ROLE AND EXTENT OF PELVIC LYMPH NODE DISSECTION IN PSMA ERA

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Financial Relationships

Commercial Interest:	**Nature of Relationship:**
Elucida Oncology	*Co-inventor of intellectual property focused on tumor imaging nanoparticle technology licensed to Elucida Oncology*

The Association Between Total and Positive Lymph Node Counts, and Disease Progression in Clinically Localized Prostate Cancer

Timothy A. Masterson, Fernando J. Bianco, Jr., Andrew J. Vickers, Christopher J. DiBlasio, Paul A. Fearn, Farhang Rabbani, James A. Eastham and Peter T. Scardino*

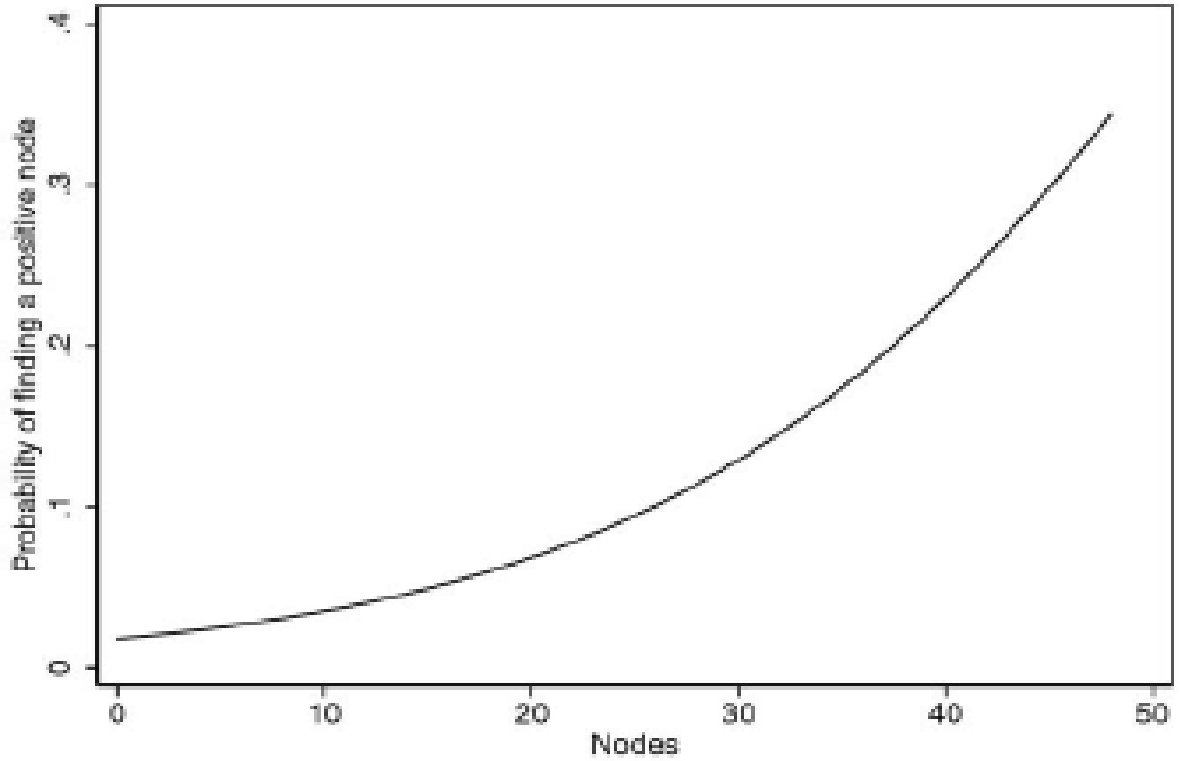
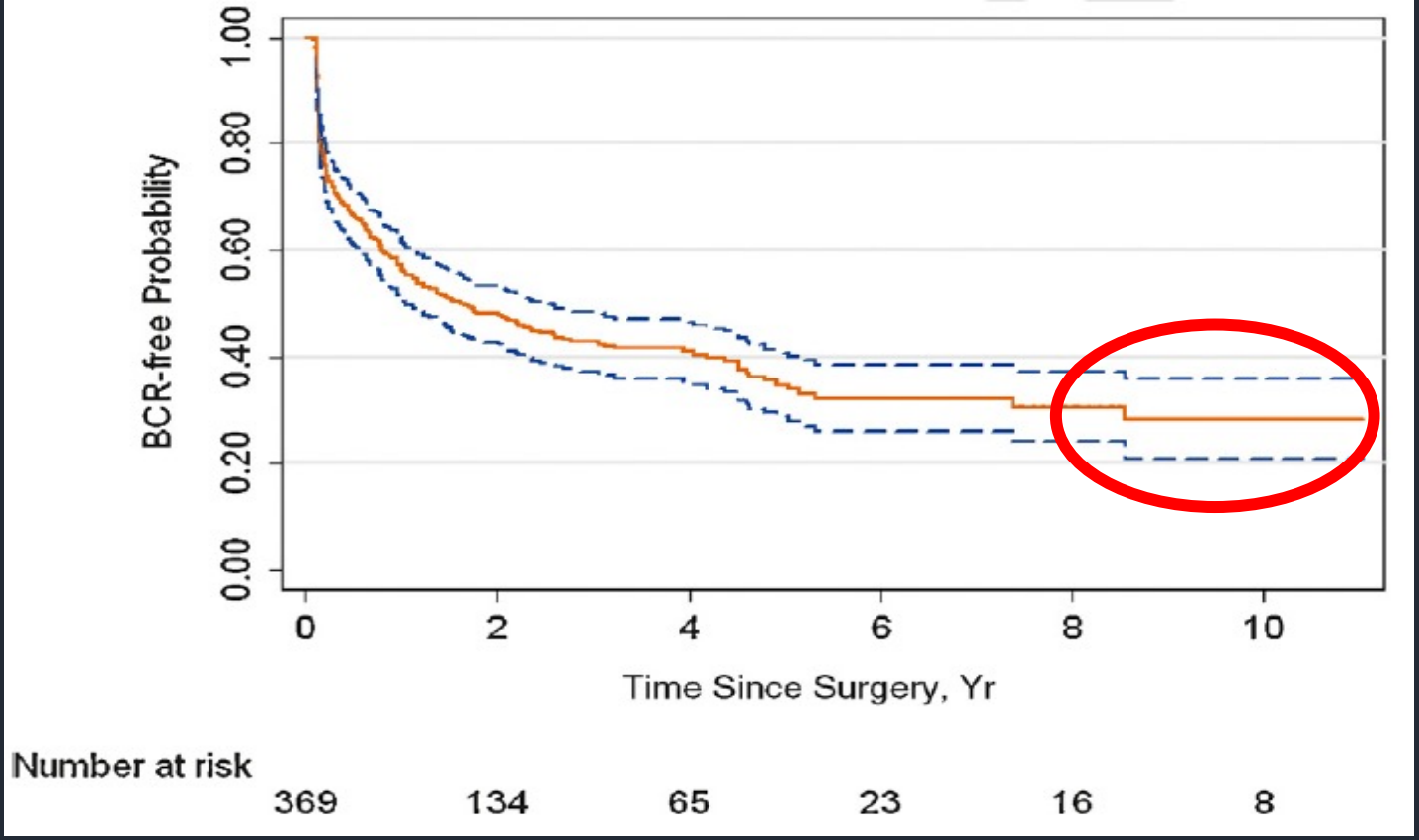
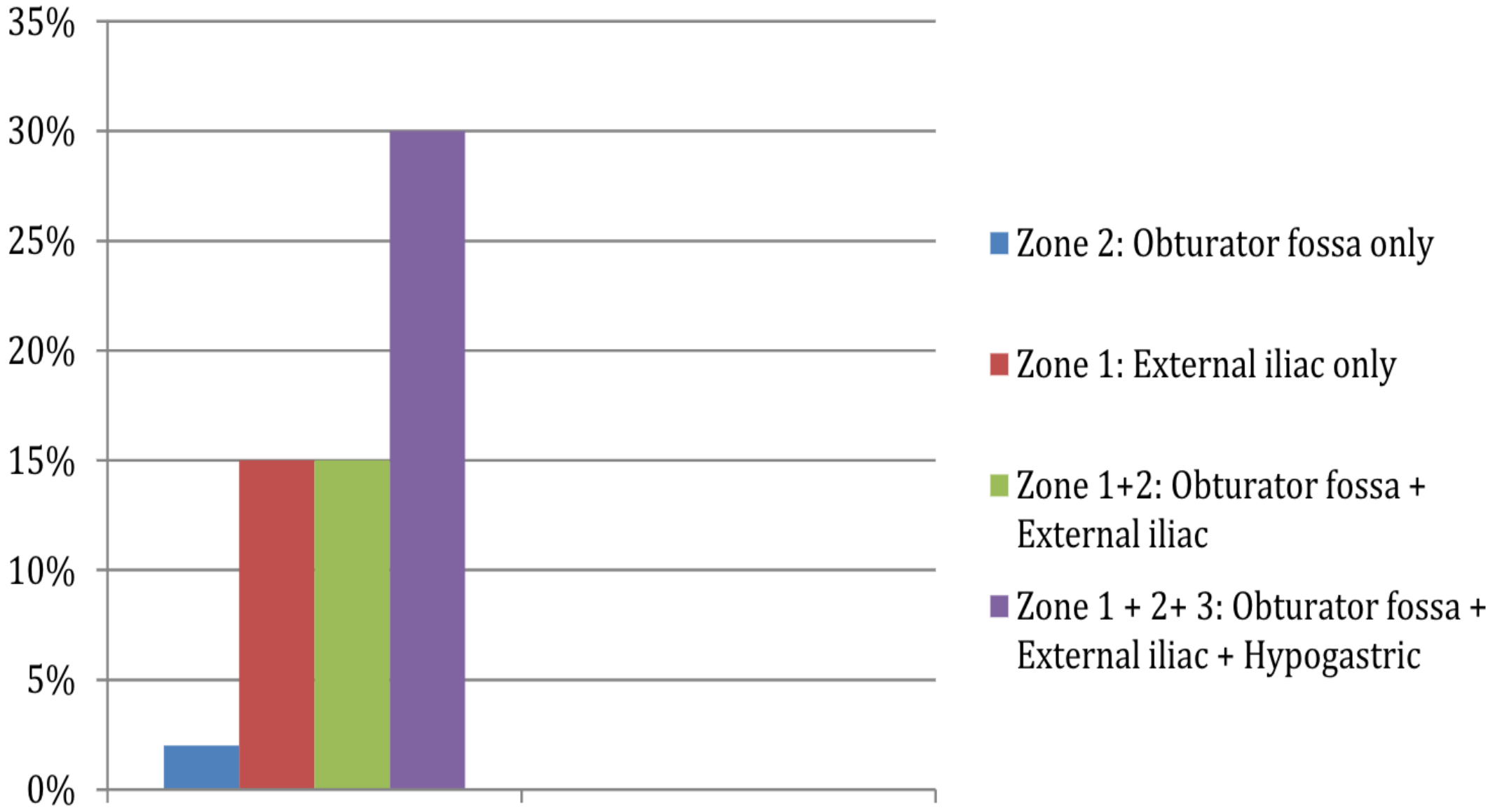


