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Title: Artificial Intelligence and computer-aided diagnosis in colonoscopy: current evidence and future directions

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Summary

Computer-aided diagnosis (CAD) offers a promising solution to reduce variation in colonoscopy performance. Pooled miss rates as high as 22% for polyps and associated interval colorectal cancers following colonoscopy are concerning. Meanwhile, the concept of 'optical biopsy' where in vivo classification of polyps based on enhanced imaging replaces histopathology has not been incorporated into routine practice, largely limited by inter-observer variability and generally meeting accepted standards only in expert settings. Real-time decision support software has been developed to detect and characterise polyps, whilst also offering feedback on the technical quality of inspection. Some of the current algorithms, particularly with recent advances in artificial intelligence techniques, now match human expert performance for optical biopsy. This article will review the current evidence in relation to the clinical applications of CAD and artificial intelligence in colonoscopy.

Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed malignancy and fourth leading cause of cancer death worldwide.[1] Colonoscopy has demonstrated efficacy in preventing CRC through the detection and removal of neoplastic lesions.[2] There is concerning variability in the diagnostic performance of colonoscopy leading to widespread efforts to improve quality and reduce operator dependence.

Adenoma detection rate (ADR) is an independent predictor for the risk of interval CRC.[3,4] This key metric has been shown to vary considerably among different endoscopists within a similar setting, even independent of patient-related factors.[5,6] The operator dependence of colonoscopy has been highlighted by a pooled miss-rate of 22% for polyps of any size in a meta-analysis including six studies involving patients undergoing two same-day colonoscopies.[7] A more recent analysis identified a post-colonoscopy cancer rate of 8.6% within three years of an apparently negative colonoscopy. Evidence suggests that these most likely represent missed cancers or incompletely resected lesions.[8,9]

A number of strategies have been developed in an attempt to improve ADR. This includes advanced imaging technologies to facilitate detection, such as virtual chromoendoscopy, although studies have failed to demonstrate conclusive increments in ADRs in average risk populations.[10] Devices aimed at increasing mucosal exposure have produced variable results. A recent meta-analysis suggested only modest improvements in ADRs for distal attachment devices, especially in low-performing endoscopists.[11]

It is increasingly recognised that a significant proportion of lesions are endoscopically subtle. Using the Paris classification to describe morphology, flat and depressed lesions are not only particularly challenging to detect but are also more likely to contain advanced histopathology.[12] Furthermore, sessile serrated lesions have endoscopic features that are difficult to differentiate from background mucosa in comparison to conventional adenomas, such as mucus capping, indistinct borders and pale colour.[13]

Although uncertain, indirect evidence supports a concept that endoscopists may fail to identify lesions even when within the endoscopic field of view. This includes the demonstration that nurse participation allowing dual observation during colonoscopy withdrawal can improve ADR.[14] Learning curves also exist for the detection flat and sessile serrated lesions.[15,16] In addition, the landmark endoscopy quality improvement programme study by Coe at al. that led to improved ADRs included pattern recognition training. [17] It is possible that the appreciation of certain visual cues may alert high level detector endoscopists to subtle lesions that may otherwise be overlooked.

Polyp characterisation during endoscopy is another area subject to inter-observer variability amongst endoscopists. The term ‘optical biopsy’ has been proposed where enhanced imaging, in conjunction with validated classification systems, allows for real-time in vivo prediction of histopathology. This application is particularly relevant to diminutive (≤5mm) polyps to differentiate between neoplastic and non-neoplastic lesions. A ‘resect and discard’ strategy has been proposed for diminutive adenomas, where in-vivo virtual chromoendoscopy-based diagnoses are used in lieu of histopathology, allowing resected adenomas to be discarded.[18] Suggested benefits include significant cost savings due to immediate surveillance interval

recommendations, with a reduced requirement for follow-up appointments and lower burden on histopathology services. A further proposal involves a 'diagnose and leave' strategy where diminutive rectosigmoid polyps optically characterised as non-neoplastic could be left in situ.

An ideal optical biopsy technique should use readily available enhanced imaging alongside a robustly validated classification system which is reproducible in widespread clinical practice. In addition, some form of accreditation scheme alongside audit processes to monitor performance should exist as highlighted by the recent National Institute for Clinical and Healthcare Excellence guidance on virtual chromoendoscopy to assess colorectal polyps.[19] The American Society for Gastrointestinal Endoscopy published the Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) standards required of a technology for a resect and discard strategy (≥90% agreement for post-polypectomy surveillance intervals when compared with histopathology) and for a diagnose and leave strategy (≥90% negative predictive value for adenomatous histology).[20] Studies have demonstrated that standards for a resect and discard strategy can be achieved in academic settings but not always in community-based practice, limiting its incorporation into routine care.[21,22] The reasons for variability in performance between 'expert' and 'non-expert' settings are unclear. Differences in training methodologies and performance feedback could be one potential explanation.

