Key research questions for implementation of artificial intelligence in capsule endoscopy

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Abstract

Background: Artificial intelligence (AI) is rapidly infiltrating multiple areas in medicine, with gastrointestinal endoscopy paving the way in both research and clinical applications. Multiple challenges associated with the incorporation of AI in endoscopy are being addressed in recent consensus documents.

Objectives: In the current paper, we aimed to map future challenges and areas of research for the incorporation of AI in capsule endoscopy (CE) practice.

Design: Modified three-round Delphi consensus online survey.

Methods: The study design was based on a modified three-round Delphi consensus online survey distributed to a group of CE and AI experts. Round one aimed to map out key research statements and challenges for the implementation of AI in CE. All queries addressing the same questions were merged into a single issue. The second round aimed to rank all generated questions during round one and to identify the top-ranked statements with the highest total score. Finally, the third round aimed to redistribute and rescore the top-ranked statements.

Results: Twenty-one (16 gastroenterologists and 5 data scientists) experts participated in the survey. In the first round, 48 statements divided into seven themes were generated. After scoring all statements and resoring the top 12, the question of AI use for identification and grading of small bowel pathologies was scored the highest (mean score 9.15), correlation of AI and human expert reading-second (9.05), and real-life feasibility-third (9.0).

Conclusion: In summary, our current study points out a roadmap for future challenges and research areas on our way to fully incorporating AI in CE reading.

Keywords: capsule endoscopy, artificial intelligence, research

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Introduction

Artificial intelligence (AI) technologies are being rapidly developed and implemented in multiple areas of medicine. In recent years, gastrointestinal (GI) endoscopy led the way, with several AI-based technologies for colonic polyp detection introduced and evaluated in clinical practice.1–8 Some of the systems are already being used routinely across the world, even though real-world implementation results are still lacking.

AI is being implemented in several other areas of GI endoscopies, such as early detection of gastric neoplasia,9,10 Barrett’s esophagus,11 endoscopic ultrasound,12,13 and grading of mucosal inflammation in ulcerative colitis.14–18 An additional
field with the fast development of AI research is capsule endoscopy (CE), with several publications evaluating deep learning for automated detection of inflammatory lesions, vascular lesions, protruding and neoplastic lesions/masses, and scoring of bowel cleanliness.

However, there are still multiple challenges in the way of implementation of the impressive experimental performance of AI in CE in clinical practice. Some of these challenges include standardization of the results, validation of established end points, creation of common datasets and computational methodology, and correlation with clinical outcomes. These challenges are partially common to other areas of GI endoscopy and medicine in general and are being addressed by expert consensus meetings and workshops providing roadmaps into future research targets and methodologies. Recently, such priority-setting statement was published for colonoscopy; the key themes were identified as the establishment of clinical trial design/end points, technological development, clinical integration, data access and annotation and regulatory approval.

The main aim of our study was to identify the top research priorities related to the implementation and further research for AI in CE.

**Materials and methods**

**Study design**

The study design was based on a modified three-round Delphi consensus online survey. The modified Delphi methodology is well known and used in medical literature for establishing research priorities related to the implementation of AI in CE in clinical practice, and auditing AI systems. Some of these challenges include standardization of the results, validation of established end points, creation of common datasets and computational methodology, and correlation with clinical outcomes. These challenges are partially common to other areas of GI endoscopy and medicine in general and are being addressed by expert consensus meetings and workshops providing roadmaps into future research targets and methodologies. Recently, such priority-setting statement was published for colonoscopy; the key themes were identified as the establishment of clinical trial design/end points, technological development, clinical integration, data access and annotation and regulatory approval.

The core group and expert group

The CG was composed of translational CE readers and data scientists (UK, RL, AK, XD, and AH) to form a key leader opinion to conduct this study. All questionnaires were sent to a panel of CE experts, including the CG, with a diversity of backgrounds including physicians CE experts’ readers and data scientists related to the CE medical field.

