Endoscopic characterization of colorectal neoplasia with different published classifications: comparative study involving CONECCT classification

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ABSTRACT

Background and study aims The aim of this study was to validate the COlorectal NEoplasia Classification to Choose the Treatment (CONECCT) classification that groups all published criteria (including covert signs of carcinoma) in a single table.

Patients and methods For this multicenter comparative study an expert endoscopist created an image library (n = 206 lesions; from hyperplastic to deep invasive cancers) with at least white light Imaging and chromoendoscopy images (virtual ± dye based). Lesions were resected/biopsied to assess histology. Participants characterized lesions using the Paris, Laterally Spreading Tumours, Kudo, Sano, NBI International Colorectal Endoscopic Classification (NICE), Workgroup serrAted polypS and Polyposis (WASP), and CONECCT classifications, and assessed the quality of

images on a web-based platform. Krippendorff alpha and Cohen's Kappa were used to assess interobserver and intra-observer agreement, respectively. Answers were cross-referenced with histology.

Results Eleven experts, 19 non-experts, and 10 gastroenterology fellows participated. The CONECCT classification had a higher interobserver agreement (Krippendorff alpha = 0.738) than for all the other classifications and increased with expertise and with quality of pictures. CONECCT classification had a higher intra-observer agreement than all other existing classifications except WASP (only describing Sessile Serrated Adenoma Polyp). Specificity of CONECCT IIA (89.2, 95 % CI [80.4;94.9]) to diagnose adenomas was higher than the NICE2 category (71.1, 95 % CI [60.1;80.5]). The sensitivity of Kudo Vi, Sano IIIa, NICE 2 and CONECCT IIC to detect adenocarcinoma were statistically different (P < 0.001): the highest sensitivities were for NICE 2 (84.2 %) and CONECCT IIC (78.9 %), and the lowest for Kudo Vi (31.6 %).

Conclusions The CONECCT classification currently offers the best interobserver and intra-observer agreement, including between experts and non-experts. CONECCT IIA is the best classification for excluding presence of adenocarcinoma in a colorectal lesion and CONECCT IIC offers the better compromise for diagnosing superficial adenocarcinoma.

Introduction

Endoscopic characterization of colorectal lesions is required to predict histology and choose the best therapeutic strategy as recommended in European Society of Gastrointestinal Endoscopy guidelines [1]. Different classifications have been proposed to predict histology according to endoscopic findings; the shape of the lesion is described in the Paris classification [2], the mucosal pattern in Kudo's classification [3], and the vascular pattern using virtual chromoendoscopy in Sano's [4]. Recently, classifications combining several color and mucosal and vascular pattern criteria have been described, such as the NBI International Colorectal Endoscopic Classification (NICE) [5], and after this study was designed, the Japan narrow-band imaging (NBI) Expert Team (JNET) classification was described, [6] which corresponds to Sano's and Kudo's classifications, but without consideration of macroscopic shape (Paris, lateral spreading tumor [LST]). However, although the value of combining the Paris, Sano, and Kudo criteria has recently been reported, these classifications do not cover all published criteria [5, 6]. We created a synthetic classification called CONECCT (▶ **Fig. 1**) that groups the different criteria, including both overt (pit and vascular patterns) and covert signs of carcinoma (macronodules > 1 cm, non-granular LST). This was used initially as an educational tool and it was found to allow gastroenterology fellows and gastroenterologists to progress in histological prediction of colorectal lesions presented in the form of images [7]. The published classifications have yet to be evaluated together in a single study. Therefore, we conducted a comparative study to evaluate endoscopic characterization performance of these different classifications in terms of histological prediction and intra-observer and interobserver agreement in a group of gastroenterologists with varying levels of expertise using colorectal lesions.

Patients and methods

Participants

For this multicenter study, We based our sample size on the previous validation study of Ijspeert et al for WASP classification [8] which included 10 gastroenterologists and involved analysis of 45 lesions. We collected 206 lesions representing the five different categories. Because we wanted to compare experts, non-experts, and interns, we proposed to include a minimum of 10 participants in each group, but considering that concordance could be inferior in the group of non-expert gastroenterologists, we doubled the number of participants to 20 non-experts gastroenterologists.

We decided on a panel of 11 experts (including the the expert who collected the images and performed the first prospective evaluation before pathology) to characterize the lesions included in the study. All of the experts were physicians on the Research and Development Committee of the French digestive endoscopy society involved in a training program of endoscopic characterization for colorectal neoplasia (Société Francaise d'Endoscopie Digestive [SFED]). In addition, 20 gastroenterologists from both private and public local hospitals who were interested in colorectal neoplasia characterization and 10 gastroenterology fellows from Lyon University were invited to participate to evaluate the agreement of prediction according to their expertise. Each participant did so voluntarily and provided written consent to participate.

