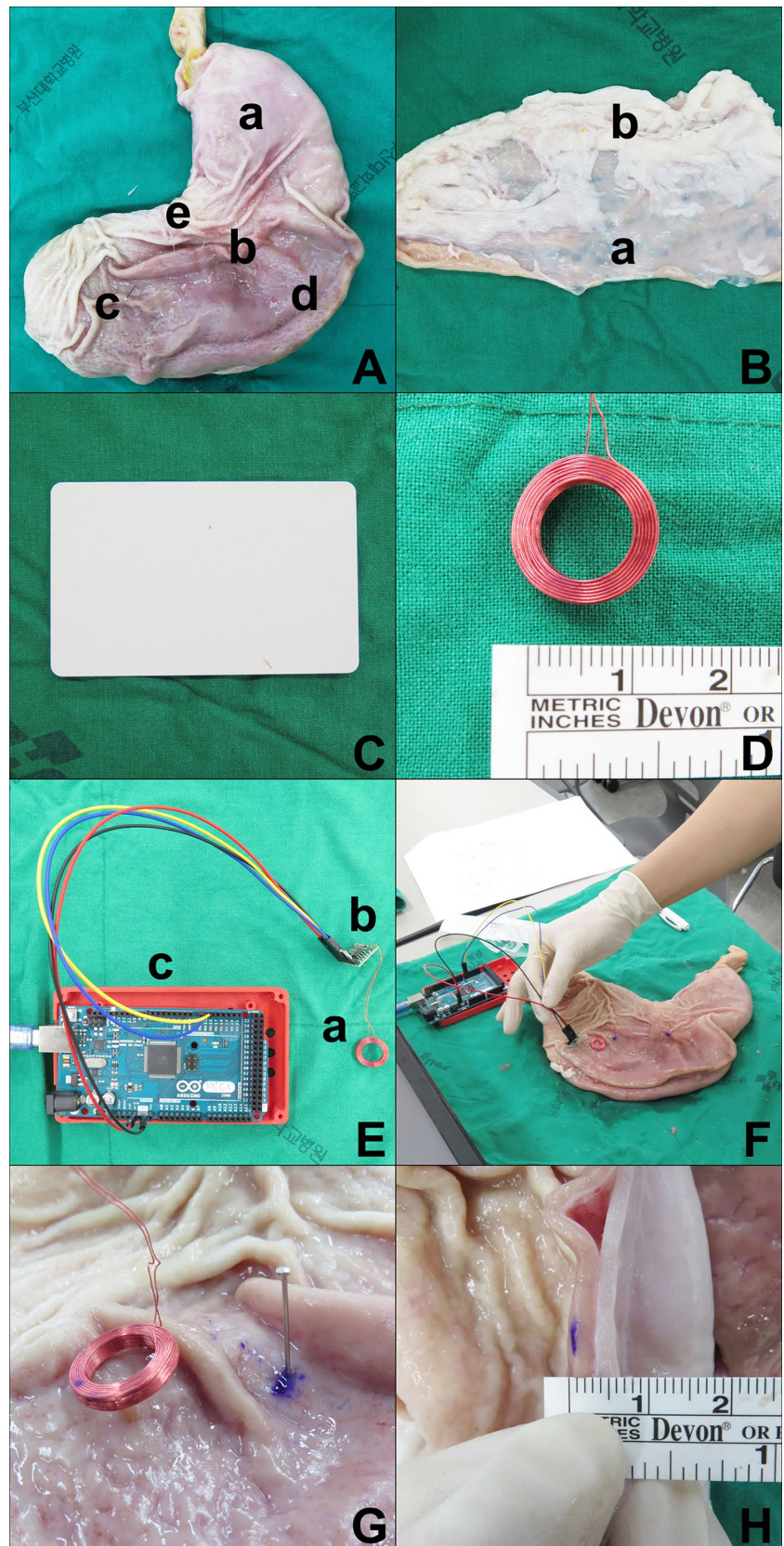
Fig. 2 Schematic of the RFID lesion detection system and operating algorithm. **A** Wireless detection system (detector). This system detects RFID tags and communicates with computers through RFID detection circuits and 802.11b modules. **B** The computer acts as a server for receiving information on the RFID tag. The speaker beeps when the tag is detected. This computing system will be embedded into a wireless stand-alone detector in a prototype. *RFID* radio-frequency identification, *MCU* micro control unit, *UDP* user datagram protocol
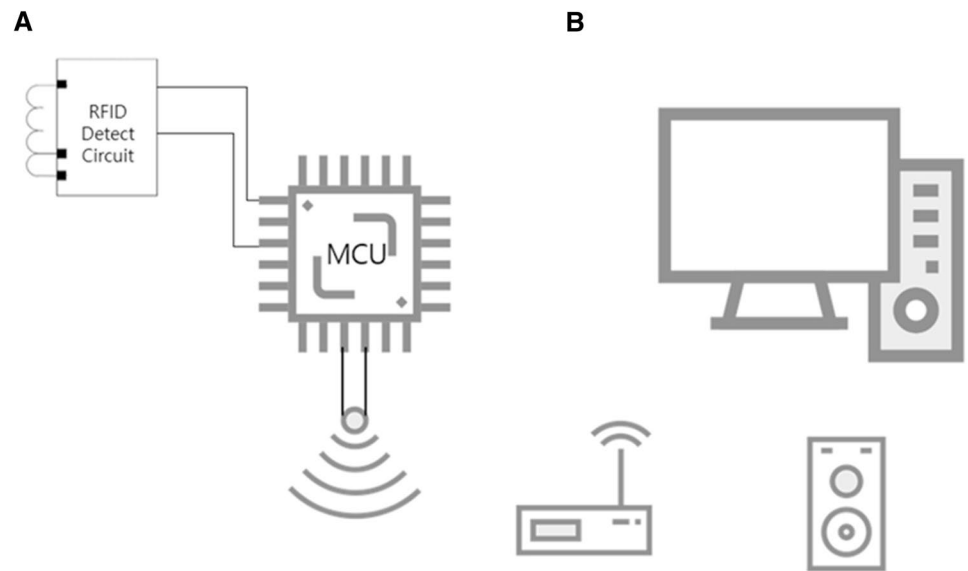