**Results**

Among the 22 experts invited to participate in this study, 21 finally answered at least one of the questionnaires. The participation rate was 90% (n=19) for the first round and 95% (n=20) for the second and third rounds, respectively. The 21 respondents were considered as the expert group (EG) and included physicians CE experts readers (76%, n=16) and data scientists (24%, n=5). Members of the EG were based in Denmark (n=3), England (n=1), France (n=4), Germany (n=1), Greece (n=1), Ireland (n=1), Israel (n=3), Italy (n=2), Norway (n=1), Portugal (n=1), Spain (n=1), and Sweden (n=2). The mean age of the experts was 49 years. The main practice setting was academic (n=18; 86%) and mixed academic/private (n=3; 14%). The physicians CE experts had a mean CE reading experience of 14 years (interquartile range [IQR]=13) and a mean number of CE read annually of 154 (IQR=150). The data scientists had a mean CE experience of 12 years.

After the review process by the CG, the first round generated 48 statements divided into seven themes (Table 1). These statements were then considered for scoring in the second round. In round two, considering the wider scale from 1 (very low priority) to 10 (very high priority), the mean score obtained for the 48 statements ranged from 4.6 to 9.2 (Table 1). Then the top 12 statements, including tied scores, were identified from three themes including performances metrics, AI in CE in clinical practice, and auditing AI systems. The final 12 statements were considered for rescoring in the third round. Results of the third round showed a mean score ranging from 7.63 to 9.15 (Table 2).
Discussion

The current study is the first attempt to prioritize and standardize the research challenges and questions in the application of AI in CE. The consensus was facilitated by a modified three-stage Delphi process through an established group of CE experts and data engineers with extensive experience on the subject.

AI is rapidly being incorporated into multiple fields in medicine, with GI endoscopy being among the leading disciplines. In colonoscopy, AI-based systems for the facilitation of polyp detection are already commercially available and have been proven successful in improving polyp detection rate by up to 40%. In CE, comparative research is not yet available; however, detection of multiple types of small bowel (SB) and colonic pathologies is accurate and feasible. CE is perhaps an even more attractive target for AI research, as there is no need for real-time diagnosis, and the variety of pathology types is somewhat limited: thus, identification of most SB pathologies by AI was very accurate, with AUC above 90%. In future models of CE, strong incorporation of AI modules with automated lesion markup can be expected. However, the incorporation of AI into clinical practice and clinical trials requires a huge leap in terms of standardization, quality assessment, reproducibility, and workflow integration. In a recent large European survey encompassing 380 gastroenterologists (of them 88% experienced capsule readers), a majority of the responders agreed that AI would positively impact CE, shorten CE reading time, help standardize reporting in CE, and characterize lesions seen in CE; however, the likelihood of complete replacement of human readers by AI was deemed to be low.

We aimed to map and prioritize the main challenges for further research and integration into clinical practice. Our EG was comprised of 76% physicians and 24% data scientists, all of them with a vast track record of CE reading and research. It appears that the highest scores issued in this EG were still those referring to accuracy in detection of findings in both SB and colon, as well as the optimal threshold for accuracy of the algorithm. The next group of statements addressed the feasibility and accuracy in a real-world setting. Indeed, to date, no real-world model for the utilization of AI in CE has been published. Identification of specific lesions by AI may be introduced into capsule reading software of any of capsule producers/vendors; nonetheless, clinical decision-making or predictive models based on AI capsule reading (either complete videos or still images) are still missing.

Most of the available studies included images obtained with a specific capsule model or brand. Widespread utilization of AI will require brand/model-spanning algorithms that are still very rare. Similarly, a clinical algorithm would be required to detect multiple types of pathologies at the same time and on the same still image, regardless of the location of the image (SB/colon). An additional issue of concern is whether AI would be able to completely replace a human reader, and what degree of human supervision/auditing will be required. This challenge is closer to those originating from the worlds of imaging and pathology; AI in colonoscopy may augment human judgment but will not replace it completely as the human is still behind the scope and is instrumental to the obtainment of quality images. CE diagnosis is completely in post-acquisition, and human intervention is not required for anything but the reading itself. Nevertheless, CE reading is a tedious and lengthy task, especially for colonic capsules; AI can shorten the reading time by at least 95%; however, real-life accuracy data that could support this model in clinical practice are completely lacking. This issue could be critical for the uptake of colonic CE that is currently hampered by long reading time and subsequent devaluation of the economic model for this potentially appealing screening modality. An additional temporary compromise could be to...
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utilize AI to remove normal images, in similarity to the current features of ‘Quickview’ or top-100; currently, these features are insufficiently accurate; however, future hardware and software improvements may change that.