FIG. 2. Predicted probability of finding positive LN by number of nodes removed.

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

Karim A. Touijer [a,b,], Clarisse R. Mazzola [a], Daniel D. Sjoberg [c], Peter T. Scardino [a,b], James A. Eastham [a,b]*




35%
30%
25%
20%
15%
10%
5%
0%
Zone 2: Obturator fossa only
Zone 1: External iliac only
Zone 1+2: Obturator fossa + External iliac
Zone 1 + 2+ 3: Obturator fossa + External iliac + Hypogastric

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

Karim A. Touijer[a,*], Daniel D. Sjoberg[b], Nicole Benfante[a], Vincent P. Laudone[a], Behfar Ehdaie[a], James A. Eastham[a], Peter T. Scardino[a], Andrew Vickers[b]

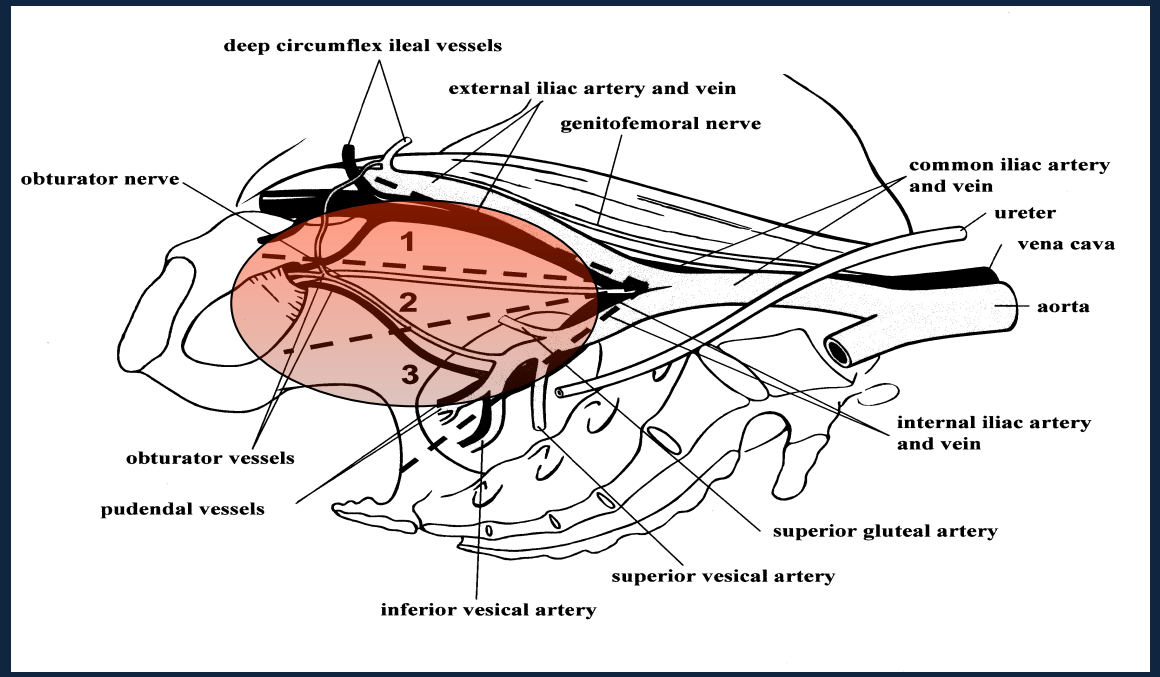
[a]Urology Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA

