

Predictive rules for optical diagnosis of <10-mm colorectal polyps based on a dedicated software

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ABSTRACT

Background The BASIC classification for predicting in vivo colorectal polyp histology incorporates both surface and pit/vessel descriptor domains. This study aimed to define new BASIC classes for adenomatous and hyperplastic polyps.

Methods A video library (102 still images/videos of <10-mm polyps using white-light [WLI] and blue-light imaging [BLI]) was reviewed by seven expert endoscopists. Polyps were rated according to the individual descriptors of the three BASIC domains (surface/pit/vessel). A model to predict polyp histology (adenomatous or hyperplastic) was developed using multivariable logistic regression and subsequent “leave-one-out” cross-validation. New BASIC rules were then defined by Delphi agreement. The overall accuracy of these rules when used by experts was evaluated according to the level of confidence and light type.

Results The strength of prediction for adenomatous histology from 2175 observations assessed by area under the curve (AUC; 95% confidence interval) was poor-to-fair for the surface descriptors (0.50 [0.33–0.69] for mucus; 0.68 [0.57–0.79] for irregular surface), but stronger for pits (0.87 [0.80–0.96] for featureless/round/not round) and vessels (0.80 [0.65–0.87] for not present/lacy/pericryptal). By combining the domains, a good-to-excellent prediction was shown (AUC 0.89 [0.81–0.96]). After the definition of new BASIC rules for adenomatous and hyperplastic polyps, accuracy for high confidence BLI predictions was 90.3% (86.3%–93.2%), which was superior to high confidence WLI (83.7% [77.3%–87.7%]) and low confidence BLI predictions (77.7% [61.1%–88.6%]).

Conclusions Based on the strength of prediction, the new BASIC classes for adenomatous and hyperplastic histology show favorable results for accuracy and confidence levels.

Introduction

Detection rates for neoplastic lesions at screening colonoscopy are increasing rapidly owing to improvements in endoscopist performance and technology [1–3]. Up to 84% of screening colonoscopies end up with the detection of at least one polyp,

which in most cases is a diminutive lesion (≤ 5 mm) [1]. Until recently, it was recommended that all retrieved specimens were sent to histology in order to classify such diminutive lesions as either hyperplastic or adenomatous [4]. However, the risk of advanced neoplasia and invasive cancer in these lesions is marginal, being rare and exceptional, respectively [5].

Electronic chromoendoscopy associated with high definition colonoscopy and, possibly, optical magnification emphasizes the vascular and glandular pattern of colorectal lesions leading to an *in vivo* prediction of the histological diagnosis [6]. The adequate accuracy achieved by these methodologies in preliminary studies resulted in official recommendations for its use as the standard of care in clinical practice [6–8]. In detail, “resect and discard” and “leave-in-situ” strategies based on high confidence optical predictions have been recommended for diminutive adenomas and rectosigmoid hyperplastic polyps, respectively [6, 7].

In order to standardize optical diagnosis, international classifications for *in vivo* prediction of polyp histology, such as the narrow-band imaging (NBI) international colorectal endoscopic (NICE) and Japan NBI Expert Team (JNET) classification, have been validated and incorporated into clinical practice [9–11]. These classifications are mainly based on vascular and glandular patterns, and differing results have been shown with their implementation in the endoscopic community [9, 12].

Recently, specific features of the polyp surface have also been shown to predict polyp histology. The valley sign – a slight pseudodepression on the edge of the polyp – has been shown to be highly specific for the diagnosis of adenoma [13], while a cloudy or irregular appearance and indistinct borders have been associated with sessile serrated polyp histology [14].

By incorporating both surface and vascular/pit patterns, we created a new classification – the blue-light imaging (BLI) adenoma serrated international classification (BASIC) – for optical prediction of polyp histology [15].

The aim of this validation study was to quantify analytically the strength of the BASIC descriptors individually and when combined in predicting polyp histology, and to use these data to create new BASIC rules for classification of adenomas and hyperplastic polyps. The secondary aim was to evaluate the diagnostic accuracy of such rules for the diagnosis of adenomas when used by experts.

Methods

Study design

With the use of dedicated software, seven endoscopists who were expert in advanced endoscopic imaging anonymously and independently scored the individual descriptors of the BASIC classification in a prospectively collected video library in two different phases:

1. scoring only for the presence/absence of each descriptor, without providing a final prediction
2. scoring for the presence/absence of each descriptor and providing a final prediction.

