Imaging di precisione per la diagnosi, la stadiazione e il monitoraggio dei tumori:
Il contributo dell'Intelligenza Artificiale

UNIVERSITÀ DEGLI STUDI DI MILANO

Prof. Giuseppe Petralia[1-3]

1. *Division of Radiology, IEO - Milan*
2. *Department of Oncology and Hemato-Oncology, University of Milan*
3. *Icahn School of Medicine at Mount Sinai, New York*

Icahn School of Medicine at Mount Sinai

*By 2030 □ **76 million** deaths caused by the modelled* cancers*

2000
- **10 Mln**
- New cases

2020 prediction
- **15 Mln**
- Increase by 50%

2020
- **19.3 Mln**
- New cases

2030 prediction
- **22.4 Mln?**
- New cases

Global cancer pandemic

*microsimulation model of 11 cancers

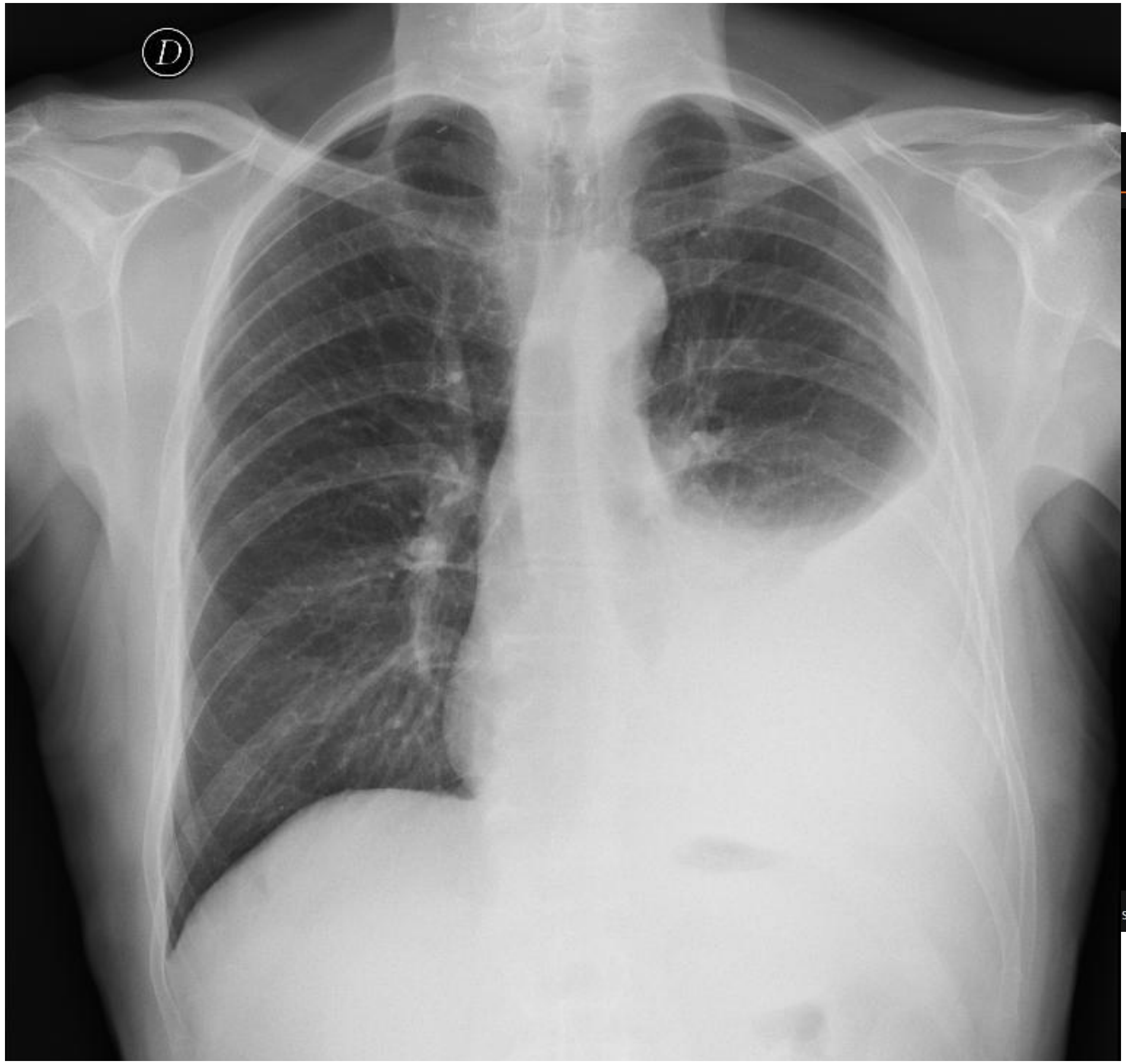
The Lancet Oncology 2021 22e136-e172DOI: (10.1016/S1470-2045(20)30751-8)

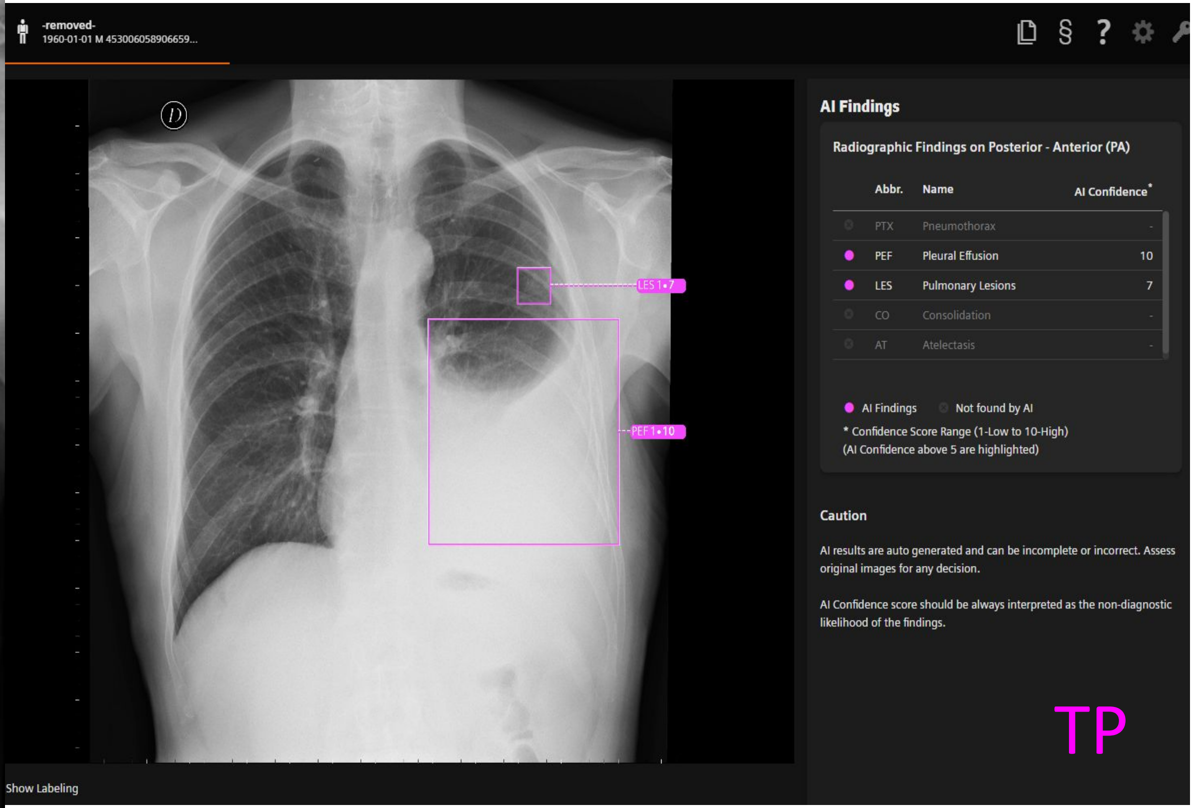
AI for cancer detection & screening

Why? How? Who?

Chest X-ray (AI challenge)

Cheap, available, low radiation □ Elevated workload □ AI solution





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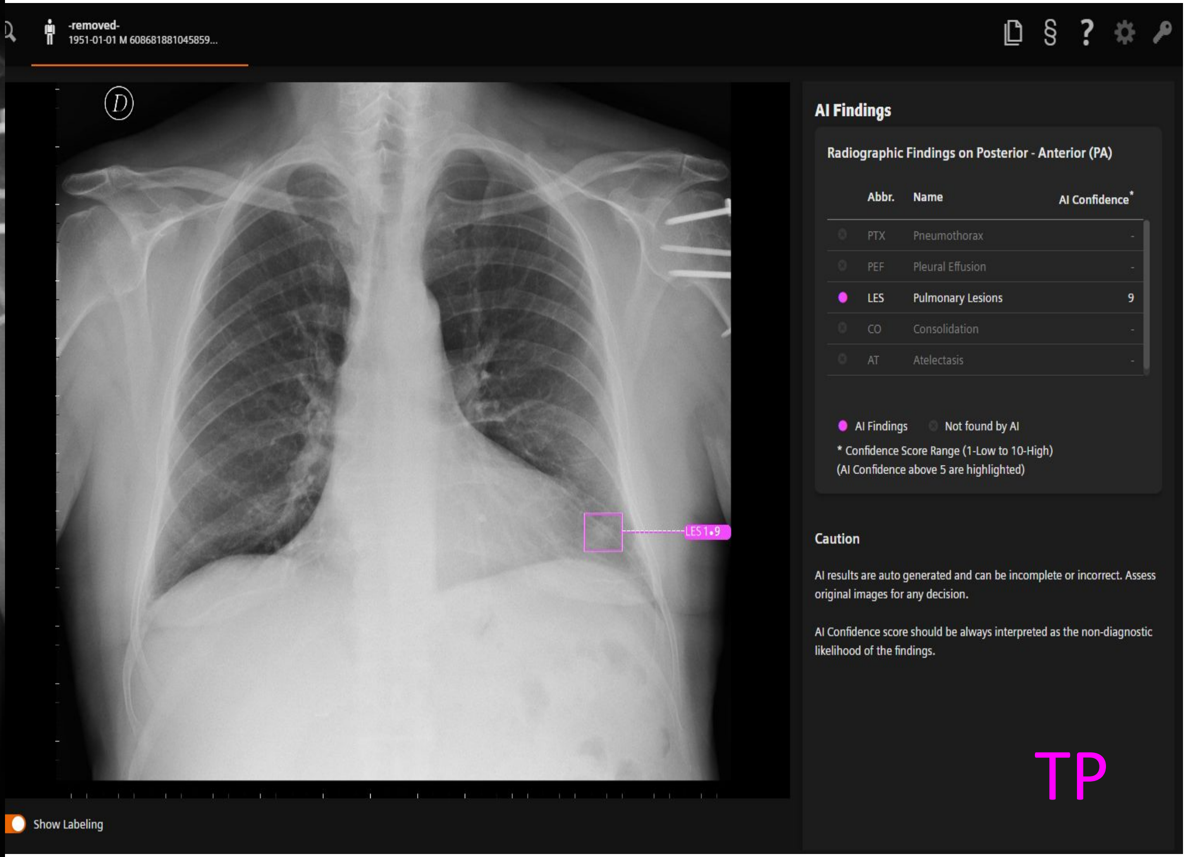


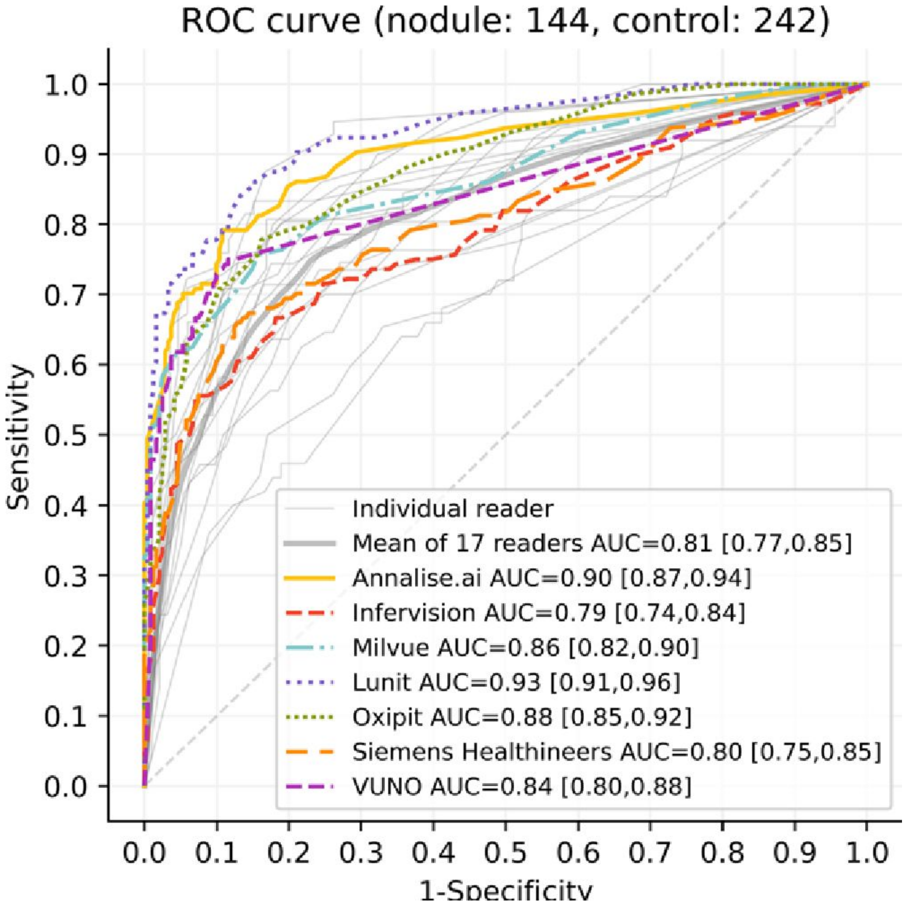
Comparison of Commercial AI Software - Lung Nodule Detection

404 cases / 7 centres[1]

- Human readers (n = 17)
  - Mean AUC = 0.81 (95% CI: 0.77, 0.85)

- Superior performance for:
  - Annalise.ai (AUC, 0.90 [95% CI: 0.87, 0.94]; P < .001)
  - Lunit (AUC, 0.93 [95% CI: 0.91, 0.96]; P < .001)
  - Milvue (AUC, 0.86 [95% CI: 0.82, 0.90]; P = .04)
  - Oxipit (AUC, 0.88 [95% CI: 0.85, 0.92]; P = .005)

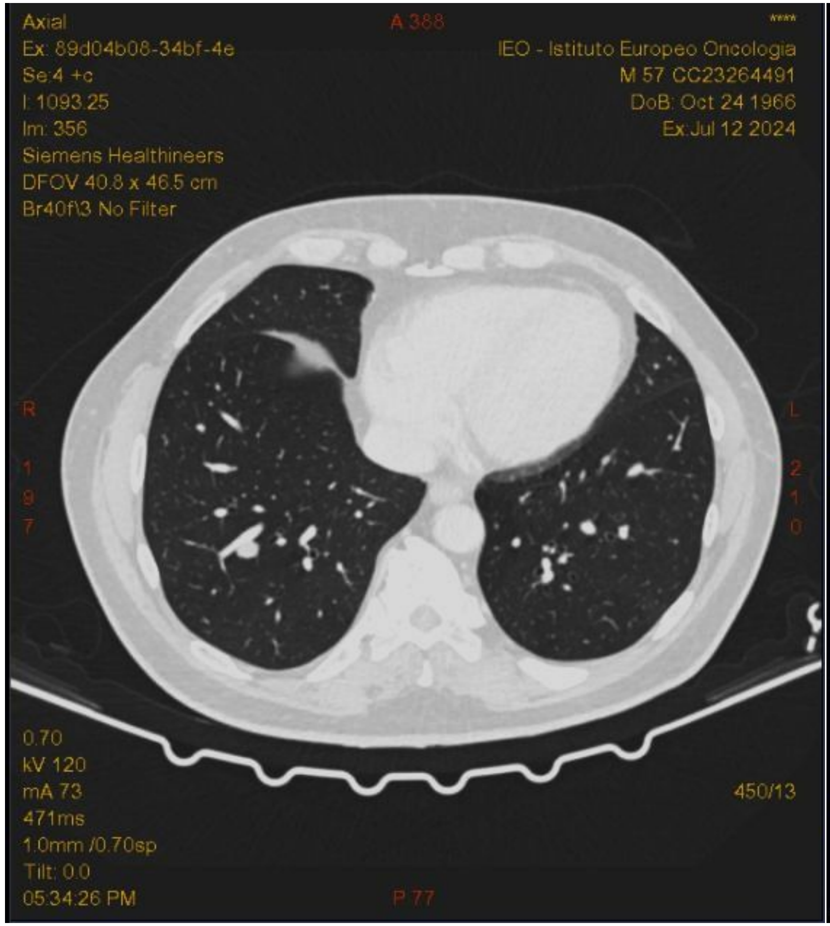
- No difference for:
  - Infervision (AUC, 0.79 [95% CI: 0.74, 0.84]; P = .33)
  - Siemens (AUC, 0.80 [95% CI: 0.75, 0.85]; P = .60)
  - VUNO (AUC, 0.84 [95% CI: 0.80, 0.88]; P = .26).