Fig. 3 Lesion localization using the RFID tag. **A** Low-frequency cylindrical RFID tag (passive, 125 kHz). **B** Modified metal clips. **C** Application of clip and RFID tag to the mucosal surface of the stomach. **D** Localization of RFID tag using the wireless detector. *RFID* radio-frequency identification
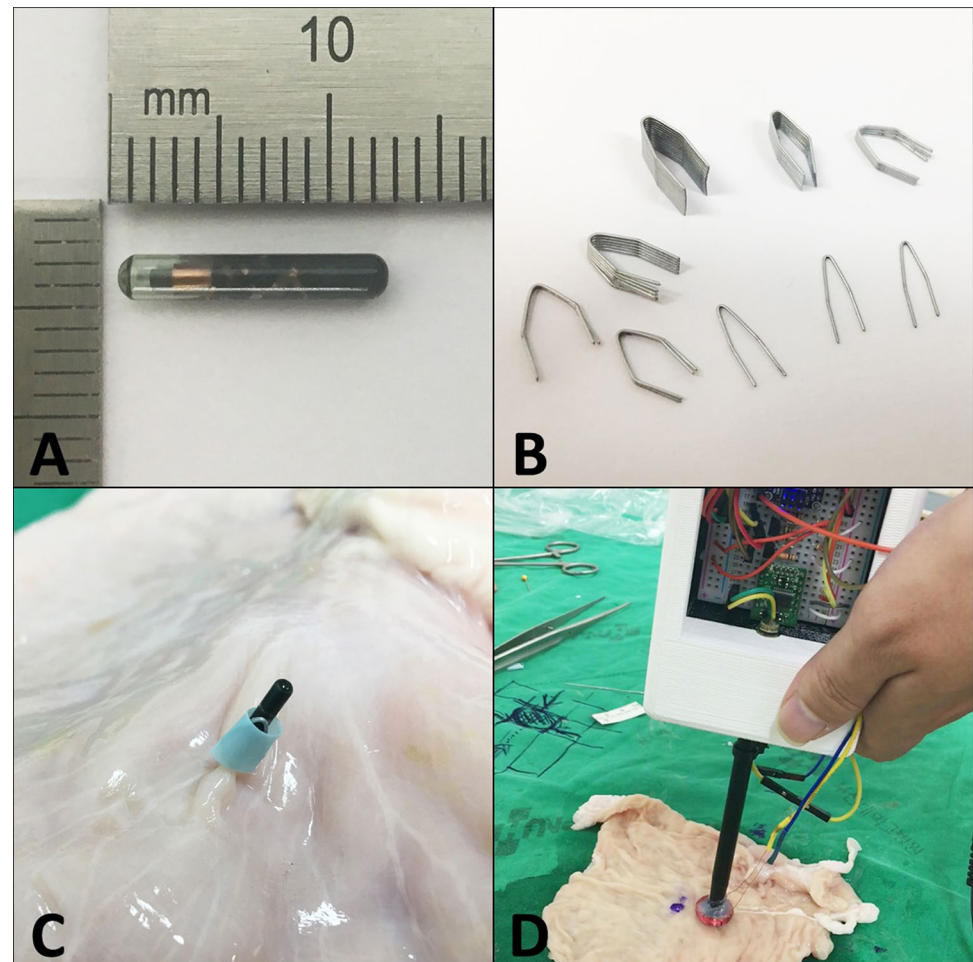
for visualization of the detection distance. In this process, we used scatterplot jittering with the following formula: [Measured value] $+ (R - 0.5) \times 0.9$, where "$R$" is a random number from zero to one. In addition, we derived virtual ellipses from this scatterplot jittering and calculated their area for

