Prostate Imaging

Jelle Barentsz
Dept. of Medical Imaging
Andros Clinics, NL

j.barentsz@andros.nl
www.mri-prostate-barentsz.nl

ANDROS
CLINICS

Unpaid Advisor SPL Medical

ANDROS
CLINICS

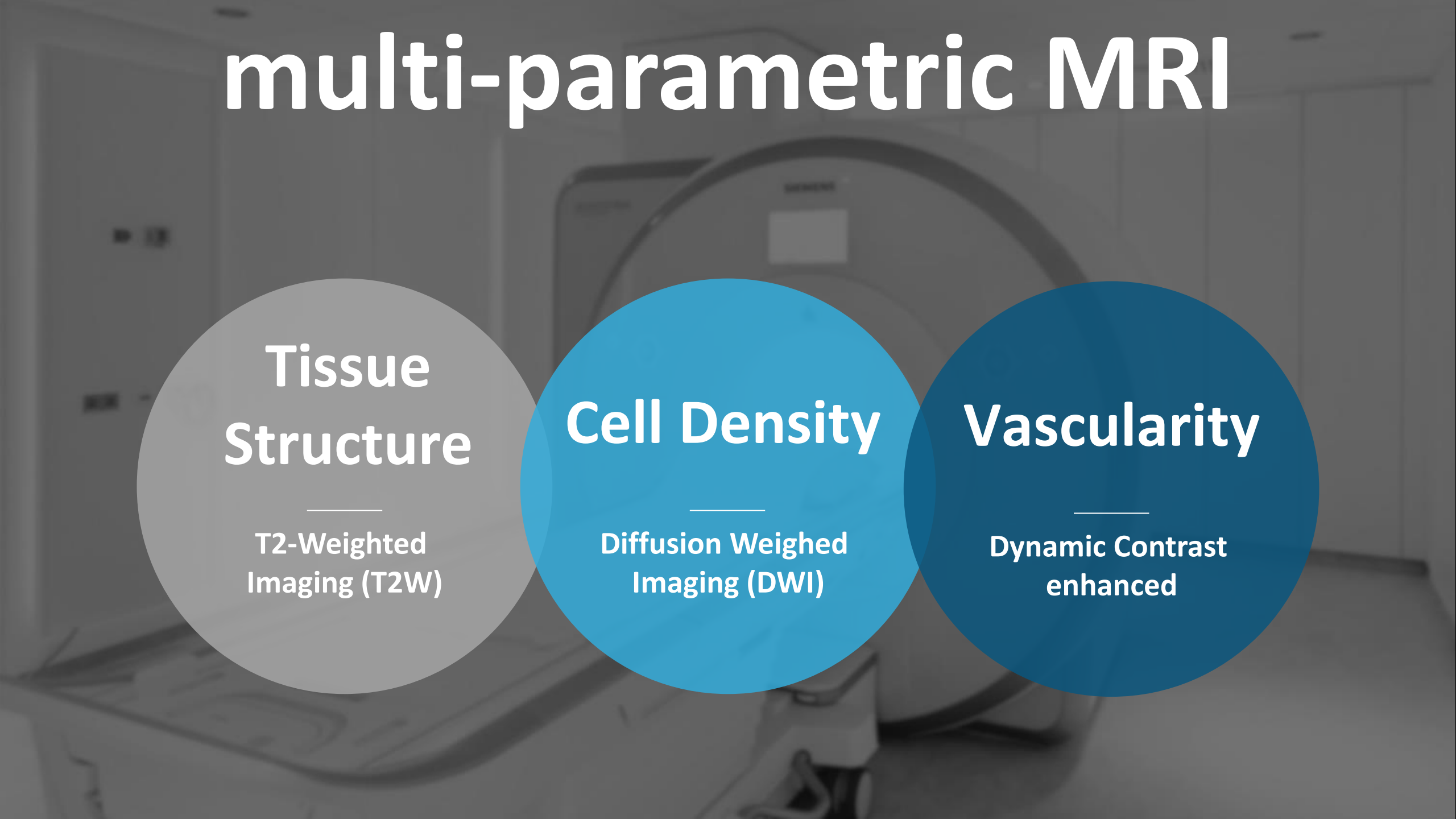
PROSTATE CANCER

1 Local

WHAT IS MULTI-PARAMETRIC MRI

Integration of 3 techniques

multi-parametric MRI



Tissue Structure

T2-Weighted Imaging (T2W)

Cell Density

Diffusion Weighed Imaging (DWI)

Vascularity

Dynamic Contrast enhanced

PI-RADS v1

Prostate Imaging Reporting and Data System

Eur Radiol (2012) 22:746–757
DOI 10.1007/s00330-011-2377-y

UROGENITAL

ESUR prostate MR guidelines 2012

Jelle O. Barentsz · Jonathan Richenberg · Richard Clements · Peter Choyke · Sadhna Verma · Geert Villeirs · Olivier Rouviere · Vibeke Logager · Jurgen J. Fütterer

Received: 16 October 2011 / Revised: 23 November 2011 / Accepted: 2 December 2011 / Published online: 10 February 2012

Barentsz, Eur Radiol 2012;22: 746-757

GUIDELINES

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Review – Prostate Cancer

Editorial by XXX on pp. x–y of this issue

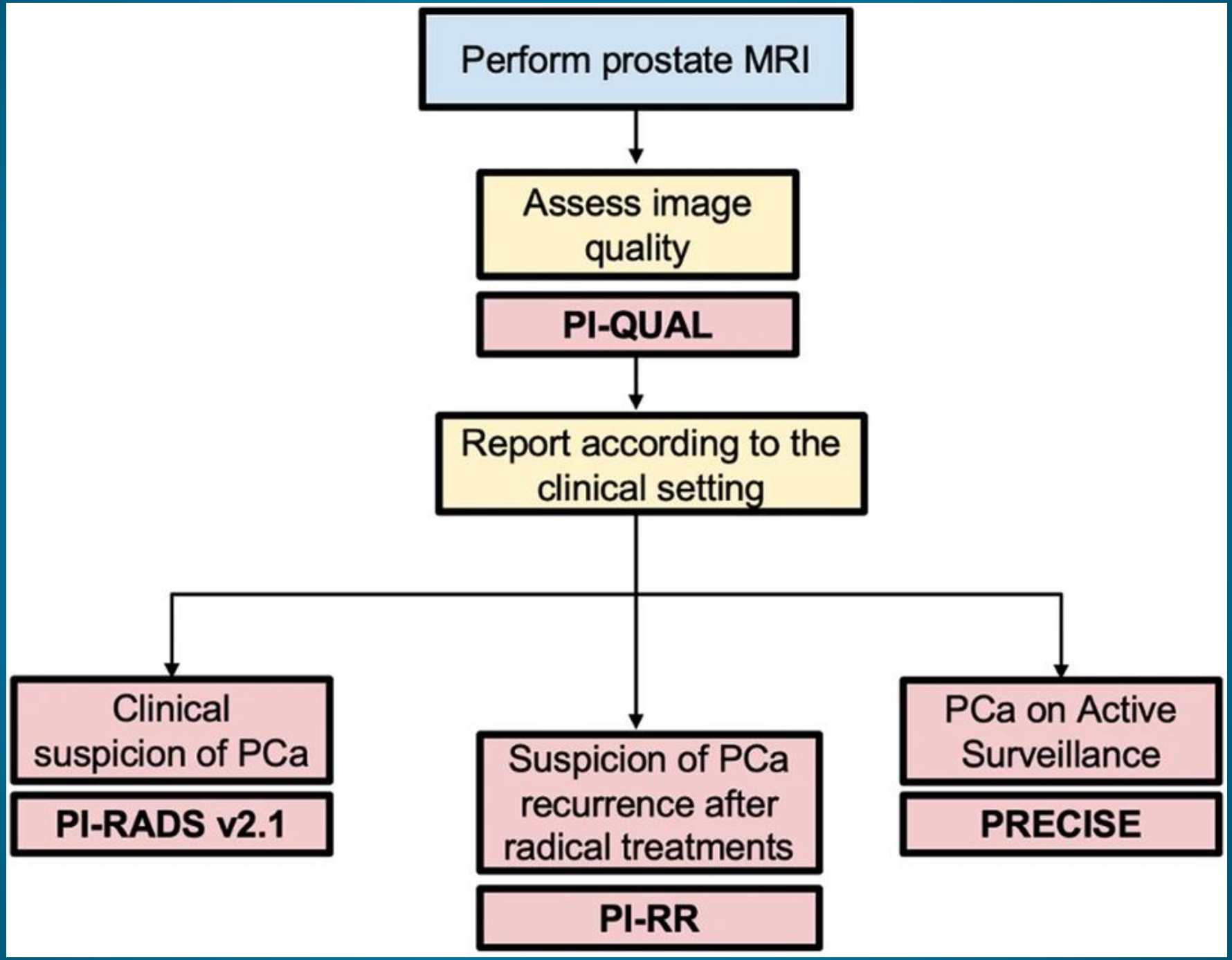
Prostate Imaging Reporting and Data System Version 2.1: 2019 Update of Prostate Imaging Reporting and Data System Version 2

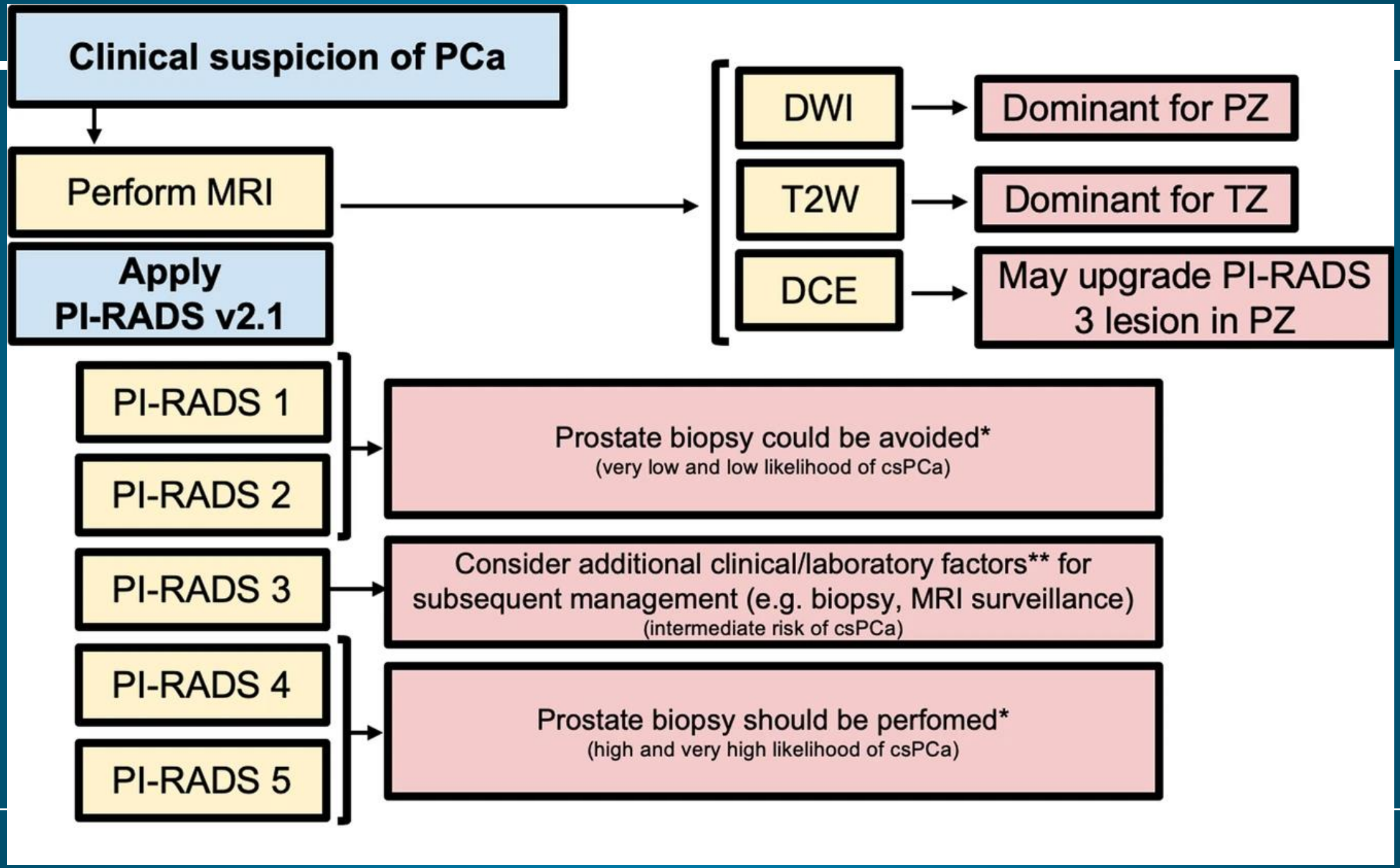
Baris Turkbey[a,†,*], Andrew B. Rosenkrantz[b,†,*], Masoom A. Haider[c], Anwar R. Padhani[d], Geert Villeirs[e], Katarzyna J. Macura[f], Clare M. Tempany[g], Peter L. Choyke[a], Francois Cornud[h], Daniel J. Margolis[i], Harriet C. Thoeny[j], Sadhna Verma[k], Jelle Barentsz[l,‡], Jeffrey C. Weinreb[m,‡]

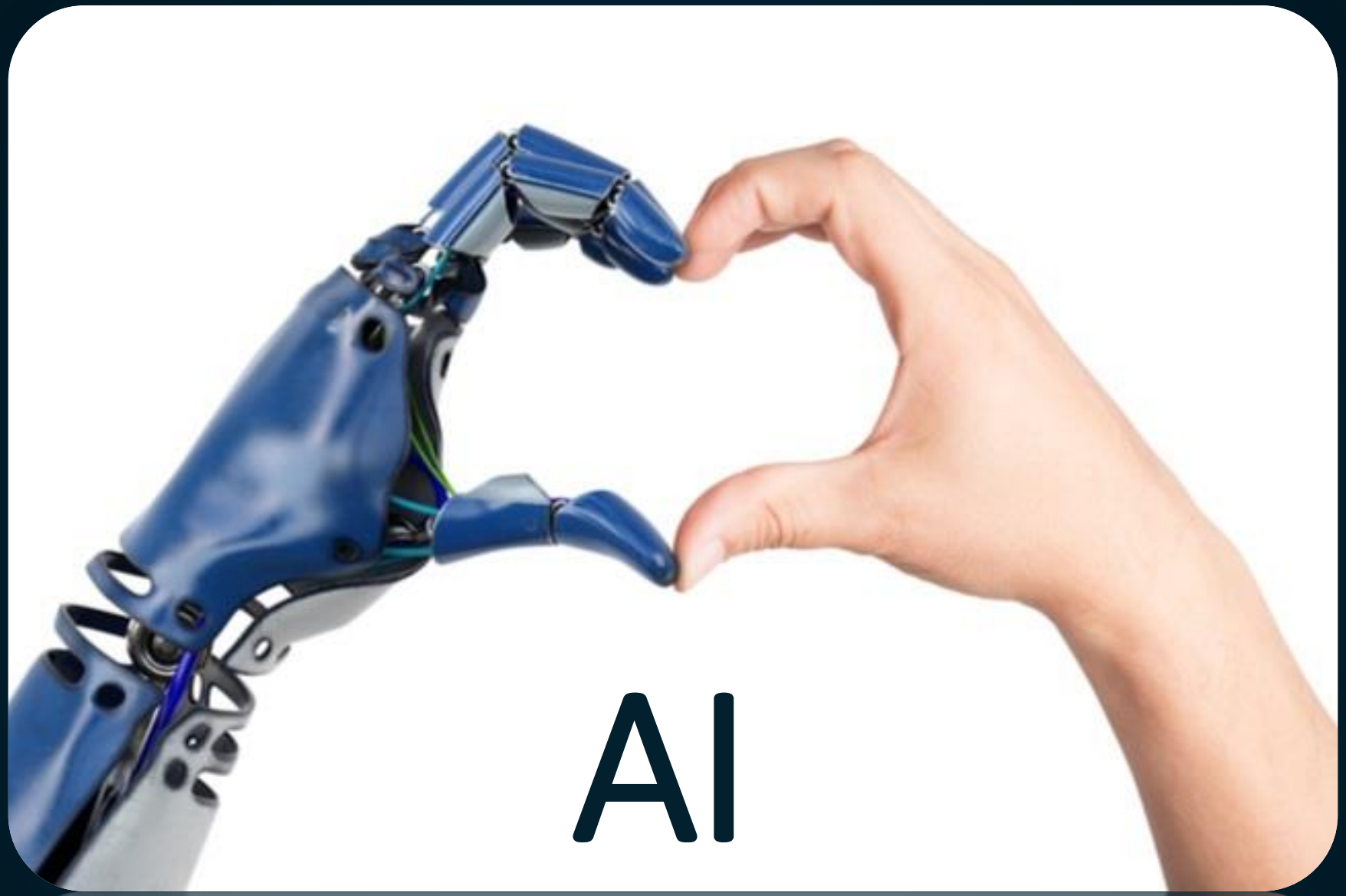
PI-RADS v2.1: Assessment Categories

Each lesion is assigned a PI-RADS Assessment Category using a **5-point Likert-scale** based on the likelihood (probability) that findings on:
T2W (anatomy), DWI (cell-density), and DCE (vascularity) correlate with the presence of a **clinically significant cancer** at a particular location

1	**very low**	clinically significant cancer **highly unlikely**
2	**low**	clinically significant cancer **unlikely**
3	**intermediate**	clinically significant cancer **equivocal**
4	**high**	clinically significant cancer **likely**
5	**very high**	clinically significant cancer **highly likely**

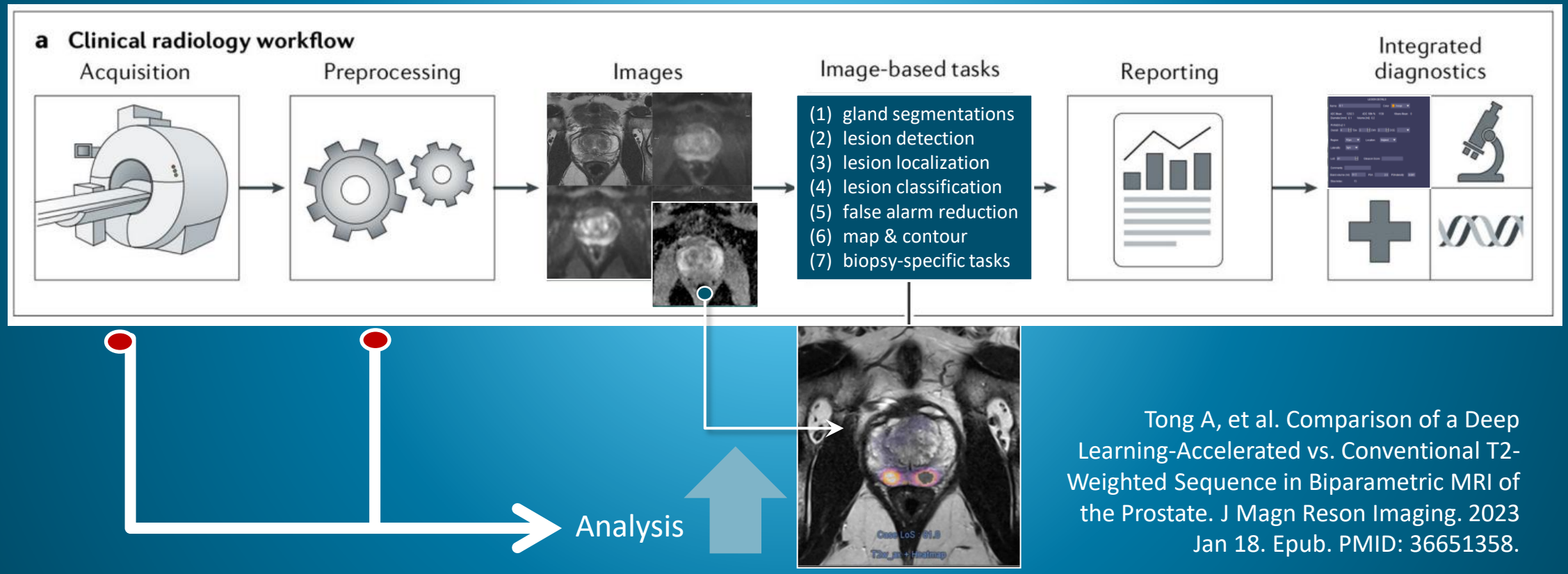

Perform prostate MRI
Assess image quality
PI-QUAL
Report according to the clinical setting
Clinical suspicion of PCa
PI-RADS v2.1
Suspicion of PCa recurrence after radical treatments
PI-RR
PCa on Active Surveillance
PRECISE


Clinical suspicion of PCa
Perform MRI
Apply PI-RADS v2.1
DWI
Dominant for PZ
T2W
Dominant for TZ
DCE
May upgrade PI-RADS 3 lesion in PZ
PI-RADS 1
PI-RADS 2
Prostate biopsy could be avoided*
(very low and low likelihood of csPCa)
PI-RADS 3
Consider additional clinical/laboratory factors** for subsequent management (e.g. biopsy, MRI surveillance)
(intermediate risk of csPCa)
PI-RADS 4
PI-RADS 5
Prostate biopsy should be perfomed*
(high and very high likelihood of csPCa)



Acquisition

AI in MRI prostate cancer diagnosis workflow

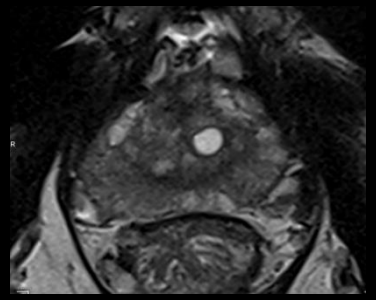


Tong A, et al. Comparison of a Deep Learning-Accelerated vs. Conventional T2-Weighted Sequence in Biparametric MRI of the Prostate. J Magn Reson Imaging. 2023 Jan 18. Epub. PMID: 36651358.

“Prostate on Speed” – 15-min time slot (prep/acquisition)
Deep-Learning for image reconstruction on sparse data

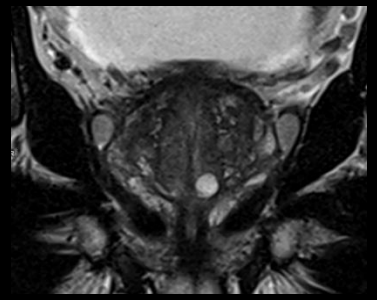
SIEMENS Healthineers

Standard mpMRI

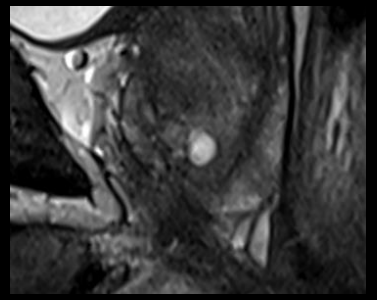


TSE ax
TA 2:59 min

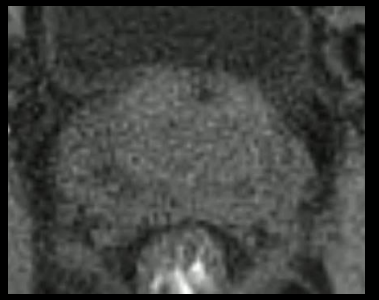
ZOOMit^{PRO}
TA 3:50 min



TSE cor
TA 2:50 min



TSE sag
TA 2:50 min



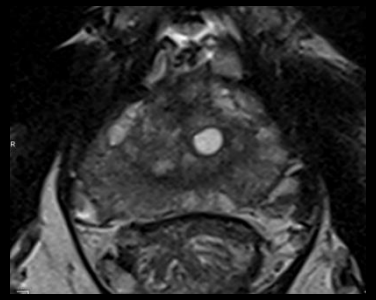
15:29

Courtesy of Karl-Heinz Engelhard, Martha Maria Hospital, Nuremberg, Germany. The product is still under development and not commercially available yet worldwide. It is not for sale in the US. Its future availability cannot be ensured.

“Prostate on Speed” – 15-min time slot (prep/acquisition)
Deep-Learning for image reconstruction on sparse data

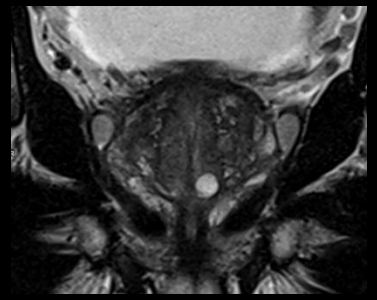
SIEMENS Healthineers

Standard mpMRI

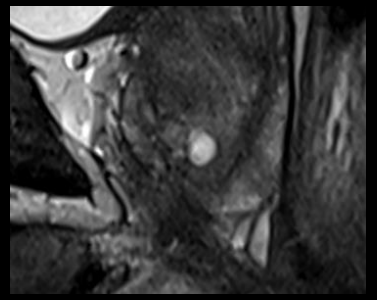


TSE ax
TA 2:59 min

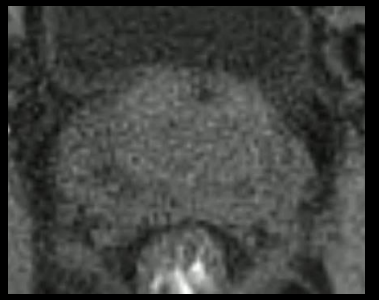
ZOOMit^{PRO}
TA 3:50 min



TSE cor
TA 2:50 min

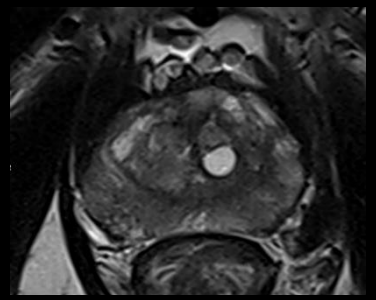


TSE sag
TA 2:50 min



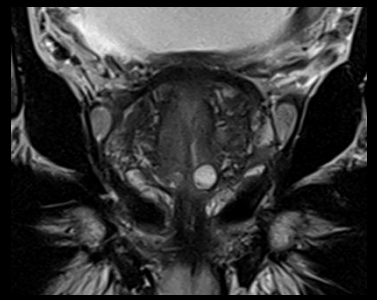
15:29

Deep Resolve Boost for TSE and planned DL EPI*

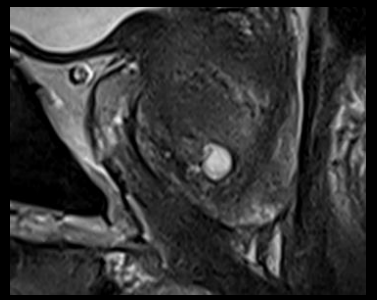


DRB TSE ax
TA 1:10 min

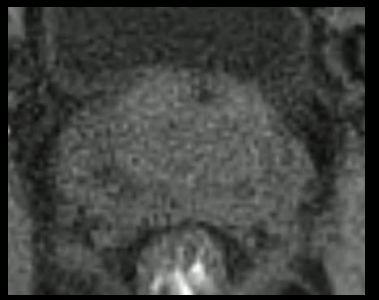
DL ZOOMit^{PRO}
TA 2:05 min



DRB TSE cor
TA 1:10 min



DRB TSE sag
TA 1:10 min



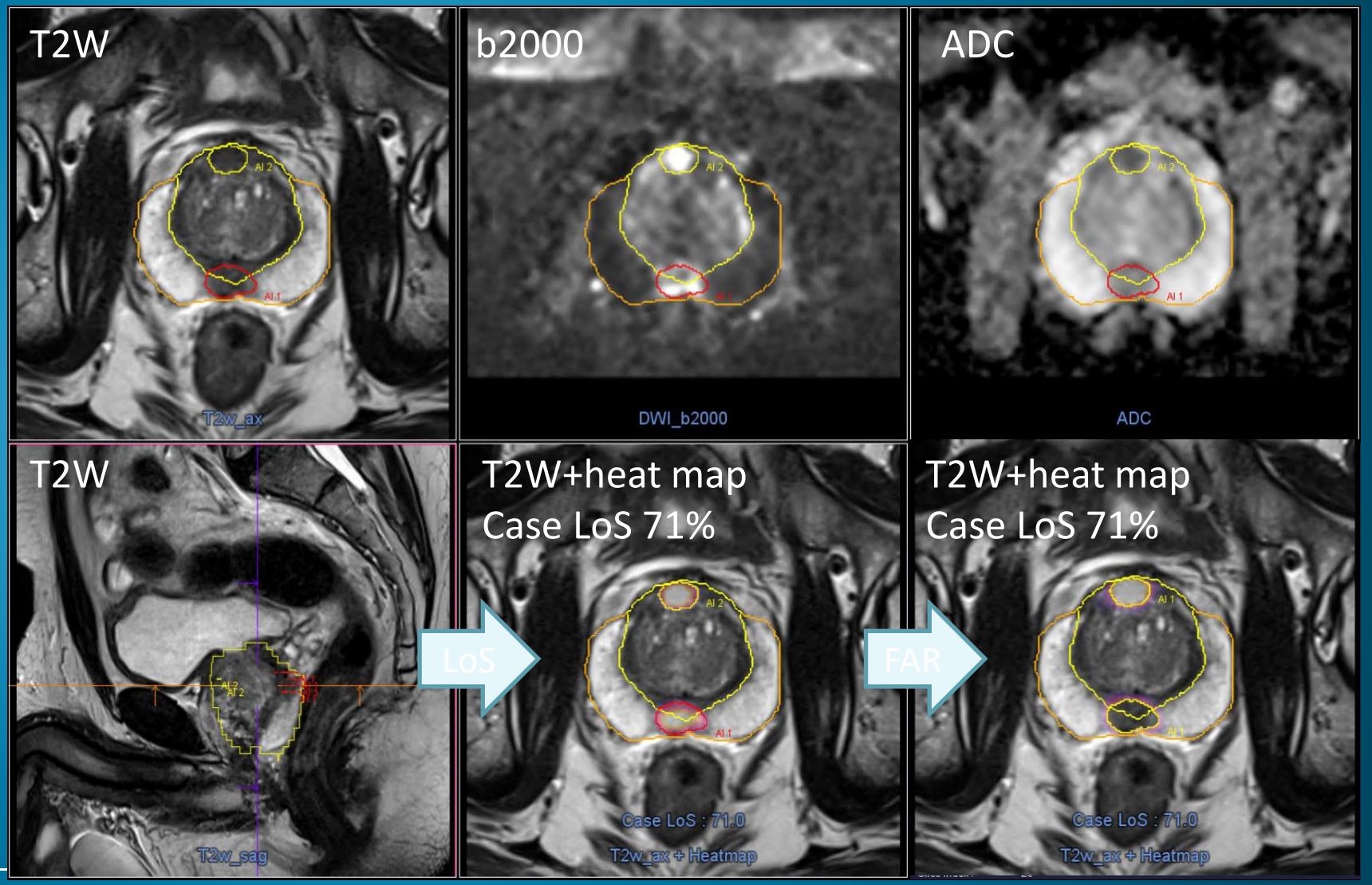
DCE
TA 3:00 min

8:35

Courtesy of Karl-Heinz Engelhard, Martha Maria Hospital, Nuremberg, Germany. The product is still under development and not commercially available yet worldwide. It is not for sale in the US. Its future availability cannot be ensured.