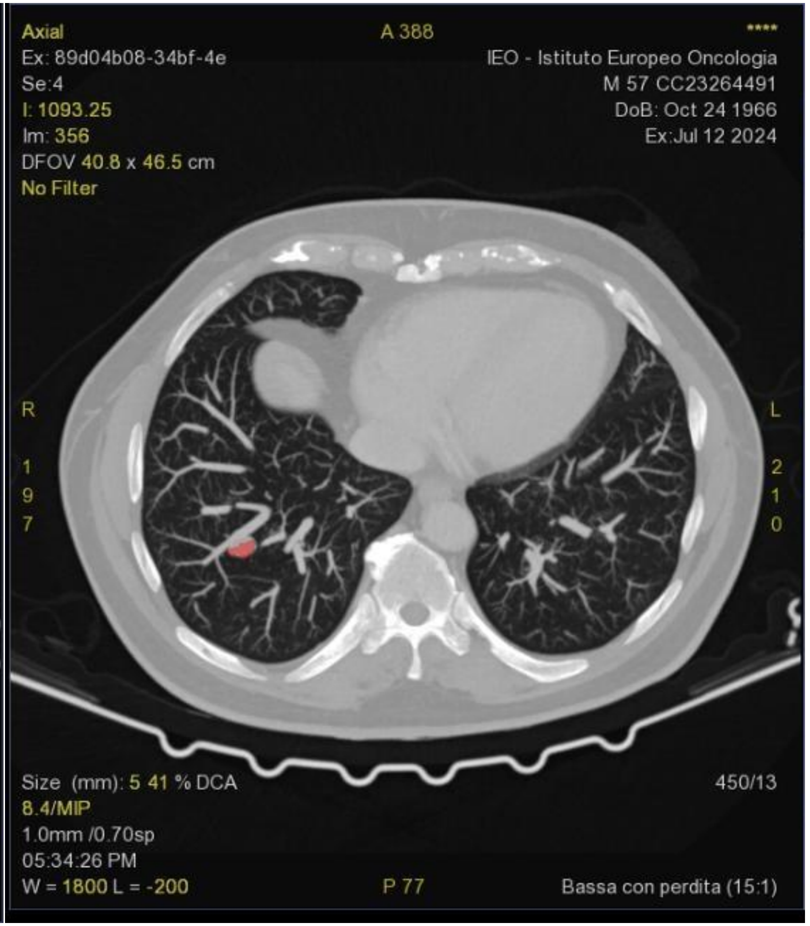


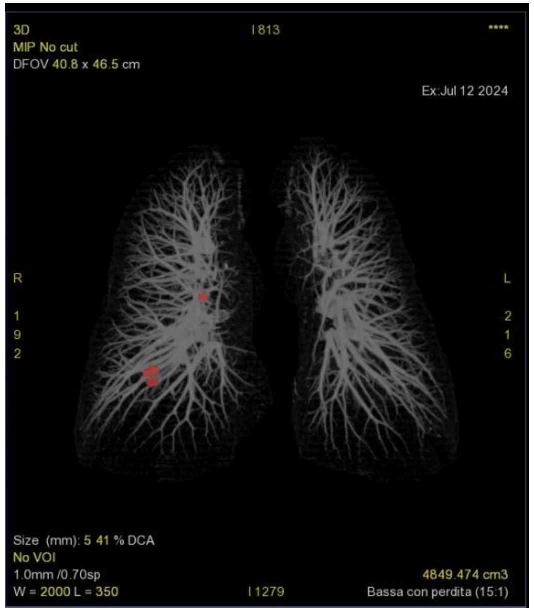
1. Kicky G., et al. Radiology 2024; 310(1):e230981

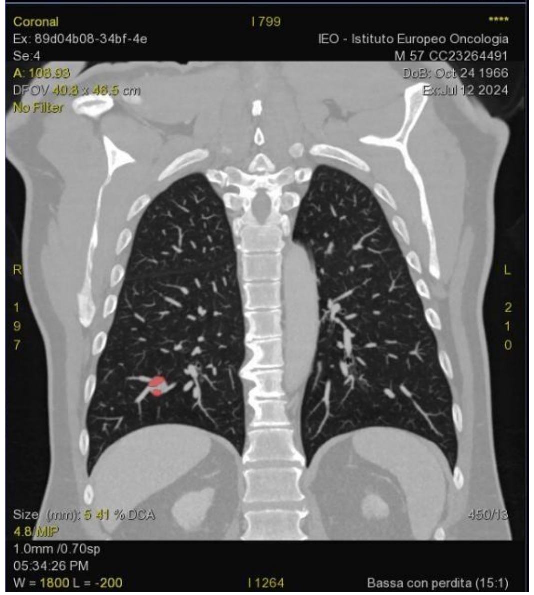
Lung cancer screening with low-dose CT (<1mSV)

Established programmes worldwide (including Lombardia)





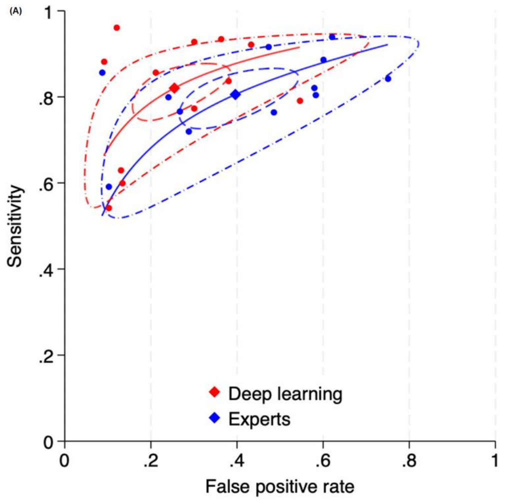


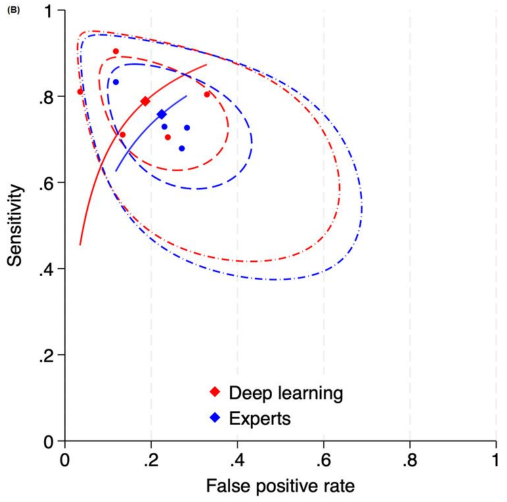


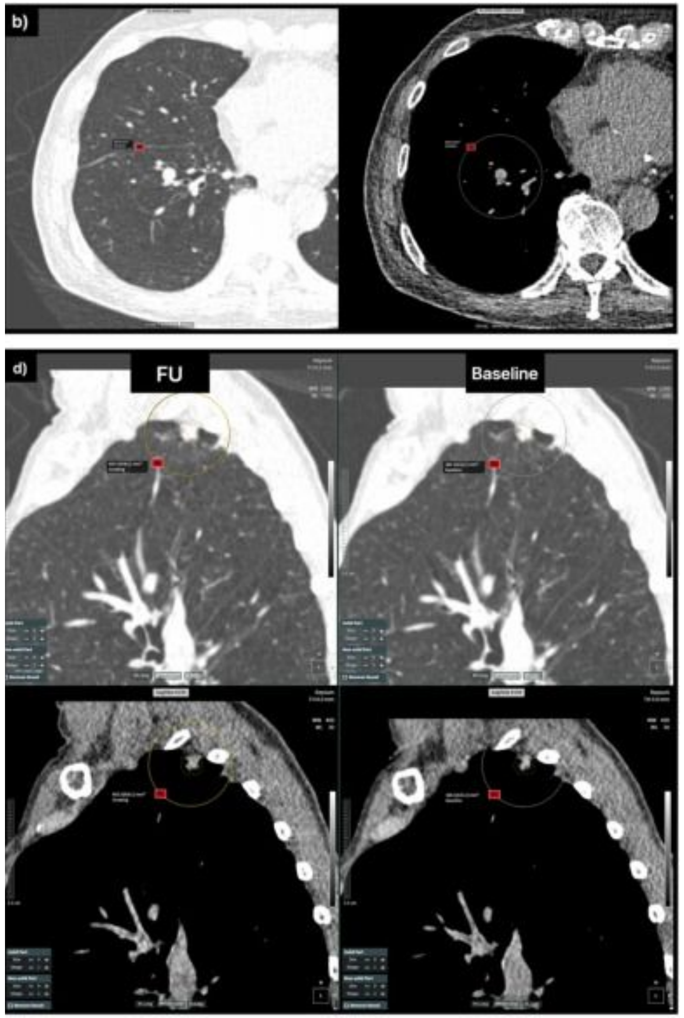
Lung cancer screening with low-dose CT (<1mSV)

AI outperforms radiologists

- Review on 20 studies[1]
  - DL algorithms exhibited superior SE (82%) and SP (75%) compared to human experts (SE 81%, SP 69%)
    - Difference in SP was statistically significant
- Multicentre prospective study (3678 CT scans)[2]
  - Radiologists, as first reader, would have led to 11.8 % missed referrals, higher than the 2.9 % of AI
    - AI significantly less negative missclassifications



