Table 3 Comparison of diiagnositic performance for neoplastic and non-neoplastic lesions between white light colonoscopy, chromoendoscopy and NBI

Author	Year	Evaluation method	Institute	No. endoscopists	*n* (polyp/pts)	NBI system	Magnification	Comparison	Endopoints	Assessment	Results
H Machida	2004	Pilot study	Single	2	43/34	RGB sequential illuination	+	NBI vs CE vs WLI	Differential diagnosis	Pit pattern (Kudo's classification) and vascular network	NBI = CE > WLI
MY Su	2006	Feasibility test	2 hospitals	3	110/78	RGB sequential illuination	–	NBI vs CE	Differential diagnosis	Pit pattern (Kudo's classification)	NBI = CE
HM Chiu	2007	Retrospective image review	2 hospitals	4	180/133	RGB sequential illuination	+	NBI vs CE vs WLI	Differential diagnosis	Pit pattern (Kudo's classification)	NBI = CE > WLI
M Hirata	2007	Retrospective study	Single	2	189/163	RGB sequential illuination	+	NBI alone	Prediction of histology	Vascular thickness & vascular iregularity	NBI can predict histologic grade and depth of invasion
M Hirata	2007	Retrospective study	Single	Not described	148/99	RGB sequential illuination	+	NBI alone	Differential diagnosis	Pit pattern (Kudo's classification)	NBI = CE
JJW Tischendorf	2007	Prospective RCT	Single	2	200/99	color CCD chip	+	NBI vs CE	Differential diagnosis	Pit pattern (Kudo's classification) and vascular intensity and shape	Pit patten (NBI = CE) Vascular pattern (NBI > CE)
JN Rogart	2007	Prospective polyp series	Single	4	265/131	color CCD chip	–	NBI vs WLI	Differential diagnosis	Pit pattern (Kudo's classification) and vascular color intensity	NBI = WLI
JE East	2008	Prospective polyp series	Single	1	33/20	RGB sequential illuination	+	NBI vs CE	Differential diagnosis	Pit pattern (Kudo's classification) and vascular pattern intensity	NBI = CE
T Katagiri	2008	Prospective polyp series	Single	1	139/104	RGB sequential illuination	+	NBI alone	Prediction of histology	Micro vessel shape	NBI capillary pattern can assess the degree of atypia
Y Sano	2008	Prospective polyp series	Single	1	150/92	RGB sequential illuination	+	NBI alone	Differential diagnosis	Visibility of meshed capillary pattern	NBI meshed capillary pattern is useful for differential diagnosis
S Sikka	2008	Retrospective image review	Single	2	80/31	color CCD chip	–	NBI vs WLI	Prediction of histology	Modified Kudo's classification and vascular markig	NBI > WLI
A Rostagi	2008	Feasibility test	Single	1	123/40	color CCD chip	–	NBI vs WLI	Prediction of histology	Mucosal and vascular pattern	NBI can predict histologic diagnosis

CCD, charge coupled device; CE, chromoendoscopy; NBI, narrow band imaging; RGB, red-green-blue; WLI, white light image.

when a high resolution magnifying endoscope is combined with a RGB sequential illumination NBI system, the adenoma detection rate appears to be significantly increased. In contrast, if a non-magnifying endoscope is used, the adenoma detection rate will not improve, even by using high resolution. However, NBI is useful to detect additional adenomas in the back-to-back fashion after white light observation.[62,65] To date, there are no data on direct comparison of detection of neoplasms in the colon (and also other parts of the gastrointestinal tract) between the RGB sequential illumination NBI system and color CCD chip NBI system. Therefore, investigation is required to establish whether there are any differences of detection power between these technologies, using large-scale multicenter prospective randomized control studies.

Overlooking neoplastic colonic polyps has been one of the major problems to solve in CRC screening programs; such oversight can lead to the development of colon cancer within a few years after an apparently complete colonoscopy. While Kaltenbach *et al.*[67] reported that NBI did not reduce the miss rate of colorectal neoplasms compared with white light observation, Uraoka *et al.*[66] reported that the miss ratio of both flat and polypoid neoplasic lesions decreased by the use of NBI compared with white light observation. It is unclear whether this difference depends on the difference of NBI systems. A ratio of high detection rates and low missing rates is ideal for any cancer screening test. Therefore, the future challenge is to investigate which system (RGB sequential or color chip) is superior for decreasing the missing rate of colorectal neoplasms.

Machida *et al.*[13] first evaluated the diagnostic performance of the NBI system for colorectal lesions. In their pilot study, NBI with magnifying endoscope achieved better visualization of the mucosal vascular network pattern than conventional white light imaging. Further, the accuracy for diagnosing neoplastic polyps by NBI was equivalent to chromoendoscopy. To date, 12 studies[13,65,68–77] on diagnostic performance of NBI have been published (Table 3). Of them, eight studies were aimed at differential diagnosis, six showed comparable performance between NBI and chromoendoscopy, three showed superiority of NBI to white light imaging, and one study showed the superiority of NBI to chromoendoscopy when assessment had been based on microvascular pattern. One study showed that NBI 'meshed capillary pattern' was useful for differential diagnosis. The remaining four studies were aimed at prediction of polyp histology. All four reported that NBI assessment based on vascular pattern was useful in predicting histology of colorectal polyps.

A recent meta-analysis showed that, in the colon, there was no significant difference in diagnostic accuracy for neoplasm between NBI and chromoendoscopy, but NBI was significantly more accurate than white light observation alone.[78] In addition, this meta-analysis showed that simple assessment of the microvasculature is enough to make an accurate diagnosis of colonic neoplasm. This means that NBI could become the standard endoscopic procedure for detection and diagnosis of colonic neoplasms.

Conclusions

Narrow band imaging is now a promising endoscopic technology to improve the detection and diagnostic accuracy of neoplastic lesions in the head and neck region and the gastrointestinal tract. However, most studies have been conducted at a single institution and carried out by one or a few observers. Thus, we should confirm these data with a large scale prospective randomized trial to standardize both technological aspects and precise indications for NBI.

