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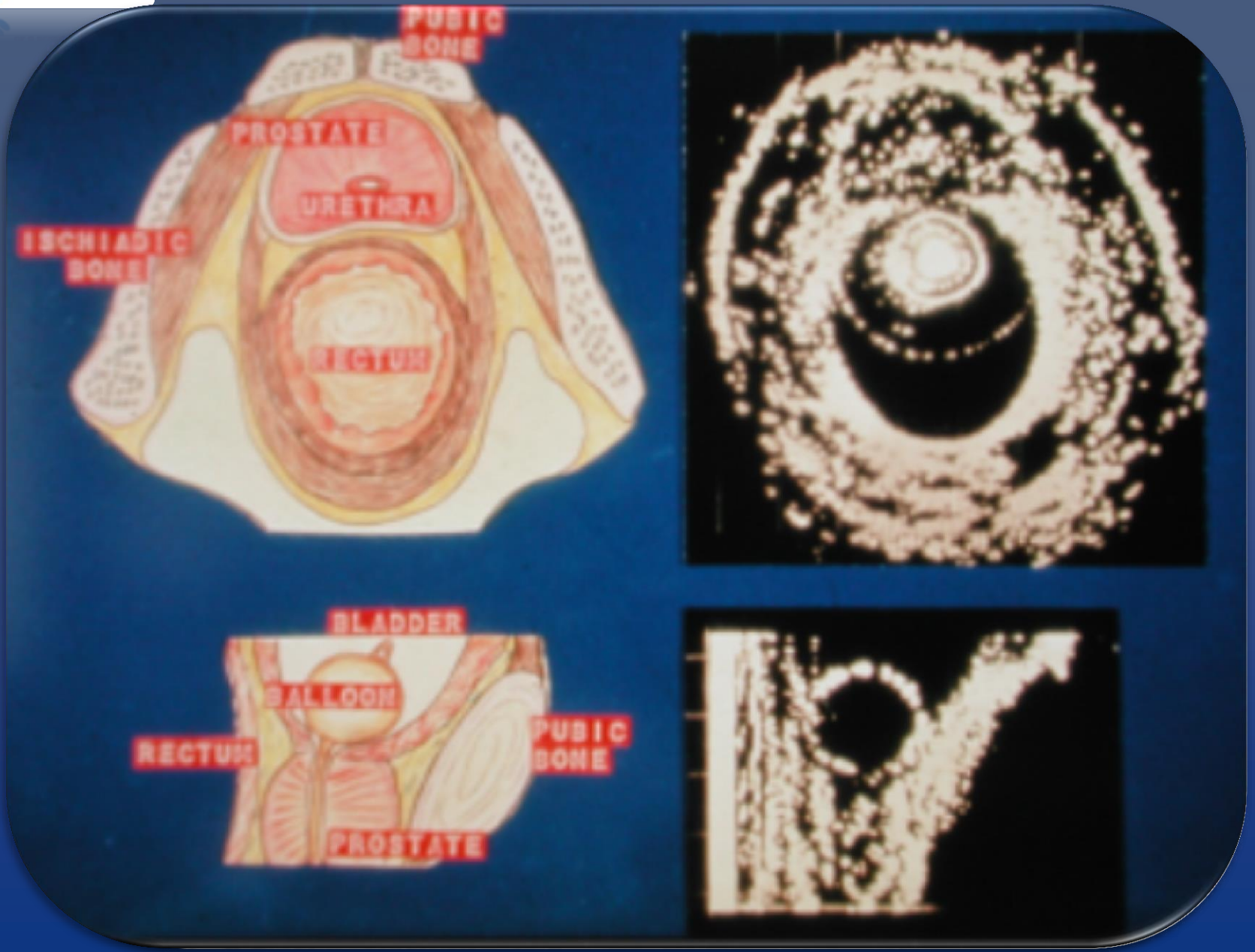
UK & Ireland Conference 2017

Brachytherapy Imaging Update

Brendan Carey

Leeds

Belfast 2017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PROSTATE

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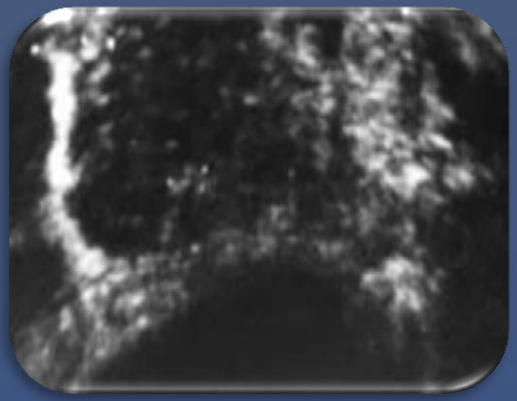
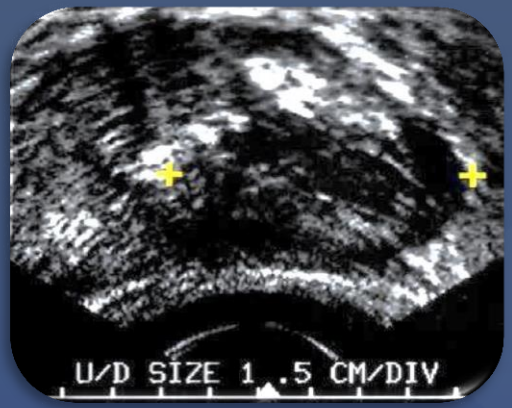
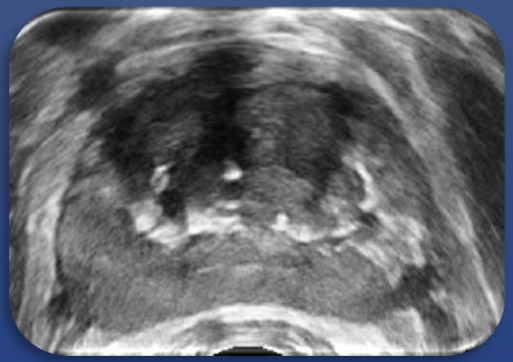
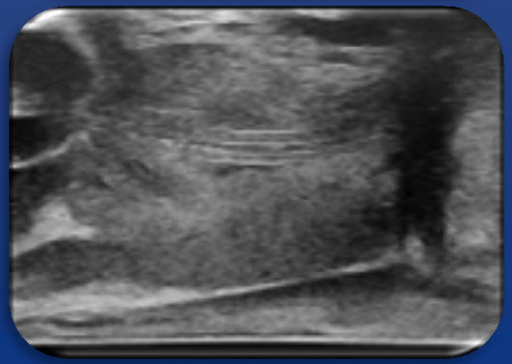
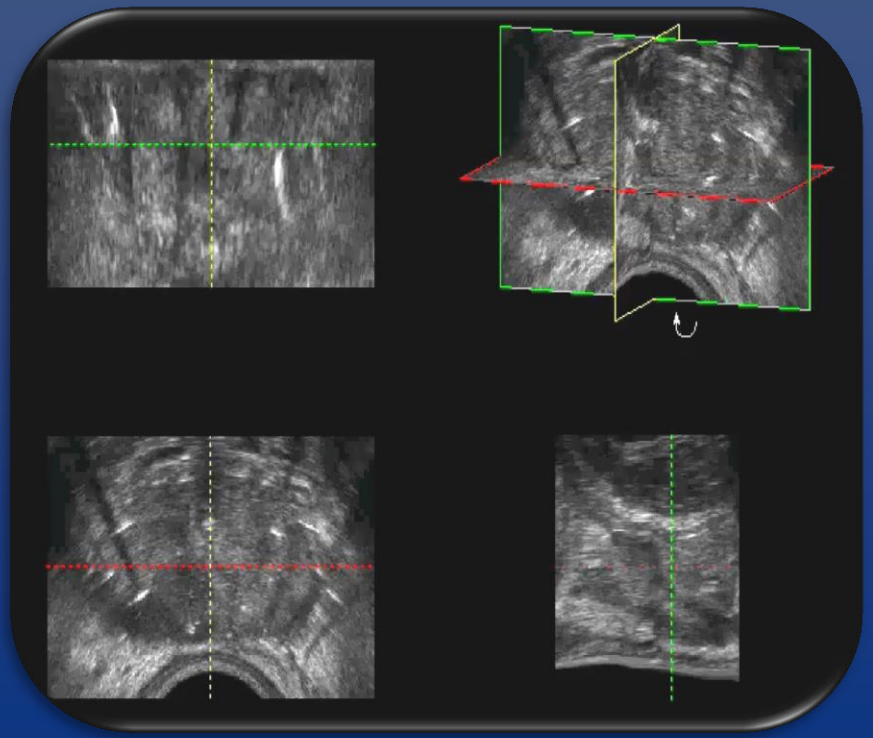


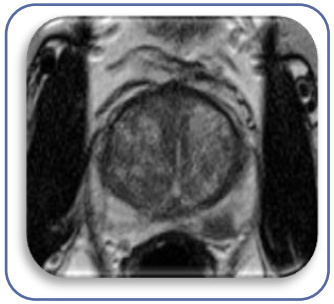


2017

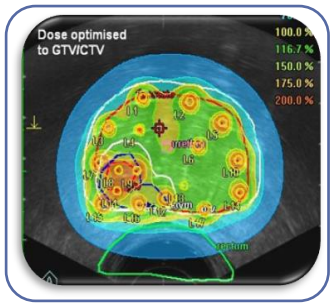




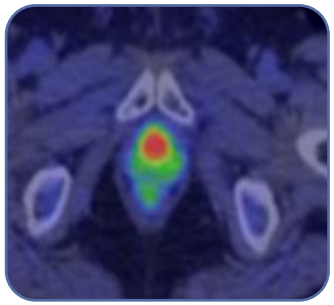




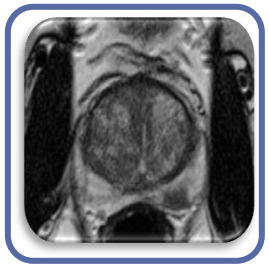
Imaging for Patient Selection



Tumour Location for Boost / Focal Brachytherapy



Recurrence Detection & Salvage Brachytherapy



Imaging for Patient Selection

- **More Accurate Tumour Staging**

- **Treatment stratification**
  - *LDR or HDR*
  - *Monotherapy or Boost*
  - *Focal Boost or Whole gland Boost*
  - *Focal Monotherapy*
  - *Dose modulation*
  - *Salvage*

- **More Accurate Tumour Staging**
- **Treatment stratification**
  - *LDR or HDR*
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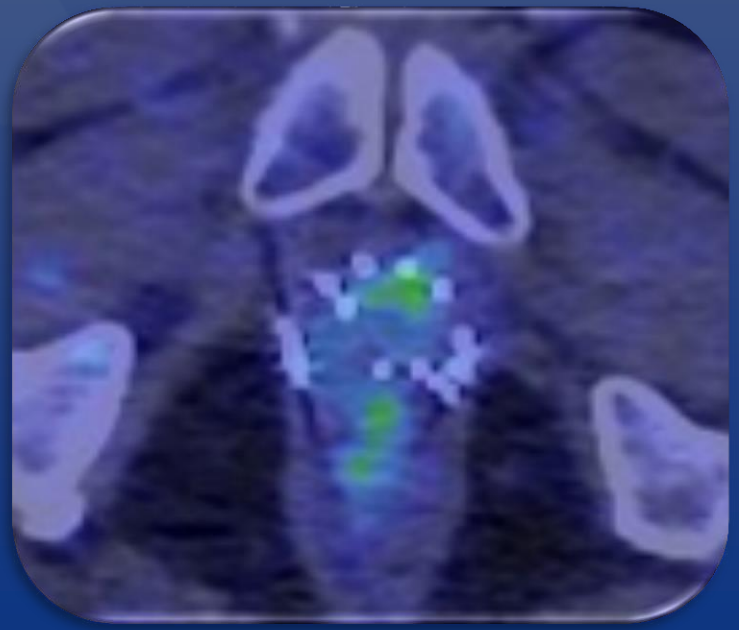
  - *Focal Boost or Whole gland Boost*
  - *Dose modulation*
  - *Salvage*

- Multiparametric MRI
- Multiparametric TRUS
- PET CT



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Multiparametric MRI : Brachytherapy
Can we locate cancer ?

