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Pelvic Lymph Node Dissection in Prostate Cancer: Update from a RCT of Limited vs Extended Dissection

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Original Article

Editorial by Matthew J. Roberts, Philip Cornford, Derya Tilki on pp. 261–263 of this issue

Pelvic Lymph Node Dissection in Prostate Cancer: Update from a Randomized Clinical Trial of Limited Versus Extended Dissection

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AIM

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

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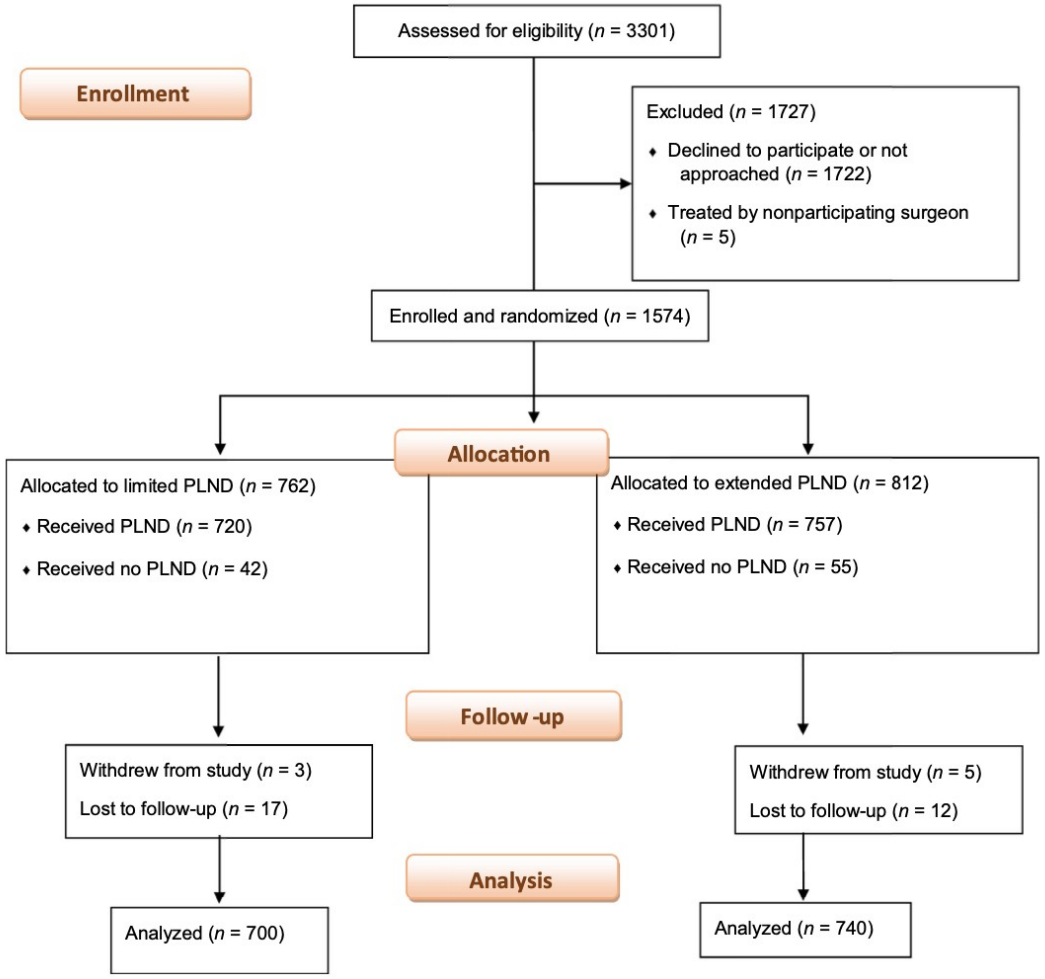
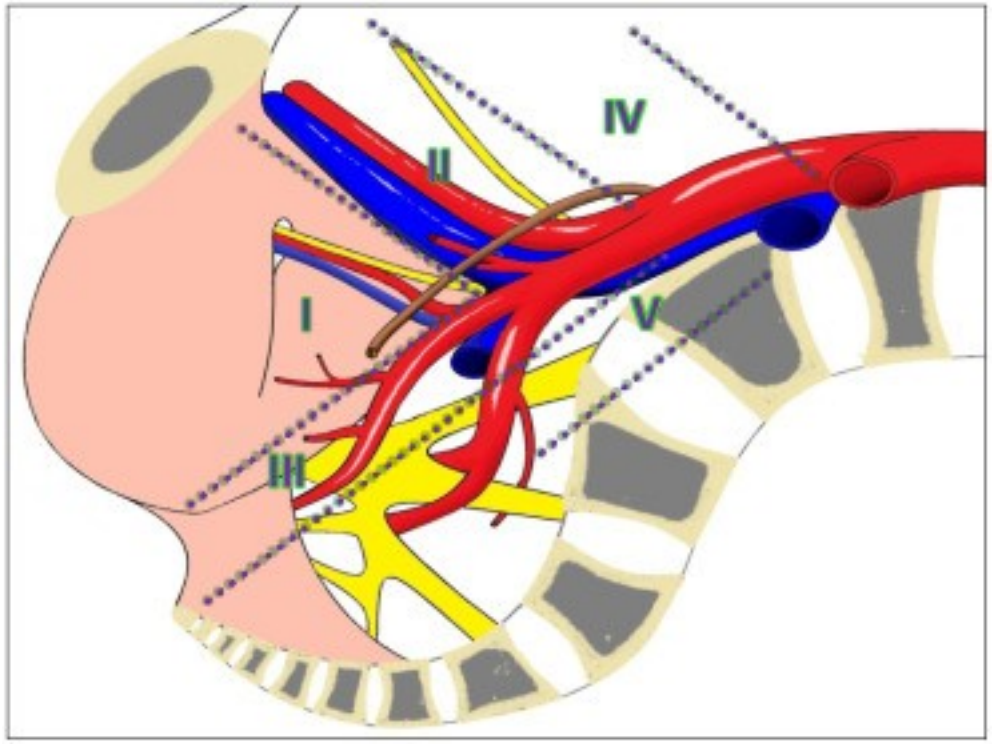
RCT comparing **limited vs extended pelvic LND (PLND)** during radical prostatectomy previously reported **comparable biochemical recurrence (BCR) rates.**