Table 1 Detection range of the card-shape RFID tag at each site in porcine stomach and colon (pilot study)

Viscera name	Location	Wall thickness (mm)	Distance[a] (mm)		
			1st	2nd	3rd
Stomach	Cardia	7	8	9	7
	Body	5	9	9	11
	Antrum	6	10	10	11
	Body/GC	8	11	7	10
	Body/LC	4	11	15	14
Colon	Thin	2	13	19	22
	Thick	5	11	11	10

GC greater curvature, *LC* lesser curvature

[a]Distance is the lengths from the edge of the transceiver field to the tag measured three times each
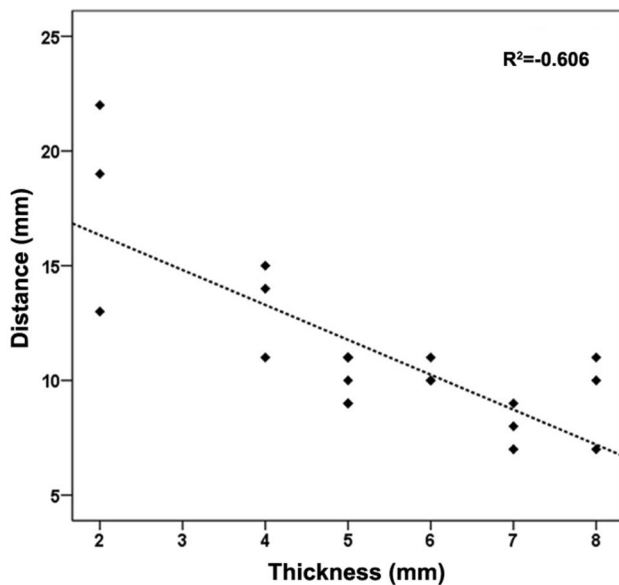
Fig. 4 Correlation between intestinal thickness and detection distance (logistic regression analysis, $R^2 = -0.606$)

each site. The software used for the statistical analysis was SPSS, version 22.0 for Windows (SPSS, Inc., Chicago, IL).