All the scores were incorporated into a regression model in order to assess the strength of prediction of each descriptor individually and in combination. The two phases were separated by an expert meeting at which, based on the results of the first phase, the individual descriptors were assigned to a specific histological type (i.e. adenomatous or hyperplastic) to define BASIC classes specific for such lesions. Analogously to our pre-

vious study on interobserver agreement [15], no final diagnosis was performed during phase 1, in order to allow the endoscopists to purely focus on the individual descriptors, without any interference/anticipation from an eventual clinical classification. In contrast, the results of phase 2 were used to assess the accuracy of the endoscopists when using the new classes of the BASIC classification. (Institutional review board approval: ICH 477/16, 1 December 2016.)

Library

A video library of polyps <10 mm was prospectively created for the purpose of this study, as previously detailed [15]. Briefly, for each lesion, we collected videos/still images, with and without optical magnification, both in white-light imaging (WLI) and BLI modes (ELUXEO VP-7000 and BL-7000; Fujifilm), both as still image and videos. Overall, there was a mean of five images per polyp (more details in **Table 1s**, see online-only Supplementary material). All polyps were resected and sent for histopathological examination, which was used as the gold standard for our analysis and was performed by experienced gastroenterology pathologists according to the revised Vienna classification [16]. Only adenomatous and hyperplastic polyps of <10 mm were included in our analysis, with sessile serrated polyps being excluded.

BASIC classification

The BASIC classification has been detailed elsewhere. Briefly, it consists of three main domains (surface, pit, and vascular patterns) divided into subdomains and individual descriptors (► **Table 1** and ► **Fig. 1**). A detailed explanation of the BASIC descriptors is provided in **Table 2s**. The BASIC classification has a branched structure to be incorporated into the dedicated software (**Fig. 1s**). Although the classification was created for prediction of all the main histological types (i.e. serrated or invasive cancer), we decided to limit the present analysis to differentiation between adenomatous and hyperplastic histology [15], excluding alternative histological types (i.e. sessile or traditional serrated adenomas) from our analysis.

Creation of new BASIC rules

Based on the prediction strength assessed in the regression model at the end of the phase 1 (see below), individual predictors were eventually assigned to either the adenomatous or hyperplastic histology classes using the same modified Delphi criteria adopted previously [15]. Further specification of the individual predictors based on the phase 1 results was also allowed in this phase. Following this, we assessed the accuracy of the classification when used by the expert endoscopists, including the level of confidence (low vs. high), the light adopted (WLI vs. BLI), the use of optical magnification, and the type of media used (video vs. still image). The accuracy assessments were based on the final diagnoses provided by the endoscopists for each case in phase 2 of the study.

Software

Videos/still images of each polyp (► **Fig. 1**) were anonymously uploaded on a specifically developed application for high reso-

► **Table 1** Explanation for the BASIC descriptors and terminology. Domains (bold), subdomains (italics), and descriptors are reported according to the same conditional structure that was used to develop the software application. A detailed definition of each descriptor is reported in **Table 2s**.

Domain	Subdomains and descriptors
1 Surface	<i>a) Presence of mucus</i>
	▪ Yes
	▪ No
	<i>b) Regularity</i>
	▪ Regular
	▪ Irregular
	<i>(1) Presence of depression</i>
	(a) True
(b) Pseudo	
2 Pit pattern	<i>a) Featureless</i>
	▪ Yes
	▪ No
	<i>(1) Type</i>
	(a) Round, dark
	(b) Round, not dark
	(c) Non-Rounded
	<i>(2) Distribution</i>
	(a) Homogeneous
	(b) Heterogeneous
	<i>(1) Focal loss</i>
	(i) Yes
(ii) No	
3 Vessels	<i>a) Presence</i>
	▪ Yes
	(1) Lacy
	(2) Pericryptal
	(3) Irregular
	▪ No

lution iPad (Apple). The software was built in order to force the endoscopist to rate the presence/absence of each descriptor for each of the three main domains, and to indicate the correct diagnosis and the level of confidence (0–5 on a Likert scale).

Statistical analysis

R statistical software, version R version 3.3.2, was used for all analyses (R Development Core Team, Vienna, Austria, 2011). Significance was assigned for a *P* value of less than 0.05.

