

SN-GISCO R STUDY

MULTICENTRIC PROSPECTIVE STUDY “PREDICTIVE VALUE OF SENTINEL NODES (SN) IN STAGING EARLY COLORECTAL CANCER”

Main investigator

Bruno Andreoni
Division General Surgery - European Institute of Oncology
Via Ripamonti 435 – 20141 Milano
e-mail: bruno.andreoni@ieo.it

Organizational Coordinators

Paolo Pietro Bianchi
General Surgery Unit - Istituto Clinico Humanitas
Via Manzoni 56 – 20089 - Rozzano (Milano)
e-mail: marco.montorsi@humanitas.it paolopietro.bianchi@fastwebnet.it

Pathology

Angelica Sonzogni
Division of Pathology - European Institute of Oncology
e-mail: angelica.sonzogni@ieo.it

Endoscopy

Cristiano Crosta
Division of Endoscopy - European Institute of Oncology
e-mail: cristiano.crosta@ieo.it

Data Management

Antonella Perilli / Darina Tamayo
Division General Surgery - European Institute of Oncology
e-mail: antonella.perilli@ieo.it; darina.tamayo@ieo.it

DATA COLLECTION FORM MULTICENTRIC STUDY - *SN-GISCoR*

**"PREDICTIVE VALUE OF SENTINEL NODE
IN STAGING EARLY COLORECTAL CANCER (STAGES i-ii)**

Allotted by the Coordinating Center

Center No / _/_/_/_/_/

Patient N° / _/_/_/_/_/

Patient's Data

Initials / _/_/_/_/_/

Sex M F

Date of birth / _/_/_/ / _/_/_/ / _/_/_/

Informed consent form*:

YES

NO

** Patients can only be enrolled if
the informed consent form has been signed*

Previous colonic resection

YES

NO

Date endoscopic diagnosis

/ _/_/_/ / _/_/_/ / _/_/_/

Site of lesion

1. right colon
2. flessura destra
3. transverse colon
4. left Flexure
5. descending colon
6. sigmoid colon
7. recto-sigmoid junction

Radioactive tracer

YES NO

No. Hot nodes /_/_/_/

Length SN procedure /_/_/_/ minutes

Not Recognized

- 1. no SN visualization
- 2. Technical difficulties

Which ones:-----

Pathology

Total lymphadenectomy + SN /_/_/_/ + /_/_/_/

No. Marked nodes (sentinel) /_/_/_/

No. Blue nodes /_/_/_/

No. Hot nodes /_/_/_/

Sentinel:

Blue	Total No.	Positive No.	If positive:	1. Metastasis
E&E	/_/_/_/	/_/_/_/		2. Micro
IIC (Immunohistochemistry)	/_/_/_/	/_/_/_/		3. ITC
Hot	Total No.	Positive No.	If positive:	1. Metastasis
E&E	/_/_/_/	/_/_/_/		2. Micro
IIC (Immunohistochemistry)	/_/_/_/	/_/_/_/		3. ITC

If Micro or ITC (1^a)

Level /_/_/_/ (section)
Following /_/_/_/ (for how many more levels)
Position (only in one half) (in both halves)
Dimension /_/_/_/ (in micron)
Type Parenchimal Capsular Caps. and extracaps. Embolic

If Micro or ITC (2^a)

Level /_/_/_/ (section)
Following /_/_/_/ (for how many more levels)
Position (only in one half) (in both halves) |
Dimension /_/_/_/ (in micron)
Type Parenchimal Capsular Caps. and extracaps. Embolic |

If Micro or ITC (3^a)

Level /_/_/_/ (section)
Following /_/_/_/ (for how many more levels)
Position (only in one half) (in both halves)
Dimension /_/_/_/ (in micron)
Type Parenchimal Capsular Caps. and extracaps. Embolic

If Micro or ITC (4^a)

Level /_/_/_/ (section)
Following /_/_/_/ (for how many more levels)
Position (only in one half) (in both halves)
Dimension /_/_/_/ (in micron)
Type Parenchimal Capsular Caps. and extracaps. Embolic

	Total	Positive
<i>N in resection sample</i>	/_/_/	/_/_/

Final histology
Report -----

TNM -----
Dukes -----
Grading -----

INFORMATION TO THE PATIENT
AND INFORMED CONSENT FORM

(USE OF DYE)

Multicentric prospective study: "PREDICTIVE VALUE OF SENTINEL NODE IN STAGING EARLY COLORECTAL CANCER"

Dear Sir, / Madam,

our Institute takes part in a clinical research involving several Italian centers. The study evaluates the value of sentinel node detection in neoplastic diseases of the colon. The sentinel node is the first node draining lymph from the disease site. Its utility has already been proven in breast and skin cancers. The absence or presence of disease in this lymph node is highly predictive of the status of other lymph nodes. In case no disease is found in the sentinel node, it is highly probable that there is no disease in distant nodes. Therefore, sentinel nodes can heavily influence the following therapeutic approach.

