

The future of APC imaging

Stefano Fanti



Disclosures

AAA

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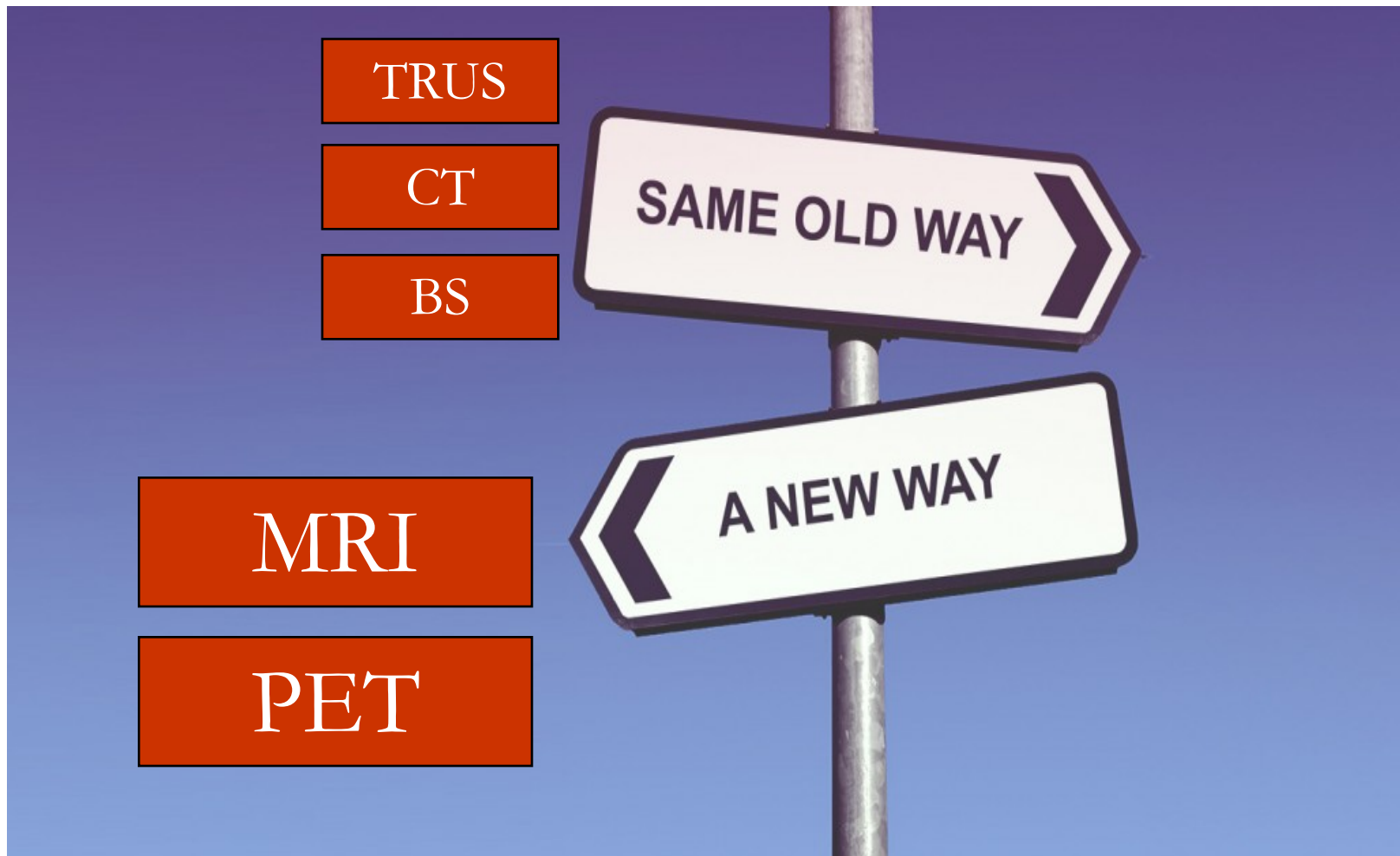
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GE HEALTHCARE





The Present of Prostate Cancer Imaging



The Future of Prostate Cancer Imaging

Radiology

REVIEWS AND COMMENTARY • REVIEW

Imaging Diagnosis and Follow-up of Advanced Prostate Cancer: Clinical Perspectives and State of the Art

Raquel Perez-Lopez, MD, PhD • Nina Tunariu, MD, FRCR* • Anwar R. Padhani, MBBS, FRCR • Wim J. G. Oyen, MD, PhD • Stefano Fanti, MD • Hebert Alberto Vargas, MD • Aurelius Omlin, MD • Michael J. Morris, MD • Johann de Bono, MBChB, PhD • Dow-Mu Koh, MD, FRCR*

The management of advanced prostate cancer has changed substantially with the availability of multiple effective novel treatments, which has led to improved disease survival. In the era of personalized cancer treatments, more precise imaging may help physicians deliver better care. More accurate local staging and earlier detection of metastatic disease, accurate identification of oligometastatic disease, and optimal assessment of treatment response are areas where modern imaging is rapidly evolving and expanding. Next-generation imaging modalities, including whole-body MRI and molecular imaging with combined PET and CT and combined PET and MRI using novel radiopharmaceuticals, create new opportunities for imaging to support and refine management pathways in patients with advanced prostate cancer. This article demonstrates the potential and challenges of applying next-generation imaging to deliver the clinical promise of treatment breakthroughs.