The data were thoroughly inspected using univariate analyses (descriptive statistics and univariate logistic regression)



► **Fig. 1** The user-friendly software has a rating for each descriptor to the right of the screen, including the three main domains of BASIC and the confidence of the diagnosis. Video/still images of the polyp were anonymously displayed at the center of the screen in a predefined randomized sequence for each individual rater. In the case shown, the surface domain was rated as no mucus and irregular surface with a central pseudodepression and conserved pit pattern; the pit pattern domain was characterized as non-round pits with tubular strictures and homogeneous distribution; the vascular domain was characterized as non-continuous pericryptal vessels. The lesion was a diminutive IIa tubular adenoma with low grade dysplasia on histology.

and multivariable logistic regression analysis to combine the descriptors to develop a prediction model of polyp histology (adenoma or hyperplastic polyp).

Descriptive statistics

Categorical data were reported as frequencies with proportions. The strength of association between the selected covariates and the outcome was modeled using logistic regression. Results are expressed as an odds ratio (OR) with 95% confidence interval (CI).

Model development and internal validation

The model used the polyp histology (i.e. adenoma or hyperplastic polyp) as the outcome, and all BASIC descriptors were used as predictor variables. We used leave-one-out cross-validation (LOOCV) to select the optimal number of descriptors in the final model (**Appendix 1s**). Regression analysis was performed using a multilevel approach to account for dependencies of the data due to multiple images of the same polyp and multiple observations of the same image by more than one observer; polyps and readers were considered as random cross-classifications, with the descriptors considered as fixed factors.

The ability of the model to perform in an independent cohort was then assessed by receiver operating curve (ROC) analysis; the area under the ROC curve (AUC), validated internally using the LOOCV technique (detailed in next paragraph). Bootstrap analysis was used to calculate the distribution and CIs for the AUCs. AUC values >0.9 were interpreted as excellent, 0.8–0.9 as good, 0.7–0.8 as fair, 0.6–0.7 as poor, and <0.6 as having no discrimination. The value associated with the highest

sensitivity and specificity cutoff values was chosen for dichotomization into adenomas and hyperplastic polyps.

As all of the lesions were used for the model generation, the performance of the model may be overoptimized. To correct this bias, we performed a LOOCV. First, the LOOCV procedure removes one sample (including all observations for a given polyp) to form a test set, and the remaining samples are used for model construction (Fig. 2s). The constructed model is then tested using the removed sample. After all samples have been left out and tested in turn, the final classification error is obtained by the fraction of errors over the total number of training samples. This gives a better idea of the ability of the model to predict outcome, because the probability of each polyp being an adenoma is computed without using their data.

Model validation was performed for each of the two phases of the study. However, as the results were similar, we decided to report in the main text only the cumulative results of the two phases. To better understand the contribution of the individual descriptors to the predictive strength of the model, ROC curves were also generated for each BASIC descriptor, and for different subsets of descriptors (Fig. 2s).

The accuracy of the new BASIC rules when used by experts

A secondary analysis was performed to evaluate the diagnostic accuracy of the new BASIC classification when used by experts. The analysis included data from the second phase of the study. The accuracy for each expert was calculated considering the histological diagnosis as the reference standard. Multilevel logistic regression was used to model the influence of type of light (BLI vs. WLI), polyp confidence level (high vs. low), and the use of optical magnification on the odds of a correct diagnosis of polyp histology (correctly diagnosed as an adenoma/hyperplastic polyp vs. not). Data are presented as ORs and 95% CIs.

Results

Polyp characteristics

The video library cumulatively included a total of 102 polyps of < 10 mm (59 for the first phase; 43 for the second). The characteristics of the included polyps and related observations are given in Fig. 3s and Tables 3s and 4s. The prevalence of adenomas at histology was 69.6% (71/102). Overall, 67 (65.7%) and 35 (34.3%) were diminutive (≤ 5 mm) and small (6–9 mm), respectively, while 87 (85.3%) and 15 (14.7%) were polypoid and non-polypoid, respectively. In addition, 73 (71.6%) and 29 (28.4%) were located in the proximal and distal colon, respectively.