Optical diagnosis of malignant colonic polyps is another important clinical application, where recognition of early invasive cancers and prediction of depth of invasion is key to selecting the optimal treatment strategy. In cases of superficial invasive carcinoma, en-bloc endoscopic treatments can be curative. Polyps harbouring deep submucosal invasion are at higher risk of lymphovascular invasion and in these cases referral for surgical resection is recommended. Validated classification systems based on advanced imaging using magnifying chromoendoscopy and narrow band imaging have been developed to predict submucosal invasion. These include the Kudo pit pattern, Sano capillary pattern, Hiroshima and NBI International Colorectal Endoscopic Classifications.[23] The majority of studies have evaluated experts within Japan. Western data are limited but image analysis studies suggest that accurate diagnosis represents a challenge.[24]

The use of 'computer-aided diagnosis', using advances in artificial intelligence and especially recent deep learning techniques, offers a promising solution to provide decision support during colonoscopy to address human variation in performance.

This review article evaluates the current literature in relation to the clinical applications of computer-aided diagnosis and artificial intelligence in colonoscopy addressing current evidence, limitations and future prospects.

Computer-Aided Diagnosis & Deep Learning

Computer-aided detection and diagnosis (CAD) systems are designed to assist clinicians in interpreting medical images. Over the last few decades there have been significant technological advances in the methods applied within this field. Machine

learning is a type of artificial intelligence (AI), that allows systems to automatically learn from data and improve performance without prediction rules being explicitly programmed.

Early image-based CAD systems were based on traditional machine learning approaches that require human researchers to design meaningful image features which would then be fed to a trainable prediction algorithm such as a classifier. Deep learning overcomes this obstacle by discovering the informative features, in a trainable manner, that optimally represent the data for the specific task. Deep learning models rely on artificial neural networks, that are biologically inspired by the concept of neurons and synapses in the human brain. Within the field of image analysis, the best results to date have been achieved with a particular type of model known as convolutional neural networks (CNNs), consisting of multiple layers of relatively simple computational nodes but with complex connections simulating the action of the human visual cortex, allowing learning of increasingly higher-level features.

Deep-learning based approaches are now gaining unprecedented interest and success in relation to medical imaging due to advances in the development of algorithms, availability of enhanced computational power with graphics processing units (GPU) and access to large sets of data ('big data').[25-27] Algorithms have been shown to exceed human performance in tasks such as object recognition in natural images and playing strategic games.[28-29] This successful combination is highlighted within medical imaging by the example of a CNN, trained on 129,450 skin images, that was able to match the performance of expert dermatologists in differentiating benign from malignant lesions.[30] In another study, deep-learning algorithms evaluated as part of a competition, were comparable in accuracy to an expert pathologist assessing 129 pathology slide images for the presence of breast cancer metastases within sentinel axillary lymph node specimens.[31] More importantly, the top-performing algorithms achieved a superior diagnostic performance on the test set when compared to 11 pathologists taking part in a time-limited exercise designed to simulate real-life clinical practice.

Polyp Detection

Early work led by computer scientists focussed on techniques guided by polyp features such as colour, shapes or textures in comparison to the surrounding mucosa.

Karkanis et al. used a colour feature based analysis on colonoscopy videos.[32] The test set consisted of 1200 randomly selected still frames from video sequences from 66

patients all containing polyps. Expert endoscopists manually annotated image regions within frames that corresponded to polyps and normal background tissue. The best performing model demonstrated a sensitivity of 93.6% and specificity of 99.3%. Wider application of the model was limited by significant variations in polyp colours and lighting conditions during colonoscopy.[33]

Other methodologies have analysed shapes and boundaries. Hwang et al. developed a technique focussing on elliptical shape features.[34] Relying on elliptical shape can lead to challenges where other structures such as the lumen or artefacts can be misinterpreted as polyps.

Fernandez-Esparrach et al. , used a Window Median Depth of Valleys Accumulation (WM-DOVA) energy maps system to highlight the specific region of an image containing a polyp.[35] This system modelled polyps as protrusions in the mucosa and defined their boundaries. They analysed 24 colonoscopy videos containing 31 different polyps labelled by expert endoscopists. Polyp detection was achieved with a sensitivity of 70.4% and specificity of 72.4%. Of note the WM-DOVA method was particularly useful for small flat (Paris 0-II) lesions and was not negatively affected by bowel preparation which was graded using the Boston Bowel Preparation Scale. The authors suggested that since the model did not use texture or colour cues, only solid faeces would mimic a polyp appearance, but other forms of faecal material would not have an impact. Limitations of the model included detection errors caused by lateral views of the polyps and other structures (colonic folds and blood vessels).

Wang et al. developed an algorithm that extracted features for polyp edge detection and tracked these within 'polyp shots'.[36] A polyp shot is defined as a sequence of images covering the same polyp. The software correctly detected 42 out of 43 polyp shots (97.7%) on 53 randomly selected videos from two different endoscopy processors. There were 31 videos that did not contain any polyps within the test set. A performance metric consisting of the total number of falsely alerted polyp shots as a proportion of the total number of tested videos was used to evaluate the false positive rate. The system operated in near real-time but produced an average of 36.2 false positives per video. The performance was not assessed against polyp morphology or bowel preparation quality.

