Identifying the optimal candidates for pelvic lymph node dissection during prostatectomy

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QUID EST HOMO?

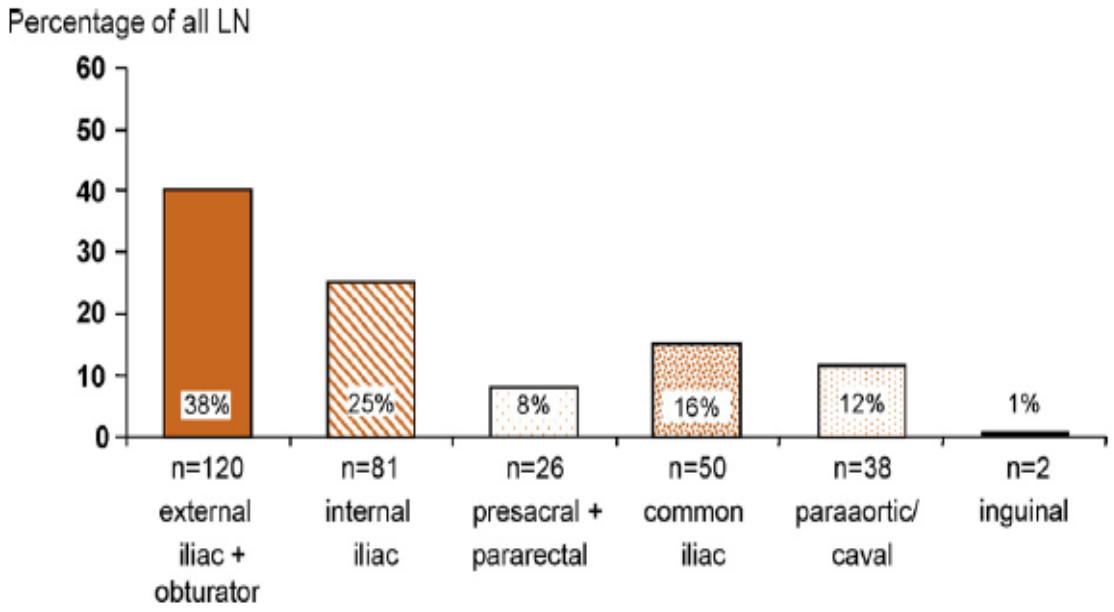
Disclosures

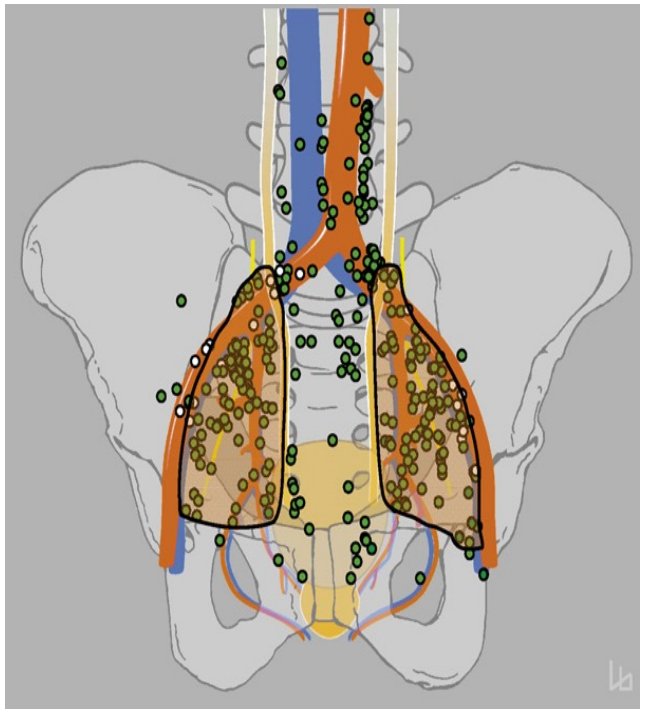
Astellas Pharma Janssen-Cilag, OPKO Health, MDx Health, Bayer, miR Scientific, LLC ("miR"), A3P biomedical, MSD/Astrazeneca, Ferring, Pfizer, Sandoz-Novartis, Telix Pharmaceuticals

PLND in prostate cancer : a purely staging procedure.. However..

- ✓ Not all men are candidate to ePLND
- ✓ The easiest thing we may say is that this is a useless procedures : we have no evidence
- ✓ Fine but we do also too many useless prostatectomies!!!
- ✓ Be balanced in your judgement : it is not only removing nodes
- ✓ If you had 35% patient chaces of having positive nodes what would you decide for yourself? Just observe and treat in the salvage setting? Fine you reduce overtreatment but may undertreat those 35%

What Is the Optimal Extent of PLND?

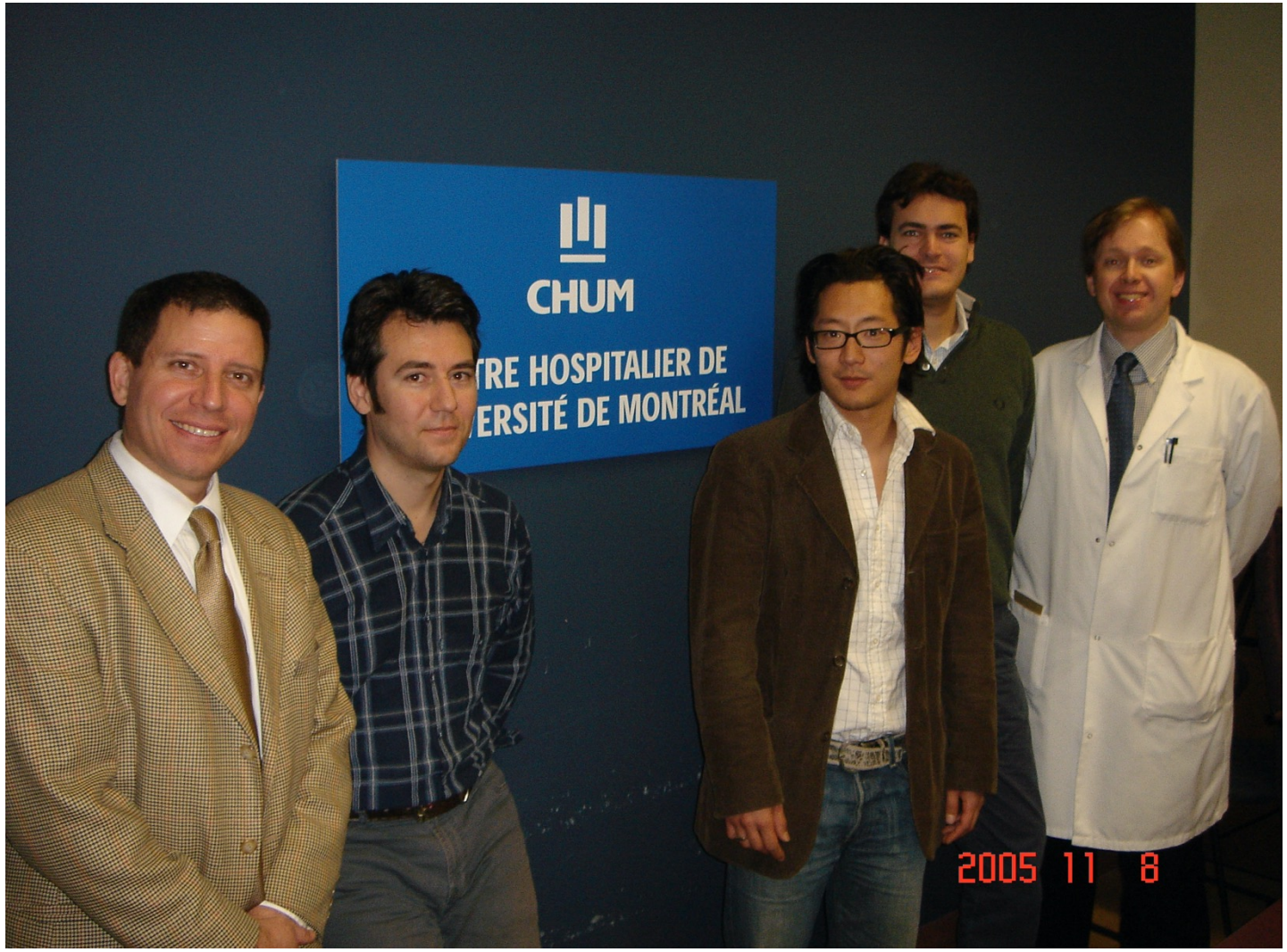




By extending the dissection along common iliac vessels at least up to the ureteric crossing 75% of all nodes potentially harbouring LNI can be removed

Mattei A et al, Eur Urol, 52:126-32 2008

Know your data and how to analyse them!
Only by doing so you find important answers for your patients!



CHUM

Centre hospitalier
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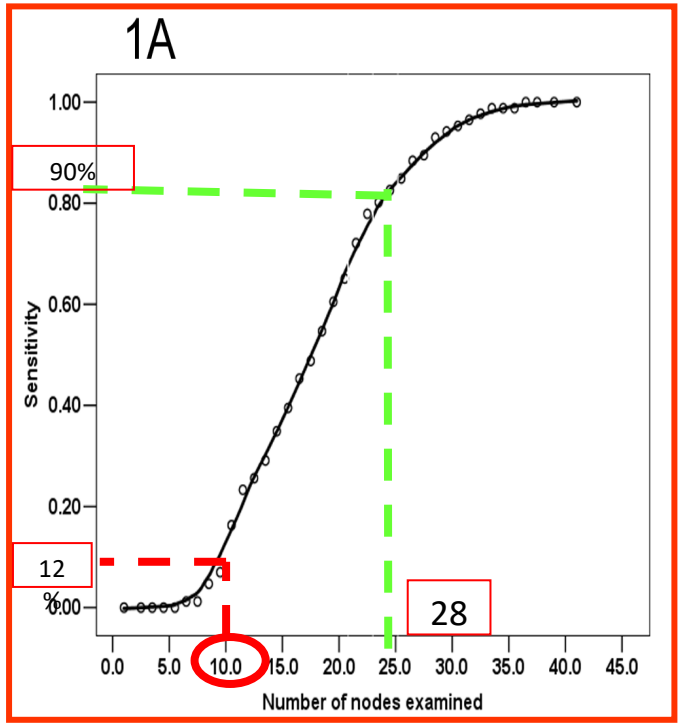
Professor Pierre I. Karakiewicz

Outline

- ✓ Current indications for ePLND in Prostate Cancer
- ✓ Can imaging replace ePLND?
- ✓ Outcomes of ePLND
- ✓ Novel approaches for individualized PLNDs

THE MORE YOU REMOVE THE HIGHER RATES OF LNI

NCCN (CAGGIANOS) NOMOGRAM: BASED ON LIMITED PLND



Briganti A et al Urology 69:147-51,2007

- Total PSA at diagnosis : 5.4 ng/mL
- Clinical stage: T1c
- Biopsy Gleason score : 7 (4+3)

Risk of LNI

3%

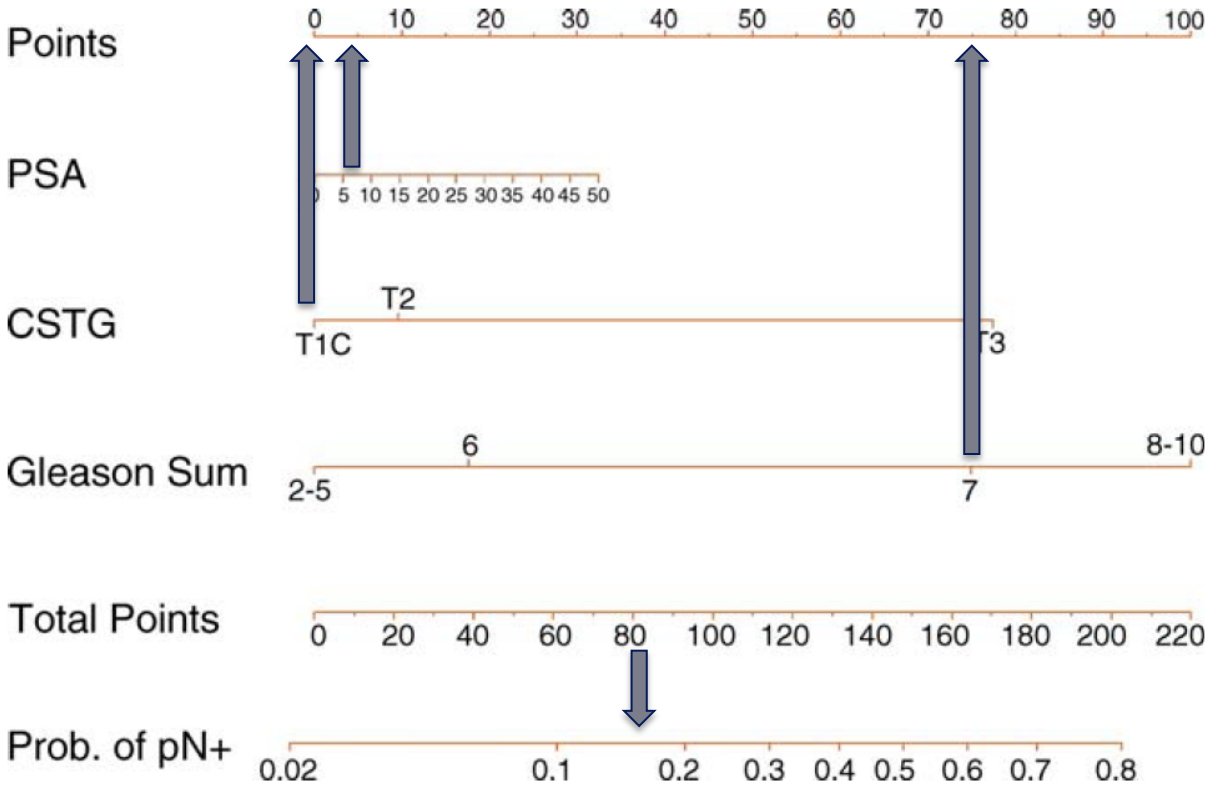
According to

Caggianos' nomogram*

http://www.mskcc.org/mskcc/html/10088.cfm

**Caggianos et al, J Urol 170:1798-803, 2003*

IMPORTANCE OF THE EXTENT OF PLND IN THE DIAGNOSIS OF PROSTATE CANCER NODAL METASTASES



PSA 5 (5 pts)