Univariable association between BASIC descriptors and polyp histology

A dataset of 2175 observations (1653 from the second phase) was subjected to logistic regression to assess the predictive value of the BASIC descriptors. On univariable analysis, all descriptors were statistically significant predictors for the diagnosis of adenomas: mucus presence (no vs. yes: OR 5.0, 95%CI 3.9–7.1), irregular surface (vs. regular: OR 5.9, 95%CI 4.6–7.7), featureless appearance (no vs. yes: OR 7.7, 95%CI 6.3–10.0), non-

round pits (vs. not present: OR 21.2, 95%CI 15.9–28.3), round pits (vs. not present: OR 1.9, 95%CI 1.4–2.5), heterogeneous distribution of pits (OR 1.5, 95%CI 1.2–1.7), and pericryptal vessels (vs. not present or lacy: OR 2.0, 95%CI 1.5–2.6).

Predictive strength for adenoma prediction models based on each BASIC descriptor in isolation

The predictive strength of each domain of BASIC for predicting adenomatous histology is given in Table 2.

a) Surface domain descriptors

i) Mucus With application of the LOOCV validation method, the performance of the mucus criterion alone for predicting adenomas (vs. hyperplastic polyps) was poor with values for AUC, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 0.50, 91.5%, 41.9%, 73.6%, and 70.0%, respectively (Table 2).

ii) Regularity The AUC, sensitivity, specificity, PPV, and NPV were 0.68, 62.0%, 88.5%, 88.5%, and 47.9%, indicating a fair agreement with the histological diagnosis. There was a trend toward higher predictive strength for this predictor as compared with mucus ($P=0.08$ for difference in AUC) (Table 2). The AUC from the combination of mucus and regularity (M2) was 0.76 (95%CI 0.66–0.86).

b) Pit domain descriptors

i) Featureless appearance The AUC, sensitivity, specificity, PPV, and NPV for this descriptor were 0.81, 80.3%, 84.0%, 92.6%, and 64.5% indicating good agreement with the histological diagnosis. This criterion tended to outperform both mucus and regularity ($P=0.004$ vs. mucus presence; $P=0.09$ vs. regular surface) (Table 2)

ii) Round (dark/non-dark) vs. non-round pits The AUC, sensitivity, specificity, PPV, and NPV were 0.87, 74.6%, 93.5%, 96.0%, and 61.9%, respectively. Pit appearance showed a higher predictive strength than mucus and surface regularity. The AUC resulting from the combination of pit appearance and featureless appearance (0.87, 95%CI 0.80–0.96) was also higher than that obtained by combining the surface descriptors (0.76, 95%CI 0.66–0.85; $P=0.06$).

iii) Distribution of pits (homogeneous vs. non-homogeneous) The AUC, sensitivity, specificity, PPV, and NPV were 0.81, 83.1%, 77.4%, 90.0%, and 67.5%, respectively, indicating good agreement with the histological diagnosis of adenoma. The AUC value of this criterion alone was found to be comparable to that of pit appearance (round vs. not round) (0.81 vs. 0.87; $P=0.20$). (Table 2).

c) Vessel domain descriptor

Pericryptal and/or lacy vessels With application of the LOOCV method, the performance of the vessels criterion alone was good, with an AUC, sensitivity, specificity, PPV, and NPV of 0.80, 84.5%, 74.2%, 88.2%, and 66.7%, respectively. The AUC resulting from the combination of pit appearance, featureless

► **Table 2** Summary of the area under the curve (AUC) and measures of diagnostic performance of the individual BASIC descriptors¹ for predicting adenomatous histology. Models were trained and tested using a leave-one-out cross-validation.

	AUC (95%CI)	Sensitivity (95%CI), %	Specificity (95%CI), %	Positive predictive value (95%CI), %	Negative predictive value (95%CI), %
Surface domain					
Mucus: yes/no ²	0.50 (0.33–0.69)	91.5 (69.0–98.6)	41.9 (22.6–64.5)	73.6 (78.4–84.0)	70.0 (44.6–91.7)
Surface: regular/irregular ³	0.68 (0.57–0.79)	62.0 (38.0–78.0)	88.5 (61.3–100)	88.5 (80.8–100)	47.9 (39.0–59.2)
Pits					
Featureless ⁴	0.81 (0.70–0.91)	80.3 (67.8–90.1)	84.0 (71.1–96.8)	92.6 (86.2–98.0)	64.5 (53.5–78.8)
Pits: non-round/round	0.87 (0.80–0.96)	74.6 (63.4–94.4)	93.5 (67.0–100)	96.0 (86.7–100)	61.9 (52.6–87.0)
Distribution: hetero/homogeneous	0.81 (0.71–0.91)	83.1 (69.0–93.0)	77.4 (61.3–90.3)	90.0 (83.6–95.0)	67.5 (54.5–82.1)
Vessels					
Vessels: not present ^{5,6} or lacy/pericryptal	0.80 (0.65–0.87)	84.5 (69.0–89.0)	74.2 (61.0–93.0)	88.2 (79.3–95.0)	66.7 (49.0–81.2)

¹ Accuracy values refer to each of the individual BASIC descriptors in isolation.

