


# The Role of Artificial Intelligence in Surveillance in Barrett's Esophagus and Gastric Intestinal Metaplasia

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## Abstract

Artificial Intelligence (AI) has been increasingly applied in medical imaging for improved accuracy and efficiency. One area that has seen significant advances is the use of AI in the detection of Barrett's esophagus (BE) and gastric intestinal metaplasia (GIM). BE is a pre-cancerous condition that occurs in the esophagus and can lead to esophageal adenocarcinoma, while GIM is a precancerous lesion that occurs in the stomach. In this review article, we will provide an overview of current AI techniques used in the detection and diagnosis of BE and GIM, including computer-aided diagnosis (CAD) systems, deep learning algorithms, and image analysis techniques. The performance of AI in detecting these conditions will be evaluated and compared to traditional methods. The challenges and limitations of using AI in the diagnosis of BE and GIM will also be discussed. The article aims to provide a comprehensive understanding of the use of AI in BE and GIM detection and to guide future research in this field.

## Keywords

artificial Intelligence, Barrett's esophagus, gastric intestinal metaplasia, gastric cancer, computer aided detection

## Introduction

A growing marriage between medicine and technology is being complemented by artificial intelligence (AI), an emerging field that is being studied and implemented across several frontiers in gastroenterology, including clinical decision-making tools, image-based diagnostics, and targeted biopsies. Within the field of gastroenterology, AI is being used for polyp detection,<sup>1</sup> identification of small bowel lesions during WCE,<sup>2</sup> as well as identification of dysplastic Barrett's esophagus (BE)<sup>3,4</sup> and gastric intestinal metaplasia (GIM).<sup>5</sup> A sub-branch of AI, that is, computer vision is being used to detect mucosal pattern. AI in gastroenterology is aimed at developing and validating this technology for the diagnosis of pathological mucosal patterns using computer assisted detection.

## What is the Technology That Is Used in Clinical AI Tools?

AI is an umbrella term that involves computer aided diagnosis based on image pattern recognition such as computer vision as well as deep learning, machine learning, and use of neural networks. While a deep dive into these are beyond the scope of this article and have been discussed elsewhere, readers are encouraged to peruse through some of the references.<sup>6</sup>

## Why Use AI in BE and GIM?

Endoscopy of the upper gastrointestinal (UGI) tract is a commonly used procedure for diagnosing, screening, and monitoring a variety of pathologies. However, the quality of the examination varies based on the technology and the operator. Such variations translate to significantly different clinical outcomes and missed rates for precancerous lesions and cancer leading up to missed cancers. Despite efforts to improve detection with image-enhancing technology, overall detection rates of early cancers and precancers remain poor. Missed diagnoses of gastric cancer have been estimated at 11%, ranging from 4% to 26%.<sup>7-9</sup> EGDs missed 2.3% to 13.9% of upper GI cancers in the West, and more than 20% of gastric cancers were missed in Asia.<sup>7,8,10</sup> In a meta-analysis, the pooled miss rate for esophageal adenocarcinoma (EAC) was 25.3% overall and 23.9% in patients with no dysplasia. These results were consistent across time, but with correction for publication bias, the

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pooled miss rate was 33.2%.<sup>11</sup> Another recent meta-analysis that examined the rate of Barrett's neoplasia after an initial negative endoscopy (defining a lesion detected at the first exam or within 6 months as prevalent Barrett's neoplasia, a lesion detected between 7 months and 3 years after the index endoscopy as interval neoplasia and any neoplasia found 36 months or more after a negative first exam as incident or new) found that the largest category is prevalent neoplasia.<sup>12</sup> This implies that early EAC or dysplasia was missed during previous surveillance endoscopies.

Particular importance should be paid to esophageal adenocarcinoma, with its increasing incidence and poor 5 year survival rates of less than 20%<sup>13</sup> with 50% of patients diagnosed at stage 2 or later. The current standard of care in most community gastroenterology practices is white light high-resolution endoscopy with sampling of the Barrett's segment every 2 cm from all 4 quadrants, known as the Seattle protocol, which has been shown in studies to sample less than 5% of the mucosal surface.<sup>14</sup> Additionally, biopsies are taken from lesions that appear suspicious, such as raised or depressed lesions, nodular areas, and foci of ulceration. Random as well as targeted biopsies have the inherent disadvantage of sampling errors, inability to identify sub-squamous changes and there can be subtle changes in mucosal patterns imperceptible to the human eye due to improper and inadequate examination.