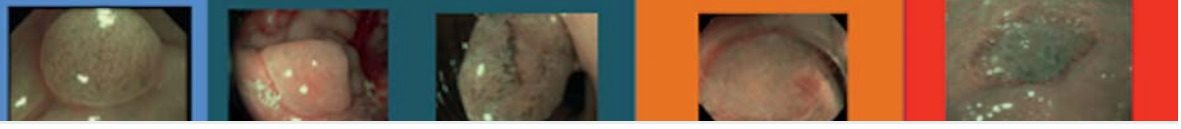
CONECCT classification

To elaborate on this classification, only validated criteria were used and included in a single table, facilitating characterization of all colorectal neoplasia.

Most hyperplastic polyps (CONECCT IH) develop in the rectum and the sigmoid and have the following features described in the NICE classification [5]: color is clear or close to that of the background mucosa; the pits are round with a whitish or clear center; and lacy vessels go across the lesion without surrounding the mucosal pits. These lesions are usually small and multiple and have no risk of becoming cancer. Thus, guidelines do not recommend that these polyps be resected after endoscopic characterization using virtual chromoendoscopy.

Sessile serrated lesions (SSLs) (CONECCT IS) are totally different from hyperplastic polyps and were characterized using specific criteria called WASP [8]. Two of the following criteria were required: mucus cap, irregular edges, cloud aspect, and

CONECCT	IH Hyperplastic	IS Sessile serrated lesions	IIA Adenoma	IIC High risk adenoma or superficial adenocarcinoma	III Deep invasive adenocarcinoma
Macro	Small < 10 mm usually Aspect IIa Paris	Paris IIa or IIb Plateau aspect, unclear margins	Paris Ip, Is Or IIa Rarely depressed	Often IIc Ou IIa + IIc Or LST Non granular Or macronodule (> 1 cm) on granular LST	Often III Or IIc with nodule in the depression **Spontaneous bleedings**
Color (NBI)	Clear or equivalent to background	Variable Yellow mucus (red with NBI)	Darker than background	Often dark	Heterogenous, dark or clear in amorphous area
Vessels (NBI or equivalent)	Lack of visible vessels or thin vessels across the lesion not following pits	Sometimes Absents Dark spots in the bottom of pits	**Regulars** Following pits	**Irregular but persisting** No avascular area	Irregulars Large interrupted vessels Or absent vessels (avascular areas)
Pits (chromo endoscopy real or virtual)	Round shape Whitish pits	Round shape Dark dots (NBI)	Elongated or branched crypts, cerebriform aspect	**Irregular but maintained** No amorphous area	**Absent, amorphous destroyed** Or irregular (clear demarcation)
Resection proposed	No resection	**EN BLOC R0 if possible But PIECE MEAL ok**		**EN BLOC R0** (EMR or ESD (>20 mm)	**Surgery with lymphadenectomy**