Results

Pilot study

The detection range is shown in Table 1. The greater curvature of the body was the thickest at 8 mm, and the thin colon was the thinnest at 2 mm. The detection distance varies from 7 to 22 mm and its dependency with intestinal thickness is shown in Fig. 4 ($R^2 = -0.606$). The RFID tag was read more closely with increasing intestinal wall thickness due to its torus-shaped magnetic field of the card-shaped tag.

Add-on clip RFID lesion detection system

The detection distance for each site and area calculated from the derived ellipses is presented in Table 2 and is visualized with a jittered scatterplot (Fig. 5). Unlike the results of the pilot study, there was relatively large variation among the organ sites and approach directions. In the upper body, the value measured from the upper direction was greater than the other values (12.5 ± 0.7 mm). In the antrum, although there was not large deviation among the values, the detection distance was smallest from the lower direction (3.7 ± 0.5 mm). The thin colon showed the greatest detection distance in the upper direction at 9.7 ± 0.7 mm. The thick colon showed the largest detection distance in the lower direction at 9.8 ± 0.5 mm and smallest detection distance in the right direction at 3.5 ± 0.8 mm. Overall, mean detection distance in each direction is 7.2 ± 1.9 mm, 5.7 ± 0.9 mm, 10.2 ± 1.8 mm, and 4.8 ± 1.4 mm, respectively (right, left, upper, and lower side). The thickness of the upper gastric wall, antrum, thin colon, and thick colon was measured as 4.0 mm, 6.0 mm, 3.0 mm, and 8.0 mm, respectively. And there was not associated between intestinal thickness and detection distance. The area of the ellipse derived from the detection distance was smallest for the antrum (83.7 mm^2) and similar for the other sites (150.6, 154.7, and 157.7 mm^2 for the upper body, thin colon, and thick colon, respectively).

Table 2 Detection range of RFID tag add-on clip according to porcine organ (mm, $M \pm SD$)

	Variable	Thickness	Right	Left	Upper	Lower	Major axis	Minor axis	Area (mm^2)
Stomach	Upper body	4.0	4.5 ± 0.9	5.6 ± 0.7	12.5 ± 0.7	5.3 ± 0.5	18.1	10.6	150.62
	Antrum	6.0	5.8 ± 0.7	6.9 ± 0.5	5.6 ± 0.5	3.7 ± 0.5	12.5	8.5	83.86
Colon	Thin	3.0	6.3 ± 0.5	5.0 ± 0.5	9.7 ± 0.7	6.4 ± 0.4	14.7	13.4	154.67
	Thick	8.0	3.5 ± 0.8	6.6 ± 0.5	8.4 ± 0.6	9.8 ± 0.5	15.0	13.4	157.74