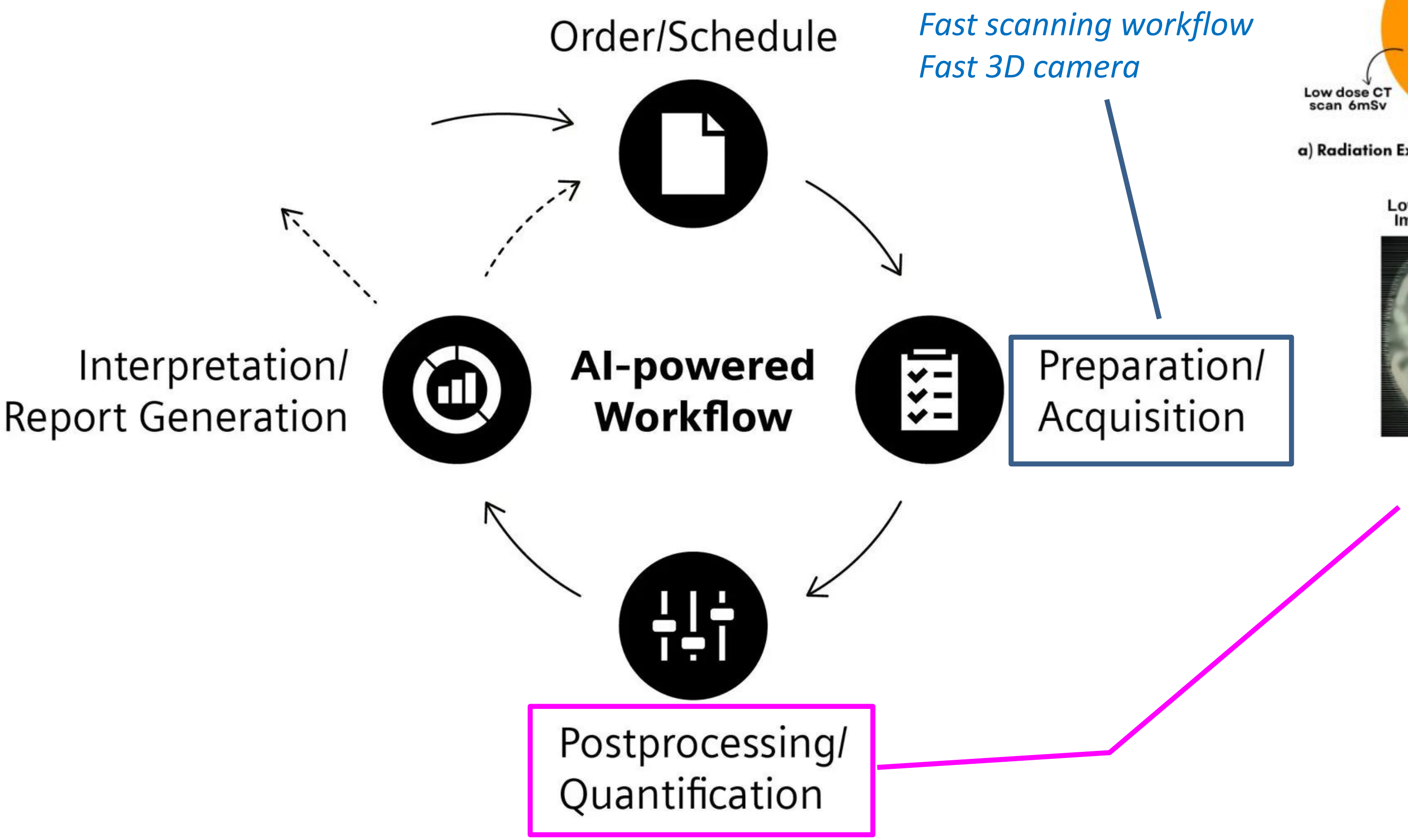


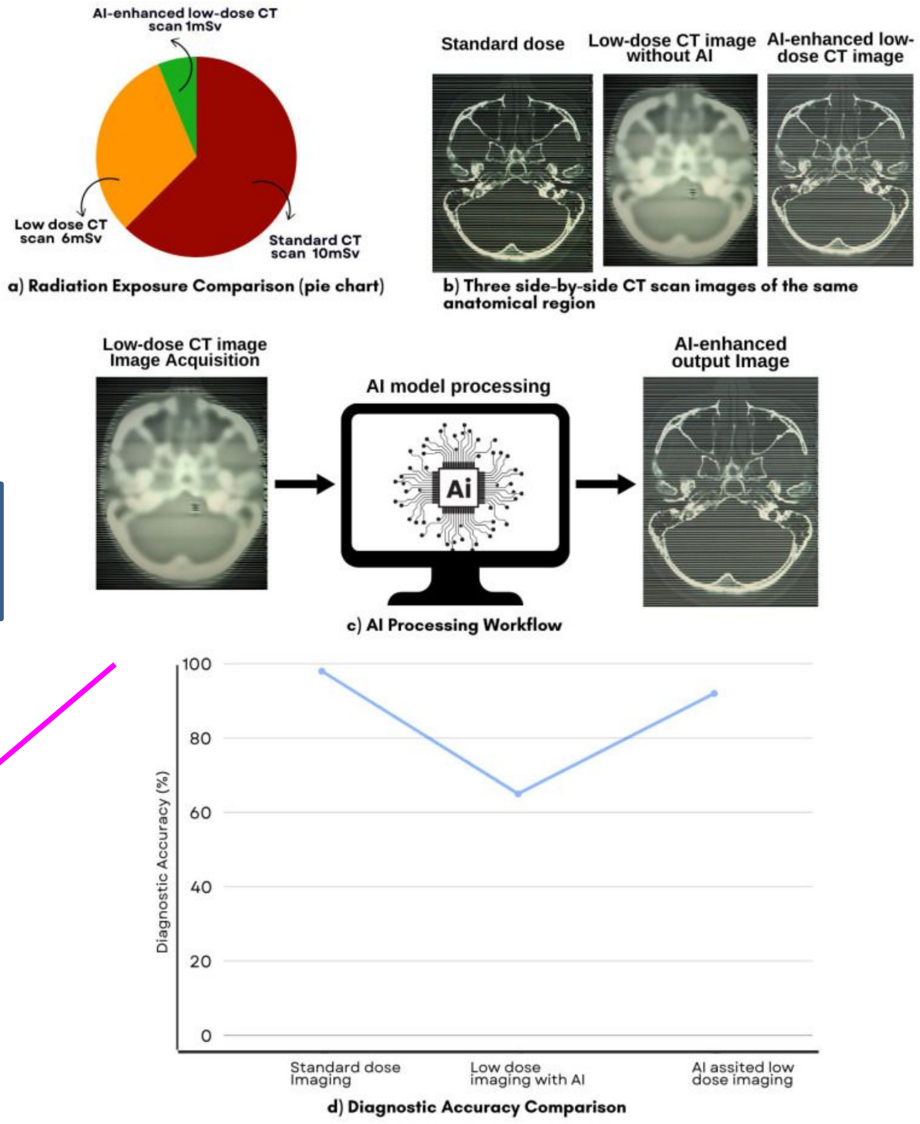


1. Wang TW, et al. Eur Radiol 2024 Nov;34(11):7397-7407
2. Walstra AN, et al. Eur J Cancer 2025 Feb 5:216:115214

AI Minimizes Radiation at Every Step of the Imaging Workflow

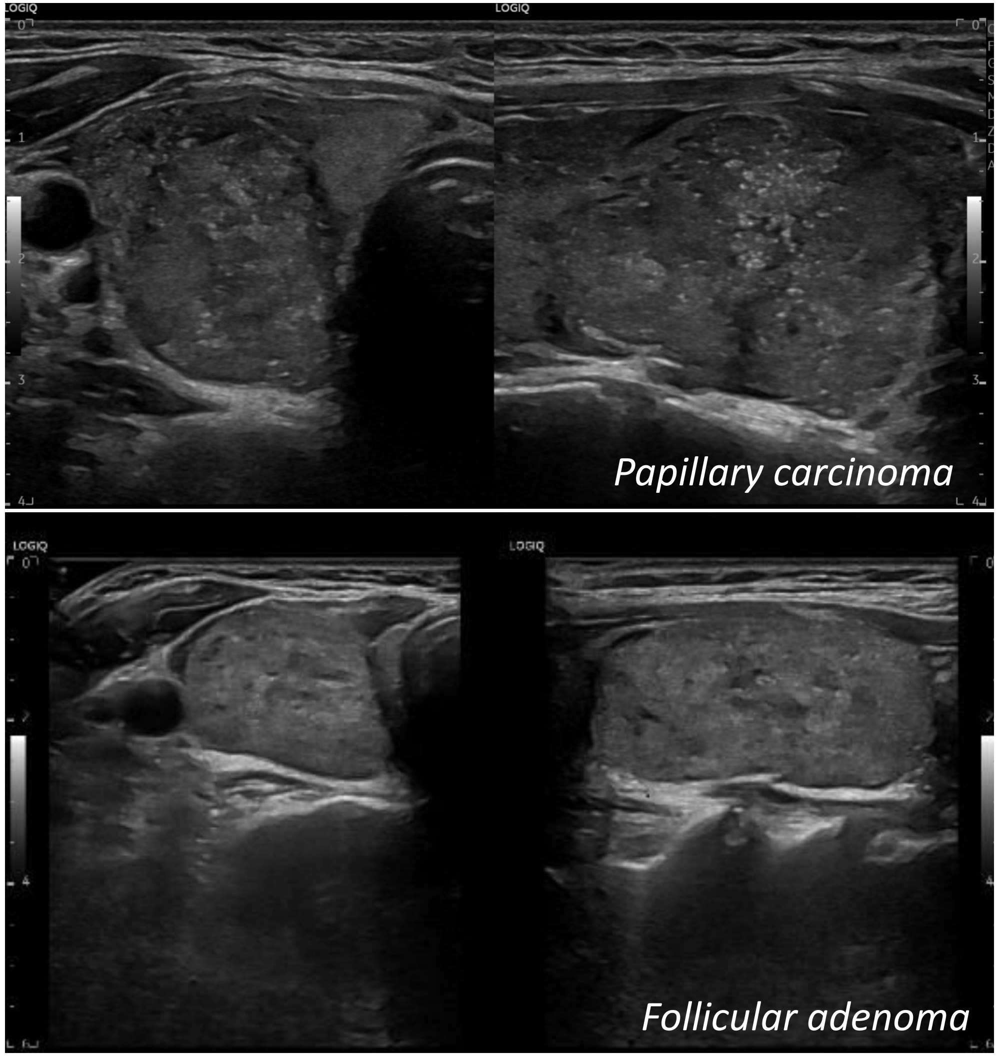
More efficient workflow enables safer CT Imaging





Thyroid cancer diagnosis with US is challenging

Complex assessments (TI-RADS 1-5), time consuming, variability, too many biopies



Thyroid Assistant, powered by Koios DS™
Analysis return examples

Benign

Not suspicious

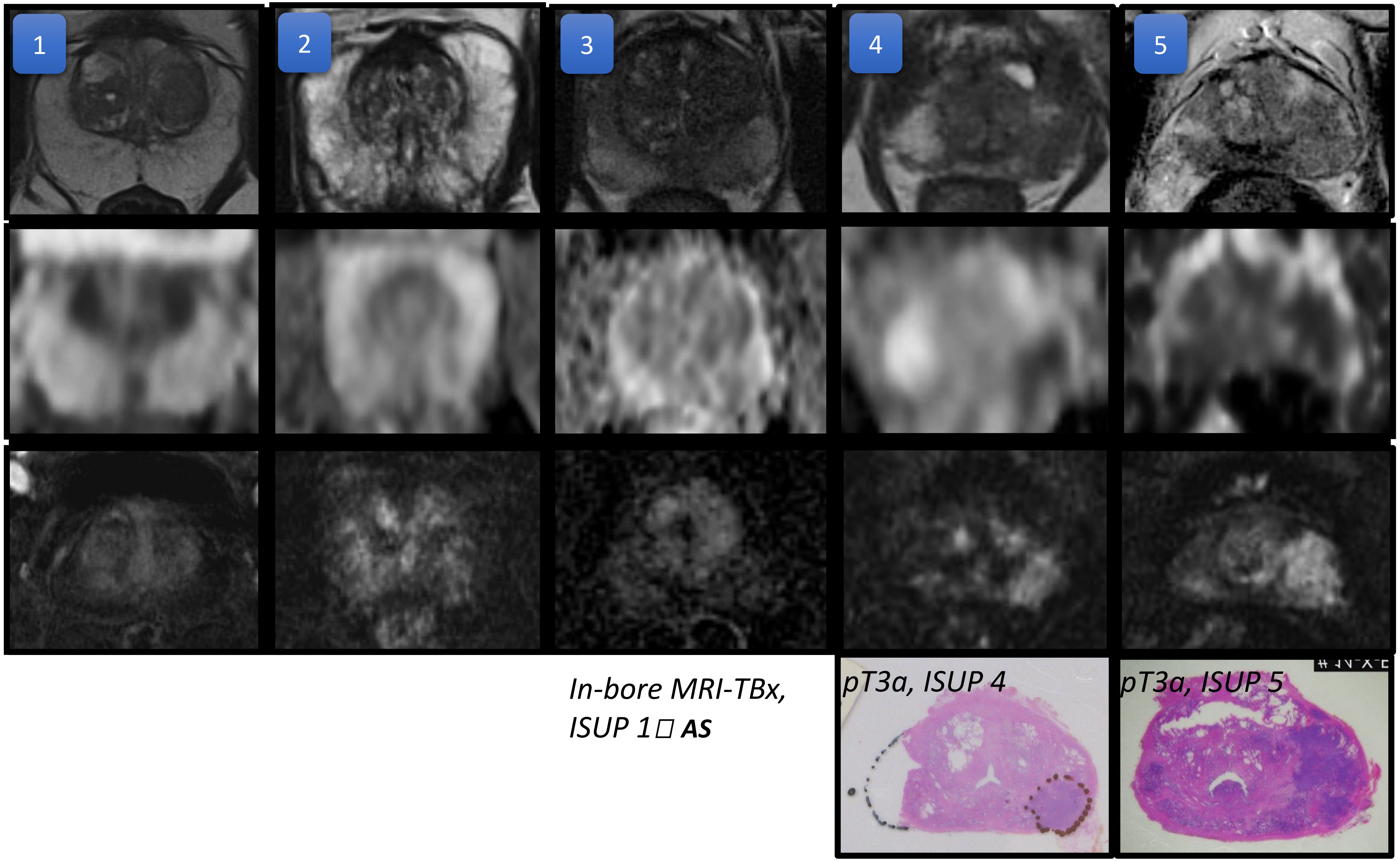
Mildly suspicious

Moderately suspicious

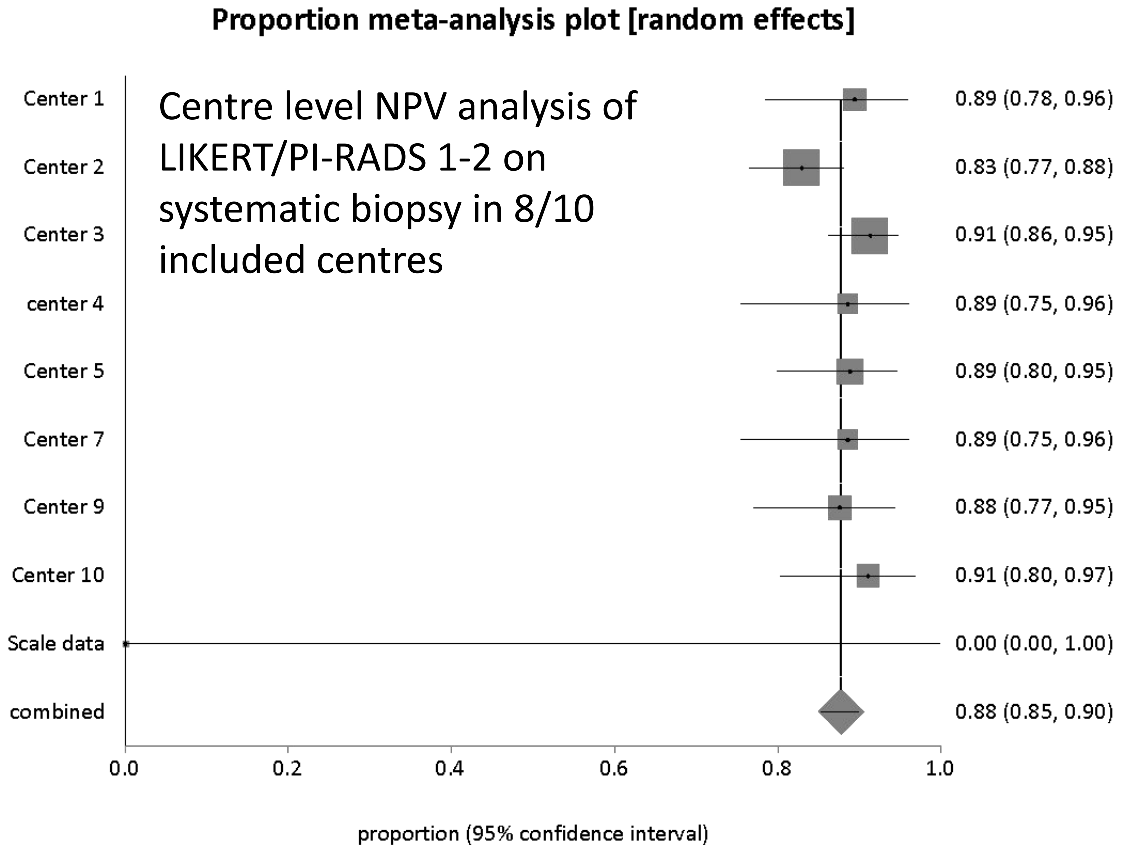
Highly suspicious

Multiparametric MRI of the prostate

Complex assessments (PI-RADS 1-5), time consuming, variability, too many biopies

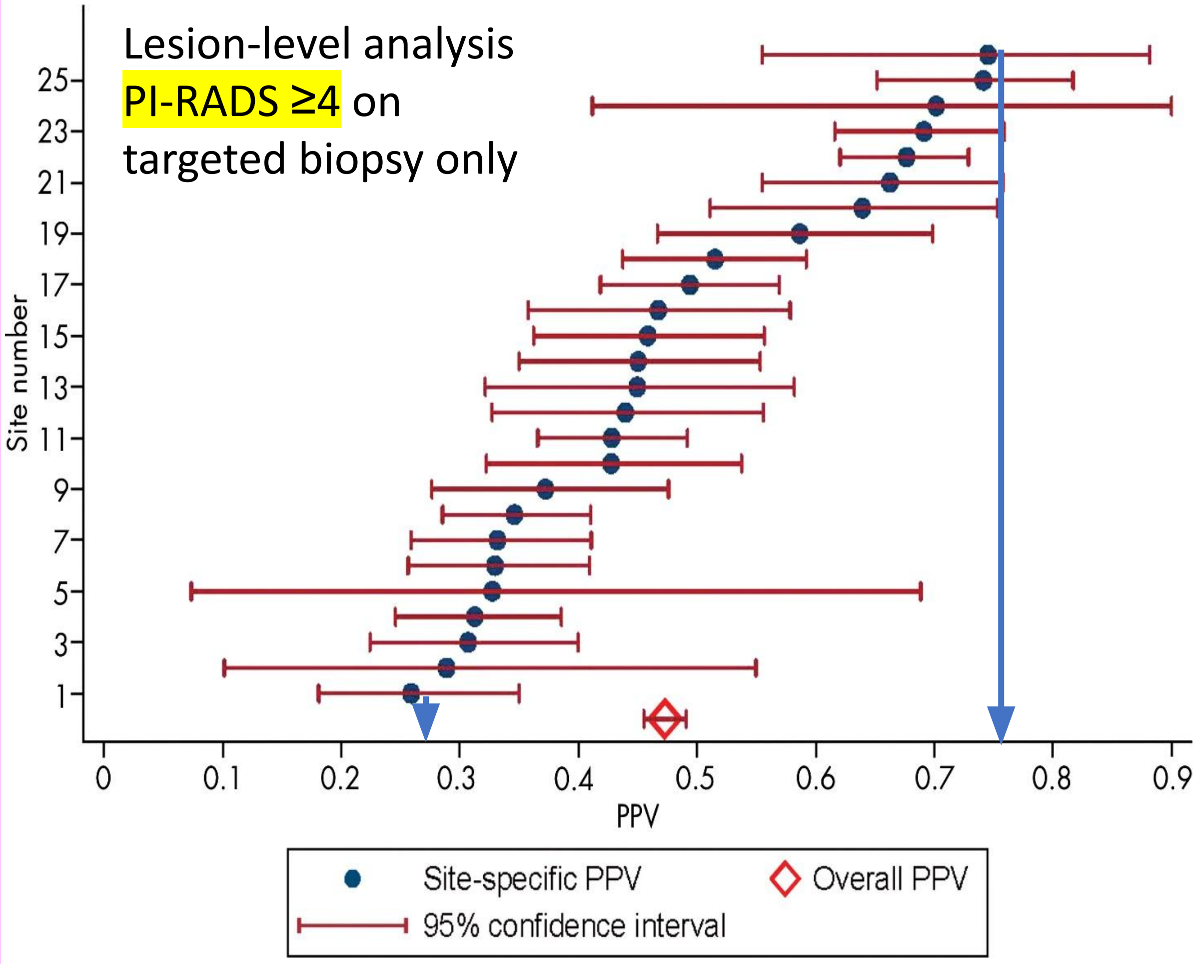


High sensitivity (low FNR) and NPV with low variability → consistent biopsy avoidance



Stonier T, et al. The “Is mpMRI Enough” or IMRIE Study: A Multicentre Evaluation of Prebiopsy Multiparametric MRI Compared with Biopsy. Eur Urol Focus 2020; S2405-4569(20)30271-6.

