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Appendix Tables e1 – e7
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ABSTRACT

Background and study aim Advanced endoscopic imaging has revolutionized the characterization of lesions during colonoscopy. The aim of this study was to create a new classification for differentiating subcentimetric hyperplastic and adenomatous polyps, and deeply invasive malignant lesions using blue-light imaging (BLI) with high definition, with and without optical magnification, as well as to assess its interobserver concordance.

Methods A video library consisting of 48 videos/still images (with/without optical magnification) from 24 histologically verified polyps/cancer with BLI was prospectively created. In the first step, seven endoscopists with experience in electronic chromoendoscopy reviewed 12 BLI videos/still images with/without magnification representative of the different histotypes, and individually identified possible descriptors. In the second step, these descriptors were categorized and summarized with a modified Delphi methodology. In the third step, the seven endoscopists independently reviewed the remaining 36 videos/still images with/without optical magnification, and the interobserver agreement for the new descriptors was assessed. The interobserver agreement between endoscopists was assessed using Gwet's AC1.

Results By reviewing the initial 12 videos/still images, 43 descriptors were proposed. By a modified Delphi process, the endoscopists eventually agreed on summarizing 12 descriptors into three main domains. The main domains identified were: polyp surface (mucus, yes/no; regular/irregular; [pseudo]depressed, yes/no), pit appearance (featureless, yes/no; round/nonround with/without dark spots; homogeneous/heterogeneous distribution with/without focal loss), and vessels (present/absent, lacy, pericryptal, irregular). Interobserver agreement for the polyp surface domain appeared to be almost perfect for mucus (AC1 0.92 with and 0.88 without optical magnification), substantial for the regular/irregular surface (AC1 0.67 with and 0.66 without optical magnification). For the pit appearance domain, interobserver agreement was good for featureless (AC1 0.9 with and 0.8 without optical magnification), and round/nonround (AC1 0.77 with and 0.69 without optical magnifica-

tion) descriptors, but less consistent for the homogeneity of distribution (AC1 with/without optical magnification 0.58). Agreement was almost perfect for the vessel domain (AC1 0.81 – 0.85).

Conclusions The new BASIC classification takes into account both morphological features of the polyp, as well as crypt and vessel characteristics. A high concordance among the observers was shown for most of the summarized descriptors. Optical magnification had a beneficial effect in terms of interobserver agreement for most of the descriptors.

Introduction

Colorectal cancer (CRC) represents a major cause of morbidity and mortality in Western countries [1, 2]. Screening has been shown to reduce CRC incidence and mortality [3, 4], and organized programs have been widely implemented.

Colonoscopy is currently regarded as the "gold standard" for the detection of polyps and cancers in the colon [5]. The efficacy of colonoscopy in preventing CRC has been mainly attributed to the removal of adenomas [6, 7]. However, the removal of hyperplastic polyps has been generally regarded as a "false-positive" result, except for larger hyperplastic or other serrated lesions. Because of the suboptimal accuracy of white-light endoscopy in predicting polyp histology, endoscopists are forced to remove all detected polyps for pathological characterization. However, this "resect-and-characterize" policy has several drawbacks. The cost of pathological examination for small hyperplastic polyps negatively affects the cost-effectiveness of the procedure [8, 9]. This is worsened by the evidence that the possibility of harboring a hyperplastic histology is much higher in the small lesions (< 10 mm) than in the large lesions, and it is also higher in diminutive polyps (≤ 5 mm) than in polyps of 6 – 9 mm. Conversely, the prevalence of advanced neoplasia and invasive cancer is associated with polyp size, being extremely infrequent in diminutive adenomas [10, 11]. Diminutive and small polyps account for over 80 % of all the polypoid lesions [10, 12]. Thus, the clinical outcome of referring small and diminutive polyps to pathology is marginal, whereas the exploitation of human and financial resources is substantial.

The field of advanced endoscopic imaging, which aims to reliably predict histology of colorectal lesions based on endoscopic features [13 – 16], was revolutionized by the development of electronic or virtual chromoendoscopy. In order to differentiate between neoplastic (adenomatous) and non-neoplastic (hyperplastic) lesions, chromoendoscopy exploits the neo-angiogenesis of neoplastic lesions. In a recent meta-analysis including all of the available technologies, promising results were reported for the differentiation of different histologies [17]. This has prompted the development of the "resect-and-discard" strategies, with no resection and/or histopathology assessment being undertaken for clinically irrelevant diminutive lesions [18]. In addition, chromoendoscopy-based characterization has recently been shown to differentiate between superficial and deeply invasive neoplasia [19], in alignment with different types of endoscopic interventions, such as endoscopic submucosal dissection [20, 21], and surgical referrals.

