Prostate Biopsy - The Beginning of the End?

Mark Emberton FMedSci
Division of Surgery and Interventional Sciences
University College London

The pace of change

- It was not that long ago that we did a biopsy on everyone at risk
- Today about half the men with raised PSA are offered a biopsy
- Is this trend likely to continue?

April 2019 – NICE declared that all men should have an MRI prior to biopsy

What is driving the trend?

- Cost
- Clinical efficiency
- Harm reduction
- Change in our conceptual framework
  - From a histopathological phenotype to an imaging phenotype

Biopsies confer harm: they incur delays, cost and imprecision

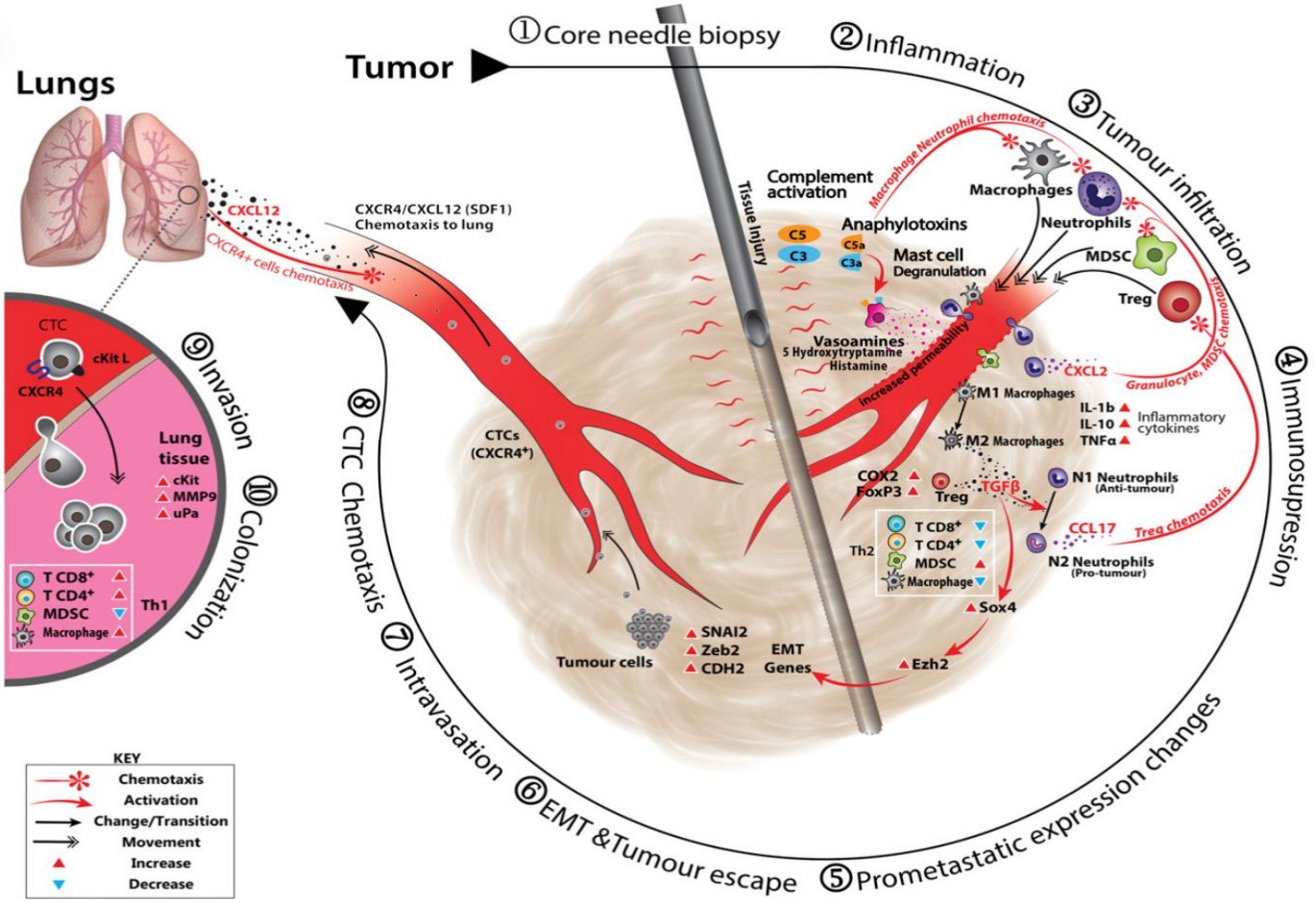
- Discomfort, bleeding, infection, sepsis requiring hospital admission (1:500), death (0.01% at 120 days)
- Delays: to biopsy, path result, definitive care
- Cost $2,000 rising to $4,000 with one complication*
- Missed diagnoses, miss-classified diagnoses (downward and upward)

**Weiner AB et al. Urol Pract 2020*

Does the process of biopsy confer negative oncological outcomes

- Mechanical manipulation of tumour can cause metastases in animal models (murine sarcoma model)
- Needle tract seeding of prostate cancer has been reported
- Modern targeted biopsy induce more disruption/trauma to the tumour than ‘systematic biopsies’

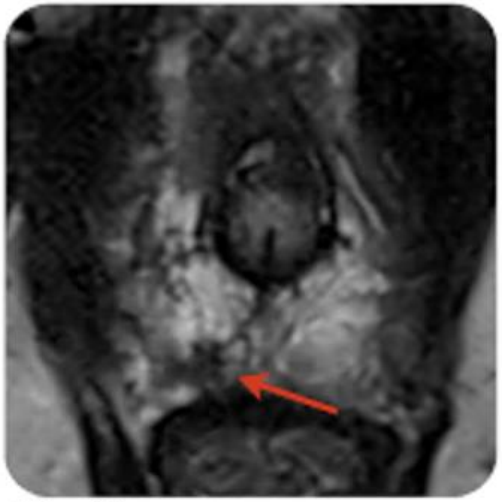
Pathological and metabolic response to injury



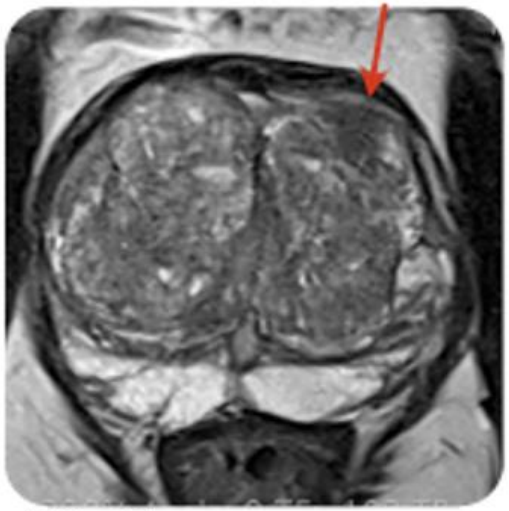
Mathenge EG *et al.* Neoplasia 2014

A recent case

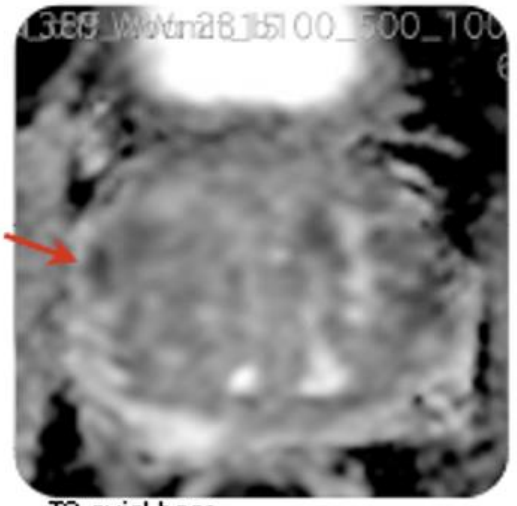
Targeted biopsies - patient A



T2 axial apex



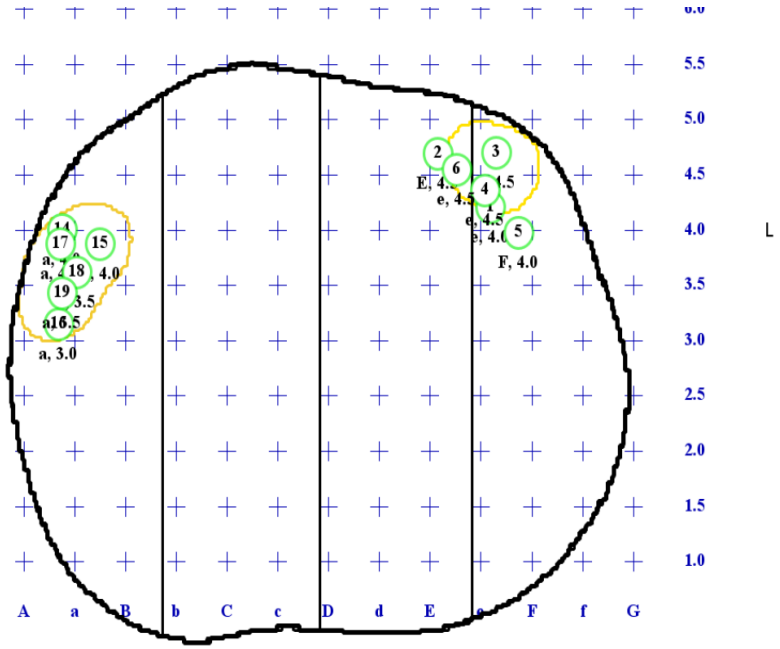
ADC axial apex

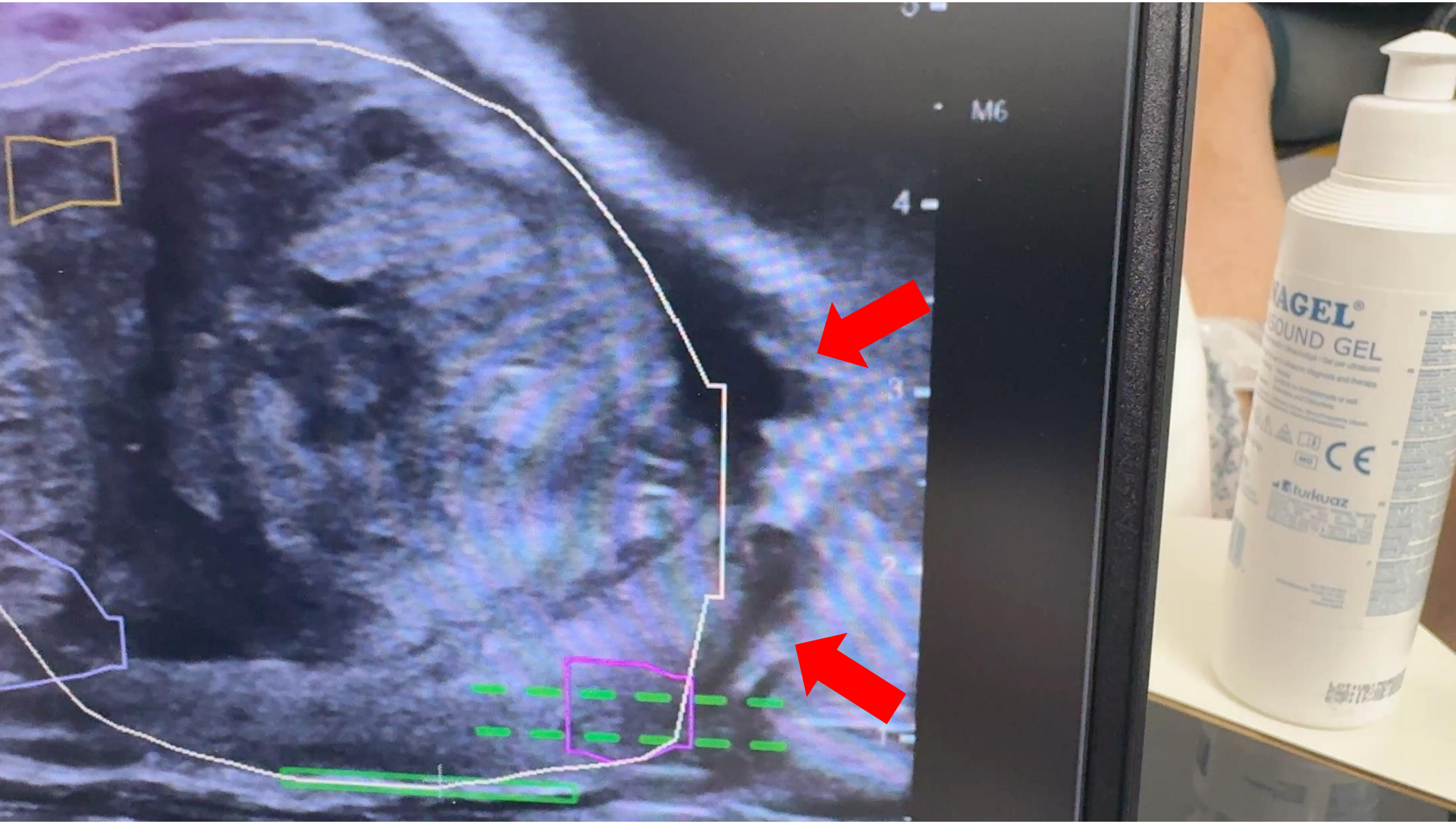


T2 axial base

A recent case

Targeted biopsies - patient A




M6
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turkuaz

Do we have any evidence that cancer cells get in blood after biopsy?

Clinical Chemistry 66:1
161–168 (2020)

Cancer Diagnostics

Tumor-Associated Release of Prostatic Cells into the Blood after Transrectal Ultrasound-Guided Biopsy in Patients with Histologically Confirmed Prostate Cancer

Simon A. Joosse,[1] Burkhard Beyer,[2†] Christin Gasch,[1†] Paulina Nastały,[1†] Andra Kuske,[1†] Hendrik Isbarn,[2] Ludwig J. Horst,[1] Claudia Hille,[1] Tobias M. Gorges,[1] Laure Cayrefourcq,[3] Catherine Alix-Panabières,[3] Pierre Tennstedt,[4] Sabine Riethdorf,[1] Thorsten Schlomm,[2] and Klaus Pantel[1*]

Josse SA *et al.* Clin Chem 2020

Table 2. ORs of CTC increase for biopsy and PCa status.[a]

	Univariable analysis				Multivariable analysis			
Covariate	Coefficient (b_i)	OR [exp(b_i)]	95% CI	*P* value	Coefficient (b_i)	OR [exp(b_i)]	95% CI	*P* value
Biopsy	0.8532	2.3470	1.6610–3.3165	<0.0001	1.6217	5.0617	3.2674–7.8413	<0.0001
PCa status	0.2433	1.2754	0.5828–2.7910	0.5409	1.0962	2.9928	1.0762–8.3220	0.0358
Biopsy[b] * PCa					1.3405	3.8210	1.6213–9.0009	0.0023
Biopsy: PCa−	−0.8467	0.4288	0.1797–1.0235	0.1260[c]				
Biopsy: PCa+	2.0646	7.8821	4.8443–12.8250	<0.0001[c]				

[a] Estimated coefficient of CTC increase with corresponding OR, 95% CI, and *P* value in univariable and multivariable analyses, corrected for age. Depicted are the effects of biopsy and PCa status on CTC count, as well as their interaction effect (Biopsy * PCa) and the effect of biopsy in PCa negative (Biopsy: PCa−) and PCa positive (Biopsy: PCa+) separately.
[b] Biopsy = time point of blood collection (before biopsy/after biopsy).
[c] Bonferroni adjusted *P* value.

