

Artificial Intelligence in *Cancer*

Quarterly Volume 5 Number 1 July 18, 2024





Artificial Intelligence in Cancer

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Quarterly Volume 5 Number 1 July 18, 2024

EDITORIAL

Tombesi P, Cutini A, Grasso V, Di Vece F, Politti U, Capatti E, Labb F, Petaccia S, Sartori S. Past, present, and future perspectives of ultrasound-guided ablation of liver tumors: Where could artificial intelligence lead interventional oncology? *Artif Intell Cancer* 2024; 5(1): 96690 [DOI: [10.35713/aic.v5.i1.96690](https://doi.org/10.35713/aic.v5.i1.96690)]

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AIC mainly publishes articles reporting research results obtained in the field of artificial intelligence in cancer and covering a wide range of topics, including artificial intelligence in bone oncology, breast cancer, gastrointestinal cancer, genitourinary cancer, gynecological cancer, head and neck cancer, hematologic malignancy, lung cancer, lymphoma and myeloma, pediatric oncology, and urologic oncology.

INDEXING/ABSTRACTING

The AIC is now abstracted and indexed in Reference Citation Analysis, China Science and Technology Journal Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Wen-Bo Wang*, Production Department Director: *Xiang Li*, Cover Editor: *Jin-Lei Wang*.

NAME OF JOURNAL

Artificial Intelligence in Cancer

ISSN

ISSN 2644-3228 (online)

LAUNCH DATE

June 28, 2020

FREQUENCY

Quarterly

EDITORS-IN-CHIEF

Mujib Ullah, Massoud Mirshahi, Cedric Coulouarn

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2644-3228/editorialboard.htm>

PUBLICATION DATE

July 18, 2024

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<https://www.wjgnet.com/bpg/GerInfo/288>

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<https://www.wjgnet.com/bpg/gerinfo/208>

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<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Past, present, and future perspectives of ultrasound-guided ablation of liver tumors: Where could artificial intelligence lead interventional oncology?

Paola Tombesi, Andrea Cutini, Valentina Grasso, Francesca Di Vece, Ugo Politti, Eleonora Capatti, Florence Labb, Stefano Petaccia, Sergio Sartori

Specialty type: Oncology

Provenance and peer review:

Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B

Novelty: Grade B

Creativity or Innovation: Grade B

Scientific Significance: Grade B

P-Reviewer: Chowdhury D

Received: May 14, 2024

Revised: June 26, 2024

Accepted: July 10, 2024

Published online: July 18, 2024

Processing time: 63 Days and 17.1 Hours



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Abstract

The first ablation procedures for small hepatocellular carcinomas were percutaneous ethanol injection under ultrasound (US) guidance. Later, radiofrequency ablation was shown to achieve larger coagulation areas than percutaneous ethanol injection and became the most used ablation technique worldwide. In the past decade, microwave ablation systems have achieved larger ablation areas than radiofrequency ablation, suggesting that the 3-cm barrier could be broken in the treatment of liver tumors. Likewise, US techniques to guide percutaneous ablation have seen important progress. Contrast-enhanced US (CEUS) can define and target the tumor better than US and can assess the size of the ablation area after the procedure, which allows immediate retreatment of the residual tumor foci. Furthermore, fusion imaging fuses real-time US images with computed tomography or magnetic resonance imaging with significant improvements in detecting and targeting lesions with low conspicuity on CEUS. Recently, software powered by artificial intelligence has been developed to allow three-dimensional segmentation and reconstruction of the anatomical structures, aiding in procedure planning, assessing ablation completeness, and targeting the residual viable foci with greater precision than CEUS. Hopefully, this could lead to the ablation of tumors up to 5-7 cm in size.

Key Words: Artificial intelligence; Fusion imaging; Percutaneous thermal ablation; Microwave ablation; Radiofrequency ablation; Ultrasound; Contrast-enhanced ultrasound

Core Tip: Starting from the first experiences with ethanol injection, constant technical improvements in both thermal ablation and ultrasound imaging have led clinicians in interventional oncology to break the so-called 3-cm barrier in the percutaneous treatment of primary and secondary liver tumors. At present, advanced software powered by artificial intelligence has been developed to precisely target tumor margins and/or residual viable tumor tissue, opening the way to the percutaneous ablation of tumors up to 5-7 cm in size.

Citation: Tombesi P, Cutini A, Grasso V, Di Vece F, Politti U, Capatti E, Labb F, Petaccia S, Sartori S. Past, present, and future perspectives of ultrasound-guided ablation of liver tumors: Where could artificial intelligence lead interventional oncology? *Artif Intell Cancer* 2024; 5(1): 96690

URL: <https://www.wjgnet.com/2644-3228/full/v5/i1/96690.htm>

DOI: <https://dx.doi.org/10.35713/aic.v5.i1.96690>

INTRODUCTION

Surgery was the only curative option for the treatment of liver cancer for a long time. However, in the early 1980s percutaneous ethanol injection (PEI) under real-time, grayscale ultrasonography (US) guidance suggested that small hepatocellular carcinomas (HCCs) could effectively be treated with minimally invasive techniques[1,2].

Ethanol injected into the tumor through very fine needles (from 19 to 21 gauge) induces rapid dehydration of cytoplasmic proteins with subsequent coagulation necrosis of the tumoral tissue, necrosis of endothelial cells with platelet aggregation and thrombosis of small vessels, and tissue ischemia. Moreover, the presence of peripheral capsula in most HCCs, their hypervascularity, and the high density of the cirrhotic tissue surrounding the tumor allow ethanol to achieve high intratumoral concentrations, making PEI an effective, safe, and cheap treatment for HCC lesions under 2 cm in diameter[3-5].

However, PEI has shown some major limitations. First, the volume of ethanol that could be injected in a single session was low, leading to multiple treatment sessions even for small lesions. The attempts of injecting large volumes of ethanol in a single session under general anesthesia yielded questionable results and some severe complications, with mortality rates up to 4.5%-5.0%[6,7]. Second, PEI was not effective to treat HCC satellites. Therefore, local tumor progression (LTP) was not infrequent. Finally, PEI was proven to be unsuccessful in the treatment of liver metastases due to their poor vascularity and absence of a peripheral capsule[8].

Some preliminary reports on other attempts of chemical ablation with acetic acid[9] or hot saline[10] were not followed by larger trials with longer follow-up, and these methods were abandoned. As a result, PEI remained the only percutaneous technique that was used worldwide until the early 1990s. However, PEI was limited to the treatment of small HCC lesions not suitable for surgery due to patient comorbidity or poor liver function.

THERMAL ABLATION

The shift from chemical to thermal ablation represented a milestone in the percutaneous treatment of liver tumors, in particular with the “hot” approach. Despite the interesting physical characteristics and good cytotoxic effect of the “cold” approach of thermal ablation, cryoablation was only sporadically used to treat liver tumors due to its high rates of severe complications and high costs[11,12].

The first “hot” technique introduced in clinical practice was interstitial laser photocoagulation. This technique converts light absorption into heat, provoking tissue coagulation[13]. However, interstitial laser photocoagulation produced small thermal lesions (20 mm or less) and was technically challenging because multiple, regularly-spaced laser fibers had to be inserted into the tumor. Therefore, it had limited clinical diffusion, mainly in the treatment of small multiple liver metastases[14,15].

The first experiences with radiofrequency ablation (RFA) in the 1990s on both animals and humans changed the history of thermal ablation of liver tumors[16,17]. Radiofrequency waves induce ionic agitation resulting in production of heat by friction because the surrounding tissue opposes resistance to the current of the flow. Heat is generated within the tissue rather than at the tip of the probe. The heat produced inside the tumor results from the difference between the heat generated by radiofrequency waves and the entity of heat dispersion, depending on tissue conductivity and proximity of blood vessels (the so-called heat-sink effect).

