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## Prediction of Polyp Pathology Using Convolutional Neural Networks Achieves ‘Resect and Discard’ Thresholds

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### Abstract

**Introduction**—Reliable *in situ* diagnosis of diminutive ( < 5 mm) colorectal polyps could allow for “resect and discard” and “diagnose and leave” strategies resulting in one billion dollars in cost savings per year in the U.S. alone. Current methodologies have failed to consistently meet the Preservation and Incorporation of Valuable endoscopic Innovations (PIVI) initiative thresholds. Convolutional neural networks (CNN) have the potential to predict polyp pathology and achieve PIVI thresholds in real-time.

**Methods**—We developed a CNN-based optical pathology (OP) model using Tensorflow and pre-trained on ImageNet, capable of operating at 77 frames per second. 6223 images of unique colorectal polyps of known pathology, location, size, and light source (white light [WL] or narrow band imaging [NBI]) underwent 5-fold cross training (80%) and validation (20%). Separate fresh validation was performed on 634 polyp images. Surveillance intervals were calculated, comparing OP vs. true pathology (TP).

**Results**—In the original validation set, the negative predictive value (NPV) for adenomas was 97% among diminutive rectum/rectosigmoid polyps. Results were independent of use of NBI or WL. Surveillance interval concordance comparing OP and TP was 93%. In the fresh validation set, NPV was 97% among diminutive polyps in the rectum and rectosigmoid and surveillance concordance was 94%.

**Conclusion:** This study demonstrates the feasibility of *in situ* diagnosis of colorectal polyps using CNN. Our model exceeds PIVI thresholds for both “resect and discard” and “diagnose and

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leave” strategies independent of NBI use. Point-of-care adenoma detection rate and surveillance recommendations are potential added benefits.

## Keywords

Deep Machine Learning; Colorectal Cancer Screening; PIVI; Optical Pathology

## INTRODUCTION

Colorectal cancer (CRC) is the 2nd leading cause of cancer deaths in the United States [1]. The majority of colorectal cancers start as benign precancerous polyps, such as adenomas [2]. Colonoscopy remains the gold standard for finding adenomas and is the only intervention capable of removing adenomas short of surgery. The National Polyp Study (NPS) showed that 70%-90% of colorectal cancers are preventable with polyp removal [3]. The same NPS colonoscopy cohort had a 53% decrease in CRC mortality compared to the SEER population, in whom an unknown percentage had colonoscopy [2].

Approximately 80% of polyps removed during colonoscopy are diminutive (< 5 mm) and rarely demonstrate advanced pathology [4]. Among 36,107 diminutive polyps in a large prospective database, only 0.3% of colonic polyps demonstrate high grade dysplasia and none were cancers [5][6]. Pathologic analysis of diminutive polyps contributes \$1 billion annually to colonoscopy costs in the United States [7]. A reliable means to ‘optically’ diagnose diminutive polyps *in situ* could allow for “resect and discard” and “diagnose and leave” strategies resulting in significant cost savings, while also providing surveillance interval recommendations and calculation of adenoma detection rate (ADR) at point of care.

In 2011, the American Society for Gastrointestinal Endoscopy (ASGE) initiative titled “Preservation and Incorporation of Valuable endoscopic Innovations” (PIVI), developed performance thresholds required to “resect and discard” and/or “diagnose and leave” diminutive polyps [8]. “Resect and discard” requires an optical biopsy system with >90% concordance in recommended surveillance intervals compared to true histology for all diminutive polyps throughout the colon [8]. “Diagnose and leave” applies to diminutive non-adenomatous polyps in the rectosigmoid and requires > 90% negative predictive value (NPV) for adenomas. Numerous attempts have been made to reach both PIVI thresholds however these studies have had a number of limitations.

Deep machine learning has the potential to diagnose colorectal polyps *in situ* and meet optical biopsy PIVI criteria independent of setting, operator motivation, skill or training. Our goal was to create a deep learning algorithm capable of *in situ* diagnosis of diminutive colorectal polyps and to test its performance against PIVI thresholds under both NBI and white light (WL) without uninterpretable “low confidence” polyps.