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Imaging Diagnosis and Follow-up of Advanced Prostate Cancer: Clinical Perspectives and State of the Art

Raquel Perez-Lopez, MD, PhD • Nina Timariu, MD, FRCR* • Anwar R. Padhani, MBBS, FRCR • Wim J. G. Oyen, MD, PhD • Stefano Fanti, MD • Hebert Alberto Vargas, MD • Aurelius Omlin, MD • Michael J. Morris, MD • Johann de Bono, MBChB, PhD • Dow-Mu Koh, MD, FRCR*

Essentials

- Conventional imaging with CT and bone scanning has limited sensitivity to depict nodal and bone disease in prostate cancer.
- Next-generation imaging, including whole-body diffusion-weighted MRI with novel radiopharmaceuticals for combined PET and CT and combined PET and MRI, is more accurate in defining the presence and extent of disease.
- Next-generation imaging enables earlier initiation of treatment in patients with occult metastatic disease at CT and bone scanning; optimal change in treatment via earlier detection of disease progression; detection of oligometastatic state (limited metastatic disease), which may be treated more aggressively; guidance of tissue biopsies for molecular tumor characterization; and development of novel predictive and prognostic biomarkers to guide therapies.



The diagnostic accuracy of CT and MRI in the staging of pelvic lymph nodes in patients with prostate cancer: a meta-analysis

A.M. Hövels^{a,*}, R.A.M. Heesakkers^b, E.M. Adang^a, G.J. Jager^b,
S. Strum^c, Y.L. Hoogeveen^b, J.L. Severens^d, J.O. Barentsz^b

First author	Publication year	N	Sensitivity	Specificity
CT				
Benson ¹⁵	1981	23	50%(1/2)	66%(14/21)
Golimbu ¹⁶	1981	46	31%(5/17)	92%(27/29)
Levine ¹⁷	1981	16	94%(7/7)	83%(7/8)
Morgan ¹⁸	1981	9	36%(2/6)	95%(10/10)
Giri ¹⁹	1982	12	75%(4/5)	81%(6/7)
Emory ²⁰	1983	27	27%(3/12)	97%(15/15)
Sawczuk ²¹	1983	8	25%(1/5)	88%(3/3)
Weinermann ²²	1983	19	68%(7/10)	75%(7/9)
Flanigan ²³	1985	35	50%(3/6)	98%(29/29)
Mukamel ²⁴	1986	10	50%(0/0)	59%(6/10)
Biondetti ²⁵	1987	7	83%(2/2)	92%(5/5)
Hricak ²⁶	1987	85	25%(2/9)	99%(76/76)
Platt ²⁷	1987	32	8%(0/5)	95%(26/27)
Engeler ²⁸	1992	160	5%(2/47)	100%(113/113)
Van Poppel ²⁹	1994	285	77%(35/45)	96%(232/240)
Flanigan ³⁰	1996	173	27%(3/12)	97%(156/161)
Rorvik ³¹	1998	64	28%(2/8)	97%(44/45)
Borley ³²	2003	13	5%(0/9)	90%(4/4)



WHICH PATIENTS WITH NEWLY DIAGNOSED PROSTATE CANCER NEED A RADIONUCLIDE BONE SCAN? AN ANALYSIS BASED ON 631 PATIENTS

NANCY LEE, M.D.,* RASHID FAWAAZ, M.D.,[†] CARL A. OLSSON, M.D.,[‡] MITCHELL C. BENSON, M.D.,[‡]
DANIEL P. PETRYLAK, M.D.,[§] PETER B. SCHIFF, M.D., PH.D.,* EMILIA BAGIELLA, PH.D.,^{||}
ARUN SINGH,* AND RONALD D. ENNIS, M.D.*

Purpose: Although radionuclide bone scans are frequently recommended as part of the staging evaluation for newly diagnosed prostate cancer, most scans are negative for metastases. We hypothesized that Gleason score, prostate-specific antigen (PSA), and clinical stage could predict for a positive bone scan (BS), and that a low-risk group of patients could be identified in whom BS might be omitted.

Methods: All patients who had both pathologic review of their prostate cancer biopsies and radionuclide BS at our institution between 1/90 and 5/96 were studied. Gleason score, PSA, and clinical stage (AJCC, 4th edition) were evaluated by univariate and multivariate analyses for their ability to predict a positive BS. Groups analyzed were Gleason of 2–6 vs. 7 vs. 8–10; PSA of 0–15 vs. greater than 15–50 vs. greater than 50; and clinical stage of T1a–T2b vs. T2c–T4. Univariate analysis using χ^2 and multivariate analysis using logistic regression were performed.

Results: Of the 631 consecutive patients, 88 (14%) had positive BS. Multivariate analysis (64 excluded due to missing PSA and/or clinical stage) showed Gleason score, PSA, and clinical stage to be significant independent predictors for positive BS ($p < 0.002$, $p < 0.001$, $p < 0.001$, respectively). The odds ratios were 5.25 (confidence interval [CI], 3.43–8.04) for PSA > 50 vs. 0–15; 2.25 (CI, 1.43–3.54) for Gleason of 8–10 vs. 2–6; 2.15 (CI, 1.54–2.99) for clinical stage T2c–T4 vs. T2b or less. Three of 308 (1%) had a positive BS in patients with Gleason 2–7, PSA of 50 or less, and clinical stage of T2b or less. In the subset of the same risk group with PSA of 15 or less, all 237 had negative bone scans. In patients with PSA greater than 50, 49/99(49.5%) had positive BS.