The size and shape of the coagulation area depend on the diameter of the electrode, length of the exposed needle tip, temperature around the exposed tip, and time of application[18]. However, charring of the tissue surrounding the needle tip hampers heat propagation within the tumor, remarkably reducing the size of the necrotic area. To solve this problem, probes with an internal cooling system were introduced in 1995[19], and further technical improvements aimed at increasing the size of the thermal lesion (multiprobe cooled tip arrays, perfusion needles, probes with side-deployed arrays, and so on) were launched into clinical practice[20].

Several randomized trials and meta-analyses showed that RFA was superior to PEI in the treatment of small HCC in terms of primary technique efficacy rate, LTP, and overall survival (OS)[21-24]. Indeed, in tumors under 3 cm in size, RFA frequently obtained a 0.5-1.0 cm safety margin, significantly reducing LTP rates and achieving OS rates comparable to surgical resection[25]. Based on these results, it was included with the curative treatment options for early-stage HCC [26]. Unlike PEI, RFA is also effective in the treatment of small liver metastases[19,27,28]. A phase II randomized trial reported that systemic chemotherapy combined with RFA significantly prolonged OS compared to chemotherapy alone in patients with colorectal liver metastases[29]. However, despite the ongoing technical improvements, RFA remains poorly effective in the treatment of nodules ≥ 3 cm in size. Moreover, the heat sink effect limits its efficacy when the tumor is close to large blood vessels.

In the late 1990s, microwave ablation (MWA) was proposed as an alternative to RFA[30]. Microwave energy applied to tumor tissue creates a rapidly alternating electromagnetic field, and polar molecules (primarily H_2O) are forced to continuously realign with the oscillating electric field. Their kinetic energy increases, which increases the tissue temperature and causes coagulation necrosis. Microwaves are produced by a generator that works at a wavelength of 915 or 2450 MHz and are delivered to tissues through needle-like antennas. Due to the radiating nature of the antenna, direct heating occurs in a volume of tissue around the antenna.

This mechanism of heating differs substantially from RFA and offers some advantages. RFA heating requires an electrically conductive path, is limited in areas of low electrical conductivity, and heats only tissues immediately adjacent to the electrode. Conversely, microwaves are capable of propagating through tissues with low electrical conductivity, high impedance, or low thermal conductivity and are not influenced by the heat sink effect. Therefore, larger ablation volumes and a more predictable shape of the ablation volume should be expected[31].

Despite these theoretical advantages, the first experiences with MWA did not yield better results than RFA[32,33]. The main limit of the first-generation MWA systems was the back heating effect due to reflected waves along the antenna. The effects of this were the need to deliver energy at low power for a short time, small coagulation areas, and the requirement of multiple antennas to treat HCC lesions up to 2 cm[32,33].

Technical improvements, such as a cooling jacket around the antenna to decrease cable heating, and the introduction in the distal portion of the antenna of a miniaturized device for microwave confinement to minimize the back heating effect enabled the delivery of high-power energy for a longer time, achieving large ablation areas. The first *in vivo* randomized comparison between the most recent generation of the MWA system and an internally cooled RFA system found significantly larger ablation areas for MWA than for RFA[34]. Subsequent studies confirmed the efficacy of MWA in the treatment of both HCC and liver metastases from 3-5 cm in size, suggesting that the so-called 3-cm barrier was finally going to be broken[35-38].

US-GUIDANCE: FROM GRAYSCALE TO FUSION IMAGING

Grayscale US was the first imaging technique used to guide needle placement in the percutaneous ablation of liver tumors[1,2,17,19], and US still remains the most used guidance tool worldwide. However, confident visualization of the lesions can sometimes be poor because of small size, deep location, obscuration by overlying structures, or patient characteristics such as obesity or meteorism[39].

Computed tomography (CT) provides a larger field of view and better visualization of the target lesion and is less limited by patient characteristics. However, it requires radiation exposure, does not allow real-time visualization of intrahepatic vessels, and offers a limited angle for needle insertion[39]. Magnetic resonance imaging (MRI) is the most sensitive imaging technique to detect small liver lesions, does not require radiation exposure, and allows near real-time thermal monitoring to adjust power settings and optimize treatment duration. However, it is expensive, its availability is limited, and the ablation procedure is complex and time-consuming[39].

Therefore, despite the limits of US guidance, the vast majority of interventional oncology centers still consider US the first-choice to guide percutaneous ablation. Indeed, US guidance is cheap, readily available, does not require radiation exposure, enables real-time monitoring of each step of the ablation procedure, and allows the placement of the patient in the most suitable position to reach the target area.

In the late 1990s, the implementation of harmonic imaging, which exploits non-linear propagation of US waves through the tissues, decreased reverberation artifacts and improved the signal-to-noise ratio, providing better quality images compared to conventional US[40]. However, a major advancement in US imaging was the introduction of second-generation US contrast media that consisted of small (3-7 μm) gas-containing microbubbles with an external lipidic, proteic, or polymeric shell. Intravenous microbubbles are confined to the blood pool and when they are exposed to the ultrasound beam experience a resonance phenomenon with a frequency from 2-15 MHz[41].

Exploiting this non-linear interaction of the US wave with microbubbles and using low mechanical index, contrast-specific techniques to minimize microbubble destruction, it is possible to achieve continuous, real-time imaging of macrovessels and microvessels in normal and pathologic tissues. Contrast-enhanced US (CEUS) dramatically improved both characterization and detection of liver lesions not visible upon conventional US to such an extent that it is similar to CT or MRI[42]. Even more importantly in interventional oncology, CEUS can differentiate perfused, viable tissues from necrotic tissues enabling the assessment of the completion of the ablation after the end of the procedure and guiding the immediate retreatment of residual viable foci in the tumor tissue, which significantly reduces LTP rates[43,44].

Unfortunately, CEUS unavoidably shares some limitations similar to conventional US. First, US wave penetration is decreased in obese or meteoric patients or in presence of fatty liver. Second, small and deep lesions or lesions at the hepatic dome are extremely difficult to visualize. Third (and most important) in the assessment of ablation completion,

CEUS images are two-dimensional, but the tumor and thermal lesion are three-dimensional, leading to the possibility of missing residual viable foci[45].

Therefore, further advancements are still needed for US and CEUS to remain the first-choice to guide percutaneous ablation. Recent technical advancements such as navigation systems and fusion imaging (FI) (*i.e.* the fusion of real-time US and CEUS with previously acquired CT or MRI scans) are moving in this direction. They enable precise localization (Figure 1A), allow characterization and correct targeting (Figure 1B and C) of lesions that are difficult to visualize (thus expanding the indications for US-guided or CEUS-guided ablation of tumors missed at US or CEUS), and lead to visualization of tumors in high-risk locations (Figure 2A). Moreover, FI provides a better assessment of the ablation area (Figure 2B), which improves the evaluation of ablation completion and permits the treatment of large tumors with multiple needle insertions[46-48].

The complete workflow of FI consists of acquiring baseline images, registering and creating a fusion image, validating the fused image, employing the fused image for real-time guidance during the procedure, and evaluating the post-procedural result of the treatment. FI originates from both different (*i.e.* CT-US or MRI-US) and identical imaging modalities (*i.e.* US-US) acquired before, during, and after thermal ablation[46]. FI is mostly based on the fusion of real-time US images with pre-ablation CT or MRI, but interesting results have also been reported for three-dimensional US-US FI. In this regard, US-US FI has been recently reported to achieve a higher successful registration rate than multimodality FI due to the higher anatomical consistency in monomodality imaging[49].

Regardless of imaging modalities used, intraprocedural real-time FI improves safety and efficacy of percutaneous ablation. A systematic review that analyzed 22 studies confirmed the usefulness of FI in planning and guiding the treatment as well as in monitoring treatment efficacy[47]. In particular, some studies reported immediate technical success rates ranging from 80.7% to 100% and LTP rates ranging from 0% to 14.8%[50,51]. Moreover, other authors reported an improved one-time ablation rate and OS rate as well as a decreased major complication rate[48]. Furthermore, FI allows the identification of incomplete ablation. This leads to accurate and safe guidance of either retreatment or additional needle insertions when large tumors are treated.

