# ENDOSCOPY

## When and How To Use Endoscopic Tattooing in the Colon: An International Delphi Agreement



Lucía Medina-Prado,\* Cesare Hassan,<sup>‡</sup> Evelien Dekker,<sup>§</sup> Raf Bisschops,<sup>||</sup> Sergio Alfieri,<sup>¶</sup> Pradeep Bhandari,<sup>#</sup> Michael J. Bourke,<sup>\*\*</sup> Raquel Bravo,<sup>‡‡</sup> Marco Bustamante-Balen,<sup>§§</sup> Jason Dominitz,<sup>|||</sup> Monika Ferlitsch,<sup>¶¶</sup> Paul Fockens,<sup>§</sup> Monique van Leerdam,<sup>##</sup> David Lieberman,<sup>\*\*\*</sup> Maite Herráiz,<sup>‡‡‡</sup> Charles Kahi,<sup>§§§</sup> Michal Kaminski,<sup>|||||</sup> Takahisa Matsuda,<sup>¶¶¶</sup> Alan Moss,<sup>###</sup> Maria Pellisé,<sup>\*\*\*\*</sup> Heiko Pohl,<sup>‡‡‡‡</sup> Colin Rees,<sup>§§§§</sup> Douglas K. Rex,<sup>||||||</sup> Manuel Romero-Simó,<sup>¶¶¶¶¶</sup> Matthew D. Rutter,<sup>####</sup> Prateek Sharma,<sup>\*\*\*\*\*</sup> Aasma Shaukat,<sup>‡‡‡‡‡</sup> Siwan Thomas-Gibson,<sup>§§§§§</sup> Roland Valori,<sup>|||||||||</sup> and Rodrigo Jover<sup>\*</sup>

\*Servicio de Medicina Digestiva, <sup>1111</sup>Unidad de Coloproctología, Servicio de Cirugía General, Hospital General Universitario de Alicante, Instituto de Investigación Biomédica Instituto de Investigación Sanitaria y Biomédica de Alicante, Alicante, Spain; <sup>‡</sup>Digestive Endoscopy, Nuovo Regina Margherita Hospital, Rome, Italy; <sup>§</sup>Department of Gastroenterology and Hepatology, Amsterdam University Medical Centers, Location Academic Medical Center, Amsterdam, The Netherlands; Department of Gastroenterology and Hepatology, University Hospitals Leuven, KU Leuven, Belgium; <sup>1</sup>Surgery Department, Fondazione Policlinico A. Gemelli, Istituto di Ricovero e Cura a Carattere Scientifico, Università Cattolica del Sacro Cuore, Rome, Italy; <sup>#</sup>Department of Gastroenterology, Queen Alexandra Hospital. Portsmouth Hospital NHS Trust, Portsmouth, United Kingdom; \*\*Department of Gastroenterology and Hepatology, Westmead Hospital, Sydney, Australia; <sup>‡‡</sup>Department of Gastrointestinal Surgery, \*\*\*\*Gastroenterology Department, Institute of Digestive and Metabolic Diseases, Hospital Clinic, Institut d'Investigacions Biomèdiques August Pi i Sunver, Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas, University of Barcelona, Centro Esther Koplowitz, Cellex Biomedical Research Center, Barcelona, Catalonia, Spain;  $^{\$\$}$ Gastrointestinal Endoscopy Unit, Gastrointestinal Endoscopy Research Group, Health Research Institute (Instituto de Investigación Sanitaria La Fe. NHS: National Health Service), Hospital Universitari i Politècnic La Fe, Valencia, Spain; <sup>III</sup>Gastroenterology Department, VA Puget Sound Health Care System, University of Washington, Seattle, Washington; <sup>¶¶</sup>Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Medical University of Vienna, Wien, Austria; \*\*Department of Gastroenterology and Hepatology, Netherlands Cancer Institute, Amsterdam, The Netherlands; \*\*\*Division of Gastroenterology and Hepatology, Oregon Health and Science University, Portland, Oregon; ##Departamento de Digestivo, Clínica Universitaria de Navarra, Pamplona, Spain; <sup>§§§</sup>Roudebush VA Medical Center, <sup>[[]][]</sup>Division of Gastroenterology and Hepatology, Indiana University School of Medicine, Indianapolis, Indiana; <sup>[[]]]</sup>Department of Gastroenterological Oncology, Maria Sklodowska-Curie Memorial Cancer Center, Institute of Oncology, Warsaw, Poland; <sup>1111</sup>Endoscopy Division, National Cancer Center Hospital, Tokyo, Japan; <sup>###</sup>Department of Endoscopic Services, Western Health, Melbourne Medical School Western Precinct, The University of Melbourne, St. Albans, Victoria, Australia; <sup>±±±±</sup>Department of Gastroenterology and Hepatology, VA Medical Center, White River Junction, Vermont; Dartmouth Geisel School of Medicine, Hanover, New Hampshire; <sup>\$§§§</sup>Department of Gastroenterology, South Tyneside NHS Foundation Trust, South Shields, United Kingdom; \*\*\*\*\* University Hospital of North Tees, Stockton on Tees, United Kingdom; Northern Institute for Cancer Research, Newcastle University, Newcastle-upon-Tyne, United Kingdom; \*\*\*\*\*Department of Gastroenterology and Hepatology, VA Medical Center, University of Kansas School of Medicine, Kansas City, Kansas; <sup>#####</sup>Section of Gastroenterology, Department of Medicine, Minneapolis VA Medical Center, University of Minnesota, Minneapolis, Minnesota; <sup>§§§§§</sup>Wolfson Unit for Endoscopy, St. Mark's Hospital, Harrow, and Imperial College, London, United Kingdom; <sup>[[[]]]]</sup>Gloucestershire Hospitals National Health Service Foundation Trust, Gloucestershire, United Kingdom

