Use of Endoscopic Impression, Artificial Intelligence, and Pathologist Interpretation to Resolve Discrepancies From Endoscopy and Pathology Analyses of Diminutive Colorectal Polyps

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Conflicts of Interest

Neal Shahidi: No conflicts of interest to disclose.

Douglas K Rex: Consultant: Olympus Corporation, Boston Scientific, Medtronic, Aries Pharmaceutical, Braintree Laboratories; Research Support: EndoAid, Olympus Corporation, Medivators; Shareholder: Satisfai Health

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Author Contributions

Study concept and design: Neal Shahidi, Douglas Rex, Michael Byrne

Acquisition of data: Douglas Rex

Analysis and interpretation of data: Sina Hamidi Ghalehjegh

Drafting of the manuscript: Neal Shahidi

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Study supervision: Michael Byrne

Introduction

With the introduction of high-definition colonoscopes and virtual chromoendoscopy, evaluating the surface pit pattern and vascular pattern of colorectal lesions is now possible. This has empowered endoscopists, through the utilization of established optical evaluation criteria[1, 2], to reliably diagnose and distinguish between diminutive adenomatous and hyperplastic polyps.

However, with the widespread adoption of virtual chromoendoscopy, a common occurrence after high-confidence optical diagnosis of a diminutive adenoma is a conflicting pathologic diagnosis[3]; whereby the pathologist has only identified normal colorectal tissue. This discrepancy is of critical importance, given its inherent effect on surveillance colonoscopy recommendations[4], and therefore its potential impact on interval colorectal cancer. In a recent study by Ponugoti and colleagues[5], 644 consecutive colorectal lesions ≤ 3mm were diagnosed as adenomas with high-confidence by an experienced endoscopist with expertise in optical evaluation. On pathology, 15.4% were diagnosed as normal mucosa. Two blinded optical evaluation experts subsequently reviewed high-quality lesion images and agreed with the endoscopic diagnosis in 94% and 100% of cases, respectively. These findings directly question pathology as the gold-standard for diagnosing lesions ≤ 3mm in size.

Recently, artificial intelligence (AI) has showcased an impressive ability to diagnose diminutive adenomatous polyps[6, 7]. Therefore, we sought to evaluate the discrepancy between endoscopic and pathologic diagnoses of lesions ≤ 3mm using an established real-time AI clinical decision support solution (CDSS).

Methods

From April 2016 to August 2017 consecutive colorectal lesions ≤ 3mm, diagnosed during optical evaluation as adenatomous with high-confidence by a single experienced endoscopist with expertise in optical evaluation (DKR), were considered for inclusion[5]. A size restriction of ≤ 3mm was selected, as these lesions were perceived to have a substantial risk of failed pathologic identification.

Endoscopy was performed using high-definition Olympus 190 series colonoscopes (Olympus America Corp., Pennsylvania, USA) with evaluation under white-light, narrow-band imaging (NBI) and near-focus, when available. High-confidence optical diagnosis was performed using the NBI International Colorectal Endoscopic (NICE) classification[1]. After image capture, the lesion was removed either by cold forceps or cold snare polypectomy. Specimen collection and preparation was protocolized, in accordance with the College of American Pathologists. Pathology review was performed by one of 17 board-certified pathologists. Blinded to pathology, one endoscopist (DKR) reviewed all captured images and removed those of suboptimal quality. Institutional review board (IRB) approval was obtained.

Our CDSS, using a deep convolutional neural network, was previously trained, validated and tested on routine unaltered videos of normal mucosa and colorectal polyps captured by Olympus 190 series high-definition colonoscopes[7]. It allows for real-time NICE classification for both images and videos with published performance achieving the American Society for Gastrointestinal Endoscopy (ASGE) Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) 2 recommendation[8]. The

image dataset was evaluated by our CDSS, which was blinded to the endoscopic and pathologic diagnoses.

Our primary outcome was to assess the frequency of agreement between endoscopic, pathologic and CDSS diagnoses (Figure 1). SPSS version 25.0 (IBM Corp, New York, USA) was used for data analysis.

Results

900 consecutive colorectal lesions ≤ 3mm, with a high-confidence optical diagnosis of adenoma were evaluated. 256 lesions were excluded due to sub-optimal image quality.

Of the remaining 644 lesions, 458 (71.1%) had a concordant pathologic diagnosis. Discrepancy between endoscopic and pathologic diagnoses occurred in 186 (28.9%) lesions. This included a pathologic diagnosis of hyperplastic polyp, sessile serrated polyp and normal mucosa in 85 (13.2%), 2 (0.3%), and 99 (15.4%), respectively.

Endoscopic, pathologic and CDSS diagnoses are provided in supplementary table 1. Overall, CDSS agreed with the endoscopic diagnosis in 577 (89.6%) lesions. Concerning discordant endoscopic and pathologic diagnoses, CDSS agreed with the endoscopic diagnosis in 168 (90.3%) lesions. Of those lesions identified on pathology as normal mucosa, CDSS agreed with the endoscopic diagnosis in 90 (90.9%).

