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OS	SORLEA, S., COROȘ, M.F., GEORGESCU, R., GYÖRGY-FAZAKAS, I., BRÂNZANIUC, Klara, MILUTIN, D., PAVAI, Z. and COPOTOIU, C., Immunohistochemical Evaluation of Sentinel Lymph Nodes in Colon Cancer. <i>Acta Medica Marisiensis (AMM)</i> , <b>57</b> (2). 2011. 113-115.
OA	KELDER, W. Lymph node staging in colon cancer. Thesis. Univ.Groeningen. 2007.

## Incidența minimă a suspiciunii / Minimum incidence of suspicion

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Prin notația p.113:09 - p.113:21 se înțelege că fragmentul de text preluat fără indicarea provenienței în opera suspicionată este cuprins integral între rândul 9 al pag.113 și rândul 21 al pag.113.

**Documente care se referă la faptele de plagiat probate:****A<sup>1</sup>.**

Consiliul Național de Etică a Cercetării Științifice, Dezvoltării Tehnologice și Inovării (CNECSDTI) a înregistrat cu nr. 255/9.03.2012 adresa cu nr. 8304/6.03.2012 trimisă de Ministerul Educației, Cercetării, Tineretului și Sportului (MECTS), Direcția Generală de Învățământ Superior.

În această adresă se solicită soluționarea memoriilor înregistrate la MECTS cu nr. 8304 / 13.02.2012 și nr. 8304bis/21.02.2012, cu privire la posibile abateri grave de la buna conduită în cercetarea științifică și activitatea universitară. În sesizarea cu nr. 8304 / 6.03.2012 adresată Ministrului Educației, Cercetării, Tineretului și Sportului, reclamantul dorește „să atragă atenția asupra actelor de plagiat ale rectorului Copotiu, ale prorectorului Brânzaniuc și ale decanului Azamfirei de la Universitatea de Medicină și Farmacie Târgu Mureș”.

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... Prin urmare, CNECSDTI constată că autorii A. Ivănescu, R. Melinte, A. Solyom, L. Moraru, M. Petrisor și K. Brânzaniuc au expus într-o operă scrisă texte, expresii și idei extrase dintr-o altă operă scrisă, fără a menționa acest lucru și fără a face trimitere la sursele originale. Având în vedere prevederile articolului 2, litera a), și articolului 4, aliniatul (1), litera d) din Legea 206/2004 cu modificările și completările ulterioare, CNECSDTI constată că semnatarul articolului incriminat se face vinovați de abaterea de la normele de bună conduită în activitatea de cercetare privind articolul Hayan R., Gicquel P., Schneider L., Karger C., Clavert J.M., Juvenile osteochondritis of femoral condyles: treatment with transchondral

<sup>1</sup> Consiliul Național de Etică a Cercetării Științifice, Dezvoltării Tehnologice și Inovării. Raportul final nr.977/ 26.09.2012. Disponibil la: <http://cne.ancs.ro/wp-content/uploads/2012/11/Raportul-final-nr.-977.pdf>

drilling. Analysis of 40 cases, din: J Child Orthop, No. 4, 2010, pp. 39-44 și articolul D. Karataglis, M.A. Green, D.J.A. Learmonth, Autologous osteochondral transplantation for the treatment of chondral defects of the knee, din The Knee 13 (2006), pp. 32-35.

CNCSDTI constată că a fost publicată o erată la acest articol A2 în Acta Medici Marisiensis 2011, 57(4): 383 — 385.

Pentru articolul A3: The presence of Nucleated Red Cells in the Blood of Critical Care Patients is Associated with an Increased Mortality Risk, autori: Duțu M., Negoită S., Manolescu R., Calu V., Corneci D., Georgescu A., Togănel C., Azamfirei L. a fost analizat de către Comisia de Etică a UMF Târgu Mureș la data de 17.09.2012,

CNCSDTI constată că a fost publicată o erată la acest articol A3 în Acta medici Mari-siensis 2022, 58(2): 132.

În concluzie, CNECSDTI constată că lucrările:

A1. Immunohistochemical Evaluation of Sentinel Lymph Nodes in Colon Cancer, autori: Șorlea S., Coros M.F., Georgescu R., Gyrgy-Fazakas I., Brânzaniuc K., Milutin D., Pavai Z., Copotoiu C.

A2. Transchondral drilling and osteochondral autograft (Mosaicplasty) inknee articular cartilage defects, autori: Ivănescu A., Melinte R., Solyom A., Moraru L., Petrisor M., Brânzaniuc K.

A3. The presence of Nucleated Red Cells in the Blood of Critical Care Patients is Associated with an Increased Mortality Risk, autori Duțu M., Negoita S., Manolescu R., Calu V., Corneci D., Georgescu A., Toganel C., Azamfirei L., nu respectă normele de bună conduită în activitatea de comunicare, publicare diseminare și popularizare științifică.

