

LYMPH NODE MAPPING AND SENTINEL NODE DETECTION IN EARLY STAGE OF CERVICAL CARCINOMA WITH COMBINATION OF ^{99m}Tc-NANOCOLLOID AND PATENT BLUE

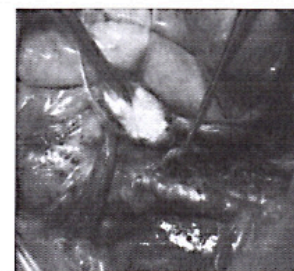
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Introduction: Lymphatic spreading of the cervical cancer and the lymphonodes status is the most significant negative prognostic factor of the disease with a direct impact on the curative plan. There is no suitable non-invasive examination method of the involvement of the regional lymphonodes. Lymphatic mapping with identification of sentinel nodes combined with ultrastaging by histological and immunohistochemistry examination has been proven to be essential for correct staging of the regional lymphatic nodes.

Background and aims: The aim of the study is to analyse the feasibility of intraoperative sentinel lymph node (SLN) detection using gamma detection probe and Blue dye (BD) in patients undergoing radical hysterectomy for treatment of cervical cancer (CC).

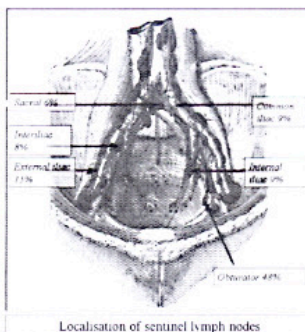


Blue SLN with blue coloured efferent lymphatic vessels

Patients and methods: In the period from May 2004 to February 2005 77 patients with histologically proven cervical cancer, mean age 48.8 years, range 24-78 years, referred to our department for radical surgery were included into the study. Patients were divided into three groups according to tumor volume with tumor diameter less than 20 mm, with tumor diameter more than 20 mm and stadium IB2. The most frequent histological type was squamous cell carcinoma, 34 patients underwent preoperative coisation and 6 patients received neoadjuvant chemotherapy.

After assigned informed consent 50 MBq SENTI-SCINT (FJC National Research Institute for Radiobiology and Radiohygiene, Budapest, Hungary) was injected intracervically superficially in each quadrant around the tumor at 3, 6, 9 and 12 o'clock position using 27 gauge hypodermic needle 2 hours before surgery. Static scintigraphy is performed 1 hour after injection using a gamma camera to identify sentinel nodes. At the time of surgery in general anesthesia after pelvic exploration during the laparotomy, 4 ml of blue dye was injected superficially around the tumor at the same locations as the tracer. SLN were identified intraoperatively by using a handheld gamma detection probe after marking of lymphatic vessels with blue dye. Next the systematic lymph node dissection was done and all tissue was examined visually for blue staining and radioactive counts. If the counts were at least 10-fold above background levels, the node was considered sentinel. All sentinel nodes recorded by their position to the pelvic vessels were labeled as blue, hot or hot and blue positive. SLN were histologically and immunohistochemically analysed. For the final pathological analysis, serial sectioning of the sentinel node was performed to include four sections every 5 µm perpendicular to the long axis of the node. Each level was stained for hematoxylin and eosin and examined by immunohistochemistry with an anticytokeratin antibody cocktail (Monoclonal Mouse Anti-human Cytokeratin: AE/AE3, Code M. Dako).

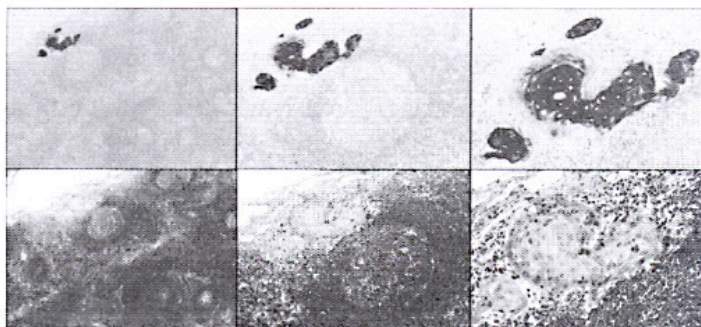
FIGO stage	No. of patients	Detection rate of SLN per patient	Detection rate of SLN per site	No. of patients with positive SLN	No. of patients with positive LN
IA2-IB1 < 2 cm	42	41 (97,6%)	85,7%	5 (11,9%)	6 (14,3%)
IB1 > 2 cm	29	27 (93,1%)	87,9%	18 (62,0%)	20 (70,0%)
IB2	6	5 (83,3%)	66,7%	3 (50,0%)	5 (83,3%)
Total	77	73 (94,8%)	85,1%	26 (33,7%)	31 (40,2%)



Results: A total number of 2 764 lymph nodes with an average 36 per patient and 202 sentinel lymph nodes with an average 2,6 per patient were identified. The SLN detection rate was 94,8 % per patient and 85,1% for the side of dissection and depends of the tumor volume. False negative rate was 3%, sensitivity and negative predicted value calculated per patient were 92,3% and 95,7% respectively.

Sentinel nodes were identified in obturator area in 48%, external iliac in 15 %, common iliac and internal iliac both in 9%, internal iliac in 8 %, sacral region in 6% and parametrial region in 5 % of cases. Metastatic disease was detected in 31 (40,0 %) patients. SLN was only site of metastasis in 12 (15,6 %) patients.

Micrometastasis in the subcapsular sinus in a sentinel node stained by immunohistochemistry (magnification 31x, 76x, 156x)



Micrometastasis in the subcapsular sinus in a sentinel node stained by H&E (magnification 31x, 76x, 156x)

Discussion: The treatment of choice in early-stage node-negative cervical cancer is radical hysterectomy and pelvic lymph node dissection, in the event of proven lymphatic metastases the primary treatment is chemoradiation. A radical surgery followed by radiation leads to substantially more morbidity than either treatment alone, without clearly better survival. Non-invasive staging of the regional lymph nodes in these patients is false negative in approximately 20%.

In cases, where lymphatic spreading is confirmed by positivity of the sentinel node, the primary surgical treatment will be avoided, as it would have followed by adjuvant radiotherapy.

In cases, where the lymphatic spreading of the tumor will be excluded by the negativity of the sentinel node, there is no need to perform systematic regional lymphadenectomy and thus patient morbidity will be decreased.

Conclusions: Intraoperative lymphatic mapping using combination of technetium-99-labeled nanocolloid and blue dye are feasible, safe and accurate techniques to identify SLN in stage IA2-IB1 of cervical cancer.

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