

Endoscopic tattooing

The American Society for Gastrointestinal Endoscopy (ASGE) Technology Committee provides reviews of existing, new, or emerging endoscopic technologies that have an impact on the practice of GI endoscopy. Evidence-based methodology is used, with a MEDLINE literature search to identify pertinent clinical studies on the topic and a MAUDE (U.S. Food and Drug Administration Center for Devices and Radiological Health) database search to identify the reported complications of a given technology. Both are supplemented by accessing the "related articles" feature of PubMed and by scrutinizing pertinent references cited by the identified studies. Controlled clinical trials are emphasized, but in many cases, data from randomized, controlled trials are lacking. In such cases, large case series, preliminary clinical studies, and expert opinions are used. Technical data are gathered from traditional and Web-based publications, proprietary publications, and informal communications with pertinent vendors.

Technology Status Evaluation Reports are drafted by 1 or 2 members of the ASGE Technology Committee, reviewed and edited by the committee as a whole, and approved by the Governing Board of the ASGE. When financial guidance is indicated, the most recent coding data and list prices at the time of publication are provided. For this review, the MEDLINE database was searched through January 2010 for articles related to endoscopic tattooing by using the Keywords tattooing, colonic, endoscopic, India ink, indocyanine green in different search term combinations.

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BACKGROUND

The intraoperative identification of lesions previously detected by endoscopy is often difficult, particularly during laparoscopic surgery.¹ Estimation of the tumor site at

colonoscopy can be imprecise, with as many as 14% of tumor locations incorrectly identified.^{1,2} Lesions that may be difficult to identify by inspection or palpation at surgery include small or flat neoplasms, polypectomy sites, diverticula, arteriovenous malformations, and Dieulafoy lesions. The lack of accurate lesion identification during laparoscopy may lead to resection of the wrong segment of bowel.³ Endoscopic tattooing of colonic lesions to assist in operative localization was first described in 1975.⁴ Tattooing is also used to facilitate identification of subtle mucosal lesions or endoscopic resection sites at the time of subsequent endoscopy.^{4,5}

TECHNOLOGY UNDER REVIEW

Suspensions of carbon particles are the most commonly used substance for endoscopic tattooing. India ink, used for writing in India dating back to the 4th century BC, has been used for endoscopic tattooing since the 1970s.⁶ It is composed of a colloidal suspension of carbon particles in a solution of organic and inorganic substances used as stabilizing diluents and surfactants. Some preparations of India ink contain ethylene glycol, phenol, shellac, and animal products (eg, gelatins) that may cause inflammatory reactions in local tissue. Nonsterile India ink diluted with normal saline solution may be rendered sterile by on-site autoclaving (20 minutes at 110-121°C at 27.6 kPa pressure)⁷ or by passage through a bacteriostatic Millipore filter (0.22 μ m).

A sterile and biocompatible suspension containing highly purified, very fine carbon particles (Spot; GI Supply, Camp Hill, Pa) was developed and is marketed specifically for endoscopic tattooing. It is the only product approved by the U.S. Food and Drug Administration (FDA) for this purpose. Each sterile syringe contains 5 mL of the marker and is prediluted and ready to use. The composition of Spot includes water, glycerol, polysorbate 80, benzyl alcohol, simethicone, and high-purity carbon black. It does not contain phenols, shellacs, or ammonia that are present in suspensions of India ink.

Other dyes that have been assessed as endoscopic tattooing agents include methylene blue, indigo carmine, toluidine blue, isosulfan blue, hematoxylin, eosin, and indocyanine green (ICG). These agents are less useful compared with India ink with respect to safety, efficacy, and ease of use. Animal studies have shown that only India ink and ICG are visible at the injection site longer than 48 hours, whereas other dyes are reabsorbed within

24 hours.⁸ ICG is a vital stain originally used for quantifying cardiac output. ICG cannot be used in patients with allergy to iodine.