More recent systems have utilised hybrid methods such as Tajbakhsh et al., where shape information was combined with the image appearance of polyp boundaries.[37] The system was evaluated using a free-response receiver operator characteristic analysis. It achieved a sensitivity of 48% in their own image database and 88% in an external dataset, with an average of 0.1 false positives per frame. The authors suggested the variation of the performance may be attributed to an insufficient number of images within the external dataset including an absence of images without a polyp. The datasets analysed, however, contained only 10 and 15 polyps respectively. The total number of frames evaluated included 5,500 polyp and 14,200 non-polyp images.

Deep-learning based methods using CNNs have started to feature more frequently in the literature. Park and Sargent, developed a CNN to extract image descriptor features representing polyps.[38] The model was an advance on their previous work that used anatomical features which was susceptible to error from variations in viewing angles and image quality factors. The algorithm demonstrated 86% sensitivity and 85%

specificity when evaluated on a training set of 11802 still images from 35 videos. A limitation of is that the algorithm did not incorporate relationships in adjacent video frames into the CNN.

Misawa et al. conducted a pilot study using a dataset consisting of 73 colonoscopy video sequences running from caecal intubation to scope withdrawal across anus which included a total of 155 polyps.[39] Flat lesions accounted for 64.5% of the dataset. Each frame containing a polyp was retrospectively annotated by two expert endoscopists acting as the reference for polyp presence. The dataset was divided into 155 polyp positive and 391 polyp negative short videos which were randomly used for training and testing the CNN. A cut-off value of 15% was set for the probability of detecting a polyp based on a receiver operating characteristic analysis. The system achieved a sensitivity, specificity and accuracy of 90.0%, 63.3% and 76.5% respectively on an image-frame based analysis using a test set of 135 short videos.

More recently, Urban et al. evaluated a CNN on a dataset of 8641 hand-selected colonoscopy images from over 2000 patients consisting of 4088 unique polyp images and 4553 images without polyps. [40] Polyp containing images were annotated by a team of colonoscopists. The CNN detected polyps with a cross-validation accuracy of 96.4% and area under the receiver operating characteristic curve (ROC-AUC) value of 0.991. A further analysis of two colonoscopy video datasets was performed. Three colonoscopists deemed to be experts (ADR≥50%) identified frames containing polyps without the assistance of the CNN. A senior expert (ADR≥50% and >20K colonoscopies) also reviewed the videos with a CNN-overlay consisting of a superimposed green box over polyps detected in frames with a probability greater than 95%. A confidence level (high or low) was assigned by the senior expert for true polyp presence which was used as a reference. The first dataset consisted of nine videos where 28 polyps were removed by the original colonoscopists. The three experts reviewing the unaltered videos identified a total of 36 polyps (8 additional). With the CNN overlay on videos, a total of 45 polyps were identified, of the 9 additional polyps found with CNN assistance the senior expert confidence value was low for 6 and high for 3 polyp encounters. A second dataset was evaluated consisting of eleven videos containing 73 polyps, where the colonoscopist did not close in on already identified polyps during withdrawal to purposefully simulate missed polyp scenarios. The CNN identified 67 of 73 polyps with a frame-by-frame false positive rate of 5%. This important feasibility study using CNN video overlay supports the concept that CNN assistance offers promise in improving ADR by highlighting polyps that could potentially be missed.

A much-needed global initiative, as part of the Medical Imaging Computing and Computer Assisted Intervention (MICCAI) 2015 conference, highlighted the key challenges for automated polyp detection and sought to define performance metrics on publically annotated databases to allow comparisons of multiple methodologies.[41] Results from the challenge competition demonstrated that CNNs were state of the art and a combination of methods led to improvements in performance. Several groups have since used the annotated datasets to enhance methods.[42,43] Figure 1 illustrates the polyp detection performance of different CNNs. Results from the subsequent 2017 challenge await publication. Table 1 provides a summary of the key recent studies for polyp detection.

CAD based systems for polyp detection, particularly using deep learning techniques, provide great promise in offering real-time support for clinicians potentially reducing human variation in performance. No system has currently been trialled or adopted in a clinical setting. General application is lacking as most methodologies are validated on small datasets, often consisting of high quality still images, lacking variability in polyp morphologies and commonly use a single type of endoscopy processor. Furthermore, few studies address the potential effect of other quality parameters on performance such as bowel preparation and withdrawal time. It is possible that CAD polyp detection performance might vary depending on operator characteristics such as speed of withdrawal and quality of inspection. To overcome these challenges, clinician and computer scientist collaborative initiatives leading to more readily available large annotated datasets with consistent performance evaluation metrics are an absolute necessity.

Polyp Characterisation

Computer-aided classification for colonic polyps has largely been developed for use with advanced imaging modalities such as magnifying NBI, endocytoscopy and laser auto-fluorescence. More recent methods have integrated advanced computer vision techniques including deep learning into non-magnification conventional endoscopy. The key studies for polyp characterisation are summarised in table 2.