Conclusion: Gleason score, PSA, and clinical stage were independent predictors for a positive radionuclide BS in newly diagnosed prostate cancer patients. PSA is the major predictor for positive BS. About one-half of the patients analyzed were in the low-risk group (Gleason 2–7, PSA ≤ 50 , clinical stage \leq T2b) and elimination of BS in these patients would result in considerable economic savings. © 2000 Elsevier Science Inc.



STAGING

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EAU - EANM -
ESTRO - ESUR - SIOG
Guidelines on
Prostate Cancer

5.3.4 *Summary of evidence and practical considerations on initial N/M staging*

The field of non-invasive nodal and metastatic staging of PCa is evolving very rapidly. Evidence shows that choline PET/CT, PSMA PET/CT and MRI provide a more sensitive detection of LN and bone metastases than the classical work-up associating bone scan and abdominopelvic CT. It could be tempting to conclude that bone scan and abdominopelvic CT must be replaced by more sensitive tests in all patients undergoing initial PCa staging. Yet, the clinical benefit of detecting metastases at an earlier time-point remains unclear [318].

The prognosis and ideal management of patients diagnosed as metastatic by these more sensitive tests is unknown. In particular, it is unclear whether patients with metastases, detectable only with PET/CT or MRI, should be managed using systemic therapies, or whether they should be submitted to aggressive local and metastases-directed therapies [319].

Results from RCTs evaluating the management and outcome of patients with (and without) metastases detected by choline PET/CT, PSMA PET/CT and MRI are awaited, before a decision can be made to treat patients based on the results of these tests [320].