It is likely that in the near future we will witness several AI systems for CE, some incorporated in the reading software and others as standalone suites. There is a need to compare the accuracy of these and other forthcoming systems and a requirement for benchmarking parameters for both clinical trial and real-world use.

In inflammatory bowel diseases, CE has a potential major advantage of being able to access the panenteric inflammatory burden. The importance of mucosal healing as a therapeutic target in inflammatory bowel diseases has been well described. However, the concept of mucosal healing in IBD is almost constantly addressing the colon and the terminal ileum. Nonetheless, mucosal responsiveness of different gut segments to medical treatment is not identical. In addition, in Crohn’s disease patients in clinical remission, some residual SB inflammation is very common and has major clinical implications on the likelihood of long-term remission. Surprisingly, only a handful of studies to date utilized CE for evaluation of mucosal healing prospectively. In the last few years, several studies reported the use of colonic capsules for panenteric evaluation; recently a specialized Crohn’s disease capsule (Pillcam Crohn, Medtronic, Minneapolis, MN, USA) has been released. AI-read CE could be a potentially safe and accurate modality for the assessment of mucosal inflammation in clinical trials in IBD.

Table 2. Results of the top 12 ranked statements third round with the top 12 ranked statements.

| Rank | Statements                                                                                                                                                                                                 | Total score | Mean score |
|------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|------------|
| 1    | AI for automatic detection, identification, characterization (type, size, severity), and differentiation of SB lesions: inflammatory lesions (erosion, ulceration, edema, etc.), vascular lesions, bulges, atrophy. | 174         | 9.15       |
| 2    | How do the overall results of AI and expert reading correlate (for all lesions/relevant lesions)?                                                                                                           | 172         | 9.05       |
| 3    | Feasibility and accuracy in the real-world setting.                                                                                                                                                            | 171         | 9.00       |
| 4    | AI for automatic detection/identification, characterization (type, size, severity), and differentiation of colon lesions: ulcers, vascular lesions, polyps.                                                   | 157         | 8.26       |
| 5    | Auditing of CE systems after incorporation in clinical practice.                                                                                                                                             | 155         | 8.15       |
| 6    | How to reduce the false-positive rate without decreasing sensitivity?                                                                                                                                        | 155         | 8.15       |
| 7    | Creation of algorithms for simultaneous identification of multiple lesion types.                                                                                                                             | 151         | 7.94       |
| 8    | Adoption of AI by clinicians.                                                                                                                                                                               | 150         | 7.89       |
| 9    | What are the optimal clinical end-points for the evaluation of AI software?                                                                                                                                  | 149         | 7.84       |
| 10   | What are the optimal clinical trial design and end-points to compare different AI systems for CE?                                                                                                           | 149         | 7.84       |
| 11   | How accurate should AI be to be incorporated in clinical trials?                                                                                                                                             | 147         | 7.73       |
| 12   | What accuracy parameters are potential targets for AI utilization?                                                                                                                                              | 145         | 7.63       |

AI, artificial intelligence; CE, capsule endoscopy; SB, small bowel.
pending further benchmarking and standardization. To date, no studies evaluating complete film AI-augmented reading were published. This challenge may require a very different analytical approach.

Our study has several limitations. Primarily, this was a Delphi survey of a predefined group of AI and CE experts. The group was limited in size however included participants with a significant track record in the field. Attitudes toward AI in CE in a larger and more representative group of gastroenterologists were previously evaluated by our group. In addition, our objective was to raise and solicitate research questions; the suggestions of the participating experts merit further research efforts in the years to come.

Conclusion
In summary, our current study points out a roadmap for future challenges and research areas on our way to fully incorporate AI in CE reading. These statements are useful not only for research but also for AI medical education.

Declarations

**Ethics approval and consent to participate**
Not applicable.

**Consent for publication**
Not applicable.

**Author contribution[s]**

**Romain Leenhardt:** Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Writing – original draft; Writing – review & editing.