In vivo endoscopic characterization of polyps by chromoendoscopy has been mainly based on vascular and surface patterns, as summarized in the narrow-band imaging (NBI) International Colorectal Endoscopic (NICE) classification [22]. For instance, a diminutive polyp is mainly identified as hyperplastic when characterized by a pale color in the absence of surface and vascular patterns [22]. Despite being prospectively validated, the NICE classification offered suboptimal performance when tested in a real-life setting [23]. Meanwhile, new evidence supported the usefulness of morphological criteria in differentiating between polyps. Clouded surface, indistinct borders, and irregular shape were shown in vivo to characterize a sessile serrated polyp (SSP) [24]. More recently, a slight depression with sloppy edges and preservation of the vascular pattern has been shown to be highly specific for small and diminutive adenomatous polyps [25].

Additional uncertainty in the field of in vivo polyp characterization is represented by the technology adopted. For instance, the NICE classification was developed exclusively for the NBI technology [22], and it did not appear to be fully reproducible when a different technology was used [26]. In addition, such classification was based only on images obtained without magnification [22]. Nowadays, optical magnification, in association with high definition, is spreading in Western countries, similarly to the expansion seen several years ago in Japan. There is also uncertainty over whether the use of video rather than still images would affect the robustness of chromoendoscopy-based classifications, as this represents a scenario that is closer to real-life assessment.

The aim of our study was to create a new classification for differentiating between subcentimetric hyperplastic and adenomatous polyps, as well as between superficially and deeply invasive lesions by using blue-light imaging (BLI) with high definition, with and without optical magnification, as well as with both still images and videos. We also aimed to assess the interobserver agreement across the participating endoscopists for the final descriptors.

Methods

A video library of polyps < 10 mm, as well as larger lesions, characterized with BLI technology, was prospectively created for the purpose of this study. Seven experienced endoscopists revised these videos and still images in order to identify variables asso-

ciated with polyp histology. All institutions participating in this noninterventional clinical study obtained the appropriate institutional review board approval (ICH 477/16, date: 1/12/2016).

Study sample

The images and videos were taken from consecutive adult patients who were referred to undergo elective outpatient colonoscopy between June and December 2016. Study exclusion criteria were inflammatory bowel disease, a personal history of polyposis syndrome, diverticulitis or toxic megacolon, and a history of radiation therapy to the abdomen or pelvis. Patients with a history of severe cardiovascular, pulmonary, liver or renal disease, as well as those with coagulation disorders or use of anticoagulants were also excluded.

Technology

BLI is based on the direct (i. e. not filtered) emission of blue light with short wavelength (410 nm), which is selectively absorbed by hemoglobin. Optical magnification allows gradual zoom of up to × 135. However, only low optical magnification was used for the purpose of the present study.

Video library

Seven expert endoscopists recorded high definition still images and videos of consecutive polyps diagnosed during the study period. All endoscopies were performed with Fujifilm colonoscopes series ELUXEO TM 700 with BLI enhancement system (ELUXEO, VP-7000, BL-7000; Fujifilm, Tokyo, Japan). The following records were made for each lesion.

1) 5 – 10 second video with BLI without optical magnification
2) 5 – 10 second video with BLI with optical magnification
3) 2 – 3 still images with BLI with optical magnification
4) 2 – 3 still images with BLI without optical magnification.

All polyps were resected and sent for histopathological examination, the results of which were used as the gold standard for our analysis. Histopathological assessment was performed by experienced gastrointestinal pathologists according to the revised Vienna classification [27].

New classification

During a meeting of the seven endoscopists in Munich in January 2017, the following actions were undertaken.

Step 1 – A PowerPoint presentation summarized the available chromoendoscopy classifications from Western or Asian literature, including NICE [22], Japan NBI Expert Team (JNET) [28], Sano [29], Hiroshima [30], and the workgroup serrated polyp and polyposis classification (WASP) [24].

Step 2 – 12 videos/still images (6 with and 6 without optical magnification) from 6 colorectal lesions representative of different type of polyps were reviewed. Each endoscopist described, in his own words, what features/descriptors were present. From this, a cumulative list of descriptors was generated.

Step 3 – A modified Delphi process (required agreement: > 80 %) was used to summarize and define the final descriptors. Structured discussion and voting were used to assure equal participation and to achieve consensus [31]. At least two rounds of voting were undertaken to accept or ignore certain descriptors and definitions, with agreement of > 80 % required for acceptance. If agreement was not achieved after the first voting, the descriptors and definitions were adapted until final rejection or acceptance was obtained after the second voting round. In the final step, accepted descriptors and definitions were summarized into domains and subdomains for assessment; these were also discussed and required > 80 % agreement in order to be accepted.

