Innovation in Prostate Surgery Webinar

Improving patient outcomes through advances in surgical techniques, diagnostics and AI-powered decision support

21st May 2025

This webinar will be recorded

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Agenda

Agenda Items	Lead	Time
Chair welcome	**Mr Tom Leslie,** Consultant Urological Surgeon, Oxford University Hospitals NHS FT; Urology Clinical Advisory Group Lead, Thames Valley Cancer Alliance	**12:30 - 12:35**
Introduction to University of Oxford Prostate Cancer Research Programme	**Professor Freddie Hamdy** CBE, Professor of Surgery, Nuffield Department of Surgical Sciences, University of Oxford; Consultant Urological Surgeon	**12:35 – 12:45**
The TRANSLATE Trial	**Professor Richard Bryant,** Chief Investigator, TRANSLATE Associate Professor of Urology, University of Oxford Honorary Consultant Urologist, Oxford University Hospitals NHS FT	**12:45 – 13:00**
Mapping prostate cancer: insights from spatial transcriptomics and 3D imaging	**Dr Sandy Figiel,** Postdoctoral Research Scientist, Nuffield Department of Surgical Sciences, University of Oxford	**13:00 – 13:15**
The PART Trial	**Mr Tom Leslie,** PART Principle Investigator, Churchill Hospital, Oxford, Nuffield Department of Surgical Sciences, University of Oxford	**13:15 – 13:30**
Intraoperative molecular targeted fluorescence imaging and radical prostatectomy	**Mr Aaron Leiblich DPhil FRCS (Urol),** Consultant Urological Surgeon, Oxford University Hospitals	**13:30 – 13:45**
Q&A session	**Facilitated by Mr Tom Leslie and Professor Freddie Hamdy**	**13:45 – 13:55**
Chair summary	**Mr Tom Leslie**	**13:55 – 14:00**
End of Session		**14:00**

Introduction to University of Oxford Prostate Cancer Research Programme

Professor Freddie Hamdy CBE, Professor of Surgery, Nuffield Department of Surgical Sciences, University of Oxford; Consultant Urological Surgeon

The TRANSLATE Trial

Professor Richard Bryant, Chief Investigator TRANSLATE
Associate Professor of Urology, University of Oxford;
Honorary Consultant Urologist, Oxford University Hospitals NHS FT

TRANSLATE: Local anaesthetic transperineal biopsy versus transrectal prostate biopsy in prostate cancer detection a multicentre, randomised, controlled trial.

Richard Bryant
Chief Investigator, TRANSLATE

Associate Professor of Urology, University of Oxford
Honorary Consultant Urologist, Oxford University Hospitals NHS Foundation Trust

May 2025

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THE LANCET Oncology

Local anaesthetic transperineal biopsy versus transrectal prostate biopsy in prostate cancer detection (TRANSLATE): a multicentre, randomised, controlled trial

Richard J Bryant, Ioana R Marian, Roxanne Williams, J Francisco Lopez, Claudia Mercader, Mutie Raslan, Christopher Berridge, Jessica Whitburn, Teresa Campbell, Steve Tuck, Vicki S Barber, Jessica Scaife, Aimi Hewitt, Amy Taylor, Alexander Ooms, Filipa Landeiro, Matthew Little, Jane Wolstenholme, Sukanya Ghosh, John M Reynard, Freddie C Hamdy, Matthew P C Liew, Tom A Leslie, James W F Catto, Derek J Rosario, Altan Omer, Daniel W Good, Robert HR Gray, Sashi Kommu, Daniel Chung, Hannah Wells, Krishna Narahari, Ruth E Macpherson, Clare Verrill, Ben Eddy, Hide Yamamoto, Alastair D Lamb*, for the TRANSLATE Trial Study Group†*

Lancet Oncol 2025; published online first March 23. https://doi.org/10.1016/S1470-2045(25)00100-7

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Introduction

- Diagnostic prostate biopsies traditionally via transtrectal route (TRUS) under local anaesthetic (LA) with ultrasound guidance, after MRI.
- LA transperineal (LATP) biopsy in clinic is gaining popularity.
- 3 recent RCTs published in 2024:
  - ProBE-PC (Mian); n=763; 1º: 30-day infections; 9 (2.6%) TRUS vs 10 (2.7%) LATP, *p*=0.99
  - PREVENT (Hu); n=658; 1º: infection; 4 (1.4%) TRUS vs 0 LATP; *p*=0.059
  - PERFECT (Ploussard); n=270: 1º: Gleason grade group (GGG) ≥2; 47.2% LATP vs 54.2% TRUS; *p*=0.6235
- Uncertainty regarding cancer detection, infection, other complications, cost-effectiveness for LATP biopsy vs TRUS.
- TRANSLATE is an RCT comparing LATP vs TRUS prostate biopsy.

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Patients & Methods [1]

- 1,126 participants randomised 1:1 to LATP or TRUS biopsy
- 10 hospitals in the UK (in England, Scotland and Wales)
- Primary intention-to-treat (ITT) outcome:
  - Detection of GGG ≥2 prostate cancer.
    - 90% power to detect 10% uplift from 45% for TRUS [(1)] to 55% for LATP [(2)]; 2-sided α 0.05.

[(1)] Bryant 2019 THE JOURNAL of UROLOGY [(2)] Lopez 2021 BJUI BJU International

- Secondary outcomes:
  - Infection-related complications and/or related hospitalisation
  - Other complications (bleeding, urinary retention, pain)
  - Tolerability; patient-reported outcome measures – urinary (IPSS) & sexual (IIEF)
  - Health-related quality of life (EQ-5D)
  - Cost-effectiveness

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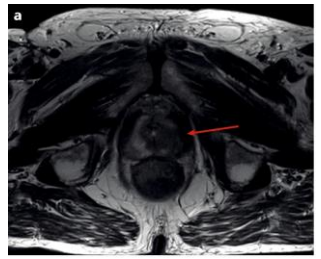
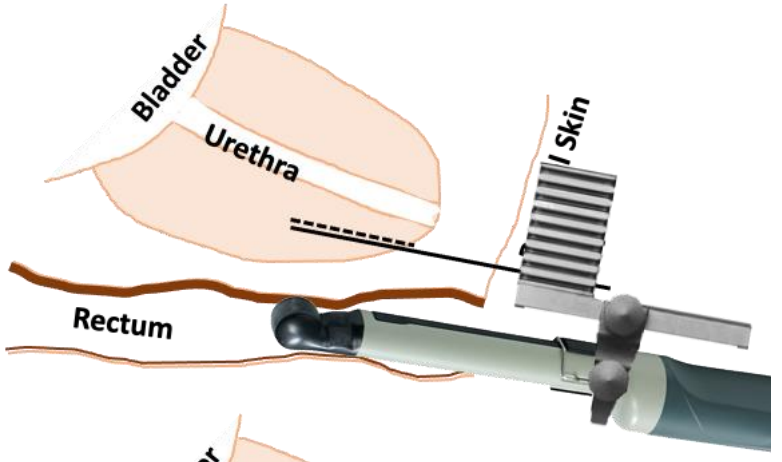
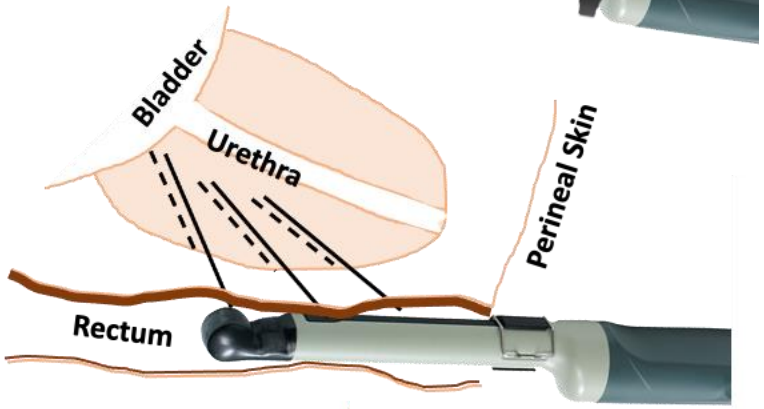
Patients & Methods [2]

- **Inclusion criteria**
  - Biopsy-naïve; ≥18 years; elevated PSA or abnormal DRE; pre-biopsy MRI.
- **Exclusion criteria**
  - Previous biopsy; PSA≥50 ng/ml; extensive disease on MRI.
  - Inability for either biopsy; current/recent UTI; enhanced antibiotic prophylaxis.
- **LATP biopsy**
  - Chlorhexidine-based skin prep; no antibiotics.
  - $\bar{x}$ 12 systematic biopsies (6 sectors); 3-5 ($\bar{x}$ 4) cognitive target biopsies.
- **TRUS biopsy**
  - Pre- and post-biopsy antibiotics.
  - $\bar{x}$ 12 systematic biopsies (6 per side); 3-5 ($\bar{x}$ 4) cognitive target biopsies.
- **Patient-reported outcome measures**
  - Post-procedure (ProBE questionnaire); 7 & 35 days; 4 months.



Nat Rev Urol 2020;17(1):41-61





Results [1]: Baseline demographics

	LATP (n=562)		TRUS (n=564)		Total (n=1126)	
White British Ethnicity	527	93.8%	517	91.7%	1044	92.7%
Charlson Comorbidity Index Score	559	2 (2, 3); 2.4 (1.3)	557	2 (2, 3); 2.5 (1.4)	1116	2 (2, 3); 2.5 (1.3)
Anticoagulants	27	4.8%	28	5.0%	55	4.9%
Finasteride	14	2.5%	13	2.3%	27	2.4%
PSA (ng/ml)	561	7 (5, 10); 8.8 (7.5)	559	7 (5, 10); 8.8 (6.8)	1120	7 (5, 10); 8.8 (7.1)
Age (years)	562	66 (60, 72); 66.1 (8.1)	564	66 (61, 71); 66 (7.3)	1126	66 (61, 72); 66.1 (7.7)
IIEF (Domain A)	531	19 (3, 29)	530	18 (4, 28)	1061	19 (4, 29)
I-PSS	468	7 (3, 13)	461	7 (3, 13)	929	7 (3, 13)
DRE result pre-biopsy						
Benign	249	44.4%	289	51.7%	538	48.0%
Suspicious	148	26.4%	119	21.3%	267	23.8%

Numbers: n (%)
n, median (IQR), mean (SD)
n, median (IQR)

- 97% of participants accepted their allocated biopsy
- Equal $\bar{x}$ systematic & cognitive target biopsy core numbers between LATP & TRUS biopsy

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Results [2]: Primary Outcome

	LATP (n=562)		TRUS (n=564)		Adjusted Odds Ratio (95% CI)	*p*-value
Primary Outcome						
Gleason Grade Group ≥2 prostate cancer detection						
Intention-to-treat Population	**329**/547	**60.1%**	**294**/540	**54.4%**	**1.32 (1.03, 1.7)**	**0.031**
Per-protocol Population	**323**/539	**60.3%**	**273**/509	**53.6%**	**1.38 (1.06, 1.78)**	**0.016**

5.7% ↑ detection GGG ≥2 disease for LATP vs TRUS biopsy, ITT analysis, $p = 0.031$

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Results [3]: Infection

	LATP (n=562)		TRUS (n=564)		Adjusted Odds Ratio (95% CI)
Infection Rate					
Primary definition (infection causing hospitalisation)					
Overall	6	1.1%	13	2.3%	0.45 (0.17, 1.20)
By 7 days	1	0.2%	7	1.2%	0.14 (0.02, 1.15)
By 35 days	2	0.4%	9	1.6%	0.22 (0.05, 1.01)
By 4 months	6	1.1%	13	2.3%	0.45 (0.17, 1.20)
Secondary definition (symptoms and signs +/- hospitalisation)					
Overall	113	20.1%	120	21.3%	0.93 (0.7, 1.25)
By 7 days	54	9.6%	72	12.8%	0.73 (0.5, 1.06)
By 35 days	85	15.1%	102	18.1%	0.81 (0.59, 1.11)
By 4 months	113	20.1%	120	21.3%	0.93 (0.7, 1.25)

- Fewer infection-related events for LATP vs TRUS biopsy (not statistically significant)
- 88% of LATP biopsies performed without antibiotics

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Results [4]: Other Secondary Outcomes

Other complications / PROMs / Quality of life / Alternative pathology

	LATP (n=562)		TRUS (n=564)		Odds Ratio (95% CI)
Reported biopsy to be painful or embarrassing	**216**	**38.4%**	**153**	**27.1%**	1.84 (1.4, 2.43)
Procedure-related symptoms 7 days after biopsy	**99**	**17.6%**	**140**	**24.8%**	0.59 (0.44, 0.80)
IPSS (at 7 days)	479	8.0 (4, 14)	448	7.0 (3, 13)	0.41 (-0.30, 1.13)
IIEF (Domain A) (at 7 days)	464	4.0 (3, 12)	437	4.0 (3, 13)	0.21 (-0.90, 1.32)
One or more biopsy-related complication (by 4 months)	454	80.8%	436	77.3%	1.23 (0.93, 1.65)
Urinary retention requiring catheter (by 4 months)	35	6.2%	27	4.8%	
Visible blood in bowel movements (by 4 months)	62	11.0%	174	30.9%	
Urology admission due to haematuria (by 4 months)	0	0%	0	0%	
Urology admission due to pain (by 4 months)	1	0.2%	2	0.4%	
Procedure time (minutes)	553	12 (10, 15)	508	8 (6, 10)	
Gleason Grade Group ≥3 prostate cancer detection	123	21.9%	129	22.9%	0.93 (0.70, 1.24)

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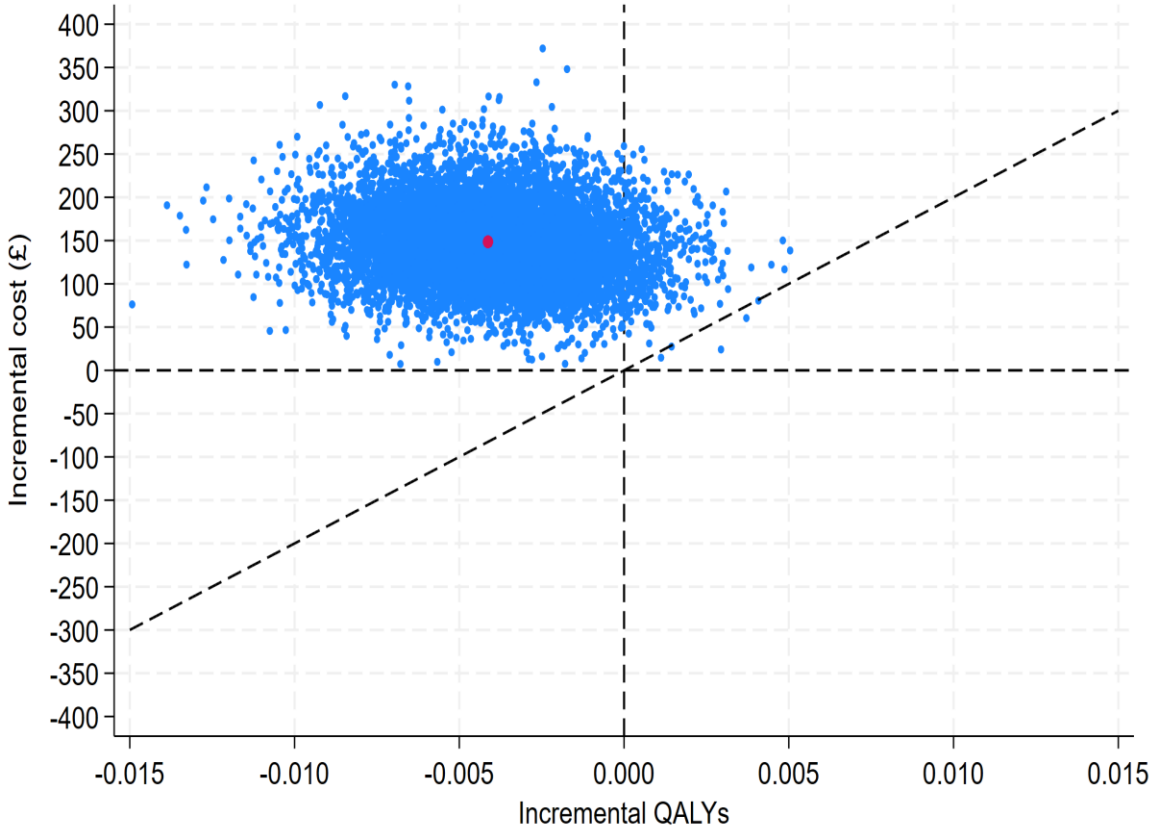
Results [5]: Health Economics

Cost-effectiveness (unpublished preliminary data)

- Cumulative total mean costs £1064 in the LATP arm versus £915 in the TRUS arm
  - **Adjusted mean difference: £149**
  - 95% CI £61 to £236, *p* = 0.001
- Cumulative total mean QALYs 0.282 in the LATP arm versus 0.284 in the TRUS arm
  - **Adjusted mean difference: -0.004**
  - 95% CI -0.009 to 0.001, *p* = 0.098
- **At 4 months post biopsy, LATP dominated**
  - **0.1% probability of LATP being cost-effective, assuming a cost-effectiveness threshold of £20,000**



- Top & left = cost-effectiveness ratio > £20,000 per QALY gained
- Below & right = cost-effectiveness < £20,000 per QALY gained

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Conclusions

- LATP biopsy compared against TRUS biopsy results in:
  - Greater detection of GGG≥2 prostate cancer
  - No difference in detection of GGG≥3 prostate cancer
  - Fewer infection-related complications
  - Higher immediate post-procedure pain and embarrassment
  - Fewer procedure-related symptoms beyond 7 days
- LATP biopsy takes longer to perform than TRUS biopsy (procedure, & clinic time)
- LATP biopsy has 0.1% probability of being cost-effective versus TRUS biopsy in the first 4 months post-procedure in the NHS setting (preliminary data)
- TRANSLATE provides the evidence necessary when considering trade-offs and deciding which biopsy to adopt

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Acknowledgements

Oxford: Richard J Bryant, Alastair D Lamb, Tom A Leslie, Ioana R Marian, Roxanne Williams, J Francisco Lopez, Claudia Mercader, Mutie Raslan, Teresa Campbell, Vicki S Barber, Jessica Scaife, Aimi Hewitt, Amy Taylor, Alexander Ooms, Filipa Landeiro, Matthew Little, Jane Wolstenholme, John M Reynard, Freddie C Hamdy, Ruth E Macpherson, Clare Verrill

Maidstone: Sukanya Ghosh, Hide Yamamoto

Canterbury: Ben Eddy, Sashi Kommu

Cardiff: Daniel Chung, Hannah Wells, Krishna Narahari

Coventry: Christopher Berridge, Altan Omer

High Wycombe: Jessica Whitburn, Robert HR Gray

Milton Keynes: Tom A Leslie

Sheffield: Derek J Rosario, James W F Catto

Wigan: Matthew P C Liew

Edinburgh: Daniel W Good

PPI Lead: Steve Tuck, for the TRANSLATE Trial Study Group.