BACKGROUND & AIMS:	There is a lack of clinical studies to establish indications and methodology for tattooing, therefore technique and practice of tattooing is very variable. We aimed to establish a consensus on the indications and appropriate techniques for colonic tattoo through a modified Delphi process.
METHODS:	The baseline questionnaire was classified into 3 areas: where tattooing should not be used (1 domain, 6 questions), where tattooing should be used (4 domains, 20 questions), and how to perform tattooing (1 domain 20 questions). A total of 29 experts participated in the 3 rounds of the Delphi process.
RESULTS:	A total of 15 statements were approved. The statements that achieved the highest agreement were as follows: tattooing should always be used after endoscopic resection of a lesion with suspicion of submucosal invasion (agreement score, 4.59; degree of consensus, 97%). For a

Abbreviation used in this paper: EMR, endoscopic mucosal resection.

Most current article

© 2021 by the AGA Institute 1542-3565/\$36.00 https://doi.org/10.1016/j.cgh.2021.01.024 colorectal lesion that is left in situ but considered suitable for endoscopic resection, tattooing may be used if the lesion is considered difficult to detect at a subsequent endoscopy (agreement score, 4.62; degree of consensus, 100%). A tattoo should never be injected directly into or underneath a lesion that might be removed endoscopically at a later point in time (agreement score, 4.79; degree of consensus, 97%). Details of the tattoo injection should be stated clearly in the endoscopy report (agreement score, 4.76; degree of consensus, 100%).

**CONCLUSIONS:** 

This expert consensus has developed different statements about where tattooing should not be used, when it should be used, and how that should be done.

 $T_{\rm future\ localization\ of\ malignant\ and\ premalignant\ lesions\ in\ the\ digestive\ tract.\ The\ endoscopic\ orientation\ within\ the\ colon\ is\ complicated\ by\ the\ absence\ of\ reliable\ internal\ anatomic\ landmarks\ between\ the\ ileocecal\ valve\ and\ anal\ verge,\ and\ numerous\ reports\ have\ stated\ low\ accuracy,\ especially\ in\ localization\ of\ lesions\ in\ the\ left\ and\ transverse\ colon.^1$ 

A significant difference between the location of colorectal cancers reported by gastroenterologists during endoscopy and the actual anatomic location in surgery or surgical specimens at pathology has been reported.<sup>2</sup> For this reason, tattooing is particularly important for identification of colonic lesions to enable surgical treatment of neoplasia and for future endoscopic localization of lesions and post-treatment scars.<sup>3,4</sup>

However, there is a lack of clinical studies to establish the indications and methodology for tattooing, and the technique and practice of tattooing remains highly variable and conducted largely on an individual basis without clear recommendations or consensus for its use.<sup>5</sup> Therefore, important inconsistencies between reported and actual practices have been described.<sup>6</sup> This uncertainty may lead to unfavorable outcomes, such as misleading guidance from endoscopists to surgeons, which may affect surgical outcomes adversely. Alternatively, inappropriate injection of the tattoo too close to a polyp or polypectomy site may result in fibrosis beneath the polyp.<sup>7,8</sup> This may significantly impair the ability to remove the polyp, increases the risk of adverse events during polypectomy, and may prevent adequate treatment of possible recurrence at surveillance colonoscopy.

For this reason, we sought to establish a consensus on the indications and appropriate techniques for colonic tattoo placement.

## Methods

#### Study Design

This study was based on the Delphi process methodology and was developed through a web application (http://calite-revista.umh.es/delphi). The Delphi process is a structured technique designed to build consensus among experts about a topic in which the available scientific evidence may not be robust enough to develop definitive conclusions.<sup>9</sup> In this process, a steering committee developed a baseline questionnaire with multiple statements, and then each member of an expert group reviewed and indicated a level of agreement with each specific item. Successive rounds identified those elements for which a high degree of consensus was achieved.

## Steering Committee

The steering committee was composed of 4 gastroenterologists with expertise in colonoscopy (R.J., C.H., E.D., and R.B.). This steering committee developed the baseline questionnaire and its subsequent versions.

#### Baseline Questionnaire

The baseline questionnaire was developed based on literature review. The search terms were as follows: colonoscopy, tattooing, surveillance, polypectomy, laparoscopic surgery identification. Members of the steering committee conducted an extensive literature search for relevant English language articles on these topics, up until January 2019, in the Medline, Scopus, and Cochrane databases. This search included relevant polypectomy guidelines<sup>4,10</sup> and cross-references. The initial questionnaire items were formulated exclusively by the members of the steering committee. After the questionnaire was finalized, the voting process commenced.

The questionnaire included 3 domains and 46 individual statements. The domains were classified into 3 areas: where tattooing should not be used (1 domain, 6 questions), where tattooing should be used (4 domains, 20 questions), and how to use tattooing (1 domain 20 questions).

## Expert Panel

A total of 33 experts were invited to participate in the successive rounds of the Delphi process, together with the steering committee members; finally, 29 experts answered these rounds. The criteria for inclusion in the expert panel was knowledge and expertise shown by previous or current research on colonoscopy technique and quality, peer-reviewed publications in the field, and/ or participation in national and international guideline

Descargado para Anonymous User (n/a) en Valencian School of Health Studies de ClinicalKey.es por Elsevier en enero 26, 2024. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2024. Elsevier Inc. Todos los derechos reservados.

development. For specific questions, 5 experts in abdominal surgery also were invited. (These questions can be seen in Tables 1 and 2.) The expert selection made an effort to ensure representation from Europe, the United States, and the Asia-Pacific region.

## The Delphi Rounds and Consensus Meeting

The agreement with each statement was scored using a Likert scale with 5 possible answers (strongly disagree, 1 point; disagree, 2 points; neither agree nor disagree, 3 points; agree, 4 points; strongly agree, 5 points). Participants were allowed to include personal opinions as well as to propose revised wording for each item.