+

Stage T1 (0 pts)

+

Gleason 4+3 (75 pts)

=

Total 80 pts

Risk of LNI

15%

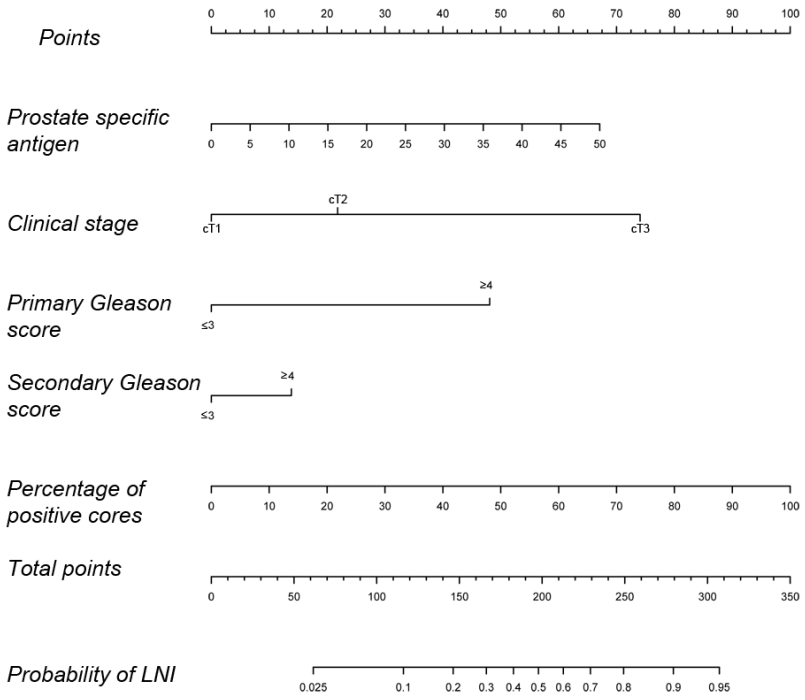
Briganti et al. Eur Urol 49:1019-1026,2006

LIMITATIONS OF THE 2006 MODEL

- ✓ Assumption that all positive biopsies are of the same grade
- ✓ No data on tumor volume (proxy?)
- ✓ No data on Imaging (mpMRI) – cstage done with DRE, no targeted biopsy
- ✓ No sensitive imaging (no PSMA PET)

Updated Nomogram Predicting Lymph Node Invasion in Patients with Prostate Cancer Undergoing Extended Pelvic Lymph Node Dissection: The Essential Importance of Percentage of Positive Cores

- 588 patients undergoing an anatomically defined ePLND



PSA 5 (45 pts)
+
Stage T1 (0 pts)
+
Gleason 4+3 (40 pts)

20% positive cores<5%

90% positive cores:19%

Patients with a LNI risk<5% might be spared ePLND (sparing 67% of ePLNDs while losing 1.2%of men with LNI)

Cut-off confirmed in the external validation setting^

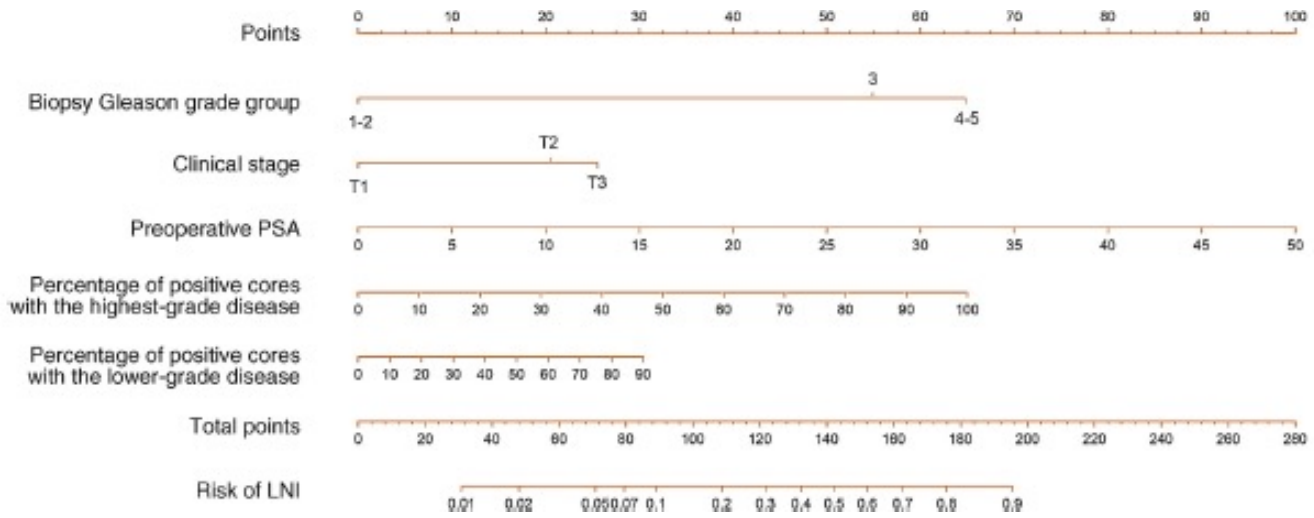
Briganti A et al Eur Urol ,61:480-7, 2012

LIMITATIONS OF THE 2012 MODEL

- ✓ Assumption that all positive biopsies are of the same grade
- ✓ No data on tumor volume (proxy?)
- ✓ No data on Imaging (mpMRI) – cstage done with DRE, no targeted biopsy
- ✓ No sensitive imaging (no PSMA PET)

Can We Further Reduce the Number of Useless PLNDs?

- 2017 update of the Briganti nomogram
- 681 patients undergoing an anatomically defined ePLND with detailed biopsy information

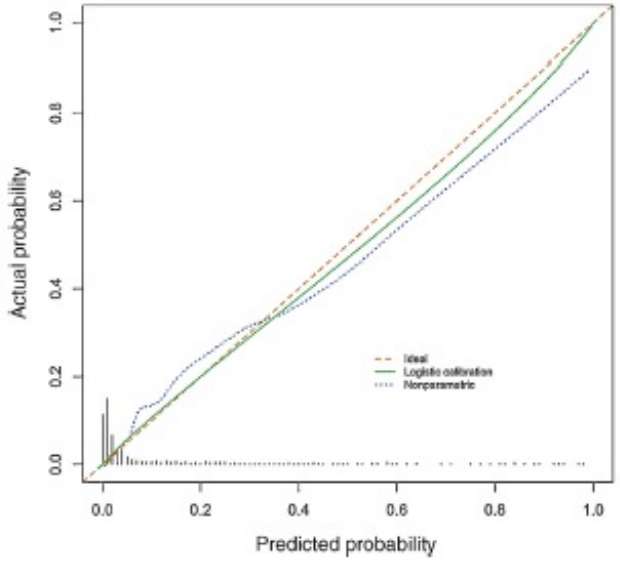


Nomogram calculated probability of LNI, cutoff (%)	Patients in whom PLND is not recommended according to the cutoff (below cutoff)	Patients below cutoff without histologic LNI	Patients below cutoff with histologic LNI	Patients in whom PLND is recommended according to the cutoff (above cutoff)	Patients above cutoff without histologic LNI	Patients above cutoff with histologic LNI
1	38 (5.6)	38 (6.3)	0 (0)	643 (94)	564 (88)	79 (100)
2	264 (39)	264 (44)	0 (0)	417 (61)	338 (81)	79 (100)
3	362 (53)	359 (60)	3 (0.8)	319 (47)	243 (76)	76 (96)
4	406 (60)	402 (67)	4 (1.0)	275 (40)	200 (72)	75 (95)
5	446 (66)	441 (73)	5 (1.1)	235 (35)	161 (69)	74 (94)
6	464 (68)	458 (76)	6 (1.3)	217 (32)	144 (66)	73 (92)
7	471 (69)	464 (77)	7 (1.5)	210 (31)	138 (66)	72 (91)
8	482 (71)	474 (79)	8 (1.7)	199 (29)	128 (64)	71 (90)
9	491 (72)	482 (80)	9 (1.8)	190 (28)	120 (63)	70 (89)
10	496 (73)	486 (81)	10 (2.0)	185 (27)	116 (63)	69 (87)

LNI = lymph node invasion; PLND = pelvic lymph node dissection.

Table 4 – Clinical implications according to treatment option (novel nomogram vs Briganti nomogram vs MSKCC nomogram)

Treatment option	Patients in whom PLND is not recommended according to the cutoff (below cutoff)	Patients below cutoff without histologic LNI	Patients below cutoff with histologic LNI	Patients in whom PLND is recommended according to the cutoff (above cutoff)	Patients above cutoff without histologic LNI	Patients above cutoff with histologic LNI
Novel nomogram, 7% cutoff	471 (69)	464 (99)	7 (1.5)	210 (31)	138 (66)	72 (34)



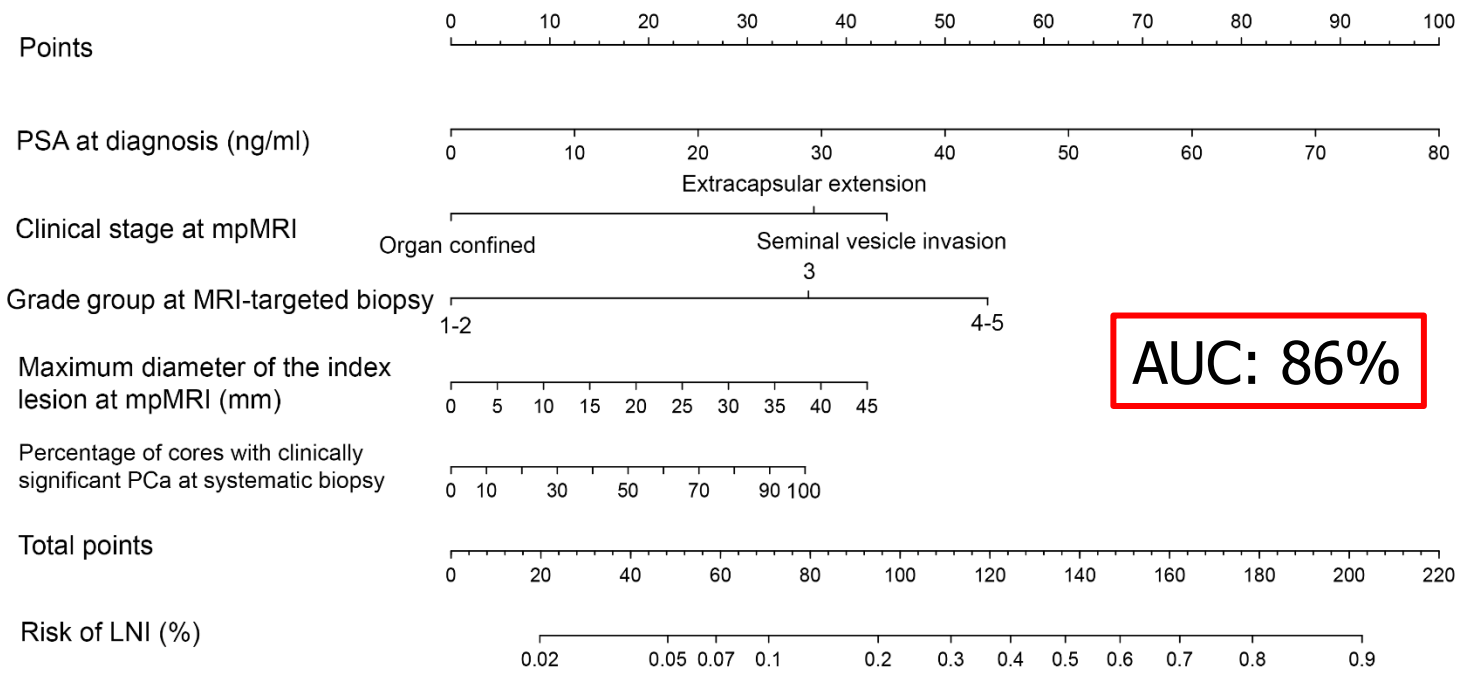
Gandaglia et al., Eur Urol 2017;72:632-40

LIMITATIONS OF THE 2017 MODEL

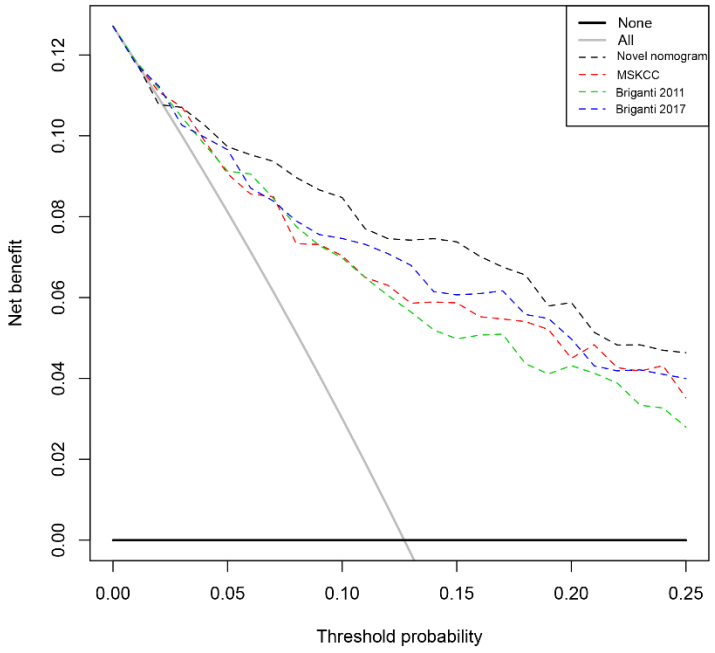
- ✓ Assumption that all positive biopsies are of the same grade
- ✓ No data on tumor volume (proxy?)
- ✓ No data on Imaging (mpMRI) – cstage done with DRE, no targeted biopsy
- ✓ No sensitive imaging (no PSMA PET)

When Should We Consider an ePLND?