Our 1126 participants

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THE LANCET Oncology

TRANSLATE

SITU SURGICAL INTERVENTION TRIALS UNIT

OCTRU Oxford Clinical Trials Research Unit

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@TranslateTrial

Local anaesthetic transperineal biopsy versus transrectal prostate biopsy in prostate cancer detection (TRANSLATE): a multicentre, randomised, controlled trial

Richard J Bryant, Ioana R Marian, Roxanne Williams, J Francisco Lopez, Claudia Mercader, Mutie Raslan, Christopher Berridge, Jessica Whitburn, Teresa Campbell, Steve Tuck, Vicki S Barber, Jessica Scaife, Aimi Hewitt, Amy Taylor, Alexander Ooms, Filipa Landeiro, Matthew Little, Jane Wolstenholme, Sukanya Ghosh, John M Reynard, Freddie C Hamdy, Matthew P C Liew, Tom A Leslie, James W F Catto, Derek J Rosario, Altan Omer, Daniel W Good, Robert HR Gray, Sashi Kommu, Daniel Chung, Hannah Wells, Krishna Narahari, Ruth E Macpherson, Clare Verrill, Ben Eddy, Hide Yamamoto, Alastair D Lamb*, for the TRANSLATE Trial Study Group*

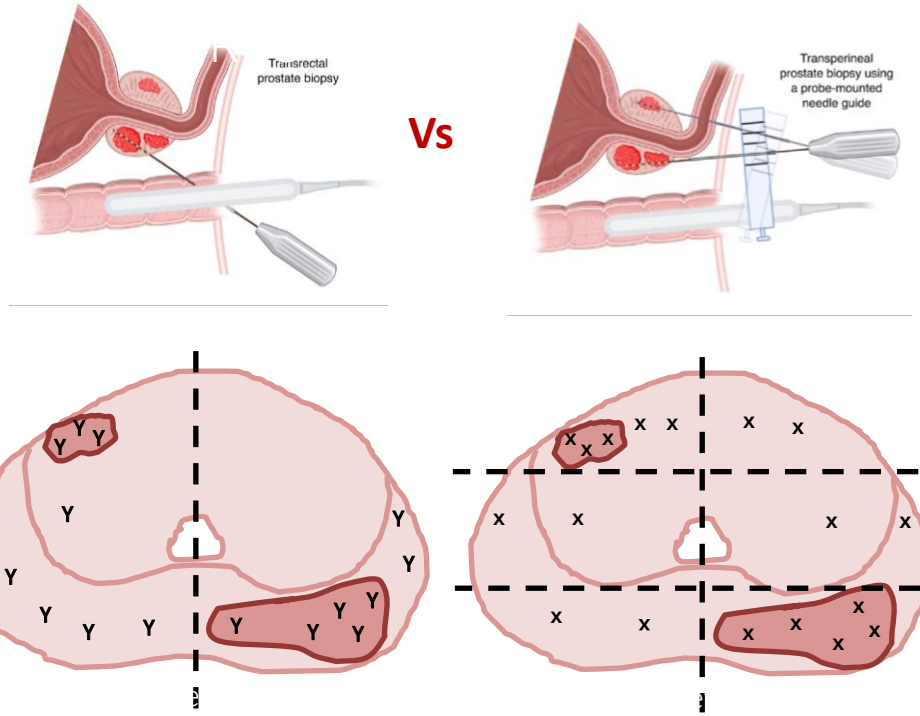
Outcomes:

- **1º detection GGG≥2: LATP 60.1%, TRUS 54.4% (ITT)**
- 2º infection (hospitalⁿ@7d): LATP 1 (0.2%), TRUS 7 (1.2%)
- 2º retention: LATP 35 (6.2%), TRUS 27 (4.8%)
- 2º histology GGG≥3: no difference
- 2º PROMS: LATP more immediately painful / embarrassing
- 2º PROMS: TRUS more symptoms >7d (bowel, haem, pain)
- 2º Health Econ: LATP takes longer, <1% chance cost-effective

Design:

- n = 1126 pts
- All with MRI, & biopsy naïve
- 1:1 RCT, ITT, LATP vs TRUS
- Equal biopsy core number
- 10 UK centres
- 2021 - 2024

- Abx - TRUS: local SOC
  - LATP: 88% without



Conclusion:

LATP 5.7% ↑ GGG≥2 (OR 1.32; *p*=0.031)

Limitations:

- 93% White British
- Fewer systematic LATP cores than 'normal' Ginsburg protocol
- Clinical significance of 5.7% uplift in GGG≥2 unknown
- Health Economics specific to NHS

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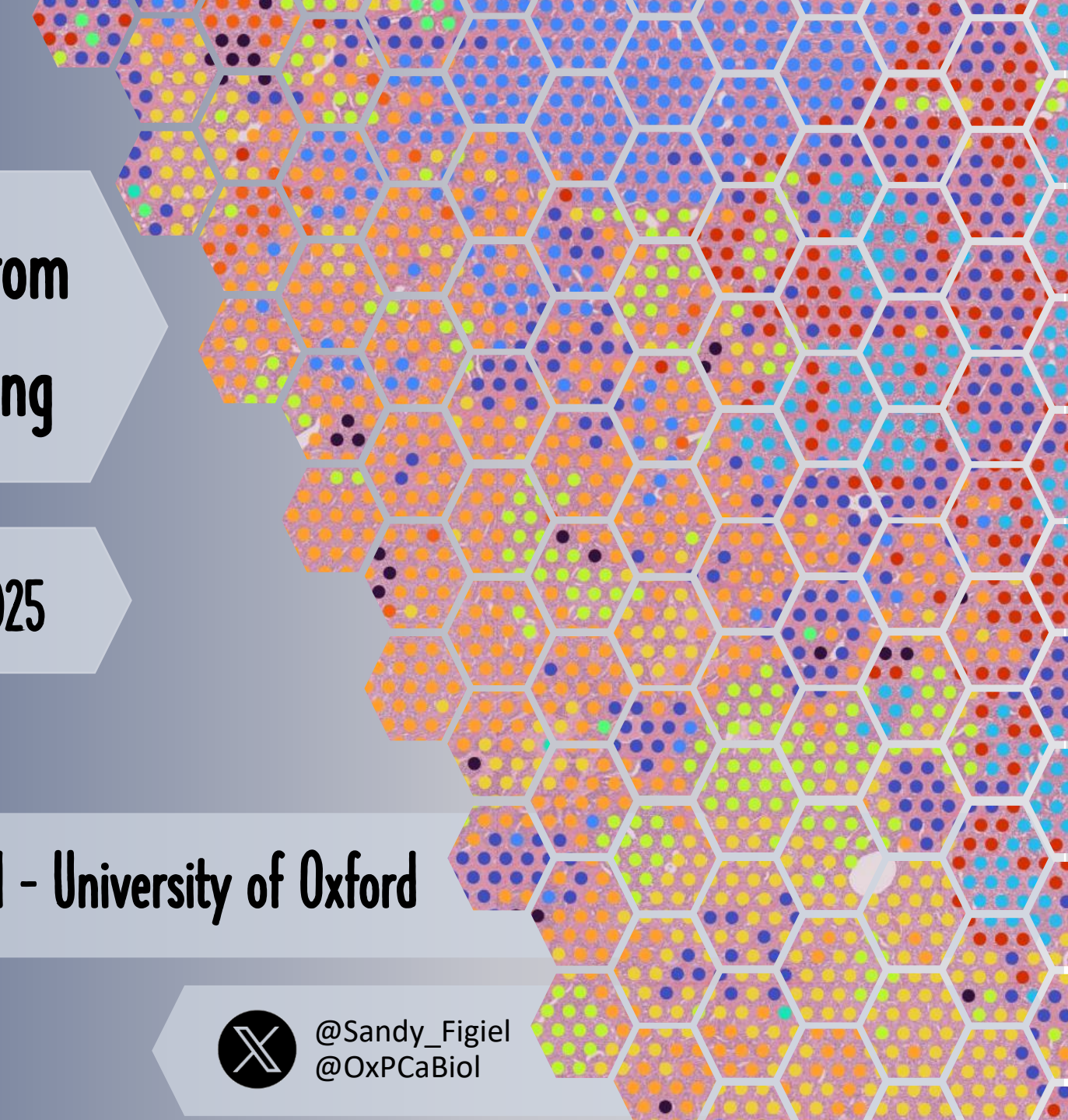
Mapping prostate cancer: insights from spatial transcriptomics and 3D imaging

Dr Sandy Figiel, Postdoctoral Research Scientist, Nuffield Department of Surgical Sciences, University of Oxford

Mapping prostate cancer : insights from spatial transcriptomics and 3D imaging

Innovation in Prostate Surgery Webinar - May 2025



Sandy Figiel - University of Oxford

@Sandy_Figiel
@OxPCaBiol

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Background

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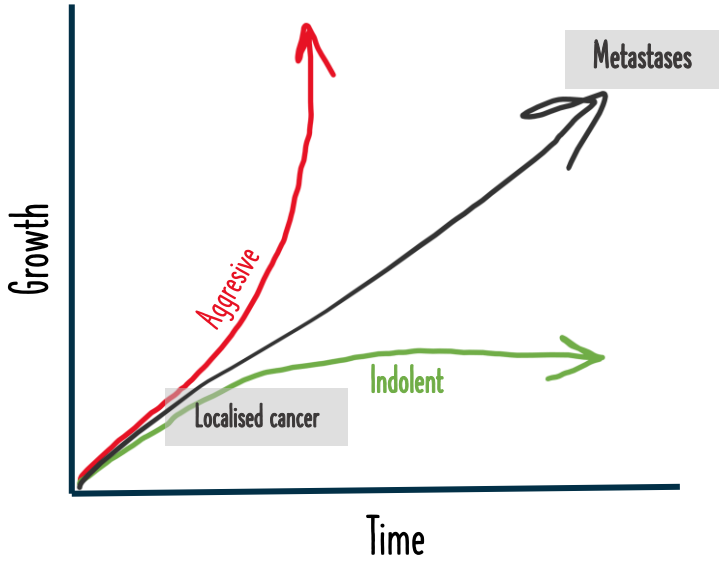
- Prostate cancer is heterogeneous
- Disease progression is unpredictable.

Why do some cancers become aggressive and spread, while others remain indolent?



Tumour heterogeneity

Role of the tumour microenvironment

Spatial omics

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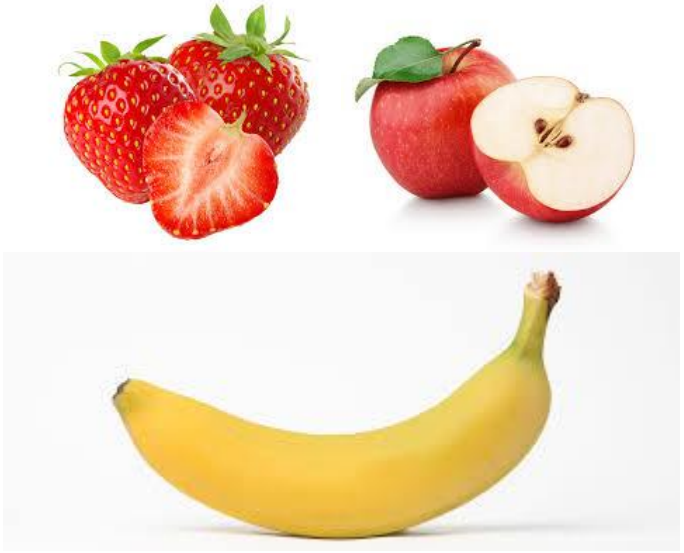
Bulk

Single cell



Spatial

Spatial omics

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EUROPEAN UROLOGY xxx (xxxx) xxx–xxx

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

European Association of Urology

Rapid Review

Clinical Implications of Basic Research: Exploring the Transformative Potential of Spatial 'Omics in Uro-oncology

Sandy Figiel [a], Anthony Bates [b], David A. Braun [c], Renu Eapen [d], Markus Eckstein [e], Brandon J. Manley [f], Matthew I. Milowsky [g], Tom J. Mitchell [h], Richard J. Bryant [a,b], John P. Sfakianos [i], Alastair D. Lamb [a,b,]*

[a] *Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK;* [b] *Department of Urology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK;* [c] *Center of Molecular and Cellular Oncology, Yale Cancer Center, Yale School of Medicine, New Haven, CT, USA;* [d] *Department of Genitourinary Oncology & Division of Cancer Surgery, Peter MacCallum Cancer Centre, The University of Melbourne, Victoria, Australia;* [e] *Institute of Pathology, University Hospital Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg & Bavarian Cancer Research Center (BZKF), Erlangen, Germany;* [f] *Department of Genitourinary Oncology, H. Lee Moffitt Cancer Center, Tampa, FL, USA;* [g] *Department of Medicine, University of North Carolina, Chapel Hill, NC, USA;* [h] *Early Detection Centre, University of Cambridge, Cambridge, UK;* [i] *Department of Urology, Ichan School of Medicine at the Mount Sinai Hospital, New York, NY, USA*

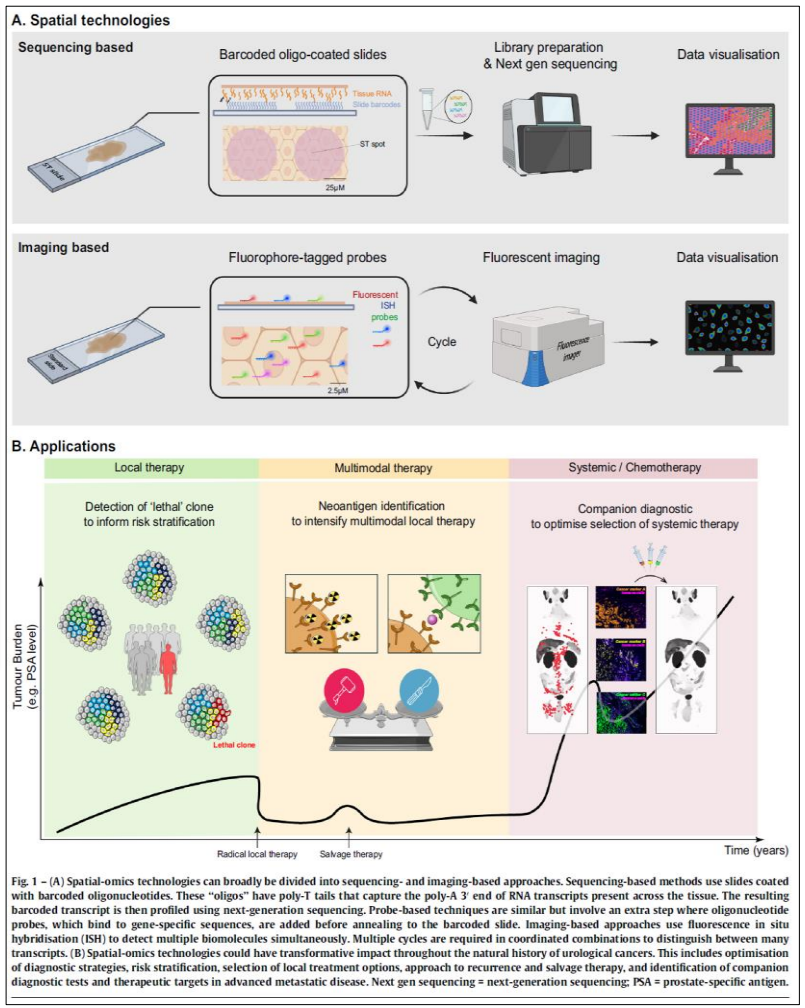

Fig. 1 – (A) Spatial-omics technologies can broadly be divided into sequencing- and imaging-based approaches. Sequencing-based methods use slides coated with barcoded oligonucleotides. These "oligos" have poly-T tails that capture the poly-A 3′ end of RNA transcripts present across the tissue. The resulting barcoded transcript is then profiled using next-generation sequencing. Probe-based techniques are similar but involve an extra step where oligonucleotide probes, which bind to gene-specific sequences, are added before annealing to the barcoded slide. Imaging-based approaches use fluorescence in situ hybridisation (ISH) to detect multiple biomolecules simultaneously. Multiple cycles are required in coordinated combinations to distinguish between many transcripts. (B) Spatial-omics technologies could have transformative impact throughout the natural history of urological cancers. This includes optimisation of diagnostic strategies, risk stratification, selection of local treatment options, approach to recurrence and salvage therapy, and identification of companion diagnostic tests and therapeutic targets in advanced metastatic disease. Next gen sequencing = next-generation sequencing; PSA = prostate-specific antigen.

Table 1 – An overview of spatial-omics methods and platforms

Platform	Omics type	Method	Sample	Resolution	Coverage	Cost*	Pros	Cons	Ref
Visium, 10X genomics	RNA	Sequenced-based, probe-based	FF, FFPE	FF/FFPE: 55 µm HD: 8 µm	18 000 +	+++	+ Whole transcriptome + Little specialised equipment required + High number of reads per ROI	- Requires careful sample preparation - Limited sensitivity for low-abundance transcripts - Data storage & bioinformatics needs	[35]
Slide-seq/Slide-seq V2	RNA	Sequenced-based	FF, FFPE	10 µm	18 000 +	+	+ Whole transcriptome	- Low RNA capture efficiency - Low number of reads per ROI	[36]
Xenium, 10X genomics	RNA	Image-based	FF, FFPE	Subcellular	100	+++	+ High sensitivity + Lower false discovery rate (FDR)	- Limited number of genes profiled - Requires specialised equipment - Relatively low throughput compared to sequencing-only approaches	[37]
GeoMx DSP, NanoString Technologies	RNA, protein	Probe-based	FF, FFPE	10 µm	18 000 +	++	+ Whole transcriptome + Protein co-detection	- Need to select region of interest - Requires specialised equipment - Low number of reads per ROI	[38,39]
MERSCOPE, Vizgen	RNA, protein	Image-based	FF, FFPE	Subcellular	1 000	++	+ High RNA capture efficiency + Protein co-detection	- Limited number of genes profiled - Requires specialised equipment - Low signal-to-background ratio	[40]
CosMx SMI, NanoString Technologies	RNA, protein	Image-based	FF, FFPE	Subcellular	600 / 6K	+++	+ Number of genes assayed compared to others image-based technology + Protein co-detection	- Workflow requires multiple data processing steps and a specialised equipment - Lack of field of view stitching - Bioinformatics needs (CoxMx 6K)	[41]
Phenocycler, Akoya Biosciences	Protein	Image-based	FF, FFPE	Single cell	100	+++	+ Faster imaging, shorter cycles	- Custom modification of each antibody and extensive optimisation. - Requires specialised instrument	[42]
Cell DIVE, Leica Microsystems	Protein	Image-based	FF, FFPE	Single cell	21	+	+ Use of a commercially available antibody	- Slower cycles - Requires specialised instrument	[43]
IMC & MIBI	Protein, metabolites	Image-based, MCI	FF, FFPE	1 µm for IMC 300 nm for MIBI	50	+++	+ Metabolites detection + Higher resolution, higher sensitivity compared to MSI	-Heavy instrumentation	[44,45]
MSI	Protein, metabolites	Image-based, MSI	FF, FFPE	10 µm	2 000	+++	+ Quantitative antibody-free approach + Metabolites detection + Greater coverage compared to MCI	- Decreased sensitivity for protein > 15 kDa - Heavy instrumentation - Non standardised workflow	[46]

DSP = digital spatial profiler; FF = freshly frozen; FFPE = formalin-fixed paraffin embedded; HD = high definition; IMC = imaging mass cytometry; MCI = mass cytometry imaging; MIBI = multiplexed ion beam imaging; MSI = mass spectrometry imaging; Ref = reference; ROI = region of interest; SMI = spatial molecular imager.
* Cost range: + = < £100; ++ = £100-£1000 +++ = >£1000 per sample