Josse SA *et al.* Clin Chem 2020

Progression rates increased in CTC+ after Bx

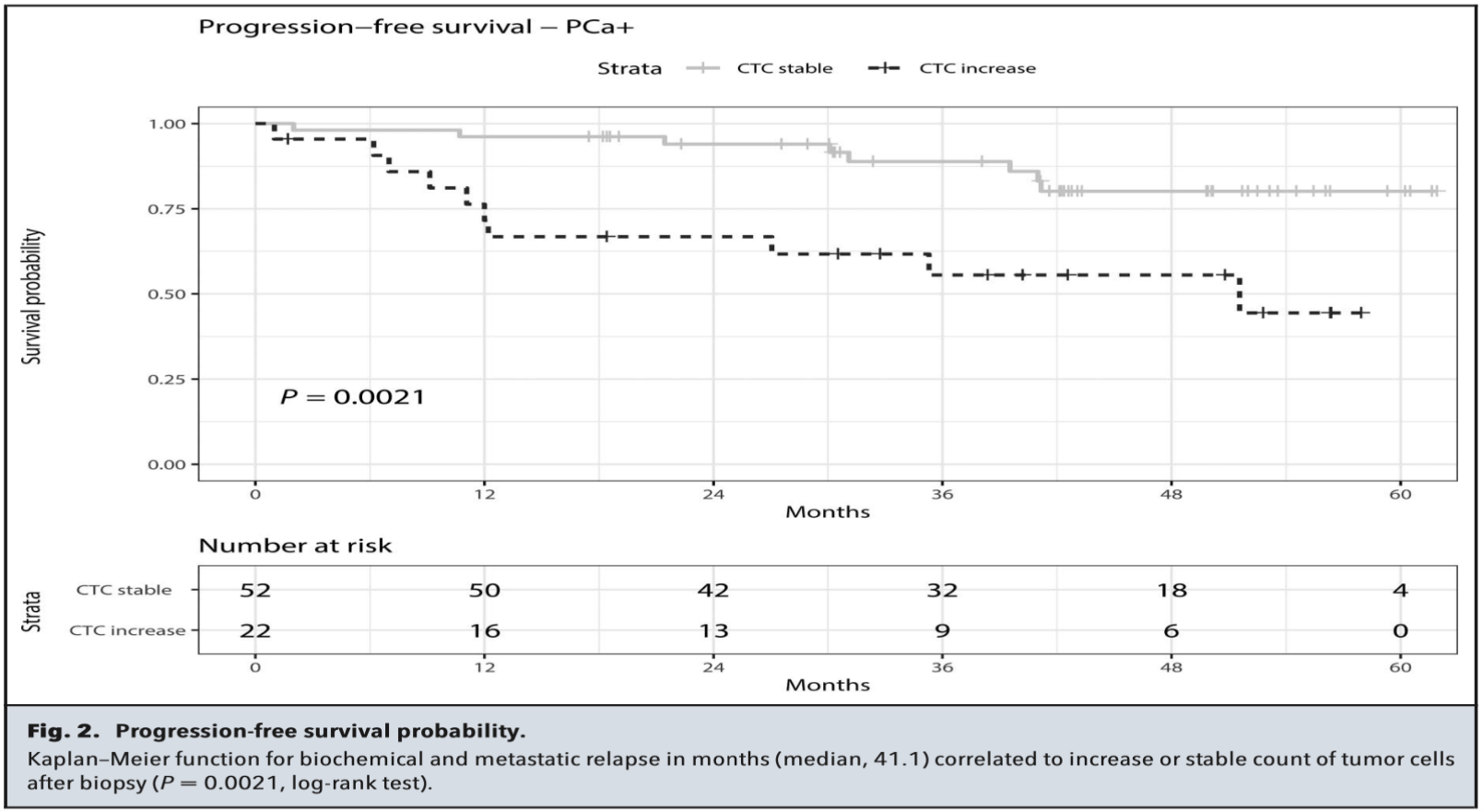


Fig. 2. Progression-free survival probability.
Kaplan–Meier function for biochemical and metastatic relapse in months (median, 41.1) correlated to increase or stable count of tumor cells after biopsy ($P = 0.0021$, log-rank test).

Josse SA *et al.* Clin Chem 2020

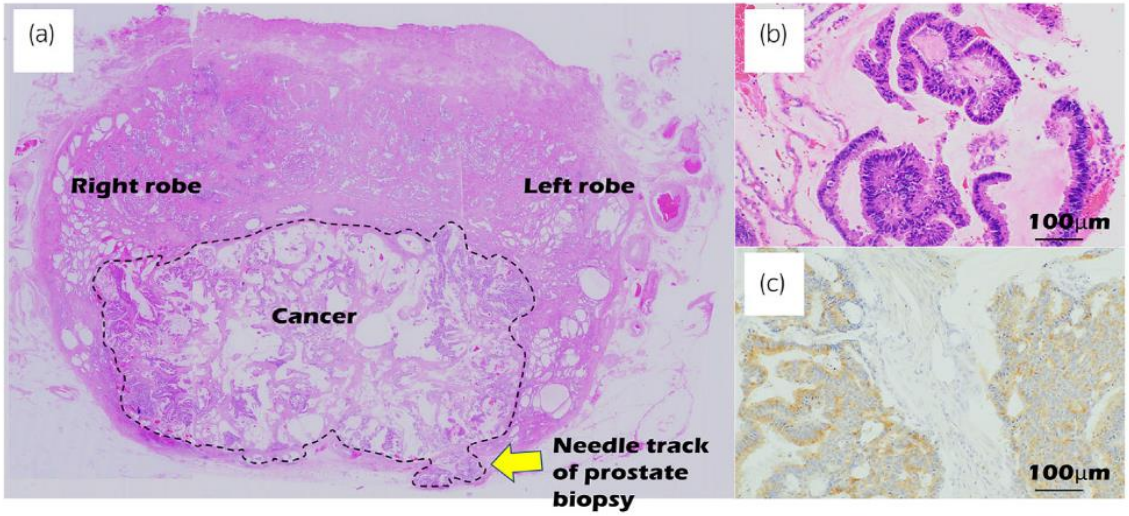
Do we have any evidence that cancer cells can migrate down the needle tract?

Case Report

Recurrence of mucinous prostate cancer in rectal wall due to needle-track seeding from previous transrectal prostate biopsy

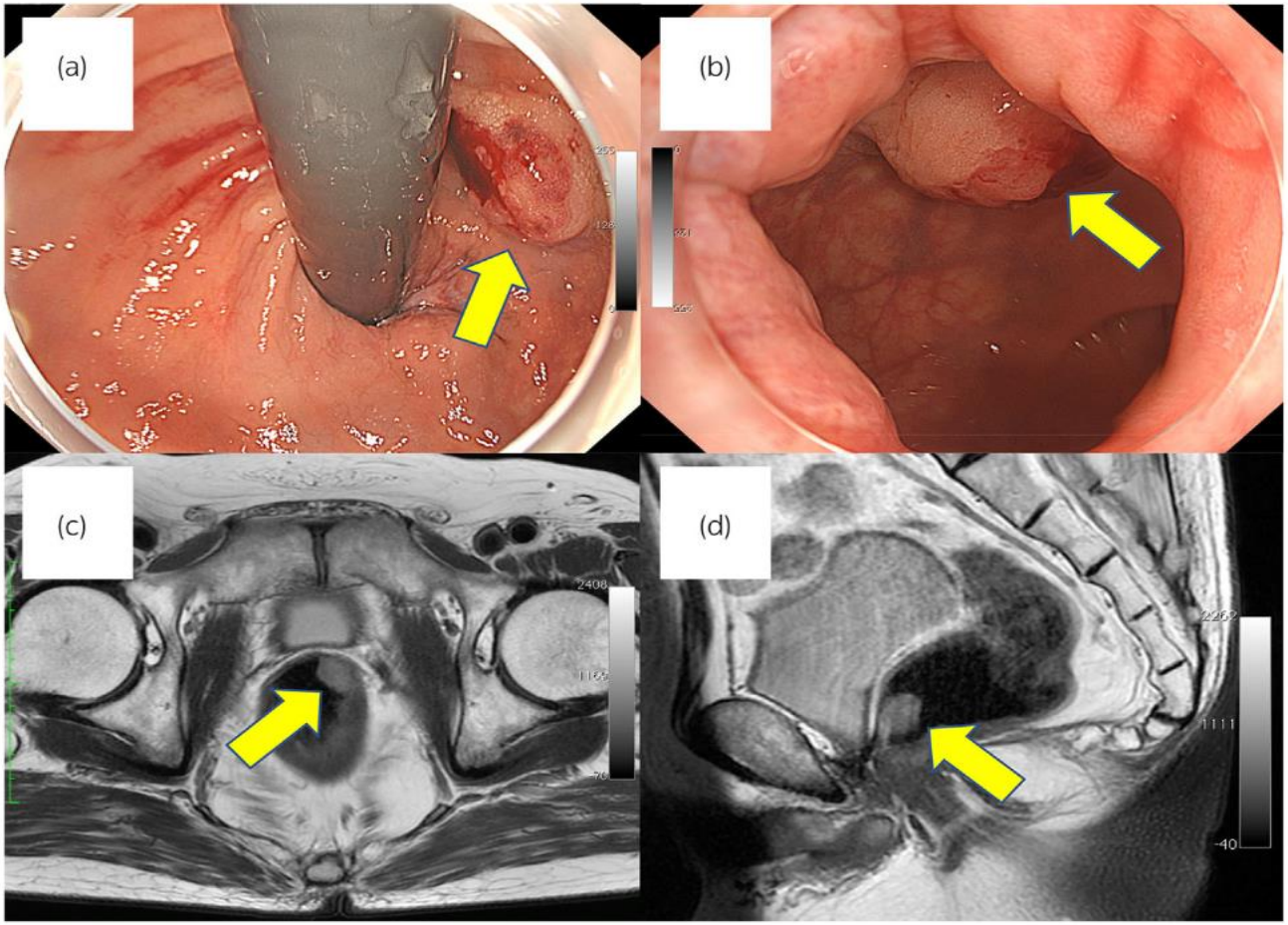
Tomoaki Hakariya,[1] Kazune Teshima,[1] Daiyu Aoki,[1] Naoki Nishimura,[1] Tetsuro Tominaga,[2] Takashi Nonaka,[2] Shunsuke Sato,[3] Nozomi Ueki,[4] Masahiro Nakashima[4] and Ryoichi Imamura[5]

Division of [1]Urology and [3]Pathology, Japan Community Health Care Organization, Isahaya General Hospital, Departments of [2]Surgical Oncology, and [5]Urology, Nagasaki University Graduate School of Biomedical Sciences, and [4]Departments of Tumor and Diagnostic Pathology, Atomic Bomb Disease Institute, Nagasaki University, Nagasaki, Japan



Gleason 4 plus 4

Hakariya T *et al.* IJU Case Reports 2024



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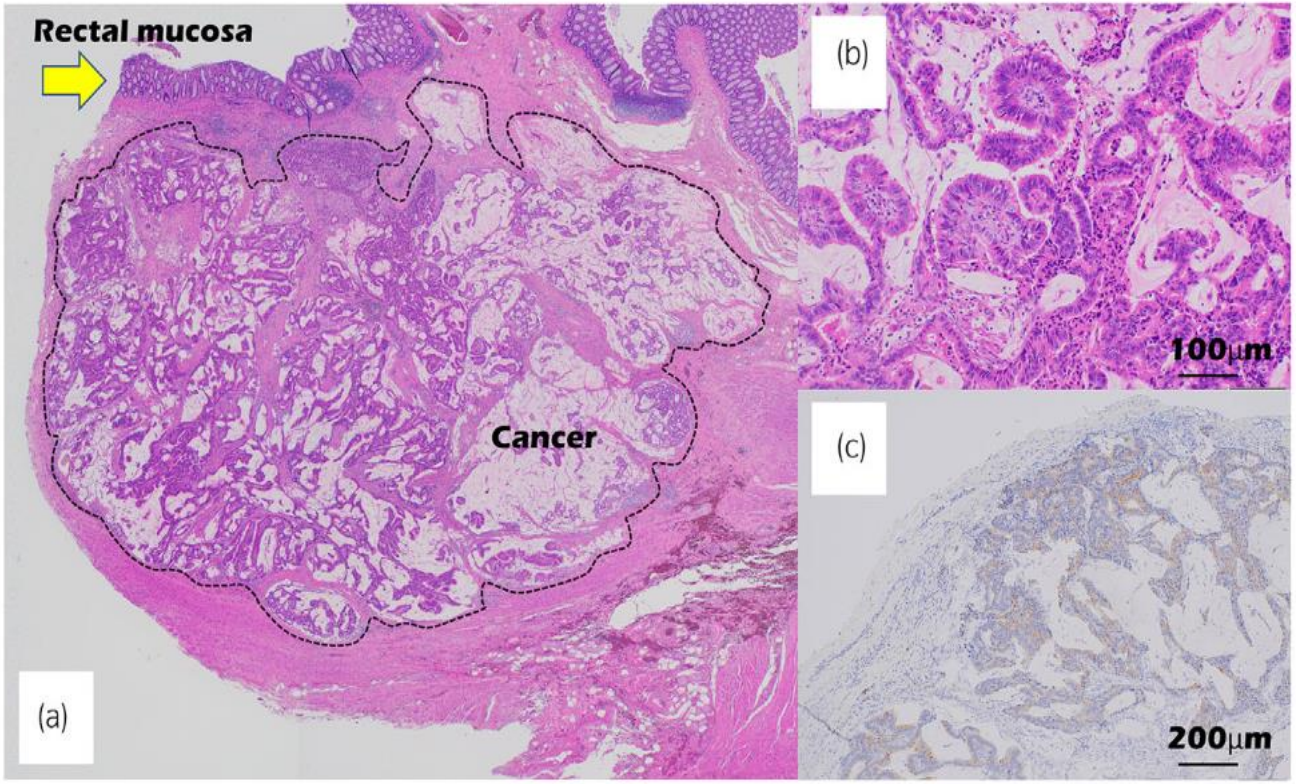
PSA positive adenocarcinoma, not arising from rectal mucosa



