Results

Group 2 lymph nodes were judged as SNs in 52 patients (32%; Table 1). Distal gastrectomy was performed in almost two-thirds of the 52 patients and the extent of lymph node dissection was D1+α in 58% of these patients.

The most common lymphatic basin of the cancer in the upper one-third of the stomach was the left gastric artery area (eight patients), while the most common location of SNs in cancer in the upper one-third of the stomach was station No. 7 (seven patients; Table 2). However, one patient had an SN in No. 4d.

For cancer in the middle one-third of the stomach, mainly the lymphatic compartments around both the left gastric artery and the right gastric artery were stained. Thirty-one of these patients had SNs in the No. 7 area, but in 7 patients, staining with ICG was seen in No. 9, 11p, 12a, or 14v.

Gastric cancers in the lower one-third of the stomach predominantly drained to the right side, around the right gastroepiploic artery and the right gastric artery. Common locations of SNs were stations No. 7 and No. 8a (11 patients). However, SNs were also observed in the areas of No. 1, 11p, and 14v.

Lymphatic basins positive for ICG, in relation to the cancer location, are shown in Table 2. Only two patients had no drainage to the left gastric artery area. For cancers in the middle and lower one-thirds of the stomach, the most common drainage in the lymphatic basins was to the left gastric artery and the right gastroepiploic artery areas.

Two patients had lymph node metastasis (Fig. 2). Case 1 had a 45 × 23-mm submucosal signet ring cell carcinoma in the greater curvature of the middle one-third of the stomach, which had three lymphatic basins (left gastric artery, right gastric artery, and right gastroepiploic artery areas) and SNs in No. 3, 4sb, 4d, 7, and 11p. Metastatic lymph nodes were located in No. 3 and No. 7, which were all SNs. Group 2 lymph nodes, No. 8a and No. 11p, were dissected. Case 2 had a 23 × 12-mm submucosal signet ring cell carcinoma in the anterior wall of the lower one-third of the stomach, which had two lymphatic basins (left gastric artery and right gastroepiploic artery areas) and SNs in No. 1, 3, 4d, and 6. A metastatic lymph node was located in No. 4d, and this was an SN. D1+α resection was performed.

Table 1. Characteristics of patients with Group 2 lymph nodes judged to be SNs

Age (years)	59.7 ± 10.0 (35–76)
Sex ratio (M:F)	37:15
Tumor location	
Upper one-third	7
Middle one-third	33
Lower one-third	12
Extent of resection	
Proximal gastrectomy	2
Distal gastrectomy	33
Total gastrectomy	4
Pylorus-preserving gastrectomy	5
Segmental gastrectomy	5
Wedge resection	3
Extent of dissection	
D1+α	30
D1+β	6
D2	9
LBD	7

LBD, Lymphatic basin dissection; SN, sentinel lymph node

Table 2. Lymphatic basins positive for ICG, in relation to the cancer location

Location of tumor	Lymphatic basin		Location of SNs	
Upper one-third	LGA alone	4	No. 7	7
	LGA and PGA	2	No. 4d	1
	LGA, LGEA, and PGA	1		
	LGA, LGEA, and RGEA	1		
Middle one-third	LGA alone	11	No. 7	31
	LGA and RGEA	16	No. 8a	4
	LGA and RGA	2	No. 9	1
	LGA, LGEA, and RGEA	1	No. 11p	4
	LGA, RGEA, and RGA	1	No. 12a	1
	LGA, LGEA, RGEA, and RGA	1	No. 14v	1
Lower one-third	LGA alone	1	No. 7	6
	RGE alone	2	No. 8a	5
	LGA and RGEA	2	No. 1	2
	LGA and RGA	1	No. 11p	1
	RGA and RGEA	2	No. 14v	3
	LGA, RGA, and RGEA	4		

LGA, Left gastric artery; RGA, right gastric artery; PGA, posterior gastric artery; LGEA, left gastroepiploic artery; RGEA, right gastroepiploic artery

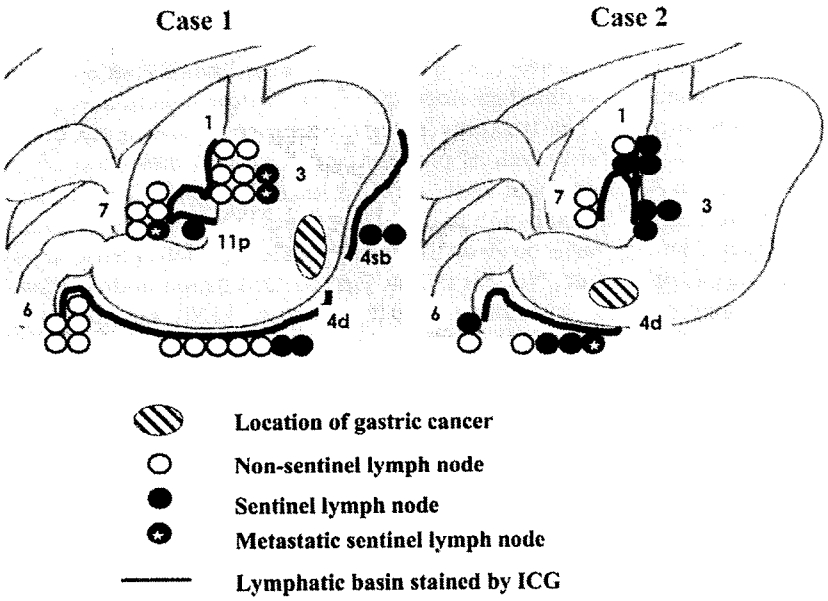

Fig. 2. Details of the two patients who had metastatic lymph nodes. Case 1 had a 45 × 23-mm submucosal signet ring cell carcinoma in the greater curvature of the middle one-third of the stomach, which had three lymphatic basins, in the left gastric artery (LGA), right gastric artery (RGA), and right gastroepiploic artery (RGEA) areas, and sentinel lymph nodes (SNs) in stations No. 3, 4sb, 4d, 7, and 11p. Metastatic lymph nodes were located in No. 3 and No. 7; these were all SNs (n2 [3/29] No. 1, 0/2; No. 3, 2/6; No. 4sb, 0/2; No. 4d,, 0/7; No. 5, 0/1; No. 6, 0/5; No. 7, 1/5; No. 11p, 0/1). Case 2 had a 23 × 12-mm submucosal signet ring cell carcinoma in the anterior wall of the lower one-third of the stomach, which had two lymphatic basins (LGA and RGEA) and SNs in No. 1, 3, 4d, and 6. A metastatic lymph node was located in No. 4d, and this was an SN (n1 [1/16] No. 1, 0/4; No. 3, 0/3; No. 4d, 1/4; No. 6, 0/2; No. 7, 0/2; No. 8a, 0/1). *IGC*, indocyanine green

All the SNs in Group 2 lymph nodes were detected with IREE plus ICG. Skip metastasis was not observed, and metastatic lymph nodes were judged to have been dissected by the D1 + α procedure. There were no cases of postoperative metastasis or recurrence.

Discussion

According to the treatment guidelines of the JGCA, endoscopic mucosal resection (EMR) or modified gastrectomy is indicated for stage IA (T1N0) disease as the routine practice [5]. In addition, local resection and segmental resection are proposed for clinical trials [5]. These recommendations are based on the large amounts of data obtained from patients who have undergone gastrectomy in Japan. Although the guidelines were developed based on as much evidence as possible, the guideline-developing committee did face difficulties because of the lack of evidence for various aspects of treatments [7].

During SNNS using ICG, we sometimes encountered SNs in the Group 2 lymph node area. These findings suggest that even early gastric cancer may be associated with metastasis to the Group 2 lymph node area, or skip metastasis. Therefore, we were faced with the following question: "Is D1+α lymph node dissection really enough for T1N0 gastric cancer?"

As to the skip metastasis of gastric cancer, Park et al. [8] analyzed findings in 14 patients with such metastasis among 266 patients who had undergone more than D2 lymph node dissection. The incidence of skip metastasis was 5.3%, and only 1 patient with early gastric cancer had such metastasis. The lymph node stations of the skip metastasis were No. 7, 8a, 9, 11p, and No. 1. The survival rate did not show any statistically significant difference between those with and those without skip metastasis. Park et al. [8] concluded that D2 lymph node dissection should be performed until sentinel lymph node (SN) detection became feasible and reliable, and that the potential risk from skip metastasis was not great, and therefore skip metastasis itself should not be a major consideration in therapeutic decisions.