It is known that the LTP rate strongly depends on tumor size: As it increases, its spatial shape becomes more complex, making it more difficult to obtain adequate ablation margins and increasing the risk of thermal damage to adjacent structures[48,52,53]. Moreover, ablation planning is more difficult, and multiple needle insertions are needed to cover the entire volume of the tumor. Using FI guidance, Yang *et al*[48] achieved a technical success rate of 97.1% in the treatment of primary and secondary liver tumors 3-7 cm in size. They were able to use FI to stereoscopically define the profile of both the lesions and surrounding structures and to guide the optimal needle insertion, correctly stating the ablation volume and avoiding thermal damage. Interestingly, no difference in technique efficacy rate was found between 3.0-5.0 cm and 5.1-7.0 cm nodules[48], suggesting that US FI might play a key role in the treatment of medium to large-sized liver tumors, particularly using MWA systems.

ARTIFICIAL INTELLIGENCE APPLIED TO US GUIDANCE SYSTEMS: WHERE COULD IT LEAD PERCUTANEOUS ABLATION OF LIVER TUMORS?

Artificial intelligence (AI) is revolutionizing the landscape of modern medicine, assisting physicians in complex interventional procedures that rely on advanced imaging modalities such as MRI, CT, and US.

AI for automatic registration in abdominal FI

It is well recognized that real-time FI can increase safety and efficacy of percutaneous ablation, but achieving perfect synchronization between the two selected imaging modalities is crucial to improve treatment outcomes. Synchronization requires very skilled operators and is complex and time-consuming. AI can aid clinicians in this crucial phase. Machine learning algorithms can work like a very expert clinician who has performed many evaluations. These algorithms are trained to understand and optimize the integration of data from various imaging modalities in real-time. By automating the synchronization process, AI ensures precise alignment and registration of imaging data, enabling the lesion to be targeted more accurately and permitting the precise placement of the needle, ultimately improving the overall accuracy of the ablative procedure[54].

In this regard, an innovative tool introduces a sophisticated approach to FI (AutoSync®; Esaote S.p.A., Genova, Italy). This system utilizes a three-dimensional camera positioned over the patient's abdomen to capture detailed photographs of the skin surface (Figure 3). Subsequently, an advanced algorithm conducts a pixel-by-pixel comparison between these images and the three-dimensional volume derived from CT or MRI datasets, achieving precise alignment and registration. AutoSync® can enable clinicians to promptly verify registration accuracy and to proceed with fine-tuning adjustments using conventional tools, particularly focusing on areas of interest. This system significantly expedites the initial phase of imaging synchronization and has the advantage of being independent of patient positioning. The algorithm comprehensively recognizes the entire surface of datasets, allowing synchronization even with patients positioned in lateral decubitus and ensuring seamless integration and alignment.

AI for post-procedure control of ablation volume

A concentric ablative margin of at least 5 mm significantly decreases the LTP rate[27,55]. Post-procedure CEUS and FI between pre-ablation CT and post-ablation CEUS can help assess the completeness of the ablation and the size of the safety margin to guide further needle insertions[43,44,46-48]. Nevertheless, the side-by-side comparison between pre-

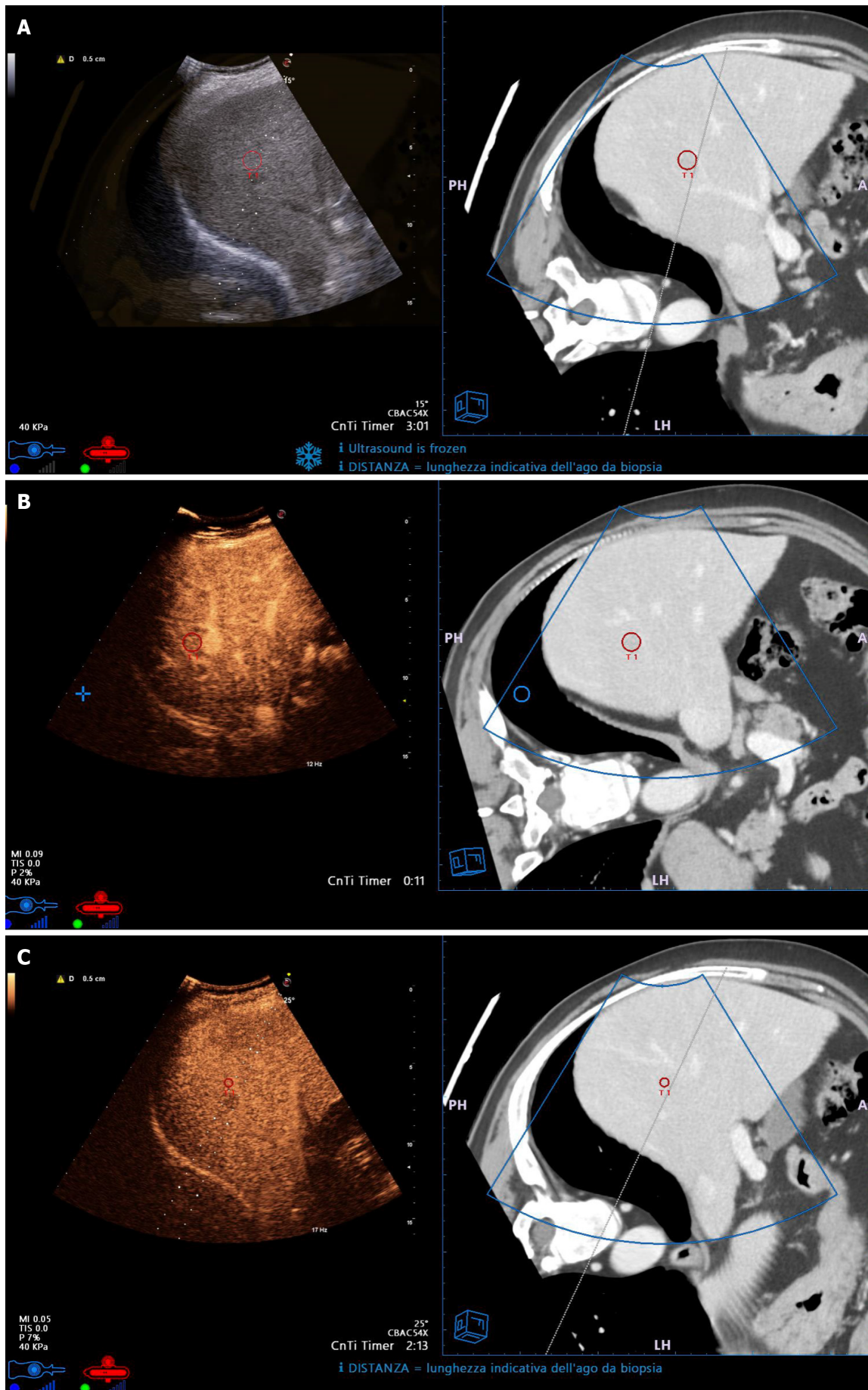


Figure 1 Small hepatocellular carcinoma with low visibility on ultrasound. A: Fusion Imaging (FI) allows to precisely identify and target the lesion (red

circlet in both left and right sides of the split screen); B: Contrast-enhanced ultrasound (CEUS) shows hyperenhancement in the arterial phase (left side of the split screen); C: CEUS shows wash-out in the portal-venous phase (left side of the split screen). FI allows correct guidance of the needle electrode insertion for thermal ablation (dotted line in CEUS images, continuous line in Computed Tomography images).

