

**Received:** 2004.06.11  
**Accepted:** 2004.08.09  
**Published:** 2005.07.15

## Sentinel node mapping in gastric cancer

**Arkadiusz Jeziorski**

Oncological Surgery Department, Medical University in Łódź

Proceedings from the I Symposium "Sentinel Node", Poznań, 26 March 2004.

### Summary

This article is a review of literature of what we know in the field of sentinel node mapping in gastric cancer.

The current status of lymphatic mapping and sentinel node (SN) biopsy in the treatment of patients with gastric carcinoma is a matter of intense discussion.

One of the most simplest and not expensive technique is intraoperative peri-tumoral subserosal injection of the blue dye and real time observation.

An alternative method is radioquided detection with the use of 99 m Technetum fin colloid.

The third method is technique described by Wong.

Identification of SN in patients with gastric cancer may lead to modification of the status of the disease in the pTNM system, which can help in better qualification for adjuvant treatment. Intensive studies are needed to solve some burning problems concerning this subject and at present it is still too early to recommended one of these above techniques in routine clinical practice.

### Key words

**gastric cancer • sentinel node • controversies**

**Full-text PDF:** <http://www.rpor.pl/pdf.php?MAN=7617>

**Word count:** 2004

**Tables:** –

**Figures:** 4

**References:** 18

### Author's address:

Arkadiusz Jeziorski, Oncological Surgery Department, Paderewskiego 4 Str., 93-509 Łódź, Poland,  
e-mail: jeziorski@post.pl

## BACKGROUND

The first possible site of metastases via a lymphatic chain from a primary lesion was described as sentinel node (SN). Morton demonstrated the concept of sentinel nodes in patients with melanoma [1]. Multicentre trials with breast cancer have been carried out and the prediction of a node status in the majority of centers now exceeds 95% [2,3]. The feasibility of sentinel node mapping in gastric cancer and its diagnostic reliability are still unclear. Lymphatic drainage of the stomach is much more complicated than in other sites [4,5], therefore reports of the distribution of solitary lymph node metastases demonstrate unpredictable patterns [6,7]. For these reasons, the majority of surgeons are still sceptical about the concept of sentinel node in gastric cancer [4,5,8].

## ANATOMY OF THE LYMPHATIC SYSTEM OF THE STOMACH

The lymphatic vessels form several levels in the gastric wall: the lymphatic rete of mucous membrane, the lymphatic rete of submucous membrane, the lymphatic rete of muscular membrane and the lymphatic rete of serous membrane. The rete of mucous membrane is divided into subepithelial and subglandular membranes which fuse to form dense network surrounding gastric glands. By means of perpendicular vessels lymphatic rete of mucous coat are joined with the rete of the submucous coat, which is formed by narrow lymphatic vessels forming several loops varied in length. The lymphatic rete of the muscular coat consists of three layers: the lymphatic rete of longitudinal fibres, the lymphatic rete of circular fibres and the lymphatic rete of oblique fibres. Numerous short vessels connect the lymphatic rete of the muscular coat to the lymphatic rete of submucous membrane on the inside and to the lymphatic rete of serous membrane on the outside. The minor lymphatics extend from the serous coat to the greater and lesser curvature of the stomach. The lymphatic rete of serous coat forms Teichmann's plexus from where lymph is carried through lymphatic vessels directly to regional lymph nodes.

There are six areas of lymph flows and six groups of the first level regional lymph nodes. The first (cardiac) area embraces cardia and the abdominal part of the esophagus. Lymph passes from this part to the pericardiac lymph nodes (precardiac and retrocardiac). The second area includes the lesser curvature of anterior and posterior walls of

the organ; lymph passes to the right gastric nodes. The third area embraces both surfaces of the stomach located in the pyloric portion; lymph passes to the pyloric and hepatic nodes. Lymph which is passed from the fourth area embracing the pyloric portion adjacent to the greater curvature of the stomach is carried to pyloric nodes and to the right gastroepiploic nodes. Lymph from the part of the anterior and posterior surfaces of the stomach which adjoin the greater curvature (the fifth area) passes to the left gastroepiploic nodes. The sixth area is located around the fundus of the stomach. The pancreatosplenic nodes form a regional lymphatic system of this area.