Kikuchi et al. [9] analyzed the topographical pattern of lymph node metastasis for pN1 patients with curative resection. Skip metastasis occurred in 5%, and the common stations for such a metastasis were No. 7 and No. 8a. This pattern of metastasis was found in 14% of the patients with single positive nodes. Kikuchi et al. [9] noted that although perigastric nodes were important first sites of drainage, the distribution of positive nodes depended on the tumor location.

Accordingly, in view of both the complexity of the lymphatic circulation and skip metastasis, previous studies have recommended the routine use of systemic D2 dissection [9–11]. However, the feasibility and reliability of SNNS is a prerequisite for limited gastric resection [9–11].

In western countries, Roviello et al. [12], in their multicenter retrospective study, confirmed nodal involvement to be a significant prognostic factor for early gastric cancer. In view of the trend to a lower risk of recurrence when more than 15 nodes were retrieved and the better staging achieved, they concluded that D2

lymphadenectomy was the treatment of choice. However, Degiuli et al. [13], in their retrospective analysis, reported that the survival benefit of D2 gastrectomy for early gastric cancer was not documented either in the overall population or in subset analyses of patients with increased risk of nodal metastasis.

Recently, reports on SNNS for gastric cancer have increased, in which technical improvements have been documented [14–20]. Using infrared ray electronic endoscopy (IREE), we previously reported a sensitivity of 100%, specificity of 67%, positive predictive value of 29%, and negative predictive value of 100% for the detection of SNs [6].

In the present study, common locations of SNs were stations No. 7 and No. 8a. During the SNNS, if these lymph nodes were stained green, we were afraid that they may have been the stations of skip metastasis, as reported by others [9,10]. Interestingly, in the middle- and lower-thirds of the stomach, stations No. 11p and No. 14v (which are necessary to include for more than D2 dissection) were included as SNs. However, metastatic lymph nodes were located in stations No. 3 and No. 7 in one patient, and in No. 4d in another patient. They were all SNs. Furthermore, skip metastasis were not observed and metastatic lymph nodes were considered to have been dissected by the D1+α procedure.

In T1N0 stage disease, the first sites of metastasis are the perigastric nodes, and skip metastasis seems to occur rarely. In previous studies, almost all patients with skip metastasis had advanced cancer [8,9,10,11]. As mentioned previously, in the study by Park et al. [8], only one patient with early gastric cancer had skip metastasis.

As to the lymphatic basins that were positive for ICG, we found that the left gastric artery compartment was the most common area, regardless of the location of the cancer. Furthermore, as many as 61.5% of the patients in our study had more than one lymphatic basin positive for ICG, including the left gastric artery area (mainly the left gastric artery and right gastroepiploic artery areas).

Miwa et al. [20] advocated the concept of lymphatic basin dissection with SNNS, using patent blue as a tracer. The sensitivity and accuracy of their method were 85% and 98%, respectively. They reported that T1 gastric cancer involved a single lymphatic basin in 42% of their patients with gastric cancer, two lymphatic basins in 47%, and three in 12%. Similar to findings in our study, they found that the most common drainage lymphatic basins were the left gastric artery and right gastroepiploic artery areas, especially for cancers in the middle and lower one-thirds of the stomach. In their series, patients with one or two basins were treated with limited gastric resection with en-bloc dissection of the blue lymphatic basins, and none developed recurrence or died of cancer.

If SNs are detected in Group 2 lymph nodes during modified gastrectomy (such as local resection, segmental gastrectomy, pylorus-preserving gastrectomy, or distal as well as proximal gastrectomy), dissection of the lymphatic basin positive for ICG would identify metastatic lymph nodes. In patients in whom the lymphatic basin positive for ICG includes the left gastric artery area, No. 7 is the most important lymph node station.

Therefore, for patients with T1N0 gastric cancer, modified gastrectomy (D1+α dissection), combined with SNNS, is suitable; however, for those whose Group 2 lymph nodes have been judged as SNs, additional dissection of the ICG-positive lymphatic basin, detected by SNNS, should be performed to confirm the absence of lymph node metastasis.

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特集 センチネルリンパ節理論の消化器癌への応用

2 センチネルリンパ節の同定
(3) 赤外光の応用

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Key words：早期胃癌，インドシアニングリーン，赤外線腹腔鏡システム，腹腔鏡下手術，センチネルリンパ節ナビゲーション手術

要 旨

赤外観察下でのSNNS(センチネルリンパ節ナビゲーション手術)は従来の色素法に比べて明瞭にセンチネルリンパ節(SN)の同定ができた．とくに腹腔鏡下では他の方法に比べて有用かつ実用的である．今後，endoscopic submucosal dissection(ESD)と腹腔鏡手術のコラボレーションに際しての有用性が期待される．

はじめに

本稿では，センチネルリンパ節(SN)の同定法の一つである赤外光観察について述べる．とくに，われわれの胃癌における赤外法の成績をもとに，従来の色素やアイソトープ法との比較，腹腔鏡下胃癌手術への応用，endoscopic mucosal resection(EMR)やendoscopic submucosal dissection(ESD)とのコラボレーションの可能性について考察した．

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**柏健診クリニック

Ⅰ．SNNSの臨床研究の現状

この項のポイント
- ICGはわが国でもっとも使いやすく安価で安全な色素である．
- ICGを用いたSNNSは実際には視認しづらいが，赤外線観察で明瞭に観察できる．

消化器癌，とりわけ胃癌におけるセンチネルリンパ節ナビゲーション手術(以下，SNNS)の臨床研究は，現在わが国を中心にトレーサーとして色素やアイソトープを用いたり，それぞれの弱点を補うべく併用で行われ，良好な成績が報告されてきた[1)~3)]．また，色素のなかでもっともわが国で手に入りやすく，安価かつ安全であるindocyanine green(ジアグノグリーン，第一製薬，東京；以下，ICG)を用いたSNNSにおいてもその有用性が報告された[4),5)]．そこでわれわれは，2000年5月から経内視鏡的にICGを局注しSNNSを行った．SN同定率は6例中3例，50%で，6例中2例にリンパ節転移を認めたが，いずれも偽陰性であった．ラーニングカーブは20例ほどとされているが，green nodeが薄い場合の視認は困難であった．

ICGの吸収波長は805 nmと，赤外光の波長

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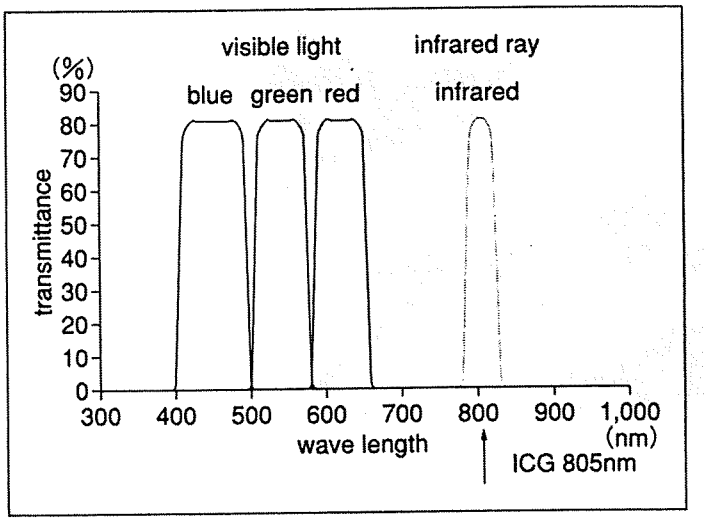

図1　赤外線観察の原理
〔二村浩史，他：消化器内視鏡　17；738-741，2005[7]より引用〕

と一致している[6),7)](図1)．その性質を利用して，赤外線内視鏡を用いてSNNSを行ったところ，不可視のICG陽性リンパ管やリンパ節が観察できた[8)]．そこでわれわれ独自の方法である赤外法，すなわちICGをトレーサーとして赤外光観察下でのSNNSの臨床研究を始めた．

Ⅱ．赤外法の実際

この項のポイント

- 術中内視鏡の前に空腸をクランプすることが，腹腔鏡下のSNNSのやりやすさや安全性につながる．
- 赤外線観察でのSN同定にはリンパ流域切除が必要である．

まず術中に，トライツ靭帯の近傍の空腸を鉗子でクランプし小腸に送気されないようにし，上部消化管内視鏡を施行する．術前に内視鏡下で，癌の辺縁に4個クリップをした部位の粘膜下に5 mg/m*l*のICGを0.5 m*l*ずつ計2 m*l*を23もしくは25ゲージの穿刺針で局注する．その後20分間，赤外線腹腔鏡システム(infrared ray laparoscopy system，オリンパスメディカルシステムズ，東京；以下，IRLS)(図2)を用いて通常光と赤外光で胃壁周囲を観察する(図3a，b)．20分間でもっとも遠くに流れたICG陽性リンパ管およびICG陽性リンパ節を遠位端とし，その部分までの脂肪組織を一括で切除するリンパ流域切除（lymphatic basin dissection；LBD)[9)]を施行するか，クリップや針糸でマーキングをしておき，胃切後にサイドテーブルでその脂肪組織内のリンパ節を取り出し，再度，赤外線で観察しICG陽性リンパ