Intermediate specificity (FPR) and PPV with high variability → inconsistent biopsy yields

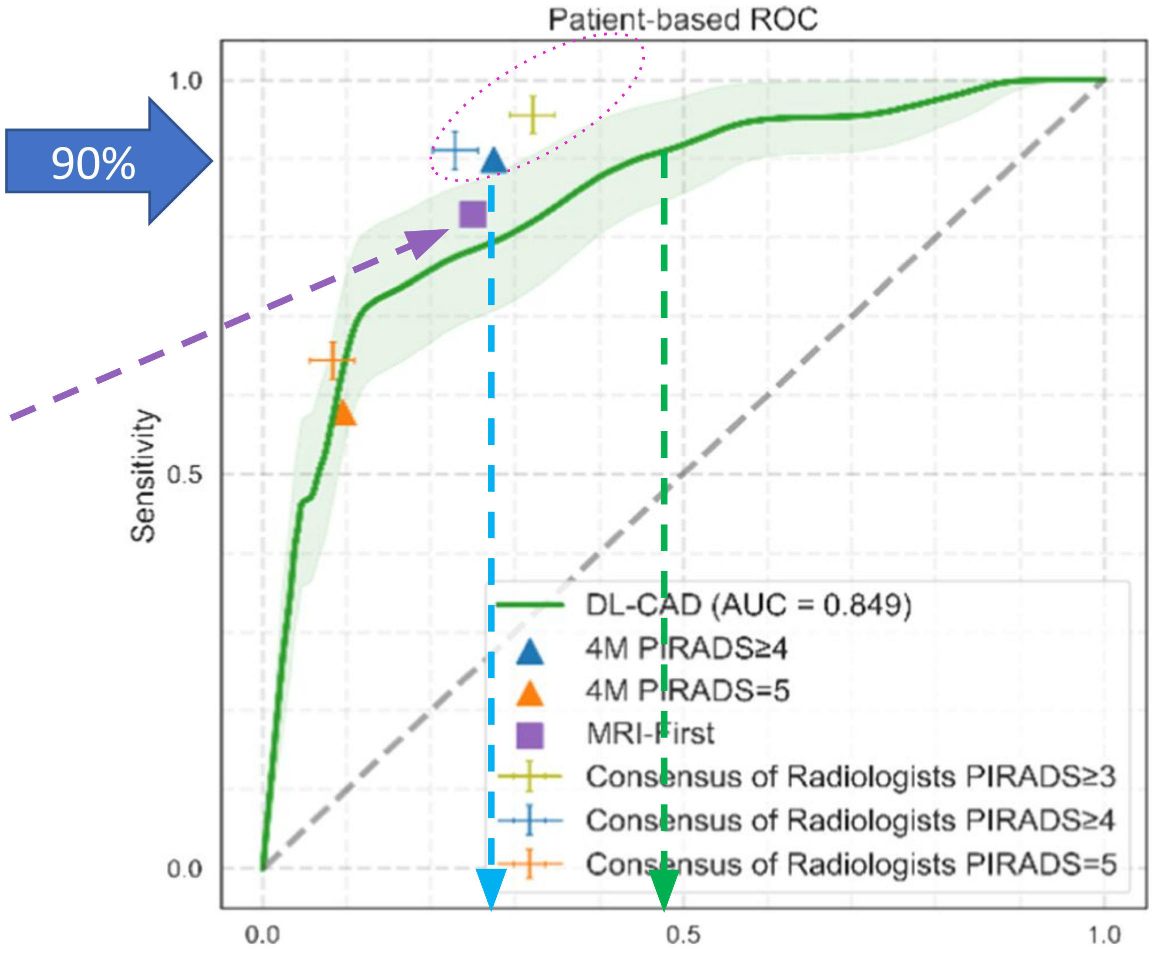


@ProfPadhani

Focus on excluding patients unlikely to have csPCa

Highest SE/NPV possible

- Cohort (2438 cases vs Radiologist)
  - 1586 training
  - 852 validation
- External validation
  - 296 mpMRI exams followed by biopsy*
- Matches general radiologists[2]
- Below the expert level[3]
  - DL-CAD shows higher FPR
- Moderate agreement with radiologist
  - k=0.53 □ comparable to the inter-reader agreement



False-positive rate

* All patients had systematic Bx, PI-RADS 3-5 in-bore MR-TBx

1. Hosseinzadeh M, et al. Eur Radiol. 2022 Apr;32(4):2224-2234.
2. Rouvière O, et al. Lancet Oncol. 2019 Jan;20(1):100-109.
3. van der Leest M, et al., Eur Urol. 2018 Nov 23.

100 cases with GG≥2 prevalence of 56% reviewed by 7 radiologists

- High accuracy for PI-RADS 4-5 patient-level detection (93%); average false detection/case 0.7
- Improves consistency between readers
- Reduces reading times

Performance metric	Radiologist	Radiologist with AI	P-value
AUC for PI-RADS ≥4 lesion detection	0.84	0.88	+4%; P=0.01
Inter-reader concordance (kappa)	0.22	0.36	P=0.003
Median reading time	103 seconds	81 seconds	-21%; P<0.001

Winkel DJ, et al. A Novel Deep Learning Based Computer-Aided Diagnosis System Improves the Accuracy and Efficiency of Radiologists in Reading Biparametric MRI of the Prostate: Results of a Multireader, Multicase Study. Invest Radiol. 2021; 56:605-613

WB-MRI can detect the most common cancers

Top-ten 2024[1]

- The most common (Screened already)
  1. Prostate / Breast
  2. Lung
  3. Colon & rectum
  4. Uterine corpus

- Other top-ten cancers (Not screened)
  - Urinary bladder
  - Kidney
  - NHL
  - Pancreas, Liver, etc.

Estimated New Cases

Male			Female		
Prostate	299,010	29%	Breast	310,720	32%
Lung & bronchus	116,310	11%	Lung & bronchus	118,270	12%
Colon & rectum	81,540	8%	Colon & rectum	71,270	7%
Urinary bladder	63,070	6%	Uterine corpus	67,880	7%
Melanoma of the skin	59,170	6%	Melanoma of the skin	41,470	4%
Kidney & renal pelvis	52,380	5%	Non-Hodgkin lymphoma	36,030	4%
Non-Hodgkin lymphoma	44,590	4%	Pancreas	31,910	3%
Oral cavity & pharynx	41,510	4%	Thyroid	31,520	3%
Leukemia	36,450	4%	Kidney & renal pelvis	29,230	3%
Pancreas	34,530	3%	Leukemia	26,320	3%
All sites	**1,029,080**		**All sites**	**972,060**	

Estimated Deaths

Male			Female		
Lung & bronchus	65,790	20%	Lung & bronchus	59,280	21%
Prostate	35,250	11%	Breast	42,250	15%
Colon & rectum	28,700	9%	Pancreas	24,480	8%
Pancreas	27,270	8%	Colon & rectum	24,310	8%
Liver & intrahepatic bile duct	19,120	6%	Uterine corpus	13,250	5%
Leukemia	13,640	4%	Ovary	12,740	4%
Esophagus	12,880	4%	Liver & intrahepatic bile duct	10,720	4%
Urinary bladder	12,290	4%	Leukemia	10,030	3%
Non-Hodgkin lymphoma	11,780	4%	Non-Hodgkin lymphoma	8,360	3%
Brain & other nervous system	10,690	3%	Brain & other nervous system	8,070	3%
All sites	**322,800**		**All sites**	**288,920**	

Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

1. CA A Cancer J Clinicians, Volume: 74, Issue: 1, Pages: 12-49, First published: 17 January 2024, DOI: (10.3322/caac.21820)

WB-MRI in high-risk individuals (cancer predisposition syndromes)

Recommended by International guidelines □ Measurable benefit

Syndromes	Age
Li-Fraumeni syndrome (LFS)[1-8]	Any *(Annual)*
Hereditary Paraganglioma-Pheocromocytoma syndromes (HPP)[9-10]	From 6-8yy *(Every 2 years)*
Constitutional mismatch repair deficiency syndrome (CMMRD)[11-14]	From 6-8yy *(Annual)*
Hereditary retinoblastoma[15]	From 8yy *(Annual)*

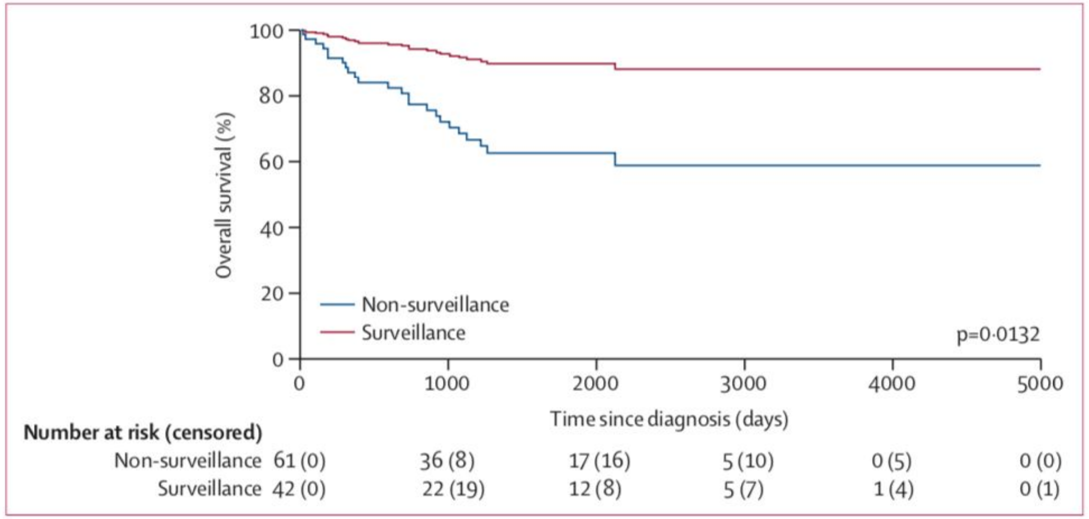


Figure 1: **Overall survival in the surveillance and non-surveillance groups**
Number at risk refers to the number of tumours, not individuals.

1. TORONTO protocol
2. ESMO guidelines
3. ESO-ESMO guidelines
4. NCCN guidelines
5. GENTURIS guidelines
6. UKCGG Consensus Group guidelines
7. Kumamoto et al.
8. Australian Reccommendations
9. Rednam SP et al
10. Garcia-Carbonero et al
11. AACR
12. US task force
13. C4CMMRD
14. IRRD consortium
15. Greer MC, et al.

WB-MRI in low-risk individuals (general population)

Benefit not yet measured, but increasingly used

- Challenges
  - Abnormal findings Up to 99%
    - How to *minimise harm*?
      - Trust a negative WB-MRI
      - Do not over-investigate
      - High NPV & low prevalence of cancer
  - Cancer About 1-2%
    - How to *maximise potential*?
      - Oncological expertise in multi-organ evaluations

	Subjects	***Cancer***	***Abnormal findings***
Bamberg F et al. (2015)	30,000	*Ongoing*	*Ongoing*
Hegenscheid K et al. (2013)	2,500	*5,9%**	*/*
Hu YS et al. (2024)	2064	***1.2 %***	***99%***
Baumgart D et al. (2007)	1007	***0.44 %***	***/***
Cieszanowski A et al. (2014)	666	***1.05 %***	***99%***
Basar Y et al. (2021)	576	***2.6 %***	***/***
Goede SC et al. (2005)	298	***0.33 %***	***/***
Lee SY et al. (2018)	229	***0.8%***	***93%***
Lo GG et al. (2008)	132	***1.5 %***	***94%***
Ulus S et al. (2016)	118	***1.7 %***	***72%***
Tarnoki DL et al. (2014)	22	***4.5 %***	***91%***

* No histological confirmation

Radiology

Oncologically Relevant Findings Reporting and Data System (ONCO-RADS): Guidelines for the Acquisition, Interpretation, and Reporting of Whole-Body MRI for Cancer Screening

Giuseppe Petralia, MD • Dow-Mu Koh, MD • Raj Attariwala, MD, PhD • Joseph J. Busch, MD • Ros Eeles, MD • David Karow, MD, PhD • Gladys G. Lo, MD • Christina Messiou, MD • Evis Sala, MD, PhD • Hebert A. Vargas, MD • Fabio Zugni, MD • Anwar R. Padhani, MD

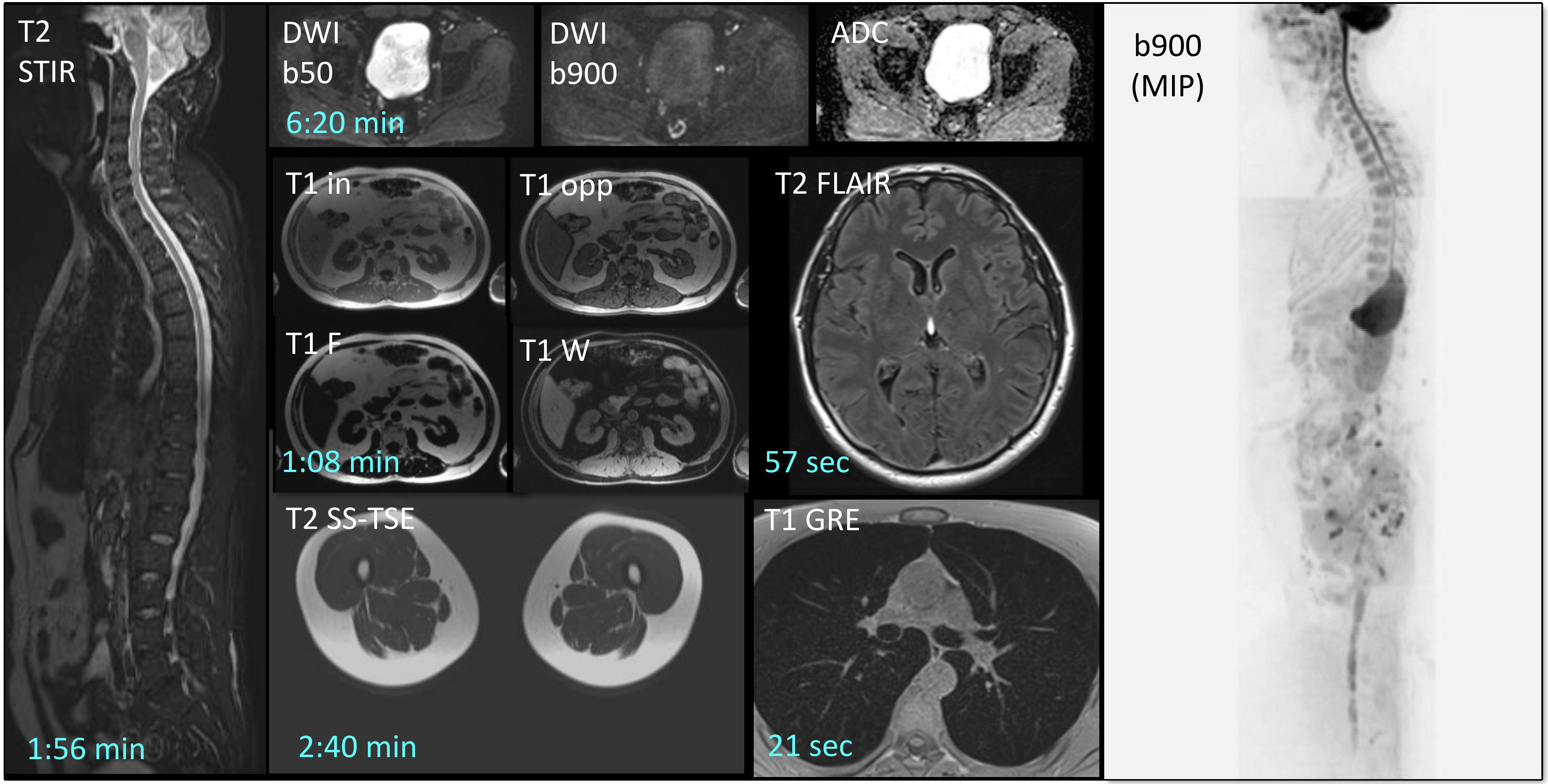
From the Precision Imaging and Research Unit, Department of Medical Imaging and Radiation Sciences (G.P.), and Department of Radiology (F.Z.), IEO European Institute of Oncology IRCCS, Via Giuseppe Ripamonti 435, 20141 Milan, Italy; Department of Oncology and Hemato-Oncology, University of Milan, Italy (G.P.); Department of Radiology, Royal Marsden Hospital and Institute of Cancer Research, Sutton, England (D.M.K., C.M.); AIM Medical Imaging, Vancouver, Canada (R.A.); Busch Center, Alpharetta, Ga (J.J.B.); The Institute of Cancer Research and Royal Marsden NHS Foundation Trust, London, England (R.E.); Human Longevity, San Diego, Calif (D.K.); Department of Diagnostic & Interventional Radiology, Hong Kong Sanatorium & Hospital, Hong Kong (G.G.L.); Department of Radiology and Cancer Research, UK Cambridge Center, Cambridge, England (E.S.); Department of Radiology, Memorial Sloan-Kettering Cancer Center, New York, NY (H.A.V.); and Paul Strickland Scanner Centre, Northwood, England (A.R.P.). Received April 24, 2020; revision requested June 16; revision received November 5; accepted November 17. **Address correspondence to** G.P. (e-mail: *giuseppe.petralia@ieo.it*).