References

1 Gono K, Yamazaki K, Doguchi N *et al.* Endoscopic observation of tissue by narrow band illumination. *Opt. Rev.* 2003; **10**: 1–5.
2 Gono K, Obi T, Yamaguchi M *et al.* Appearance of enhanced tissue feature in narrow-band endoscopic imaging. *J. Biomed. Opt.* 2004; **9**: 568–77.
3 Sano Y, Kobayashi M, Hamamoto Y *et al.* New diagnostic method based on color imaging using narrow-band imaging (NBI) system for gastrointestinal tract [abstract]. *Gastrointest. Endosc.* 2001; **53**: AB125.
4 Kudo S, Hirota S, Nakajima T *et al.* Colorectal tumours and pit pattern. *J. Clin. Pathol.* 1994; **47**: 880–5.
5 Inoue H, Honda T, Nagai K *et al.* Ultra-high magnification endoscopic observation of carcinoma *in situ* of the oesophagus. *Dig. Endosc.* 1997; **9**: 16–18.
6 Kumagai Y, Inoue H, Nagai K, Kawano T, Iwai T. Magnifying endoscopy, stereoscopic microscopy, and the microvascular architecture of superficial esophageal carcinoma. *Endoscopy* 2002; **34**: 369–75.
7 Yao K, Oishi T. Microgastroscopic findings of mucosal microvascular architecture as visualized by magnifying endoscopy. *Dig. Endosc.* 2001; **13**: S27–33.
8 Yao K, Oishi T, Matsui T, Yao T, Iwashita A. Novel magnified endoscopic findings of microvascular architecture in intramucosal gastric cancer. *Gastrointest. Endosc.* 2002; **56**: 279–84.
9 Muto M, Nakane M, Katada C *et al.* Squamous cell carcinoma *in situ* at oropharyngeal and hypopharyngeal mucosal sites. *Cancer* 2004; **101**: 1375–81.
10 Muto M, Katada C, Sano Y, Yoshida S. Narrowband imaging: a new diagnostic approach to visualize angiogenesis in the superficial neoplasm. *Clin. Gastroenterol. Hepatol.* 2005; **3**: S16–20.
11 Muto M, Ugumori T, Sano Y, Ohtsu A, Yoshida S. Narrow band imaging combined with magnified endoscopy for the cancer at the head and neck region. *Dig. Endosc.* 2005; **17**: S23–S24.
12 Shibuya K, Hoshino H, Chiyo M *et al.* High magnification bronchovideoscopy combined with narrow band imaging could detect capillary loops of angiogenic squamous dysplasia in heavy smokers at high risk for lung cancer. *Thorax* 2003; **58**: 989–95.
13 Machida H, Sano Y, Hamamoto Y *et al.* Narrow-band imaging in the diagnosis of colorectal lesions: a pilot study. *Endoscopy* 2004; **36**: 1094–8.
14 East JE, Tan EK, Bergman JJ, Saunders BP, Tekkis PP. Meta-analysis: narrow band imaging for lesion characterization in the colon, oesophagus, duodenal ampulla and lung. *Aliment. Pharmacol. Ther.* 2008; **28**: 854–67.
15 Adler A, Pohl H, Papanikolaou IS *et al.* A prospective randomized study on narrow-band imaging versus conventional colonoscopy for adenoma detection: does NBI induce a learning effect. *Gut* 2008; **57**: 59–64.
16 Yoshida T, Inoue H, Usui S, Satodate H, Fukami N, Kudo SE. Narrow-band imaging system with magnifying endoscopy for superficial esophageal lesions. *Gastrointest. Endosc.* 2004; **59**: 288–95.
17 Watanabe A, Tsujie H, Taniguchi M, Hosokawa M, Fujita M, Sasaki S. Laryngoscopic detection of pharyngeal carcinoma *in situ* with narrowband imaging. *Laryngosocpe* 2006; **116**: 650–4.
18 Watanabe A, Taniguchi M, Tsujie H, Hosokawa M, Fujita M, Sasaki S. The value of narrow band imaging endoscope for early

head and neck cancers. *Otolaryngol. Head Neck Surg.* 2008; **138**: 446–51.
19 Ugumori T, Muto M, Hayashi R, Hayashi R, Kishimoto S. Prospective study of early detection of pharyngeal superficial carcinoma with the narrowband imaging laryngoscope. *Head Neck* 2009; **31**: 189–94.
20 Slaughter DP, Southwick HW, Smejkal W. Field cancerization in oral stratified squamous epithelium: clinical implications of multicentric origin. *Cancer* 1953; **6**: 963–8.
21 Ioue H, Rey JF, Lightdale C. Lugol chromoendoscopy for esophageal squamous cell cancer. *Endoscopy* 2001; **35**: 75–9.
22 Mori M, Adachi Y, Matsushima T, Matsuda H, Kuwano H, Sugimachi K. Lugol staining pattern and histology of esophageal lesions. *Am. J. Gastroenterol.* 1993; **88**: 701–5.
23 Muto M, Saito Y, Ohmori T *et al.* Multicenter prospective randomized controlled study on the detection and diagnosis of superficial squamous cell carcinoma by back-to-back endoscopic examination of narrowband imaging and white light observation. *Gastrointest. Endosc.* 2007; **65**: AB110.
24 Lee YC, Wang CP, Chen CC *et al.* Transnasal endoscopy with narrow-band imaging and Lugol staining to screen patients with head and neck cancer whose condition limits oral intubation with standard endoscope (with video). *Gastrointest. Endosc.* 2009; **69**: 408–17.
25 Kiesslich R, Kanzler S, Vieth M *et al.* Minimal change esophagitis: prospective comparison of endoscopic and histological markers between patients with non-erosive reflux disease and normal controls using magnifying endoscopy. *Dig. Dis.* 2004; **22**: 221–7.
26 Sharma P, Wani S, Bansal A *et al.* A feasibility trial of narrow band imaging endoscopy in patients with gastroesophageal reflux disease. *Gastroenterology* 2007; **133**: 454–64.
27 Lee YC, Lin JT, Chie HM *et al.* Intraobserver and interobserver consistency for grading esophagitis with narrow-band imaging. *Gastrointest. Endosc.* 2007; **66**: 230–6.
28 Wj B, Devesa SS, Kneller RW *et al.* Rising incidence of adenocarcinoma of the esophagus and gastric cardia. *JAMA* 1991; **265**: 1287–9.
29 Devesa SS, Blot WJ, Fraumeni JF *et al.* Changing pattern in the incidence of oesophageal and gastric carcinoma in the United States. *Cancer* 1998; **83**: 2049–53.
30 Working Party of the British Society of Gastroenterology. Guidelines for the diagnosis and management of Barrett's columnar-lined oesophagus: A report from the Working Party of the British Society of Gastroenterology, August 2005. Cited 5 August 2009. Available from URL: http://www.bsg.org.uk/clinical-guidelines/oesophageal/guidelines-for-the-diagnosis-and-management-of-barrett-s-columnar-lined-oesophagus.html; www.bsg.org.uk/.
31 Egger K, Wermer M, Meining A *et al.* Biopsy surveillance is still necessary in patients with Barrett's esophagus despite a new endoscopic imaging technique. *Gut* 2003; **52**: 18–23.
32 Kara MA, Peters FP, Rosmolen WD *et al.* High-resolution endoscopy plus chromoendoscopy or narrow-band imaging in Barrett's esophagus: a prospective randomized crossover study. *Endoscopy* 2005; **37**: 929–36.
33 Hamamoto Y, Endo T, Nosho K, Arimura Y, Sato M, Imai K. Usefulness of narrow-band imaging endoscopy for diagnosis of Barrett's esophagus. *J. Gastroenterol.* 2004; **39**: 14–20.
34 Kara MA, Ennahachi M, Fockens P, Kate FJ, Bergman JJ. Detection and classification of the mucosal and vascular patterns (mucosal morphology) in Barrett's esophagus by using narrow band imaging. *Gastrointest. Endosc.* 2006; **64**: 155–66.
35 Sharma P, Bansal A, Mathur S *et al.* The utility of a novel narrow band imaging endoscopy system in patients with Barrett's esophagus. *Gastrointest. Endosc.* 2006; **64**: 167–75.
36 Goda K, Tajiri H, Ikegami M, Urashima M, Nakayoshi T, Kaise M. Usefulness of magnifying endoscopy with narrow band imaging for the detection of specialized intestinal metaplasia in columnar-lined esophagus and Barrett's adenocarcinoma. *Gastrointest. Endosc.* 2007; **65**: 36–46.
37 Anagnostopoulus GK, Yao K, Kaye P, Hawkey CJ, Ragunath K. Novel endosocpic observation in Barrett's oesophagus using high resolution endoscopy and narrow band imaging. *Aliment. Pharnacol. Ther.* 2007; **26**: 501–7.
38 Singh R, Anagnostopoulus GK, Yao K *et al.* Narrow-band imaging with magnification in Barrett's esophagus: validation of simplified grading system of mucosal morphology pattern against histology. *Endoscopy* 2008; **40**: 457–3.
39 Wolfsen H, Crook JE, Krishna M *et al.* Prospective, controlled tandem endoscopy study of narrow band imaging for dysplasia detection in Barrett's esophagus. *Gastroenterology* 2008; **135**: 24–31.
40 Busuttil RA, Boussioutas A. Intestinal metaplasia: a premalignant lesion involved in gastric carcinogenesis. *J. Gastroenterol. Hepatol.* 2009; **24**: 193–201.
41 Uedo N, Ishihara R, Iishi H *et al.* A new method of diagnosing gastric intestinal metaplasia: narrow band imaging with magnifying endoscopy. *Endoscopy* 2006; **38**: 819–24.
42 Bansal A, Ulusarac O, Mathur S, Sharma P. Correlation between narrow band imaging and non-neoplastic gastric pathology: a pilot feasibility trial. *Gastrointest. Endosc.* 2008; **67**: 210–16.
43 Yao K, Iwasita A, Tanabe H *et al.* Novel zoom endoscopy technique for diagnosis of small flat gastric cancer: A prospective, blind study. *Clin. Gastroenterol. Hepatol.* 2007; **5**: 869–78.
44 Yao K, Iwashita A, Tanabe H *et al.* White opaque substance within superficial elevated gastric neoplasia as visualized by magnification endoscopy with narrow-band imaging: a new optical sign for differentiating between adenoma and carcinoma. *Gastrointest. Endosc.* 2008; **68**: 574–80.
45 Nakayoshi T, Tajiri H, Matsuda K, Kaise M, Ikegami M, Sasaki H. Magnifying endoscopy combined with narrow band imaging system for early gastric cancer: correlation of vascular pattern with histopathology. *Endoscopy* 2004; **36**: 1080–4.
46 Sumiyama K, Kaise M, Nakayoshi T *et al.* Combined use of a magnifying endoscope with a narrow band imaging system and a multibending endoscope for en bloc EMR of early stage gastric cancer. *Gastrointest. Endosc.* 2004; **60**: 79–84.
47 Tamai N, Kaise M, Nakayoshi T *et al.* Clinical and endoscopic characterization of depressed gastric adenoma. *Endosocpy* 2006; **38**: 391–4.
48 Uchiyama Y, Imazu H, Kazutani H *et al.* New approach to diagnosing ampullary tumors by magnifying endoscopy with a narrow-band imaging system. *J. Gastroenterol.* 2006; **41**: 483–90.
49 Itoi T, Tsuji S, Sofuni A *et al.* A novel approach emphasizing preoperative margin enhancement of tumor of the major duodenal papilla with narrow-band imaging in comparison to indigo carmine chromoendoscopy (with videos), 21 November 2008. *Gastrointest. Endosc.* 2009; **69**: 136–41.
50 Vogelstein B, Fearon ER, Hamilton SR *et al.* Genetic alterations during colorectal-tumor development. *N. Engl. J. Med.* 1988; **319**: 525–32.
51 Winawer S, Zauber A, Ho M *et al.* Prevention of colorectal cancer by colonoscopic polypectomy: the National Polyp Study Workgroup. *N. Engl. J. Med.* 1993; **329**: 1977–81.
52 Jemal A, Siegle R, Ward E *et al.* Cancer statistics. *CA Cancer J. Clin.* 2006; **56**: 106–30.
53 Rockey DC, Paulson E, Niedzwiecki D *et al.* Analysis of air contrast barium enema, computed tomographic colonoscopy, and colonoscopy: prospective comparison. *Lancet* 2005; **365**: 305–11.