Magnification Endoscopy

Computer-aided classification of colorectal polyps using NBI magnification images with zoom endoscopes, was first evaluated by Tischendorf et al. [44] In this prospective pilot study, 209 polyps were analysed from 128 patients using a computer algorithm. The images were initially pre-processed to provide contrast between blood vessels and polyp surface. Calculations based on three features were used for classification: mean vessel length, vessel circumference and mean brightness within detected blood vessels. This analysis achieved a sensitivity of 90% and specificity of 70.2% in differentiating neoplastic from non-neoplastic images when compared to histopathology as gold standard. The model was inferior to classification by human observers. The authors improved on this with a further prospective study analysing a total of 434 polyps (10mm or smaller) from 214 patients.[45] This algorithm evaluated nine classification features achieving 95% sensitivity, 90.3% specificity and 93.1% accuracy. This performance was comparable to an expert group analysis and superior to the non-expert group. Both studies however analysed the images retrospectively and the algorithm did not operate at real-time.

There have been a number of subsequent studies in Japan using magnification imaging. Takemura et al. developed image analysis software to classify pit patterns that quantified 6 shape descriptors for each pit.[46] Using 134 retrospectively collected chromo-endoscopy images containing polyps stained with crystal violet, validated by a single expert endoscopist, their computer algorithm achieved an overall accuracy of 98.5%. A major limitation was that the system was only semi-automated requiring a manual processing step for some images and took several minutes to provide a decision.

A further retrospective study by this group used a computer-based system to characterise 371 polyps into neoplastic and non-neoplastic categories based on the Hiroshima classification.[47] This classification divides the surface structure and micro-vessels based on NBI into types A (non-neoplastic) and types B-C (neoplastic). The software achieved an accuracy of 97.8%, sensitivity and specificity of 97.8% and 97.9% respectively for a diagnosis of neoplastic lesions (type B-C3). Two experienced endoscopists also reviewed the images, and when compared to the computer-based algorithm results there was agreement in 98.7% of images. The methods however still required the selection and manual extraction of regions of interest by experts.

An improved version of this software was subsequently analysed prospectively, this time being able to provide support vector machine real-time decision outputs operating at 20 frames per second.[48] Support vector machines are supervised machine learning algorithms that analyse data for classification. The system was tested on 118 colorectal lesions from 41 patients providing an overall accuracy of 94.9% for all lesions in comparison to histopathology and a concordance of 97.5% with expert endoscopic diagnoses. Whilst promising, a significant limitation is the lack of generalisability of this system given that magnification colonoscopy is not accessible to the majority of endoscopy centres worldwide.

Endocytoscopy (EC) allows in vivo cellular imaging by contact microscopy, providing ultra-magnification capability (x450) for visualisation of nuclei. Mori et al. assessed a computer-aided diagnostic system for the endocytoscope (EC-CAD) in a pilot study involving 152 patients.[49] This integrated prototype colonoscope provides a standard videoendoscope mode which can be switched to EC mode using a hand operated lever. EC images were collected after staining with crystal violet and methylene blue. The EC-CAD was based on automatic extraction of features from nuclei based on six features leading to a predicted pathological classification decision in 0.3seconds. Retrospectively collected still EC images from 176 small polyps (≤10mm) were evaluated by the software and compared to 2 expert and 2 trainee endoscopists. EC-CAD achieved a sensitivity of 92.0% and accuracy of 89.2% in identifying neoplastic polyps. This performance was comparable to experts and superior to trainees. Specificity was 79.5% with no significant difference in comparison to the expert or trainee groups. A diagnosis could not be provided by EC-CAD in 4.5% of the images due to insufficient staining and inability to extract nuclei.

A second-generation EC-CAD was evaluated by the same group using a web-based study of images.[50] This more advanced algorithm now focussed on both nuclei and gland duct lumens, extracted 296 features and used a support vector machine to classify polyps as non-neoplastic, adenoma or invasive cancer with a probability prediction. High confidence was defined as a probability exceeding 90%. Time to diagnostic output was 0.2 seconds. EC-CAD was evaluated on 205 small polyps (including 139 diminutive polyps) and compared with 3 experts and 10 non-experts. EC-CAD was accurate for 89% of polyps, with a sensitivity of 89% and specificity of 88%. Once again performance was equivalent to experts and significantly better than non-experts. EC based post-polypectomy surveillance outcomes were also predicted for diminutive polyps and compared with decisions based on pathological assessment. EC-CAD based predictions provided agreement rates of 98% and 96% with European and American guidelines respectively.

The same EC-CAD system was subsequently used to distinguish invasive cancer from adenomatous lesions on images extracted from a database.[51] This differentiation is important in guiding therapy, as endoscopic treatment will not be curative in the setting of deep submucosal invasion. The test set consisted of 200 EC images with endoscopic or surgical histopathology acting as a reference. EC-CAD provided a sensitivity, specificity and accuracy of 89.4%, 98.9% and 94.1% respectively for 188 images that were suitable for analysis. There was no comparison with NBI imaging or endoscopy operators.