Conflicts of interest are listed at the end of this article.

Radiology 2021; 000:1–14 • https://doi.org/10.1148/radiol.2021201740 • Content codes: OI MR

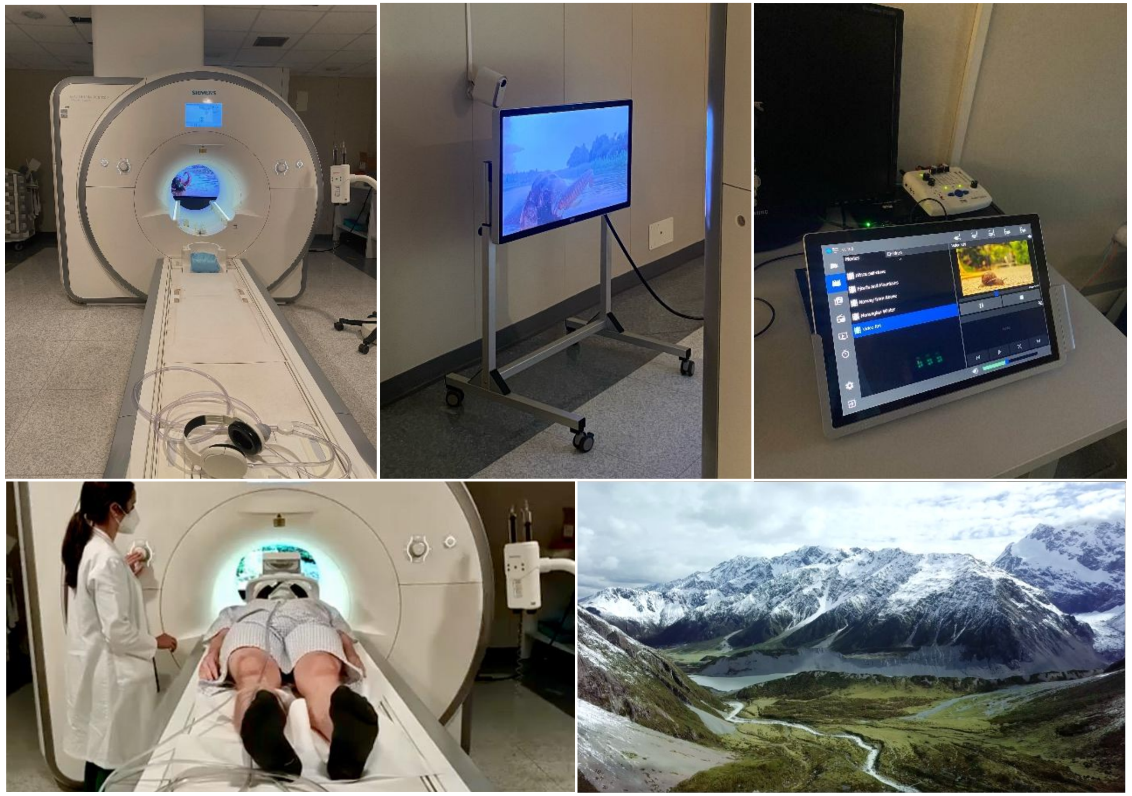
1. Acquisition

WB-MRI protocol @ 1.5 & 3T (35-40mins) (TA = 13:22 sec @1.5T with AI)



How to make acquisition easier?

Communication / Music / TV

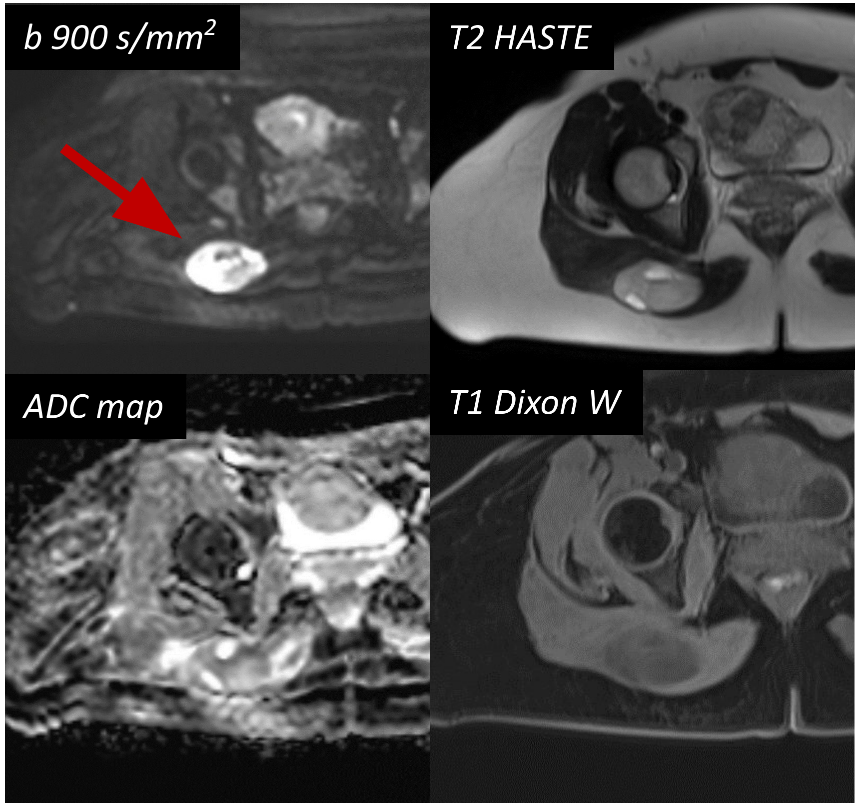


62 individuals	Acceptability	Comfort	Satisfaction
AV Vs Standard	t(105)=3.8 p<0.05	t(105)=2.35 p<0.05	t(105)=4.1 p<0.01
AV vs Music	t(105)=0.69 p=0.82	t(105)=1.37 p=0.39	t(105)=2.2 p<0.05
Music Vs Standard	t(88)=2.72 p<0.05	t(88)=0.95 p=0.26	t(88)=1.79 p=0.33

2. Interpretation

Abnormal findings assigned to one of the 7 body regions (bone, head, neck, chest, abdomen, pelvis, limbs)

- ONCO-RADS category (1 to 5)
  - ONCO-RADS 1: normal
  - ONCO-RADS 2: benign finding highly likely
  - ONCO-RADS 3: benign finding likely
  - ONCO-RADS 4: malignant finding likely
  - ONCO-RADS 5: malignant finding highly likely

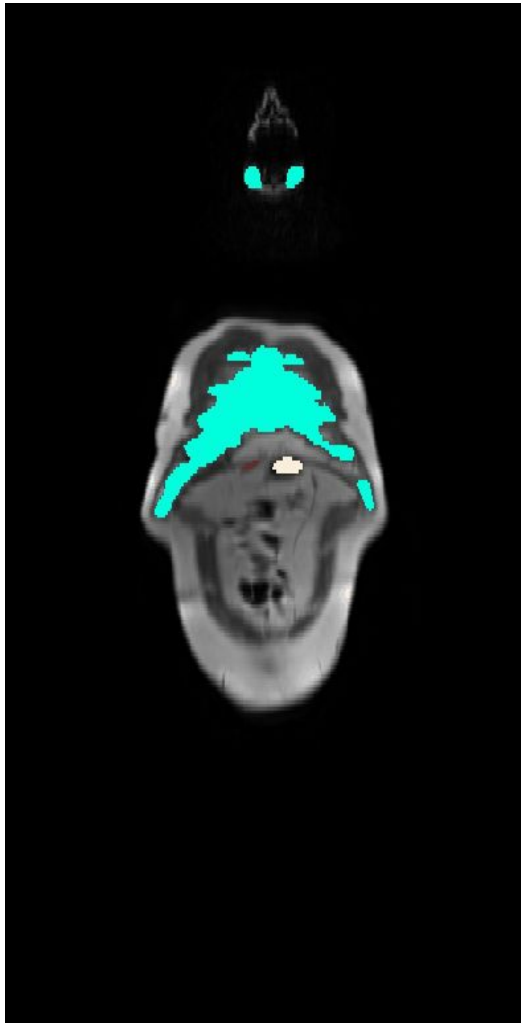


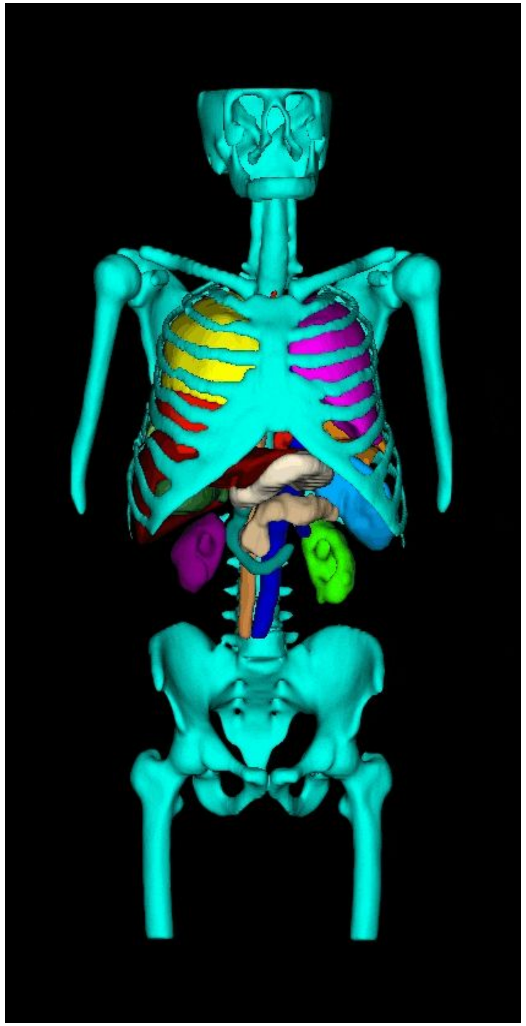
- 29yo, F (LFS)
  - 2013 Breast cancer
  - 2017 Right inguinal dermatofibrosarcoma protuberans
  - 2018 Recurrence (Surgery + RT)
  - 2020 WB-MRI for cancer screening

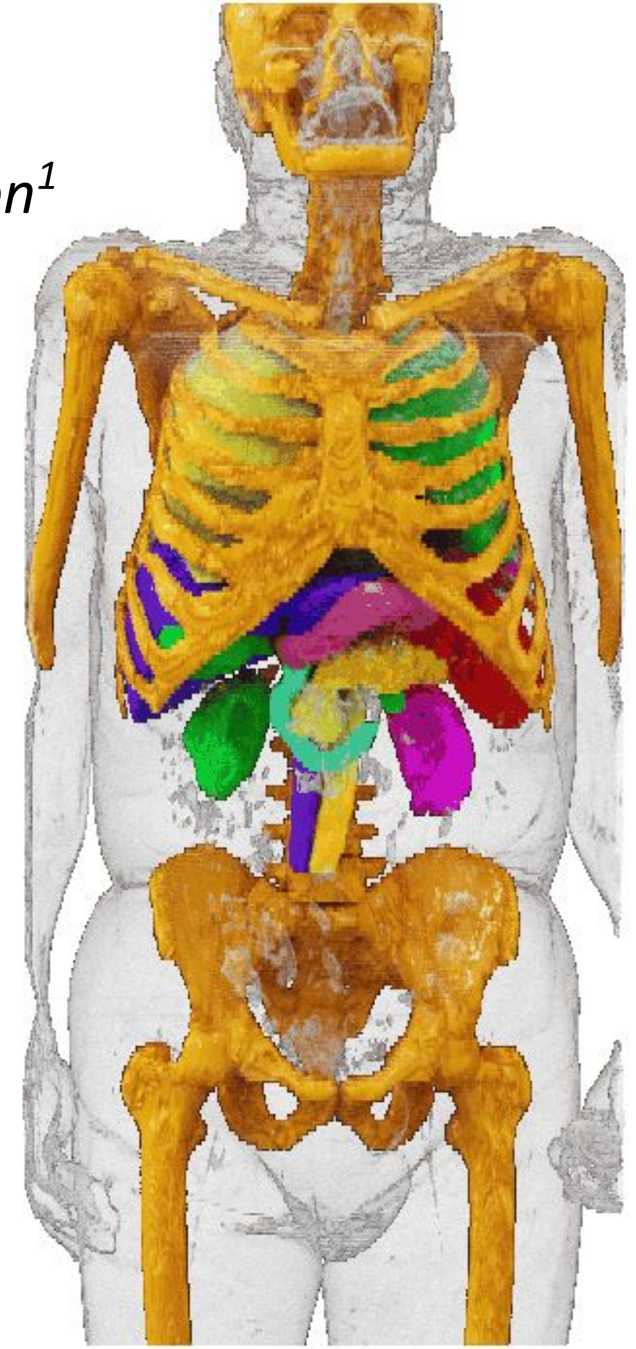
ONCO-RADS 5 Surgery / Biopsy

How to make interpretation easier?

AI assisted ONCO-RADS assessments Bone & organ segmentation[1]





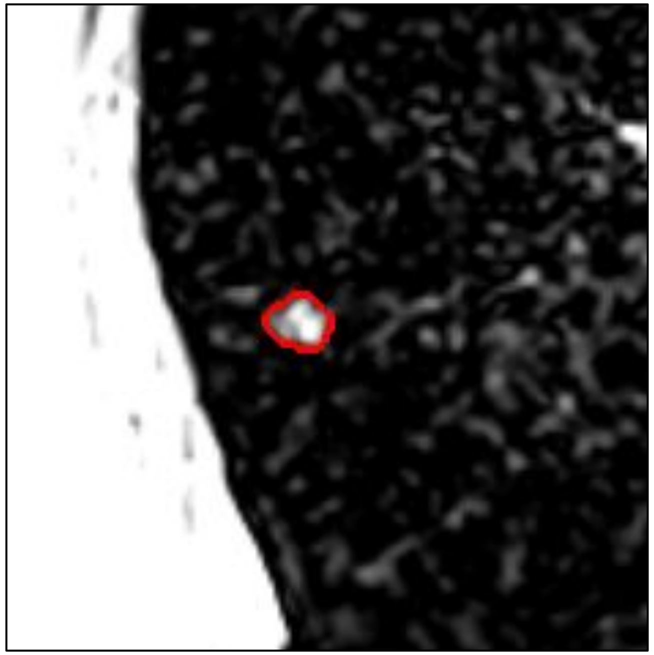


1. *Cornelius Jacob, IEO & Siemens Healthineers*

How to make interpretation easier?