54 Rex DK, Cutler CS, Lemmel GT *et al.* Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. *Gastroenterology* 1997; **112**: 24–8.

55 Van Rijn JC, Reitsma JB, Stoker J, Bossuyt PM, van Deventer SJ, Dekker E. Polyp miss rate determined by tandem colonoscopy: a systematic review. *Am. J. Gastroenterol.* 2006; **101**: 343–50.

56 Heresbach D, Barrioz T, Lapalus MG *et al.* Miss rate for colorectal neoplastic polyps: a prospective multicenter study of back-to-back video colonoscopies. *Endoscopy* 2008; **40**: 284–90.

57 Roberts-Thomson IC, Teo E. Colonoscopy: art or science? *J. Gastroenterol. Hepatol.* 2009; **24**: 180–4.

58 Kiesslich R, von Bergh M, Hahn M, Hermann G, Jung M. Chromoendoscopy with indigocarmine improves the detection of adenomatous and nonadenomatous lesions in the colon. *Endoscopy* 2001; **33**: 1001–6.

59 Brooker JC, Saunders BP, Hah SG *et al.* Total colonic dye-spray increases the detection of diminutive adenomas during routine colonoscopy: a randomized controlled trial. *Gastrointest. Endosc.* 2002; **56**: 333–8.

60 Hurlstone DP, Cross SS, Slater S, Sanders DS, Brown S. Detecting diminutive colorectal lesions at colonoscopy: a randomised controlled trial of pan-colonic versus targeted chromoscopy. *Gut* 2004; **53**: 376–80.

61 Rex DK, Helbig CC. High yields of small and flat adenomas with high-definition colonoscopes using either white light or narrow band imaging. *Gastroenterology* 2007; **133**: 42–7.

62 East JE, Suzuki N, Saunders BP. Comparison of magnified pit pattern interpretation with narrow band imaging versus chromoendoscopy for diminutive colonic polyps: a pilot study. *Gastrointest. Endosc.* 2007; **66**: 310–16.

63 Adler A, Pohl H, Papanikolaou IS *et al.* A prospective randomised study on narrow-band imaging versus conventional colonoscopy for adenoma detection: does narrow-band imaging induce a learning effect? *Gut* 2008; **57**: 59–64.

64 Inoue T, Murano M, Murano N *et al.* Comparative study of conventional colonoscopy and pan-colonic narrow-band imaging system in the detection of neoplastic colonic polyps: a randomized, controlled trial. *J. Gastroenterol.* 2008; **43**: 45–50.

65 Rastogi A, Bansal A, Wani S *et al.* Narrow-band imaging colonoscopy—a pilot feasibility study for the detection of polyps and correlation of surface patterns with polyp histologic diagnosis. *Gastrointest. Endosc.* 2008; **67**: 280–6.

66 Uraoka T, Saito Y, Matsuda T *et al.* Detectability of colorectal neoplastic lesions using a narrow-band imaging system: A pilot study. *J. Gastroenterol. Hepatol.* 2008; **23**: 1810–15.

67 Kaltenbach T, Friedland S, Soetikno R. A randomized tandem colonoscopy trial of narrow band imaging versus white light examination to compare neoplasia miss rate. *Gut* 2008; **57**: 1406–12.

68 Su MY, Hsu CM, Ho YP, Chen PC, Lin CJ, Chiu CT. Comparative study of conventional colonoscopy, chromoendoscopy, and narrow-band imaging systems in differential diagnosis of neoplastic and non-neoplastic colonic polyps. *Am. J. Gastroenterol.* 2006; **101**: 2711–16.

69 Chiu HM, Chang CY, Chen CC *et al.* A prospective comparative study of narrowband imaging, chromoendoscopy, and conventional colonoscopy in the diagnosis of colorectal neoplasia. *Gut* 2007; **56**: 373–9.

70 Hirata M, Tanaka S, Oka S *et al.* Magnifying endoscopy with narrow band imaging for diagnosis of colorectal tumors. *Gastrointest. Endosc.* 2007; **65**: 988–95.

71 Hirata M, Tanaka S, Oka S *et al.* Evaluation of microvessels in colorectal tumors by narrow band imaging magnification. *Gastrointest. Endosc.* 2007; **66**: 945–52.

72 Tischendorf JJW, Wasmuth HE, Koch A, Hecker H, Trautwein C, Winograd R. Value of magnifying chromoendoscopy and narrow band imaging (NBI) in classifying colorectal polyps: a prospective controlled study. *Endoscopy* **39**: 1092–6.

73 Rogart JN, Jain D, Siddiqui UD *et al.* Narrow-band imaging without high magnification to differentiate polyps during real-time colonoscopy: improvement with experience. *Gastrointest. Endosc.* 2008; **68**: 1136–45.

74 East JE, Suzuki N, Stavrinidis M, Guenther T, Thomas HJW, Saunders BP. Narrow band imaging for colonoscopic surveillance in hereditary nonpolyposis colorectal cancer. *Gut* 2008; **57**: 65–70.

75 Katagiri A, Fu KI, Sano Y *et al.* Narrow band imaging with magnifying colonoscopy as a diagnostic tool for predicting the histology of early colorectal neoplasia. *Aliment. Pharmacol. Ther.* 2008; **27**: 1269–74.