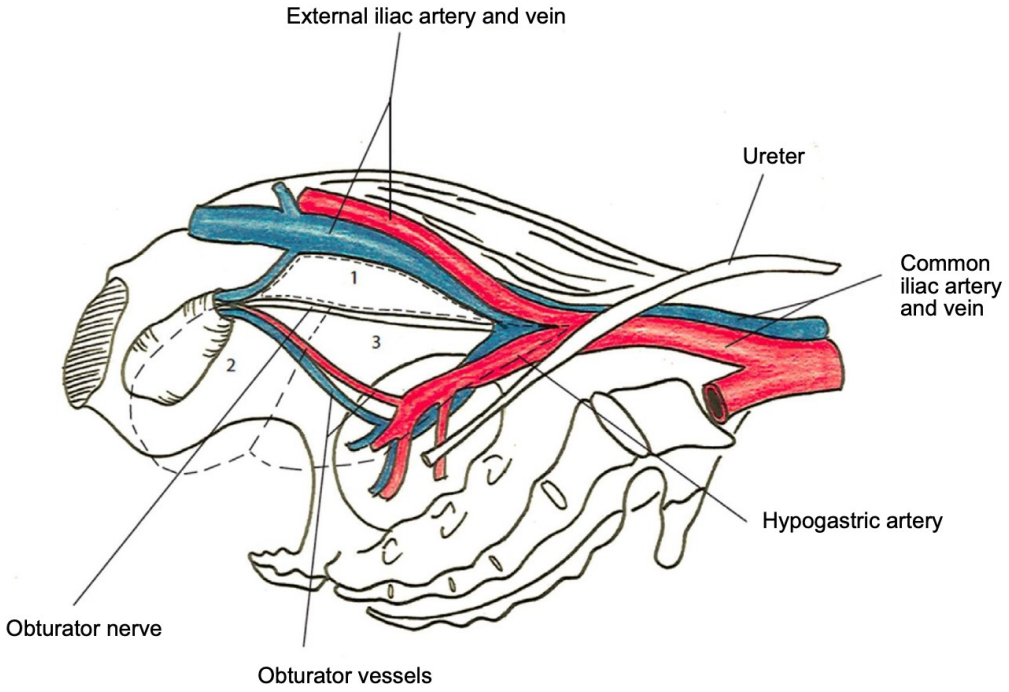
To report **updated BCR rates and compare rates of metastasis between the study arms.**