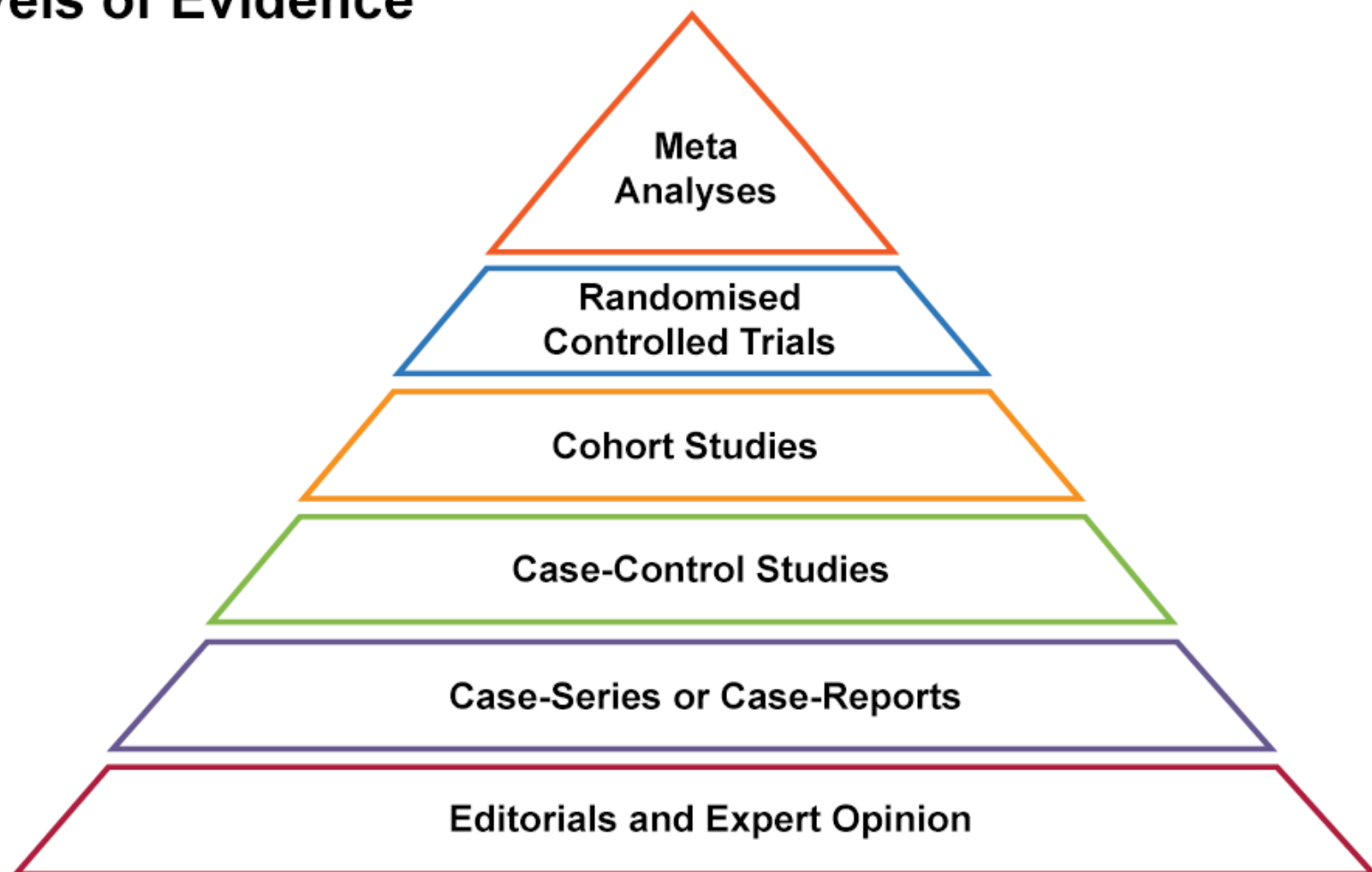


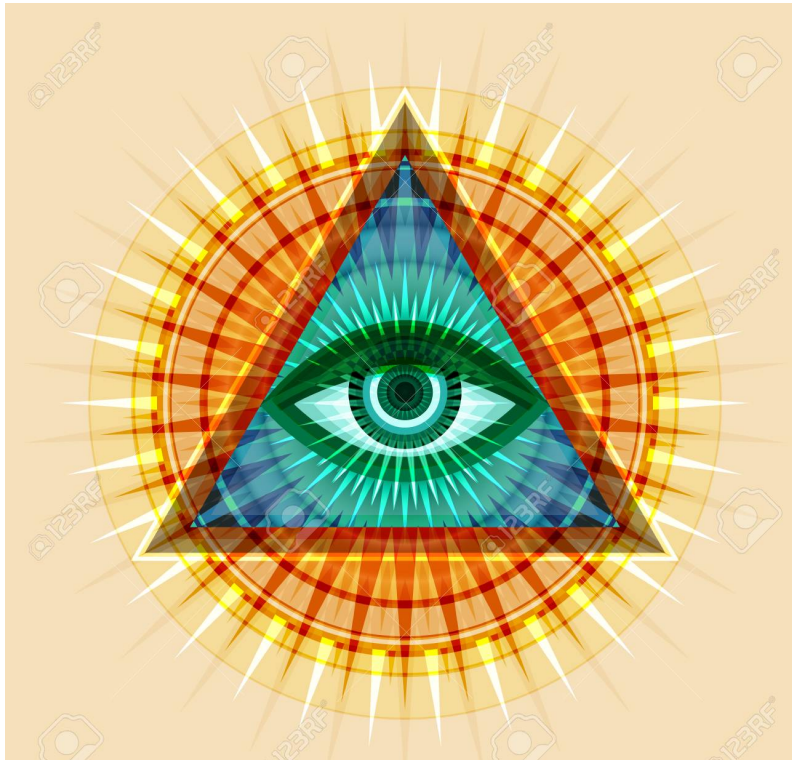


CLINICAL BENEFIT



Levels of Evidence





The Future of Prostate Cancer Imaging

DIAGNOSIS

STAGING

BIOCHEMICAL RECURRENCE

THERAPY PLANNING

THERAPY MONITORING



DIAGNOSIS

EAU - EANM - ESTRO - ESUR - SIOG Guidelines on Prostate Cancer

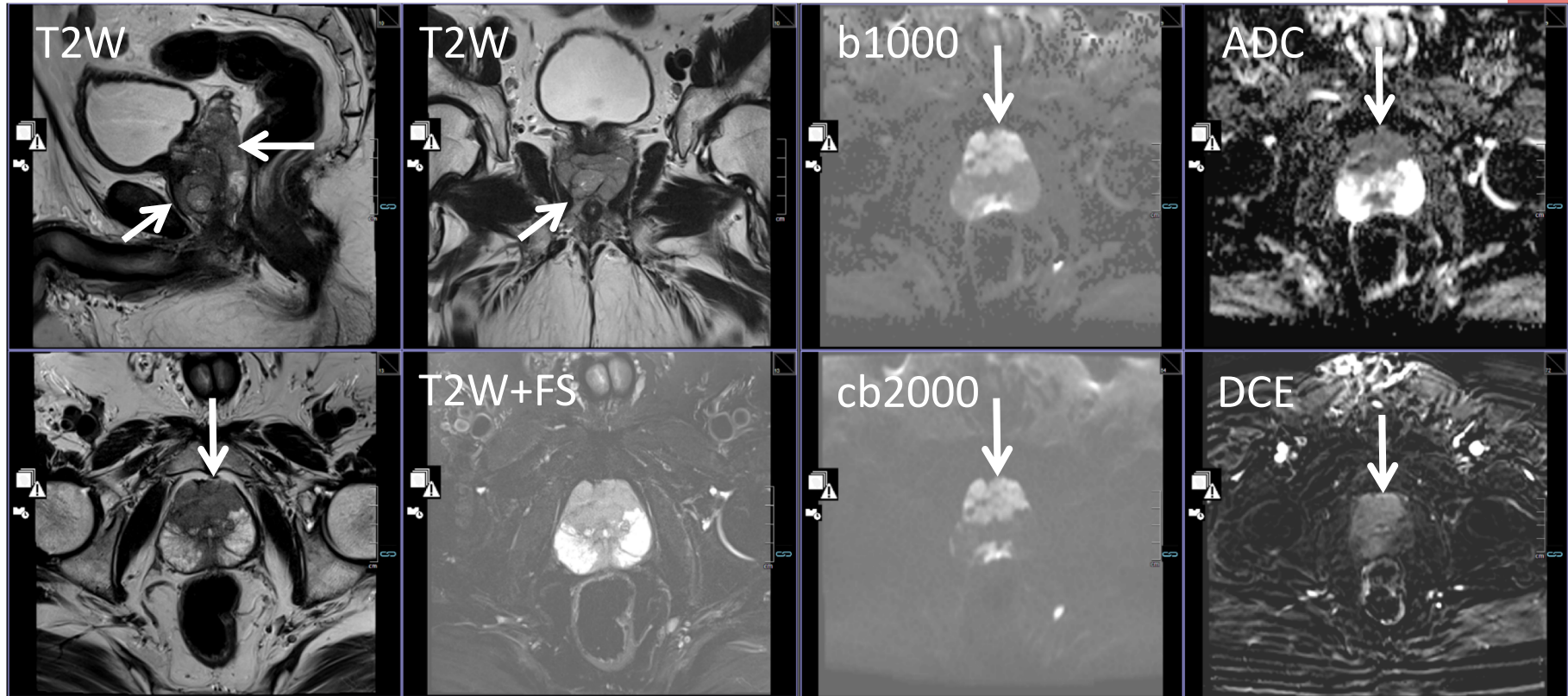
Recommendations in biopsy-naïve patients	LE	Strength rating
Perform mpMRI before prostate biopsy.	1a	Weak
When mpMRI is positive (i.e. PI-RADS ≥ 3), combine targeted and systematic biopsy.	2a	Strong
When mpMRI is negative (i.e. PI-RADS ≤ 2), and clinical suspicion of prostate cancer is low, omit biopsy based on shared decision making with the patient.	2a	Weak