Figiel et al & Lamb, Eur Urol 2024

EUROPEAN UROLOGY

Tumour heterogeneity

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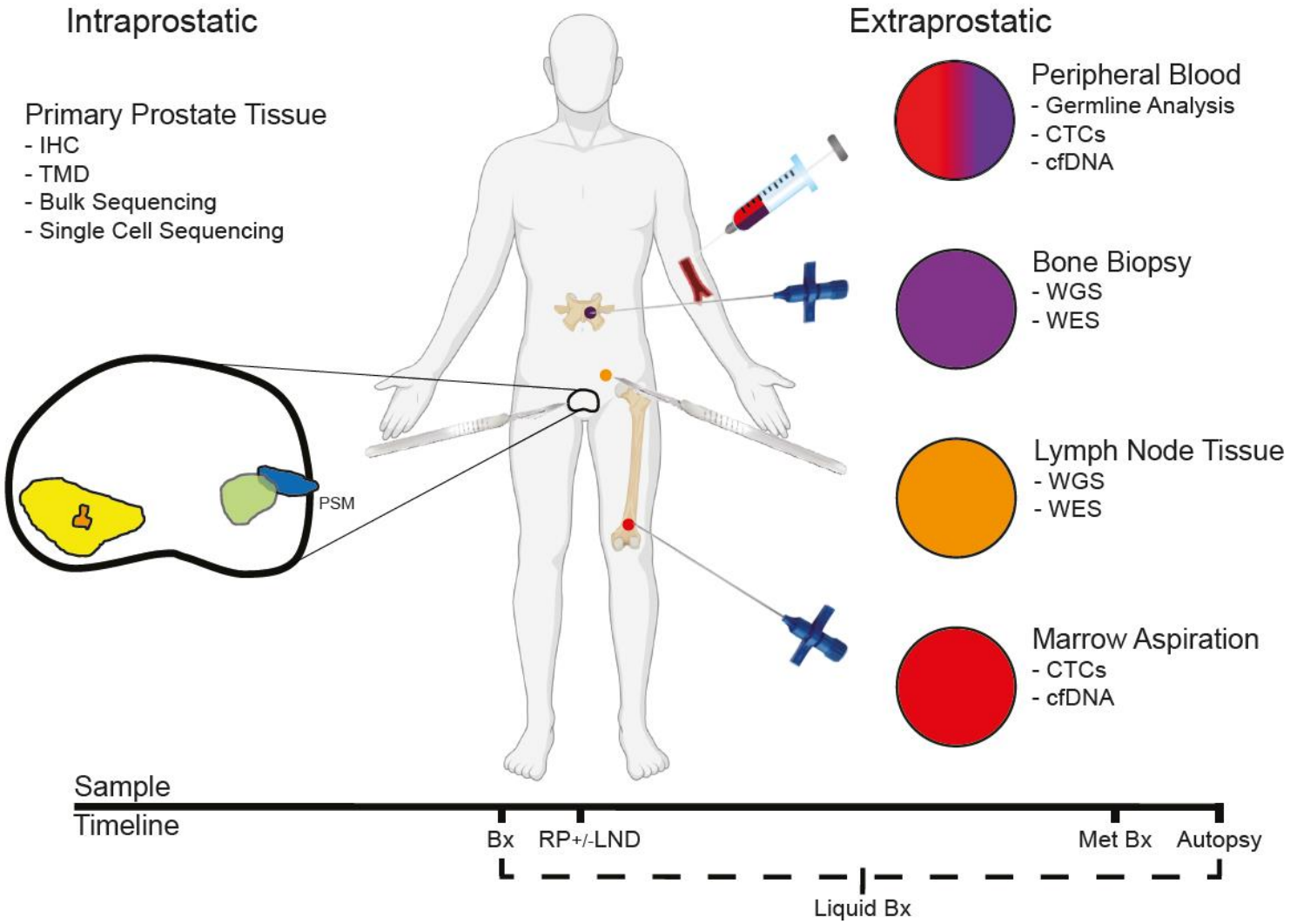

Erickson et al, EU Oncol 2021

Rapid Review – Prostate Cancer

A Systematic Review of Prostate Cancer Heterogeneity: Understanding the Clonal Ancestry of Multifocal Disease

Andrew Erickson[a], Alicia Hayes[a,g], Timothy Rajakumar[a], Clare Verill[a,c,d,g], Richard J. Bryant[a,e,g], Freddie C. Hamdy[a,e,g], David C. Wedge[f], Dan J. Woodcock[a,b], Ian G. Mills[a,g], Alastair D. Lamb[a,e,g,]*

Tumour heterogeneity

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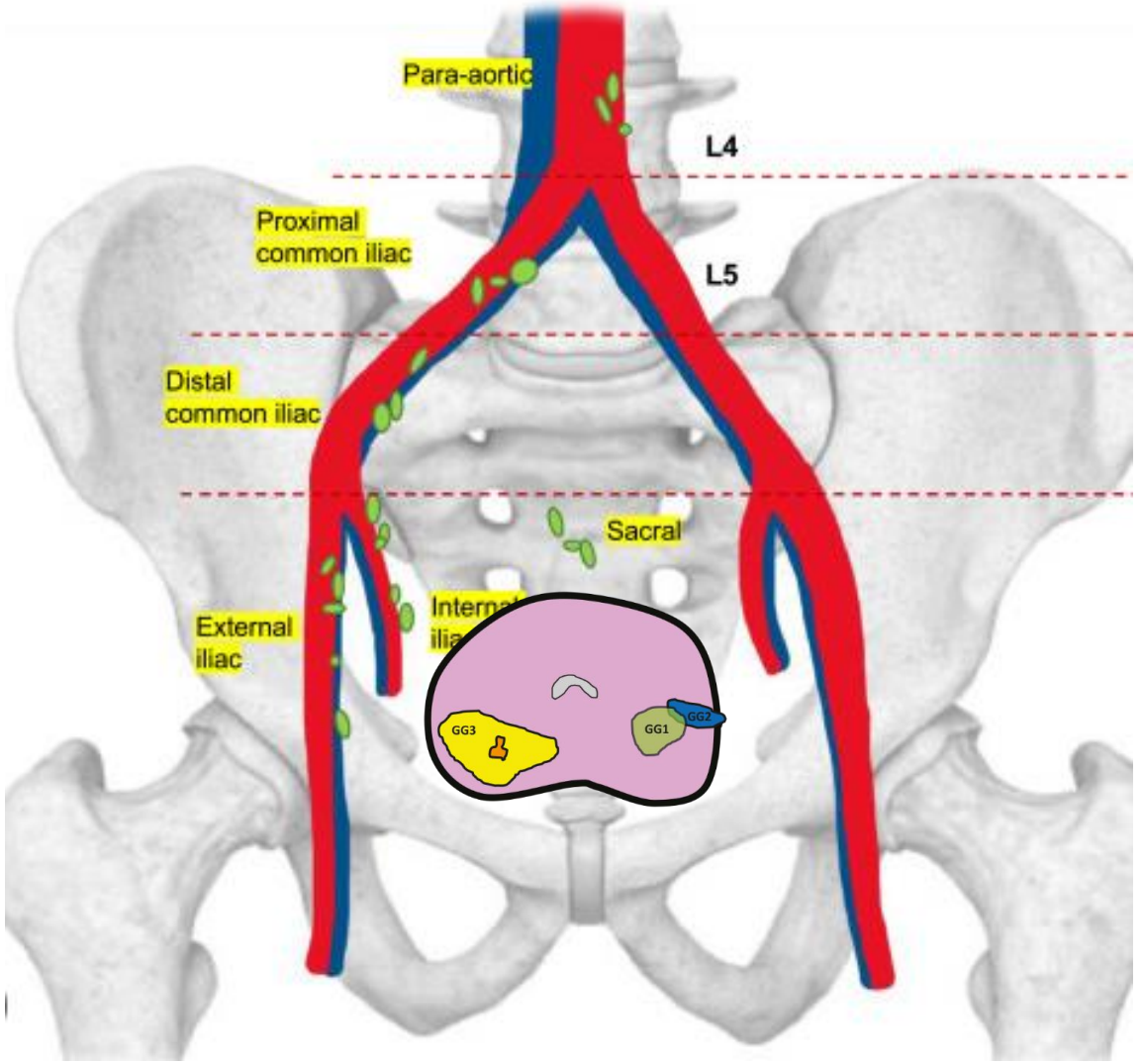

Hunting the lethal clone

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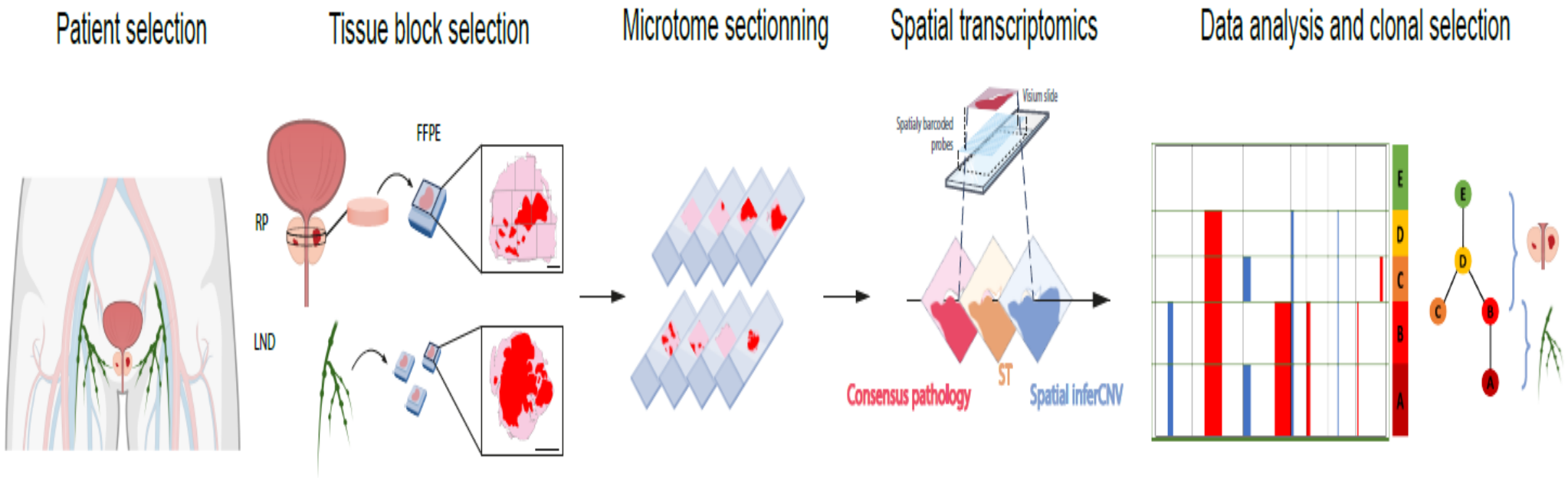
Spatial transcriptomics → define clonal heterogeneity


Alastair Lamb — Joakim Lundeberg

S.P.A.C.E. — SciLifeLab



Hunting the lethal clone

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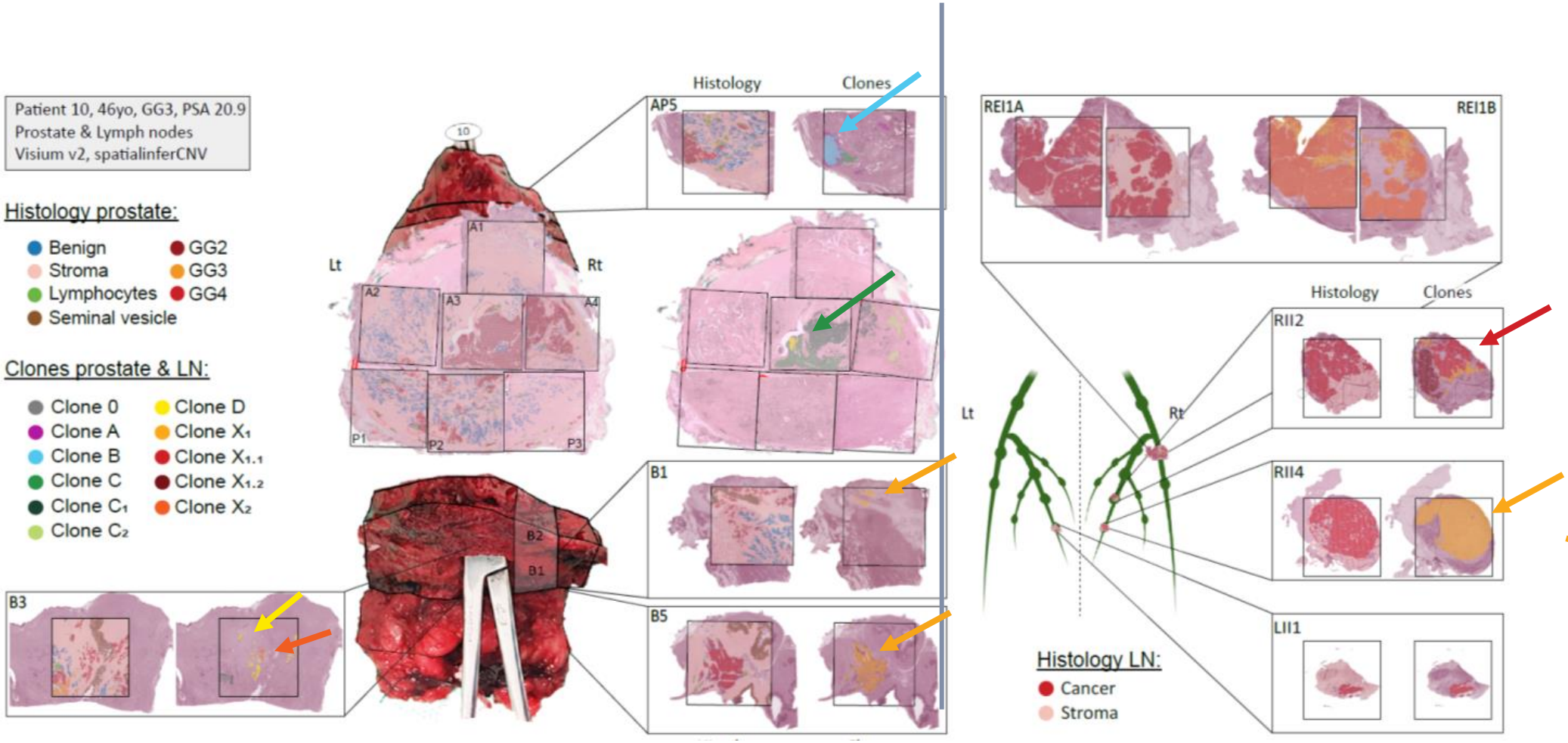
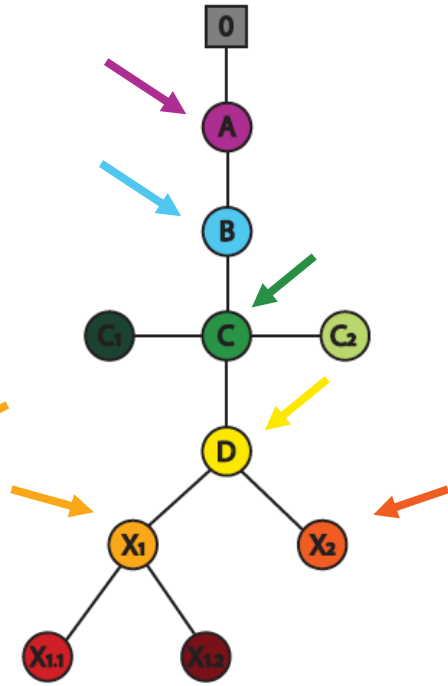


Clone tree



Investigating the tumour microenvironment

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Does the stromal profile differ based on disease severity?

Investigating the stroma around distinct tumour clones:

- Radial distance analysis - stroma changes with distance from the tumour
- Cell-cell communication analysis
- Spatial immune profiling to map the immune landscape

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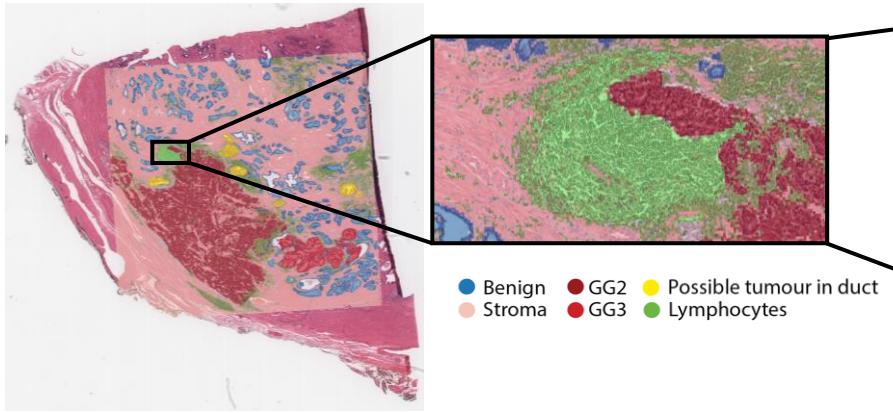
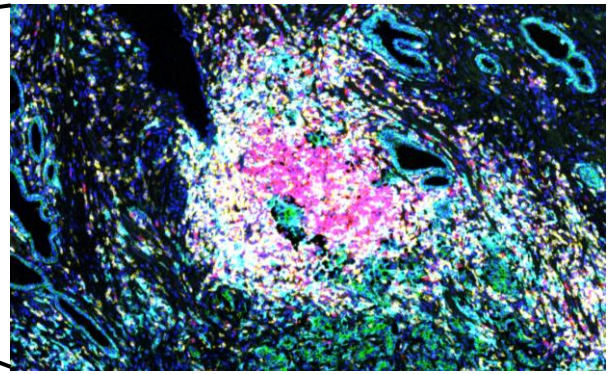
Visium HD (resolution 8 µm)



Multiplex imaging - spatial proteomics



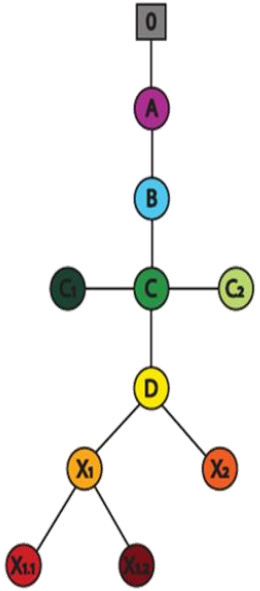
Karl Smith-Byrne

OXFORD POPULATION HEALTH CEU

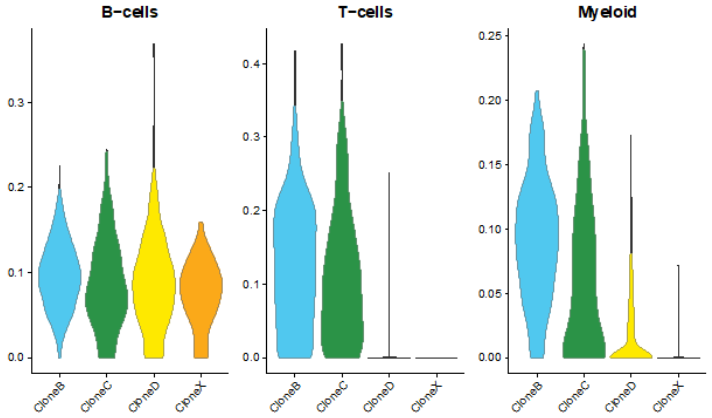
SciLifeLab

Charlotte Stadler

Investigating the tumour microenvironment

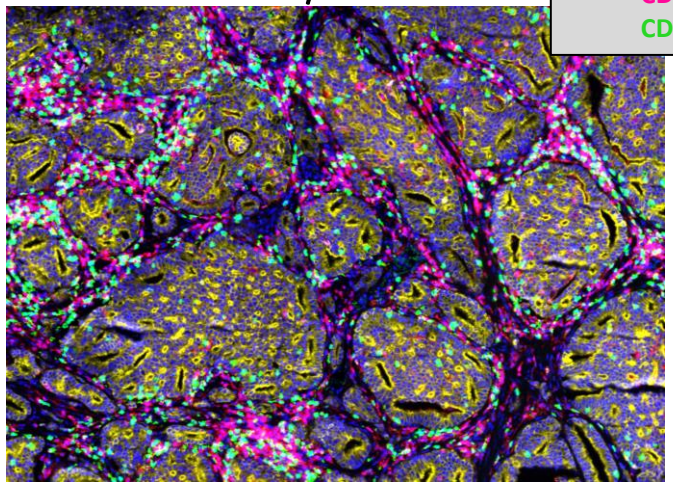


Immune cell proportions of clone border spots

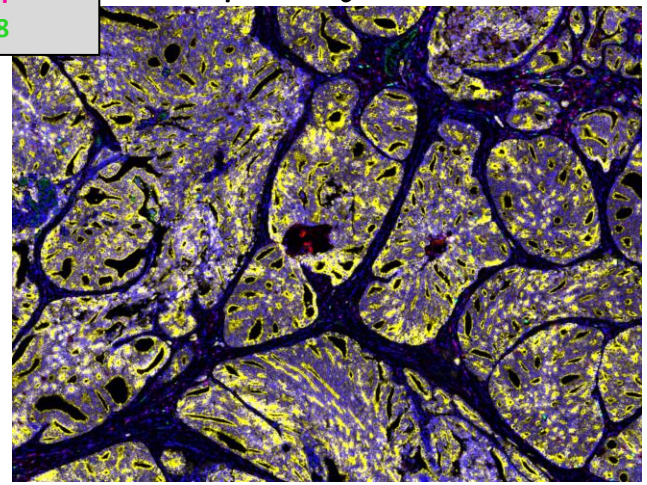


DAPI
Keratin 8/18
CD4
CD8

Early clone



Spreading clone



Generation of 3D images

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Generation of 3D images

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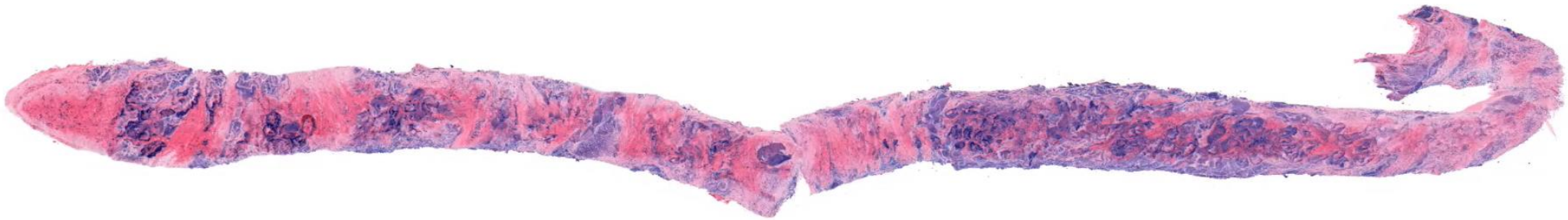
Freddie Hamdy