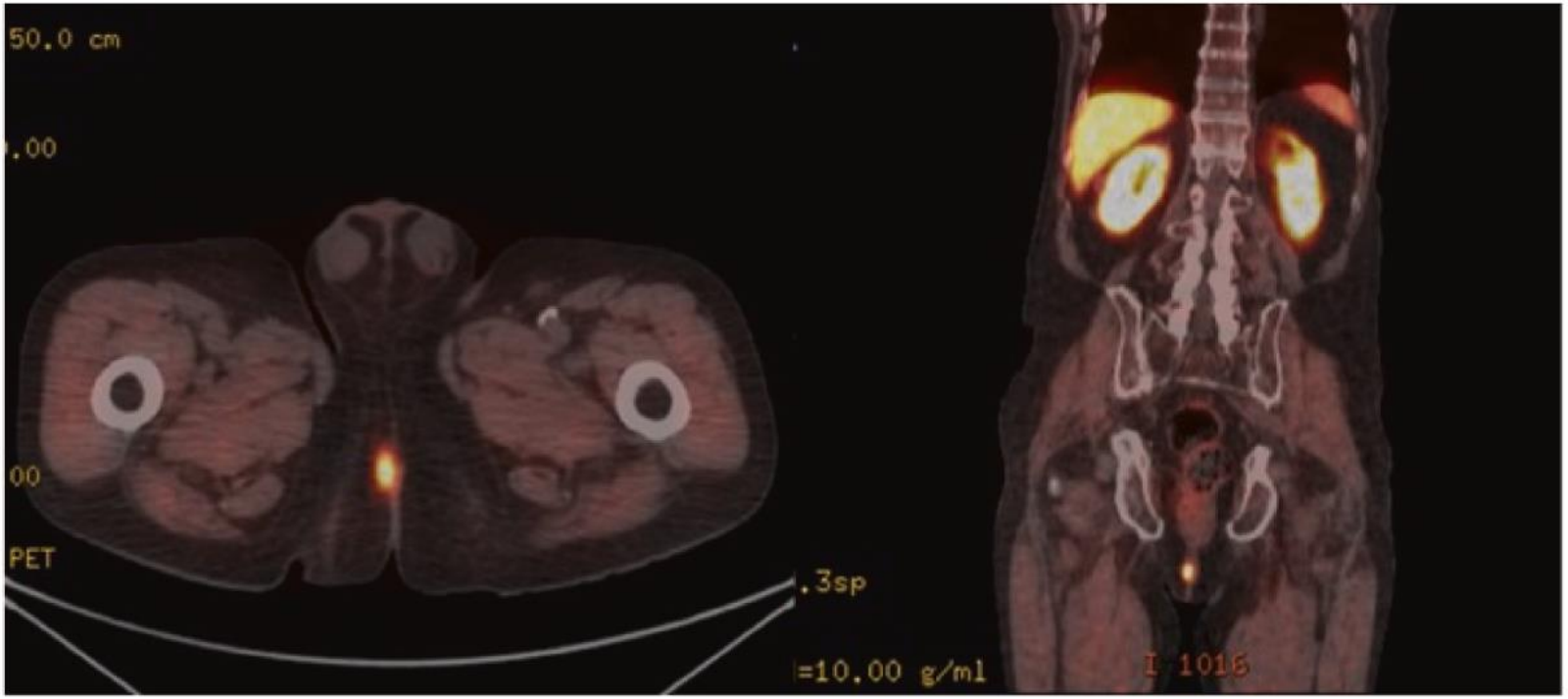
Hakariya T *et al.* IJU Case Reports 2024

Oncology

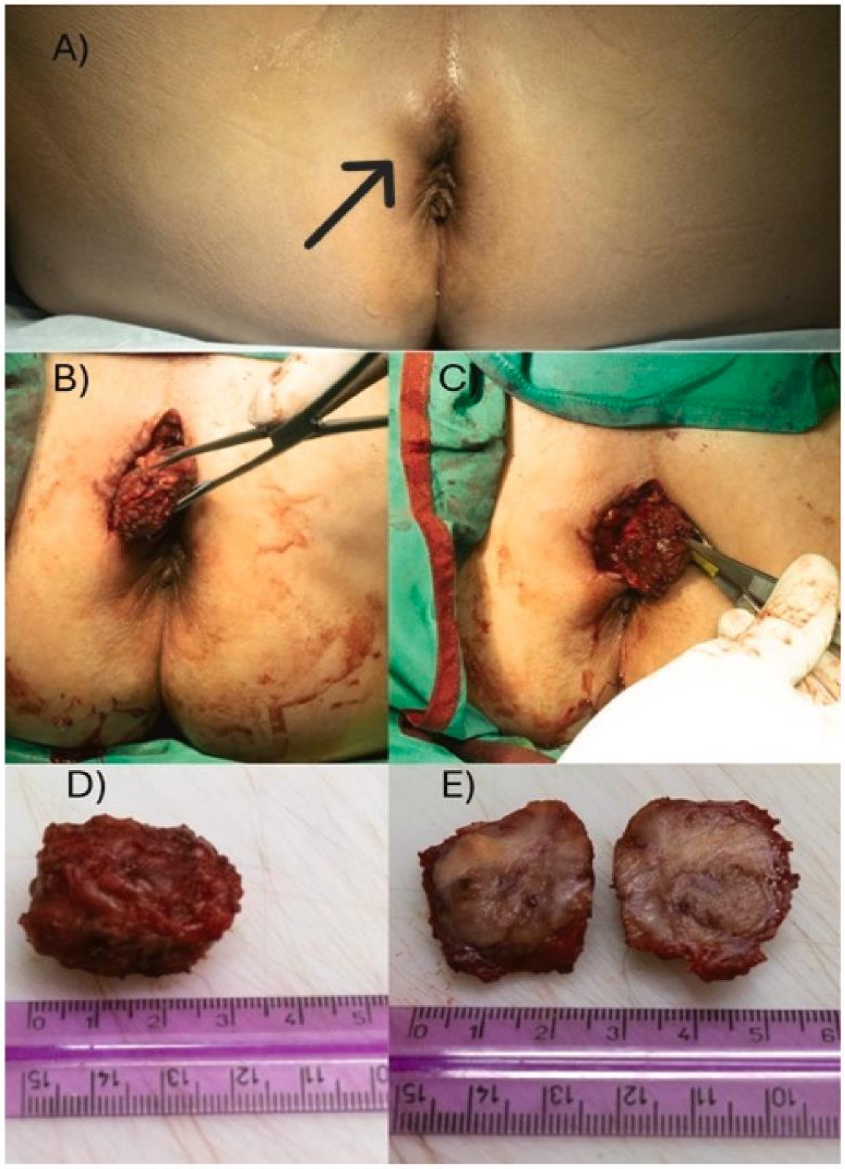
A challenging diagnosis of prostate cancer seeding in the perineal needle-tract after transperineal biopsy: is PET-CT the imaging of choice?

Claudia Fede Spicchiale [a], Federico De Leonardis [a], Luca Orecchia [a], Stefano Germani [a], Anastasios D. Asimakopoulos [a], Roberto Miano [b,*]

[a] *Urology Unit, AOU Policlinico Tor Vergata, Rome, Italy*
[b] *Department of Surgical Sciences, Urology Unit, University of Rome Tor Vergata, AOU Policlinico Tor Vergata, Rome, Italy*



Resection of perineal lesion revealed Gleason 4 plus 3 adenocarcinoma



What can we learn from other cancers?

Contents lists available at ScienceDirect

Pathology - Research and Practice

journal homepage: www.elsevier.com/locate/prp

Core needle biopsy changes the expression of TGFβ1 and TGFβRII at protein level, and the distribution of CD4 and CD8 positive T cells in primary breast cancer

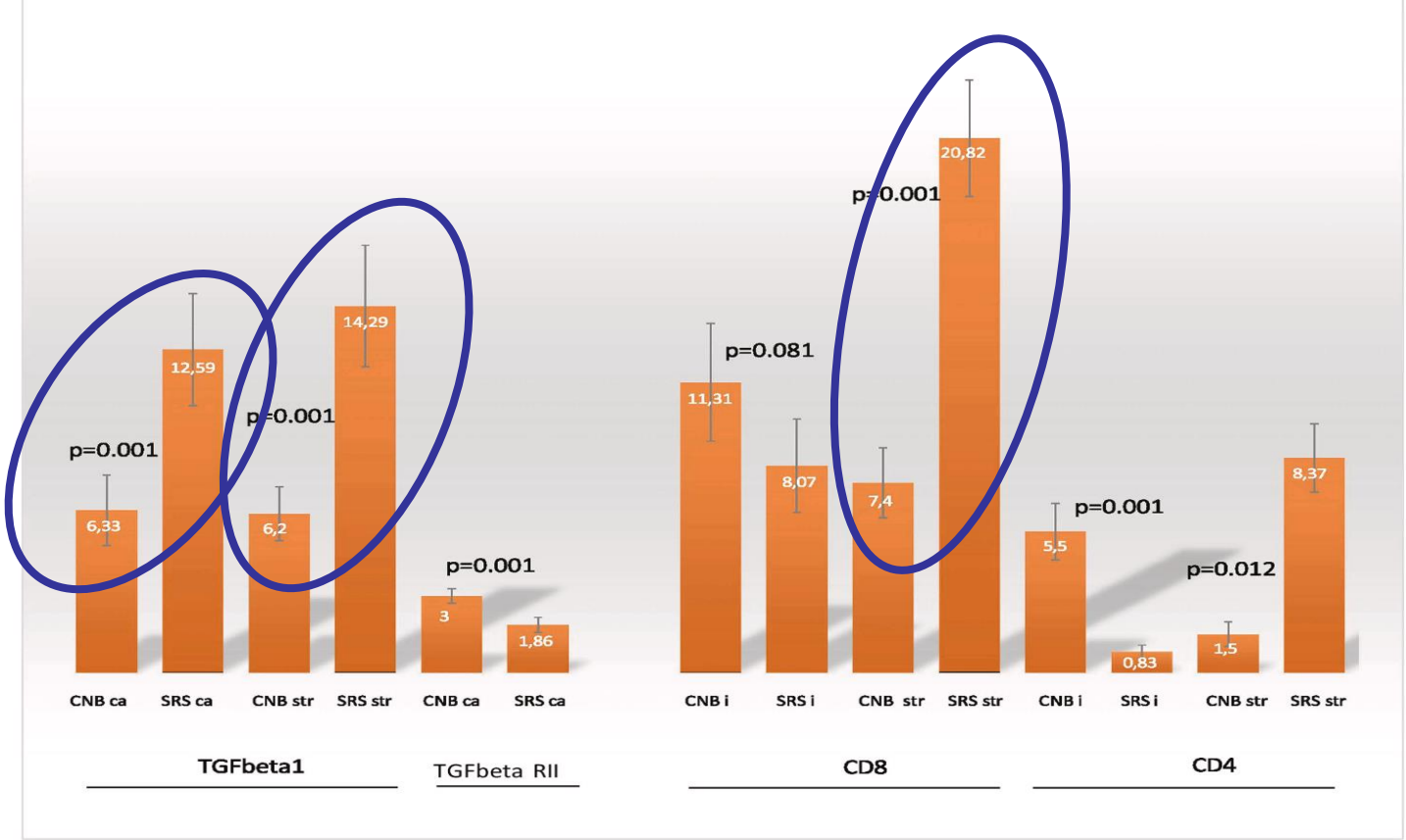
Kristiina Joensuu *, Marja Heiskala, Päivi Heikkilä

Department of Pathology and HUSLAB, Helsinki University Hospital and University of Helsinki, Helsinki FIN-00290, Finland

Compared formalin fixed, paraffin embedded samples from core needle biopsies (mean 4.3) with surgical specimen (biopsy to resection time median 25 days) in 49 women with confirmed breast cancer.

Joensuu K *et al.* Path Res Pract 2024

Core biopsy alters host immune response in women with breast cancer



Joensuu K *et al.* Path Res Pract 2024

Needle biopsy accelerates pro-metastatic changes and systemic dissemination in breast cancer: Implications for mortality by surgery delay

Hiroyasu Kameyama,[1] Priya Dondapati,[1] Reese Simmons,[1] Macall Leslie,[1] John F. Langenheim,[2] Yunguang Sun,[3] Misung Yi,[4] Aubrey Rottschaefer,[1] Rashmi Pathak,[1] Shreya Nuguri,[1] Kar-Ming Fung,[5] Shirng-Wern Tsaih,[6] Inna Chervoneva,[4] Hallgeir Rui,[2] and Takemi Tanaka[1,5,7,*]

[1]Stephenson Cancer Center, University of Oklahoma Health Sciences Center, 975 NE 10th St., Oklahoma City, OK 73104, USA

[2]Department of Pharmacology, Physiology & Cancer Biology, Sidney Kimmel Cancer Center, Thomas Jefferson University, 233 S 10th St., BLSB 1008, Philadelphia, PA 19107, USA

[3]Department of Pathology, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, USA

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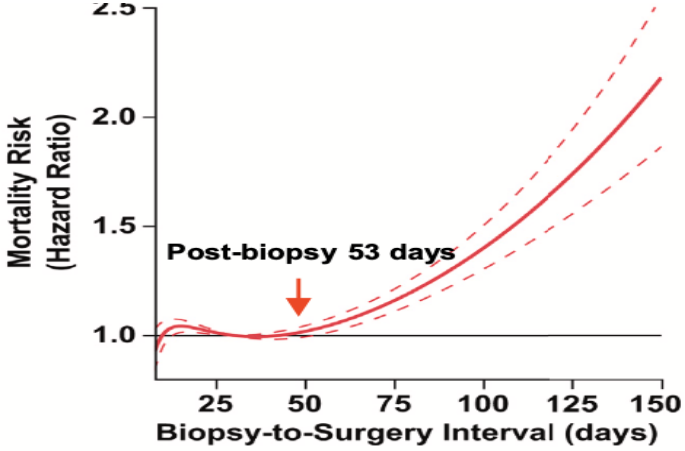
[6]Department of Obstetrics and Gynecology, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, USA

