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# A Specific Mapping Study Using Fluorescence Sentinel Lymph Node Detection in Patients with Intermediate- and High-risk Prostate Cancer Undergoing Extended Pelvic Lymph Node Dissection

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**Abstract**

Sentinel lymph node (SLN) detection techniques have the potential to change the standard of surgical care for patients with prostate cancer. We performed a lymphatic mapping study and determined the value of fluorescence SLN detection with indocyanine green (ICG) for the detection of lymph node metastases in intermediate- and high-risk patients undergoing radical prostatectomy and extended pelvic lymph node dissection. A total of 42 patients received systematic or specific ICG injections into the prostate base, the midportion, the apex, the left lobe, or the right lobe. We found (1) that external and internal iliac regions encompass the majority of SLNs, (2) that common iliac regions contain up to 22% of all SLNs, (3) that a prostatic lobe can drain into the contralateral group of pelvic lymph nodes, and (4) that the fossa of Marcille also receives significant drainage. Among the 12 patients who received systematic ICG injections, 5 (42%) had a total of 29 lymph node metastases. Of these, 16 nodes were ICG positive, yielding 55% sensitivity. The complex drainage pattern of the prostate and the low sensitivity of ICG for the detection of lymph node metastases reported in our study highlight the difficulties related to the implementation of SNL techniques in prostate cancer.

***Patient summary:*** There is controversy about how extensive lymph node dissection (LND) should be during prostatectomy. We investigated the lymphatic drainage of the prostate and whether sentinel node fluorescence techniques would be useful to detect node metastases. We found that the drainage pattern is complex and that the sentinel node technique is not able to replace extended pelvic LND.



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The role of pelvic lymph node dissection (PLND) during radical prostatectomy (RP) remains a matter of continuous debate [1]. Sentinel lymph node (SLN) detection has been advanced as a potential alternative to PLND. In prostate cancer (PCa), the technique was first described using technetium Tc 99m bound to a colloid [2]; however, radioguided SLN detection has not come into widespread use. The use of the fluorescent dye indocyanine green (ICG)

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may open the door to broader acceptance of SLN techniques in PCa surgery [3]. Against this background, we provided a comprehensive description of lymphatic landing sites per anatomic region of the prostate using this SLN technique. We also evaluated the sensitivity of ICG-based fluorescence SLN detection to detect lymph node metastases in intermediate- and high-risk patients.

Detailed information on patient selection and detection technique is found in Supplement 1. From November 2012 through September 2015, 42 patients presenting with clinically localized intermediate- or high-risk PCa and scheduled for RP gave written informed consent to participate in our prospective study. ICG (Pulsion Medical Systems, Feldkirchen, Germany) was injected transrectally shortly prior to laparotomy. The first 12 patients enrolled received sextant injections (six injections into base, midportion, and apex of each prostatic lobe peripheral zone). The next 30 patients received injections into one of these sites: prostate base bilaterally, midportion bilaterally, apex bilaterally, left lobe (base, midportion, apex), or right lobe (base, midportion, apex). A near-infrared–sensitive probe (Fluobeam; Fluoptics, Grenoble, France) was used to collect fluorescence generated in the tissue under real-time image guidance. Independent of the findings of fluorescence SLN detection, an extended PLND was subsequently performed. An ex vivo fluorescence examination of all dissected lymph nodes was then carried out. Lymphatic landing sites per anatomic region of the prostate were depicted graphically. Diagnostic statistics assessed the value of ICG in detecting lymph node metastases.

Baseline characteristics of the patients are summarized in Supplementary Table 1. All 42 patients had one lymph node or more detected by fluorescence. The lymphatic mapping study showed the following results (Fig. 1; Supplementary Table 2): (1) The external and internal iliac regions encompassed the majority of SLNs; (2) the common iliac regions contained up to 22% of all SLNs; (3) a prostatic lobe can drain into the contralateral group of pelvic lymph nodes; (4) the fossa of Marcille also received significant drainage; and (5) practically all sites of the prostate can drain to different regions of the pelvis bilaterally.

The drainage pattern did not show that distinct lymphatic pathways exist per prostatic anatomic region. Our results also underscored that lymphatics cross over to the opposite side and that the common iliac regions and the fossa of Marcille should not be overlooked during PLND, as combined, they may contain up to a third of all SLNs. The multitude of lymphatic landing sites as well as the individual variability of lymphatic drainage may represent obstacles to intraoperative SLN detection. In contrast to breast cancer, lymph node metastases in PCa do not follow a predefined pathway of metastatic spread, and there is no certainty that the histologic status of the SLN reflects the status of the entire pelvic node basin.