INDICATIONS AND EASE OF USE

Endoscopic tattooing is indicated to facilitate localization of a luminal abnormality at the time of surgery or repeat endoscopic examination. The tattooing agent is delivered by an injection needle advanced through the working channel of the endoscope.⁹ The needle should be inserted at an oblique angle to the bowel wall to avoid penetrating the serosa.¹⁰ Transmural injection may result in diffuse staining of the peritoneal surface. Once the needle's bevel is within the submucosa, the agent is injected to raise a bleb, usually in 0.5- to 1.0-mL aliquots. Four-quadrant injection around the circumference of the bowel has been suggested to optimize operative localization.¹¹ This is particularly important in the colon because it is difficult to identify the location intraoperatively if the tattoo is only placed on the mesenteric or retroperitoneal side of the colon.¹² The use of 2 injections to bracket a lesion for subsequent endoscopic inspection has also been described.⁵ When using India ink, it must be sterilized and diluted before use, whereas the FDA-approved Spot is prediluted and ready to use.

More recently, "saline test injection" techniques have been described to define the submucosal plane to prevent dye infiltration of the muscularis propria or spillage into the peritoneum.¹³ In one technique, saline solution is first injected into the submucosa to ensure formation of a submucosal bleb.¹⁴ The syringe with saline solution is then replaced by a syringe containing India ink while the needle is still in the submucosal plane. After injection of the ink, the saline solution syringe is reattached and used to expel the residual India ink in the injection catheter. This method was used in 55 cases and was more effective for operative identification than the conventional technique (54/55 vs 31/36; $P = .034$). The same method was used in another study using Spot.¹² This study confirmed that the technique was safe and effective for operative tumor localization (61/63; 96.8%). A 2-step variation of this technique has been described in which saline solution is first injected to create a submucosal elevation.¹⁵ This is followed by a separate puncture of the bleb with a needle containing India ink and injection of a small amount of India ink. Leakage of residual India ink from the 2 puncture sites resulted in smaller, more precise tattoos without broad tissue staining based on subjective operative findings.

India ink has been used for endoscopic marking of esophageal lesions, in particular Barrett's esophagus. In a prospective study, 19 patients with Barrett's esophagus had India ink tattoos placed at the most proximal level of the squamocolumnar junction.¹⁶ Of the 15 patients who remained in the study, all had good tattoo persistence at 36

months. No complications related to esophageal tattooing were reported.

Mucosa marking targeting biopsy has been described as a method for longitudinal follow-up in multifocal atrophic gastritis and precancerous lesions in the stomach. In this technique, tattooing of biopsy sites is used as a means to identify previously sampled areas.¹⁷ Endoscopic tattooing has also been used during deep enteroscopy (eg, double-balloon enteroscopy) to mark the extent of antegrade inspection for identification during subsequent retrograde enteroscopy.¹⁸

Another reported application of endoscopic tattooing based on limited case series is EUS-guided fine-needle tattooing using India ink or ICG for the preoperative localization of pancreatic lesions.¹⁹⁻²¹

OUTCOMES AND COMPARATIVE DATA

Various concentrations of India ink were studied in an animal model.²² Undiluted and 1:10 dilution resulted in mucosal ulceration. Tattoos created with 0.5-mL aliquots of 1:100 India ink produced no gross inflammation and were seen consistently at colonoscopy, laparoscopy, and laparotomy for as long as 5 months.

The safety and efficacy of Spot were evaluated in a study of 113 patients.²³ Fever, abdominal pain, or signs or symptoms of inflammation did not develop in any of the patients. Ten patients with colon polyps deemed endoscopically unresectable or malignant appearing had the area surrounding the lesions tattooed and subsequently underwent surgical resection. At operation, the tattoos were visible in all cases, and none of the resected specimens exhibited necrosis or abscess formation on histopathology. An additional 103 patients underwent colonoscopic tattooing and subsequently underwent colonoscopy or underwent surgery at another hospital. In the 42 patients who underwent subsequent colonoscopy 3 to 12 months after tattooing, all tattoos were readily identifiable.

Endoscopic tattooing with ICG in 12 patients was visible at surgery 36 hours after injection and resulted in only minimal inflammation.²⁴ In another study of 39 patients, ICG was visible intraoperatively in all 29 patients having surgery within 8 days. In the remaining 10 patients who underwent surgery more than 8 days after tattooing, staining was seen in only 2 patients.²⁵

An animal study considered the safety and efficacy of various dilutions of India ink and ICG.¹⁹ Although the tattoo with 1:100 dilution of India ink was seen consistently for as long as 5 months with only a mild submucosal reaction, ICG was visible only on day 1 and caused mucosal ulceration and mild to severe inflammation at both the concentrated and diluted injection sites. To enhance detection of tattoos created with lower concentrations of ICG, fluorescence imaging with light-emitting, diode-activated ICG has been described.²⁶ Although this new technique is reported to be safe and effective, it will add