² Accuracy values refer to no mucus as predictor of adenomatous histology.

³ Accuracy values refer to "irregular" as a predictor of adenomatous histology.

⁴ Accuracy values refer to no featureless as predictor of adenomatous histology.

⁵ Includes featureless cases.

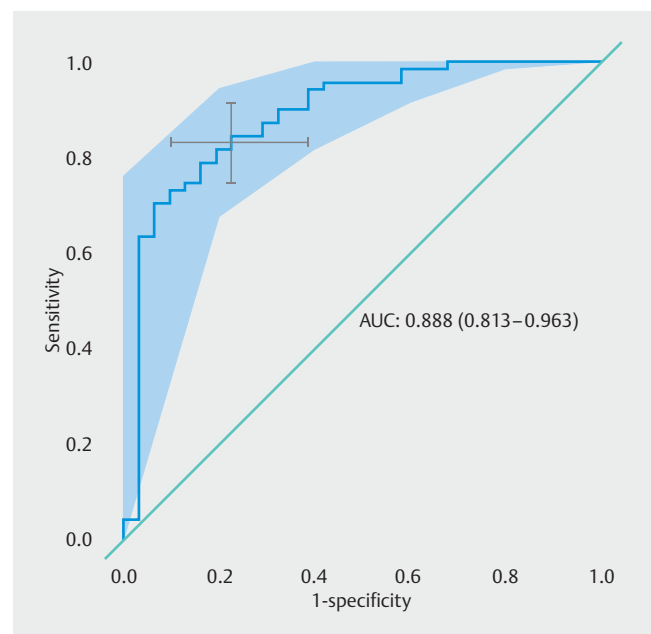
⁶ Accuracy values refer to pericryptal as predictor of adenomatous histology.

appearance, and vessel descriptors (0.87, 95%CI 0.81–0.96) was significantly higher than that for the combination of the surface descriptors (0.76, 95%CI 0.66–0.85; $P=0.009$).

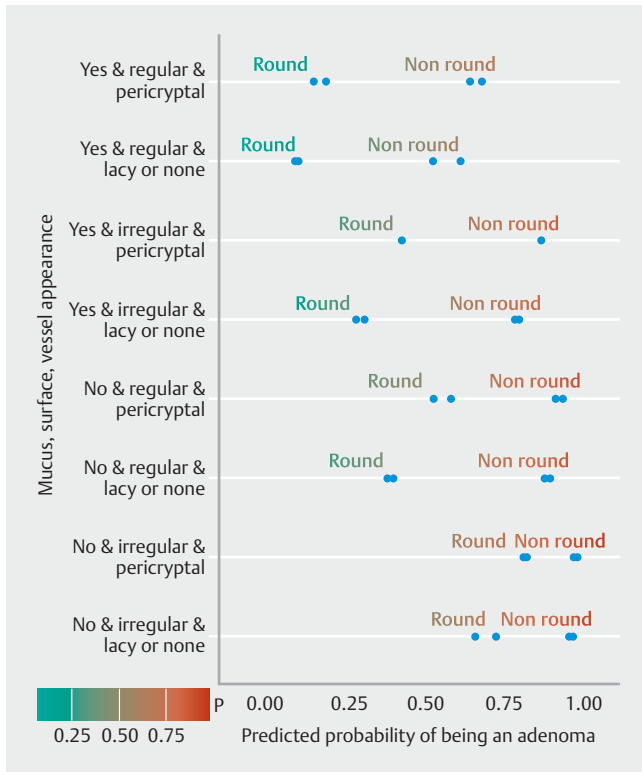
Predictive performance of combining the BASIC domains: a multivariable model to predict adenomas

To compare the predictive ability of different subsets of the descriptors, a series of ROC curve analyses were performed and differences in the AUCs obtained by LOOCV were calculated. The final model including polyp surface, pit appearance, featureless appearance, and vessels gave an AUC of 0.89 (95%CI 0.81–0.96) when tested using LOOCV (► **Fig. 2**). The AUC resulting from the final model was significantly higher than those obtained with other descriptor subsets, indicating that all descriptors were informative (**Fig. 2s**). The ROC analysis identified 0.58 as the best cutoff point. A probability of 0.58 gave a sensitivity of 87.0% (95%CI 69.0%–94.0%) and a specificity of 84% (95%CI 71.0%–94.9%).