NBI imaging combined with EC (EC-NBI) was developed to overcome the limitation of pre-staining of lesions with dyes that was required before analysis with standard EC.[52] Custom software was subsequently developed to evaluate EC-NBI images and evaluated on 100 images (50 neoplastic and 50 non-neoplastic) that were randomly extracted from a database.[53] The CAD system provided a diagnostic output within 0.3 seconds yielding an overall accuracy of 90.0%, sensitivity of 84.5% and specificity of 97.6%. The accuracy improved further when a high confidence threshold was applied to the algorithm which was possible for 65% of the images.

A CNN was created for polyp classification using the concept of transfer learning by Zhang et al. [54]To address to some extent the limitation of small labelled datasets that exists in the medical field, transfer learning involves building on the knowledge acquired by the model for solving one visual task in a large unrelated or loosely related dataset and adapting this to the task at hand using the small available dataset. The endoscopy dataset consisted of 1930 images (1104 non-polyp, 263 hyperplastic polyp and 563 adenomatous polyp). The images were collected from a total of 215 polyps (65 hyperplastic and 150 adenomatous). The authors state that images were taken under white light and NBI imaging using zooming and optical magnification. 50 images were used for each category for CNN testing. The best model for polyp characterisation on average achieved an accuracy of 85.9%(sensitivity 87.6% and PPV 87.3%). This performance was better than endoscopists evaluated on the same dataset.

More recently, Chen et al. developed a deep-neural network CAD (DNN-CAD) system to characterise diminutive polyps using NBI images captured from colonoscopes with an optical magnification function.[55] For training purposes, still images observing polyps at the maximum magnification power were collected retrospectively from 1476 neoplastic polyps and 681 hyperplastic polyps. Regions of interest were manually selected from high-quality images by two endoscopists. The DNN-CAD was then tested on 96 hyperplastic and 188 neoplastic diminutive polyp images collected prospectively with the same image criteria for the training set. Histology was used as the reference standard. The DNN-CAD differentiated neoplastic from hyperplastic polyp images with 96.3% sensitivity, 78.1% specificity and 90.1% accuracy (NPV 91.5%, PPV 89.6%). The performance of the algorithm was superior when compared to 4 novice endoscopists defined as having less than 1 year of colonoscopy experience. The DNN-CAD provided a diagnosis in 0.45 seconds, in a shorter time period compared to endoscopists (expert group 1.54 seconds and non-experts 1.77 seconds).

Laser induced auto-fluorescence

Laser-induced auto-fluorescence spectroscopy (LIFS) allows for the optical biopsy of colorectal polyps using an optical fibre that is incorporated into the biopsy forceps (WavSTAT, Pentax Medical, Tokyo, Japan). Laser light is emitted by the fibre and absorbed by the tissue. A computer software algorithm analyses the resulting autofluorescence signal from the polyp to provide an in vivo prediction of neoplasia. An initial study evaluating 207 polyps (≤9mm) in comparison to histopathology as reference, demonstrated an accuracy and negative predictive value for WavSTAT3 of 74.4% and 73.5% respectively.[56] A technically improved version, WavSTAT4, which provides a decision output within one second, was assessed on 137 diminutive polyps in a prospective observational study, yielding an accuracy of 84.7% (sensitivity 81.8%, specificity 85.2%, negative predictive value 96.1%).[57] Agreement between the WavSTAT4 and histopathology based United States guidelines for surveillance intervals reached 88.9%.

Non-magnification endoscopy

Mesejo et al. created a framework combining machine learning and computer vision algorithms to classify 76 polyp lesions from colonoscopy videos, using white light and narrow band imaging, into three classes: hyperplastic, serrated adenoma and adenoma.[58] Reference standard was based on histology results. The best performing model produced an average accuracy of 82.46%, sensitivity of 72.74% and specificity of 85.88% for the three classes of polyp. The system was human competitive, performing better than experts on average.

Byrne et al. developed a CNN to differentiate diminutive adenomas from hyperplastic polyps on unaltered NBI videos from a previous study using standard colonoscopy (Olympus 190 series, Olympus America, Center Valley, PA).[59] Polyps were detected in the normal 'far focus' mode and then viewed in the near focus mode before being resected and retrieved. NBI frames used were a mixture of normal focus and near focus. The training set consisted of 223 polyp videos (all size ranges including many >10mm) in NBI (29% type 1, 53% type 2 according to the NICE classification and 18% normal mucosa with no polyp). Further validation was performed on 40 videos. The final test set consisted of 125 consecutively identified diminutive polyps (74 adenomas and 51 hyperplastic polyps). The deep learning model operated in quasi real-time on videos at rate of 50ms per frame. A probability score was calculated along with the classification according to NICE criteria. The model did not build enough confidence to predict the histology in 19 polyps, for the remaining 106 polyp videos, the overall accuracy achieved was 94% (sensitivity 98%, specificity 83%, PPV 90%, NPV 97%). The videos used for the model were all collected retrospectively by a single expert operator. The authors commented on further studies to evaluate the algorithm in a live patient clinical trial setting.