Step 4 – The abovementioned descriptors were incorporated into an assessment algorithm using Excel.

Step 5 – The described descriptors were reassessed for the six polyps that were used for developing the descriptors, with feedback by each member.

Step 6 – interobserver agreement was assessed using a series of 36 videos/still images (18 with and 18 without optical magnification) from 18 colorectal lesions. To prevent operator-related bias, each endoscopist rated only the videos/still images recorded by the other six endoscopists; these were viewed in a random sequence.

Study outcomes

Assessment of interobserver agreement involved comparison of interpretations with and without optical magnification for each study variable. For this purpose, video and still images were considered as a single asset. Accuracy was not an end point in this meeting, in order to allow the endoscopists to focus purely on individual descriptors, without any interference/anticipation of an eventual clinical classification.

Data analysis

interobserver reliability for the final descriptors was calculated using the alternative chance-correlated coefficient (AC1) statistic, with 95 % confidence intervals (CIs) [32 – 34]. Although the kappa statistic is frequently used to test interobserver reliability (i. e. measurement of the extent to which raters assign the same score for the same variable), it does have some limitations. In particular, the kappa statistic is affected by the prevalence of the finding under consideration to a similar extent as predictive values are affected by the prevalence of the considered disease. For rare findings, very low values of kappa may not necessarily reflect low rates of overall agreement [32 – 34]. The Gwet measure AC1 is supposed to deal with the apparent "paradox" of low agreement values despite a large percentage agreement. Interpretation of the AC1 statistic is similar to the kappa statistic: AC1 ranges from – 1.00 (perfect disagreement) to + 1.00 (perfect agreement), with a value of zero indicating reliability equivalent to chance. Accordingly, interobserver reliability was classified using criteria established by Landis and Koch: less than chance (< 0.00), slight (0.00–0.20), fair (0.2 – 0.40), moderate (0.41–0.60), substantial (0.61–0.80), and almost perfect (0.81–0.99) [32]. An additional level of classification – perfect (1.00) – was also added. Percentage agreement, with 95 % CIs, was also calculated.

The pair-wise AC1 s across all possible pairs of endoscopists and assets were then analyzed using linear regression. Linear regression models were also used for comparing the average AC1 s of interpretation with and without optical magnification.

All evaluations were done using the statistical package R, Version 3.3.2 (2016 – 10 – 31).

Results

Video library creation of BLI cases

Overall, 24 polyps were included in this analysis. These included, 7 hyperplastic polyps (29.2 %), 2 SSPs (8.3 %), 13 adenomas (54.2 %), and 2 invasive cancers (8.3 %; 1 superficial, 1 deep). In addition, 16 polyps (66.7 %) were diminutive (< 5 mm), 5 (20.8 %) were small (6 – 9 mm), and 3 (12.5 %) were large (> 10 mm). Regarding the location, 10 polyps (41.7 %) were located in the rectosigmoid tract, whereas the others were more proximal.

For each polyp, a video and a still image (regarded as a single asset) were recorded, with and without optical magnification, corresponding cumulatively to a video library of 48 cases (24 with and 24 without magnification).

BASIC classification

Step 1

From the review of existing classifications, it was clear that it would be necessary to consider both surface/vascular patterns and morphological criteria, such as the WASP criteria, and other irregularities of the polyp surface.

Step 2

From the review of 12 videos and still images (6 with and 6 without magnification) from 6 colorectal lesions (2 hyperplastic polyps, 2 adenomas, 1 SSP, 1 invasive cancer), 5 main raw descriptors with 43 possible definitions were proposed by the participating endoscopists. These descriptors are cumulatively presented in the **Supplemental material** (Appendix ▶ **Table e1**, available online).

Step 3

After the modified Delphi process, the following domains and subdomains were included in the final classification.

- Surface
  - Presence of mucus
  - Regular/irregular
  - Presence of depression/pseudodepression
- Pit pattern
  - Featureless
  - Type (round/nonround)
  - Round with/without dark spots
  - Distribution (homogeneous/heterogeneous)
    - Heterogeneous with/without focal loss
- Vessels
  - Presence (yes/no)
  - When present
    - Lacy
    - Pericryptal
    - Irregular

Step 4

A simple algorithm to score all of the descriptors for each polyp was created on an Excel file. For each analyzed variable, the ratings were provided by each study endoscopist. A majority rating, which was based on the mode of raters' distribution of scores, was also recorded.

Step 5

To minimize the variability among the endoscopists, analytical definitions of the different possibilities for each descriptor were created, as reported in the **Supplemental material** (Appendix ▶ **Table e2**, available online). Examples on how to apply the BASIC classification on hyperplastic and adenomatous polyps are provided in ▶ **Fig. 1**.