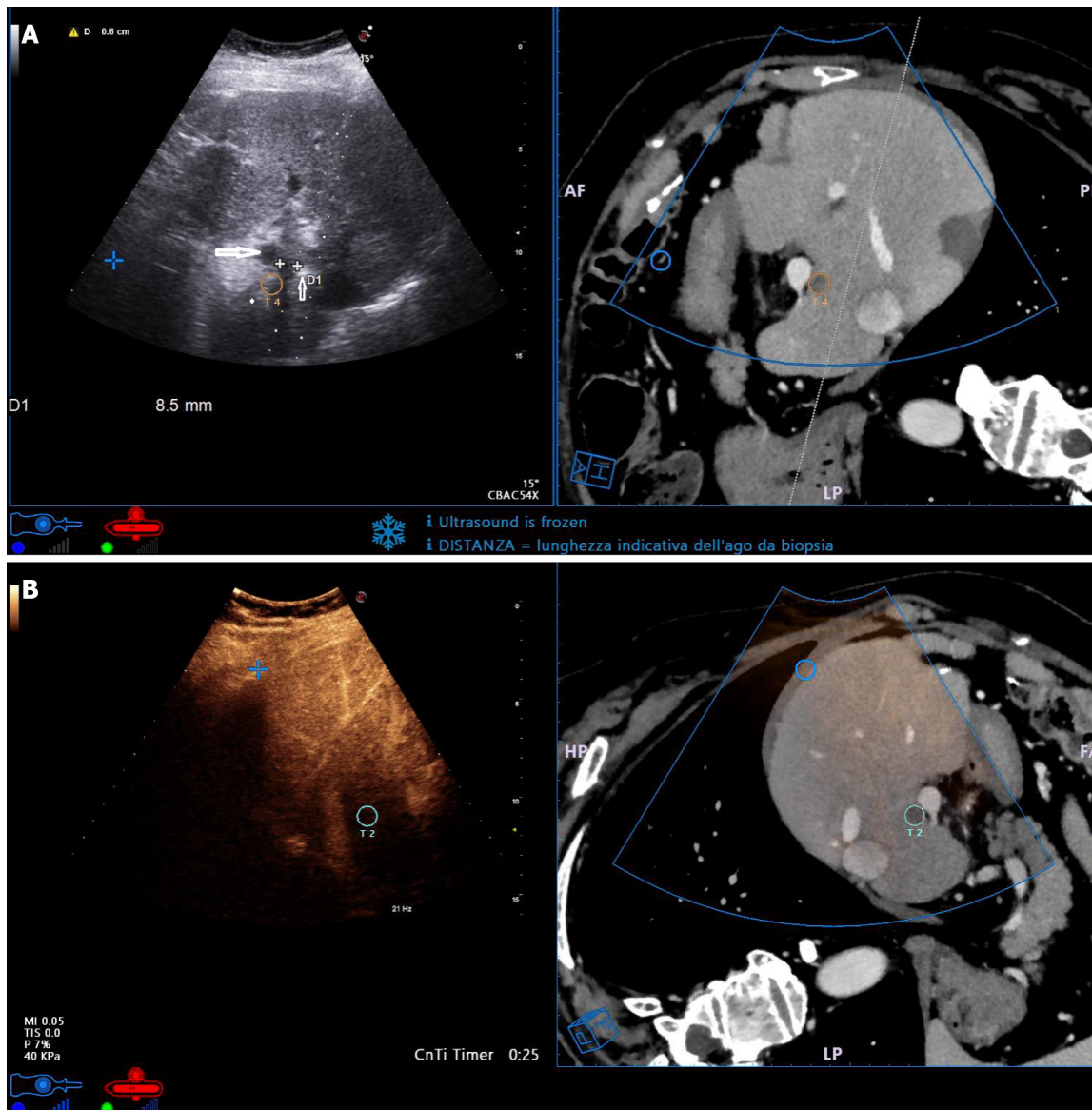


Figure 2 Fusion imaging of small metastasis from colorectal cancer in difficult and high-risk location. A: The lesion was close to the portal vein (white cross-shaped markers in ultrasound image, yellow circle in computed tomography image). The needle tip was correctly placed lateral of the lesion (thin arrow) to maintain a safe distance from the portal vein (large arrow); B: CEUS scan performed 10 min after thermal ablation (with ultrasound transducer orientation inverted compared to Figure 3A) showed complete necrosis. Fusion imaging confirmed the presence of safety ablation margins around the targeted lesion.

procedure and post-procedure contrast-enhanced cross-sectional images is undoubtedly more reliable[20]. However, it too relies on visual evaluation by clinicians and has a non-negligible margin of error because of the misalignment of the liver due to the patient's position and breath movements as well as the tissue biomechanical changes after ablation[56].

Recently, various software have been developed to provide objective and precise assessment of ablation margins using the non-rigid registration of pre-procedure and post-procedure CT or MRI[57,58]. These tools are becoming mandatory for the precise assessment of the technical success of percutaneous ablation. However, they are external to the US machine, are not user-friendly, and are time-consuming. These limits have led to the development of a new technology. The Augmented Ablation Suite (AuAS[®]; Esaote, Genova, Italy) integrates a pre-ablation and post-ablation control software directly into the most advanced Esaote US machines (Figure 4). Powered by AI, AuAS[®] combines pre-ablation and post-ablation CT datasets through an elastic registration, which follows a preliminary segmentation of the abdominal organs. Afterwards, it compares the pre-procedure planned margins (Figure 5) with the necrotic area obtained by ablation (Figure 6), identifying and quantifying any residual viable tumor tissue or insufficient safety margin (Figures 7 and 8) and displaying them as a new target. The development and introduction of this technology will very likely allow



Figure 3 Three-dimensional camera positioned over the patient's abdomen captured detailed images of the skin surface.



Figure 4 Augmented Ablation Suite. Pre-ablation and post-ablation computed tomography datasets are displayed on the monitor of the ultrasound machine.

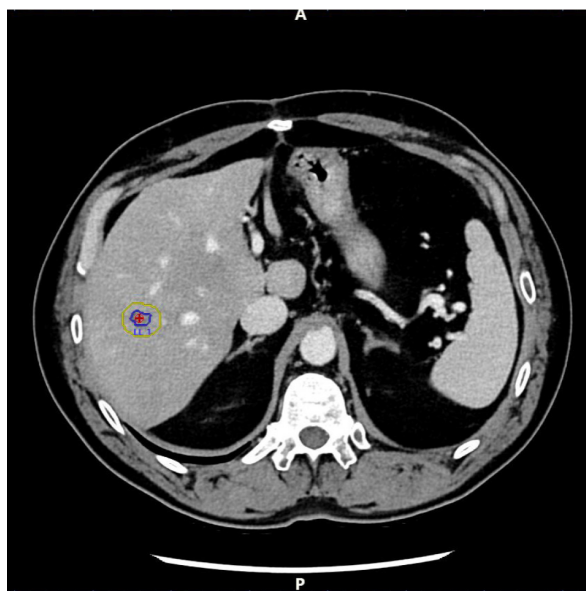


Figure 5 Pre-ablation two-dimensional computed tomography. The target lesion (red circle) was circumscribed scan by scan by the operator (blue line), and the software calculated the safety margin (yellow line).