[7]Lead contact

*Correspondence: takemi-tanaka@ouhsc.edu

https://doi.org/10.1016/j.xcrm.2023.101330



Kameyama H *et al.* Cell Reports Med 2023

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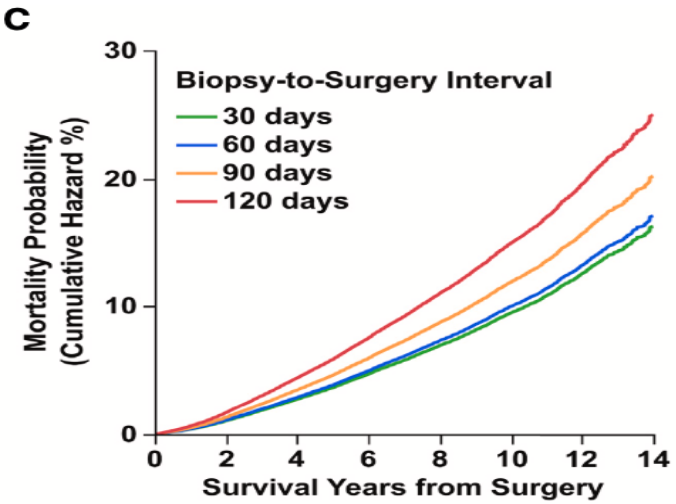
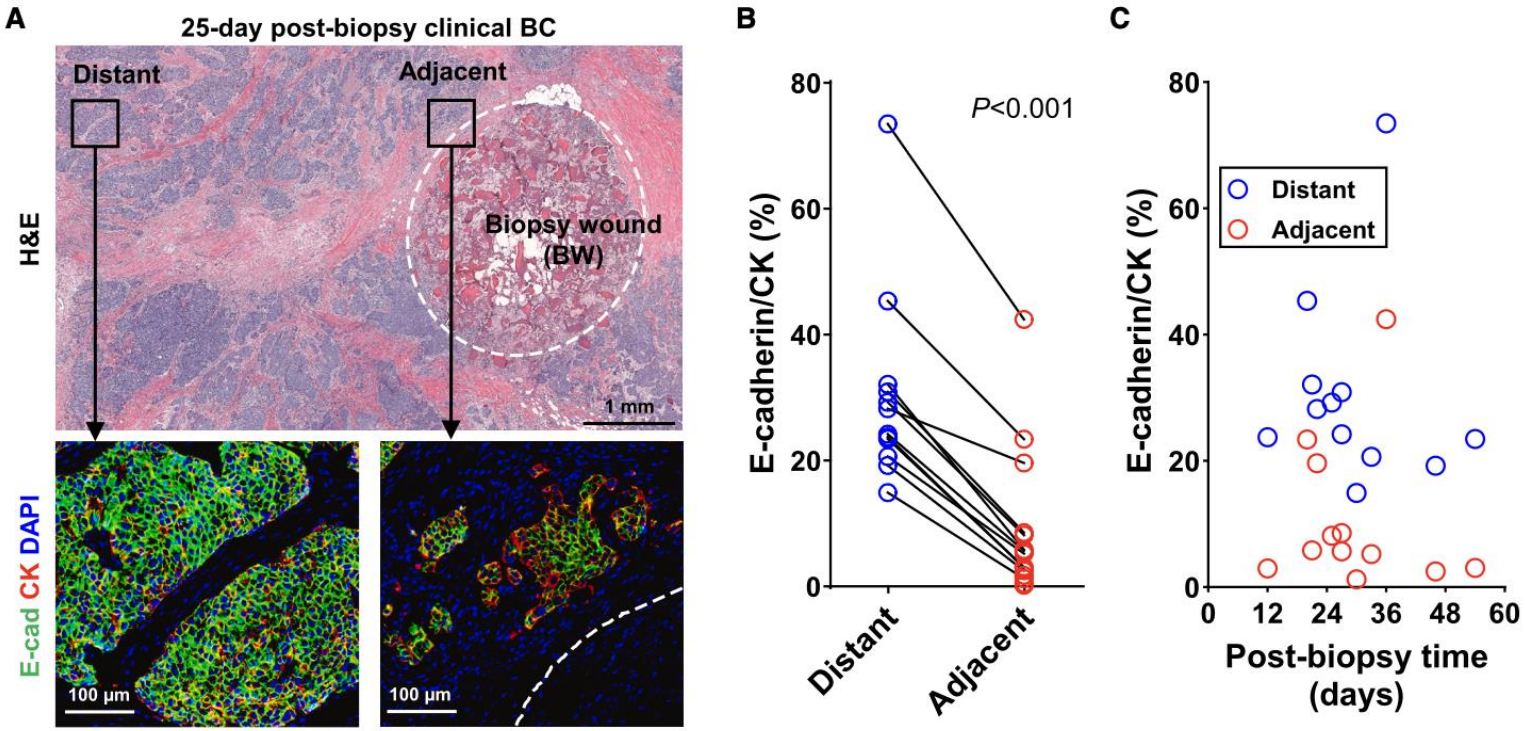


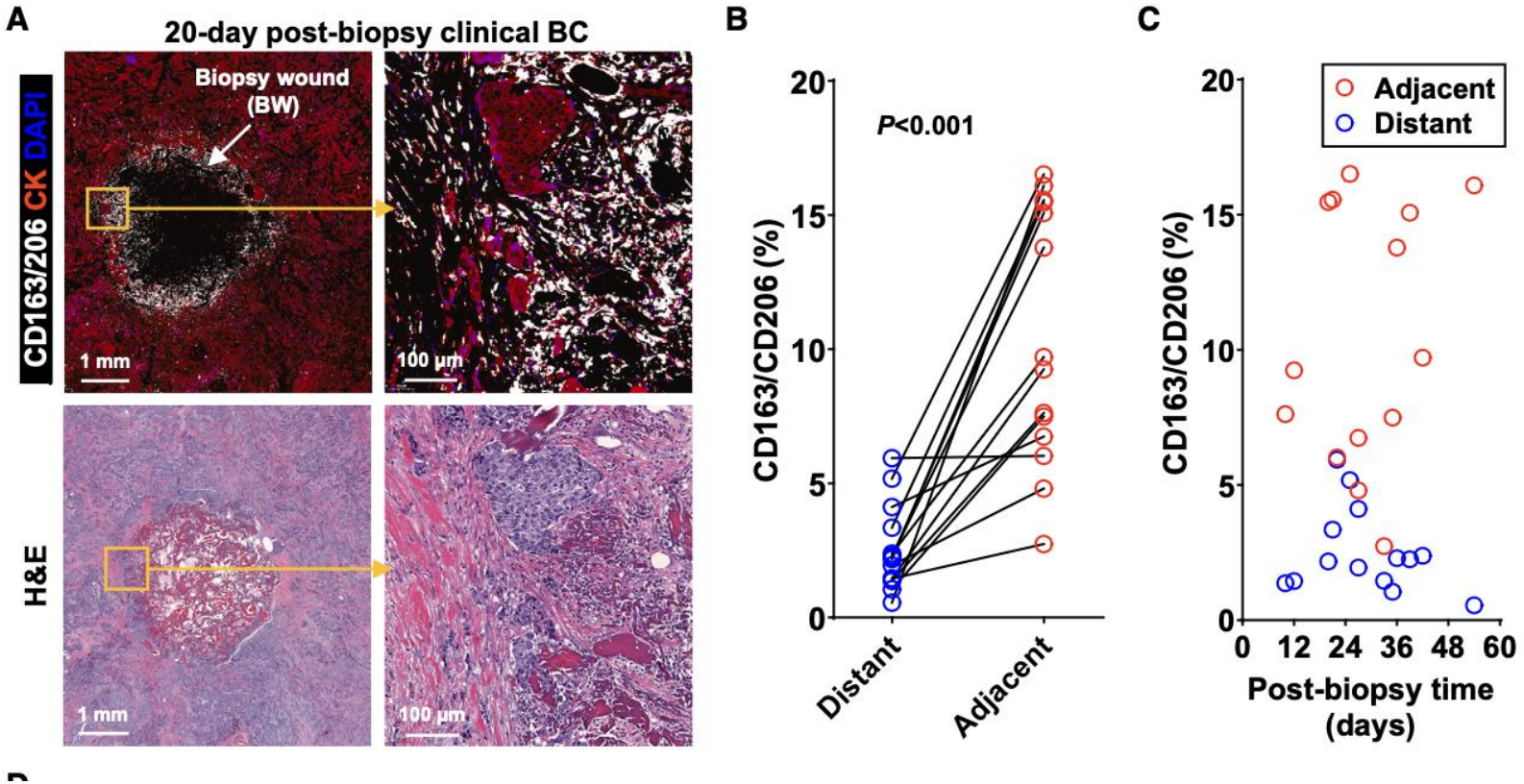
Kameyama H *et al.* Cell Reports Med 2023

Reduction in E-cadherin+/CK+ cells adjacent to biopsy compared with distant sample



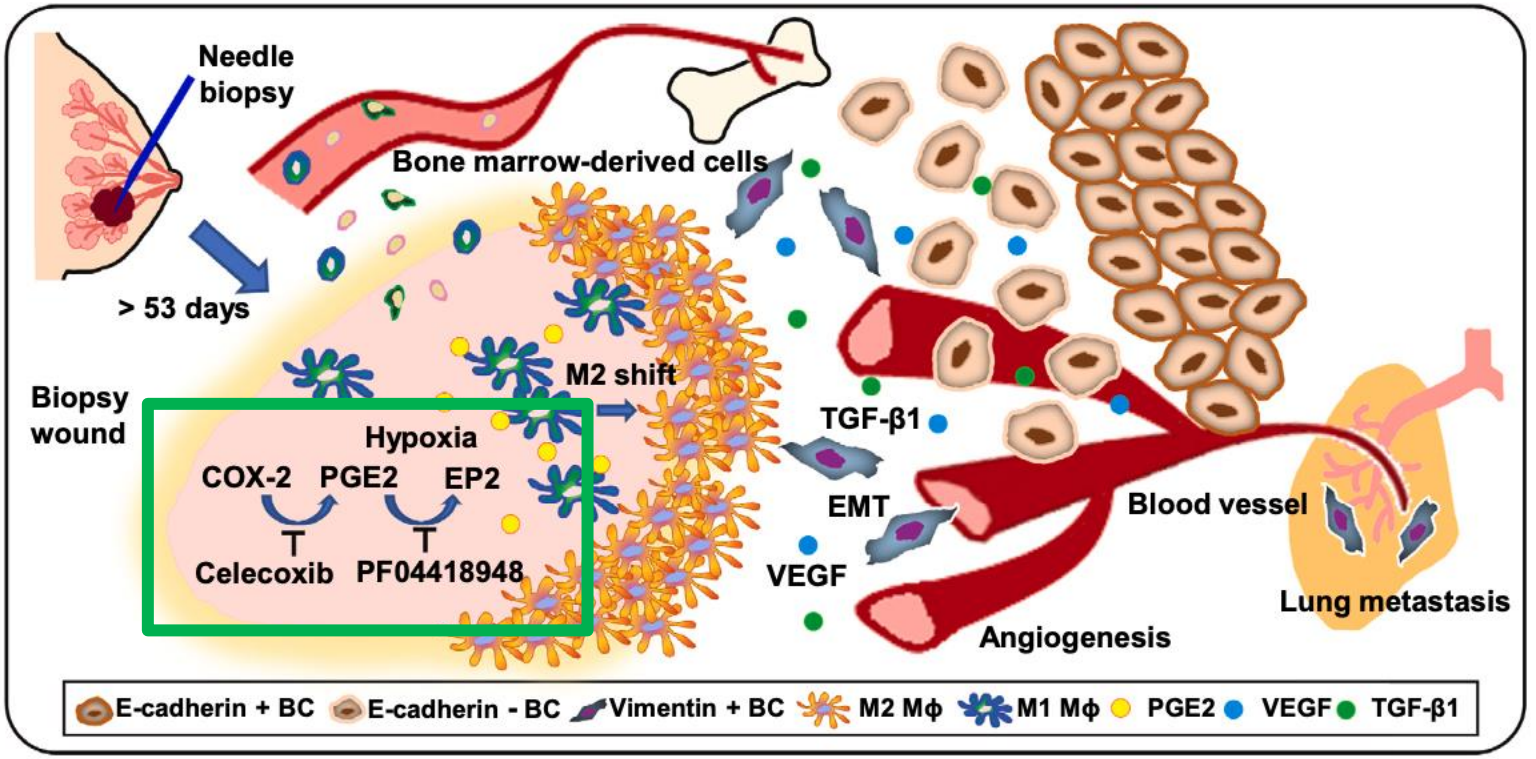
Kameyama H *et al.* Cell Reports Med 2023

Increase in CD163+/CD206+ M2-like macrophages adjacent to biopsy compared with distant sample



Kameyama H *et al.* Cell Reports Med 2023

Graphic hypothesis of biopsy induced metastases and pharmacological interception



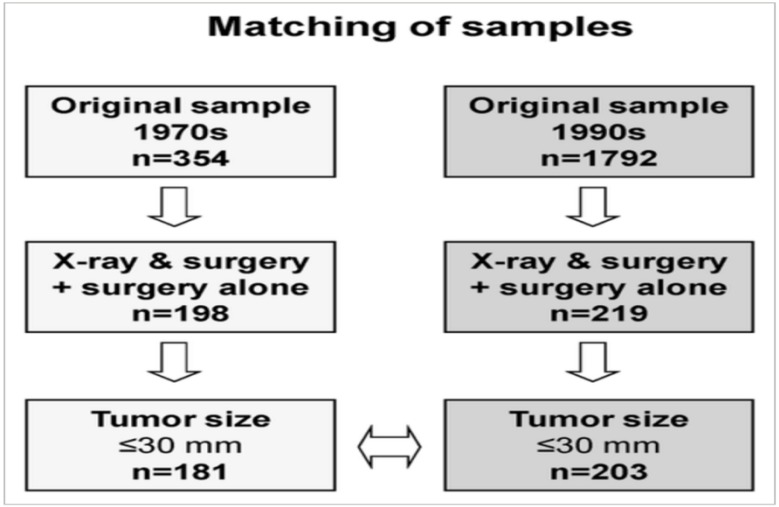
Kameyama H *et al.* Cell Reports Med 2023

Original Article | Free Access

Core-needle biopsy of breast cancer is associated with a higher rate of distant metastases 5 to 15 years after diagnosis than FNA biopsy

Roland B. Sennerstam MD, PhD, Bo S. H. Franzén PhD, Hans O. T. Wiksell PhD, Gert U. Auer MD, PhD

First published: 24 August 2017 | https://doi.org/10.1002/cncy.21909 | VIEW METRICS



Sennerstam RB et al. Cancer Cytopathol 2017

Investigators were diligent in their matching

Analysis of Tumor Size	No. of Patients		*P*
	FNAB Cohort, n = 230	CNB Cohort, n = 219	
No. with unknown tumor size (not included)	21	0	
No. with multiple tumors (not included)	11	0	
No. with tumors ≤20 mm	120	121	NS
Mean tumor size ± SD, mm	13.3 ± 1.44	12.7 ± 3.91	
No. with tumors ≤30 mm[b]	181	203	NS
Mean tumor size ± SD, mm	18.3 ± 7.13	18.2 ± 7.1	
No. with tumors > 30 mm (not included)	17	15	.056
Mean tumor size ± SD, mm	56.9 ± 10.1	46.2 ± 19.9	
Total no. with tumor size registered	198	219	
No. included in the analysis[b]	181	203	

Sennerstam RB et al. Cancer Cytopathol 2017

Core needle biopsy cohort had more exposure to radiation

Tumor Size ≤ 30 mm	Postoperative RTP + Surgery: No. of Patients (%)	*P*	Surgery Alone: No. of Patients (%)	Σ
FNAB cohort	96 (53)	0.46 (NS)	83 (47)	n = 181
P	< .02		.05	
CNB cohort	140 (69)	< .005	63 (31)	n = 203

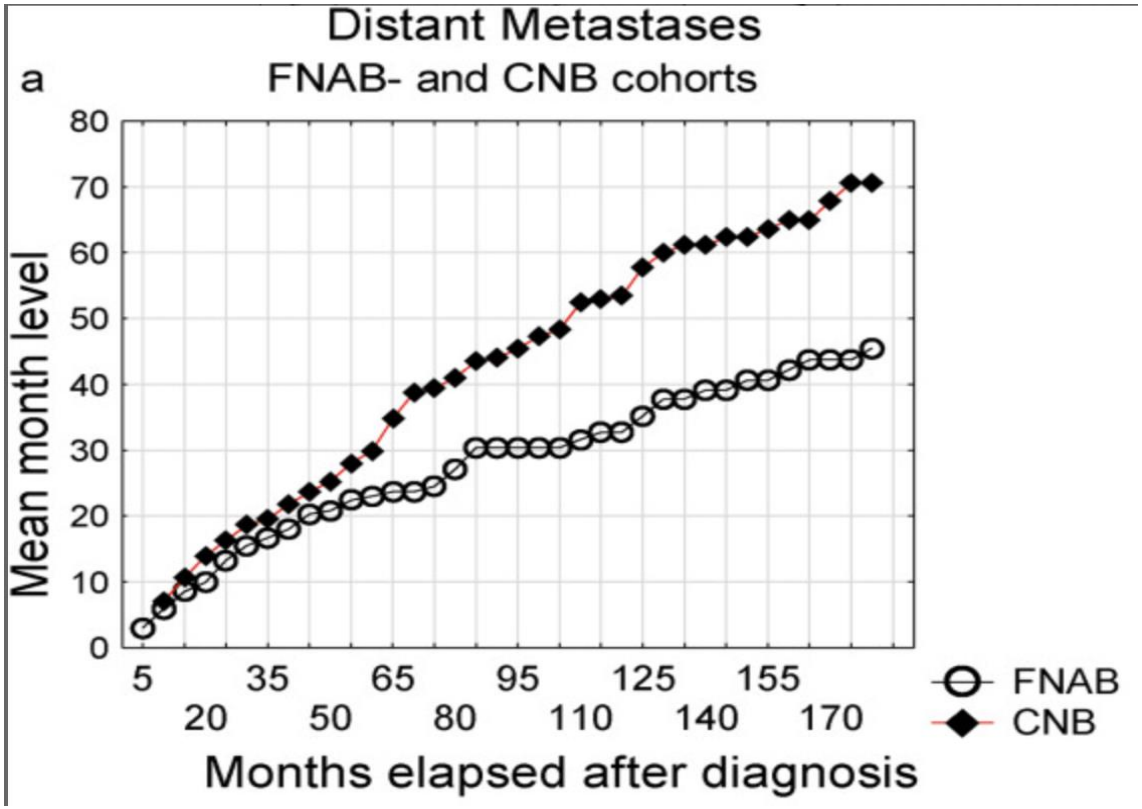
Sennerstam RB et al. Cancer Cytopathol 2017