TARGET ACCRUAL 1400 PATIENTS OVER 5 YEARS

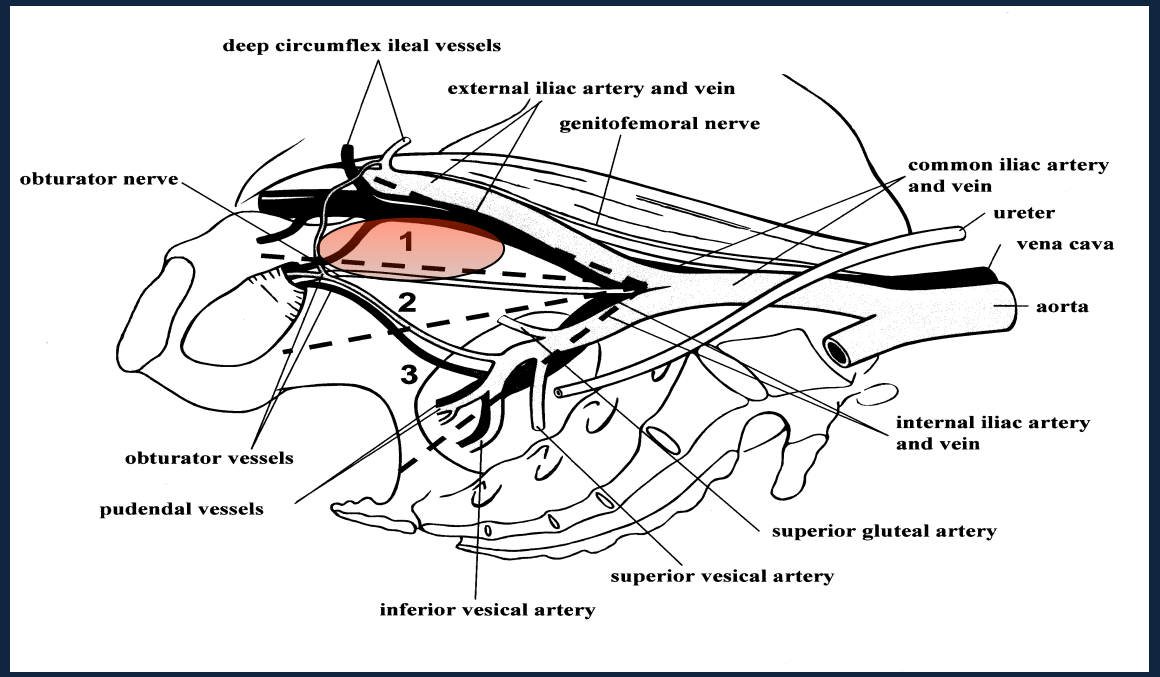
ONE YEAR FOLLOW-UP AFTER THE FINAL ACCRUAL

EXPECTED RECURRENCE RATE AT 5 YEARS OF 23%

EXTENDED



LIMITED (Ext. Iliac)