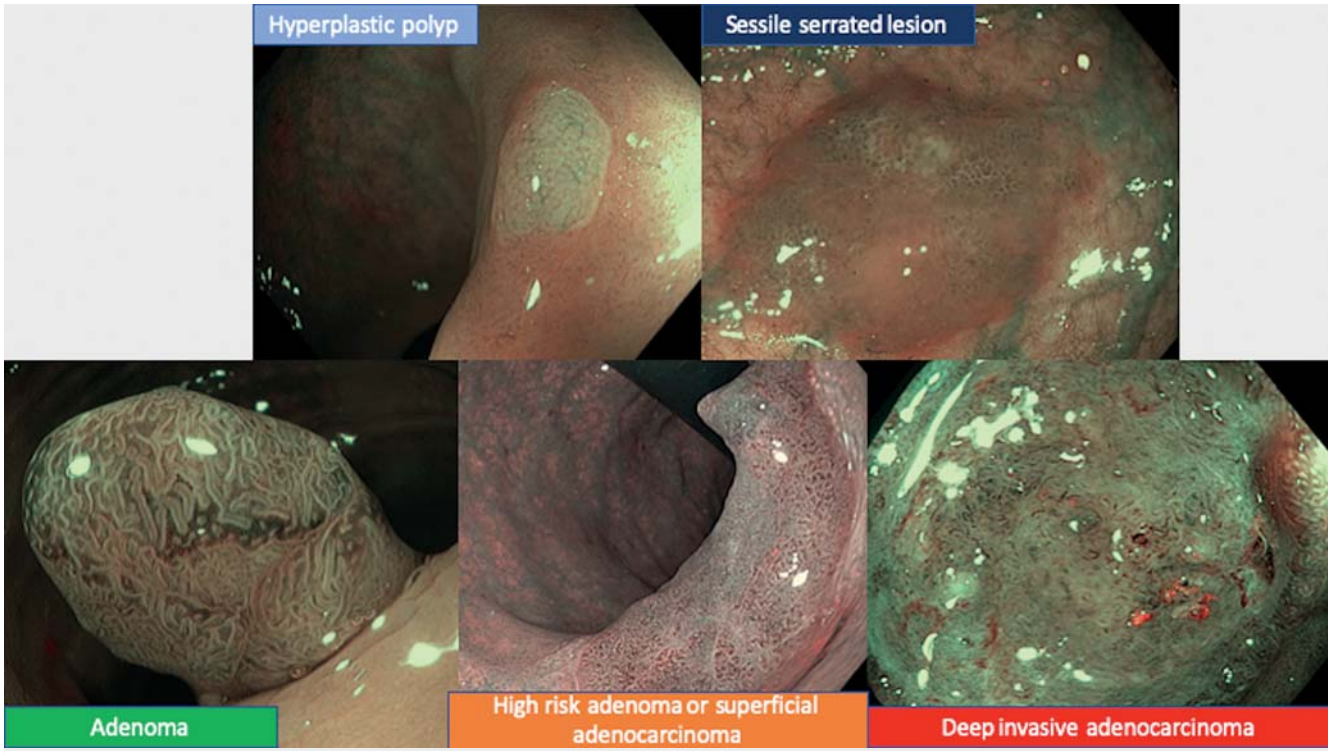
▶ **Fig. 1** CONECCT classification.

round shape pits with dark dot at the center. Because they have a risk of becoming cancer in patients with a *BRAF* mutation, resection is recommended. Nevertheless, most of those lesions are not dysplastic and reports of SSL with an invasive carcinoma component are rare. Thus, low-risk endoscopic resections are recommended using cold snare resection, en bloc if possible or piecemeal endoscopic mucosal resection (EMR), or endoscopic en bloc piecemeal mucosal resection to reduce perforation risk.

Adenomas with very low risk of invasive adenocarcinoma (CONECCT IIa) include those with very low risk of adenocarcinoma (< 1 %), which justifies SSL for low-risk endoscopic resection such as with a cold snare [9, 10], en bloc EMR, or EPMR. These lesions present with adenomas features: Paris macroscopic shape sessile (Is), pedunculated (Ip), flat (IIa or IIb) pit pattern with Kudo types IIIs, IIIL, or IV, and vascular pattern Sano II with regular vessels following pits. These lesions do not meet any of the following criteria of risky adenomas (CONECCT IIc), superficial carcinomas (CONECCT IIc), and deeplly invasive ones. Granular homogenous LST G without any macroscopic nodules are considered as very low risk of adenocarcinoma and can be resected with EPMR [11].

Adenomas with risk of undetected adenocarcinoma and superficial adenocarcinoma (CONECCT IIc) include two different types of lesion. First are lesions without evidence of adenocarcinoma but with high risk (> 5 %) of invasive carcinoma because of their shape. For example, non-granular LST (LST NG) and LST G with large nodules (> 1 cm) have high risk of invasive carcinoma (> 5 %) [11]. Given that risk, en bloc resection is required to ensur that the specimen for pathologic examination is sufficient to avoid underestimation of the invasion depth. The second type are lesions with evidence of adenocarcinoma but without any clear features of deep submucosal invasion. For example, presence of a depressed Paris IIc component, a type V irregular pit pattern (irregular mucosal pattern without any amorphous area and without demarcation line), or irregular vessels without avascular areas (Sano's IIIa) are associated with high risk of invasive components. These lesions should be resected en bloc with margins to avoid a truncated pathology examination and noncurative resection.