RFID radio-frequency identification, *M* mean value, *SD* standard deviation
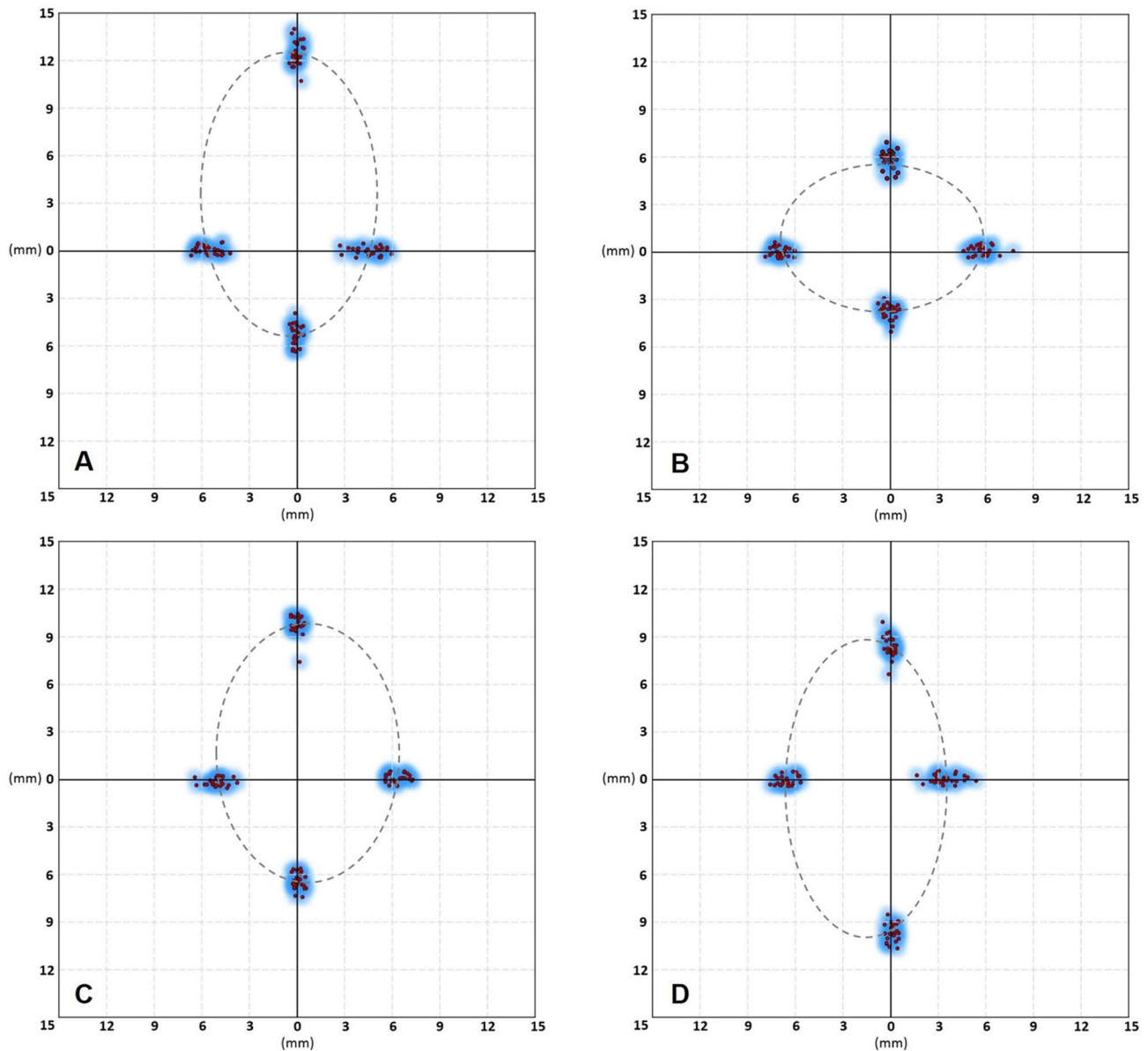
Fig. 5 Visualization of the detection range at each location on the porcine organ. Virtual ellipses were derived from four points of measurement for calculating the area. **A** Upper body (stomach). **B** Antrum (stomach). **C** Thin colon. **D** Thick colon

Discussion

During laparoscopic surgery, it is impossible to confirm the location of early cancer with the naked eye because the lesion is not present on the serosal surface. This is also true for various benign tumors that grow into the lumen of the intestine (endophytic growths). As minimally invasive surgery has become popular, the directions and trends of surgery have also changed. However, the basis of cancer surgery is ensuring oncological safety by obtaining a clear margin through exact resection.