Based on the sentinel technique in other diseases, its detection is being tested also in other, less superficial organs such as colon. The present study assesses identified sentinel nodes through specific evaluation methods. **In order to identify sentinel nodes, during the surgical procedure some dye (2 ml) will be injected** around the neoplastic tissue. This dye is drained to a number of nodes through the lymphatic vessels. The first nodes to be reached and become blue are called sentinel nodes.

These nodes will be marked and sent separately to the pathologists, so as to be studied more accurately. The surgical procedure will then be completed according to the standard technique by radical removal of all nodes. The dye used (isosulfan blue) is well tolerated, although mild unwanted side effects due to an allergic reaction to the dye have been reported in 1% of cases.

Having read the information form, I had the chance to ask all the questions about the protocol that I deemed necessary and I accept to participate in the study.

Date _____

The Patient

The study investigator

.....

.....

I Consent

I do not consent

that all my clinical information are given to my General Practitioner, Dr.

.....

The patient

.....

RATIONALE

Nodal staging is the most important prognostic factor in colorectal cancer. Five-year survival drops from 80% in N0 patients to about 50% in N1 patients. There is no proven added benefit from adjuvant chemotherapy (CT), although 20% to 40% of them will develop metastatic disease over the following 5 years. Node-positive patients treated with adjuvant CT, on the other hand, have a 33% proven benefit in survival. Nodal metastases occur in about 45% of patients with colorectal cancer. Preoperative staging methods still have low sensitivity. Standard nodal staging therefore requires radical lymphadenectomy. To date, colorectal resection needs to extend to the entire lymphatic drainage. The high percentage of N0 patients who will eventually develop disease progression lead to surmise that traditional staging methods may understage a number of cases. The main problem is therefore accuracy in nodal staging and reducing the risk of understaging. Detecting the highest number of nodes is crucial, as is the detection method used by the pathologist. The most detection methods (multilevel sections, immunohistochemistry and molecular biology) cannot be used on all identified nodes because of the high cost and the time necessary. Sentinel Node (SN) study in colon surgery is part of a strategy to select nodes to be studied more accurately.

Role of sentinel nodes in colonic surgery and review of literature

Over the last 8 years, SN evaluation has become the standard procedure in staging breast cancer and skin melanoma. Important clinical trials have proven that SN evaluation has a 97% accuracy in predicting nodal status in these neoplasms. Identifying the first draining node(s) may avoid an extended resection with radical excision. Thuption is valid for all tumors with a linear nodal metastatization, such as melanoma and breast cancer. The procedure is less effective whenever lymphatic diffusion skips a station.

Literature data regarding SN evaluation in colorectal surgery are very varied. The percentages of SN detection vary from 58% to 98%, although in the largest studies the percentage of detection is over 90%. An accurate analysis of the studies easily explains such variability: early technical mistakes; inclusion of medial and inferior rectum cancers, where a large rectal mobilization is necessary, with a possible damage to lymphatic routes; timing of nodal pickup and effect of neoadjuvant therapy. A second data emerges from literature, that is the percentage of false negatives (FN), the so called skip metastases. Percentages vary from 0% to 60% in different studies when nodal status is studied through the traditional method of hematoxylin/eosin dyeing (H/E). When considering also nodes examined by several methods, the percentage of FN decreases to 18%, adding data from the main studies. This large variability can also be explained by the same reasons as before, especially the enrollment of advanced neoplasms (T4 or N1), where SN evaluation has no meaning. In the largest series on 198 patients, published by Saha, a 10% of FN is reported. In a recent review by Mulrow, revising the largest published series, the percentage of overstaged patients in 11 series after studying SNs with methods different than H/E dyeing is 19%. Sentinel node proved to be the only site of metastases in 35% of cases, while in 5.5% of cases SN study allowed a lymphadenectomy different from the standard procedure.

In summing up literature data it can be concluded that SN evaluation in colorectal surgery has a good percentage of nodal detection and plays an important role in overstaging the disease, also considering that the real prognostic value of micrometastases has not yet been proven. The incidence of FN is considerably lower when stage I and II cases are selected. Lymphatic mapping also allows a more precise SN-guided lymphadenectomy.

