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# Sentinel node lymphoscintigraphy: new applications, new challenges

**R.A. Valdés Olmos (Amsterdam)**

The evolution of the sentinel node procedure to the standard of care for both cutaneous melanoma and breast cancer has led to an increasing use of lymphoscintigraphy for other malignancies. For all current applications the role of lymphoscintigraphy includes identification of draining lymph node fields at risk for metastases as well as the detection of lymph nodes in unpredictable locations. To accomplish these purposes lymphoscintigraphy has been gradually optimized with regard to methodology and image interpretation. This cumulative experience constitutes the basis for the development of the new clinical applications

**New challenges for tracer administration**

The administration of the tracer has evolved from sentinel node procedures performed by nuclear medicine independently to procedures performed in cooperation with other disciplines. (1) In the first group, tracer administration, guided by palpation or visual examination, is directly possible for the nuclear physician and is characterized by optimal timing between injection and gamma camera acquisition. The two first applications in this group were melanoma and palpable breast cancer. Subsequently the procedure was applied for penile carcinoma, vulvar carcinoma, testicular cancer and oral cavity malignancies. Particularly for penile and vulvar malignancies the application of a spray containing xylocaine or a lidocaine-based cream 30 min before tracer administration ensures that subsequent tracer injections are relatively easy to perform and well tolerated. The second group concerns tracer administration guided by ultrasound, stereotaxis, CT, endoscopy or endoscopic ultrasonography. These procedures require a close cooperation with the radiologist or the endoscopist, and are characterized by more demands for the start of the gamma camera acquisition as well as for radiation hygiene. One of the first clinical applications in this group was non-palpable breast cancer, followed by lung cancer, prostate cancer, bladder carcinoma, deep located head and neck malignancies (e.g. larynx), and gastrointestinal malignancies (e.g. stomach). For radiology-assisted procedures the use of a fine spinal needle and small tracer volumes followed by flushing with air mostly leads to a successful administration. A critical aspect of tracer injection under endoscopy-guidance is the use of long needles. An adequate 3-way connection for the syringe containing the radiotracer and for a second syringe containing saline is necessary in order to enable flushing of the needle.

**New dimension in lymphatic mapping and sentinel node localization**

To match the sentinel concept lymphoscintigraphy must be able to visualize the lymphatic channels and identify the lymph nodes receiving direct drainage from the tumour. Traditionally gamma camera acquisition has included a dynamic initial study which aims to identify lymphatic vessels when a rapid drainage from the injection site is expected (e.g. melanoma, penis, vulva, superficial injection in breast cancer) and subsequent static images at 20-30 minutes and 2 hours as well as 4-6 hours when sentinel nodes are not clearly visualized or when a slow migration from the injection site is expected. Static images are important to differentiate the further lymphatic drainage and to identify sentinel nodes with delayed filling at unexpected sites. Particularly for superficial located lymph node basins, the current standard requires the use of planar images with simultaneous transmission scanning by means of a flood source of $^{57}$Co or $^{99m}$Tc to outline the body contour.

For malignancies with deep lymphatic drainage, complementary SPECT/CT, mostly performed after delayed planar images, appears to improve the preoperative localization of sentinel lymph nodes. Particularly for anatomical areas such as the pelvis (urogenital and rectal malignancies), upper abdomen (gastric cancer), mediastinum (lung cancer), and neck SPECT/CT is able to provide surgeons with spatial information for the localization of the sentinel node. This 3D anatomical mapping may be of help particularly for intra-operative procedures with laparoscopic gamma probes.

In pelvic malignancies (uterus, prostate, bladder) lymphoscintigraphy is becoming indispensable to detect sentinel nodes outside the standard lymphadenectomy areas. (2) However, principally due to practical

reasons preoperative gamma camera imaging is being used only by 50 % of the investigators in lung cancer (3) and has been omitted in protocols concerning colorectal malignancies. (4) A possible solution in this issue is the use of intraoperative gamma camera imaging and an important future challenge for nuclear medicine will be the validation of small-imaging devices for use during surgery.

**Advances in other aspects**

Various aspects characterize the practice of lymphoscintigraphy today. The large geographical tracer variability led to validation of numerous radiopharmaceuticals in different countries and/or continents. Simultaneously, the mechanism of lymph node uptake based on a receptor-mediated phagocytosis of the colloid particles by the macrophages became better understood in the light of these clinical applications. However, the present generation of colloid tracers has some objective limitations in depicting the real number of sentinel nodes. Very large particles will be trapped in the interstitial space and never enter the lymphatic system. Due to this decreased migration from the injection site, its use may lead to underestimation of the number of sentinel nodes. Smaller particles are mostly associated to optimal lymph channel visualization and lymph node uptake. However, more second echelon lymph nodes may be observed, which may lead to an overestimation of the number of sentinel nodes. (5) An advance in this field is the introduction of $^{99m}$Tc-DTPA-manosyl-dextran which combines a small particle size with a high receptor affinity. This may lead to a fast migration from injection site combined with an improved extraction of the particles during the first pass through the sentinel lymph node.

With respect to sentinel node detection new advances include the use of hand-held gamma- cameras to assist gamma-probe detection during surgery principally for identification of sentinel nodes located close to the injection site. This device may also be helpful in cases with lymph node clustering or non-visualization on standard gamma camera imaging as well as for skin marking of superficial located sentinel nodes or for ex-vivo imaging of radioactive surgical lumpectomie specimens at the operation room.

**References**

1. Nieweg OE, Estourgie S, Valdés Olmos RA. Lymphatic mapping and sentinel node biopsy. In: Nuclear medicine in diagnosis and treatment. Ell PJ, Gambhir SS, Eds, Churchill Livingstone., New York, 2004:229-260.
2. Gipponi M. Clinical applications of sentinel lymph-node biopsy for the staging and treatment of solid neoplasms. Minerva Chir 2005; 60:217-233
3. Minamiya Y, Ogawa J. The current status of sentinel lymph node mapping in non-small cell lung cancer. Ann Thorac Cardiovasc Surg 2005;11:67-72
4. Saha S, Dan AG, Viehl CT, Zuber M, Wiese D. Sentinel lymph node in colon and rectal cancer: its impact on staging, limitations, and pitfalls. Cancer Treat Res 2005;127:105-122.
5. Wilhem AJ, Mijnhout GS, Franssen EJF. Radiopharmaceuticals in sentinel lymph-node detection – an overview. Eur J Nucl Med 1999; 26 (Suppl): S36-S42.