Artificial intelligence: The new wave of innovation in EUS

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INTRODUCTION

During the past four decades, EUS has developed rapidly and has established itself as a vital tool in the diagnosis and treatment of digestive system diseases.[1] Nevertheless, there are still some limitations related to image-related interpretation such as overlap of various diagnoses, interobserver variability, false positives, and false negatives.[2] Recent improvements in deep learning (DL) techniques and computing power have made computer-aided diagnosis (CAD) system, a useful tool in the field of medical imaging.[3] Furthermore, artificial intelligence (AI)-related image processing techniques have widely penetrated in various medical fields and have achieved some promising initial results.[4-6] Processing and analyzing EUS images utilizing AI-related CAD (AI-CAD) may overcome limitations of diagnostic EUS and improve differentiation of benign and malignant processes as well as decrease interobserver variability in endosonography which is an operator-dependent technique.

WHAT IS ARTIFICIAL INTELLIGENCE?

AI can be simply described as "a computer program that can learn and utilize data to accomplish specific goals and tasks flexibly and appropriately."[7] Machine learning (ML),[8] as an important branch of AI, mainly includes three types of learning: supervised, unsupervised, and reinforcement. Supervised learning is mainly applied in the study of diagnostic imaging, such as artificial neural networks (ANNs) and support vector machines (SVMs). An ANN is a mathematical model that is meant to mimic the characteristics of a biological neural network. ANNs achieve this through simulating the process of stimulation and inhibition of neurons in a complex human neural network and applying this format to the operation of complex data. As a result, ANNs have become a popular classification model for diagnoses based on EUS images and have been widely applied in medical imaging recognition, analysis, and processing. A series of previous studies on tumor imaging analysis based on an ANN suggested that the ANN contributed

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to the segmentation, recognition, and detection of tumor imaging. Based on the principle of margin maximization,[9] SVMs classify the data into two categories by creating a boundary, which is referred to as a separating hyperplane to complete the pattern recognition. Compared with ANNs, SVMs have the advantages of high training efficiency and repeatability. Nevertheless, researchers need to mark classification features manually, and when the number of samples increases, the learning time will be correspondingly prolonged. DL is developed from ML,[10] in which convolutional neural networks (CNNs) served as a DL algorithm based on the processing of human visual signals. In contrast to the traditional CAD algorithms, which require manual trial and error, CNNs utilize the image itself as input and automatically learn to identify the most appropriate features. There has been a wide range of AI application in analyzing medical imaging, including the detection of colon polyps, the differentiation of benign and malignant tumors, and the evaluation of tumor invasion depth.[11]

OVERVIEW OF ARTIFICIAL INTELLIGENCE IN DIAGNOSTIC EUS

Norton *et al.*[12] in 2001 first reported on the use of a CAD system based on digital imaging analysis (DIA) to distinguish focal pancreatitis images from those of pancreatic cancer (PC) on EUS. When the sensitivity of the malignant diseases was set at 100% to minimize the chance of missed malignant tumor diagnosis, its overall diagnostic accuracy was 80%, which was similar to diagnostic accuracy of 85% using the traditional EUS examination and 83% using a blinded method. These findings suggested that utilizing DIA to analyze EUS images was both feasible and accurate compared with other human diagnostic results. Although the above DIA was not complicated and with small sample size and poorer EUS image resolution compared to the current times, some may not even call this technique as AI-CAD in contemporary terms. However, this project successfully laid the foundation for further investigation of AI in EUS imaging. Hence, the concept of digital analysis of EUS images is not that new and is 20 years old. However, the DIA of EUS images did not reach routine clinical application over the past two decades. As stated by Bhutani in 2008,[13] "until a DIA program is commercialized, standardized, and integrated into standard, conventional EUS equipment, it may only stay as a promising research tool and will not gain widespread clinical acceptance by the busy endoscopist."

The interest in DIA was probably somewhat dormant until recently when there have been marked advances in applying AI in all areas of medicine including other areas gastrointestinal endoscopy such as colon polyp detection, Barrett's esophagus, detecting early gastric cancer, and capsule endoscopy of small bowel.[14] This has also awakened the sleeping giants in EUS in academia and industry to pursue AI in EUS with renewed gusto and enthusiasm. Research on the application of AI in EUS is still in early stages and of development. This editorial highlights some possible applications of AI in EUS that can potentially the diagnostic capabilities of EUS.