EUROPEAN UROLOGY 68 (2015) 1045–1053

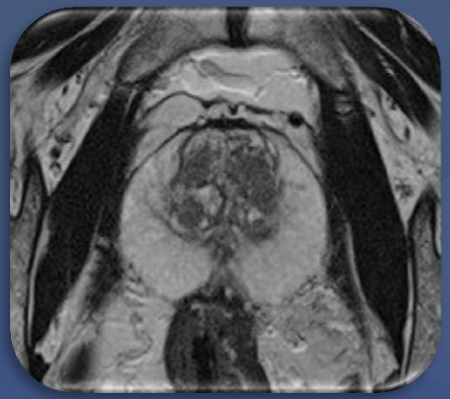
available at www.sciencedirect.com
journal homepage: www.europeanurology.com

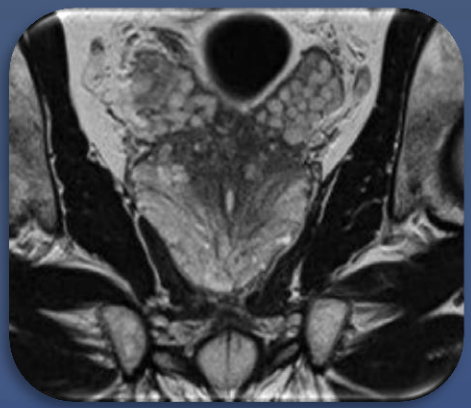
European Association of Urology

Collaborative Review – Prostate Cancer

Can Clinically Significant Prostate Cancer Be Detected with Multiparametric Magnetic Resonance Imaging? A Systematic Review of the Literature

Jurgen J. Fütterer[a,], Alberto Briganti[b], Pieter De Visschere[c], Mark Emberton[d], Gianluca Giannarini[e], Alex Kirkham[f], Samir S. Taneja[g], Harriet Thoeny[h], Geert Villeirs[c], Arnauld Villers[i]*





The negative predictive value for exclusion of significant disease ranged from 63% to 98%

Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study

Hashim U Ahmed, Ahmed El-Shater Bosaily*, Louise C Brown*, Rhian Gabe, Richard Kaplan, Mahesh K Parmar, Yolanda Collaco-Moraes, Katie Ward, Richard G Hindley, Alex Freeman, Alex P Kirkham, Robert Oldroyd, Chris Parker, Mark Emberton, and the PROMIS study group†*

Summary

Background Men with high serum prostate specific antigen usually undergo transrectal ultrasound-guided prostate biopsy (TRUS-biopsy). TRUS-biopsy can cause side-effects including bleeding, pain, and infection. Multi-parametric magnetic resonance imaging (MP-MRI) used as a triage test might allow men to avoid unnecessary TRUS-biopsy and improve diagnostic accuracy.

Lancet 2017; 389: 815–22
Published Online
January 19, 2017
http://dx.doi.org/10.1016/S0140-6736(16)32401-1

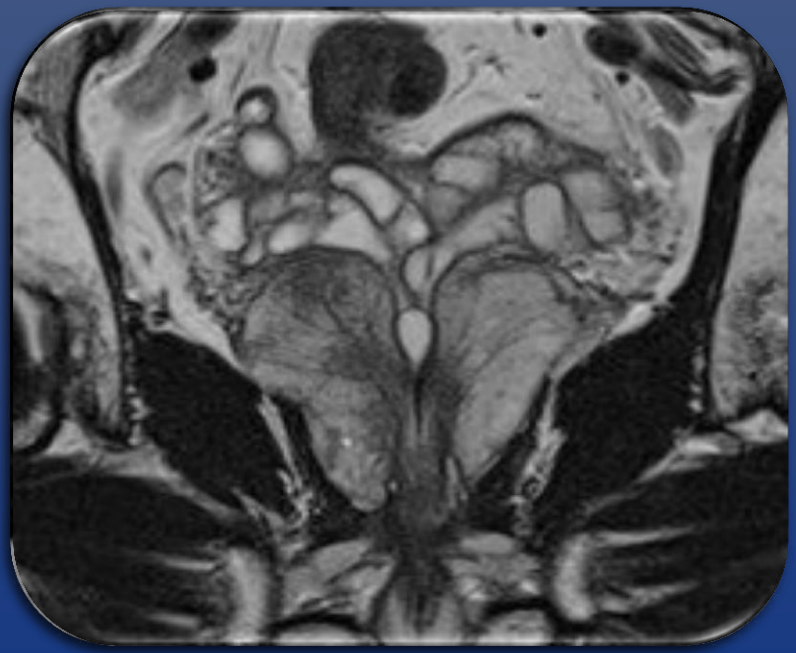
Any Gleason score 7 (≥3+4), prevalence of clinically significant cancer 308 (53%, 49–58%)

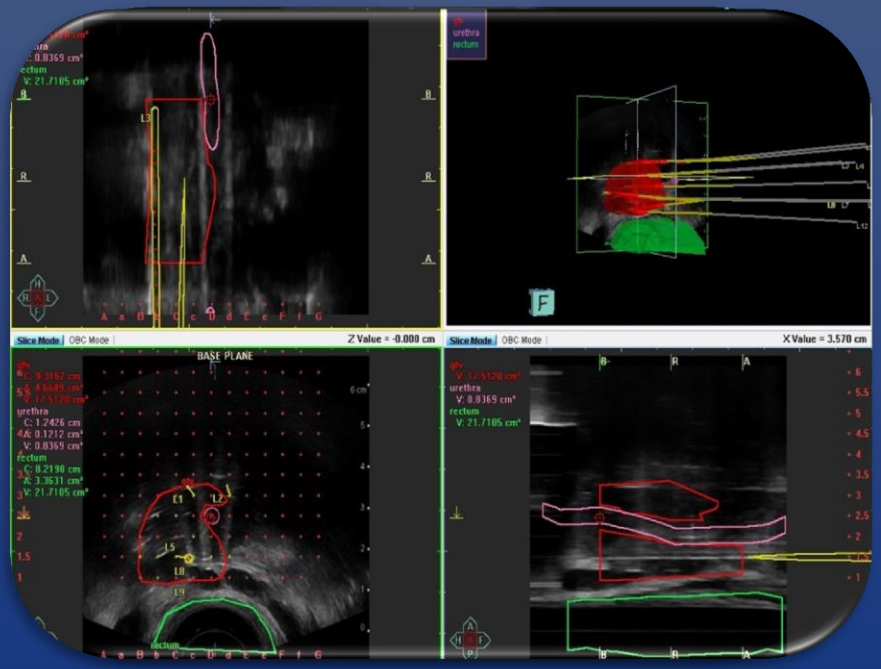
Sensitivity test	88 (84–91)	48 (43–54)	0·55 (0·49–0·62)	p<0·0001
Specificity test	45 (39–51)	99 (97–100)	2·22 (1·94–2·53)	p<0·0001
PPV	65 (60–69)	99 (95–100)	40·8 (10·2–162·8)	p<0·0001
NPV	76 (69–82)	63 (58–67)	0·53 (0·38–0·73)	p<0·0001

Prevalence of disease on TPM-biopsy, N (%, 95% CI) *McNemar test to compare sensitivity and specificity present ratio of proportions. TPM-biopsy=template prostate mapping biopsy. MP-MRI=multi-parametric-MRI. TRUS-biopsy=transrectal ultrasound-guided prostate biopsy. PPV=positive predictive value. NPV=negative predictive value. General Estimating Equation logistic regression model to compare PPV and NPV present odds ratios. All ratios presented as TRUS relative to MRI.

Table: **Diagnostic accuracy of TRUS-biopsy and MP-MRI in the detection of clinically significant prostate cancer using alternative secondary definitions of clinically significant cancer**

- **More Accurate Tumour Staging**
- **Treatment stratification**
  - *LDR or HDR*
  - *Monotherapy or Boost (Focal or Whole Gland)*
  - *Focal Boost or Whole gland Boost*
  - *Dose modulation*
  - *appropriate for salvage*





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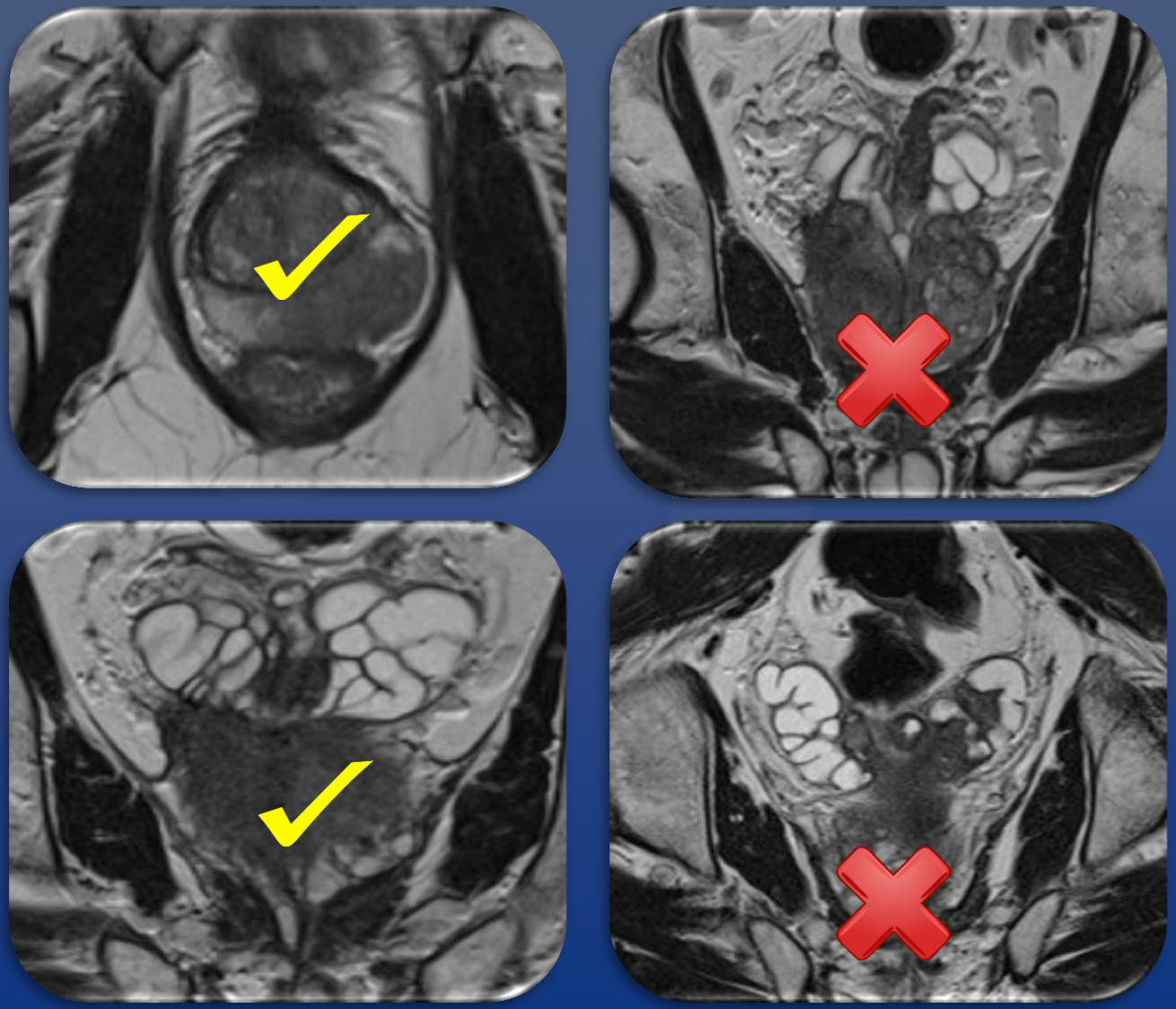
Extent of T3 tumour : is HDR Brachytherapy feasible ?