Methods

- **Study Design:**
  - Single-center, cluster-randomized trial (limited vs. extended PLND).
  - Surgeons randomized for 3-month periods.
- **Participants:**
  - 1432 patients undergoing radical prostatectomy (2011–2017) for clinically localised cancer
- **Interventions:**
  - **Limited PLND:** External iliac nodes.
  - **Extended PLND:** External iliac, obturator, and hypogastric nodes.
- **Endpoints:**
  - Primary: BCR (PSA ≥0.2 ng/mL).
  - Secondary: Any metastasis (regional and distant), distant metastasis.







Limited PLND – ON
Std PLND – O +EI
ePLND – O + EI + II
sePLND – ePLND + CI + PS

Limited PLND – Region 1 (Ext. Iliac Nodes)

- node packet under the external iliac vein and above the obturator nerve

Extended PLND – Region 1 (Ext. Iliac Nodes) + Region 2 (Obturator Fossa Nodes) + Region 3 (Hypogastric Nodes)

Patient Characteristics

Median number of nodes removed, *n* (IQR)	12 (8–17)	14 (10–20)
Number of positive nodes removed, *n* (%)		
0	619 (88)	640 (86)
1	41 (5.9)	51 (6.9)
2	18 (2.6)	14 (1.9)
≥3	22 (3.1)	35 (4.7)

The patient groups were **comparable** with respect to

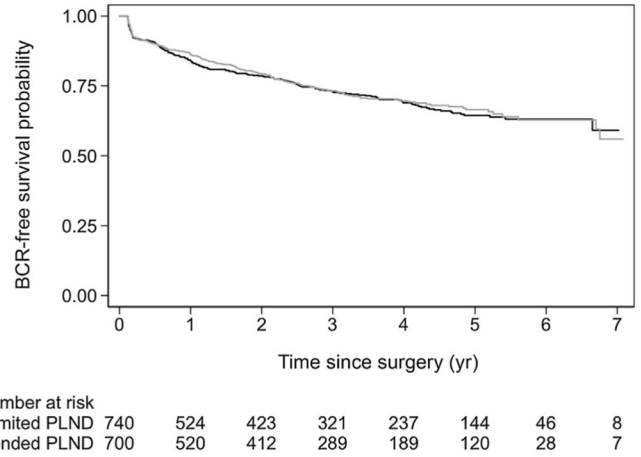
- Demographics
- Staging (clinical and pathological)
- Histopathology (GG,EPE,SV,LNI)
- Number of nodes removed

Parameter	Limited PLND (*n* = 698)	Extended PLND (*n* = 734)
Median age at RP, yr (IQR)	62 (57–67)	63 (57–67)
Race, *n* (%)		
White	581 (88)	603 (86)
Black	54 (8.2)	70 (10)
Asian	18 (2.7)	20 (2.9)
Other	9 (1.4)	5 (0.7)
Unknown	36	36
Median preoperative PSA, ng/ml (IQR)	5.9 (4.3–8.7)	5.7 (4.2–8.3)
Unknown (*n*)	1	0
Biopsy Gleason grade group		
1	70 (10)	67 (9.2)
2	364 (52)	385 (53)
3	132 (19)	123 (17)
4	80 (11)	92 (13)
5	51 (7.3)	64 (8.8)
Unknown	1	3
Clinical T stage		
≤T1c	410 (59)	410 (57)
T2a	111 (16)	129 (18)
T2b	103 (15)	106 (15)
T2c	20 (2.9)	28 (3.9)
≥T3	49 (7.1)	48 (6.7)
Unknown	5	13
Median pre-RP 5-yr BCR risk, % (IQR)	15 (9–31)	15 (9–30)
Unknown (*n*)	22	26
Pathologic Gleason grade group		
1	40 (5.9)	53 (7.3)
2	400 (59)	384 (53)
3	160 (23)	172 (24)
4	26 (3.8)	45 (6.2)
5	56 (8.2)	70 (9.7)
Unknown	16	10
Extracapsular extension, *n* (%)	373 (53)	360 (49)
Seminal vesicle invasion, *n* (%)	86 (12)	86 (12)
Lymph node involvement, *n* (%)		
N0	619 (89)	638 (87)
N1	79 (11)	96 (13)
Adjuvant hormone therapy, *n* (%)	3 (0.4)	2 (0.3)
Adjuvant radiation therapy, *n* (%)	1 (0.1)	3 (0.4)