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6) 成宮徳親，二村浩史，藤崎順子，他：赤外線内視鏡システムによるsentinel lymph node観察．Gastroenterol. Endosc. 45；2338-2345，2003

赤外線内視鏡の原理やなぜICGを用いると赤外線でよく見えるのかを説明している．また，どのくらいの深さまで観察できるかを実験しており，3 mmの深さの脂肪織まで観察できるとしている．

8) Nimura, H., Narimiya, N., Mitsumori, N., et al.：Infrared ray electronic endoscopy combined with indocyanine green injection for detection of sentinel nodes of patients with gastric cancer. Br. J. Surg. 91；575-579，2004

実際に開腹手術と腹腔鏡下手術で赤外線観察SNNSを行い，赤外光観察では肉眼観察に比べて偽陰性がなく，SN同定率，感度ともに有意に優れており，赤外線観察は胃癌SNNSに有用であるとしている．

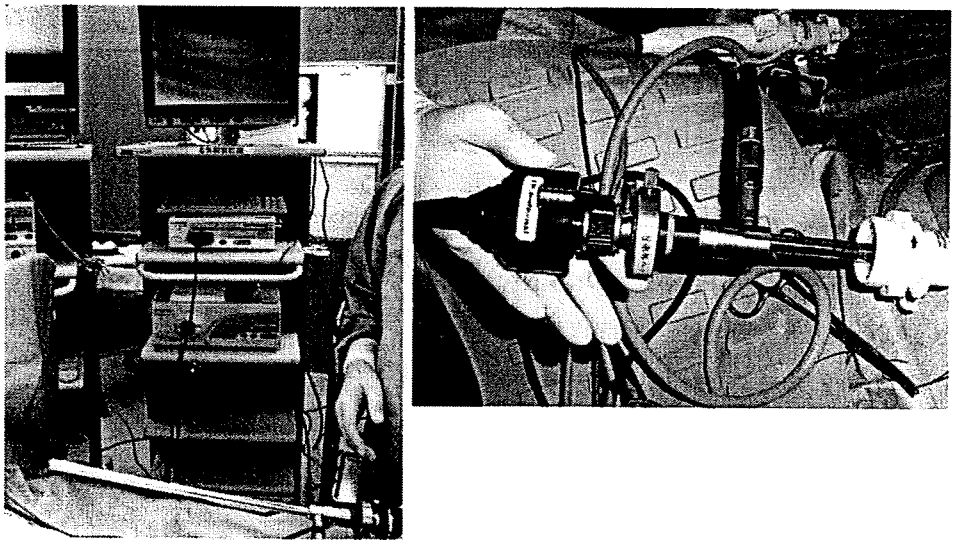
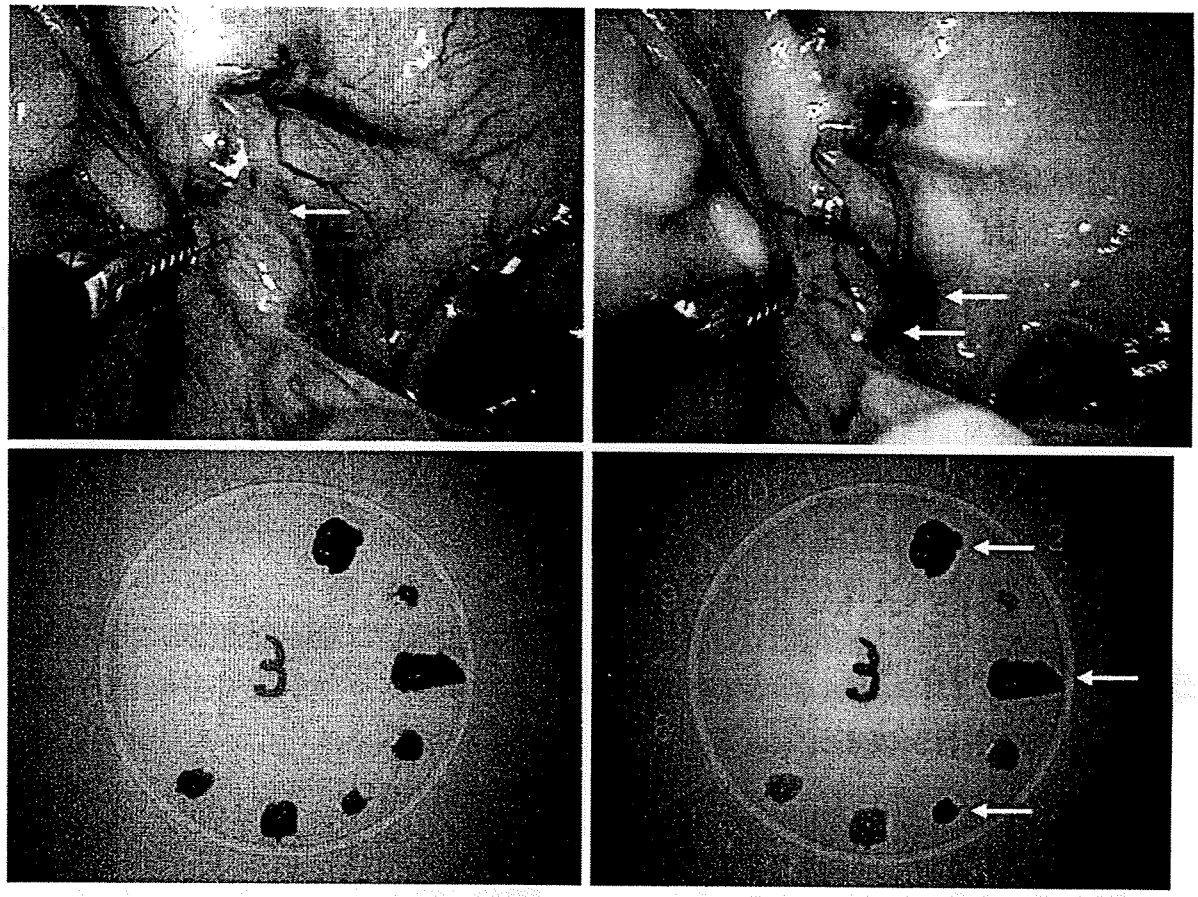


図2　赤外線腹腔鏡システム
〔二村浩史，他：消化器内視鏡　17；738-741，2005[7]より引用〕



3a | 3b
3c | 3d

図3　肉眼観察と赤外観察
a：肉眼にて green のリンパ管が観察できる．
b：赤外では明らかに明瞭にリンパ管，リンパ節が観察できる．
c：肉眼で SN は視認できない．
d：赤外では明瞭に SN の同定ができる(矢印)．

節をSNとして同定する(図3c, d).

赤外法は現在まだ臨床応用前段階であるため，全例は術中凍結迅速病理診断に出してはいない．リンパ節病理診断法は最大割面のHE染色で行う．すべてホルマリン固定後サイトケラチン免疫染色(CAM 5.2, Becton Dickinson, San Jose, CA, USA)で微小転移の有無も確認する．

Ⅲ. 赤外法におけるSNNS施行対象と検討方法

これまで赤外法によるSNNSを施行した胃癌患者195人(うち腹腔鏡手術78人)を対象とした．

開腹および腹腔鏡下での赤外法におけるSN同定率，転移リンパ節検出感度を検索した．またEMRやESD後における赤外法SNNS 13人の状況を検討した．さらに2005年7月から2006年6月まで慈恵医大4附属病院合同で行った開腹下赤外法SNNS臨床試験24人の肉眼観察と赤外光観察におけるICG陽性リンパ流域数，SN個数，SN同定率，転移リンパ節検出感度を比較検討した．

Ⅳ. 赤外法におけるSNNS施行結果と肉眼観察との比較

1. 赤外法によるSNNS(表1)

この項のポイント
- 癌で完全に占居されて色素が入っていかないリンパ節以外に，赤外線観察では偽陰性は認めなかった．
- EMR, ESD後であっても腹腔鏡下で十分SNNSは可能であった．