Step 6

Overall, 36 videos and still images (18 with and 18 without magnification) from 18 colorectal lesions (5 hyperplastic, 1 SSP, 11 adenomas, 1 invasive cancer) were reviewed. The ratings provided by each study endoscopist and the majority rating for each analyzed variable are shown in ▶ **Fig. 2**, ▶ **Fig. 3**, ▶ **Fig. 4**, ▶ **Fig. 5**, ▶ **Fig. 6**, ▶ **Fig. 7**. Concordance and degree of agreement between each pair of endoscopists are shown in the **Supplemental material** (Appendix ▶ **Tables e3 – e7**, available online). The results of reliability analysis among all pairs are reported in ▶ **Table 8**. Gwet's AC1 scores show raters, on average, to have substantial and almost perfect reliability for most variables. Polyp characteristics according to the majority rating across the evaluated assets and histology evaluation are given in ▶ **Table 9**.

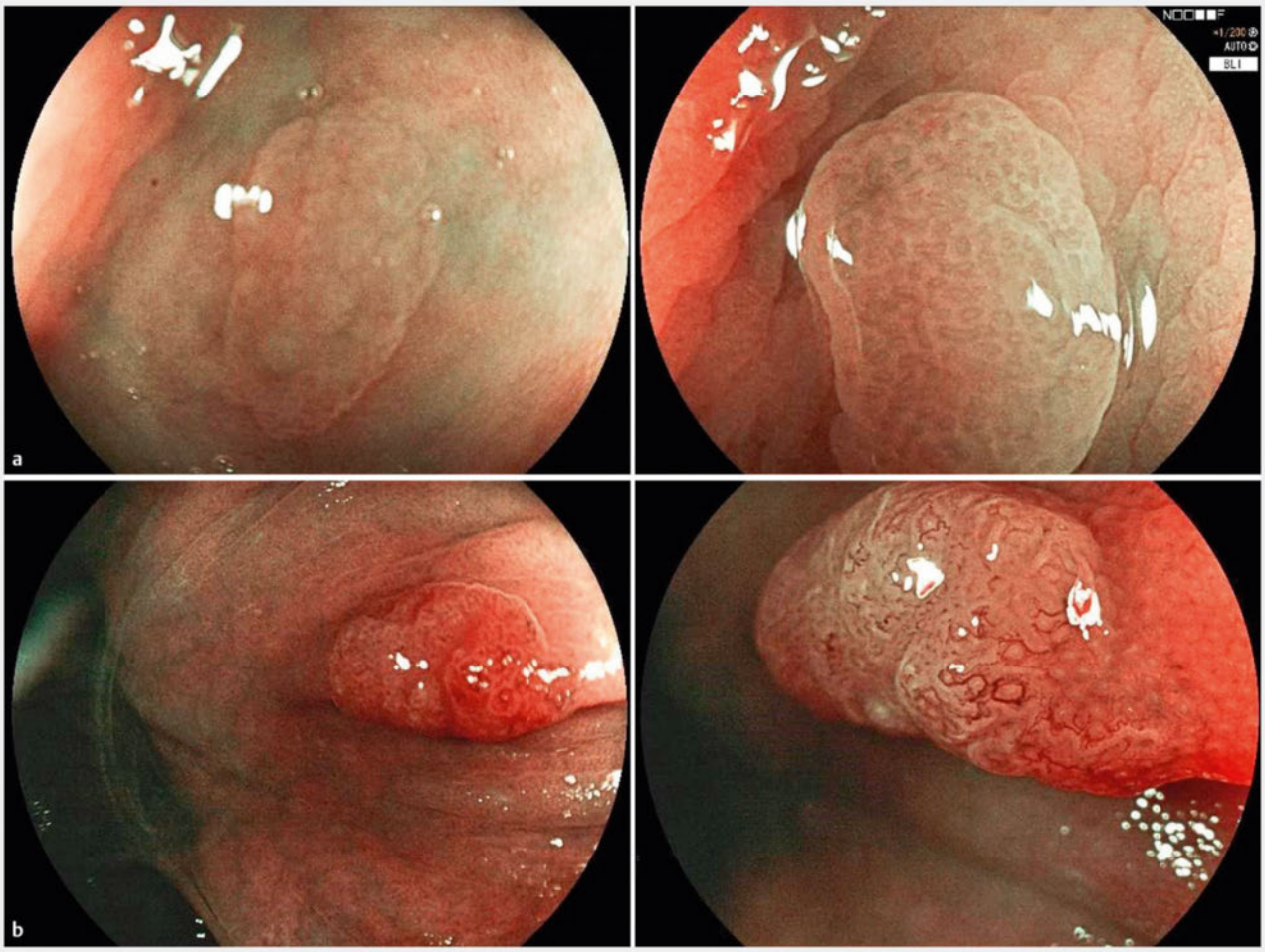
Interobserver agreement for "surface" domains