ARTIFICIAL INTELLIGENCE AND EUS ELASTOGRAPHY

EUS elastography (EUS-E) can provide supplementary information for traditional EUS, while simultaneously minimizing the examination cost without increasing patient morbidity and fatality.[15] EUS-E can convert the properties of tissue into visible images that are composed of color pixels; this is achieved based on the elastic coefficients of the analyzed tissue. As a result, endoscopic clinicians are able to detect possible pathological changes of corresponding tissues or organs according to EUS-E images. Săftoiu *et al.*[16] first conducted real-time quantitative analysis of EUS-E and found that real-time EUS-E produced ideal results because it avoided not only color perception errors and the motion artifacts caused by individual selection and manipulation bias but it also avoided the selection bias resulting from static image analyzing. In 2012, the European multicenter EUS-E group launched a prospective, blinded study to evaluate the accuracy of real-time EUS-E in the diagnosis of focal pancreatic lesions with an ANN-based CAD mode.[17] In the study, 744 EUS-E images from 258 patients with focal pancreatic lesions were included. By retrieving the color hue histogram data from the dynamic sequence of EUS-E, and then, analyzing the data in a neural network to distinguish benign and malignant patterns automatically, the results showed that the sensitivity of EUS-E was 87.6%, specificity was 82.9%, and positive predictive value (PPV) and negative predictive value (NPV) were, respectively, 96.3% and 57.2%. These results indicated that the ANN-based CAD model could provide rapid and accurate diagnosis and assist in medical decision-making.

ARTIFICIAL INTELLIGENCE, CONTRAST-ENHANCED EUS AND GUIDED FINE-NEEDLE ASPIRATION

Since EUS-FNA was reported in 1992, it has been widely applied in the diagnosis and treatment of intramural and extramural digestive tract lesions.[18] It is well known that EUS-FNA is a multistep process, that can be affected by a variety of uncertainties. It can be difficult at times to differentiate benign and malignant lesions and formulate subsequent treatment strategies based only on the clinical/imaging features and sample results of EUS-FNA.[19] For these reasons, some AI-related algorithms aimed at promoting the diagnostic accuracy and efficiency of EUS-FNA have emerged in the recent 5 years. In 2015, Săftoiu *et al.*[20] recruited 167 patients, including 112 patients with PC and 55 patients with chronic pancreatitis and mapped their time-intensity curves (TICs) using dynamic contrast-enhanced EUS (CE-EUS) data performed on solid pancreatic masses; the study further quantified the 7 parameters of TICs through a multilayer ANN. The results showed that the sensitivity, specificity, PPV, and NPV were 94.64%, 94.44%, 97.24%, and 89.47%, respectively. These findings indicated that this ANN could provide additional diagnostic value for human CE-EUS and EUS-FNA results. In 2019, Kurita *et al.*[21] used AI based on DL to build a diagnostic algorithm and retrospectively analyzed the pancreatic cystic fluid from surgical specimens or EUS-FNA specimens of 85 patients with pancreatic cystic lesions. Factors such as carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), cancer antigen 125, amylase, patient sex, cyst location, connection between pancreatic duct and cyst, cyst type, and cytology of the collected cystic fluid were closely related to the algorithm, which can also predict the malignancy. The accuracy, specificity, and sensitivity of the proposed algorithm were 92.9%, 91.9%, and 95.7%, respectively. Both the accuracy and sensitivity of the proposed algorithm were higher than those of CEA and cytology. Herein, it is reasonable to believe that the proposed algorithm can improve the diagnostic efficiency of differentiating between benign and malignant pancreatic cystic lesions.