TRIAL DESIGN

OCTOBER 2011 TO MARCH 2017

1573 MEN UNDERGOING RP AT MSKCC CONSENTED TO THE TRIAL

OPEN – LAP – ROBOTIC

Touijer et al. Eur Urol Onc, 2021,

TRIAL DESIGN

1480 PATIENTS REGISTERED

757 RANDOMIZED TO THE EXTENDED PLND

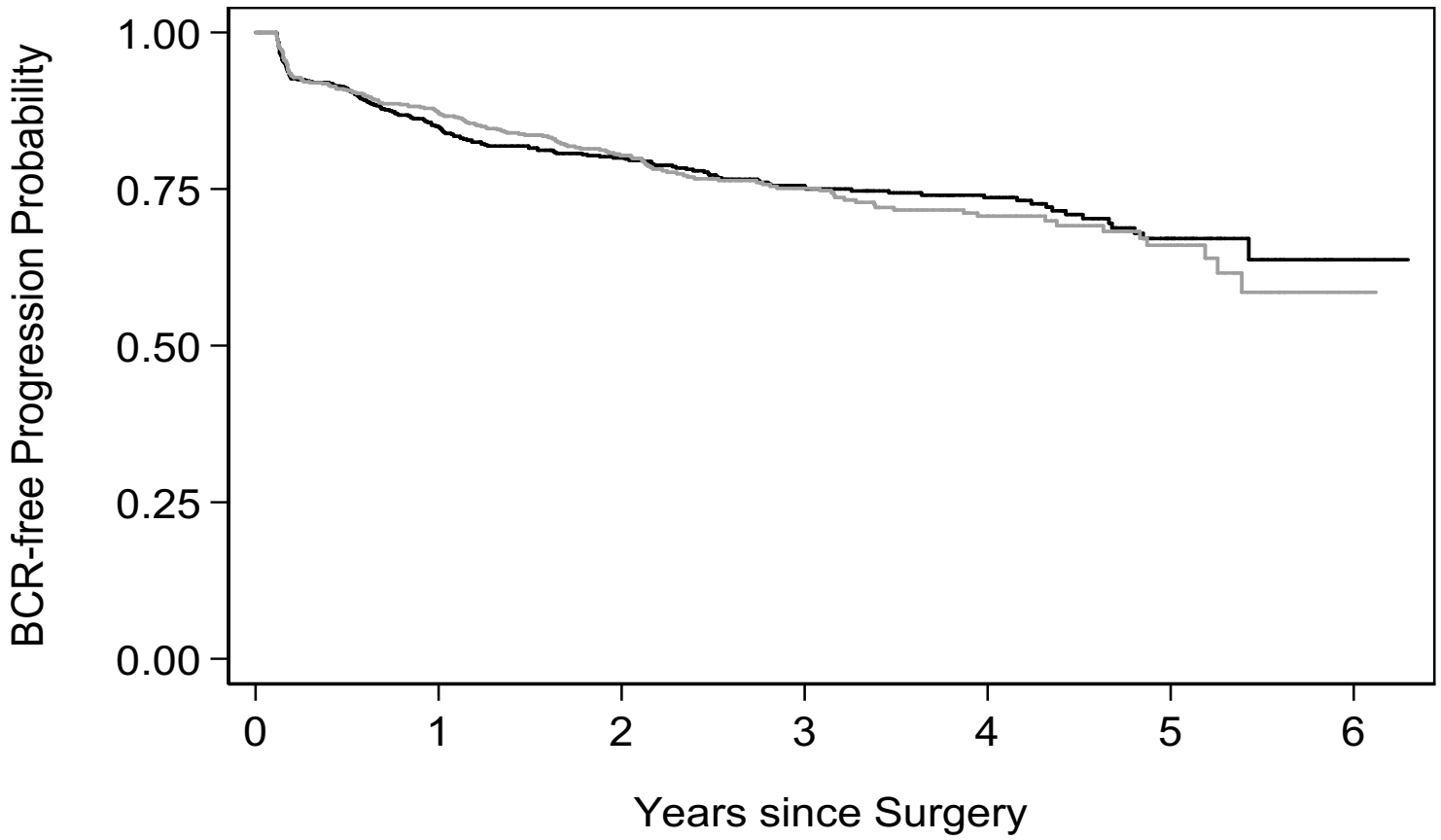
723 RANDOMIZED TO THE LIMITED PLND

Touijer et al. Eur Urol Onc, 2021,

TRIAL DESIGN

PRIMARY ENDPOINT: TIME TO BCR

Touijer et al. Eur Urol Onc, 2021,

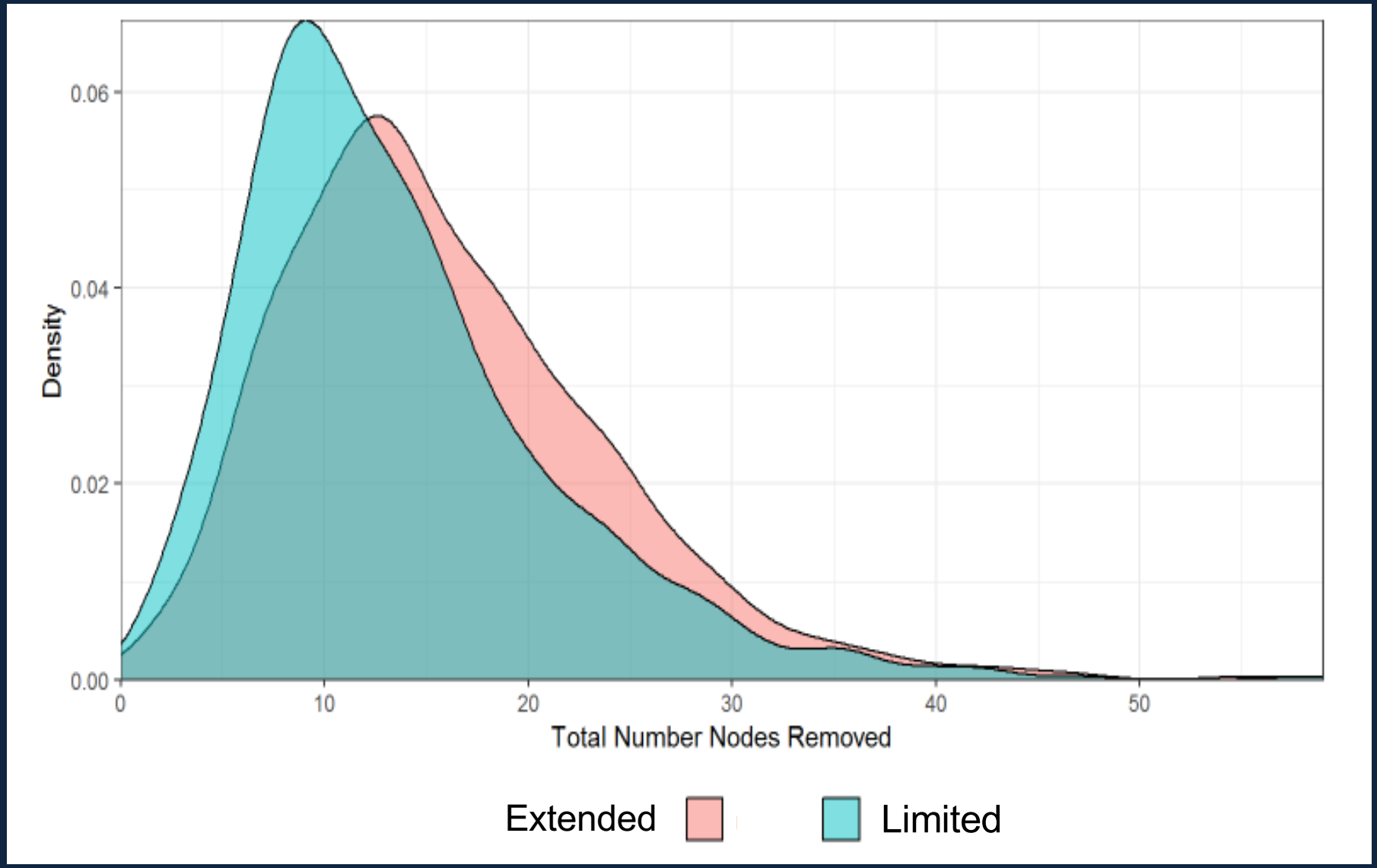


Number at risk							
Limited Template	798	570	433	276	182	58	5
Extended Template	746	559	361	223	137	53	4

Touijer et al. Eur Urol Onc, 2021,

Karim Touijer
Memorial Sloan-Kettering Cancer Center

Variable	Hazard Ratio	95% Confidence Interval	p-value
All Men in Trial	0.99	0.84, 1.17	0.9
Enrolled after June 2015	1.11	0.64, 1.93	0.7
Meta Analysis*	0.98	0.84, 1.15	0.8



Touijer et al. Eur Urol Onc, 2021,

LIMITED VS. EXTENDED PLND TRIAL

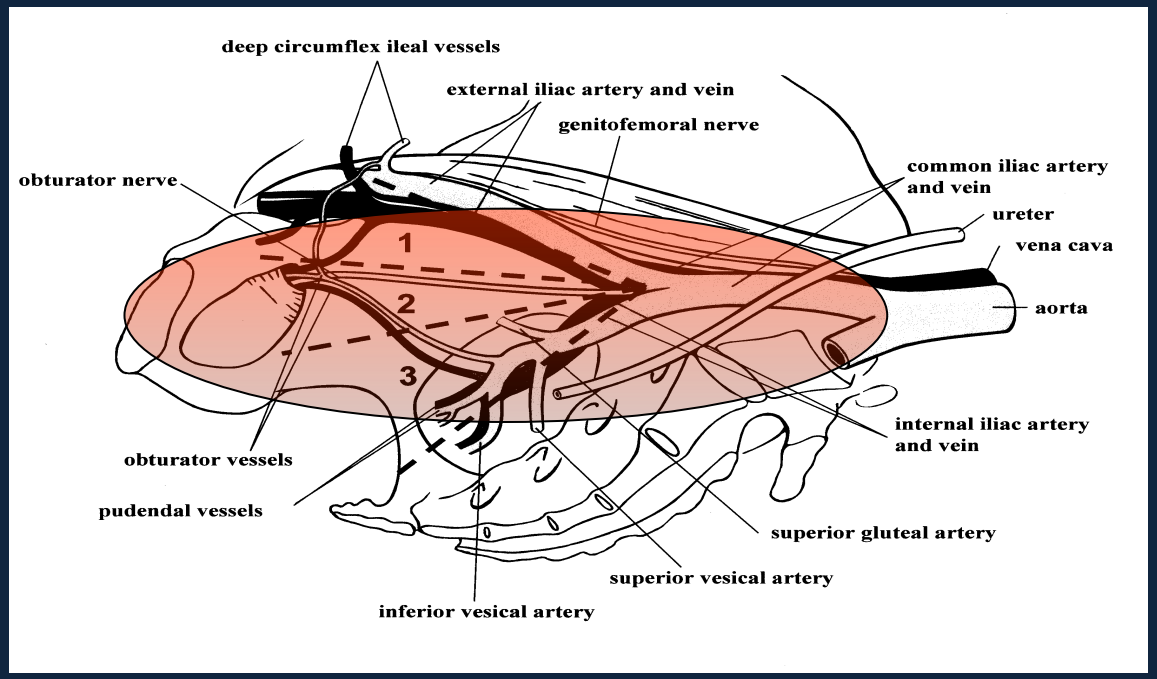
300 PATIENTS REGISTERED

150 RANDOMIZED TO THE EXTENDED PLND

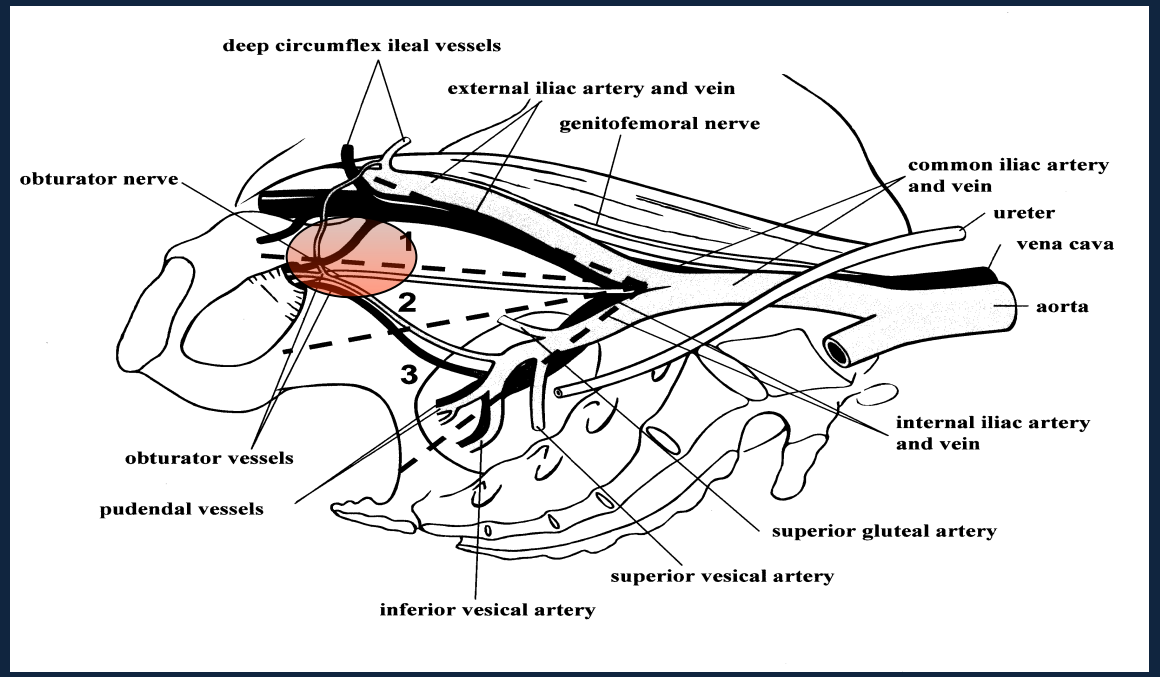
150 RANDOMIZED TO THE LIMITED PLND

Lestingi et al . Eur Urol, 2020

Superextended



Limited (obturator fossa)

