

# Application of ultrasound technology in the diagnosis and treatment of digestive tract diseases

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**Abstract.** – Ultrasound is commonly used in clinical examination which is economic, non-invasive and convenient. Ultrasound can be used for the examination of solid organs and hollow organs. Due to the presence of air, routine ultrasound examination of the digestive tract is not very appropriate. Because of the development of endosonography and its related technology, diagnosis and treatment of gastrointestinal diseases have been improved which is valuable in clinic. This review focused on the application of ultrasound technology in the diagnosis and treatment of digestive tract diseases.

*Key Words:*

Ultrasound technology, Gastrointestinal diseases, Diagnosis, treatment.

## Introduction

Imaging techniques like CT, ultrasound technology, MRI and PET are widely used in modern clinical medicine. All of these technologies can be used to take images of gastrointestinal tract. Because it is economical, non-invasive and non-radioactive features, ultrasound is favored by doctors and patients. Ultrasound has been developed to endoscopic ultrasonography, 3D/4D ultrasound, contrast-enhanced ultrasonography, ultrasonic elastography, strain rate imaging and ultrasound-guided treatment combining with other technologies has already been used in the diagnosis and treatment of digestive diseases.

### **Application of TAUS in Digestive Diseases**

Because of gas in digestive tract, it is difficult to see digestive tract and organs in abdominal cavity clearly by transabdominal ultrasound.

Special conditions are required when observing the hierarchical structure of digestive tract or digestive diseases, e.g., filling liquid into the patient's stomach, which offers a way to observe the hierarchical structure of gastric wall and Gastric ulcer. Similarly, filling liquid's into the patient colon by enema, ulcerative colitis, wall-thickening diseases and colorectal cancer through transabdominal ultrasound. Besides, it is helpful in diagnosing appendicitis by observing the hierarchical structure of appendix. Compared with transabdominal ultrasonography, high-frequency ultrasound is much improved in the observation of digestive tract. Nylund et al<sup>1</sup> has accomplished ultrasound imaging and thickness-testing recently by 8-12 MHz ultrasound, an average thickness of 0.9-1.2 mm from jejunum to sigmoid colon, 2.1 mm of antrum and 1.6 mm of duodenum. Due to the interference of intestinal contents, it is not easy to see small intestine and the colon wall clearly.

### **Application of IDUS in Digestive Diseases**

Ultrasound endoscope, combining ultrasonography with endoscope, does gastrointestinal examination by putting the ultrasonic probe deep into the digestive tract. Ultrasonic probe provides a more accurate and clearer image. If working together with high-frequency ultrasound or HRUS, a more meticulous observation can be provided.

### **Image-Forming Principle of Normal Digestive Tract Wall**

After the ultrasonic emits by ultrasonic probe reflected by human tissue, the back wave, received by ultrasonic probe, forms images on the ultrasonic instrument. Ultrasound beam forms bright echoes when meet with collagen and fat;

on the contrary, forms dim hypoechoes when meet with muscles. Besides, as different tissues have different acoustic resistance, interface ultrasound forms at the interface between different tissues. Interface ultrasound becomes wider or narrower by the ultrasound of lower organization. It can be observed by 7.5-12.5 MHz ultrasound that there is a 5-layer sound image structure of the digestive tract wall. The first layer observed by ultrasound endoscope comes from the interface between gastrovascular cavity water layer and the surface of mucosa. The first layer can hardly be seen when water sacs around ultrasonic sensor are filled with water and stick to the mucosa. The second layer, corresponding to the rest of mucosa, has a hypoecho. The third layer, corresponding to the lower part of mucosa, has a strong echo. The fourth layer, corresponding to muscularis propria, has a hypoecho. The fifth layer mainly corresponds to subserosa and outer membrane. According to the ultrasound images, however, the third layer is thicker than the lower part of mucosa, and the fourth layer is thinner than the muscularis propria. Kimmey MB et al<sup>2</sup> compared tissue sections of digestive tract wall, which come from operation excisions or corpse excisions, with the corresponding ultrasonography. They found that the actual corresponding relations of the five-layer ultrasonography of normal digestive tract wall and tissues are surface mucosa, deep mucosa, submucosa and the boundary echo layer between submucosa and muscularis propria, muscularis propria except for the boundary echo layer between muscularis propria and submucosa, serosa and the fat layer under serosa. The thickness of boundary echoes relates to the longitudinal resolution of the ultrasonic detector. The thickness of the high frequency probe is about 300  $\mu$ . The structure of mucosa is actually complicated, including superficial mucosa, muscularis mucosae and submucosa. However, these complicated structure cannot be distinguished by low-frequency ultrasound, as the acoustic thickness of normal muscularis mucosae is thinner than the boundary echo area between muscularis mucosae and muscularis propria, which results a blurred echo of muscularis mucosae by the boundary echo. Besides the compounded echo of submosa, only the third layer of low-frequency ultrasound can be formed. When high-frequency ultrasound (above 20 MHz) is adopted or the muscularis mucosae become thicker, different parts of the original third layer can be ob-