Similarly, gastric cancer has a significant burden, being the third most common cause of cancer related mortality and the fifth most common cancer globally. The Lauren classification divides gastric cancer into diffuse type of gastric cancer and the intestinal type of gastric cancer.<sup>9</sup> While the diffuse type of gastric cancer does not have well defined pre-cursor lesions that can aid early image-based detection, the intestinal type develops from a well described progression from chronic gastritis to chronic atrophic gastritis to GIM and then to dysplasia which eventually leads to gastric adenocarcinoma.

Both BE and GIM are pre-cursor lesions and have a lag time to malignant progression and hence early detection of these lesions offers a relatively large window for surveillance, early treatment, and thereby improves patient outcomes.

## Status of AI in BE and GIM

### Use of AI in BE

The development and validation of data sets allowing the identification of precursor lesions such as dysplasia in BE has been a significant development. However, at present, no FDA-approved imaging system is available for diagnosing dysplasia in Barrett's esophagus.

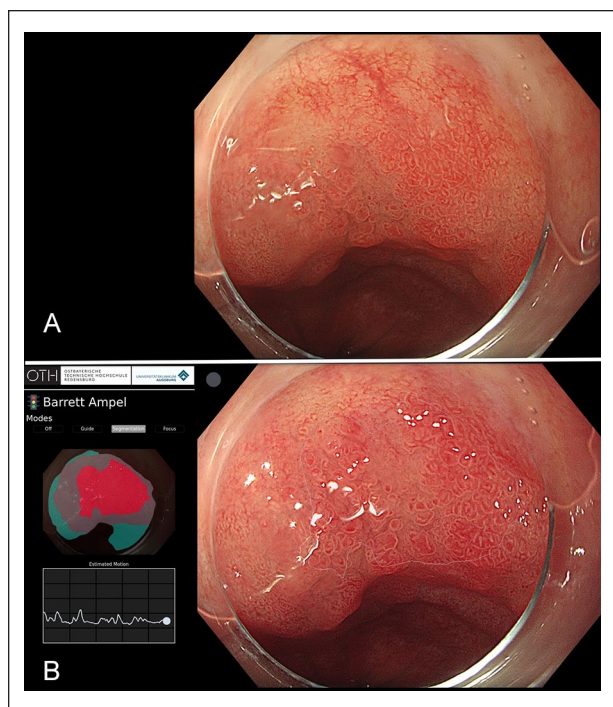
AI in endoscopy could be helpful to endoscopists in two ways: —(1) lesion detection and (2) lesion classification.

## AI in Detection of BE

The use of AI for endoscopic image recognition of BE has been evaluated by several studies. In one of the first in-vivo study for computer aided detection for BE, de Groof et al<sup>3</sup> developed a computer-aided detection (CAD) system. The CAD system was trained with multilevel, BE-specific imagery, containing 1544 images of Barrett's neoplasia and nondysplastic BE (NDBE). The CAD system was then tested during a prospective endoscopic procedure in 10 patients with NDBE and 10 patients with confirmed Barrett's neoplasia. White-light endoscopy images were obtained at every 2-cm level of the Barrett's segment and immediately analyzed by the CAD system, providing instant feedback to the endoscopist. At every level, 3 images were evaluated by the CAD system with an accuracy, sensitivity, and specificity of 90%, 91%, and 89%, respectively. In summary, 9 of 10 neoplastic patients were correctly diagnosed. AI based algorithms were also used for Narrow band imaging (NBI). Boschetto et al published data on an AI trained to detect intestinal metaplasia on NBI images of the esophagus with an accuracy, sensitivity, and specificity of 83.9%, 79.2%, and 82.3%, respectively.<sup>15</sup>