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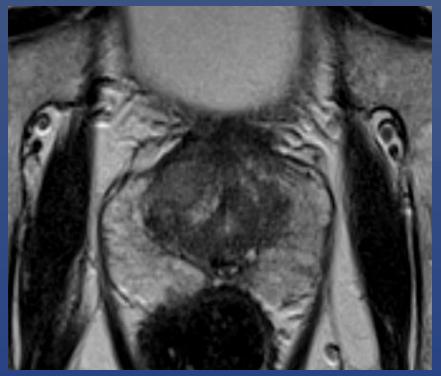
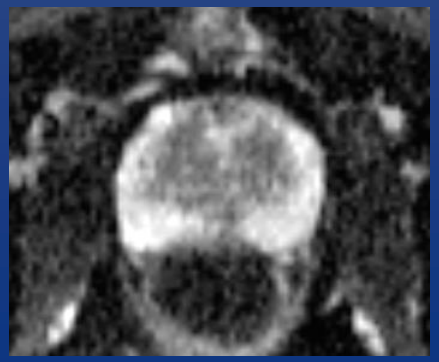
Textural Analysis

? Better GTV definition for Brachytherapy

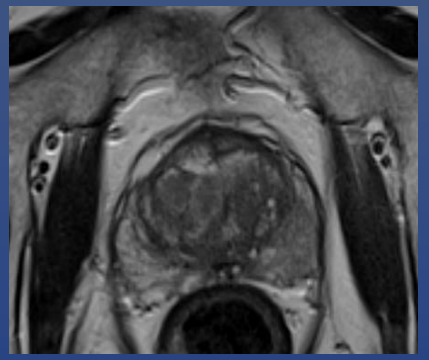
Texture analysis is a technique for the quantification of image texture

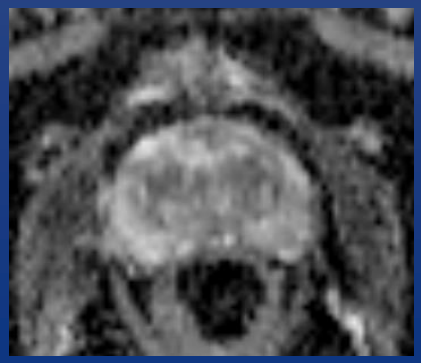
Can be used in MRI as a computer-aided diagnostic tool for the quantification of the intrinsic heterogeneity of prostate tissue imperceptible to the human eye





- **Texture analysis describes a wide range of techniques for quantification of grey-level patterns on MRI images**
- **Potential for dose modulation with Brachytherapy**





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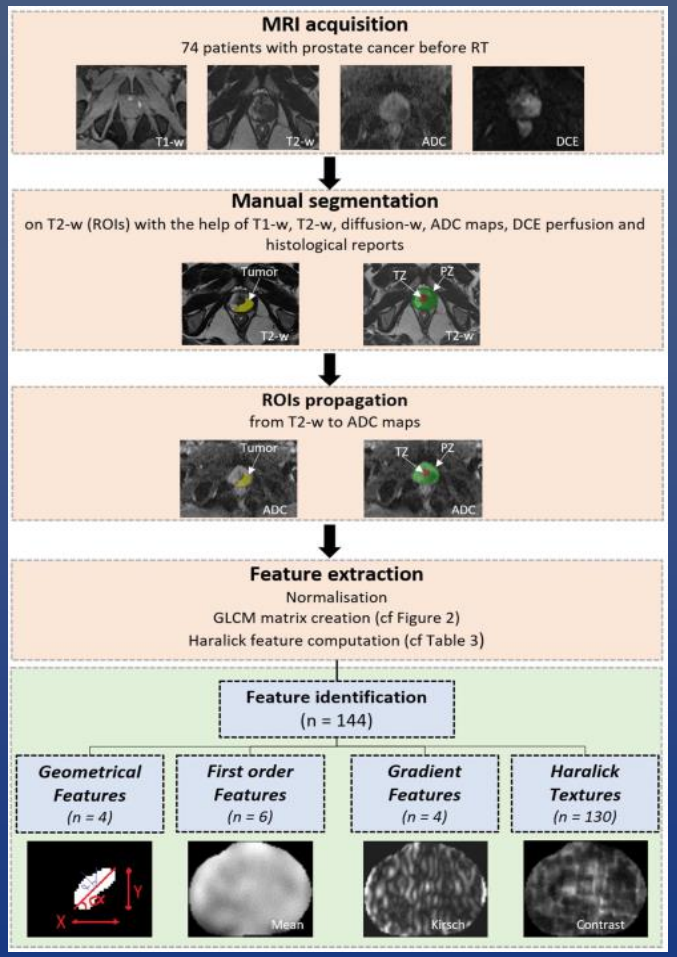
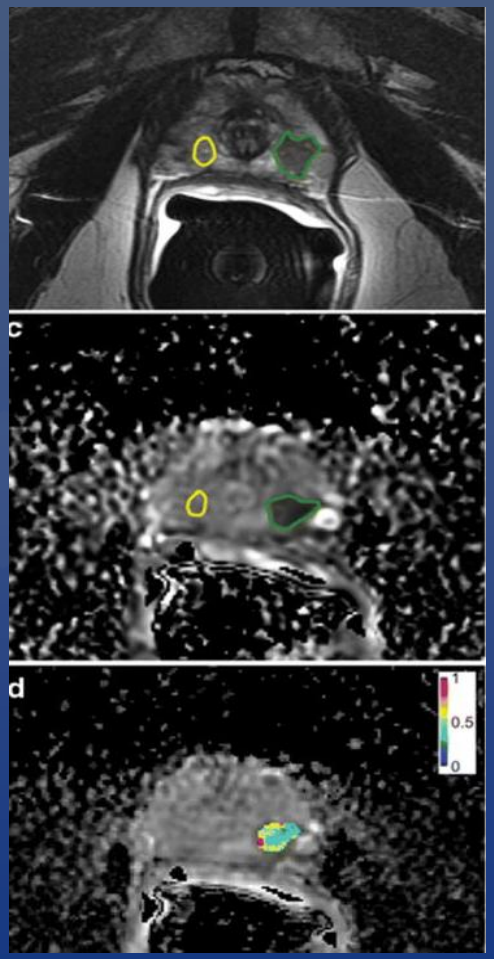
MRI *T2* Haralick textural features, along with geometrical parameters, were shown to be strongly associated with biochemical recurrence following radiotherapy, particularly in the high-risk prostate cancer group





Gnep 2017 *JMRI*
Wibner 2015 *Eur Urol*

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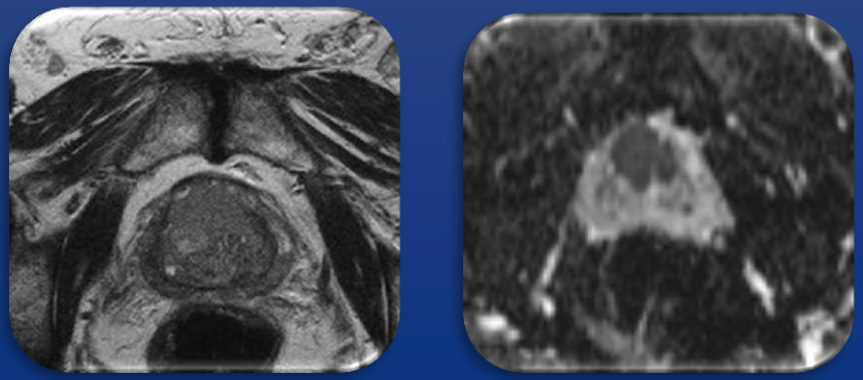
Diffusion MRI
role in Brachytherapy

measures the mobility of protons within tissue at cellular level

mediated by the volume fraction of water in the intra/extra-cellular compartments

sensitive marker for alterations in tumour cellularity and the early assessment of treatment response

locate the Dominant Cancer
Boost / Monotherapy (LDR /HDR)



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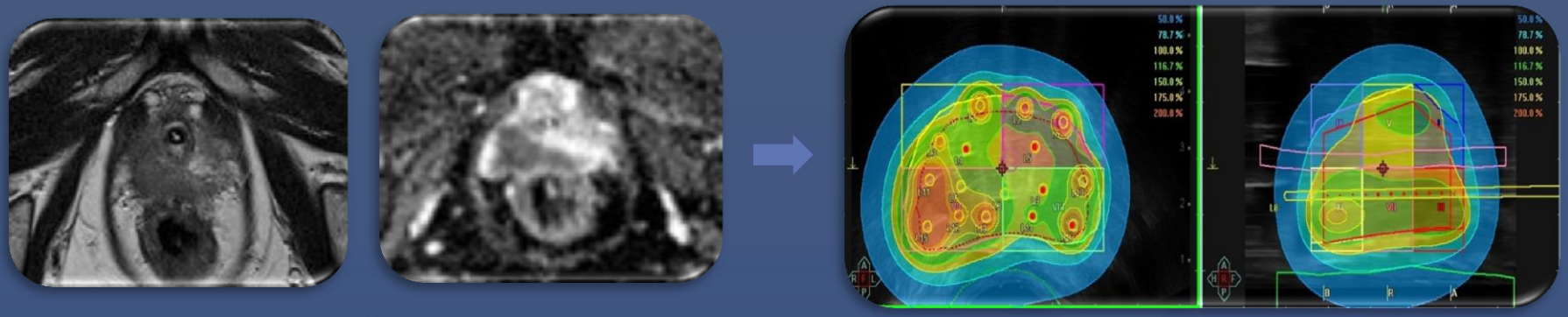
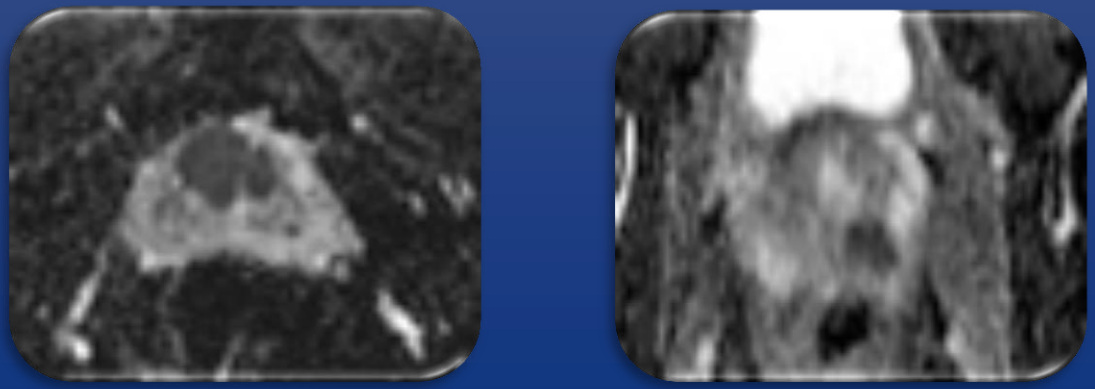
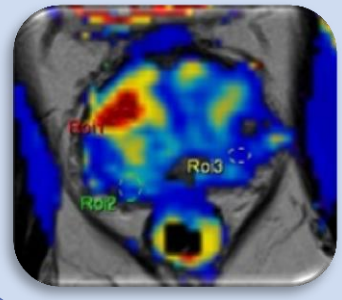
Brachytherapy can deliver intentionally non-uniform dose distributions to the target volume



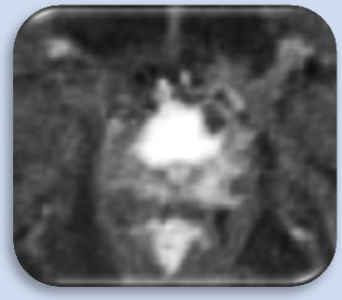
Better OAR sparing may be possible to combine dose escalation to primary tumour with dose de-escalation to areas of the prostate where no macroscopic tumour is visible





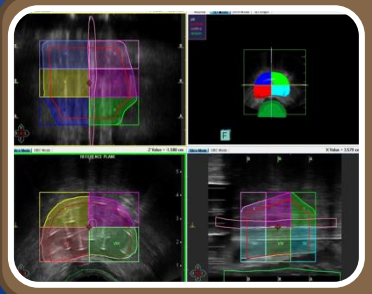
Tumour heterogeneity is one of the most important factors in tumour progression and recurrence after therapy

- Subvolumes within the CTV can be identified reflecting hypoxic tissue which may benefit from higher / modulated RT doses