served. Two echoes will appear below the mucosa: the superficial one with a strong echo is a boundary echo between muscularis propria and muscularis mucosae, while the deeper one with a dim echo is the muscularis mucosae itself<sup>3,4</sup>. Besides, it is found that there is a high level echo appears in the place where the low level echo used to be in the fourth layer by high-frequency ultrasound. This is probably the echoes of fibrous texture between internal-circular muscles external-longitudinal muscles or the boundary echoes between the two layer muscles. However, it is not proved that it will benefit the diagnosis of digestive tract clinical diseases if observation of a few more layers is provided.

### ***Ultrasound endoscope Technology***

Usually in clinical treatment, the quality of echo and echo-location are used to diagnose lesions and find out the cause of disease<sup>5,6</sup>. For example, ultrasonography can be used a basis in the diagnosis of lipoma and cyst. If by high-frequency ultrasound, depth of tumor invasion can be tested accurately. The research shows that the accuracy of gastrointestinal tumor T stage diagnosis has reached 90%<sup>7-9</sup>. However, in other circumstances, ultrasonography can be only used as secondary evidence of differential diagnosis. For example, hypoecho in the third or the fourth layer may have different clinical significance. The accuracy of ultrasonography is only 50% these variations. In these cases, biopsy is still needed<sup>10</sup>. Generally speaking, leiomyoma of muscularis mucosae and granular cell tumor are performed as hypoecho block of the second or the third layer. Meanwhile, lymphangioma is performed as hypoecho block in the third or the fourth layer. Stromal tumor, leiomyoma of muscularis propria and neurilemmoma are in the fourth layer, while lipomyoma and fibroma are in the third layer. High frequency ultrasound endoscope can also obtain detailed information of digestive tract movement<sup>11</sup>. Taniguchi et al<sup>12</sup> recorded the variations of the esophageal wall layers when the esophagu swallowed and moved by 20 MHz ultrasonic probe. The research showed that the thickness of different esophageal wall layers change with cavity pressure. Using high-frequency IDUS to check digestive tract movement can learn the irritation of bowel by intestinal allergen. Arslan et al<sup>13</sup> made a clinical test that by inserting a 20MHz micro probe into duodenum cavity to record clinical manifestation, tunica mucosa, submu-

cosa and muscular thickness before and after the irritation. About 75% percent of the patient showed that their mucosae became thicker, the bowels contracted and the numbers of acoustic image layers changed.

### **Ultrasonic Elastography**

As other organic diseases, the difficulty in diagnosing lesions of gastrointestinal tract is to distinguish benign and malignant lesions, such as in diagnosing adenoma, myoma, ulceration and inflammation. Recently, a new kind of ultrasound technology based on elastoplasticity called ultrasonic elastography or real-time strain imaging technology has come into being. The rationale of ultrasonic elastography is to exert an internal or external static/quasi-static stimulation. By combining ultrasonic imaging with digital signal processing or digital picture processing technique, changes inside tissues can be estimated and elasticity modulus inside tissues can be reflected directly or indirectly. As a result, ultrasonic elastography can distinguish the hard part and the soft part on the digestive tract wall, finding out the distribution of tissues of different hardness. Ultrasonic elastography functions as guidance in determining benign tissues and malignant tissues, showing the boundary between normal tissues and abnormal tissues, for fibrosis makes tissues become harder when canceration<sup>14</sup>. According to types of stimulation, ultrasonic elastography can be divided into static compression/quasi static compression elastography, blood vessel elastography, myocardial elastography, low-frequency vibrating stimulating ultrasonic elastography, instant or pulse elastography based on pulsed excitation and fast ultrasonic system, acoustic radiation force pulse elastography by acoustic radiation force excitation, radiation force imaging, USVA by ultrasonic excitation and shear wave elastography. Ultrasonic elastography facility currently used is the combination of elastography and B-mode ultrasonic, mainly used in diagnosing breast, thyroid and prostate lesions. A research<sup>15</sup> on digestive system showed that the sensibility, specificity, PPV, NPV and accuracy of ultrasonic elastography is 93.4%, 66.0%, 92.5%, 68.9% and 85.4% in diagnosing pancreatic masses. Research by Rustemovic N<sup>16</sup> also showed that Crohn's Diseases in active phase has a higher strain rate than active ulcerative colitis. By using elastography to monitor the movement of stomach, functional gastrointestinal disorder and functional dyspepsia can be diagnosed. However,

as the digestive tract wall is a thin layer structure with tension contracting slowly, SRI is facing challenges in the application of digestive tract treatment<sup>17,18</sup>.