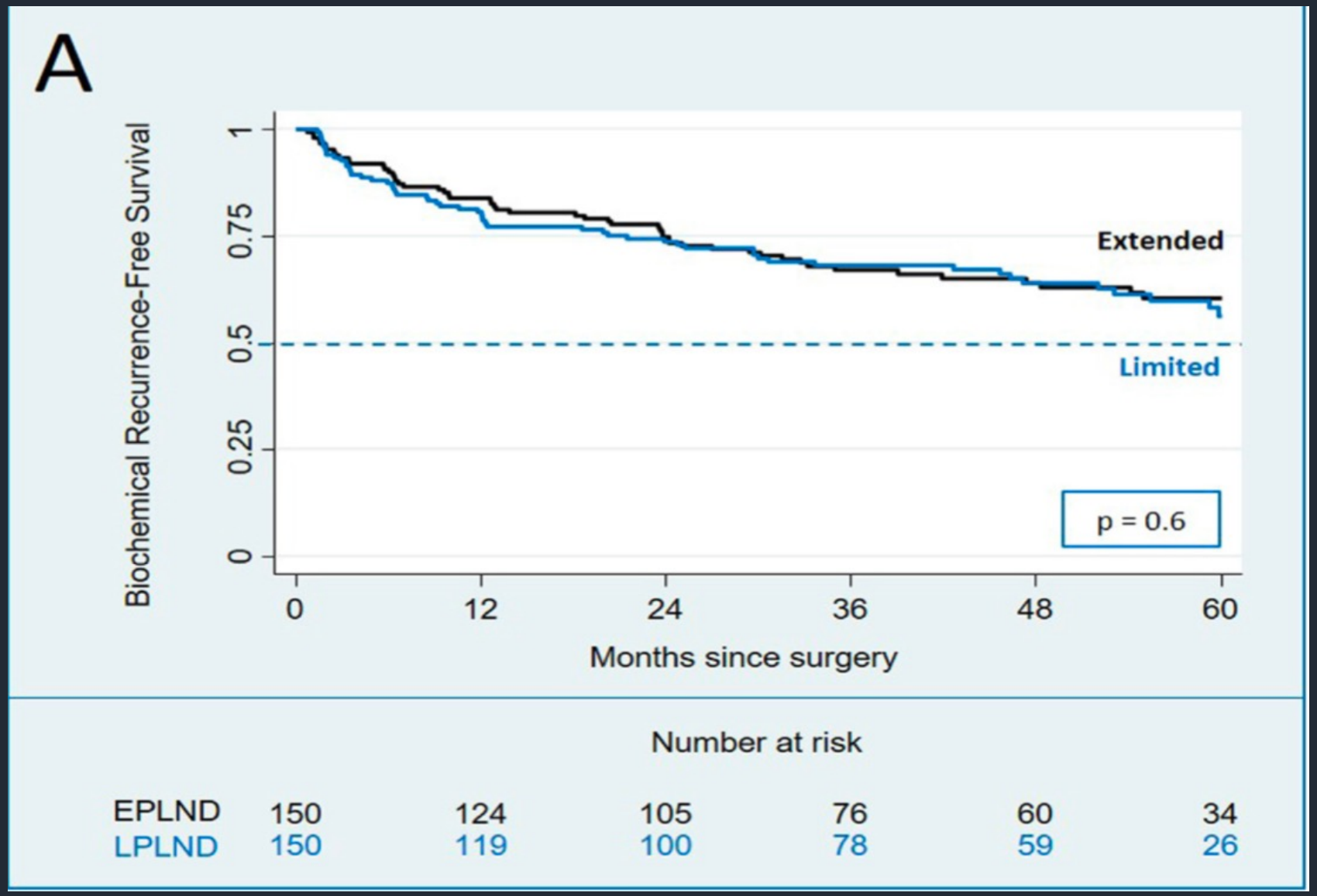


Lestingi et al . Eur Urol, 2020

Karim Touijer
Memorial Sloan-Kettering Cancer Center

Parameter	EPLND	LPLND	*p* value
Prostatectomy Gleason score, *n* (%)			
6 (ISUP GG1)	4 (2.7)	6 (4)	0.8 **
7 (3+4; ISUP GG2)	83 (55)	73 (49)	
7 (4+3; ISUP GG3)	45 (30)	46 (31)	
8 (4+4; ISUP GG4)	2 (1.3)	1 (0.7)	
9, 10 (4+5, 5+4, 5+5; ISUP GG5)	16 (11)	23 (15)	
Median percentage of tumor volume, % (IQR)	16 (10–25)	16 (10–29)	0.5 *
pT stage, *n* (%)			NA
T0	0	1 (0.7)	
T2	61 (41)	57 (38)	
T3a (extraprostatic extension)	67 (45)	64 (43)	
T3b (seminal vesicle involvement)	21 (14)	27 (18)	
T4	1 (0.7)	1 (0.7)	
Positive surgical margins, *n*/*N* (%)	65 (44)	55 (37)	0.2 **
T2 with positive surgical margins	17/61 (28)	12/57 (21)	0.3 **
≥T3 with positive surgical margins	49/89 (55)	43/92 (47)	0.2 *
Number of lymph nodes dissected			<0.001 *
Median, *n* (IQR)	17 (13–24)	3 (2–5)	
Mean, *n* (standard deviation)	18.5 (9.8)	4.5 (4)	
Patients with lymph node metastasis (N+), *n* (%)	25 (17)	5 (3.4)	<0.001 **
D'Amico intermediate risk (N+), *n*/*N* (%)	10/91 (11)	0	0.001 **
D'Amico high risk (N+), *n*/*N* (%)	15/57 (26)	5/55 (9)	0.017 **

