TechFlash: Artificial intelligence for real-time detection of polyps during colonoscopy

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This report comprises a review of abstracts identified through a search of the recent biomedical literature and does not constitute a comprehensive analysis. The report focus is on clinical evidence and outcomes.

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Technology overview and status

Artificial intelligence (AI) is a disruptive technology with numerous rapidly emerging uses in radiology and diagnostic imaging. An AI-based system for computer-assisted detection of polyps during colonoscopy is now available. This AI algorithm analyzes each frame of the live colonoscopy video. By recognizing and highlighting potential lesions in real-time, AI can provide a "second set of eyes" to assist the colonoscopist during the procedure. This AI application may improve the quality of colonoscopy exams by increasing the adenoma detection rate and potentially reducing the incidence of preventable colorectal cancer.

There are many AI platforms in development with two primary applications for colonoscopy: computer-aided polyp detection (CADe) and computer-aided polyp characterization (CADx).[1-6] The AI algorithms for colonoscopy are based on the convolutional neural network (CNN) programming architecture. CNNs are comprised of many linked "deep" or "hidden" programming layers that detect different image features, like colors, shapes and elevations. After a CNN algorithm has been trained on many thousands of images annotated with the correct findings by a human expert, it "learns" to recognize lesions of interest.

The GI Genius™ intelligent endoscopy module, developed by Cosmo Pharmaceuticals (Dublin, Ireland) and distributed by Medtronic, is the first commercially available CADe system for colonoscopy in the US. It received Food and Drug Administration (FDA) *de novo* marketing clearance in April 2021 (DEN200055) and is in the early adoption phase in the US. It has been available in select European countries since 2019.

The GI Genius module consists of a small box with computer hardware and AI software. The box takes input video from the endoscope and passes it through to a conventional video display monitor. AI detection software is simultaneously run on the input video. If a lesion is detected, the system superimposes a green box (see Figure 1) around the lesion on the monitor in real time. An audible alert indicator is also used. The system is able to detect both sessile (flat) and pedunculated (stalk) polyps.

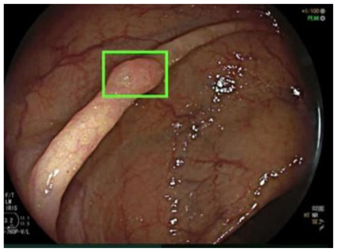

Figure 1. GI Genius detection alert box. Medtronic, Inc.

The AI-assisted colonoscopy procedure is conducted in the same manner as a conventional procedure. Thus, it remains up to clinician judgment to visually inspect any lesions identified by the AI system. Standard criteria are also used to determine lesion sampling, testing and/or removal.

An incrementally-improved version (v2.0.0) of GI Genius received FDA 510(k) marketing clearance on July 23, 2021 (k211951). Improvements to optimize algorithm speed and energy efficiency were noted. The algorithm was also trained on a larger data set with reported improvement in detection accuracy.[7] FDA labeling states "…GI Genius System is a computer-assisted reading tool designed to aid endoscopists in detecting colonic mucosal lesions (such as polyps and adenomas) in real time during standard white-light endoscopy examinations of patients undergoing screening and surveillance endoscopic mucosal evaluations. This device is not intended to replace clinical decision making."

Technology significance

Colorectal cancer (CRC) is the third most common cancer and the second leading cause of cancer death, accounting for ~ 150,000 new cases and 50,000 deaths annually in the US.[8] Since most cases of CRC progress from adenomatous polyps to invasive adenocarcinoma, early polyp detection may have a significant positive effect on morbidity and mortality outcomes. The US Preventive Services Task Force (USPSTF) now recommends screening start at age 45 years (B-level recommendation) in average risk adults.[9] Though adherence to screening guidelines is suboptimal for various reasons, an estimated 19 million screening colonoscopies are currently performed annually in the US.[10, 11]

The quality of colonoscopy is directly related to the adenoma miss rate (AMR). AMRs as high as 25% to 30% have been reported.[12, 13] Several intrinsic factors may contribute to AMR, including polyp location, color, shape and size.[14] Other factors that may contribute to AMR include: adequacy of bowel cleansing, type of sedation, cecal intubation rate and use of advanced endoscope technology and techniques. Human factors, such as operator training and experience, endoscope withdrawal time, concentration and procedure time-of-day could also affect AMR.[15] High miss rates may, in part, explain the occurrence of interval CRCs, i.e., cancers diagnosed in the interval after a screening exam and before the next scheduled exam.