## METHODS

### Colonoscopy and Polyp Image Dataset

We utilized an anonymized version of our prospectively collected Colonoscopy Quality Database inclusive of all GIQuIC quality measures (GI Quality Improvement Consortium,

Ltd.), polyp location, size, morphology, and linked images. The database includes over 180,000 polyp and non-polyp images acquired from Olympus 190 (90%), Olympus 180 (7%) -and Pentax i10 series colonoscopes (3%). The polyp images are categorized by light source (WL vs NBI) and image quality (excellent, adequate, poor). Only adequate-to-excellent quality polyp images linked to specimens with a single pathology were included. A total of 6223 high quality images of unique diminutive polyps (one image per polyp) with known unique pathology were identified.

### Convolutional Neural Network Architecture

We developed and designed our CNN model architecture from two primary modules: Feature Extraction and Classification. The ‘base’ module of our algorithm is responsible for automated feature extraction and borrows from the Inception-ResNet-v2 algorithm developed by Google AI that achieves “state-of-the-art” accuracy on popular image classification benchmarks. The ‘head’ module of our algorithm is designed for transforming extracted features from the base layers (50mm+ parameters) into a graded scale that allows for pathologic classification. The sigmoid activation function maps the model’s output logits into a float value ranging between 0 - 1. An Nvidia Gtx 1070 GPU was used for algorithm development. Running inference on a frame requires 13 ms (77 frames per second), essentially ‘real time’.

### Binary Classification: Adenomatous vs Serrated Lesions

We developed a binary CNN classifier consisting of: 1) adenomatous polyps (tubular adenoma, tubulovillous adenomas, villous adenomas and flat adenomas); vs 2) serrated polyps (hyperplastic and sessile serrated polyps). Our rationale for using this binary classification was based on three factors:

1. the vast majority of colorectal polyps can be categorized as either adenomas or serrated lesions [9];
2. pathologists (our “ground truth”) demonstrate excellent agreement distinguishing adenomatous versus serrated polyps but have fair to poor agreement separating hyperplastic polyps (non-neoplastic/surveillance-irrelevant lesions [SILs]) and sessile serrated polyps (precancerous/surveillance-relevant lesions [SRLs]) [10];
3. there were insufficient numbers of other polyp types in our data set to develop a robust “multiclass” model.

After excluding 945 images of polyps that did not meet our binary classification, the training dataset consisted of 5278 diminutive polyp images (3310 adenomatous polyps and 1968 serrated polyps).

### Convolutional Neural Network Training and Validation

Convolutional neural network (CNN) training and validation proceeded in three stages: pre-processing, training, and inference. In the pre-processing stage, data was formatted for input in the algorithm by resizing images, normalizing pixels, and then using transfer learning to help initiate the base layer imaging weights. The base layer imaging weights were pre-trained on ImageNet, which is a large visual database designed for object recognition

software. In the training stage, the CNN was trained with Tensorflow, an open-source machine learning framework. 5278 polyp images were partitioned into 5 equal-sized subsamples for 5-fold cross validation with training (80%) and validation (20%). Data augmentation provided standardization for training data “on-the-fly” including various image adjustments. In the Inference stage, the data produced by the training were used to generate test set predictions. Various augmentations to the test set generated an additional layer of predictions. Predictions are then averaged to create a composite probability, and then fed into an Adam optimizer to produce a binary result between 0-0.5 and 0.5-1 for final polyp classification data. Any value  $\geq 0.5$  is classified as adenoma. Any value  $< 0.5$  is classified as serrated.

### Conditional Validations:

The CNN model was then tested for performance under three separate conditions:

1. NBI vs WL performance: Optical Pathology (OP) was compared to True Pathology (TP) for all adenomatous vs serrated polyps of all sizes and locations.
2. “Diagnose and leave” performance: OP compared to TP among all diminutive polyps in the rectum and rectosigmoid.
3. “Resect and discard” performance: Surveillance intervals were compared based on OP vs TP of all diminutive polyps throughout the colon on a per procedure basis.