TABLE 1. Tattooing agents

Tattooing agent	Manufacturer	FDA-approved for tattooing	Price	Special features
Indocyanine green (Cardiogreen)	Sigma-Aldrich Inc, St. Louis, Mo	No	\$46.70 for 25 mg, \$80.60 for 50 mg	Available in powder form, not readily soluble in saline solution, soluble in water
India ink (Endomark)	PMT/Permark Inc, Chanhasen, Minn	No	10-mL vials, \$30 each; box of 9 for \$225	Sterile, diluted 1:50 with normal saline solution
Spot	GI Supply Inc, Camp Hill, Pa	Yes	5-mL syringe, box of 10 for \$199	Sterile, ready-to-use, prepackaged syringes

significant cost because the imaging requires a special light and camera.

Alternative localization techniques have included metal clips, fluoroscopy, barium enema, CT colonography, magnetic resonance imaging, and intraoperative colonoscopy.^{27,28} There are no studies comparing endoscopic tattooing with these alternative methods of localization.

SAFETY

Injection of appropriately diluted and sterile solutions is generally safe, with most complications related to transmural injection. A retrospective study of 195 patients undergoing 4-quadrant tattooing with 0.2- to 0.5-mL aliquots of sterile 1:100 India ink found no short-term complications.²⁹ A retrospective analysis of 447 cases of colonic tattooing by using various India ink preparations found a complication in only 1 patient in whom abdominal pain, tenderness, and fever developed after tattooing a cautery-induced ulcer.⁶ In a prospective study of India ink tattooing in 55 patients, no clinical complications were noted.³⁰ After an average of 36 months of follow-up, there were no endoscopically visible inflammatory changes and evaluation of 74 biopsy specimens from these patients revealed no histologic changes at the tattoo sites in 48 patients, mild chronic inflammation in 6 patients, and hyperplastic changes in 1 patient. Other case reports of complications after colonic tattooing with India ink include an isolated case of idiopathic inflammatory bowel disease, 3 abdominal abscesses, 2 cases of inflammatory pseudotumor, 1 case of focal peritonitis, and instances of peritoneal staining.^{5,31-35} In all these case reports, India ink was injected either undiluted or at a 1:1 or 1:10 dilution.

In a study of 63 patients who had tattooing with Spot, 6 patients (9.5%) had peritoneal leakage based on findings at surgery; mild peritonitis developed in only 1 patient.¹² Another case study of 3 patients who underwent endoscopic tattooing by using this agent reported intraoperative identification of black macular patches or streaks at extraintestinal sites including the peritoneum and mesentery. This is thought to be caused by either intraperitoneal spillage of the dye from deep injection or migration of

pigment-laden macrophages via lymphatic channels.³⁶ A MAUDE database search for Spot resulted in 1 report of a patient I whom fever, abdominal pain, and abnormal liver enzymes developed after injection at the hepatic flexure.³⁷

In a single case report, injection of dye too close to a malignant lesion or contacting the tumor with the needle tip during tattooing was reported to cause needle-track implantation at a site distinct from the tumor.¹³

FINANCIAL CONSIDERATIONS

The list prices of currently available sterile preparations of tattooing agents are listed in Table 1. The CPT (Current Procedural Terminology)* codes for “directed submucosal injection(s), _any substance” are used for endoscopic tattooing. For esophagoscopy with directed submucosal injection(s), report CPT 43201; for EGD, the CPT code is 43236. For sigmoidoscopy, the applicable code is 45335, and for colonoscopy, proximal to the splenic flexure; with directed submucosal injection(s), any substance, the code is 45381. In other intestine sites, use of code 44799 (unlisted service, intestine) would be appropriate, providing the report and a cover letter to the payer requesting payment equivalent to the services denoted by the specific CPT codes noted. National correct coding bundling edits exclude same-day reporting of the base codes within these sections (eg, 45330 or 43235) but do not require specific modifiers to report separate services such as biopsy and polypectomy. Payment is typically based on multiple-procedure (51 modifier) or family of code (59 modifier) rules, but varies with the payer. More guidance is provided in the ASGE *Coding Primer, A Guide for Gastroenterologists* (2009).³⁸

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AREAS OF FUTURE RESEARCH

Spot is the only FDA-approved endoscopic tattooing agent. The data on long-term safety and effectiveness of this agent are limited. Studies comparing different tattooing agents are needed. In addition, other localization techniques using endoscopic metallic clips or CT-colonography should be compared with tattooing techniques. The utility of shorter length needles should be evaluated to prevent inadvertent deep intestinal injection leading to peritoneal spillage. Finally, more studies are needed to define the added benefit of EUS-guided fine-needle tattooing relative to preoperative localization using imaging alone.