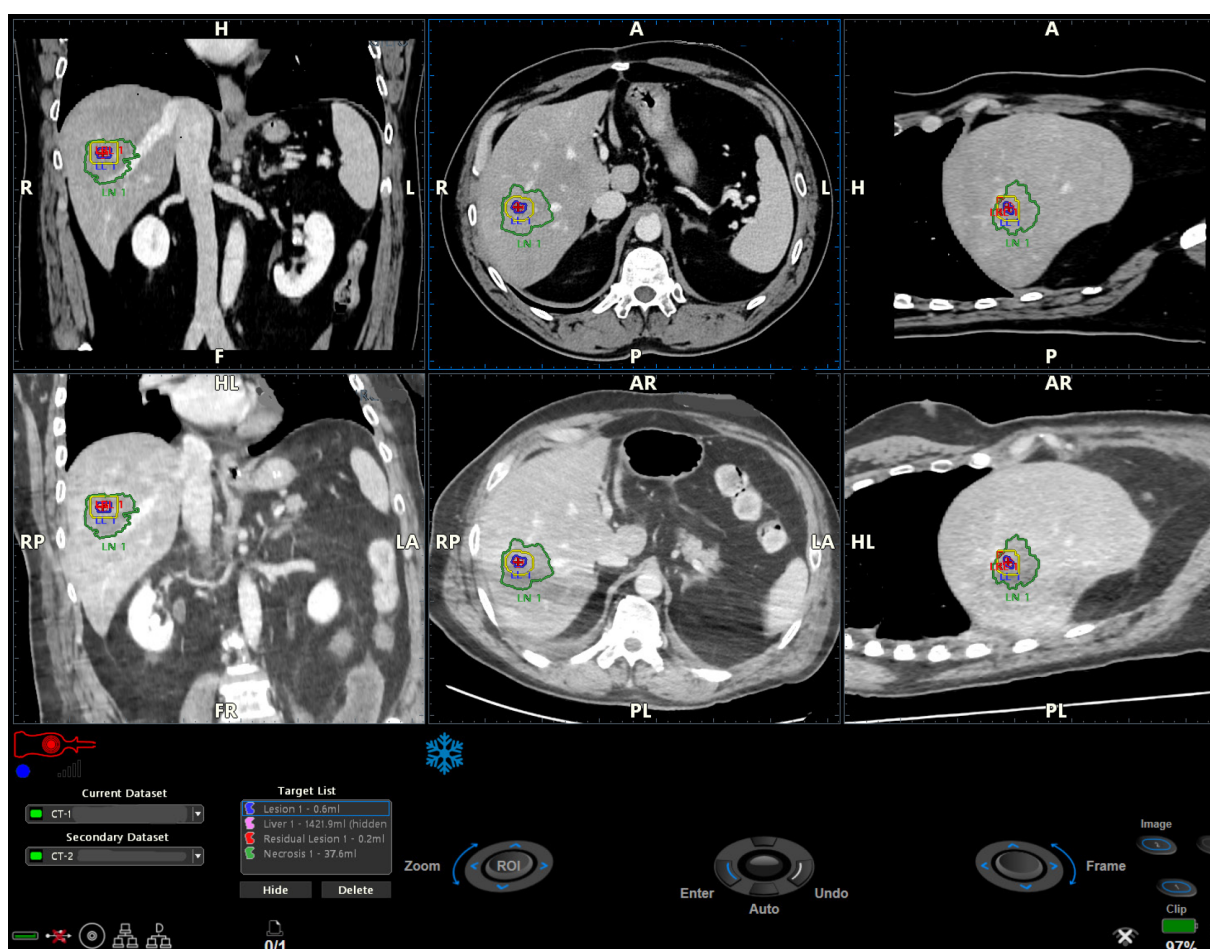


Figure 6 Detail of Figure 4: The pre-ablation dataset (upper series), the post-ablation dataset (lower series), the lesion (red circle and blue line), the safety margin calculated by the software (yellow perimeter), and the necrosis area (green perimeter) are displayed in the three plans.

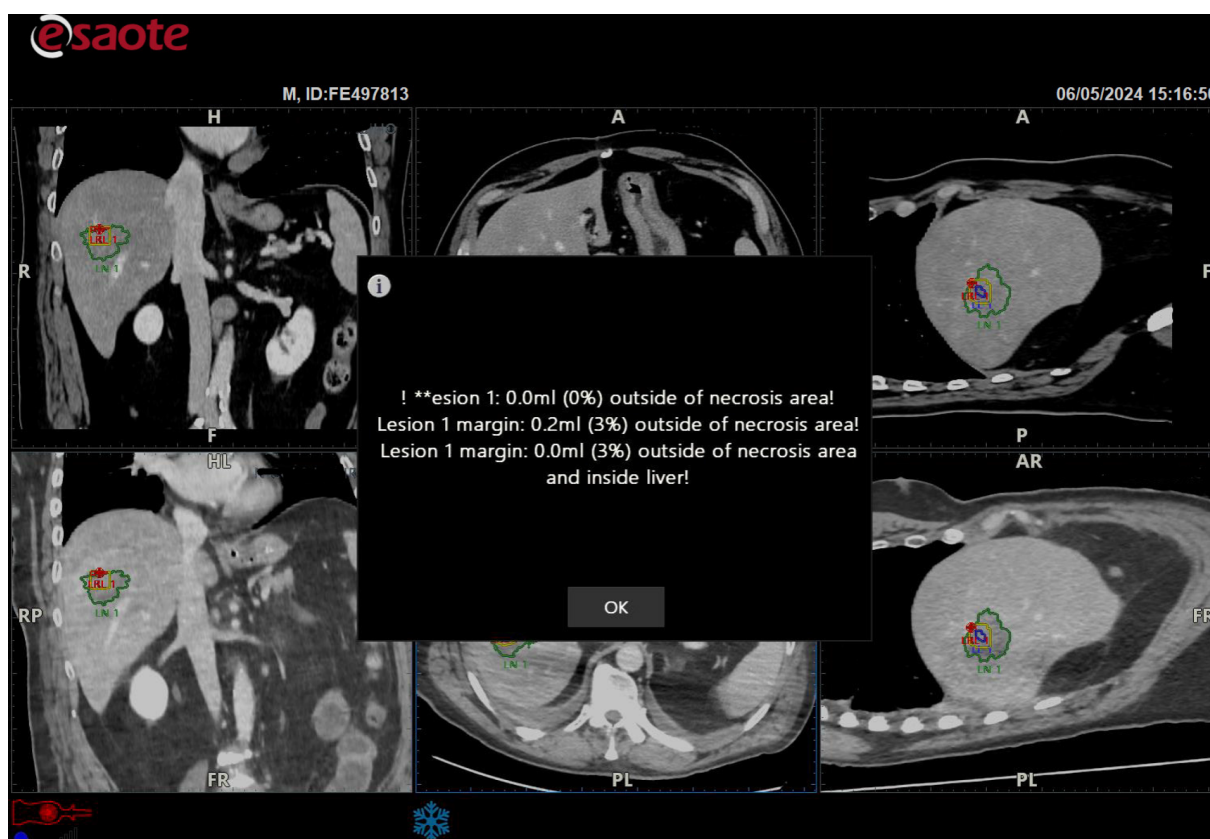


Figure 7 The target lesion was within the necrotic area, but the software warned that the safety margin was insufficient (red spot).