Mucus

Individual scoring for this descriptor is reported in ▶ **Fig. 2**. According to the majority of the ratings, no polyp was scored as "mucus" present (▶ **Table 9**). Among all pairs of raters, the grading of this descriptor was identical in 30/36 (83.3 %) cases. For this variable, an AC1 of 0.92 (95 %CI 0.89 – 0.95) and 0.88 (95 %CI 0.85 – 0.90) with and without optical magnification, respectively, was observed ($P = 0.002$), corresponding to a percentage of observed agreement of 93 % and 90 % with and without optical magnification, respectively; thus, the reliability was considered to be "almost perfect."

Regular/irregular

Individual scoring for this descriptor is reported in ▶ **Fig. 3**. According to the majority of the ratings, 72.2 % of the lesions – including 90.0 % of the hyperplastic polyps and 66.7 % of the adenomas – were scored as "regular" surface (▶ **Table 9**). Grading of surface appearance (i. e. regular vs. irregular) was identical in 16/36 cases (44.4 %) and showed substantial agreement, with no difference between optical magnification and no optical magnification assessments, corresponding to AC1 coefficients of 0.67 (95 %CI 0.63 – 0.71) and 0.66 (95 %CI 0.58 – 0.68), respectively. No interobserver agreement was measured for the presence of depression/pseudodepression, as this fea-



▶ **Fig. 1** Blue-light imaging technology (BLI). **a** Hyperplastic polyp. Without optical magnification (left), according to the BASIC classification, the surface of this lesion is regular and without mucus, and the pit and vascular pattern are both featureless. With optical magnification (right), no change in the surface and vascular pattern occurs, while a round dark pit appearance with homogeneous distribution becomes visible. **b** Adenomatous polyp. Without optical magnification (left), according to the BASIC classification, the surface of this lesion is irregular and without mucus. With optical magnification (right) a heterogeneous distribution of both nonround and round nondark pits may be observed. In addition, noncontinuous perycriptal vessel may be observed across all the lesions.

ture was present in only 1 – 2 cases according to all of the endoscopists.

Interobserver agreement for "pit pattern" domains

Featureless

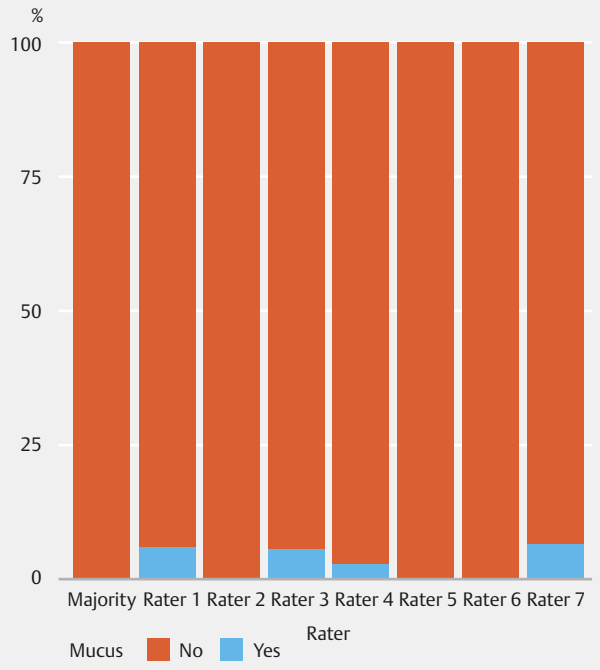
Individual scoring for this descriptor is reported in ▶ **Fig. 4**. According to the majority of the ratings, only 2.8 % of the lesions – corresponding to 1 SSP without optical magnification – were scored as "featureless" (▶ **Table 9**). The grading of featureless appearance was identical in 30/36 cases (83.3 %), and there was substantial to almost perfect agreement without (AC1 0.8; 95 %CI 0.77 – 0.83) and with (AC1 0.9; 95 %CI 0.87 – 0.93) optical magnification (P < 0.001).

Round/Nonround

Individual scoring for this descriptor is reported in ▶ **Fig. 5**. According to the majority of the ratings, 36.1 % of the lesions – corresponding to 90.0 % of the hyperplastic polyps and 12.5 % of the adenomas – were scored as "round" pits (▶ **Table 9**). In 28/36 cases (77.8 %), the grading of polyp type (i. e. round vs. nonround) was identical, and the interobserver agreement was substantial, corresponding to an AC1 of 0.77 (95 %CI 0.69 – 0.83) and 0.69 (95 %CI 0.62 – 0.77) with and without optical magnification, respectively (P = 0.02).