S. Șorlea nu a respectat normele de bună conduită în cercetare prin includerea în lista de autori a unei publicații științifice a două persoane fără acordul acestora. A fost sancționat de Comisia de Etică a UMF Târgu Mureș cu suspendarea, pe o perioadă de 12 luni, a dreptului de înscriere la un concurs pentru ocuparea unei funcții didactice superioare ori a unei funcții de conducere, de îndrumare și de control, ca membru în orice comisie de doctorat, de master sau de licență, sancțiune regăsită.

A. Ivănescu nu a respectat aceleași norme de bună conduită în cercetare incluzând trei persoane fără acordul acestora pe lista de autori a unei publicații științifice. A fost sancționat de Comisia de Etică a UMF Târgu Mureș cu avertisment scris.

Dr. Duțu M. nu a respectat normele de bună conduită în cercetare prin includerea prof. L. Azamfirei ca ultim autor al articolului A3 fără acordul acestuia. A fost sancționată de Comisia de Etică a UMF Târgu Mureș cu avertisment scris.

Prof. C. Copotoiu și prof. K. Brânzaniuc nu pot fi făcuți responsabili de nerespectarea normelor de bună conduită în cercetare din articolul A1, întrucât nu li s-a cerut acordul de a face parte din lista de autori.

Prof. Azamfirei L. nu poate fi făcut responsabil de nerespectarea normelor de bună conduită din articolul A3, întrucât nu i s-a cerut acordul de a face parte din lista de autori.

#### 4) Sancțiuni și recomandări

##### 4.1. CNECSDTI stabilește următoarele sancțiuni:

Avertisment scris, în baza Legii 206/2004 cu modificările și completările ulterioare, art. 14, alin.(1), lit. a), coroborat cu Legea 1/2011, art. 324, litera a) pentru doamna prof dr. K. Bânzaniuc.

...

# Retraction

The editors retract the following article:

## **Immunohistochemical Evaluation of Sentinel Lymph Nodes in Colon Cancer**

Sorlea S, Coroş MF, Georgescu R, György-Fazakas I, Brînzaniuc Klara, Milutin Doina, Pávai Z, Copotoiu C

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# ACTA MEDICA MARISIENSIS

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# Immunohistochemical Evaluation of Sentinel Lymph Nodes in Colon Cancer

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**Background:** Lymph node status is the most important predictive factor in the treatment of colic cancer. As sentinel lymph node (SLN) biopsy might upstage stage II colon cancer, it could have therapeutic consequences in the future.

**Aim:** To investigate and evaluate nodal microstaging and ultrastaging using cytokeratin immunohistochemistry.

**Material and methods:** In 20 consecutive patients operated on First Surgery Clinic of the County Hospital Mures for colon cancer, subserosal injection with Patent Blue dye was used for SLN detection. In searching for occult micrometastases, each SLN was examined. In tumor-negative SLNs at routine hematoxylin-eosin (H&E) examination (pN0) we performed cytokeratin(CK) immunohistochemistry (IHC).

**Results:** The procedure was successful in 19 out of 20 patients (95%). The SLN was negative in 12 patients detected by H&E and IHC, in 10 patients the non-SLN was also negative, leading to a negative predictive value of 89% and an accuracy of 93%. In 6 patients with SLN negative by HE was positive by IHC, leading to a 33% value of upstaging.

**Conclusions:** The SLN concept in colon carcinoma using Patent Blue V is feasible and accurate. It leads to upstaging of nodal status in 6 cases (33%) when IHC techniques are involved. The clinical value of the method will be evaluated by postoperative chemotherapy efficiency.

1 - 83%

**Keywords:** sentinel lymph node, colon, carcinoma

## Introduction

Colorectal carcinoma is the most common gastrointestinal malignancy. Lymph node status as the most important predictor of outcome indicates the use of adjuvant chemotherapy. The reported 5-year survival rate is 70–80% for patients with node negative disease (st. I–II), but only 45–50% for those with node positive tumors (st. III) [1]. Adjuvant chemotherapy significantly improves the 5-year survival in patients with node positive disease. Despite the favorable prognosis of patients with localized colon cancer without regional lymph node metastasis, 20–30% of these patients will develop recurrent disease, after apparently curative resection. It is therefore necessary to perform a more detailed histological examination of negative lymph nodes by histological examination with haematoxylin-eosine staining (HE) and immunohistochemistry with cytokeratin (CK). Understaging may be the result of inadequate numbers of examined lymph nodes, missing some metastases [1,2,3]. For adequate staging and treatment of patients with colon cancer, meticulous examination of at least 12 nodes harvested by pathological analysis is mandatory [4].

Sentinel node technique was described by Cabanas in 1977 in penile cancer, and Morton Giuliano introduced the method for melanoma and breast cancer. In colon cancer the sentinel lymph node is defined as the first tumor draining lymph node, with the highest potential to harbor metastatic disease [5,6,7]. This allows a targeted examination of a smaller number of nodes that can be examined

2 - 72%

2 - 72%

with multiple sections and immunohistochemistry for the accurate detection of metastases and micrometastases and to provide a better staging of colon cancer.

We used methylene blue dye to identify sentinel lymph nodes and examined them with haematoxylin-eosine staining and immunohistochemical technique with cytokeratin. In tumor-negative SLN's at routine hematoxylin-eosin (H&E) examination (pN0) we performed CK8/CK18 immunohistochemistry (IHC).