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References
1. Pannala R, Krishnan K, Melson J, et al. Artificial intelligence in gastrointestinal endoscopy. VideoGIE 2020; 5: 598–613.
2. Tontini GE, Rimondi A, Vernero M, et al. Artificial intelligence in gastrointestinal endoscopy for inflammatory bowel disease: a systematic review and new horizons. Therap Adv Gastroenterol 2021; 14: 17562848211017730.
3. Yang YJ. The future of capsule endoscopy: the role of artificial intelligence and other technical advancements. Clin Endosc 2020; 53: 387–394.
4. Ahmad OF. Deep learning for colorectal polyp detection: time for clinical implementation? Lancet Gastroenterol Hepatol 2020; 5: 330–331.
5. Ahmad OF, Mori Y, Misawa M, et al. Establishing key research questions for the implementation of artificial intelligence in colonoscopy: a modified Delphi method. Endoscopy 2021; 53: 893–901.
6. Repici A, Badalamenti M, Maselli R, et al. Efficacy of real-time computer-aided detection of colorectal neoplasia in a randomized trial. Gastroenterology 2020; 159: 512.e7–520.e7.
7. Repici A, Spadaccini M, Antonelli G, et al. Artificial intelligence and colonoscopy experience: lessons from two randomised trials. Gut 2021; 71: 757–765.
8. Topol EJ. Welcoming new guidelines for AI clinical research. Nat Med 2020; 26: 1318–1320.
9. Wu L, Xu M, Jiang X, et al. Real-time artificial intelligence for detecting focal lesions and diagnosing neoplasms of the stomach by white-light endoscopy (with videos). Gastrointest Endosc 2021; 95: 269–280.
10. Klang E, Barash Y, Levartovsky A, et al. Differentiation between malignant and benign endoscopic images of gastric ulcers using deep learning. Clin Exp Gastroenterol 2021; 14: 155–162.
11. Struyvenberg MR, de Groof AJ, van der Putten J, et al. A computer-assisted algorithm for narrow-band imaging-based tissue characterization in Barrett’s esophagus. Gastrointest Endosc 2021; 93: 89–98.
12. Goyal H, Mann R, Gandhi Z, et al. Application of artificial intelligence in pancreaticobiliary diseases. Ther Adv Gastrointest Endosc 2021; 14: 2631774521993059.
13. Kuwahara T, Hara K, Mizuno N, et al. Usefulness of deep learning analysis for the diagnosis of malignancy in intraductal papillary mucinous neoplasms of the pancreas. Clin Transl Gastroenterol 2019; 10: 1–8.
14. Gottlieb K, Requa J, Karnes W, et al. Central reading of ulcerative colitis clinical trial videos using neural networks. Gastroenterology 2021; 160: 710.e2–719.e2.
15. Ghoshal UC, Rai S, Kulkarni A, et al. Prediction of outcome of treatment of acute severe ulcerative colitis using principal component analysis and artificial intelligence. JGH Open 2020; 4: 889–897.
16. Takenaka K, Ohtsuka K, Fujii T, et al. Development and validation of a deep neural network for accurate evaluation of endoscopic images from patients with ulcerative colitis. Gastroenterology 2020; 158: 2150–2157.

17. Yao H, Najarian K, Gryak J, et al. Fully automated endoscopic disease activity assessment in ulcerative colitis. Gastrointest Endosc 2021; 93: 728.e1–736.e1.

18. Stidham RW, Liu W, Bishu S, et al. Performance of a deep learning model vs human reviewers in grading endoscopic disease severity of patients with ulcerative colitis. JAMA Netw Open 2019; 2: e193963.

19. Klang E, Barash Y, Margalit RY, et al. Deep learning algorithms for automated detection of Crohn’s disease ulcers by video capsule endoscopy. Gastrointest Endosc 2020; 91: 606.e2–613.e2.

20. Klang E, Grinman A, Soffer S, et al. Automated detection of Crohn’s disease intestinal strictures on capsule endoscopy images using deep neural networks. J Crohns Colitis 2020; 15: 749–756.

21. Klang E, Kopylov U, Mortensen B, et al. A convolutional neural network deep learning model trained on CD ulcers images accurately identifies NSAID ulcers. Front Med 2021; 8: 656493.

22. Barash Y, Azaria L, Soffer S, et al. Ulcer severity grading in video capsule images of patients with Crohn’s disease: an ordinal neural network solution. Gastrointest Endosc 2021; 93: 187–192.

23. Aoki T, Yamada A and Koike K. The exceptional performance of deep learning for capsule endoscopy: will such quality be maintained in clinical scenarios? Gastrointest Endosc 2021; 93: 365–366.