Ian Mills


Jens Rittscher

Open-top light-sheet (OTLS) microscopy



A.K. Glaser, et al., *Nature Biomedical Engineering* (2017)

Background

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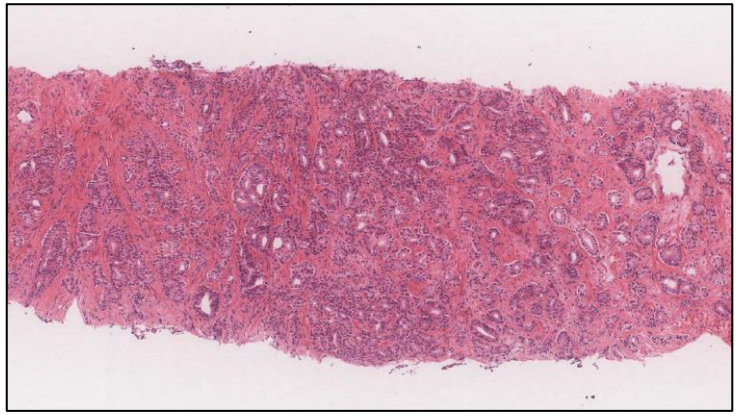
Nuclear features as prognostic indicators *have only been examined in 2D*



2D imaging

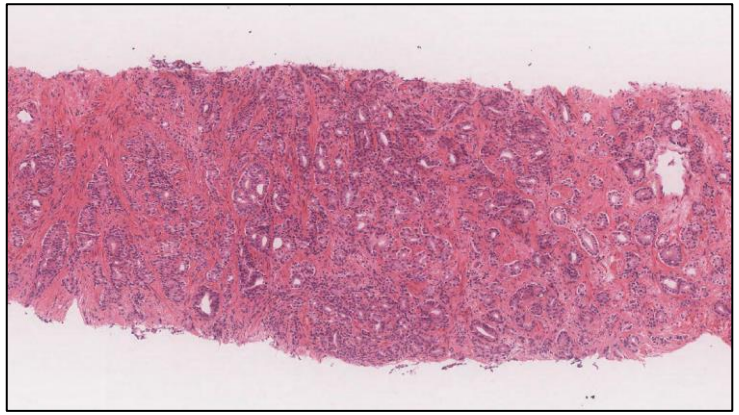
Simplicity
Established methods
Quick analysis & comparison

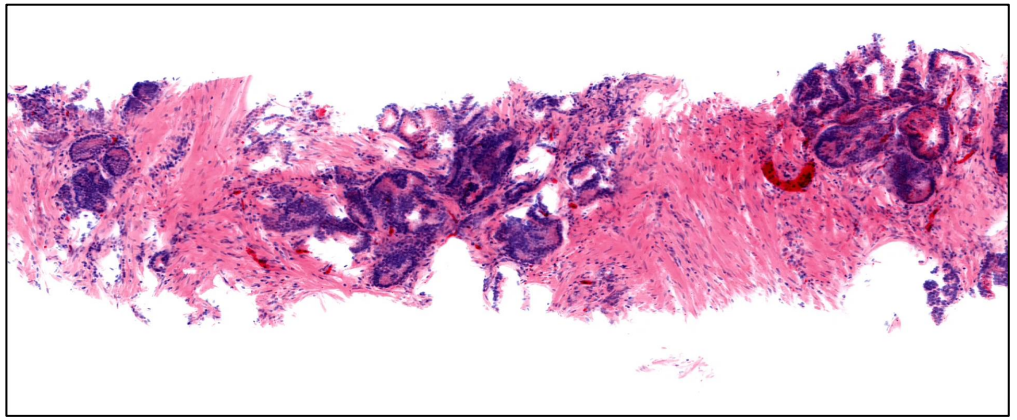
Sampling bias
Limited information

Background

NUFFIELD DEPARTMENT OF SURGICAL SCIENCES

Nuclear features as prognostic indicators *have only been examined in 2D*





2D imaging

Simplicity
Established methods
Quick analysis & comparison

Sampling bias
Limited information

3D imaging

Comprehensive sampling
Quantify cell morphology & context
Detection of rare events

No established tools and workflows
Longer processing time

AK Glaser et al., Nat. Biomed. Eng., 2017

Background

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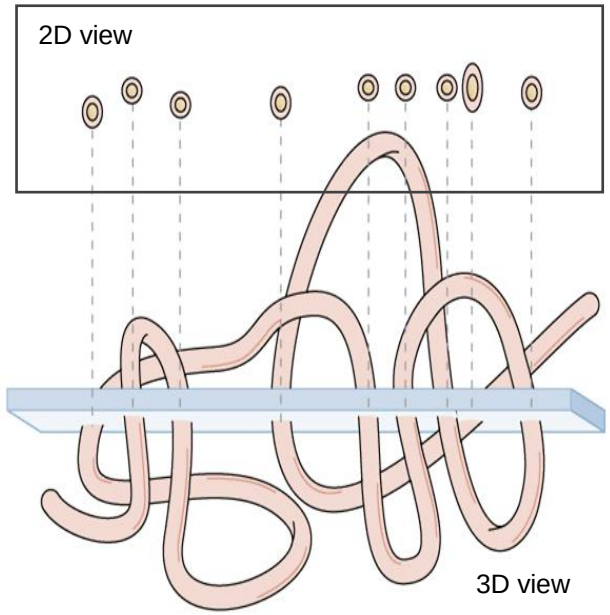
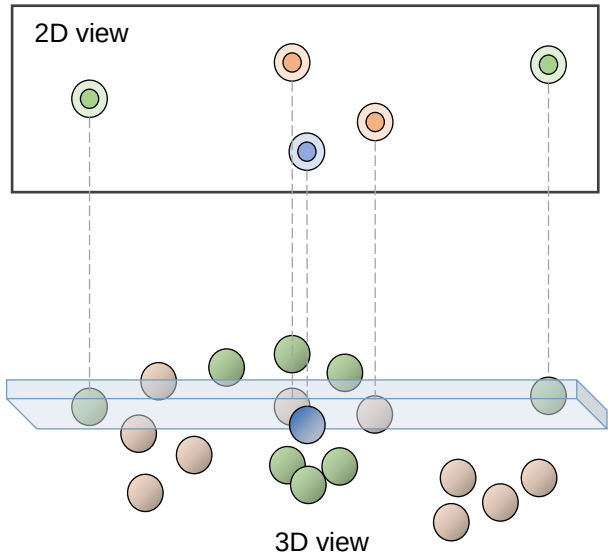
Convoluted structures



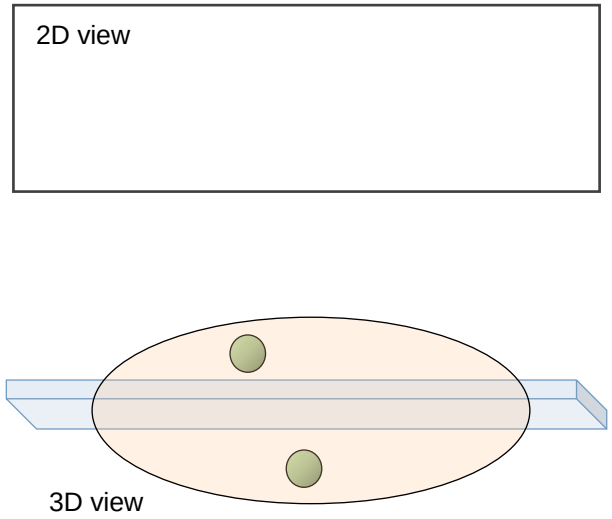
3D imaging of the prostate glandular network for prognostication

Complex distributions



Quantification of the tumor-immune microenvironment for predicting response to immunotherapies

Sparse / rare objects



Quantification of lympho-vascular invasion for prognostication and treatment stratification

JTC Liu et al., *Nat. Biomed. Eng*., 2021

Background

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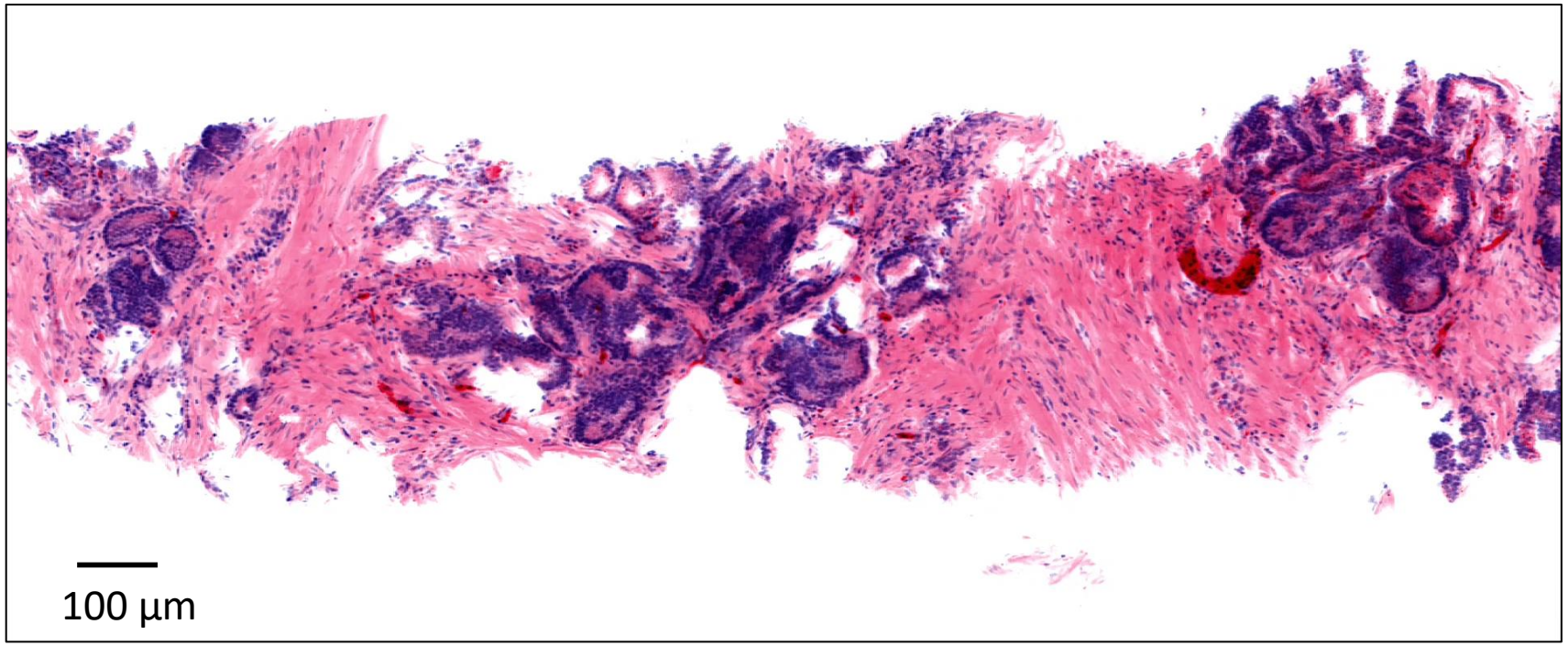
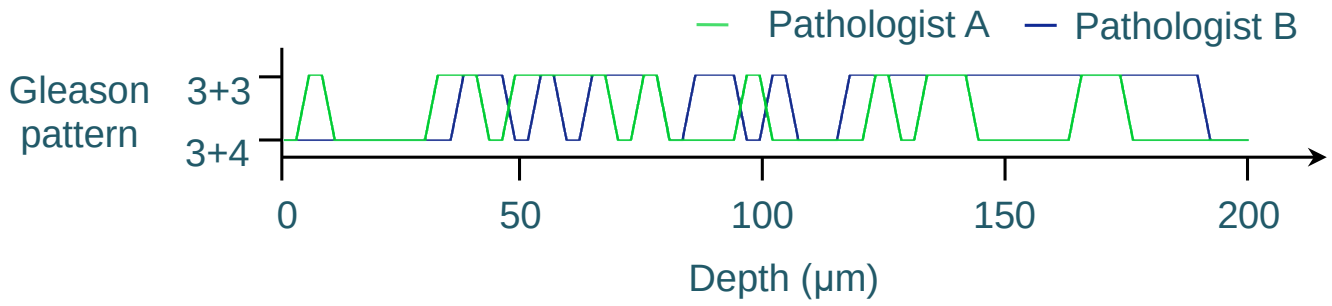
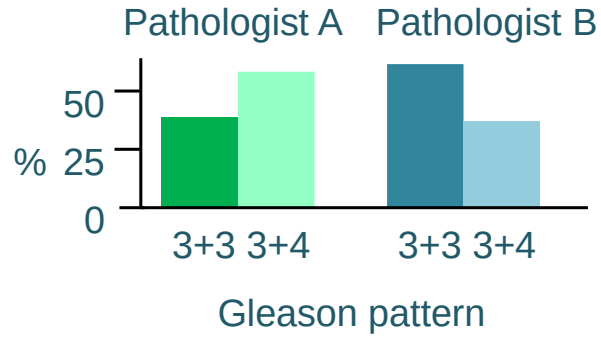


Variable grading with depth





AK Glaser et al., Nat. Biomed. Eng., 2017

Background

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CellPress

Cell

Article

Analysis of 3D pathology samples using weakly supervised AI

Andrew H. Song,[1,2,3,4] Mane Williams,[1,3,4,5,18] Drew F.K. Williamson,[1,2,3,4,18] Sarah S.L. Chow,[6] Guillaume Jaume,[1,2,3,4] Gan Gao,[6] Andrew Zhang,[1,3,4,7] Bowen Chen,[1,2,3,4] Alexander S. Baras,[8,9] Robert Serafin,[6] Richard Colling,[10,11] Michelle R. Downes,[12] Xavier Farré,[13] Peter Humphrey,[14] Clare Verrill,[10,11,15] Lawrence D. True,[16] Anil V. Parwani,[17] Jonathan T.C. Liu,[6,19,*] and Faisal Mahmood[1,2,3,4,19,20,*]

Highlights

- TriPath is a 3D pathology deep learning platform for clinical endpoint prediction
- Patient prognostication with 3D tissue volume outperforms 2D slice-based approaches
- 3D prognostication outperforms pathologist baselines, suggesting its clinical potential
- Larger tissue volume mitigates sampling bias and accounts for tissue heterogeneity

Generation of 3D images

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Objective: Develop a 3D platform that integrates

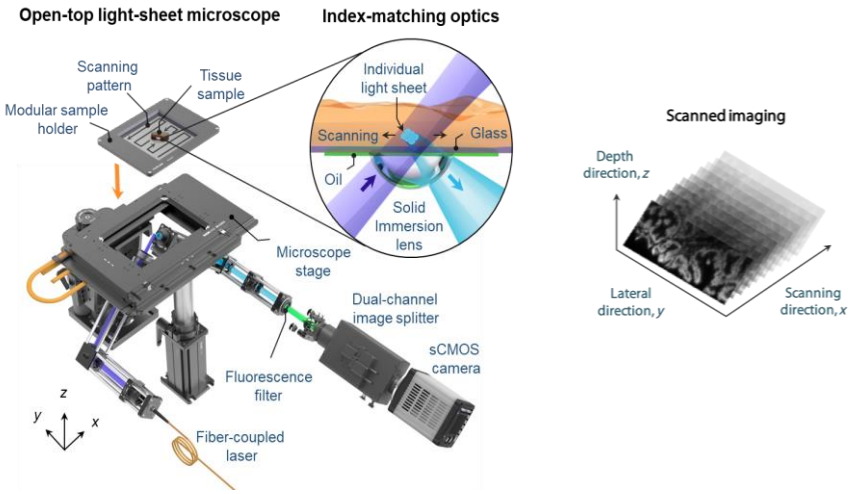
- **High-resolution optical imaging** – to reconstruct tumour architecture.
- **Multiplexed molecular analysis** – to visualise key biomarkers in 3D
- **Advanced visualisation & analysis** – to extract meaningful patterns

wellcome

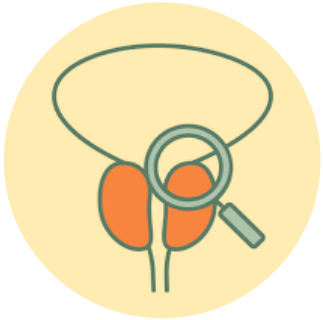

Freddie Hamdy

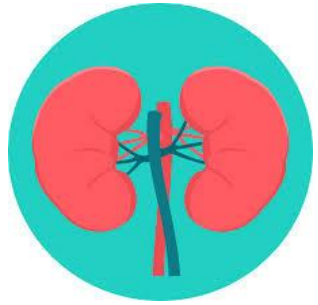

Ian Mills

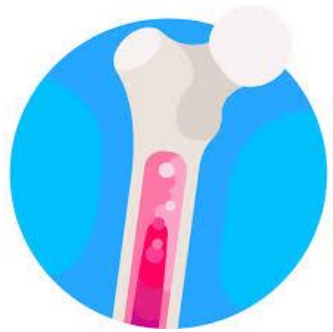

Jens Rittscher



AK Glaser et al., Nat. Biomed. Eng., 2017







Conclusion

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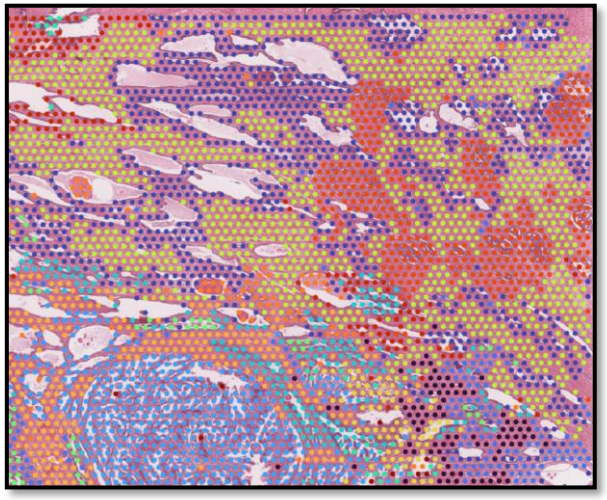
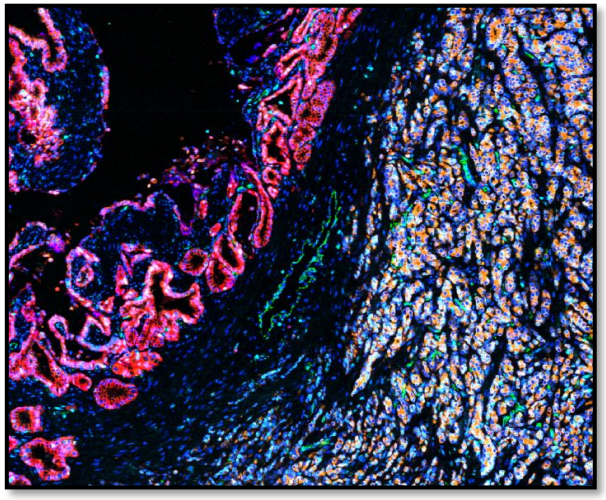
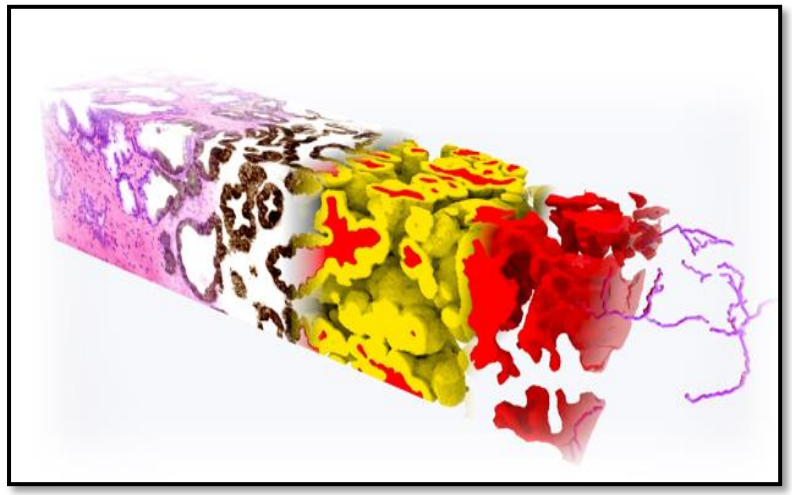
Spatial transcriptomics