Surveillance intervals were calculated based on U.S. Multi-Society Task Force guidelines, accounting for procedure indication and polyp number, size, location and pathology (OP vs TP). We adopted the concept that serrated polyps proximal to the rectosigmoid are “surveillance relevant” (see Table 1 for calculations) [9]. The number of cases for which surveillance intervals were lengthened, shortened or unchanged by OP were analyzed.

### Validations against new polyp images:

To address validity of our model against fresh datasets, we utilized images of polyps with known pathology previously unexposed to the CNNs. These included 542 polyp images from 286 colonoscopies in our colonoscopy quality database, and 92 polyp images from 50 colonoscopies performed at an independent ambulatory surgical center (ASC).

## RESULTS

### CNN-predicted Optical Pathology vs True Pathology

Among the original validation set, the distribution of raw CNN OP outputs vs TP is shown in Figure 1. 96% of true adenomas were predicted by OP to be adenomas (prediction bins  $\geq 0.5$ ) and the 90% of true serrated polyps were predicted by OP to be serrated (prediction bins  $< 0.5$ ). Figure 1 also shows the distribution of “other” polyps (i.e. non-adenomatous non-serrated polyps) across raw CNN OP outputs. The majority of surveillance-relevant lesions (SRLs) such as traditional serrated adenomas (27/37), hamartomas (9/11), lymphomas (5/5), and juvenile polyps (5/6) were predicted by OP to be adenomatous lesions.

### **Effect of NBI vs WL on Optical Pathology Performance**

Among the original validation set, performance of OP across all polyp sizes and locations was compared between NBI and WL. Overall accuracy of OP was 93.6% (92.9-94.2% [95% CI])% with an NPV of 92.6% (91.5-93.8% [95% CI]) for adenomatous polyps. Positive predictive value was 94.1% (93.3-94.9% [95% CI]); sensitivity was 95.7% (95.1-96.4% [95% CI]) and specificity was 89.9% (88.6-91.3% [95% CI]). OP accuracy was 91.9% (90.2-93.6% [95% CI]) under WL and 94.0% (93.2-94.7% [95% CI]) under NBI (Figure 2). Among the fresh set of polyp images, under WL, accuracy was 92.8% (91.5-94.1% [95% CI]) and under NBI, accuracy was 93.1% (91.6-94.6% [95% CI]). A Pearson's chi squared test showed that OP performance under WL and NBI was not significantly different in the original or fresh validation sets.

### **Optical Pathology Performance Against "Diagnose and Leave" Strategy**

The PIVI threshold to "diagnose and leave" non-adenomatous polyps requires a >90% NPV for adenomatous polyps  $\leq$  5 mm in the rectosigmoid. Under these size and location stringencies, OP achieved an NPV for adenomas of 97.3% (95.8-98.8% [95% CI]) under both WL and NBI with an overall accuracy of 91.5% (89.3-93.8% [95% CI]) in the original validation set (see Table 2). In the fresh set of polyp images, NPV was 96.5% (94.8-98.2% [95% CI]) with an accuracy of 88.9% (86.6-91.3% [95% CI]) (see Table 3).

### **Optical Pathology Performance Against "Resect and Discard" Strategy**

The PIVI threshold for "resect and discard" requires 90% concordance for recommended surveillance intervals between OP and TP of polyps  $\leq$  5 mm throughout the colon. Among all polyps  $\leq$  5 mm (regardless of location or use of WL or NBI) surveillance interval concordance between TP and OP was 93.4% (92.4-94.4% [95% CI]) in the original validation set, and 94.1% (91.3-96.9% [95% CI]) in the fresh set of polyp images. Among screening and surveillance cases in the original validation set, surveillance interval concordance was 90.8% (89.3-92.3% [95% CI])% and 96.4% (95.3-97.5% [95% CI]) respectively, and was 90.8% (86.2-95.4% [95% CI]) and 98.3% (96.0-100% [95% CI]), respectively in the fresh validation set.