Discussion

Discordance between endoscopic and pathologic diagnoses for colorectal lesions is not infrequent. This represents a clinically and fiscally meaningful scenario where the endoscopist must decide on the appropriate surveillance interval. Our findings further support those of Ponugoti et al.[5], and represent a paradigm shift; pathology should not be viewed as the gold standard for diagnosing colorectal lesions ≤ 3mm.

Potential sources for this discrepancy are many. Although optical misclassification, and erroneously resecting adjacent normal tissue are possible, it is unlikely for them to be key players. All examinations were performed by an experienced endoscopist with expertise in optical evaluation. Likewise, a pathologist diagnosing normal colorectal mucosa when a high-confidence optical diagnosis of adenoma has been made seems improbable. Therefore, specimen retrieval and specimen processing appear to be likely culprits; whereby tissue fragmentation leads to the collection and evaluation of a single piece of normal colorectal epithelium or sub-optimal sectioning causes the pathologist to believe that only normal colorectal epithelium is present in the specimen, respectively. Further evaluations to confirm these findings, assess potential endoscopist-, pathologist- and processing-related factors for this discrepancy, address limitations of this current analysis, and assess the impact on surveillance intervals are needed. This will need to include: 1) photo-documentation of optical evaluation and appropriate tissue resection; 2) specimen quality and tissue fragmentation assessment; 3) specimen re-sectioning and 4) assessing endoscopic and pathologic inter-rater reliability.

This study is the first description of a potential future application of AI; the arbitration between endoscopist and pathologist when discordant diagnoses occur. CDSS performance will need to be optimized with evidence showcasing that it can effectively arbitrate between endoscopic and pathologic diagnoses prior to consideration for clinical practice. CDSS performance optimization is, however, inevitable, given the increasing use of deep learning methodology in the development of current AI platforms, manifesting in AI's ability to adapt with increasing data exposure.

In summary, our findings reaffirm that pathology should be questioned as the gold standard for diagnosing colorectal lesions ≤ 3mm; especially, when high-confidence optical evaluation identifies an adenoma. It is therefore imperative that all endoscopists incorporate optical evaluation, coupled with high-quality photo documentation, into clinical practice. In the interim, endoscopists should consider a more conservative approach for deciding on the appropriate surveillance colonscopy interval, when endoscopic and pathologic discrepancy is encountered.

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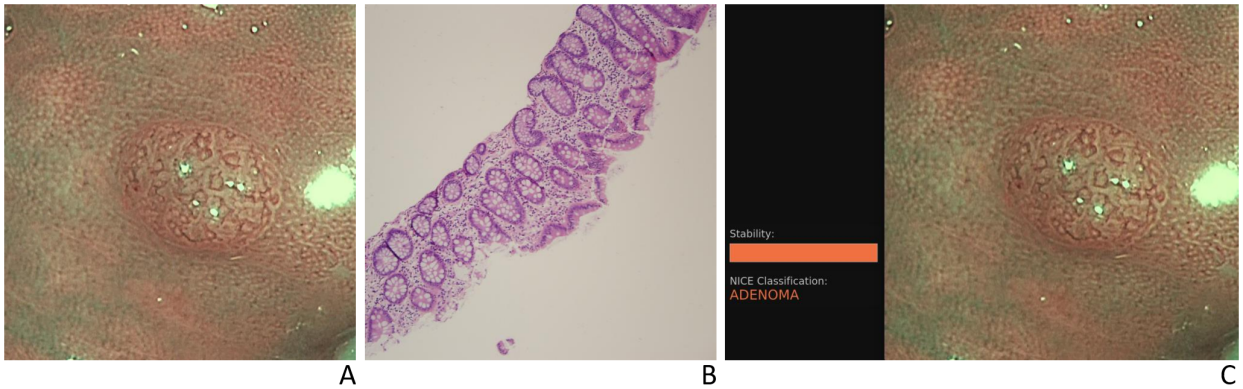
Figure Legends

Figure 1: A: 3mm colorectal lesion optically diagnosed with high-confidence as adenomatous; **B**: histopathology identifies only normal mucosa; **C**: CDSS supports the optical diagnosis



A B C

Supplementary Table 1: Pathologic and CDSS diagnoses for 644 colorectal lesions ≤ 3mm optically diagnosed as adenomatous with high-confidence

Pathologic Diagnosis	**CDSS Diagnosis**		
	Hyperplastic Polyp	Adenoma	Normal Mucosa
Adenoma (N=458)	18 (3.9%)	409 (89.3%)	31 (6.8%)
Normal Mucosa (N=99)	5 (5.1%)	90 (90.9%)	4 (4.0%)
Hyperplastic Polyp (N=85)	3 (3.5%)	76 (89.4%)	6 (7.1%)
Sessile Serrated Polyp (N=2)	0 (0.0%)	2 (100.0%)	0 (0.0%)