Recommendations in patients with prior negative biopsy	LE	Strength rating
Perform mpMRI before prostate biopsy.	1a	Strong
When mpMRI is positive (i.e. PI-RADS ≥ 3), perform targeted biopsy only.	2a	Weak
When mpMRI is negative (i.e. PI-RADS ≤ 2), and clinical suspicion of prostate cancer is high, perform systematic biopsy based on shared decision making with the patient.	2a	Strong



DIAGNOSIS

69M, PSA 10ng/mL, Asymptomatic, Routine check, DRE+ve



3TSkyra
@ProfPadhani

Anterior biopsy: GS4+5, 70% GS=4; Diffuse pattern adenocarcinoma; No small cell neuroendocrine differentiation



PSMA PET in prostate cancer staging

Risk of metastatic disease on ^{68}Ga -prostate-specific membrane antigen positron emission tomography/computed tomography scan for primary staging of 1253 men at the diagnosis of prostate cancer

John W. Yaxley^{*†‡}, Sheliyan Raveenthiran^{†‡}, François-Xavier Nouhaud^{‡§}, Hemamali Samarasinghe^{†¶}, William J. Yaxley^{†‡}, Geoff Coughlin^{*‡}, Anna J. Yaxley^{**}, Troy Gianduzzo^{††}, Boon Kua^{†‡}, Louise McEwan^{†‡} and David Wong^{†‡}

Conclusion

We have identified the ability of ^{68}Ga -PSMA PET/CT to detect metastatic prostate cancer in 12.1% of men at initial diagnosis of prostate cancer. We recommend a ^{68}Ga -PSMA PET/CT scan as the investigation of choice in men with high-risk prostate cancer. The apparent improved detection ability of ^{68}Ga -PSMA PET/CT compared to standard radiology requires confirmation with a sufficiently powered randomised trial, to evaluate the diagnostic potential, the economic impact, and significant management impact of ^{68}Ga -PSMA PET/CT scan as first-line staging above standard radiology. One such prospective multicentre trial of high-risk and primary Gleason 4 intermediate-risk prostate cancer has just finished recruitment [23] and the results are expected in early 2020.



STAGING



78 yo

PSA (oct 2018)= 94,08
ng/mL

biopsy (nov 2018) = PCa GS
4+4, 60-100% del core
bioptico.

STAGING

PSMA PET in prostate cancer staging

NIH U.S. National Library of Medicine

ClinicalTrials.gov

27 Studies found for: **psma staging** | **prostate cancer**

1	<input type="checkbox"/>	Not yet recruiting	Place of 68Ga-PSMA-11 PET-CT in the Therapeutic Decision at the End of the Initial Staging for High Risk Prostate Cancer Patients	<ul style="list-style-type: none"> Prostate Cancer 	<ul style="list-style-type: none"> Diagnostic Test: 68Ga-PSMA-11 Diagnostic Test: 18F-Choline PET-CT 	<ul style="list-style-type: none"> Central hospital Nancy Nancy, France
2	<input type="checkbox"/>	Recruiting	Novel Imaging in Staging of Primary Prostate Cancer	<ul style="list-style-type: none"> High Risk Prostate Cancer 	<ul style="list-style-type: none"> Diagnostic Test: Whole body contrast enhanced computer tomography Diagnostic Test: 99mTc-HMDP planar bone scintigraphy (BS) Diagnostic Test: 99mTc-HMDP single photon emission computer tomography/computer tomography (and 2 more...) 	<ul style="list-style-type: none"> Department of Urology Turku, Finland
3	<input type="checkbox"/>	Recruiting	A Study of the Value of Hybrid PET/MR and PET/CT in Prostate Cancer	<ul style="list-style-type: none"> Prostate Cancer PET/MR PET/CT 	<ul style="list-style-type: none"> Diagnostic Test: 68Ga-PSMA-11 and/or 18F-FDG PET/MR, PET/CT 	<ul style="list-style-type: none"> Xiaoli Lan Wuhan, Hubei, China
4	<input type="checkbox"/>	Recruiting	Mp-3TMRI and 68Ga-PSMA PET/CT Guided Prostate Biopsy and Tumor Node Metastasis (TNM) Staging	<ul style="list-style-type: none"> 68Ga-PSMA PET/CT Guided Prostate Biopsy Mp-3TMRI Guided Prostate Biopsy Prostate Cancer (and 2 more...) 	<ul style="list-style-type: none"> Diagnostic Test: pelvic MRI Diagnostic Test: 68Ga-PSMA PET/CT 	<ul style="list-style-type: none"> Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) Meldola, FC, Italy
5	<input type="checkbox"/>	Recruiting	Clinical Application of 68Ga-PSMA PET in Prostate Cancer	<ul style="list-style-type: none"> Prostate Cancer 	<ul style="list-style-type: none"> Diagnostic Test: Ga-68 PSMA PET 	<ul style="list-style-type: none"> National Taiwan University Hospital Taipei, Taiwan