Since the introduction of laparoscopic-assisted gastrectomy by Kitano in 1994, it has become the standard treatment for early gastric cancer, and many favorable results have been reported even for advanced gastric cancer [11, 12]. Because early gastric cancer does not show any indication on the serosa, most surgeons install a hemostatic clip near the lesion through the endoscope preoperatively and indirectly confirm the lesion by palpating the clip by hand during surgery [13]. However, in totally laparoscopic gastrectomy, which has been introduced recently, it is difficult to detect the lesion because the entire surgical procedure, including the dissection and anastomosis, is performed

within the abdominal cavity. Therefore, many researchers have reported various techniques for identifying lesions.

Hyung et al. introduced a technique using laparoscopic ultrasonography for gastric submucosal tumors. Although this method has several advantages that allow it to be easily and safely performed, surgeons need to be proficient in ultrasonography, and it might fail to identify lesions because of the small clip [7]. In 2011, Kim et al. reported a method for identifying the location of clips applied preoperatively in 80 early gastric cancer patients through intraoperative plain abdomen radiography [8]. In 2014, Kim et al. also reported a technique for detecting lesions through plain abdominal radiography using radio-opaque gauze during the surgery [14]. Several methods using intraoperative endoscopy have been introduced. The autologous blood tattooing method has been reported by Jeong et al. This method takes blood from the patient before surgery and injects it into the gastric submucosal layer during the surgery [15]. Xuan et al. also suggested a method for identifying mark presented on the serosa by injecting a dye in the submucosa via intraoperative endoscopy without the application of a hemoclip before surgery [9]. However, these various techniques are not widely used in the clinical field because intraoperative radiology or endoscopy presents the risk of contaminating the aseptic surgical field, prolonging the operation time, and needing to manipulate an unconscious patient under general anesthesia.

RFID is a technology that can transmit data without physical contact using the energy of the RF spectrum. The basic RFID system consists of an RFID tag and RFID reader (or RFID detector). The RFID tag can be passive or active depending on the presence of a power supply. An active tag operates by receiving power and has a very long detection distance (~ 100 m). A passive RFID tag consists of an RFID antenna and an IC chip containing unique data; these tags are advantageous for miniaturization because they operate only with the induction current of the RFID detector without a power supply. If the RFID detection range is too long, it is difficult to know the exact location of the lesion. Therefore, to narrow the detection range of the lesion and miniaturize the device, a low-frequency passive RFID tag was chosen for this study. The radio-frequency and design of the antenna in the detector determine the detection distance. If the RFID detection distance can be precisely controlled by the design of the coil structure of the antenna, clinical utilization would be increased.

A pilot study was conducted to evaluate the feasibility of clinically applying this RFID system. Because we used a card-shaped tag, the RFID tag was placed directly under the intestine without any movement or torsion of the axis. The antenna coil of the card-shaped tag is flat. Therefore, the detection field of the RFID tag forms the shape of a torus or a perforated orb (Fig. 6A), and the detection range was constant in all directions and correlated with the thickness

of the field. In addition, the detection range decreased with increasing intestinal wall thickness. Because the detection range was within 20 mm, which was an acceptable result for clinical use, we planned the next study.

The results of the experiment with the RFID add-on clip were slightly different from those of the pilot study, and there was no correlation between detection range and intestinal thickness. The ideal RFID detection field of a cylindrical coil antenna used for this study is shown in Fig. 6B. However, the actual detection field was in the shape of an elongated sphere (Fig. 6C) because the antenna was not coiled infinitely in a vertical direction (x-axis). These results suggest that the detection fields of the RFID tag form obliquely with respect to the direction in which the clip is placed while the RFID tag is clipped to the intestinal surface. It may be difficult to find the actual location of the clip due to the axis deviation of this elongated sphere. Figure 6D shows why this difference in distance occurs between the predicted and actual location of the clip.