A total of 3 voting rounds were performed between May 2019 and February 2020 (Figure 1). Participants received feedback about the results after each round (average agreement score and degree of consensus for each statement). Consensus was defined using 2 measures: first, as an average score for the agreement (agreement score) in the range from 1 to 5, with the statement equal or higher than 4 points (agree-strongly agree), or equal or lower than 2 points (disagree-strongly disagree); and, second, as a degree of consensus between panelists, defined by the percentage of responses of agree and strongly agree. If the agreement score was equal to or higher than 4 points, and the consensus of agree and strongly agree was equal or higher than 80%, the statement was accepted. On the other hand, when the agreement score was equal to or lower than 2 points, the statement was taken out. Statements with an intermediate agreement score (2-4 points) were adapted in the subsequent round. When consensus was not reached, statements were rephrased based on participant comments and panel discussions, and resubmitted for possible consensus in a following voting round. In these successive rounds, a decision on statements that scored close to the threshold for acceptance was adopted after discussion by the steering committee.

## Results

Accepted and nonaccepted statements are summarized in Tables 1 and 2, respectively, including their corresponding agreement scores and degree of consensus. Successive rounds of questions were performed, as can be seen in Figure 1.

Here, we summarize the findings and conclusions of the Delphi process.

## Contraindications and Indications for Tattooing

**Contraindications.** Statement 1: Tattooing should not be used in the cecum (agreement score, 4.37; degree of consensus, 85%).

## What You Need to Know

## Background

Tattooing is particularly important for identification of colonic lesions to enable surgical or future endoscopic treatment of lesions. There is a lack of clinical studies to establish indications and methodology for tattooing.

## **Findings**

This expert consensus has identified several areas of agreement regarding the appropriate use of colorectal tattooing, developing different clear statements about where tattooing should not be used, and when and how it should be used. This was not an experimental study. More robust evidence is needed to support the indications and technique of tattooing. Nevertheless, these statements set the baseline for future research on this topic.

## Implications for patient care

Adoption of the recommendations of this consensus statement will avoid consequences of inadequate localization of colorectal cancer at surgery, incorrect treatment of polyps or polypectomy scars, as well as potential complications of this technique.

Statement 2: In general, tattooing should not be performed in the rectum (agreement score, 4.10; degree of consensus, 79%).

We obtained quick consensus on not to perform tattooing in the cecum because there already is a natural landmark for this location such as the ileocecal valve and appendiceal orifice. On the other hand, consensus was not obtained as easily about the use of tattooing in the rectum. Finally, after 2 rounds, agreement was reached on the statement that, in general, tattooing should not be performed in the rectum. We did not succeed in reaching an agreement on the exceptions to this general advice. Mostly, it seemed a matter of local agreement between endoscopists and surgeons.

Tattooing in the rectum is controversial because of the higher rate of mesorectal spilling of tattooing, which for some surgeons is considered inconvenient because it may complicate subsequent surgeries. Moreover, the location readily can be measured from the anal verge. Rectal surgery requires precision to avoid stoma and optimize functional results, and tattooing is fairly imprecise. In addition, the submucosal dispersion of tattoo cannot be predicted with any great accuracy. However, there also have been reports showing some advantages of tattooing in the rectum, such as the reduction of preventive ileostomy rates<sup>11</sup> or a higher rate of retrieved lymph nodes in patients receiving neoadjuvant chemoradiotherapy.<sup>12</sup>

**Indications for tatooing.** We described 4 scenarios: (1) deep invasive cancer, (2) resected superficial

## Table 1. Statements With Consensus

		Degree of consensus,		
Domain	Sentence	Agreement score	%	SD
1. When should tattooing not be used? <sup>a</sup>	Tattooing should not be used in the cecum	4.37	85	0.84
	In general, tattooing should not be performed in the rectum	4.10	79	1.11
2. When should tattooing be used? (see exceptions, part 1)				
2A. When should tattooing be used in case of deep invasive cancer? <sup>a</sup>	Tattooing should be used in case of an endoscopic diagnosis of deep invasive cancer	4.52	97	0.57
2B. When should tattooing be used inTattooing should always be used aftercase of superficial neoplasia at riskendoscopic resection of a lesion with suspicion of submucosal invasion		4.59	97	0.57
2C. When should tattooing be used in case of superficial neoplasia that examination?For a colorectal lesion that was left in situ but considered suitable for subsequent endoscopic resection, the lesion is considered difficult to detect in a future endoscopy		4.62	100	0.49
2D. In which of these scenarios would you put a tattoo after polyp removal because of the need for future surveillance?	In which of these scenarios would in piecemeal with additional predictors of polyp removal recurrence because of the need for future surveillance?		84	1.06
3. How should tattoos be placed?	Technique of tattoo, a saline bleb in the submucosal layer should be created before tattooing	4.17	79	0.87
	For the localization of polyps or scars, tattoos should be placed 3–5 cm distal (anal side) of the lesion	3.93	79	0.72
	For localization of lesions referred for surgery, 2 or 3 tattoos should be placed circumferentially at necessary sites <sup>a</sup>	4.17	93	0.66
	A tattoo should never be injected directly into or underneath a lesion that may be removed endoscopically at a later point	4.79	97	0.49

#### Table 1. Continued

Domain	Sentence	Agreement score	Degree of consensus, %	SD
	For the localization of polyps or scars at a subsequent endoscopy, in general only 1 tattoo is needed	4.03	83	0.82
	The volume of each tattoo should be enough to ensure adequate visualization at later procedures and generally not exceed 1 mL per injection site	3.96	85	0.65
	Details of the tattoo injection should be stated clearly in the endoscopy report	4.76	100	0.44
	The tattoo should be photodocumented in the endoscopy report	4.30	90	0.67
	An institutional protocol for tattooing should be implemented at each center	4.45	93	0.74

SD, standard deviation.