DL-CAD steps for prostate cancer detection (multistage architecture)

Gland/zonal segmentations

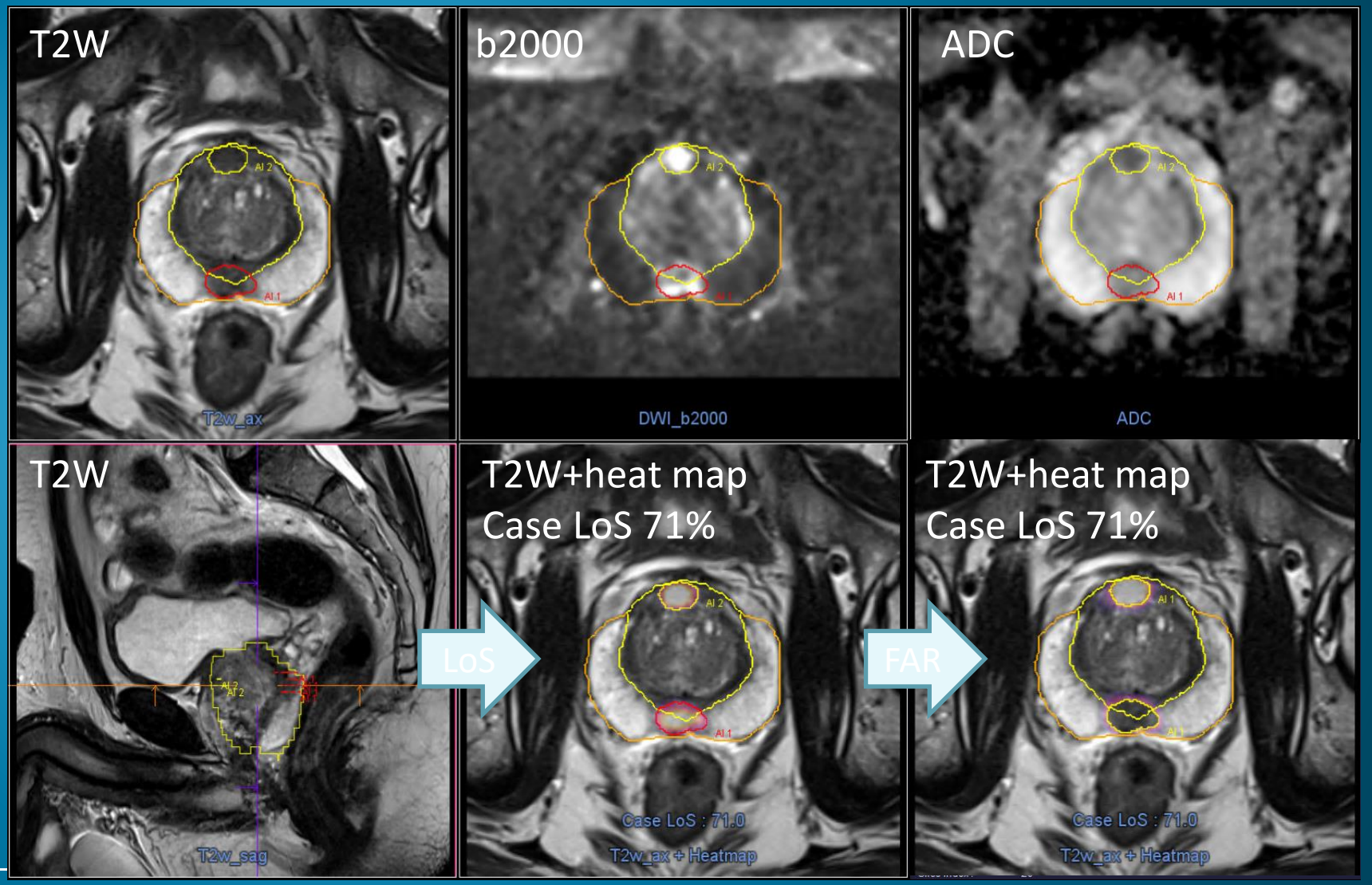


58 yo. GP. Family history positive; BRAC1 carrier; PSA 8.7 ng/mL; GG2 on template biopsy.

DL-CAD steps for prostate cancer detection (multistage architecture)

Gland/zonal segmentations

Lesion detection-localization



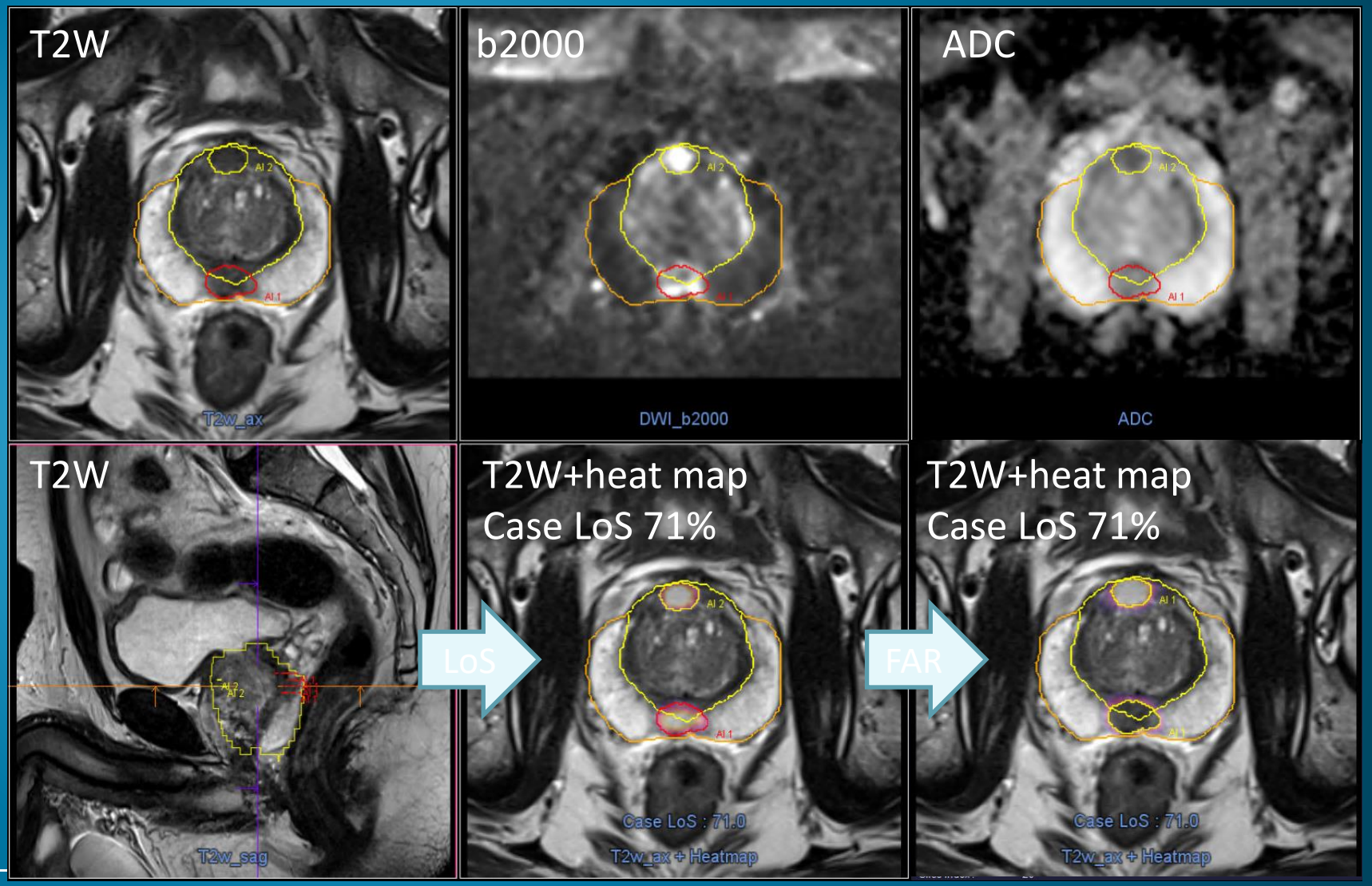
58 yo. GP. Family history positive; BRAC1 carrier; PSA 8.7 ng/mL; GG2 on template biopsy.

DL-CAD steps for prostate cancer detection (multistage architecture)

Gland/zonal segmentations

Lesion detection-localization

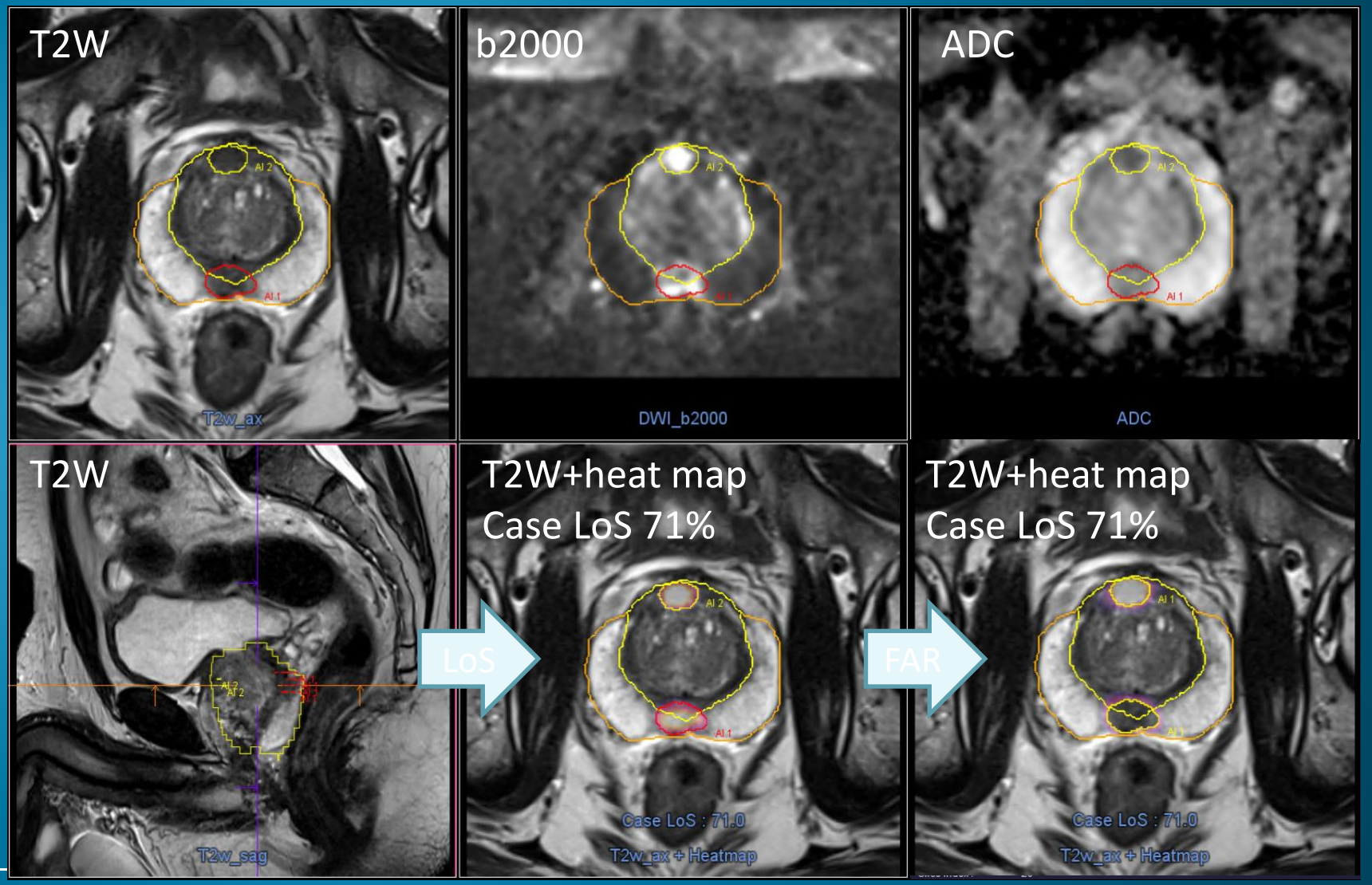
Lesion classification
(level of suspicion; LoS



58 yo. GP. Family history positive; BRAC1 carrier; PSA 8.7 ng/mL; GG2 on template biopsy.

DL-CAD steps for prostate cancer detection (multistage architecture)

- Gland/zonal segmentations
- Lesion detection-localization
- Lesion classification (level of suspicion; LoS
- False alarm reduction (FAR)



58 yo. GP. Family history positive; BRAC1 carrier; PSA 8.7 ng/mL; GG2 on template biopsy.

DL-CAD steps for prostate cancer detection (multistage architecture)

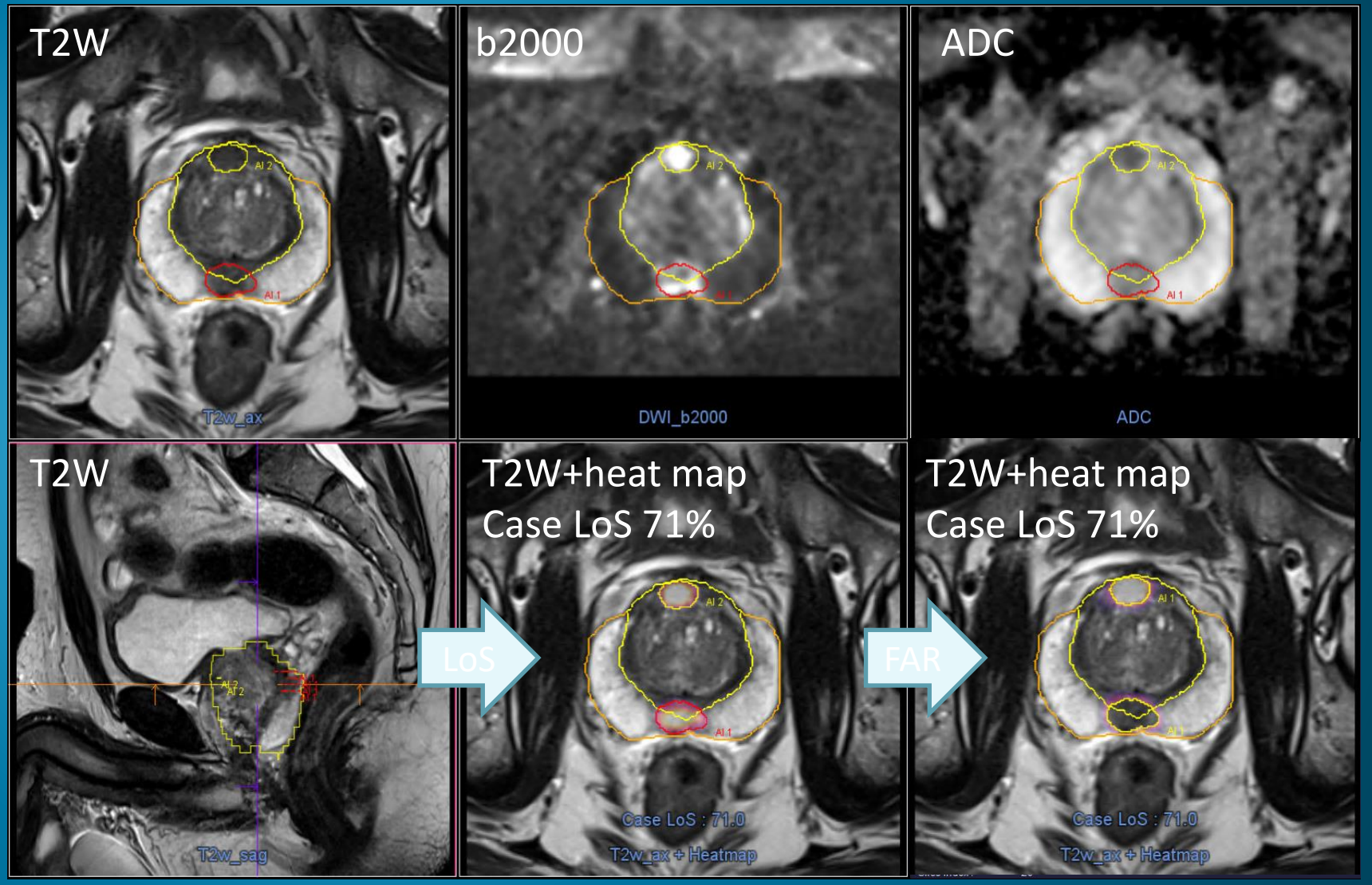
Gland/zonal segmentations

Lesion detection-localization

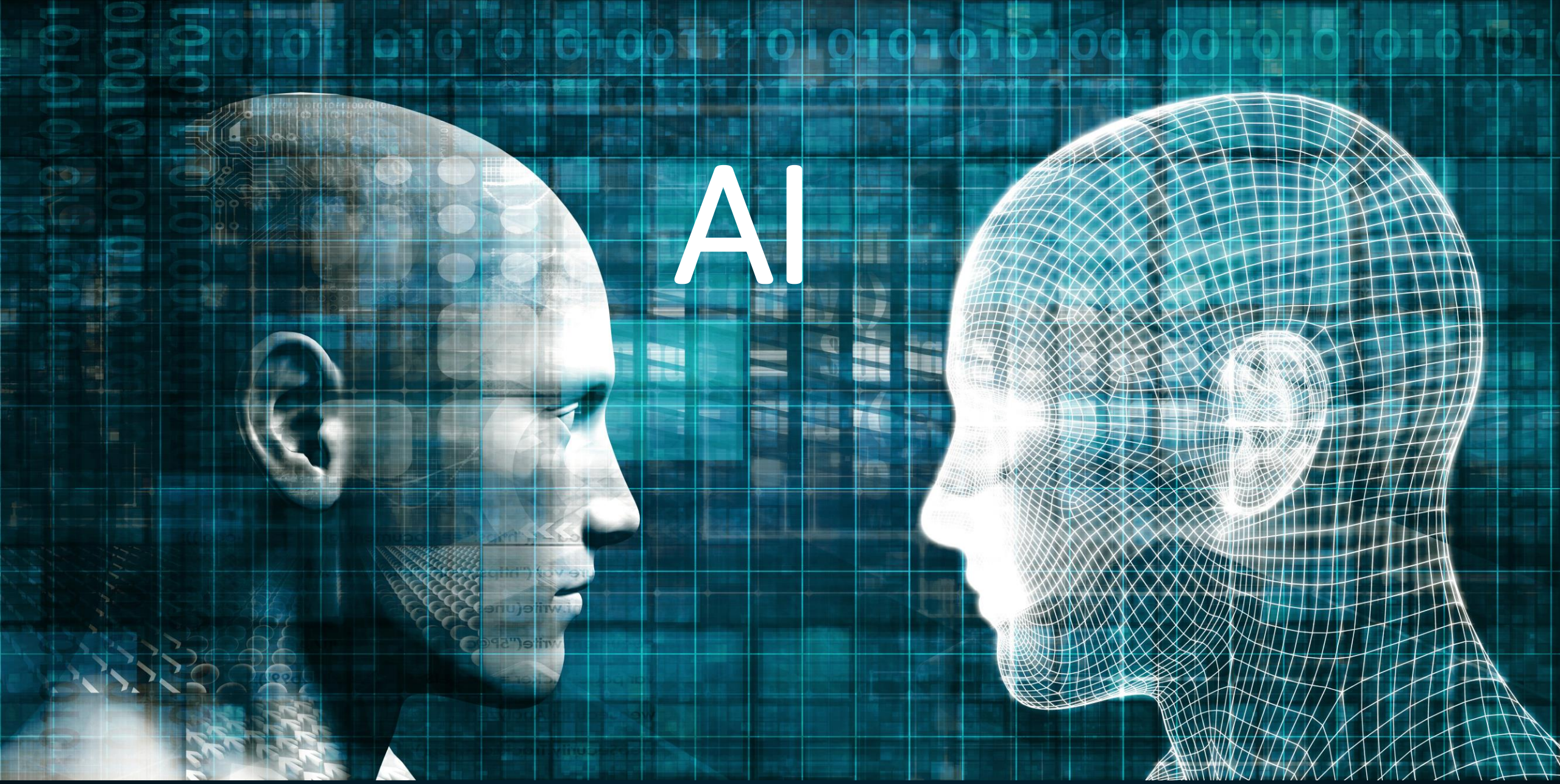
Lesion classification
(level of suspicion; LoS)

False alarm reduction (FAR)

Mapping & contouring



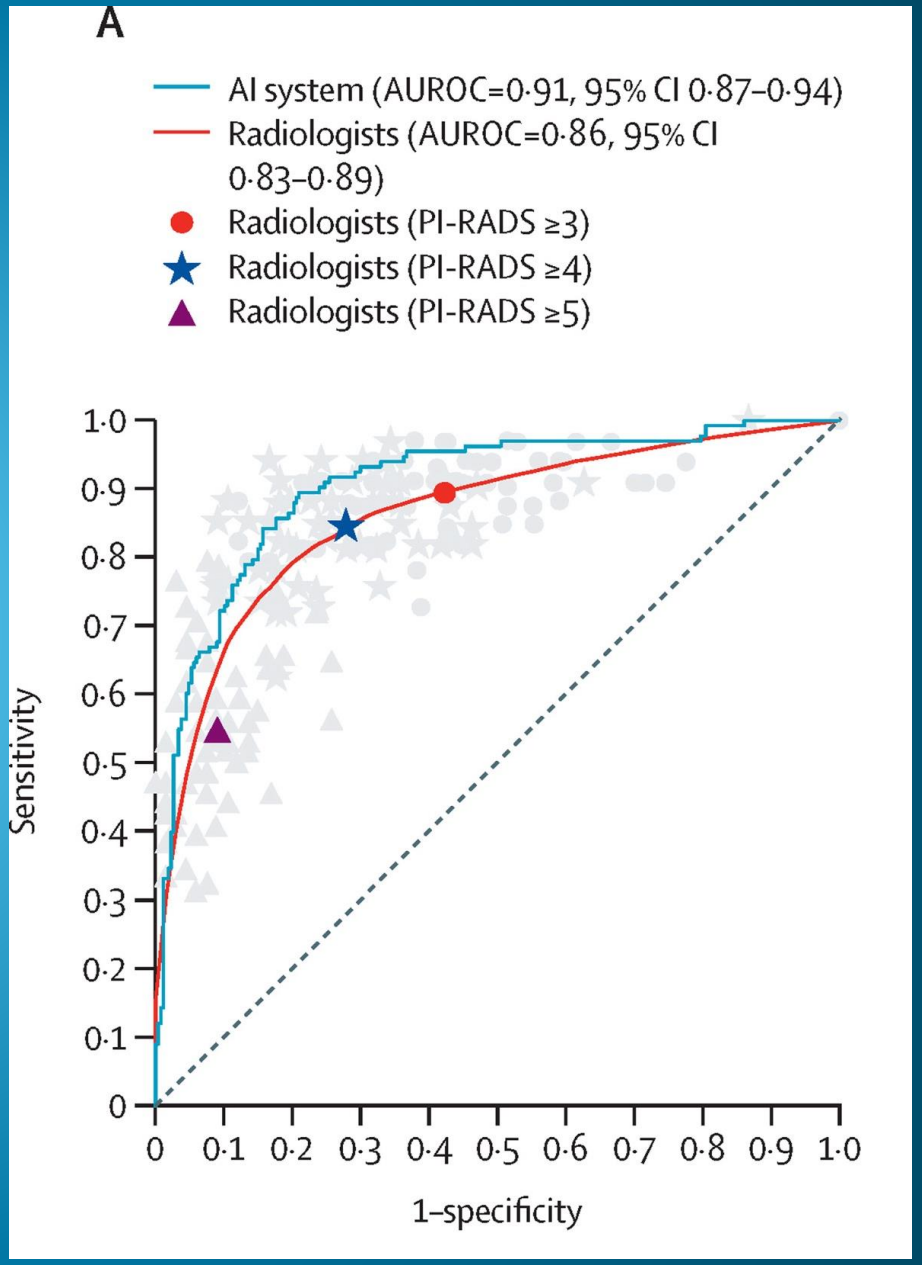
58 yo. GP. Family history positive; BRAC1 carrier; PSA 8.7 ng/mL; GG2 on template biopsy.



Interpretation

AI-system, trained on >10.000 cases

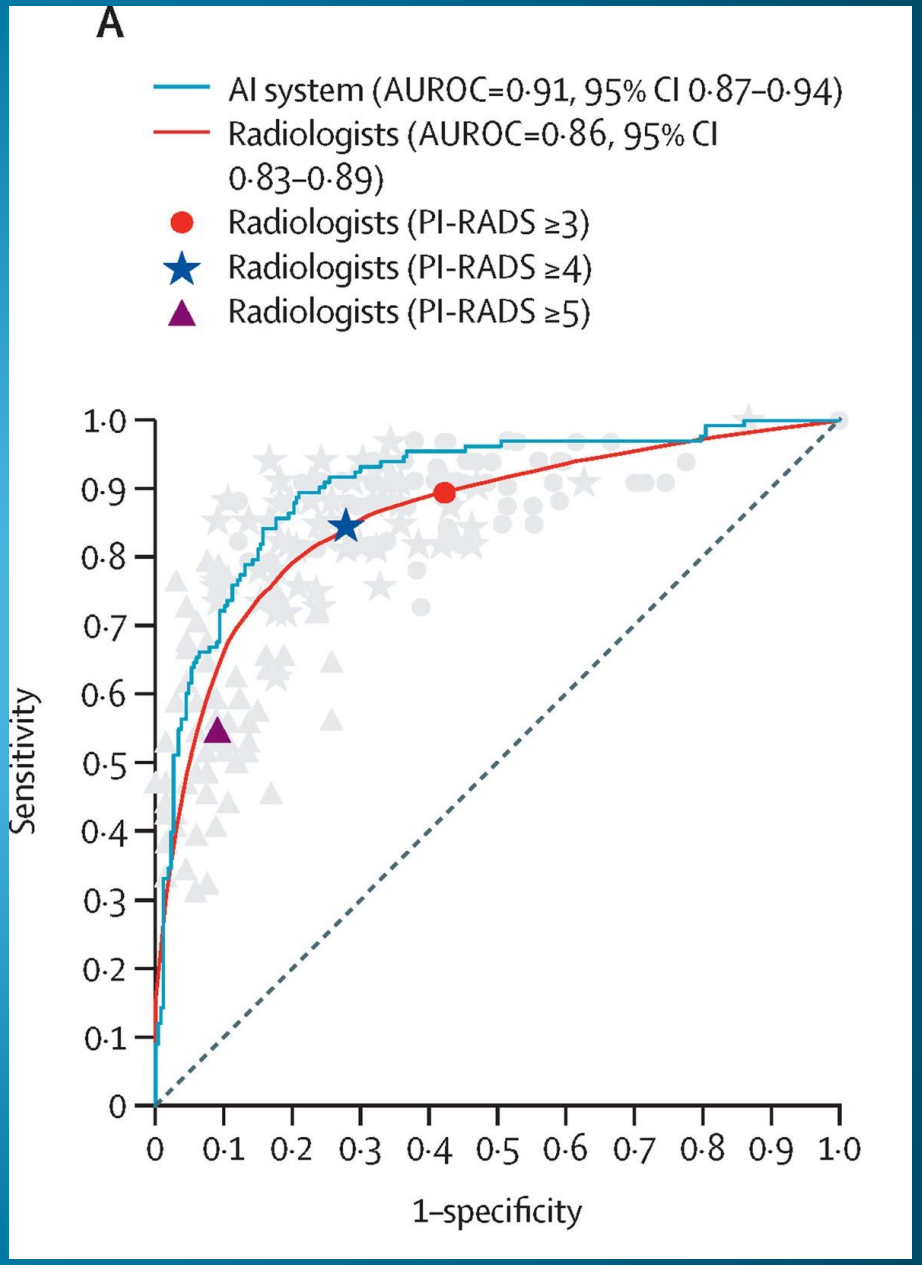
- Scoring 400 cases; non-contrast MRI



Saha, Lancet Oncology 2024

AI-system, trained on >10.000 cases

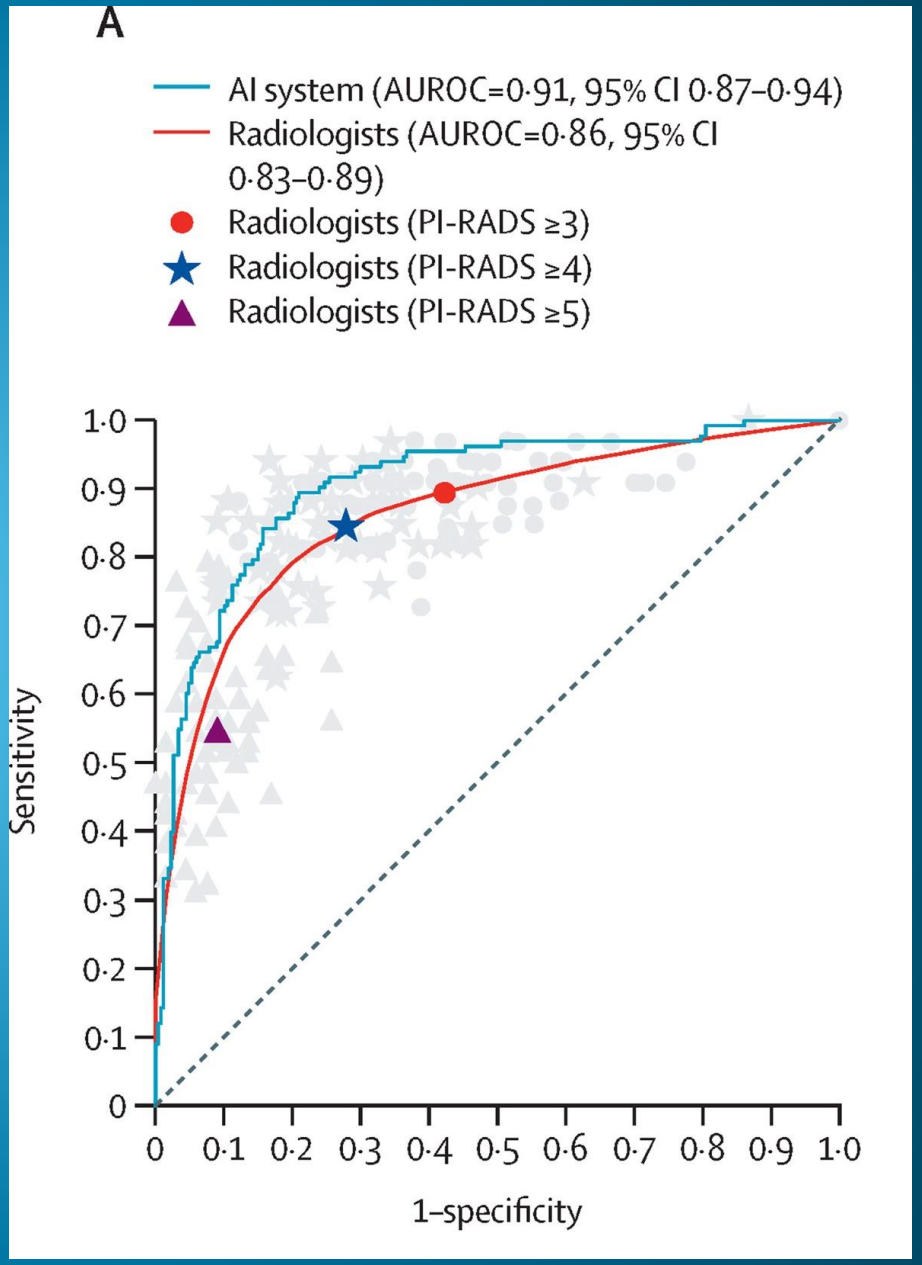
- Scoring 400 cases; non-contrast MRI
- AUROC AI: 0.91; 62 radiologists 0.86



