Comment

Artificial intelligence in gastrointestinal endoscopy: how intelligent can it get?

An array of artificial intelligence software is being incorporated in the equipment or devices that are used in day-to-day life. The first commercial artificial intelligence system in endoscopy called EndoBRAIN, which was developed in collaboration with academic endoscopists from Showa University Northern Yokohama Hospital (Yokohama, Japan), was recently launched on March 4, 2019, by Olympus.[1] This software allows for artificial intelligence-assisted differentiation of neoplastic and non-neoplastic colon polyps during real-time colonoscopy.[2] Artificial intelligence is here to stay; however, it is important that endoscopists and clinicians have in-depth understanding of its application and limitations in modern endoscopy. Artificial intelligence in its simplest form is machine learning. This learning can be either supervised or unsupervised. In supervised learning, the computer is fed with input and output datasets, which are interpreted. In unsupervised learning, the computer is able to interpret data in addition to the trained inputs based on deep learning like the human neural network. Diagnostic endoscopy operates on three basic principles: detection, delineation, and characterisation. Whatever aid we develop in diagnostic endoscopy, it should support these three applications. In the past decade, advanced imaging techniques have been introduced that included manipulating and filtering the illumination wavelength, post-processing image augmentation software algorithms, endoscopic microscopy and cystoscopy.[3] However, these techniques are not used in the real world universally. Hence, in the real world, clinicians rely on good quality, high-definition white light endoscopy for routine endoscopy. In *The Lancet Oncology*, the study by Huiyan Luo and colleagues[4] has focused on the application of artificial intelligence in white light upper gastrointestinal endoscopy in real-life practice by experts and non-experts from both tertiary and community hospitals in China. This study highlights the complexity of the use of artificial intelligence in diagnostic endoscopy. This study is the first to have incorporated a mammoth 1 036 496 endoscopy images from 84 424 individuals

to develop and validate a gastrointestinal artificial intelligence system for diagnosis of upper gastrointestinal cancer. A study of this magnitude requires participation by multiple institutions and funding by a national body. The Gastrointestinal Artificial Intelligence Diagnostic System (GRAIDS) developed by this group was based on retrospective collection of clinical endoscopy images and validated both internally and externally in a prospective manner. Converting still image to video analysis is a big step in artificial intelligence that was overcome by GRAIDS. Video endoscopy runs at minimum 24 frames per second and can be up to 60 frames per second in high-definition videos. GRAIDS is capable of processing a minimum of 25 images per second with a latency of less than 40 ms during real-time video analysis. This level of performance can be incorporated in routine clinical endoscopy with minimal training for endoscopists. In this study, GRAIDS improved the accuracy of diagnosis by the trainee endoscopist (from diagnostic accuracy of 0·886 [0·875–0·897] to 0·904 [95% CI 0·894–0·914]) and the sensitivity of GRAIDS was similar to that of the expert endoscopist (0·942 [95% CI 0·924–0·957] *vs* 0·945 [0·927–0·959]). The diagnostic sensitivity and negative predictive value for the GRAIDS was consistently more than 90% for the internal and external validation sets, which is adequate for a tool that essentially acts like a warning screening tool. It is important that the clinicians understand that this is the current extent of use of such tools (ie, to be used to assist in diagnosis, rather than to be the sole means of diagnosis), because artificial intelligence will not and cannot replace the human element of clinical medicine. The authors have also created a website providing free access to GRAIDS. This website is designed to view as well as upload images, thus providing a useful resource for learning that can also be used for second opinion.

The challenge in upper gastrointestinal endoscopy, unlike with colon polyps, is that the morphology can vary substantially. The pathology also varies between Asia and Europe and North America. For example, Barretts-related neoplasia is common in Europe

and North America, where squamous neoplasia is common in Asia. One key limitation of this study is that the pathology incorporated was limited to the Chinese population and hence cannot be generalised to other countries. Nevertheless, this is an important step towards use of artificial intelligence in real-time gastrointestinal endoscopy.

There is a lot of excitement in the medical community; however, uncertainty and anxiety about artificial intelligence in medicine is also evident.[5] A global unified approach is necessary for the development of such artificial intelligence systems develop and validate artificial intelligence platforms, so that all ethnicities and pathologies are represented and tested. The level of intelligence that can be achieved by artificial intelligence ultimately depends on our enthusiasm in perfecting these systems before announcing victory.

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3 Beg S, Wilson A, Ragunath K. The use of optical imaging techniques in the gastrointestinal tract. *Frontline Gastroenterol* 2016; **7:** 207–15.
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Are neutralising anti-VEGF or VEGFR2 antibodies necessary in the treatment of *EGFR*-mutated non-small-cell lung cancer?

The NEJ026 study[1] in patients with *EGFR*-positive non-small-cell lung cancer (NSCLC) showed that the combination of erlotinib (150 mg/day) plus intravenous bevacizumab (15 mg/kg once every 21 days) yields a median progression-free survival of 16·9 months (95% CI 14·2–21·0) compared with 13·3 months (11·1–15·3) in patients treated with erlotinib alone (p=0·016). The trial was permissive, allowing patients with CNS metastases (32% in each group) and an Eastern Cooperative Oncology Group performance status of 2 or lower to enroll. Median progression-free survival was also longer in patients with Leu858Arg mutations in the erlotinib and bevacizumab group (17·4 months [95% CI 12·6–not estimable]) than in the erlotinib group (13·7 months [8·8–15·5]). However, no significant differences were found between treatment groups in patients with *EGFR* exon 19 deletions.[1] In *The Lancet Oncology*, Kazuhiko Nakagawa and colleagues[2] report the results of a phase 3 trial (RELAY) assessing the combination of erlotinib 150 mg/day plus ramucirumab (an anti-VEGFR2 antibody) 10 mg/kg intravenously every 2 weeks versus erlotinib 150 mg/day plus

intravenous placebo every 2 weeks. Median progression-free survival was 19·4 months (95% CI 15·4–21·6) in the erlotinib plus ramucirumab group versus 12·4 months (11·0–13·5) in the erlotinib plus placebo group (hazard ratio 0·59 [95% CI 0·46–0·76], p<0·0001). Grade 3 hypertension occurred in 52 (24%) of the 221 patients in the erlotinib plus ramucirumab group safety population. In the previous NEJ026 study,[1] in the erlotinib plus bevacizumab group, grade 3 hypertension also occurred in 23% of the patients. Both trials shed light on the convenience of combining EGFR tyrosine kinase inhibitors with other drugs. However, several questions arise, because in both trials, the proportion of patients attaining a complete response was very low in the combination group: three (1%) of 224 in RELAY and eight (7%) of 112 in NEJ026.

Notably, invasion and metastases increase after the inhibition of VEGF signalling in preclinical tumour models of glioblastoma and pancreatic neuroendocrine tumours. Treatment with a neutralising anti-VEGF antibody reduces tumour burden, but also augments tumour hypoxia, hypoxia-inducible

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