Table 4 shows the effect of OP on recommend surveillance interval based on the 2499 procedures in our original validation dataset. Among the 192 colonoscopies for which OP shortened surveillance intervals, 167 were attributed to right-sided surveillance irrelevant polypoid lesions (154 normal, 27 lymphoid aggregates, 12 inflammatory polyps, and 1 mucosal prolapse) classified by OP as surveillance-relevant serrated polyps (44%) or adenomas (56%). The remaining 25 cases for which OP shortened surveillance intervals were attributed to OP misclassification of diminutive rectosigmoid hyperplastic polyps as adenomas. The 8 cases for which OP produced longer surveillance intervals were attributed to rectosigmoid adenomas or SSPs misclassified by OP as surveillance-irrelevant serrated polyps. Table 5 shows the effect of OP on recommend surveillance interval based on the 272 procedures in our fresh validation dataset with similar results.

## DISCUSSION

Reliable *in situ* diagnosis of polyp pathology could reduce pathology costs, provide patients with immediate surveillance recommendations, streamline physician workflow and improve cost-effective patient care. We created a CNN-based deep learning model with an overall accuracy of 94% for distinguishing adenomas and serrated polyps. Performance was unaffected by use of WL or NBI. Among diminutive polyps in the rectum/rectosigmoid, the NPV was 97% for adenomas, which is well over the “diagnose and leave” PIVI threshold of 90%. When considering all diminutive polyps removed throughout the colorectum under the indications of screening or surveillance, the surveillance interval concordance between OP and TP was 93%, for original data, and 94% for the fresh data, which are greater than the “resect and discard” PIVI threshold of 90%. To our knowledge, this methodology is the first to successfully achieve and surpass both PIVI thresholds independently of light source, human-based visual criteria or expertise.

There have been numerous attempts to achieve PIVI guideline thresholds using different optical modalities [11][12]. The NICE Criteria, created by the ‘Colon Tumor NBI Interest Group’, separates hyperplastic polyps (Type 1), tubular adenomas (Type 2), and invasive carcinoma (Type 3) based on color, vessels, and surface pattern under NBI without magnification [13]. In 2015, the ASGE performed a meta-analysis assessing the ability of NICE criteria to achieve PIVI standards [7]. Overall an NPV of 91% for adenomas was obtained, however post-polypectomy surveillance interval agreement was only 89%. Performance depends on the practice setting (community vs. academic), operator experience (novice vs. experienced endoscopists), and confidence level. For example, expert endoscopists from academic settings with high confidence could obtain an NPV of 95% with a post-polypectomy surveillance interval agreement of 93% [7], whereas community physicians trained on the NICE criteria were unable to reach PIVI thresholds [11][14].

Other real-time advanced imaging techniques applied to predict polyp histology include magnifying NBI, endocytoscopy, and laser-induced autofluorescence spectroscopy [15]. These technologies are limited by requirements for specialized training, access to expensive equipment, and inability to reach both PIVI thresholds [16][17][18][19]. Failure to consistently achieve PIVI thresholds is multifactorial and includes the subjectivity intrinsic to human-based criteria, e.g., NICE, and the numerous polyps that do not fit into human-based criteria [20].

Deep learning provides a new approach to overcome these limitations. CNNs determine their own criteria based on training sets of polyp images with known pathology. The resulting CNN provides a consistent ‘objective’ output independent of colonoscopist’s training, experience, and skill. Fatigue, loss of motivation, and inability to concentrate are not problems for a deep learning system.