76 Sano Y, Ikemastu H, Fu KI *et al.* Meshed capillary vessels by use of narrow-band imaging for differential diagnosis of small colorectal polyps. *Gastrointest. Endosc.* 2009; **69**: 278–83.

77 Sikka S, Ringold DA, Jonnalagadda S, Banerjee B. Comparison of white light and narrow band high definition images in predicting colon polyp histology, using standard colonoscopes without optical magnification. *Endoscopy* 2008; **40**: 818–22.

78 East JE, Tan EK, Bergman JJ *et al.* Meta-analysis: narrow ban imaging for lesion characterization in the colon, oesophagus, duodenal umpulla and lung. *Aliment. Pharmacol. Ther.* 2008; **28**: 854–67.

Teleteaching endoscopy: the feasibility of real-time, uncompressed video transmission by using advanced-network technologies

Tonya Kaltenbach, MD, MS, Manabu Muto, MD, PhD, Roy Soetikno, MD, MS, Parvati Dev, PhD, MS, Koji Okamura, PhD, Joonsoo Hahm, MD, Shuji Shimizu, MD, PhD

Palo Alto, California, USA

Background: Teleteaching of endoscopy has been limited by the exorbitant cost and time inherent in high-quality digital endoscopy video transmission. The Digital Video Transport System (DVTS) transmitted over advanced networks, such as Internet2 and the Asia-Pacific Advanced Network (APAN), provides a unique infrastructure for sharing uncompressed digital videos of endoscopy. This may allow high-quality, real-time, international training of diagnostic and therapeutic endoscopy techniques at a low cost.

Objective: To test the proof of concept of long-distance teaching through live, interactive, high-resolution video transmission by using advanced networks and the DVTS. We used teleteaching of image-enhanced endoscopy techniques as a model.

Design: Prospective multicenter pilot study.

Setting and Participants: Trainees, faculty, and staff at 3 international endoscopy units.

Intervention: An image-enhanced endoscopy video lecture with advanced-network technologies.

Main Outcome Measurements: We compared image-based prelecture and postlecture test scores and secondarily assessed technical feasibility and quality.

Results: The DVTS transmitted over advanced networks successfully transmitted uncompressed, high-resolution, digital lectures with endoscopic video (digital video format 720 × 480 pixels). Postsession scores improved. Participants highly rated the technical and informational quality. The majority reported a definite interest in participating in future sessions, with a mean rating (out of 5 [scale 1-5]) of 4.7 ± 0.5.

Limitations: Pilot study with a limited number of participants and sessions.

Conclusion: The DVTS transmitted over advanced networks such as Internet2 and APAN can provide the infrastructure for transmission of high-resolution, uncompressed video endoscopy for the purpose of teleteaching endoscopy.

Progress in endoscopy requires the efficient and effective transfer of knowledge. A promising method of transferring knowledge is through teleteaching.[1-4] Teleteaching of endoscopy has been limited by the exorbitant cost and amount of time inherent in high-quality, digital endoscopy video transmission.[5,6] The development of high-bandwidth networks—Internet2 and the Asia-Pacific Advanced Network (APAN)—coupled with a specialized program to transmit high-resolution, uncompressed video, such as the Digital Video Transport System (DVTS), may provide the ability to teleteach endoscopy to academic centers worldwide.

The advanced networks, such as Internet2 and APAN, are a nonprofit consortium, which develops and deploys applications and technologies for high-speed intensive data transfer within the research and education community. The physical network combines several robust,

Abbreviations: APAN, Asia-Pacific Advanced Network; DVTS, Digital Video Transport System; IEE, image-enhanced endoscopy.

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logistically distinct but related networks to create a super-broadband Internet line with a backbone of up to 10 gigabits per second—key to the effective and efficient transfer of large-bandwidth data (ie, real-time conferencing, high-definition video). Internet2 is available at more than 210 U.S. and 1000 Asian institutions and is connected globally to other similar networks. The client software for DVTS is freely available, simple, and inexpensive. It is designed for high-quality video and audio transmission over the Internet, with minimal image compression and low latency between sites during videoconferencing.[7] Video compression typically requires a powerful computer processor and time to render. Eliminating compression allows the utilization of commercially available personal computers and a minimal time lag between sending and receiving images, respectively. Thus, the use of the DVTS transmitted over an advanced network is a potential vehicle for teleteaching high-quality video endoscopy with live participant interaction.

We aimed to test the proof of concept of long-distance teleteaching through live, interactive, high-resolution video transmission by using advanced networks and the DVTS. We used teleteaching of image-enhanced endoscopy (IEE) techniques as a model, whereby dye, optical, and electronic methods are applied during endoscopic examination to augment the detection and diagnosis of subtle, precancerous lesions and early GI mucosal cancers.[8]

METHODS

Participants and study design

We conducted a prospective, multicenter, pilot study. Endoscopy units at 3 international sites—Veterans Affairs Palo Alto and Stanford University, USA; Kyoto University, Japan; and Kyushu University, Japan—participated. Hanyang University, South Korea, served as a technical site. We provided participants with written information about the approved study as requested by our institutional review board.

Teleteaching technology and content

We connected sites to high-speed networks with large bandwidths and used the DVTS for bidirectional video and audio. Two streams signaled from each site—the participants obtained by a digital video camera and the lecture and video images from the computer processor—without display or transfer of personally identifiable information.

Kyushu researchers led the system configuration. They connected stations with the DVTS by using the QualImage/Quatre server software (Information Services International-Dentsu, Ltd, Tokyo, Japan), and distributed uncompressed images. Upon request, they merged the 4 DVTS signals onto 1 screen and then returned the signal to the other centers for display (Fig. 1) or, alternatively, from the speaker or video images only (Fig. 2).

Capsule Summary

What is already known on this topic

- Information on advanced endoscopic techniques is often difficult to disseminate because of the limited number of experts, costs of travel, and deficiencies in learning in a text-based, didactic lecture.

What this study adds to our knowledge

- Image-based, prelecture and postlecture test scores from trainees, faculty, and staff at 3 international endoscopy units revealed that digital video transmitted over advanced networks resulted in effective endoscopy training.

Over a 6-week period, we organized four 1-hour sessions on the use of IEE in the detection and diagnosis of precancerous lesions and early GI cancers. Experts in IEE provided the lectures, in English, at 1600 Pacific standard time and 0800 Japan time.

Endpoints and statistics

We aimed to determine the teaching efficacy by using the DVTS transmission system of high-resolution images and video over advanced networks. Participants completed image-based, prelecture and postlecture tests in real-time (Appendix, available online at www.giejournal.org). We secondarily assessed the technical feasibility and quality (Appendix).

In this pilot study, we were careful to perform inferential statistical analyses. We focused on descriptive analyses and primarily used histograms for data illustration.

RESULTS

Participants (n = 42) showed overall improvement from 57% ± 25% prelecture test scores to 83% ± 17% postlecture test scores. Scores improved across sessions: 35% (53% ± 27% to 88% ± 15%; n = 15) in session 2, 31% (46% ± 23% to 77% ± 20%; n = 12) in session 3, and 13% (70% ± 18% to 83% ± 17%; n = 15) in session 4. Figure 3 illustrates the learning trend over each session and site. Participants highly rated the usefulness of the endoscopy images and videos (5.0 ± 0.4 [scale 1-5]), the commentary from remote and local faculty (4.8 ± 0.5), and the interactions with remote (4.9 ± 0.4) and local audiences (4.8 ± 0.5).

The large bandwidth (about 100 megabits per second) provided network stability during the televideo conference. The measured latency between sites is shown in Table 1. One interruption of the transmission occurred during the first (practice) session from Kyoto University because of a laptop malfunction and required network reconnection. The other 3 sites remained connected during the 8-minute period.