With deep invasive adenocarcinoma (CONECCT III), some features are associated with high risk of deep submucosal invasion (> 95 %) and are indicative of a need for first-intention coloectomy with lymphadenectomy. Characteristics include Paris



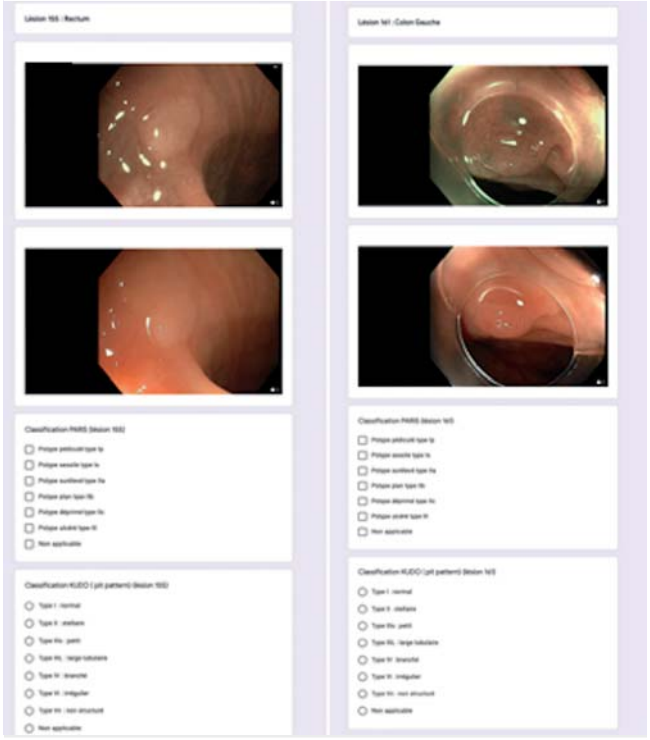
▶ **Fig. 2** Examples of the five different types of lesions in the questionnaire.

shape type III with deep ulcer, nodule or pseudomass into a depressed LST NG and areas without any pit pattern (Kudo Vn) or with irregular pattern in a demarcated area (Vi invasive) or with avascular areas (Sano's IIIB). The avascular and amorphous areas are also included in the NICE classification type III.

Study design

Each participant received an email with a PowerPoint (Microsoft, Redmond, Washington United States) created by the expert who detected and resected the lesions that contained a presentation about the study and an oral explanation on the different endoscopic classifications, including Paris, LST, Kudo, Sano, NICE, and CONECCT classifications. The email also contained a link to the training questionnaire constructed using Google Forms (Google LLC, Mountain View, California, United States); the five lesions referenced were not included in the study questionnaire.

After each participant completed the training questionnaire and then received a second email containing links to six similarly designed study questionnaires about 206 lesions (▶ **Fig. 2**, ▶ **Fig. 3**). The lesion images were recorded prospectively and were different from those used for the first educational study for the CONECCT classification [7]. For each lesion, at least one white light image and one virtual or natural chromoendoscopic image were provided. We also provided the location of the lesion in the colorectum (rectum, descending, transverse, or ascending colon). Participants were asked to complete the questionnaires in a certain order, which was random to avoid any learning bias between the first and last lesions characterized. All the classifications were provided in a pdf in the first email sent to the participants, who could use this material at any point during the study. The 11 experts independently completed the six questionnaires in a dedicated session in Paris. The



▶ **Fig. 3** Example of questions using Google form.

other 30 participants were able to complete the questionnaires on their own at home, but they had to reply within 1 week (to avoid any training bias).

Six months later, the first nine volunteers among the 40 participants (3 experts, 3 gastroenterologists, 3 gastroenterology fellows) were asked to complete the same questionnaires (in a different random order) to evaluate intra-observer agreement. Because the study was long, it was not feasible to obtain the participation of all the initial participants. The responses of the first three people who answered from the three subgroups were used for the intra-observer agreement evaluation.

Questionnaires

Physicians had to describe each lesion according to the Paris classification and the classification of LST, which are based on the macroscopic aspect of polyps [2]; Kudo's classification, which is based on the mucosal pit pattern [3, 7]; Sano's classification, which is based on the vascular pattern [4]; the NICE classification, which is based on the combination of color, vascular pattern, and mucosal pattern [5]; the Workgroup serrAted polypS and Polyposis (WASP) classification[8] to diagnose the Sessile serrated adenoma polyp (SSAP) lesions; and the CONECCT classification that combines criteria of the Paris, NICE, Kudo, LST and Sano classifications [4].

For each lesion, they could answer "not applicable" when an image was not sufficient to allow an answer to the question (blurred lesion, missing information). They also were asked to evaluate the quality of the images for each lesion, rating them from 1-very bad to 4-excellent quality.