Distribution

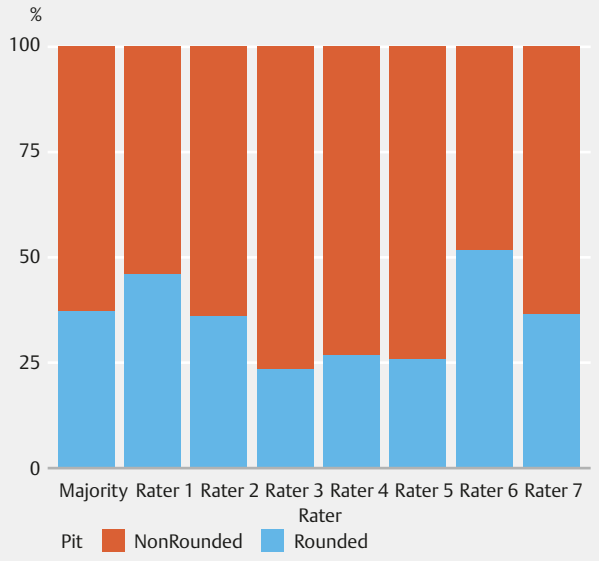
Individual scoring for this descriptor is reported in ▶ **Fig. 6**. According to the majority of the ratings, 88.9 % of the lesions – corresponding to 90.0 %/91.7 % of hyperplastic/adenomatous polyps – were scored as "homogeneous" distribution of the pits (▶ **Table 9**). However, AC1 scores (AC1 0.58 [95 %CI 0.50 – 0.62) with and 0.58 [95 %CI 0.50 – 0.62] without optical magni-



▶ **Fig. 2** Individual scores in percentage for each of the seven endoscopists for the presence of mucus on the polyp surface, as well as the majority rating (mode values across the raters).

▶ **Fig. 3** Individual scores in percentage for each of the seven endoscopists for the regular/irregular descriptor of the polyp surface, as well as the majority rating (mode values across the raters).

▶ **Fig. 4** Individual scores in percentage for each of the seven endoscopists for the presence of featureless appearance in the pit domain, as well as the majority rating (mode values across the raters).



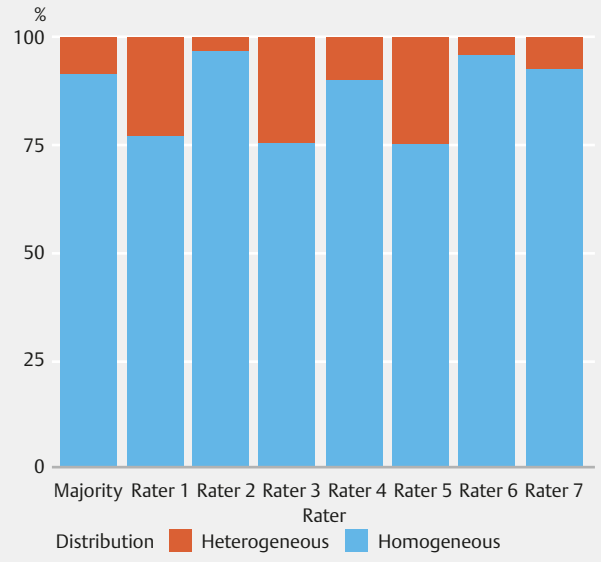
▶ **Fig. 5** Individual scores in percentage for each of the seven endoscopists for the presence of a round type of the pits, as well as the majority rating (mode values across the raters).

fication) indicated that endoscopists achieved only a moderate agreement in rating pit distribution (i. e. homogeneous vs. heterogeneous). Across the study raters, the observed probability of agreement varied significantly from 33.0 % to 83.3 %.

Interobserver agreement for “vascular” domain

Presence (yes/no)

Individual scoring for this descriptor is reported in ▶ **Fig. 7**. According to the majority of the ratings, 86.1 % of the lesions – corresponding to 70.0 % of hyperplastic and 100 % of adenomatous polyps – were scored as presence of “vessels” (▶ **Table 9**). The grading of vessels was identical in 23/36 cases (63.9 %) and



▶ **Fig. 6** Individual scores in percentage for each of the seven endoscopists for the presence of a homogeneous distribution of the pits, as well as the majority rating (mode values across the raters).

▶ **Fig. 7** Individual scores in percentage for each of the seven endoscopists for the presence of vessels, as well as the majority rating (mode values across the raters).