BCR = biochemical recurrence; IQR = interquartile range; PLND = pelvic lymph node dissection; PSA = prostate-specific antigen; RP = radical prostatectomy.

Results

BCR Rates



- **no difference** in BCR rate (HR 1.05, 95% CI 0.97–1.13; p = 0.3)

Metastatic Disease

- The median follow-up among participants who did not develop any metastasis was 5.4 yr (IQR 2.4–8.1) with 123 events.
- A significant **protective effect of ePLND** against
  - **Any metastasis (HR 0.82**, 95% CI 0.71–0.93; p = 0.003
  - **Distant metastasis (HR 0.75**, 95% CI 0.64–0.88; p < 0.001)
- The **metastasis-free survival rate at 10 yr** was **85%** (95% CI 81–89%) in the limited template group

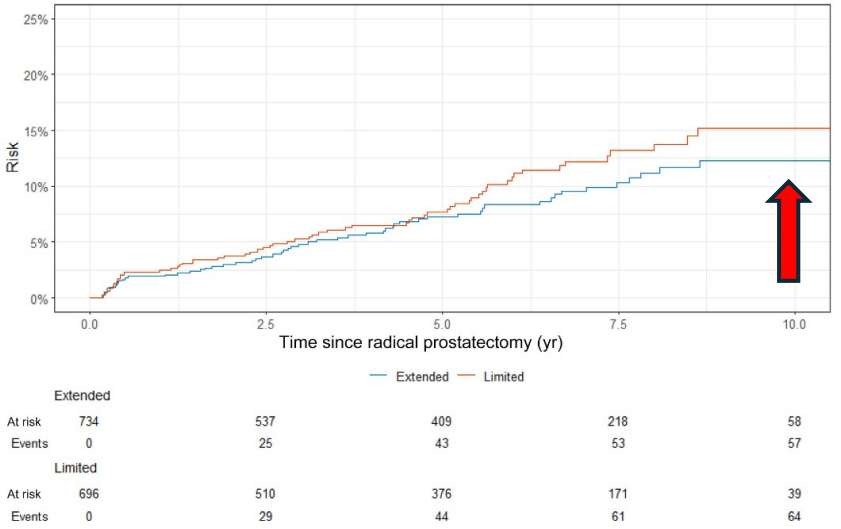


Fig. 1 – Cumulative incidence of any metastasis in the extended and limited pelvic lymph-node dissection arms.

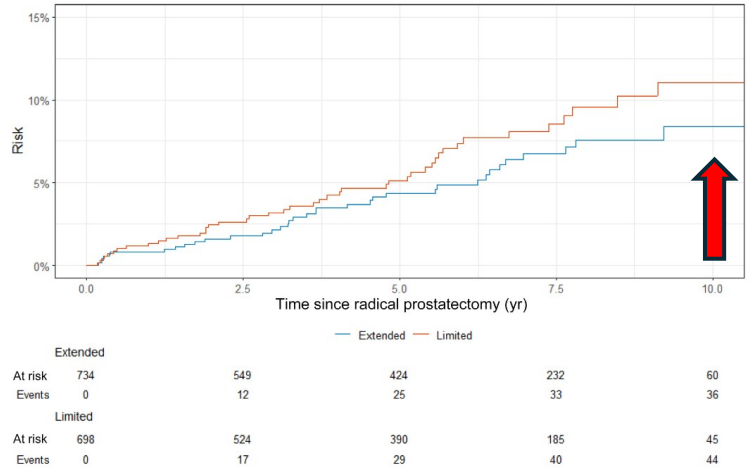


Fig. 2 – Cumulative incidence of distant metastasis in the extended and limited pelvic lymph-node dissection arms.