SUMMARY

Endoscopic tattooing is an effective means to enable subsequent endoscopic and surgical localization of luminal digestive tract lesions. India ink has been used effectively in a large number of cases over several decades. When diluted (1:100 with normal saline solution) and injected tangentially in small aliquots (0.5-1 mL), India ink tattooing is safe and long-lasting. One purified carbon particle suspension is the only FDA-approved agent for this indication and its ready-to-use formulation offers convenience. ICG has been used less frequently and appears to be safe but provides a less durable tattoo.

REFERENCES

1. Cho YB, Lee WY, Yun HR, et al. Tumor localization for laparoscopic colorectal surgery. *World J Surg* 2007;31:1491-5.
2. Vignati P, Welch JP, Cohen JL. Endoscopic localization of colon cancers. *Surg Endosc* 1994;8:1085-7.
3. Wexner SD, Cohen SM, Ulrich A, et al. Laparoscopic colorectal surgery—are we being honest with our patients? *Dis Colon Rectum* 1995;38:723-7.
4. Ponsky JL, King JF. Endoscopic marking of colonic lesions. *Gastrointest Endosc* 1975;22:42-3.
5. Shatz BA, Thavorides V. Colonic tattoo for follow-up of endoscopic sessile polypectomy. *Gastrointest Endosc* 1991;37:59-60.
6. Nizam R, Siddiqi N, Landas SK, et al. Colonic tattooing with India ink: benefits, risks, and alternatives. *Am J Gastroenterol* 1996;91:1804-8.
7. Salamon P, Berner JS, Wayne JD. Endoscopic India ink injection: a method for preparation, sterilization, and administration. *Gastrointest Endosc* 1993;39:803-5.
8. Hammond DC, Lane FR, Welk RA, et al. Endoscopic tattooing of the colon: an experimental study. *Am Surg* 1989;55:457-61.
9. ASGE Technology Committee: Conway JD, Adler DG, Diehl DL, et al. Endoscopic hemostatic devices. *Gastrointest Endosc* 2009;69:987-96.
10. Fennerty MB, Sampliner RE, Hixson LJ, et al. Effectiveness of India Ink as a long-term colonic mucosal marker. *Am J Gastroenterol* 1992;87:79-81.
11. Hyman N, Wayne JD. Endoscopic four quadrant tattoo for the identification of colonic lesions at surgery. *Gastrointest Endosc* 1991;37:56-8.
12. Park JW, Sohn DK, Hong CW, et al. The usefulness of preoperative colonoscopic tattooing using a saline test injection method with pre-packaged sterile India ink for localization in laparoscopic colorectal surgery. *Surg Endosc* 2008;22:501-5.
13. Raju GS. What is new in tattooing? Custom tattooing. *Gastrointest Endosc* 2004;59:328-9.
14. 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;33:687-91.
15. Sawaki A, Nakamura T, Suzuki T, et al. A two-step method for marking polypectomy sites in the colon and rectum. *Gastrointest Endosc* 2003;57:735-7.
16. Shaffer RT, Francis JM, Carrougner JG, et al. India ink tattooing in the esophagus. *Gastrointest Endosc* 1998;47:257-62.
17. Sun L, Si J, Chen S, Liu W, et al. The establishment and clinical appliance of technique of mucosa marking targeting biopsy. *Hepatogastroenterology* 2009;56:59-62.
18. Akahoshi K, Kubokawa M, Matsumoto M, et al. Double-balloon endoscopy in the diagnosis and management of GI tract diseases: methodology, indications, safety, and clinical impact. *World J Gastroenterol* 2006;12:7654-9.
19. Price N, Gottfried MR, Clary E, et al. Safety and efficacy of India ink and indocyanine green as colonic tattooing agents. *Gastrointest Endosc* 2000;51:438-42.