胃癌全体ではSN同定率195人中194人(99%)，感度33人中32人(97%)であった．同定できなかった1人は胆石術後で癒着強固の患者であった．また転移リンパ節がICG陰性であった1人は，肉眼および触診で明らかに癌で置換されており，術中病理診断にても癌細胞による占居で転移診断された患者である．腹腔鏡下ではSN同定率78人中78人(100%)，感度10人中10人(100%)であった．とくに腹腔鏡下では薄いgreen nodeやICG陽性リンパ管の同定は困難であり，赤外法は有用であった(図3)．

表1 赤外観察SNNS

	赤外線観察SNNS		計
	開腹下	腹腔鏡下	
患者数	117	78	195
SN同定率	116(99%)	78(100%)	194(99%)
リンパ節転移例	23	10	33
転移検出感度	22(96%)	10(100%)	32(97%)

EMR, ESD後であってもSN同定率は13人中13人(100%)，感度は3人中3人(100%)であった．いずれも周囲臓器と癒着を認めたり，局注に際して粘膜下が切除後瘢痕による硬化で色素が入りづらいことがある．13人中7人に腹腔鏡下SNNSを施行したが，SNNSは十分可能であった．

2. 肉眼観察と赤外光観察の比較(表2)

この項のポイント
- 肉眼観察では偽陰性が生じるが，赤外光観察では癌で置き換わったリンパ節以外は偽陰性は認めなかった．
- 肉眼ではICG陽性リンパ流域を見逃す危険性がある．

慈恵医大4附属病院合同臨床研究での開腹下でのICG陽性リンパ流域数は，肉眼では24人中18人(75%)に観察でき，平均0.9流域(0～2流域)であった．赤外観察では24人中24人

表2　慈恵医大4附属病院合同開腹下赤外観察SNNS臨床試験

	肉眼観察	赤外観察
ICG陽性リンパ管同定率	18/24(75%)	24/24(100%)
ICG陽性リンパ流域数	0.9(0～2)	1.7(1～4)
SN同定率	16/24(67%)	24/24(100%)
SN個数	2.8(0～13)	8.5(3～28)
転移検出感度	3/8(38%)	7/8(88%)

(100%)に観察でき，平均1.7流域(1～4流域)であった．SN同定率は，肉眼24人中16人(67%)に対し，赤外では24人中24人(100%)であった．SN個数は，肉眼で平均2.8(0～13)個，赤外で平均8.5(3～28)個であった．転移リンパ節検出感度は，肉眼8人中3人(38%)に対して赤外では8人中7人(88%)であった．赤外で感度陰性であった1人は，先に述べた癌で置換されて色素が入っていけない転移リンパ節の患者である．

V．考察—赤外線腹腔鏡システムの有用性

胃癌SNNSにおいて色素法はもっとも簡便であり，とくにICGはわが国では安価で安全性も保たれており，使用しやすい色素である．しかし，表2のように肉眼のみでは明らかに視認できないICG陽性リンパ管やSNがあり，偽陰性となる危険性が高い．また，他の色素でも時間の経過とともにwash outされて視認できなくなってしまうという欠点がある．他の色素で偽陰性の報告もある[10]．その点，赤外観察は，ICGの濃度が薄くても黒く明瞭に視認できるため確実にSNの同定ができる[6)~8)]．とくに腹腔鏡下ではすべてのgreen nodeを視認することは困難であり，ICGを用いるならば赤外観察が必要と考える[8),11)]．そのうえ腹腔鏡下では部屋を暗くしなくてもよく，また一連の腹腔鏡観察の流れのなかでワンタッチで赤外観察に切り替えることができ，煩雑さがない．赤外観察でSN以外に転移を認めたとする報告がある[11]．また癌に占居されて色素が入らない転移リンパ節は偽陰性となるが，LBDを施行し掘り出したリンパ節を赤外観察したり，触診することで解決できると考える．アイソトープ法では視認できないため色素の併用が必要[3)]であり，煩雑なうえアイソトープ室が必要である．さらに腹腔鏡下では側方線量のため同定が困難なことがある[12]．今後，一般病院においてもSNNSを応用するならば，赤外線腹腔鏡システムは有用と考えられる．

VI．EMR，ESDと腹腔鏡手術の接点

現在，ESDの進歩により内視鏡治療の適応が広がりつつある[13]．今後，ESDと腹腔鏡手術の接点が生まれるが，リンパ節郭清の必要性を判断するうえでSNNSが必要と考えられる．EMR後ICG肉眼観察のみの腹腔鏡下リンパ節郭清の報告もある[14]．われわれのデータからは偽陰性となる可能性が否定できない．アイソトープ法によるEMR後の機能温存縮小手術への応用も報告されている[15]．赤外観察は腹腔鏡下でリンパ流域が明瞭に観察でき，LBDの範囲が明確にできる点でも今後，ESDとのコラボレーションにおいてもっとも期待できる方法であろう．

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Summary

Detection of Sentinel Lymph Node—Observation with Infrared Ray

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Compared to the conventional dye method, SNNS with infrared ray observation allows easy, much improved identification of SN. With this technique, the usefulness of combining ESD techniques and laparoscopic surgery is expected.

Key words : early gastric cancer, indocyanine green, infrared ray laparoscopy system, laparoscopic surgery, sentinel lymph node navigation surgery

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2. 消化器癌
b) 胃癌——SNNS導入による胃癌治療の変化*

二村浩史　矢永勝彦**

〔要旨〕胃癌センチネルノードナビゲーション手術(SNNS)は本邦から発信された臨床研究であり，その有用性が報告されている．リンパ流域切除は郭清範囲を術中に個別に同定することで，郭清と同等の効果が期待できる．内視鏡的粘膜下層剥離術後にリンパ節転移の可能性が否定できない場合を含め，今後の早期胃癌治療はSNNSと腹腔鏡下手術の融合によってSN転移陰性例に対する腹腔鏡下手術による手術の低侵襲化や縮小手術の個別化などを可能にすると見込まれる．

はじめに

1992年にMorton ら[1]が早期悪性黒色腫に対してセンチネルノードナビゲーション手術(SNNS)をはじめて臨床応用した．その後，乳癌での検証が行われており，今や乳癌手術においてはSNNSが標準治療となりつつある[2]．

本稿では，胃癌におけるSNNSの現状と導入後における胃癌治療の変化について述べる．

I. 胃癌SNNSの現状

胃癌SNNSは本邦から発信された臨床研究であり，良好な成績が報告されている[3~8]．2007年12月現在，PubMedで「sentinel node(SN)」で検索すると5,808件の論文がヒットする．このうち2006年以降は1,553件である．SNに検索用語「breast cancer」を加えると2,974件，うち2006年以降では687件で，SNに「gastric cancer」を加えると165件，2006年以降では43件がヒットする．このようにSNに関する英文論文ではその約半数が乳癌に関するものであり，胃癌に関するものはわずか3%にすぎない．これは欧米諸国に胃癌が少ない特徴からして当然のことかと考えられるが，2006年以降の胃癌SNNS 43件中29件が本邦からの報告であり，したがって胃癌SNNSに関してはわが国が主体となって研究がすすめられているといえる．今後胃癌SNNSは，SN生検と腹腔鏡下手術の融合により，SN転移陰性例に対して腹腔鏡下手術による低侵襲手術，個別化縮小手術の実践を目指していくものと考えられる．

現在わが国では，臨床応用に向けた胃癌SN生検手技の多施設共同臨床試験が二つ進行している．一つはトレーサーに色素indocyanine green(ICG)を用いて開腹下で胃の漿膜に注入する方法である，Japan Clinical Oncology Group

キーワード：胃癌，SNNS

* Changes in the surgical strategy for early gastric cancer by sentinel node navigation surgery(SNNS)

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a．肉眼観察．ICG陽性リンパ管やリンパ節は視認できない．

b．赤外光観察．ICG陽性リンパ管，リンパ節が明瞭に観察できる．

図1．腹腔鏡下観察所見(肉眼 vs 赤外光)