Multiparametric imaging can identify hypoxic elements within the tumour which can be imported into a brachytherapy planning system

- DCE /BOLD MRI and DWI can be used to identify hypoxic subvolumes and areas of necrosis



Dose painting as a non-uniform dose distribution is a feasible strategy in brachytherapy

- The ultimate goal of dose painting is to achieve dose escalation within the relatively resistant biological subvolumes

Hoskin 2015 *Acta Oncologica*

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Radiotherapy and Oncology 121 (2016) 310–315

Contents lists available at ScienceDirect

Radiotherapy and Oncology

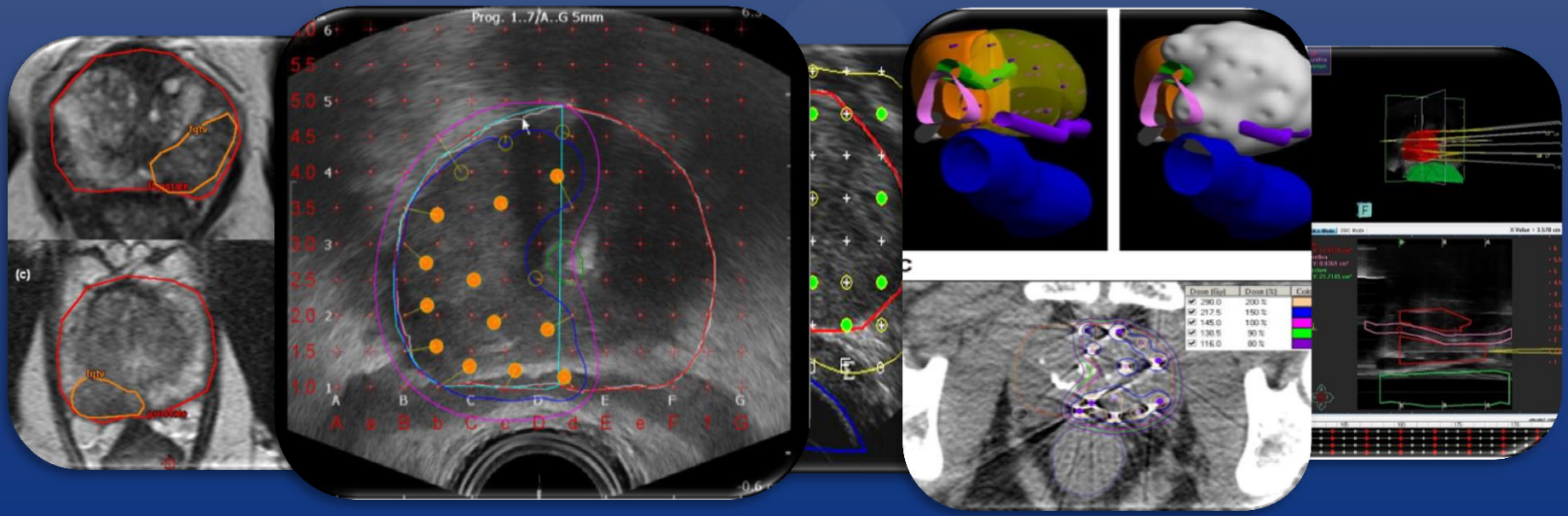
journal homepage: www.thegreenjournal.com

Prostate brachytherapy

Hemi-gland focal low dose rate prostate brachytherapy: An analysis of dosimetric outcomes

Robert Laing*, Adrian Franklin, Jennifer Uribe, Alex Horton, Santiago Uribe-Lewis, Stephen Langley

St. Luke's Cancer Centre, Guildford, UK



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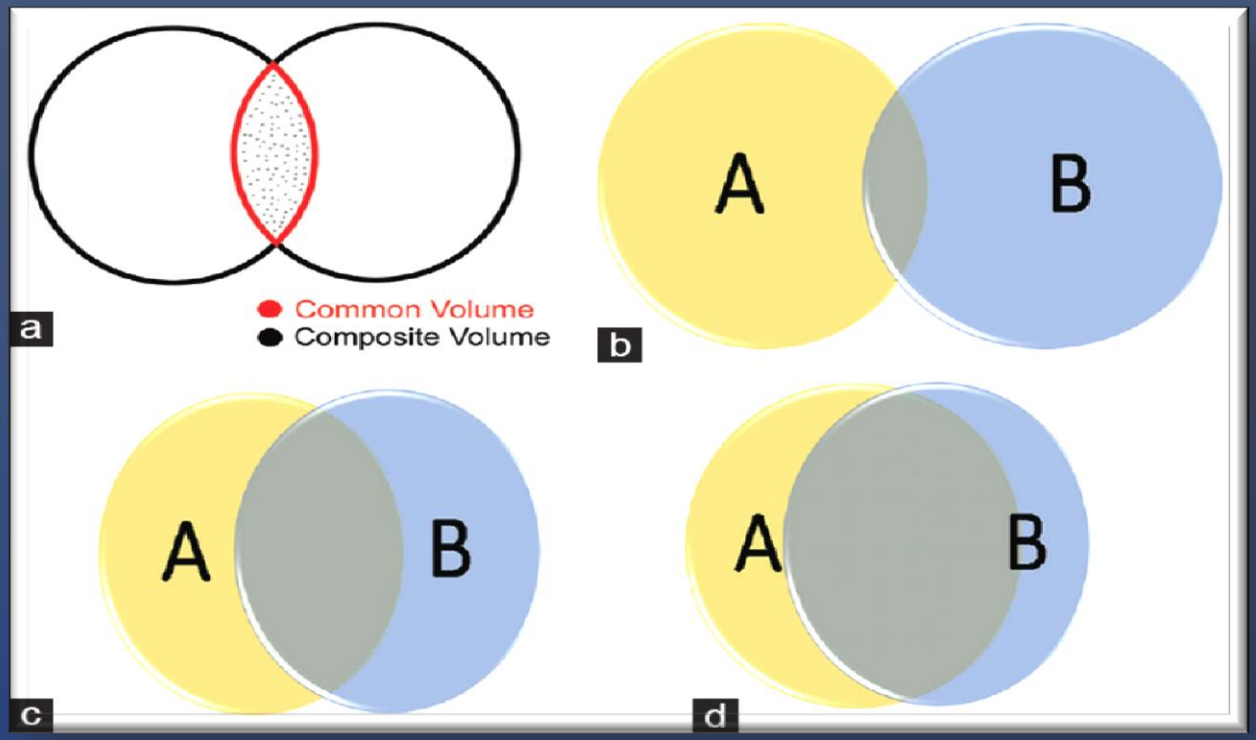
Dealing with overlapping data from mpMRI
- defining the Target



The ratio of the common and composite volume is designated as the Concordance Index

The Overlap is evaluated as the Dice Similarity Coefficient

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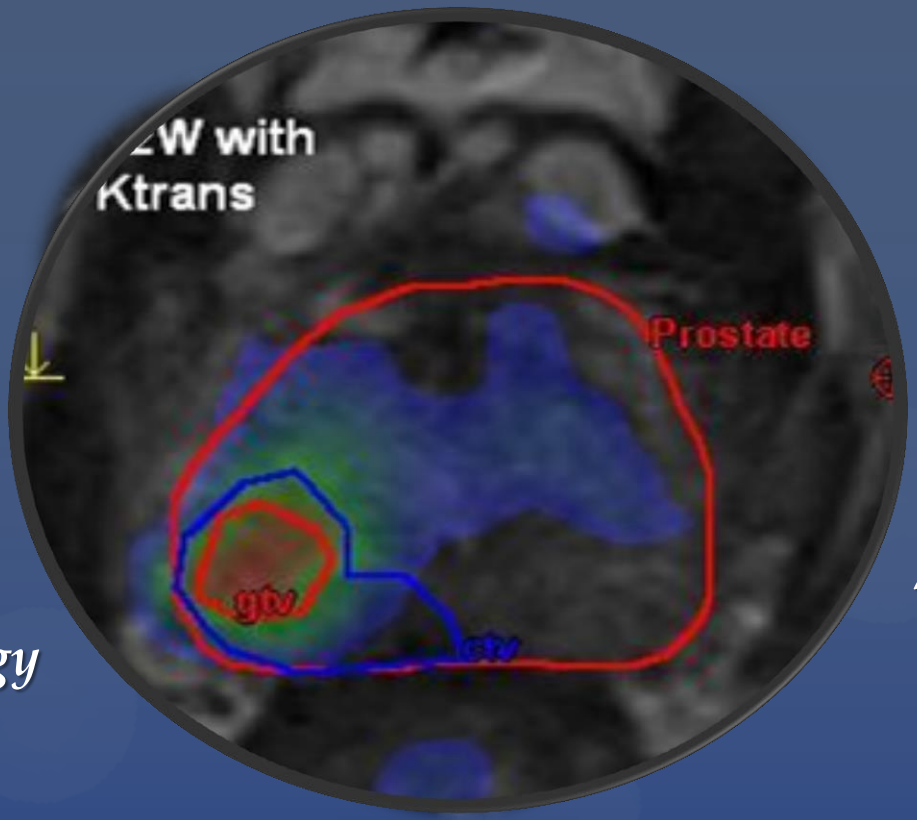
Combining
abnormal anatomy
+
abnormal physiology



What is the true "Tumour Target" ?