<sup>a</sup>Surgeons were allowed to participate in the consensus for these questions.

neoplasia at risk of submucosal invasion, (3) neoplasia left in situ that would be resected at a following occasion, and (4) a resected polyp with an indication for surveillance of the polypectomy site.

*Deep invasive cancer.* Statement 3: Tattooing should be used in case of an endoscopic diagnosis of deep invasive cancer (agreement score, 4.52; degree of consensus, 97%).

In case of an endoscopic diagnosis of deep invasive cancer, surgical treatment commonly is indicated and tattooing is used to facilitate tumor location, especially in case of laparoscopic surgery.<sup>1</sup> At minimally invasive surgery, the tumor is not palpable by the surgeons, and therefore the tumor location must be determined before the patient's arrival in the operating room. A blind resection may lead to resection of the wrong colonic segment, an unexpected change in the previously planned procedure, or a permanent ostomy. Although deep invasive cancer is a clear indication for tattooing and there was significant agreement on that, large variability has been described in clinical practice.<sup>6</sup> It is important to remark that in case of suspected cancer, the tattoo should be placed before the biopsy of the lesion to avoid inadvertent contamination of the needle with malignant cells via the biopsy channel of the scope and subsequent cancer inoculation into another colonic site.<sup>13</sup>

Superficial neoplasia at risk of submucosal invasion after resection. Statement 4: Tattooing always should be used after endoscopic resection of a lesion with suspicion of submucosal invasion (agreement score, 4.59; degree of consensus, 97%).

Consensus was reached about tattooing all of the endoscopically identified neoplasia where the endoscopist has a suspicion of potential submucosal invasion. This recommendation is in line with polypectomy guidelines,<sup>4,10</sup> and there is consensus that these lesions always should be tattooed independently of their shape, size, or the chance of redetecting the location at a next endoscopy. Given the potential need of follow-up treatment by surgery, circumferential tattooing should be placed at the first colonoscopy.

Neoplasia that is referred for resection at a subsequent colonoscopy. Statement 5: For a colorectal lesion that is left in situ but considered suitable for endoscopic resection, tattooing may be used if the lesion is considered difficult to detect at a subsequent endoscopy (agreement score, 4.62; degree of consensus, 100%).

In this case, consensus was reached on tattooing only those that are considered difficult to detect at a subsequent colonoscopy. No agreement was achieved in terms of shape or size of these lesions, so this indication is based on the judgment of the endoscopist. Although injection of appropriately diluted and sterile solutions generally is safe, with rare complications mainly related to transmural injection,<sup>14</sup> unnecessary tattooing must be avoided. This is for safety reasons, as well as to preclude multiple markings in the colon for the future, which potentially could complicate endoscopic identification of



Figure 1. Flow-chart of the Delphi process.

one specific target lesion. Special mention should be made regarding the transverse colon because unique aspects of length, relative mobility, and often significant shortening of this colonic segment during colonoscopy make it particularly subject to variable performance characteristics at subsequent colonoscopy, challenging timely and accurate lesion localization. The same can be considered for the sigmoid colon, although to a much lesser extent.

Resected polyp that needs future surveillance of the polypectomy scar. Statement 6: A tattoo should be placed for polyps 20 mm or larger resected piecemeal with additional predictors of recurrence (agreement score, 4.04; degree of consensus, 84%).

Tattoo ink may be placed after finishing an endoscopic mucosal resection (EMR) to enable future detection of the scar, which is not always readily apparent at endoscopy. Scars appear as white discolorations of the colonic wall, associated with disruption of the mucosal vascular pattern and haustral folds. In addition, this indication has a wide variability in clinical practice. Only one possibility reached consensus: lesions larger than 20 mm with additional predictors of recurrence. In cases with uncertainty about completeness of the resection, the statement "A tattoo should always be placed when there is uncertainty about the completeness of the resection (either after piecemeal EMR or after a nonradical resection)" obtained an agreement score of 4.00, but the degree of consensus was only 71%, which was below the accepted threshold. However, this situation also may be considered as a potential indication for tattooing.

Additional predictors of recurrence can be considered<sup>11</sup>: lesions larger than 40 mm, use of complementary thermal techniques for resection, prior failed attempts at resection and size, morphology, site, and access scale level.<sup>10</sup> After EMR of large polyps, residual neoplasia should be excised using hot and cold avulsion. Use of thermal ablation of visible residual neoplasia is a strong predictor of recurrence.<sup>15-18</sup> However, thermal ablation of the mucosal defect margin with argon plasma or soft coagulation can be used as adjuvant treatment for invisible recurrence, having been proven as safe and highly effective.<sup>19</sup> No consensus was reached on the size or method of resection as the only criteria for tattoo placement, for instance, in all lesions larger than 20 mm resected piecemeal.

## Methodology of Tattooing

## Technique of tattooing

Statement 7: Technique of tattoo: a saline bleb in the submucosal layer should be created before tattooing (agreement score, 4.17; degree of consensus, 79%).

Statement 8: A tattoo should never be injected directly into or underneath a lesion that might be endoscopically removed at a later point in time (agreement score, 4.79; degree of consensus, 97%).

Statement 9: The volume of each tattoo should be enough to ensure adequate visualization at later procedures and generally not to exceed 1 mL per injection site (agreement score, 3.96; degree of consensus, 85%).