### **Contrast-Enhanced Ultrasound**

CEUS (contrast-enhanced ultrasound) is a kind of imaging technology that injects UCA into blood vessels to enhance imaging. Microbubbles of UCA vibrate under ultrasound and scatter strong ultrasonic signals, which make itself the most important characteristic of UCA. The first generation of UCA has air in its microbubbles, which are commonly used as UCA today, with its envelopes made of polymer such as ALB and galactose. The second generation of UCA has high-density inert gas wrapped inside, with its diameter shorter than 6  $\mu\text{m}$ . CEUS makes it possible to get the picture of revascularization, which benefits the evaluation of tissue vitality, the identification of acute/chronic inflammation and the treatment of tumor blood supply<sup>19</sup>. Girlich et al<sup>20</sup> found that the perfusion of normal intestinal wall and inflamed intestinal wall are different. Schreyer et al detected the activity of Crohn's disease using contrast harmonic ultrasound with quantitative analysis of time-intensity curve<sup>21,22</sup>. CEUS can also evaluate the efficiency of anti gastrointestinal tumor drug by evaluate the signal intensity curves after the injection of UCA. Lassau et al<sup>23</sup> evaluates Gilvec's research on digestive tract stromal tumor by CEUS. Generally speaking, UCA is safe, except for the pregnant. Anaphylaxis is rare and nephrotoxicity has not yet been reported.

### **3D and 4D Ultrasound**

3D ultrasound, more direct than two-dimensional image, demonstrates the spatial form of observation object. The technology means 3D reconstruction of ultrasound data by using a software that contains different coloring schemes, thus any sections can be divided or calculated<sup>24</sup>. Intestinal 3D ultrasound reconstruction performs well in imaging hernia, ulcerative colitis, Crohn's disease, intestinal abscess and tumor. As the development of computer data processing, real-time 3D ultrasound has been achieved, which brings about the so-called 4D ultrasound. The layer structure of the digestive tract wall and bowel movement can be presented dynamically by 4D ultrasound.

### **Ultrasonic Guided Intervention**

High-frequency ultrasound is suitable for the diagnosis and evaluation before the operation of digestive tract endoscopic surgery or minimally invasive surgery, for the imaging of soft tissue in submillimeter level can be achieved by this technology. For example, evaluation of lesion invasion depth is needed before the surgery on colonic polyp loop and endoscopic mucosal resection of digestive tract tumor. However, the application of ultrasound endoscope in the treatment of endoscopic mucosal resection and high-level Barrett digestive tract with atypical hyperplasia is still controversial. A research showed that the accuracy of ultrasound endoscope in confirming the submucosal tumor invasion is no more than 70%<sup>25,26</sup>. Besides, high-frequency ultrasound can guide puncture needle and other devices in intervention treatment of digestive tract diseases, with the whole process showing on the ultrasound screen. By using TAUS guidance, ordinary intervention especially parenchymatous organ intervention can be made. However, to small lesions in the digestive tract wall ultrasound endoscope is usually adopted. Ultrasound endoscope is safer in digestive tract surgery when Doppler is attached to locate blood vessels and observe their distribution<sup>27</sup>. Doppler ultrasound can also help with the diagnosis and treatment of digestive tract varices and vascular malformation<sup>28,29</sup>. Tissue samples can be acquired by ultrasound guidance if lesion of intestinal wall is large, which is very important to clinical diagnosis. If the lesion is deep, small or inconvenient to resect, ultrasound guided EBUS-FNA is needed. Ultrasound guided EBUS-FNA is a kind of intervention commonly used. The needle can be monitored real time and a short-distant, safe and effective puncture path can be established to get the samples of cells or body fluid. FNA under ultrasound guidance can be used in not only the biopsy of pancreas or mediastinal lymph nodes outside the digestive tract, but also intraluminal lesions like tumor and cyst. Besides, ultrasound can also achieve targeted improvement on drug release and absorption. Active ingredient of drugs and even gene segment, wrapped in special mechanical chemical shell, are injected into blood, forming microbubble sediment. When these microbubbles reach the target section, they are exposed in high-energy ultrasonic. At this moment, the shell of drugs fall apart and the active ingredient is released. In this way, local drug concentration is promoted, with the systemic toxicity re-

duced<sup>30,31</sup>. Ultrasound with high energy can make cell membranes shortly open to transmembrane drugs, promoting drug ingestion, which is called "Sonoporation"<sup>32,33</sup>.

### **Conclusions**

Generally speaking, the development of ultrasound technology has improved the diagnosis and treatment of digestive tract diseases. The application of puncture under ultrasonic guidance and ultrasound endoscope has been well-developed. At the same time, ultrasonic elastography and ultrasonic inductive local drug delivery and absorption are still to be improved and clinically assessed.

### **Conflict of Interest**

The Authors declare that there are no conflicts of interest.

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