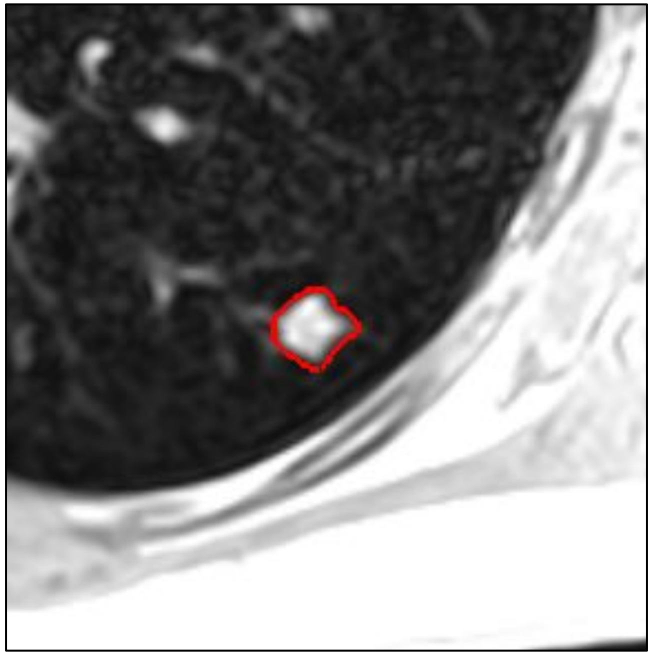
AI assisted ONCO-RADS assessments □ Deep learning model for lung nodule detection[1]

Lung Nodule of **4 mm**



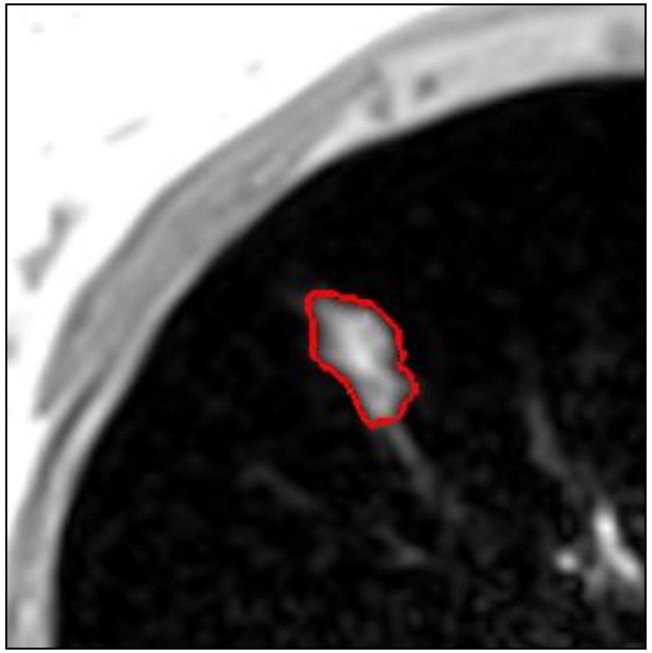
□ ONCO-RADS 2
(< 6 mm)

Lung Nodule of **7 mm**



□ ONCO-RADS 3
(≥ 6 mm and < 8 mm)

Lung Nodule of **14 mm**



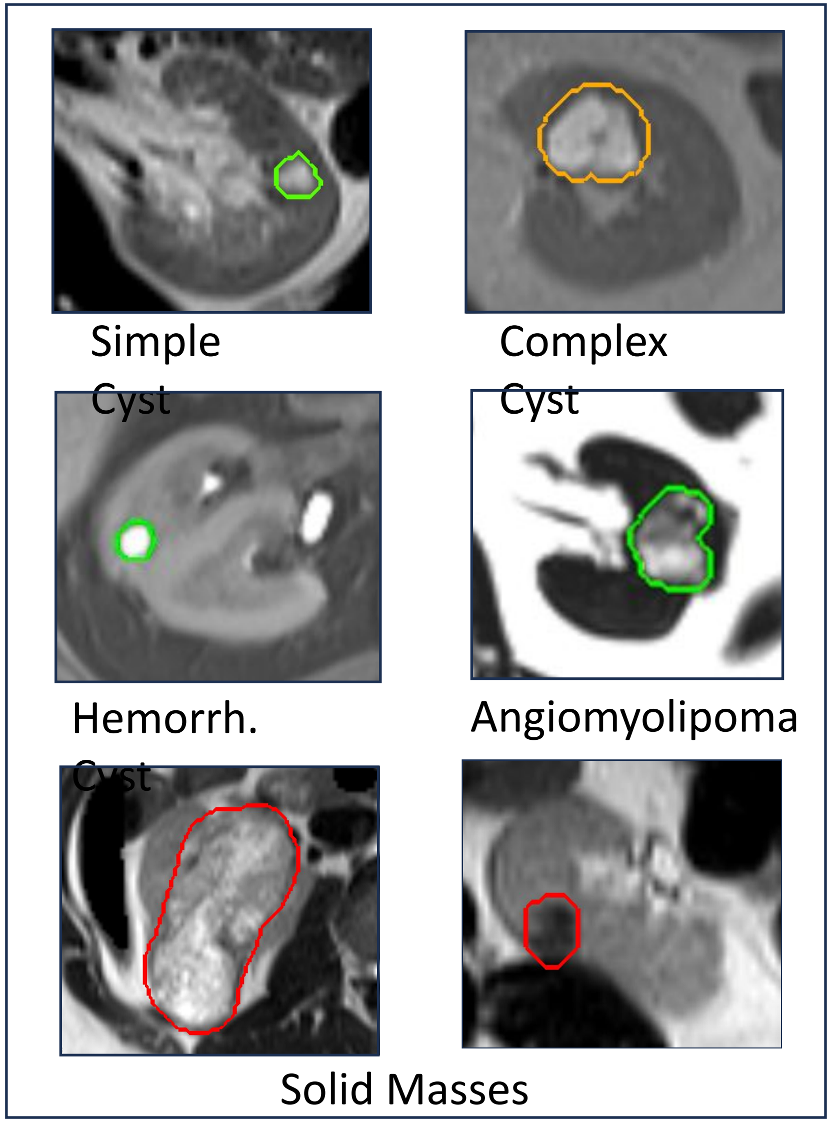
□ ONCO-RADS 4
(≥ 8 mm)

1. *ECR 2025, Cornelius Jacob, IEO & Siemens Healthineers*

How to make interpretation easier?

AI assisted ONCO-RADS assessments □ Deep learning model for kidney lesion detection[1]

- Simple Cysts (ONCO-RADS 2)
- Complex Cysts (ONCO-RADS 3)
- Hemorrhagic Cysts (ONCO-RADS 2)
- Angiomyolipoma (ONCO-RADS 2)
- Solid Masses (ONCO-RADS 4-5)

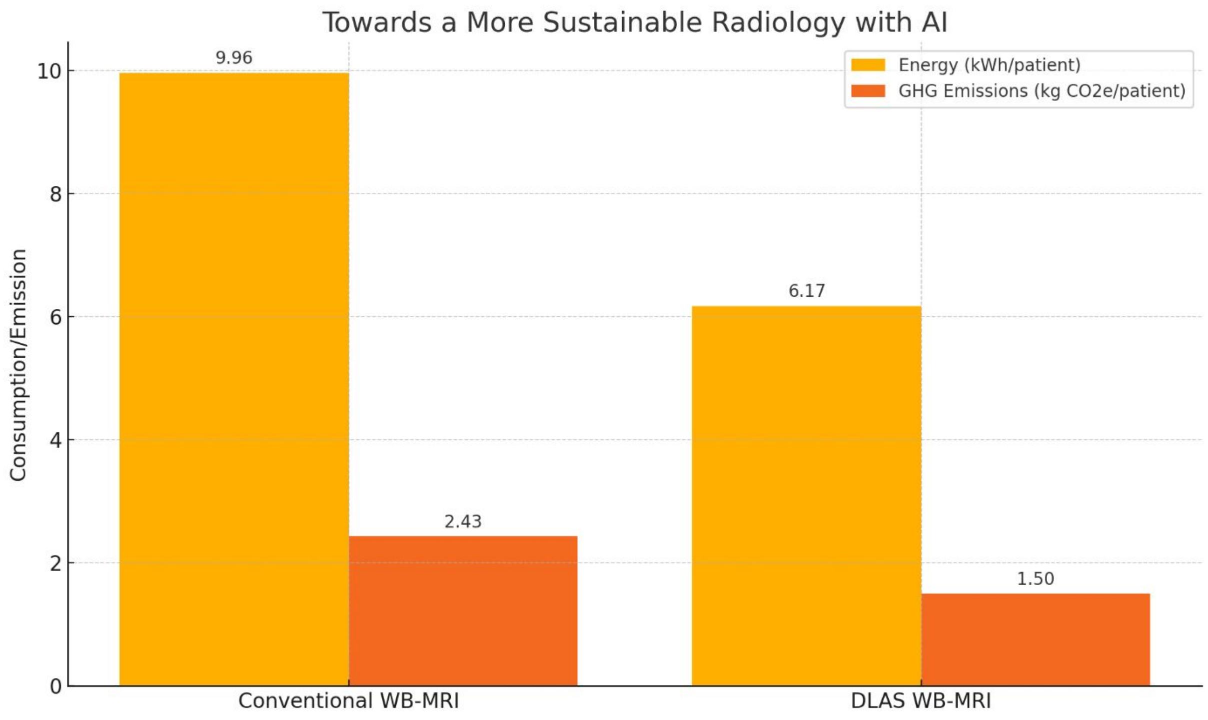


1. *Cornelius Jacob, IEO & Siemens Healthineers*

Towards a more sustainable radiology with AI

WB-MRI examinations performed with deep learning–accelerated sequences (DLAS)

- WB-MRI DLAS vs WB-MRI conv
  - 38% reduction in both energy consumption and greenhouse gas emissions
    - GHG emissions: 1.50 vs 2.43 $kgCO_2e$/patient ($p < .05$)
    - Energy: 6.17 vs 9.96 kWh/patient ($p < .05$)



Cancer staging

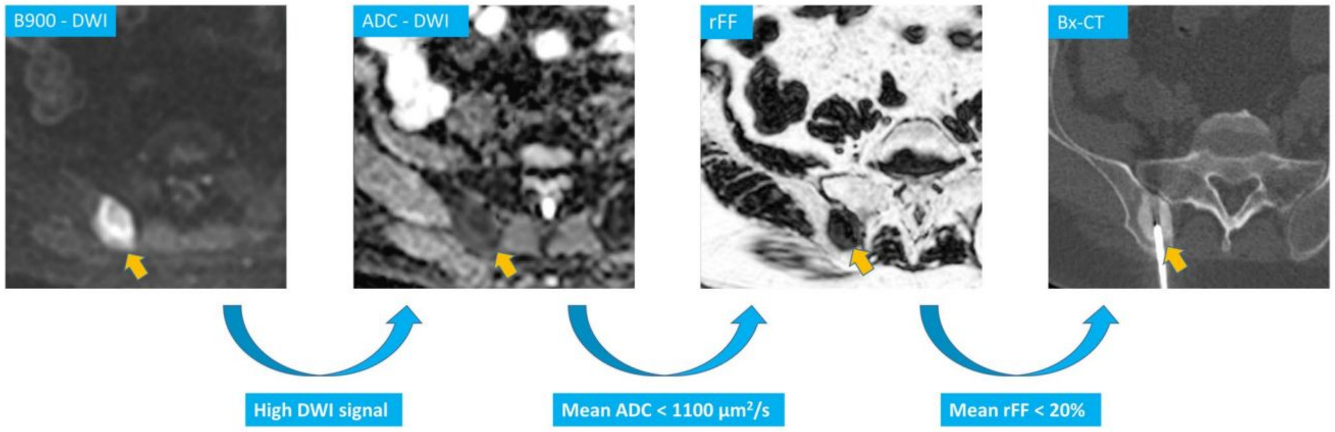
Mostly osteotropic cancers (prostate / breast / multiple myeloma)

Other cancers (lung, colon, ovarian)

Multiparametric analysis of the bone □ Improves both SE & SP

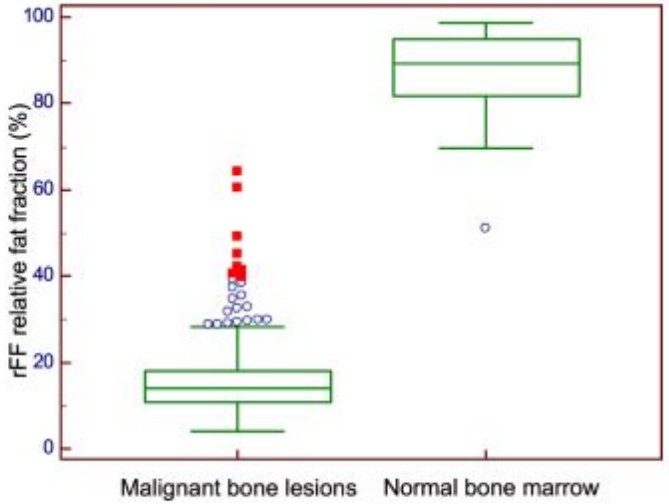
*Active bone disease □ Hyper-DWI **<u>and</u>** ADC <1000 μm²/s /**<u>and</u>** rF% < 20%*

- PPV = 93%[1]
  - No overlap in values (rF%)[2]
- Excellent interobserver agreement (0.95)[2]



WB-MRI	ICC between observers (95% confidence interval)
Cervicothoracic spine	0.98 (0.96–0.98)
Lumbosacral spine	0.95 (0.92–0.97)
Pelvis	0.95 (0.92–0.97)
Extremity	0.93 (0.89–0.97)
Whole skeleton	0.95 (0.94–0.96)

ICC, intraclass correlation coefficient; WB-MRI, whole-body MRI.