Subgroup Analysis

- Significant benefit in node-positive patients (HR 0.49 for distant metastasis).

Table 2 – Results from interaction analyses investigating the interaction between pathologic N stage and limited versus extended PLND (*p* value for interaction presented) and subsequent analyses for BCR and metastasis performed separately for pN0 and pN1 subgroups

Outcome for extended	N0				N1				Interaction
vs limited PLND	Pts	Events	HR (95% CI)	*p* value	Pts	Events	HR (95% CI)	*p* value	*p* value
BCR	1257	312	1.04 (0.92–1.18)	0.5	175	140	0.95 (0.72–1.25)	0.7	0.6
Any metastasis	1257	58	0.81 (0.63–1.04)	0.11	173	63	0.68 (0.48–0.96)	0.029	0.2
Regional metastasis	1257	40	0.68 (0.48–0.97)	0.034	173	42	0.88 (0.45–1.72)	0.7	0.6
Distant metastasis	1257	33	1.01 (0.75–1.36)	>0.9	175	47	0.49 (0.37–0.65)	<0.001	0.005

BCR = biochemical recurrence; HR = hazard ratio; CI = confidence interval; PLND = pelvic lymph node dissection; Pts = patients.

Post Hoc Analyses to Understand Metastasis vs. BCR Discordance

1. No Difference in Salvage Treatment Timing or Type

- **Time to salvage therapy** after BCR was similar between extended vs. limited PLND (difference: **2–3 weeks**, *p* = NS).
- Node-positive **(N1) patients received salvage therapy slightly sooner** (HR = 1.15), but this small difference did not explain metastasis reduction.
- **No between-group differences** in **salvage treatment** modalities

2. Identical PSA Profiles at BCR

- **Median PSA at first rise:** 0.13 ng/mL (IQR 0.10–0.24) for both groups (*p* = 0.6).
- **PSA velocity:** 0.11 vs. 0.10 ng/mL/yr (limited vs. extended PLND, *p* = 0.3).
- Metastasis reduction is **not driven by differences in PSA response** post-surgery.

3. Strong Interaction with Nodal Status

- **Node-positive (N1) patients:**
  - **HR 0.49 (95% CI 0.37–0.65)** for distant metastasis (*p* < 0.001) with extended PLND.
  - **No benefit in node-negative (N0) patients** (HR 1.01, *p* > 0.9).
- **U-shaped risk curve:** Metastasis risk varied nonlinearly with node count, but **template benefit persisted across counts**

4. Surgeon Technique/Experience Did Not Influence Outcomes

- **No heterogeneity** in treatment effects across surgeons for:
  - BCR (*p* = 0.9), any metastasis (*p* > 0.9), or distant metastasis (*p* > 0.9).
- **Consistency:** Extended PLND’s benefits were **independent of individual surgeon skill/experience**

Discussion

1. Contrast with Prior Literature

- Most previous RCTs found **no significant benefit** for extended PLND, likely due to **underpowered studies**.
- This trial (n=1,432) had **greater statistical power** than prior studies (e.g., n=81–401).

2. Biological Mechanism: Tumor Self-Seeding Hypothesis

- **Node-positive patients** showed the strongest benefit from extended PLND.
- Suggests **lymph nodes may act as reservoirs** for circulating tumor cells, promoting metastasis.
- Removal of occult micrometastases in extended nodes may disrupt this process.

3. No Difference in Biochemical Recurrence (BCR)

- **Primary endpoint (BCR)** did not differ between groups.
- But **metastasis reduction** was significant, implying PLND affects **later-stage progression**.

4. Clinical Guidelines & Implications

- Supports **NCCN/EAU guidelines** recommending extended PLND when lymphadenectomy is performed.
- **PSMA PET/CT limitations:** Even with negative imaging, **13% risk of occult nodal disease** remains.

