

Supplementary Patients and Methods

1. Patient selection

The study protocol underwent preliminary assessment by the Ethics Committee of the Canton of Bern, which approved the project as a quality control study of an established procedure (pelvic lymph node dissection [PLND]), and waived the requirement for a full board review. All candidates for a radical prostatectomy underwent staging with magnetic resonance imaging and/or computed tomography of the abdomen and pelvis as well as a bone scintigraphy regardless of preoperative prostate-specific antigen (PSA) level or biopsy Gleason score. All patients included in the study had biopsy-proven, clinically localized intermediate- or high-risk prostate cancer (PSA ≥ 10 mg/l and/or biopsy Gleason score ≥ 7). Exclusion criteria included prior hormonal or radiation therapy, or known allergy to indocyanine green (ICG) or to iodides (ICG contains sodium iodide). During the study period, a total of 78 patients were excluded: 17 had Gleason score 6 prostate cancer in the preoperative biopsy, four had received hormonal or radiation therapy prior to radical prostatectomy, 22 underwent robotic radical prostatectomy, and 35 either refused to participate or could not be included because none of the physicians trained to use the ICG device (DPN, PMH, TAM, GNT) was present on the day of surgery. All data were prospectively entered into an anonymized, password-protected database.

2. Fluorescence imaging and PLND

Under general anesthesia, ICG (Pulsion Medical Systems, Feldkirchen, Germany; 1 ml of a 5 mg/ml solution resuspended in 9 ml of sterile aqueous water; 0.5 mg/ml) was injected shortly prior to laparotomy in 1-ml aliquots with a Chiba needle (0.70 x 220 mm) under transrectal ultrasound guidance. A handheld near-infrared-sensitive (800-900 nm) probe (Fluobeam®,

Fluoptics, Grenoble, France) was used to collect fluorescence generated in the tissue and assist in SLN detection under real-time image guidance. The excitation is provided by a class 1 expanded laser source at 780 nm. The fluorescence signal is collected by a charge-coupled device through a high pass filter with a high transmittance for wavelength >800 nm. The head of the device is held at 20-25cm from the surgical field and the surgeon assesses the location of fluorescent lymph nodes on a deported screen. Independent of the findings of fluorescence SLN detection, an extended PLND was performed in all patients. To ensure that all fluorescent SLNs were detected, an ex-vivo fluorescence examination of all dissected lymph nodes was carried out. Similarly, the PLND surgical site was systematically inspected for remaining fluorescent activity.

Recommended limits of extended PLND at the University of Bern are: the mid-common region where the ureter crosses the iliac vessels cranially, the circumflex iliac vein and femoral canal distally, the upper limit of the external iliac vein laterally, the bladder medially and the floor of the obturator fossa and the internal iliac vessels dorsally. At first, dissection is performed along the external iliac vein up to the ureter crossing and down to the circumflex iliac vein and femoral canal, using the split and roll technique. The obturator fossa is then cleared while preserving the nerve and vessels. Next, skeletonization of the tissue medial (presacral/pararectal region) and lateral to the internal iliac vessels is done. Finally, lymph nodes located in the fossa of Marcille, that is, dorsolateral to the proximal external iliac vessels and dorsal to the junction of the ureters with the common iliac vessels, are removed.