Techniques to identify SNs

The most commonly used technique is the intraoperative subserosa injection of vital dye. The most widely used dye is Lymphazurin 1%. This method is highly specific, easy to use with a

short learning curve, while side effects are minimal and costs rather low. When a radioactive tracer is used, the day before surgery ^{99m}Tc -radiolabelled human albumin is endoscopically injected around the lesion. During the surgical procedure a probe identifies all radioactive sentinel nodes. The procedure seems to have some advantages, namely: a slower effusion of the tracer along the draining routes with a consequent higher precision, a lower risk of missed identification in obese patients. Some studies report a higher success rate with a combined technique.

Regarding mini-invasive surgical procedures, there are only two studies reported in literature that prove the technique applicable also in laparoscopic surgery, although their number are very small.

Conclusions

Based on favorable experiences in sentinel-node detection in the treatment of breast cancer and melanoma, it is of high interest to verify the potential applicability of the technique in colorectal cancer.

The main advantages offered by the procedure, in case its predictive value is confirmed, may be:

- possibility to selectively examine sentinel nodes through pathological multilevel and immunohistological analysis, so as to detect micrometastases and improve staging;
- correct identification through lymphatic mapping of spreading routes, thus allowing a more selective lymphadenectomy, extended to nodal sites not included in standard technique whenever necessary;
- in case of malignant polyps, possibility to remove the sentinel node through minimally-invasive technique and to help decide the better treatment strategy: resection or conservative treatment.

Our protocol aims to evaluate the predictive value of sentinel nodes in staging stage I and II colorectal cancer, excluding clinical stage III, where identifying sentinel nodes seems clinically less relevant. Furthermore, stage III cases have the higher number of false negative responses.

KIND OF STUDY

Multicentric prospective study

STUDY DESIGN

MAIN OBJECTIVE

To determine the predictive value of sentinel node detection in terms of sensitivity, specificity and accuracy in staging non metastatic colonic cancer.

In case a significant predictive value is demonstrated, studying sentinel nodes (detected through minimally-invasive procedure) in malignant colorectal polyps after “complete” polypectomy may help choose the correct clinical strategy: surgical resection vs endoscopic surveillance.

SECONDARY OBJECTIVES

- 1) To standardize technique and evaluate feasibility.
- 2) To evaluate the effectiveness of minimally-invasive procedures in sentinel-node pick up.

- 3) To determine the role of sentinel nodes in staging malignant polyps after endoscopic polypectomy.
- 4) To determine false negative rate (skip metastases) in colon cancer.
- 5) To determine the incidence of nodal micrometastases (upstaging) through sentinel node evaluation with multilevel sectioning and immunohistochemistry.
- 6) To find the most effective technique for identifying sentinel nodes (radioimmunoguided technique, vital blue dye, combined technique).

INCLUSION CRITERIA

- a) Histological diagnosis of stage I and II colon carcinoma or endoscopic excision of high-risk malignant polyps of the colon.
- b) Age 18 or over
- c) Staging through colonoscopy, chest X-rays, whole-abdomen US or CT scan
- d) Anesthesiology risk ASA 1-3
- e) Informed consent

EXCLUSION CRITERIA

- a) Confirmed or suspect distant or nodal metastases
- b) Previous colonic resection
- c) Contraindication to general anesthesia (ASA 4)
- d) Psychic or neurological conditions that may impair informed participation to a clinical trial

PROCEDURES

Phase I – Evaluation of vital-dye technique [(Patent blue V Guerbet (injectable solution 2.5%)].

*** Laparoscopy**

- Complete examination of the peritoneum and liver parenchyma. Identification of the colonic lesion. Intraoperative liver ultrasound whenever possible.

*** Laparotomy**

- Visual and manual examination of the liver; identification of the neoplastic lesion. Intraoperative liver ultrasound whenever possible.

*** Laparoscopy/laparotomy**

- Peritumoral injection of 2 ml isosulphan blue dye. (blue patent V Guerbet).
- Identification of the first blue-dyed nodes (4 at the most) and their marking with a stitch or metallic clip.
- No surgical dissection before injecting the dye. In obese patients, where seeing the blue nodes may be difficult, accurate dissection of the mesum in order to expose the lymphatic drainage.
- Standard colon resection with radical lymphadenectomy. The lymphadenectomy should be extended to any blue nodes outside standard sites.