In addition, with the innovation of AI image recognition technique and the development of cytopathology, some researchers have applied AI-related algorithms to the analysis of EUS-FNA specimen pathology results.[22] Inoue *et al.*[23] proposed an ML-based automated visual inspection method to assist in rapid on-site evaluation (ROSE) of EUS-FNA. In this method, the stationary Gaussian mixed model (GMM) was used to classify the local statistics of the specimens, aiming to clarify the relationship between the tumor cell content grade and the quality of the EUS-FNA specimens. The results showed that the method could effectively display the regions containing tumor cells, thus assisting the ROSE with EUS-FNA. In a retrospective analysis, Hashimoto *et al.*[24] grouped the 2015 EUS-FNA specimens at their center and then used a CNN algorithm to carry out sequential transfer learning on them. The results showed that the sensitivity, specificity, and accuracy of the algorithm for the first group of specimens were 78%, 60%, and 69%, respectively. The accuracy, sensitivity, and specificity of the second group were 80%, 80%, and 80%, respectively. These findings preliminarily indicated that the algorithm can improve its diagnostic performance in a step-by-step manner and further improve the efficiency of ROSE with EUS-FNA through higher training and more effective system development.

ARTIFICIAL INTELLIGENCE AND ENDOBRONCHIAL ULTRASONOGRAPHY

Endobronchial ultrasonography (EBUS) involves the insertion of a small ultrasonic probe into the bronchoscope to effectively distinguish tumorous lesions from the surrounding tissues, blood vessels, and lymph nodes through real-time ultrasound imaging.[25] EBUS can also be applied to the biopsy of mediastinal-occupying lesions and lymph nodes to obtain a histologic or cytologic pathological diagnosis. EBUS has become an important method for the differential diagnosis of hilar and mediastinal enlarged lymph nodes.[26] A study designed by Fujiwara *et al.*[27] showed that a well-defined, rounded, tumor configuration, inhomogeneous echo, and abundant blood flow were independent predictors of malignant lymph nodes under EBUS. However, these criteria could only be used to correctly distinguish benign from malignant lymph nodes in approximately 25% of cases.

Based on the previously mentioned reasons, Tomlinson *et al.*[28] performed genome-wide transcriptional profiling and laboratory evaluation of mediastinal lymph node samples from 88 patients using a new SVM algorithm applied in the transcriptional profiling analysis. The results suggested that the algorithm could distinguish between granuloma and granulomatous diseases, cancer, and reactive lymphadenopathy, and the diagnostic

sensitivity of each test above was nearly 90%, which was higher than the existing tuberculous and cancer detection method. The findings confirmed that the SVM algorithm may significantly promote the clinical application of EBUS-mediated biopsy. Ozcelik *et al.*[29] developed an AI diagnostic model using ANN. First, the EBUS images of 345 lymph nodes were obtained and divided into two groups of 300 and 45 lymph nodes, which were, respectively, used as input and output variables to verify the algorithm. The best diagnostic accuracy was 82%, with a sensitivity 89%, a specificity of 72%, and an area under the curve of 78.2%. In summary, the results suggest that the diagnostic model could improve the ability of better evaluate both benign and malignant lymph nodes in EBUS images, but further studies will require more EBUS images to be used as input data.

EXPECTATION

With the development of EUS equipment and the innovation of image-processing techniques, the application of AI in diagnostic EUS has been increasingly broadened. As a highly specialized imaging technique, the future direction of AI is not only focused on its use in various ultrasound procedures to accurately identify tumorous lesions but also to provide relevant interventional treatments based on the integration of various procedures. Of note, there are some limitations to the application of AI in EUS imaging.[30] For instance, the number of EUS images is overwhelmingly lower than that of traditional imaging methods such as computed tomography and magnetic resonance imaging, and the use of EUS to identify and diagnose rare and atypical diseases needs further study.[31] These challenges can be met by establishing a multicenter collaborative EUS image database at the national or global level. Moreover, there is a fatal "black box effect" in AI,[32] which means that computer judgment and recognition are invisible. In the context of evidence-based medicine, this is an urgent problem for physicians and AI researchers. Future AI visualization techniques may be helpful in solving these dilemmas. In summary, to achieve the ideal integration of AI techniques into EUS with clinical diagnosis and treatment, more rigorous study and repeated verification in the clinical environment are still required.

Conflicts of interest

There are no conflicts of interest.

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