## AI and Dysplasia Detection in BE Segment

The next step after lesion identification is lesion characterization. The visual detection of early esophageal neoplasia (high-grade dysplasia [HGD] and T1 cancer) in BE with white light or virtual chromoendoscopy still remains challenging. It is estimated that the neoplasia detection rate (NDR) on index endoscopy ranges between 4% and 10%.<sup>16</sup> Hashimoto et al<sup>17</sup> conducted a pilot study on the visual detection of early esophageal neoplasia using 916 images from 65 patients of histology -proven early esophageal neoplasia. A convoluted neural network (CNN) algorithm was pretrained on ImageNet and then fine-tuned providing a binary classification of "dysplastic" or "nondysplastic." In addition, the object detection algorithm was able to draw a localization box around the areas of dysplasia with high precision and at a speed that allows real time implementation. The CNN analyzed 458 test images (225 dysplasia and 233 non dysplasia) and correctly detected early neoplasia with sensitivity of 96.4%, specificity of 94.2%, and accuracy of 95.4%. deGroof et al<sup>4</sup> further developed a hybrid ResNet-UNet model CAD system using 5 independent endoscopy data sets. Then they used 1704 unique esophageal high-resolution images of rigorously confirmed early-stage neoplasia in BE and nondysplastic BE, derived from 669 patients. CAD system classified images as containing neoplasms or nondysplastic BE with 89% accuracy, 90% sensitivity, and 88% specificity. The CAD system



**Figure 1.** White light appearance of BE in Panel A with corresponding boundaries of the Barrett's segment detected by AI.

Source. We sincerely thank Dr. Alana Ebigo from the Department of Gastroenterology, University of Augsburg, Germany for permission to use provided images.

achieved higher accuracy than any of the individual 53 nonexpert endoscopists. The CAD system identified the optimal site for biopsy of detected neoplasia in 97% and 92% of cases in the 2 data sets used for assessing system performance.

Another study by Hussein et al<sup>18</sup> used a CNN based on proprietary I-scan optical chromoendoscopy available on Pentax endoscopes. They used a CNN which was trained using 148,936 video frames (31 dysplastic patients, 31 NDBE, and 2 normal esophagus), validated on 25,161 images from 11 patient videos and tested on 264 I-scan-1 images from 28 dysplastic and 16 NDBE patients which included expert delineations. To localize targeted biopsies/delineations, a second directly supervised CNN was generated based on expert delineations of 94 dysplastic images from 30 patients. This was tested on 86 I-scan images from 28 dysplastic patients. CNN achieved a per image sensitivity in the test set of 91%, specificity 79%, area under receiver operator curve of 93% to detect dysplasia. Per-lesion sensitivity was 100%. Mean assessment speed was 48 frames per second (fps). 97% of targeted biopsy predictions matched expert and histological assessment at 56 fps. The AI system performed better than 6 endoscopists.

## AI in Image Enhancing Techniques for Barrett's Dysplasia Detection

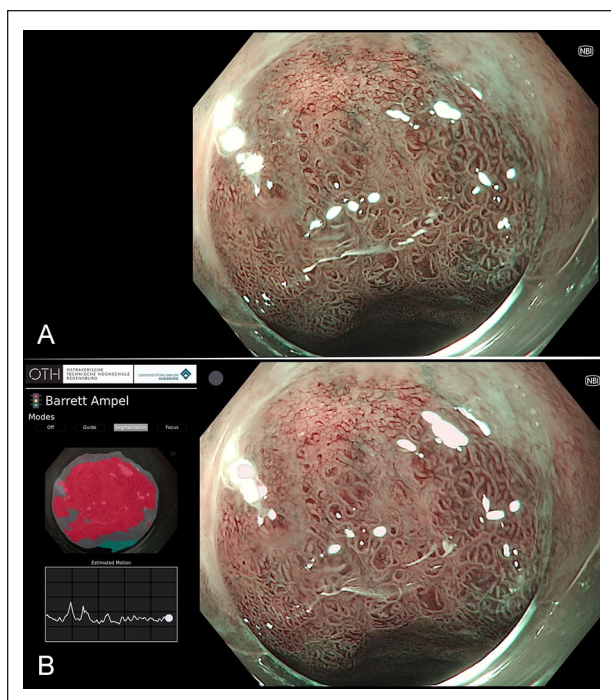
The use of AI to augment the diagnostic performance of an endoscopist while using image enhancing techniques has also been studied. Volumetric laser endomicroscopy (VLE) is an advanced endoscopic imaging tool that can improve dysplasia detection in BE. However, VLE scans generate 1200 cross-sectional images that can make interpretation difficult. While various scoring systems have been devised, each requires the endoscopist to correctly identify imaging features. In response, an AI algorithm called Intelligent Real-time Image Segmentation (IRIS) has been developed and incorporated into the VLE console system to automatically highlight VLE features known to be associated with dysplasia<sup>19, 21</sup>. These include epithelial glands, loss of layering, and increased surface signal intensity. A similar, recently-developed computer-aided detection (CAD) algorithm was developed and tested on targeted regions of interest (ROI), showing an impressive 85% accuracy in neoplasia detection.<sup>20</sup> When IRIS-enhanced VLE was used as the first interpretation modality, 100% of dysplastic ROI's were identified, compared with 76.9% when unenhanced VLE was used as the first interpretation modality ( $P=.06$ ) (Figures 1–3).