Concordance Index

Dice Similarity Coefficient

- volume metrics

- still need a measure of dimension / shape / surface variation

Metric error

- poor sensitivity

-outliers

-class imbalance

-agreement by chance

Basis for Image Registration/Fusion for Brachytherapy Planning

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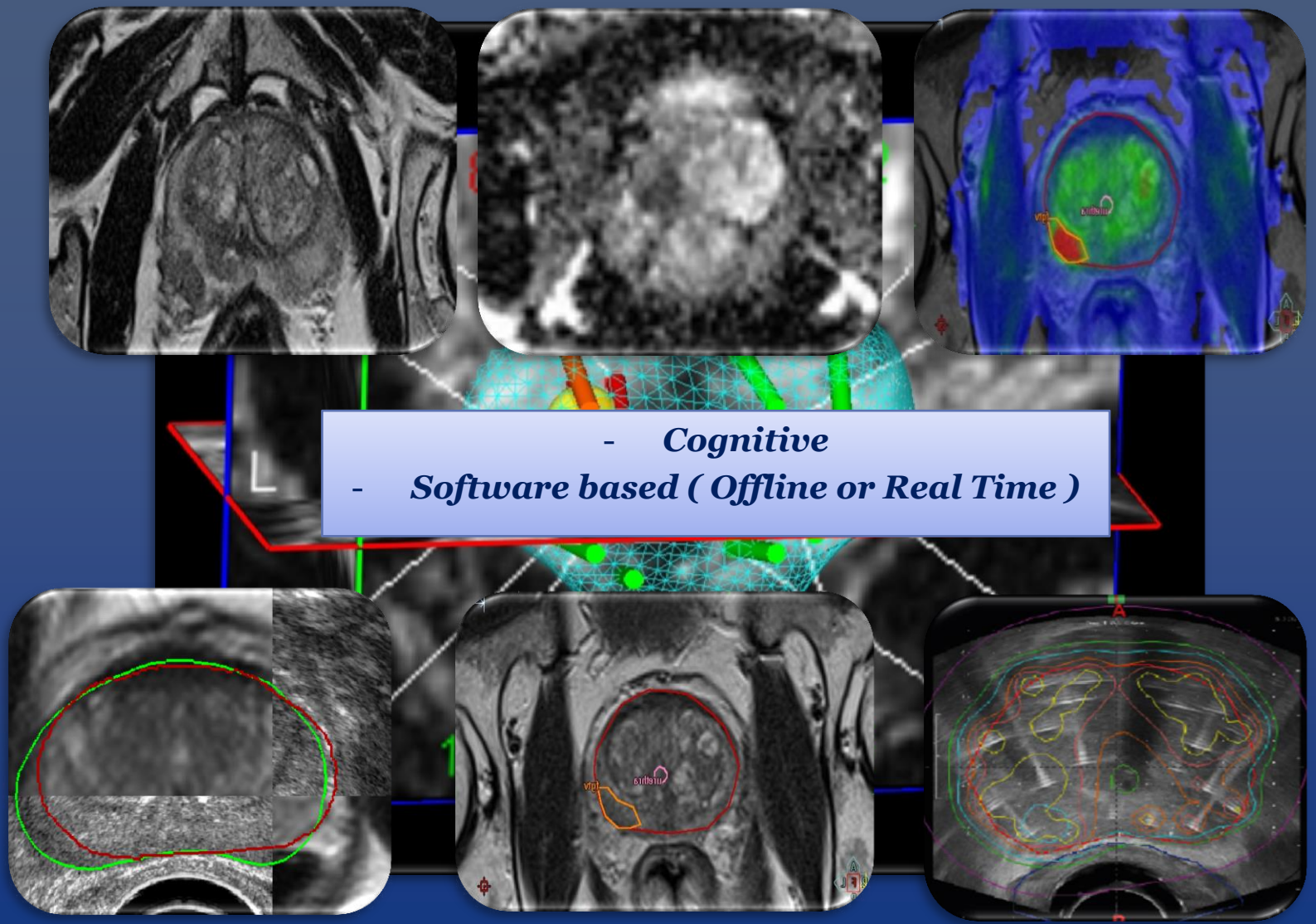
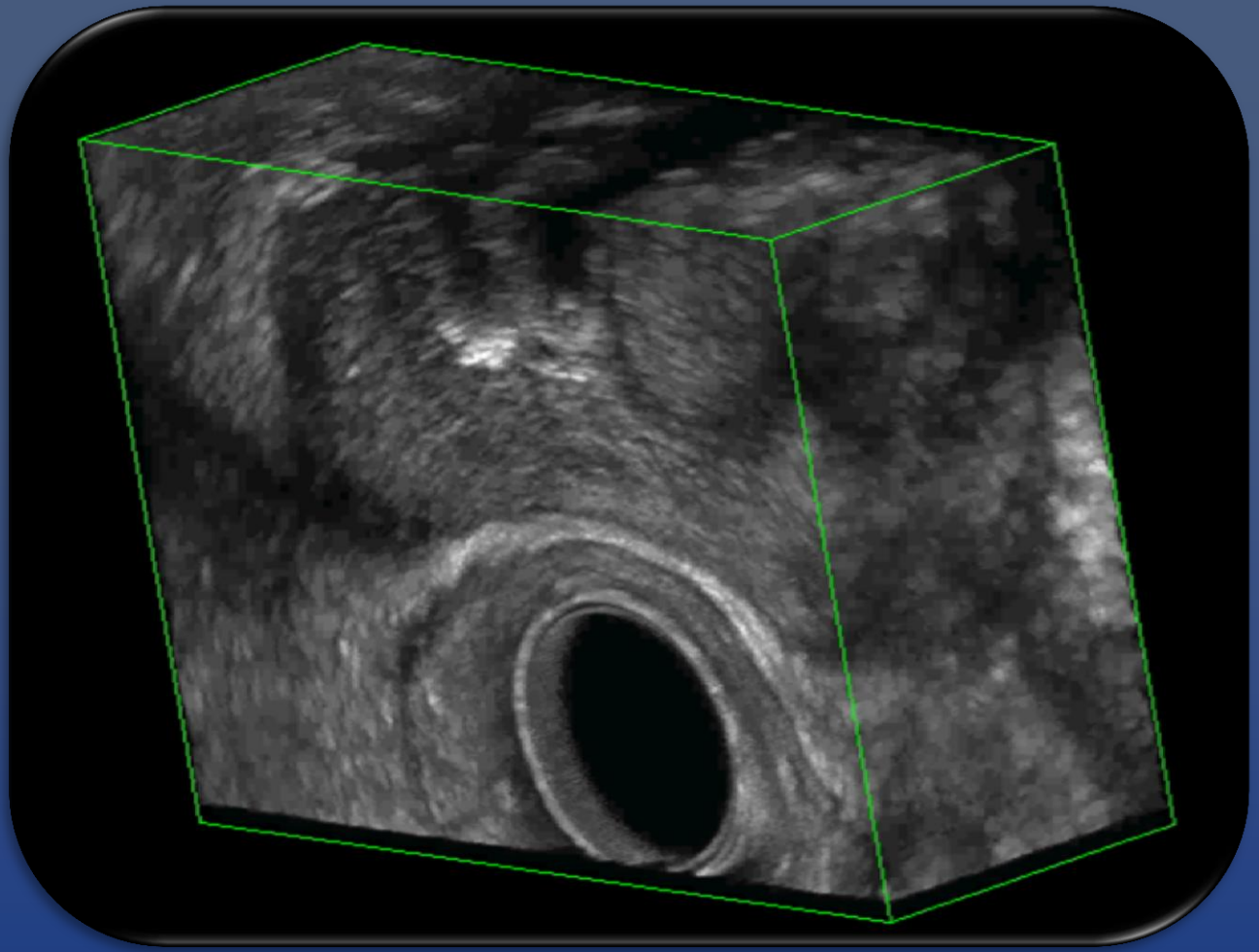
Medical Image Fusion for Brachytherapy



- ***Cognitive***
- ***Software based (Offline or Real Time)***



Conventional TRUS mode imaging has limited sensitivity and specificity between 40 to 50% for cancer detection

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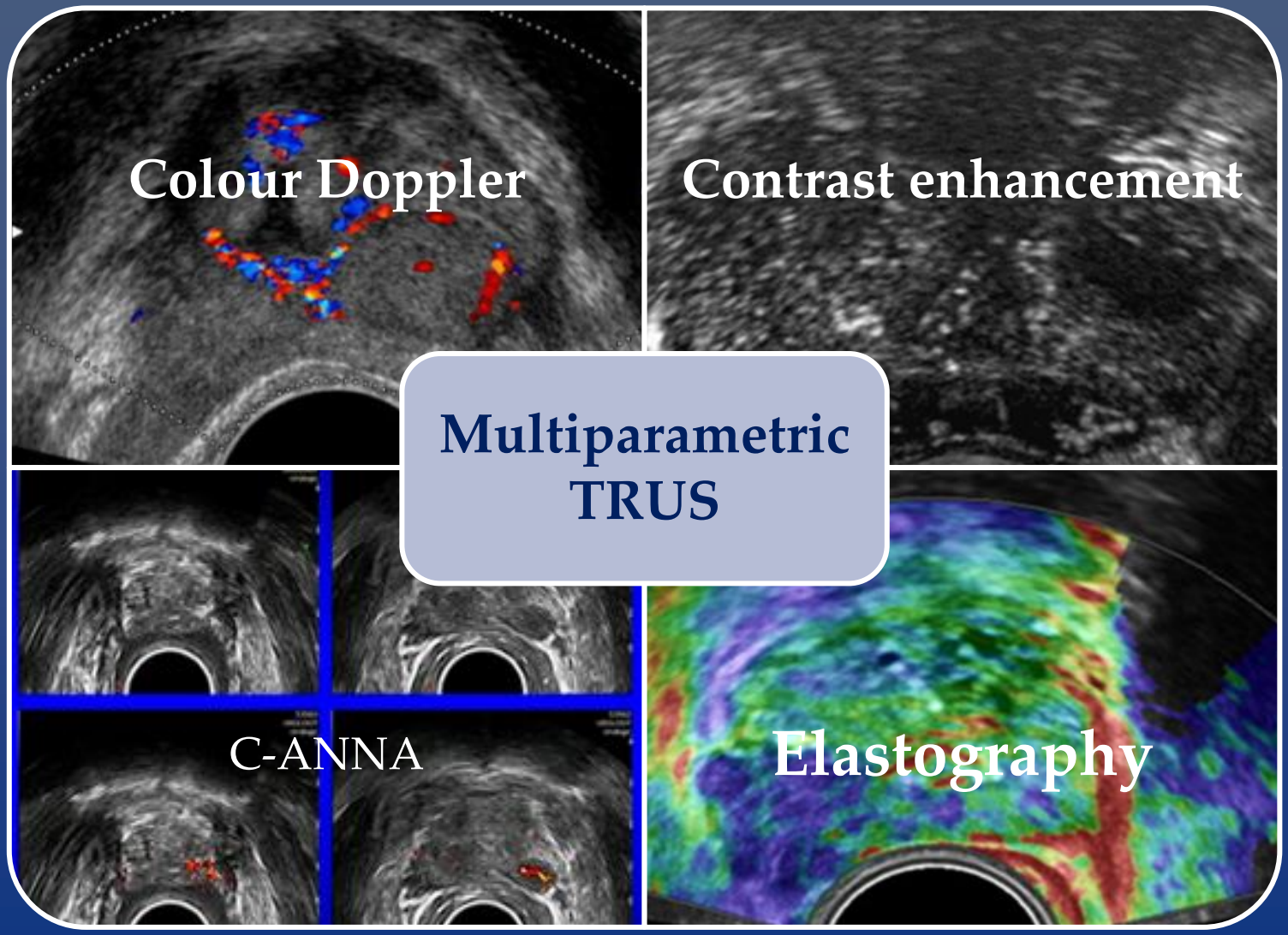
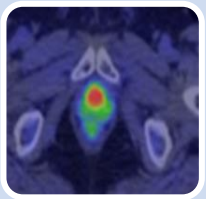
Identify the Dominant Cancer with TRUS
- Focal / Boost therapy





Recurrence Detection & Salvage Brachytherapy

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New Nuclear-Imaging Tests Show Promise in Locating Cancer

New tests could lead to more accurate prognosis and treatment of prostate cancer

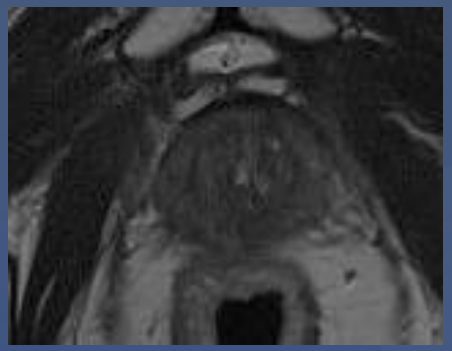
Axumin imaging at work, showing areas of cancer in red.

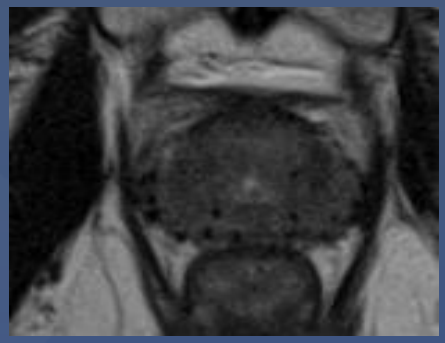
Data on salvage brachytherapy after primary brachytherapy is extremely limited

Much of the data in the current literature comes from patients that were included in series treated with primary EBRT

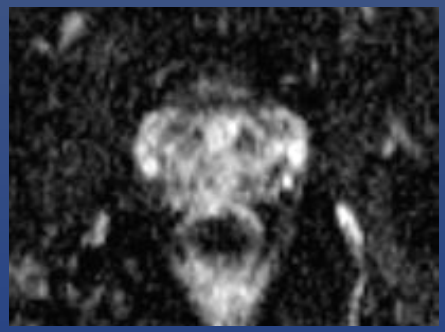
MRI post Radiotherapy

- The prostate and seminal vesicles show decreased size and diffusely decreased signal on T2
- Loss of zonal architecture

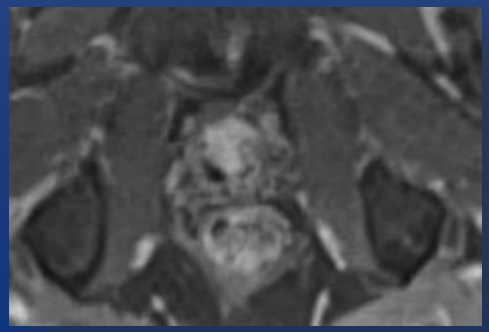




- The significant difference in ADC values between tumour and benign tissues before radiotherapy may disappear after radiotherapy