- ✓ 659 patients who received mpMRI-targeted biopsy with concomitant systematic biopsy at 5 Centers



AUC: 86%

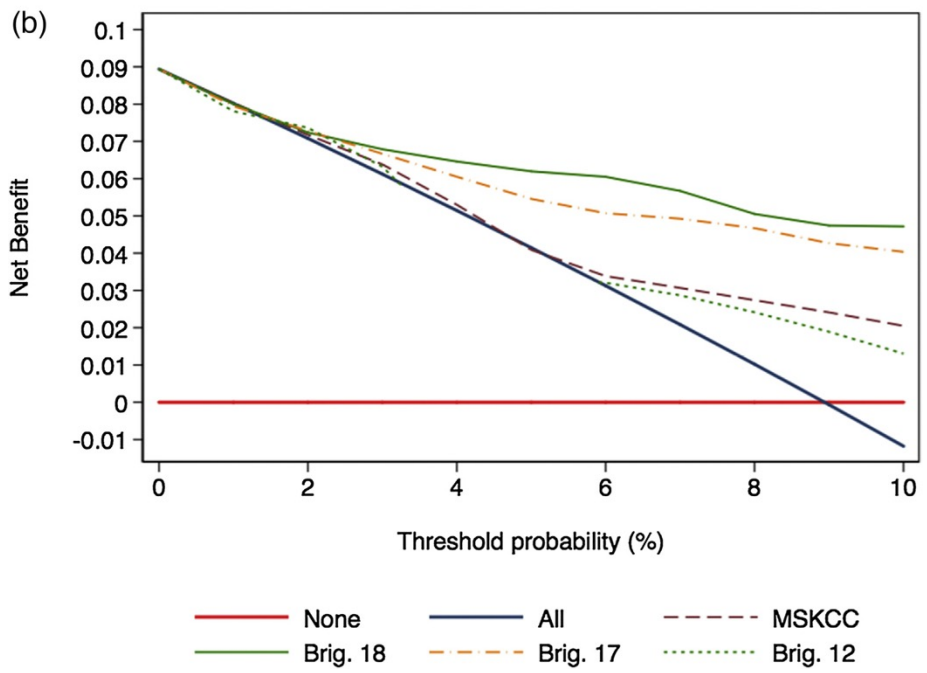


- ✓ Using the **7% cut-off, 244 (57%) ePLNDs would be spared and a lower number of LNIs (1.6%)**

Gandaglia, Briganti et al. Eur Urol 2019;75:506-14

Can We Apply Models Developed in Systematic Biopsy to Contemporary Men Diagnosed with MRI-Targeted Biopsy?

Treatment option	Patients in whom PLND is not recommended according to the cut-off (below cut-off)	Patients below cut-off with histologic LNI
Novel nomogram, 7% cut-off	244 (57%)	4 (1.6)
Briganti 2017, 7% cut-off	290 (60%)	13 (4.5)
Briganti 2012, 5% cut-off	268 (54%)	9 (3.4)
MSKCC, 2% cut-off	157 (31%)	1 (0.6)



The 2019 Briganti nomogram had a higher AUC as compared to the 2012 and 2017 Briganti nomograms as well as the MSKCC risk calculator (78% vs. 75% vs. 65% vs. 74%) at external validation

Gandaglia, Briganti et al. Eur Urol 2020;78:138-142

When Should We Consider an extended PLND?

ePLND provides important information for staging and prognosis which cannot be matched by any other currently available procedure

Intermediate risk

Extended pelvic lymph node dissection (ePLND)	Perform an ePLND based on predicted risk of lymph node (LN) invasion (validated nomogram, see Section 6.1.2.3.2.)	Weak

High risk/locally advanced

ePLND	Perform an ePLND in high-risk PCa.	Strong
	Do not perform a frozen section of nodes during RP to decide whether to proceed with, or abandon, the procedure (see Section 6.2.4.1).	Strong

An updated nomogram has been externally validated in men diagnosed based on MRI followed by MRI-targeted biopsy [401]. Using this nomogram, patients could be spared an ePLND if their risk of nodal involvement was less than 7%; which would result in missing only 1.5% of patients with nodal invasion [401, 403]. However, 70% of patients would still undergo an unnecessary ePLND as they would have no LN involvement [364]. This is problematic due to the risk of complications of PLND (see below) as well as the additional operative time required.

EAU Guidelines on Prostate Cancer; 2023 update

While waiting for oncological results of RCTs, Too Many ePLNDs Are Still Performed!

Study	Setting	Percentage of patients at high risk of LNI requiring an ePLNDs	Rate of LNI	Unnecessary ePLNDs performed
Briganti et al. Eur Urol 2012	Patients diagnosed with systematic biopsy	34%	21%	79%
Gandaglia et al. Eur Urol 2019	Patients diagnosed with MRI-targeted biopsy	49%	24%	76%
Diamond et al. World J Urol 2020	Intermediate- and high-risk patients	54%	20%	80%

LIMITATIONS OF THE 2017 MODEL

- ✓ Assumption that all positive biopsies are of the same grade
- ✓ No data on Imaging (mpMRI)
- ✓ No central revision
- ✓ No sensitive imaging (no PSMA PET)

Conventional imaging vs PSMA PET/CT
ProPSMA study

- ✓ Multicentre, two-arm, randomized study, biopsy-proven prostate cancer and high-risk features
- ✓ 320 Patients were randomly assigned to:
  - ✓ Conventional imaging with CT and bone scanning
  - ✓ Gallium-68 PSMA-11 PET-CT

	Lesion-based accuracy			
	Sensitivity	Specificity	PPV	NPV
Overall	71%	99%	91%	98%
>3 mm	82%	99%	92%	99%

	Sensitivity (%)	Specificity (%)	Accuracy (%)
Overall			
PSMA PET/CT	85	98	92
Conventional imaging	38	91	65
Pelvic nodes			
PSMA PET/CT	83	99	95
Conventional imaging	23	96	77

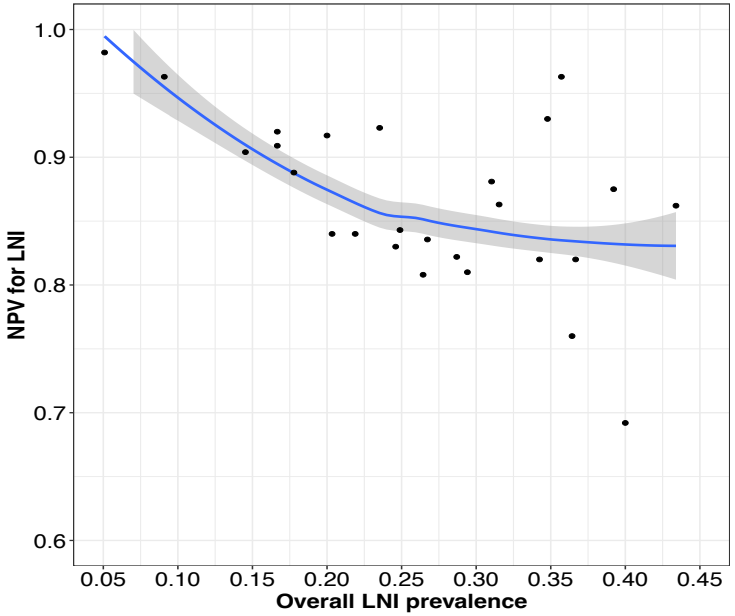
Diameter of nodal mets	Detection rate at PSMA	Prevalence at ePLND
<2	0%	20%
2-5	60%	40%
>5	86%	40%

Hofman et al., Lancet 2020;395:1208
Van Leuween et al. BJU Int 2017;119:209-15
Sprute et al. J Nucl Med 2020; in press
Briganti et al. Unpublished data

Is there a role for PSMA PET in intermediate risk patients?

- ✓ **NPV ranged from 98 to 84%** between 5 and 45% risk of LNI
- ✓ In those studies where LNI prevalence ranged between 5 and 20%, the NPV of PSMA PET/CT remained steadily above 90%.
- ✓ The PPV increased significantly as the LNI prevalence increased (from 54% to 90%).

A staging ePLND might be omitted in patients with a nomogram predicted risk of LNI < 20% and a negative PSMA PET/CT test.

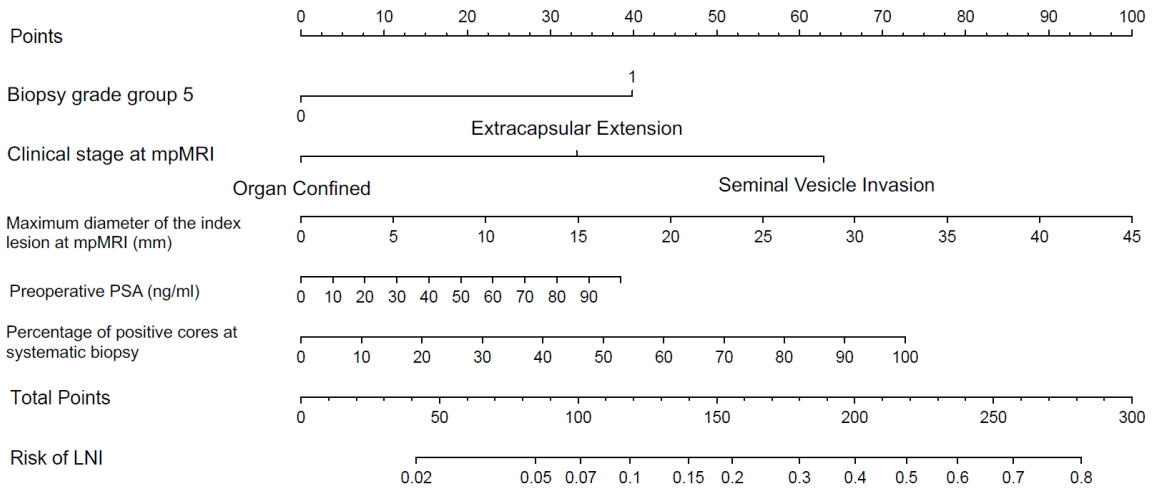


Stabile et al., Eur Urol Oncol, 5:1-17, 2022

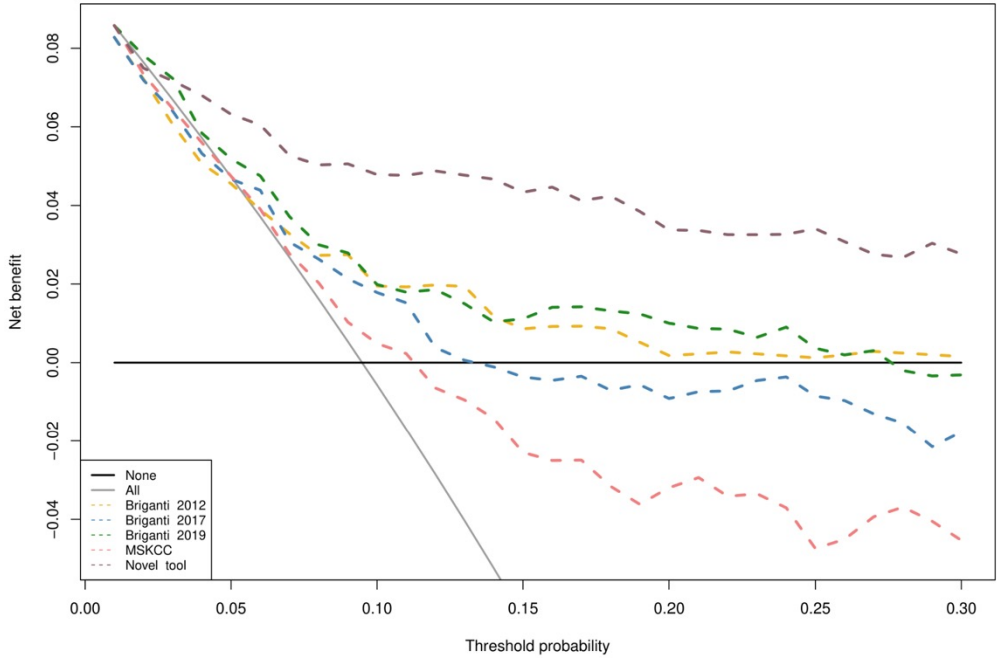
Development of a Novel Nomogram

The AUC of available nomograms did not exceed 70%. At internal validation, a novel model depicted an AUC of **81%, better calibration**, and **higher net-benefit** compared to available nomograms. The use of a 5% cut-off would have spared 47% ePLNDs (vs. 16% for the Briganti 2019 nomogram) at the cost of missing only 2% LNIs.

Novel coefficient-based nomogram predicting LNI in miN0M0 patients at PSMA-PET imaging.