▶ **Table 8** Summary measures for interobserver agreement, as measured by crude agreement. Gwet's AC1, for the final descriptors of the BASIC classification. Data are provided separately for the use of optical magnification.

	With optical magnification			Without optical magnification			P value
	Crude agreement (95 %CI)	Gwet's AC1	95 %CI	Crude agreement (95 %CI)	Gwet's AC1	95 %CI	
Mucus	0.93 (0.91 – 0.95)	0.92	0.89 – 0.95	0.90 (0.88 – 0.92)	0.88	0.85 – 0.90	0.002
Surface pattern (regular vs. irregular)	0.80 (0.78 – 0.83)	0.67	0.63 – 0.71	0.82 (0.80 – 0.84)	0.66	0.58 – 0.68	0.12
Featureless appearance (yes vs. no)	0.91 (0.89 – 0.94)	0.90	0.87 – 0.93	0.86 (9,84 – 0.88)	0.80	0.77 – 0.83	<0.001
Round pit (yes vs. no)	0.88 (9.85 – 0.91)	0.77	0.69 – 0.83	0.84 (0.79 – 0.88)	0.69	0.62 – 0.77	0.02
Distribution (homogeneous vs. heterogeneous)	0.75 (0.72 – 0.79)	0.58	0.50 – 0.62	0.75 (0.72 – 0.79)	0.58	0.50 – 0.66	0.88
Vessels pattern (no vs. yes)	0.86 (0.84 – 0.88)	0.85	0.83 – 0.88	0.88 (0.86 – 0.90)	0.81	0.78 – 0.83	0.02

CI, confidence interval.

the mean observed agreement was 85.8 %. An AC1 of 0.85 (95 % CI 0.83 – 0.88) and 0.81 (95 %CI 0.78 – 0.83) with and without optical magnification, respectively (P = 0.02) indicated almost perfect agreement for this variable.

Discussion

By using a modified Delphi process, we created a new classification for polyp characterization that incorporates the main features of polyp surface with those of pit and vascular patterns. In addition, we showed a substantial to almost perfect agreement across the seven expert endoscopists for most of the descriptors proposed, and demonstrated the additional value of optical magnification in further improving the interobserver agreement. The proposed BASIC classification is relevant for the following four reasons.

First, unlike previous Western and Japanese classifications [19, 22, 28 – 30], we decided to add one specific domain on polyp surface, based on these main assumptions. First, according to the WASP classification, clouded surface, irregular shape,

▶ **Table 9** Distribution of BASIC criteria according to histology evaluation. Each descriptor was scored according to the majority of the ratings from the 36 assets (18 videos and still images with and 18 without optical magnification) taken from the initial population of 18 polyps.[1]

			Hyperplastic (n = 10)	SSP (n = 2)	Adenoma (n = 24)	Total (n = 36)
Polyp surface, n (%)	Mucus	Yes	0	0	0	0 (0)
		No	10 (100)	2 (100)	24 (100)	36 (100)
	Surface	Regular	9 (90.0)	1 (50.0)	16 (66.7)	26 (72.2)
		Irregular	1 (10.0)	1 (50.0)	8 (33.3)	10 (27.8)
Pit appearance, n (%)	Featureless	Yes	0 (0)	1 (50.0)	0 (0)	1 (2.8)
		No	10 (100)	1 (50.0)	24 (100)	35 (97.2)
	Type Round	Yes	9 (90.0)	1 (100)	3 (12.5)	13 (36.1)
		No	1 (10.0)	0[2]	21 (87.5)	22 (61.1)
	Distribution	Homogeneous	9 (90.0)	1 (100)	22 (91.7)	32 (88.9)
		Heterogeneous	1 (10.0)	0[2]	2 (8.3)	3 (8.3)
Vessels pattern, n (%)	Vessels	No	3 (30.0)	2 (100)	0	5 (13.9)
		Yes	7 (70.0)	0	24 (100)	31 (86.1)

SSP, sessile serrated polyp.
[1] 5 hyperplastic, 1 SSP, 12 adenomas. For the purpose of this analysis, the only case of superficially invasive cancer was included in the adenoma category.
[2] One case reported as featureless was not available for the analysis of this descriptor.

and vague borders were associated with a SSP phenotype [24]. Second, the "valley sign" has been shown to be highly specific for an adenomatous phenotype [25]. Third, presence of real depression on polyp surface (i. e. IIc Paris classification) has been intimately related to an increased risk of deep cancer invasion, especially when associated with the loss of pit pattern [35]. When agreeing on the descriptors, we decided to summarize all of this evidence into two main descriptors, namely presence/absence of mucus, and regular/irregular surface. Of note, the concordance among the endoscopists was very high for the "mucus" descriptor, and substantial for the "regular/irregular" descriptor. This slight difference was not fully unexpected, when considering that in a previous study, concordance among the experts on the Paris classification was also only moderate [36].