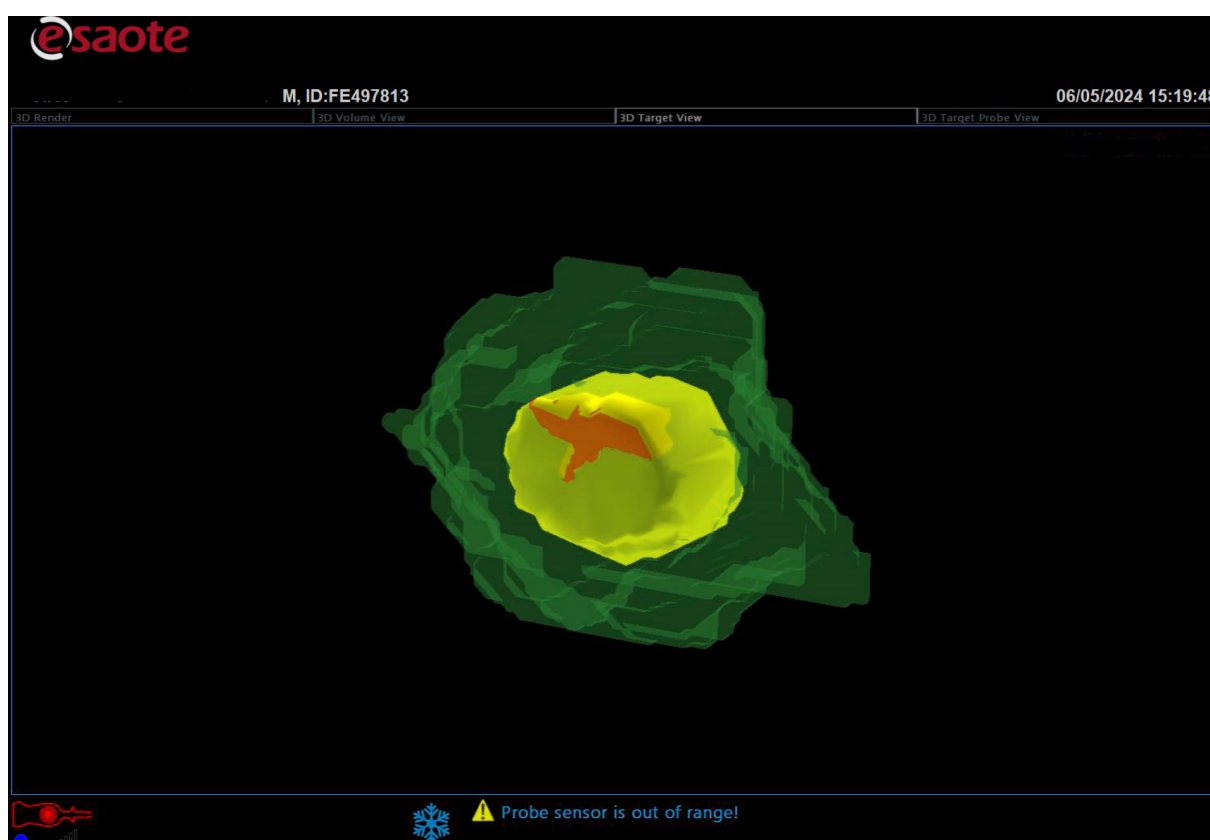


Figure 8 Three-dimensional reconstruction of the ablation result showed the necrotic volume (deep green), planned safety margin (yellow), completely necrotic lesion (light green), and planned safety margin outside of necrosis volume (red).

significant increases in precision targeting of percutaneous ablation, optimizing technical success and patient outcomes.

CONCLUSION

Starting from grayscale US-guided PEI of small HCC lesions, constant technical advancements in both thermal ablation and US imaging have led interventional oncology clinicians to break the so-called 3-cm barrier in the percutaneous treatment of primary and secondary liver tumors^[35-38]. The latest generation of MWA systems and advanced software powered by AI can precisely target tumor margins and/or residual viable tumor tissue to enable us to attack the 5-cm (and hopefully the 7-cm) barrier.

Interventional oncologists are ready to fight!

ACKNOWLEDGEMENTS

The authors acknowledge Dr. Emanuela Mo for her outstanding contribution to the assembly work of this manuscript.

FOOTNOTES

Author contributions: Tombesi P, Cutini A, Grasso V, Di Vece F, Politti U, Capatti E, Labb F, Petaccia S, and Sartori S equally contributed to conception and design of the study, literature review and analysis, drafting and critical revision and editing, and final approval of the final version.

Conflict-of-interest statement: All authors declare no conflicts of interest related to this publication.

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S-Editor: Liu JH

L-Editor: A

P-Editor: Wang WB

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Artificial Intelligence in *Cancer*

Quarterly Volume 5 Number 2 September 8, 2024





Artificial Intelligence in Cancer

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AIMS AND SCOPE

The primary aim of *Artificial Intelligence in Cancer* (AIC, *Artif Intell Cancer*) is to provide scholars and readers from various fields of artificial intelligence in cancer with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

AIC mainly publishes articles reporting research results obtained in the field of artificial intelligence in cancer and covering a wide range of topics, including artificial intelligence in bone oncology, breast cancer, gastrointestinal cancer, genitourinary cancer, gynecological cancer, head and neck cancer, hematologic malignancy, lung cancer, lymphoma and myeloma, pediatric oncology, and urologic oncology.

INDEXING/ABSTRACTING

The AIC is now abstracted and indexed in Reference Citation Analysis, China Science and Technology Journal Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Xiao-Mei Zheng*, Production Department Director: *Xiang Li*, Cover Editor: *Jin-Lei Wang*.

NAME OF JOURNAL

Artificial Intelligence in Cancer

ISSN

ISSN 2644-3228 (online)

LAUNCH DATE

June 28, 2020

FREQUENCY

Quarterly

EDITORS-IN-CHIEF

Mujib Ullah, Cedric Coulouarn, Massoud Mirshahi

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<https://www.wjgnet.com/2644-3228/editorialboard.htm>

PUBLICATION DATE

September 8, 2024

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STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

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Role of artificial intelligence in gastrointestinal surgery

Ankit Shukla, Rajesh Chaudhary, Nishant Nayyar

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B

Novelty: Grade B

Creativity or Innovation: Grade B

Scientific Significance: Grade B

P-Reviewer: Hilendarov AD

Received: May 28, 2024

Revised: July 11, 2024

Accepted: July 17, 2024

Published online: September 8, 2024

Processing time: 100 Days and 2.9 Hours



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Abstract

Artificial intelligence is rapidly evolving and its application is increasing day-by-day in the medical field. The application of artificial intelligence is also valuable in gastrointestinal diseases, by calculating various scoring systems, evaluating radiological images, preoperative and intraoperative assistance, processing pathological slides, prognosticating, and in treatment responses. This field has a promising future and can have an impact on many management algorithms. In this minireview, we aimed to determine the basics of artificial intelligence, the role that artificial intelligence may play in gastrointestinal surgeries and malignancies, and the limitations thereof.

Key Words: Machine learning; Gastrointestinal surgery; Radiology; Artificial neural network; Deep learning

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Core Tip: Artificial intelligence (AI), a term coined by John McCarthy in 1955, is the new-kid-on-the-block in the medical arena, with immense potential to revolutionize how patients may be managed in coming years. It is a science of creating machines with capability to reason and solve problems like human beings. The principal subfields of AI are: (1) Machine learning; (2) artificial neural networks; (3) natural language processing; and (4) computer vision. AI is improving the fields of gastrointestinal surgery and medicine immensely, assisting in diagnoses as well as management of gastrointestinal diseases. As with any new technology, AI has limitations and drawbacks.

Citation: Shukla A, Chaudhary R, Nayyar N. Role of artificial intelligence in gastrointestinal surgery. *Artif Intell Cancer* 2024; 5(2): 97317

URL: <https://www.wjgnet.com/2644-3228/full/v5/i2/97317.htm>

DOI: <https://dx.doi.org/10.35713/aic.v5.i2.97317>

INTRODUCTION

The platform of artificial intelligence is revolutionizing the medical field and changing approaches to reach a definitive diagnosis. Furthermore, artificial intelligence is expanding its horizons not only in clinical diagnoses, but also in the operative management of patients. Leonard *et al*[1] and John Hopkins University have shown this by developing the Smart Tissue Autonomous Robot (STAR) to perform *ex vivo* and *in vivo* anastomosis of the small bowel in porcine models [2]. Artificial intelligence can be vaguely defined as the study of sets of algorithms giving machines the ability to perform reasoning and solve problems, along with image, object, and word identification[3,4]. Another innovation in the surgical field was Gestonurse, which is a robotic scrub nurse used to hand instruments to the operating surgeon[5].

The index application of artificial intelligence in gastrointestinal surgery was documented in 1976, when it was introduced to aid computer analysis for acute abdominal pain[6]. The term artificial intelligence was coined by McCarthy *et al*[7] in 1955 during his summer research project. However, its origin can be traced back to 1950, when Turing[8], a British mathematician, used a computer to display human-like behavior in the Turing test.