Deep learning for polyp pathology prediction is rapidly emerging in the literature. In 2017, Byrne et al published their CNN deep learning model trained on NICE classification of polyps. When tested on 106 polyp videos, they achieved an accuracy of 94%, and NPV of 97%. Surveillance concordance was not published. Notable limitations included a dataset

collected by one expert endoscopist, dependency on NBI, and exclusion of 19 polyps due to lack of high confidence results from their NICE-based deep learning model [21]. In 2018, Mori et al. published data on the use of deep learning combined with endocytoscopy and reported an NPV >90% for left colon adenomas after exclusion of low confidence polyps [22]. Their data was collected by experts in the use of the endocytoscopy which limits applicability in the community setting and bypasses the cost saving potential of deep learning.

We challenged our deep learning algorithm to differentiate adenomatous and serrated polyps on unaltered endoscopic images at standard magnification using conventional colonoscopes inclusive of WL and NBI imaging. The resulting model performed equally well under both light settings, and therefore independent of Olympus NBI technology. Because our data set was collected from endoscopists at various levels of training ranging from first year GI fellows to endoscopists with 30+ years' experience, we expect that its performance will be user-independent as well as applicable in both community and academic settings. Our validation subset at a community ASC supports this conjecture.

An optimal OP technology will reliably distinguish surveillance relevant lesions (SRLs) from surveillance-irrelevant lesions (SILs). CNNs, however, can only be as good as the "ground truth" on which they are trained [23]. Our CNN was based on pathology, derived from our academic pathologists who cluster tightly in their classification rates of adenomas and serrated polyps but vary widely in their classification rates of the two primary sub-classifications of serrated polyps (HPs [SILs] and SSPs [SRLs]) [24][25]. This is in line with several studies showing poor agreement among pathologists distinguishing hyperplastic (SILs) and sessile serrated polyps (SRLs) [26]. This current limitation of pathology coupled with data suggesting that diminutive proximal HPs are associated with synchronous advanced neoplasia [27], supports suggestions that any serrated polyp proximal to the sigmoid should be considered an SRL [28].

We therefore trained our CNN on the best "ground truth" pathology (adenoma vs serrated), and adopted the rule that any serrated polyp proximal to the sigmoid is considered a SRL. Our binary approach (serrated vs adenoma) and surveillance model means that any polyp, including normal and lymphoid aggregates proximal to the sigmoid will be categorized as an SRL (serrated vs. adenoma) by our CNN. This strategy therefore biases toward OP-shortened surveillance intervals and discordance with TP. In fact, 84% of surveillance interval discordance by our OP was attributed to 167 SILs classified as SRLs by OP, 154 of which were diagnosed as "normal" colonic mucosa by our pathologists. Even so, our CNN exceeded the PIVI "resect and discard" threshold of 90% concordance. It is especially interesting that this level of concordance is achieved by combining OP for rectosigmoid polyps with a simple OP-independent rule: all diminutive polyps proximal to the sigmoid are SRLs.

Development of an OP system to further reduce surveillance discordance will require separate categories of SILs (HPs, normal, lymphoid aggregates, inflammatory, mucosal prolapse). We are currently generating a multiclass CNN to accomplish this, realizing that its performance will be limited by poor "ground truth" for separating proximal serrated polyps

into HP and SSP categories. Furthermore, the category of “normal” may include a significant number of diminutive SRLs, such as adenomas, that were missed on tissue sectioning [23].

A key limitation of our study is that it is retrospective and based on static images. We currently are able to run multiple CNNs in real time during live colonoscopies without noticeable frame drops or lag. Additionally, we are optimizing live OP feedback during colonoscopy in conjunction with our polyp detection algorithm in real time [29]. Future prospective multicenter validation studies during colonoscopy are being planned.

In summary, we demonstrate the promise of real-time *in situ* diagnosis of colorectal polyps using deep learning. We show that *in situ* diagnosis is possible without dependency on specific light source, potentially applicable across multiple scope manufacturers. Deployment does not require specialized scopes or processors and only needs an off-the shelf computer with standard graphic processing unit with connections to the video source and viewing monitor. The future will bring a new deep learning assistant to the endoscopy suite to find and diagnose polyps in real time. For the patient, this means that polyps in view are found, removed, and diagnosed without unnecessary pathology fees, followed by accurate recommendations for follow-up at point-of care. Deep learning cannot replace the colonoscopist, who must drive the scope effectively and safely, clean away debris, inspect all mucosal surfaces, make sound judgements on what pathologies they find, and apply their knowledge and skill during intervention. Deep machine learning technology will continually learn from the endoscopists, leading to continual improvements in quality patient care delivery.