Quality Assessment

A number of quality assessment indicators have been introduced by professional societies in order to provide assurance that high quality colonoscopy is performed. Key quality metrics relating to the quality of mucosal inspection include caecal intubation rate, mean withdrawal time and adenoma detection rates.[60,61] Low ADRs are associated with high rates of post-colonoscopy colorectal cancers.[4] Diligent mucosal inspection is vital in ensuring screening colonoscopy achieves its primary purpose, the detection of neoplastic lesions and subsequent removal which provides protection against CRC.

These quality metrics are only reviewed post procedure which limits performance improvement to future colonoscopy. Furthermore, whilst prolonged withdrawal time has been associated with an increased ADR, it has been suggested that this crude metric does not necessarily reflect the quality of inspection. This may explain the failure of mandatory minimal withdrawal times to significantly improve ADR in some studies, although specific instructions about how prolonged withdrawal time should be used was often absent from negative studies.[62,63]

Computer software based systems allow real-time quality analysis of colonoscopy videos and feedback during procedures. Filip et al. developed software to provide automated outputs in three key areas: 1) Real-time visual feedback of image quality taking into account blurriness and changing velocity 2) Post procedure statistics including % time of adequate visualisation and withdrawal times 3) automated bowel preparation documentation.[64] In this study, 14 screening colonoscopy videos were analysed by the software and compared to three gastroenterologists who rated the videos using a scale for overall quality, withdrawal velocity, bowel preparation and image quality. The automated overall quality rating was strongly correlated with the reviewers' overall quality rating, although there was no correlation with mean endoscopists image quality rating.

Stanek et al. developed another real-time image analysis software feedback system for colonoscopy videos.[65] Procedure image analysis was performed using the following modules: 1) blurry frame detection (distinguishing informative from non-informative frames) 2) real-time stool detection 3) assessing the degree of inspection by counting the withdrawal spiral motions of the endoscope. This involves a feedback mechanism whereby the image is divided into four quadrants and a green marker is displayed when each quadrant has been inspected, leading to an increase in score with sequential inspection of all four quadrants. The authors report that the software led to an improvement in the quality of colonoscopy when evaluated on third-year GI trainees.

It is therefore possible that novel quality indicators and metrics to assess quality of mucosal inspection could be developed based on CAD systems. In addition, some pilot studies have developed CAD software to evaluate other existing quality indicators including confirmation of caecal intubation and automated bowel preparation scoring.[66]

Challenges and Future Directions

Artificial intelligence and CAD technology must overcome a number of challenges before it enters routine clinical practice. The key stages for implementation of CAD technology into routine colonoscopy have been highlighted elsewhere, particularly by Mori et al. where the following steps are described: product development and feasibility studies, clinical trials, regulatory approval and insurance re-imbursement. [67,68]

The majority of the studies described for CAD in colonoscopy are currently limited to the early stages and most are retrospective in design. This leads to uncertainty about the true efficacy of CAD in 'real-world' practice which will only become apparent with future clinical trials. The lack of available large datasets required for effective deep learning represents a significant obstacle to progression. Efforts are underway in other areas of medicine to address this, such as the Cancer Imaging Archive.[69] It should be noted that it is not purely a matter of quantity of data but also the additional quality of labelling or annotation from experts or on the basis of pathology results.

Additional information that clinicians use for diagnostic purposes is also not always available for image analysis, where algorithms focus on the images alone. For example, including metadata on the location and size of polyps along with patient clinical information may be incorporated into future deep learning strategies. The concept of class imbalance is also challenging. In deep learning, there is a requirement to find classes of data for a specific task, an abnormal class may be difficult to find for example, images of subtle flat colonic lesions where this morphology type may be under-represented in colonoscopy image databases. This may limit the efficacy of an automated polyp detection algorithm arguably where it is required most in clinical practice. Technological advances in deep learning may reduce the data requirements in the future. Strategies such as transfer learning and data augmentation have been developed to partially address this.

Concerns are often expressed about the lack of transparency and complexity involved in deep learning methodology. Once a CNN has been trained, it can be difficult to understand the decision-making processes of a network. For clinical use, it would be important for any CAD system to justify its analysis particularly if there were concerns about unreliable predictions. Visualisation techniques have been developed in an attempt to gain insight into the function of intermediate layers of the CNN and understand what the network is perceiving to make decisions.[70]

The exact position of CAD in relation to colonoscopy workflow and endoscopist decision making is unclear. This is particularly important for polyp characterisation, where such an algorithm could provide decision support via a concurrent or second read.[71] The possibility of CAD completely replacing human endoscopist decision making is unlikely at this stage. Should CAD technology be utilised as part of the 'resect and discard' strategy for diminutive polyps then the medico-legal issue of photo-documentation with high definition images marked with CAD decisions needs to be addressed. As new validated classification systems are developed, particularly those that might be applicable across different imaging modalities and processors, it would be interesting to determine whether CAD can continue to provide decision support and match human 'expert' performance. Moreover, the emergence of deep learning methodologies with increased availability of larger datasets may reduce the

need for human derived classification systems which are often created by expert consensus and can be challenging to integrate into wider clinical practice.