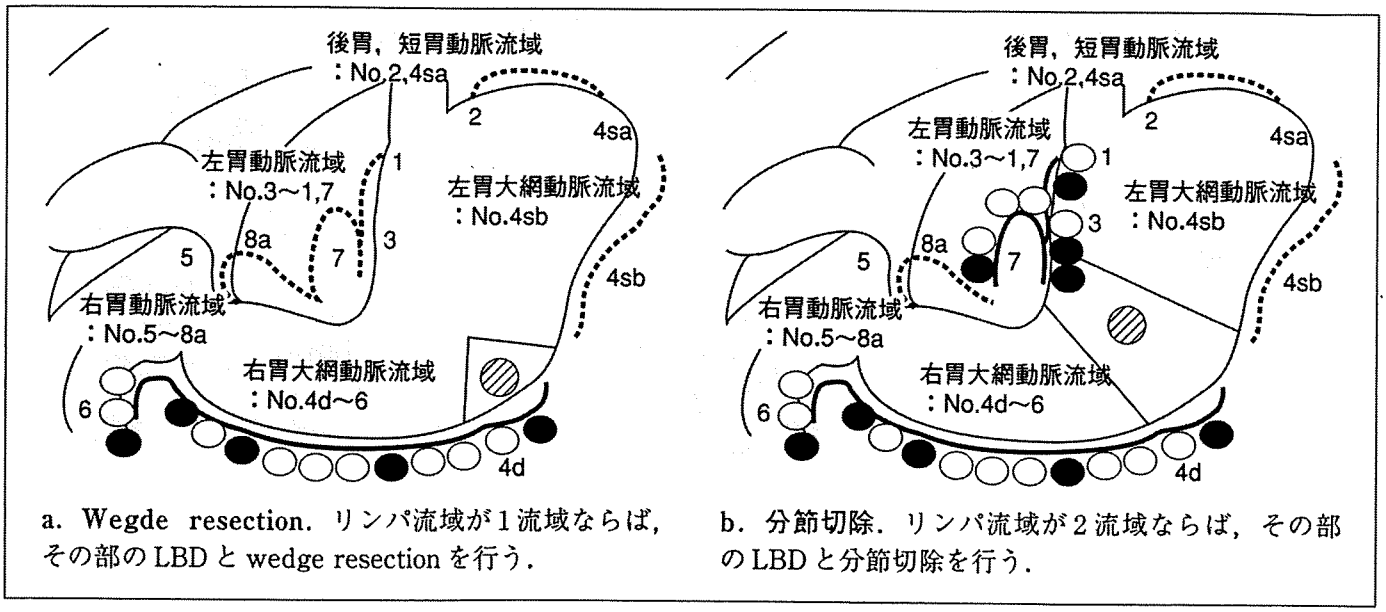
(JCOG)胃癌外科グループの「早期胃癌におけるセンチネルリンパ節生検の妥当性に関する研究(JCOG0302)」[9]であり，もう一つはトレーサーとして色素isosulfan blue(Lymphazurin)＋アイソトープ(RI)^{99m}Tcスズコロイドを用いて内視鏡にて癌周囲に局注する方法である，SNNS研究会・厚生労働省がん研究助成金研究班の多施設共同研究[10]である．それぞれトレーサーや投与経路，同定方法が違うので一概に単純比較はできないが，SNNSが胃癌で臨床応用できるか否かの重要な研究であることには間違いない．最終結果が待たれるところである．ただし，JCOGスタディで使用されるICGは，視認性に劣るため肉眼観察のみでは偽陰性率が高いと報告されている[8,11,12]．

われわれは偽陰性の発生を防ぐ目的で，ICGの吸収波長が赤外光の波長と一致する性質を利用して赤外線観察でのSNNSを行い，良好な成績を報告してきた(図1)[8,11,13~15]．乳癌では蛍光ICG赤外線観察の報告がある[16]．最近胃癌でもこの方法を応用したSNNSの報告もあり，各施設で偽陰性をなくすための新たなSN同定法が開発されてきている[17]．

しかし，これらの研究で有用性が証明されても胃癌におけるリンパ節の微小転移診断の有用性や意義が明確でないため，胃癌SNNSの術中転移診断法については議論の余地のあるところである[18~20]．

II. SNNS導入後における胃癌治療の変化

これまでわが国では，胃癌治療はD2郭清が標準術式であり，早期胃癌ではリンパ節郭清の一部を省略する縮小手術α，βがガイドラインで示されている[21]．先にも述べたが，SNNS導入後はSN転移陰性例に対して腹腔鏡下手術による低侵襲手術，個別化縮小手術へと治療が変化してくるものと考えられる．なお腹腔鏡下SNNSを色素＋RIで行う場合，色素染色リンパ節とRI集積リンパ節は必ずしも一致しない点[7]，開腹に比べていわゆるshine throughによる影響を強く受ける点[22]に注意を要する．これまで偽陰性とされた多くの症例は同一のリンパ流域(lymphatic basin)内にSNが同定されていること[23,24]，赤外線腹腔鏡システムを使用してもpick up法では偽陰性を生じること[25]，サイトケラチン染色やPCRでの検索でSN以外の微小転移リンパ節も同じbasin内にあるため，リンパ流域切除(lymphatic basin dissection：LBD)をすれば転移リンパ節の取り残しはないと報告されている[26]．このため，最近ではLBD法[27]によるSN同定が行われることが多くなってきた．胃の動脈リンパ領域から早期胃癌の至適郭清範囲を設定する報告[28]があるが，LBDは郭清範囲を術中に個別に同定し郭清することと



a. Wegde resection．リンパ流域が1流域ならば，その部のLBDとwedge resectionを行う．

b．分節切除．リンパ流域が2流域ならば，その部のLBDと分節切除を行う．

図2．リンパ流域に基づく胃癌縮小手術
実線：リンパ流域，●：SN，○：流域内の非SN，▨：癌部

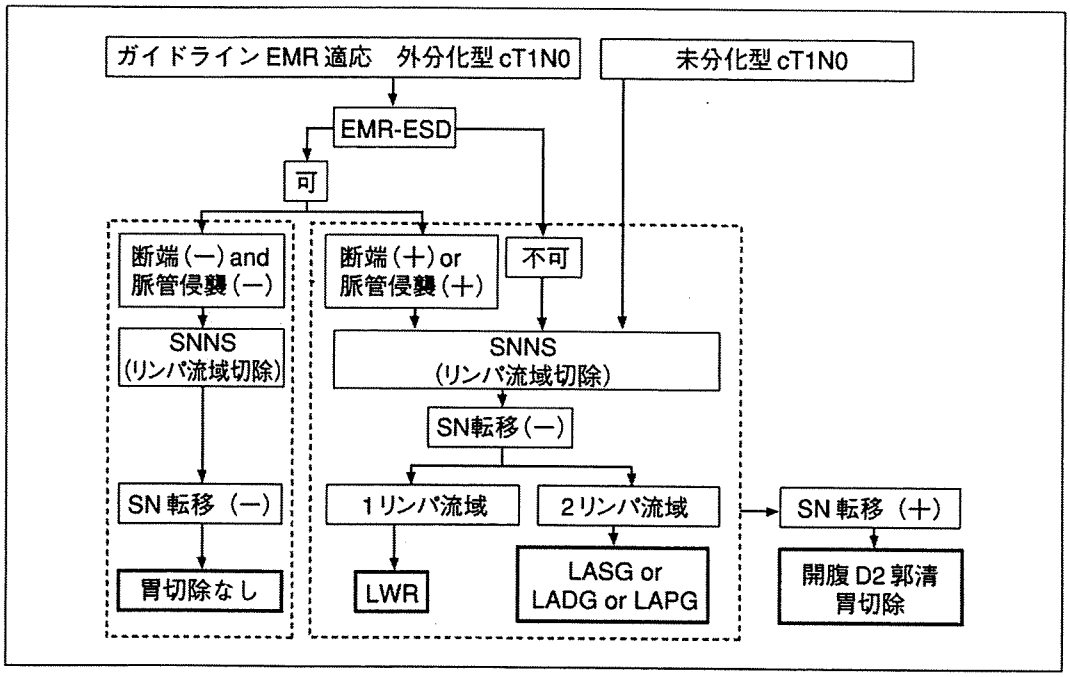


図3．今後のc0IIc胃癌の治療方針
LWR：laparoscopic wedge resection，LASG：laparoscopy-assisted segmental gastrectomy，LAPG：laparoscopy-assisted proximal gastrectomy

同等の効果が得られると考えられる．

すなわち，腹腔鏡下SNNSをLBDで行い，リンパ流域が1方向で術中リンパ節転移がなければwedge resection(図2a)，2方向で術中転移がなければ分節切除(図2b)，3方向なら幽門側胃切除，また術中に転移を認めた場合は定型手術に移行するという術式設定が成り立つ(図3)．現にこれに準じた手術を施行している施設もある[29,30]．

さらに，内視鏡的粘膜下層剝離術(ESD)の適応拡大に伴い，リンパ節転移の可能性があるカテゴリー，すなわちSM1・分化型・3 cm以内・脈管侵襲なしの条件を満たさない場合に腹腔鏡下SNNSを施行し，図3のような術式設定をすることができる[31]．このESD切除標本の病理検索，特にHE染色でリンパ管侵襲を見逃さないためにD2-40染色を施行したり，先進部が未分化型に変化していないかを確実に診断する必要がある[32,33]．最近術中にESDとリンパ節郭清を組み合わせて，胃を切除しないとする報告もある[34]．しかしわれわれは，連続切片ではじめてリンパ管侵襲陽性の診断がついて，SNNSによる手術の結果，切除胃にリンパ管侵襲陽性の遺残を認めた症例を経験している[35]．術中の脈管侵襲診断ができない以上，現時点ではまずESDを先行させて，断端陰性，脈管侵襲がないとされた先進部未分化型のもの以外は，basinに流れる胃壁内のリンパ管を切除するために図3のような胃切除は必要と考えられる．

おわりに

SNNS導入後は個別化により必要最小限の胃癌治療が可能となってくると考えられる．

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Original Articles

The Possibility of Performing a Limited Resection and a Lymphadenectomy for Proximal Gastric Carcinoma Based on Sentinel Node Navigation

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Abstract

Purpose. This study examined the possibility of performing a limited resection and a lymphadenectomy with sentinel node navigation surgery (SNNS) for the treatment of proximal gastric carcinoma.