The adenoma detection rate (ADR) is inversely correlated with AMR and is a readily calculated, validated and widely used quality metric for colonoscopy.[16, 17] ADR is defined as the proportion of patients with at least one colorectal adenoma detected during average risk first-time screening colonoscopy. An established benchmark for the minimum ADR is 25%. However, ADRs ranging from ~7% to 52% among different endoscopists has been reported.[18] Importantly, every 1% increase in ADR is associated with a 3% decrease in the risk of cancer development and a 5% reduction in cancer mortality.[18, 19]

The use of AI for polyp detection is intended to improve AMR and ADR and reduce performance variability.[20-24] The AI algorithms can serve as an additional "observer" and this redundancy may improve detection rates. In addition, AI may be more objective and not affected by human factors, like fatigue or stress; thus, reducing some causes of variability. Colonoscopy quality improvement through use of AI may be most helpful for inexperienced endoscopists and those with low baseline ADR metrics.

Despite potential advantages, AI is also associated with implementation barriers often common to novel emerging medical technologies. These typically include limitations in the clinical evidence base demonstrating safety, efficacy and appropriate indications for usage. Cost and reimbursement are also significant issues. The optimal coordination of workflow between AI and endoscopist is another potential hurdle. The endoscopist could rely too much or too little on the AI and this could affect detection rates. Further, an AI algorithm that presents too many false positives could lead to "alarm fatigue" and increase workload for the endoscopist and/or increase procedure times.

Current practice and alternatives

There are a variety of screening tests used for detection of colorectal cancer and adenomatous polyps.[25-27] These may be divided into 2 broad categories: stool tests and structural exams. The former includes various types of fecal occult blood tests (FOBTs) and fecal immunochemical tests (FITs). The latter includes colonoscopy, sigmoidoscopy, wireless capsule endoscopy (PillCam), computed tomography (CT) colonography and double contrast barium enema. Each of these techniques has limitations, advantages and disadvantages. For example, the stool tests may be preferred by patients and can increase the screening rate for patients hesitant about colonoscopy.

FIT is a commonly-used, simple laboratory test using engineered antibodies to detect human blood proteins in a non-invasively collected stool sample. FIT has high sensitivity for the detection of CRCs, but may be less accurate for pre-cancerous lesions due to their lower rate of bleeding.[25] It is low cost (< $50 to $100), usually covered by insurance and may be repeated annually. More frequent utilization due to low cost and non-invasiveness is a significant advantage of this test over alternatives and may be expected to improve diagnostic utility.

A similar non-invasive at-home test kit (Cologuard; Exact Sciences Corp., Madison, Wisconsin) analyzes a stool sample for both occult hemoglobin and neoplasia associated DNA markers derived from cells exfoliated from the intestinal lining. Cologuard has high sensitivity for CRC (>90%) and moderate sensitivity for large precancerous polyp detection (~40%), which may be better than FIT but lower than colonoscopy.[28]

Cologuard costs around $500 and is typically covered by insurance in patients meeting criteria of average to low risk for CRC. This test may be repeated every 3 years rather than annually.

Colonoscopy (without AI) is considered the gold-standard for both screening and diagnosing CRC and is frequently required if any of the other screening tests have a positive result. A colonoscopy procedure involves significant pre-procedure at-home bowel cleansing, conscious sedation during the procedure and use of a long, flexible endoscope to visualize the rectum and entire colon. A major advantage of colonoscopy is that detected lesions may be immediately biopsied for analysis and pre-cancerous polyps can be removed during the procedure as a preventive measure. Complications are rare, but may occur secondary to the bowel cleansing regimen, sedation or biopsy.

Colonoscopy is recommended in average risk adults beginning at age 45 and repeated every 10 years in those without significant findings.[9] Costs may range from ~$1,000 to $2,000 and are typically covered by most insurance when used in accordance with guidelines.

Various advanced endoscope technologies and techniques are available that may also improve ADR.[29, 30] These include distal attachments (e.g., endocap, endocuff, endoring) that flatten and stretch the mucosa, enhanced optics including magnification, narrow-band imaging using various different wavelengths of light and chromoendoscopy using different dyes or staining procedures. Some of these advanced technologies may be helpful for better in situ lesion characterization as well.