Clinical trials with CAD may address the uncertainty surrounding factors that lead to missed polyps particularly the relative contribution of inadequate mucosal exposure versus failure to identify subtle polyps that are present within the endoscopic field of view. Real-time overlays of CNN alerts during video-colonoscopy would highlight potential missed lesions present in the field of view, whilst future systems may also objectively assess the quality of mucosal inspection.

Conclusion

Artificial intelligence and CAD technology offers great promise for colonoscopy. Strong collaborations are required between clinicians and computer scientists to break through translational barriers and overcome challenges. An evaluation of clinician acceptance and minimal disruption on procedure workflow are crucial for wider implementation. Robust clinical trials will be required to provide evidence demonstrating improvements in performance. Increasing industry involvement and governmental incentives should lead to dramatic advances within the next few years. It is not inconceivable that artificial intelligence based software will analyse video colonoscopy in the future to support not only lesion detection and characterisation but also assess technical quality. By providing real-time feedback, this could prove to be a useful adjunct in improving ADR, guiding therapeutic decision making and reducing the significant variation observed in the quality of colonoscopy.

Search strategy and selection criteria

A literature search was conducted using MEDLINE (1946-2018), EMBASE (1980-2018), Engineering Village and the Cochrane Library Databases. The following medical subject terms and keywords were used; “colonoscopy”; “endoscopy”; “polyps”; “artificial intelligence”; “computer-assisted diagnosis” and “neural networks”. Only fully published journal articles in English were reviewed. Reference lists of publications were manually searched for additional relevant studies and searches were conducted for authors the team recognised as experts in the field. The latest date of this search was July 2018. A narrative review was performed using this search strategy highlighting key studies within three clinical areas: automated polyp detection, polyp characterisation and colonoscopy quality assessment.

Contributors

All authors contributed to the concept, structure, drafting of the manuscript, critical revisions and the final approval of the submitted work.

Declaration of interests

All authors declare no competing interests.

Figure 1

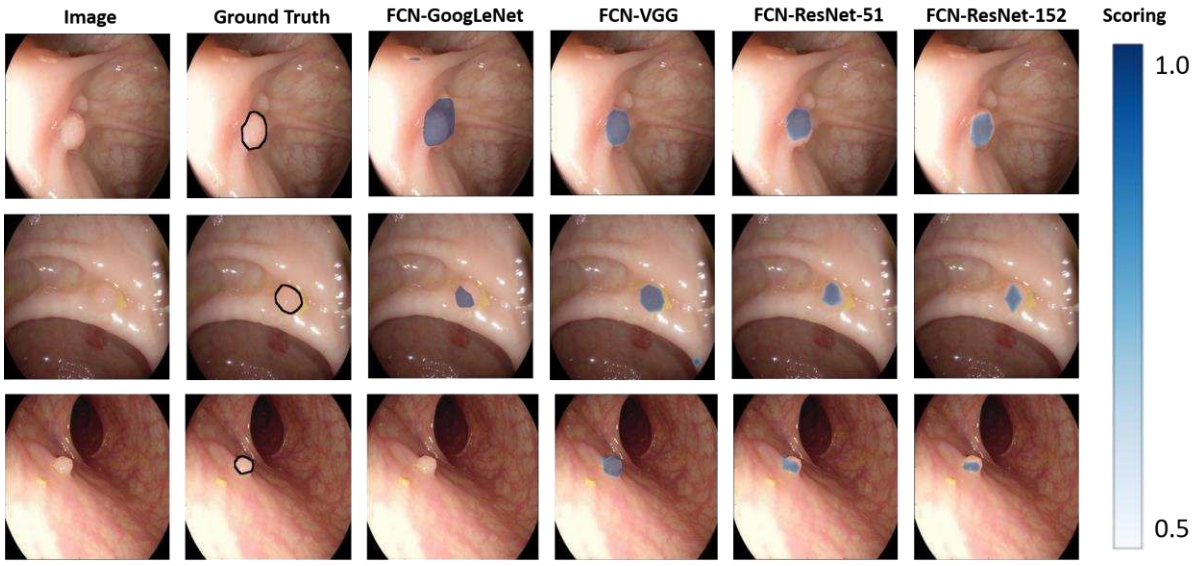
Image
Ground Truth
FCN-GoogLeNet
FCN-VGG
FCN-ResNet-51
FCN-ResNet-152
Scoring
1.0
0.5

Figure 1: Examples of three different scored polyp detection and segmentation images produced by four fully connected convolutional networks (FCNs). The colour bar defines the scoring probability of each pixel representing a polyp and can be compared to the ground truth image which acts the reference standard. Images provided by P.Brandao using methodology outlined in Brandao et al. [43]