Saha, Lancet Oncology 2024

AI-system, trained on >10.000 cases

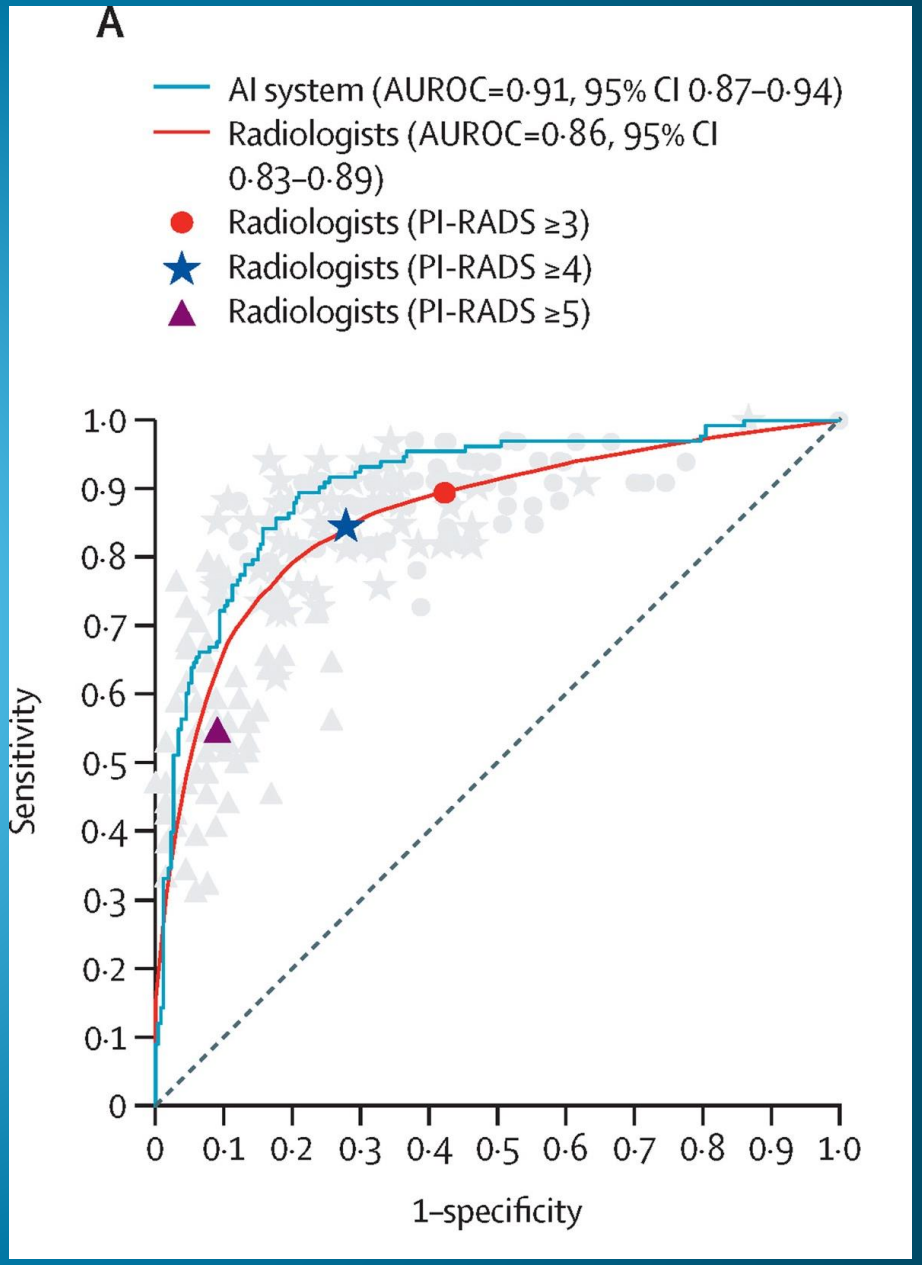
- Scoring 400 cases; non-contrast MRI
- AUROC AI: 0.91; 62 radiologists 0.86
- AI: ↑6.8% ≥GG2



Saha, Lancet Oncology 2024

AI-system, trained on >10.000 cases

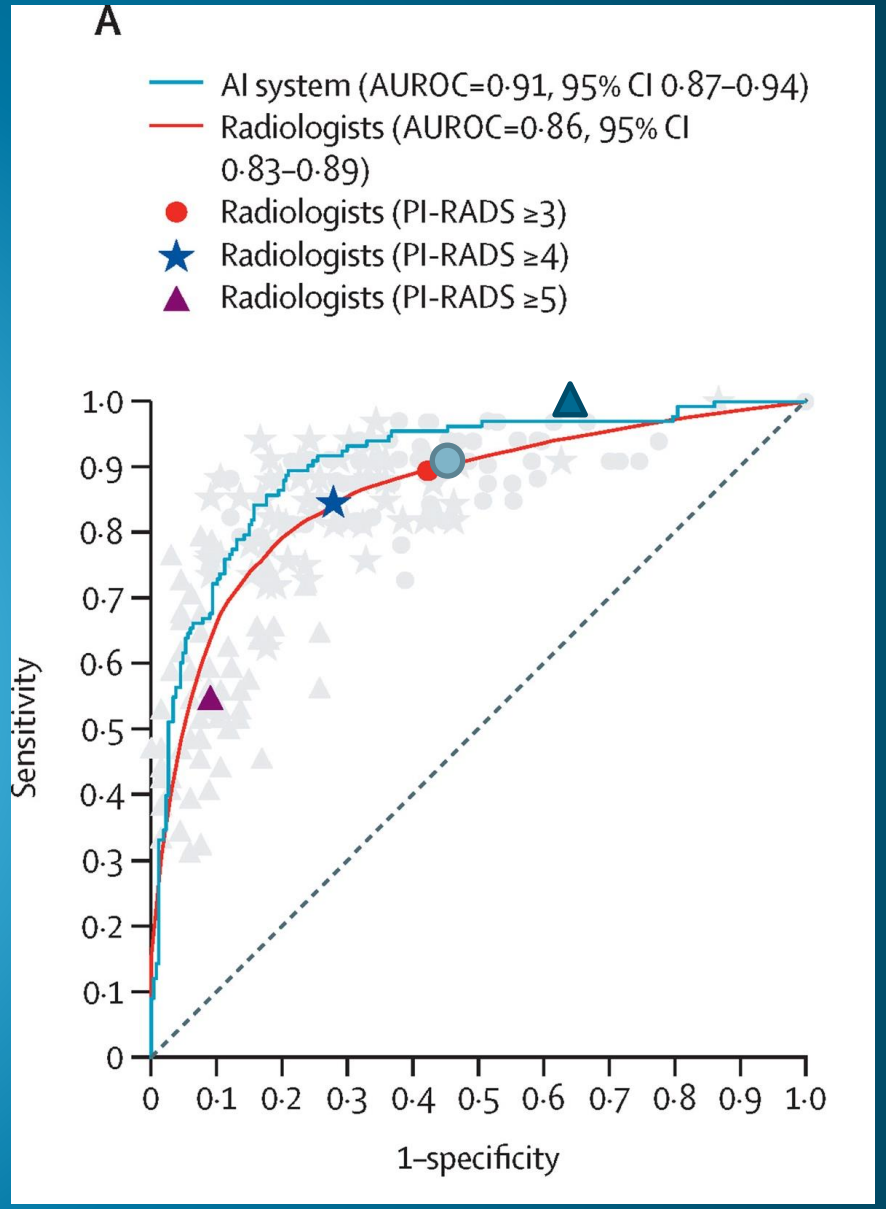
- Scoring 400 cases; non-contrast MRI
- AUROC AI: 0.91; 62 radiologists 0.86
- AI: ↑6.8% ≥GG2
- ↓50% FP, ↓20% GG1, ↔ ≥GG2



Saha, Lancet Oncology 2024

Performance for ≥GG2

Study		Sen	Spec
AI		94%	68%
62 radiologists		90%	53%
4M (≥4)	▲	96%	68%
PROMIS	●	88%	45%

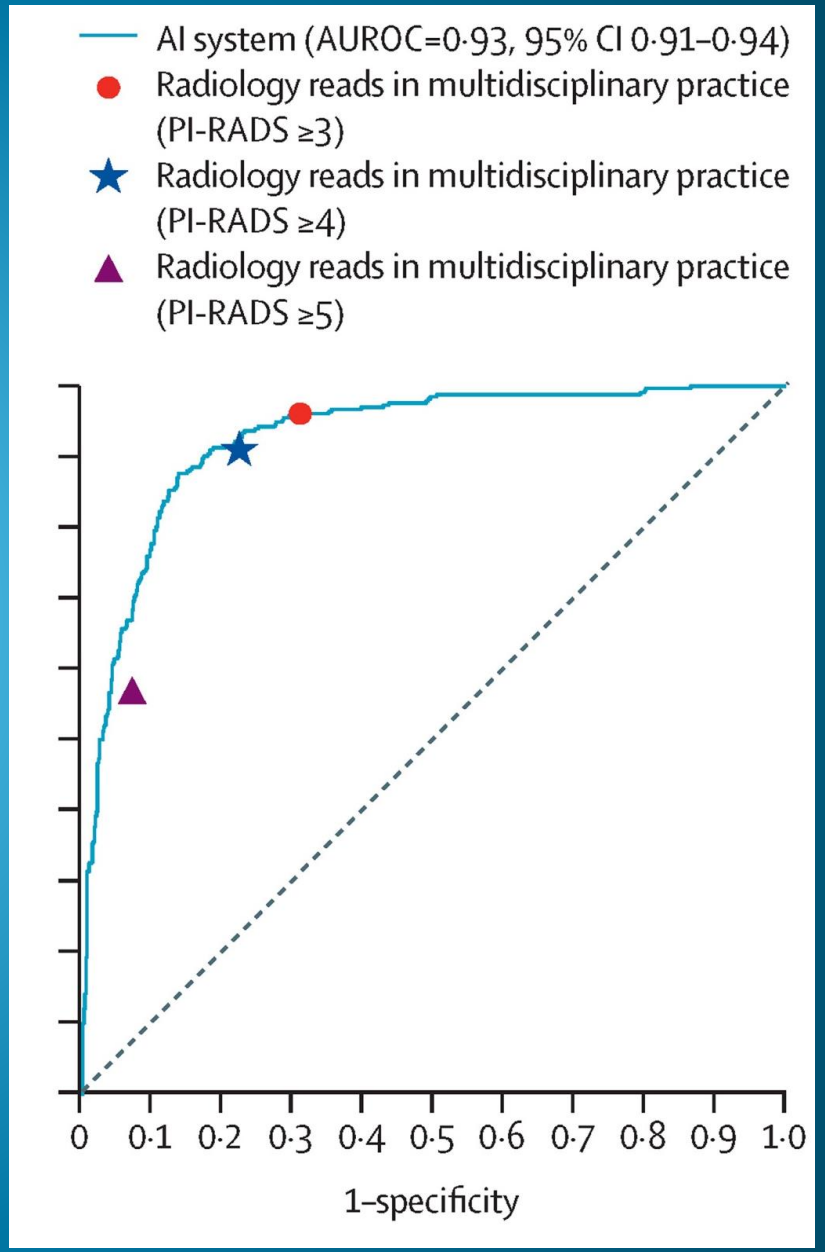


Hosseinzadeh M, et al. Deep learning-assisted prostate cancer detection on bi-parametric MRI: minimum training data size requirements and effect of prior knowledge 2022 Apr;32(4):2224-2234

Saha A, et al. End-to-end prostate cancer detection in bpMRI via 3D CNNs: Effects of attention mechanisms, clinical priori and decoupled false positive reduction. Med Image Anal. 2021 Oct;73:102155. [Epub]

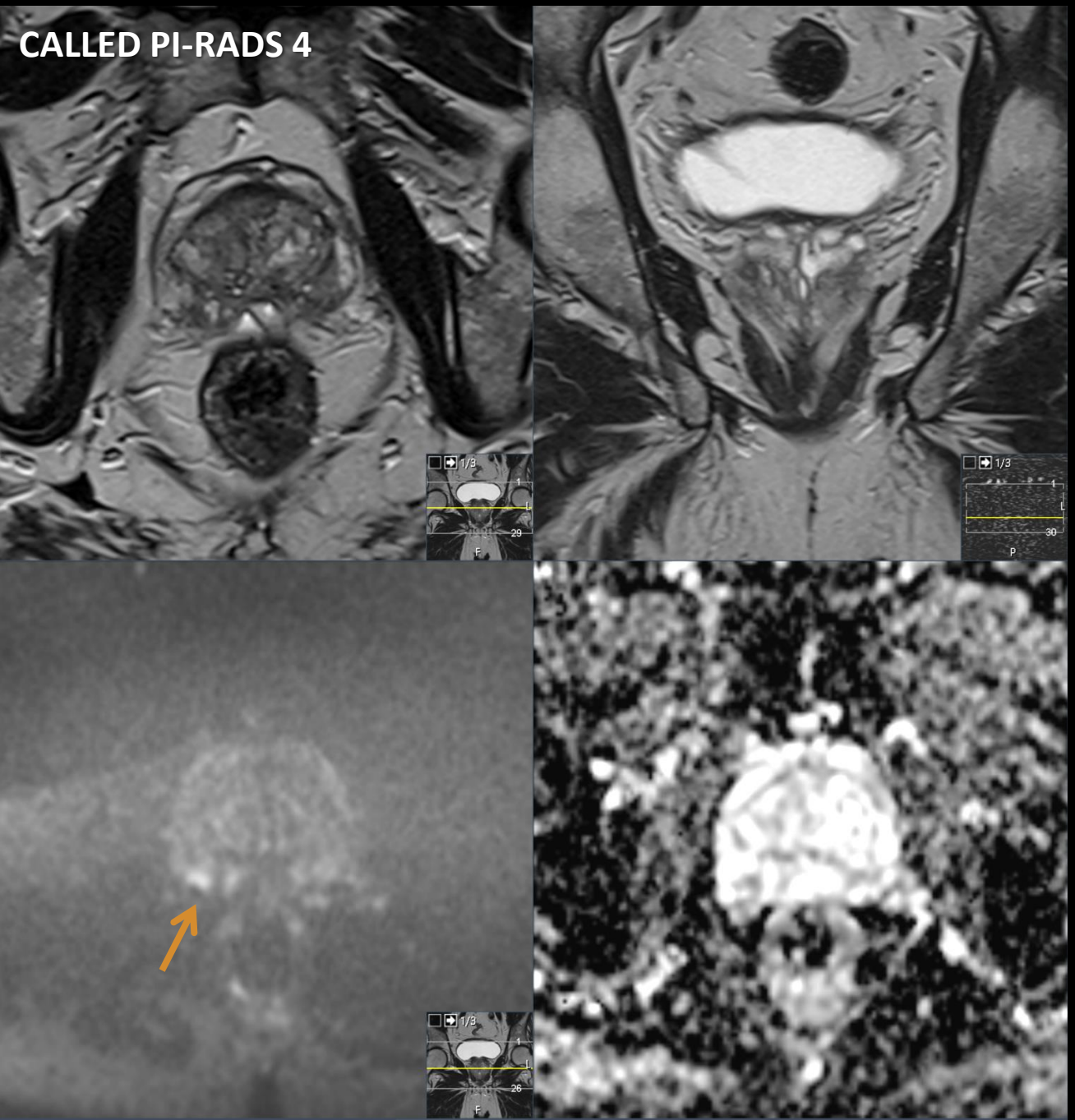
AI-system, trained on >10.000 cases

- 1000 cases
- AI vs radiologist + clinical data: AUROC 0.93
  + slightly lower specificity

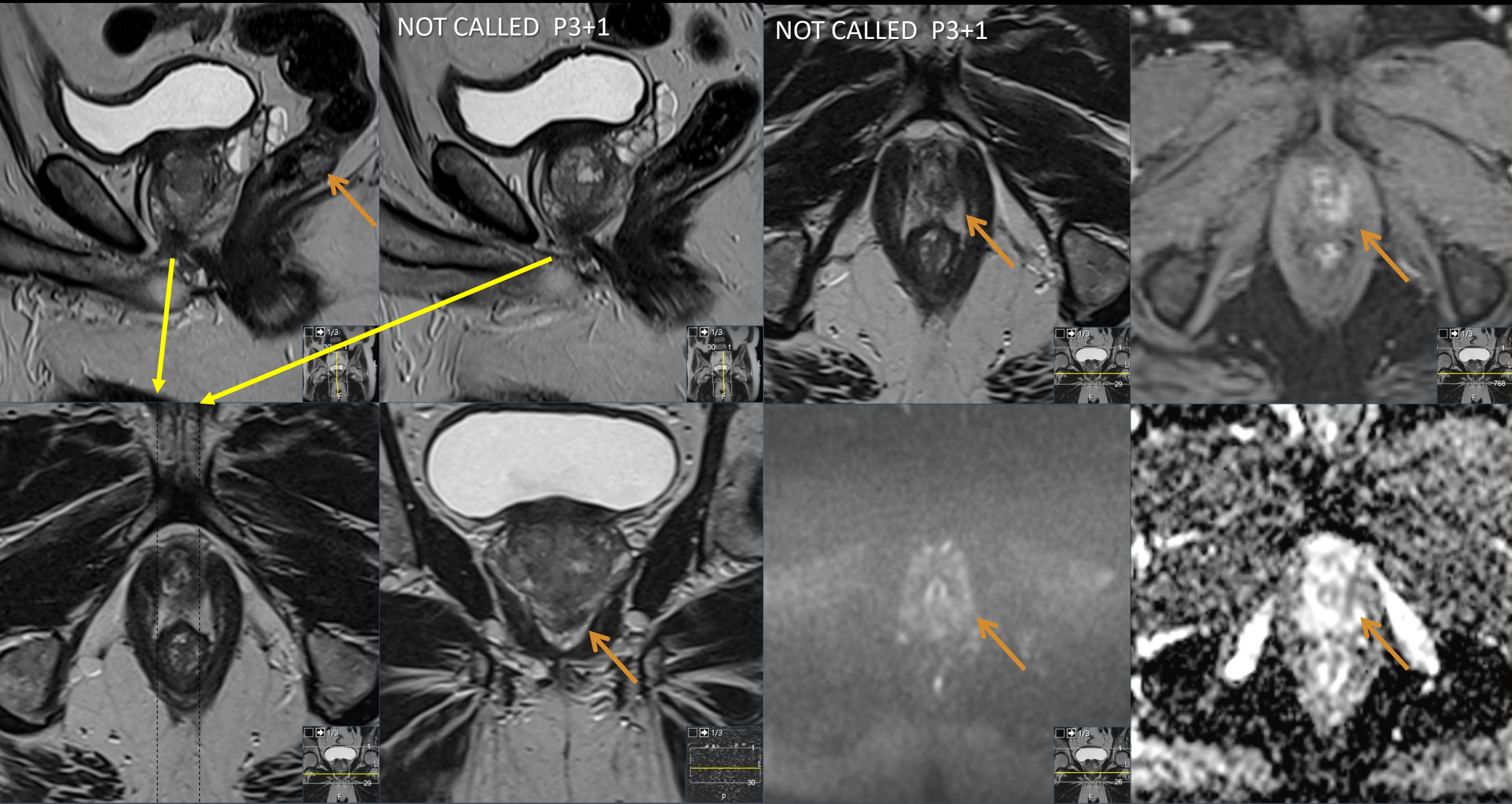


Saha, Lancet Oncology 2024

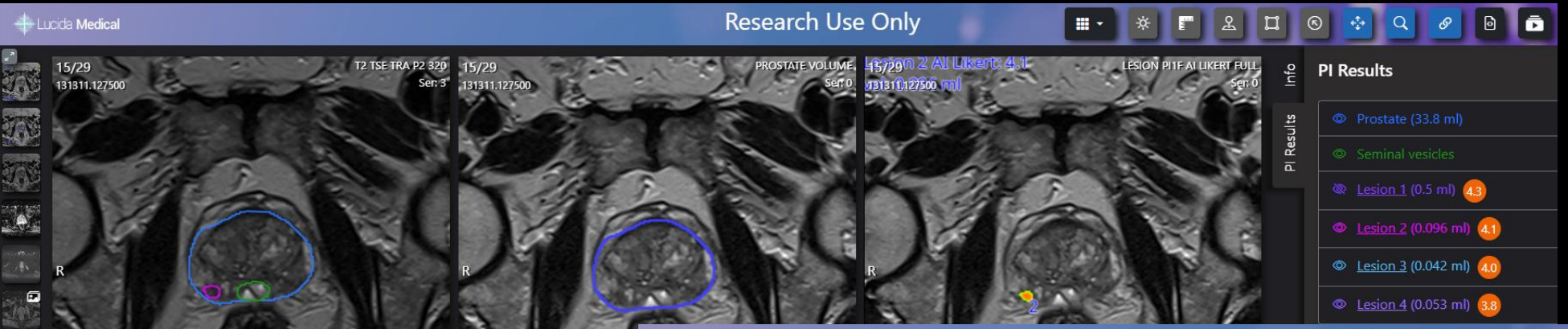
70M. Asymptomatic. PSA 2.67 2013; 3.13 2018; 6.38 Aug 21.

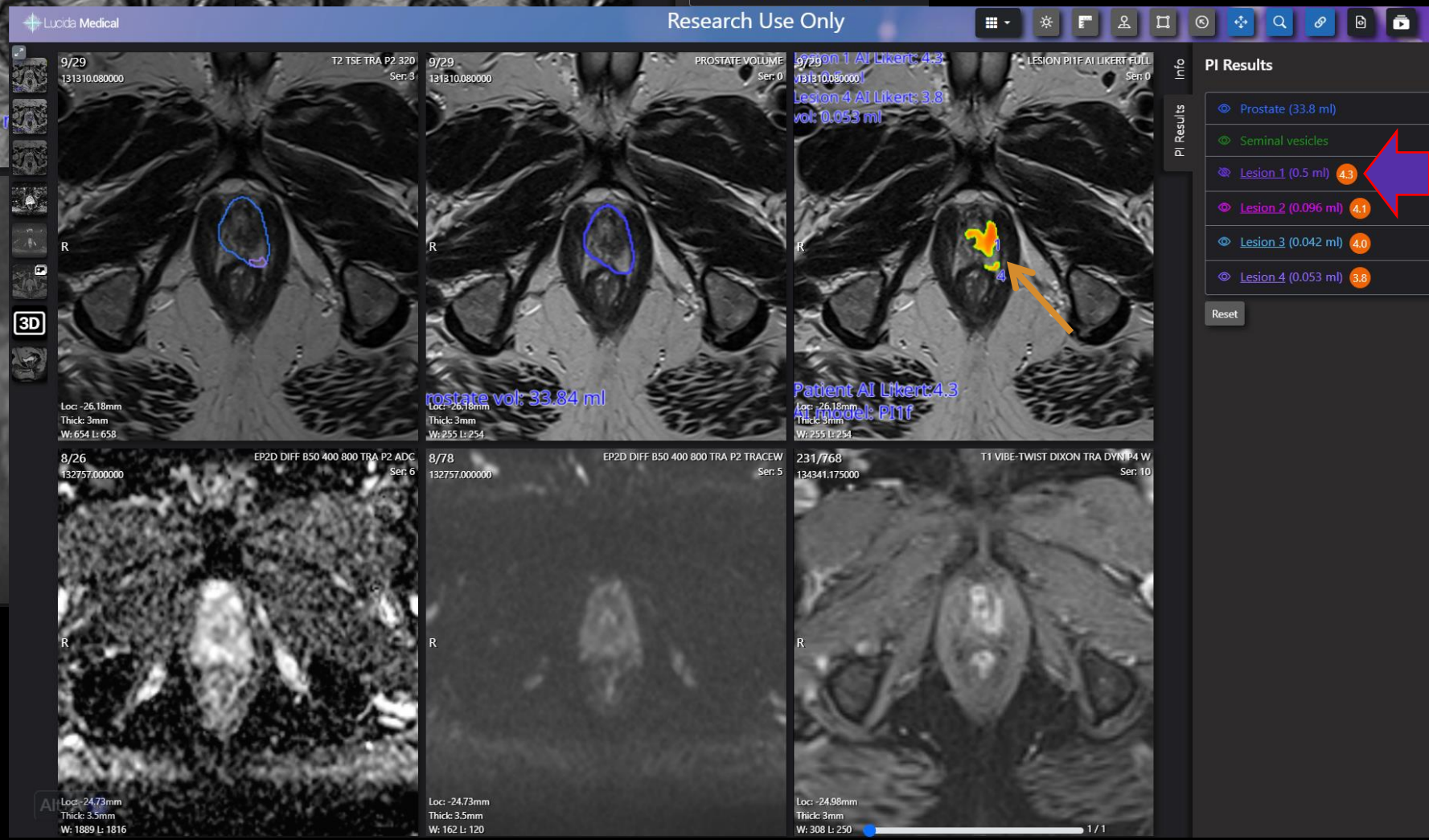


70M. Asymptomatic. PSA 2.67 2013; 3.13 2018; 6.38 Aug 21. GS 3+4 pT3a, R1 left apex margin.



70M. Asymptomatic.
PSA 2.67 2013; 3.13 2018; 6.38 Aug 21.
Mid-rectal polyp also.





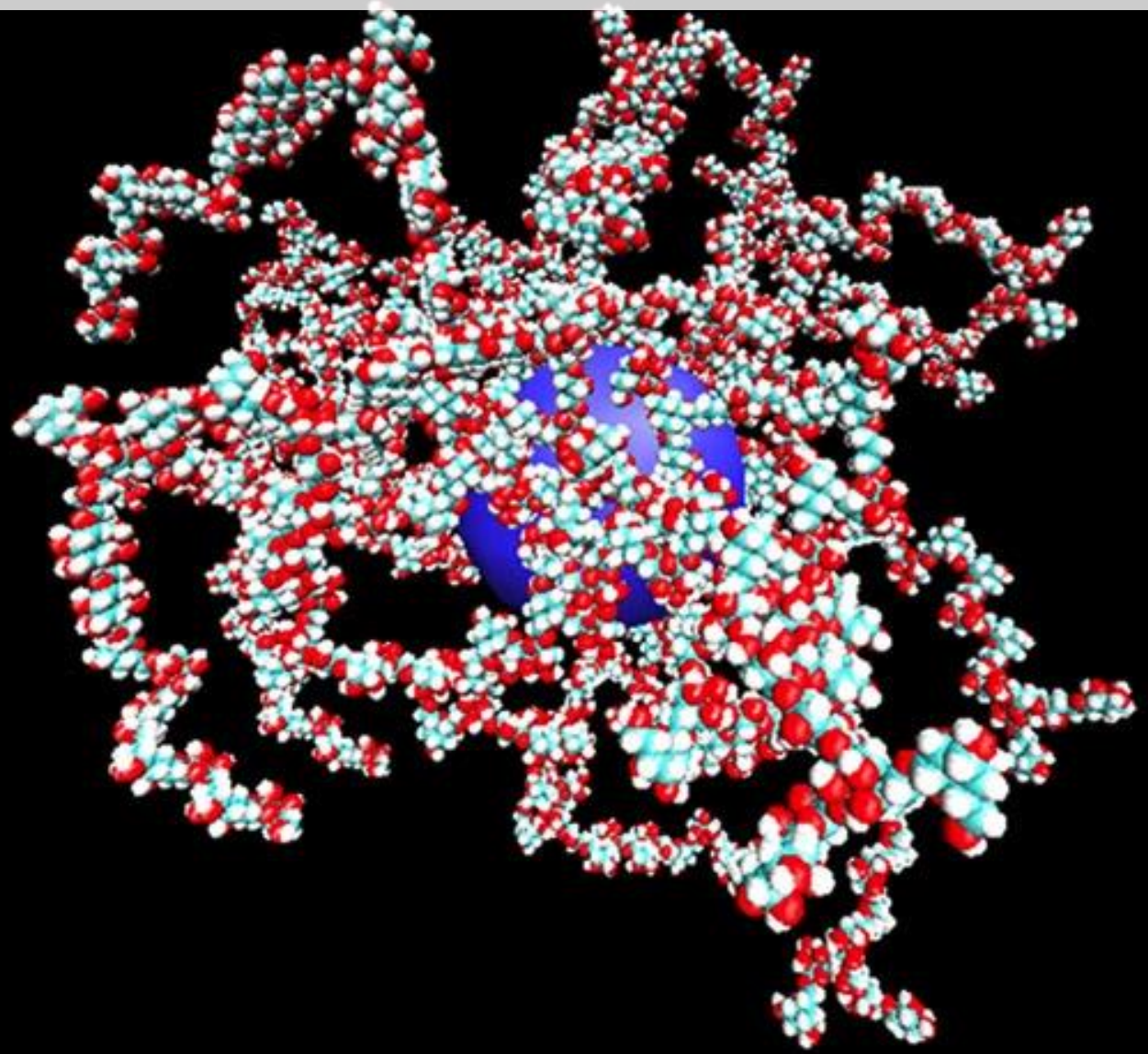
70M. Asymptomatic.
PSA 2.67 2013; 3.13 2018; 6.38 Aug 21.
Mid-rectal polyp also.
GS 3+4 pT3a, R1 left apex margin.

Can the Radiologists be replaced by AI?