BIOCHEMICAL RECURRENCE

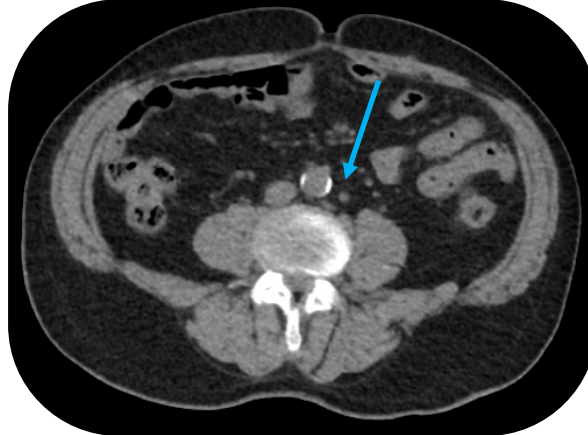
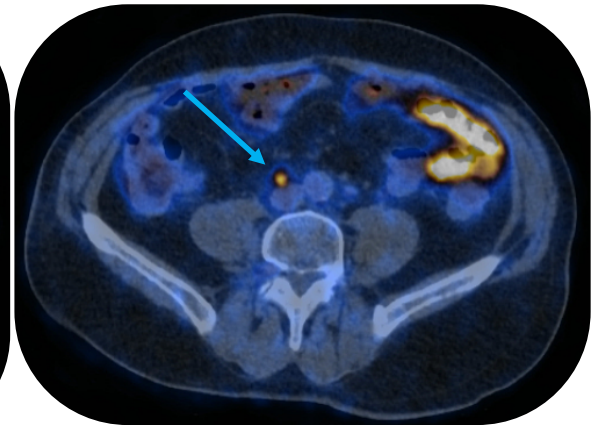
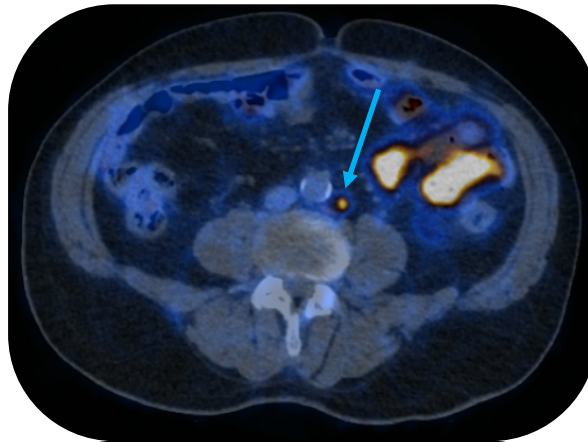
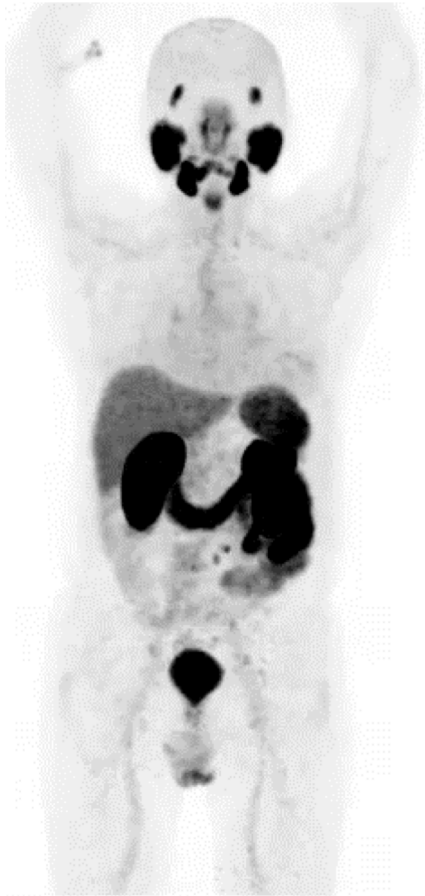
EAU - EANM -
ESTRO - ESUR - SIOG
Guidelines on
Prostate Cancer

6.3.4.4 Guidelines for imaging in patients with biochemical recurrence

Prostate-specific antigen (PSA) recurrence after radical prostatectomy	LE	Strength rating
Perform prostate-specific membrane antigen (PSMA) positron emission tomography (PET) computed tomography (CT) if the PSA level is > 0.2 ng/mL and if the results will influence subsequent treatment decisions.	2b	Weak
In case PSMA PET/CT is not available, and the PSA level is ≥ 1 ng/mL, perform fluciclovine PET/CT or choline PET/CT imaging if the results will influence subsequent treatment decisions.		Weak
PSA recurrence after radiotherapy		
Perform prostate multiparametric magnetic resonance imaging to localise abnormal areas and guide biopsies in patients fit for local salvage therapy.	3	Strong
Perform PSMA PET/CT (if available) or fluciclovine PET/CT or choline PET/CT in patients fit for curative salvage treatment.	2b	Strong



BIOCHEMICAL RECURRENCE



Courtesy University of Zurich



PSMA PET in prostate cancer RT planning

Prostate. 2017 Jun;77(8):920-927. doi: 10.1002/pros.23347. Epub 2017 Mar 20.

68 Ga-PSMA-PET for radiation treatment planning in prostate cancer recurrences after surgery: Individualized medicine or new standard in salvage treatment.