All detection ranges measured were within approximately 10 mm (3.5–12.5 mm), these results indicate that RFID can be used as a strong tool for identifying the location of lesions more precisely. However, this error may cause the concern regarding the exact resection for obtaining a safety margin despite many debates about that issue. Japanese gastric cancer group suggested the proximal margin of 2–3 cm in early gastric cancer and 5 cm in advanced gastric cancer [16]. And NCCN guideline recommended a proximal resection margin more than 4 cm [17]. Also, there are some reports that margin length is not associated with prognosis of cancer [18, 19]. Actually, margin length in final pathology is reported with a very wide range and may be different from the intention of the operator. Therefore, we believe that these differences in distance may not affect the final result of the surgery. In addition, since the deviation between the center of the measured ellipse and the actual location of the clip is small (2–3 mm), it is expected that predicting the precise location of a lesion using the suggested RFID detection system is highly feasible.

This study has some limitations, such as the ex vivo test, in which several environmental conditions were not controlled. First, there may be bias in the detection distances due to the manual measurements. Therefore, we tried to reduce this bias through measurement of 25 times in each of the four directions based on the location of the pin (total 100 times per site). This large number of measurements may decrease the error and increase the reliability of the results. Second, the area of ellipses that can be derived from the four points may be larger; however, because the lines from the upper to lower regions and from left to right were set to be perpendicular to each other based on the pin, these lines can be assumed to be parallel to the major and minor axes of the ellipse, respectively. Therefore, the area of the derived and

Fig. 6 Shape of the detection field according to tag design and difference in the detection distance between the real and predicted location of the clip. **A** Torus (flat RFID). **B** Cylindrical (ideal RFID detection field). **C** Elongated sphere (actual RFID detection field). **D** Illustration of deviated detection field axis. *RFID* radio-frequency identification
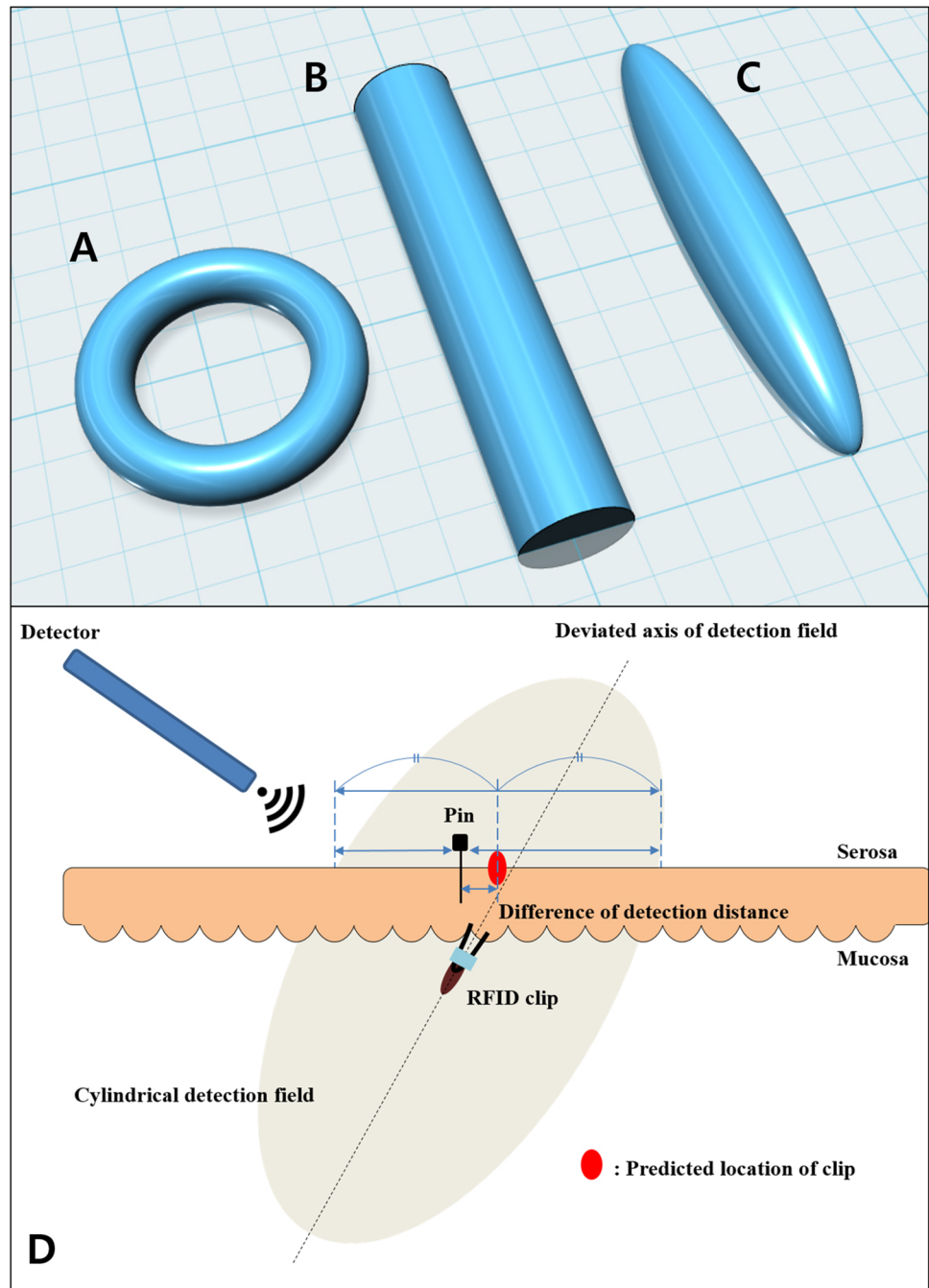
actual ellipse would not show a large difference. Because the RFID tag is an intuitive and semi-permanent device, it is user-friendly and will yield similar results for different users without any bias. In addition, the surgeon can finish alone all the procedures related to detecting a lesion without any necessary cooperation from other departments or patient manipulation during the surgery. Thus, this approach could lead to shortened operative times.