Lestingi et al . Eur Urol, 2020



Lestingi et al . Eur Urol, 2020

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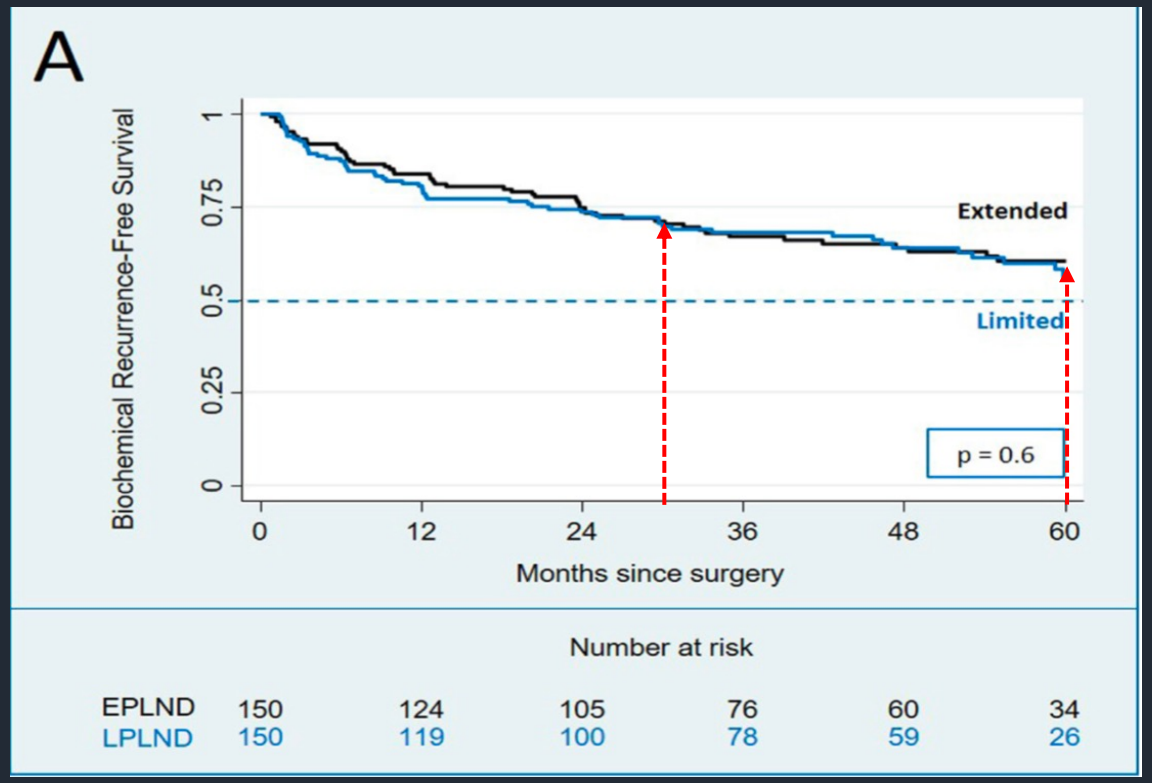
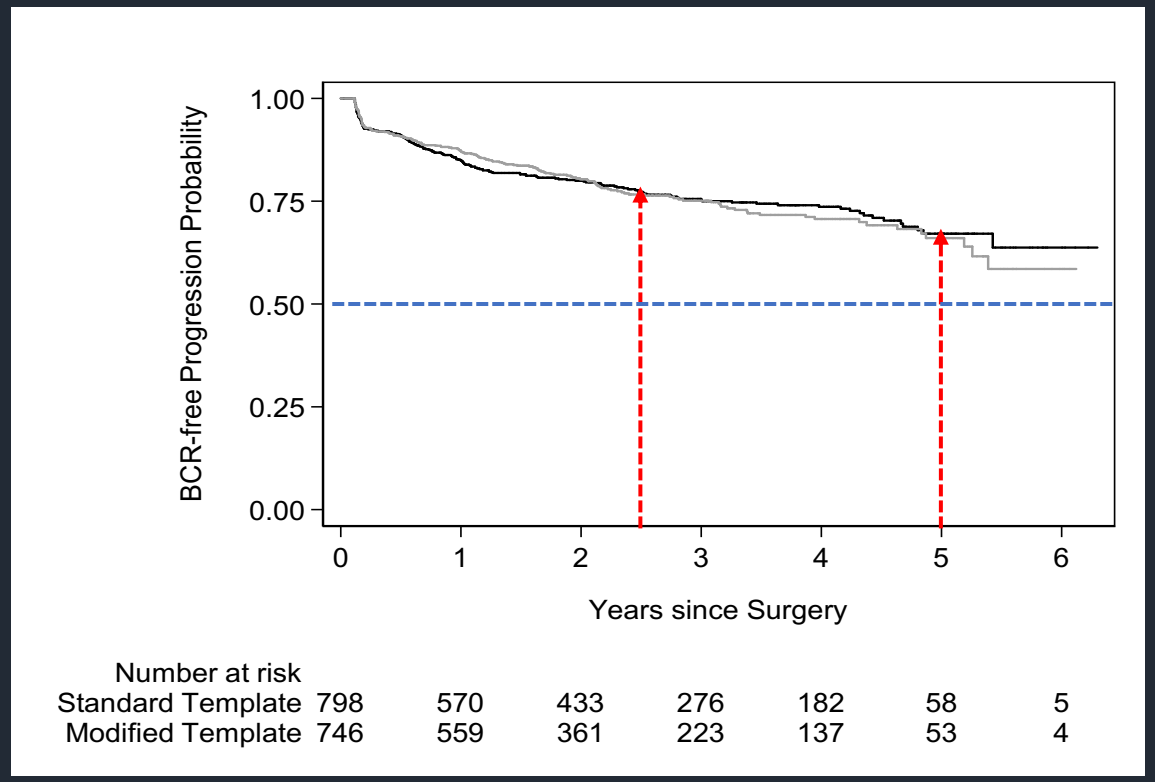
Sao Paulo, Br.

HR: 0.91, 95% CI: 0.63 – 1.32 p=0.6



MSKCC

HR: 0.99, 95% CI: 0.84 – 1.17 p=0.9



Touijer et al. Eur Urol Onc, 2021,

Lestingi et al . Eur Urol, 2020

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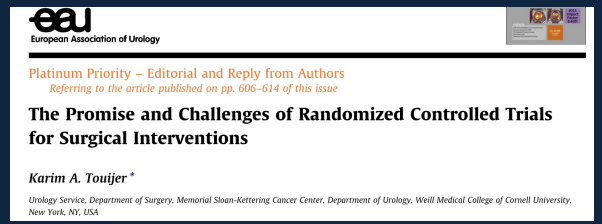
CHALLENGES OF SURGICAL TRIALS OF LYMPHADENECTOMY

UNDERPOWERED

LACK OF BLINDING

SURGICAL IMPRECISION


European Association of Urology

Platinum Priority – Editorial and Reply from Authors

Referring to the article published on pp. 606–614 of this issue

The Promise and Challenges of Randomized Controlled Trials for Surgical Interventions

Karim A. Touijer *

Urology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, Department of Urology, Weill Medical College of Cornell University, New York, NY, USA

Blencowe NS, et al. Standardizing and monitoring the delivery of surgical interventions in randomized clinical trials. *The British journal of surgery* 2016; **103**(10): 1377-84.
Landheer ML, Quality assurance in surgical oncology (QASO) within the European Organization for Research and Treatment of Cancer (EORTC): current status and future prospects. *European journal of cancer (Oxford, England : 1990)* 2001; **37**(12): 1450-62

PLND vs. NO PLND RCT - MSKCC. NCT01407263

Results:

- From July 2020 - Jan 2023; we've enrolled 600 + patients
- Our trial is on track to complete accrual within our 5-year goal.

^{68}Ga- PSMA to Detect Metastatic Lymph Nodes Prior to RP

Meta-analysis

11 STUDIES

- **^{68}Ga-PSMA by Patients:**

Sensitivity	33 % – 100%
Specificity	80% - 100 %

- **^{68}Ga-PSMA by LN fields:**

Sensitivity	24 % – 96%
Specificity	98% - 100 %

Luiting et al. BJU Int. 2020;125:206-216

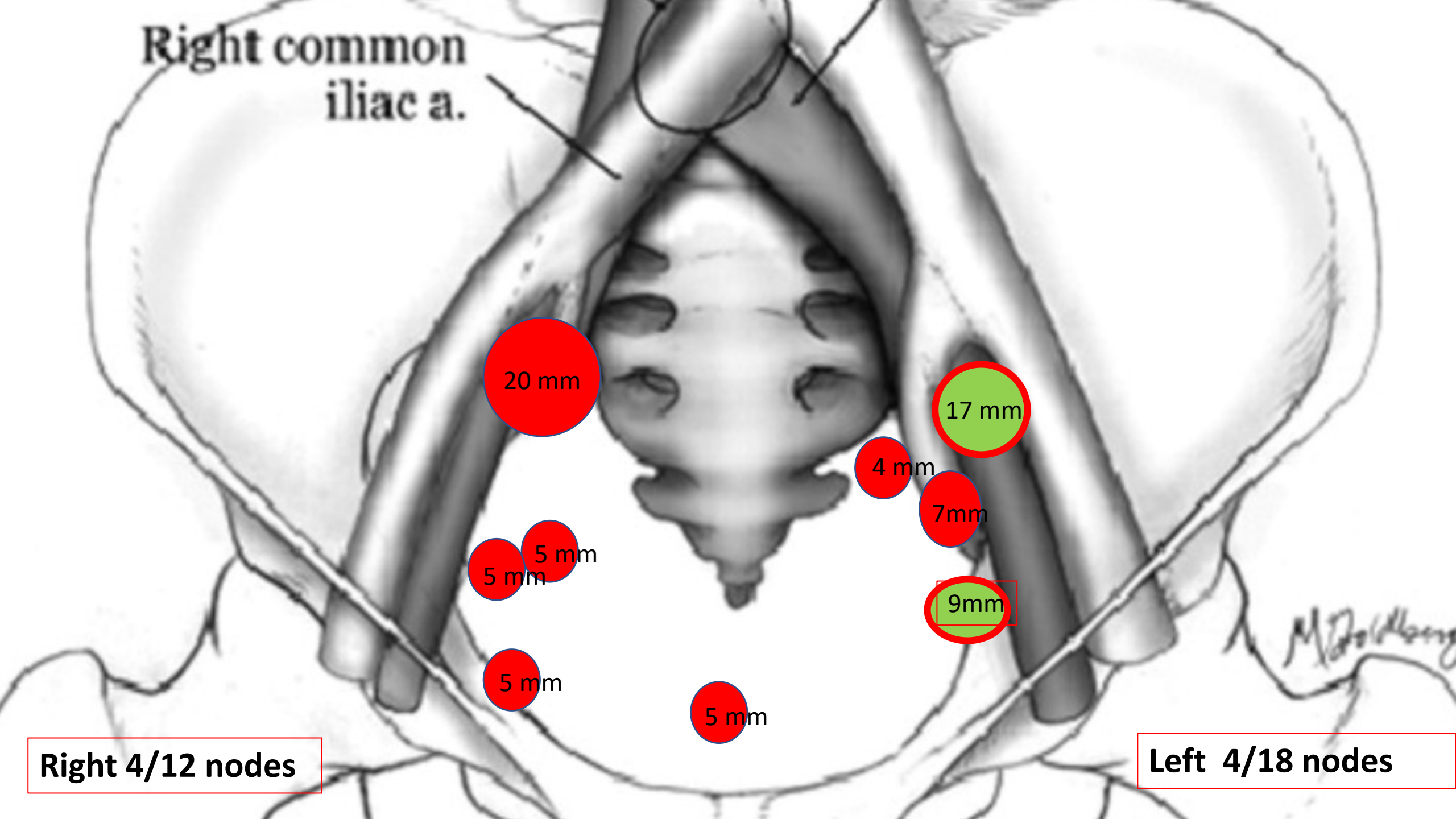
Targeting PSMA to Detect and Localize Metastatic Lymph Nodes Prior to RP