Most of the initial advancements of artificial intelligence are depicted in the field of dermatology, radiology, and pathology, noted by an increase in Food and Drug Administration approvals for artificial intelligence devices in these fields[9]. Also, in pathology, a reduction in error rates from 3.4% to 0.5% was seen with the help of artificial intelligence [10]. Artificial intelligence has also seeped deeply into our lives in the form of daily assistance devices such as Siri, Alexa, chatbots, Google assistant, smart homes, navigation apps, autonomous vehicles, *etc.* Similarly, machine and deep learning is assisting physicians in diagnosing various gastrointestinal diseases, liver tumors, pancreatic neoplasms, and various infections.

Applying artificial intelligence to large and complex data is also helping to identify new variables and their associations, shaping changes in today's clinical practices. In the surgical field, the surgeon must associate with data scientists to unfold the role of artificial intelligence. In the future, human roles may be limited to only supervision and authentication of different models of artificial intelligence.

METHODOLOGY

Search strategy

We performed a PubMed search for relevant articles, and then searched the article reference lists for additional appropriate studies. The keywords and combinations included in the search were as follows: "Artificial intelligence" and "radiology"; "artificial intelligence" and "pathology"; "artificial intelligence" and "endoscopic management"; "artificial intelligence" and "gastrointestinal surgery"; "artificial intelligence" and "gastric cancer"; "artificial intelligence" and "colorectal malignancy"; "artificial intelligence" and "pancreatic cancer"; and "artificial intelligence" and "robotic surgery". The search was limited to publications in English. All the authors agreed that the articles selected for review were relevant.

FUNDAMENTALS OF ARTIFICIAL INTELLIGENCE

The basis and advances of artificial intelligence relies on machine learning and deep learning. Artificial intelligence has found many uses in surgical diseases, from diagnosis and scoring systems to preoperative and intraoperative planning and assistance, as well as in surgical training and robotics[11-13]. Principal subfields of artificial intelligence are: (1) Machine learning; (2) artificial neural networks; (3) natural language processing; and (4) computer vision (Figure 1).

The purpose of machine learning is to equip machines to learn and predict by identifying similar patterns[14]. Machine learning is based on the ability to do a task with the help of a set of algorithms without programming, and is further subdivided into supervised, unsupervised, and reinforced learning[4]. Supervised learning is beneficial to train machine learning algorithms to differentiate an anticipated sequence, whereas unsupervised learning is beneficial in identifying patterns in the given data[14]. An advantage of machine learning is noted in finding minute patterns in large data, which may be missed by human analysis, with the aid of complex and indirect nonlinear relationships or multivariate effects [15]. In surgical site infection analysis, machine learning has surpassed logistic regression with the help of nonlinear regression patterns, including multiple data resources like diagnosis, treatment, and blood tests[16]. An analogy of supervised learning is equipping a device to identify gastrointestinal metaplasia utilizing a large data set of lesions formerly recognized by a pathologist as gastrointestinal metaplasia. Comparatively, an example of unsupervised learning is tissue sample clustering derived from similar gene expressions, as it is based on finding patterns rather than algorithms [14].

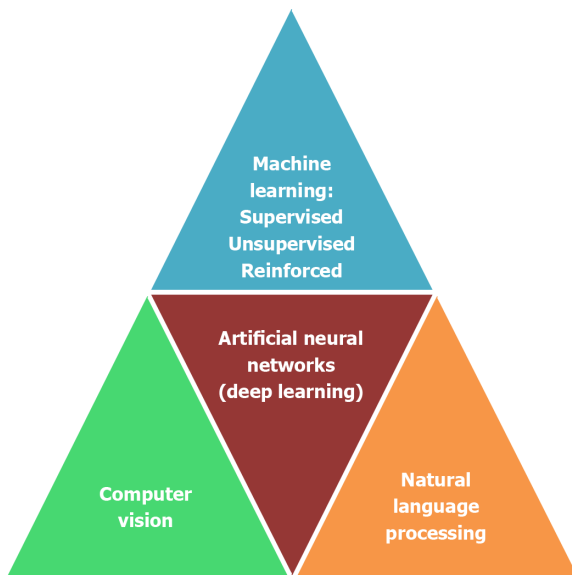


Figure 1 Principal subfields of artificial intelligence.

Reinforced learning is a type of machine learning wherein the device makes decisions to achieve the most optimal results. It is similar to the trial and error learning process that humans use to fulfill their goals. An example of such a module is an artificial pancreas device used to accurately measure and inject doses of insulin for diabetic patients[17]. Another use of machine learning is precisely predicting mortality, sepsis, and acute kidney injury with the help of an intraoperative database[18,19].

An artificial neural network applying binary threshold functions was conceived in 1943 by McCulloch and Pitts[20]. It is the subdivision of artificial intelligence persuaded by the human nervous system and applied in various medical applications. Deep learning is a new type of artificial intelligence based on artificial neural networks. The deep learning neural network is composed of multiple layers, which enables them to learn minuscule patterns from the given datasets in comparison to simple or two-layered neural networks[21]. In deep learning, every network subgroup of inputs leads to various concealed subgroups in response to distinct characteristics of inputs, which allows for an in-depth understanding of datasets similar to multiple neuronal connections occurring in the human brain[22,23]. In the arena of clinical applications, the artificial neural network has shown high accuracy and sensitivity and specificity in predicting in-hospital mortality following abdominal aortic aneurysms. Similarly, its application in acute pancreatitis to assess severity has surpassed conventional APACHE II scoring (sensitivity and specificity of 80% and 85%, respectively), with a sensitivity and specificity of 89% and 96%, respectively[24]. To analyze images, convolutional neural networks are a type of deep neural network used in the detection of gastrointestinal malignancy within endoscopic images, radiologic images, and pathologic specimen assessments[14,25].

Computer vision, a subtype of artificial intelligence, portrays the ability of a device or machine to obtain and interpret images or videos like humans. It has been widely used in axial imaging for virtual colonoscopy, computer aided diagnosis, and decision making in surgery[26]. Real time assessments of minimally invasive laparoscopic sleeve gastrectomy videos have identified unplanned or forgotten surgical steps with 93% accuracy using computer vision[27].

Natural language processing is the subfield of artificial intelligence dealing with interpretation of text form and voice data from electronic health records[28]. It has a role in both preoperative and postoperative assessments of surgical patients to predict risks, outcomes, and complication rates. It is used in the surgical field to follow up on patients and monitor complications[29]. One of the most frequent applications of natural language processing is to foretell the risk of surgical site infection in various surgical procedures[30-32].

ARTIFICIAL INTELLIGENCE IN GASTROINTESTINAL SURGERY

Artificial intelligence is improving the field of gastrointestinal surgery, and helping in the diagnosis and management in many gastrointestinal diseases where images (endoscopy, radiology, and pathology) are used such as in Barrett's esophagus, esophageal cancers, gastric cancer, Helicobacter infection, pancreatic diseases, liver tumors, colonic polyps, and malignancies. It also helps in identifying precancerous lesions more efficiently and to reduce missing small lesions. In comparison to other fields, the diagnosis of surgical diseases require more dynamic and complex algorithms, sometimes involving real time decision making, similar to differences in artificial intelligence software used to recognize faces and to drive autonomous vehicles.

In abdominal wall hernia repair, artificial intelligence uses supervised machine learning algorithms and preoperative computed tomography images to anticipate risks and requirements of component separation techniques. In a study, this model was found to be superior to a panel of consultant surgeons[33]. Artificial intelligence has been used in convolutional neural network-based algorithms to find stomach malignancy with endoscopic images since 2018[34]. One

multicenter study introduced the Gastrointestinal Artificial Intelligence Diagnostic System model to diagnose upper gastrointestinal cancers in late 2019, comparing its accuracy with a specialist and trainee endoscopist, and noticed it to be better than the trainee and similar to the specialist in diagnosing stomach carcinoma[35]. Convolutional neural networks using narrow band imaging in endoscopy have been used to differentiate stomach cancer and gastritis with an upper limit of sensitivity of 95% and positive predictive value of 91%[36]. In studies of Barrett's esophagus, deep learning model algorithms have been used to find neoplastic changes based on datasets of images, showing superior accuracy to amateur endoscopists, along with the optimum site for biopsy in 97% cases[37]. Another study using a convolutional neural network-based model was found to be more accurate in detecting early gastric carcinoma than a specialist endoscopist [38]. Other studies have used deep learning modules along with biomarkers, histologic images, and radiologic images to anticipate liver and lymph node spread in stomach carcinoma[39,40]. Various studies have also used evolved models anticipating risk stratification of stomach carcinoma and its survival prediction[41,42]. In esophageal carcinoma, deep learning models have been developed to find squamous cell carcinoma of the esophagus using narrow band imaging as the input; models anticipating depth of esophageal malignancy have also been developed[43-45].