5. Addressing Potential Objections

- **Ascertainment bias unlikely:** Metastasis curves diverged by >1 year, unlikely due to scan timing bias.
- **Node location matters:** Extended templates likely remove **high-risk nodal basins** missed in limited PLND.

6. Trial Strengths

- **Single-center, high accrual** (1,500+ patients in 5.5 years) due to pragmatic, clinically integrated design.
- **Minimal patient burden:** No extra visits/tests, enhancing participation.

7. Limitation

- The **metastatic workup** was conducted at the **discretion of the treating medical oncologist** (consisted of bone scan and CT of the chest, abdomen, and pelvis, or whole-body MRI and/or PET (FDG/Choline/PSMA)

Conclusion

- Extended PLND (obturator/hypogastric nodes/Ext. Iliac) **reduces metastasis risk.**
- **Node-positive** patients benefit most.
- Extended PLND's **metastasis reduction is linked to nodal disease biology** (eliminating micro-metastatic reservoirs) rather than altering PSA-driven recurrence.
- **3% absolute reduction** in metastasis at 10 years ($p < 0.001$).
- **Supports current guidelines** recommending extended PLND for high-risk patients.

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Platinum Priority Prostate Cancer
Editorial by XXX on pp. x-y of this issue.

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

Jean F.P. Lestingi[a,], Giuliano B. Guglielmetti[a], Quoc-Dien Trinh[b], Rafael F. Coelho[a], Jose Pontes Jr.[a], Diogo A. Bastos[a], Mauricio D. Cordeiro[a], Alvaro S. Sarkis[a], Sheila F. Faraj[a], Anuar I. Mitre[a], Miguel Srougi[a], William C. Nahas[a]*

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Study Design:

Phase 3 RCT at a single center (Brazil, 2012–2016).

Participants: 300 men with intermediate-/high-risk localized prostate cancer (D'Amico criteria).

Interventions:

LPLND: Obturator nodes only.

EPLND: Obturator, external/internal/common iliac, and presacral nodes.

Endpoints:

Primary: 5-year BRFS (PSA ≥0.2 ng/mL).

Secondary: MFS, CSS, histopathological

Pathological Findings:

EPLND detected **5× more lymph node metastases** (17% vs. 3.4%, *p* < 0.001).

Median nodes removed: **17 (EPLND) vs. 3 (LPLND)**.

Oncological Outcomes:

No difference in BRFS (HR 0.91, 95% CI 0.63–1.32; *p* = 0.6).

No difference in MFS/CSS (too few events).

Subgroup Analysis:

EPLND improved BRFS in ISUP grade group 3–5 patients (HR

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Review – Prostate Cancer

Oncologic Outcome of the Extent of Pelvic Lymph Node Dissection During Radical Prostatectomy: A Systematic Review, Meta-analysis, and Network Analysis

David E. Hinojosa-Gonzalez[a,*], *José I. Nolazco*[a,b], *Gal Saffati*[a], *Shane Kronstedt*[a], *Jeffrey A. Jones*[a,c], *Dov Kadmon*[a], *Justin Badal*[a], *Jeremy R. Slawin*[a]

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Systematic review and of 12 studies (2 RCTs, 10 retrospective; n = 4,570 patients).

Meta-analysis for BCR, nodal y rates.

Bayesian netw compare dissec

Key Definition

IPLND: Obturator nodes only.

ePLND: Obturator + internal/external iliac ± common iliac/presacral nodes.

BCR Rates:

Overall: ePLND reduced BCR risk (HR 0.68, 95% CI 0.52–0.88; *p* = 0.003).

By Study Type:

RCTs: No benefit (HR 1.03, 95% CI 0.92–1.14; *p* = 0.61).

Retrospective Studies: Significant benefit (HR 0.59, 95% CI 0.43–0.81; *p* = 0.0009).

By Anatomical Extent:

Key Findings:

Retrospective data favor ePLND for BCR reduction, but **RCTs show no benefit**.

Common iliac/presacral dissection may improve outcomes (network analysis).

more nodes (*p* < 0.00001).

Node-Positive Rates: ePLND detected **3.44× more positive nodes** (*p* < 0.0001).

Thank you!