Methods. Thirty patients with cT1N0 ($n = 23$) and cT2N0 ($n = 7$) proximal gastric carcinoma that was located primarily in the U area (the upper third of the stomach) were enrolled. indocyanine green (ICG; 0.5 ml) was injected endoscopically into the submucosa of the four quadrants encompassing the cancer. Twenty minutes after injection, infrared ray electronic endoscopy (IREE) was used to identify the lymph nodes that were stained with ICG (sentinel nodes, SNs) around the serosa and surrounding fat tissue.

Results. One hundred percent of the SNs were identified with our SNNS method. The most common location of SNs was No. 3 (T1: 78%, T2: 100%). The main route of lymphatic drainage was from No. 1 or No. 3 to No. 7 (T1: 95%, T2: 100%). In T1 cancer, Indocyanine green was not distributed to the right gastric area, and no patients had SNs in No. 5 or No. 8a. Four cT2 cancer patients had lymph node metastases, all of which were SNs. There were no cases of postoperative metastasis or recurrence.

Conclusions. For the cT1 proximal gastric carcinoma patients, limited dissection of the ICG tracer-positive lymphatic areas alone by SNNS using IREE may be acceptable. The main lymphatic drainage route of proximal gastric carcinoma is the left gastric artery area (Nos. 1, 3, and No. 7) and dissection of this area is important.

Key words Limited gastrectomy · Sentinel node navigation surgery · Proximal gastric carcinoma

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Introduction

Although the overall incidence of gastric cancer has been declining in both Western and Eastern countries, the incidence of adenocarcinoma of the proximal third of the stomach has been increasing at an alarming rate.[1] Owing to an aging population and an increasing proportion of early gastric cancers,[2] Japanese surgeons may be faced with treating a greater number of early cancers in the upper third of the stomach in the future.[3]

An analysis of the outcomes of such patients treated by the standard Japanese D2 total gastrectomy in the 1980s demonstrated that nodal metastasis in the distal perigastric nodes was rare.[3,4] Recently, more attention has been paid to improving the postoperative function and quality of life after early gastric cancer surgery without impairing the long-term outcome.[5] The treatment guidelines of the Japanese Gastric Cancer Association (JGCA) recommend endoscopic mucosal resection (EMR) or a modified gastrectomy (Modified A: D1 + No. 7, Modified B: D1 + No. 7, 8a, 9) for Stage IA (T1N0).[6]

For several years, we have performed sentinel node navigation surgery (SNNS) using infrared ray electronic endoscopy (IREE) combined with indocyanine green (ICG) injection for cT1N0 or cT2N0 gastric cancer.[7] Furthermore, we have previously reported the validity of a modified gastrectomy combined with this method for T1N0 gastric cancer.[8] The present study examined the surgical outcome of a gastrectomy combined with SNNS using IREE combined with ICG for proximal gastric cancer.

Patients and Methods

The protocol was approved by the Ethics Committee for Biomedical Research of the Jikei Institutional Review Board, and all patients provided written informed consent. The patients who were admitted to Jikei University Hospital with gastric cancer with no obvious metastases were prospectively enrolled.

Between July 2000 and December 2006, 135 patients with proximal gastric cancer that was located primarily in the U area (the upper third of the stomach) underwent resection with lymph node dissection. Of these, 30 patients with cT1N0 and cT2N0 gave their informed consent for SNNS and thereafter were enrolled in this study.

Sentinel node navigation surgery was performed according to the method of Nimura et al.[7] Firstly, 0.5 ml ICG (5 mg/ml; Diagnogreen; Dai-Ichi Pharma, Tokyo, Japan) was injected via an endoscope into each of the four submucosal sites surrounding the gastric cancer using an endoscopic puncture needle during open or laparoscopic surgery. Twenty minutes after the injection, the lymph nodes that were stained with ICG (sentinel nodes, SNs) were observed intraperitoneally around the serosa, and the surrounding fat tissue from the serosal side. Infrared ray electronic endoscopy (Olympus Optical, Tokyo, Japan) was used to illuminate the regional lymph nodes from the serosal side. Positive staining was confirmed by at least four surgeons or endoscopists during surgery (Fig. 1).

In principle, a lymph node dissection and a gastrectomy were performed according to the criteria established in the gastric cancer treatment guidelines of the JGCA, followed by a definitive pathological examination that included hematoxylin–eosin staining, and immunohistochemical staining with an anticytokeratin antibody (CAM 5.2; Becton Dickinson, San Jose, CA, USA). When metastases to SNs (hard or swollen SNs) were suspected, quick sections were examined pathologically. If informed consent was obtained from the cT1N0 patients, then a limited gastrectomy (wedge resection, segmental gastrectomy, or pylorus-preserving gastrectomy) with a dissection of the lymphatic area positive for ICG (lymphatic basin dissection, LBD[9]) was performed. In such cases, the SNs were examined using the frozen section diagnosis procedure. A pylorus-preserving gastrectomy or a segmental gastrectomy was performed for the patients with a lesser curvature lesion if the tumor margin was located greater than 2 cm from

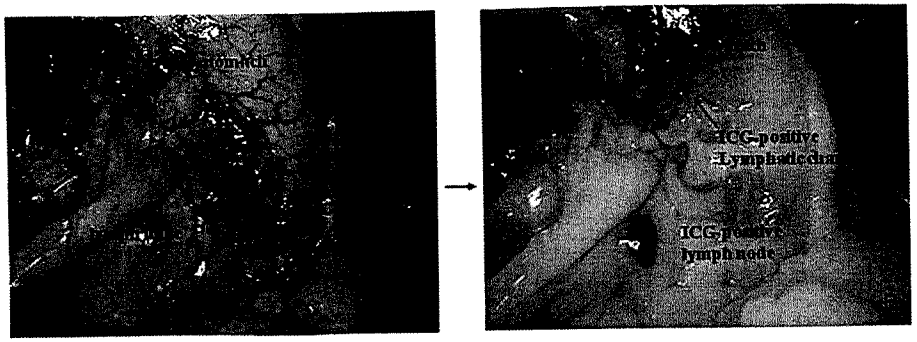

Fig. 1A,B. Intraperitoneal observation of the stomach during laparoscopic surgery, 20 min after the injection of indocyanine green (*ICG*). With infrared ray electronic endoscopy (IREE), lymph nodes (sentinel nodes) and lymphatic vessels positive for ICG were clearly detected. **A** Ordinary light. **B** IREE

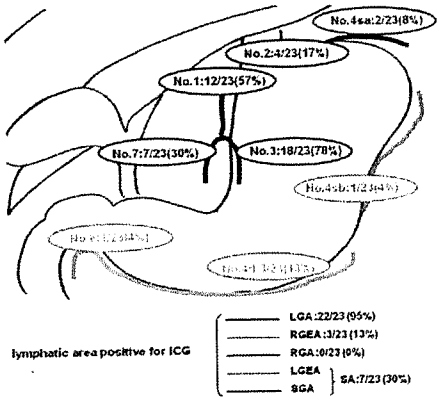

Fig. 2. Location of identified sentinel nodes (SNs) and lymphatic areas positive for ICG in T1 cancer cases. *LGA*, left gastric artery area; *RGEA*, right gastroepiploic artery area; *RGA*, right gastric artery area; *LGEA*, left gastroepiploic artery; *SGA*, short gastric artery; *SA*, splenic artery area