Study endpoints

The primary endpoint was interobserver agreement when using current endoscopic classifications and the CONECCT classification. Secondary endpoints included interobserver agreement according to the level of expertise (experts, gastroenterologists from private/local hospitals, or gastroenterology fellows) and the quality of endoscopic images. Then, intra-observer agreement according to the level of expertise (experts, gastroenterologists in private/local hospitals, and gastroenterology fellows) was investigated. In addition, the sensitivity and specificity of the classifications for prediction of histology was evaluated, using the answer most frequently given by the participants overall. The categories of classifications evaluated were those that correspond to a specific lesion histology, diagnosed by an expert pathologist in the field: NICE I, Sano I and CONECCT IH for hyperplastic polyps; WASP and CONECCT IS for SSAP; NICE 2 and CONECCT IIA for adenomas; CONECCT IIC, Kudo Vi, NICE 2, and Sano 3a for superficial adenocarcinomas (intramucosal and sm superficial invasion); and NICE 3, Kudo Vn, Sano 3b, and CONECCT III for adenocarcinomas with deep submucosal invasion. For accurate assessment of a specific lesion histology, sensitivity was defined relative to the specific lesion histology, and specificity relative to all other lesion histologies.

Statistical analyses

With 15 % discordant pairs, a significance level of 5 %, and a power of 90 %, 135 observations were needed per group for paired analysis. To confirm that a variety of observers scored the same set of polyps, an inflation factor was calculated using the formula $1+(n-1)\rho$, which is commonly used for clustered matched-pair data. Assuming an intrarater correlation of 0.05 and using 206 observations per participant, the inflation factor was calculated to be three, resulting in at least 2025 observations (10 participants) needed for paired analysis in each subgroup (experts, non-experts and interns). Because the experience of non-expert gastroenterologists could have varied, and because it was feasible, we chose to double the number in that subgroup.

The interobserver agreement was assessed by the Krippendorff alpha coefficient: 1 indicates a perfect agreement, 0 indicates an agreement obtained by simple chance, and a negative coefficient indicates a systematic discordance. The coefficient penalizes deviations more when they are high. Interobserver agreement was estimated for each classification overall, then according to level of expertise, and according to the quality of the images.

Concerning the quality of the photos, for each lesion, the most probable value reported by all the assessors was taken into account.

Intra-observer agreement was assessed with Cohen's Kappa coefficient. A Kappa coefficient was determined for each evaluator and then a mean value calculated for each classification for all participants together, then according to their level of expertise.

Finally, the majority response from evaluators was cross-referenced with the histological result for each lesion, to calculate the sensitivity and specificity (with the associated 95 % confidence intervals [95 %CI]) of the different classifications for detection of hyperplastic polyps, SSAP, adenoma, superficial adenocarcinoma and deep invasive adenocarcinoma. Comparisons of sensitivity and specificity between classifications were performed using a logistic mixed model to take into account multiple evaluations per lesion; the associated *P* values correspond to overall *P* values, i. e. testing if at least one category differs from the others.

Statistical analyses were performed using R software version 4.0.2.

Registration

This study was conducted following the declaration of Helsinki with approval from the Institutional Review Board (Comité d'éthique des Hospices Civils de Lyon, Lyon, France; N°19–107) on 26 August 2019 and was reported to the national clinical trials database in August 2019 (NCT 04048447).

Results

A total of 40 physicians participated; 11 experts, 19 gastroenterologists (among the 20 were invited, one did not participate), and 10 gastroenterology fellows. For intra-observer re-

▶ **Table 1** Impact of the assessor level on interobserver agreement.

Classification							
Krippendorff alpha coefficient	Paris	LST	Kudo	Sano	NICE	WASP	CONECCT
Overall	0.281	0.599	0.490	0.528	0.559	0.682	0.738
Expert	0.356	0.607	0.580	0.589	0.545	0.770	0.799
Gastroenterologist	0.292	0.645	0.500	0.619	0.612	0.657	0.733
Intern	0.209	0.507	0.399	0.341	0.467	0.654	0.692

LST, lateral spreading tumor; NICE, International Colorectal Endoscopic Classification; WASP, Workgroup serrAted polypS and Polyposis; CONECCT, COlorectal NEoplasia Classification to Choose the Treatment; CONECCT, COlorectal NEoplasia Classification to Choose the Treatment.

▶ **Table 2** Impact of image on interobserver agreement.

Classification							
	Paris	LST	Kudo	Sano	NICE	WASP	CONECCT
Krippendorff alpha coefficient							
Overall	0.281	0.599	0.490	0.528	0.559	0.682	0.738
Excellent quality (4)	0.289	0.164	0.843	0.939	0.974	1.000	0.952
Good quality (3)	0.279	0.619	0.494	0.536	0.571	0.729	0.751
Bad quality (2)	0.256	0.330	0.308	0.306	0.283	0.135	0.460

LST, lateral spreading tumor; NICE, International Colorectal Endoscopic Classification; WASP, Workgroup serrAted polypS and Polyposis; CONECCT, COlorectal NEoplasia Classification to Choose the Treatment.

producibility, nine volunteers (3 experts, 3 non-expert gastroenterologists and 3 gastroenterology fellows) among the 40 participants completed the same questionnaires 6 months later.