They have to learn this “new” modality

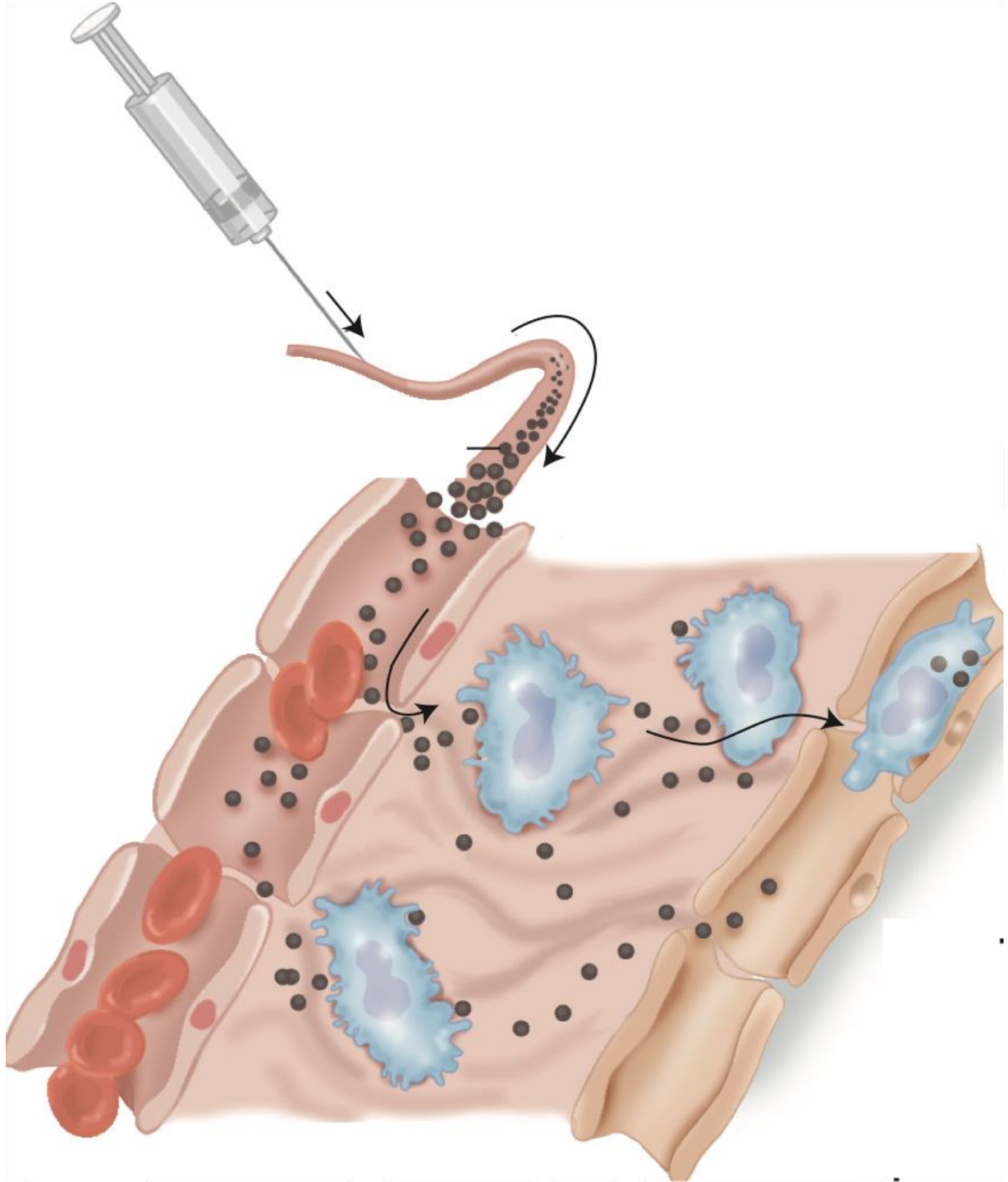
2 Nodes

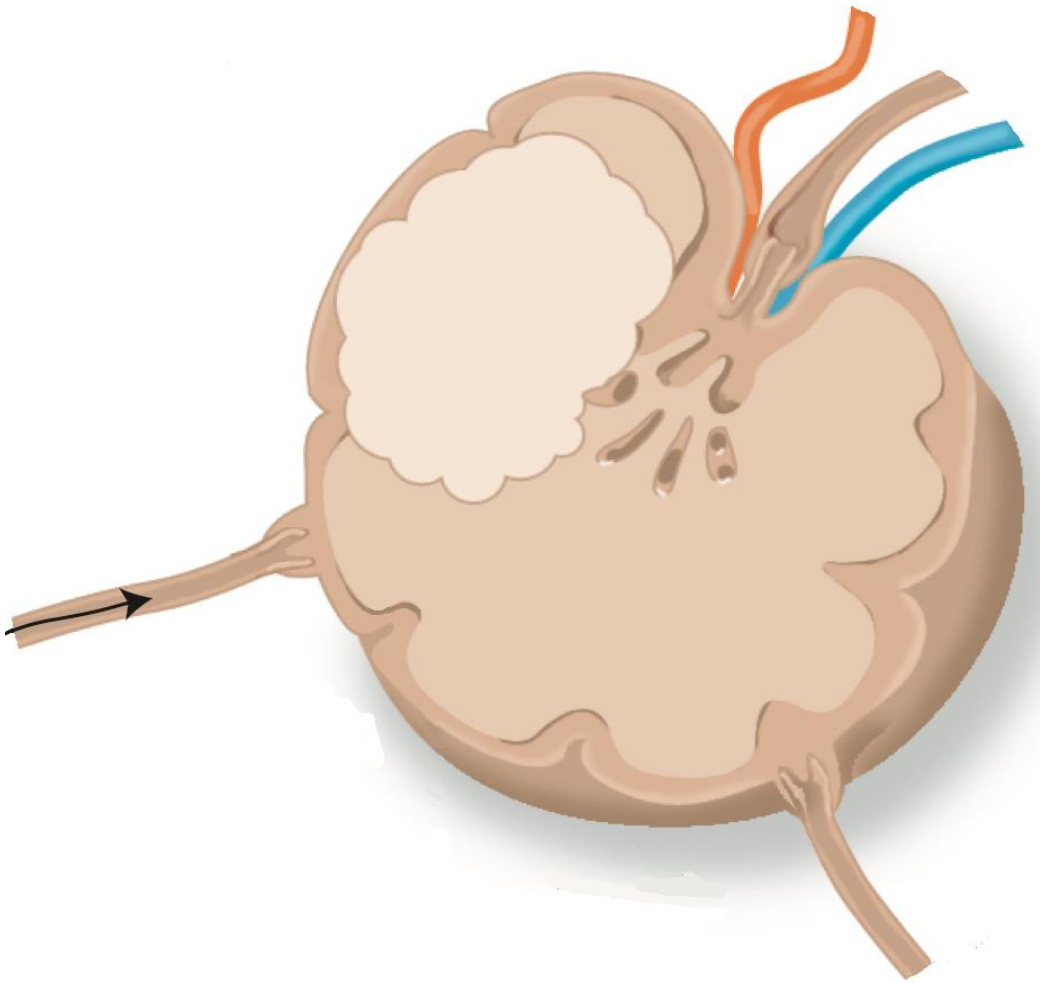
Nano-particle (Ferrotran) MRI

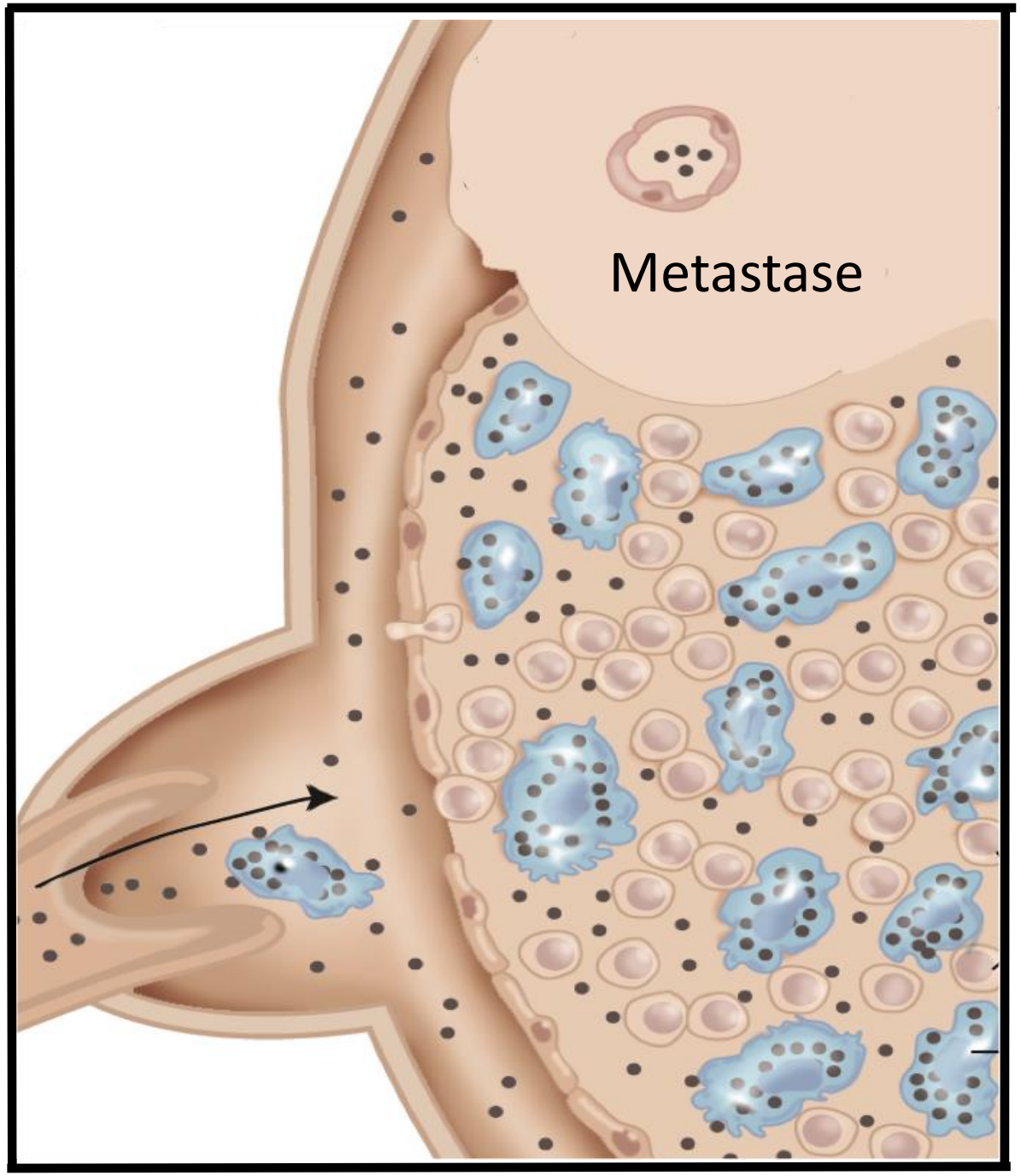


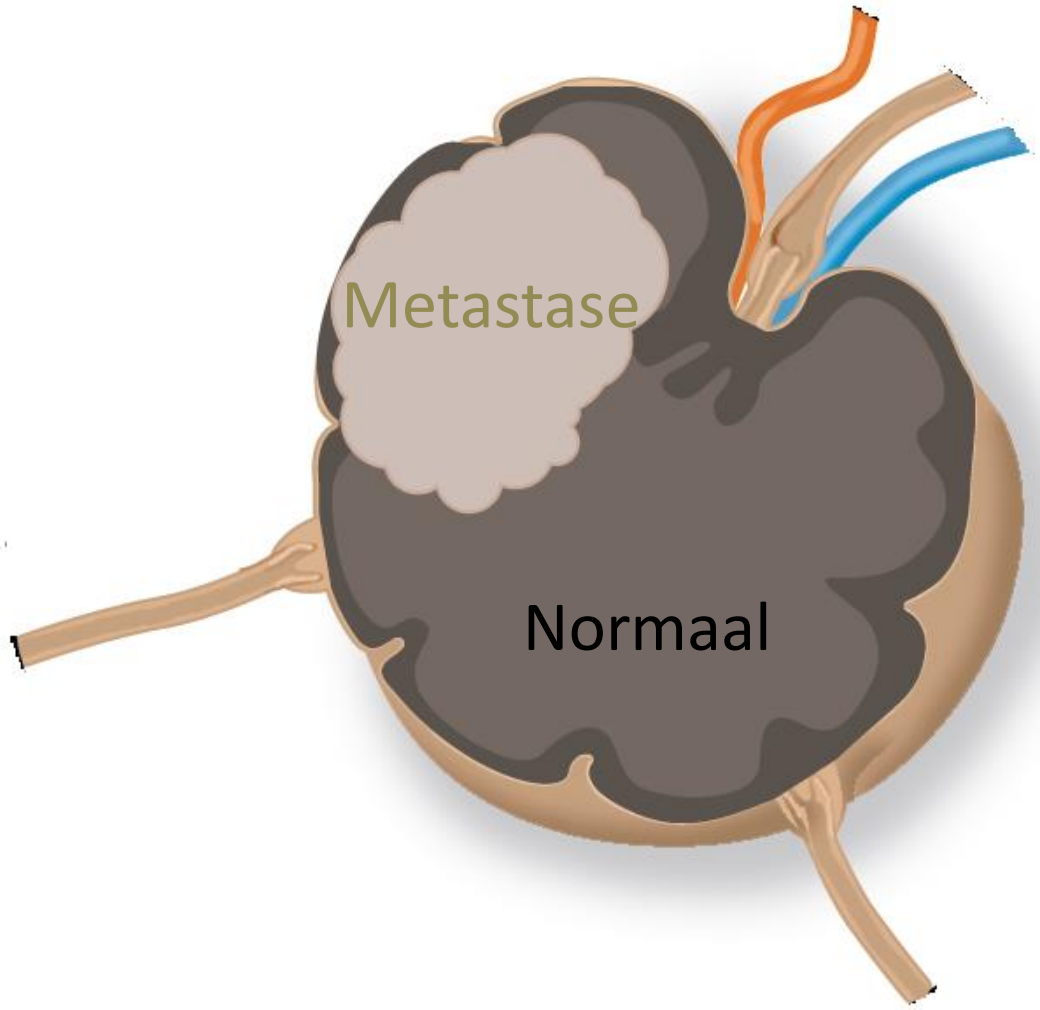
Nano-particle (Ferrotran) MRI

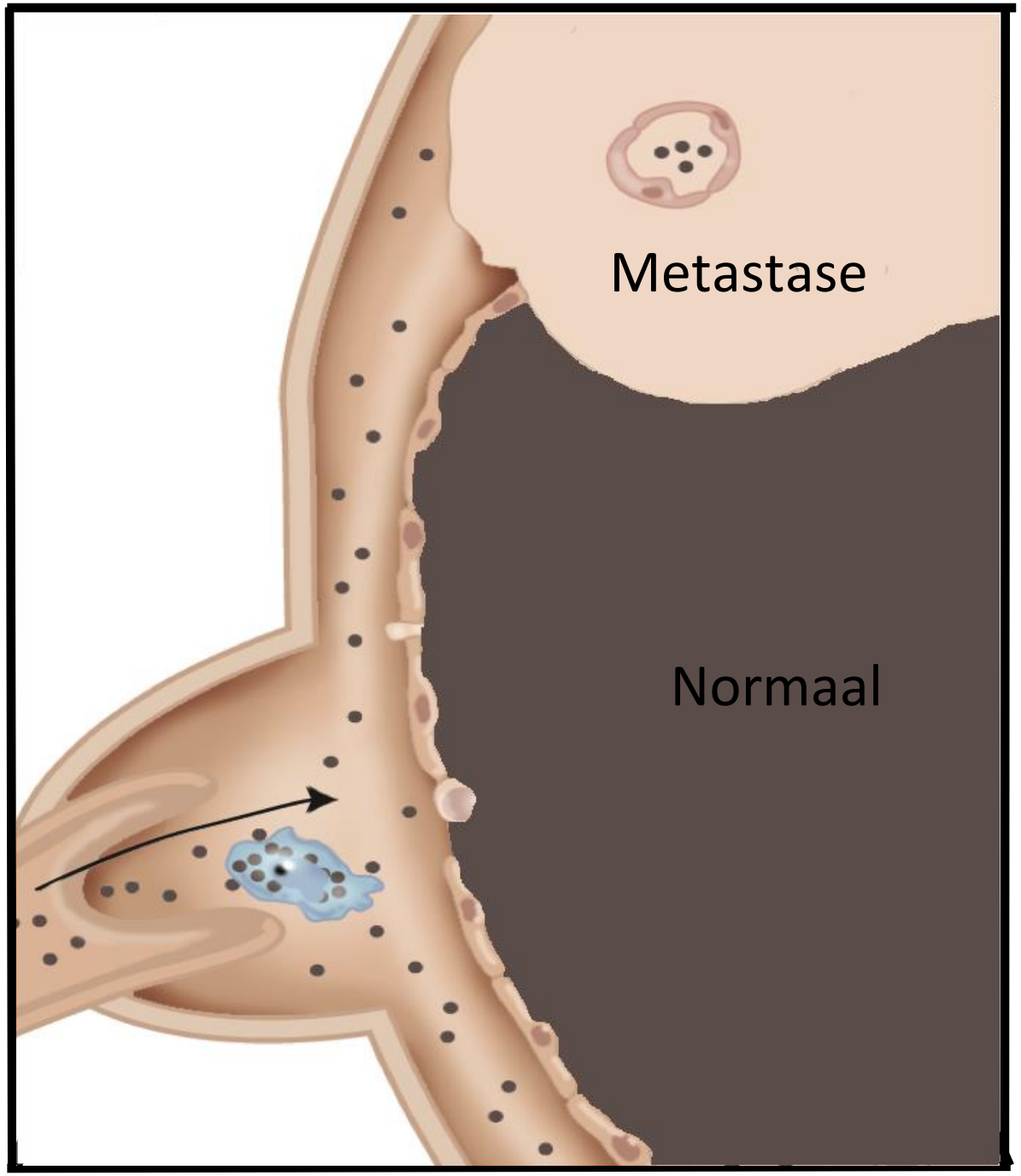
Radboudumc

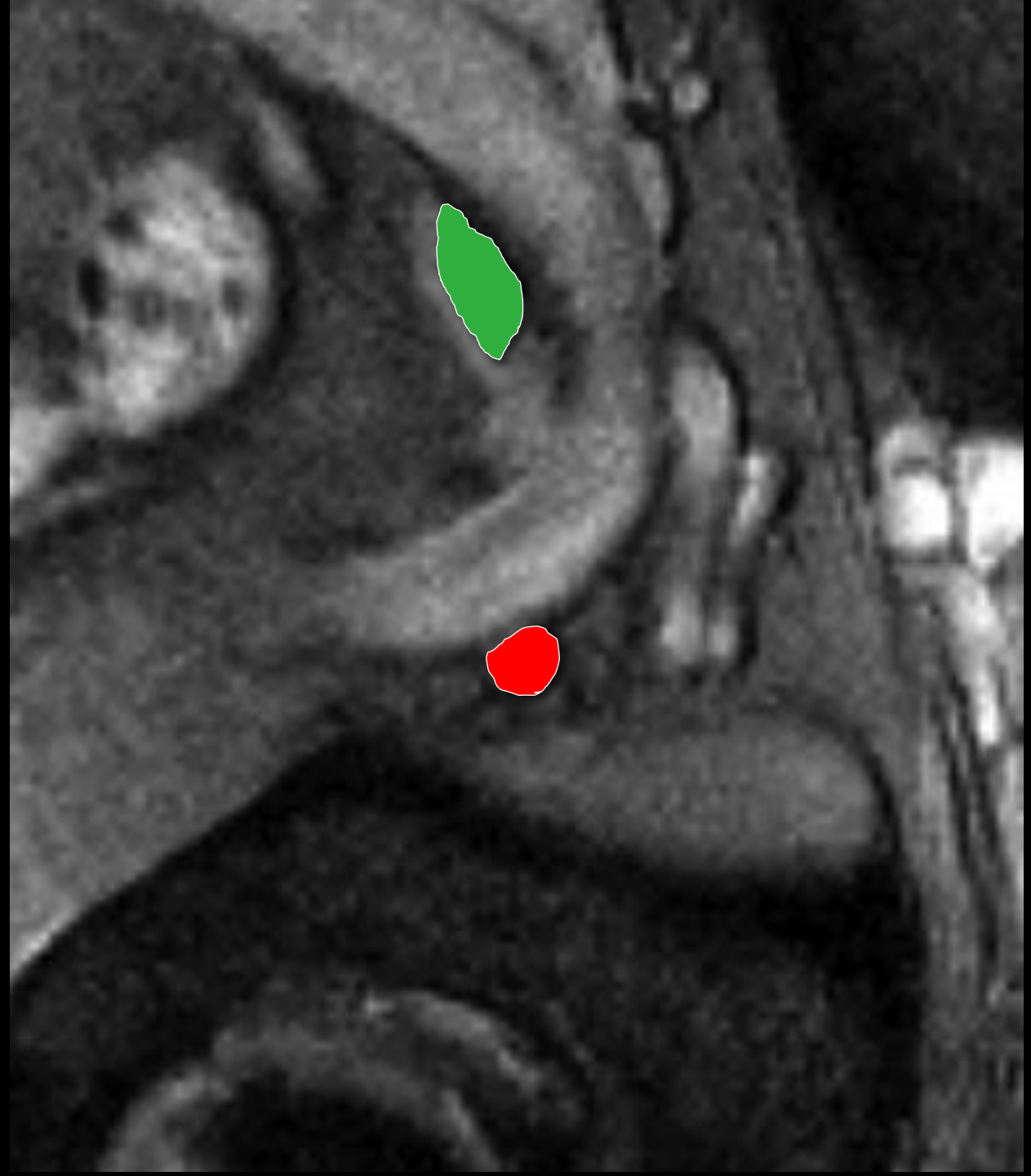


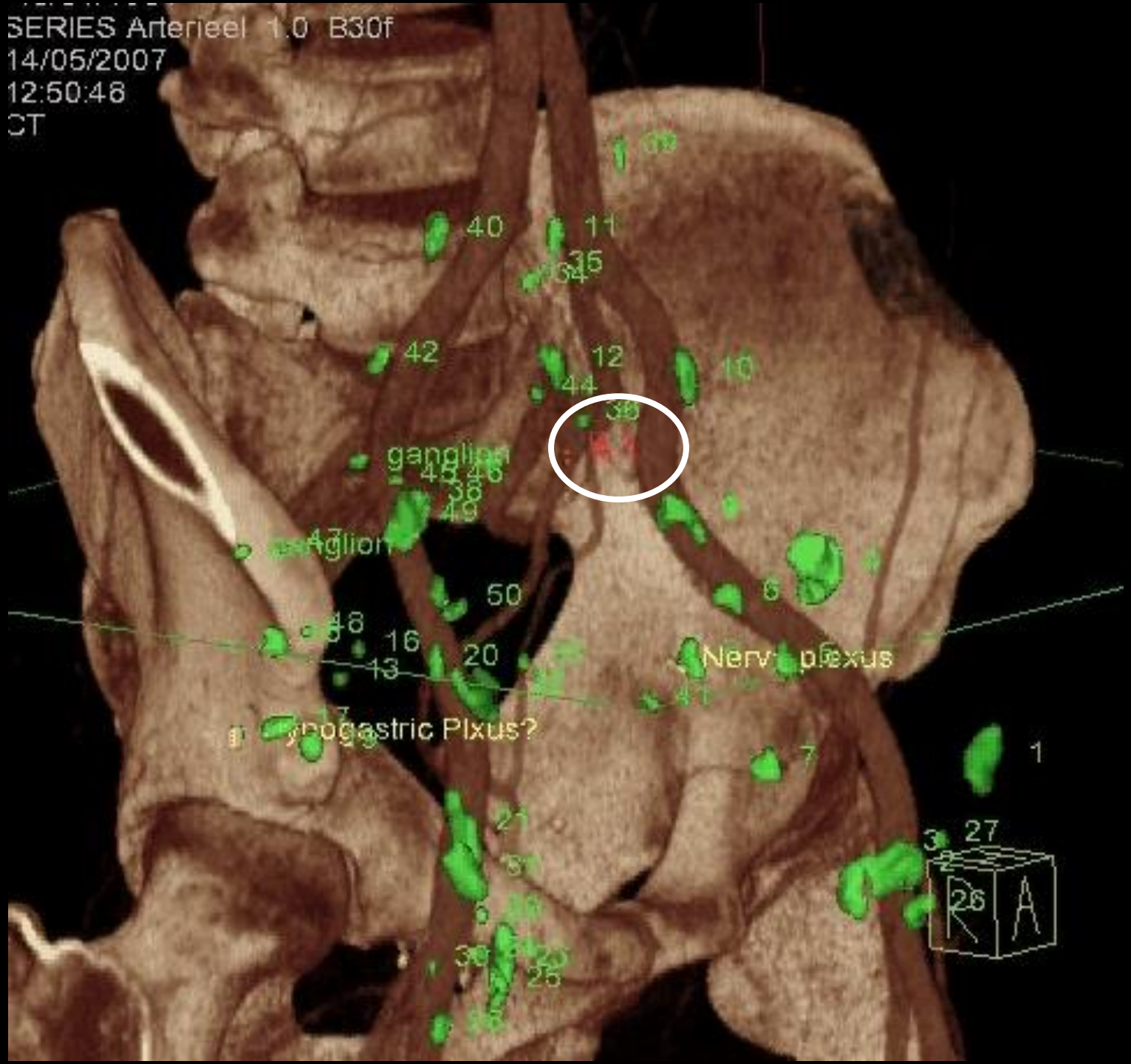


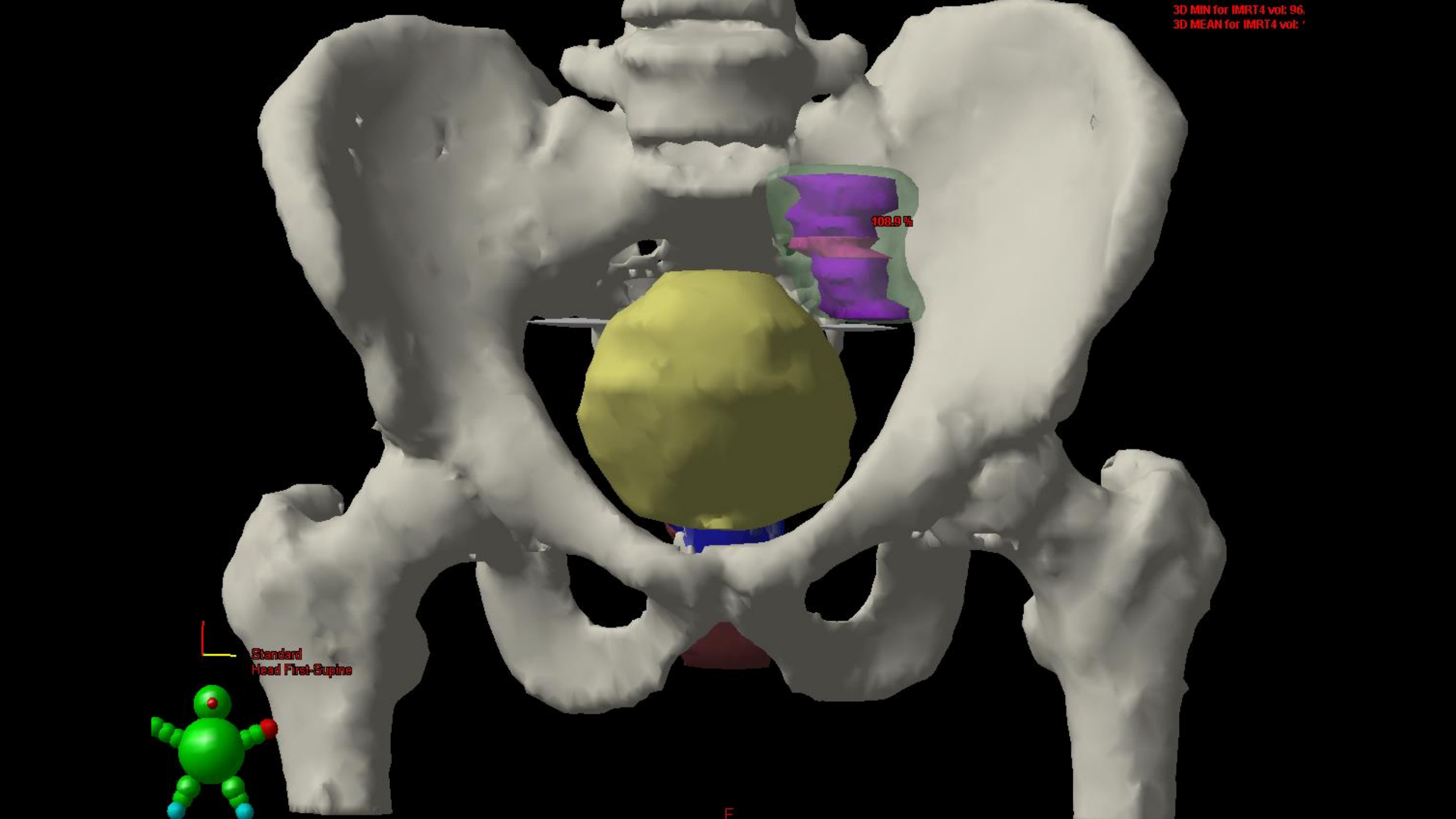

Metastase


Metastase
Normaal

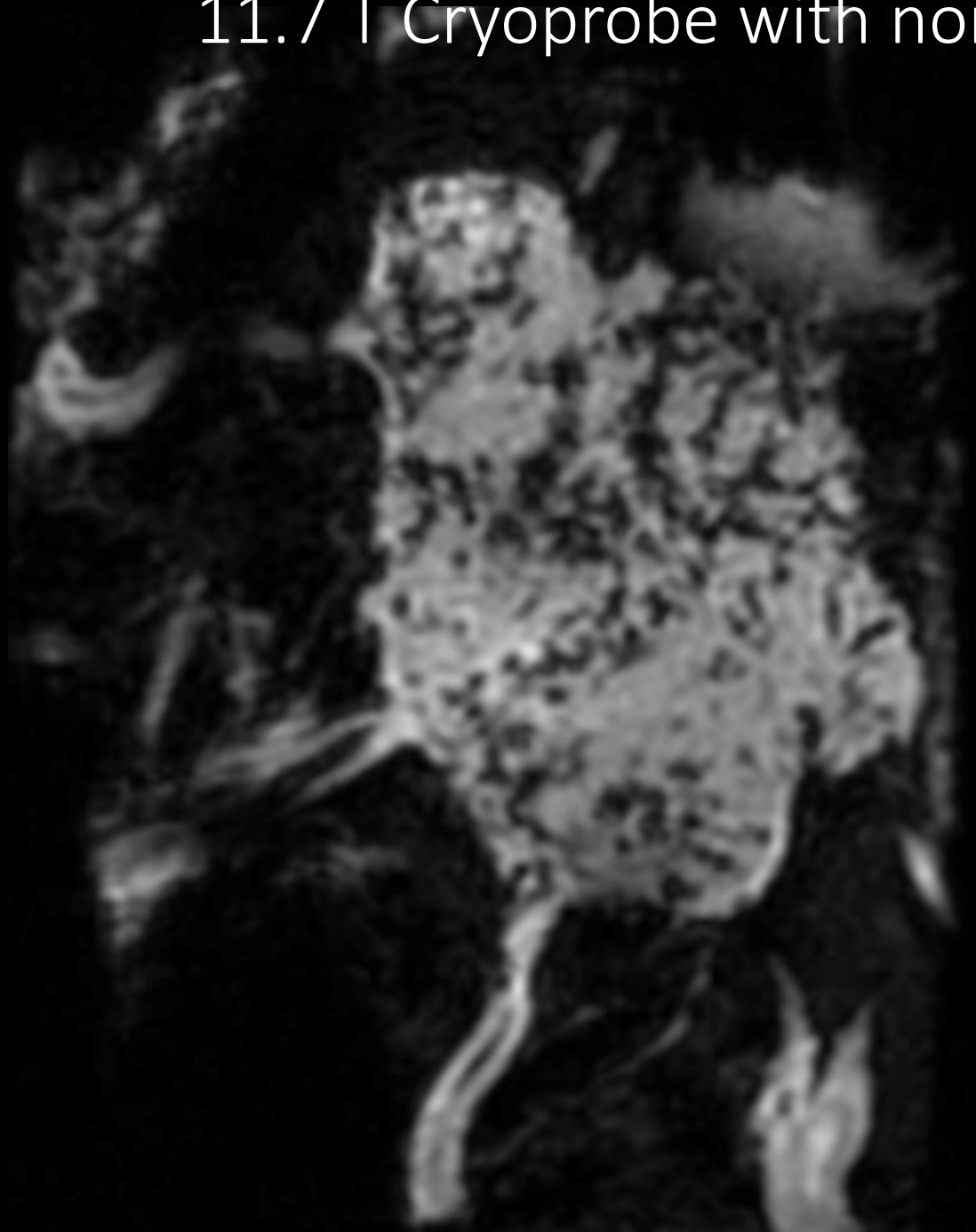

Metastase
Normaal




SERIES Arterieel 1.0 B30f
14/05/2007
12:50:48
CT
40
11
35
42
12
10
ganglion
50
16
20
Nerv plexus
ypogastric Plxus?
1
27
R
A