Spatial proteomics



3D imaging



Conclusion

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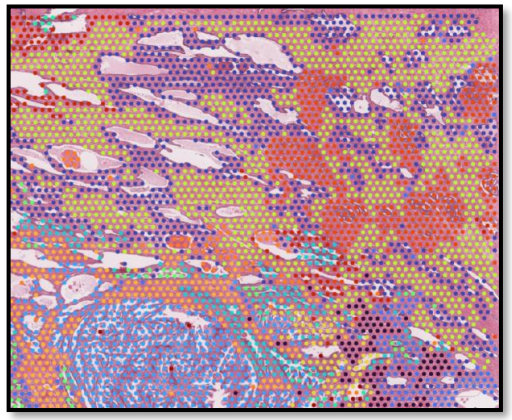
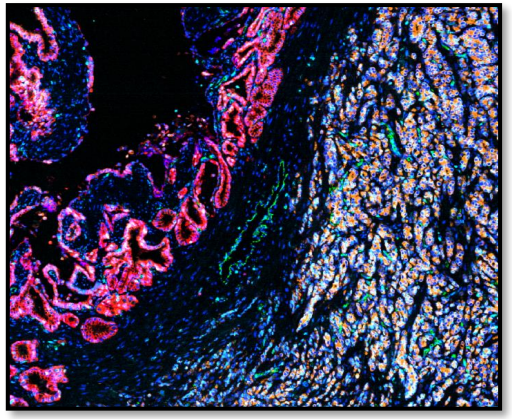
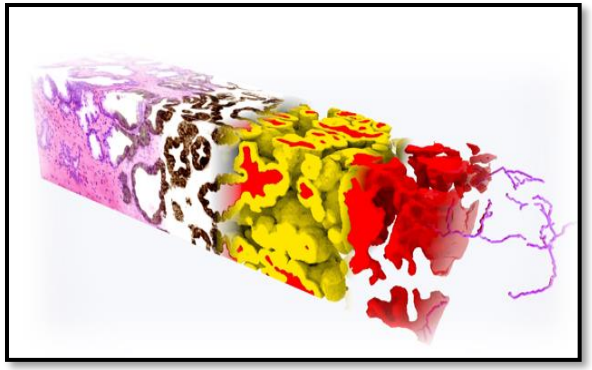
Spatial transcriptomics





Spatial proteomics



3D imaging

Acknowledgments


Ian Mills


Alastair Lamb


Freddie Hamdy


Jens Rittscher


Clare Verrill


Richard Colling


Daniel Royston


Rosalin Cooper


Renuka Teague


Katherine Bull


Richard Bryant


Dan Woodcock


Ruth Travis


Karl Smith-Byrne


Willem Bonnaffe


Yang Hu


Wencheng Yin


Andrew Erickson


Thineskrishna Anbarasan


Nithesh Ranasinha


Sophia Abusamra


Joakim Lundeberg


Charlotte Stadler


Mengxiao He


Eleanor O'Roberts


Emmanouela Perisynaki


Leire Alonso Galicia


Jonathan Liu


Kevin Bishop


Rob Serafin


Lindsey Barner


Tuomas Mirtti


İbrahim Kulaç

THE HANSON RESEARCH TRUST

European Research Council

CANCERFONDEN Swedish Cancer Society

NIHR | Oxford Biomedical Research Centre

wellcome

PROSTATE CANCER UK

The John Black Charitable Foundation

CANCER RESEARCH UK

NHS Oxford University Hospitals NHS Foundation Trust

The PART Trial

Mr Tom Leslie, PART Principle Investigator, Churchill Hospital, Oxford, Nuffield Department of Surgical Sciences, University of Oxford

FUNDED BY

NIHR | National Institute for Health and Care Research

PART

A randomised controlled trial of **P**artial prostate **A**blation versus **R**adical **T**reatment in intermediate risk, unilateral clinically localised prostate cancer

Mr Tom Leslie

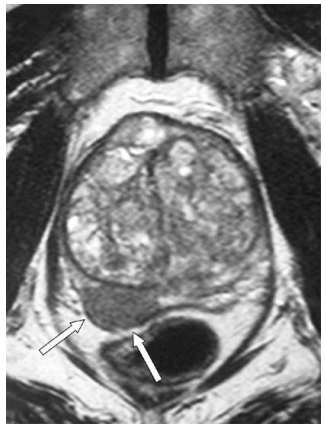
PART Principle Investigator

Churchill Hospital, Oxford

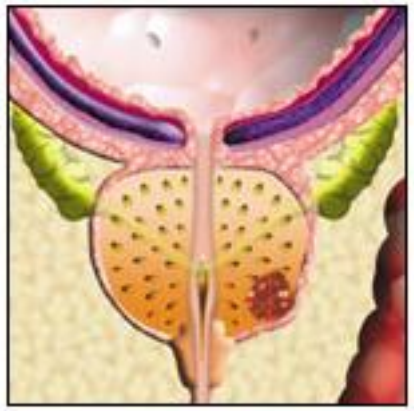
&

Nuffield Department of Surgical Sciences, University of Oxford

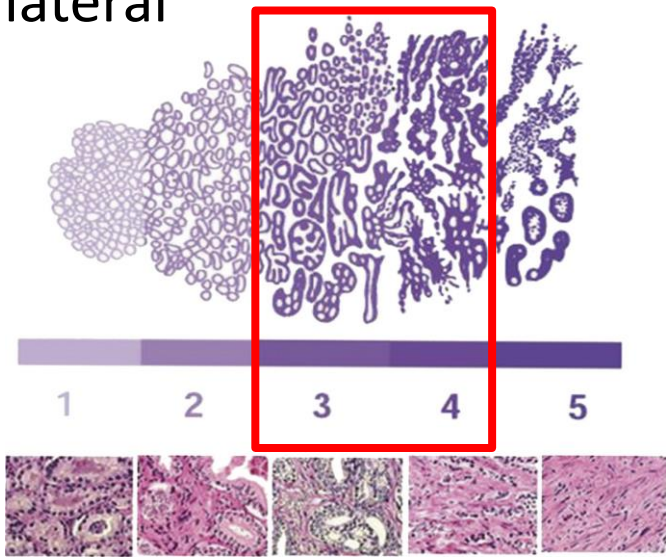
Radical treatment for intermediate-risk localised prostate cancer



Unilateral



T2



Gleason grade group 2-3

Radical prostatectomy

External beam radiotherapy

Brachytherapy

Focal Therapy / Partial Ablation

Several minimally invasive focal therapy / tissue ablative technologies developed:

- High intensity focussed ultrasound (HIFU)
- Irreversible Electroporation (IRE)
- Cryotherapy
- Vascular Targeted Photodynamic therapy (VTP)

Aim for organ preservation & reduced side effects versus radical therapy, with acceptable oncological outcomes

Eur Urol 2022;81:407-413

Cancer Control Outcomes Following Focal Therapy Using High-intensity Focused Ultrasound in 1379 Men with Nonmetastatic Prostate Cancer: A Multi-institute 15-year Experience

Deepika Reddy [a,b,*], Max Peters [c], Taimur T. Shah [a,b], Marieke van Son [c], Mariana Bertoncelli Tanaka [b], Philipp M. Huber [d], Derek Lomas [e], Arnas Rakauskas [f], Saiful Miah [g], David Eldred-Evans [a], Stephanie Guillaumier [h,i], Feargus Hosking-Jervis [a], Ryan Engle [a], Tim Dudderidge [j], Richard G. Hindley [k,l], Amr Emara [k,x], Raj Nigam [m,n], Neil McCartan [h,i], Massimo Valerio [f], Naveed Afzal [o], Henry Lewi [p], Clement Orczyk [h,i], Chris Ogden [q], Iqbal Shergill [r], Raj Persad [s], Jaspal Virdi [t], Caroline M. Moore [h,i,u,v], Manit Arya [b,h,i], Mathias Winkler [a,b], Mark Emberton [h,i,u,v,y], Hashim U. Ahmed [a,b,v,w,y]

- n=1379 with ≥ 6 months prospective F/U in HEAT registry (largest such reported focal therapy cohort)
- 13 UK centres 2005-2020
- ≥5 years F/U for 325 (24%) patients
- 65% intermediate-risk; 28% high-risk
- Overall median F/U = 32 (17-58) months
- For those with ≥5 years F/U, the median F/U was 82 (72-94) months

Table 1 – Baseline characteristics for patients undergoing focal HIFU for nonmetastatic prostate cancer

Characteristic	*n* = 1379
Age (yr), median (IQR)	66 (60–71)
Missing age data, *n* (%)	7 (0.5)
Pre-HIFU PSA (ng/ml), median (IQR)	6.9 (4.9–9.4)
Pre-HIFU PSA group, *n* (%)	
<10 ng/ml	1061 (77)
10–20 ng/ml	272 (20)
>20 ng/ml	24 (1.7)
Missing PSA data	22 (1.6)
Pre-HIFU prostate volume (ml), median (IQR)	36 (28–48)
Missing data, *n* (%)	154 (11)
Gleason score, *n* (%)	
3 + 3 = 6	257 (19)
3 + 4 = 7	851 (62)
4 + 3 = 7	225 (16)
≥8	17 (1.2)
Missing data	29 (2.1)
Pretreatment HIFU T stage, *n* (%)	
T1	95 (7)
T2	1023 (74)
T2a	276 (20)
T2b	140 (10)
T2c	209 (15)
Missing T2 subclassification	398 (29)
T3a/b	151 (11)
Missing data	110 (8.0)
D'Amico risk, *n* (%)	
Low	84 (6.1)
Intermediate	896 (65)
High	386 (28)
Missing data	13 (0.9)
Gleason 3 + 3 = 6, MCCL <6 mm, rT1	20 (1.5)
Ablative pattern, *n* (%)	
Quadrant	850 (62)
Hemiablation	487 (35)
Hockey-stick	42 (3.0)
Year of treatment, *n* (%)	
2005–2009	166 (12)
2010–2014	613 (45)
2015–2020	600 (44)

HIFU = high-intensity focused ultrasound; IQR = interquartile range; MCCL = maximum cancer core length; PSA = prostate-specific antigen.

- Failure-free survival (FFS) defined as no evidence of disease requiring salvage or systemic therapy, and no development of metastatic disease or PCa-specific mortality

- Kaplan-Meir 7-yr FFS 69% (64-74%)

- 7-yr FFS in intermediate- & high-risk disease 68% (62-75%) & 65% (56-74%)

- Metastasis-free survival & PCa-specific mortality 100% at 7 yr

- 1/5 needed a 2nd focal HIFU in 7 yrs

- Limited data on post-treatment biopsy, location of recurrence, or PROMs

<u>Conclusion:</u>

Focal HIFU in well-selected patients with localised csPCa has good cancer control in the medium term (7 years).

Table 2 – Kaplan-Meier estimates for failure outcomes after primary focal HIFU in patients with nonmetastatic prostate cancer and at least 6-mo follow-up

Kaplan-Meier estimate, % (95% confidence interval)							
	1 yr	2 yr	3 yr	4 yr	5 yr	6 yr	7 yr
Failure-free survival [a]	100 (100–100)	96 (95–98)	93 (91–95)	88 (85–90)	82 (79–86)	75 (71–79)	69 (64–74)
By D'Amico risk class							
Low	100 (100–100)	99 (96–100)	99 (96–100)	94 (88–100)	91 (84–100)	91 (84–100)	88 (77–99)
Intermediate	100 (100–100)	97 (96–98)	93 (91–95)	88 (85–91)	83 (79–87)	75 (70–81)	68 (62–75)
High	100 (99–100)	95 (93–97)	91 (88–94)	85 (81–90)	79 (73–85)	69 (62–78)	65 (56–74)
Salvage local whole-gland or systemic treatment-free survival	100 (100–100)	97 (96–98)	93 (91–95)	89 (86–91)	85 (83–88)	80 (77–84)	75 (71–80)
By D'Amico risk class							
Low	100 (100–100)	99 (96–100)	99 (96–100)	99 (96–100)	99 (96–100)	99 (96–100)	95 (87– 100)
Intermediate	100 (100–100)	97 (96–99)	94 (91–96)	89 (86–92)	84 (80–88)	79 (74–84)	73 (67–80)
High	100 (99–100)	95 (93–98)	91(87–94)	86 (82–91)	84 (79–89)	78 (71– 85)	73 (65–82)

HIFU = high-intensity focused ultrasound.

[a] Failure-free survival defined by transition to whole-gland salvage treatment, third focal therapy treatment, systemic treatment, development of prostate cancer metastases, or prostate cancer–specific death.

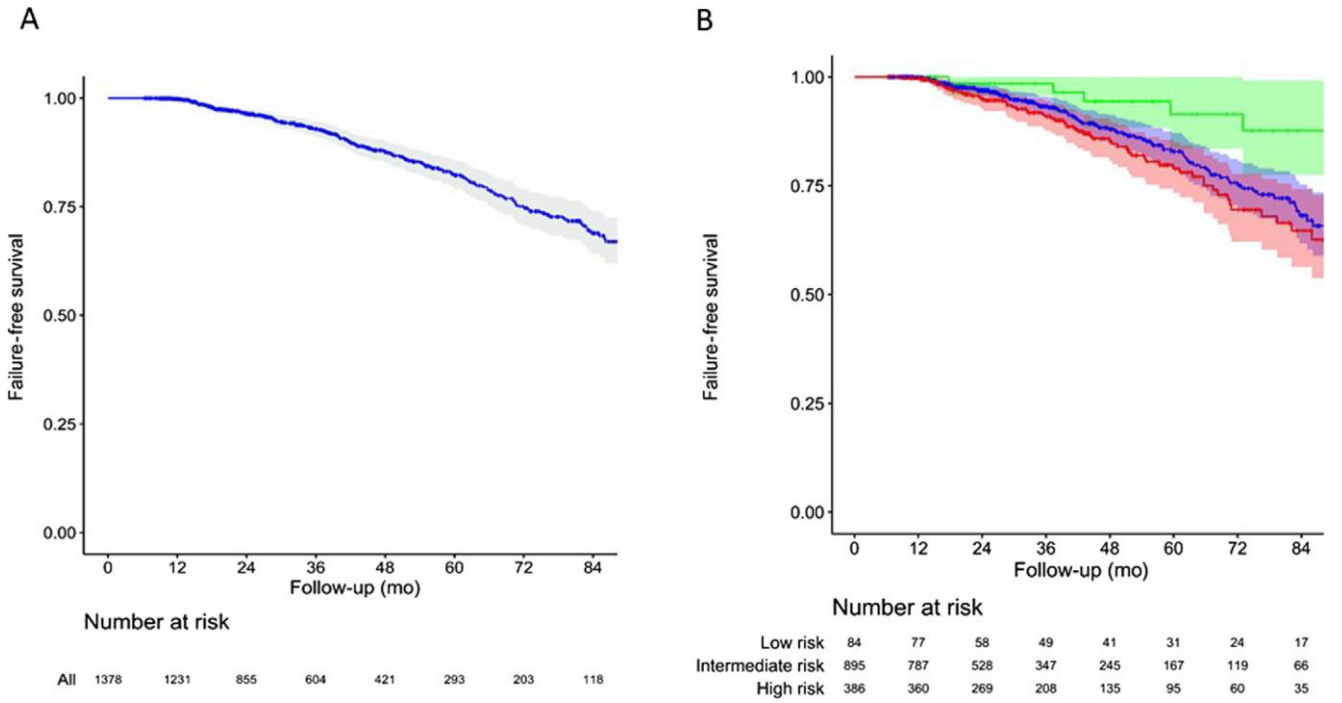


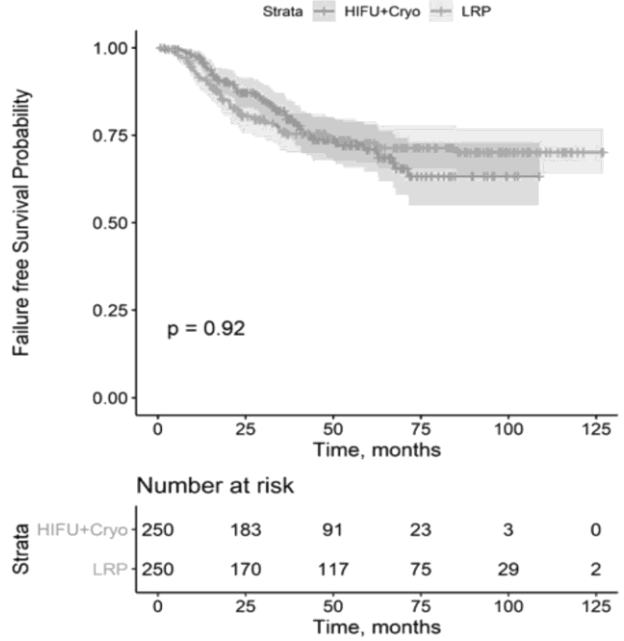
Fig. 1 – Kaplan-Meier curves of failure-free survival (FFS) with 95% confidence intervals. FFS is defined as transition to whole-gland salvage treatment or third focal therapy treatment, systematic treatment, and/or development of prostate cancer metastases and/or prostate cancer–specific death for (A) all patients with at least 6 mo of follow-up and (B) 1365 patients stratified per D'Amico low-risk (green line), intermediate-risk (blue line), and high-risk (red line) group (log-rank analysis of D'Amico intermediate- vs high-risk disease $p = 0.3$).