Decision Curve Analysis



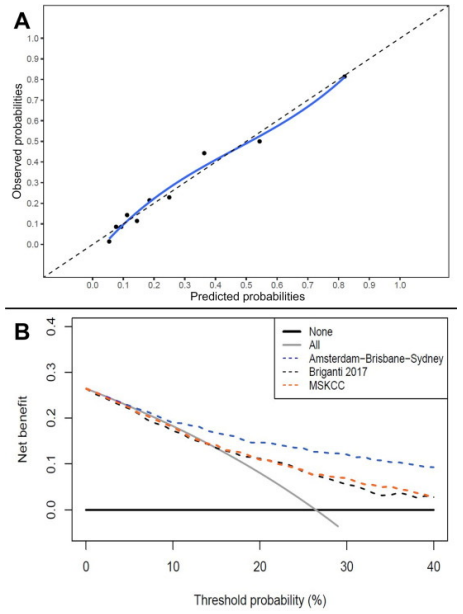
Gandaglia et al , Eur Urol Oncol, 2023;6:543-552

Development of a Novel Nomogram

	Patients in whom PLND is not recommended according to the cut-off (below cut-off)	Patients below cut-off with histologic LNI	Patients in whom PLND is recommended according to the cut-off (above cut-off)	Patients above cut-off with histologic LNI
Novel nomogram[a], 5%cut-off	184 (47.2)	4 (2.1)	206 (52.8)	35 (17)
Novel nomogram[a], 7%cut-off	238 (61)	8 (3.4)	152 (39)	31 (20.4)
Briganti 2012[b], 5% cut-off	54 (13.7)	1 (1.9)	340 (86.3)	39 (11.5)
Briganti 2012[b], 7% cut-off	97 (24.6)	2 (2.1)	297 (75.4)	38 (12.8)
Briganti 2017[c], 5% cut-off	35 (10.8)	1 (2.8)	288 (89.2)	34 (11.8)
Briganti 2017[c], 7% cut-off	50 (15.5)	3 (6)	273 (84.5)	32 (11.7)
Briganti 2019[d], 5% cut-off	40 (13)	0 (0)	267 (87)	26 (9.7)
Briganti 2019[d], 7% cut-off	54 (17.6)	0 (0)	253 (82.4)	26 (10.3)
MSKCC[e], 5% cut-off	27 (6.7)	1 (3.7)	379 (93.3)	43 (11.3)
MSKCC[e], 7% cut-off	40 (9.9)	2 (5)	366 (90.1)	42 (11.5)

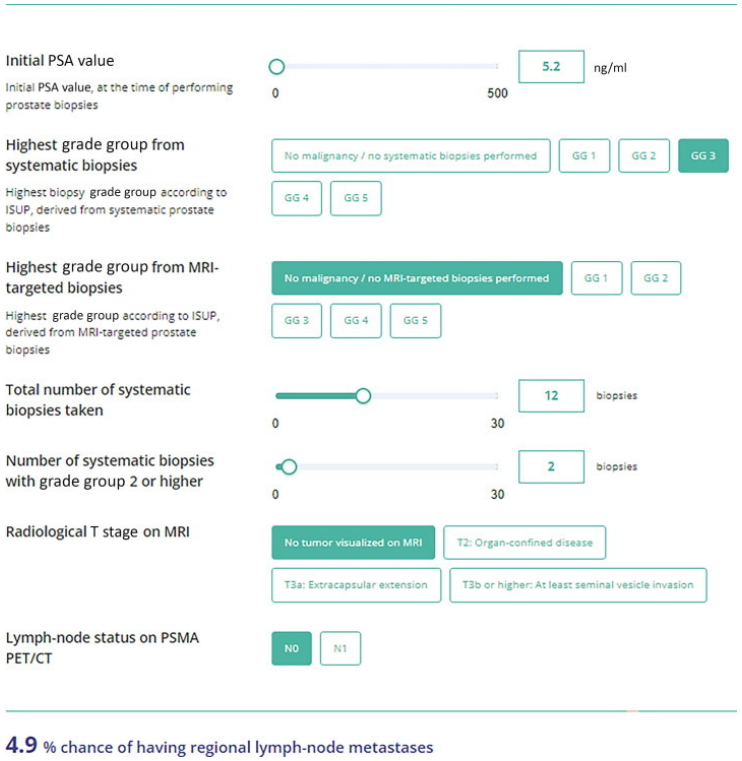
Development and External Validation of a Novel Nomogram to Predict the Probability of Pelvic Lymph-node Metastases in Prostate Cancer Patients Using MRI and PSMA PET

- ✓ 700 eligible patients who underwent RARP and ePLND were included in the model-building cohort
- ✓ The external validation cohort consisted of 305 surgically treated patients
- ✓ Logistic regression with backward elimination was used to select variables for the Amsterdam-Brisbane-Sydney nomogram
- ✓ Performance of the final model was evaluated using the AUC, calibration plots, and decision-curve analyses
- ✓ Models were subsequently validated in an external population



76: miN1

Of these, 22 (29%) were pN0



AUC 0.81

increased net benefit at a threshold probability of ≥4%.

Vis et al. Eur Urol Oncol 2023;6:553-63

External Validation of the Available Nomograms for the Identification of Candidates for a Staging Extended Pelvic Lymph Node Dissection at the Time of Radical Prostatectomy in Prostate Cancer Patients Preoperatively Staged with PSMA PET

267 miN0 PCa patients treated with RP and ePLND

- ✓ Individual LNI risk was calculated relying on the coefficients of the MSKCC, Amsterdam-Brisbane-Sydney, Briganti 2012-2017-2019 and 2023 nomograms.
- ✓ 28 (10%) patients harbored LNI at final pathology.
- ✓ The MSKCC, Amsterdam-Brisbane-Sydney, Briganti 2012-2017-2019 nomograms were associated with a risk of overestimation.
- ✓ The C-index for the MSKCC, Amsterdam-Brisbane-Sydney, Briganti 2012-2017-2019 and 2023 nomograms were 65, 67, 69, 64, 74 and **79%.**

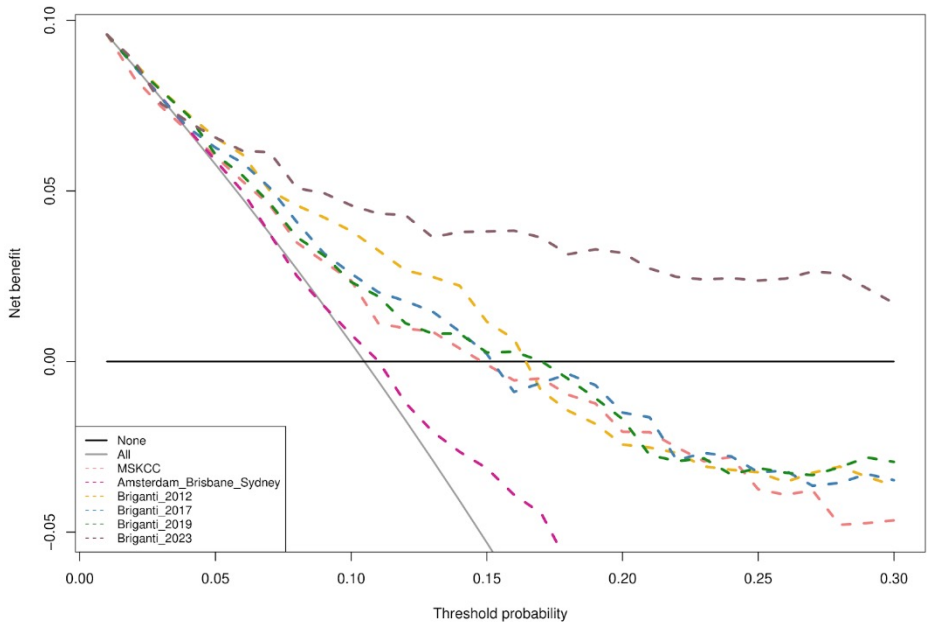


Figure: Decision curve analysis evaluating the net benefit of different ePLND thresholds according to different nomograms.

Conclusions

Internal validation (Gandaglia G, et al, 2023)

- ✓ *5% cutoff : 47% ePLND procedures spared (vs 13% for the Briganti 2019 nomogram) at the cost of missing only 2.1% LNI cases.*

External validation (current abstract)

- ✓ The use of the recent Briganti 2023 nomogram in miN0 patients is associated with 45% ePLNDs spared with only 3% LNI missed.

Gandaglia et al, EAU meeting, 2024

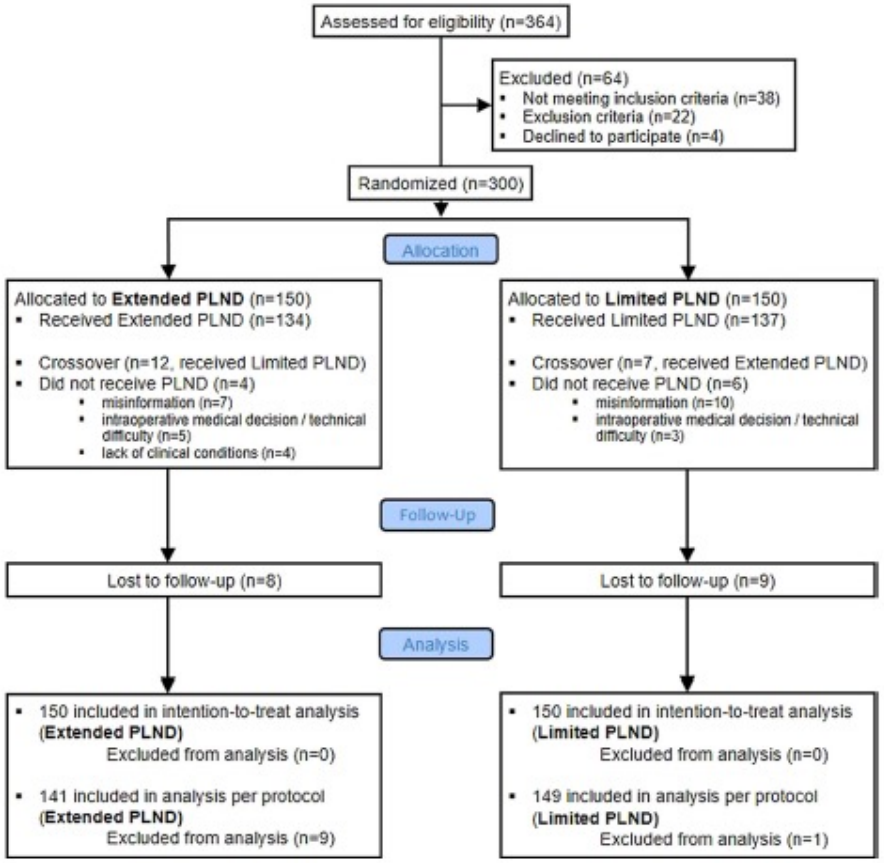
(Weak) Data from RCTs

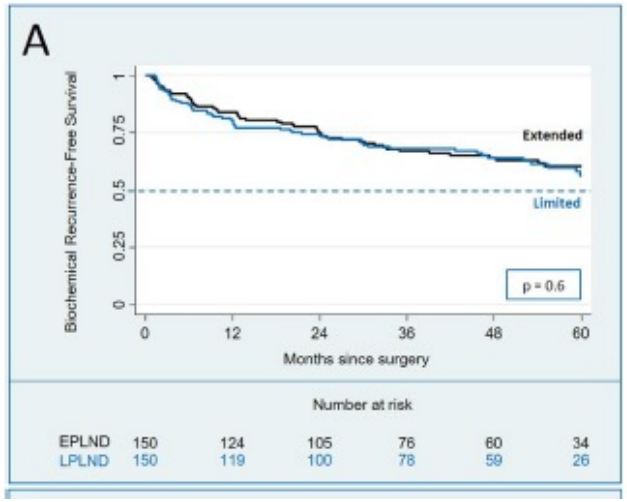
Sponsor	Study	Clinicaltrials.gov	Patients included	Study groups	N. Of patients	Estimated Completion Date	Results
University of San Paolo, Brazil	**LFD**	NCT01812902	Intermediate- and high-risk patients	Extended vs. Limited PLND	260	2020	Full report available
Association of Urologic Oncology (AUO), Germany	**SEAL AUO AP 55/09**	NCT01555086	Intermediate- and high-risk patients	Extended vs. Limited PLND	500	August 2017 (results not released)	**EAU2014**: 244 randomized patients; descriptive statistics presented
Swiss Group for Clinical Cancer Research	**-**	NCT03921996	Intermediate- and high-risk patients	Extended vs. no PLND	900	September 2023	NA
MSKCC	**–**	–	Intermediate- and high-risk patients	Extended vs. Limited PLND (surgeon randomized)	1,573	2020	Full report availble

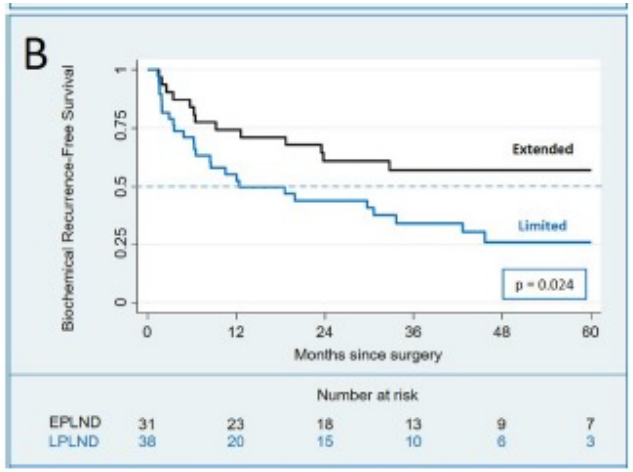
Extended Versus Limited Pelvic Lymph Node Dissection During Radical Prostatectomy for Intermediate- and High-risk Prostate Cancer: Early Oncological Outcomes from a Randomized Phase 3 Trial

In total, 300 patients were randomized 1:1 to:

- ✓ LPLND (obturator nodes n=150)
- ✓ EPLND (obturator, external iliac, internal iliac, common iliac, and presacral nodes n=150) bilaterally