Diameter of LN.	Detection rate PSMA
0.1 mm - 1.9 mm	0%
2.0 mm - 4.9 mm	60%
>= 5 mm	86%

Van Leeuwen et al. BJU Int. 2016

Patients	PET Node status	Path node status	Number of missed nodes	Size of missed nodes
1	N1 (2 nodes)	N1 (9/30)	7	4mm – 20 mm
2	N1 (5 nodes)	N1 (5/22)	2	3.5mm – 8 mm
3	N1 (1)	N1 (2/18)	1	5mm
4	N0	N1 (2/23)	2	1mm – 6mm
5	N0	N1 (1/23)	1	3mm
6	N0	N1 (1/22)	1	8mm
7	N0	N1 (1/44)	1	6mm
8	N0	N1 (1/28)	1	5mm
9	N0	N1 (1/38)	1	11mm
10	N0	N1 (1/29)	1	8mm

277 nodes removed , 24 positive on path and **8/24** detected by PSMA PET. (33%)


Right common
iliac a.
20 mm
17 mm
4 mm
7mm
5 mm
5 mm
9mm
5 mm
5 mm
Right 4/12 nodes
Left 4/18 nodes

Right pelvic lymph nodes:

Metastatic prostatic adenocarcinoma
Number of lymph nodes examined: 11
Number of lymph nodes with metastatic disease: 2
Size of the largest lymph node involved by tumor: 1.8cm.
Size of the largest metastatic focus : 0.5 cm

Left pelvic lymph nodes:

Metastatic prostatic adenocarcinoma, see comment
Number of lymph nodes examined: 19
Number of lymph nodes with metastatic disease: 11
Size of the largest lymph node involved by tumor: 3.5cm.
Size of the largest metastatic focus : 1.6 cm.

Interaorta cava

Metastatic
Number o
Number of lymph nodes with metastatic disease: 31
Size of the largest lymph node involved by tumor: 1.8cm.
Size of the largest metastatic focus : 1.7 cm.

84/105 positive lymph nodes

oma
ed: 15
Number of lymph nodes with metastatic disease: 15
Size of the largest lymph node involved by tumor: 2.4cm.
Size of the largest metastatic focus : 2.4 cm

Presacral bilateral common iliac nodes:

Metastatic prostatic adenocarcinoma
Number of lymph nodes examined: 13
Number of lymph nodes with metastatic disease: 13
Size of the largest lymph node involved by tumor: 2.4cm.
Size of the largest metastatic focus : 2.0 cm.

Left common iliac posterior lateral nodes:

Metastatic prostatic adenocarcinoma
Number of lymph nodes examined: 12
Number of lymph nodes with metastatic disease: 12
Size of the largest lymph node involved by tumor: 1.8cm.
Size of the largest metastatic focus : 1.8 cm.

Pelvic Lymph Nodes, left:

Metastatic prostate adenocarcinoma

Number of lymph nodes examined: 8
Number of lymph nodes with metastatic disease: 2
Size of the largest lymph node involved by tumor: 0.5cm.
Size of the largest metastatic focus : 0.2 cm.