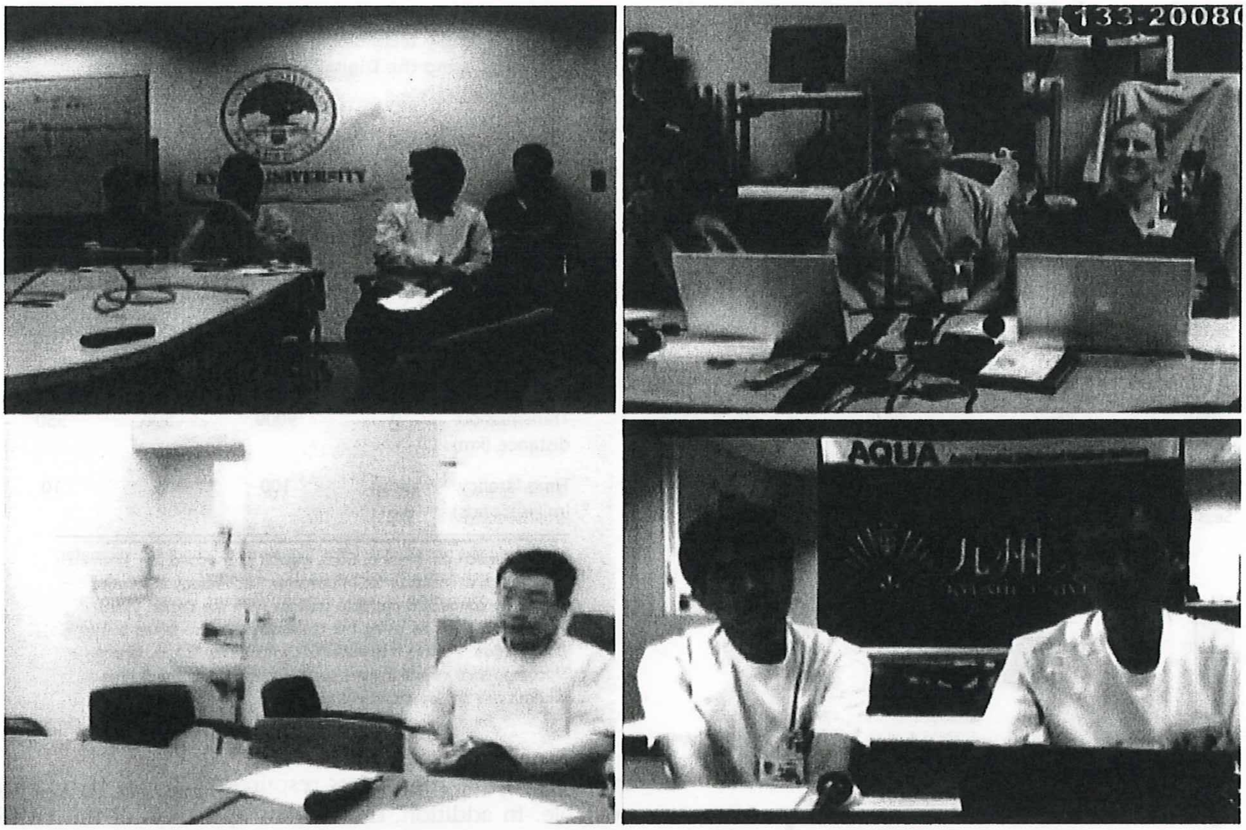

Figure 1. Screen capture of a composite image from the 4 participating centers. The original program was transmitted at 720 × 480 pixels digital video resolution with 30 frames per second.

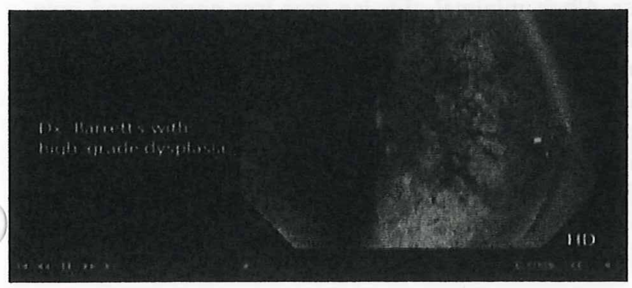

Figure 2. Screen capture from a video lecture display during one of the programs.

The majority of participants reported a definite interest in participating in future, similar sessions—mean rating of 4.7 ± 0.5 (range 3-5). Participants highly rated the technical quality of the endoscopic images and audio and video teleconferencing, with a mean rating of 4.7 ± 0.5, 4.5 ± 0.6, and 4.7 ± 0.5, respectively.

DISCUSSION

Progress in endoscopy requires the dissemination of information about technique and technology. The global availability of, demand for, and practice of endoscopy poses an increasing challenge to effectively and efficiently disseminate the art and science of endoscopic techniques and technologies. It is important to meet this challenge; otherwise, the potential benefit of endoscopy to more patients cannot be realized. Over the years, we have provided resources for learning endoscopy through self-study multimedia programs, publications, and lectures. Recently, we explored an interactive education mechanism—one that would allow us to interactively teach and learn endoscopy through real-time sharing of high-resolution endoscopy images and videos with other endoscopy centers at a minimal cost.

Herein, we describe a potential use of the super-broadband Internet connection for transmitting information (intensive endoscopic movies) for the purpose of teaching diagnostic and therapeutic endoscopy techniques that require images with fine details. We report that the infrastructure that is currently available to most academic centers worldwide can support such an effort by using advanced networks, such as Internet2, and the DVTS. The effort appears to be promising, as evidenced by participants' increasing understanding of a spectrum of concepts of IEE. The use of advanced networks and the DVTS is also highly efficient. It would have been otherwise costly and time prohibitive for the numerous speakers of the 4 IEE

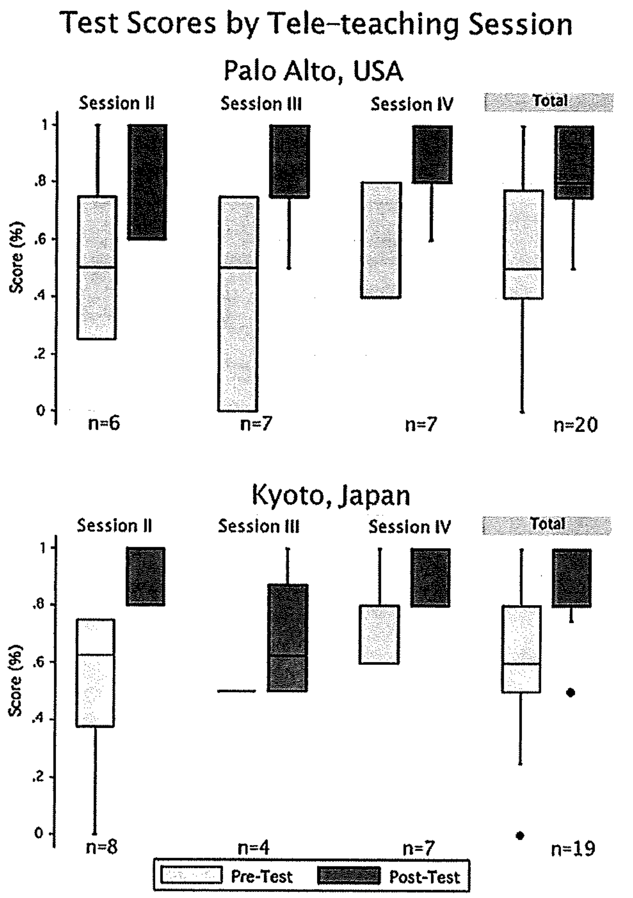

Figure 3. Distribution of participants' prelecture and postlecture scores, according to session number and site location. The height of the "box" displays the interquartile range (IQR), with the 25th and 75th percentiles representing the lower and upper edges of the box, respectively. The middle horizontal line across the box is the median. Error bars extend from the box to show the minimum and maximum data points (whiskers). The lower whisker represents the 25th percentile minus 1.5× IQR, and the upper whisker represents the 75th percentile plus 1.5× IQR. Values outside of the whiskers are defined as outliers.