CT colonography, also called virtual colonoscopy, is another screening option in patients reluctant or contraindicated to undergo colonoscopy due to invasiveness, sedation or structural disease. The procedure takes only about 10 minutes to perform and uses a conventional CT scanner. Like colonoscopy, it requires standard pre-procedure bowel cleansing. Other disadvantages include air insufflation during the procedure and the use of ionizing radiation. High accuracy has been reported for detecting polyps of biologic importance.[31] Unlike colonoscopy, however, significant findings will require a secondary procedure for polyp biopsy or removal. Third-party payer reimbursement for CT colonography is inconsistent as a first-line screening exam and follow-up may be recommended at 5 years in patients with no significant findings.

There are a number of alternative AI-based colonoscopy platforms similar to GI Genius in development and many of these are now commercially available in Japan, China and/or the European Union.[32, 33] These include ai4gi (Satisfai/Imagia/Olympus), CAD-Eye (Fujifilm Medical), Discovery (Pentax Medical), EndoBrain-Eye (Cybernet/Olympus), Wise Vision (NEC) and Wision AI (China). Notably, in addition to highlighting when a polyp is detected, some have a characterization mode that predicts whether the polyp is neoplastic or hyperplastic. Some of these AI platforms may be expected to gain commercial marketing clearance in the US in the near future.

Clinical evidence summary

The Medline/PubMed bibliographic database was searched in September 2021 to identify clinical evidence related to the use of GI Genius during colonoscopy. Keywords used in the literature search strategy included*: artificial intelligence, deep learning, convolutional neural network, colonoscopy, polyp, adenoma, screening* and/or product/manufacturer names.

Key performance indicators of interest include the AMR and ADR. Mean number of polyps and adenomas detected per procedure may also be reported in some trials. Statistics may sometimes be broken down by polyp type. For example, polyps can be classified as neoplastic (adenoma) or non-neoplastic (hyperplastic). The latter are not pre-cancerous and do not require resection. Other sub-classifications may account for polyp size, morphology and location. For example, diminutive polyps, measuring between 1 and 5 mm, are most frequently missed and may account for ~75% of colorectal polyps encountered during screening colonoscopy. Secondary outcomes in trials may include performance metrics, like scope withdrawal and procedure time.

Overall, the literature search identified a large and rapidly growing body of published clinical evidence. Evidence summaries are available in a number of recent systematic reviews and meta-analyses.[34-39] Eight randomized controlled trials (RCTs) comparing conventional colonoscopy to CADe have been conducted including more than 5,000 patients.[4] However, most of the RCTs were performed in China or Japan where patient characteristics and endoscopy practices may be different from the US. A meta-analysis including non-randomized trials identified 48 applicable studies of AI in CADe.[37]

Despite some study limitations, it is notable that all of the RCTs have noted improvements in ADR and the mean number of adenomas detected per procedure.[34] A recent meta-analysis including data from 5 select RCTs (4,354 patients) reported a 44% improvement in pooled ADR using AI (36.6% vs. 25.2%; P<0.01).[35] The adenomas detected per procedure was 70% higher (0.58 vs. 0.36; P<0.01). Pooled subset analysis in this meta-analysis noted statistically significant improvement in all polyp size groups, locations and morphology.

GI Genius was initially validated using retrospective colonoscopy video from a previously conducted RCT.[40] The dataset included 840 patients with 2,684 histologically confirmed polyps. In a training subset, sensitivity per lesion was 99.7% and false positives were reported in <1% of activations. In addition, the reaction time for recognition of a lesion was reportedly faster for the algorithm in ~82% of cases compared to the endoscopist. The average difference in reaction time was 1.27 seconds.

Safety and efficacy was next tested in an Italian RCT enrolling 700 patients at 3 centers who were undergoing colonoscopy for screening, surveillance, positive FIT test or possible CRC symptoms (The AID study, NCT04079478). Results from this study showed a higher ADR for the CADe group compared to controls (54.8% vs. 40.4%), representing a 14% absolute difference and 30% relative increase in ADR.[41] The adenoma per colonoscopy rate was also higher in the CADe group (1.05 vs. 0.7; 46% relative increase). Adenomas of ≤5 and 6–9 mm were detected in a statistically significant higher proportion in the CADe group compared to controls.

No significant differences in the overall average withdrawal time were noted in this study. However, a post-hoc analysis in a subset of patients reported an average of 27.3 false positive alarms per colonoscopy.[42] Expert manual review ascribed most of these to artifacts in the bowel wall or bowel content and most of these were reportedly immediately discarded by the endoscopist without further exploration. In 5.7% of false activations, additional investigation required about 4.8 seconds per incident which accounted for only a 1% increase in the total withdrawal time. False activations are undergoing further study in the NOISE study (NCT04399590).