Habl G^{1,2}, Sauter K¹, Schiller K¹, Dewes S¹, Maurer T³, Eiber M^{4,5}, Combs SE^{1,2}.

Author information

Abstract

BACKGROUND: ⁶⁸ Ga-PSMA-PET imaging is a novel promising diagnostic tool to locate early biochemical failure after radical prostatectomy (RP) in prostate cancer (PC) patients. Exact knowledge of the relapse location may result in changes of the therapy concept aside from changes to the TNM stage. To gain data for this approach, we evaluated PC patients receiving ⁶⁸ Ga-PSMA-PET imaging before salvage radiotherapy (RT).

METHODS AND MATERIALS: In this study, 100 patients with biochemical failure after RP± prior RT who underwent ⁶⁸ Ga-PSMA PET/CT or PET/MRI were evaluated undergoing salvage RT in our department. We analyzed TNM staging changes due to ⁶⁸ Ga-PSMA-PET imaging and its influence on RT planning and treatment.

RESULTS: Uptake indicative for tumor recurrence in ⁶⁸ Ga-PSMA-PET was found in 76% of the patients with biochemical recurrent PC. Median PSA level was 1.0 ng/mL (range 0.12-14.7 ng/mL). Of these, 80% showed no morphological correlate in the corresponding CT or MRI. A 43% of all patients experienced a change in TNM stage due to ⁶⁸ Ga-PSMA-PET imaging. Patients had changes from Tx to rcT+ (28%), 12% from pN0 to rcN1, 1% from pN0/cM0 to rcM1a, and 8% from cM0 to rcM1b. Due to the additional knowledge of ⁶⁸ Ga-PSMA-PET imaging, initial planned RT planning was adapted in 59% of all cases. An additional simultaneous integrated boost (SIB) to the prostate bed or lymph nodes was given to 32% and 63%, respectively. Ten patients received stereotactic body RT (SBRT) to single bone metastases.

CONCLUSION: ⁶⁸ Ga-PSMA-PET imaging showed a high clinical impact on staging and RT management in patients with biochemically recurrent PC, even at low serum PSA levels. With 43% changes in staging and 59% in radiotherapy planning ⁶⁸ Ga-PSMA-PET could lead to an indispensable tool in guiding radiation treatment in recurrent PC.



THERAPY PLANNING



50 yo
Gs 9 iPSA 34ng/ml
RP (Dec 2018) T3b N1 M0
PSA 3.1 ng/ml February 2019
SRT planning



THERAPY PLANNING

PSMA PET in prostate cancer RT planning

NIH U.S. National Library of Medicine

ClinicalTrials.gov

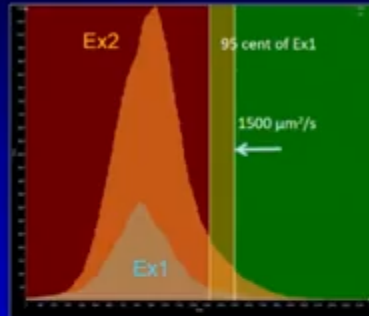
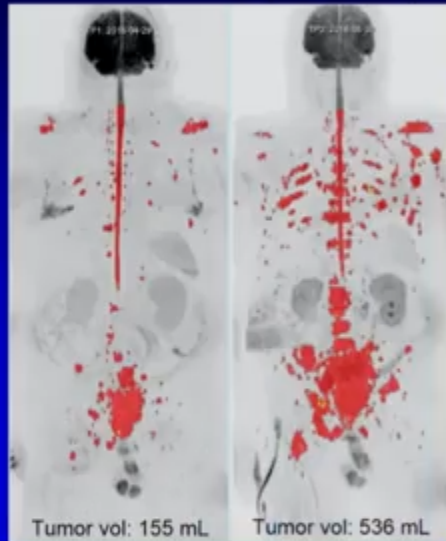
11 Studies found for: **psma radiotherapy planning | Prostate Cancer**

1	<input type="checkbox"/>	Recruiting	Trial of 68Ga-PSMA-11 PET/CT Molecular Imaging for Prostate Cancer Salvage Radiotherapy Planning [PSMA-SRT]	<ul style="list-style-type: none"> Recurrent Prostate Carcinoma 	<ul style="list-style-type: none"> Drug: 68Ga-PSMA-11 	<ul style="list-style-type: none"> UCLA Los Angeles, California, United States
2	<input type="checkbox"/>	Recruiting	PSMA-PET Guided Radiotherapy	<ul style="list-style-type: none"> Prostate Cancer 	<ul style="list-style-type: none"> Radiation: PSMA -PET/CT simulation Radiation: Standard-care simulation 	<ul style="list-style-type: none"> Centre Hospitalier de l'Université de Montréal Montréal, Quebec, Canada
3	<input type="checkbox"/>	Recruiting	Fluciclovine F18 or Ga68-PSMA PET/CT to Enhance Prostate Cancer Outcomes	<ul style="list-style-type: none"> Prostate Adenocarcinoma 	<ul style="list-style-type: none"> Procedure: Computed Tomography Drug: Fluciclovine F18 Radiation: Gallium Ga68-labeled PSMA-11 Procedure: Positron Emission Tomography 	<ul style="list-style-type: none"> Grady Health System Atlanta, Georgia, United States Emory University Hospital/Winship Cancer Institute Atlanta, Georgia, United States Emory Saint Joseph's Hospital Atlanta, Georgia, United States
4	<input type="checkbox"/>	Recruiting	Interest of Trimodality PET-CT Choline MRI Before Radiotherapy in High Risk Prostate Cancer	<ul style="list-style-type: none"> Prostate Cancer 	<ul style="list-style-type: none"> Procedure: imaging in trimodality 	<ul style="list-style-type: none"> Centre Henri Becquerel Rouen, France