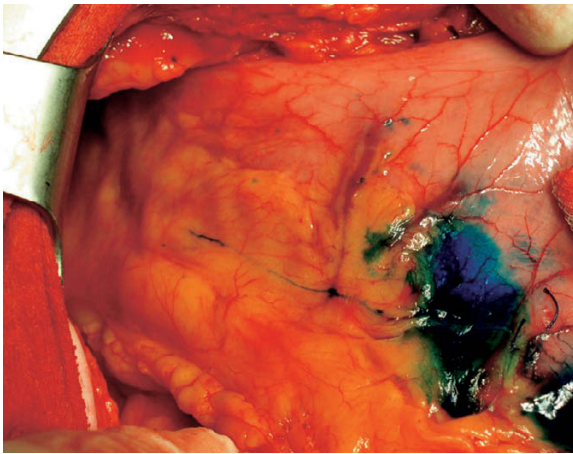
The second level of lymph nodes consists of celiac nodes (lymph nodes surrounding the celiac axis), and nodes accompanying the splenic artery, the common hepatic artery, the proper hepatic artery, the hepatoduodenal ligament and the left renal vein. Then the lymph passes through the lumbar lymph nodes and ultimately via lumbar lymph plexus flows into the thoracic duct.

It seems necessary to mention the presence of the lymph route passing to the left supraclavicular lymph nodes (Virchow's node) which is enlarged and palpable in only 10% of gastric cancer patients.

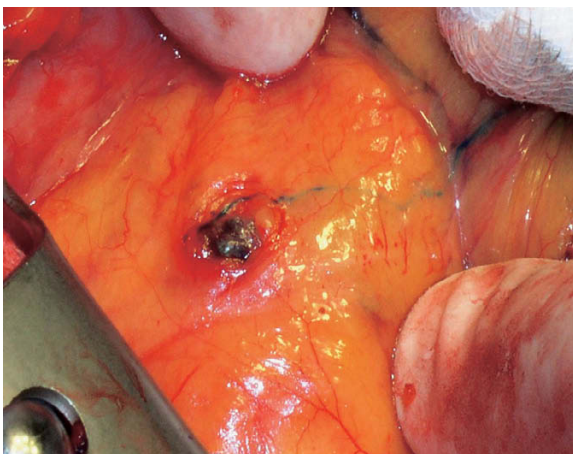
Due to the presence of numerous anastomoses between the layers of the gastric lymphatic networks, lymph can pass easily from the mucous rete to the serous rete. The lines bordering each area of the lymph flow were established. It would seem fairly simple to determine the direction of lymph flow in regard to the tumour localisation especially in early gastric cancer, which it is true in most cases. However, when the tumor is located in the interdivisional zones, the direction of lymphatics is hard to predict. Moreover, the borders of particular areas vary from patient to patient. Therefore metastases of gastric cancer can spread to different groups of lymph nodes. Hence the idea of sentinel lymph node (SLN) biopsy in gastric cancer.

## MAPPING TECHNIQUE

After laparotomy, the stomach is mobilized from the lesser and greater omenta and from the duodenum. When the tumour is visible or palpable 1 ml of blue-dye is injected into the subserosal layer at two points: 1 cm distally and 1 cm proximally of the gastric carcinoma. If the tumour is non palpable, the standard upper gastrointestinal panendoscopy is inserted into the stomach and the loca-



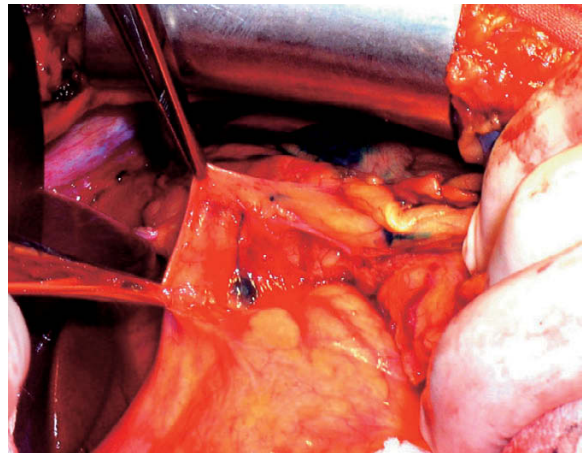
**Figure 1.** Blue lymphatic vessels along right epiploic artery.



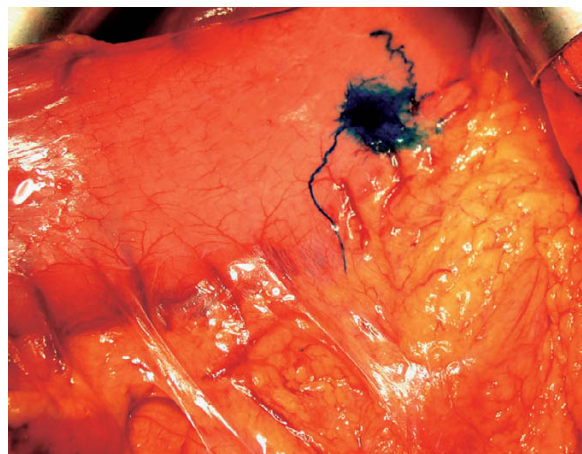
**Figure 2.** A sentinel node at the end of a lymphatic vessel.

tion of the lump is established. Then the marker is injected subserosally at one point: just above the point showed by an endoscope. If the tumour is located in the anterior or posterior wall in the border line area a blue dye is administrated circumferentially around the neoplasm. In each case the lymphatic channel is visualized within a couple of minutes: the blue dye appeared as coloured lines on the gastric serosal surface. Figure 1 illustrates the lymphatic basins along the right gastroepiploic artery which ends in one lymph node.