Experts agree on the technique of creating a saline bleb (Figure 2)<sup>16</sup> to ensure adequate submucosal injection of the tattoo ink and to prevent dye infiltration of the muscularis propria or a transmural injection, which leads to diffuse staining and potential spillage into the peritoneum.<sup>20</sup> This technique has been associated with fewer errors in localization.<sup>1</sup> Agreement also was achieved regarding the advice of avoiding direct injection into lesions, especially when future endoscopic treatment is expected, to avoid submucosal fibrosis that could hamper or prevent future endoscopic resection of lesions,<sup>8</sup> or even facilitate the spread of malignant cells if they are injected directly during tattoo placement.<sup>21,22</sup> There also was agreement about a maximum volume of 1 mL per injection site to avoid unwanted tattoo dispersion, although data to support this are absent.

#### Table 2. Statements in Which Consensus Was Not Reached

		Degree of consensus,	
Sentence	Agreement score	%	SD
Tattooing should not be used in the right colon	1.93	11	1.14
Tattooing should not be used proximal to the splenic flexure	1.37	0	0.63
Tattooing could be used in the rectum in case of deep invasive cancer	2.63	30	1.24
Tattooing could be used in the rectum in case of superficial neoplasia at risk of submucosal cancer after resection	3.11	59	1.22
Tattooing could be used in the rectum for detection of potential recurrence after endoscopic resection	3.11	56	1.34
Tattooing should be used in the rectum in case of neoadjuvant chemoradiotherapy treatment	2.52	19	1.01
Tattooing could be considered in the rectum when required for localization at surgery or neoadjuvant treatment	3.52	66	1.33
Tattooing always should be used	2.85	41	1.13
Tattooing should be used only if referred for surgery	2.74	33	1.23
Tattooing should be used only if the cancer is considered difficult to identify at surgery	2.85	38	1.35
Tattooing should be used only for a nonpedunculated lesion	2.41	15	1.12
Tattooing should be used only if the lesion is considered difficult to identify in future procedures	2.74	30	1.23
	<ul> <li>Tattooing should not be used in the right colon</li> <li>Tattooing should not be used proximal to the splenic flexure</li> <li>Tattooing could be used in the rectum in case of deep invasive cancer</li> <li>Tattooing could be used in the rectum in case of superficial neoplasia at risk of submucosal cancer after resection</li> <li>Tattooing could be used in the rectum for detection of potential recurrence after endoscopic resection</li> <li>Tattooing could be used in the rectum in case of neoadjuvant chemoradiotherapy treatment</li> <li>Tattooing could be used in the rectum when required for localization at surgery or neoadjuvant treatment</li> <li>Tattooing should be used only if referred for surgery</li> <li>Tattooing should be used only if the cancer is considered difficult to identify at surgery</li> <li>Tattooing should be used only if the lesion is considered difficult to identify in future procedures</li> </ul>	SelfenceAgreement scoreTattooing should not be used in the right colon1.93Tattooing should not be splenic flexure1.37Tattooing could be used in the rectum in case of deep invasive cancer2.63Tattooing could be used in the rectum in case of superficial neoplasia at risk of submucosal cancer after resection3.11Tattooing could be used in the rectum for detection of potential recurrence after endoscopic resection3.11Tattooing should be used in the rectum in case of neoadjuvant chemoradiotherapy treatment2.52Tattooing always should be used3.52Tattooing should be used for localization at surgery or neoadjuvant treatment2.85Tattooing should be used only if referred for surgery2.85Tattooing should be used only if referred for surgery2.85Tattooing should be used only if referred for surgery2.85Tattooing should be used only if referred for surgery2.41Tattooing should be used only for a nonpedunculated lesion2.74Tattooing should be used only for a nonpedunculated lesion2.74	Tattooing should not be used proximal to the splenic flexure1.9311Tattooing could be used in the rectum in case of deep invasive cancer2.6330Tattooing could be used in the rectum in case of accord and the rectum in case of accord after resection3.1159Tattooing could be used in the rectum in case of accord after resection3.1156Tattooing could be used in the rectum in case of neoadjuvant the rectum in case of neoadjuvant treatment3.1156Tattooing could be used in the rectum in case of neoadjuvant the rectum in case of neoadjuvant treatment3.5266Tattooing should be used only if referred for surgery reatment2.8541Tattooing should be used only if referred for surgery2.8538Tattooing should be used only if referred for surgery2.8538Tattooing should be used only if referred for surgery2.4115Tattooing should be used only if referred for surgery2.4115only if referred for surgery2.7430Tattooing should be used only if the cancer is considered dificult to identify at surgery2.7430Tattooing should be used only if the lesion is considered dificult to identify at surgery2.7430Tattooing should be used only if the lesion is considered dificult to identify at surgery2.7430Tattooing should be used only if the lesion is considered dificult to identify in future procedures2.7430 </td

## Table 2. Continued

			Degree of consensus,	
Domain	Sentence	Agreement score	%	SD
	Tattooing should be used in all lesions >20 mm because they could be considered as suspicious of invasive CRC	2.85	44	1.38
2C. When should tattooing be used in case of superficial neoplasia that needs to be resected at the next examination?	Tattooing always should be used	2.44	30	1.37
	For a colorectal lesion that is left in situ but considered suitable for subsequent endoscopic resection, tattooing always should be performed (see exceptions. part 1)	2.79	31	1.29
	Tattooing should be used only if referred for surgery	2.37	19	1.18
	Tattooing should be used only if referred for endoscopic treatment	2.07	11	0.96
	Tattooing should be used only if >20 mm	2.19	11	0.92
	Tattooing should be used only if >10 mm	2.19	11	0.96
	Tattooing should be used only for nonpedunculated lesions	2.41	22	1.15
2D. In which of these scenarios would you put a tattoo after polyp removal because of the need for future surveillance?	Polyps >10 mm resected in piecemeal	2.60	20	0.91
	Any resected polyp >20 mm	3.04	42	1.20
	Polyps >20 mm resected in piecemeal	3.48	64	1.29
	Any resected polyp, irrespective of the size, when the scar could be considered difficult to identify in future procedures	3.31	50	1.35