Prostate Cancer and Prostatic Diseases (2021) 24:567–574
https://doi.org/10.1038/s41391-020-00315-y

ARTICLE

Focal therapy compared to radical prostatectomy for non-metastatic prostate cancer: a propensity score-matched study

Taimur T. Shah[1,2] · Deepika Reddy[1,2] · Max Peters[3] · Daniel Ball[2] · Na Hyun Kim[2] · Enrique Gomez Gomez[4] · Saiful Miah[5] · David Eldred Evans[1,2] · Stephanie Guillaumier[6] · Peter S. N. van Rossum[3] · Marieke J. Van Son[3] · Feargus Hosking-Jervis[1] · Tim Dudderidge[7] · Richard Hindley[8] · Amr Emara[8] · Stuart McCracken[9,10] · Damian Greene[11] · Raj Nigam[12] · Neil McCartan[6] · Massimo Valerio[13] · Suks Minhas[2] · Naveed Afzal[14] · Henry Lewi[15] · Chris Ogden[16] · Raj Persad[17] · Jaspal Virdi[18] · Caroline M. Moore[6] · Manit Arya[2,6] · Mark Emberton[6] · Hashim U. Ahmed[1,2] · Mathias Winkler[1,2]



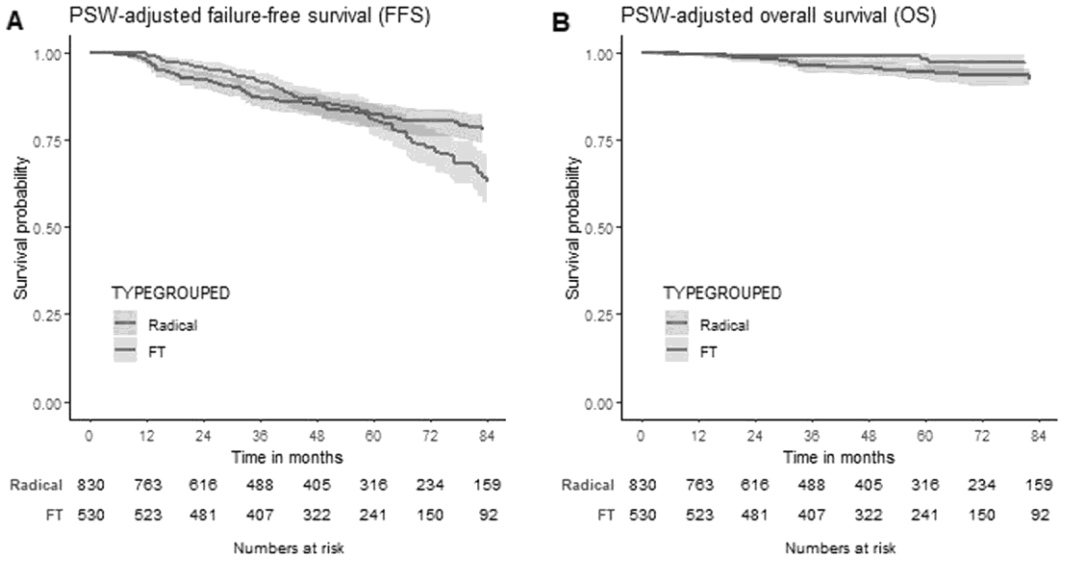
Prostate Cancer and Prostatic Diseases (2021) 24:1120–1128
https://doi.org/10.1038/s41391-021-00369-6

ARTICLE

Clinical Research

Conventional radical versus focal treatment for localised prostate cancer: a propensity score weighted comparison of 6-year tumour control

Marieke J. van Son[1,2,3] · Max Peters[1,2] · Deepika Reddy[1] · Taimur T. Shah[1,4] · Feargus Hosking-Jervis[1] · Stephen Robinson[5] · Jan J. W. Lagendijk[2] · Stephen Mangar[6] · Tim Dudderidge[7] · Stuart McCracken[4] · Richard G. Hindley[8] · Amr Emara[8] · Raj Nigam[9] · Raj Persad[10] · Jaspal Virdi[11,12] · Henry Lewi[13] · Caroline Moore[14,15] · Clement Orczyk[14,15] · Mark Emberton[14,15] · Manit Arya[1,6,11,12,15] · Hashim U. Ahmed[1,6] · Jochem R. N. van der Voort van Zyp[2] · Matt Winkler[1,6] · Alison Falconer[1,6]



- Propensity-matched analysis of focal therapy (HIFU or cryotherapy) versus radical treatment (radical prostatectomy or radical radiotherapy).
- No clinically relevant differences in FFS.

NICE National Institute for Health and Care Excellence

NICE guideline

Focal therapy using high-intensity focused ultrasound for localised prostate cancer

Interventional procedures guidance [IPG756] Published: 05 April 2023 Register an interest

1 Recommendations

1.1 Evidence on the safety of focal therapy using high-intensity focused ultrasound for localised prostate cancer is adequate, but evidence on its efficacy is limited. Therefore, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research. Find out what special arrangements mean on the NICE interventional procedures guidance page.

1.2 Clinicians wanting to do high-intensity focused ultrasound for localised prostate cancer should:

- Inform the clinical governance leads in their healthcare organisation.
- Give people (and their families and carers, as appropriate) clear written information to support shared decision making, including NICE's information for the public. Use the recommendations in NICE's guideline on diagnosing and managing prostate cancer for information on treatment options and decision support.
- Ensure that people (and their families and carers, as appropriate) understand the procedure's safety and efficacy, and any uncertainties about these.
- Audit and review clinical outcomes of everyone having the procedure. The main efficacy and safety outcomes identified in this guidance can be entered into NICE's interventional procedure outcomes audit tool (for use at local discretion).
- Discuss the outcomes of the procedure during their annual appraisal to reflect, learn and improve.

1.3 Healthcare organisations should:

- Ensure systems are in place that support clinicians to collect and report data on outcomes and safety for everyone having this procedure.
- Regularly review data on outcomes and safety for this procedure.

1.4 Patient selection should be done by a multidisciplinary team.

1.5 Further research could include registry data or randomised trials. It should include details of patient selection, including size and classification of tumour, technique used and long-term outcomes such as quality of life.

EAU - EANM - ESTRO - ESUR - ISUP - SIOG Guidelines on

Prostate Cancer

N. Mottet (Chair), P. Cornford (Vice-chair), R.C.N. van den Bergh, E. Briers, Expert Patient Advocate (European Prostate Cancer Coalition/Europa UOMO), D. Eberli, G. De Meerleer, M. De Santis, S. Gillessen, J. Grummet, A.M. Henry, T.H. van der Kwast, G.J.L.H. van Leenders, M.D. Mason, S. O'Hanlon, I.M. van Oort, D.E. Oprea-Lager, G. Ploussard, O. Rouvière, I.G. Schoots. J. Stranne, D. Tilki, T. Wiegel
Guidelines Associates: T. Van den Broeck, A. Farolfi, G. Gandaglia, N. Grivas, M. Lardas, M. Liew, E. Linares Espinós, P-P.M. Willemse

6.2.2.4 Other options for the primary treatment of intermediate-risk PCa (experimental therapies)

6.2.2.4.1 Focal therapy

A prospective study on focal therapy using HIFU in patients with localised intermediate-risk disease was published but the data was derived from an uncontrolled single-arm case series [789]. There is a paucity of high-certainty data for either whole-gland or focal ablative therapy in the setting of intermediate-risk disease. Consequently, neither whole-gland ablative treatment nor focal treatment can be considered as standard therapy for intermediate-risk patients and, if offered, it should only be in the setting of clinical trials or prospective registries [778].

Recommendation	Strength rating
Other therapeutic options	
Only offer whole-gland ablative therapy (such as cryotherapy, high-intensity focused ultrasound, etc.) or focal ablative therapy within clinical trials or registries.	Strong
Do not offer ADT monotherapy to asymptomatic men not able to receive any local treatment.	Weak

EAU Guidelines on Focal Therapy for Prostate Cancer

2022

6.1.6 General guidelines for the treatment of prostate cancer
Offer focal therapy within a clinical trial setting or well-designed prospective cohort setting.

HOW IT WAS APPLIED TO YOUR PRACTICE

Research ethics comittee, legally sponsored trial only

2023

Section 6.1.5.3
Currently, focal therapy using HIFU or cryotherapy should be performed within the context of a prospective registry. All other ablative modalites should only be offered in a well-designed prospective trial setting.

6.1.6 General guidelines for the treatment of prostate cancer
Only offer focal therapy with high-intensity focused ultrasound or cryotherapy within a clinical trial or prospective registry.

HOW TO APPLY TO YOUR PRACTICE

HIFU or cryotherapy within prospective registry
ALL other modalities: research ethics comittee, legally sponsored trial only

Aim

- Assess focal therapy in the context of an important unmet clinical need – i.e. unilateral intermediate-risk localised prostate cancer
- Pragmatic trial design, to allow for the fast moving diagnostic pathway and changes in treatment modalities
- Combine the ProtecT team experience of a large multi-centre RCT with the leading focal therapy trialists
- Embed training and quality assurance for the delivery of Partial Ablation in centres interested in adopting this in a protocolised programme within a multi-centre RCT, thus growing the expertise in high-quality delivery of this treatment modality

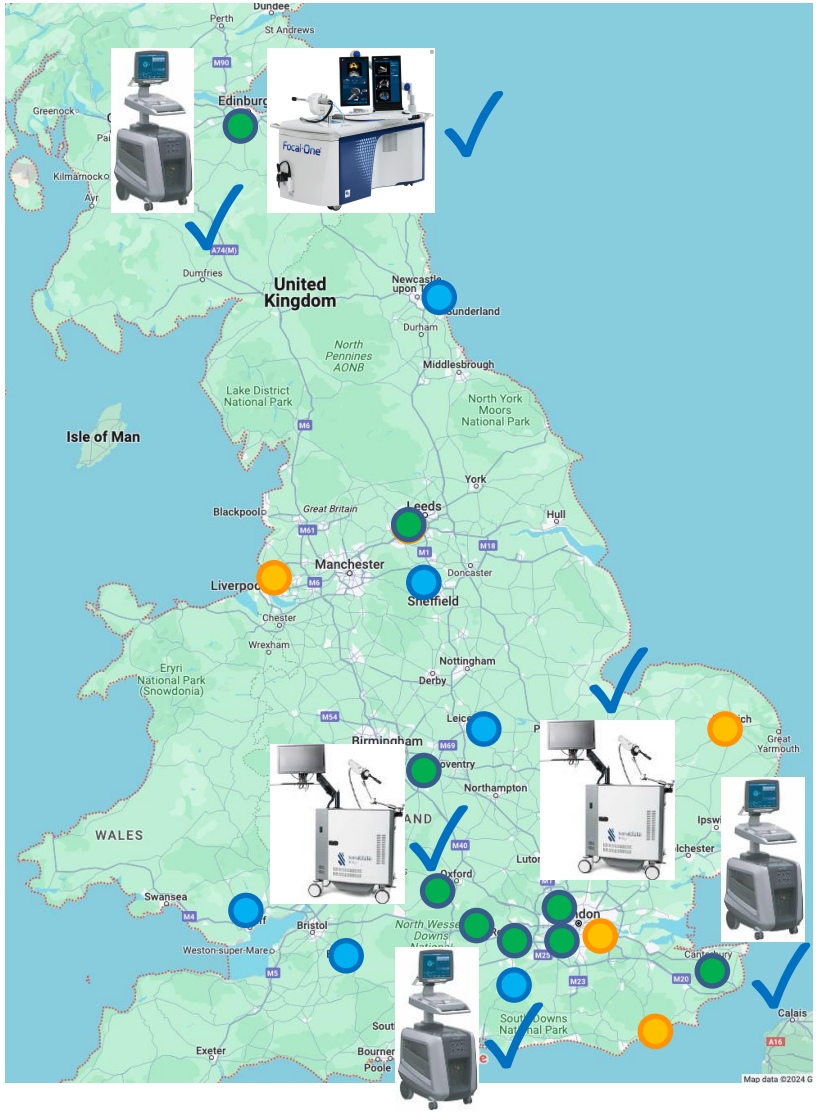
Trial Design

Aim:

The aim of the PART study is to determine whether partial ablation for unilateral intermediate-risk prostate cancer provides effective oncological outcomes compared with radical treatment, with the added benefits of reduced side effects, and an improved patient reported outcomes profile.

Design:

- Multi-centre, two arm, parallel design, randomised controlled clinical study.
- An embedded QuinteT Recruitment Intervention will be used to understand, monitor and address barriers to participation.
- 800 Participants (400 in each of the 2 study arms) with PCa from approximately 10 sites in the UK.



Current sites open to recruitment:

- Churchill Hospital, Oxford
- Royal Berkshire Hospital, Reading
- East Kent Hospital, Canterbury
- UCL, London
- NHS Lothian, Edinburgh
- Imperial, London
- Wexham Park Hospital, Slough
- Coventry and Warwickshire
- Leeds Royal Infirmary

Highlights of the PART Feasibility Study

- Recruiting and randomising men with intermediate-risk, unilateral, clinically localised prostate cancer to Partial Ablation or Radical Prostatectomy is feasible.
- Support from NIHR HTA to extend the recruitment period has been pivotal in optimising recruitment rates and demonstrating feasibility.
- This feasibility study has shown a good response rate to the patient-reported outcome measures (PROMs) survey pack and self-reported resource use diary.
- The QuinteT Recruitment Intervention contributed to the increase in recruitment rates from 1.4 patients per month to 3.9 patients per month.

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PART Main Trial

HYPOTHESIS: Partial Ablation for unilateral intermediate-risk prostate cancer is a safe and beneficial alternative to Radical Therapy, with improved quality of life and a reduced cost, without unduly compromising treatment effectiveness. More specifically, we hypothesise that:

1) Partial Ablation offers equivalent benefit to whole gland Radical Treatment in prostate cancer control

2) The side-effect profile of Partial Ablation is favourable compared with Radical Therapy

3) The 'trade-off' between side-effects and oncological outcomes for men with localised prostate cancer favours Partial Ablation compared with Radical Therapy.

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Main Trial - Outcome Measures

Primary outcome:

- Primary treatment failure, defined as the need for whole gland treatment (RP or RRT) following Partial Ablation (in which case the organ-preservation strategy will have failed), or secondary treatment after Radical Therapy (initial RP, RRT or LDR-B)

Secondary outcomes:

- Health-related QoL using standard, validated PROMs questionnaires (IPSS, EQ-5D-5L, PORPUS, MAX-PC, EPIC)
- Health resource utilisation and cost-effectiveness in terms of cost per QALY
- Short, medium and long-term adverse events related to treatments
- Disease progression including development of metastases
- The accuracy of mpMRI imaging and biopsy protocols in determining suitability of patients for Partial Ablation
- Disease-specific and all-cause mortality.

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Partial Ablation & PART

1) HIFU

- (Focal One / Sonablate)
- Focal One – EDAP TMS
- Successful PART feasibility based on HIFU
- Well-established technology –over three decades
- Non-invasive
- Recommended by NICE for clinical research
- Expertise available within recruiting centres

edap tms
Bringing New Horizons to Therapy

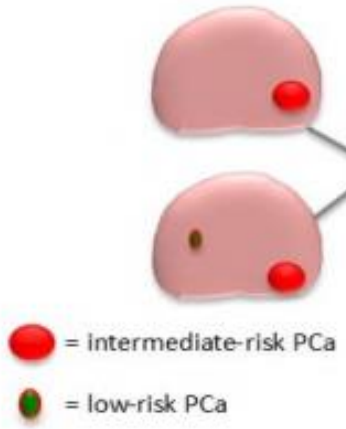
https://www.edap-tms.com/en/products-services/prostate-cancer/focal-one

Partial Ablation & PART

2) IRE

- Nanoknife - Angiodynamics
- Established for tissue ablation and FDA approved
- Needle based approach, no drugs
- Ample evidence of safety and efficacy in treating prostate cancer
- Local expertise available in the UK

https://nanoknife.com/



Patient referred to urology/oncology clinic and undergoes mpMRI and biopsy as per local SOP

Diagnosis of: Unilateral intermediate-risk OR
Dominant unilateral intermediate-risk + small contralateral low-risk foci

MDT: Patient discussed, eligibility considered

Patient routine visit: Treatment options discussed, PART Trial introduced by Consultant and/or Research Nurse

Study visit: Informed consent, Confirm eligibility, Patient questionnaires (HRQoL and resource use), baseline data collection. Randomisation

PARTIAL ABLATION (PA) ARM
HIFU treatment **OR**
IRE treatment
(as recommended by the PA planning team)

RADICAL TREATMENT (RT) ARM
Treatment option from one of the following:
Radical prostatectomy **OR**
Radical radiotherapy **OR**
Low dose-rate brachytherapy

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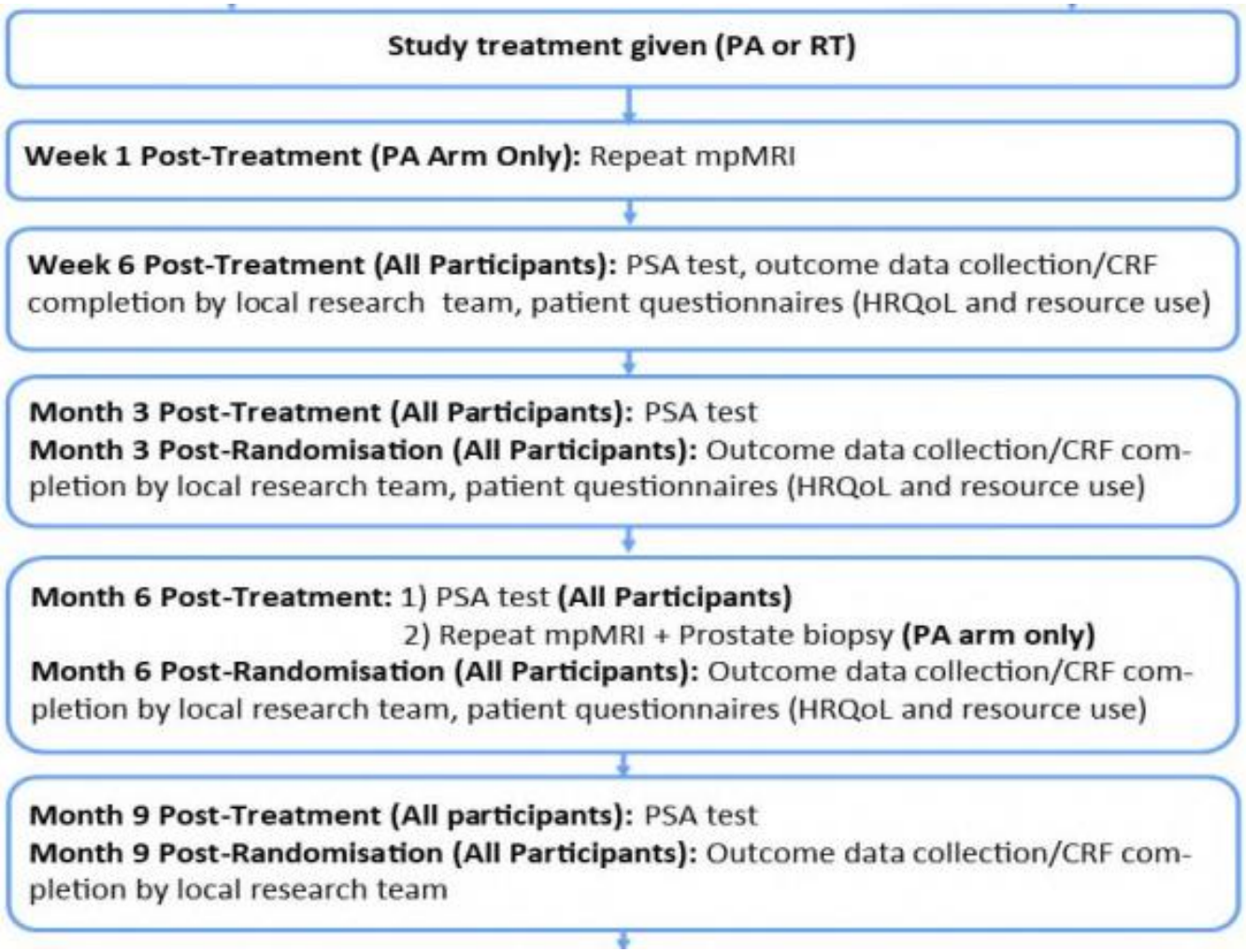

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Month 12 Post-Treatment: 1) PSA test **(All Participants)**
2) Repeat mpMRI + Prostate biopsy **(PA arm only)**
Month 12 Post-Randomisation (All Participants): Outcome data collection/CRF completion by local research team, patient questionnaires (HRQoL and resource use)

Month 24 Post-Treatment (All participants): PSA test
Month 24 Post-Randomisation (All Participants): Outcome data collection/CRF completion by local research team

Month 36 Post-Treatment: 1) PSA test **(All Participants)**
2) Repeat mpMRI + Prostate biopsy **(PA arm only)**
Month 36 Post-Randomisation (All Participants): Outcome data collection/CRF completion by local research team, patient questionnaires (HRQoL and resource use)

Annually post-treatment until end of trial (All Participants): PSA test
Annually post-randomisation until end of trial (All Participants): outcome data collection/CRF completion by local research team, patient questionnaires (HRQoL and resource use)

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Intraoperative molecular targeted fluorescence imaging and radical prostatectomy

Mr Aaron Leiblich DPhil FRCS (Urol), Consultant Urological Surgeon, Oxford University Hospitals