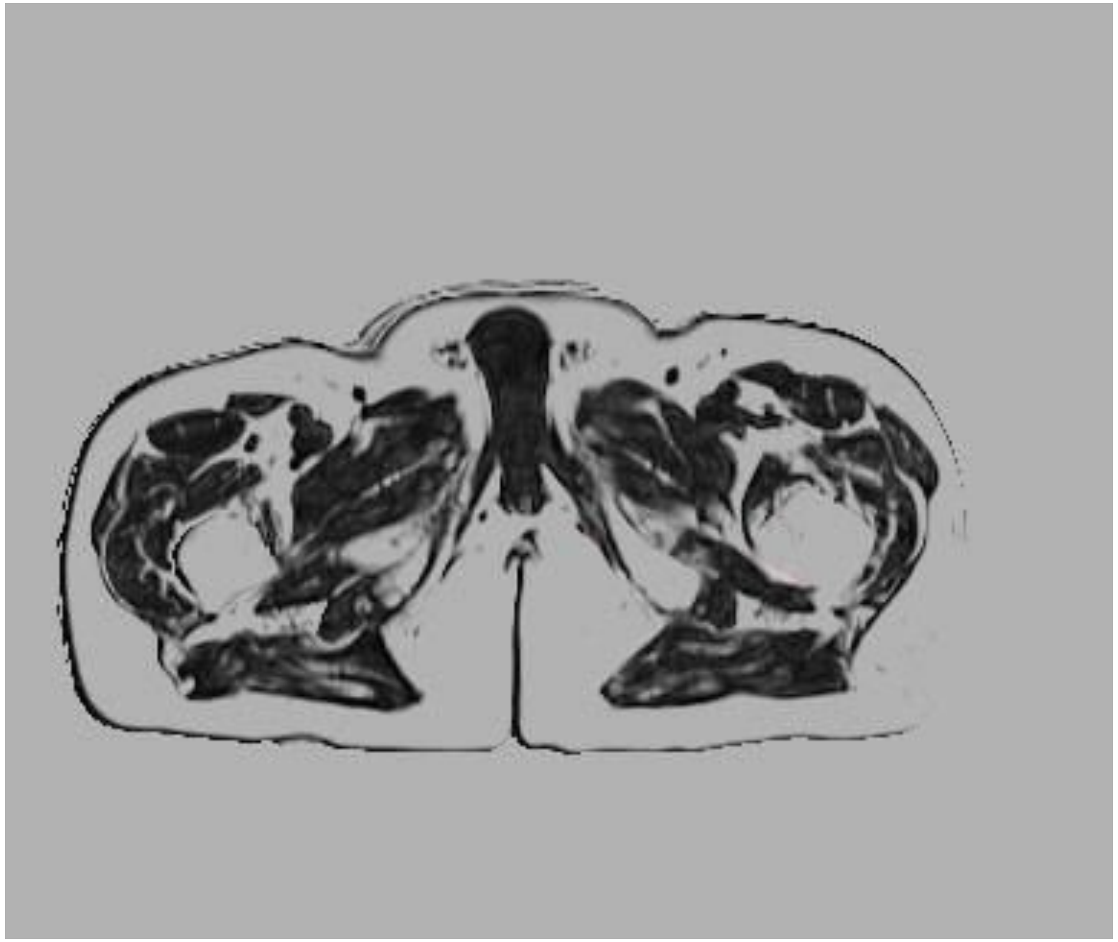


1. Donners R, et al. Eur radiol. 2022 Jul;32(7):4647-4656.
2. Castagnoli F, et al. BJR. 2023 Dec;96(1152):20230240.

Welcome to a new era with AI

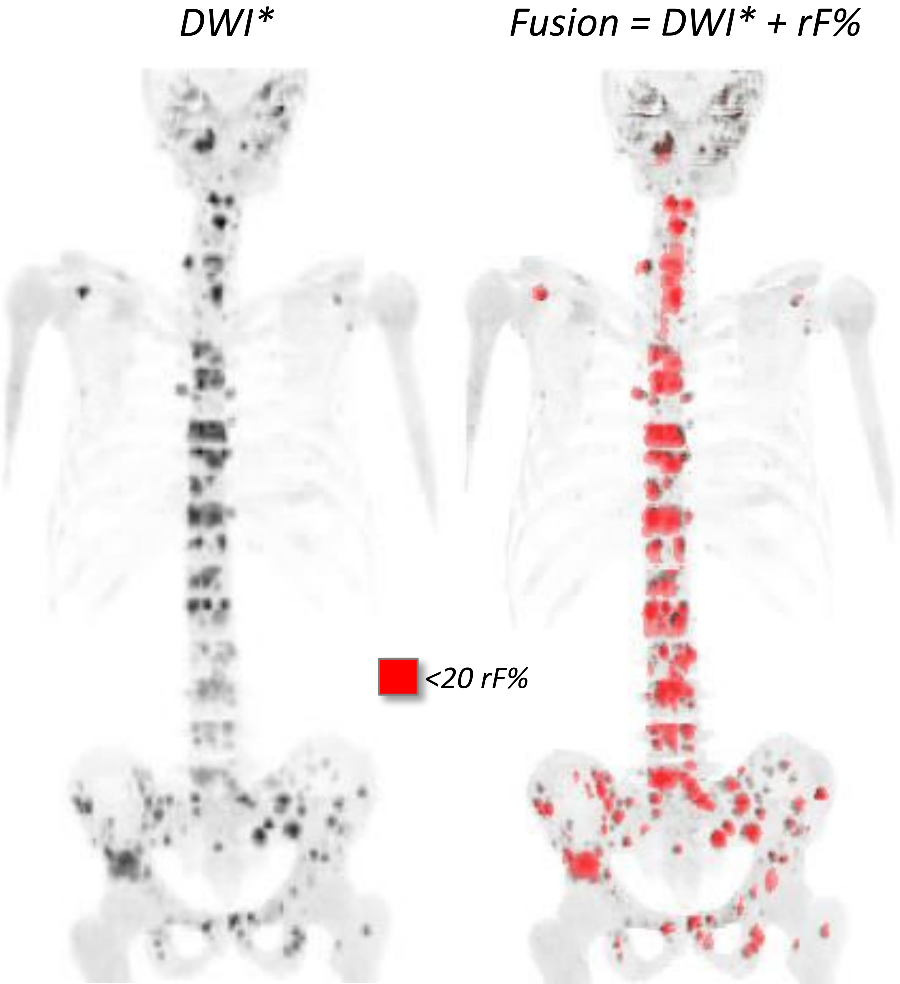
From multiple to single image reading

Active metastastic volume = 104mL



Fusion = DWI + rF%*

**b = c1400 s/mm²*



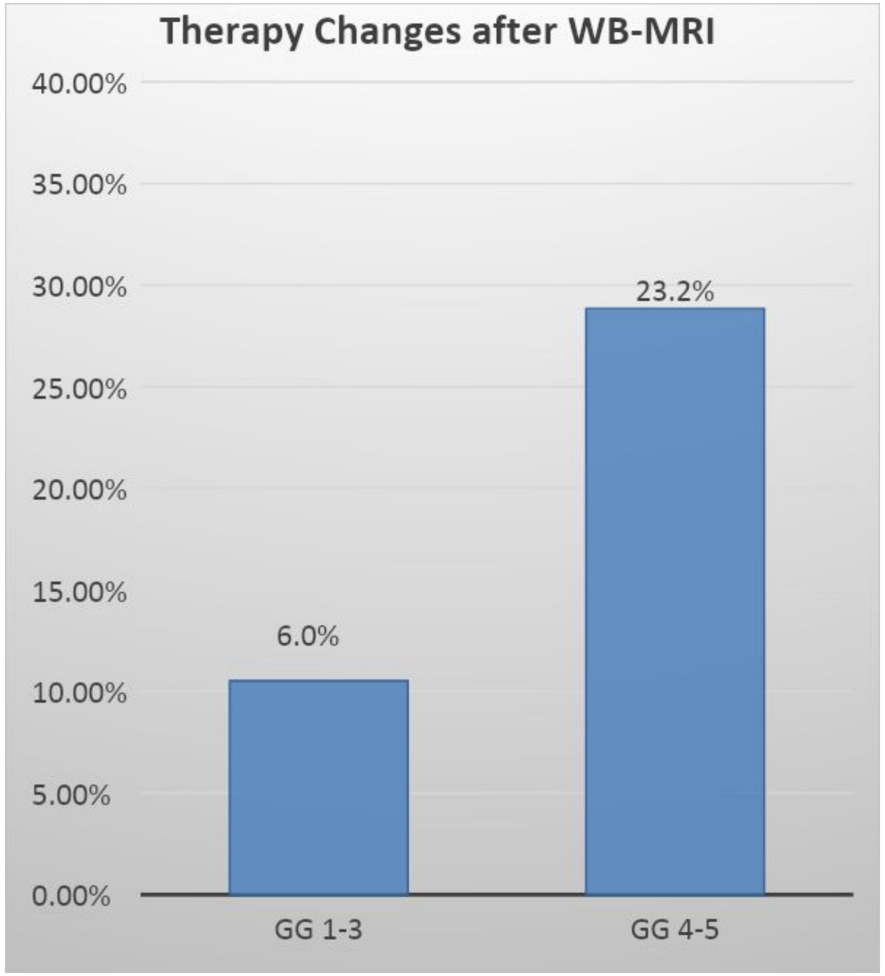
Cornelius Jacob, IEO & Siemens Healthineers

Prostate cancer «All-in-one» staging with WB-MRI[1]

Multicentre (IEO, AOUV, SCB), prospective, interventional study

	TOTAL	Therapy UNCHANGED	Therapy CHANGED
Patients	152	131 (86.2%)	21 (13.8%)
CONCORDANT	109 (71.7%)	108 (71.0%)	1 (0.7%)
UPSTAGING	26 (17.1%)	13 (8.5%)	13 (8.5%)
DOWNSTAGING	17 (11.2%)	9 (5.9%)	8 (5.3%)

Data relative to IEO (Milan) and Spedali Civili (Brescia)



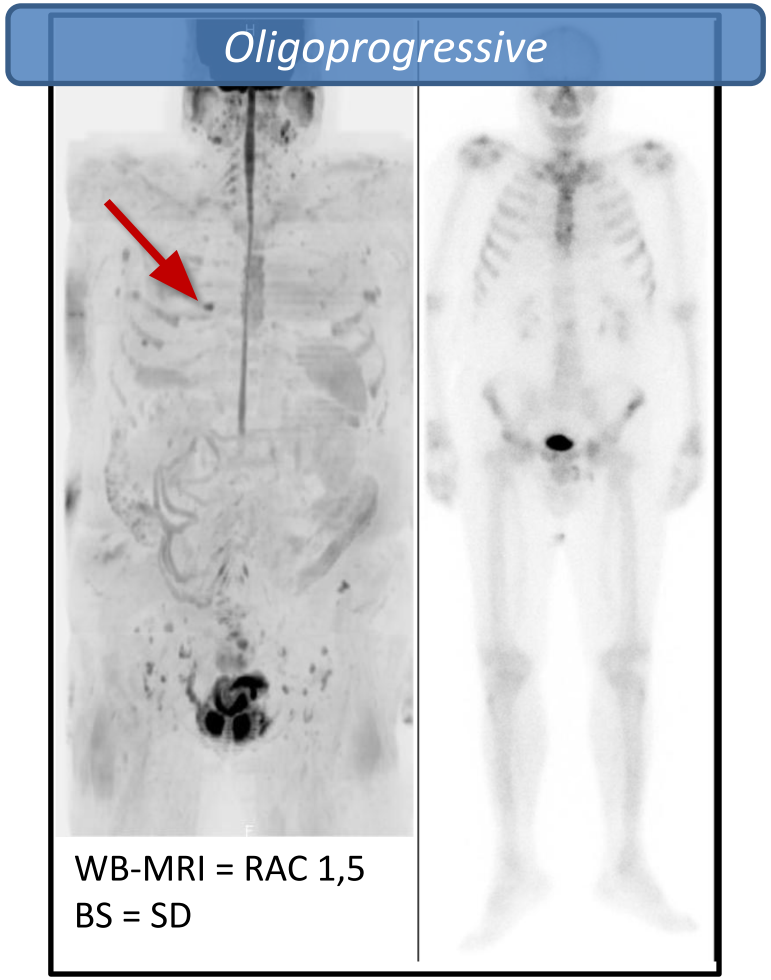
1. ClinicalTrials.gov Identifier: NCT06071195

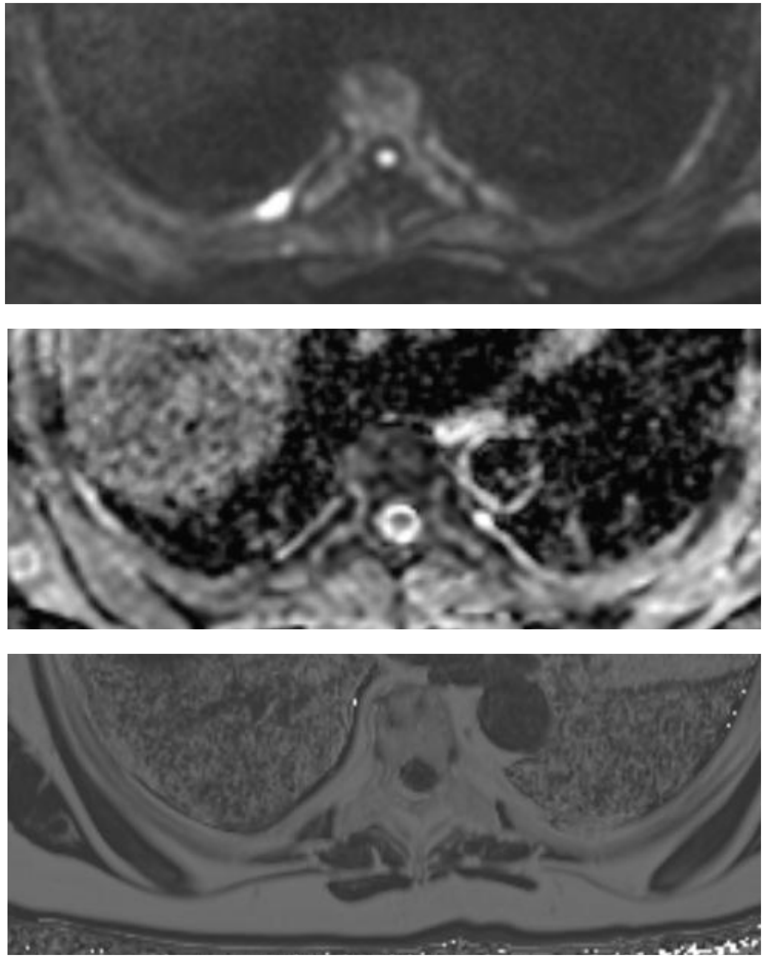
Cancer therapy monitoring

mCRPC □ Abiraterone

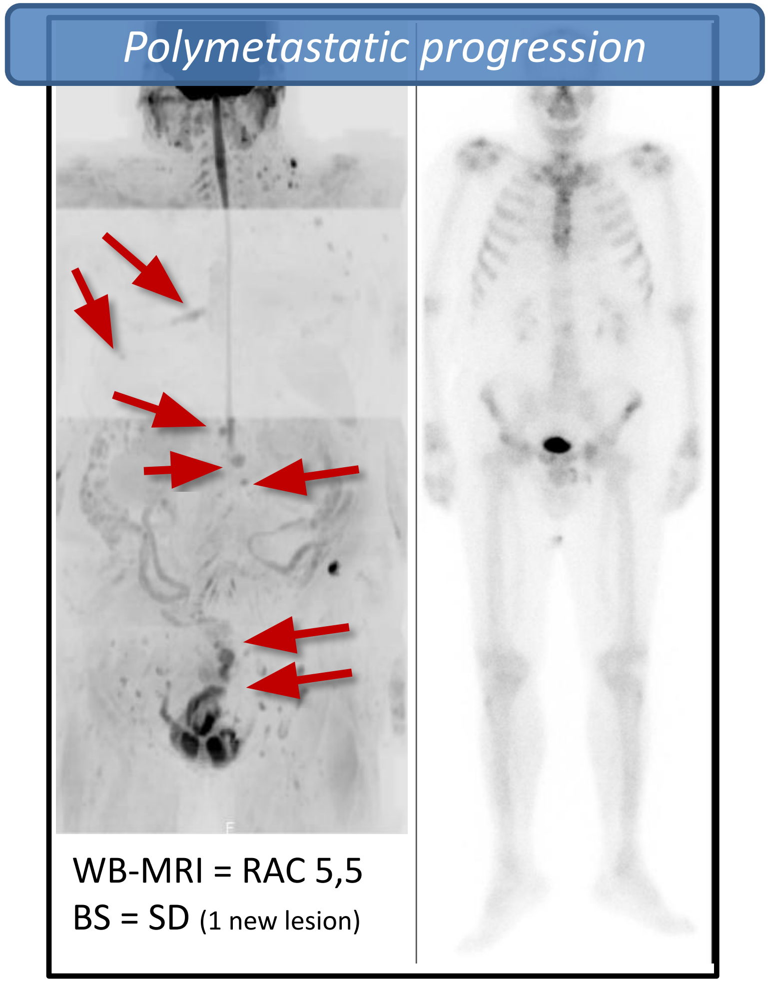
WB-MRI detects PD earlier than BS

24 weeks – PSA = 0.56 ng/mL





36 weeks – PSA = 2.42 ng/mL



RESPECT prostate study: prospective, non-inferiority study evaluating anticancer therapies in mCRPC with bone disease with WB-MRI versus BS/CT scans

31 men with mCRPC with bone disease starting new line of therapy

12 weekly follow-up with CT + BS, WB-MRI, clinic visits, blood tests

Endpoint: test that defines progressive disease (PD)

- 11/25 (44%) → PD on WB-MRI only
- 14/25 (56%) → PD on CT + BS & WB-MRI simultaneously
- No patient → PD only on CT + BS