3D MIN for IMRT4 vol: 96.
3D MEAN for IMRT4 vol:
108.9 %
Standard
Head First-Supine
F

11.7 T Cryoprobe with nomal lymph node post Ferrotran IV



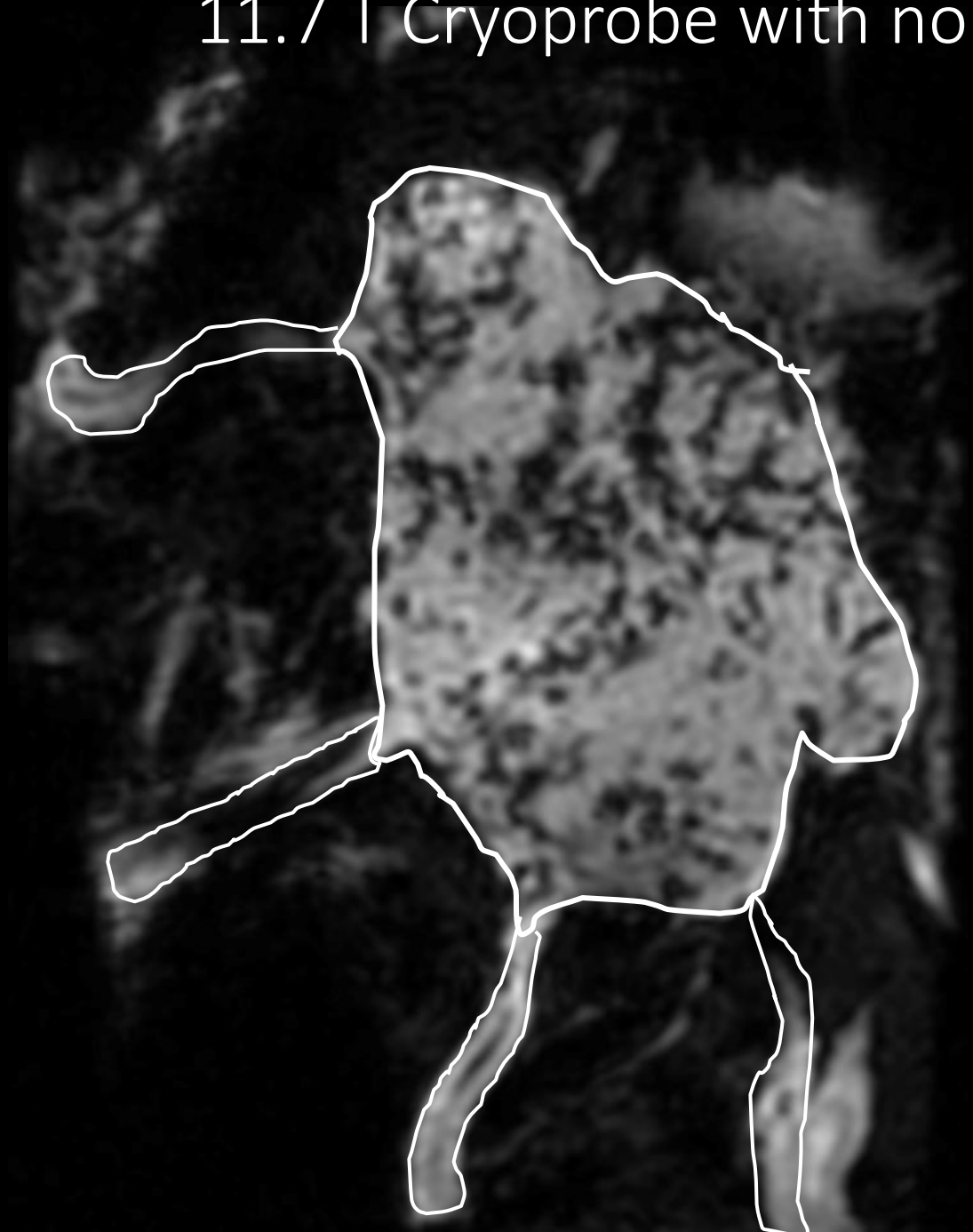
Resolution:

63 micron (isotropic)

Black dots

-> individual macrophages

11.7 T Cryoprobe with nomal lymph node post Ferrotran IV

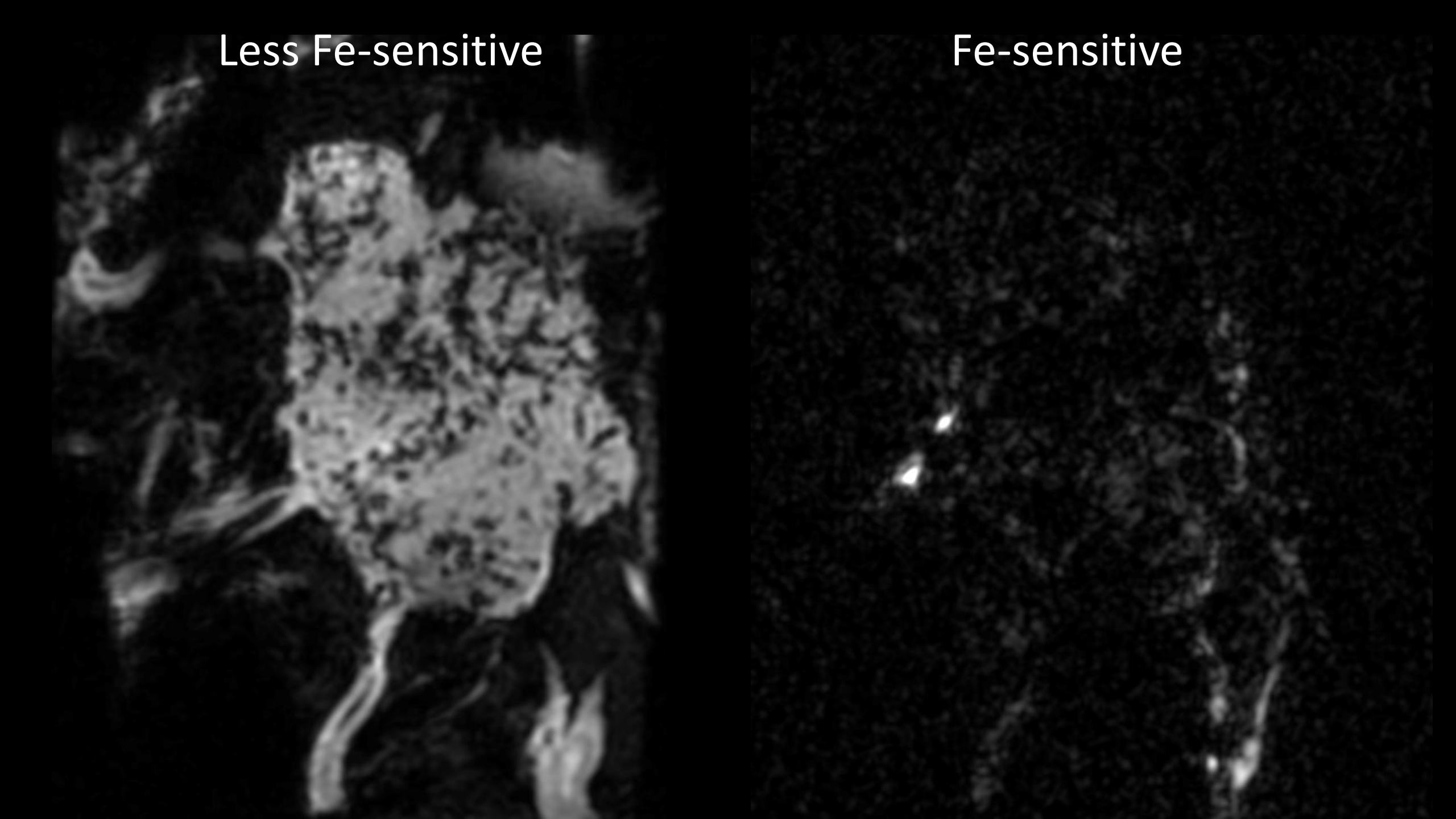


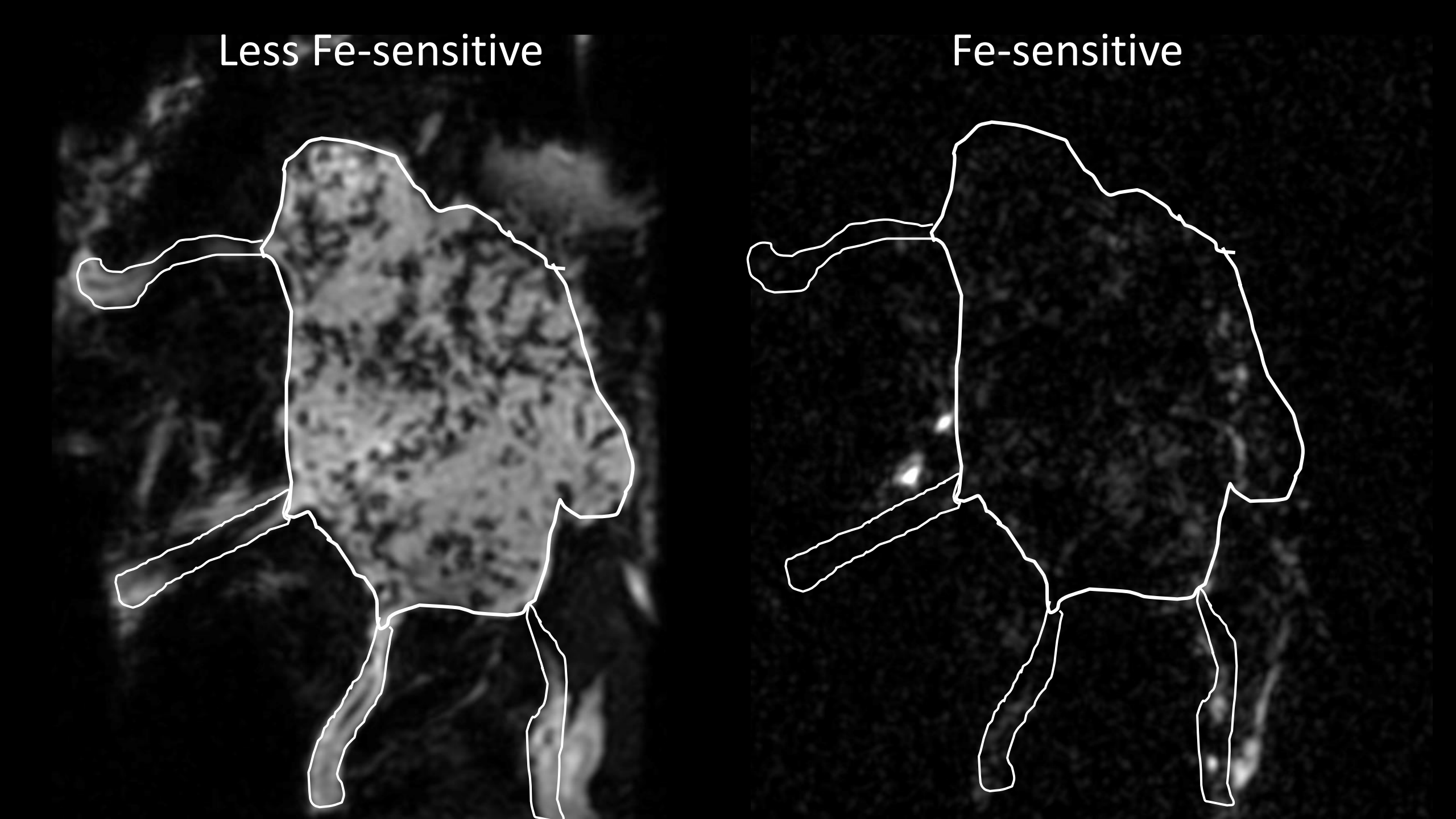
Resolution:

63 micron (isotropic)