- DCE is a critical sequence to detect recurrence following radiotherapy



BioMed Research International 2014
Barchetti

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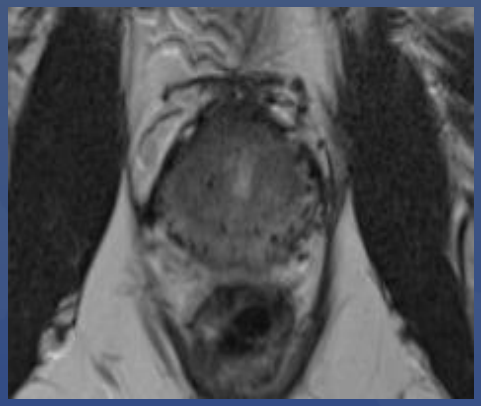
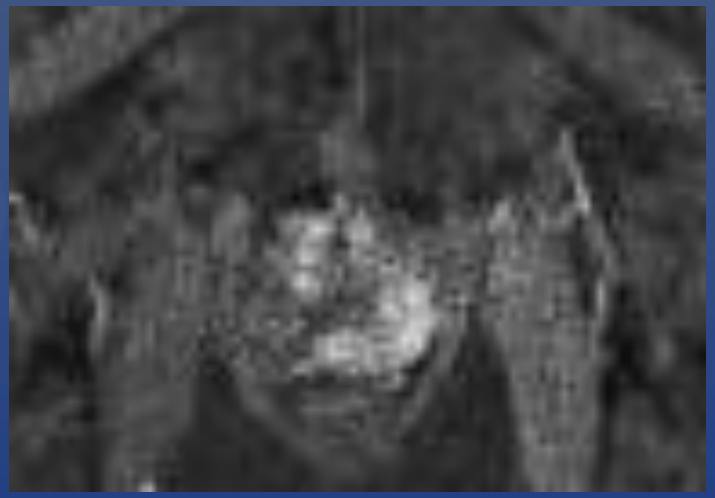
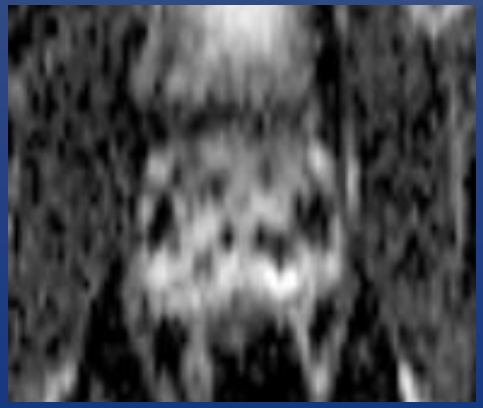
DWI is particularly suboptimal following LDR brachytherapy because the metallic seed implants may create susceptibility artefacts and image distortion



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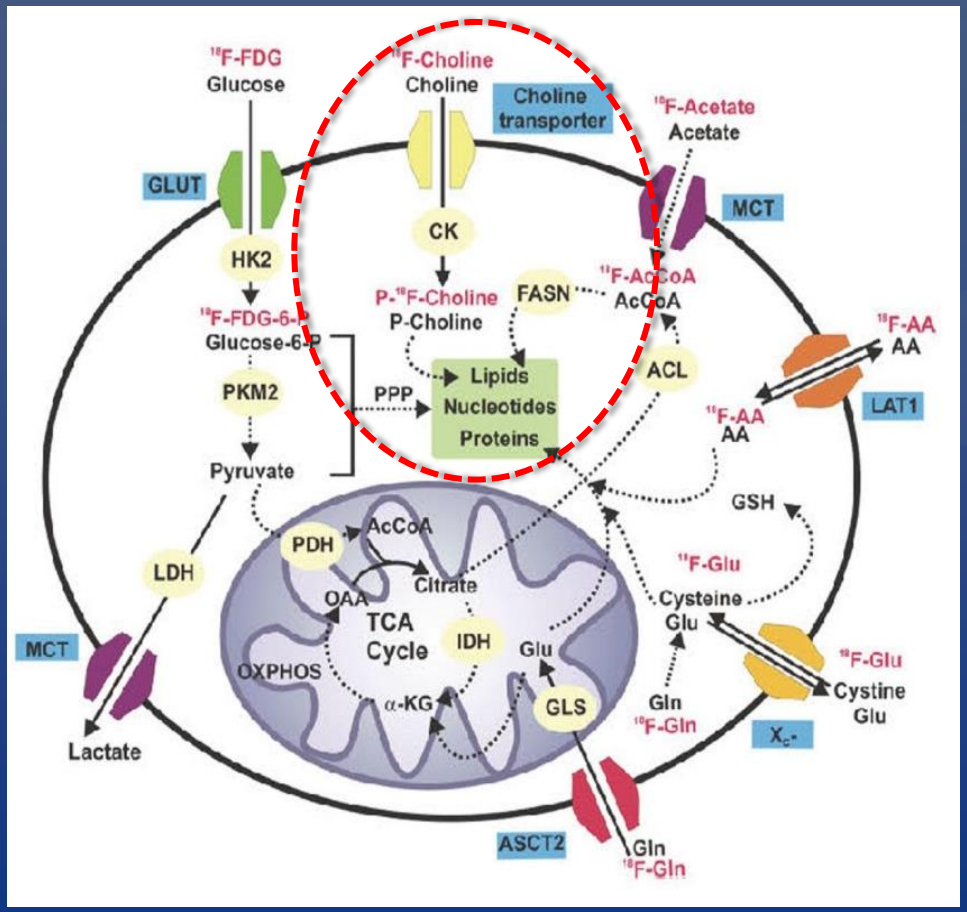
Molecular imaging for Prostate Cancer

- *increased metabolic needs of cancer cells*
- *tumour-specific expression of androgen receptors and membrane protein*
- *osteoblastic reaction adjacent to bone metastases.*



Choline is the precursor for the biosynthesis of phospholipids in the cell membrane and enters the cell through choline transporters

Choline uptake by prostate cancer cells appears to be influenced by their sensitivity to and the presence of androgens

18F-FCH PET/CT is useful to detect recurrence or metastases in patients with rising PSA

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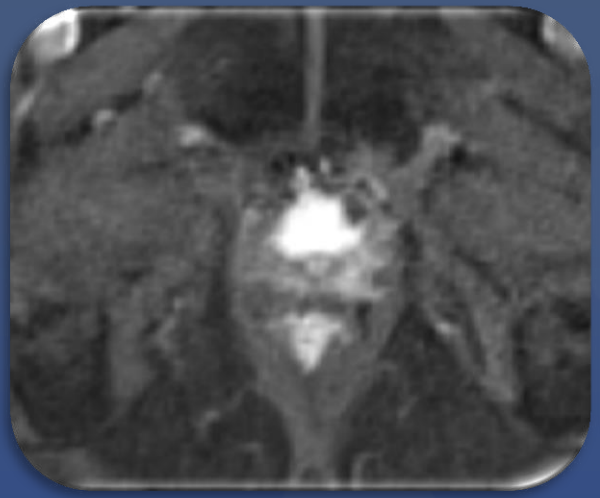
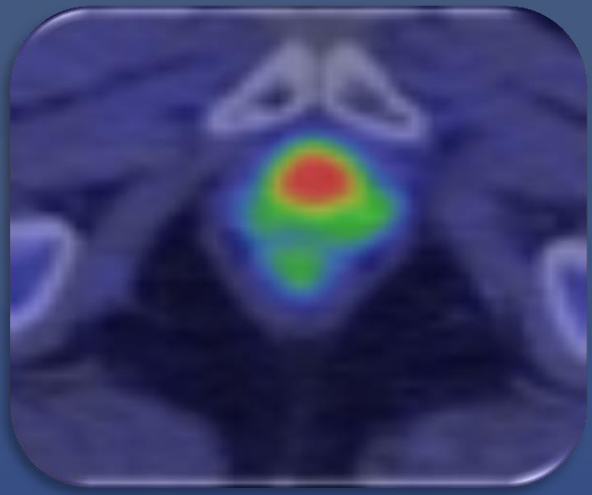
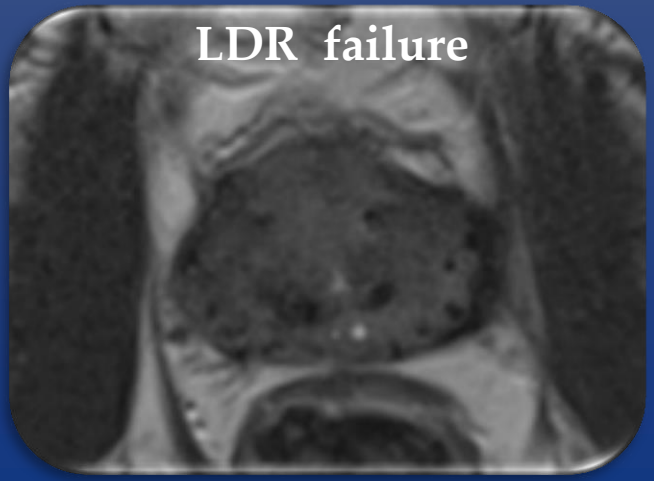
Molecular Imaging in patient selection for salvage brachytherapy