Although this is the result of a basic experiment and conceptual RFID add-on clip in this study cannot be applied in humans now, it suggests several clues related to the

utilization of RFID technology for detecting the lesion location during the laparoscopic surgery. Our final goal is developing the product that can be used in the clinical field through linkage with the medical industry. In the current status, we have a lot of technical and ethnic hurdles to overcome. However, hyper-small RFID is already commercially available, and endoscopic hemoclip technology is also matured enough. Because of the patent issue, we have a plan to design RFID integrated endoscopic clip newly for a finished product, which would be used in the same way as the current endoscopic clip system. So. the RFID add-on

clip is expected to have good persistence after applying on the intestinal wall during the diagnostic endoscopy and be secure enough to remain until the operation day. It will give a higher satisfaction to both the patient and surgeon. We think that it has a high possibility of productization (regardless of its commercial value) and this detection system would be a useful clinical tool.

The RFID add-on clip is expected to have good persistence after applying on the intestinal wall during the diagnostic endoscopy and be secure enough to remain until the operation day. The patient's and surgeon's satisfaction will be higher due to no additional endoscopy for lesion localization. The clip part would be made of titanium. However, a cooper would be used for RFID tag (coil), which may have some risk for magnetic resonance image test. Consequently, it will be not problematic after surgery, because RFID add-on clip will be removed during the surgery with the specimen. And it is also safe using intraoperative diathermy because the clip is applied to the intragastric wall.

Conclusion

A lesion detection system using low-frequency RFID that could be used to easily and quickly locate the clip within a narrow detection range was developed and evaluated in ex vivo test. Correlation between the detection range and RFID's shape of the magnetic field is investigated and explained by using an ellipse model. However, additional data regarding the clipping force, persistence, and difference between the real and predicted clip locations are needed to verify the results of this study. A prototype of the integrated RFID clip and detector system that can be used in the clinical field is in preparation.

Compliance with ethical standards

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