TABLE 1. Study technology characteristics of advanced networks using the Digital Video Transport System

Technology	Kyushu University* Fukuoka, Japan	VA Palo Alto,Stanford University, Palo Alto, California, USA	Kyoto University, Kyoto, Japan	Hanyang University, Seoul, South Korea
Bandwidth				
Local	100 Mbps	1 Gbps	100 Mbps	1 Gbps
Remote	10 Gbps	1 Gbps	10 Gbps	1 Gbps
Transmission distance (km)	0	9000	500	550
Time latency (milliseconds)	about 0.01	100	5	10

Mbps, Megabit per second; *Gbps*, gigabit per second; *km*, kilometer.
*The Research Institute for Information Technology at Kyushu University connected multiple stations with the Digital Video Transport System by using the QualImage/Quatre server software (Information Services International-Dentsu, Ltd; Tokyo, Japan). Uncompressed digital images were distributed to the 3 sites without any analog conversion.

sessions to travel to the participating sites of this study. Comparatively, the annual Internet2 university membership dues and network participation fee is $60,000,[9] and the DVTS is free software. The hardware consists of an off-the-shelf digital video camera, audio gear, and a computer with Firewire-400 port and display monitor. Furthermore, once the technology infrastructure is in place, it can support numerous applications, such as distance learning, real-time clinical consultation, and live case demonstrations.[7,10]

We recognize a number of potential limitations of the use of advanced networks, such as Internet2 and APAN, and the DVTS. Namely, the robust technology has intensive bandwidth requirements. We used infrastructures of a super-broadband Internet line that was already available in our respective institutions. Though this infrastructure exists at most academic centers worldwide, the deployment and application of its resources may not be readily available. In addition, the current operation of the DVTS requires a supporting technician, rather than operating as a turn-key system. Although the line used is super broad, there was a limitation because of the lag time required for the data to be transmitted from one site to another. Albeit minimal, this lag time was appreciated only during conversation.

In summary, we have described our preliminary experience of using a new communication tool and system to potentially disseminate endoscopy effectively and efficiently. Further efforts to explore the use of the already available super-broadband Internet network for televideo endoscopy teaching are needed.

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Information Technology group, Naoto Kume, PhD, of Kyoto University, Hanglak Lee, MD, of Hanyang University, and Youngsung Lee, MD, of MEDRIC Institute in Chong Buk, Korea.

REFERENCES

1. Strode SW, Gustke S, Allen A. Technical and clinical progress in telemedicine. JAMA 1999;281:1066-8.
2. Demartines N, Otto U, Mutter D, et al. An evaluation of telemedicine in surgery: telediagnosis compared with direct diagnosis. Arch Surg 2000;135:849-53.
3. Cook A, Salle JL, Reid J, et al. Prospective evaluation of remote, interactive videoconferencing to enhance urology resident education: the genitourinary teleteaching initiative. J Urol 2005;174:1958-60.
4. Stain SC, Mitchell M, Belue R, et al. Objective assessment of videoconferenced lectures in a surgical clerkship. Am J Surg 2005;189:81-4.
5. Rabenstein T, Maiss J, Naegele-Jackson S, et al. Tele-endoscopy: influence of data compression, bandwidth and simulated impairments on the usability of real-time digital video endoscopy transmissions for medical diagnoses. Endoscopy 2002;34:703-10.
6. Heatley DJ, Bell GD. Telemedicine in gastrointestinal endoscopy. Endoscopy 2003;35:624-6. author reply 627-8.
7. Shimizu S, Nakashima N, Okamura K, et al. International transmission of uncompressed endoscopic surgery images via superfast broadband Internet connections. Surg Endosc 2006;20:167-70.
8. Kaltenbach T, Sano Y, Friedland S, et al. American Gastroenterological Association (AGA) Institute technology assessment on image-enhanced endoscopy. Gastroenterology 2008;134:327-40.
9. Internet2 annual membership dues and network participation fees. http://www.internet2.edu/membership/dues.html. Accessed June 15, 2009.
10. Digital Video Transport System http://www.internet2.edu/pubs/DVTS-infosheet.pdf. Accessed June 15, 2009.

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Current affiliations: Division of Gastroenterology (T.K., R.S.), Veterans Affairs Palo Alto Health Care System and Stanford University School of Medicine, Palo Alto, California, USA, Departments of Gastroenterology and Hepatology (M.M.), Kyoto University Hospital, Kyoto, Japan, Medical Media and Information Technologies (P.D.), Stanford University School of Medicine, Palo Alto, California, USA, Department of Endoscopic Diagnostics and Therapeutics (K.O., S.S), Kyushu University Hospital, Fukuoka, Japan, Department of Medicine (J.H.), Hanyang University Medical College, Seoul, South Korea.

Reprint requests: Tonya Kaltenbach, MD, MS, VA Palo Alto Health Care System, 3801 Miranda Ave, GI-111, Palo Alto, CA 94304.

Live Teaching of Image Enhanced Endoscopy using High Resolution Digital Video Transport System and Internet2 - The IEE International Teaching Project

Session IV:
Image Enhanced Endoscopy in the Colon

The July 10th (July 9th at Stanford) event is one of a series of sessions to test the concept of teaching and sharing gastrointestinal endoscopic knowledge between major hospitals over long distances. The teaching session between Kyoto University,Japan; Stanford University, USA; Kyushu University, Japan; and Hanyang University Medical Center, South Korea builds on experience from similar events that have been run between surgeons in Kyushu and surgeons at many other sites in Japan, Korea and other Asian countries.

The focus at this event will be on its efficacy in teaching diagnostic principles in the endoscopic detection and diagnosis of early gastrointestinal cancer in the colon. You will participate in a collaborative presentation and discussion, and you will evaluate the efficacy of this as a learning event.

Pre-Test Questions

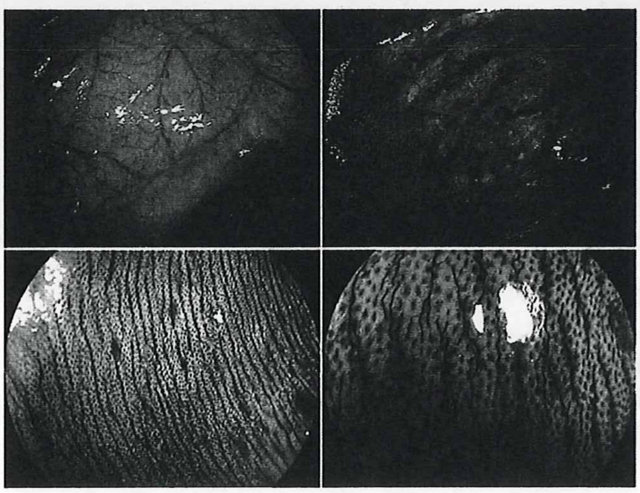
Please answer the five questions below BEFORE the lecture session.

講義の前に以下の５つの質問に答えてください。

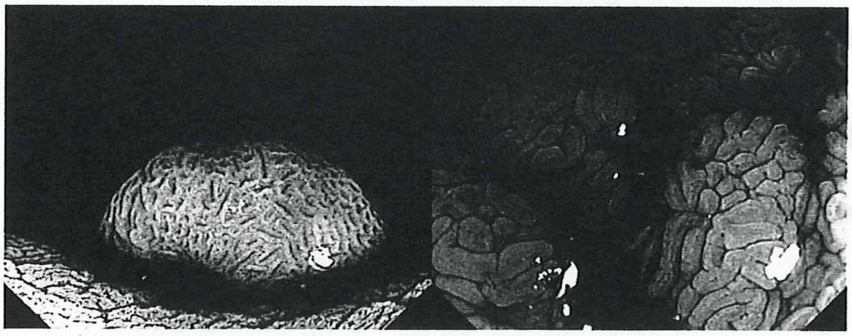
Participant Number: ______ Name of Institution: ______

1. What colonic lesion morphology is most likely to harbor high grade dysplasia/ carcionoma in situ, at the time of detection, irrespective of the lesion size?
   A. Pedunculated
   B. Sessile
   C. Superficially elevated
   D. Completely flat
   E. Depressed

2. Identify any suspicious abnormality in this image. Please outline (using a pen) entire area that appears abnormal. If the image below appears normal and no abnormality is suspected, then please do not mark, and leave the image blank.