PD – highly likely (RAC5*) in 25 patients (68% bone only; 24% bones & extra-osseous; 8% extra-osseous only)

82% of men progressing in bone were not detected on bone scan

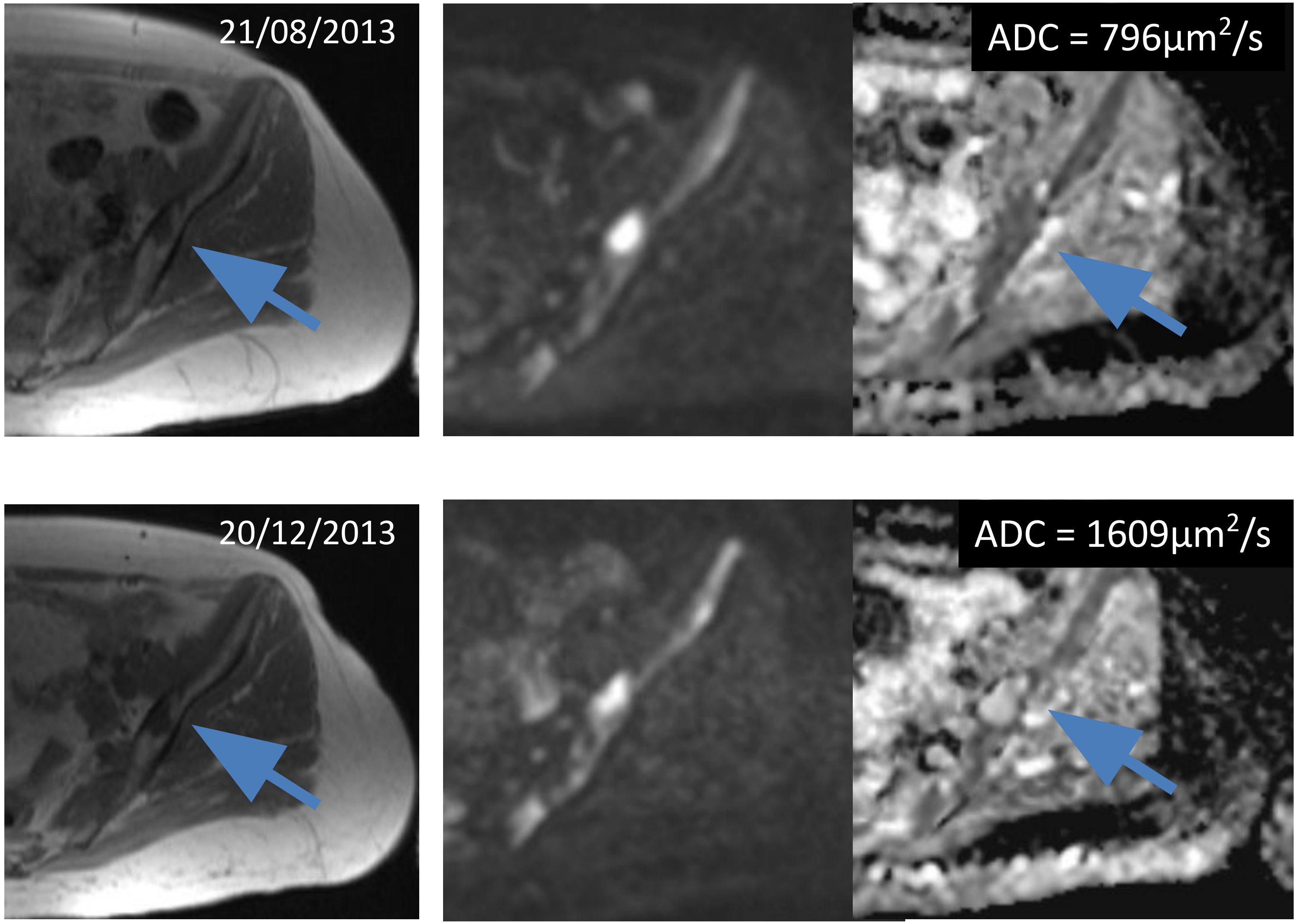
Ongoing – ad interim results

Prof. G. Petralia – P.I. of the RESPECT prostate study – UID 2243, ongoing at IEO-European Institute of Oncology, Milan

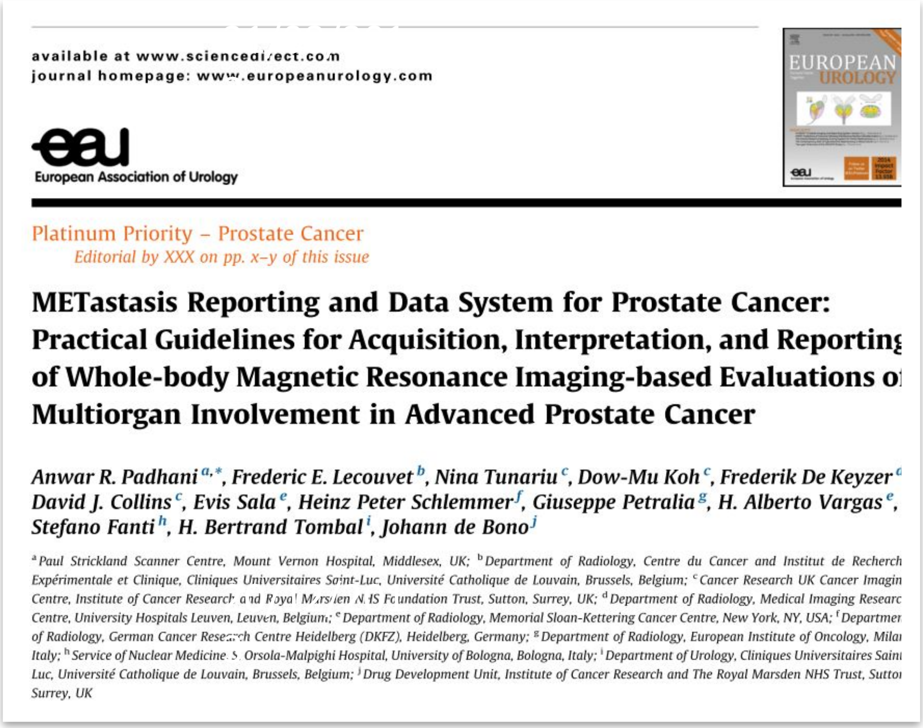
*Padhani AR. MET-RADS. Practical Guidelines for Acquisition, Interpretation, and Reporting of WB-MRI based Evaluations of Multiorgan Involvement in Advanced Prostate Cancer. Eur Urol 2017; 71:81-92

Imaging guidelines already published (MET-RADS)

To overcome limitations of RECIST 1.1 for assessing metastatic bone disease



After Docetaxel



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journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Prostate Cancer
Editorial by XXX on pp. x–y of this issue

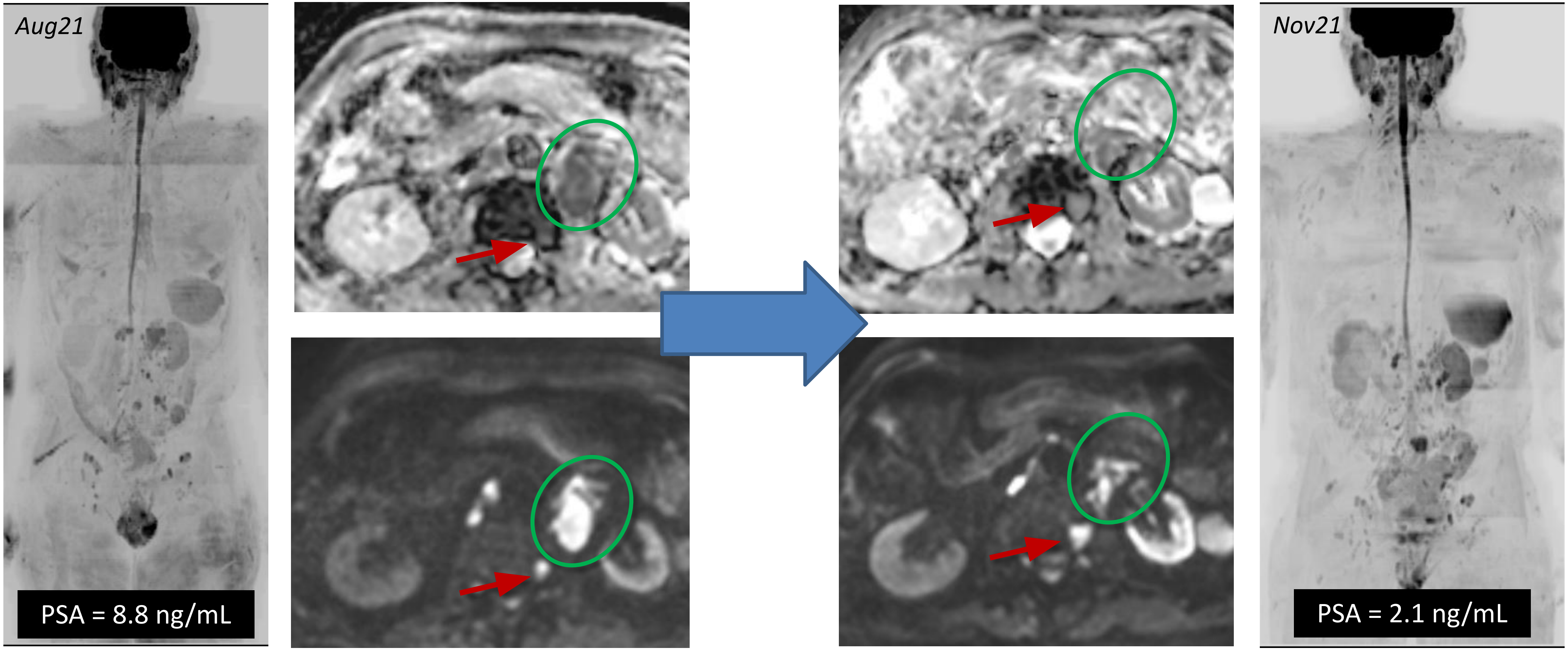
METastasis Reporting and Data System for Prostate Cancer: Practical Guidelines for Acquisition, Interpretation, and Reporting of Whole-body Magnetic Resonance Imaging-based Evaluations of Multiorgan Involvement in Advanced Prostate Cancer

Anwar R. Padhani [a,], Frederic E. Lecouvet [b], Nina Tunariu [c], Dow-Mu Koh [c], Frederik De Keyzer [d], David J. Collins [c], Evis Sala [e], Heinz Peter Schlemmer [f], Giuseppe Petralia [g], H. Alberto Vargas [e], Stefano Fanti [h], H. Bertrand Tombal [i], Johann de Bono [j]*

[a] Paul Strickland Scanner Centre, Mount Vernon Hospital, Middlesex, UK; [b] Department of Radiology, Centre du Cancer and Institut de Recherch Expérimentale et Clinique, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium; [c] Cancer Research UK Cancer Imagin Centre, Institute of Cancer Research and Royal Marsden NHS Foundation Trust, Sutton, Surrey, UK; [d] Department of Radiology, Medical Imaging Researc Centre, University Hospitals Leuven, Leuven, Belgium; [e] Department of Radiology, Memorial Sloan-Kettering Cancer Centre, New York, NY, USA; [f] Departmen of Radiology, German Cancer Research Centre Heidelberg (DKFZ), Heidelberg, Germany; [g] Department of Radiology, European Institute of Oncology, Milan Italy; [h] Service of Nuclear Medicine S. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy; [i] Department of Urology, Cliniques Universitaires Saint Luc, Université Catholique de Louvain, Brussels, Belgium; [j] Drug Development Unit, Institute of Cancer Research and The Royal Marsden NHS Trust, Sutton Surrey, UK

Imaging guidelines already published (MET-RADS)

To enable recording of the presence, location & extent of discordant responses



mCRPC under Abiraterone (2^{nd} line)

Lumbar spine = RAC 5

Para-aortic node = RAC 2

Welcome to a new era with AI

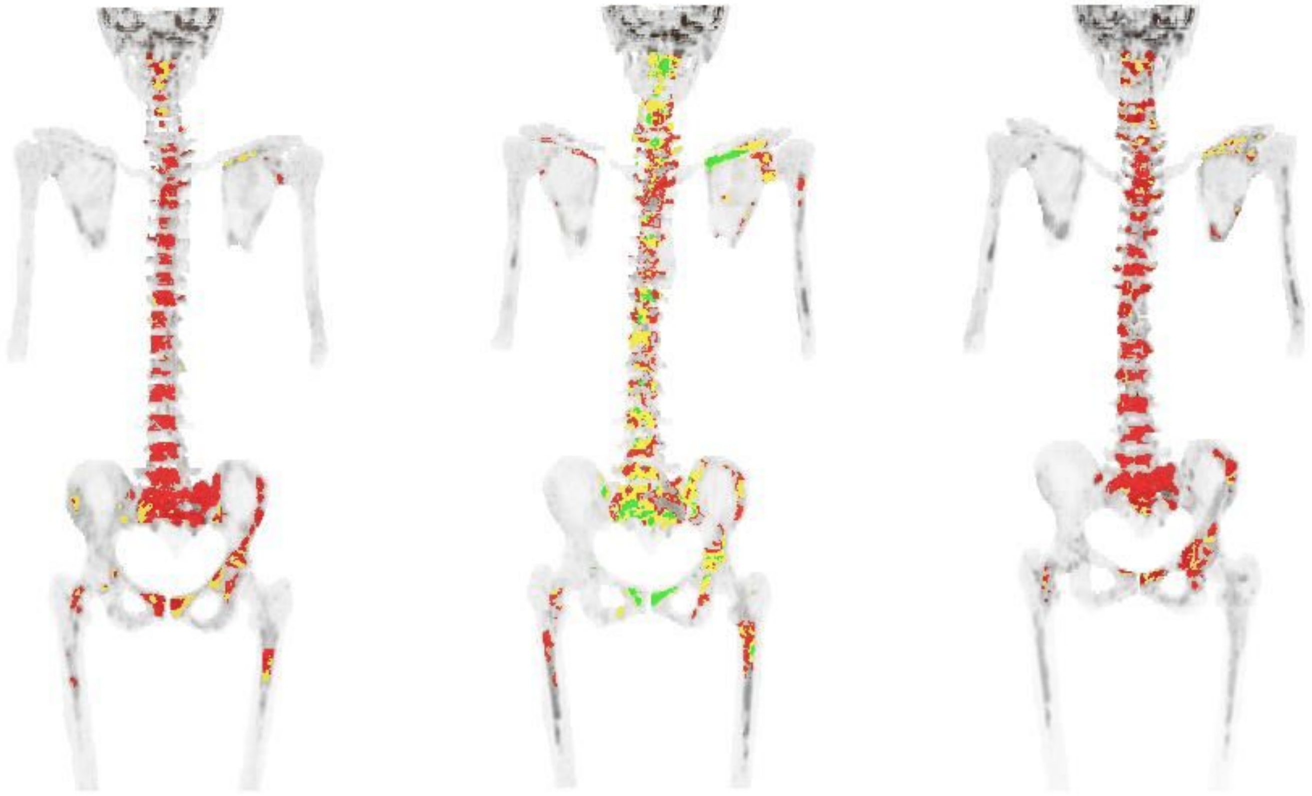
From old response categories to habitat imaging

ADC classes	
	Active (650-1000*)
	Dying (1000-1400*)
	Dead (>1400*)

*values displayed in $\mu m^2/s$

Active metastastic volume

163mL *21mL* *181mL*



TP1: 2017/05/22 TP2: 2017/09/07 TP3: 2017/11/23

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AI promotes PRECISION IMAGING in cancer patients

1. Streamlines imaging workflow
2. Reduces human error in routine examinations (e.g.. chest radiography)
3. Lowers radiation in CT and scan duration + CO_2 emissions in MRI
4. Minimizes inter-reader variability and shorten reporting times
5. Requires expert radiologists to ensure optimal patient outcomes

right treatment, right patient, right time, right duration