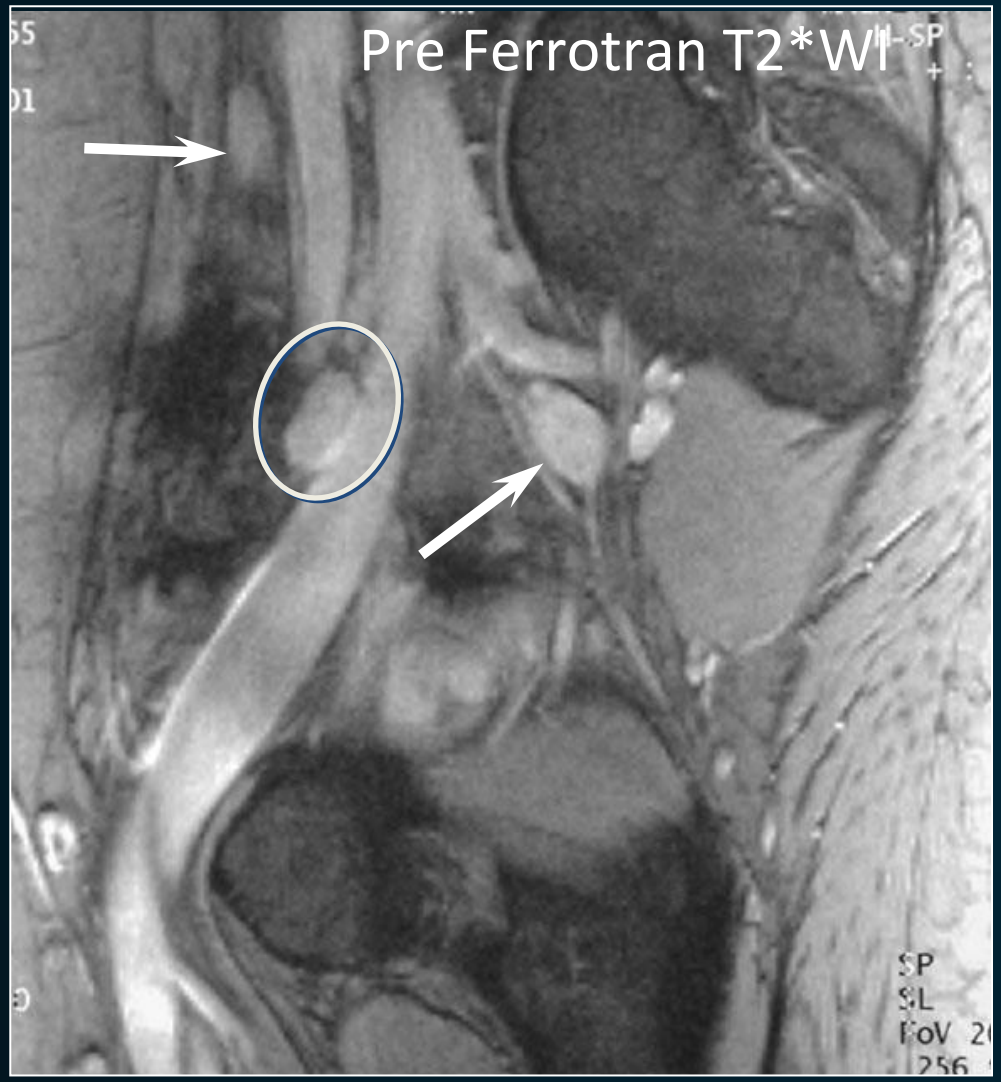
Black dots

-> individual macrophages

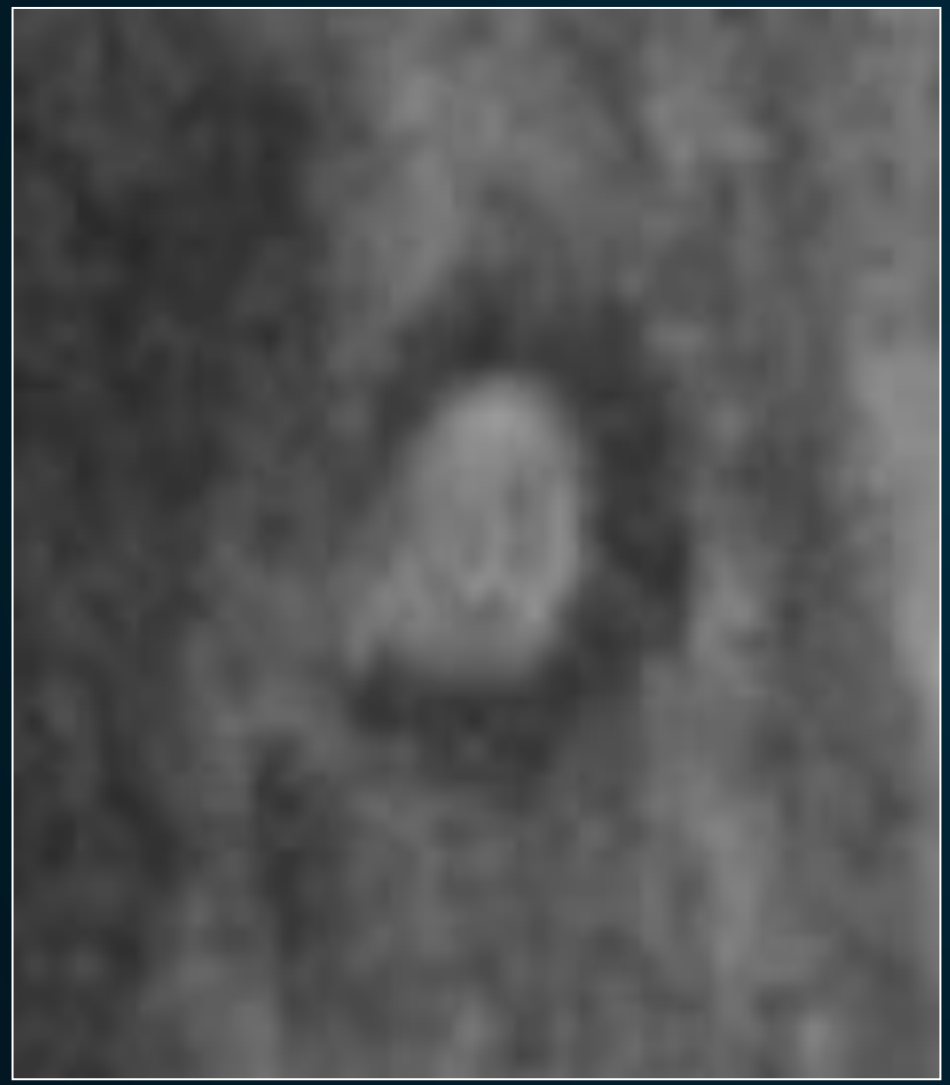

Less Fe-sensitive
Fe-sensitive

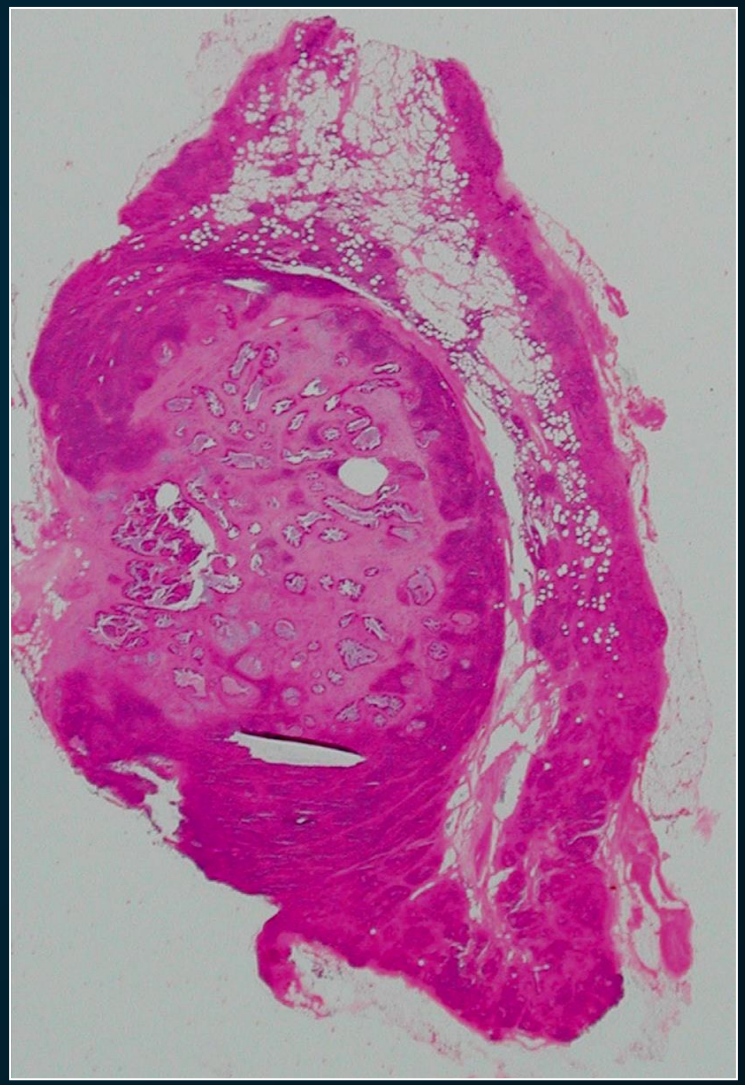

Less Fe-sensitive
Fe-sensitive

1 Partially abnormal LN, 2 normal LN's

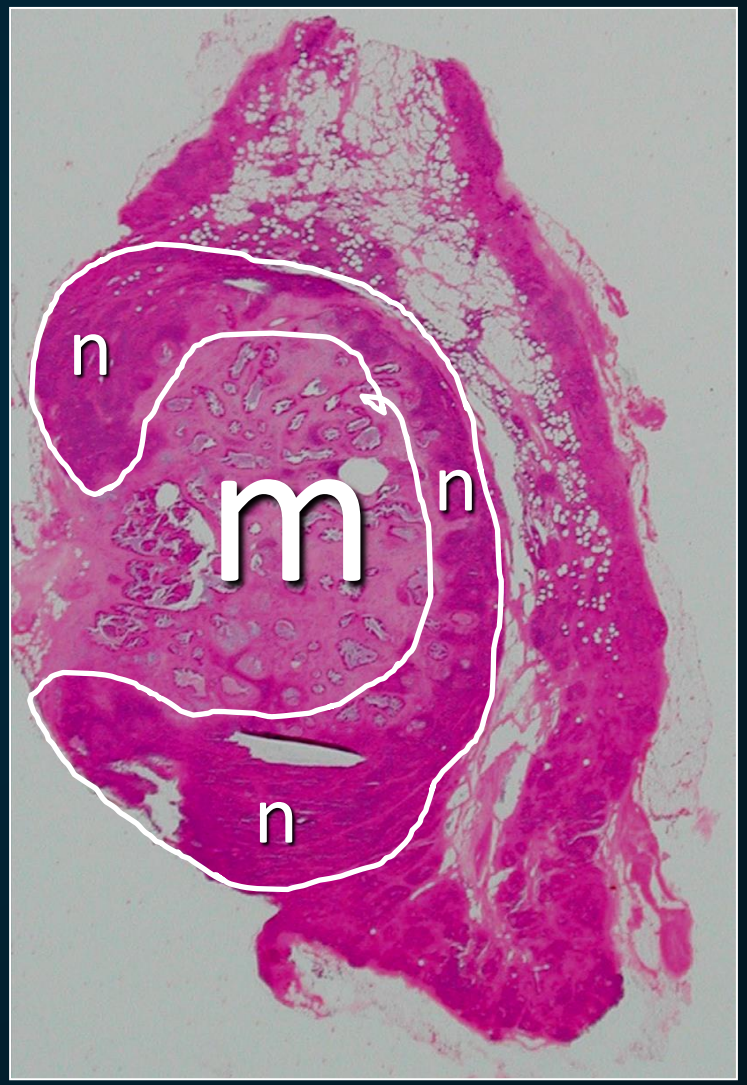


Partially positive LN

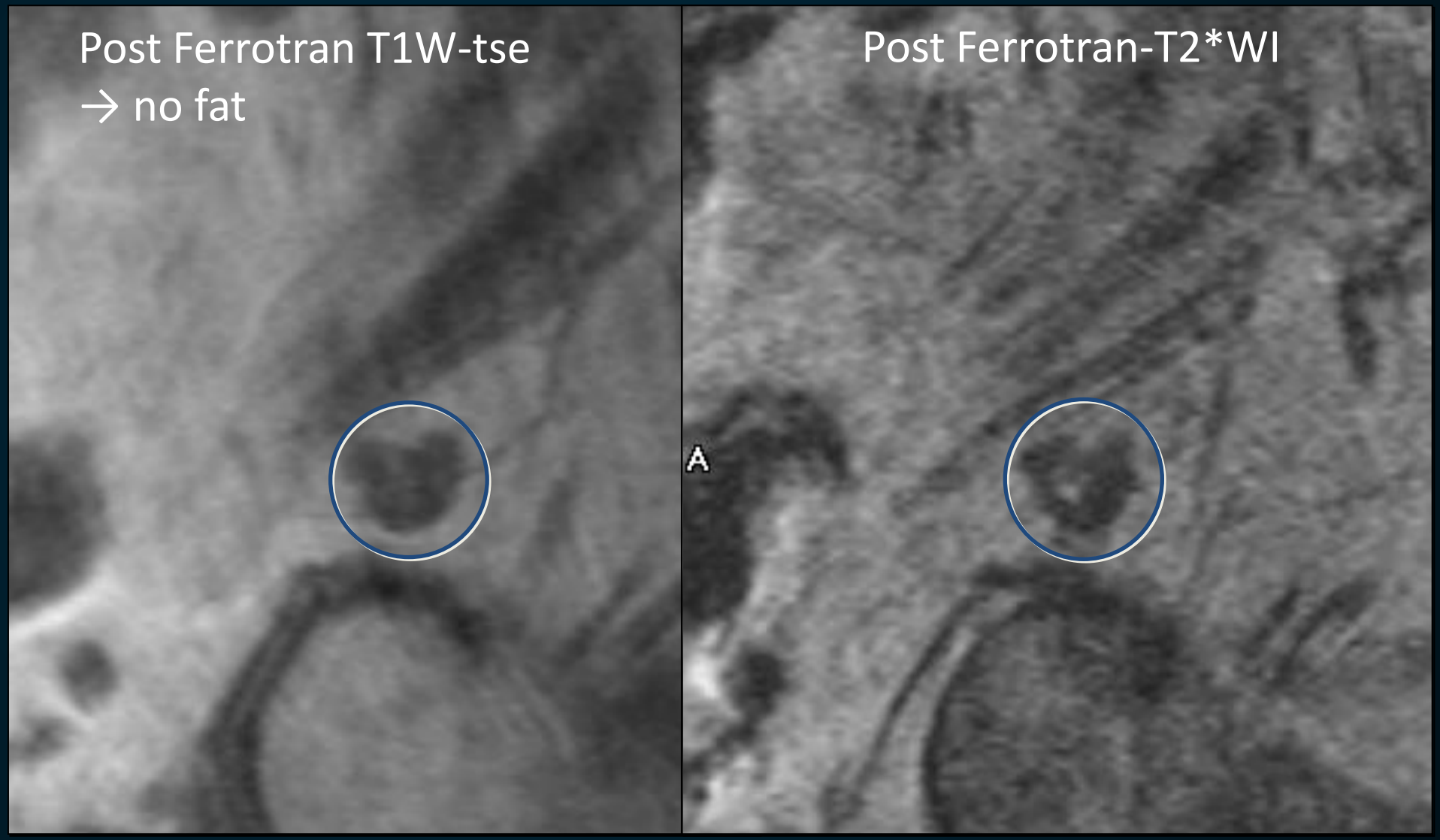




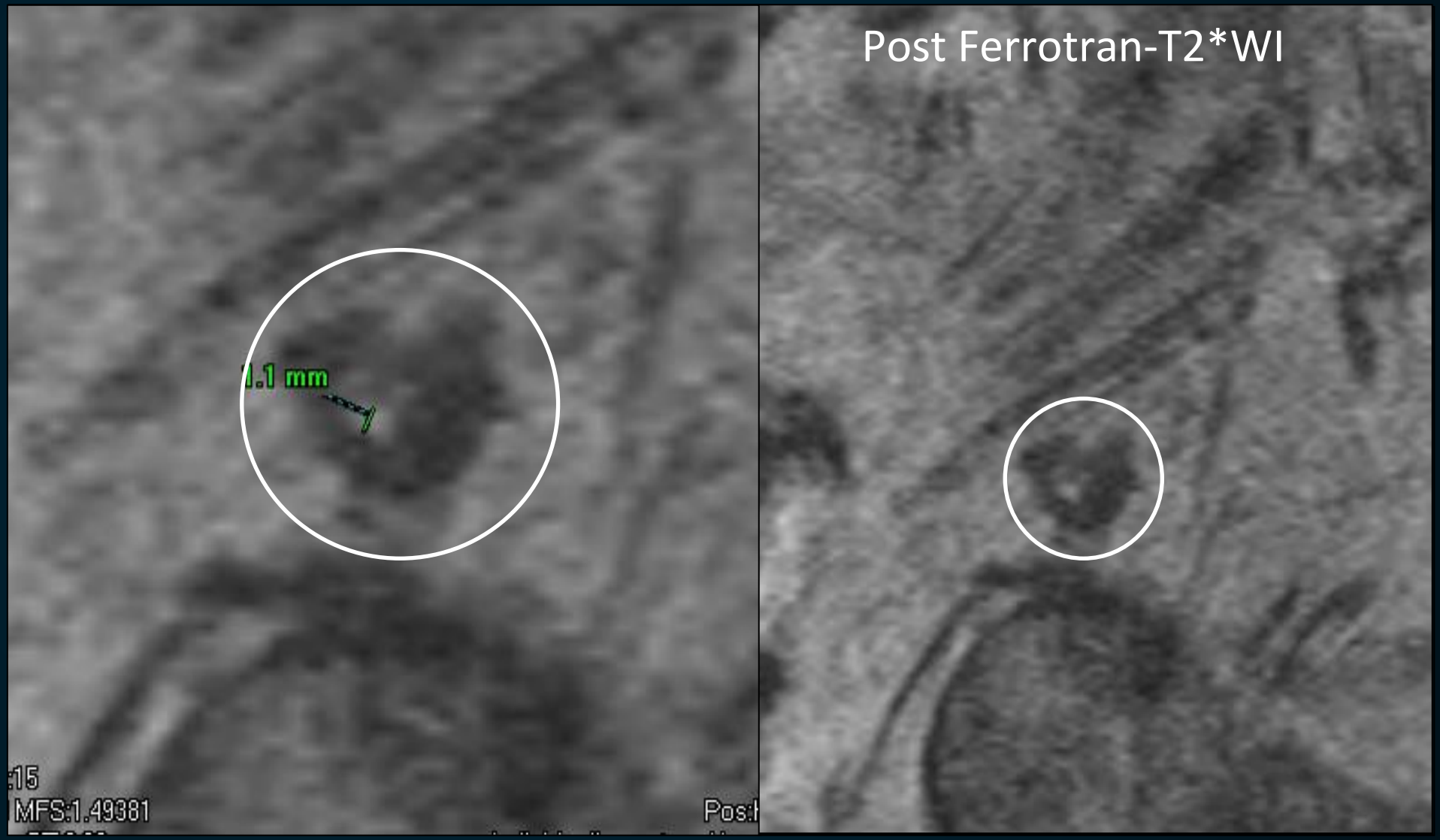
Partially positive LN



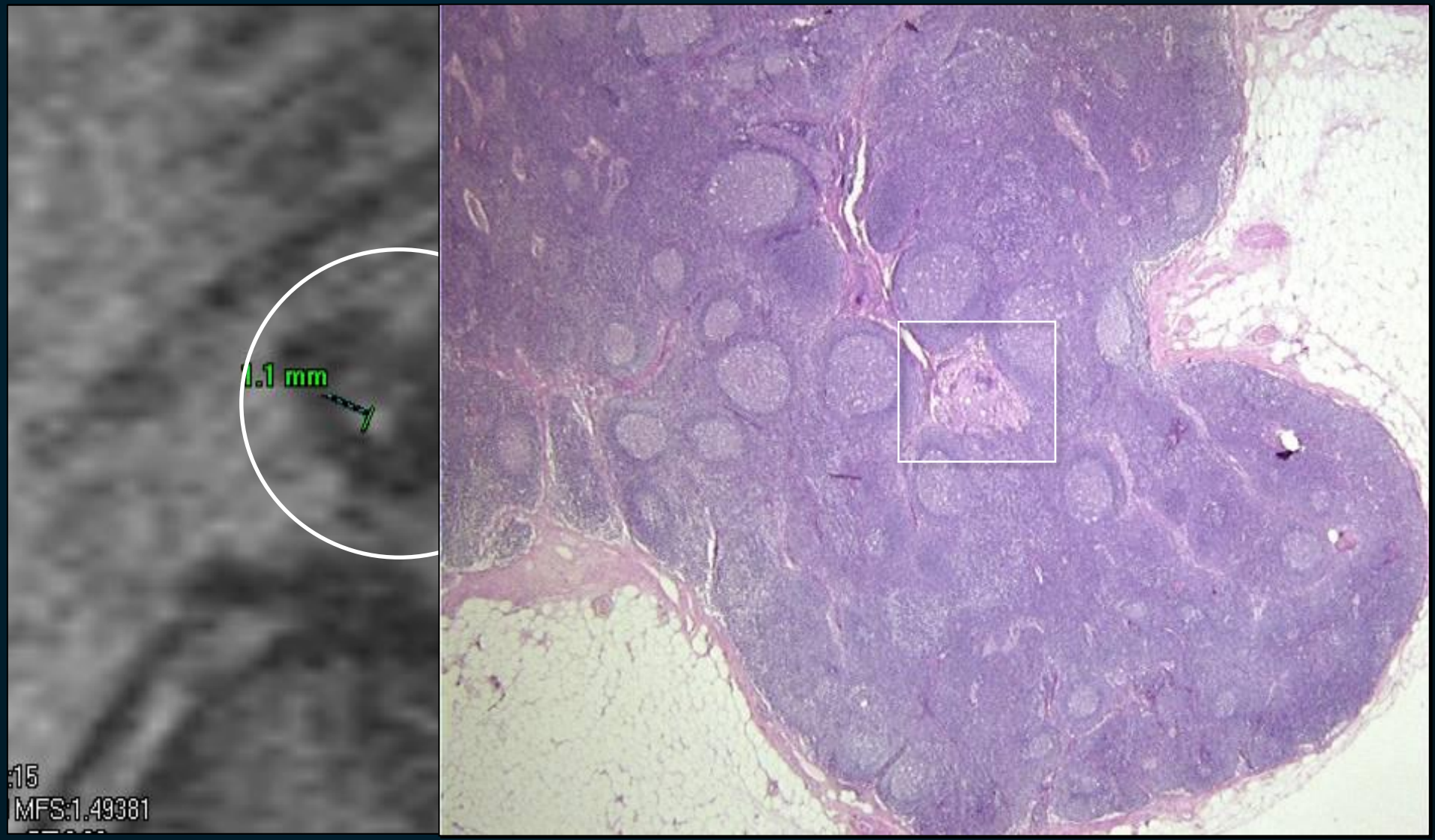
1.1 mm central LN metastasis (1.5T)



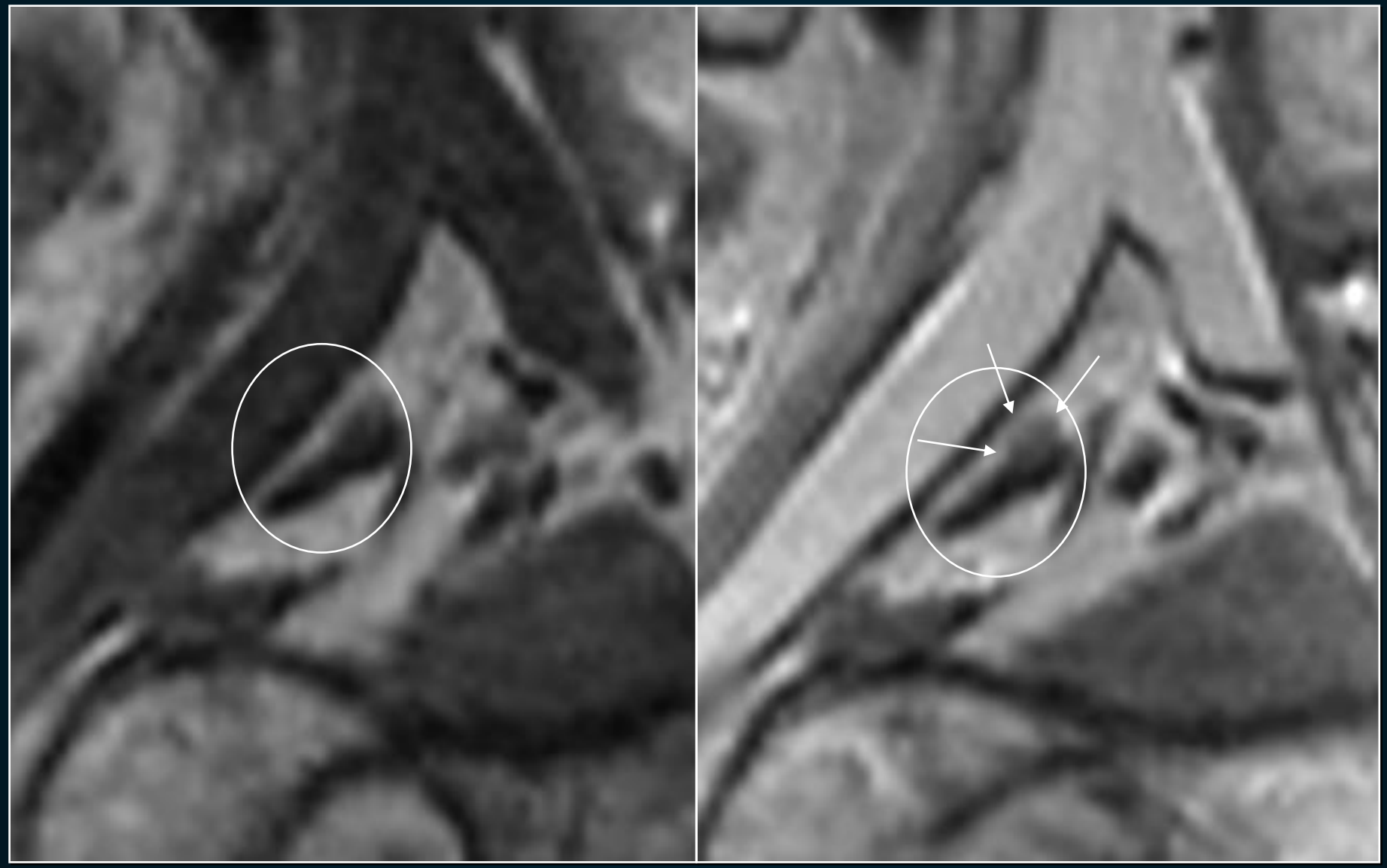
1.1 mm central LN metastasis (1.5T)



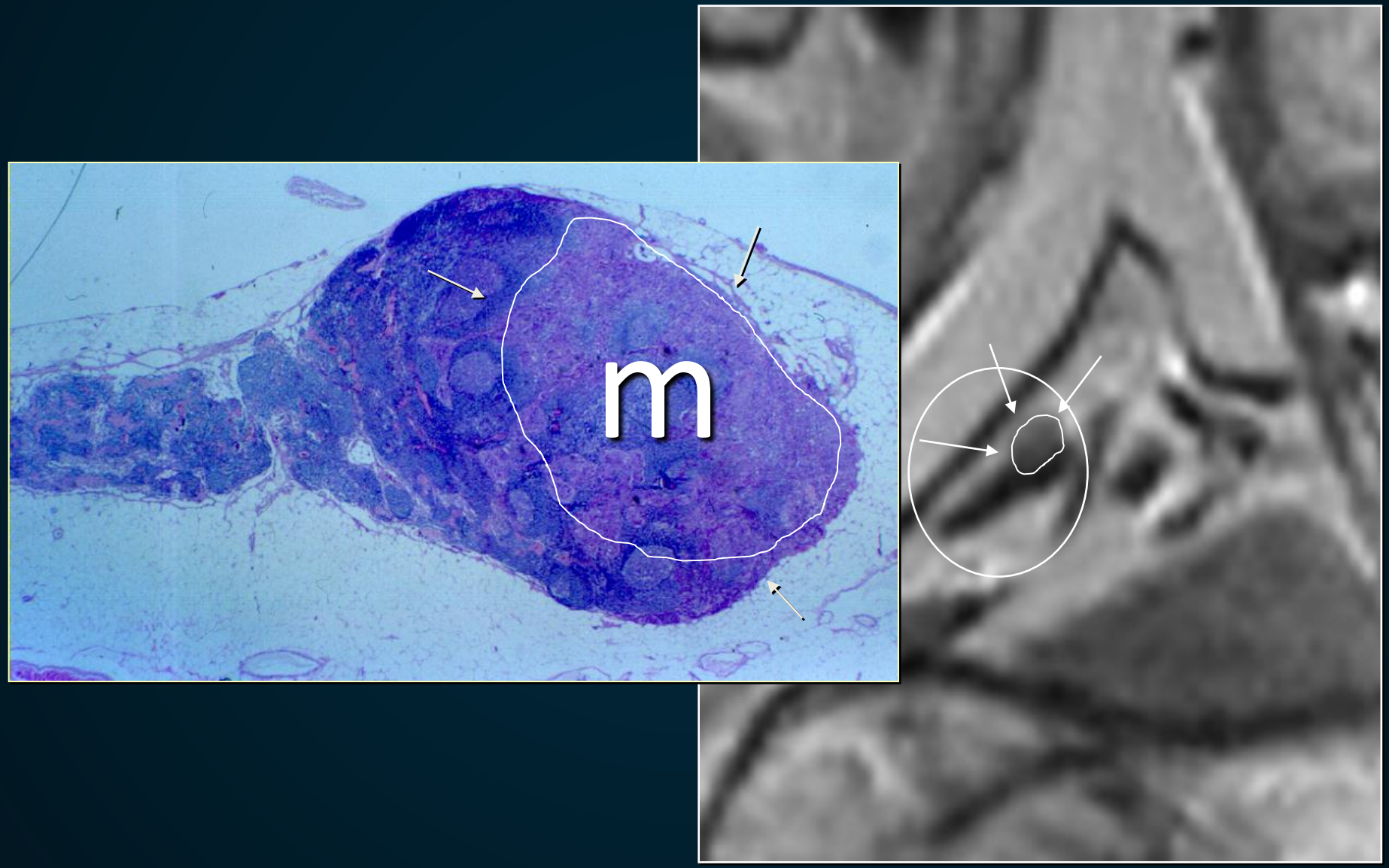
1.1 mm central LN metastasis

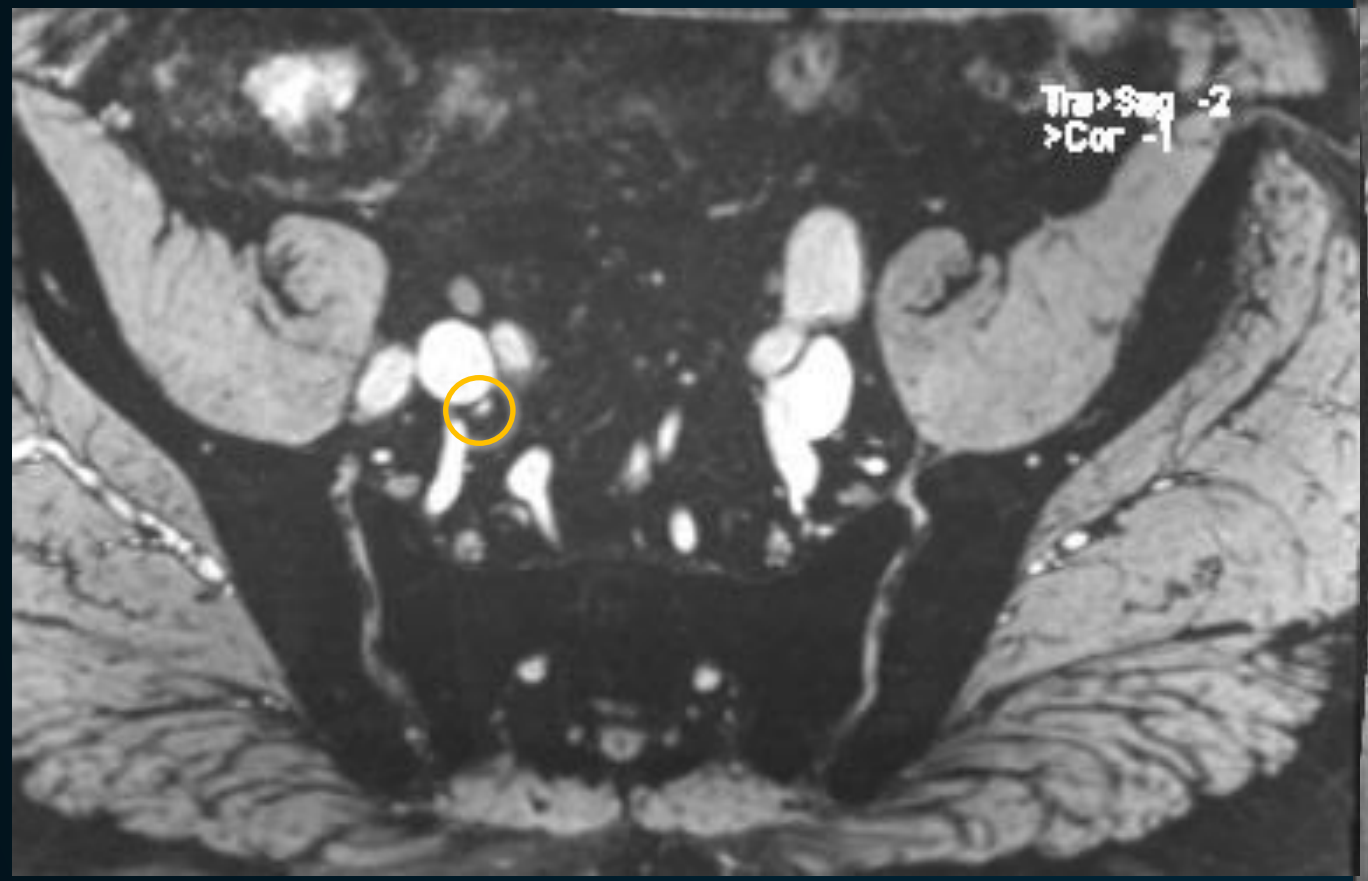


Obturator node (1.5T)