► **Fig. 3** shows the predicted probability of an adenoma based on the model. Polyps with mucus, featureless appearance, and no or lacy vessels (with either round or non-round pits) have a lower probability of being an adenoma than those with no mucus, irregular shape, and pericryptal vessels (either round or non-round pits). Round pits suggest a lower probability of a polyp being an adenoma than non-round ones assuming all other descriptors remain the same.



► **Fig. 2** Receiver operating characteristic curve showing the area under the curve (AUC) and 95% confidence interval (CI) for the final model including pit appearance, vessel type, mucus presence, and surface regulatory descriptors. The leave-one-out cross-validation AUC was 0.89 (95%CI 0.81–0.96).



► **Fig. 3** Model showing predicted probability (*P*) of a lesion being an adenoma. Red colors indicate high probabilities, while green colors indicate low probabilities.

► **Table 3** New types A (adenomatous) and H (hyperplastic) of the BASIC classification. Descriptors for each category are listed. Descriptors in bold were agreed as defining “major” criteria as they were strongly associated with the histological outcome at regression analysis.

	Type A	Type H
Surface	Irregular surface	Regular surface
	No mucus	Mucus
Pit	Round (non-dark) or non-round pits	Featureless
		Round dark or non-dark pits
	Heterogeneous pit distribution ¹	Homogeneous pit distribution
Vessel	Pericryptal vessels (A)²	No or lacy vessels
		Pericryptal vessels (H) ²

¹ Heterogeneous is defined as pits that are irregular in size or a combination of different (Kudo-based) pit patterns.

² Non-continuous or thick pericryptal vessels are typical of adenomas, while thin and continuous pericryptal vessels are typical of hyperplastic lesions.

Definition of new BASIC-based predictive rules for diagnosis of adenoma vs. hyperplastic polyp

According to the strength of prediction measured in the full model, individual descriptors of the three domains were divided into major and minor, and assigned to the newly defined types A (i.e. adenomatous) and H (i.e. hyperplastic) of the BASIC classification, as listed in ► **Table 3**.

While non-round pits were identified as a major feature for type A, and a featureless or round appearance with dark pits was identified as a major feature for the type H, we searched for additional consensus for lesions with round (non-dark) pits and with pericryptal vessels, as both features were weak predictors for a specific histology (► **Fig. 4**). It was then decided to further characterize pericryptal vessels in the adenomatous (non-continuous, thick; major criteria) and hyperplastic types (continuous, thin, usually depicted with zoom), and to incorporate these into the classification. It was also decided that a diagnosis could be rated as being high confidence only when at least one major criterion was present, as well as when the quality of the image allowed definition of the three main domains (surface, pit, and vessel) of the BASIC classification.

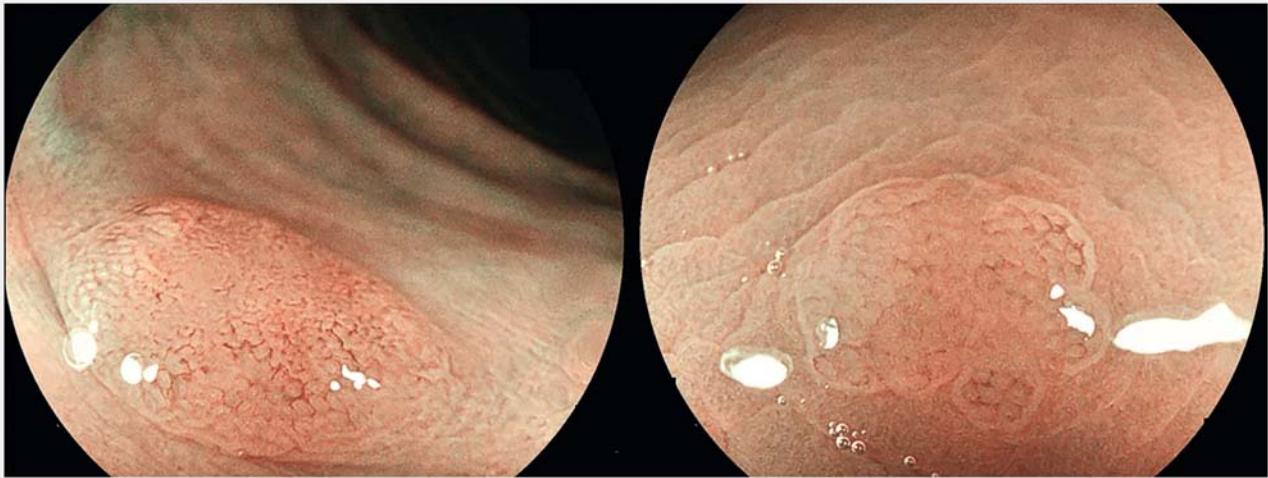
Diagnostic accuracy of experts for the diagnosis of adenoma