THERAPY MONITORING

67 yo male with metastatic castrate resistant prostate cancer
Abiraterone and zoledex
Progression on morphology & DWI/ADC maps



Parameter	09/12/2018 (14:45)	09/12/2018 (14:45)
Volume (cm³)	155.0	536.0
Mean	100.0	100.0
SD	100.0	100.0
Median	100.0	100.0
Min	100.0	100.0
Max	100.0	100.0
Volume (cm³)	155.0	536.0
Mean	100.0	100.0
SD	100.0	100.0
Median	100.0	100.0
Min	100.0	100.0
Max	100.0	100.0



20:03 / 21:50



Conclusion





The Future of Prostate Cancer Imaging

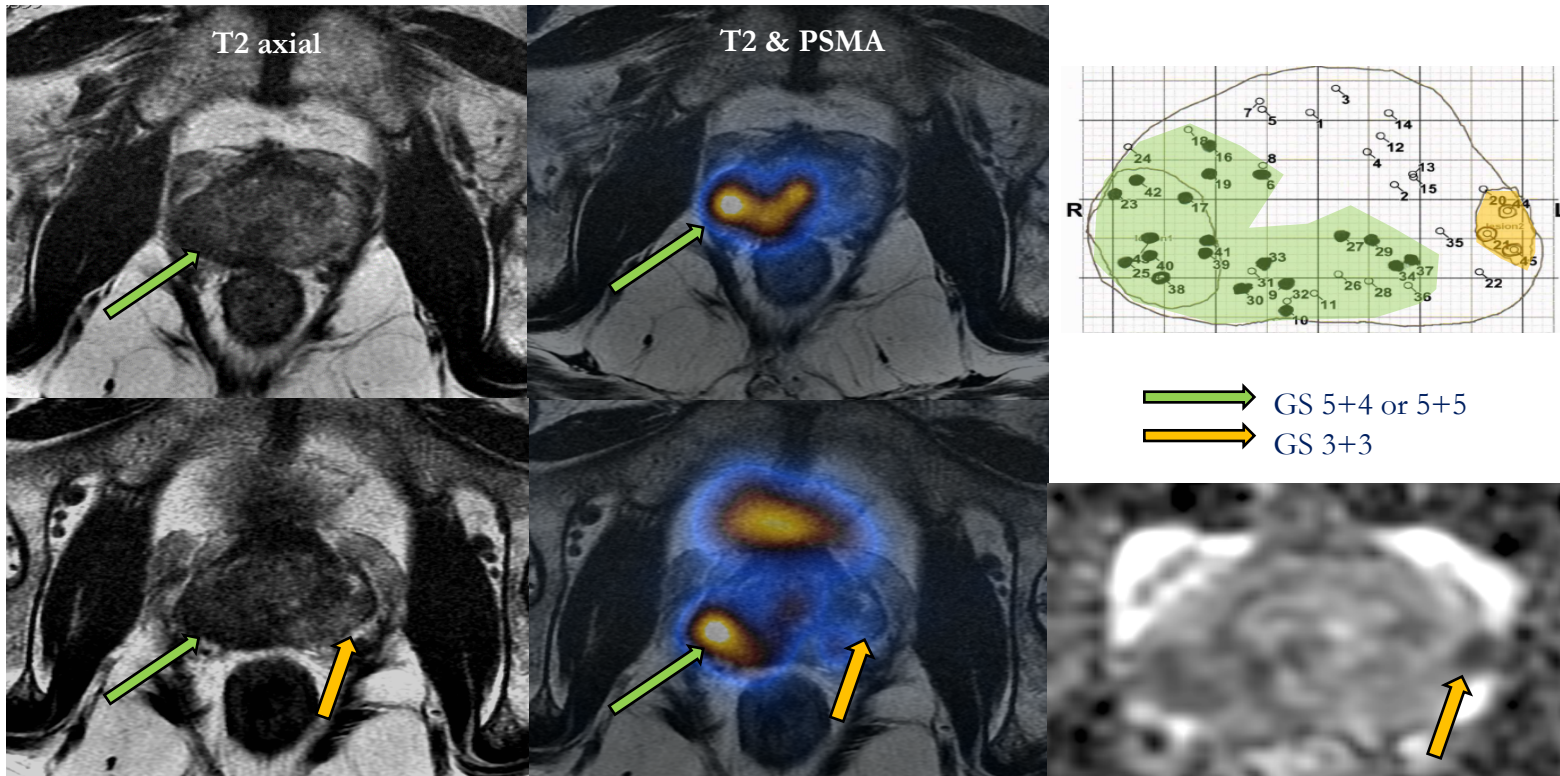
THE
FUTURE
IS NOW

PET

MRI



The Future of Prostate Cancer Imaging



Courtesy University of Zurich Hospital, Switzerland



The Future of Prostate Cancer Imaging



The Future of Prostate Cancer Imaging



ABC

Abandon the obsolete imaging approaches

Be aware of capabilities and limits of NGI

Consider NGI whenever patient management is
to be modified





THE TIME IS NOW THE FUTURE IS HERE



ADVANCED PROSTATE CANCER
CONSENSUS CONFERENCE: APCCC 2019
29-31 August 2019, Basel/Switzerland