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### Study Highlights

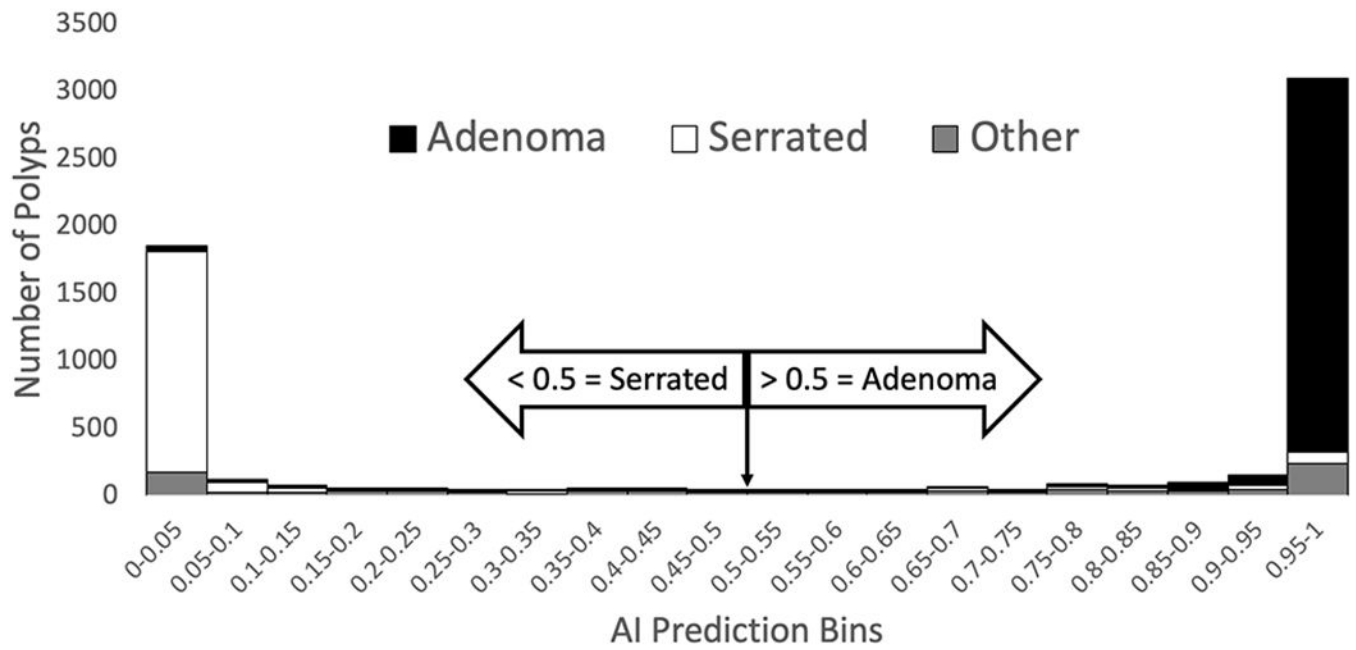
#### WHAT IS KNOWN:

- The Preservation and Incorporation of Valuable endoscopic Innovations (PIVI) guidelines provide criteria for adoption of “resect and discard” and “diagnose and leave” strategies for optical pathology.
- Convolutional Neural Networks (CNNs) show promise in achieving accurate real-time optical pathology.

#### WHAT IS NEW HERE:

- We demonstrate that our CNN-based optical pathology exceeds both PIVI thresholds when applied to polyp images obtained during colonoscopy.
- Accuracy was achieved using images from standard colonoscopes performed by novice and expert colonoscopists using white light or NBI.