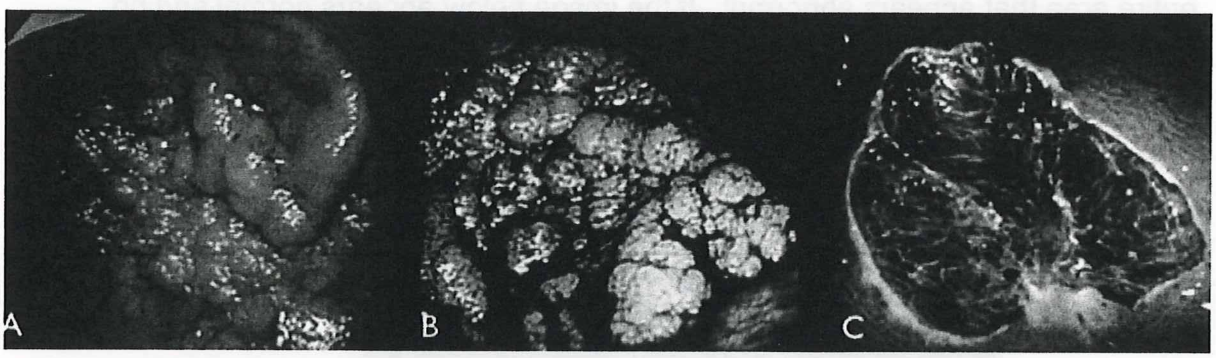


3. What is the suspected histopathology of the lesion identified in the image below?



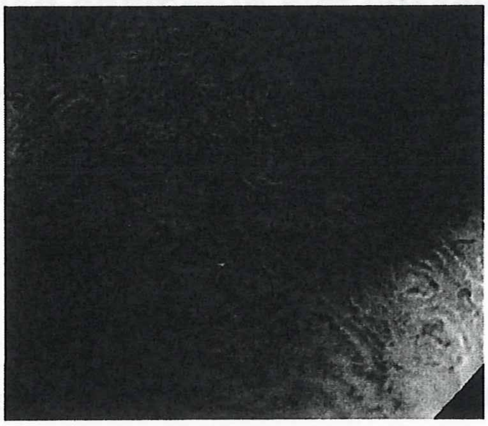
A. Normal.
B. Hyperplastic.
C. Adenoma.
D. High grade dysplasia/carcinoma in situ.
E. Invasive Adenocarcinoma.

4. A nonpolypoid colorectal lesion is seen in white light (A) and indigo carmine (B). Based on the immediate post mucosectomy site (C), what would be your next step?



A. Magnification.
B. Biopsy.
C. Closure of mucosal defect.
D. Repeat EMR.
E. Continue withdrawal examination.

5. What is the suspected histopathology of the colonic lesion shown using NBI in the image below?



A. Normal.
B. Hyperplastic.
C. Adenoma.
D. High grade dysplasia/carcinoma in situ
E. Invasive Adenocarcinoma.

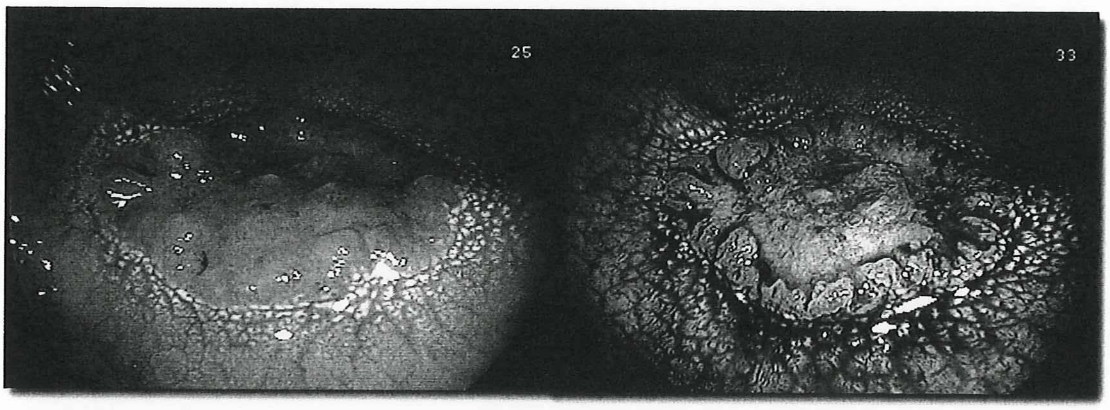
POST-Test Questions

Please answer the five questions below only AFTER the lecture session.

講義の後に以下の5つの質問に答えてください。

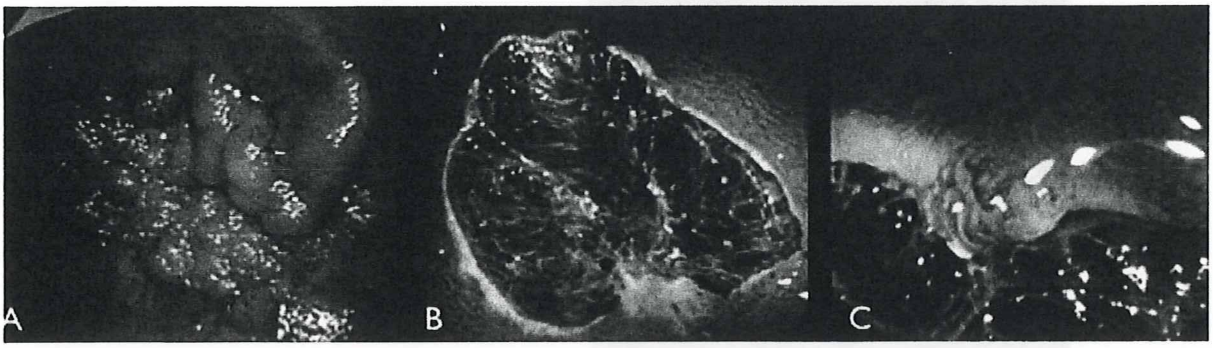
Participant Number: _______ Name of Institution: ________

1. What is the suspected histopathology of the lesion identified in the image below?



A. Normal.
B. Hyperplastic.
C. Adenoma.
D. High grade dysplasia/carcinoma in situ.
E. Invasive Adenocarcinoma.

2. A nonpolypoid colorectal lesion is seen (A). Based on the immediate post mucosectomy site (B) with magnification (C), what would be your next step?

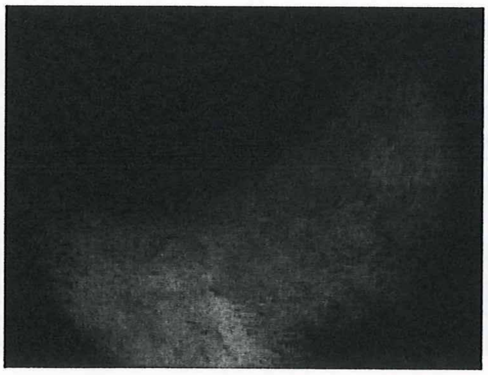


A. Increase magnification.
B. Image enhanced endoscopy technique.
C. Removal of residual lesion.
D. Closure of mucosal defect.
E. Continue withdrawal examination.

3. What colonic lesion morphology is most likely to harbor invasive cancer, at the time of detection, irrespective of the lesion size?