Table 1. Patients' characteristics

Age (years)	62.9 ± 9.14 (43–84)*
Sex (M:F)	23:7
Tumor size (mm)	42.6 ± 32.1 (7–160)*
Depth of invasion	
m	13
sm	10
mp	3
ss	2
se	2
Lymph node metastasis	
n0	26
n1	3
n2	1
Anatomical subsite	
Lesser curvature	15
Greater curvature	4
Anterior wall	3
Posterior wall	8

*Mean ± SD (range)

Table 2. Identification of sentinel node (SN) and lymph node (LN) metastasis

	T1 (n = 23)	T2 (n = 7)
SN identification	23 (100%)	7 (100%)
LN metastasis	0	4
Sensitivity	—	100%

the gastroesophageal junction in order to preserve the cardia. The gastric lymphatic area was divided into the left gastric artery (LGA) area, the right gastric artery area (RGA), the right gastroepiploic artery area, and the splenic area according to the criteria of Roviere[10] and Coller et al.[11]

Results

The patients' characteristics are listed in Table 1. The pathological findings included the depth of invasion and lymph node metastasis. Of the 30 proximal gastric cancer patients examined by SNNS, 23 patients were pT1 and 6 patients were pT2. All of the 4 patients with lymph node metastasis had T2 cancer. Our SNNS methods permitted an accurate identification of SNs and metastatic lymph nodes (Table 2). The number of SNs per patient was 4.8. Although the maximum tumor size was 160 mm, the SNs could be identified. The operative data are listed in Table 3. A wedge resection combined with a dissection of the lymphatic area positive for ICG was performed for 4 patients. The SNs of these 4 patients was examined by a frozen section, and they were confirmed to be free of any metastasis.

Table 3. Operative procedures

Type of gastrectomy	
Open	27
Laparoscopically assisted	3
Extent of resection	
Proximal gastrectomy	8
Total gastrectomy	16
Pylorus-preserving gastrectomy (segmental gastrectomy)	2
Wedge resection	4
Extent of dissection	
D1	4
D1 + α	15
D1 + β	2
D2	5
LBD	4

LBD, lymphatic basin dissection

The locations of the identified SNs and the lymphatic areas positive for ICG are shown in Figs. 2 and 3. In T1 cancer patients, the most common lymphatic area of the upper third cancer was the LGA area (22 patients, 95%), and No. 3 was the most common location of the SNs (18 patients, 78%), while No. 1 was the second most common location (12 patients, 57%). The main route of lymphatic drainage was from No. 1 or No. 3 to No. 7. Nevertheless, in some patients, the lymphatic area positive for ICG was in the right gastroepiploic artery or the left gastroepiploic artery area despite the presence of a lesser curvature lesion. Indocyanine green was not distributed to the right gastric area, and no patients had SNs in No. 5 or No. 8a.

As in the T1 cancer cases, in T2 cancer cases the most common lymphatic area was the LGA, and No. 3 was the most common SN location. In comparison to the T1 cancer cases, there was an increase in the number of cases with the lymphatic area in the greater curvature. Furthermore, the SNs were Nos. 8a and 11p.

The mapping of the four patients with lymph node metastases is shown in Fig. 4. All patients had cT2 cancer. The postoperative pathological examination showed that the depth of the tumor in Case 1 was SE. Cases 1, 2, and 4 underwent a standard total gastrectomy with a D2 dissection. However, Case 3 received a proximal gastrectomy with D1 + α, which was insufficient according to the criteria of the JGCA guidelines, because this patient did not want a total gastrectomy, but gave informed consent for a limited gastrectomy and a dissection for ICG-positive lymphatic areas. In all four patients, all metastatic lymph nodes were positive for ICG. After a median follow-up of 61 months, none of the patients had either postoperative metastases or recurrence.

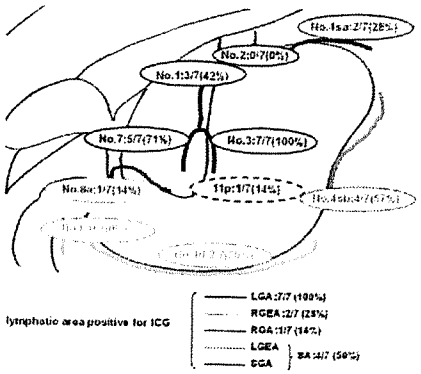

Fig. 3. Location of identified SNs and lymphatic areas positive for ICG in T2 cancer cases. *LGA*, left gastric artery area; *RGEA*, right gastroepiploic artery area; *RGA*, right gastric artery area; *LGEA*, left gastroepiploic artery; *SGA*, short gastric artery; *SA*, splenic artery area

Discussion

With respect to a lymph node dissection for proximal gastric carcinoma, Kobayashi et al. mapped the arterial areas of lymphatic drainage by studying the cases of single lymph node metastasis, in which the left gastric arterial area was reported to be the main stream, extending to the whole stomach except for the greater curvature of the upper one-third of the stomach or pylorus.[12] Furthermore, these investigators classified lymph nodes No. 5 and No. 8a in the right gastric arterial area, and reported that this arterial area was small and included only the lesser curvature of the antrum. Ohta et al. analyzed the appropriate indications for a proximal gastrectomy for cancer in the upper third of the stomach.[13] They concluded that localized, superficial lesions less than 30 mm in size, or other macroscopic types including differentiated and undifferentiated lesions with neither lymph node metastasis nor a serosal involvement, have no lymph node metastasis in No. 4d, No. 5, and No. 6. Nevertheless, these studies were based on the results of a postoperative histopathologic examination.

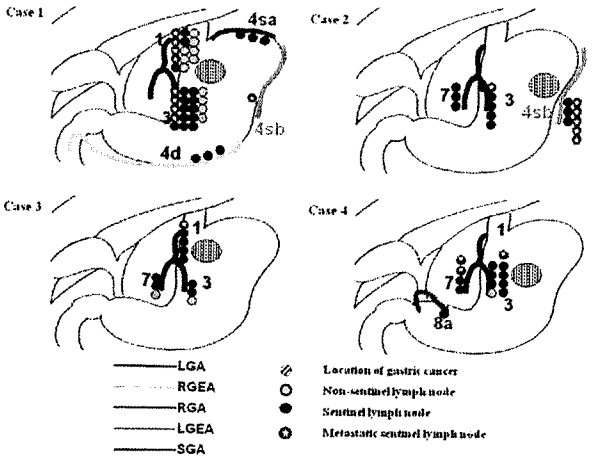

Fig. 4. Patients who had metastatic lymph nodes. *Case 1* had a 65-mm, SE mucinous carcinoma in the anterior wall, which had three lymphatic areas (LGA, SA, RGEA) and SNs in Nos. 1, 3, 4sa, 4sb, and 4d. The metastatic lymph nodes were located in Nos. 1, 3, and 4sb, which were all SNs. *Case 2* had a 25-mm, MP well-differentiated adenocarcinoma in the greater curvature, which had two lymphatic areas (LGA) and SNs in Nos. 3, 4sb, and 7. The metastatic lymph nodes were located in Nos. 3 and 4sb, which were all SNs. *Case 3* had a 62-mm, MP poorly differentiated adenocarcinoma in the lesser curvature, which had one lymphatic area (LGA) and SNs in No. 1. A metastatic lymph node was included in No. 1, which was an SN. *Case 4* had a 75-mm, SS moderately differentiated adenocarcinoma in the posterior wall, which had two lymphatic areas (LGA, RGA) and SNs in Nos. 3, 7, and 8a. The metastatic lymph nodes were included in Nos. 3 and 7, which were all SNs. *LGA*, left gastric artery area; *RGEA*, right gastroepiploic artery area; *RGA*, right gastric artery area; *LGEA*, left gastroepiploic artery; *SGA*, short gastric artery

In the present intraoperative study with SNNS, the most common location of SNs was No. 3, and the main lymphatic drainage was LGA (from No. 1 or No. 3 to No. 7). These results are in agreement with previous reports that described the importance of the dissection of LGA for proximal gastric carcinoma.[12,13]

None of the T1 cancer patients had SNs in No. 5 or No. 8a, and none of the No. 5 or No. 8a lymph nodes that were dissected contained metastatic lymph nodes. Furthermore, the maximum size of the T1 tumors was 68 mm. Therefore, it seems unnecessary to dissect these lymph nodes in early cancers that occur primarily in the upper third if the tumor does not extend to the lesser curvature of the antrum. A proximal gastrectomy, segmental gastrectomy, or wedge resection is possible if the surgical margin can be secured. In fact, in the present study, no postoperative metastases or recurrences were observed after either a wedge resection, pylorus-preserving gastrectomy (segmental gastrectomy), or proximal gastrectomy.