### Distribution of Polyp Pathologies by OP Predictions (0-0.5 = Serrated, 0.5-1.0 = Adenoma)



**Figure 1.** Histogram depicting distribution of polyp pathologies by OP Predictions.

<b>NBI + WL</b>			<b>WL</b>			<b>NBI</b>					
		<b>TPath</b>				<b>TPath</b>					
		<b>Adenoma</b>	<b>Serrated</b>			<b>Adenoma</b>	<b>Serrated</b>				
<b>OPath</b>	<b>Adenoma</b>	3169	198	<b>OPath</b>	<b>Adenoma</b>	585	47	<b>OPath</b>	<b>Adenoma</b>	2582	151
	<b>Serrated</b>	141	1770		<b>Serrated</b>	34	333		<b>Serrated</b>	107	1434
<b>Sensitivity</b>		0.96		<b>Sensitivity</b>		0.95		<b>Sensitivity</b>		0.96	
<b>Specificity</b>		0.90		<b>Specificity</b>		0.88		<b>Specificity</b>		0.90	
<b>PPV</b>		0.94		<b>PPV</b>		0.93		<b>PPV</b>		0.94	
<b>NPV</b>		0.93		<b>NPV</b>		0.91		<b>NPV</b>		0.93	
<b>Accuracy</b>		0.94		<b>Accuracy</b>		0.92		<b>Accuracy</b>		0.94	

**Figure 2.**  
Confusion matrices of adenomas and serrated polyps under *WL* white light and *NBI*.

**Table 1.**

Surveillance Intervals Calculations Based on US Multi-Society Task Force Guidelines. Final surveillance interval was defined as the lowest surveillance number combining personal history and findings at colonoscopy, comparing SRL status determined by true path (TP) vs optical path (OP) of polyps  $\geq$  5 mm. *SRL*: Surveillance Relevant Lesions. *FHx*: Family History. *Hx*: History. Lynch: Lynch syndrome. *FAP*: Familial Adenomatous Polyposis Syndrome. *PJ*: Peutz-Jeghers Syndrome.

Personal History		Findings at Colonoscopy	
Risk Category	Years	# of SRLs	Years
Avg. Risk	10	0	10
Hx Adenoma(s)	5	1-2	5
FHx CRC	5	3-9	3
Lynch/FAP/PJ	1	>9	1
		<b>Size (mm)</b>	
		1-9	5
		10-19	3
		>19	1

**Table 2.**

Confusion matrix for “diagnose and leave” criteria comparing diminutive adenomas to non-adenomas in the rectosigmoid and rectum.

		True Path	
		Adenoma	Non-Adenoma
Optical Pathology	Adenoma	107	38
	Serrated Polyp	12	434
Sensitivity		0.90	
Specificity		0.92	
PPV		0.74	
NPV		<b>0.97</b>	
Accuracy		0.92	

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**Table 3.**

Confusion matrix for “diagnose and leave” criteria comparing diminutive adenomas to non-adenomas in the rectosigmoid and rectum with fresh data.

		True Path	
		Adenoma	Non-Adenoma
Optical Pathology	Adenoma	167	60
	Serrated Polyp	16	443
Sensitivity		0.91	
Specificity		0.88	
PPV		0.74	
NPV		<b>0.97</b>	
Accuracy		0.89	

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**Table 4.**

“Resect and discard” surveillance concordance data.

Entire Colon (All polyps <6mm)					
Indications	Opath shortens interval	Unchanged	Opath lengthens interval	Totals	% Concordance
Screening	151	1223	7	1347	90.8%
Surveillance	41	1110	1	1152	96.4%
<b>Totals</b>	192	2333	8	2499	<b>93.4%</b>

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**Table 5.**

“Resect and discard” surveillance concordance for fresh data.

Entire Colon (All polyps <6mm)					
Indications	Opath shortens interval	Unchanged	Opath lengthens interval	Totals	% Concordance
Screening	9	139	5	153	90.8%
Surveillance	1	117	1	119	98.3%
<b>Totals</b>	10	256	6	272	<b>94.1%</b>

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