- Separate examination of all sentinel nodes through standard method, multilevel sectioning and immunohistochemistry if necessary.
- Comparison of the pathology report for SN with the remaining nodes.
- Evaluation of the procedure sensitivity, specificity and accuracy.

Phase II (wherever available) – Evaluation of radioimmunoguided nodal biopsy

The first 5 lymphoscintigraphies will be needed to standardize the procedure:

- Definition of the best tracer to be used with the isotope (TC99): small colloidal particles of human albumin are more quickly drained, larger ones can fix more easily within the nodes, but a longer time is required between injection and fixation;
- Definition of the right dose to be injected;
- Standardization of the digital signal for the probe revealing radiation;
- Evaluation of the right timing to identify both SN and its marking.

Technique

- The day before surgery, perilesional endoscopic injection of the tracer.
- Lymphoscintigraphy with early (15 and 30 min) and late (2 and 18 hours) scans.
- Intraoperative detection of the SN through a radioactive probe and its marking.
- Standard surgical resection with radical lymphadenectomy.
- Separate pathological study of the SN through standard technique, multilevel sectioning and immunohistochemistry if necessary
- Comparison of the pathological report for the SN with the report of all other excised nodes.
- Evaluation of sensibility, specificity and accuracy of the procedure.

Final SN Examination

- Sentinel nodes must be sent to the pathology lab in a separate container in formalin 4%
- Each SN must be isolated from the fat tissue and, after accurate cleaning, they must be cut in two along the longer axis, if thicker than 0.5 cm. Sentinel node must be sent whole if less thick than 0.5 cm.
- Samples must be put at the base of their container with the cut edge (center of the node) facing the bottom
- Samples must be included in paraffin.
- 3-5 micron thick sections, at 200 micron intervals, must be prepared until all the tissue has been used. All sections will be put on slides pretreated for immunohistochemistry.
- Sections are colored with Hematossilin and Eosin.

Examination of the remaining non-sentinel nodes

- Isolation of all remaining perivisceral nodes from the tissue sent to the pathology lab (either fixed or fresh). Sampling is made by using Carnoy clearing if necessary, so as to have at least 12 nodes.
- Cutting of the nodes in two half along the longest axis if thicker than 0.5 cm. Positioning of the two half in specific containers with the cut edge facing the bottom, trying to put nodes of the same dimensions in the same container.
- Samples must be included in paraffin.
- 3-5 micron thick sections, at 200 micron intervals, must be prepared on three levels
- Sections are colored with Hematossilin and Eosin.

Esamination through immunohistochemistry

- Sections colored with Hematosilin – Eosin where diagnostic doubt exists are used.
- Sections are colored with large-spectrum anti-CK antibody immunohistochemistry.

Criteria for measuring micrometastases

- Micrometastases must be measured along all three special axes.

PROTOCOL FINAL SUMMARY

To date, based on a review of literature, it is possible to state that sentinel nodes can be detected both by vital dye and by radioactive tracer. There are no significant data on its value in improving staging in particular regarding parameter N.

The present study aims to define the predictive value of sentinel nodes **without at present modifying standard surgical procedures** in patients suffering from “early” stage colon cancer. In case its significant predictive value is found, sentinel node examination would allow an improvement in pathological staging and would therefore help in choosing further adjuvant treatments (at present the decision whether to administer adjuvant chemotherapy depends on N+ vs N- pathological findings). Furthermore, once sentinel-node detection through minimally-invasive surgical procedure is validated, SN examination could help the therapeutic choice after “complete” polypectomy of a malignant polyp: in case of SN+, the choice would be *surgical resection with lymphadenectomy*; in case of SN-, endoscopic surveillance could be considered.

It has to be noted that the multicentric study “Predictive value of sentinel nodes in staging non metastatic colorectal cancer” will not modify what is at present the standard surgical treatment in colorectal cancer.