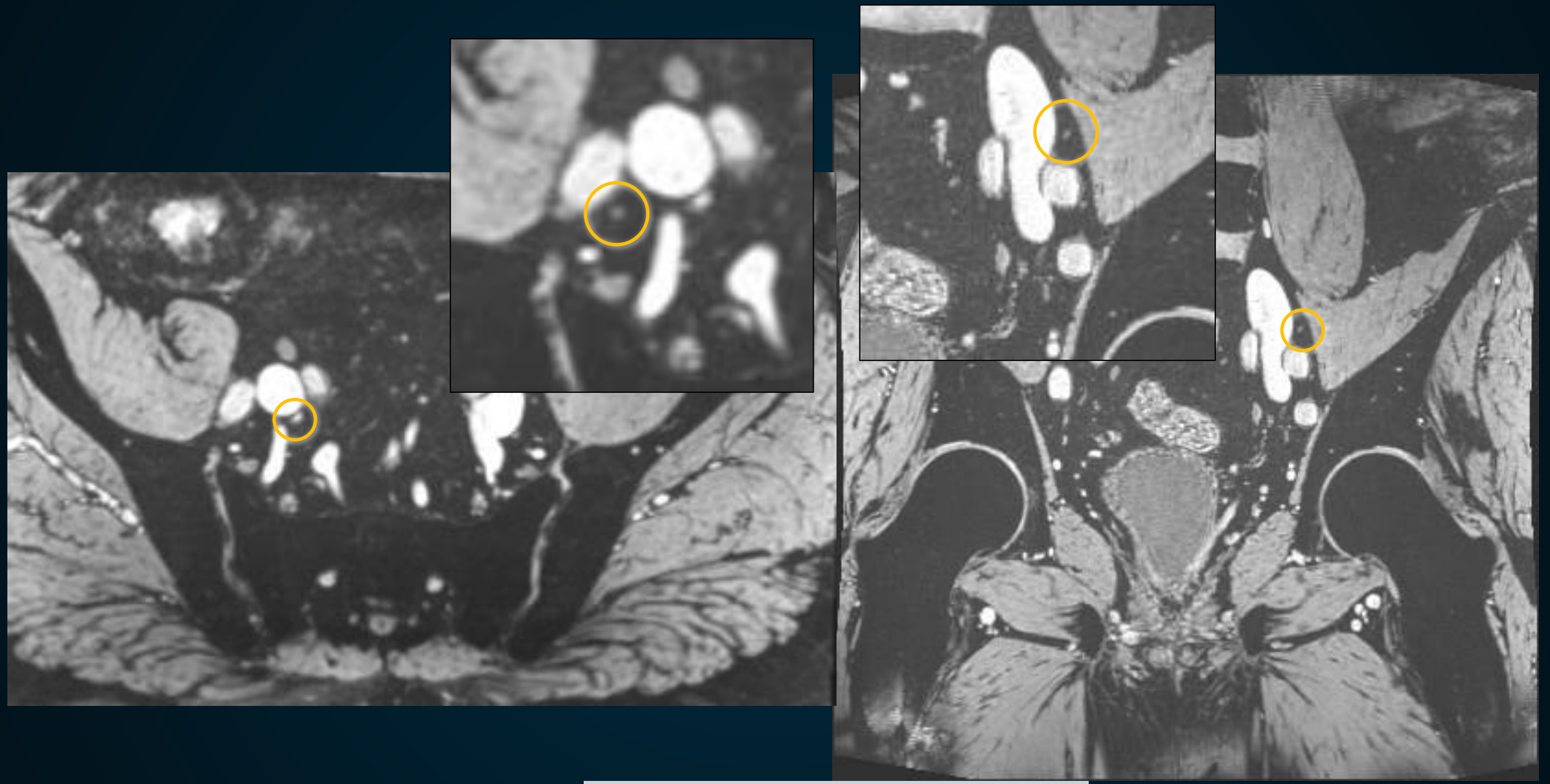


Obturator node





1.5 mm LN metastasis

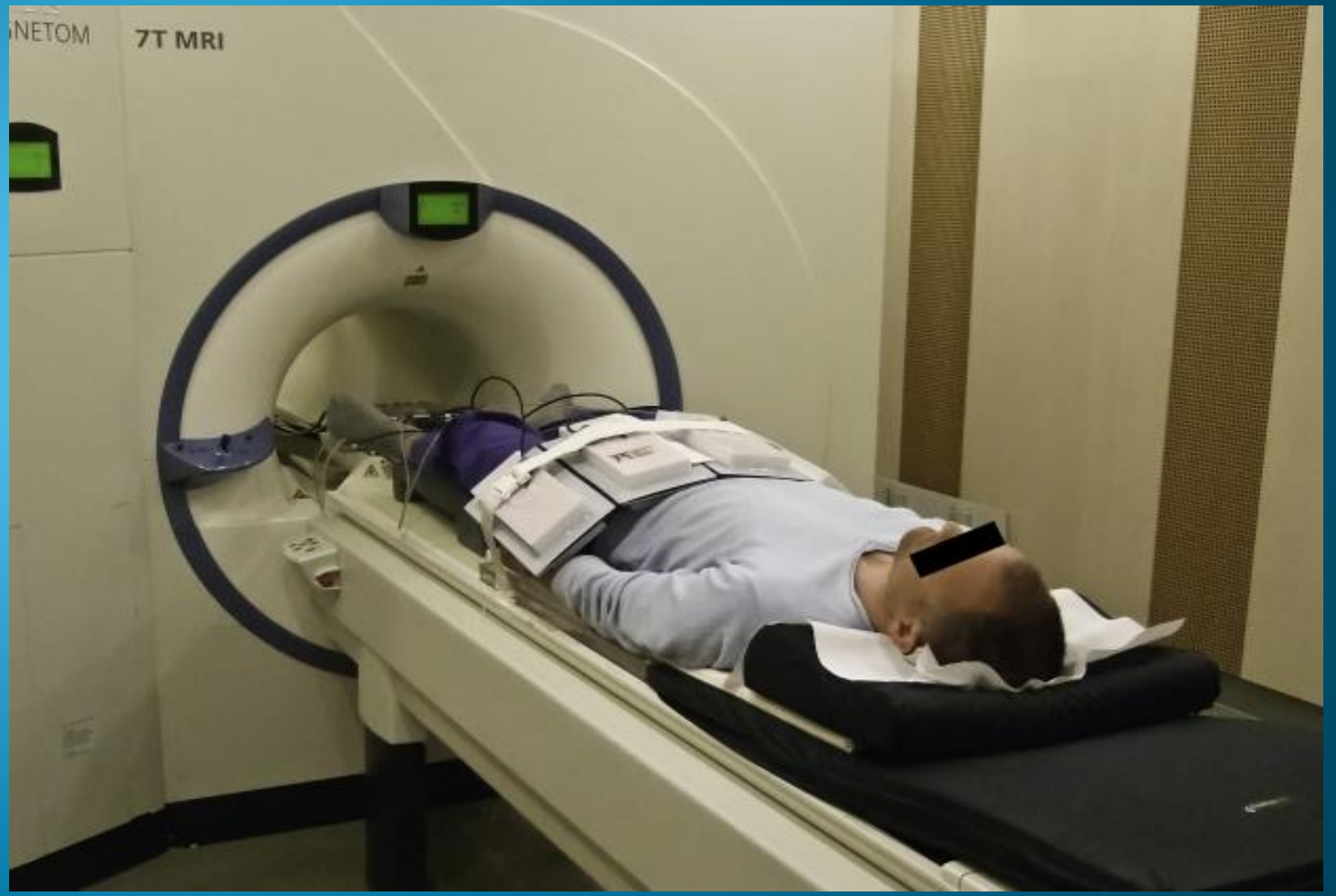


1.5 mm LN metastasis

Combidex MRI

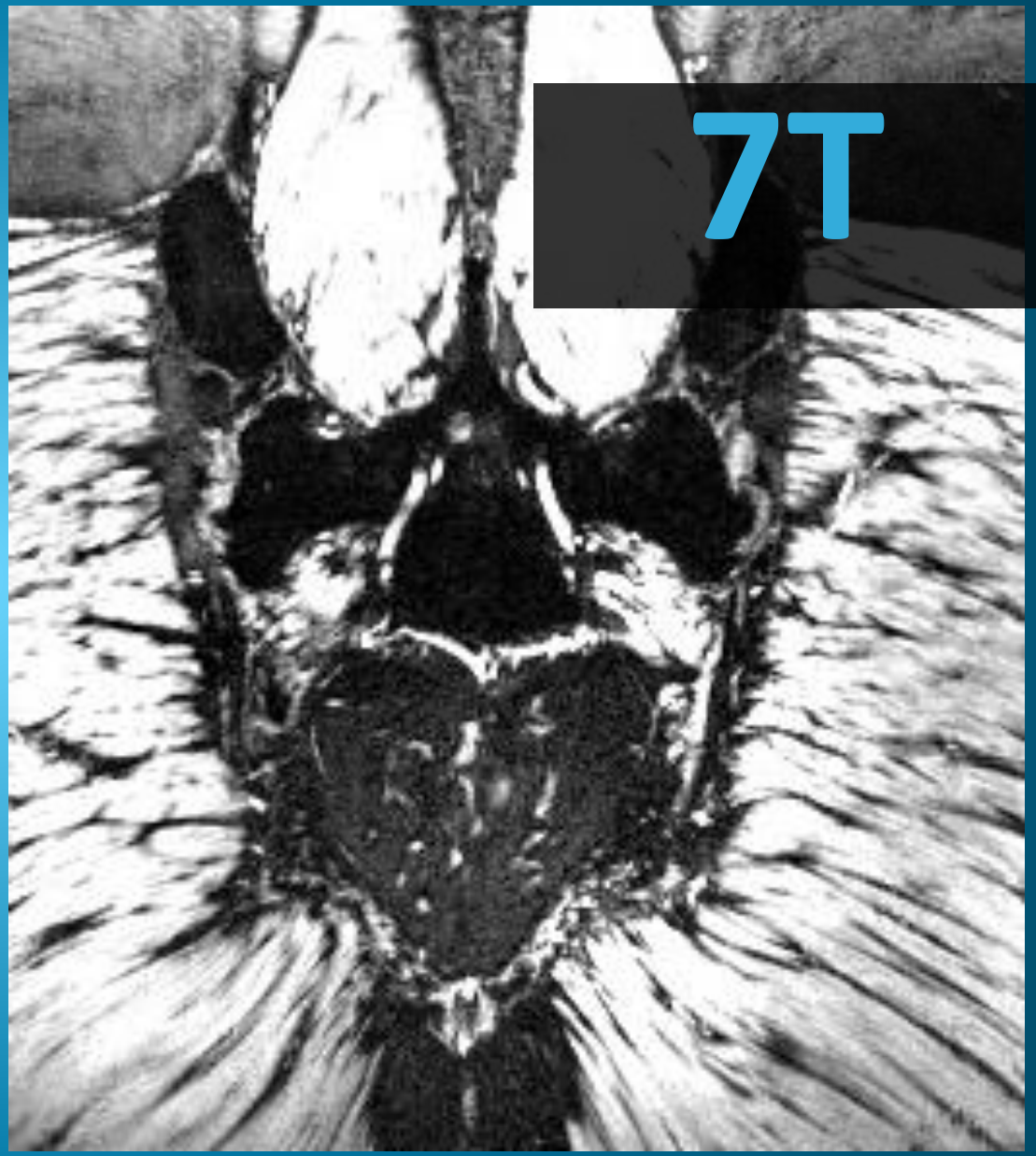
Breast & Rectal Cancer

- **Nijmegen/Essen:**
  7T vs 3T

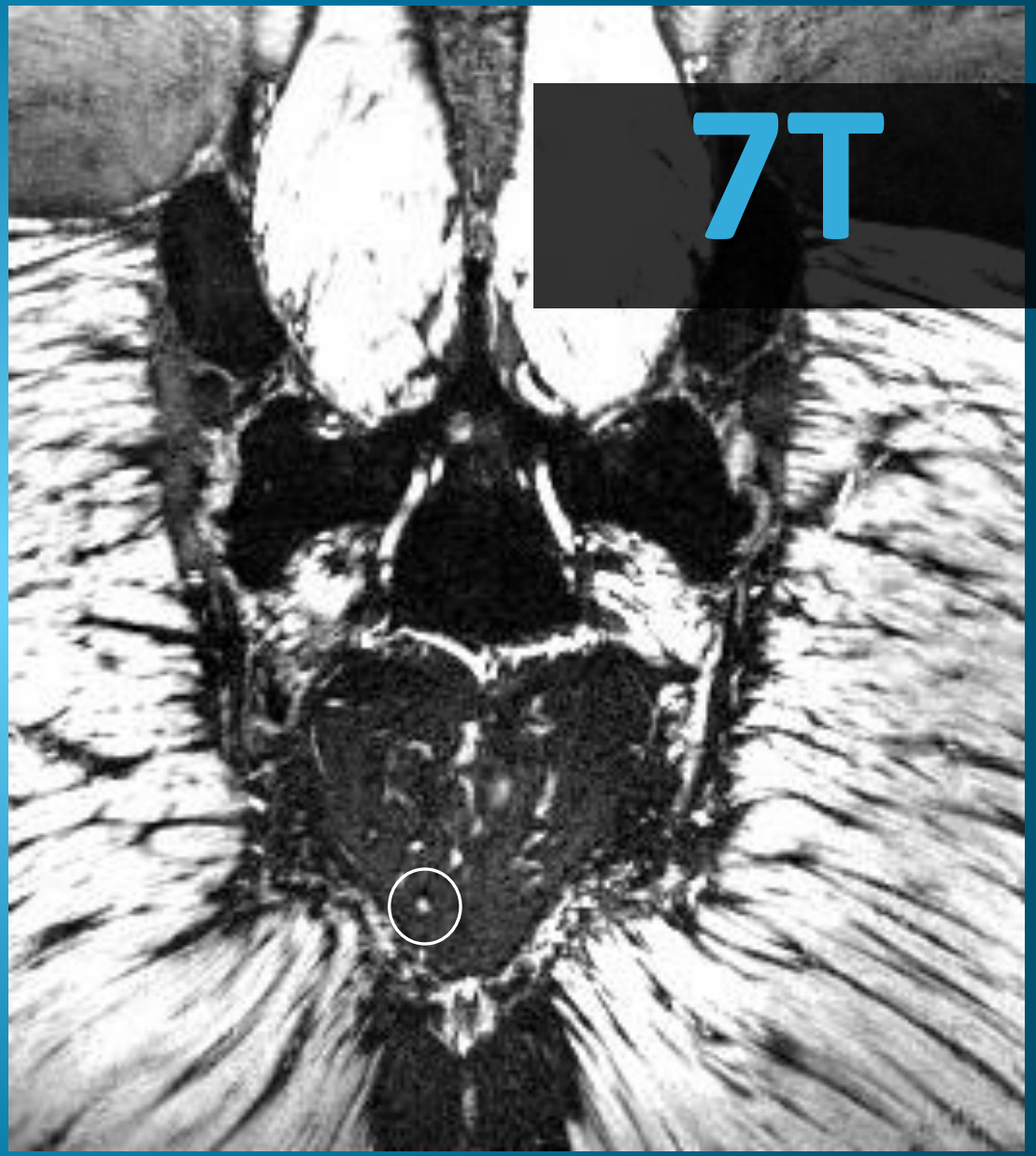


ERWIN L. HAHN INSTITUTE FOR MAGNETIC RESONANCE IMAGING

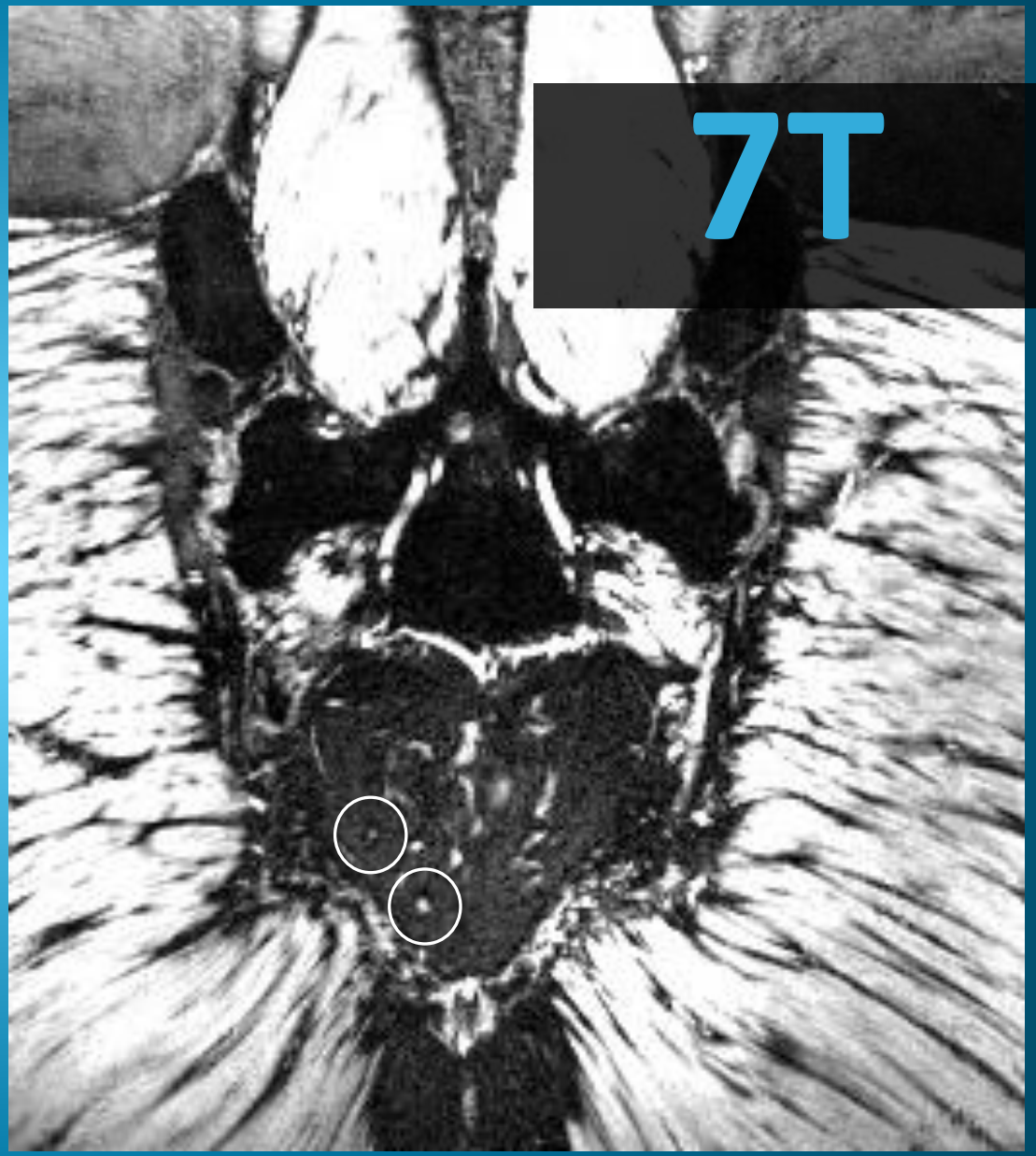

3T

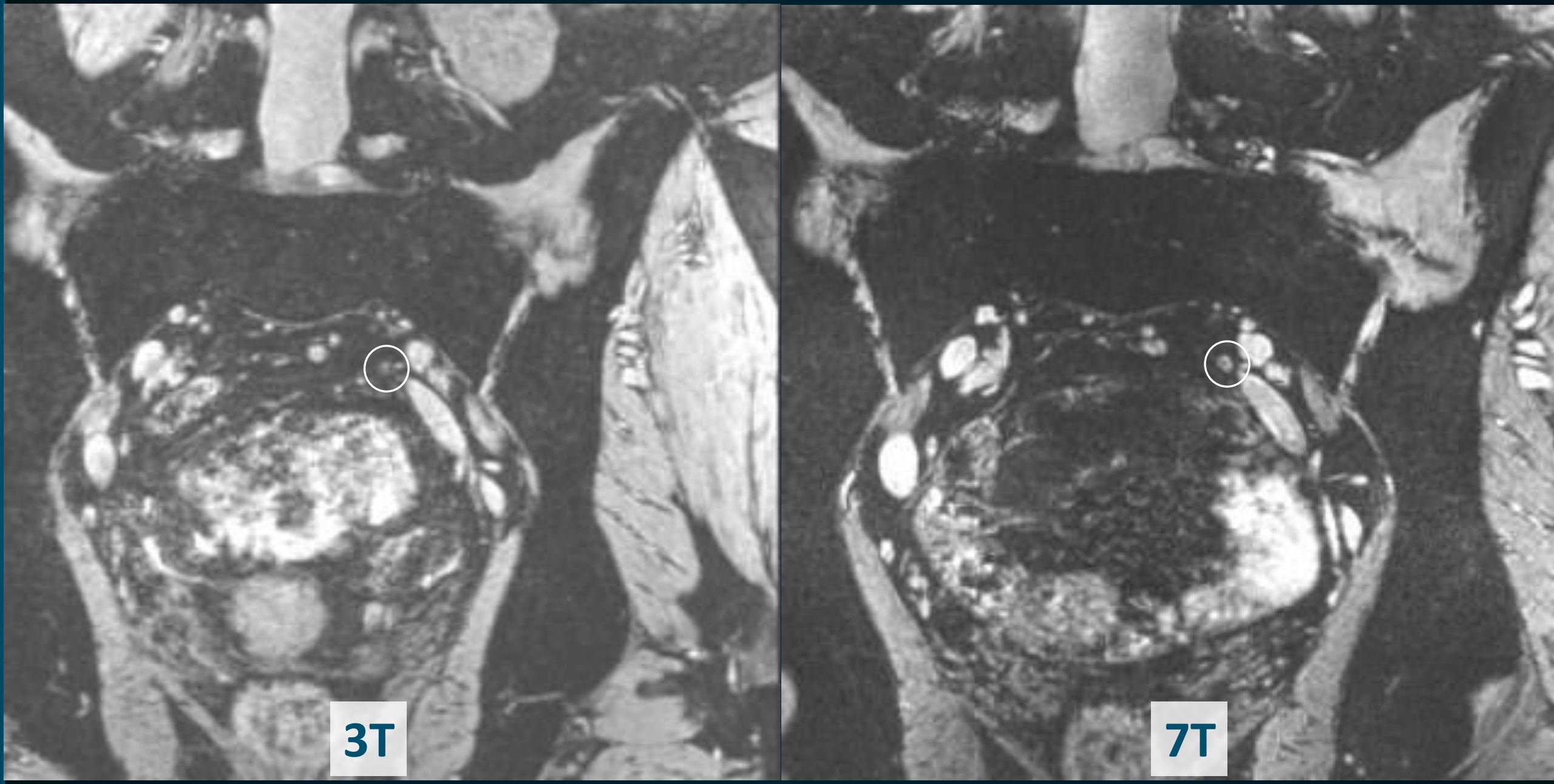

7T

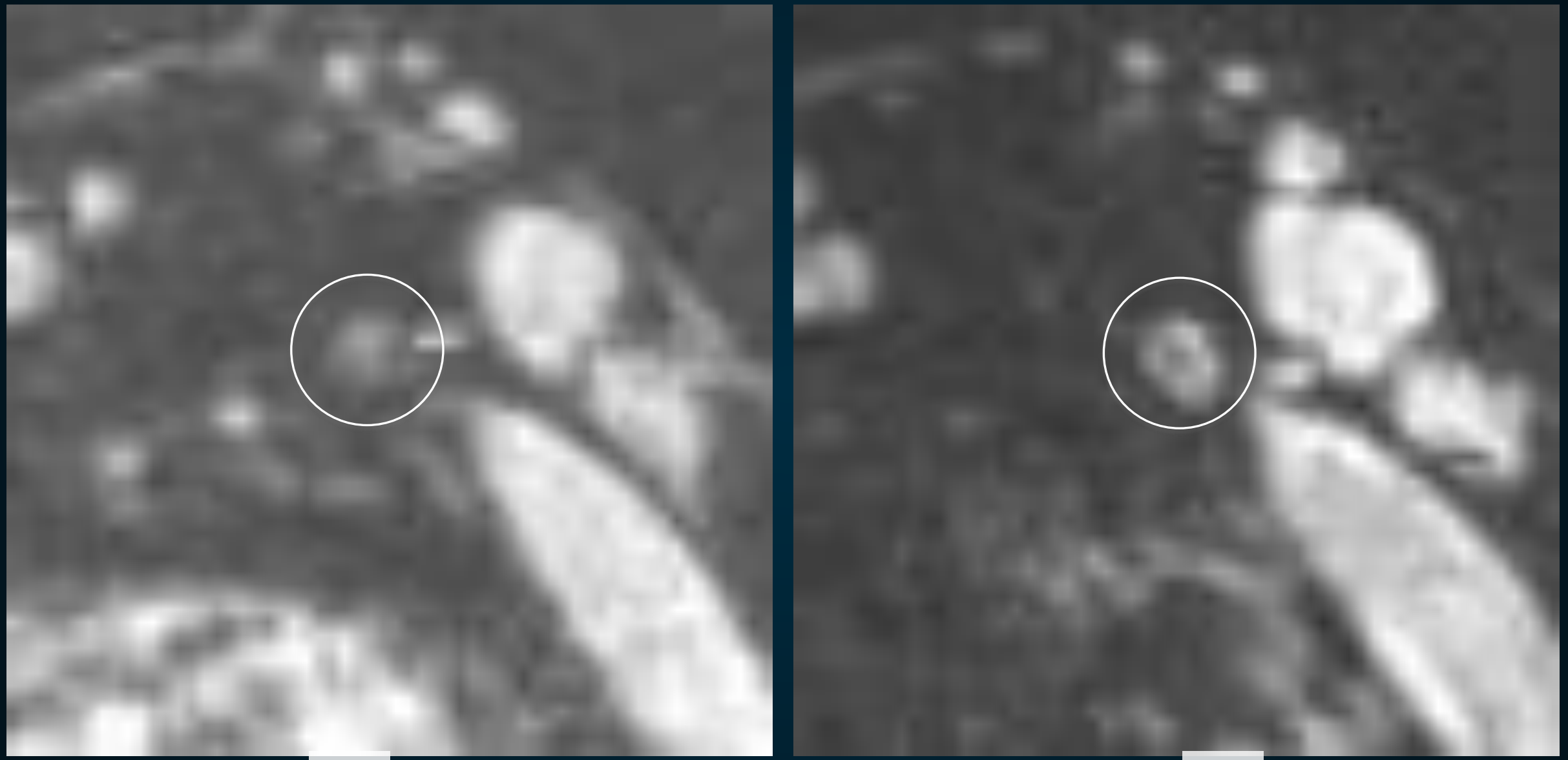

3T


7T


3T


7T


3T
7T


3T
7T

ARTICLE IN PRESS

EUROPEAN UROLOGY xxx (2023) xxx

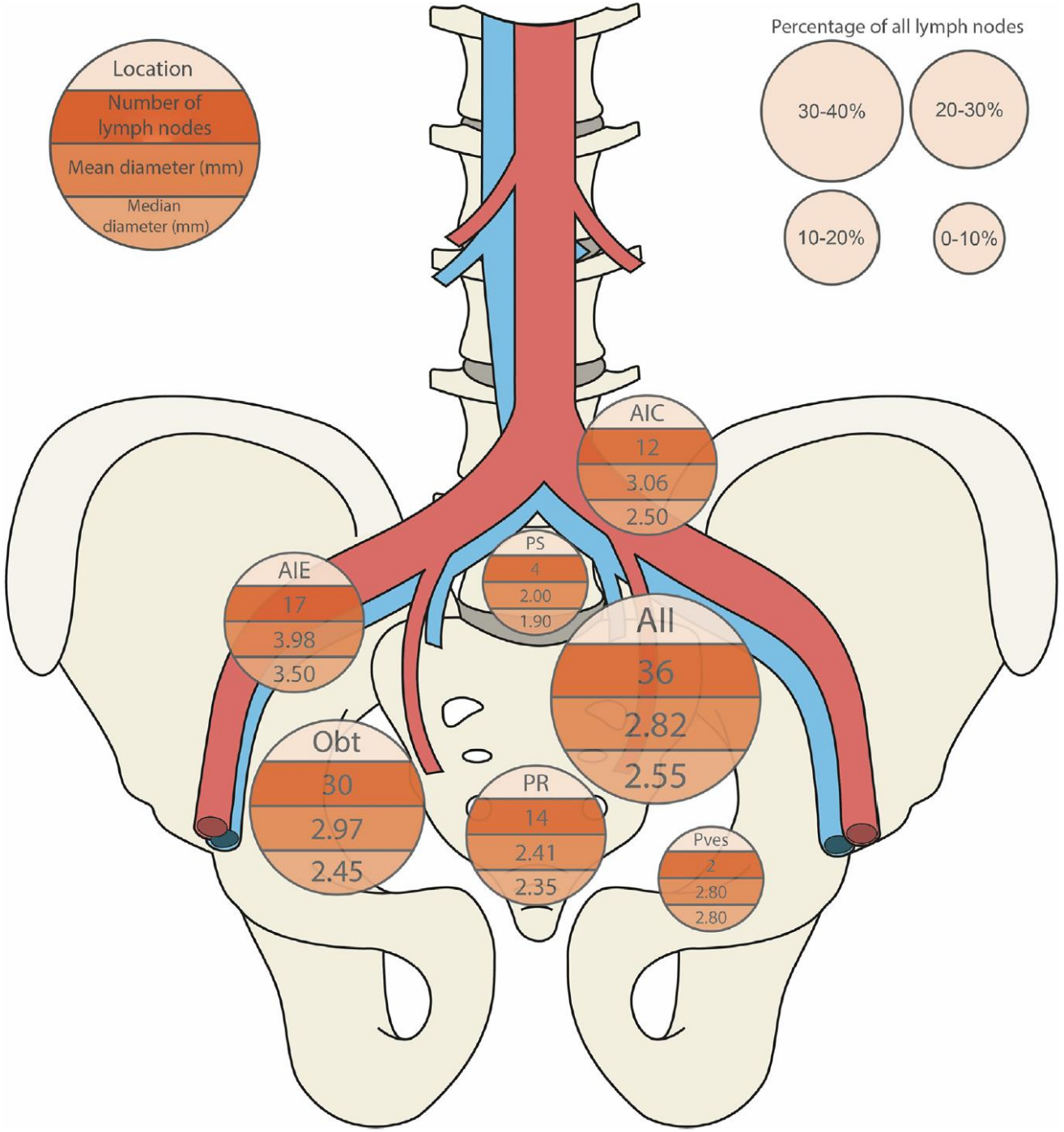
available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Research Letter

Small Suspicious Lymph Nodes Detected on Ultrahigh-field Magnetic Resonance Imaging (MRI) in Patients with Prostate Cancer with High Risk of Nodal Metastases: The First In-patient Study on Ultrasmall Superparamagnetic Iron Oxide–enhanced 7T MRI

Ansje Fortuin [a,b], *Jack van Asten* [a], *Andor Veltien* [a], *Bart Philips* [a], *Thomas Hambrock* [a], *Sören Johst* [c], *Stephan Orzada* [c,d,e], *Boris Hadaschik* [f,g], *Harald Quick* [c,d], *Jelle Barentsz* [a], *Marnix Maas* [a], *Tom Scheenen* [a,c,*]



Average short-axis 2.6 mm for suspicious LNs (range 1.3–9.5)

Nano MRI

+

^{68}Ga PSMA PET

^{68}Ga PSMA-11 PET-CT

LN Staging: meta analysis

Performance

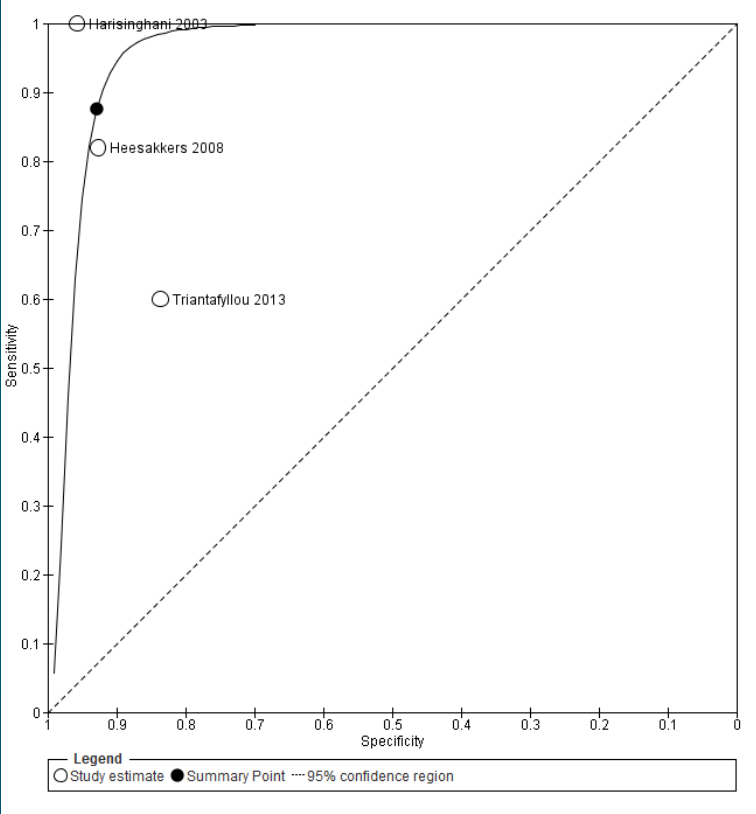
Sensitivity: 61% (95% CI: 47-72%)

Specificity: 97% (95% CI: 85-99%)

- Still low sensitivity for LN metastasis detection
- Is this sufficient to replace PLND?

Von Eyben et al, Eur Urol Focus 2017

Systematic Review: QUADAS-2



Pooled Sensitivity 93%

Pooled specificity 88%

Study	True positives	False positives	False negatives	True negatives	Specificity[95% CI]	Sensitivity [95% CI]
Harisinghani 2003	33	2	0	45	1.00 [0.89, 1.00]	0.96 [0.85, 0.99]
Heesakkers 2008	50	23	11	291	0.82 [0.70, 0.91]	0.93 [0.89, 0.95]
Triantafyllou 2013	12	9	8	46	0.60 [0.36, 0.81]	0.84 [0.71, 0.92]

Medvalue 2016

Nano MRI

+

^{68}Ga-PSMA PET

Sensitivity	93%
Specificity	97%

Comparison nano-MRI vs PSMA-PET-CT

Head-to-Head Comparison of ^{68}Ga-Prostate-Specific Membrane Antigen PET/CT and Ferumoxtran-10–Enhanced MRI for the Diagnosis of Lymph Node Metastases in Prostate Cancer Patients

Melline G.M. Schilham[*1], Patrik Zamecnik[*1], Bastiaan M. Privé[1], Bas Israël[1], Mark Rijpkema[1], Tom Scheenen[1], Jelle O. Barentsz[1], James Nagarajah[†1,2], and Martin Gotthardt[†1]

- Retrospective study
- 45 patients; primary PCa (n=9), recurrent PCA (n=36)
- all patients underwent both ^{68}Ga-PSMA PET/CT + nano-MRI
- LN metastases: size, anatomic location, and level of suspicion

Schilham/Zamecnik, J Nucl Med. 2021

Comparison nano-MRI vs PSMA-PET-CT

Results

- 179 suspicious LNs

Schilham, Zamecnik et al. J Nucl Med. 2021

Comparison nano-MRI vs PSMA-PET-CT

Results

- 179 suspicious LNs
- Significantly more suspicious LNs per patient with nano-MRI ($p < 0.001$)
  - 160/33 (nano-MRI), 71/25 PET/CT

Schilham, Zamecnik et al. J Nucl Med. 2021

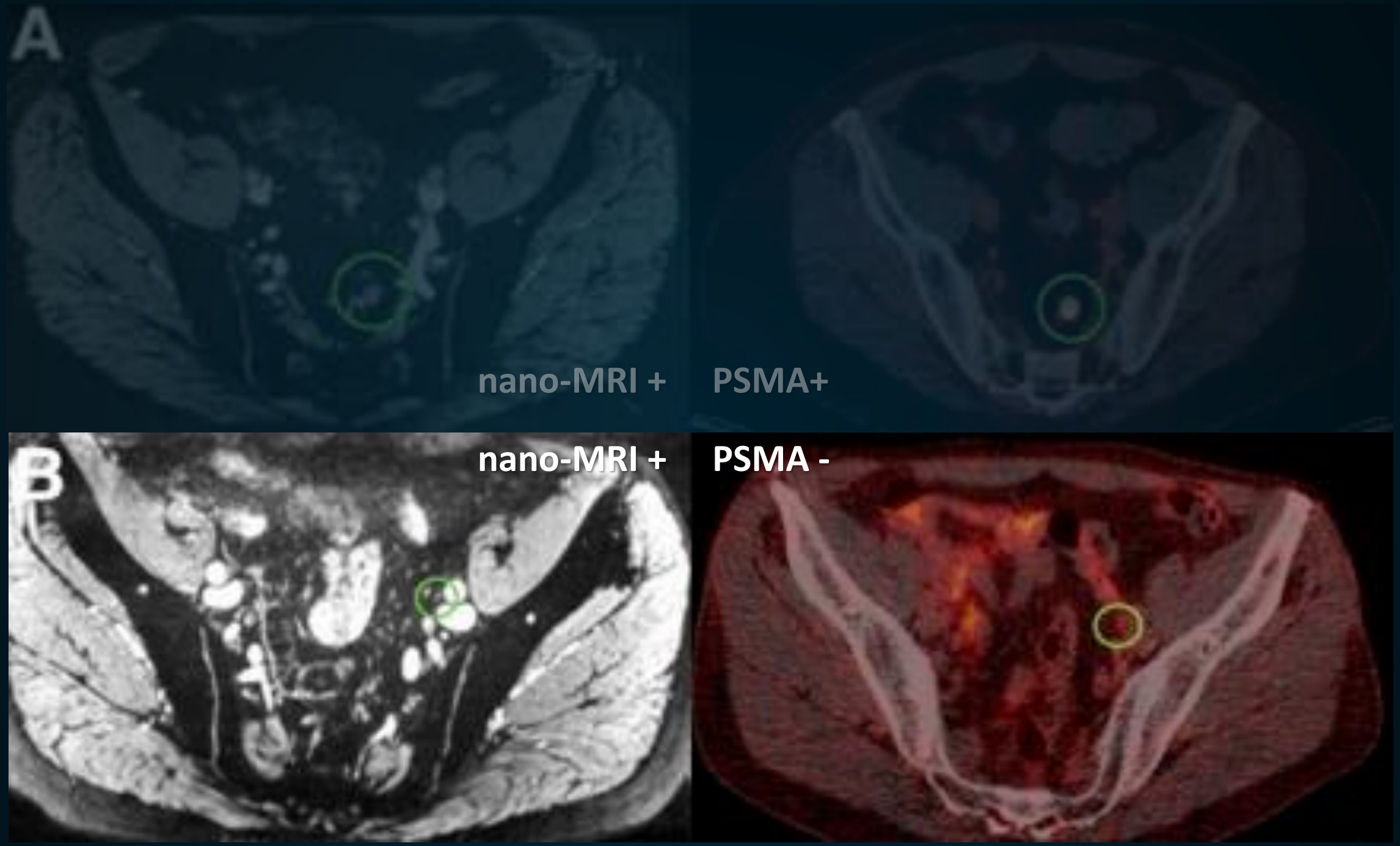
Comparison nano-MRI vs PSMA-PET-CT

Results

- 179 suspicious LNs
- Significantly more suspicious LNs per patient with nano-MRI ($p < 0.001$)
  - 160/33 (nano-MRI), 71/25 PSMA-PET/CT
- Mean size of the suspicious LNs of nano-MRI was significantly smaller (5.3 mm vs 6.0 mm, $p=0.06$)

Schilham, Zamecnik et al. J Nucl Med. 2021

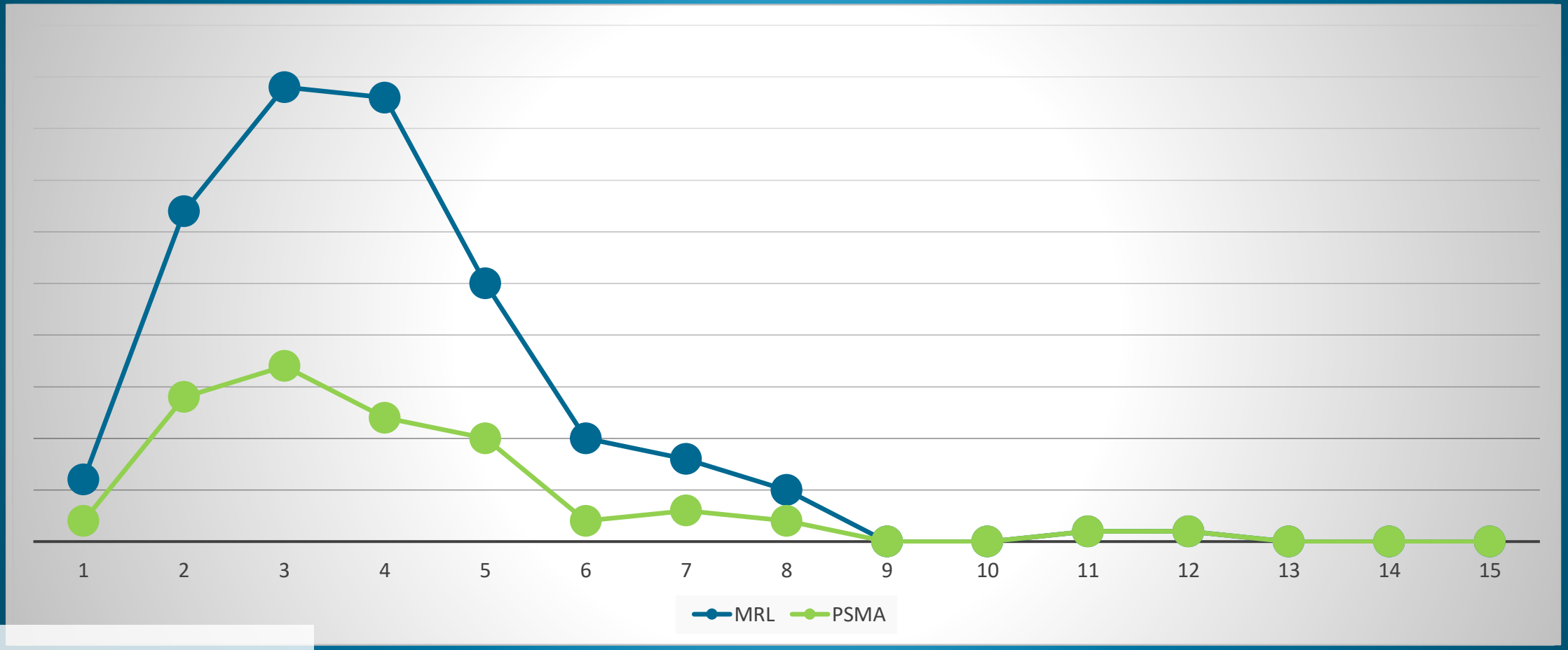

A
nano-MRI +
PSMA+


A
nano-MRI +
PSMA+
B
nano-MRI +
PSMA -

nano-MRI +

PSMA -

^{68}Ga-PSMA (2.7 mm) and nano-MRI (1.5 mm)



Nodal Size

Background

Lymph Nodes (LN): e-PLND is limited

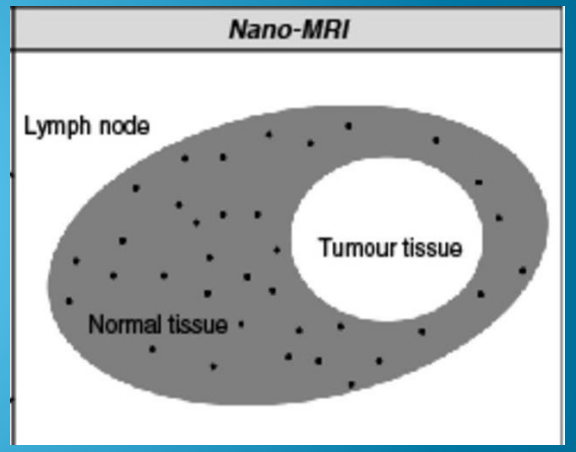
- Controversy about extent
- No Therapeutic Effect
- Significant Morbidity
- High Costs

Background

Lymph Nodes (LN): e-PLND is limited

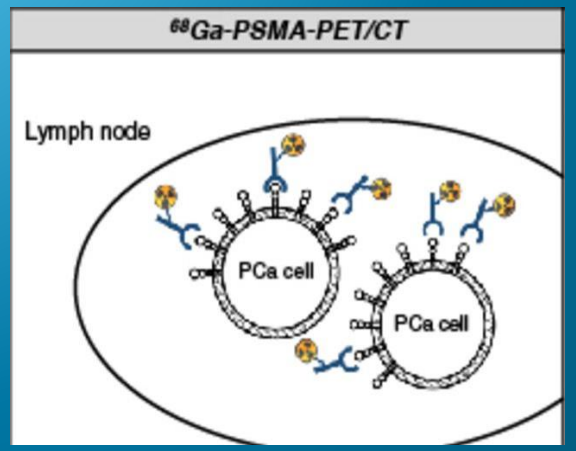
- Controversy about extent
- No Therapeutic Effect
- Significant Morbidity
- High Costs

--> Molecular Imaging



USPIO-nano-MRI

(Combidex, Ferrotran)