Intraoperative molecular targeted fluorescer imaging and radical prostatectomy

Aaron Leiblich DPhil FRCS (Urol)

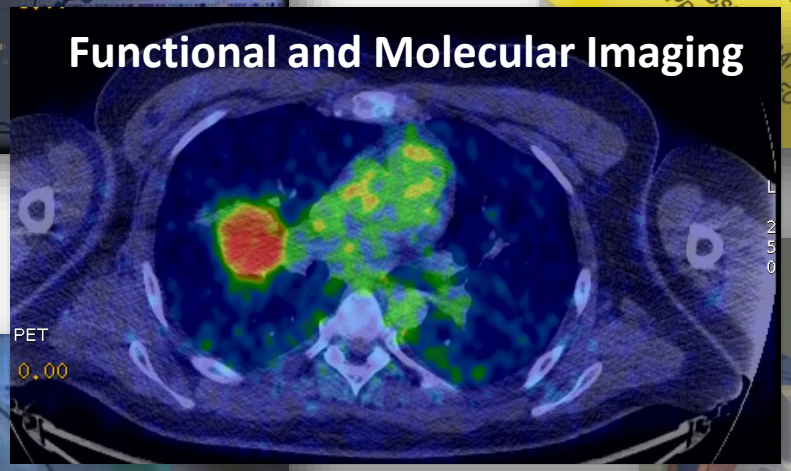
UNIVERSITY OF OXFORD

NUFFIELD DEPARTMENT OF SURGICAL SCIENCES

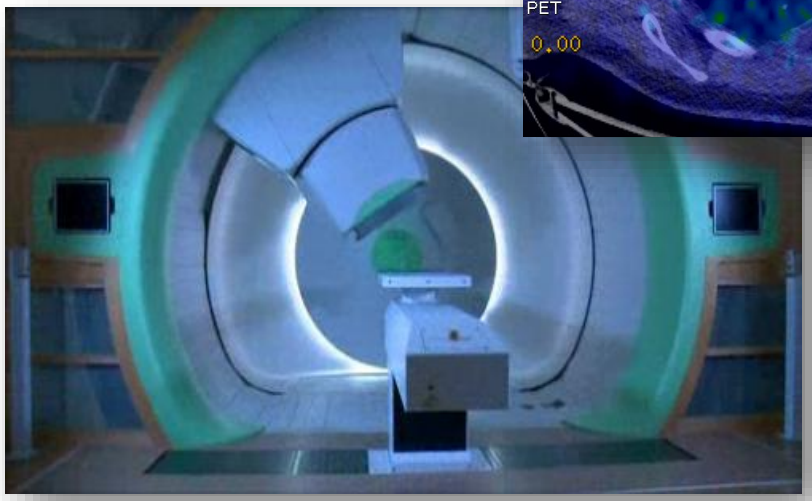
Oxford University Hospitals NHS
NHS Foundation Trust

Precision Cancer Medicine

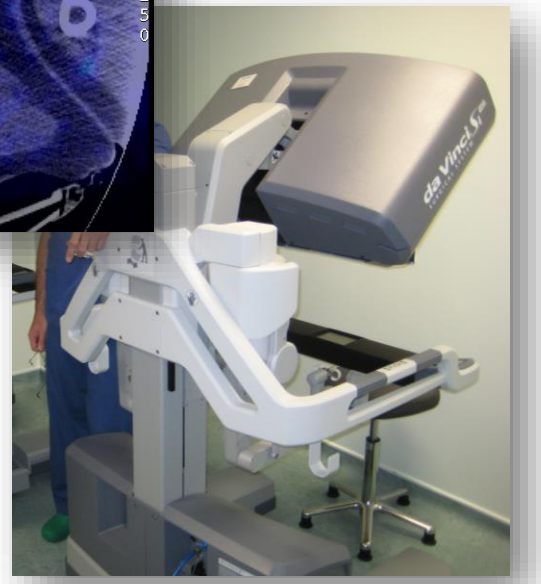
Genomics



Targeted Agents

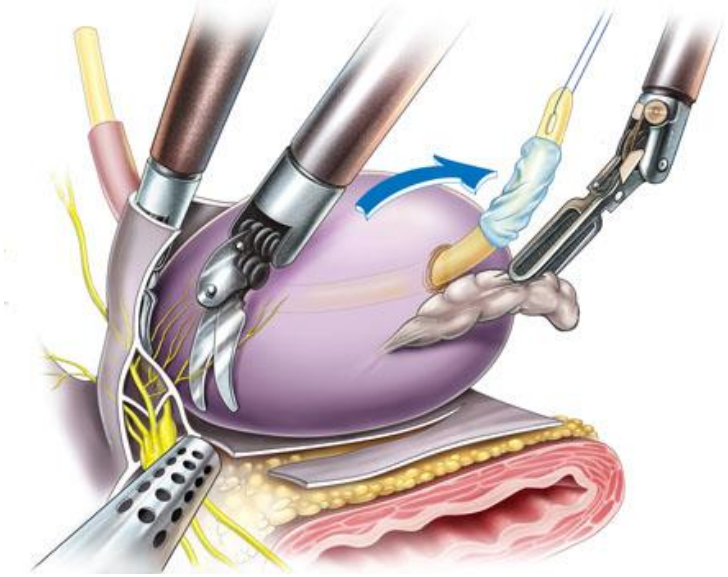


Particle Therapy



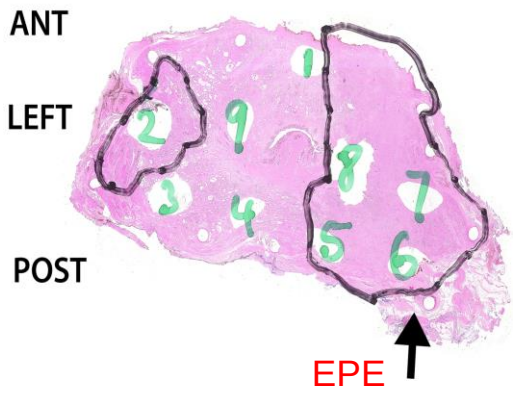
Robot-assisted Surgery

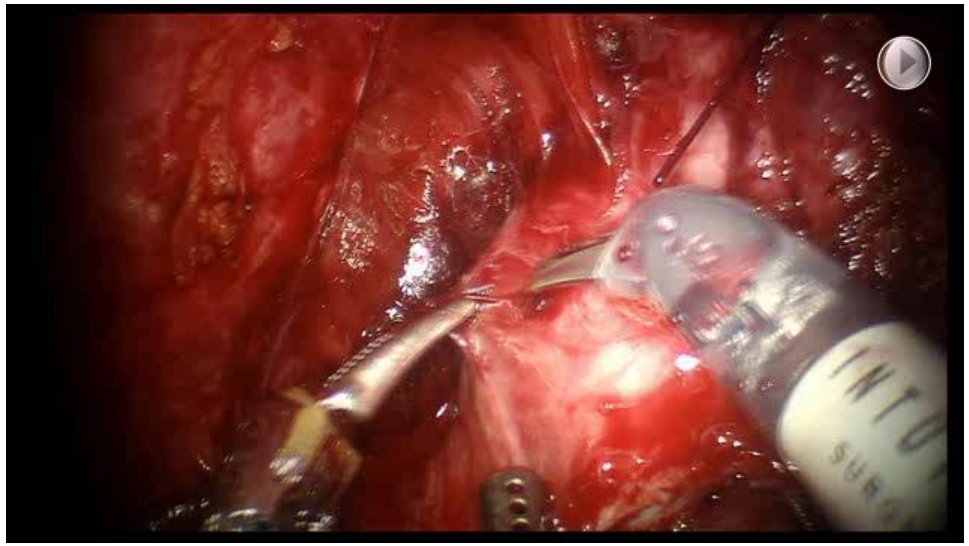
Prostate Cancer – unmet needs



- 30-40% of patients are upstaged to pathological locally advanced disease (pT3)
- 20-50% have positive surgical margins
- Margin rates and outcomes can be improved by better pre-operative, operative staging and precision surgery

Catto *et al.*, Br J Cancer 2011; 105:931-93

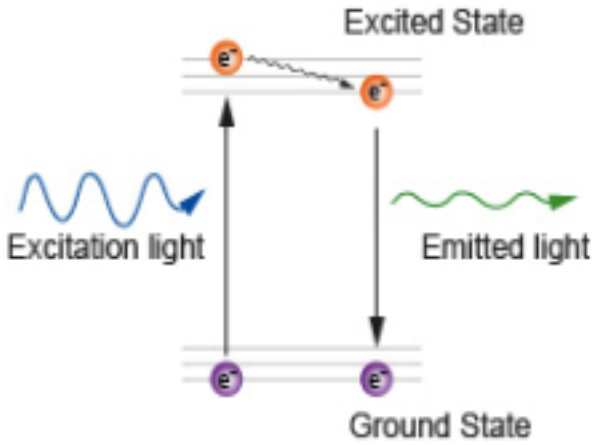


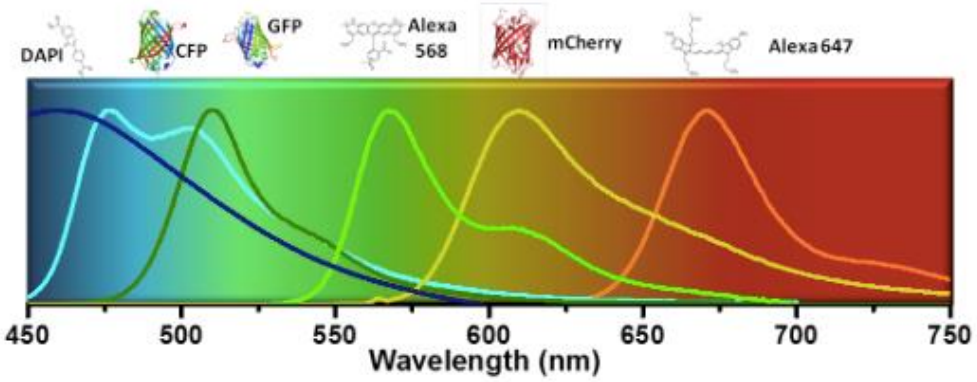


Intra-operative fluorescence
The problems

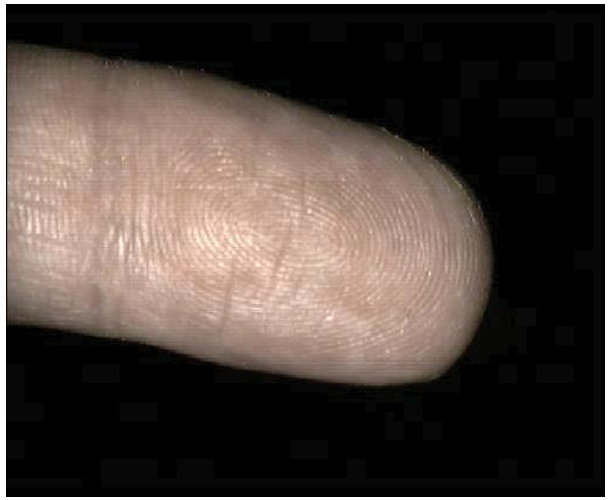
Boris Vojnovic

1. Fluorophores alone are NOT tissue specific
2. Near infra-red visualisation <u>OR</u> white light imaging <u>OR</u> fluorescence overlays

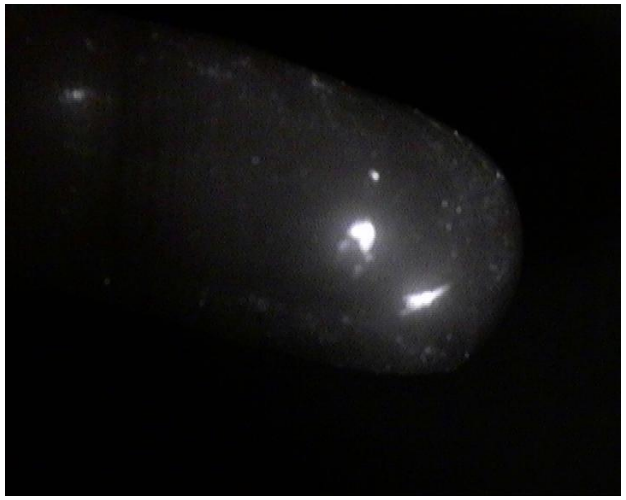




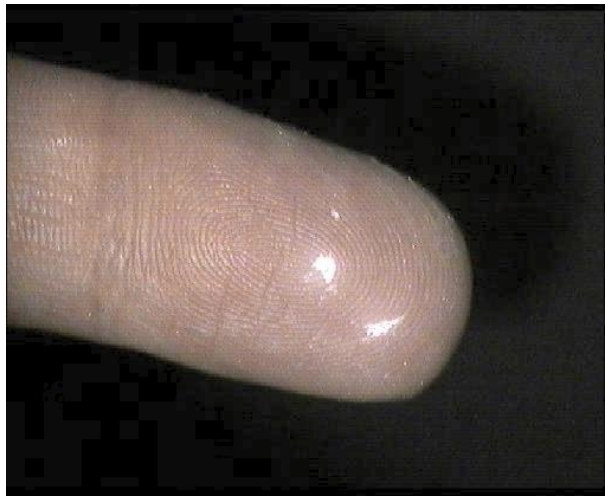
Surgical Imaging using ICG NIR **fluorescence**



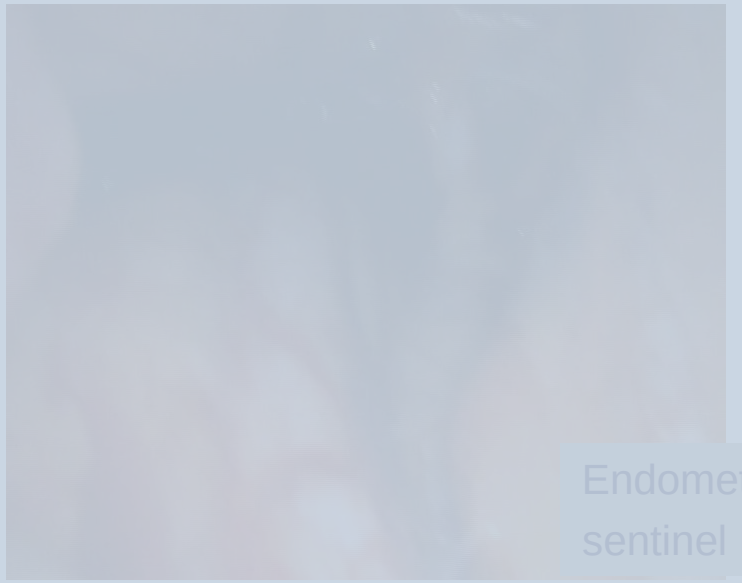
White light



NIR Fluorescence



Oxford system

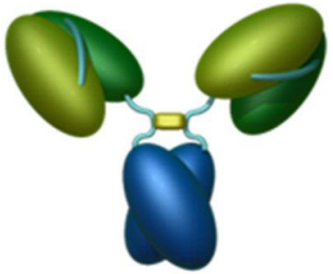


Endometrial cancer sentinel lymph node

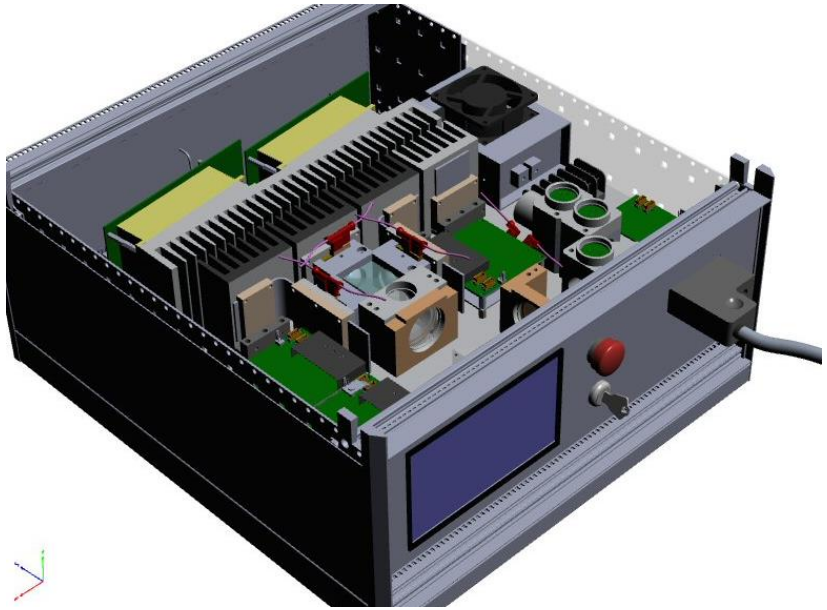
Vulval cancer sentinel lymph node

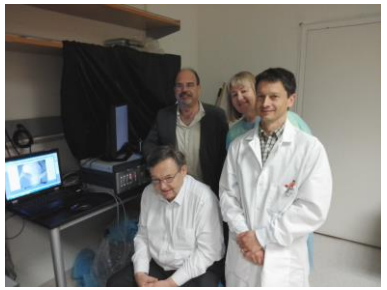
Molecularly targeted imaging of prostate cancer

ImaginAb



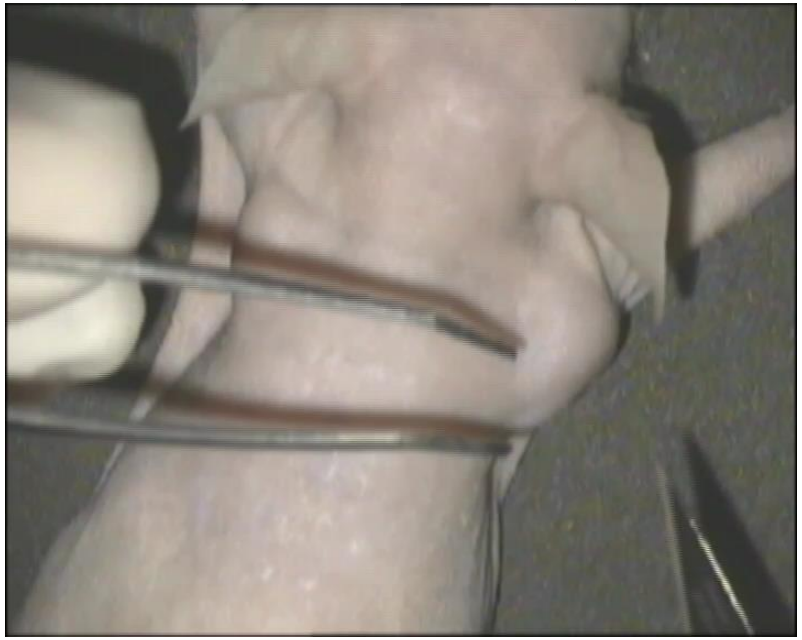
PSMA Minibody





PC3 tumour

22Rv1 tumour



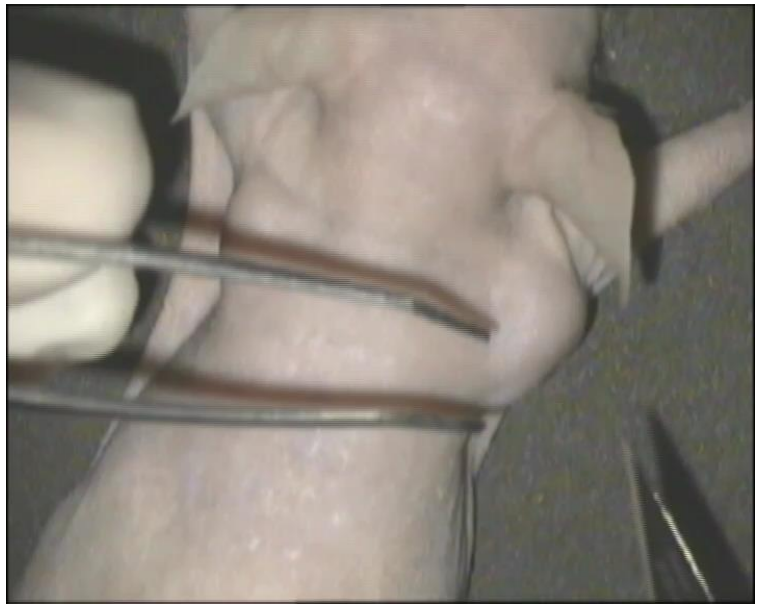
Optical Imaging with ImaginAb IRDye 800CW labelled minibody