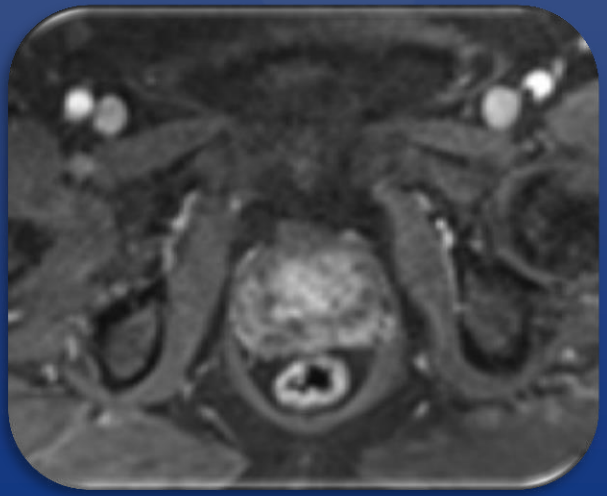
EBRT failure

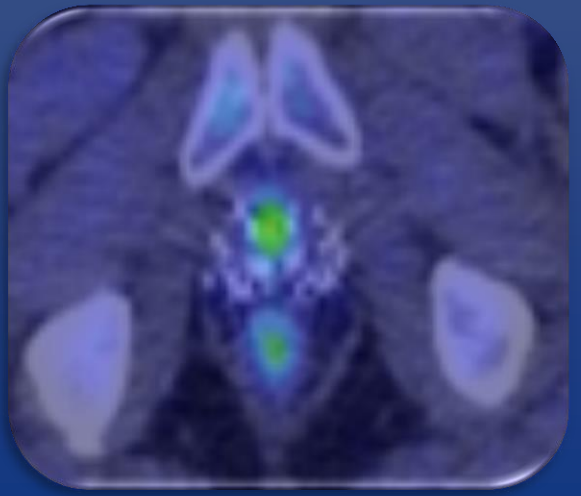


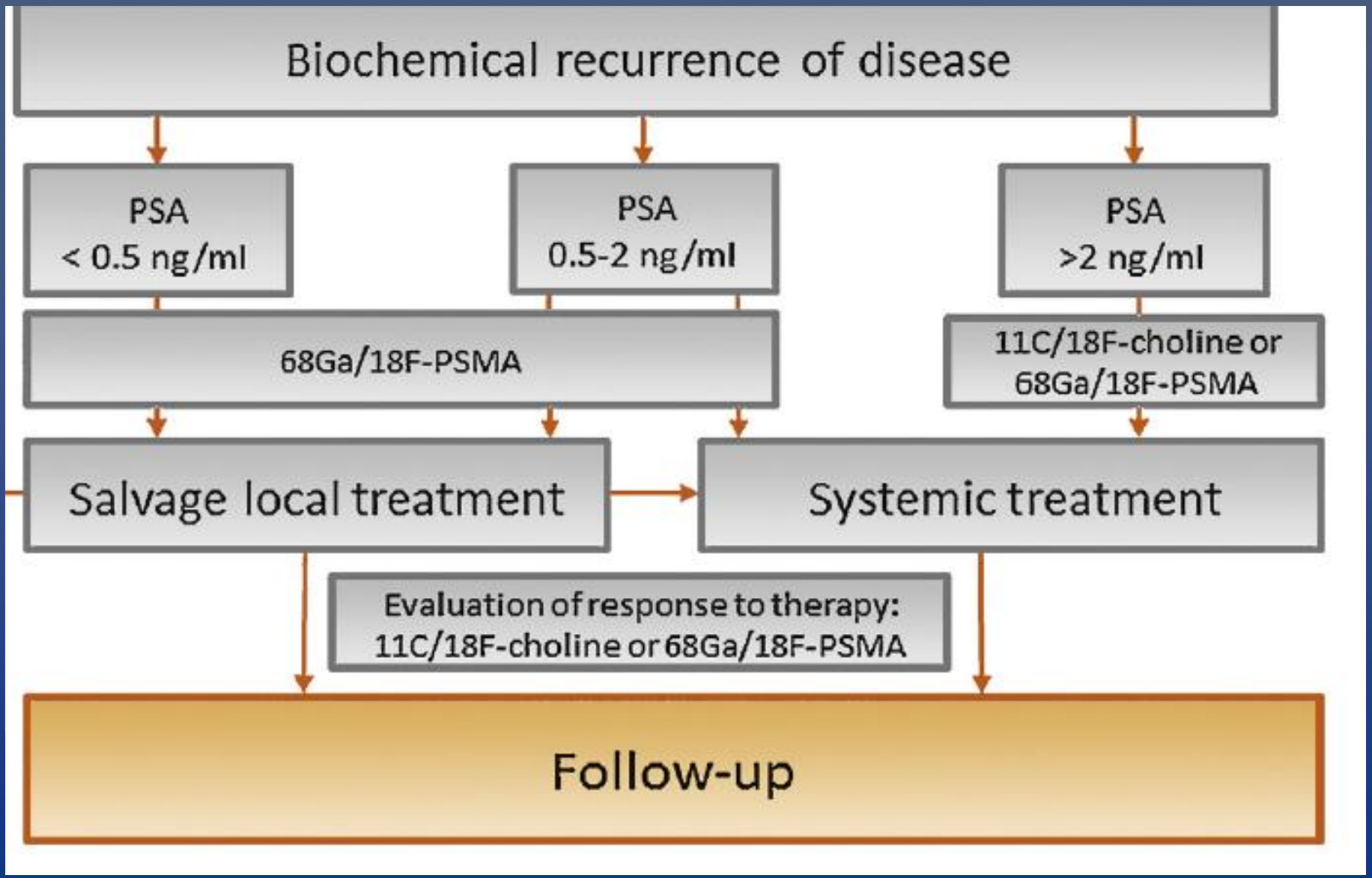


LDR failure








Biochemical recurrence of disease
PSA < 0.5 ng/ml
PSA 0.5-2 ng/ml
PSA >2 ng/ml
68Ga/18F-PSMA
11C/18F-choline or 68Ga/18F-PSMA
Salvage local treatment
Systemic treatment
Evaluation of response to therapy: 11C/18F-choline or 68Ga/18F-PSMA
Follow-up

All Sites of Prostate Cancer Recurrence

Choline PET/CT is reported to have a high sensitivity (86%) and specificity (93%) in the findings from a meta-analysis, with 18F-choline performing slightly better than 11C-choline

EUROPEAN UROLOGY 70 (2016) 161–175

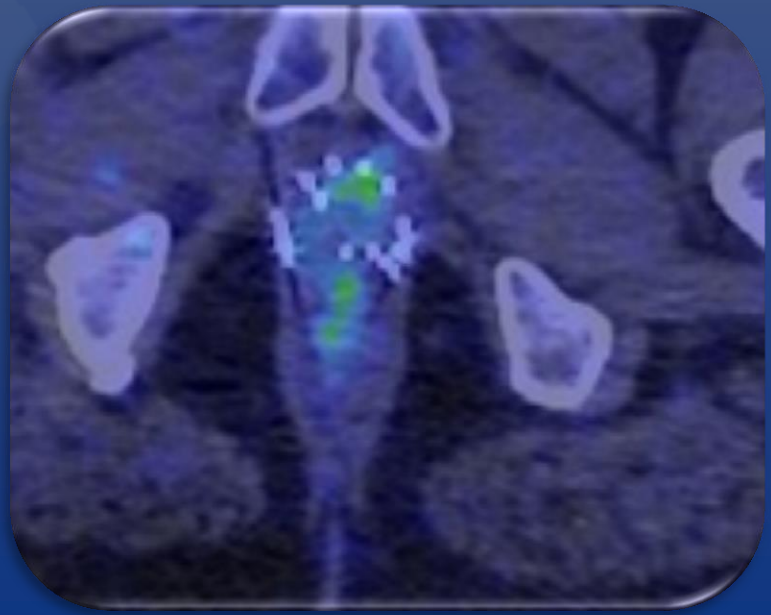
available at www.sciencedirect.com
journal homepage: www.europeanurology.com

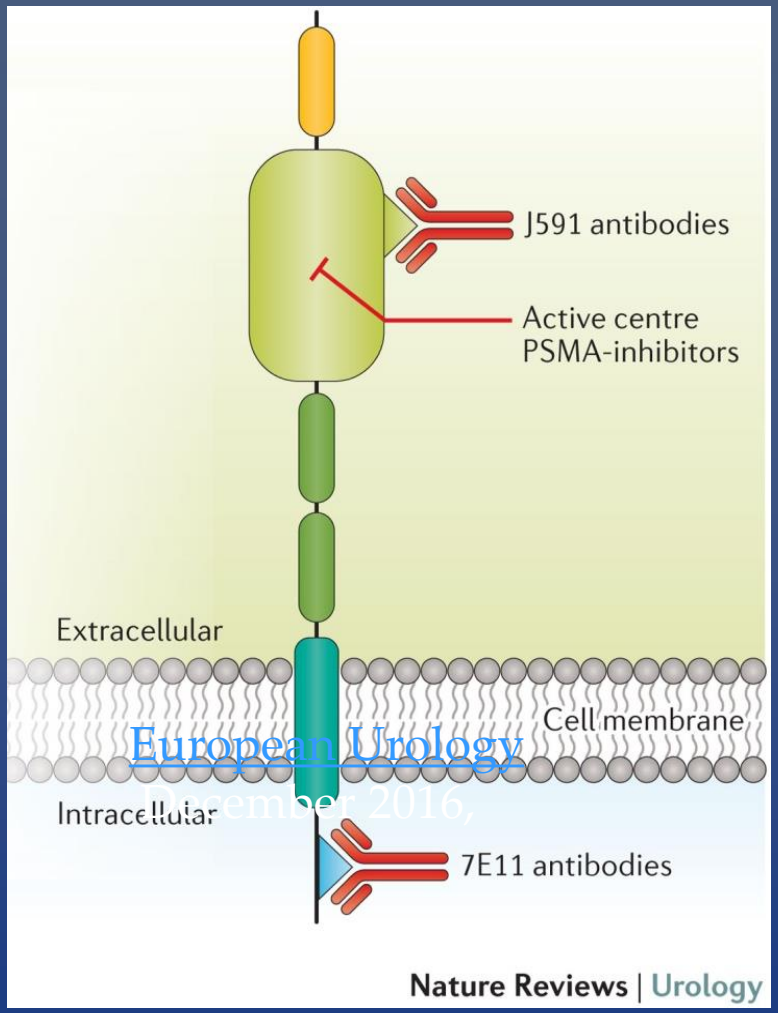
European Association of Urology

Collaborative Review – Prostate Cancer

New Clinical Indications for $^{18}F/^{11}C$-choline, New Tracers for Positron Emission Tomography and a Promising Hybrid Device for Prostate Cancer Staging: A Systematic Review of the Literature

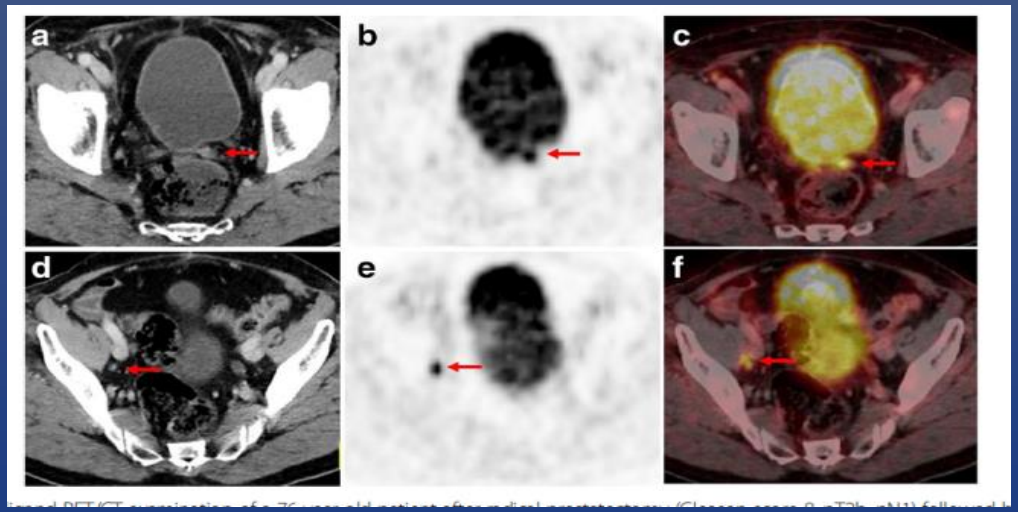
Laura Evangelista [a,], Alberto Briganti [b], Stefano Fanti [c], Stephen Joniau [d], Sven Reske [e], Riccardo Schiavina [f], Christian Stief [g], George N. Thalmann [h], Maria Picchio [i]*





Prostate-Specific Membrane Antigen is a transmembrane glycoprotein found on prostate epithelial cells

Its expression is up to 1000-fold higher in prostate cancer than in other tissues, and the degree of PMSA expression is associated with the time to tumour relapse



European Urology
December 2016,

Maurer 016 *Nat. Rev. Urol.*
Current use of PSMA–PET in prostate cancer management

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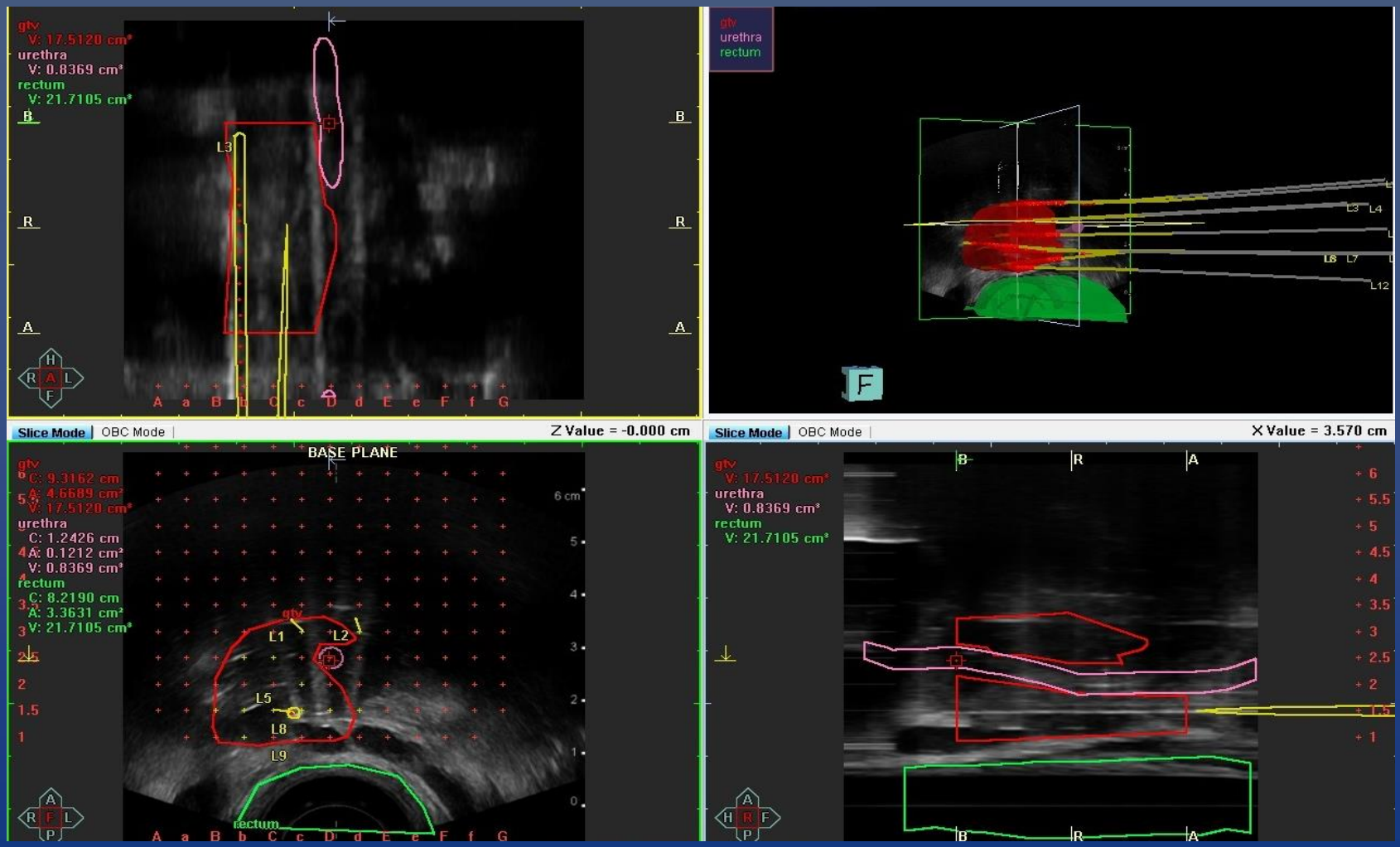
? Salvage Brachytherapy possible