20. Gress FG, Barawi M, Kim D, et al. Preoperative localization of a neuroendocrine tumor of the pancreas with EUS-guided fine needle tattooing. *Gastrointest Endosc* 2002;55:594-7.
21. Farrell JJ, Sherrrod A, Parekh D. EUS-guided fine-needle tattooing for preoperative localization of early pancreatic adenocarcinoma. *Gastrointest Endosc* 2009;69:176-7.
22. Ashida R, Yamao K, Okubo K, et al. Indocyanine green is an ideal dye for endoscopic ultrasound-guided fine-needle tattooing of pancreatic tumors. *Endoscopy* 2006;38:190-2.
23. Askin MP, Wayne JD, Fiedler L, et al. Tattoo of colonic neoplasms in 113 patients with a new sterile carbon compound. *Gastrointest Endosc* 2002;56:339-42.
24. Hammond DC, Lane FR, Mackeigan JM, et al. Endoscopic tattooing of the colon: clinical experience. *Am Surg* 1993;59:205-10.
25. Miyoshi N, Ohue M, Noura S, et al. Surgical usefulness of indocyanine green as an alternative to India ink for endoscopic marking. *Surg Endosc* 2009;23:347-51.
26. Watanabe M, Tsunoda A, Narita K, et al. Colonic tattooing using fluorescence imaging with light-emitting diode-activated indocyanine green: a feasibility study. *Surg Today* 2009;39:214-8.
27. Tabibian N, Michaletz PA, Schwartz JT, et al. Use of endoscopically placed clip can avoid diagnostic errors in colonoscopy. *Gastrointest Endosc* 1988;34:262-5.
28. Frager DH, Frager JD, Wolf EL, et al. Problems in the colonoscopic localization of tumors: continued value of the barium enema. *Gastrointest Radiol* 1987;12:343-6.
29. McArthur CS, Roayaie S, Wayne JD. Safety of preoperation endoscopic tattoo with India ink for identification of colonic lesions. *Surg Endosc* 1999;13:397-400.
30. Shatz BA, Weinstock LB, Swanson PE, et al. Long-term safety of India ink tattoos in the colon. *Gastrointest Endosc* 1997;45:153-6.
31. Gopal DV, Morava-Protzner I, Miller HAB, et al. Idiopathic inflammatory bowel disease associated with colonic tattooing with India ink preparation—case report and review of the literature. *Gastrointest Endosc* 1999;49:636-9.
32. Park SI, Genta RS, Romeo DP, et al. Colonic abscess and focal peritonitis secondary to India ink tattooing of the colon. *Gastrointest Endosc* 1991;137:68-71.
33. Coman E, Brandt LJ, Brenner S, et al. Fat necrosis and inflammatory pseudotumor due to endoscopic tattooing of the colon with India ink. *Gastrointest Endosc* 1991;37:65-8.
34. Alba LM, Pandya PK, Clarkston WK. Rectus muscle abscess associated with endoscopic tattooing of the colon with India ink. *Gastrointest Endosc* 2000;52:557-8.
35. Dell'Abate P, Iosca A, Galimberti P, et al. Endoscopic preoperative colonic tattooing: a clinical and surgical complication. *Endoscopy* 1999;31:271-3.
36. Cappell MS, Courtney JT, Amin M. Black macular patches on parietal peritoneum and other extraintestinal sites from intraperitoneal spillage and spread of India ink from preoperative endoscopic tattooing: an endoscopic, surgical, gross pathologic, and microscopic study. *Dig Dis Sci* 2009 Dec 3 [Epub ahead of print].

37. MAUDE (Manufacturer and user facility device experience) database. Available at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=879793. Accessed on January 31, 2010.
38. Littenberg G, editor. The ASGE coding primer: a guide for gastroenterologists. Oak Brook (Ill): ASGE; 2009. p. 34-42; 75.

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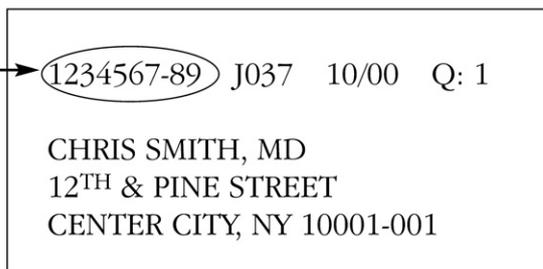
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