### Table 2. Continued

		Degree of consensus,		
Domain	Sentence	Agreement score	%	SD
	A tattoo should be placed only when there is uncertainty about the completeness of the resection (after pEMR of a nonradical resection) if future detection of the scar might be difficult (see exceptions. part 1)	3.34	59	1.32
	A tattoo always should be placed when there is uncertainty about the completeness of the resection (after pEMR of a nonradical resection)	4.00	71	1.09
3. How should tattoos be placed?	Technique of tattoo: tattoo can be made by direct injection	2.76	36	1.09
	In case of a planned ileocolonic anastomosis, only 1 site needs to be tattooed 5 cm distal (anal side) from the lesion <sup>a</sup>	3.39	57	0.96
	In case of a planned colocolonic anastomosis, 1 site 5 cm anally from the lesion and 1 site 5 cm orally from the lesion should be tattooed <sup>a</sup>	2.68	25	1.12
	In case of a planned colocolonic anastomosis, only 1 location should be marked by tattoo: 5 cm distal (anal side) from the lesion <sup>a</sup>	3.18	46	1.12
	Location of tattoo: tattoos should be placed 3–5 cm proximal to the lesion (cecal side of the lesion) <sup>a</sup>	2.22	11	0.89
	Location of tattoo: tattoos should be placed 3–5 cm in both sides of the lesion (distal and proximal) <sup>a</sup>	2.22	11	0.97
	Location of tattoo: the tattoo location does not matter as long as the location is clearly stated in the endoscopy report <sup>a</sup>	2.73	38	1.40
	Number of tattoos: just 1 tattoo on the same side of the lesion should be placed <sup>a</sup>	2.15	12	0.83

#### Table 2. Continued

		Degree of consensus,		
Domain	Sentence	Agreement score	%	SD
	Number of tattoos: just 1 tattoo on the opposite side of the lesion should be placed <sup>a</sup>	2.38	23	0.98
	Number of tattoos: at least 2 tattoos (distal and proximal) should be placed <sup>a</sup>	2.20	12	0.91
	Number of tattoos: at least 2 tattoos on opposite sides of the colonic lumen should be placed <sup>a</sup>	3.35	58	1.13
	Number of tattoos: 3–4 circumferential tattoos should be placed <sup>a</sup>	2.65	27	0.98
	Number of tattoos: the number of tattoos does not matter as long as the details are clearly stated in the endoscopy report <sup>a</sup>	2.58	33	1.06
	Number of tattoos depends on the indication for tattooing: circumferential tattooing for CRC or polyps sent to surgery; 1 tattoo is enough for polyps amenable to endoscopic review <sup>a</sup>	3.85	77	0.78
	Volume of tattooing: 1 mL of tattoo should be injected per site	3.25	50	0.94
	Volume of tattooing: 2 mL of tattoo should be injected per site	2.33	13	0.92
	Volume of tattooing: enough amount of tattoo should be injected per site to ensure adequate visualization	3.85	81	0.95

CRC, colorectal cancer; pEMR, piecemeal endoscopic mucosal resection; SD, standard deviation.

<sup>a</sup>Surgeons were allowed to participate in the consensus for these questions.

**Location and number of tattoos.** Statement 10: For the localization of polyps or scars, tattoos should be placed 3 to 5 cm distal (anal side) of the lesion (agreement score, 3.93; degree of consensus, 79%).

Statement 11: For localization of lesions referred for surgery, 2 or 3 tattoos should be placed circumferentially at necessary sites (agreement score, 4.17; degree of consensus, 93%).

Statement 12: For the localization of polyps or scars at a subsequent endoscopy, in general, only 1 tattoo is needed (agreement score, 4.03; degree of consensus, 83%).

This group of statements addressed the localization and characteristics of tattooing. In general, tattoos should be placed 3 to 5 cm distal in the anal side of the lesions for further identification; moreover, this location should be reported adequately in the endoscopy report. There are differences in the technique between marking a deep invasive cancer for surgery



Figure 2. Tattooing with saline bleb technique.

and marking a lesion for further endoscopic resection (Figure 3). For surgery it is important to place the tattoos circumferentially to facilitate laparoscopic identification in any case.<sup>23</sup> Marking at the site of the mesenteric colon may go unnoticed, a situation that is avoided with 2 to 3 tattoos.<sup>1</sup> For future endoscopic resections, it is important to establish adequate marking without increasing the risk of fibrosis. With 1 single tattoo, adequate visualization is achieved, avoiding potential risk of complications. However, this tattoo should be placed at least 3 to 5 cm anally from the lesion to avoid diffusion of ink under the lesion that may hamper future endoscopic resection. For this purpose, using a limited injection volume of 1 mL or less also is important.

**Documentation of tattooing.** Statement 13: Details of the tattoo injection should be stated clearly in the endoscopy report (agreement score, 4.76; degree of consensus, 100%).

Statement 14: The tattoo should be photodocumented in the endoscopy report (agreement score, 4.30; degree of consensus, 90%).

Statement 15: An institutional protocol for tattooing should be implemented in each center (agreement score, 4.45; degree of consensus, 93%),

Finally, consensus was reached about different aspects of the documentation of tattooing, underscoring the importance of adequately reporting details of

tattooing, such as estimated location, number, volume, or distance to the lesion, as well as photodocumentation with pictures or video that could facilitate localization of the marked lesion in future endoscopies.<sup>4,14</sup> Aside from the cecum and rectum, the location of the lesions cannot be ascertained exactly by endoscopists. Because of that, location estimated in the endoscopy report always should be considered as approximate, this being the main reason for placing tattoos. Patients who have received tattoos should be told that a tattoo is present, and future colonoscopists must be notified of the presence, reason, and location of the tattoo. It also is important that local institutional protocols are in place in endoscopy units and tumor multidisciplinary committees to make clear instructions about this important part of endoscopy.