In the large bowel, artificial intelligence has been used to find polyps and differentiate hyperplastic or adenomatous polyps based on deep learning and convolutional neural networks[46,47]. Artificial intelligence is also helpful in segregating malignant or non-malignant colonic lesions, as well as predicting depth of invasion and endoscopic resection margins[48,49]. With the aid of convolutional neural network-based deep learning, we can find real time automatic surgical phases in laparoscopic sigmoidectomy, to teach purposes and real time workflow recognition for the development of Context-Aware Computer-Assisted Surgery systems[50]. Platforms using electronic health records can anticipate perioperative risk, to improve clinical assessments using MySurgeryRisk algorithms[51]. Another similar machine learning user friendly platform for risk stratification and mortality in emergency surgery is Predictive Optimal Trees in Emergency Surgery Risk, which is based on the ACS-NSQIP dataset and is fruitful in preoperative counseling of patients and relatives[19].

Anticipation of resection of peritoneal carcinomatosis necessitates laparotomy to optimally classify the disease burden. Random forest models based on machine learning can determine resectability in this condition with accuracy to the tune of 98%, preventing unwanted laparotomies[52]. Another machine learning based model has been developed to examine intrahepatic cholangiocarcinoma patients preoperatively using various parameters, and to anticipate which patients would benefit from surgery[53,54]. Using artificial neural networks, the uterine artery can be distinguished from the ureter in laparoscopic hysterectomy, as well as other surgeries posing risk of ureteral injury[55]. In hepatic surgery, artificial intelligence helps in preoperative planning, intraoperative assistance using radiological imaging, and assessing the intricate anatomy[56]. In cases of pancreatic surgery, artificial intelligence is useful in anticipating postoperative pancreatic fistula risk following pancreatic head resection, and to help in planning management for better results[57]. In cholangiocarcinoma, computer auxiliary diagnosis systems can aid in the diagnosis and help improve the treatment plan [58].

In various gastrointestinal surgeries, postoperative management can be augmented with the help of artificial intelligence by predicting surgical site infection and blood loss requiring transfusion following pancreatic, colorectal, or hepatic surgeries[59]. After gastrointestinal surgeries like colorectal and bariatric surgery, natural language processing aids the use of variables from health records to preoperatively predict patients who have higher risks of anastomotic leak [51,60]. Artificial intelligence can also support intraoperatively using computer vision analysis of intraoperative videos and generate recommendations or warnings[61]. It can also assist in transplant surgeries both pre and post operatively by anticipating graft rejection or failure, morbidity, and survival post liver transplantation[62,63].

ROLE OF ARTIFICIAL INTELLIGENCE AND RADIOLOGY IN GASTROINTESTINAL TRACT SURGERY

Radiology assists in gastrointestinal diseases using images generated through X-ray, computed tomography, and magnetic resonance imaging, which are used by deep learning models as data inputs to identify anatomy and differentiate malignant or benign tumors[64]. Radiomics has been used to assess and differentiate the malignant potential of various tumors by assessing images *via* deep learning of shapes, texture, and histograms[65,66]. Some studies have developed survival prediction models with the help of radiomics analysis of computed tomography images. Following image segmentation, the analysis was accomplished and risk scores stratified, showing the superiority of radiomics over normal nomograms in stomach cancer patients[67,68].

In colorectal liver metastases using computed tomography and magnetic resonance imaging, radiomics have depicted splendid accuracy in finding early liver spread, which might aid in effective management and better prognosis. It is also helpful in predicting responses to chemotherapy[69]. Studies have tried to predict peritoneal spread with the help of convolutional neural networks and diagnosing metastatic lymph node spread in carcinoma of the stomach[39,70]. Three-dimensional imaging delineation of anatomy and three-dimensional reconstructions improve planning in pancreatic, liver, or biliary surgery[71-73]. Navigation systems technology helps in pre and postoperative surgeries to depict difficult anatomy, and is currently used in pancreatic, esophageal, and splenic surgeries[74-76]. Intuitive Surgical has also developed IRIS 1.0, providing segmented three-dimensional images for better analyses of anatomy and planning surgery [77]. Recently, some studies have shown use of optical coherence tomography in finding metastatic lymph nodes using artificial neural networks, which may help intraoperatively[78].

SHORTCOMINGS OF ARTIFICIAL INTELLIGENCE

As with any new technology, artificial intelligence also has limitations and drawbacks, as it depends heavily on the data provided. The quality, amount, and variation in the data used to train the model is an important aspect. Outcomes depend on the quality of the dataset provided for input, and any shortcomings will affect the results. Biases while accumulating clinical data have an impact on the kind of patterns artificial intelligence perceives and the predictions it makes[79,80]. In gastrointestinal malignancy, IBM Watson Oncology – a question-answer-based computer device – was supposed to help physicians in decision making and to keep updated with recent evidence; however, it has not lived up to the standard[81,82]. In the presence of well-devised models, depending entirely on artificial intelligence is not recommended, as a skilled endoscopist is still needed to accurately capture the data[83].

Radiological models are deficient in automatic segmentation in gastrointestinal malignancies due to large discrepancies in imaging of the gastrointestinal tract. Radiomics appears to be efficient in finding malignant probability with analyses of intratumor heterogeneity; however, it also has limitations in the form of interobserver variability during segmentation, scanning equipment, image acquisition protocols, and algorithm reconstruction[84-86]. In endoscopic imaging, most studies are retrospective in nature and do not represent real clinical scenarios, and it is not clear that artificial intelligence will be cost effective and beneficial in improving clinical results[87]. Similarly, in pathology, there is interobserver discord commonly noticed in various diagnoses among pathologists, which affects the learning or input data and the cost effectiveness of artificial intelligence[88,89].

Traditionally, the responsibility and legal implications onus was on the surgeon; however, with autonomous artificial intelligence, these need to be sorted out in respect of accountability, liability, and culpability. Only accountability can be assessed in artificial intelligence with the help of recording actions, but liability and culpability require further introspection[90]. One of the limitations is lack of sixth sense, which a machine cannot possess. Another drawback is sympathy or sensitivity toward the patient, which cannot be replaced by artificial intelligence. Ethical and legal doubts are another issue which must be dealt with. Moreover, in surgical practice, operative efficacy comes by observing and performing cases repeatedly[77]. One more issue is trust, the basis of the patient-doctor relationship, which is lacking in artificial intelligence models[91].

CONCLUSION

Artificial intelligence is advancing at a rampant pace, and is playing a major role in shaping the way patients will be managed in coming years. The implementation of artificial intelligence in diagnosing gastrointestinal disease seems to be at par with the experts; however, it is important to realize that artificial intelligence cannot totally replace humans, and will need assistance for its use, further development, and enhancement. The aim of artificial intelligence is to enrich the skills of a surgeon and not to replace him. Due to its various limitations, more must be done to use artificial intelligence to improve healthcare.

FOOTNOTES

Author contributions: All the authors performed the literature search; Shukla A wrote the first draft of the review; Chaudhary R and Nayyar N conceptualized the work, supervised the writing, and gave intellectual input; All authors critically revised the manuscript.

Conflict-of-interest statement: All authors state that they have no conflicts of interest to report.

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S-Editor: Lin C

L-Editor: Filipodia

P-Editor: Zheng XM

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