A sentinel node is that in which a lymphatic vessel ends, located most proximal to the cancer. The omental fatty tissue, including the lymphatic basin, is then mapped out from the gastric areas, and the node dissected with great care (Figure 2). Blue node or nodes are sent separately for histological examination. Than *en bloc* resection of the neoplasm and the regional lymph nodes is performed in the standard fashion. D2 involves a complete dissection of the perigastric nodes (N1)



**Figure 3.** A sentinel node found among celiac nodes, in the second level (skip metastatic phenomenon).



**Figure 4.** Two opposite directions of lymphatic spread from a primary neoplastic focus. In the left lower corner an enlarged metastatic sentinel node is visible.

as well as nodes located at suprapancreatic area, along hepatic artery, hepato-duodenic ligament and in splenic hylum (N2). If metastases are suspected in regional lymph nodes subsequent dissection of nodes along superior mesenteric vessels or para-aortic nodes in the area of left renal vein (N3) is performed (D3).

Each blue node is sliced in 0.2 mm sections and stained with hematoxylin and eosin. The remaining node tissues are processed separately in individual blocks for ordinary histological examination. The gastric specimen is fixed to a cork plate and immersed in 15 per cent formalin solution for at least 48 h.

#### **OBSERVATIONS**

Our trial is in the start line: we have carried out our studies of sentinel node in gastric cancer since

June 2003. The main indication for this procedure was early gastric cancer in T1-T2N0 stage of its development in the TNM system. Unfortunately, from the beginning the majority of our patients were in a more advanced stage, and that is why the number of patients analysed in the trial is still small. We are still on the afferent arm of the learning curve, the main idea of which is to learn the technique of blue dye injection and identification of sentinel nodes. What is interesting is that in all cases the status of SN corresponded to the status of the remaining nodes, i.e. to the disease. There were several interesting cases of lymphatic drainage. The first (Figure 3) was that in which we observed the phenomenon of skip metastases: the lump was located in the front wall of the stomach in the second area, and a SN was found among celiac nodes, which was also true to level II. An other interesting case was one with a tumour located in the front wall of the stomach, and a SN was found in the splenic hylum, so, in the consequence, splenectomy in this patient was done additionally. In still other case we found stomach cancer located in the sixth area, close to the left gastroepiploic artery, and two enlarged lymph nodes, one located in the group of parapyloic nodes (between area 3 and 4) and the other on the site of right gastric nodes (area 1 and 2) as well as on the opposite site of the stomach. After injection, we observed migration of the blue dye in two directions, exactly to these two enlarged nodes located in complete different regional groups. Both nodes were metastatic and the remaining nodes removed on D3 lymphadenectomy were clear (Figure 4).

## DISCUSSION

*In vivo* lymphatic drainage from gastric carcinoma was divided into six compartments based on their location along major gastric arteries. This is comparable to the first descriptions of the lymphatic system of the stomach made *ex vivo* by Jamieson in 1907 [9]. Gastric tumours metastasized mainly from a particular zone to a particular group of lymph nodes, but there is a high number of cases in which metastases may occur along another route. In approximately one third of these cases sentinel nodes were found in extragastric nodes [10]. Another interesting aspect associated with the concept of the sentinel node is the presence of anatomical lympho-venous shunts which connect lymphatic system with blood circulation [11]. These anastomoses provide explanation of the high risk of dissemination in patients with node metastases. This risk concerns mainly patients with locally ad-

vanced cancer in whom only the sentinel node is invaded by metastases. Some authors indicate that lymph from Teichmann's plexus can flow directly to the thoracic duct passing by the regional lymph nodes. The unexpected drainage patterns also explain also the problem of *skip metastases* which very often occur in gastric cancer. The authors emphasize that the concept of *skip metastases* is not in variance with the concept of sentinel nodes; on the contrary this technique seems to be essential in the detection of metastases and qualification for adequate pTNM classification.

Pathological examination of sentinel nodes is essential. The greater number of slices are taken the greater is the probability of finding metastases. Frozen section analysis does not permit proper diagnosis and is contraindicated in SN estimation.

