LAPAROSCOPIC RADICAL PROSTATECTOMY USING A REAL-TIME LYMPHANGIOGRAPHY WITH TRANSPERINEAL INJECTION OF INDOCYANINE GREEN: RESULTS FROM A PROSPECTIVE STUDY

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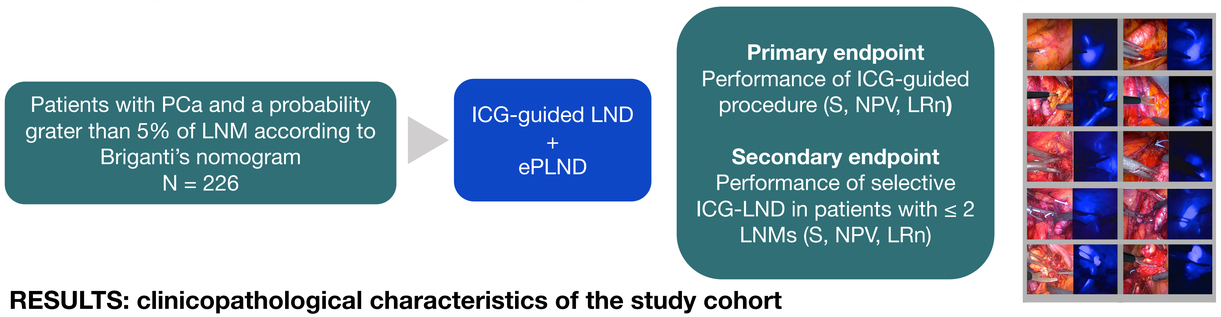
INTRODUCTION & OBJECTIVES

Current standard imaging procedures have limited ability to predict lymph node metastasis (LNM) in clinically localized prostate cancer (PCa) and extended pelvic lymph node dissection (ePLND) during radical prostatectomy (RP) remains the most accurate staging procedure. The primary aim of this study is to evaluate the effectiveness of indocyanine green (ICG)-guided ePLND to assess regional LN status in patients who underwent RP. Secondary objective is to evaluate the potential role of a selective ICG LND in patients with ≤ 2 LNMs which according to the literature are those who may more benefit from ePLND.

MATERIALS AND METHODS

Data about 226 consecutive patients underwent laparoscopic RP with ICG-guided ePLND at our Department were prospectively evaluated. A solution of 25 mg ICG in 5 ml sterile water was transperineally injected. PLND started with the ICG stained nodes followed by extended template. Primary outcome measures were sensitivity (S), negative predictive value (NPV) and likelihood ratio of a negative test (LRn) of ICG-guided procedure. To our knowledge this study shows data about the largest cohort of patients underwent ICG-guided ePLND.



RESULTS: clinicopathological characteristics of the study cohort

- Overall, median age of patients was 64.8 years with a median PSA of 6.6 ng/ml. Extracapsular disease occurred in 50.9% of patients, Gleason score ≥8 was reported in 11.9% cases and R1 rate was 24.3%.

Table 1 – preoperative, surgical and pathological data in the study population

Preoperative clinicals and demographics data	ICG-guided ePLND (n = 226)
patients, n.	226
Age (years), median (IQR)	64.6 (58.8 - 69.3)
BMI, median (IQR)	27.2 (25.1 - 29.4)
Initial PSA (ng/ml), median (IQR)	6.6 (4.9 - 9.4)
Biopsy Gleason score, n. (%)	
6	18 (8.0%)
7	179 (79.2%)
≥ 8	29 (12.8%)
Risk group, n. (%)	
low	7 (3.1%)
intermediate	149 (65.9%)
high	70 (31.0%)
Clinical stage, n. (%)	
cT1	136 (60.2%)
cT2	56 (24.8%)
cT3	34 (15.0%)
Operative and pathologicals data	
Operative time (min), median (IQR)	275.0 (240.0 - 300.0)
Locally advanced (pT3 - T4), n. (%)	115 (50.9%)
Path. Gleason score, n. (%)	
6	19 (8.5)
7	180 (79.6)
≥ 8	27 (11.9)
R1 disease, n. (%)	55 (24.3)
pN1 disease, n. (%)	58 (25.7)
ICG-stained LNs retrieved, median (IQR)	6 (4 - 9)
Overall LNs retrieved, median (IQR)	22 (16 - 27)
Follow-up (months), median (IQR)	26.3 (16.4 - 36.9)