Cancers looked very similar in terms of ploidy

DNA Ploidy	FNAB Original Cohort: No. (%), n = 354	*P*	CNB Original Cohort: No. (%), n = 1729	*P*	FNAB Final Selected Cohort: No. (%), n = 181	*P*	CNB Final Selected Cohort: No. (%), n = 203
Diploid	137 (41.1)	.53 (NS)	727 (43.9)	.62 (NS)	75 (46.9)	.45 (NS)	73 (40.8)
Tetraploid	129 (38.9)	.91 (NS)	636 (38.4)	.49 (NS)	54 (33.7)	.92 (NS)	62 (34.6)
Aneuploid	67 (20)	.64 (NS)	292 (17.6%	.80 (NS)	31 (19.4)	.59 (NS)	44 (24.6)
Σ	n = 333		n = 1655		n = 160		n = 179

Sennerstam RB et al. Cancer Cytopathol 2017

There were more metastases in the core needle biopsy group



Sennerstam RB et al. Cancer Cytopathol 2017

Reflections – none of these studies are definitive, but they do build a picture

- Very few formal investigations of this type in prostate cancer

Biopsy reduction opportunities

- Normal MRI
- Target only in PIRADS 4-5
- Diffuse PIRADS 3 changes
- PIRADS 3 changes with normal PSA density
- MRI+ve/PSMA PET-ve lesions
- Prior to radical prostatectomy

Utilization of Prediagnostic Prostate Magnetic Resonance Imaging Among Rural Americans: An Analysis of Medicare Claims for Elevated Prostate-Specific Antigen

Nathaniel Fox Hansen, Hanna Zurl, Stephan M. Korn, Jianyi Zhang, Hung-Jui Tan, Matthew E. Nielsen, Caroline M. Moore, Quoc-Dien Trinh, Adam S. Kibel, and Alexander P. Cole
View All Author Information

Conclusion:

"*Despite evidence that MRI is an extremely useful tool in the pre-diagnostic setting, fewer than 1 in 20 beneficiaries in this study received an MRI.*"

"*Rural patients were less likely than their more urban counterparts to receive MRI for evaluation of elevated PSA*."

Hansen NF *et al.* Urolo Practice 2025

Biopsy reduction opportunities

- Normal MRI
- Target only in PIRADS 4-5
- Diffuse PIRADS 3 changes
- PIRADS 3 changes with normal PSA density
- MRI+ve/PSMA PET-ve lesions
- **Prior to radical prostatectomy**

Biopsy-free prostatectomy?

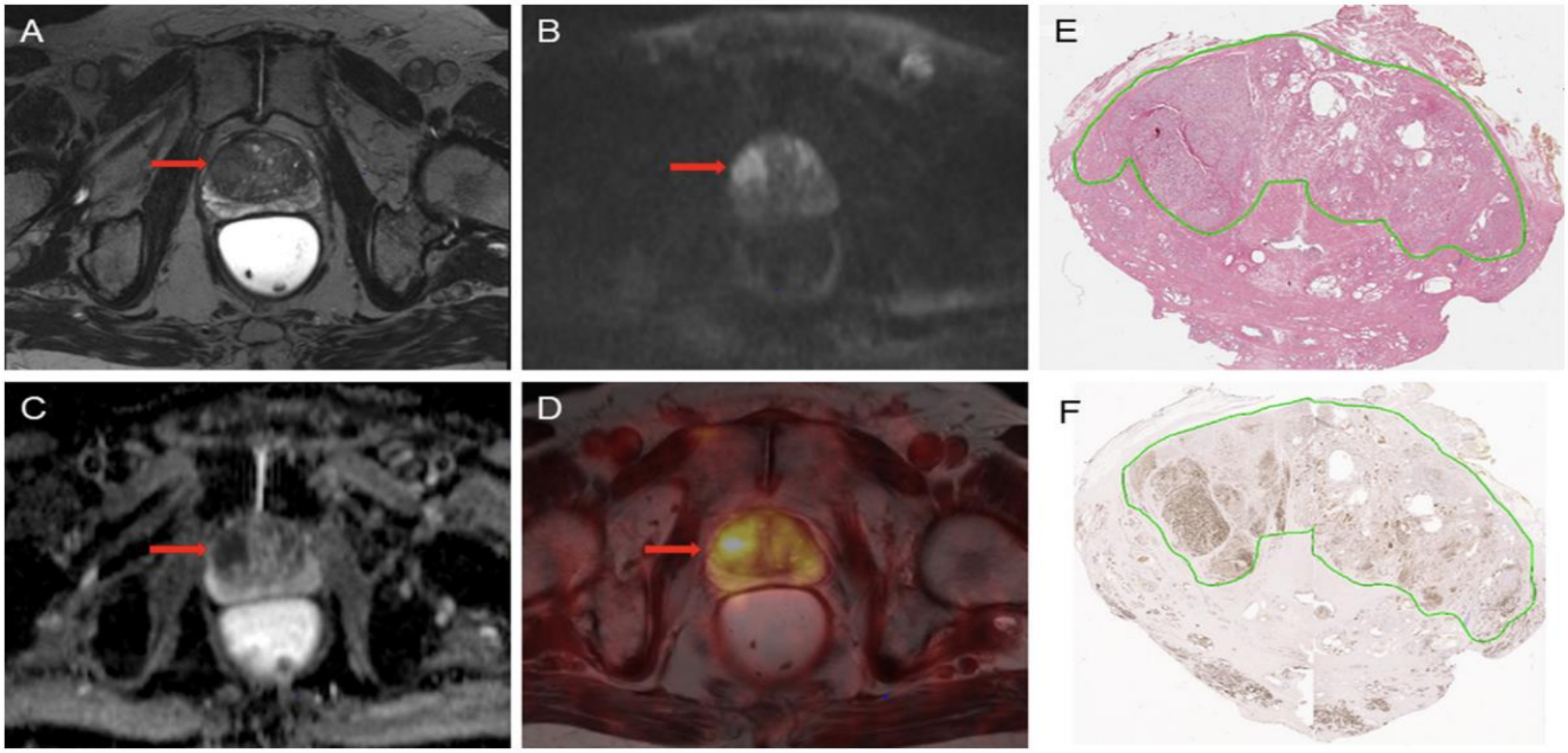
Radical Prostatectomy Without Prior Biopsy Following Multiparametric Magnetic Resonance Imaging and Prostate-specific Membrane Antigen Positron Emission Tomography

Valentin H. Meissner[a,†,], Isabel Rauscher[b,†], Kristina Schwamborn[c,†], Jan Neumann[d], Gregor Miller[e], Wolfgang Weber[b], Jürgen E. Gschwend[a], Matthias Eiber[b], Matthias M. Heck[a,*]*

- 25 patients (2015-2020) 100% sensitivity / PPV
- 52 lesions
  - For combined MRI+/PSMA+ patients:
  - Sensitivity 98% [95% CI 93–100]
  - PPV (87% [95% CI 77–97];

Meissner VH *et al.* Eur Urol Dec 2021

Biopsy-free prostatectomy?



Meissner VH *et al.* Eur Urol Dec 2021

Say no to biopsy (SNTB)

ARTICLE

Clinical Research

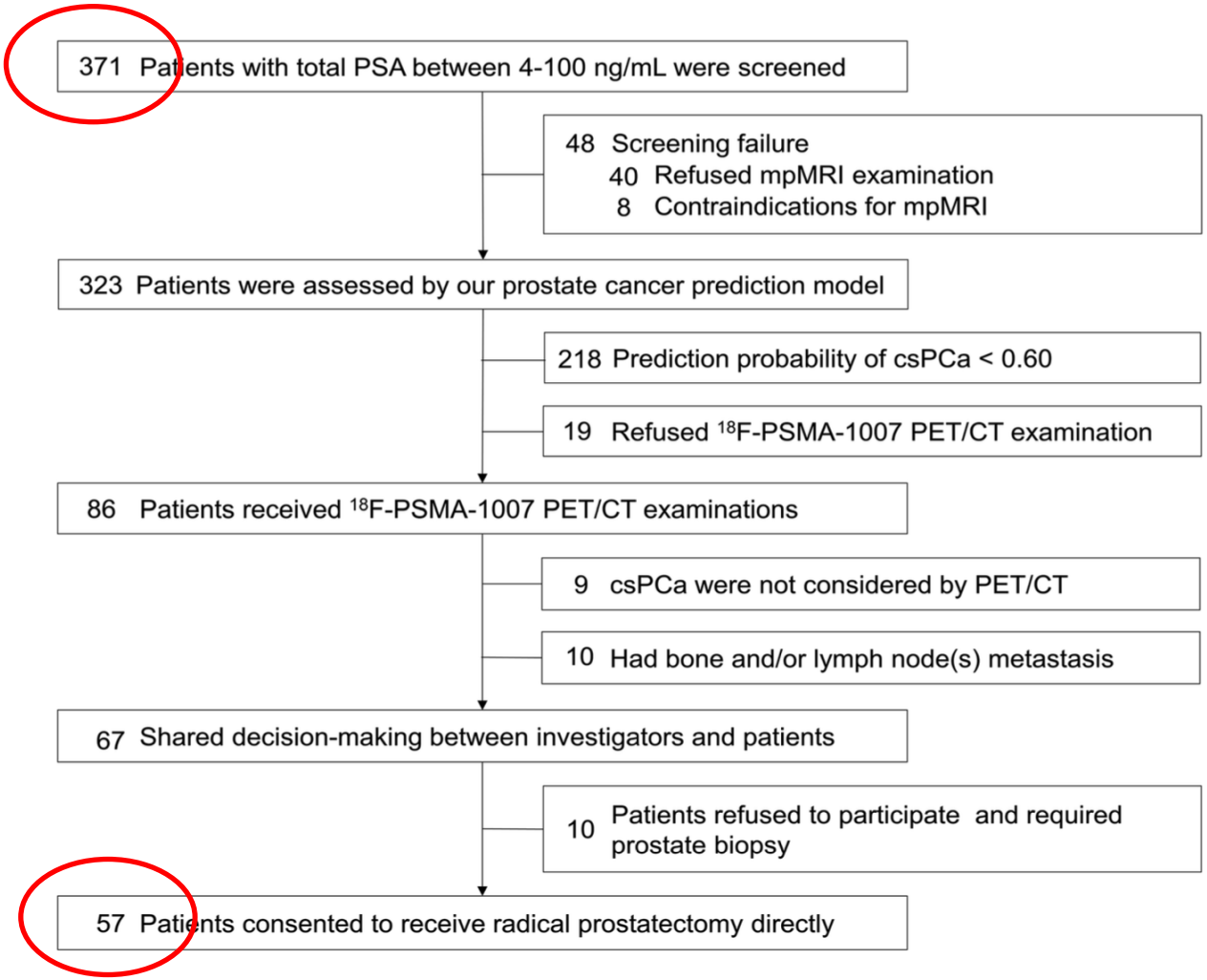
Check for updates

Radical prostatectomy without prostate biopsy based on a noninvasive diagnostic strategy: a prospective single-center study

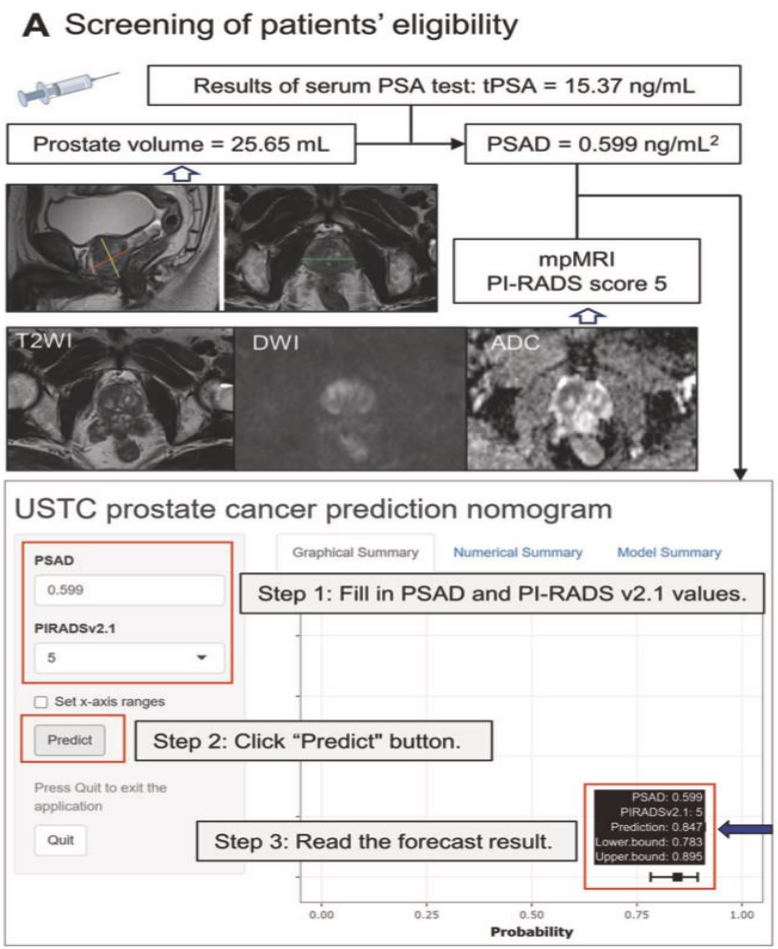
Changming Wang[1,7], Qiang Xie[2,7], Lei Yuan[3], Ming Ni[2], Dong Zhuo[4], Yukui Gao[4], Ying Liu[3], Xuehan Liu[5], Yifan Ma[1], Jun Xiao[1]✉ and Tao Tao[1,6]✉

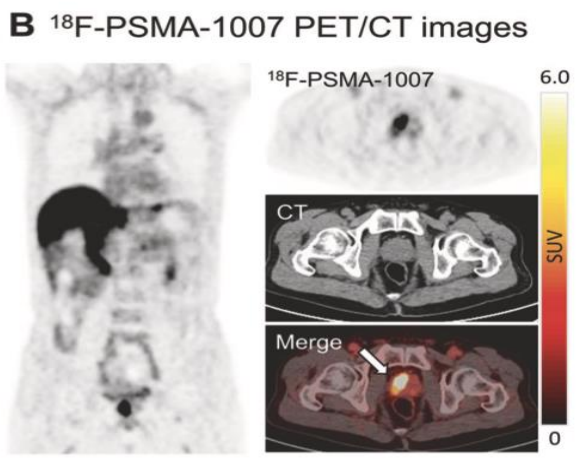
Wang C et al. Prostate Cancer and Prostate Disease 2025