24. Aoki T, Yamada A, Aoyama K, et al. Automatic detection of erosions and ulcerations in wireless capsule endoscopy images based on a deep convolutional neural network. Gastrointest Endosc 2019; 89: 357.e2–363.e2.

25. Maitner T, Brodersen JB, Herp J, et al. A deep learning framework for autonomous detection and classification of Crohn’s disease lesions in the small bowel and colon with capsule endoscopy. Endosc Int Open 2021; 9: E1361–E1370.

26. Mascarenhas Saraiva MJ, Afonso J, Ribeiro T, et al. Deep learning and capsule endoscopy: automatic identification and differentiation of small bowel lesions with distinct haemorrhagic potential using a convolutional neural network. BMJ Open Gastroenterol 2021; 8: e000753.

27. Leenhardt R, Vasseur P, Li C, et al. A neural network algorithm for detection of GI angiectasia during small-bowel capsule endoscopy. Gastrointest Endosc 2019; 89: 189–194.

28. Houdeville C, Souchaud M, Leenhardt R, et al. A multisystem-compatible deep learning-based algorithm for detection and characterization of angiectasias in small-bowel capsule endoscopy. A proof-of-concept study. Dig Liver Dis 2021; 53: 1627–1631.

29. Saito H, Aoki T, Aoyama K, et al. Automatic detection and classification of protruding lesions in wireless capsule endoscopy images based on a deep convolutional neural network. Gastrointest Endosc 2020; 92: 144.e1–151.e1.

30. Leenhardt R, Souchaud M, Houist G, et al. A neural network-based algorithm for assessing the cleanliness of small bowel during capsule endoscopy. Endoscopy 2021; 53: 932–936.

31. Langlotz CP, Allen B, Erickson BJ, et al. A roadmap for foundational research on artificial intelligence in medical imaging: from the 2018 NIH/RSNA/ACR/ The academy workshop. Radiology 2019; 291: 781–791.

32. Rees CJ, Ngu WS, Regula J, et al. European society of gastrointestinal endoscopy – establishing the key unanswered research questions within gastrointestinal endoscopy. Endoscopy 2016; 48: 884–891.

33. Sullivan P, Gupta S, Powers PD, et al. Artificial intelligence research and development for application in video capsule endoscopy. Gastrointest Endosc Clin N Am 2021; 31: 387–397.

34. Tziortziotis I, Laskaratos F-M and Coda S. Role of artificial intelligence in video capsule endoscopy. Diagnostics (Basel) 2021; 11: 1192.

35. Ferreira JPS, de Mascarenhas Saraiva MJ da QEC, Afonso JPL, et al. Identification of ulcers and erosions by the novel Pillcam™ Crohn’s Capsule using a convolutional neural network: a multicentre pilot study. J Crohns Colitis 2021; 16: 169–172.

36. Aoki T, Yamada A, Aoyama K, et al. Clinical usefulness of a deep learning-based system as the first screening on small-bowel capsule endoscopy reading. Dig Endosc 2020; 32: 585–591.

37. Dray X, Iakovidis D, Houdeville C, et al. Artificial intelligence in small bowel capsule endoscopy–current status, challenges and future promise. J Gastroenterol Hepatol 2021; 36: 12–19.

38. de Maissin A, Vallée R, Flamant M, et al. Multi-expert annotation of Crohn’s disease images of the small bowel for automatic detection using a
convolutional recurrent attention neural network. *Endosc Int Open* 2021; 9: E1136–E1144.

39. Leenhardt R, Fernandez-Urrien Sainz I, Rondonotti E, et al. PEACE: perception and expectations toward artificial intelligence in capsule endoscopy. *J Clin Med* 2021; 10: 5708.

40. Arieira C, Monteiro S, Dias de Castro F, et al. Capsule endoscopy: is the software TOP 100 a reliable tool in suspected small bowel bleeding? *Dig Liver Dis* 2019; 51: 1661–1664.

41. Freitas M, Arieira C, Carvalho PB, et al. Simplify to improve in capsule endoscopy–TOP 100 is a swift and reliable evaluation tool for the small bowel inflammatory activity in Crohn’s disease. *Scand J Gastroenterol* 2020; 55: 408–413.