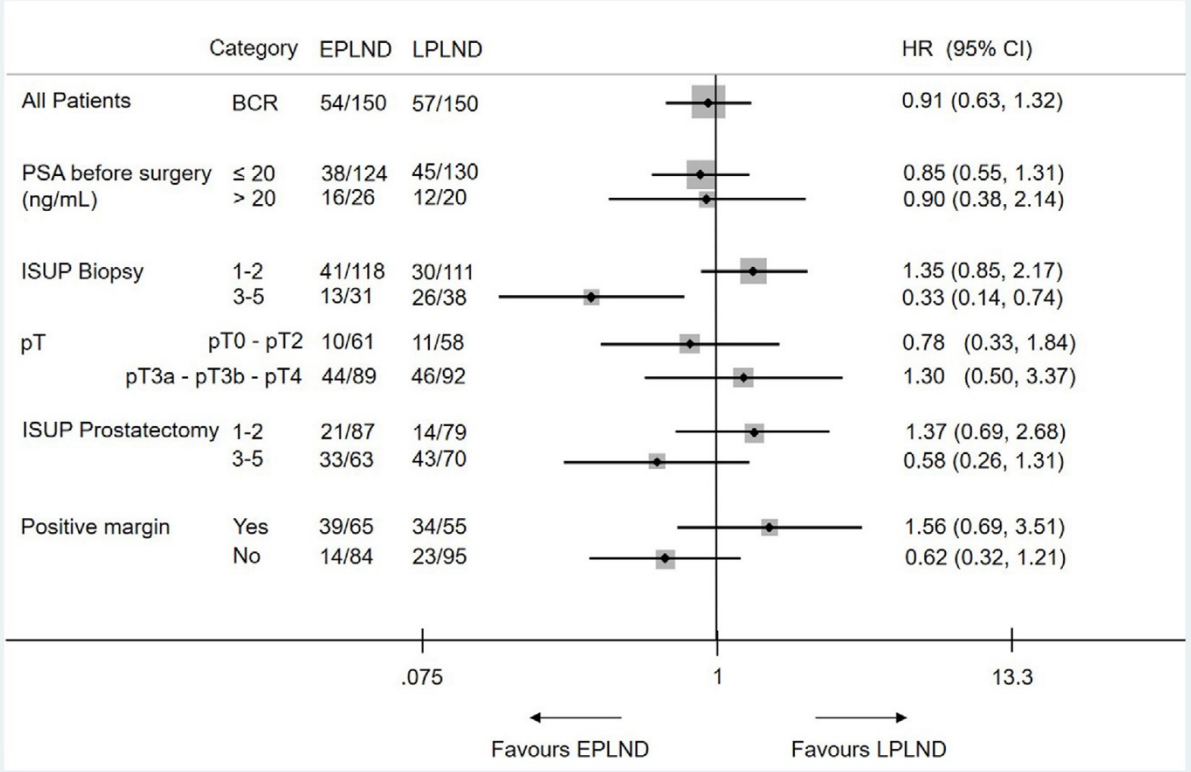




HIGH RISK PATIENTS: 38%
ROUGHLY A THIRD OF RANDOMIZED MEN HAD GLEASON 6 AT BIOPSY

Lestingi et al, Eur Urol, 779:595-64, 2021

Extended Versus Limited Pelvic Lymph Node Dissection During Radical Prostatectomy for Intermediate- and High-risk Prostate Cancer: Early Oncological Outcomes from a Randomized Phase 3 Trial



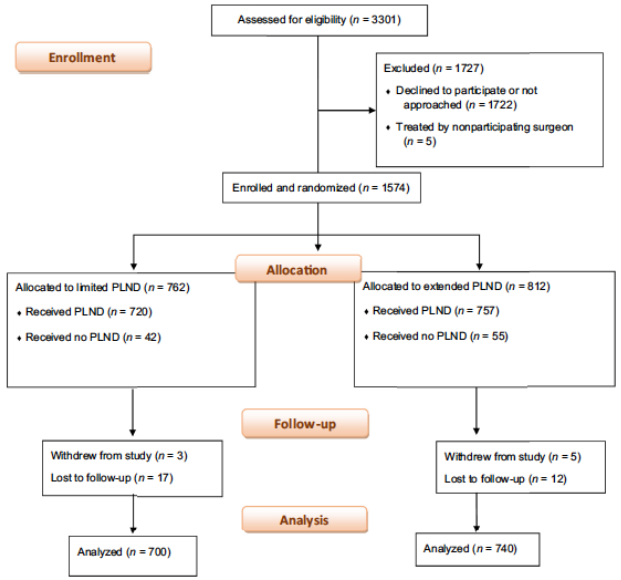
Lestingi et al, Eur Urol, 779:595-64, 2021

IS THIS TRIAL REALLY PRACTICE CHANGING?

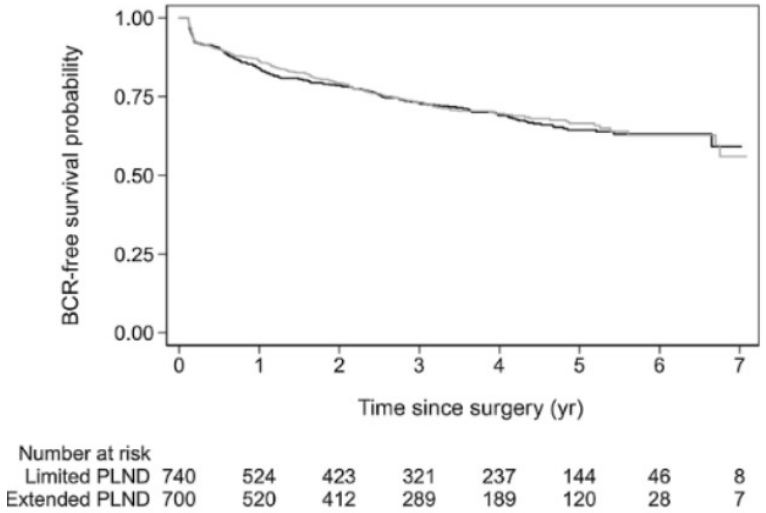
- ✓ Control group treated with limited PLND
- ✓ More than one-third of randomized men had Gleason 6 disease at biopsy.
- ✓ The effect of ePLND might have been diluted by the high positive surgical margin rate (24%) especially among pT2 cases (40% of the entire population), which might have driven BCR
- ✓ No mention about the characteristics of BCR in terms of PSA kinetics and aggressiveness

Limited versus Extended Pelvic Lymph Node Dissection for Prostate Cancer: A Randomized Clinical Trial

- ✓ Of 1440 patients included, 700 were randomized to limited PLND and 740 to extended PLND
- ✓ Median number of nodes retrieved was 12 (IQR 8–17) for limited PLND and 14 (IQR 10–20) extended PLND; the corresponding rate of positive nodes was 12% and 14% (p = 0.3).
- ✓ With median follow-up of 3.1 yr, there was no significant difference in the rate of BCR between the groups (hazard ratio 1.04, p = 0.5)
- ✓ Rates for grade 2 and 3 complications were similar at 7.3% for limited versus 6.4% for extended PLND; there were no grade 4 or 5 complications



BX GLEASON 8-10 : 20%



Touijer et al. Eur Urol Oncol 2021,;4:532-539

IS THIS TRIAL PRACTICE CHANGING?

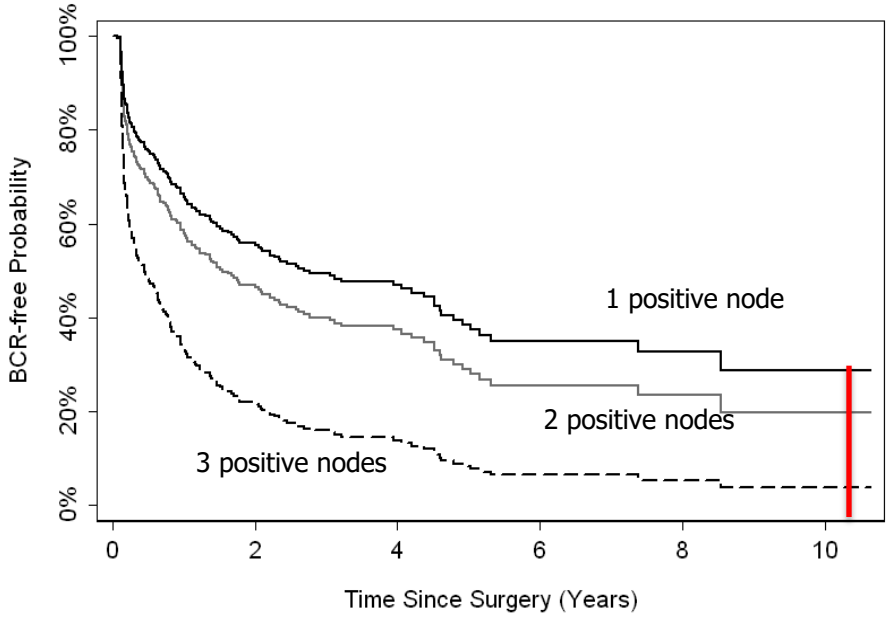
- ✓ Same number of lymph nodes retrieved between the two groups!
- ✓ Same rate of LNI between the two groups!
- ✓ Overall favourable patient characteristics
- ✓ No data on positive SM rates or adjuvant treaments

Devos et al Eur Urol Oncol, 2021, 4:540-542

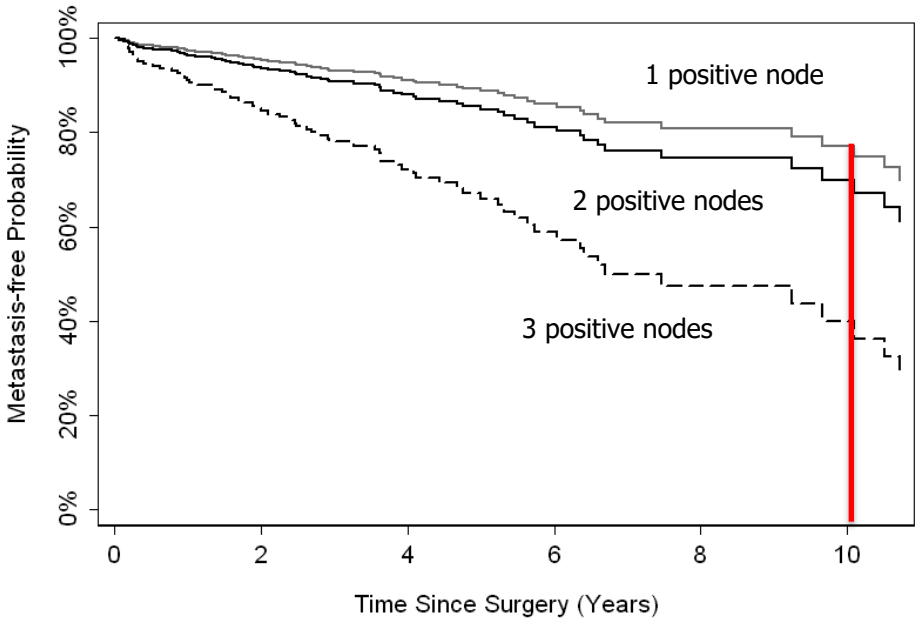
Long-term Outcomes of Patients with Lymph Node Metastasis Treated with Radical Prostatectomy Without Adjuvant Androgen-deprivation Therapy

369 patients treated with ePLND (median n. of nodes removed: 15) without adjuvant therapies

BCR FREE SURVIVAL



METASTASIS FREE SURVIVAL

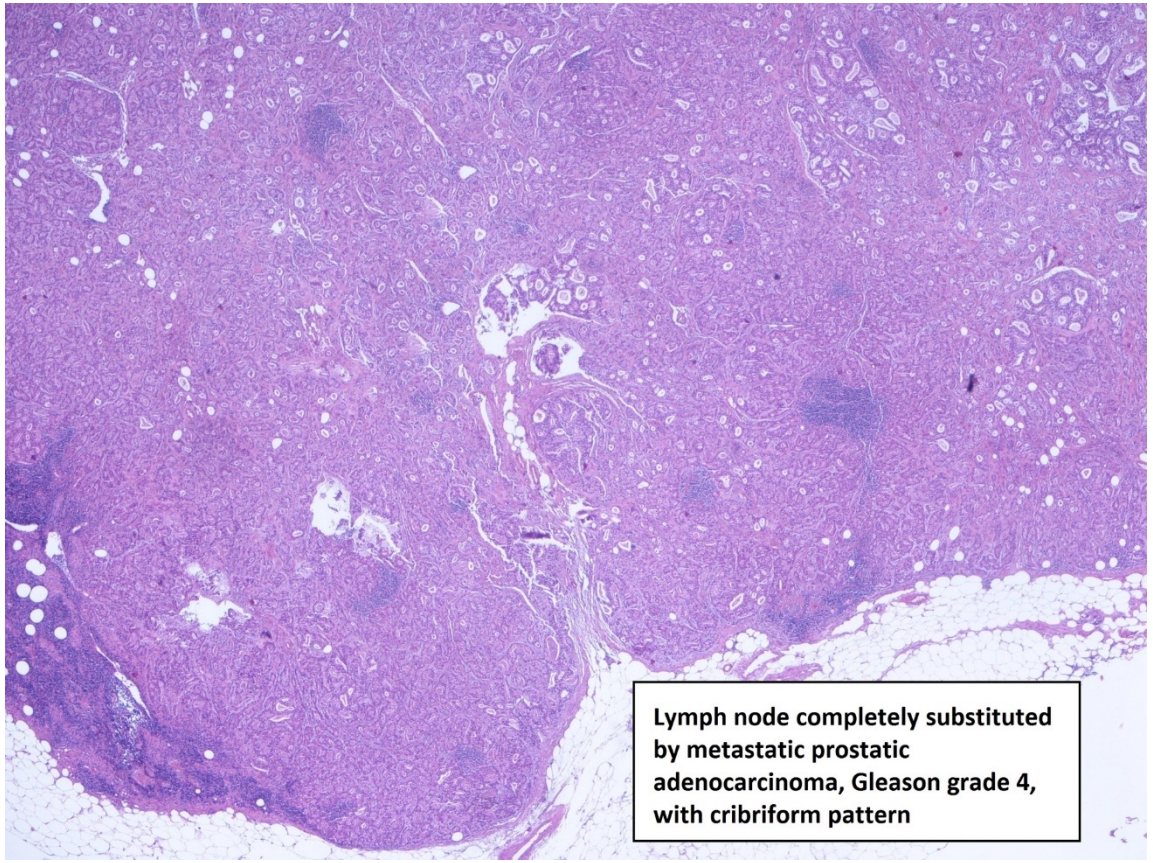


Roughly 30% of patients with <=2 positive nodes would not experience recurrence at 10-year follow-up after RP without adjuvant treatments

Toujer et al, Eur Urol 2014, 65;20-5

Is Lymphadenectomy Necessary in Prostate Cancer?