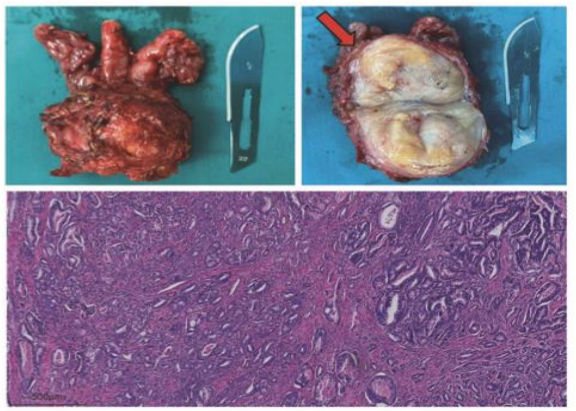
Quite difficult to do



Pathway involved double hit on visibility plus a calculator







Double hit visibility selects a high-risk group

Characteristics	Patients ($n = 57$) [a]
Age (years old)	69.8 ± 7.1
BMI (kg/m^2)	24.1 ± 2.9
DRE	
Normal	20 (35.1)
Abnormal	23 (40.4)
Suspicious	14 (24.5)
Total PSA (ng/mL)	17.2 (12.4–34.7)
Free PSA (ng/mL) [b]	2.6 (1.4–3.9)
free/total PSA [b]	0.12 (0.09–0.16)
Prostate volume (mL)	36.0 (26.3–44.7)
PSAD (ng/mL^2)	0.56 (0.42–0.82)
PI-RADS v2.1	
4	13 (22.8)
5	44 (77.2)
Prediction probability	0.81 (0.72–0.89)
SUVmax	21.6 (15.8–33.0)

Visible disease by MRI and PSMA PET seems to be ‘clinically significant’

Characteristics	Patients ($n = 57$), case (%)
Diagnostic results	
csPCa	56 (98.2)
agPCa	57 (100)
hgPCa	42 (73.7)
Benign prostatic diseases	0 (0)
Gleason score (ISUP grade)	
6 (grade 1)	1 (1.8)
7 (3 + 4, grade 2)	14 (24.6)
7 (4 + 3, grade 3)	14 (24.6)
8 (grade 4)	11 (19.3)
9 (grade 5)	17 (29.7)
Tumor stage	
pT2a	9 (15.8)
pT2b	4 (7.0)
pT2c	28 (49.1)
pT3a	6 (10.5)
pT3b	10 (17.6)
Lymph node stage	
N0[a]	57 (100)

ARTICLE

Radical prostatectomy without prior biopsy: an initial decision-making algorithm based on PSMA PET/mpMRI

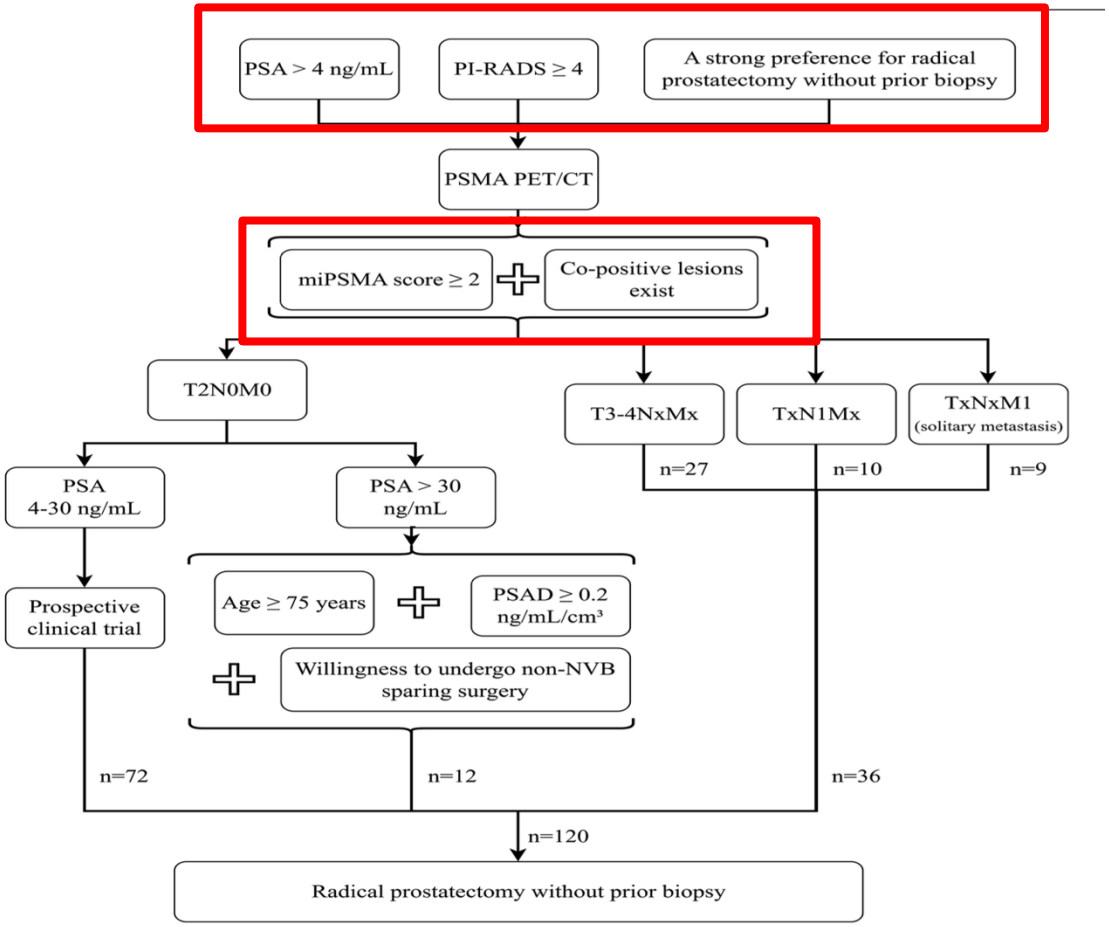
Zhuoran Li[1,2,8], Jin Luo[1,2,8], Qiwei Liu[1,2,8], Yuqi Jia[1,2], Zhiqiang Chen[1,2], Nanxin Zou[2,3], Jinqiao Li[2,3], Yujie Dong[2,4], Qiming Yang[2,4], Chao Wang[1,2], Zhuo Jia[2], Yundong Xuan[2], Xiaohui Ding[5], Honghao Xu[6], Baichuan Liu[6], Xixi Wang[1,6], Haiyi Wang[6], Yachao Liu[7], Xu Zhang[2], Weimin Ci[2], Shaoxi Niu[2]✉, Songliang Du[2]✉ and Baojun Wang[2]✉

Table 1. Basic characteristics and imaging findings of study patients.

Variables	Values
No.	120
Age, median (Q1, Q3), year	68(63, 73)
BMI, median (Q1, Q3), kg/m^2	25.3 (23.6, 27.3)
PSA, median (Q1, Q3), ng/mL	11.9 (7.7, 21.0)
Volume, median (Q1, Q3), cm^3	35.6 (28.6, 47.2)
PSAD, median (Q1, Q3), ng/mL/cm^3	0.38 (0.23, 0.59)
mpMRI PI-RADS, No. (%)	
4	35 (29.2%)
5	85 (70.8%)
SVI, No. (%)	17 (14.2%)
EPE, No. (%)	20 (16.7%)

Zhuoran L et al. Prostate Can and Prostate Disease 2026

Study flow chart



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Final pathology – all had ISUP≥2 prostate cancer

Variables	Values ($n = 120$)
Pathological concordance, No. (%)	
Discordance	0 (0%)
Hypo-concordance	4 (3.3%)
Concordance	63 (52.5%)
Hyper-concordance	53 (44.1%)
Gleason score, No. (%)	
3 + 3	0 (0%)
3 + 4	25 (20.8%)
4 + 3	38 (31.7%)
4 + 4	23 (19.2%)
5 + 3/3 + 5	3 (2.5%)
4 + 5	24 (20.0%)
5 + 4	7 (5.8%)
5 + 5	0 (0%)
ISUP grading groups, No. (%)	
1	0 (0%)
2	25 (20.8%)
3	38 (31.7%)
4	26 (21.7%)
5	31 (25.8%)

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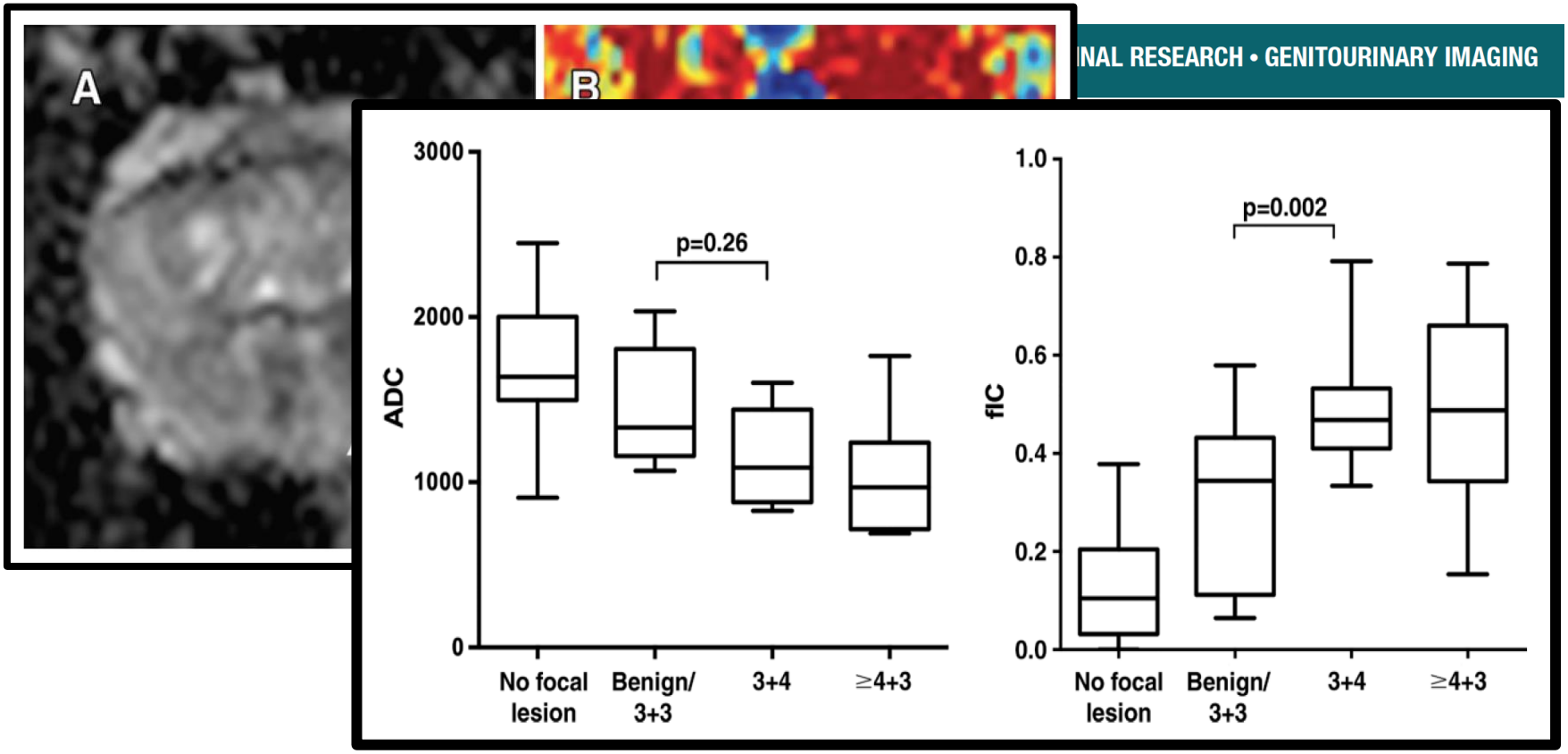
We are getting close to a ‘virtual’ biopsy

- Improved imaging
- Decreased utility of Gleason attribution
  - Poor reliability
  - Collapse of the scale
  - Biopsy associated cost/harm
- Developments in radiomics
- AI-driven feature extraction
- Companion biomarkers
- Capping of risk

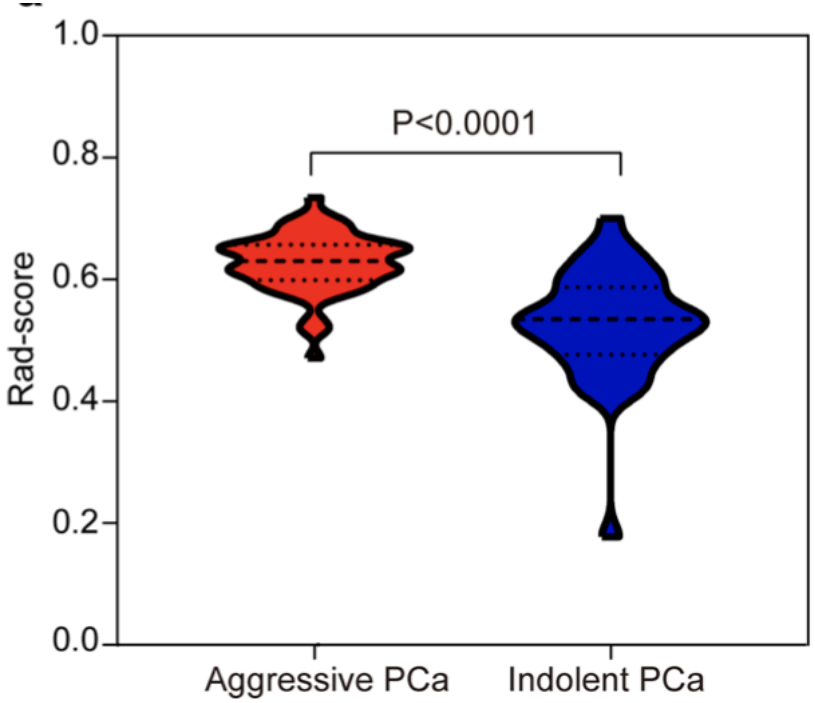
Prediction – who are the patients that might need treatment in the future?