A. Pedunculated
B. Sessile
C. Superficially elevated
D. Completely flat
E. Depressed

4. What would be your next step during a post mucosectomy surveillance colonoscopy, in the image below?



A. Continue to withdrawal.
B. Image enhanced endoscopy.
C. Biopsy.
D. Mucosectomy.

5. What is the suspected histopathology of the colonic lesion shown using NBI in the image below?

A. Normal.
B. Hyperplastic.
C. Adenoma.
D. High grade dysplasia/carcinoma in situ.
E. Invasive Adenocarcinoma.

Exit Questionnaire

Instructions:
Please answer the following questions by marking the circle that best describes your answer, or filling in the blanks.
Thank you,
The Research Team at Stanford University, SUMMIT and VA Palo Alto Heath Care System, GI Section.

Part A: Background Information

1. Year of birth: 19____ Subject Number___________

2. Mark the circle that best describes your current level of gastrointestinal training:

Intern (PGY 1)	O	Gastroenterology Fellow	O
PGY2-3	O	Attending	O
PGY4-5	O	Faculty	O
PGY6+	O	Other:	O

3. How many gastroendoscopy procedures did you perform in the last year in which you:

	Less than 5	5-9	10-14	15-19	20 or more
Served as the lead endoscopist	O	O	O	O	O
Assisted the lead endoscopist	O	O	O	O	O
Observed and/or held endoscope	O	O	O	O	O

4. Please list the 4 procedures in which you participated most frequently in the last year:

1)________________________________

2)________________________________

3)________________________________

4)________________________________

Part B: Please rate the quality of the technical components of the session:

Technical Components	Not Usable (1)	Difficult to use (2)	Degraded but still usable (3)	Some interference but usable (4)	No interference (5)
1. Quality of Endoscopy Images	O	O	O	O	O
2. Quality of Audio	O	O	O	O	O
3. Quality of Conferencing Video	O	O	O	O	O

Part C: Please rate the usefulness of the information components of the session:

Information Components	Low (1)	(2)	Medium (3)	(4)	High (5)
1. Endoscopy Images and Video	O	O	O	O	O
2. Commentary from remote faculty	O	O	O	O	O
3. Commentary from local faculty	O	O	O	O	O
4. Interaction with remote audience	O	O	O	O	O
5. Discussion within local audience	O	O	O	O	O

Part D: Please give us your opinion of the overall value of this type of live surgery events.

Overall Rating	Definitely Would Not (1)	Not Likely (2)	Not Sure (3)	Very Likely (4)	Definitely Would (5)
6. If a 45-60 minute session of this type (a remote presentation with collaborative discussion) were readily available to you at your hospital/medical school, (e.g. once a month) on a topic in your surgical area of interest, how likely would you be to watch it?	O	O	O	O	O

Part E: Addition comments.

Please write any additional comments you have:

Answer Key
Televideo Teaching Session, Image Enhanced Endoscopy – Colon:

Pre-Test Questions:
1. E. Depressed
2. None – Normal Colonic Mucosa with Innominate Grooves and Pits
3. C. Adenoma
4. A. Magnification
5. E. Invasive Adenocarcinoma

Post-Test Questions:
1. E. Invasive Adenocarcinoma
2. C. Removal of Residual Lesion
3. E. Depressed
4. B. Image Enhanced Endoscopy
5. E. Invasive Adenocarcinoma

Short Communication

Health Risk Appraisal Models for Mass Screening for Esophageal and Pharyngeal Cancer: An Endoscopic Follow-up Study of Cancer-Free Japanese Men

Akira Yokoyama,[1] Yoshiya Kumagai,[2] Tetsuji Yokoyama,[5] Tai Omori,[6] Hoichi Kato,[7,8] Hiroyasu Igaki,[8] Toshimasa Tsujinaka,[9] Manabu Muto,[10] Masako Yokoyama,[3] and Hiroshi Watanabe[4]

[1]National Hospital Organization Kurihama Alcoholism Center, Yokosuka, Kanagawa, Japan; [2]Kumagai Satellite Clinic; [3]Mitsukoshi Health and Welfare Foundation; [4]Department of Surgery, School of Medicine, Keio University, Shinjuku-ku, Tokyo, Japan; [5]Department of Human Resources Development, National Institute of Public Health, Wako, Saitama, Japan; [6]Departments of Gastroenterology and Surgery, Kawasaki Municipal Hospital, Kawasaki, Kanagawa, Japan; [7]Center for Cancer Control and Information Services, National Cancer Center and [8]Surgery Division, National Cancer Center Hospital, Chuo-ku, Tokyo, Japan; [9]Department of Surgery, National Hospital Organization Osaka National Hospital, Osaka, Osaka, Japan; and [10]Department of Gastroenterology and Hepatology, School of Medicine, Kyoto University, Kyoto, Kyoto, Japan

Abstract

Purpose: **To assess the performance of our health risk appraisal (HRA) models for screening individuals at high risk of esophageal/pharyngeal squamous cell carcinoma (EPSCC).**
Methods: **Based on the results of our previous case-control study, we invented HRA models that enable screening for EPSCC cases in Japanese men with high sensitivity and specificity based on either their aldehyde dehydrogenase-2 genotype (HRA-G model) or alcohol flushing (HRA-F model) and drinking, smoking, and dietary habits. Follow-up endoscopy combined with esophageal iodine staining (median follow-up period: 5.0 years) was done on 404 Japanese men (50-78 years) who were registered as cancer-free controls in the previous study.**
Results: **The follow-up endoscopy resulted in a diagnosis of 6 esophageal SCC (T_{is} in 5 and T_1 in 1), 1 hypopharyngeal SCC (T_2), and 1 oropharyngeal SCC (T_2). Seven and 6 of the 8 EPSCC cases were in the top 10% risk group at baseline according to the HRA-G and HRA-F models, respectively. The EPSCC detection rates per 100 person-years in the top 10% risk groups by the HRA-G and HRA-F models were 4.38 (95% confidence interval, 1.76-9.01) and 3.48 (95% confidence interval, 1.28-7.58), respectively. Their age-adjusted relative risk was 95.1- and 26.3-fold, respectively ($P < 0.0001$), higher than in the bottom 90% risk groups.**
Conclusions: **The high detection rates for EPSCC in the top 10% risk group of this preliminary follow-up study were in good agreement with those predicted by the HRA models and thus encouraged the screening based on our HRA models in larger populations of Japanese men.** (Cancer Epidemiol Biomarkers Prev 2009;18(2):651–5)

Introduction

Recent technical improvements in endoscopes and growing understanding of the endoscopic findings of early squamous cell carcinoma (SCC) in the esophagus (1, 2) and pharynx (3) have made it possible to detect esophageal/pharyngeal SCC (EPSCC) early. Treatment of early esophageal SCC by endoscopic mucosectomy has become a widespread practice in Japan and has succeeded in improving the prognosis of this high-mortality cancer (2, 4, 5), and early pharyngeal SCC can also be treated by endoscope-guided mucosectomy (6). Therefore, it is important to identify individuals at increased risk of EPSCC and offer them the opportunity to undergo detailed examination by upper aerodigestive tract endoscopy combined with esophageal iodine staining. Without using the esophageal iodine staining, more than half of intraepithelial or mucosal esophageal SCC would be missed (1, 7).

A mutant allele encoding an inactive subunit of aldehyde dehydrogenase-2 (*ALDH2*2*) is prevalent in East Asian populations (e.g., prevalence of the *ALDH2*2* allele is 24% in a Japanese population; ref. 8) and drinking a small amount of alcohol results in severe acetaldehydemia and unpleasant alcohol flushing responses in individuals with inactive ALDH2 (9). Acetaldehyde is an established carcinogen in experimental animals (10) and is suspected to play a critical role in cancer development in humans (11). Case-control studies among Japanese (12-16) and Taiwanese (13, 17, 18)

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Requests for reprints: Akira Yokoyama, National Hospital Organization Kurihama Alcoholism Center, 5-3-1 Nobi, Yokosuka, Kanagawa 239-0841, Japan. Phone: 81-46-848-1550; Fax: 81-46-849-7743. E-mail: a_yokoyama@kurihama1.hosp.go.jp

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