Second, similarly to the NICE classification [22], we included a "featureless" appearance as a strong predictor of hyperplastic histology, and we also confirmed an almost perfect agreement among the observers. We also emphasized the relevance of the "round" morphology as a predictor of a nonadenomatous phenotype, especially when dark spots are present. However, we decided to add a new descriptor on the possible heterogeneity of the pit pattern, as a possible predictor for an SSP or adenomatous histology. In addition, we anticipated that when such heterogeneity was associated with focal loss of pit pattern, the possibility of a deep submucosal invasion was substantial. However, the interobserver agreement among the endoscopists was only moderate, and it was not affected by optical magnification.

Third, similarly to the NICE classification [22], we included the presence of vessel as a possible feature to differentiate between hyperplastic and adenomatous polyps, but we also anticipated that the use of magnification would have resulted in the possibility of also identifying pericryptal vessels in hyperplastic lesions. In addition, similarly to NICE 3 phenotype [19], we incorporated the possibility of irregular vessels to predict a possible deep invasion. Of note, we demonstrated good concordance among endoscopists on this feature.

Fourth, optical magnification appeared to improve the interobserver agreement for most of the descriptors. This is not unexpected when considering that it substantially increases the chances of visualizing, with high confidence, both pit and vascular patterns.

When looking at the crude distribution of these descriptors among the 36 videos/still images used to measure the interobserver agreement, it would appear that hyperplastic polyps tend to more frequently have a regular polyp surface with round pits homogeneously distributed. However, two unexpected findings occurred in the second phase of the study. First, none of the hyperplastic polyps presented with a featureless pit pattern. This may be explained by the ability of the new endoscopes with high definition and optical magnification to systematically depict the shapes of the pits even in hyperplastic polyps. Second, 70 % of the hyperplastic polyps presented with a visible vessel pattern. Although in most of the cases, it was represented by lacy vessels (data not shown), in a few cases it was also scored as pericryptal vascular distribution. This may also be attributed to the optical magnification, which sometimes allows visualization of a vascular network in hyperplastic lesions. Conversely, adenomatous polyps tended to be more frequently associated with irregular surface, nonround pit pattern, and pericryptal vessels. The fact that the distribution of the pits

was mostly homogeneous may be explained by the fact that most lesions were diminutive or small, so that no high grade dysplasia was present.

There are limitations to the present analysis. First, we did not assess the accuracy of this new classification in predicting in vivo histology, preferring to focus on the interobserver agreement for the individual descriptors. This was to minimize the bias that the possible anticipation of a diagnosis might have had in the minds of the endoscopists when objectively describing the findings that would lead to the new classification. Second, although we included SSP and invasive cancer in the creation of the BASIC classification, our initial validation was mostly based on adenoma vs. hyperplastic < 10 mm lesions. This is due to the fact that our current methodology was based on consecutive cases of colorectal lesions, where the prevalence of SSP and invasive cancer is low. Thus, future studies adopting purposely enriched populations – such as patients with sessile serrated polyposis syndrome – are needed. However, at this stage, our aim was to assess the concordance among observers for the individual criteria irrespectively of histology. Third, this classification was based on BLI technology with optical magnification, and we cannot assure it will be fully reproducible with other technologies. However, the new incorporation of features of polyp surface in the BASIC classification is likely to be independent of the technology itself, albeit possibly linked to optical magnification. Fourth, this study was conducted in an artificial setting, and further validation in humans is needed. In particular, incorporation of optical diagnosis in clinical practice depends on several aspects, such as the availability of high definition endoscopes, adequate training in lesion recognition and characterization, intraprocedural time for optical diagnosis, patient acceptability [37], and legal issues. However, optical diagnosis is now officially recommended by scientific societies [38, 39], and a previous study confirmed its feasibility in clinical practice [40, 41]. Fifth, no direct comparison with previous classifications has been performed. However, unlike the NICE classification [22], we created individual descriptors rather than categories, so that in the future we should be able to assess the accuracy of these individual descriptors, and to select only those strongly associated with each histological diagnosis.

In conclusion, we created a new classification based on BLI technology that incorporates both morphological and pit/vessel findings in order to differentiate between the most important classes of colorectal lesions that may be detected in colonoscopy screening/surveillance. We also showed a high concordance among endoscopists on most of the new descriptors. Additional data are needed to assess the accuracy of this classification in clinical practice.

Competing interests

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