The results of the second phase (1913 observations) were included in this subanalysis. Overall, 992 (51.9%) observations were assessed using the BASIC classification with BLI and the remaining 921 (48.1%) with WLI, while 874/1913 (45.7%) were assessed using videos and 1039/1913 (54.3%) using still images. In addition, 944 (49.3%) were assessed with optical magnification, and 969 (50.7%) without. Overall, 1653/1913 observations (86.4%) – including 89.1% of BLI and 83.5% of WLI observations – received a “high” confidence of diagnosis.

The accuracies of individual endoscopists for adenoma diagnosis are reported in **Table 5s**. Among all experts, the diagnostic accuracy for the diagnosis of polyp histology with BLI was significantly superior to that estimated with WLI (90.0% vs. 80.3%). The accuracies with BLI were 90.3% (95%CI 86.3%–93.2%) and 77.7% (95%CI 61.1%–88.6%) for polyps that had been diagnosed with high and low confidence, respectively. The corresponding values using WLI were 83.7% (95%CI 77.3%–87.9%) and 67.3% (95%CI 51.3%–80.1%), respectively (► **Table 4**).

Multivariable model of the accuracy for diagnosis of adenomas

All two-way interactions between light type, polyp confidence, and zoom were non-significant and therefore were not included in the final model. In multivariable analysis, BLI (vs. WLI: OR 2.1, 95%CI 1.6–2.6) and the confidence level for polyp assessment (high vs. low: OR 5.0, 95%CI 3.4–7.1) were significantly associated with the accuracy of diagnosis of polyp histology. No association was found for the use of zoom (with vs. without: OR 1.14, 95%CI 0.90–1.43).



► **Fig. 4** Endoscopic views showing: **a** an adenomatous polyp; **b** a hyperplastic polyp. Both types present with a homogeneous appearance of round (non-dark) pits and pericryptal vessels. As these descriptors were shared by the two different histological categories, new definitions for pericryptal vessels that were distinct for each of the two polyp types were provided.

► **Table 4** Diagnostic performance of expert endoscopists for detecting adenomas by light type and confidence score.

	High confidence		Low confidence		Overall	
	BLI	WLI	BLI	WLI	BLI	WLI
Sensitivity	93.8 (89.9–96.9)	79.2 (70.4–85.9)	84.4 (66.6–93.7)	61.0 (42.2–77.1)	92.8 (89.8–95.0)	75.9 (69.7–81.1)
Specificity	84.3 (73.6–91.2)	92.1 (85.0–96.0)	70.5 (45.3–87.3)	82.8 (64.3–92.6)	82.1 (73.0–88.7)	90.1 (83.7–94.2)
PPV	92.9 (88.4–95.7)	95.3 (91.6–97.4)	77.0 (44.1–93.4)	86.7 (60.8–96.5)	91.9 (87.9–94.7)	94.2 (91.0–95.4)
NPV	85.0 (78.5–90.0)	67.3 (58.5–75.1)	77.1 (60.6–88.1)	55.4 (44.0–66.3)	83.2 (78.2–87.2)	63.5 (58.0–68.5)
Accuracy	90.3 (86.3–93.2)	83.7 (77.3–87.7)	77.7 (61.1–88.6)	67.3 (51.3–80.1)	90.0 (86.0–91.4)	80.3 (76.0–83.9)

BLI, blue-light imaging; WLI, white-light imaging; PPV, positive predictive value; NPV, negative predictive value.