42. Ding Z, Shi H, Zhang H, et al. Gastroenterologist-level identification of small-bowel diseases and normal variants by capsule endoscopy using a deep-learning model. *Gastroenterology* 2019; 157: 1044.e5–1054.e5.

43. Peyrin-Biroulet L, Sandborn W, Sands BE, et al. Selecting therapeutic targets in inflammatory bowel disease (STRIDE): determining therapeutic goals for treat-to-target. *Am J Gastroenterol* 2015; 110: 1324–1338.

44. Turner D, Ricciuto A, Lewis A, et al. STRIDE-II: an update on the selecting therapeutic targets in inflammatory bowel disease (STRIDE) initiative of the international organization for the study of IBD (IOIBD): determining therapeutic goals for treat-to-target strategies in IBD. *Gastroenterology* 2021; 160: 1570–1583.

45. Danese S, Sandborn WJ, Colombel J-F, et al. Endoscopic, radiologic, and histologic healing with vedolizumab in patients with active Crohn’s disease. *Gastroenterology* 2019; 157: 1007.e1–1018.e7.

46. Pouillon L, Rousseau H, Busby-Venner H, et al. Vedolizumab trough levels and histological healing during maintenance therapy in ulcerative colitis. *J Crohns Colitis* 2019; 13: 970–975.

47. Kopylov U, Yablecovitch D, Lahat A, et al. Detection of small bowel mucosal healing and deep remission in patients with known small bowel crohn’s disease using biomarkers, capsule endoscopy, and imaging. *Am J Gastroenterol* 2015; 110: 1316–1323.

48. Ben-Horin S, Lahat A, Amitai MM, et al. Assessment of small bowel mucosal healing by video capsule endoscopy for the prediction of short-term and long-term risk of Crohn’s disease flare: a prospective cohort study. *Lancet Gastroenterol Hepatol* 2019; 4: 519–528.

49. Hall B, Holleran G, Chin J-L, et al. A prospective 52 week mucosal healing assessment of small bowel Crohn’s disease as detected by capsule endoscopy. *J Crohns Colitis* 2014; 8: 1601–1609.

50. Hall BJ, Holleran GE, Smith SM, et al. A prospective 12-week mucosal healing assessment of small bowel Crohn’s disease as detected by capsule endoscopy. *Eur J Gastroenterol Hepatol* 2014; 26: 1253–1259.

51. Boal Carvalho P, Rosa B, Dias de Castro F, et al. PillCam COLON 2 in Crohn’s disease: a new concept of pan-enteric mucosal healing assessment. *World J Gastroenterol* 2015; 21: 7233–7241.

52. Leighton JA, Helper DJ, Gralnek IM, et al. Comparing diagnostic yield of a novel pan-enteric video capsule endoscope with ileocolonoscopy in patients with active Crohn’s disease: a feasibility study. *Gastrointest Endosc* 2017; 85: 196.e1–205.e1.

53. Hall B, Holleran G and McNamara D. PillCam COLON 2(©) as a pan-enteroscopic test in Crohn’s disease. *World J Gastrointest Endosc* 2015; 7: 1230–1232.

54. Oliva S, Aloë M, Viola F, et al. A treat to target strategy using panenteric capsule endoscopy in pediatric patients with Crohn’s disease. *Clin Gastroenterol Hepatol* 2019; 17: 2060. e1–2067.e1.

55. Cortegoso Valdivia P, Elosua A, Houdeville C, et al. Clinical feasibility of panintestinal (or panenteric) capsule endoscopy: a systematic review. *Eur J Gastroenterol Hepatol* 2019; 33: 949–955.

56. Lazaridis L-D, Tziatziou G, Toth E, et al. Implementation of European society of gastrointestinal endoscopy (ESGE) recommendations for small-bowel capsule endoscopy into clinical practice: results of an official ESGE survey. *Endoscopy* 2021; 53: 970–980.

57. Tai FWD, Ellul P, Elosua A, et al. Panenteric capsule endoscopy identifies proximal small bowel disease guiding upstaging and treatment intensification in Crohn’s disease: a European multicentre observational cohort study. *United European Gastroenterol J* 2021; 9: 248–255.

58. Eliakim R, Yablecovitch D, Lahat A, et al. A novel PillCam Crohn’s capsule score (Eliakim score) for quantification of mucosal inflammation in Crohn’s disease. *United European Gastroenterol J* 2020; 8: 544–551.