BIBLIOGRAFIA

- Parkin DM, Pisani P, Ferlay J. Estimates of the worldwide incidence of 25 major cancers in 1990. *Int J Cancer* 1999; 80: 827-841
- International Multicentre Pooled Analysis of B2 Colon Cancer Trials (IMPACT B2) investigators. Efficacy of adjuvant fluorouracil and folinic acid in B2 colon cancer. *J Clin Oncol* 1999; 17: 1356-1363
- Goldstein NS. Lymph node recoveries from 2427 pT3 colorectal resections specimens spanning 45 years: recommendations for a minimum number of recovered lymph nodes based on a predictive probabilities. *Am J Surg Pathos* 2002; 26: 179-189
- Morton DL, Wen DR, Wong JH, Economou JS, Cagle LA, Storm FK *et al.* Technical details of intraoperative lymphatic mapping for early stage melanoma. *Arch Surg* 1992; 127:392-399
- Veronesi U, Paganelli G, Galimberti V, Viale G, Zurrida S, Bedoni M *et al.* Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph-nodes. *Lancet* 1997; 349: 1864-1867

- Veronesi U, Paganelli G, Viale G, Luini A, Zurrada S, Galimberti V *et al.* A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. *N Engl J Med.* 2003 Aug7; 349(6): 546-53
- Wood TF, Tsioulis GJ, Morton DL, Ranger D, Hutchinson W Jr, Forshag LJ *et al.* Focused examination of sentinel lymph nodes upstages early colorectal carcinoma. *Am Surg* 2000; 66: 998-1003
- Saha S, Bilchik A, Wiese D, Espinosa M, Badin J, Ganatra BK *et al.* Ultrastaging of colorectal cancer by sentinel node mapping – a multicenter trial. *Ann Surg Oncol* 2001; 8(Suppl): 94S-98S
- Bilchik AJ, Saha S, Wiese D, Stonecypher, JA, Wood TF, Sostrin S *et al.* Molecular staging of early colon cancer on the basis of sentinel node analysis a multicenter phase II trial. *J Clin Oncol* 2001; 19: 1128-1136
- Wiese DA, Saha S, Badin J, Ng PS, Gauthier J, Ahsan A *et al.* Pathologic evaluation of sentinel lymph nodes in colorectal carcinoma. *Arch Pathol Lab Med* 2000; 124: 1759-1763
- Saha S, Wiese D, Badin J, Beutler T, Nora D, Ganatra BK *et al.* Technical details of sentinel node lymph node mapping in colorectal cancer and its impact on staging. *Ann Surg Oncol* 2000; 7:120 – 124
- Merrie AE, van Rij AM, Philips LV, Rossaak JL, Yun K, McCall JL. Diagnostic use of the sentinel node in colon cancer. *Dis Colon Rectum* 2001; 44: 410-417
- Wong JH, Steineman S, Calderia C, Bowles J, Namiki T. *Ex vivo* sentinel node mapping in carcinoma of the colon and rectum. *Ann Surg* 2001; 233: 515-521
- Cserni G, Vajda K, Tartan M, Bori R, Svebis M, Baltas B. Nodal staging of colorectal carcinomas from quantitative aspects. Can lymphatic mapping help staging? *Pathos Oncol Res* 1999; 5: 291-296
- Joosten JJA, Strobbe LJA, Wauters CAP *et al.* Intraoperative lymphatic mapping and the sentinel node concept in colorectal carcinoma. *Br J Surg* 1999; 86: 482-486
- Waters GS, Geisinger KR, Garske DD, Loggie BW, Levine EA. Sentinel lymph node mapping for carcinoma of the colon: a pilot study. *Am Surg* 2000; 66:943-945
- Paramo JC, Summerall J, Wilson C, Cabral A, Willis I, Wodnicki H *et al.* Intraoperative sentinel lymph node mapping in patients with colon cancer. *Am J Surg* 2001; 182:40-43
- Esser S, Reilly WT, Riley LB, Eyvazzadeh C, Arcona S. The role of sentinel lymph node mapping in patients with colon cancer. *Dis Colon Rectum* 2001; 44: 850-854
- Feig BW, Culey S, Lucci A, Hunt KK, Vauthey JN, Mansfield PF *et al.* A caution regarding lymphatic mapping in patients with colon cancer. *Am J Surg* 2001; 182: 707-712
- Bendavid Y, Latulippe JF, Younan RJ, Leclerc YE, Dube S, Heyen F *et al.* Phase I study on sentinel lymph node mapping in colon cancer: a preliminary report. *J Surg Oncol* 2002; 79:81-84