The AID-2 study (NCT04260321) was an Italian multi-center RCT studying real world usage in a group of less experienced endoscopists (10 non-experts, <2,000 colonoscopies each). Similar to AID-1, ADR was improved due to CADe (53.3% vs. 44.5%; P=0.02, relative improvement 22%) in this trial.[43] After pooling data from AID-1 and AID-2, multivariate analysis suggested endoscopist experience was not a significant factor in determining the ADR.

A single-center German, non-randomized trial enrolled 150 patients with concurrent use of AI and conventional colonoscopy.[44] Due to the set-up, the colonoscopist could not see the results from the AI and the AI was assessed by a second observer. Comparative analysis showed no difference in the AMR between the AI (6/197, 3%) and the conventional procedure (4/197, 2%). Polyp miss rate was also not statistically significant (AI: 14/311, 4.5% vs. routine colonoscopy: 17/311, 5.5%; P=0.720). ADR was 52.0% for colonoscopy and 50.7% for AI.

Financial issues

The use of AI will incrementally add to colonoscopy procedure costs. At this time (September 2021), however, there is no known additional direct reimbursement provided for the concomitant use of AI in colonoscopy. But, hospital payment rates for colonoscopy may be highly variable depending on payer, setting and other factors; thus, in some scenarios AI costs could be offset by current margins.[45] The national average Medicare reimbursement rate for colonoscopy (code 45378) in the hospital outpatient setting provides a $793 facility fee. Median commercial prices are around $1,656.[45]

Healthcare value may be added through the use of CADe secondary to the detection and removal of more adenomas. Some missed adenomas may result in interval CRC and this is associated with significant healthcare resource utilization and costs. Unfortunately, no rigorous cost-effectiveness studies have been performed yet to demonstrate this potential value.

A more straightforward effect on costs may be associated with AI systems that perform CADx.[46] For example, accurate non-invasive characterization of diminutive, non-neoplastic polyps could enable a diagnose-and-leave strategy or increase the rate of diagnose-and-discard strategies. These, in turn, may have associated savings in terms of procedural workflow and pathology costs. Further rigorous financial and clinical study of CADx will be required, however, to determine potential cost-effectiveness. Of note, no CADx system is currently cleared for marketing in the US.

Patient selection criteria

Inclusion criteria in the pivotal trial included all patients (both male and female) aged 40 to 80 years old undergoing a colonoscopy for screening, post-polypectomy surveillance, work-up due to positive FIT test or signs/symptoms of CRC.[41] Exclusion criteria included history of CRC or irritable bowel disease, inadequate bowel preparation and previous colonic resection.

Though not noted in current evidence, it is known that AI deep learning models can sometimes become overfitted to the specific characteristics of the training data and this can potentially lead to inaccuracy when the model is applied to patients with differing characteristics.[47] For example, sex, age, race or ethnicity and BMI could be factors affecting accuracy. Therefore, efforts should be made to ensure the GI Genius AI model mitigates this potential bias through appropriate training and validation in varied populations and those similar to the implementation setting.

Future developments

Further clinical studies developing proof of CADe effectiveness and appropriate usage are ongoing. Future trials are particularly needed to define the effect of AI on clinical outcomes, like the rate of interval cancer. Because of rapid developments in this field, efforts should be made to update the literature search to account for new clinical evidence.

The next phase in development, already underway, is the combination of CADe with CADx. As CADx evidence matures, it may define new strategies for managing polypectomies. Some CADx systems are currently available in Europe and introduction to the US market may be expected in the near future.

AI may also play a future role in other areas of colonoscopy quality improvement.[48] For example, AI could automatically assess and quantify the adequacy of bowel preparation to provide an objective measure of this metric. Further, AI could automatically assess the rate of cecal intubation and document colonoscopy completeness. Similarly, AI could track scope withdrawal time metrics. Feedback provided from these collected AI statistics could potentially be used for performance improvement initiatives and to standardize the final written report.

AI may also play a new role in colonoscopy education, training and accreditation. Both simulated and real-time training roles can be envisioned where AI is part of the education and assessment process. Future training should include lessons on the optimal combination of AI and endoscopist skills.