Among the 12 patients who received systematic ICG injections, a median of 15 SLNs per patient were removed (interquartile range [IQR]: 10–20). Five patients had a total of 29 lymph node metastases (Table 1). Of these, 16 were ICG positive, yielding a sensitivity for the detection of lymph node metastases of 55%. The negative predictive value was

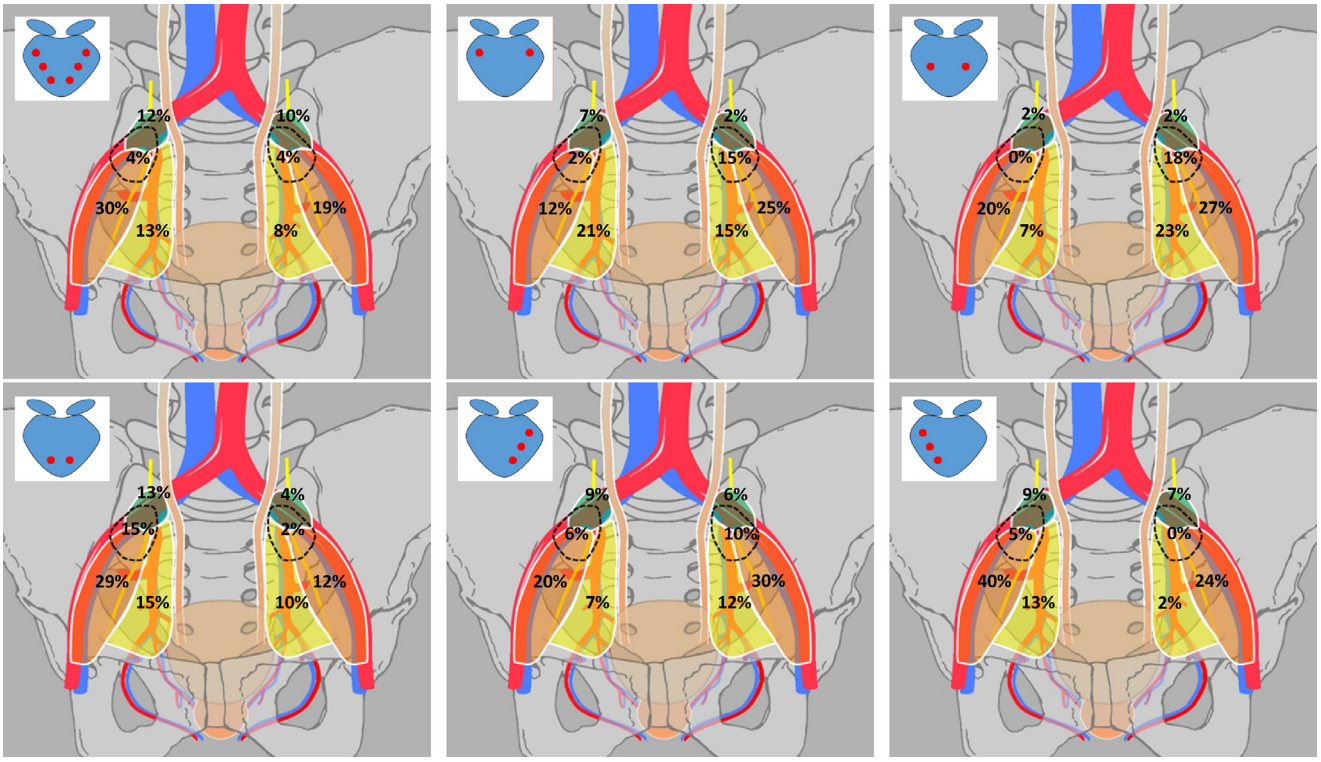


**Fig. 1 – Percentages of sentinel nodes detected per drainage region with regard to anatomic sites of the prostate. The indocyanine green injection sites are depicted in the upper right corner. The orange zones represent the external iliac regions, the yellow zones represent the internal iliac regions, the green zones represent the common iliac regions, and the regions delineated by dashed lines represent the fossa of Marcille.**

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