Intraoperative peri-tumoral subserosal injection of the blue dye and real time observation of the lymphatic flow have been widely used for mapping sentinel nodes in cancers of the gastrointestinal tract [12-14]. This technique is simple and not expensive. However some authors have noted a high percentage of false negative results in this method. A portion of the blue dye can be also injected submucosally in the area of the tumour by panendoscope inserted into the stomach. The result of this procedure is the same as the previous one in accordance with the anatomy of lymphatic chain in stomach. We should remember that the initial purpose of this procedure was to detect metastases in relatively early cases. That is why patients staged T1N0 are a proper population for this procedure. Since the early 1990s the introduction of laparoscopic surgery has provided various options in gastrointestinal surgery. It seems that a combination of laparoscopic surgery and lymphatic mapping would enable us to establish new non invasive procedures. For example, in the near future superficial gastric cancer without lymphatic metastases confirmed by sentinel mapping could be treated by laparoscopic wedge resection instead of gastrectomy with D2 lymphadenectomy.

An alternative method to sentinel mapping by blue dye in gastrointestinal tumours is radioguided detection with the use of <sup>99m</sup>Technetium tin colloid [15,16]. However based on own observations the authors conclude that, although use of a gamma probe is effective, sometimes it is difficult to find nodes located near the primary lesion because of high radioactivity at the injection site [17].

Another alternative method to *in vivo* mapping of sentinel nodes in the gastrointestinal tract has been proposed by Wong [18]. His method of *ex vivo* mapping in colon cancer is an interesting approach. However in gastric cancer we have to consider the possibility of unexpected route of lymphatic vessels. Therefore the method *in vivo* is more recommended. Also, *ex vivo* mapping might increase the probability of up-staging in some cases.

At present, it is still too early to introduce sentinel node biopsy in gastric cancer as a routine method for detecting metastases in the lymphatic chain. The method should be performed by highly qualified surgeons only at specialised centres still within the framework of controlled clinical trials.

#### REFERENCES:

1. Morton DL, Wen DR, Wong JH et al: Technical details of intraoperative lymphatic mapping for early stage melanoma. *Arch Surg*, 1992; 127: 392-99
2. Veronesi U, Paganelli G, Galimberti V et al: Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph nodes. *Lancet*, 1997; 349: 1864-67
3. Borgstein PJ, Meijer S, Pijpers R: Intradermal blue dye to identify sentinel lymph-node in breast cancer. *Lancet*, 1997; 349: 1668-69
4. Maruyama K, Sasako M, Kinoshita T et al: Can sentinel node biopsy indicate rational extent of lymphadenectomy in gastric cancer surgery? *Langenbecks Arch Surg*, 1999; 384: 149-57
5. Siewert JR, Sendlner A: Potential and futility of sentinel node detection for gastric cancer. *Recent Results Cancer Res*, 2000; 157: 259-69
6. Matsubara T, Ueda M, Kaisaki S: Localization of initial lymph node metastasis from carcinoma of the thoracic esophagus. *Cancer*, 2000; 89: 1869-73
7. Kosaka T, Ueshige N, Sugaya J et al: Lymphatic route of the stomach demonstrated by gastric carcinomas with solitary lymph node metastasis. *Surg Today*, 1999; 29: 695-700
8. Sano T, Katai H, Sasako M: Gastric lymphadenectomy and detection of sentinel nodes. *Recent Results Cancer Res*, 2000; 157: 253-58
9. Jamieson JK, Dobson JF: Lectures on the lymphatic system of the stomach. *Lancet*, 1907; i: 1061-66
10. Kitagawa Y, Fujii H, Mukai M: The role of the sentinel lymph node in gastrointestinal cancer. *Surg Clin North Am*, 2000; 157: 253-58
11. Poste G, Fidler IJ: The pathogenesis of cancer metastases. *Nature*, 1980; 283: 139-46
12. Saha S, Nora D, Wong JH: Sentinel node mapping in colorectal cancer - a review. *Surg Clin North Am*, 2000; 80: 1811-19
13. Wood TF, Tsioulis GJ, Morton DL: Focused examination of sentinel lymph nodes upstages early colorectal carcinoma. *Am Surg*, 2000; 66: 998-1003
14. Keshgar MR, Amin A, Taylor I: Intraoperative lymphatic mapping and the sentinel concept in colorectal carcinoma. *Br J Surg*, 1999; 86: 1225-26
15. Kitagawa Y, Fujii H, Mukai M et al: Radio-guided sentinel node detection for gastric cancer. *Br J Surg*, 2002; 89: 604-8
16. Mendez J, Wallace AM, Hoh CK, Vera DR: Detection of Gastric and Colonic Sentinel Nodes Through Endoscopic Administration of 99mTc-DTPA-Mannosyl-Dextran in Pigs. *J Nucl Med*, 2003; 44: 1677-81
17. Kitagawa Y, Kitajima M: Gastrointestinal Cancer and Sentinel Node Navigation Surgery. *J Surg Oncol*, 2002; 79: 188-93
18. Wong JH, Steineman S, Calderia C: *Ex vivo* sentinel node mapping in carcinoma of the colon and rectum. *Ann Surg*, 2001; 233: 515-21