- ✓ Optimal staging
- ✓ Improved oncologic control (?)
- ✓ Identification of candidates for adjuvant therapies



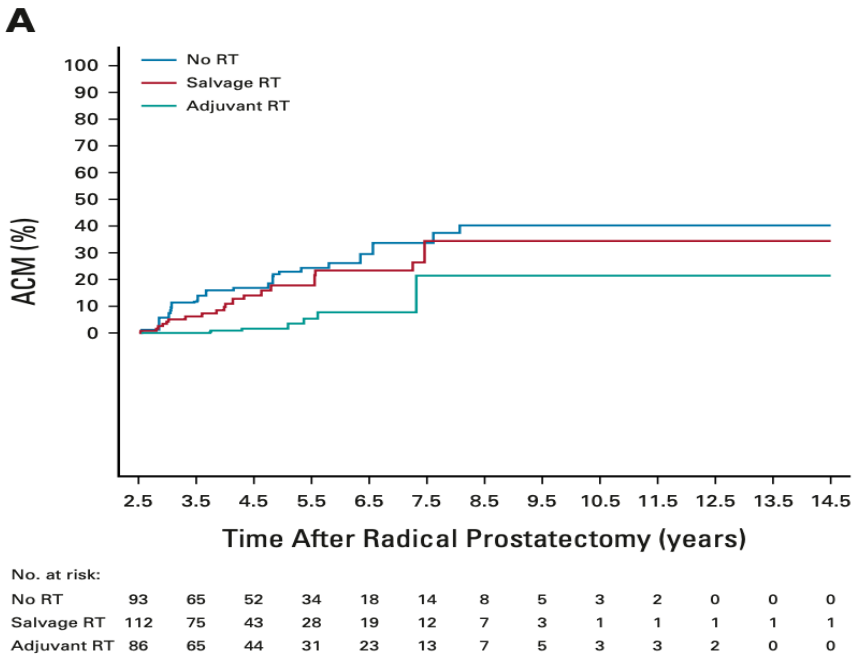
By the courtesy of Dr. Luciano' and Prof. Montironi

The impact of higher nodal metastatic burden on outcomes and its correlation with postoperative radiation therapy

Multivariable Cox regression model predicting overall mortality

Covariate	No. of Men	No. of Deaths	No. of PC deaths	Multivariable Analysis ACM AHR (95% CI)	*P*
aRT(t) *v* early sRT(t)	3,891	286	136	0.92[a] (0.85 to 0.99)	.03
No RT(t) *v* early sRT(t)	17,062	923	192	0.99[a] (0.94 to 1.04)	.68
Treatment propensity score					
Propensity score for selection of aRT *v* (early sRT or no RT)	17,913	986	223	1.016 (1.010,1.022)	< .001
Propensity score for selection of early sRT *v* (aRT or no RT)	17,913	986	223	1.015 (1.011 to 1.018)	< .001
Patient and PC prognostic factors					
Age at RP in years	17,913	986	223	1.05 (1.04 to 1.07)	< .001
No. of positive LNs	17,913	986	223	1.13 (1.08,1.19)	< .001
No. of pelvic LNs sampled	17,913	986	223	0.996 (0.99 to 1.003)	.27
Time-dependent ADT use					
Adjuvant ADT (t)	440	64	38	1.64 (1.21 to 2.23)	.002
Salvage ADT (t)	1,819	270	166	3.11 (2.60 to 3.72)	< .001

AHR represents the risk ratio of death between compared treatments per unit increase in the number of positive pelvic LNs -> aRT provide a proportional survival benefit for each additional positive node



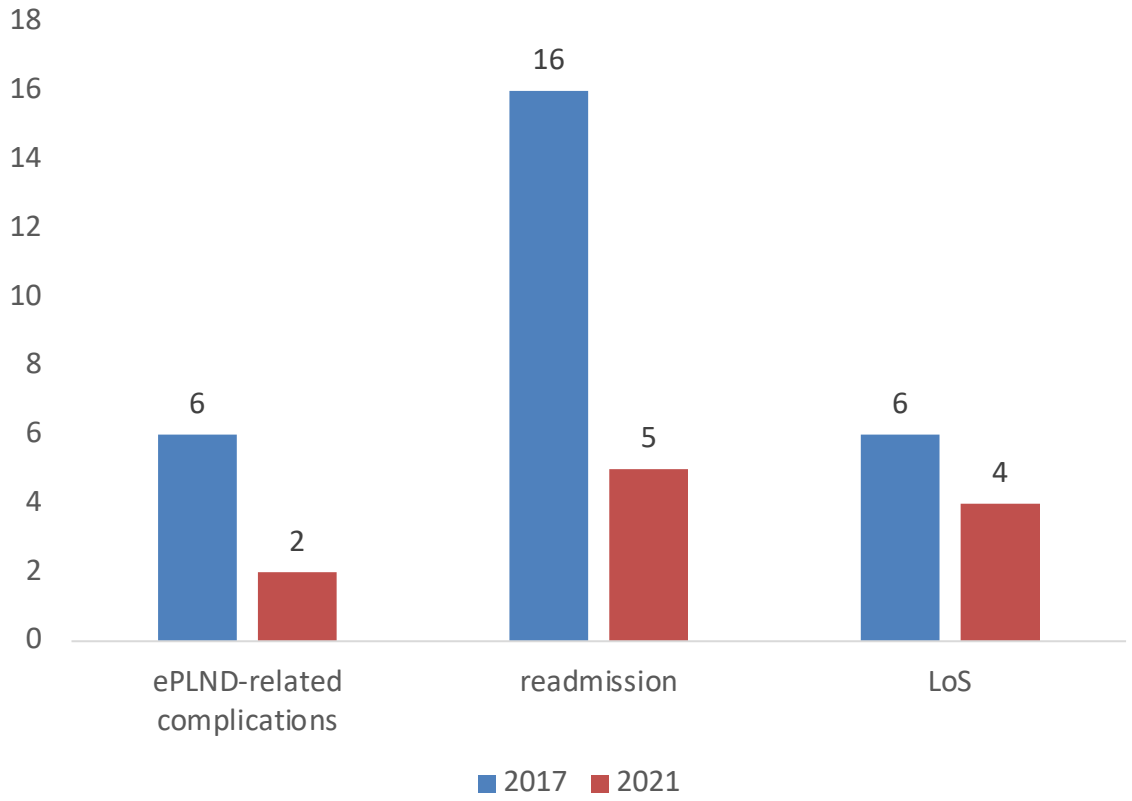
Patients **with ≥4 positive nodes** at final pathology

ART provided higher survival benefit compared to early SRT (7-yr OM 7 vs 23%, p=0.001)

Tilki et al., JCO 2022, 40(20):2186-2192.

Are Extended Pelvic Lymph Node Dissection-related complications still an issue in contemporary treated with robot assisted radical prostatectomy? A prospective Assessment using a Standardized Collection System for Perioperative Outcomes.

- ✓ We relied on prospectively collected data of 928 patients who underwent RARP ± ePLND for PCa from November 2017 to September 2021 at a tertiary center
- ✓ 661 (71%) men who received an ePLND
- ✓ The quality criteria recommended by the EAU were adopted for collecting complications. ePLND-related complications were divided in intra-operative (i.e., nerve, vessel, and ureteral injury) and post-operative at 30 and 90-days (i.e., lymphocele, lymphedema)
- ✓ A more recent year of surgery predicted with lower risk of overall and ePLND-related complications (OR: 0.96; p=0.02) and readmission (OR: 0.96; p<0.01).

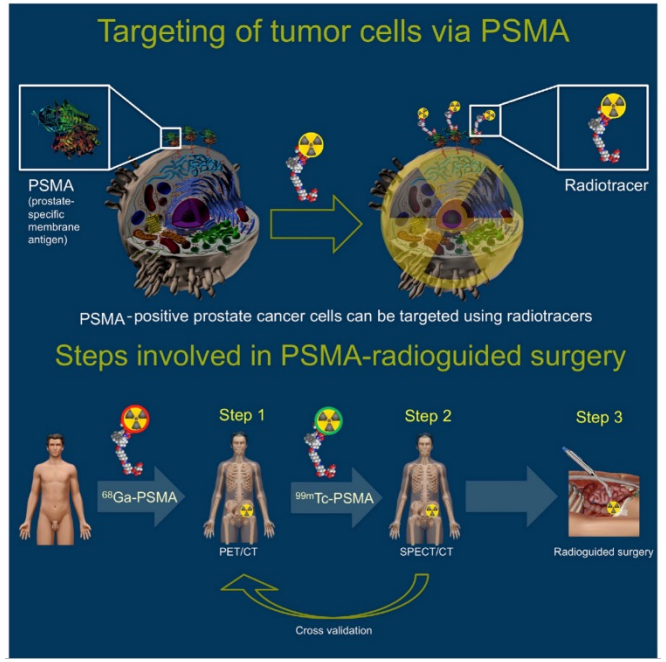


Briganti et al. EAU 2022

Novel approaches for ePLND

- ✓ PSMA Radio-Guided Surgery
- ✓ Sentinel Node Biopsy using ICG or hybrid tracer
- ✓ PSMA-based intraoperative fluorescence imaging

Can We Integrate PSMA and robotic ePLND?



Maurer et al. Eur Urol 2019;75:659-66

Technical University of Munich, Germany

Shilham et al. EAU 2021

Nijmegen, The Netherlands

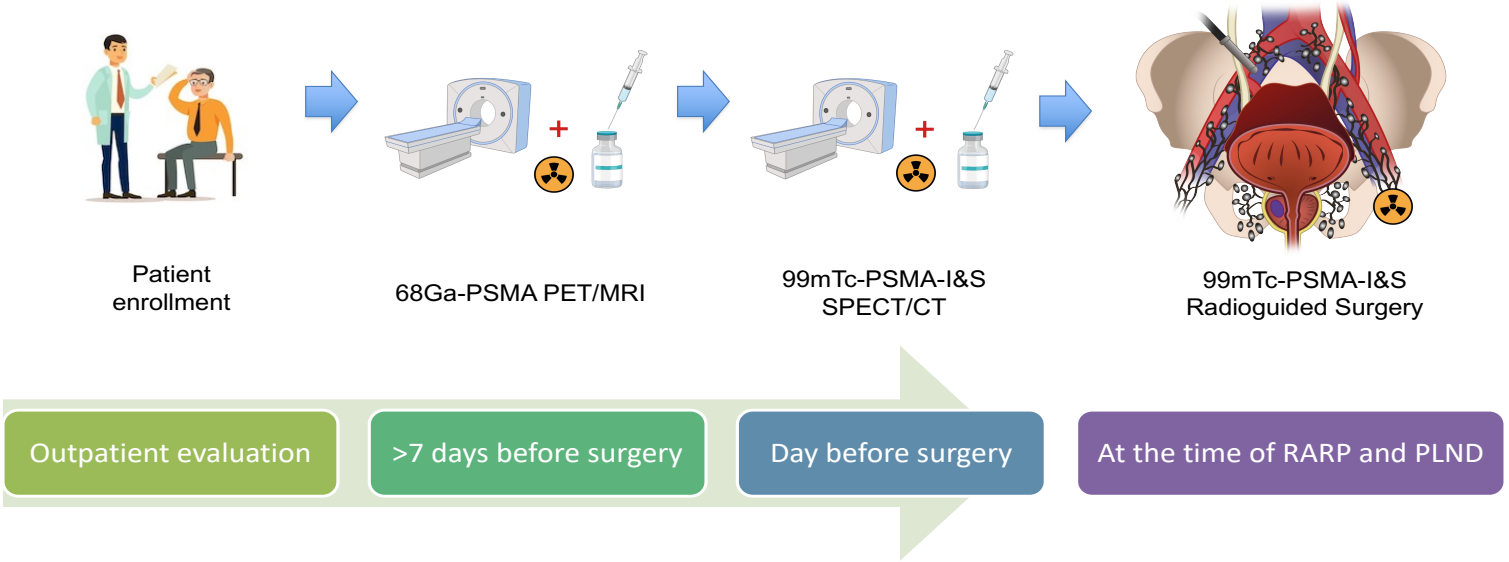
OBJECTIVES

- ✓ To optimize the synthesis of 99mTc-PSMA-I&S, to assess the safety and tolerability of the administration of 99mTc-PSMA-I&S and to describe the use of 99mTc-PSMA-radio-guided surgery (RGS) in nodal staging in PCa patients

- ✓ To assess the diagnostic accuracy of 99mTc-PSMA-RGS in the identification of LNI and to compare its predictive accuracy to preoperative 68Ga-PSMA PET/MRI and to available predictive tools such as the Briganti nomogram

PSMA Radio-Guided Surgery to Detect Nodal Metastases in PCa Patients Candidate to RARP + ePLND

- ✓ Phase 2 trial aimed at enrolling 100 patients
- ✓ Intermediate or high-risk cN0M0 PCa at conventional imaging
- ✓ LNI risk of LNI >5% (according to Briganti nomogram)
- ✓ Interim analysis of the first 21 patients.