Robotic colonoscopy is an active area of research. These devices are mostly focused on smaller less-invasive devices with different steering mechanisms that may enhance accessibility and visualization. AI could help to make steering autonomous and simultaneous CADe could help to direct the robot to lesions of interest. Similarly, CADe could play a future role in the analysis of PillCam videos.

Summary and recommendations

The following conclusions and recommendations are based on the material presented in this report:

- Colonoscopy is a potentially high-impact focus area for hospital performance improvement. More than 19 million screening colonoscopies are currently performed annually in the US and this number is expected to grow due to overall trends in aging demographics and the recent lowering of the recommended screening age from 50 to 45.
- There exists a significant amount of variation reported in colonoscopy quality metrics. Procedural adenoma miss rates of up to 30% and endoscopist adenoma detection rates ranging from 7% to 52% have been reported. Human factors, like experience, concentration/distraction and time-of-day likely account for some of the clinical variation.
- High miss rates may explain some of the occurrence of interval CRCs. One frequently cited estimate suggests that every 1% absolute increase in ADR is associated with a 3% decrease in the risk of cancer development and a 5% reduction in cancer mortality. Thus, the detection of all adenomas during colonoscopy is critical to CRC outcomes. CRC is the second leading cause of cancer death in the US.
- AI is a rapidly emerging technology for many radiology applications. AI algorithms based on CNNs and other deep learning neural networks have demonstrated high accuracy and performance comparable to human experts in multiple different diagnostic image recognition applications, including diagnosing stroke on CT images and diabetic retinopathy on fundus images. Similar algorithms have now been developed and trained for polyp detection during colonoscopy.
- GI Genius is the first AI application for colonoscopy to achieve US FDA marketing clearance with availability as of April 2021. Multiple other systems are in use in Europe and elsewhere and may be available in the US in the near future. A unique aspect AI in colonoscopy is the real-time analysis provided by the on-site combined software/hardware product. With this configuration, the time lag for AI analysis is reportedly imperceptible.
- In general, the clinical evidence for AI use in colonoscopy (all platforms) includes at least 8 RCTs and 48 non-randomized trials involving tens of thousands of subjects. One recent meta-analysis demonstrated an 11.4% absolute increase in the pooled ADR (36.6% vs. 25.2%) and a further increase in adenomas detected per procedure (0.58 vs. 0.36) with AI use. This data provides strong evidence for the use of AI as an adjunct to conventional techniques for the detection of polyps during colonoscopy.

- GI Genius specific clinical evidence includes a validation study and two Italian RCTs (type I evidence). Results from the primary study showed a 14% absolute increase in ADR (54.8% vs. 40.4%) and adenoma per colonoscopy rate (1.05 vs. 0.7). Smaller adenomas of ≤5 and 6–9 mm were comparatively better detected using AI in this study. Results from the primary trial were corroborated in a real-world RCT involving less-experienced endoscopists. False positives have been studied and do not appear to have a significant clinical impact or increase withdrawal time.
- Like many rapidly emerging innovative technologies, cost and reimbursement are barriers to implementation at this stage. Further studies are needed to determine the cost-effectiveness of adjunct AI use secondary to improved ADR and patient outcomes. This evidence may then be used by payers in coverage decisions. Development of an AI specific diagnostic code is another future milestone needed to assist reimbursement.
- AI algorithms are a medical technology used in the clinical care paradigm, hence should be reviewed through hospital processes and committees equipped to evaluate innovative new technology. Deliberative processes should include consideration of the clinical evidence, financial issues and overall hospital strategic plan.
- AI is a rapidly growing field expected to disrupt and transform many of the current healthcare paradigms within the next 5 to 10 years. Because of this, hospitals and health systems should be actively involved in learning about the technology, applications, evidence and economics. Where warranted, hospitals should proactively implement AI technologies as a strategy to maintain current and future market competitiveness.

Related links

Product page(s): GI Genius Medtronic, Cosmo Pharmaceuticals

FDA documents: April 2021 de novo approval, July 2021 510(k) approval

Literature search: PubMed Central full text articles, Google scholar full text articles, ClinicalTrials.gov trials

USPSTF recommendations for CRC screening (May 2021)

Similar alternatives: ai4gi (Satisfai/Imagia/Olympus); CAD-Eye (Fujifilm Medical); Discovery (Pentax Medical); EndoBrain-Eye (Cybernet/Olympus); Wise Vision (NEC) ; Wision AI (China)

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