Johnston E *et al.* Radiology 2019

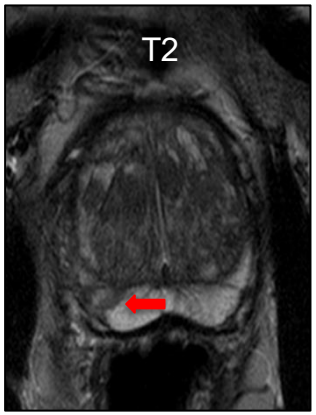
Development and validation of a multiparametric MRI-based radiomics signature for distinguishing between indolent and aggressive prostate cancer

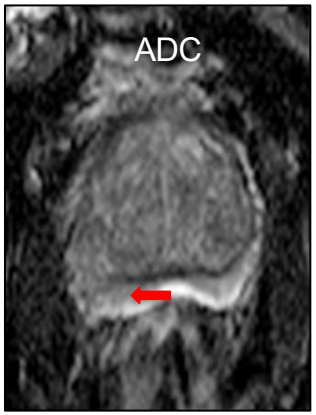
[1,2]LIUHUI ZHANG, [1]DONGGEN JIANG, [1]CHUJIE CHEN, [1]XIANGWEI YANG, [1]HANQI LEI, [3]ZHUANG KANG, [2]HAI HUANG and [1]JUN PANG

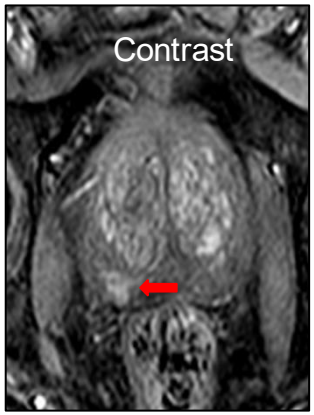


Zhang L *et al.* Br J Rad June 2021

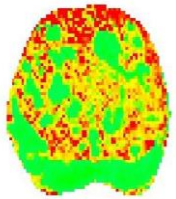
Luminal water fraction imaging (single T2 - 5 min sequence)



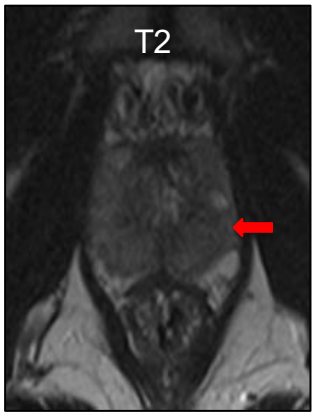


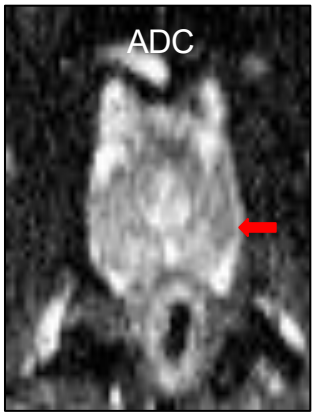


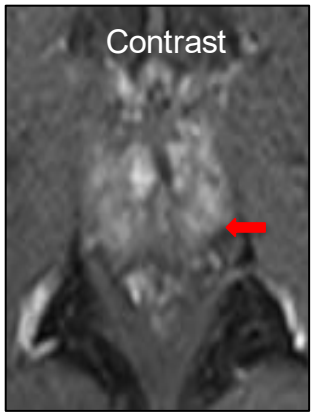
8 echo LWF map



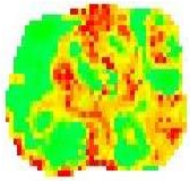
Likert: 3
Biopsy: benign
Age: 71
PSA: 6.7







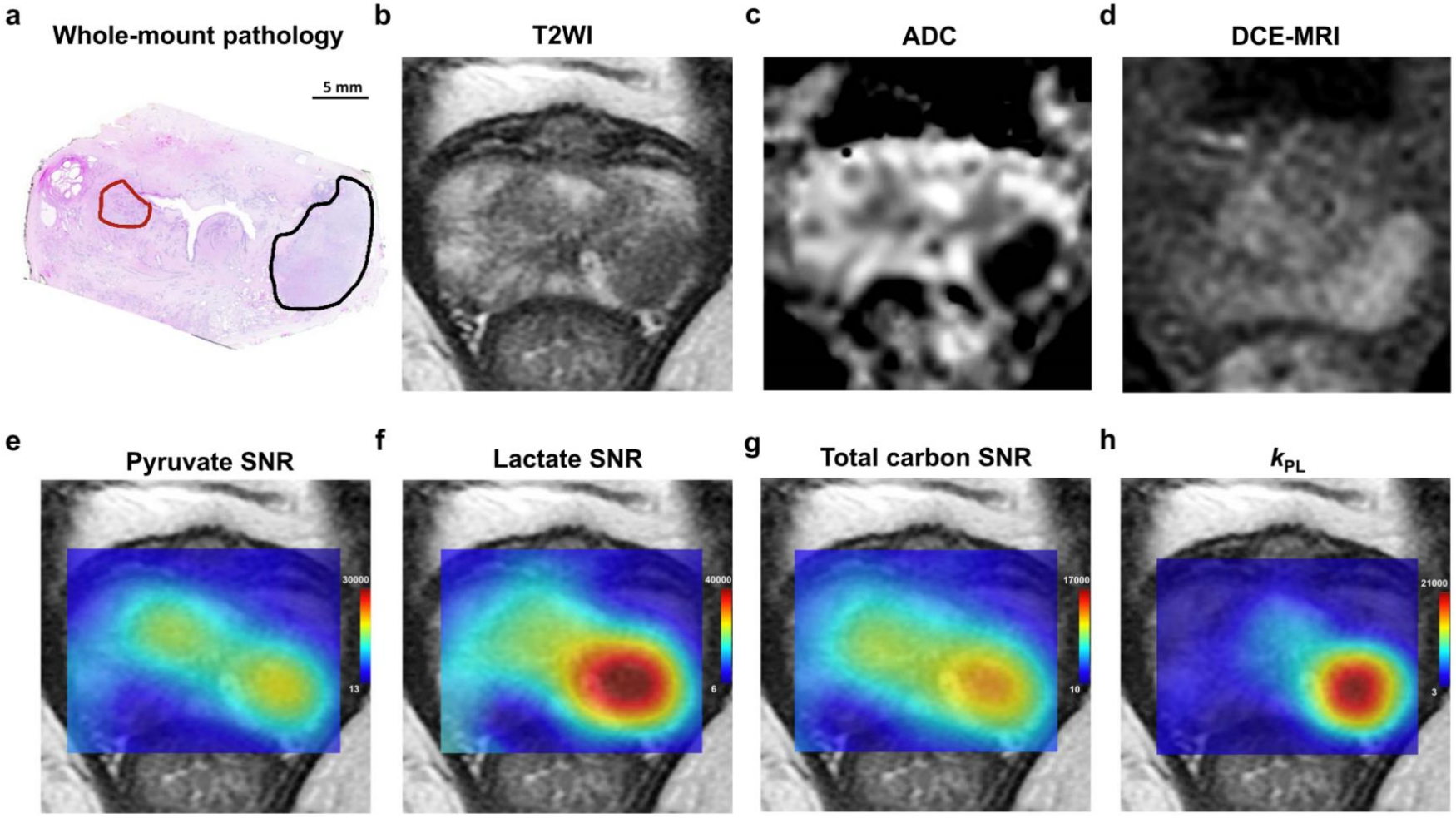
8 echo LWF map



Likert: 3
Biopsy: Gl 3+4
Age: 57
PSA: 3.89

Punwani S *et al.* ISMRM 2019 abstract #2371

13C hyperpolarized MRI



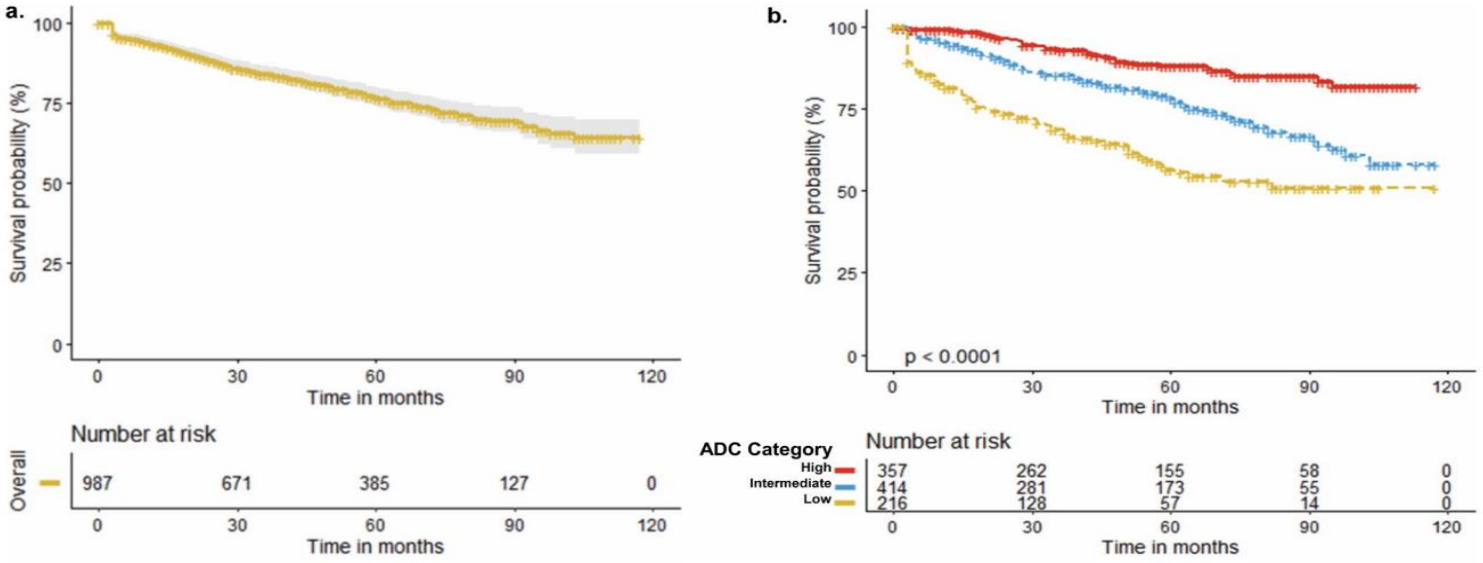
Shushentev N *et al.* Nature Comms 2022

Imaging may provide us with more direct information

- More accessible
- Can be repeated
- Greater dimensionality
- Downstream phenotype - informs us of the product of gene expression and methylation
- May be clinically more relevant

Association between mpMRI detected tumor apparent diffusion coefficient and 5-year biochemical recurrence risk after radical prostatectomy

Sarah Alessi[1] · Roberta Maggioni[1] · Stefano Luzzago[2,3] · Paul E. Summers[1] · Giuseppe Renne[4] · Fabio Zugni[1] · Maddalena Belmonte[1] · Sara Raimondi[5] · Silvano Vignati[5] · Francesco A. Mistretta[2,3] · Letizia Di Meglio[6] · Elisa D'Ascoli[6] · Alice Scarabelli[6] · Giulia Marvaso[7] · Ottavio De Cobelli[2,3] · Gennaro Musi[2,3] · Barbara Alicja Jereczek-Fossa[7,3] · Giuseppe Curigliano[8,3] · Giuseppe Petralia[1,3]



Alessi, S *et al.* Radiologia Medica, 2024

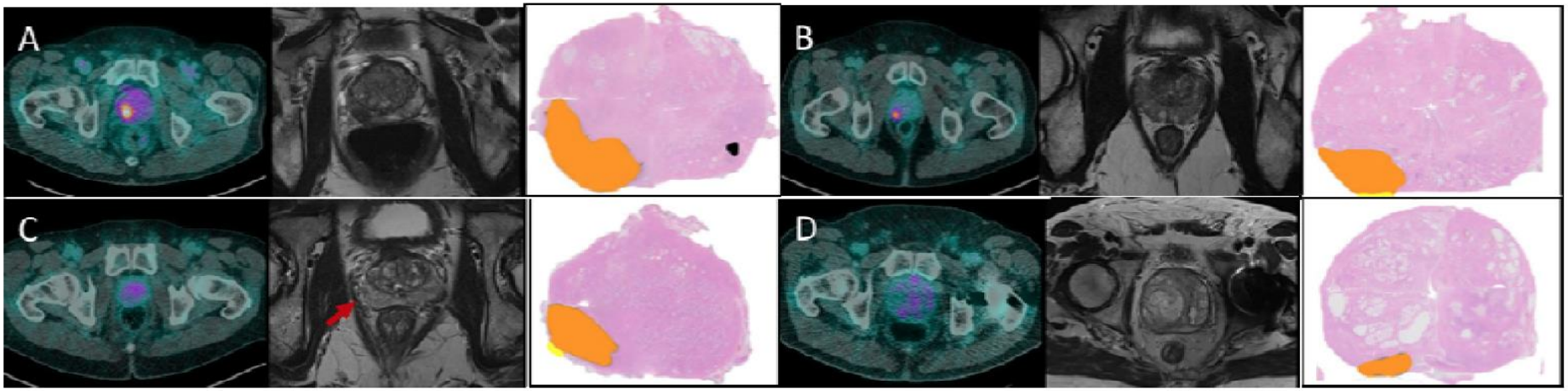
Imaging may provide us with more direct information

- More accessible
- Can be repeated
- **Greater dimensionality**
- Downstream phenotype - informs us of the product of gene expression
- May be clinically more relevant