Among the 206 lesions presented in the study, histology examination revealed that 16 were hyperplastic polyps, 30 were SSAP, 123 were adenomas without any adenocarcinoma of which 90 were low-grade dysplasia (LGD) and 33 in high-grade dysplasia (HGD), 19 were superficial adenocarcinomas, and 18 were deep invasive adenocarcinoma with an invasion of more than 1000 microns in the submucosa.

Regarding quality of photography, there were 18 lesions (8.7 %) with images of quality 2, 181 lesions (87.9 %) with images of quality 3, and seven lesions (3.4 %) with images of quality 4.

The percentage of "not applicable" answers was 0.1 % for the CONECCT classification, 0.2 % for Kudo's Classification and for the Paris classification, 0.3 % for the NICE classification and Sano's classification, 0.4 % for the LST classification, and 1 % for the WASP classification

Primary endpoint: interobserver agreement

The Krippendorff alpha coefficient was 0.281 for the Paris classification, 0.599 for the LST classification, 0.490 for Kudo's classification, 0.528 for Sano's classification, 0.559 for the NICE classification, 0.682 for the WASP classification, and 0.738 for the CONECCT classification.

Secondary endpoints

A better interobserver agreement was found among experts than among gastroenterologists or gastroenterology fellows for the Paris, Kudo, WASP, and CONECCT classifications. In each of the three groups of expertise, the Krippendorff alpha coefficient was higher for the CONECCT classification than for the other five classifications (▶ **Table 1**).

Interobserver agreement was better for very good and good-quality pictures compared to low-quality pictures for all classifications except LST (▶ **Table 2**).

The mean intra-observer agreement was highest for NICE classifications (Cohen's Kappa: 0.69), WASP (Cohen's Kappa: 0.81), and CONECCT (Cohen's Kappa: 0.76). Intra-observer agreement was higher for experts than for gastroenterologists or gastroenterology fellows for all classifications, except Kudo's and Sano's classifications. Intra-observer agreement was higher for gastroenterology fellows in the CONECCT classification (Cohen's Kappa: 0.70) than that of experts for the Paris (Cohen's Kappa: 0.51), LST (Cohen's Kappa: 0.69), Kudo's (Cohen's Kappa: 0.50) and Sano's (Cohen's Kappa: 0.61) classifications (▶ **Table 3**).

Regarding the diagnostic accuracy for histology prediction (▶ **Table 4**), for hyperplastic polyps, the sensitivities of NICE 1, Sano 1, and CONECCT IH were statistically different ($P = 0.045$), with higher sensitivity for NICE 1 and Sano 1 categories (93.8, 95 % CI [69.8;99.8] for both classifications) than for CONECCT IH (87.5, 95 % CI [61.7;98.4]) category; the specificities were also statistically different ($P < 0.001$), higher for CONECCT IH

▶ **Table 3** Intra-observer agreement for each classification: Cohen's Kappa.

	Expert	Gastro	Intern	Total
	N = 3	N = 3	N = 3	N = 9
Paris				
▪ Mean Kappa	0.51	0.49	0.34	0.44
▪ Range	0.32 – 0.60	0.38 – 0.62	0.23 – 0.42	0.23 – 0.62
LST				
▪ Mean Kappa	0.69	0.61	0.57	0.62
▪ Range	0.55 – 0.77	0.50 – 0.69	0.47 – 0.74	0.47 – 0.77
Kudo				
▪ Mean Kappa	0.50	0.51	0.52	0.51
▪ Range	0.31 – 0.65	0.38 – 0.69	0.30 – 0.73	0.30 – 0.73
SANO				
▪ Mean Kappa	0.61	0.56	0.63	0.60
▪ Range	0.52 – 0.72	0.53 – 0.62	0.51 – 0.80	0.51 – 0.80
NICE				
▪ Mean Kappa	0.79	0.64	0.64	0.69
▪ Range	0.73 – 0.85	0.55 – 0.69	0.47 – 0.91	0.47 – 0.91
WASP				
▪ Mean Kappa	0.91	0.80	0.73	0.81
▪ Range	0.90 – 0.92	0.78 – 0.83	0.58 – 0.84	0.58 – 0.92
CONECCT				
▪ Mean Kappa	0.85	0.74	0.70	0.76
▪ Range	0.74 – 0.92	0.71 – 0.75	0.64 – 0.80	0.64 – 0.92

LST, lateral spreading tumor; NICE, International Colorectal Endoscopic Classification; WASP, Workgroup serrAted polypS and Polyposis; CONECCT, COlorectal NEoplasia Classification to Choose the Treatment.