Molecular Imaging of Prostate Cancer[1]

Radiographics 2016

Andreas G. Wibmer, MD
Irene A. Burger, MD
Evis Sala, MD, PhD
Hedvig Hricak, MD, PhD
Wolfgang A. Weber, MD
Hebert Alberto Vargas, MD

Prostate cancer is the most common noncutaneous malignancy among men in the Western world. The natural history and clinical course of prostate cancer are markedly diverse, ranging from small indolent intraprostatic lesions to highly aggressive disseminated disease. An understanding of this biologic heterogeneity is considered a necessary requisite in the quest for the adoption of precise and

	Tracer				
Suspicion of Disease	Choline (Reference)*	^{11}C-Acetate	FACBC	FDG	PSMA
Any disease					
Odds ratio	1.0	1.7	1.8	0.40†	3.6‡
P value	...	.11	.16	<.001	.014
Extraprostatic					
Odds ratio	1.0	0.75	0.47	0.40†	3.1‡
P value	...	.48	.31	.001	.007
Prostatic only					
Odds ratio	1.0	2.4	2.9	0.43	0.74
P value	...	.19	.34	.075	.60
Lymph nodes					
Odds ratio	1.0	1.3	ND§	0.40†	2.2
P value	...	.43	...	.002	.053
Metastases to bone					
Odds ratio	1.0	0.78	ND§	0.62	1.5
P value	...	.53	...	.15	.40

Biomedical images contain large amounts of information that reflect underlying pathophysiology

The conversion of digital medical images into high-dimensional data that can be be analysed is known as *Radiomics*

Radiomics:
The Next Frontier in Clinical Decision Making

- Radiomics appears to offer a large volume of imaging biomarkers that could potentially aid cancer management

- Radiogenomic analysis might reveal a prognostic radiomic signature reflecting tumour heterogeneity

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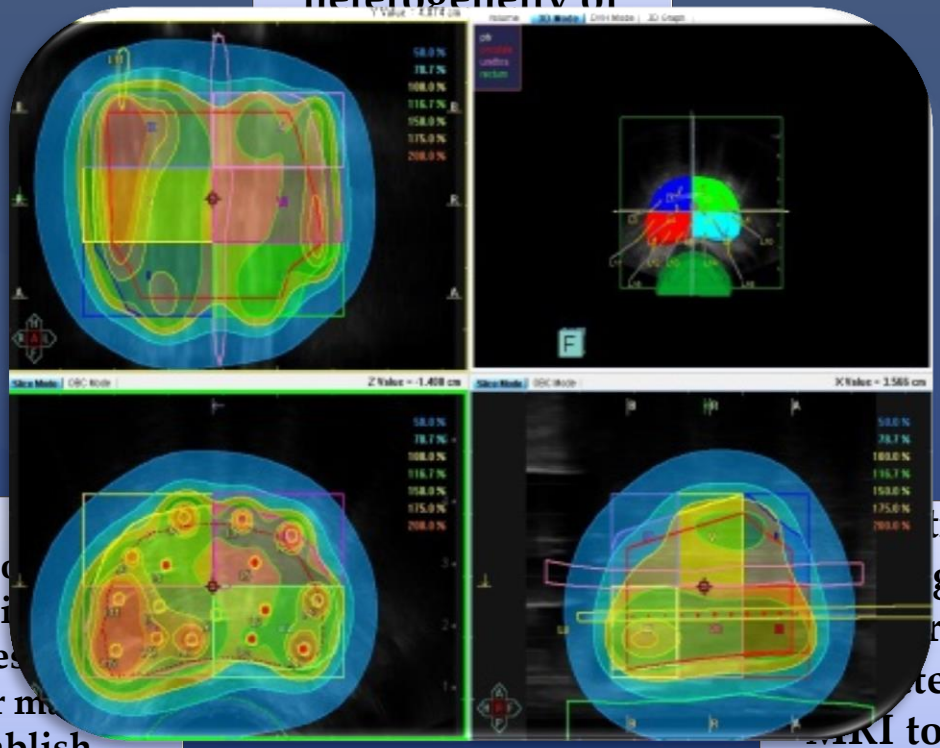
Generation of focal and whole gland focal boost treatment plans based on Radiomics-detected lesions

Genetic heterogeneity of



Associatio between i features molecular m to establish prognostic factors

titative ging res are ted from MRI to assess tumour heterogeneity

- Personalised Brachytherapy

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Clinical Radiology 72 (2017) 3–10

Contents lists available at ScienceDirect

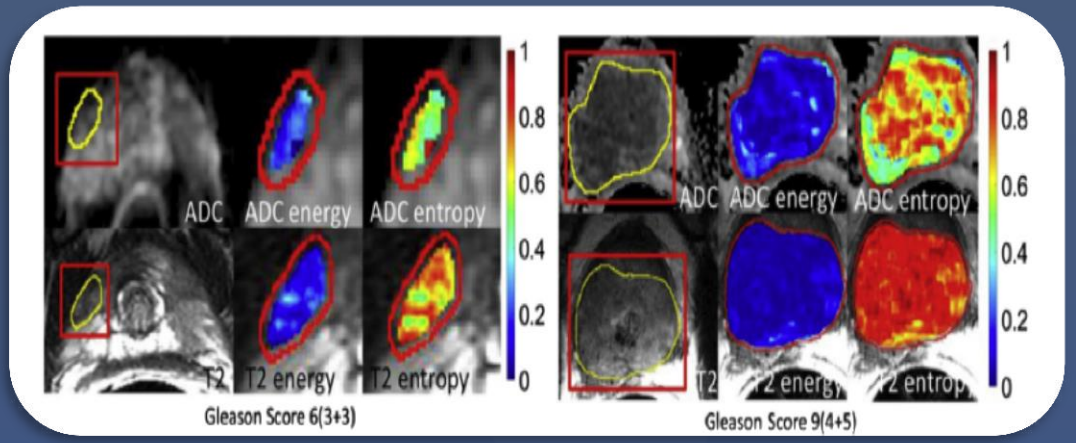
Clinical Radiology

journal homepage: www.clinicalradiologyonline.net

Review

Unravelling tumour heterogeneity using next-generation imaging: radiomics, radiogenomics, and habitat imaging

E. Sala [a,*], E. Mema [a,b], Y. Himoto [a], H. Veeraraghavan [c], J.D. Brenton [d], A. Snyder [e], B. Weigelt [f], H.A. Vargas [a]



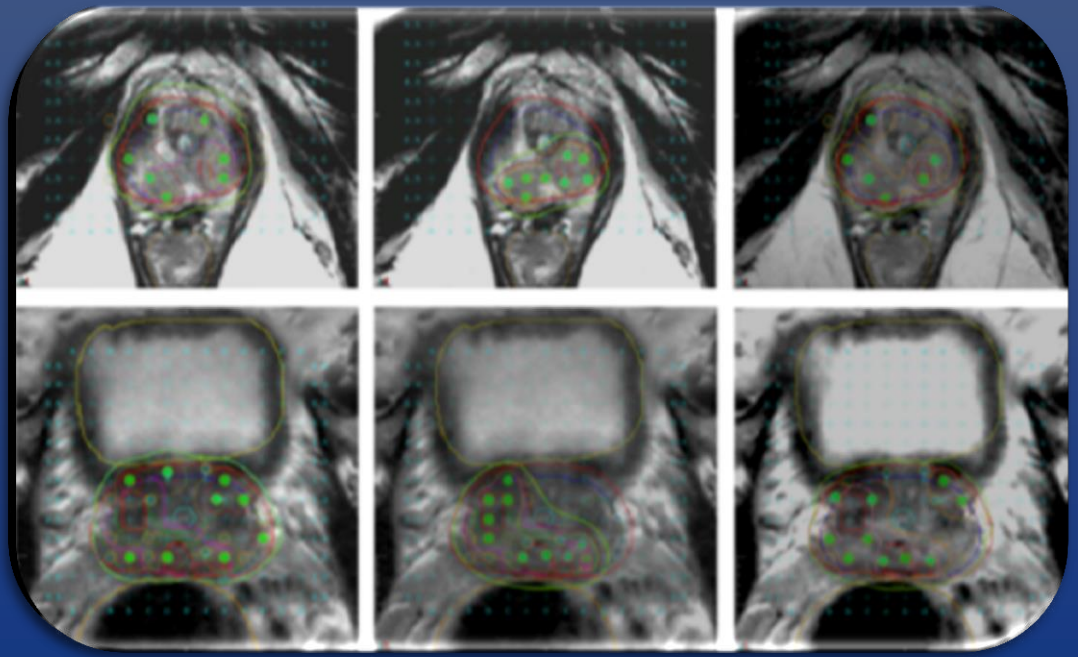
Shiradkar et al. Radiation Oncology (2016) 11:148
DOI 10.1186/s13014-016-0718-3

Radiation Oncology

RESEARCH Open Access

Radiomics based targeted radiotherapy planning (Rad-TRaP): a computational framework for prostate cancer treatment planning with MRI

Rakesh Shiradkar[1*], Tarun K Podder[2], Ahmad Algohary[1], Satish Viswanath[1], Rodney J. Ellis[2] and Anant Madabhushi[1]



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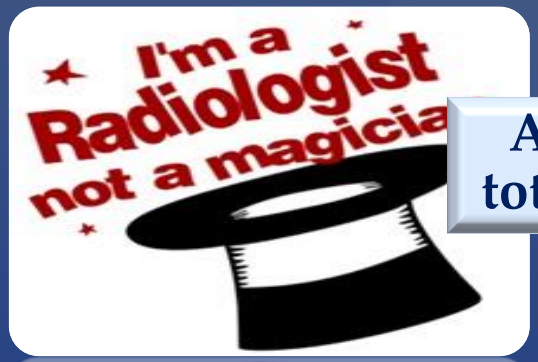
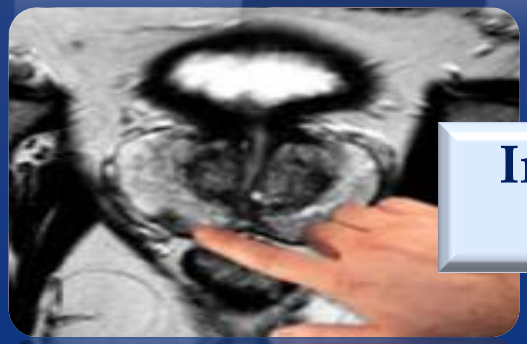
Brachytherapy Imaging Update - *summary*

Icebergs still sink ships



Any similarity to living experts is totally accidental and unintentional



Imaging is the Future for Prostate Brachytherapy