## AI and Digital Pathology in BE

Another area of rapid interest has been in the application of AI to digital pathology to enhance diagnosis. There is a critical need to improve the diagnosis of BE dysplasia, given substantial interobserver disagreement among expert pathologists and overdiagnosis of dysplasia by community pathologists. Deep learning models have been useful to predict dysplasia grade on whole-slide imaging<sup>21</sup>.

In a study by Faghani et al, a deep learning model to predict dysplasia grade on whole-slide imaging was developed. They digitized NDBE, low-grade dysplasia (LGD), and HGD histology slides. Two expert pathologists confirmed all histology and digitally annotated areas of dysplasia. Training, validation, and test sets were created (by a random 70/20/10 split). Diagnostic performance was determined for the whole slide. They digitized slides from 542 patients (164 NDBE, 226 LGD, and 152 HGD) yielding 8596 bounding boxes in the training set, 1946 bounding boxes in the validation set, and 840 boxes in the test set. When the ensemble model was used, sensitivity and specificity for LGD was 81.3% and 100%, respectively, and >90% for NDBE and HGD. The overall positive predictive value (PPV) and sensitivity metric (calculated as  $F1$  score) was 0.91 for NDBE, 0.90 for LGD, and 1.0 for HGD.<sup>22</sup>



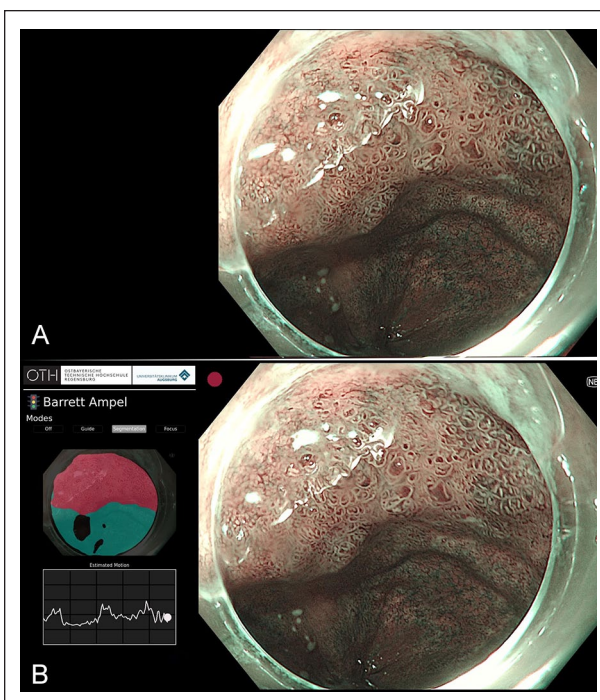


**Figure 2.** NBI appearance of BE in panel A with corresponding topographic map detecting the extent and margins of the Barrett's segment in panel B.  
 Source. We sincerely thank Dr. Alana Ebigo from the Department of Gastroenterology, University of Augsburg, Germany for permission to use provided images.

## AI in Esophageal Squamous Cell Cancer and Adenocarcinoma

Horie Y et al developed a convoluted neural network algorithm for identifying squamous and adenocarcinoma type of esophageal cancers based on WL and NBI images from a set of 8428 training images from 384 patients and a test set of 1111 images from 49 patients and 50 controls. Their CNN was able to identify all 7 small cancerous lesions less than 10mm in size. The CNN could distinguish superficial esophageal cancer from advanced cancer with an accuracy of 98%.<sup>23</sup>

A meta-analysis of the standalone performance of AI in detection of upper GI neoplasia, including squamous cell carcinoma, esophageal adenocarcinoma as well as gastric carcinoma utilized 19 studies on detection of with 218, 445, and 453 patients and 7976, 2340, and 13 562 images, respectively. AI-sensitivity/specificity/PPV/negative predictive value (NPV)/positive likelihood ratio/negative likelihood ratio for UGI neoplasia detection were 90% (CI 85%-94%)/89% (CI 85%-92%)/87% (CI 83%-91%)/91% (CI 87%-94%)/8.2 (CI 5.7-11.7)/0.111 (CI 0.071-0.175), respectively, with an overall AUC of 0.95 (CI 0.93-0.97).<sup>24</sup>



**Figure 3.** NBI appearance of BE in panel A with corresponding topographic map detecting the extent and margins of the Barrett's segment in panel B.  
 Source. We sincerely thank Dr. Alana Ebigo from the Department of Gastroenterology, University of Augsburg, Germany for permission to use provided images.