We image to elicit a range of phenotypic expression from prostate cancer

PSMA+ / MRI+

PSMA+ / MRI -



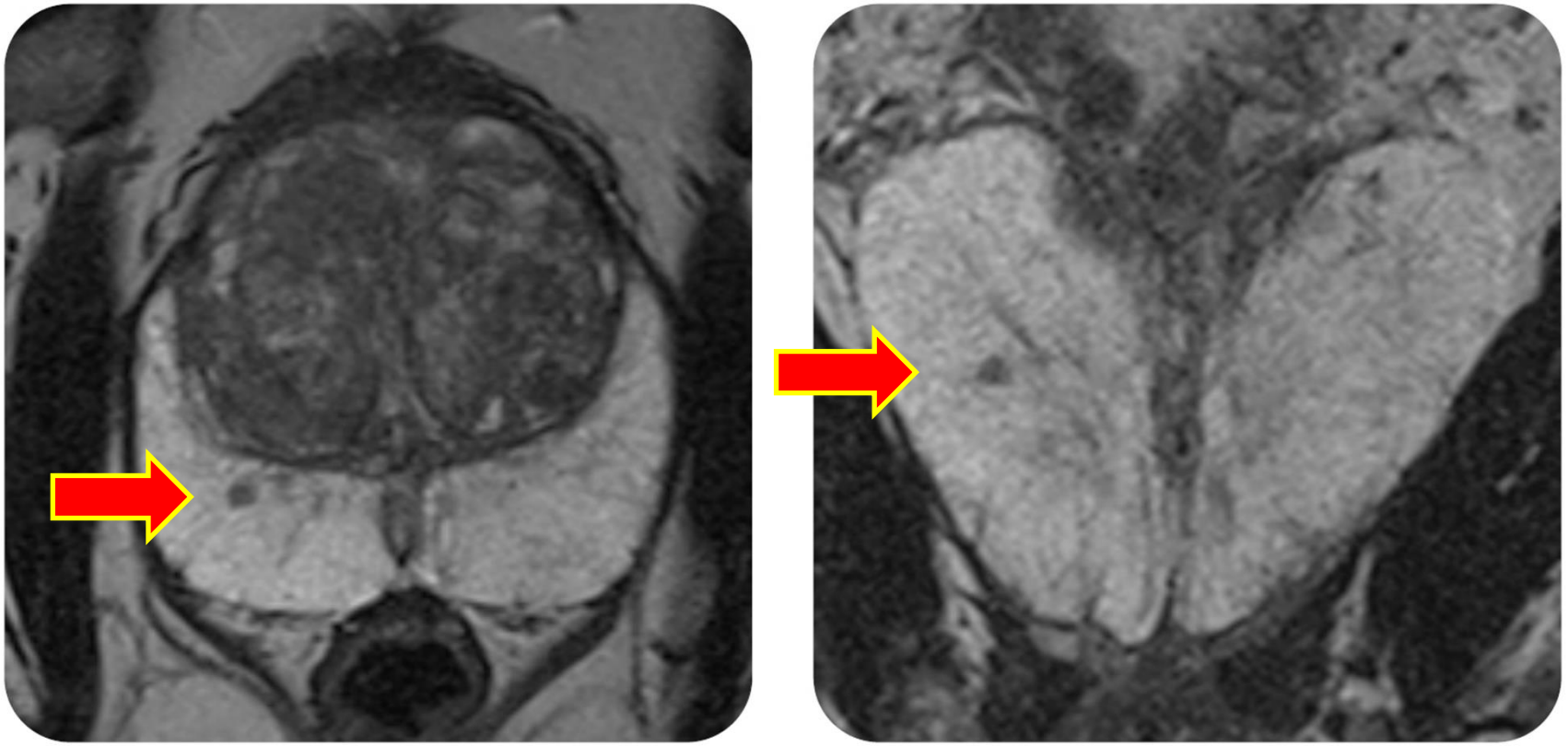
PSMA - / MRI+

PSMA - / MRI -

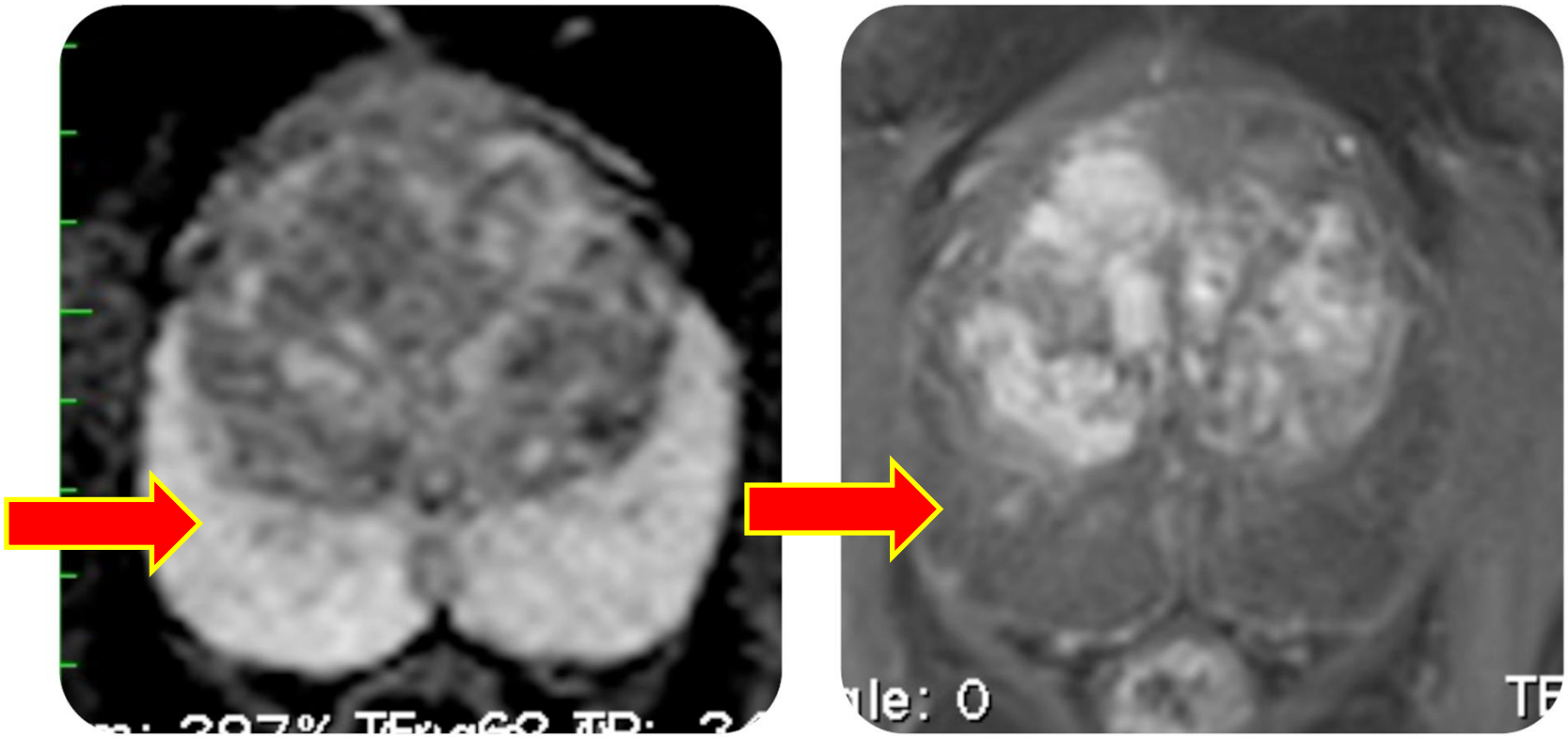
Kalapara AA *et al.* BJU Int. 2019

How might the future look?

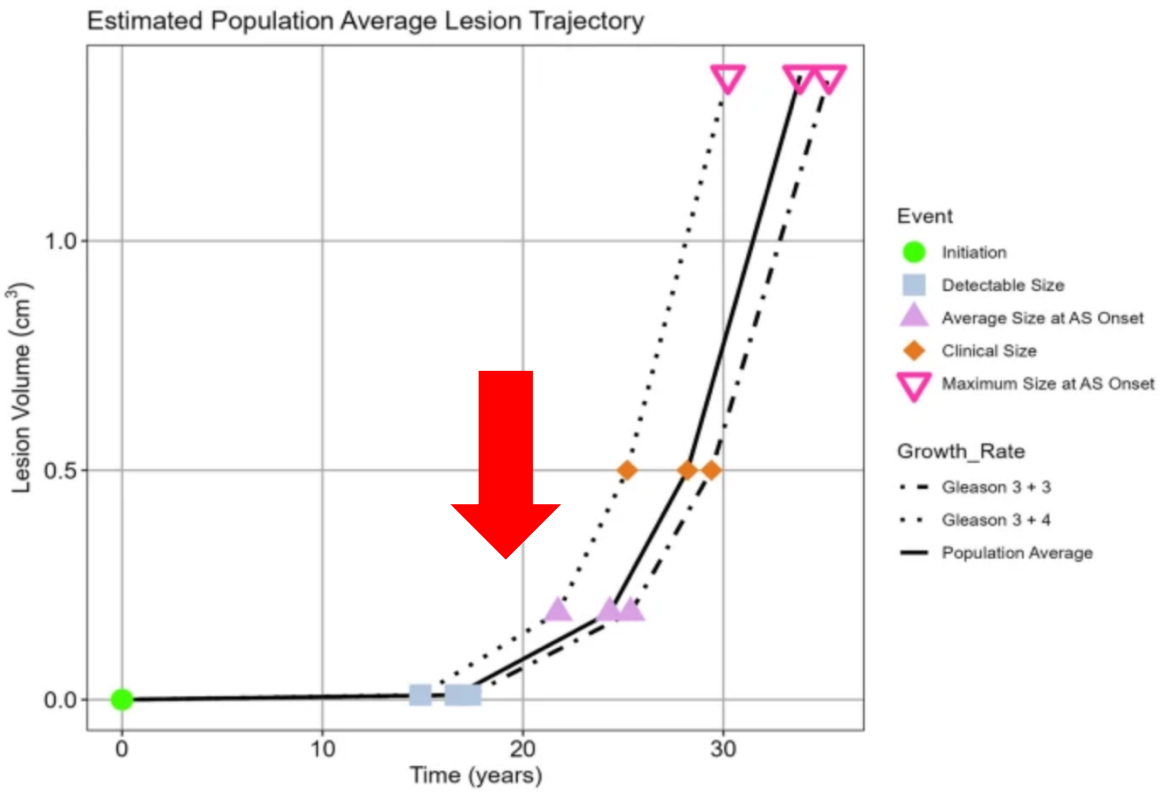
A future strategy might be the early detection of viable tumor masses



And intervention if a viable tumour mass increases in volume or signal

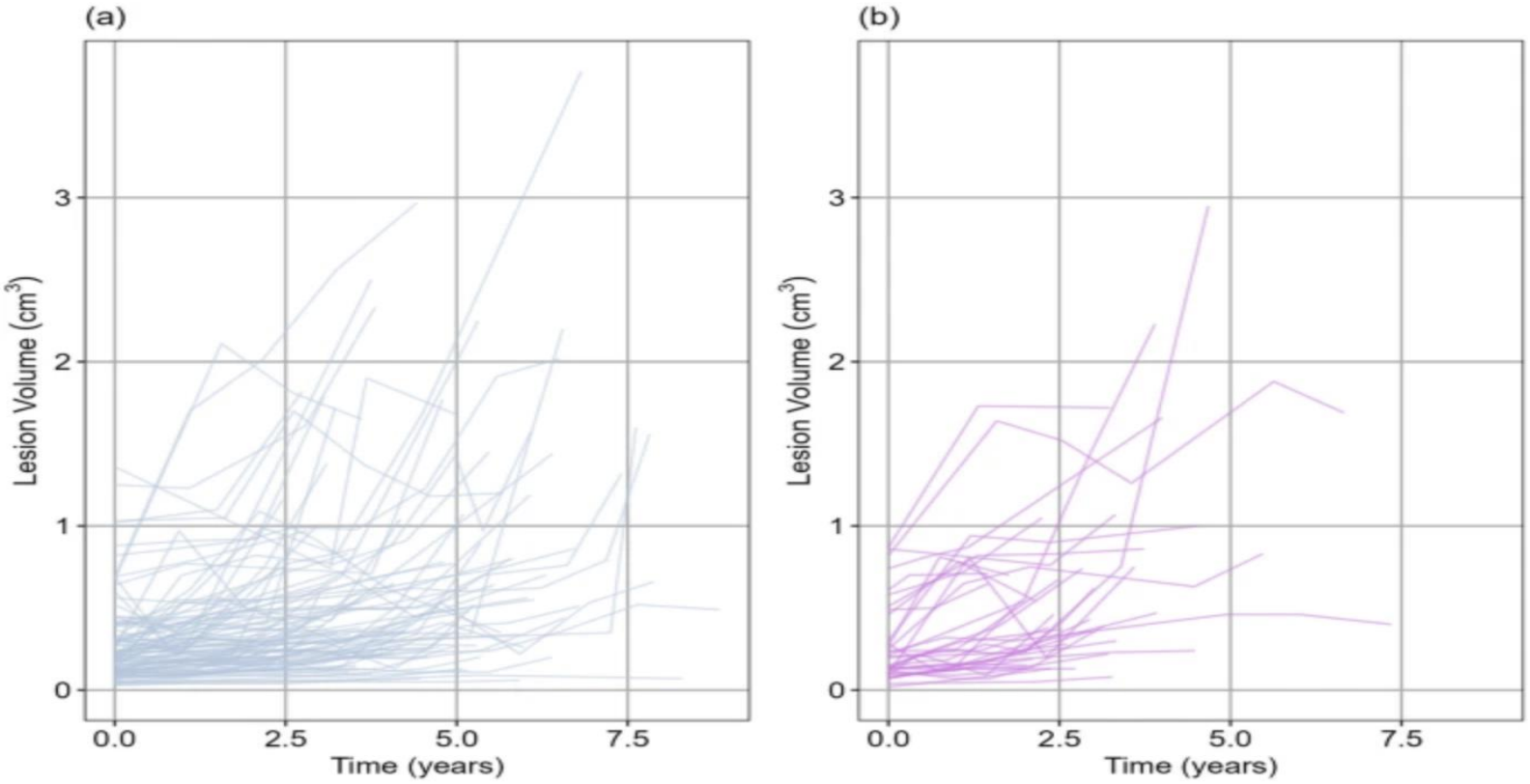


Natural history of prostate cancer evolution from single cell to detectable disease



Smith H *et al.* Eur Radiol 2026

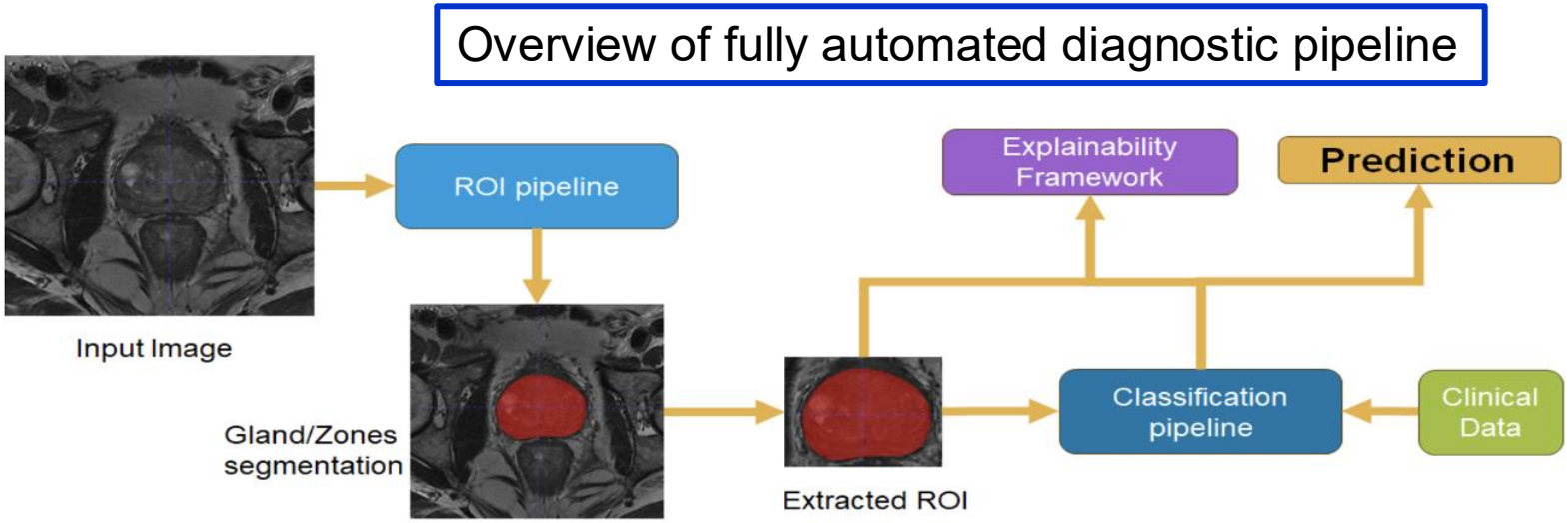
Growth rate, once established highly variable



Smith H *et al.* Eur Radiol 2026

Explainable Anatomy-Guided AI for Prostate MRI: Foundation Models and In Silico Clinical Trials for Virtual Biopsy-based Risk Assessment

Danial Khan[1, 6*], Zohaib Salahuddin[1*], Yumeng Zhang[1], Sheng Kuang[1], Shruti Atul Mali[1], Henry C. Woodruff[1, 2], Sina Amirrajab[1], Rachel Cavill[6], Eduardo Ibor-Crespo [3], Ana Jimenez-Pastor[3], Adrian Galiana- Bordera[4], Paula Jimenez Gomez[4], Luis Marti-Bonmati [4,5], Philippe Lambin [1, 2]



Khan, D *et al.* AI Model 2025

Summary

- Direction of travel is clear
- Technological advances are going to increase the opportunity to avoid biopsy in more patients
- More research is needed on the oncological harms associated with biopsy
- Clinical studies remain challenging