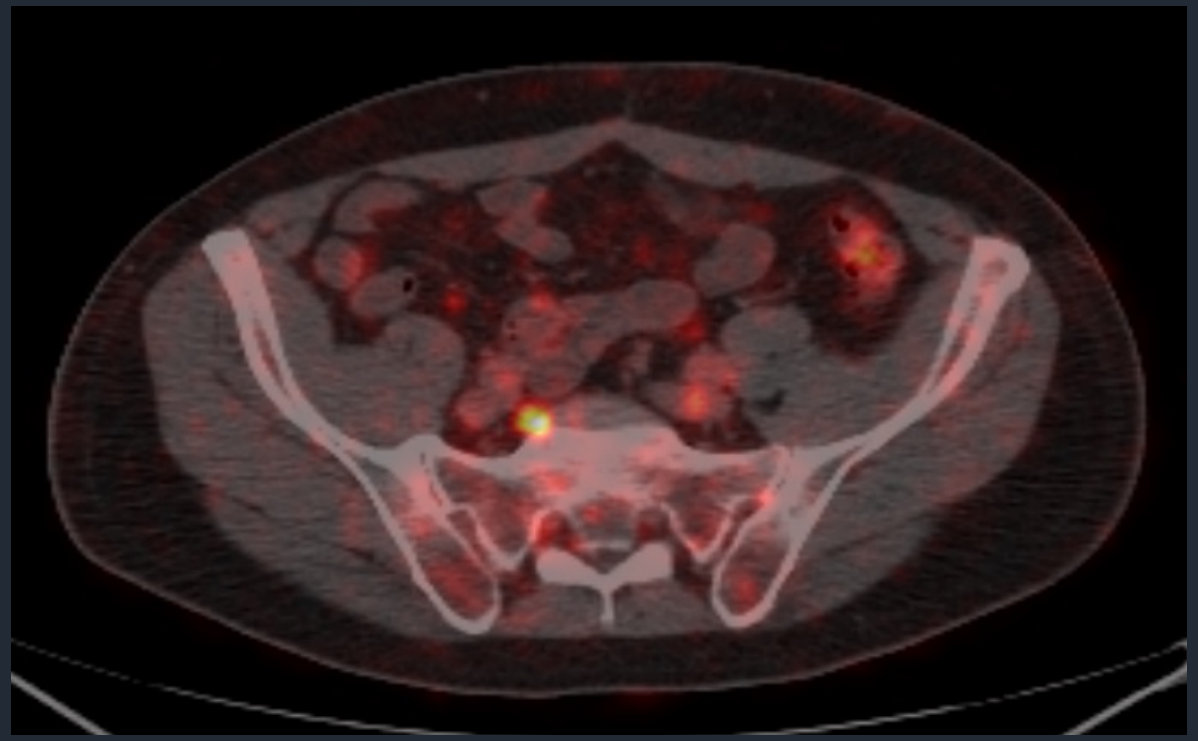
10/22 positive lymph nodes

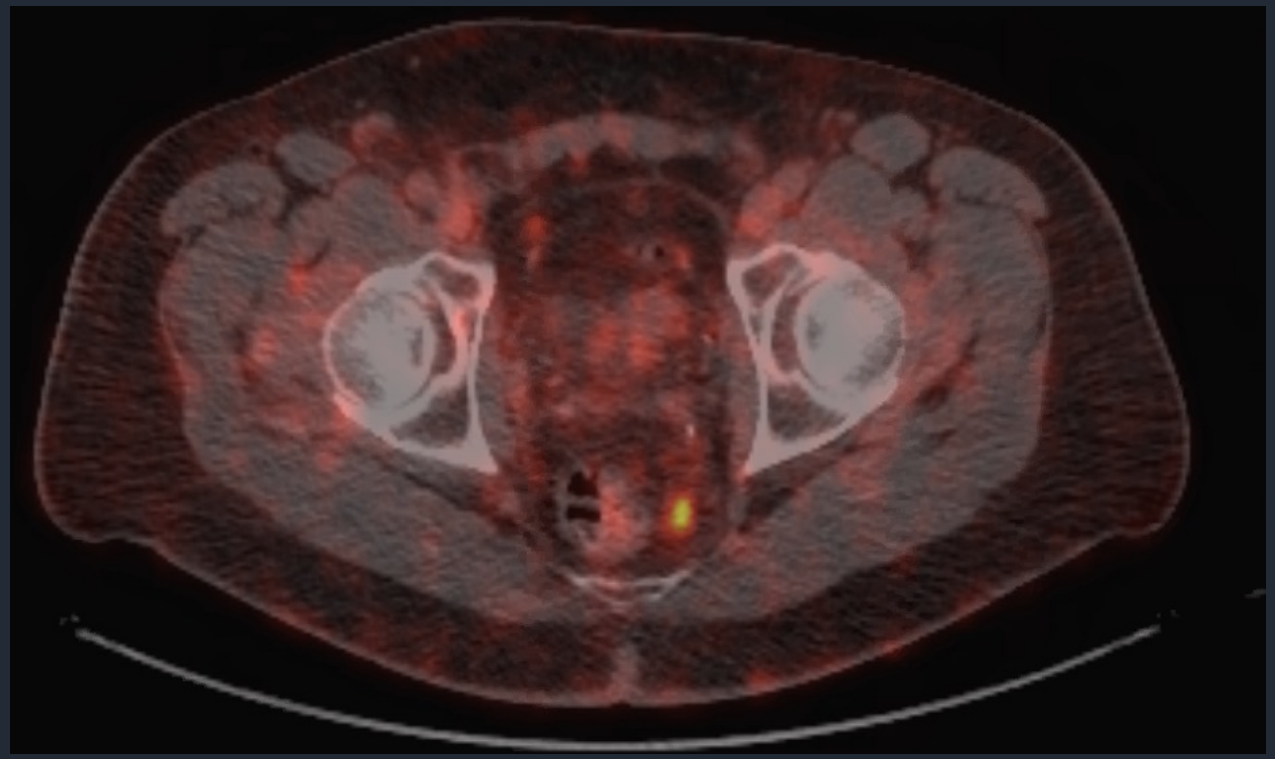
Pelvic Lymph Nodes, right:

Metastatic prostate adenocarcinoma

Number of lymph nodes examined: 14
Number of lymph nodes with metastatic disease: 8
Size of the largest lymph node involved by tumor: 1.5cm.
Size of the largest metastatic focus : 0.3 cm.

PSMA Imaging





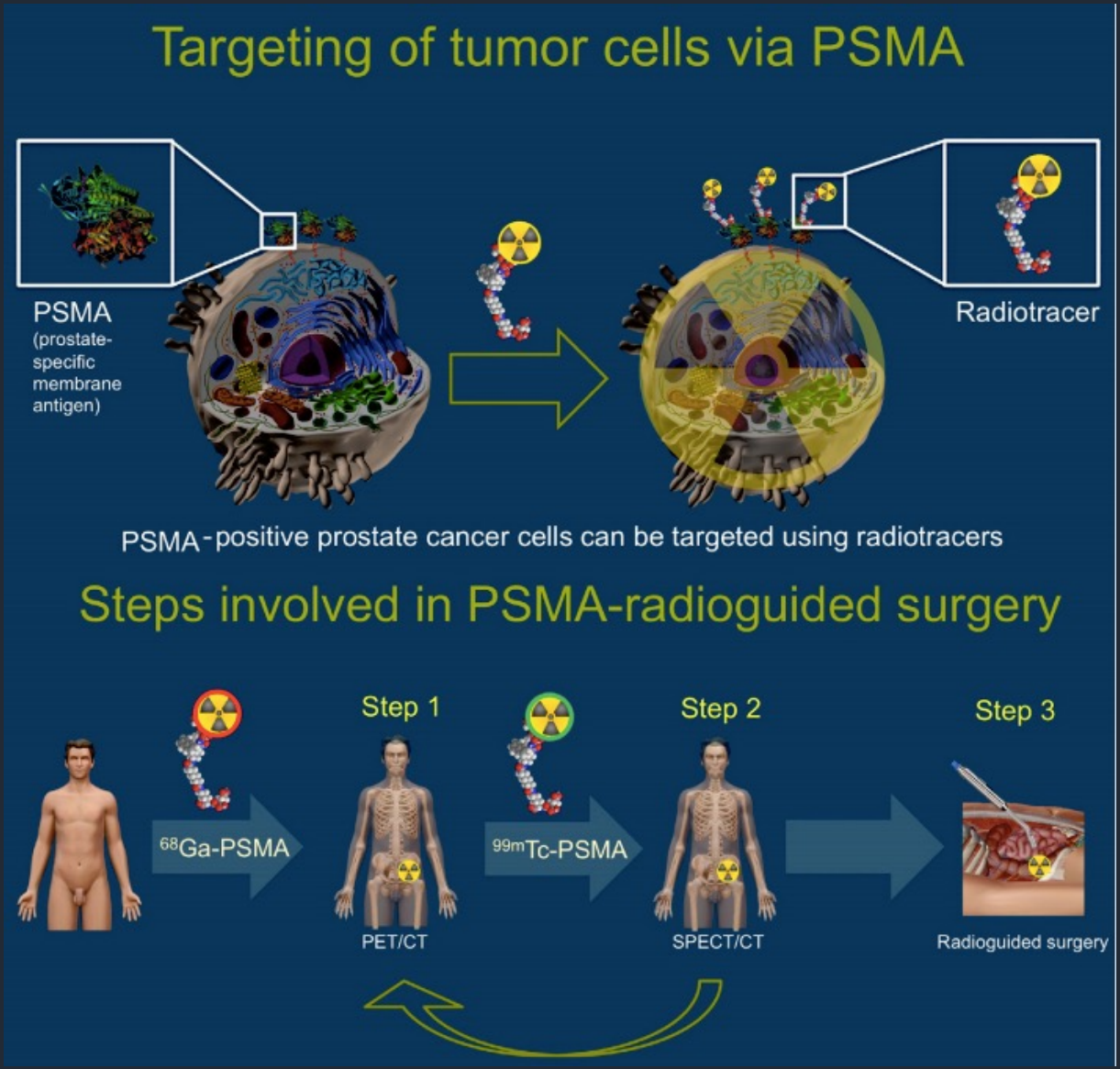
- ^{68}Ga-PSMA avid nodes outside ePLND: 28% - 48%

Franklin et al. doi:10.1111/BJU.15134

Yaxley et al. BJU Int. 2020; 124:201-407

^{99m}Technetium-based Prostate-specific Membrane Antigen–radioguided Surgery in Recurrent Prostate Cancer

Tobias Maurer[a,b,1,], Stephanie Robu[c,1], Margret Schottelius[c], Kristina Schwamborn[d], Isabel Rauscher[e], Nynke S. van den Berg[f,g], Fijs W.B. van Leeuwen[f], Bernhard Haller[h], Thomas Horn[a], Matthias M. Heck[a], Jürgen E. Gschwend[a], Markus Schwaiger[e], Hans-Jürgen Wester[c], Matthias Eiber[e]*



CONCLUSIONS

- Staging :

  PSMA IMAGING WILL IMPROVE THE STAGING CAPACITY OF PLND

  PSMA MAY NOT NOT REPLACE PLND

- Treatment Benefit ?

  PLND vs. No PLND IS A BETTER TRIAL DESIGN