## Material and methods

3 - 95%

Only patients with histological proven primary colon carcinoma were included in the study. Patients with distant metastases or gross lymph node involvement as shown by preoperative examinations or palpation during surgery were excluded.

Sentinel lymph node mapping was carried out through an open procedure by injection of 1–3 ml Blue Dye with a tuberculin syringe and 29 gauge needle subserosally in 4 quadrants around the tumor. The subserosal injection was carried out prior to vascular ligation. Within 5 to 10 minutes after the blue dye injection, the SLN's could be identified by following blue stained lymphatic vessels leading to the blue stained sentinel node [8–12]. These nodes were tagged with a long suture. Sentinel nodes were defined as the first four bluestaining nodes seen within the regional basin. After marking of the SLN's, routine resection was performed.

Table I. Sex and age distribution

Patient sex	Number of patients	Average age
Male	8	62.25
Female	12	60.91
Total	20	61.45

**3 - 95%**

The tumor and all lymph nodes were examined according to standard guidelines. If the SLN's were negative after routine hematoxylin-eosin (H&E) staining, they were sectioned at 150 µm intervals and examined at 3 levels with H&E as well as immunohistochemistry on cytokeratins (CK8/CK18). Metastases between 0.2 mm and 2 mm were referred to as micrometastases. Metastases smaller than 0.2 mm were described as isolated tumor cell 13.

A total of 20 patients were included in the study, 8 men and 12 women, with ages between 49 and 79 years old (the average age of 61.45) (Table I).

**Results**

The procedure was successful in 19 out of 20 patients (95%), but failed in one patient. The SLN was negative in 12 patients detected by H&E and IHC, in 10 patients the non-SLN was also negative, leading to a negative predictive value of 89% and an accuracy of 93% (Table II).

A total number of 275 lymph nodes from the samples were examined, with an average of 13.75 lymph nodes/sample (between 3 and 32 sampled lymph nodes). A number of 41 were marked as the SLN (an average of 2.05). The presence of metastases was detected in 6 patients, SLN was negative; the other lymph nodes from the surgical sample were also negative.

Without taking into account the SLN examination (41 marked lymph nodes), there was no spread to the lymph nodes in 14 patients (70%) staged as pN0. Out of the 6 patients (30%) with positive SLN, 4 (20%) were staged as pN1 and 2 (10%) as pN2. In 6 patients of the other 13 patients where the SLN was negative by HE, it was evidenced as positive by IHC, leading to a 33% value of upstaging. (Table III).

**Discussions**

Unlike the validated SLN concept in breast cancer and melanoma mandating lymphatic dissection, the main reason for SLN mapping in colon cancer is to focus pathologic IHC evaluation of SLN after in vivo mapping with patent blue. In colon cancer patients examination of the SLN's, will increase the accuracy of nodal staging, resulting

**4 - 92%**

Table III. Analysis of the examined lymph nodes

The analysis of the examined lymph nodes	SLN(%)	nonSLN(%)
Total lymph nodes = 275	41 (14.9)	234 (85.1)
Negative lymph nodes at HE = 185	9	176
Positive lymph nodes at HE = 90	32 (11.6)	58 (21.1)
Positive lymph nodes at HE + IHC = 108	37	61

Table II. Examination of SLN

	No.	%
Total number of patients	20	100
Total number of patients with SLN detected	19	95
Total number of patients with positive SLN at HE	6	30
Total number of patients with negative SLN at HE	13	75
Total number of patients with negative SLN at HE, and positive at IHC	6	30
Total number of patients with positive SLN and the other lymph nodes positive	6	30

**4 - 92%**

in a higher percentage of node-positive patients, who may benefit from adjuvant chemotherapy [14,15,16].

Upstaging by H&E conventional examination is difficult to measure. It might be explained by the focused examination of blue stained nodes, because these blue nodes can be very small nodes and would otherwise not have been detected. The IHC in our study was performed on cytokeratins. Most studies performed sectioning with intervals of 500 µm or immunohistochemistry on 1-4 levels in total. Increasing the number of slices for immunohistochemistry probably improves the detection rate of micrometastases smaller than 2 mm. A variety of results on this subject have been described [19,20,21] (Table IV).

We found an upstaging by immunohistochemical staining in 33% of patients. We should wait for the results after follow up in a large group of patients before assessing the real impact. If future results confirm the importance of microstaging and ultrastaging in CRC, the sentinel node concept can help the pathologist to focus the examination on one or two sentinel nodes in H&E negative cases. The detection of micrometastases might then select a subgroup of patients who could benefit from adjuvant treatment.

**Conclusions**

The sentinel node concept in colon carcinoma using Blue Dye is feasible and accurate. It leads to an upstaging of nodal status in 33 % of patients when IHC techniques are combined and may detect aberrant lymphatic drainage. This procedure can be performed in a multi-center study under adequate supervision during the learning curve and may have diagnostic and therapeutic consequences in the future.

**5 - 98%****References**

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