Gandaglia er al., Eur Urol, 2022, in press

PSMA Radio-Guided Surgery to Detect Nodal Metastases in PCa Patients Candidate to RARP + ePLND

Per-lesion analysis

Accuracy of Probe in LNI detection	Positive Pathology	Negative Pathology
PSMA RGS pos	5	1
PSMA RGS neg	3	87
Sensitivity	63%	
Specificity	99%	
PPV	83%	
NPV	96%	

Per-patient analysis

Accuracy of Probe in LNI detection	Positive Pathology	Negative Pathology
PSMA RGS pos	2	0
PSMA RGS neg	1	9
Sensitivity	67%	
Specificity	100%	
PPV	100%	
NPV	90%	

Robot-assisted PSMA-RGS in the primary staging is a safe and feasible procedure characterized by an excellent specificity but suboptimal sensitivity, missing micro-metastatic nodal disease (3 mm or less).

Gandaglia er al., Eur Urol, 2022, in press

Discordant Patients at 68Ga, 99Tc and LNI – Per Patient analyses

^{68}Ga-PSMA PET/CT	^{99}99mTc-PSMA-I&S	LNI
5 (25%)	4 (20%)	7 (35%)

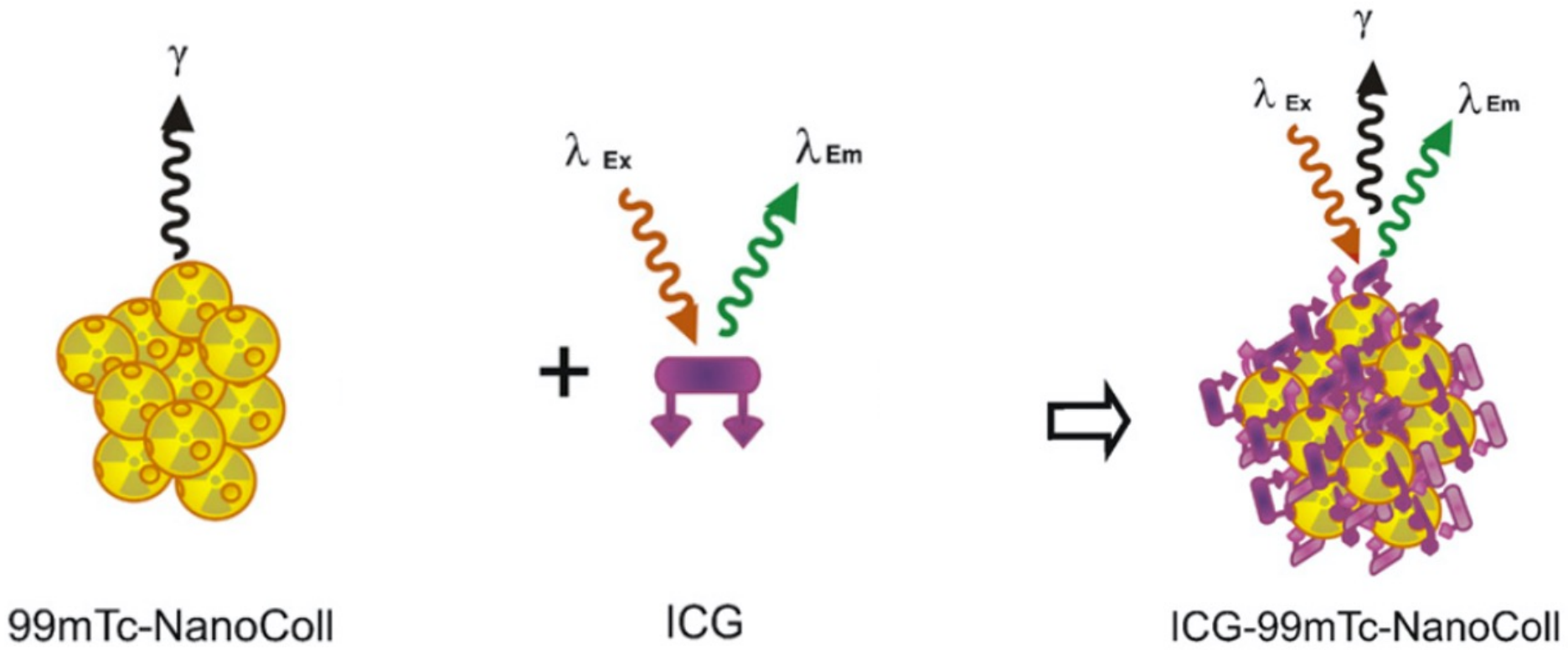
- 2 Discordant men between ^{68}Ga-PSMA and pathological report
- 1 Discordant men between ^{68}Ga-PSMA and ^{99}Tc-PSMA
- 3 Discordant men between ^{99}Tc-PSMA and pathological report

Patient	68Ga-PSMA	99-Tc PSMA	LNI
001	1	1	1
003	0	0	1
004	0	0	0
005	1	1	1
006	0	0	0
007	0	0	0
008	0	0	0
009	0	0	0
010	0	0	0
011	0	0	0
012	0	0	0
013	0	0	1
014	0	0	0
015	0	0	0
016	0	0	0
017	1	1	1
018	1	1	1
020	0	0	0
021	1	0	1
022	0	0	0

Patients diagnosed outside the boundaries of ePLND (N=7)

Patient	Briganti 2012	Briganti 2017	MRI-targeted	Site	^{68}Ga-PSMA	^{99}Tc-PSMA	LNI
001	75.8%	45.7%		Prevesical	0	0	1
003	36.4%	57.3%		Prevesical	0	0	1
013	8%	27%		Prevesical	0	0	1
015	4.8%	11.8%		Prevesical	0	0	1
017	7.30%	9.5%	12.8%	Right Common Iliac	0	0	1
				Left Common Iliac	0	0	1
				Presacral	1	0	1
018	4.4%	10.8%	10.5%	Right Common Iliac	0	0	1
				Left Common Iliac	0	1	1
021	7.7%	18.3%		Prevesical	0	0	1

Sentinel Node Biopsy using ICG or hybrid tracer in Prostate Cancer



99mTc-NanoColl was prepared by adding 1 ml pertechnetate (approximately 700 MBq) in saline to a vial containing NanoColl

0.250 mg of **ICG solution** were added to the 1-ml solution of 99mTc-Nanocoll.

Final **Hybrid ICG-99mTc-NanoColl** was prepared for intraprostatic injection

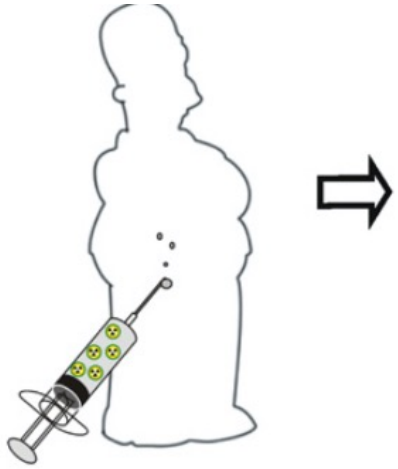
Van der Poel et al. Eur Urol. 2011

Sentinel Node Biopsy using ICG or hybrid tracer in Prostate Cancer

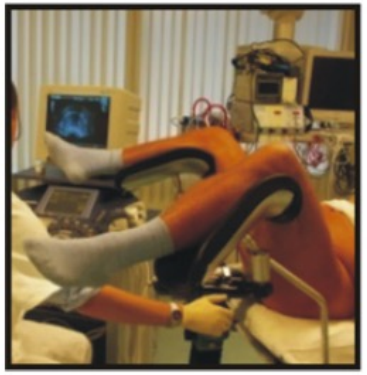
STEP 1
Intraprostatic Injection of the tracer

STEP 2
Preoperative SPECT/CT

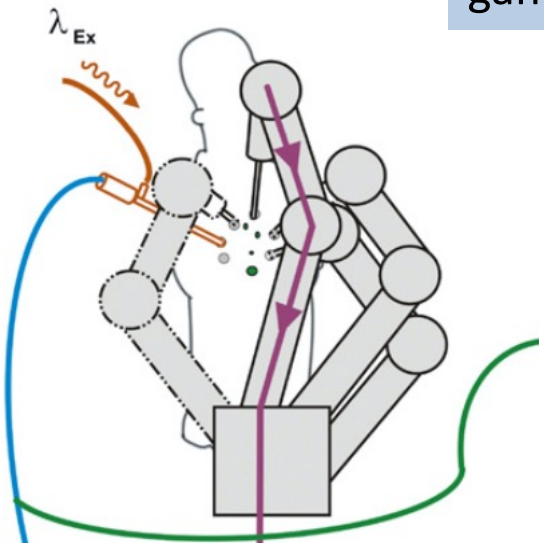
STEP 3
Intraprostatic SN detection using near-infrared fluorescence + gamma-probe



Tracer administration



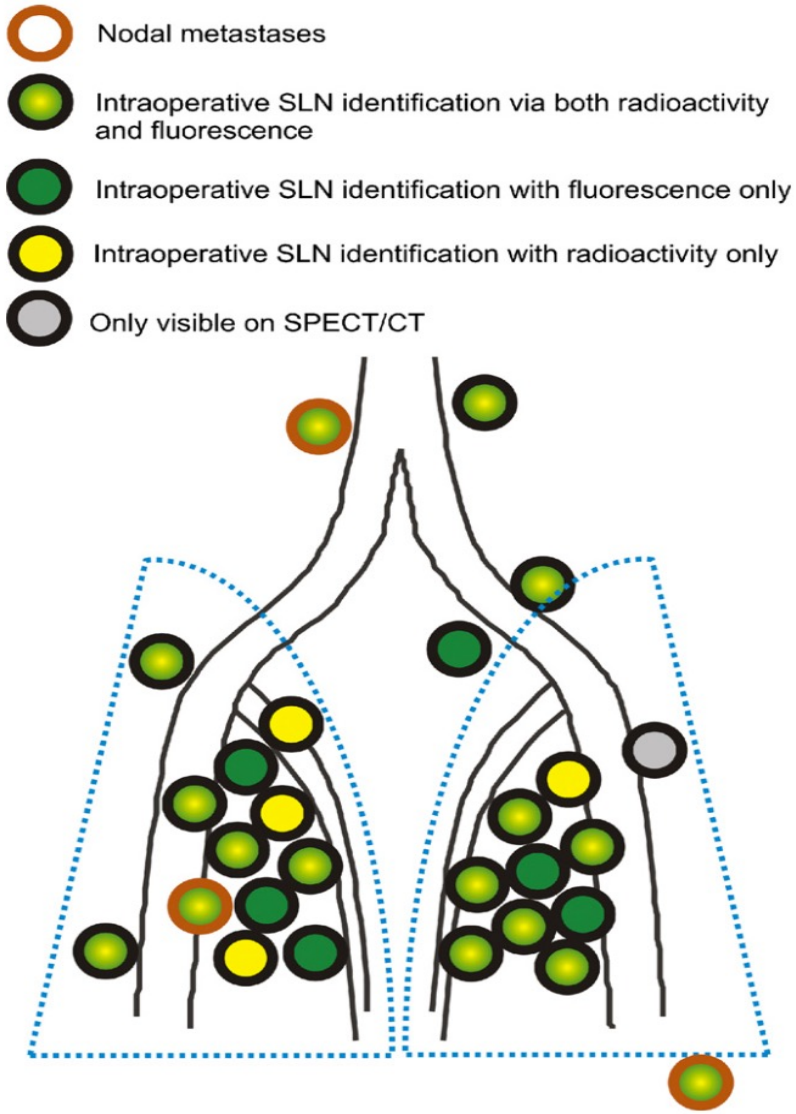
SPECT/CT



Van der Poel et al. Eur Urol. 2011

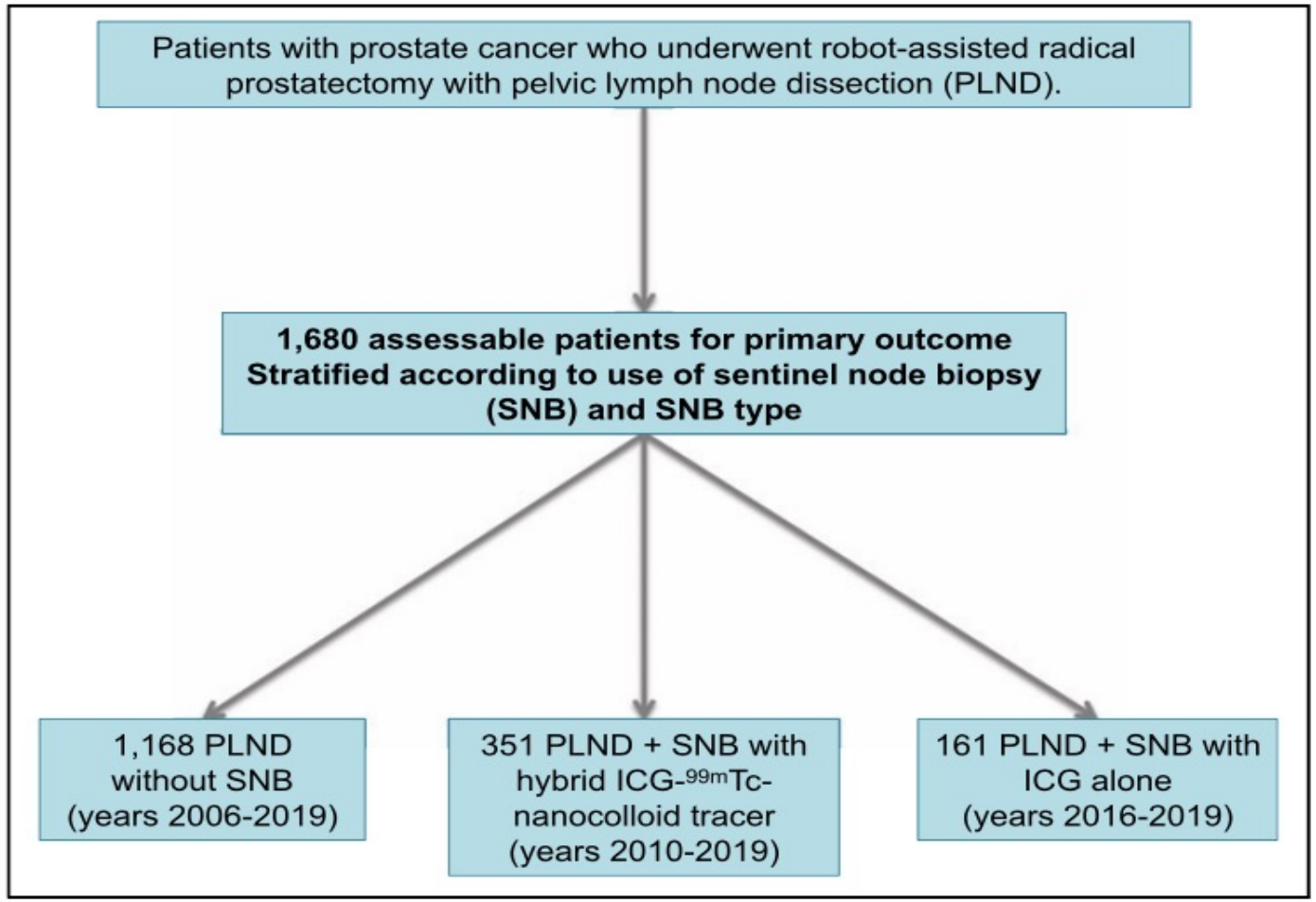
Sentinel Node Biopsy using ICG or hybrid tracer in Prostate Cancer

Modalities with which SN were identified



Van der Poel et al. Eur Urol. 2011

Sentinel Node Biopsy using ICG or hybrid tracer in Prostate Cancer: is there any clinical value?