(98.9, 95 % CI [96.2;99.9]; $P<0.001$) than for NICE 1 (82.6, 95 % CI [76.5;87.7]) and Sano 1 (82.1, 95 % CI [75.9;87.3]) categories. For SSAP, there was no difference between the CONECCT IS category and WASP classification in terms of sensitivity and specificity. For all adenomas, combining LGD and HGD, CONECCT IIA category had a significantly higher specificity (89.2, 95 % CI [80.4;94.9]) than the NICE II category (71.1, 95 % CI [60.1;80.5]; $P<0.001$). The converse was found for sensitivity, (91.9, 95 % CI [85.6;96.0]) for NICE II category and (70.7, 95 % CI [61.9;78.6]; $P<0.001$) for CONECCT IIA category. For superficial adenocarcinomas, the NICE 2, Kudo Vi, Sano IIIa and CONECTT IIC categories had statistically different sensitivities ($P<0.001$), the highest one for NICE 2 category (84.2, 95 % CI [60.4;96.6]), and the lowest one for the Vi category (31.6, 95 % CI [12.6;56.6]). The converse was found for specificity, with overall statisticall differences ($P<0.001$) being the highest for the Kudo Vi category (93.6, 95 % CI [89.1;96.6]) and the lowest for the NICE 2 category (35.3, 95 % CI [28.5;42.6]). For CONECCT IIC category, results were intermediary for sensitivity (78.9, 95 % CI [54.4;93.9]) and specificity (83.4, 95 % CI [77.3;88.4]). For deeply invasive adenocarcinomas, there was no difference between CONECCT III, Kudo Vn, Sano 3b, and NICE 3 categories in terms of sensitivity ($P=0.108$).

Discussion

The present study found that the interobserver agreement for the CONECCT classification was higher than for other published classifications, and that this was the case irrespective of the level of expertise. The intra-observer agreement for the CONECCT classification was also higher than for the other classifications, with the exception of the WASP classification. Because the latter pertains only to the histology of SSAP, this was to be expected, as the number of possible disagreements is much lower than for other classifications.

The high interobserver agreement found for the CONECCT can be explained by the use of composite criteria to classify lesions into histological subtypes and whereby a lesion that does not match a precise criterion in a given classification, it can still be assigned to a category in the CONECCT classification by

▶ **Table 4** Diagnostic performance of different classifications able to predict the correct histology using the most frequent answer as reference.

Histology	Category	Sensitivity (%) [95 % CI]	Specificity (%) [95 % CI]
Hyperplastic polyp			
	Sano I	93.8 [69.8; 99.8]	82.1 [75.9; 87.3]
	NICE 1	93.8 [69.8; 99.8]	82.6 [76.5; 87.7]
	CONECCT IH	87.5 [61.7; 98.4]	98.9 [96.2; 99.9]
P value		0.045	< 0.001
SSAP			
	WASP	90.0 [73.5; 97.9]	98.3 [95.1; 99.6]
	CONECCT IS	90.0 [73.5; 97.9]	98.3 [95.1; 99.6]
P value		1.000	1.000
Adenoma			
	NICE 2	91.9 [85.6; 96.0]	71.1 [60.1; 80.5]
	CONECCT IIA	70.7 [61.9; 78.6]	89.2 [80.4 ;94.9]
P value		< 0.001	< 0.001
Superficial adenocarcinoma			
	Kudo Vi	31.6 [12.6; 56.6]	93.6 [89.1; 96.6]
	Sano IIIa	63.2 [38.4; 83.7]	87.7 [82.1; 92.0]
	NICE 2	84.2 [60.4; 96.6]	35.3 [28.5; 42.6]
	CONECCT IIC	78.9 [54.4; 93.9]	83.4 [77.3; 88.4]
P value		< 0.001	< 0.001
Deep invasive adenocarcinoma			
	Kudo Vn	72.2 [46.5; 90.3]	98.4 [95.4; 99.7]
	Sano IIIb	77.8 [52.4; 93.6]	97.9 [94.6; 99.4]
	NICE III	77.8 [52.4; 93.6]	96.8 [93.2; 98.8]
	CONECCT III	77.8 [52.4; 93.6]	97.9 [94.6; 99.4]
P value		0.108	< 0.001