- Gandy CP, Biddlestone LR, Roe AM, O'Leary DP. Intra-operative injection of Patent Blue V dye to facilitate nodal staging in colorectal cancer. *Colorectal Dis* 2002; 4: 447-449
- Wood TF, Spirt M, Ranger D, Shen P, Tsioulis GJ, Morton DL *et al.* Lymphatic mapping improves staging during laparoscopic colectomy for cancer. *Surg Endosc* 2001; 15: 715-719
- Mulsow J, Winter DC, O'Keane C, O'Connell PR. Sentinel lymph node mapping in colorectal cancer. *Br J Surg* 2003; 90: 659-667
- Saha S, Dan A, Barman B, Wiese D, Schochet E, Barber K, Choudhri S *et al.* Lymphazurin 1% versus 99mTc sulfur colloid for lymphatic mapping in colorectal tumors: a comparative analysis. *Ann Surg Oncol* 2004; 11:21-26.
- Wong Jan H, Johnson D. Scott, Namiki T, Tauchi-Nishi P. Validation of ex vivo lymphatic mapping in hematoxylin-eosin node-negative carcinoma of the colon and rectum. *Ann Surg Oncol* 2004; 11(8): 772-777
- Morton Donald L. Sentinel node mapping and an international sentinel node society: current issues and future directions. *Ann Surg Oncol*, 11(3): 137S-143S
- Bertagnolli M, Miedema B, Redstone M, Dowell J *et al.* Sentinel node staging of resectable colon cancer. Results of a multicenter study. *Ann Surg* 2004; 240: 624-630
- Andreoni B, Crosta C, Bianchi P. *et al.* La strategia del linfonodo sentinella nel trattamento dei polipi maligni del colon retto. *Archivio ed atti della Società Italiana di Chirurgia* 2004; Volume 1°: 93-114
- Braat AE, Oosterhuis JWA, Moll FCP, de Vries JE. Successful sentinel node identification in colon carcinoma using Patent Blue V. *EJSO* 2004; 30: 633-637
- Broderick-Villa G, Amr D, Haigh PI, O'Connell TX, Danial T, Difronzo LA. Ex vivo Lymphatic mapping: a technique to improve pathologic staging in colorectal cancer. *Am J Surg* 2004; 70(11): 937-41
- Saha S, Monson KM, Bilchik A *et al.* Comparative analysis of nodal upstaging between colon and rectal cancers by sentinel lymph node mapping: a prospective trial. *Dis Colon Rectum* 2004; 47(11): 1767-72
- Andreoni B, Risio M, Segnan N, *et al.* Trattamento polipi maligni e polipi ad alto rischio del colon retto. *Atti Convegno Istituto Europeo di Oncologia*, gennaio 2004 (www.ieo.it).
- Saha S, Seghal R., Patel M, *et al.* A multicenter trial of sentinel lymph node mapping in colorectal cancer: prognostic implications for nodal staging and recurrence trial. *Am J Surg* 2006; 191: 305-10
- Redston M, Compton CC, Miedema BW, *et al.* Leukemia Group B Trial 80001. Analysis of micrometastatic disease in sentinel lymph nodes from resectable colon cancer: results of Cancer and Leukemia Group B Trial 80001. *J Clin Oncol.* 2006 20; 24: 878-83.

INFORMATION TO THE PATIENT
AND INFORMED CONSENT FORM

(USE OF DYE)

Multicentric prospective study: "PREDICTIVE VALUE OF SENTINEL NODE IN STAGING EARLY COLORECTAL CANCER"

Dear Sir, / Madam,

our Institute takes part in a clinical research involving several Italian centers. The study evaluates the value of sentinel node detection in neoplastic diseases of the colon. The sentinel node is the first node draining lymph from the disease site. Its utility has already been proven in breast and skin cancers. The absence or presence of disease in this lymph node is highly predictive of the status of other lymph nodes. In case no disease is found in the sentinel node, it is highly probable that there is no disease in distant nodes. Therefore, sentinel nodes can heavily influence the following therapeutic approach.

Based on the sentinel technique in other diseases, its detection is being tested also in other, less superficial organs such as colon. The present study assesses identified sentinel nodes through specific evaluation methods. **In order to identify sentinel nodes, during the surgical procedure some dye (2 ml) will be injected** around the neoplastic tissue. This dye is drained to a number of nodes through the lymphatic vessels. The first nodes to be reached and become blue are called sentinel nodes.

These nodes will be marked and sent separately to the pathologists, so as to be studied more accurately. The surgical procedure will then be completed according to the standard technique by radical removal of all nodes. The dye used (isosulfan blue) is well tolerated, although mild unwanted side effects due to an allergic reaction to the dye have been reported in 1% of cases.

Having read the information form, I had the chance to ask all the questions about the protocol that I deemed necessary and I accept to participate in the study.

Date _____

The Patient

The study investigator

.....

.....

I Consent

I do not consent

that all my clinical information are given to my General Practitioner, Dr.

.....

The patient

.....