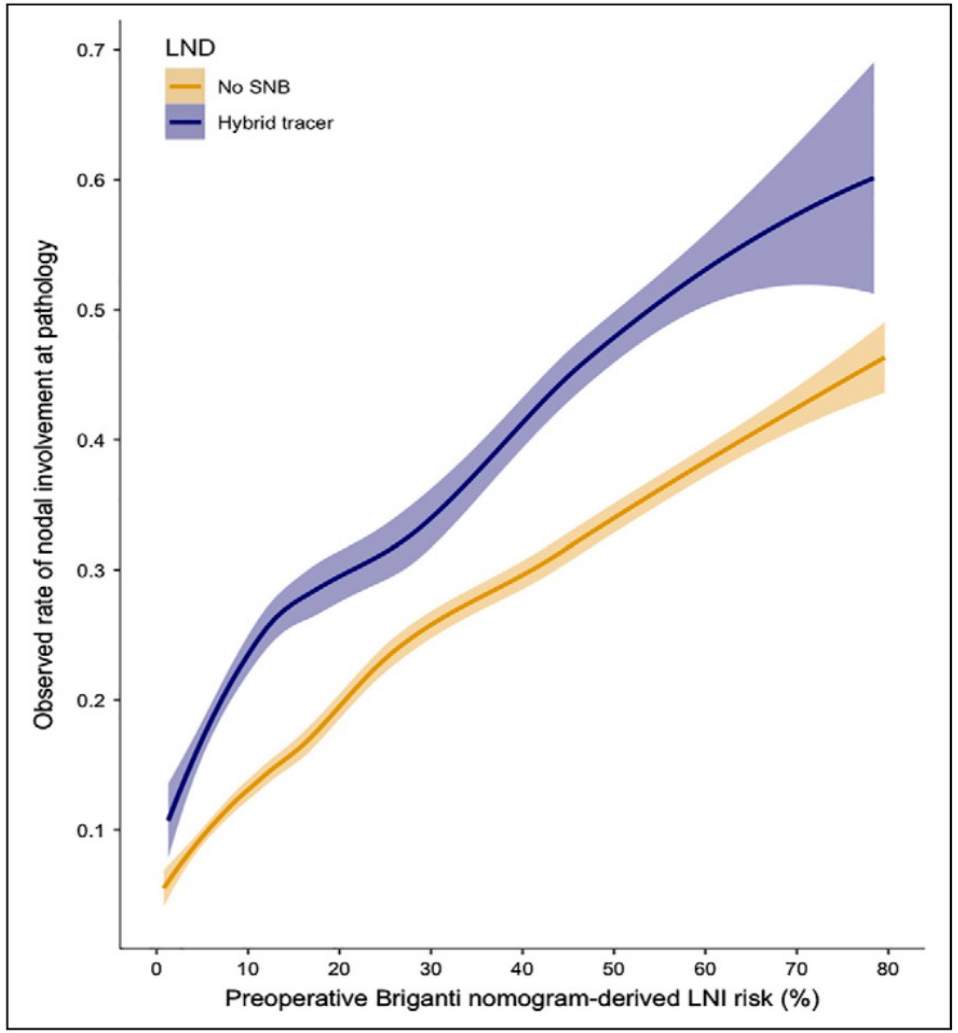


- ✓ 1,680 patients treated between 2006 and 2019 at a single institution
- ✓ Three patients' groups: PLND standard vs PLND + SNB with Hybrid tracer vs PLND + SNB with ICG alone
- ✓ Overall, patients with addition of SNB (Hybrid or ICG) had higher nodal retrieval (**median 20 vs 11 nodes removed**)

Mazzone et al. J Med Nucl. 2021; 62:1363–1371

Sentinel Node Biopsy using ICG or hybrid tracer in Prostate Cancer: is there any clinical value?

Actual LNI rate vs Predicted LNI risk

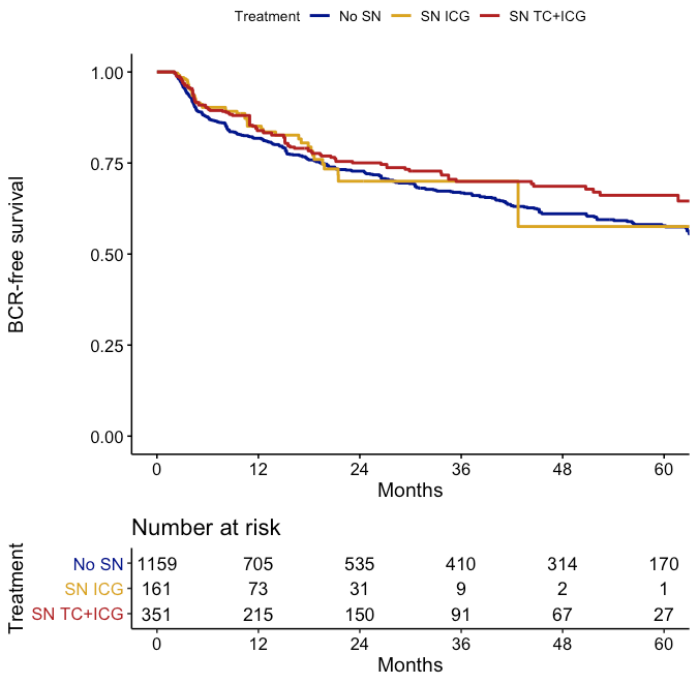


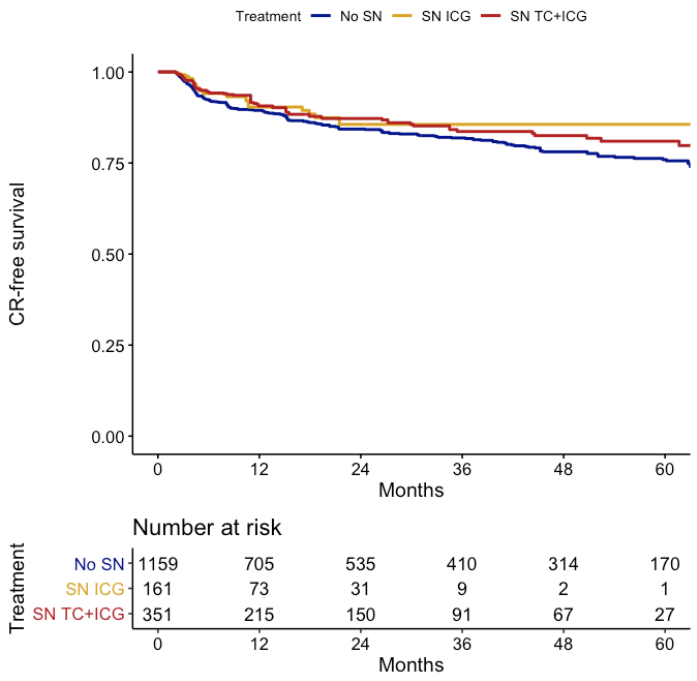
Logistic multivariable model predicting LNI

Variable	Parameter	OR	95%CI	*P*
cT stage	cT1c	Ref		
	cT2	1.14	0.74–1.79	0.4
	≥cT3	3.25	2.11–5.14	<0.001
Biopsy GS	6	Ref		
	7	1.99	1.20–3.46	0.009
	8–10	3.00	1.79–5.27	<0.001
cN stage	cNx	Ref		
	cN0	0.85	0.58–1.23	0.4
	cN1	3.02	1.84–4.98	<0.001
Percentage of positive cores		1.633	1.371–1.94	<0.001
PSA at RP		1.010	1.002–1.018	0.01
Number of removed nodes		1.032	1.015–1.049	<0.001
SNB use	Non-SNB	Ref		
	ICG SNB	1.35	0.89–2.03	0.1
	Hybrid SNB	1.61	1.18–2.20	0.002

Mazzone et al. J Med Nucl. 2021; 62:1363–1371

Sentinel Node Biopsy using ICG or hybrid tracer in Prostate Cancer: is there any clinical value?





		BCR			CR		
Variable	Parameter	HR	95%CI	*P*	HR	95%CI	*P*
SNB technique	Non-SNB	Ref					
	ICG SNB	0.84	0.61–1.15	0.2	0.73	0.49–1.11	0.1
	Hybrid SNB	0.79	0.63–0.98	0.037	0.76	0.58–0.98	0.035

Hybrid SNB technique with ICG-^{99m}Tc-nanocolloid improves detection of positive nodes and potentially lowers recurrence rates with subsequent optimization of patient management, without harming patient safety.

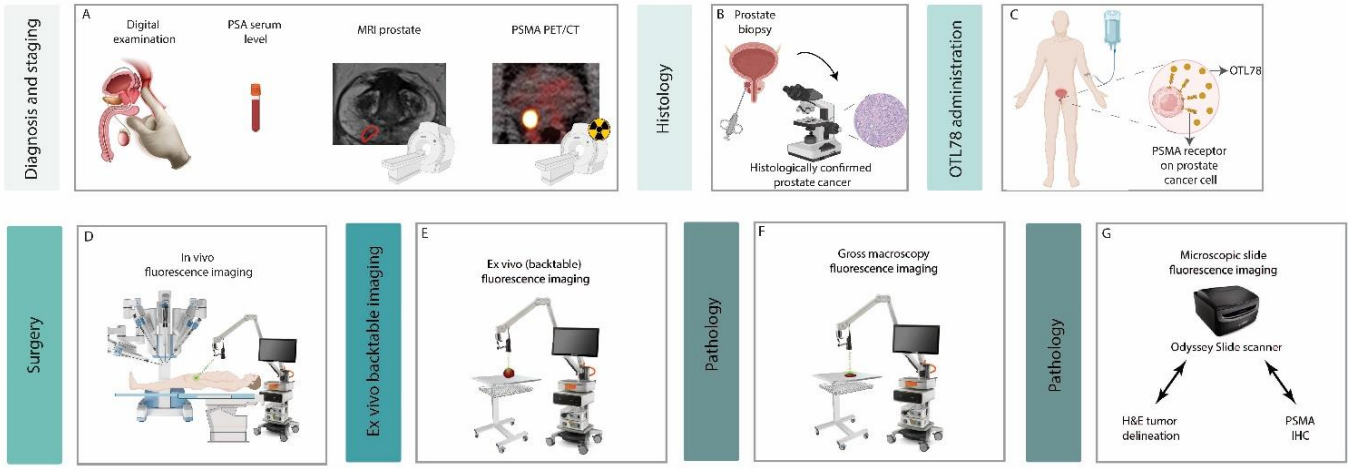
Mazzone et al. J Med Nucl. 2021; 62:1363–1371

OTL78 for intraoperative fluorescence imaging of PSMA positive prostate cancer

- ✓ Single Arm, phase 2a feasibility trial in 18 PSMA-positive patients candidates for surgery
- ✓ OTL78 : a high- affinity PSMA-targeting ligand conjugated to the near-infrared dye S0456 using a 14-atom-long polyethylene glycol-dipeptide linker.

- ✓ Single intravenous infusion of OTL78 before RARP +/- ePLND

Dose cohort 1: 0·06 mg/kg OTL78 administered 1–2 h preoperatively (dose cohort 1);
Dose cohort 2: 0·03 mg/kg OTL78 administered 1–2 h preoperatively (dose cohort 2);
Dose cohort 3: 0·03 mg/kg OTL78 administered 24 h preoperatively (dose cohort 3)



Stibbe et al Lancet Oncol 2023 ;24:457-467

OTL78 for intraoperative fluorescence imaging of PSMA positive prostate cancer

- ✓ Three serious Aes occurred unrelated to the administration of OTL78 or intraoperative fluorescence imaging
- ✓ **Optimal dosing was 0·03 mg/kg, 24 h preoperatively**
- ✓ False-positive lymph nodes (22%) were observed only when patients received OTL78 on the day of surgery and not in the 24 h dosing interval probably due to increased wash-out of OTL78 from the lymphatic system. However, this came with a higher false-negative rate for lymph nodes at in-vivo and ex-vivo backtable imaging (20% vs 100%) but very few positive LN clussters (n=7)

Stibbe et al Lancet Oncol 2023 ;24:457-467

The OSR Urology team: Thank you…!

Special THANKS to:

Giorgio Gandaglia
Vito Cucchiara
Nicola Fossati
Armando Stabile
Elio Mazzone
Carlo Bravi
Marco Bianchi
Nazareno Suardi
Marco Bandini
Giuseppe Rosiello
Firas Abdollah
Daniele Robesti