Table 1 – Summary of recent key studies for computer-aided polyp detection

Author	Methods	Dataset	Results
Wang et al.[36]	Polyp edge detection	53 colonoscopy videos (22 polyp, 31 non-polyp videos)	97.7% Recall (sensitivity) 36.2 false ('shots') positives per video on average
Fernandez-Esparrach et al.[35]	Window Median Depth of Valleys Accumulation (WM-DOVA) energy maps	24 colonoscopy videos containing 31 different polyps	70.4% Sensitivity 72.4% Specificity
Tajbakhsh et al.[37]	Hybrid context-shape approach	Internal dataset: 10 polyp positive and negative shots (5200 polyp and 14,200 non-polyp frames) External dataset: 15 polyp video sequences (300 images)	48% sensitivity (internal dataset) 88% sensitivity (external dataset) Average 0.11 false positives per frame

Park & Sargent[38]	Feature extraction using a convolutional neural network (CNN). Classification using a conditional random field model	11802 image patches extracted from 35 colonoscopy videos	86% sensitivity 85% specificity
MICCAI 2015 Endoscopic Vision Challenge Bernal et al.[41]	Various methods: 1) Hand-crafted features 2) End-to-end learning (CNNs) 3) Hybrid approaches	Video database: Training: 20 videos (10 polyp and 10 non-polyp) Testing: 18 videos (9 polyp and 9 non-polyp)	Results on all videos analysed (top performing teams): CUMED: sensitivity (recall) 71.4%, specificity 94.4%, positive predictive value (precision) 80.0% ASU: 61.1% sensitivity (recall), specificity 98.6%, positive predictive value (precision) 93.5%
Misawa et al.	CNN	73 colonoscopy withdrawal videos containing 155 polyps (1.8 million total frames) Divided into short videos for training and testing. Training: 105 polyp positive and 306 polyp negative Testing: 50 polyp positive and 85 polyp negative	Sensitivity 90% Specificity 63.3% Accuracy 76.5%
Urban et al.	CNN	Image dataset: 8641 frames (4088 polyp and 4553 non-polyp) Video dataset 1:	Image dataset: Cross-validation accuracy 96.4% and ROC-AUC 0.991

		9 videos (containing 28 polyps removed by original colonoscopists) Video dataset 2: 11 videos simulating missed polyp scenarios (containing 73 polyps)	Video dataset 1: CNN overlay led to identification of 45 polyps (additional 9 polyps over experts not using CNN assistance) Video dataset 2: 67 of 73 polyps identified with frame-by-frame false positive rate of 5% (CNN trained on 8641 images and fine-tuned with video dataset 1)

Table 2 – Summary of key studies for computer-aided polyp characterisation

Author	Imaging Modality	Dataset	Results
Tischendorf et al.[44]	Magnification NBI	209 polyps (160 neoplastic & 49 non-neoplastic) from 128 patients.	Sensitivity 90% Specificity 70.2% Accuracy 85.3%
Gross et al.[45]	Magnification NBI	434 polyps (258 neoplastic & 176 non-neoplastic) from 214 patients.	Sensitivity 95.0% Specificity 90.3% Accuracy 93.1%
Takemura et al.[46]	Magnification chromo-endoscopy	134 pit pattern images	Accuracy 98.5%
Takemura et al.[47]	Magnification NBI	371 lesions (324 neoplastic & 47non-neoplastic)	Sensitivity 97.8% Specificity 97.9% Accuracy 97.8%
Kominami et al.[48]	Magnification NBI	118 colorectal lesions (73 neoplastic & 45 non-neoplastic) from 41 patients.	Sensitivity 95.9% Specificity 93.3% Accuracy 94.9%
Chen et al.[55]	Magnification NBI	284 diminutive polyps (188	Sensitivity 96.3% Specificity 78.1%

		neoplastic & 96 hyperplastic) from 193 patients.	Accuracy 90.1%
Mori et al.[49]	Endocytoscopy	176 polyps (137 neoplastic & 39 non-neoplastic) from 152 patients.	Sensitivity 92.0% Specificity 79.5% Accuracy 89.2%
Mori et al.[50]	Endocytoscopy	205 polyps (147 neoplastic & 58 non-neoplastic) from 123 patients.	Sensitivity 89% Specificity 88% Accuracy 89%
Takeda et al.[51]	Endocytoscopy	200 images (100 adenomas & 100 invasive cancers) from 76 lesions.	Sensitivity 89.4% Specificity 98.9% Accuracy 94.1%
Misawa et al.[53]	Endocytoscopy with NBI	100 images (50 neoplastic & 50 non-neoplastic)	Sensitivity 84.5% Specificity 97.6% Accuracy 90.0%
Mesejo et al.[58]	White light & NBI	76 videos (41 adenomas, 21 hyperplastic lesions & 15 serrated adenomas)	Sensitivity 72.7% Specificity 85.9% Accuracy 82.5%
Byrne et al.[59]	NBI	125 diminutive polyp videos (74 adenomas & 51 hyperplastic polyps)	Sensitivity 98%, Specificity 83% Accuracy 94%

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