## Discussion

Accurate localization of significant neoplastic lesions within the colorectum is critical to ensure their timely identification at subsequent surveillance or treatment by colonoscopy or surgery. The placement of an indelible tattoo by submucosal injection of sterile carbon particle suspension is the major means by which this is performed. According to this Delphi multidisciplinary consensus process there is a need for clear standardization of endoscopic tattooing indications, technique, and documentation to prevent errors of lesion localization at subsequent endoscopy or surgery.

The relevance of this agreement is its comprehensive perspective, which allowed us to identify 4 possible tattoo indications, namely surgical localization for either deep or superficially invasive cancer, as well as endoscopic localization of lesions that remain in situ or postresection scar. In addition, we showed that different indications result in a different number of tattoos, mainly because of the different therapeutic approaches required.



Figure 3. Tattooing technique with different indications. GI, gastroenterologist.

#### Table 3. Questions for Future Research

#### Research questions

Usefu	Iness	of	rectal	tattooing

Should tattooing be used in rectal cancer?

- Should tattooing be used for localization after neoadjuvant chemoradiotherapy?
- Should tattooing be used in the rectum in case of potential recurrence after endoscopic resection?

Which are the complications of rectal tattooing?

When should tattoos be used in case of deep invasive neoplasia: before or after biopsies?

When should tattoos be used in suspected superficial neoplasia: always or only in selected cases? Which would be these selected cases?

When should tattoos be used in cases of future endoscopic resection: always or only if considered as difficult to detect? Always in nonpolypoid lesions >20 mm?

When should tattoos be used in cases of future surveillance: always in piecemeal endoscopic mucosal resection of lesions >20 mm? Always where there is uncertainty about the completeness of the resection?

Similarly, the proposed standard of injecting only anally and on at least 2 quadrants before referring a lesion to surgery represents an important point of transparency to prevent misunderstanding with the surgeon.

The results of this Delphi process establish expert agreement on the indications and technical aspects of tattooing of colorectal lesions. Experts were selected because of their clinical and research track record, and implicit knowledge and publications about the quality of colonoscopy, polypectomy technique, and participation in national and international guidelines. Colonic surgeons were included to provide additional expertise on the topic. The panel of experts that participated in this Delphi process include some of the most prolific and influential professionals in the field of colonoscopy. However, it is important to note that expert opinion may have the limitation of offering a different point of view in some respects from that found in community endoscopists. Our consensus set the basic indications and methodology of this useful technique, trying to avoid variability, at least in the most elemental points about when (and when not) to use it and how to perform and document tattooing. Organized expert consensus, using tools such as the Delphi process, is an optimal way to establish basic agreement in clinical practice, especially in topics in which research and sound evidence are scarce. Ultimately, this type of consensus is aimed at improving the quality of management of patients with colorectal cancer or colonic polyps. Adoption of recommendations of this consensus statement will avoid consequences of inadequate localization of colorectal cancer at surgery, incorrect treatment of polyps or polypectomy scars, as well as potential complications of this technique. Moreover, these statements set the baseline for future research on this topic (Table 3).

In summary, this expert consensus has identified several areas of agreement regarding the appropriate use of colorectal tattooing, developing different clear statements about where tattooing should not be used, when it should be used, and how that should be performed. These statements are a starting point for good clinical practice as well as for future research studies that could improve the appropriateness and utility of tattooing in endoscopy further.

#### References

- Acuna SA, Elmi M, Shah PS, et al. Preoperative localization of colorectal cancer: a systematic review and meta-analysis. Surg Endosc 2017;31:2366–2379.
- Blum-Guzman J, Wanderley de Melo S. Location of colorectal cancer: colonoscopy versus surgery. Yield of colonoscopy in predicting actual location. Endosc Int Open 2017; 05:E642–E645.
- Kaminski MF, Thomas-Gibson S, Bugajski M, et al. Performance measures for lower gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) quality improvement initiative. United European Gastroenterol J 2017; 5:309–334.
- Kaltenbach T, Anderson JC, Burke CA, et al. Endoscopic removal of colorectal lesions—recommendations by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2020;158:1095–1129.
- Azin A, Jimenez MC, Cleghorn MC, et al. Discrepancy between gastroenterologists' and general surgeons' perspectives on repeat endoscopy in colorectal cancer. Can J Surg 2016; 59:29–34.
- Spaete JP, Zheng J, Chow SC, et al. Inconsistencies in colonic tattooing practice: differences in reported and actual practices at a tertiary medical center. South Med J 2019;112:222–227.
- 7. Trindade AJ, Kumta NA, Bhutani MS, et al. Devices and techniques for endoscopic treatment of residual and fibrotic colorectal polyps (with videos). Gastrointest Endosc 2020;92:474–482.
- Kim HG, Thosani N, Banerjee S, et al. Effect of prior biopsy sampling, tattoo placement, and snare sampling on endoscopic resection of large nonpedunculated colorectal lesions. Gastrointest Endosc 2015;81:204–213.
- **9.** Jones J, Hunter D. Qualitative research: consensus methods for medical and health services research. BMJ 1995;311:376.
- Ferlitsch M, Moss A, Hassan C, et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline. Endoscopy 2017;49:270–297.
- 11. Cipe G, Cengiz MB, Idiz UO, et al. The effects of preoperative endoscopic tattooing on distal surgical margin and ileostomy rates

in laparoscopic rectal cancer surgery: a prospective randomized study. Surg Laparosc Endosc Percutan Tech 2016;26:301–303.

