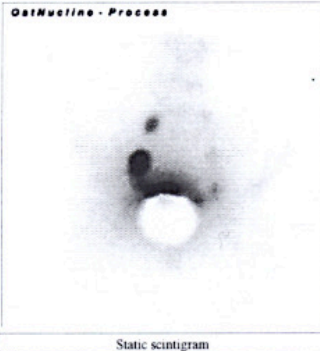


SENTINEL NODE DETECTION IN EARLY STAGE OF CERVICAL CARCINOMA

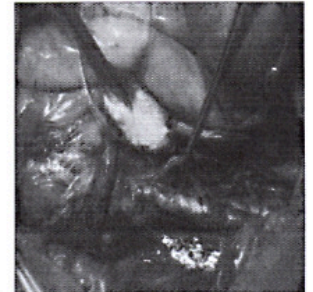
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Introduction: Lymphatic spreading of the cervical cancer and the lymphonodes status is the most significant negative prognostic factor of the disease with a direct impact on the curative plan. There is no suitable non-invasive examination method of 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.

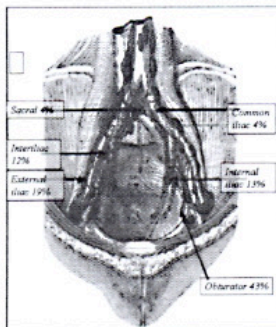
Patients and methods: The aim of the study is to analyse the feasibility of preoperative mapping of sentinel lymph nodes (SLN) by lymphoscintigraphy and intraoperative detection of SLN using gamma detection probe and blue dye (BD). In the period from May 2004 to March 2005 42 patients with histological proven cervical carcinoma, mean age 47.4 years, range 24-74 years, referred to our department for radical surgery were included into the study. Three patients had stage IA2, 34 patients stage IB1, 3 patients stage IB2 and 2 patients had stage IIA. The most frequent histological type was squamous cell carcinoma, 20 patients underwent preoperative conisation and 3 patients received neoadjuvant chemotherapy.



Blue SLN with blue coloured efferent lymphatic vessels

After assigned informed consent technetium-99-labeled nanocolloid was injected intracervically 2-16 hours before an operation and then a static lymphoscintigraphy was performed. At present we use 50 MBq SENTI-SCINT (FJC National Research Institute for Radiobiology and Radiohygiene, Budapest, Hungary) superficially injected 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 pelvis 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.

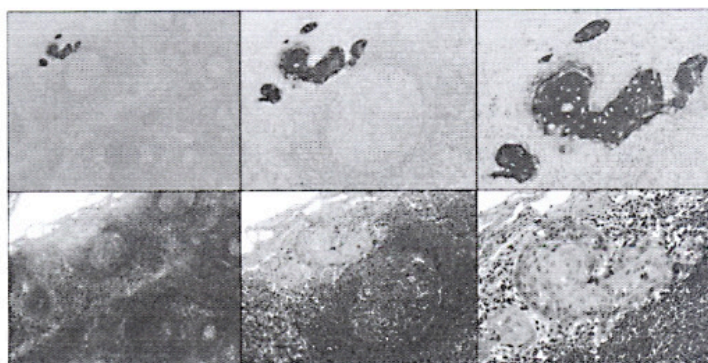
FIGO stage	Number of patients	Detection rate of SLN		Detection per site	Number of SNLs	Positive SLNs	False negative
IA2 - IB1 < 2 cm	22	21	95,5%	88,6%	55	0	0
IB1 > 2 cm	14	13	92,8%	89,3%	34	13	0
IB2	6	4	66,7%	58,3%	8	4	0
Total	42	38	90,5%	84,5%	97	17	0



Results: Patients were divided into three groups, FIGO stadium IA2- IB1 with tumor diameter less than 20 mm, stadium IB1 with tumor diameter more than 20 mm and stadium IB2. A total number of 1 545 lymph nodes with an average 36,8 per patient and 97 sentinel lymph nodes with an average 2,3 per patient were identified. Bilateral pelvic SLN was present in 87 % of the cases. The rate of SLN detection was 90,5 %, sensitivity and negative predictive value was 100%, the rate of false negative SLN was 0%. Metastatic disease was detected in 12 patients (28,6%), patients in whom SLN only site of micrometastasis were 6 (50%). Sentinel nodes were detected in common iliac region in 4 % of cases, external iliac in 19 %, interiliac in 12 %, internal iliac in 13 %, obturator in 43%, sacral region in 5% and parametrial region in 4 %.

Factor considered	Methods of SLN Localization		
	Radioisotope Alone	Blue Dye Alone	Radioisotope plus Blue Dye
Patients in whom SLNs found at surgery	66/84 78,6%	54/84 64,3%	38/42 90,5%
Sensitivity	17/17 100%	13/14 92,9%	18/18 100%
Negative predictive value	42/42 100%	59/60 98,3%	51/51 100%
Accuracy	59/59 100%	59/60 98,3%	69/69 100%
Patients in whom SLN only site of metastasis	6/13 46,2%	4/10 40%	6/12 50%

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



Micrometastasis in the subcapsular sinus in a sentinel node stained by H&E (magnify 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.