Discussion

When adopting an analytical methodology, individual surface and pit/vascular descriptors showed different strengths in the prediction of histology for <10-mm colorectal polyps, resulting in a clinically relevant hierarchy between poor-to-fair and good-to-excellent predictors for optical diagnosis with BLI technology, as shown by the wide range in AUCs (0.50–0.87) for the individual domains. This led to a stratification between major and minor criteria when clinically defining the new classes of the BASIC classification. When integrating the different descriptors, a synergistic benefit between surface and vascular/pits domains was observed, leading to a 90.3% endoscopist accuracy for high confidence diagnosis with BLI. This was further supported by a good-to-excellent power of discrimination when a regression model based on these descriptors was tested, resulting in an AUC of 0.89. The results of this model also indicated that optical diagnosis should not be considered to be a discrete black-and-white discrimination between adenomatous and hyperplastic histology, but rather a continuum of prediction prob-

abilities represented by all the possible combinations between surface and pit/vascular criteria.

The results of our study are relevant for several reasons. First, the innovative approach of combining surface and pit/vascular descriptors in the same BASIC classification resulted in a clear benefit in terms of accuracy. When restricting our analysis to surface descriptors, such benefit was mainly related to an irregular appearance of the surface of the adenomas, indirectly confirming the predictive strength of the previously described “valley sign” [13]. We preferred the term “irregular” to “valley sign” in order that we can incorporate additional findings from other categories, such as sessile serrated polyps, in the next validations of BASIC. The downgrading of the role of mucus – as shown by its poor discrimination power – is likely to be related to the exclusion of sessile serrated polyps from our study, as this criterion has been mainly associated with this particular diagnosis in the “WASP” classification [14].

We showed a hierarchy in terms of strength of prediction between pit/vascular, on one side, and surface domains, on the other. Therefore, our data argue against a high confidence di-

agnosis purely based on surface criteria, as the addition of pit/vascular descriptors substantially improved the AUC of the model.

In addition, our quantitative analysis showed a high predictive strength of non-round pits for adenomatous histology, on one side, and of featureless appearance or round with dark spots for hyperplastic polyps, on the other. Our regression model also indicated that some pits/vascular descriptors – i. e. round (non-dark) pits and pericryptal vessels – tend to overlap between the two different histological types. This is likely to be related to the systematic use of optical magnification in our study, which showed a clear pit and vascular pattern in most hyperplastic polyps, differing from the dominant featureless appearance reported in previous classifications based on non-magnified images [9]. This led us to a clinically relevant redefinition of the pericryptal vessels according to each histology, as well as to the incorporation of a heterogeneous distribution of the pits as a predictor for an adenomatous histology.

Finally, we redefined the level of confidence according to the presence of at least one major criteria of the BASIC classes to prevent a clinical misprediction when only weak criteria were identified. Despite this, approximately 90% of predictions were given with high confidence when using BLI. Finally, we showed the clinically relevant superiority of BLI over WLI, confirming the role of electronic chromoendoscopy as the clinical standard for strategies based on optical diagnosis.

The main limitation of our study is the artificial setting adopted to define the BASIC classes. However, this was critical for the analytical and quantitative approach we developed. The main biases that may have affected the study are represented by operator and selection bias. Operator bias relates mainly to the experience of the endoscopists in correctly positioning the lesion in front of the lens, also focusing on the most discriminant characteristics of the lesion. Selection bias is related to the fact that non-consecutive lesions were included. Therefore, we cannot exclude that lesions somewhat suboptimal for the purposes of this study – i. e. in an uncleaned colon or difficult position – were not included.

In addition, real-life assessment is different from an artificial setting for the multiple constraints related to patient- and technique-specific factors, such as time-limitation, patient intolerance, and unstable position. Future studies will validate BASIC classification in an *in vivo* setting. Additionally, our prediction model was not externally validated, but instead was validated internally using cross-validation. Although the results from this study are encouraging, this study should be considered a first step toward the goal of validating the BASIC criteria. Further validation studies are required to confirm the present findings and to determine the reliability of the BASIC model and its diagnostic performance in new polyp datasets.

In conclusion, an analytical quantification of the strengths of prediction of individual surface and pit/vascular descriptors for optical diagnosis with BLI led us to the development of new classes of the BASIC classification to differentiate between hyperplastic and adenomatous polyps of <10 mm with favorable effects on accuracy and confidence levels.

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Competing interests

R. Bisschops has received speaker's fees from Pentax, Olympus, and Fujifilm, and research support from Olympus and Pentax. C. Hassan has equipment on loan from Fujifilm. The remaining authors have no conflicts of interest to declare.

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