- 12. Chen YT, Wang JY, Wang JW, et al. Preoperative endoscopic tattooing technique improved lymph node retrieval in rectal cancer patients receiving neoadjuvant concurrent chemo-radiotherapy. J Clin Pathol 2020;73:267–272.
- **13.** Backes Y, Seerden TCJ, van Gestel RSFE, et al. Tumor seeding during colonoscopy as a possible cause for metachronous colorectal cancer. Gastroenterology 2019;157:1222–1232.e4.
- Kethu SR, Banerjee S, Desilets D, et al. Endoscopic tattooing. Gastrointest Endosc 2010;72:681–685.
- **15.** Hassan C, Repici A, Sharma P, et al. Efficacy and safety of endoscopic resection of large colorectal polyps: a systematic review and meta-analysis. Gut 2016;65:806–820.
- Moss A, Williams SJ, Hourigan LF, et al. Long-term adenoma recurrence following wide-field endoscopic mucosal resection (WF-EMR) for advanced colonic mucosal neoplasia is infrequent: results and risk factors in 1000 cases from the Australian Colonic EMR (ACE) study. Gut 2015;64:57–65.
- Kumar V, Broadley H, Rex DK. Safety and efficacy of hot avulsion as an adjunct to EMR (with videos). Gastrointest Endosc 2019;89:999–1004.
- Moss A, Bourke MJ, Williams SJ, et al. Endoscopic mucosal resection outcomes and prediction of submucosal cancer from advanced colonic mucosal neoplasia. Gastroenterology 2011;140:1909–1918.
- Brooker JC, Saunders BP, Shah SG, et al. Treatment with argon plasma coagulation reduces recurrence after piecemeal resection of large sessile colonic polyps: a randomized trial and recommendations. Gastrointest Endosc 2002;55:371–375.
- Fu KI, Fujii T, Kato S, et al. A new endoscopic tattooing technique for identifying the location of colonic lesions during laparoscopic surgery: a comparison with the conventional technique. Endoscopy 2001;33:687–691.
- Moss A, Bourke MJ, Pathmanathan N. Safety of colonic tattoo with sterile carbon particle suspension: a proposed guideline with illustrative cases. Gastrointest Endosc 2011;74:214–218.
- Kang HJ, Lee BI, Kim BW, et al. Potential cancer cell inoculation of tattoo site through use of a contaminated needle. Gastrointest Endosc 2006;63:884–886.
- 23. Rex DK. The appropriate use and techniques of tattooing in the colon. Gastroenterol Hepatol 2018;14:314–317.

#### **Reprint requests**

Address requests for reprints to: Rodrigo Jover, MD, Servicio de Medicina Digestiva, Hospital General Universitario de Alicante, C/Pintor Baeza 12, 03010 Alicante, Spain. e-mail: rodrigojover@gmail.com; fax: (34) 965933468.

#### **CRediT Authorship Contributions**

Lucia Medina-Prado, Researcher (Visualization: Equal; Writing - original draft: Equal; Writing - review & editing: Lead)

Cesare Hassan (Conceptualization: Lead; Data curation: Lead; Investigation: Lead; Methodology: Lead; Project administration: Lead)

Evelien Dekker (Conceptualization: Lead; Data curation: Lead; Formal analysis: Lead; Investigation: Lead; Methodology: Lead; Project administration: Lead; Validation: Equal)

Raf Bisschops (Conceptualization: Lead; Data curation: Lead; Formal analysis: Lead; Investigation: Lead; Methodology: Lead; Project administration: Lead; Supervision: Lead; Validation: Equal)

Sergio Alfieri (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal)

Pradeep Bhandari (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal) Michael J.Bourke (Data curation: Equal; Investigation: Equal; Methodology:

Equal; Validation: Equal; Visualization: Equal)

Raquel Bravo (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal)

Marco Bustamante-Balen (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal)

Jason Dominitz (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal)

Monika Ferlitsch (Data curation: Equal; Investigation: Equal; Methodology: Equal; Validation: Equal; Visualization: Equal)

Paul Fockens (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal)

Monique van Leerdam (Data curation: Equal; Formal analysis: Equal; Investigation: Equal; Methodology: Equal; Validation: Equal; Visualization: Equal)

David Lieberman (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal)

Maite Herráiz (Data curation: Equal; Investigation: Equal; Methodology: Equal; Validation: Equal; Visualization: Equal)

Charles Kahi (Data curation: Equal; Formal analysis: Equal; Investigation: Equal; Methodology: Equal; Validation: Equal; Visualization: Equal)

Michal Kaminski (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal)

Takahisa Matsuda (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal)

Alan Moss (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal)

Maria Pellisé (Data curation: Equal; Formal analysis: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal)

Heiko Pohl (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal)

Colin Rees (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Lead)

Douglas K. Rex (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal)

Manuel Romero-Simó (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal) Matthew D. Rutter (Data curation: Equal; Investigation: Equal; Validation:

Equal; Visualization: Equal)

Prateek Sharma (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal)

Aasma Shaukat (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal)

Siwan Thomas-Gibson (Data curation: Equal; Investigation: Equal; Validation: Equal; Visualization: Equal)

Roland Valori (Data curation: Equal; Investigation: Equal; Supervision: Equal; Validation: Equal)

Rodrigo Jover (Conceptualization: Lead; Data curation: Lead; Formal analysis: Lead; Investigation: Lead; Methodology: Lead; Project administration: Lead; Supervision: Lead; Validation: Equal; Visualization: Equal; Writing – original draft: Equal; Writing – review & editing: Supporting)

#### Conflicts of interest

These authors disclose the following: Rodrigo Jover and Evelien Dekker have received honorarium for consultancy and speaker's fee from GI Supply: Cesare Hassan and Raf Bisschops have received honorarium for consultancy from GI Supply; and Heiko Pohl has received research grants from Steris and Cosmo Pharmaceuticals. The remaining authors disclose no conflicts.