CI, confidence interval; SSAP, sessile serrated adenoma polyp; NICE, International Colorectal Endoscopic Classification; CONECCT, COlorectal NEoplasia Classification to Choose the Treatment; WASP, Workgroup serrAted polypS and Polyposis.

other criteria. Furthermore, the higher number of "not applicable" answers for the other classifications indicates that not all classifications could be used to describe a given lesion, despite the systematic presence of a chromoendoscopy picture. Similarly, the NICE classification, which also uses composite criteria, had better interobserver agreement than Kudo's and Sano's classifications. Furthermore, the worst interobserver agreement was found for the Paris classification, and this was likely because of the multiple choice and resulting combinations. Another point is that the interobserver agreement in the expert group was higher than in the general gastroenterologist group and the gastroenterology fellows group for CONECCT classification, but also for Kudo's, WASP, and Paris classifications. It can be assumed that more experience with these classifications leads to better agreement in endoscopic characterization. Interobserver agreement also increased based on quality of the images in all classifications, and particularly in classifications describing precise details such as microvasculature (Sano) or mucosal pattern (Kudo).

Nevertheless, fewer than 5 % of the images were of very good quality, although they were produced by an expert. This underscores the difficulty of producing high-quality images and we should probably train endoscopists in this regard to improve characterization.

The interobserver agreement for gastroenterology fellows was also better for the CONECCT classification than that between experts for the other classifications (Kudo's, Sano's, LST's, NICE). Because a document with all the classifications was provided to avoid mistakes due to forgotten criteria, with the objective of eliminating bias related to knowledge of the different classifications, understanding the CONECCT classifica-

tion was easier than the current published ones, possibly because of the composite criteria.

A more clinically relevant aspect to consider is evaluation of the performance of the different classifications for prediction of a given histology. When the CONECCT classification used only predictive criteria already used in another classification, as is the case with the WASP classification for serrated lesions or NICE 3 category for deep invasive adenocarcinomas, its performance was good but did not differ from other classifications. Conversely, when it brings composite elements into the classification, such as the macroscopic aspect of the polyp, its performance then was better than other classifications. For example, for hyperplastic polyps, the CONECCT IH category was more specific than the Sano I categories. This difference is probably related to the addition of the CONECCT macroscopic component, which describes a small, slightly elevated (Paris 0-IIa) pearl in addition to the color proposed by NICE 1 category or the pit pattern described by Sano I category. Regarding superficial adenocarcinoma, the NICE II category is more sensitive than the Kudo Vi category for detecting the presence of a superficial adenocarcinoma in the lesion. Conversely, the Kudo Vi category, which testifies to the visible presence of an irregularity zone in the lesion, is logically more specific for diagnosis of superficial cancer than NICE 2 category, which includes adenoma and superficial adenocarcinoma criteria. The CONECCT IIC category seems to be a good compromise, adding overt visible signs of adenocarcinoma (Kudo Vi category) to covert signs of carcinoma (LST NG or LST G with nodule). The strength of CONECCT is also its specificity for predicting the purely adenomatous nature of a lesion when it is classified CONECCT IIA. Thus, a CONECCT IIA lesion is very unlikely to contain adenocarcinoma foci, and this is significantly better than the NICE 2 category for the diagnosis of pure adenoma.

The study, however, HAS several limitations. First, it was a simulation using images produced by an expert endoscopist. Thus, performance could be different in real-life characterization during colonoscopy because it is linked to physician ability to produce very-good-quality pictures and for his or her analysis of the whole lesion. Second, quality of the images in the library varied and physicians could choose "not applicable" when they believe that an image did not permit them to classify the lesion using one of the classifications; nevertheless, this limitation also exists in real life. Third, the use of several classifications at the same time is also an important limitation because answers to the different questions were not independent; however, a comparative study with different groups using different classifications would also lead to bias because the participants would not have exactly the same expertise. A more general point is that the JNET classification was not evaluated because it was not widely used in Europe at the time of the study and added no criteria beyond that in Sano's classification.

Conclusions

In conclusion, the CONECCT classification currently offers the best interobserver and intra-observer agreement regardless of the level of expertise of the operators. This classification is currently a good compromise for detecting a superficial adenocarcinoma in a lesion (CONECCT IIC category) and ruling out the presence of adenocarcinoma in lesions classified CONECCT IIA. Thus, this classification should become a tool of choice for predicting histology for gastroenterologists practicing colonoscopy.

Competing interests

The authors declare that they have no conflict of interest.

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