RESULTS: diagnostic performance of ICG-guided procedure

- Median number of nodes retrieved was 22(IQR 16-27) and median number of ICG stained per patient nodes was 6(IQR 4-9).
- Overall 4939 nodes were removed and 1599(32.4%) were fluorescent in vivo.
- Node-positive disease was found in 58(25.7%), of which 53(91.4%) had some of the metastatic LNs stained by ICG, while 5(8.6%) were false negative. Therefore 97.8% of the sample was properly classified by ICG-guided ePNLD (S: 91.4%, NPV: 97.1% and LRn: 8.6%).
- Considering 209(92.5%) patients with 0, 1 or 2 metastatic LNs, 39(18.7%) had a node-positive disease of which 34(87.2%) had metastatic ICG stained LNs. Again, 97.6% were properly classified by ICG approach (S: 87.2%, NPV: 97.1% and LRn: 12.8%). These 39 node-positive patients had a total of 48 metastatic LNs and all except 9(18.8%) were fuorescent in vivo (S: 81.2%).

Table 2 – Diagnostic performance of ICG guidance at patient's level

ICG-guided ePLND	% (95% CI)
Overall	Patients (n = 226, 100.0%)
Mets. prevalence	25.7 (20.1 - 31.9)
Accuracy	97.8 (94.9 - 99.3)
Sensitivity	91.4 (81.0 - 97.1)
NPV	97.1 (93.4 - 99.1)
LRn	8.6 (3.7 - 19.9)
Intermediate risk	Patients (n = 149, 65.9%)
Mets. prevalence	20.8 (14.6 - 28.2)
Accuracy	98.0 (94.2 - 99.6)
Sensitivity	90.3 (74.3 - 98.0)
NPV	97.5 (92.9 - 99.5)
LRn	9.7 (3.3 - 28.4
High risk	Patients (n = 70, 32.0%)
Mets. prevalence	38.6 (27.2 - 51.0)
Accuracy	97.1 (90.1 - 99.7)
Sensitivity	92.6 (75.6 - 99.1)
NPV	95.6 (84.9 - 99.5)
LRn	7.4 (1.9 - 28.1)

Table 3 – Diagnostic performance of ICG guidance at node's level

ICG-guided ePLND	% (95% CI)
Overall	LNs (n = 4939, 100.0%)
Mets. prevalence	3.5 (3.0 - 4.0)
Accuracy	68.6 (67.2 - 69.9)
Sensitivity	63.4 (55.7 - 70.6)
Specificity	68.7 (67.4 - 70.1)
NPV	98.1 (97.6 - 98.6)
LRn	53.3 (43.7 - 64.9)
Intermediate risk	LNs (n = 3180, 64.4%)
Mets. prevalence	1.6 (1.2 - 2.1)
Accuracy	67.6 (65.9 - 69.2)
Sensitivity	76.6 (62.5 - 87.2)
Specificity	67.4 (65.8 - 69.1)
NPV	99.4 (99.0 - 99.7)
LRn	34.9 (21.3 - 57.3)
High risk	LNs (n = 1600, 32.4%)
Mets. prevalence	7.6 (6.3 - 9.0)
Accuracy	71.4 (69.1 - 73.6)
Sensitivity	57.9 (48.5 - 66.8)
Specificity	72.5 (70.1 - 74.7)
NPV	95.5 (94.1 - 96.6)
LRn	58.2 (47.1 - 71.8)

Table 4 – Selective ICG-LND in patients with oligometastatic nodal disease (≤ 2 LNMs)

According to patients	Patients (n = 207, 100.0%)			
	pN0	**pN+**		**% (95% CI)**
Patients with LNM in ICG LNs	0	34	Mets. prevalence	18.8 (13.8 - 24.8)
Patients without LNM in ICG LNs	168	5	Accuracy	97.6 (94.5 - 99.2)
			Sensitivity	87.2 (72.6 - 95.7)
			Specificity	100.0 (97.8 - 100.0)
			NPV	97.1 (93.4 - 99.1)
			LRn	12.8 (5.7 - 29.1)
According to nodes	LNs (n = 4470, 100.0%)			
	pN0	**pN+**		**% (95% CI)**
ICG LNs	1412	39	Mets. prevalence	1.1 (0.8 - 1.4)
Non-ICG LNs	3010	9	Accuracy	68.2 (66.8 - 69.6)
			Sensitivity	81.3 (67.4 - 91.1)
			Specificity	68.1 (66.7 - 69.4)
			NPV	99.7 (99.4 - 99.9)
			LRn	27.6 (15.3 - 49.7)

CONCLUSIONS

- ICG guidance correctly stage almost 98% of cases.
- Its high NPV may will allow to avoid ePLND as soon as an accurate intraoperative analysis is available.
- Among those patients in whom the LND may have a potentially curative role, ICG alone would have lost only 9 metastatic LNs. This suggest that maybe there is a place for selective LND in patients with limited LN metastatic burden.