CANCER RESEARCH UK

Molecularly targeted imaging of prostate cancer

Control -ve tumour

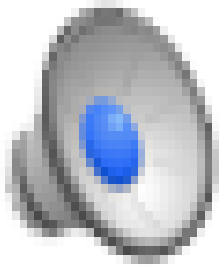
Expressing tumour



First-in-man 9 July 2018

Optical Imaging with fluorescent conjugated tissue- specific molecular target

First-in-mouse 14 May 2014



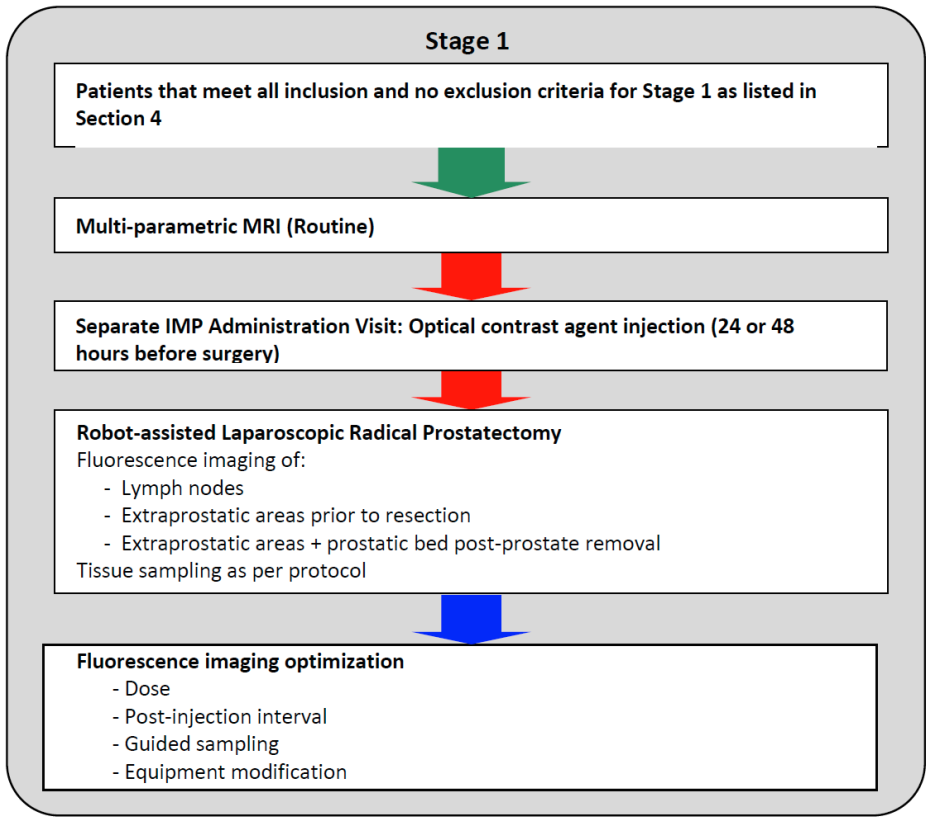
CANCER RESEARCH UK

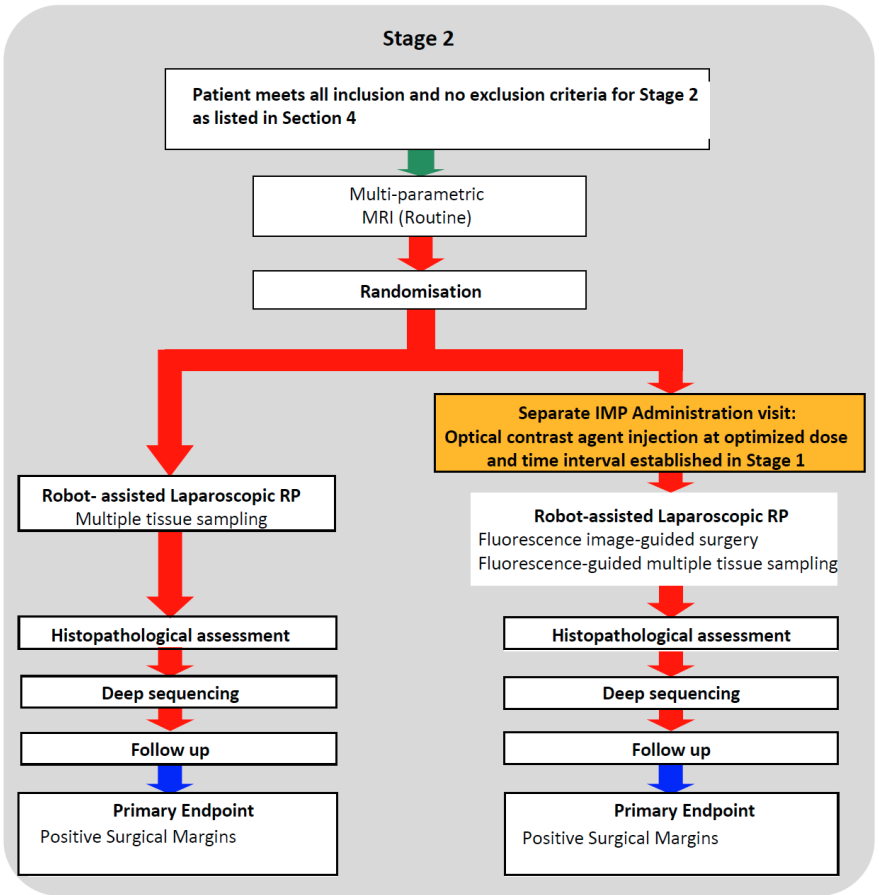
4.2. Inclusion Criteria

Men with histologically proven high-risk non-metastatic localized or locally advanced (cT3) PC with any of the following risk criteria:

Risk 1: Serum PSA 10-20ng/ml and Gleason 4+3 or greater
Risk 2: Serum PSA ≥20 ng/ml
Risk 3: Grade group 4 or 5
Risk 4: Clinical T3

confidential





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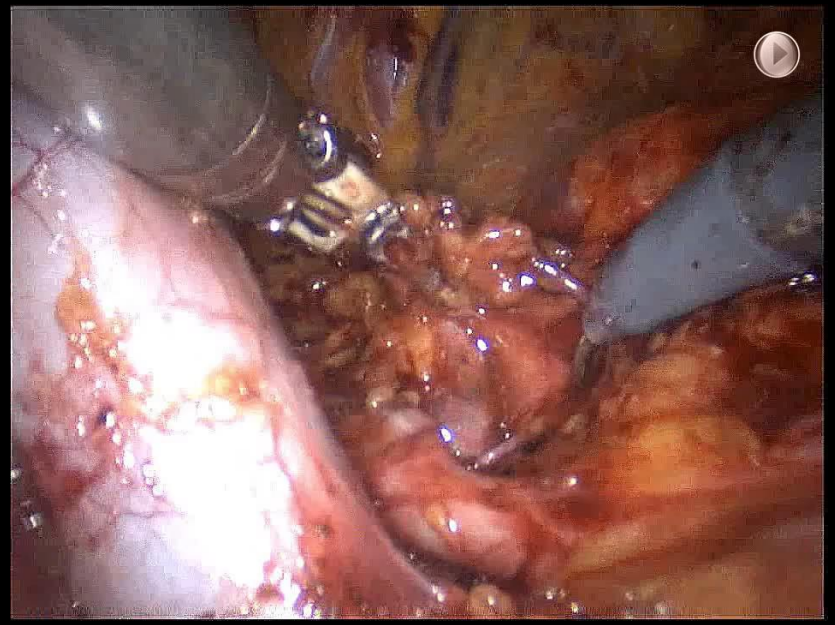
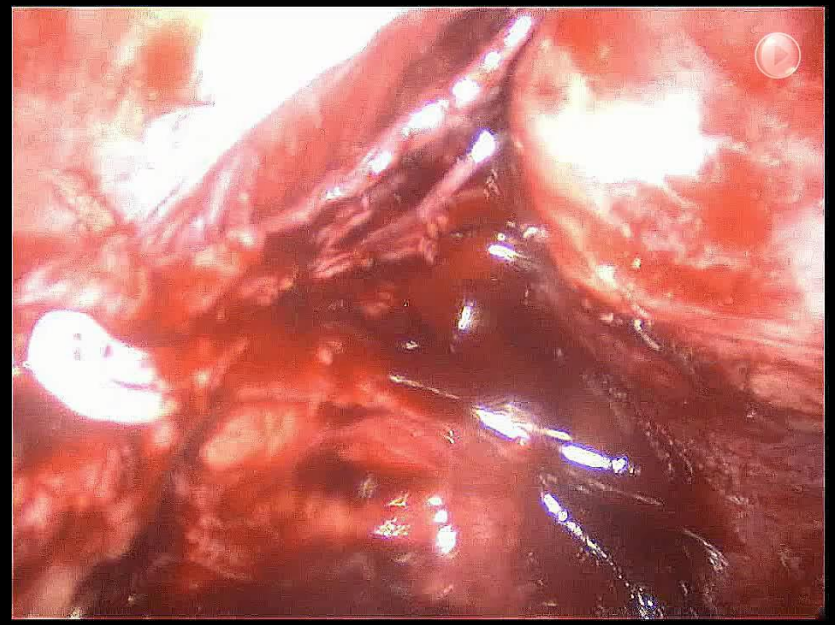


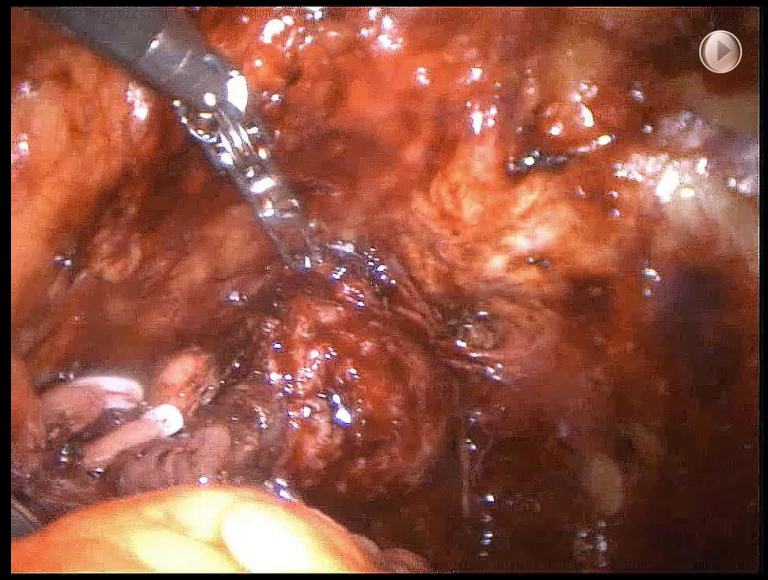
+ve lymph node [A15]



Left +ve NVB [A17]

July 2018-Jan 2020:

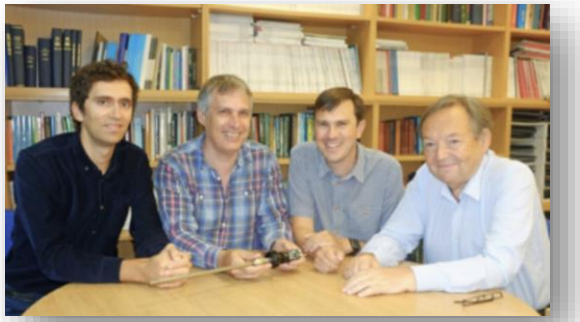
- First-in-man/Pilot
- N=23 patients
- Dose titration and interval between injection and surgery



Right –ve NVB [A14]

- Full RCT scheduled n=100 patients
- New applications: Pancreas, Kidney

ProMOTE study Team



Davide **Volpe, Iain Tullis, Paul** Barber and Boris Vojnovic,

Alastair Lamb
Tom Leslie
Aaron Leiblich

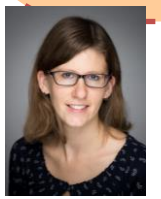
Image-guided sampling for genomic analysis

Genomics (1) PSMA expression

Genomic (2) diversity, Target Discovery

Precision Surgery

Reduce PSM, improve oncological and functional outcomes



Ines Rombach

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Monitor 3

European Journal of Nuclear Medicine and Molecular Imaging
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ORIGINAL ARTICLE

First-in-man study of the PSMA Minibody IR800-IAB2M for molecularly targeted intraoperative fluorescence guidance during radical prostatectomy

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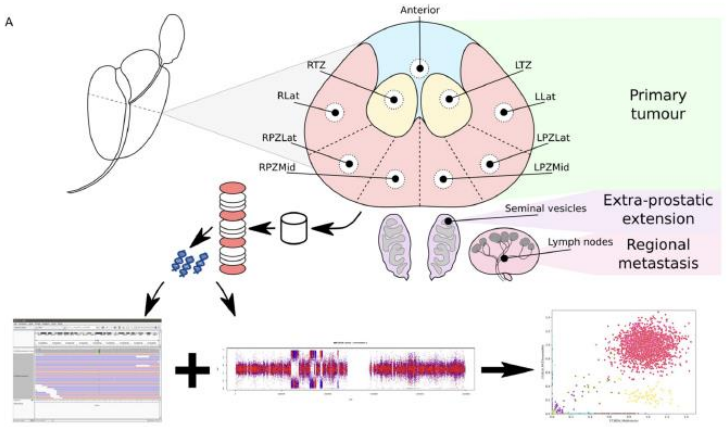


Rao et al. Genome Medicine (2024) 16:35
https://doi.org/10.1186/s13073-024-01302-x

Genome Medicine

RESEARCH Open Access

Intra-prostatic tumour evolution, steps in metastatic spread and histogenomic associations revealed by integration of multi-region whole-genome sequencing with histopathological features

Srinivasa Rao[1,5*†], Clare Verrill[1†], Lucia Cerundolo[1], Nasullah Khalid Alham[1], Zeynep Kaya[2], Miriam O'Hanlon[1], Alicia Hayes[1], Adam Lambert[1], Martha James[1], Iain D. C. Tullis[3], Jane Niederer[1], Shelagh Lovell[1], Altan Omer[1], Francisco Lopez[1], Tom Leslie[1], Francesca Buffa[3], Richard J. Bryant[1], Alastair D. Lamb[1], Boris Vojnovic[3], David C. Wedge[4], Ian G. Mills[1], Dan J. Woodcock[1], Ian Tomlinson[3] and Freddie C. Hamdy[1]

How glowing dye can help surgeons target prostate tumours

By **Colin Fernandez**
Science Correspondent

Daily Mail CAMPAIGN
END NEEDLESS PROSTATE DEATHS

SURGEONS may soon be better able to remove prostate cancer thanks to a dye that makes tumours glow.

University of Oxford experts said the dye acts as a 'second pair of eyes', lighting up cancerous tissue invisible to the naked eye.

This allows doctors to remove far more of the cancer in real time, reducing chances of the disease coming back due to cells left behind.

Cancer Research UK, which funded the scientists, said full clinical trials are under way to find out if surgery with the dye removes more prostate cancer and preserves more healthy tissue than existing surgical techniques.

In an initial study, 23 men with prostate cancer were injected with the marker dye before having surgery to remove their prostates.

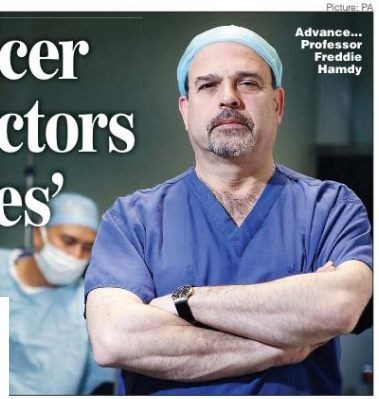
When light – white and near-infrared – was shone on the prostate and nearby regions, the fluorescent dye lit up cancer cells and where they had spread into other tissues, such as the pelvis.

Surgery professor Freddie Hamdy, from the University of Oxford and lead author of the

Dye clings to cancer cells and gives doctors 'second pair of eyes'

Exciting new hope for patients

Picture: PA



Advance... Professor Freddie Hamdy

By **Jane Kirby**

ING dye that clings to gives surgeons a "second s" in operations to eradi- ease, experts have found. nique, developed for pros- but one that could be other forms of the disease, reas of infected tissue not y the naked eye.

ws surgeons to remove far e cancer and slashes the he disease coming back.

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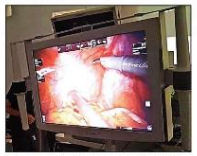

Target...dye on image during an op

where the cancer cells are and if they have spread. It's the first time we've managed to see such detail of prostate cancer in real time during surgery.

"With this technique, we can strip all the cancer away, including the cells that have spread from the tumour that could give it the chance to come back later.

"It also allows us to preserve as much of the healthy structures around the prostate as we can, to reduce unnecessary life-changing side effects, like incontinence and erectile dysfunction."

Prof Hamdy added: "We want patients to leave the operating theatre knowing that we have done everything possible to eradicate their cancer."

The technique works by combining the dye with a targeting molecule

News

Dye in cancer cells could 'fundamentally transform' surgery

Andrew Gregory
Health editor

Scientists have developed a glowing dye that sticks to cancer cells and gives surgeons a "second pair of eyes" to remove all of them in real time and permanently eradicate the disease. Experts say the breakthrough could reduce the risk of recurrence and prevent debilitating side effects.

The fluorescent dye spotlights tiny cancerous tissues that cannot be seen by the naked eye, enabling surgeons to remove every last cancer cell, which reduces the chances of recurrence while preserving healthy tissue. That could mean fewer side-effects after surgery.

The pioneering technique was developed by scientists and surgeons at the University of Oxford in collaboration with the California biotech company ImaginAb and funded by the charity Cancer Research UK.

"We are giving the surgeon a second pair of eyes to see where the cancer cells are and if they have spread," said Freddie Hamdy, a professor of surgery at Oxford. "With this technique, we can strip all the cancer away, including the cells that have spread from the tumour which could give it the chance to come back later."

In the first trial of its kind, 23 men with prostate cancer were injected with the marker dye before undergoing surgery to remove their prostates. The fluorescent dye highlighted the cancer cells and where they had spread into other tissues such as the pelvis and lymph nodes.

A special imaging system was used to shine a light on the prostate and nearby regions, making the prostate cancer cells glow. Being able to see such detail meant the surgeons could remove cancer cells while preserving healthy tissue.

The technique has been trialled in patients with prostate cancer but could be adapted to other forms of the disease. Details of the breakthrough were published today in the European Journal of Nuclear Medicine and Molecular Imaging.

"It's the first time we've managed to see such fine details of prostate cancer in real time during surgery," said Hamdy, the lead author of the ProMote study. "It also allows us to preserve as much of the healthy structures around the prostate as we can, to reduce unnecessary life-changing side-effects like incontinence and erectile dysfunction.

"Prostate surgery is life-changing. We want patients to leave the operating theatre knowing that we have done everything possible to eradicate their cancer and give them the best quality of life afterwards.

"I believe this technique makes that possibility a reality."

It works by combining the dye with a targeting molecule known as IR800 IAB2M. The dye and marker molecule attach themselves to a protein called prostate-specific membrane antigen (PSMA) found on the surface of prostate cancer cells.

David Butler, 77, a retired sales development manager from Southmoor, Oxfordshire, is cancer-free after becoming one of the 23 men to participate in the trial. Before the surgery, scans had indicated his prostate cancer had begun to spread.

Now fully recovered and healthy, Butler said he was a "lucky man" and determined to "enjoy every moment" of life. He added: "I retired early to make the most of life's pleasures, gardening, playing bowls and walking. Taking part in the ProMote study has allowed me to have many more of those pleasures for years to come."

CANCER RESEARCH UK

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Anna Wu

Independent Steering Committee:
Declan Murphy (Peter Mac, Melbourne)
Henk van der Poel (NKI, Netherlands)
Neil Bander (Columbia, NY)
Constantin Coussios (Oxford, Chair)

Our participants

CANC
RESEA
UK

Q&A session

Chair summary

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Thank you!