However, in T2 cancer cases the ICG-positive lymphatic area included the RGA area. This suggests that, in principle, a total gastrectomy with dissection of the RGA area is necessary for T2 cancer. Furthermore, all patients with lymph node metastasis had T2 cancer. Importantly, all metastatic lymph nodes were included in the ICG-positive lymphatic area and the SNs.

Recently the number of reports of SNNS for gastric cancer has increased, and such techniques have been improving.[9,14–19] Ichikura et al. reported lymphatic mapping using ^{99m}Tc-labeled tin colloid and ICG in the patients with clinical T1N0 cancer.[14] In their study, a postoperative pathologic examination revealed lymph node metastases in 3 of the 61 patients for whom the SNs were diagnosed intraoperatively as negative on the frozen section. All of their metastatic lymph nodes were included in the lymphatic areas where RI or ICG was distributed.

Ajisaka et al. analyzed micrometastases in SNNS using reverse transcription–polymerase chain reaction (RT–PCR) and immunostaining.[20] Three of the 35 patients had metastases in non-SNs, whereas all of the metastatic non-SNs were identified in the same lymphatic basin as the metastatic SNs. They concluded that the dissection of the lymphatic area containing SNs is a minimal requirement for curative resection of early-stage gastric cancer, even for patients without histologically detectable metastases in the SNs.

In most institutions, a standard total gastrectomy with D2 dissection is performed for lymph node metastasis in the SNs. Based on our results and those of previous studies, none of the patients in our study have lymph node metastasis in SNs, and a limited dissection to only the lymphatic areas where the tracers are distributed appears acceptable for cT1. For example, in the future we may be able to preserve the spleen if the tracers are not distributed to the splenic artery area. Furthermore, a limited gastrectomy such as a proximal gastrectomy, wedge resection, or pylorus-preserving gastrectomy may be indicated according to the size and the location of the cancer if the surgical margin can be defined.

In conclusion, for the patients with cT1 proximal gastric carcinoma, although a further accumulation and analysis are necessary, a limited dissection of the ICG tracer-positive lymphatic areas alone by SNNS using IREE may be acceptable. The main lymphatic drainage route of proximal gastric carcinoma is the left gastric artery area (Nos. 1, 3 to No. 7), and the dissection of this area is important when performing limited surgery.

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Tailoring Treatment for Early Gastric Cancer after Endoscopic Resection Using Sentinel Node Navigation with Infrared Ray Electronic Endoscopy Combined with Indocyanine Green Injection

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Key Words
Early gastric cancer, tailoring treatment · Endoscopic resection · Indocyanine green · Infrared ray electronic endoscopy · Sentinel node navigation surgery

Abstract
Background: This study evaluated the efficacy of sentinel node navigation surgery using infrared ray electronic endoscopy (IREE) combined with indocyanine green in patients after endoscopic treatments of early gastric cancer. ***Methods:*** 14 patients with early gastric cancer after endoscopic treatments were included. Each patient underwent sentinel node navigation surgery using IREE. Sentinel node detection rate, accuracy of sentinel node metastases and clinical efficacy including the presence or absence of recurrence were evaluated. ***Results:*** The intraoperative sentinel node detection rate was 100% (14/14), and accuracy for sentinel node metastases was 93% (13/14). Based on the results of sentinel node mapping, 2 patients received standard gastrectomy with D2 lymphadenectomy, and the remaining 12 patients underwent limited surgery with lymphatic basin dissection. After median follow-up of 32 months, no patients had tumor recurrence. ***Conclusion:*** The validity of limited surgery based on sentinel node navigation for early gastric cancer remains unclear because the results of a well-designed multicenter clinical trial of sentinel node mapping for gastric cancer have not yet been reported. However, this study suggests that sentinel node navigation surgery using IREE combined with indocyanine green is useful for early gastric cancer after endoscopic resection.

In Japan, early-stage gastric cancer now accounts for more than half of all cases. Among others, patients with mucosa-limited gastric cancer <2 cm in diameter are good candidates for endoscopic mucosal resection [1]. Advances in endoscopic therapeutic technique and development of new instruments have led to expansion of the indications for endoscopic treatments of early gastric cancer. Endoscopic submucosal dissection is a new technique developed to obtain en-bloc resection in cases of early cancer >2 cm in diameter [2, 3].

Unfortunately, a substantial percentage of patients who receive endoscopic treatment for early gastric cancer require additional treatments because of incomplete resection and/or improper indications for endoscopic re-

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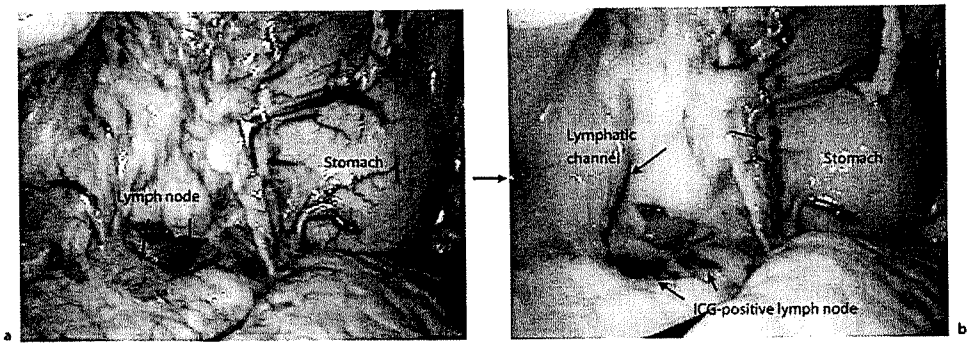

Fig. 1. a Serosal side of the stomach during laparoscopic surgery (ordinary light), 20 min after injection of ICG. **b** With IREE, lymph nodes (sentinel nodes) and lymphatic vessels positive for ICG can be identified easily.

section, such as massive submucosal invasion of cancer cells. In a large retrospective study including 445 patients who received endoscopic mucosal resection for treatment of early gastric cancer, 86 patients (19%) subsequently underwent additional surgery because of incomplete resection, local recurrence, or unclear margins in endoscopic mucosal resection specimens caused by piecemeal resection or by the electrocautery [2].

The incidence of lymph node metastasis of early gastric cancer in submucosal invasion has been reported to be about 20%, and that of metastasis to second-level lymph nodes, those around the left gastric, common hepatic, and celiac artery, has been reported to be about 4% [4]. As a result, in Japan, standard gastrectomy with D2 lymph node dissection has been advocated for early cancer with invasion to the submucosal layer, although this strategy is not accepted in Western countries. Standard gastrectomy with dissection of all first- and second-level lymph nodes (D2) is also recommended for patients who received endoscopic mucosal resection for early gastric cancer that involved the submucosal layer on subsequent histopathological examination.

However, many patients without lymph node metastasis are submitted to unnecessary extensive lymph node dissection, possibly leading to increases in postoperative morbidity and length of hospital stay. For several years, we have performed sentinel node navigation surgery using infrared ray electronic endoscopy (IREE) combined with indocyanine green (ICG) injection for patients with cT1N0 or cT2N0 gastric cancer [5], and then sentinel node navigation surgery was used for patients undergoing salvage operation after endoscopic mucosal resection. The aim of this study was to retrospectively evaluate the efficacy of sentinel node navigation surgery using IREE combined in such patients.

Patients and Methods

Among the 205 patients who underwent sentinel node navigation surgery for cT1N0 and cT2N0 gastric cancer between 2000 and 2007, 14 patients who received endoscopic resection (endoscopic mucosal resection and endoscopic submucosal dissection) as initial treatment were included in this study. The study was approved by the Ethics Committee for Biomedical Research of the Jikei Institutional Review Board, and all patients gave their written informed consent.

The methods for sentinel node mapping for gastric cancer have been previously described [5]. Briefly, each of the four submucosal sites surrounding the gastric cancer was injected with 0.5 ml ICG (5 mg/ml; Diagnogreen®; Dai-Ichi Pharm, Tokyo, Japan) through an endoscope using an endoscopic puncture needle during open or laparoscopic surgery. After 20 min, sentinel nodes stained with ICG were observed intraperitoneally around the serosa and surrounding fat tissue from the serosal side. IREE (Olympus Optical, Tokyo, Japan) was used to illuminate regional lymph nodes from the serosal side.

Positive staining was identified by at least 4 team members involved in sentinel node navigation surgery during the operation (fig. 1). The sentinel nodes were immediately examined by frozen section with hematoxylin and eosin staining. If possible, CAM5.2 (Becton Dickinson, San Jose, Calif., USA) was used for immunohistochemical staining with anticytokeratin antibody. During surgery, two sections were examined by both HE and immunohistochemical staining.