PSMA-PET/CT

Material and Methods

- Prospective, multicenter, multi-reader
- PSMA-PET/CT and nMRI 4 weeks before ePLND
- Imaging results were compared with ePLND-histopathology

Material and Methods

- Prospective, multicenter, multi-reader
- PSMA-PET/CT and nMRI 4 weeks before ePLND
- Imaging results were compared with e-PLND histopathology

-> Unique in this study:
Repeat MRI was performed 6 weeks post-ePLND,
to evaluate extent of LN-removal

Results

- 38 patients included, total 915 LN (median per patient 21)
- 22/915 LN were metastatic: 5/22 ⊕ on PSMA, 13/22 on nMRI
- Missed ⊕ LN: <3.5 mm with PSMA, nMRI <1.5 mm

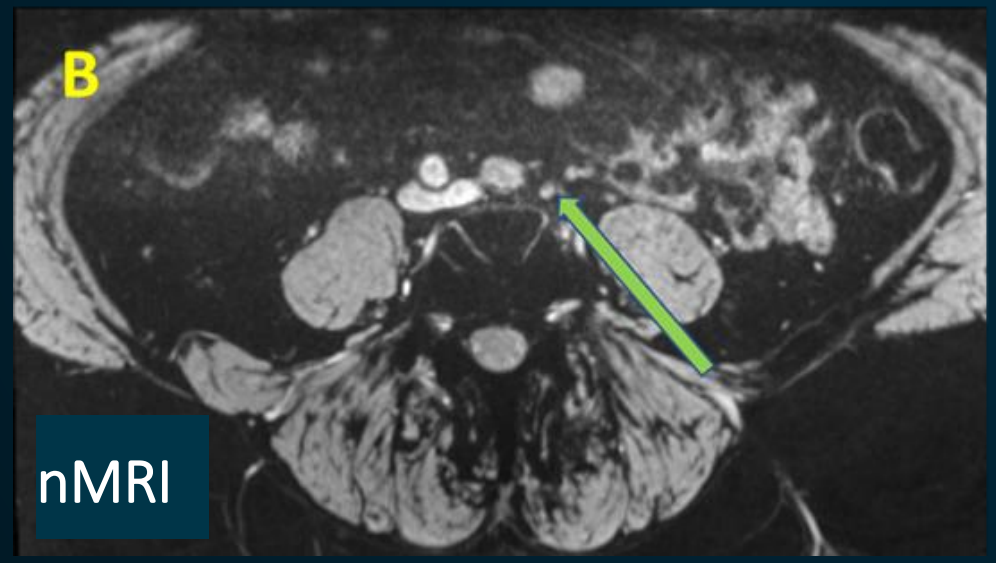
Results

- 38 patients included, total 915 LN (median per patient 21)
- 22/915 LN were metastatic: 5/22 ⊕ on PSMA, 13/22 on nMRI
- Missed ⊕ LN: <3.5 mm with PSMA, nMRI <1.5 mm

--> Post-operative MRI showed 80% non-dissected imaging ⊕ LN:
- 79% (23/29) on PSMA-scans
- 80% (53/73) on nMRI

Results

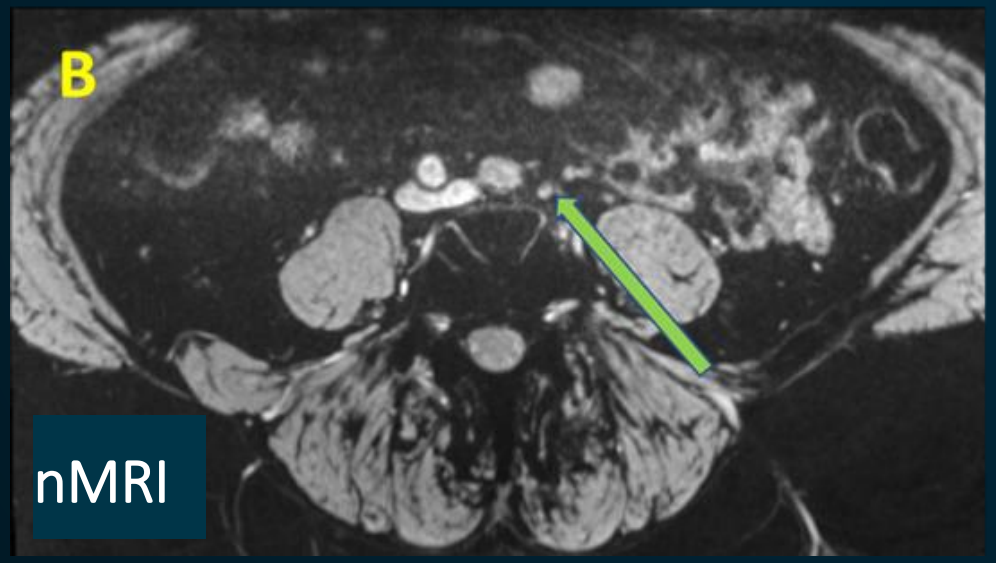
Pre ePLND



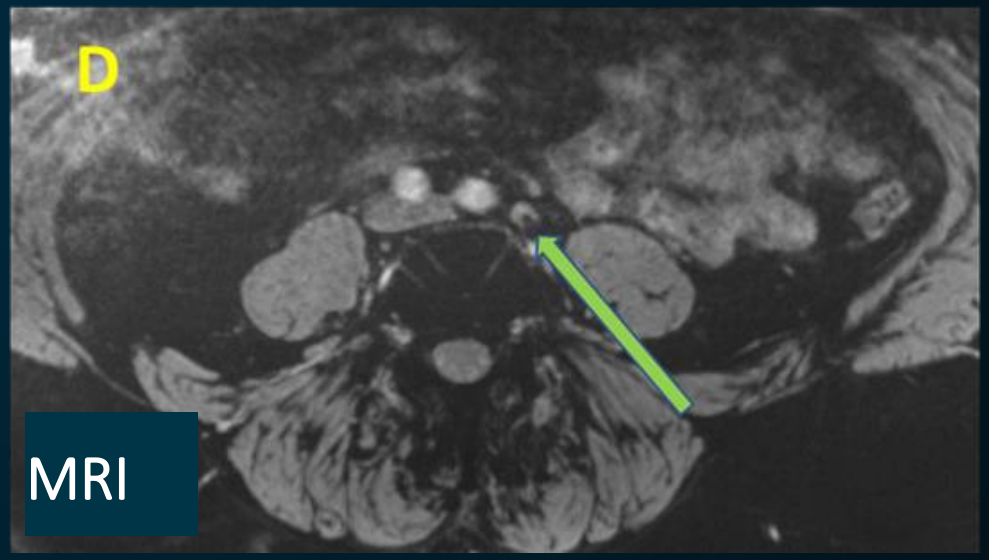
PSMA and nano-MRI ⊕ LN (5 mm)

Results

Pre ePLND



Post ePLND



Non removed CI-LN (5 mm), positive on PSMA and nMRI

Conclusions

- 80% of imaging ⊕ LN were not removed, despite adequate e-PLND (21 LN per patient removed)

→ Role of ePLND as reference standard needs to be rethought.

Conclusions

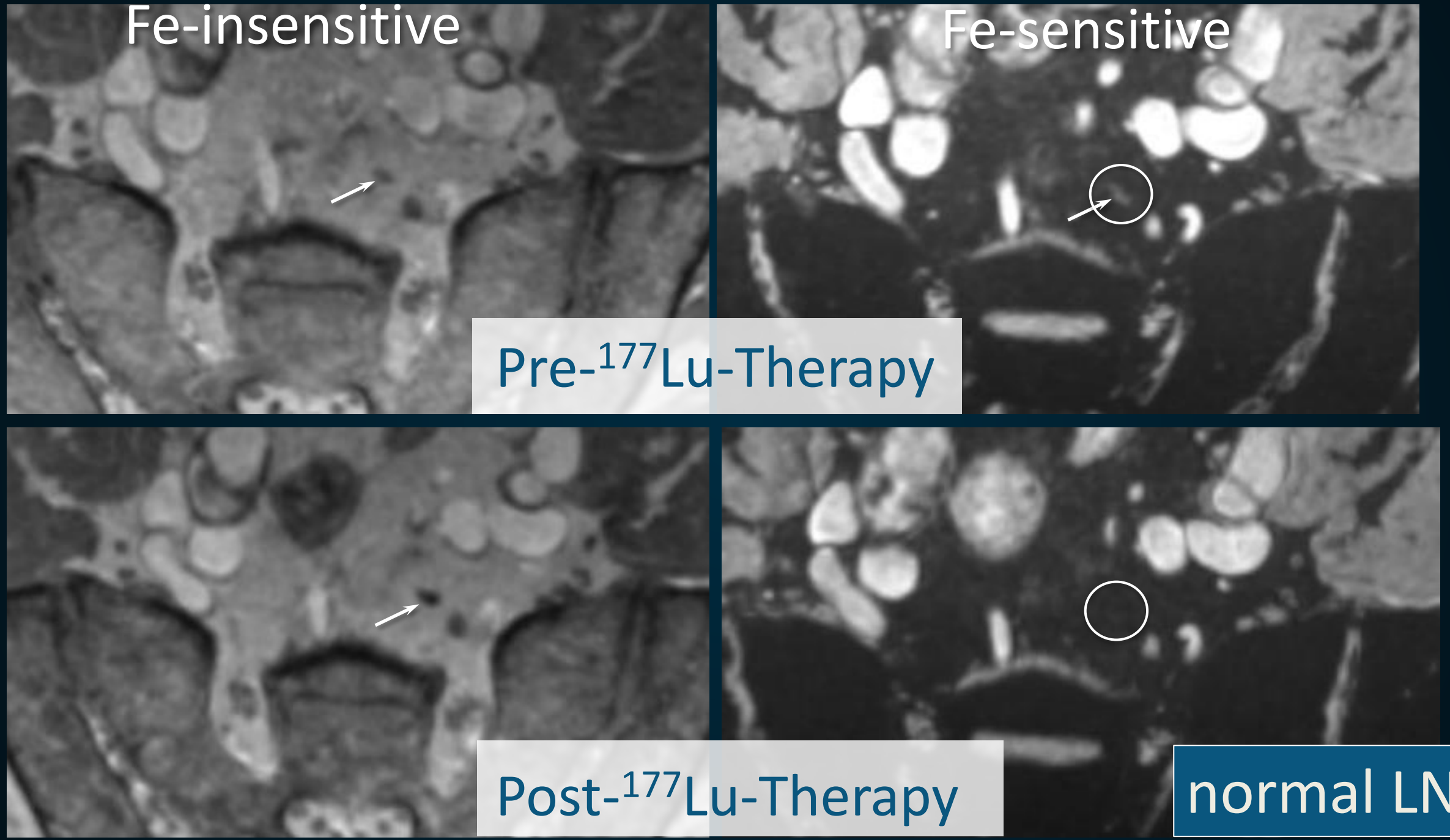
- 80% of imaging ⊕ LN were not removed → role of ePLND requires rethinking

- Imaging has also limitations (detecting 3.5 and 1.5 mm LNM for PSMA and nMRI), but can help with patient stratification for surgery and radiotherapy

Small positive node (white) on nMRI
→ no macrophages, thus positive

No ^{68}Ga-PSMA-PET/CT uptake

Patient received 1 cycle Lu-PSMA


Fe-insensitive
Fe-sensitive
Pre-^{177}Lu-Therapy
Post-^{177}Lu-Therapy
normal LN

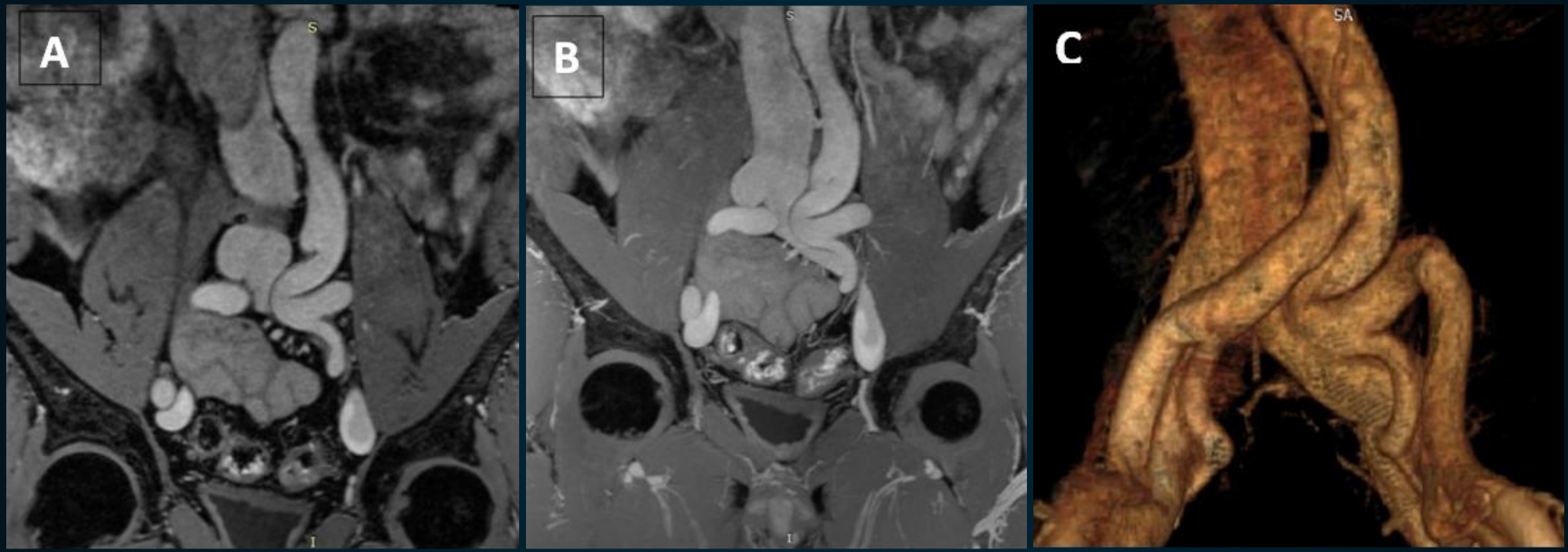
^{177}Lu-PSMA-Therapy: small LN normalised

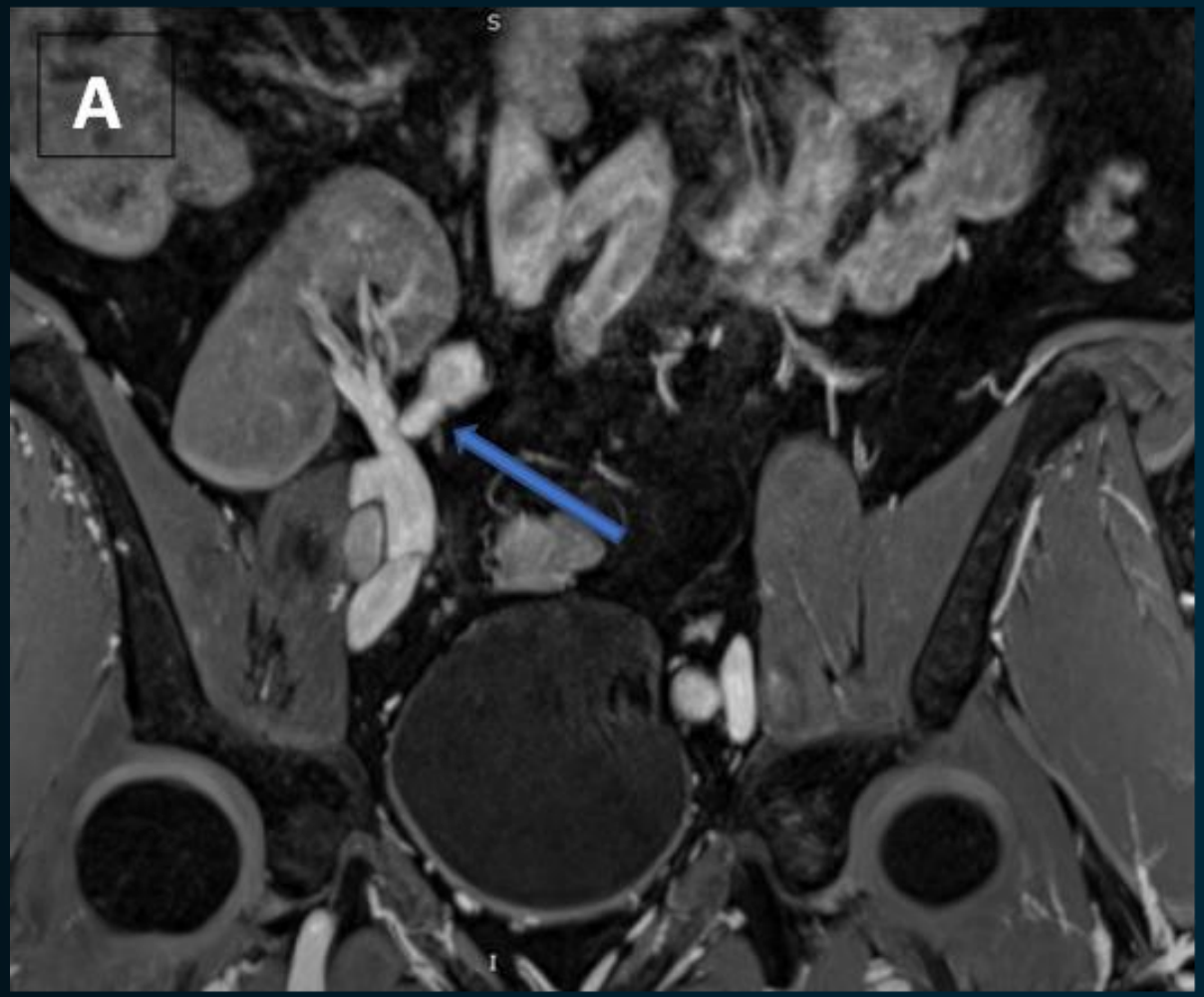
Explanation: Boost of immune system → normal LN

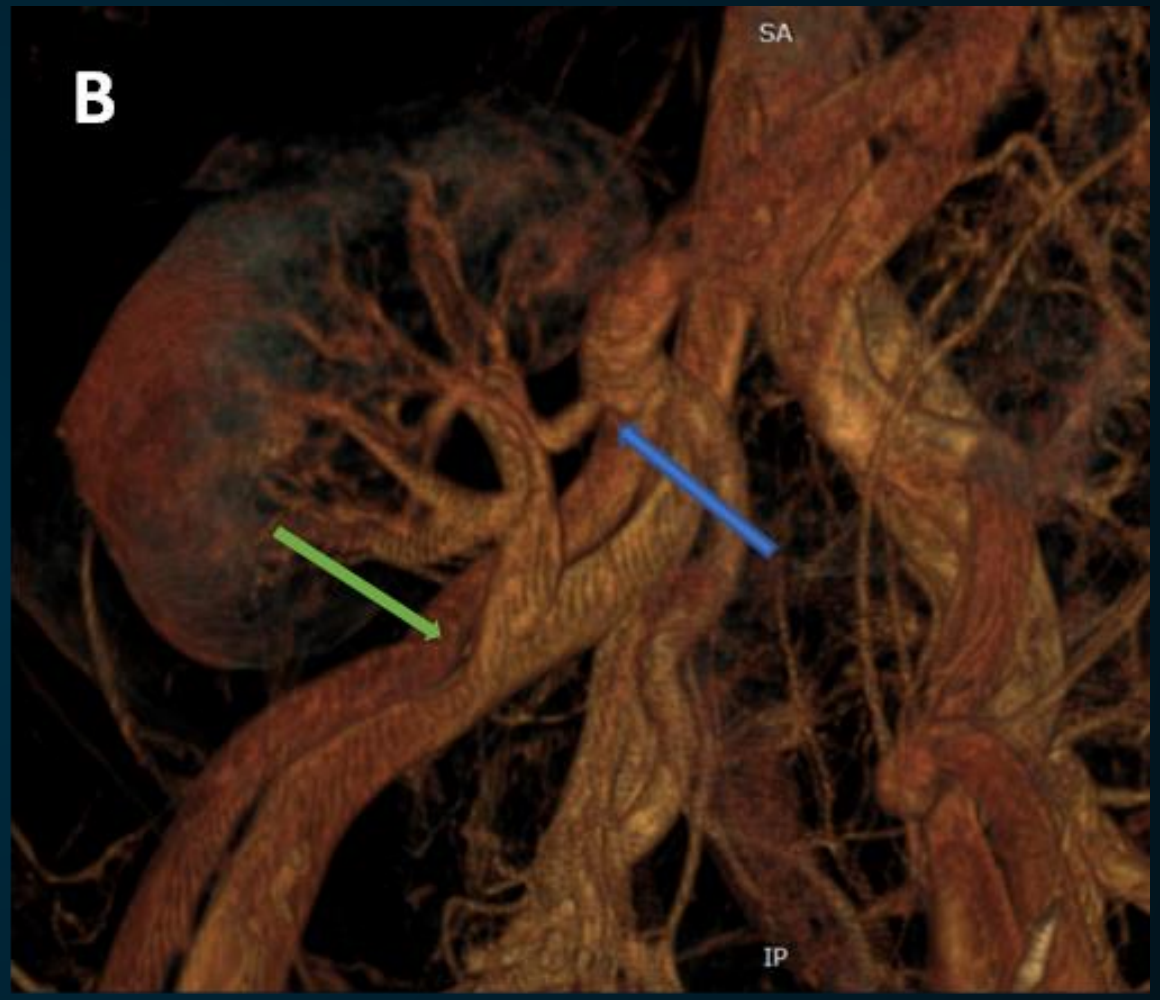
Contrast nMRI (MR-Angiograpy) with Results

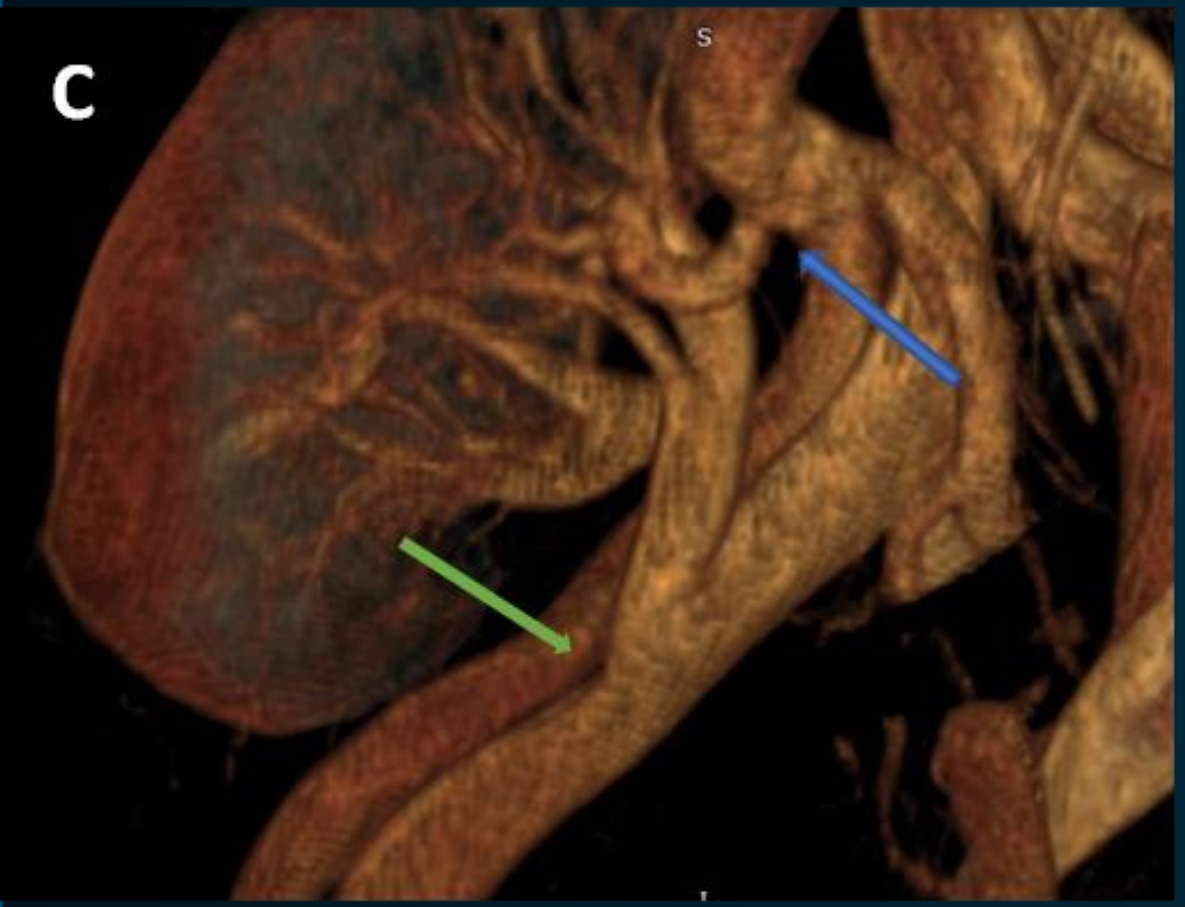
- 98% data sets had good to excellent image quality
- 98% of all vessel segments had good to excellent visibility of vessels
- Can be given with impaired renal function (Fe!)

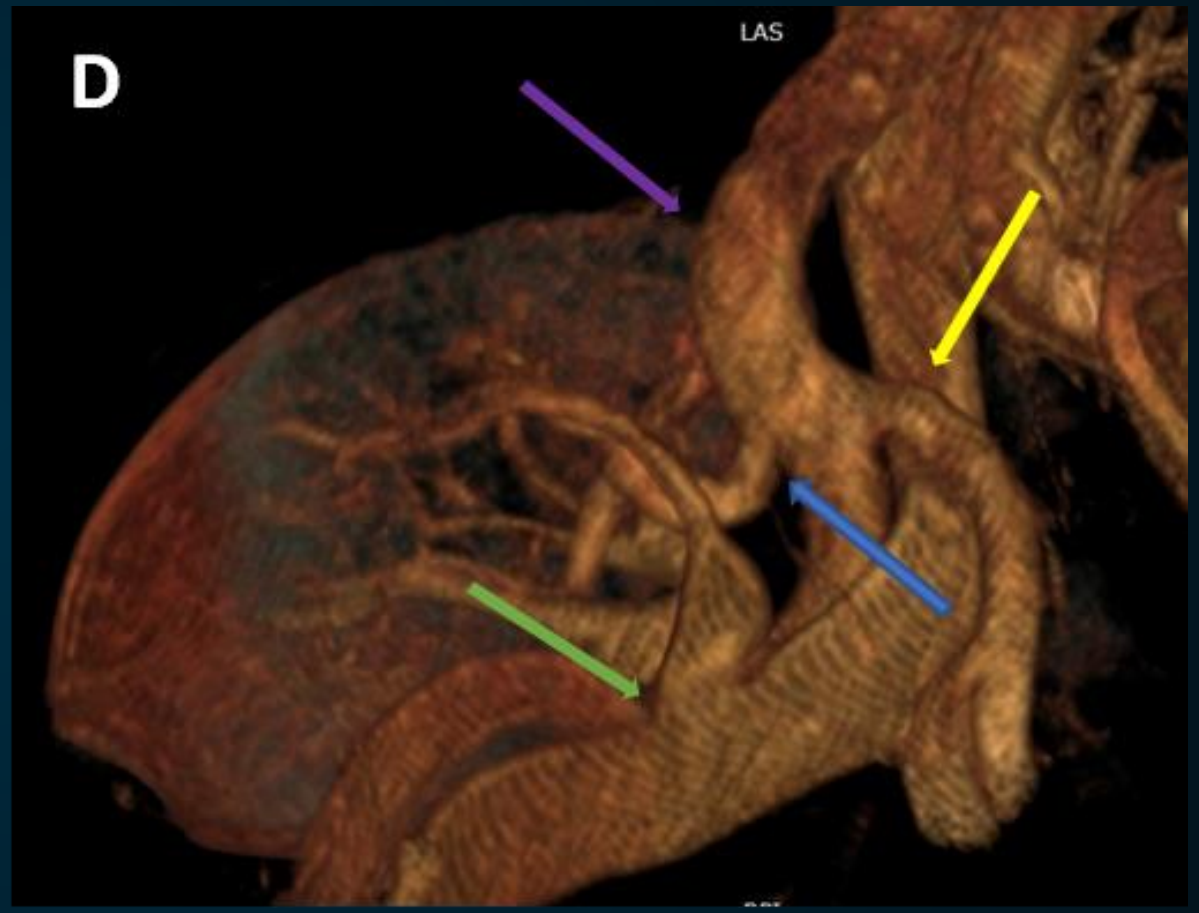
Zamecnik et al. Eur Urol Focus. 2022


A
B
C


A
S
I


B
SA
IP


C
S


D
LAS

REGULATORY ISSUES

Current Regulatory Status

- Named Patient Use procedure in NL (Nijmegen) and CH (Zürich)

Current Regulatory Status

- Named Patient Use procedure in NL (Nijmegen) and CH (Zürich)
- Pivotal trial (registration) in NL, D, CH almost finished (indication: N-staging in PCa)

Current Regulatory Status

- Named Patient Use procedure in NL (Nijmegen) and CH (Zürich)
- Pivotal trial (registration) in NL, D, CH almost finished (indication: N-staging in PCa)
- scientific studies running at the moment in NL, FIN and CH

Current Regulatory Status

- Named Patient Use procedure in NL (Nijmegen) and CH (Zürich)
- Pivotal trial (registration) in NL, D, CH almost finished (indication: N-staging in PCa)
- scientific studies running at the moment in NL, FIN and CH
- Available for investigator initiated studies

Fe-nanoparticle-MRI

- Detects smaller LNMs (1.5 mm) than PSMA (3.5 mm)

Fe-nanoparticle-MRI

- Detects smaller LNMs (1.5 mm) than PSMA (3.5 mm)
- Detects more positive LNMs

Fe-nanoparticle-MRI

- Detects smaller LNMs (1.5 mm) than PSMA (3.5 mm)
- Detects more positive LNMs
- Good quality e-PLND left 80% imaging positive LNs

Fe-nanoparticle-MRI

- Detects smaller LNMs (1.5 mm) than PSMA (3.5 mm)
- Detects more positive LNMs
- Good quality e-PLND left 80% imaging positive LNs
- High-quality MRA even in impared renal function

Fe-nanoparticle-MRI

- Detects smaller LNMs (1.5 mm) than PSMA (3.5 mm)
- Detects more positive LNMs
- Good quality e-PLND left 80% imaging positive LN
- High-quality MRA even in impared renal function
- Can show immune response (LNM turns into normal)

Nano (Ferrotran)MRI MRI

Other Potential indications

- All Cancers: gynacologic- lung-, pancreas cancer,.....
- Multiple sclerosis: shows early active area and not scar
- Other neuro-degenerative diseases: Parkinson, Alzheimer?
- Epilepsy: focus
- Vessels: vulnerable plaque

Roel Mus

Radboudumc
university medical center

MULTI PARAMETRIC MRI OF PROSTATE CANCER

PI-RADS V.2 HANDS-ON COURSE
COURSEBOOK RSNA 2018

www.mri-prostate-barentsz.nl