## AI in Early Esophageal Neoplasia Management During Endoscopic Eradication Treatment

One of the important aspects pertaining to early detection and resection of precancerous lesions is determination of the depth of the lesion. In a set of 230 white light endoscopic images, (108 T1a and 122 T1b), Ebigo et al<sup>25</sup> also used a deep learning system to distinguish T1a from T1b lesions, however the sensitivity, specificity, and accuracy using AI was 0.77, 0.64, and 0.71, respectively, which was not very different from experts, suggesting that more work was needed in predicting the depth of submucosal invasion using AI.

## Use of AI in the Diagnosis of GIM

Gastric cancer is the sixth most common cancer worldwide with over 1 million new cases made in 2018.<sup>26</sup> As with esophageal cancer, the prognosis of gastric cancer is poor with a 5-year survival rate of about 20%.<sup>27</sup> Due to the subtle nature of early gastric lesions, it is crucial to identify these lesions clearly at surveillance endoscopy so

that targeted biopsies can be taken, and diagnostic yield can be improved. In addition, determining the depth of invasion of gastric cancer is one of the most important criteria for determining whether to perform a surgical or endoscopic resection. However, this still remains a challenge.

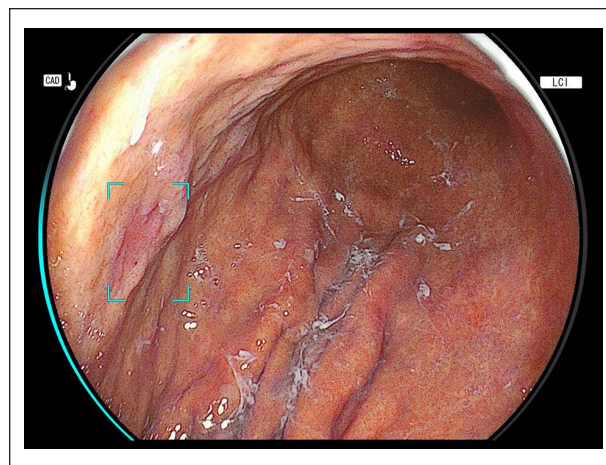
Yan et al<sup>28</sup> retrospectively collected 1880 endoscopic images (1048 GIM and 832 non-GIM) via biopsy from 336 patients confirmed histologically as GIM or non-GIM and developed a CNN with these images using a modified. A separate test dataset containing 477 pathologically confirmed images (242 GIM and 235 non-GIM) from 80 patients was used to test the performance. The area under the receiver operating characteristic curve was 0.928 for the pre-patient analysis of the system, while the sensitivities, specificities, and accuracies of the system against those of the human experts were (91.9% vs 86.5%,  $P=1.000$ ; 86.0% vs 81.4%,  $P=.754$ ), and (88.8% vs 83.8%,  $P=.424$ ), respectively. Even though the 3 indices of the system were slightly higher than those of the human experts, there were no significant differences.

Similarly, Lin et al<sup>29</sup> used total of 7037 endoscopic images from 2741 participants to develop the CNN for recognition of atrophic gastritis (AG) and/or GIM. The AUC for recognizing AG was 0.98 (95% CI 0.97-0.99) with sensitivity, specificity, and accuracy of 96.2% (95% CI 94.2%-97.6%), 96.4% (95% CI 94.8%-97.9%), and 96.4% (95% CI 94.4%-97.8%), respectively. The AUC for recognizing GIM was 0.99 (95% CI 0.98-1.00) with sensitivity, specificity, and accuracy of 97.9% (95% CI 96.2%-98.9%), 97.5% (95% CI 95.8%-98.6%), and 97.6% (95% CI 95.8%-98.6%), respectively.

Another group<sup>30</sup> using deep-learning (DL) approach for the diagnosis of atrophic gastritis developed and trained using real-world endoscopic images from the proximal stomach. The model achieved an accuracy of 93% (area under the curve (AUC): 0.98;  $F$ -score 0.93) in an independent data set, outperforming expert endoscopists.

## AI in Detection of Gastric Cancer

Hirasawa et al used a CNN that was trained using 13584 endoscopic images of gastric cancer. To evaluate the diagnostic accuracy, an independent test set of 2296 gastric images collected from 69 consecutive patients with 77 gastric cancer lesions was applied to the constructed CNN. The CNN required 47 seconds to analyze 2296 test images. The CNN correctly diagnosed 71 of 77 gastric cancer lesions with an overall sensitivity of 92.2%, and 161 non-cancerous lesions were detected as gastric cancer, resulting in a PPV of 30.6%. Seventy of the 71 lesions (98.6%) with a diameter of 6 mm or more as well as all invasive cancers were correctly detected. All missed lesions were superficially depressed and differentiated



**Figure 4.** AI aided detected of gastric cancer on upper endoscopy.

Source. We sincerely thank Fujifilm Healthcare Americas Corporation for permission to use the provided image.

type intramucosal cancers that were difficult to distinguish from gastritis even for experienced endoscopists.<sup>5</sup>

Magnified NBI can provide granular analysis of the lesion for the endoscopist. However, these techniques require a significant learning curve and are currently being used by a limited number of endoscopists. AI guided analysis might bridge this gap. Several studies have evaluated the role of AI in detection of early gastric cancer using magnifying NBI. The AI system was trained using 66 images of early gastric cancer and 60 images of noncancer and this algorithm performed with an accuracy of 96.3%<sup>31</sup>. Miyaki et al<sup>32</sup> evaluated the use of AI with blue light imaging using 100 images and this algorithm was able to detect 84.6% of the gastric cancer lesions.

Zhu et al<sup>33</sup> developed an AI algorithm to predict depth analysis of wall invasion of gastric cancer. They developed a DL algorithm that enabled identification of SM2 from M/SM1. A total of 790 conventional endoscopic images of gastric cancers were used for machine learning, while an additional 203 images, which were completely independent from the learning material, were used as a test set. The AI model showed 76% sensitivity and 96% specificity in identifying “SM2 or deeper” cancers, resulting in significantly higher sensitivity and specificity than those achieved with endoscopists’ visual inspection (Figure 4).

## Future Directions

Development of CADe and CADx in upper endoscopy is rapidly maturing. AI relies on large datasets; however, not all are appropriate for AI use. AI observes patterns in the data (images as an example) that are fed into them and attempt to reproduce a version of truth that is inherently

dependent on their input and the operator-defined version of “ground truth.” Moreover, diverse large datasets with varied image resolution<sup>34</sup> are needed for model training. Moreover, for clinical implementation, AI algorithms must be interpretable and explainable. It is part of human nature to not trust what one cannot understand. One of the major criticisms of AI in medicine is the inability to interpret the output of a Machine Learning (ML) algorithm. Another hurdle to clinical implementation is the “reproducibility” of the ML models. ML models can be trained and designed to model highly complex relationships in their training datasets, often providing excellent predictions in the same cohorts, however these models might not perform to the same level of accuracy in external datasets due to “overfitting” of the models. Hence, once trained and internally validates, AI/ ML algorithms should be compared to the current standard of care in well-designed, prospective, controlled trials.

## Conclusions

The use of computer-based diagnosis for UGI endoscopy is a rapidly growing area of research being explored for its potential application in diagnosing various diseases, including BE, esophageal squamous cell carcinoma, gastric cancer, and *Helicobacter pylori* infection. The advantages of CAD in clinical gastroscopy can be anticipated given the high performance offered by state-of-the-art technology of DL. Larger diverse datasets and well-designed prospective trials could lead to the implementation of this novel technology for UGI endoscopy in the near future.

## Abbreviations

AI: Artificial Intelligence  
 AUC: Area under the curve  
 BE: Barrett’s esophagus  
 CAD: Computer aided diagnosis  
 CNN: Convoluted neural network  
 DL: Deep learning  
 EAC: Esophageal adenocarcinoma  
 ESCC: Esophageal squamous cell carcinoma  
 GIM: Gastric intestinal metaplasia  
 HGD: High grade dysplasia  
 IRIS: Intelligent Real-time Image Segmentation  
 LGD: Low grade dysplasia  
 ML: Machine Learnings  
 NBI: Narrow band imaging  
 NDBE: Non dysplastic Barrett’s esophagus  
 NPV: Negative predictive value  
 PPV: Positive predictive value  
 UGI: Upper gastrointestinal  
 WLE: White light endoscopy

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