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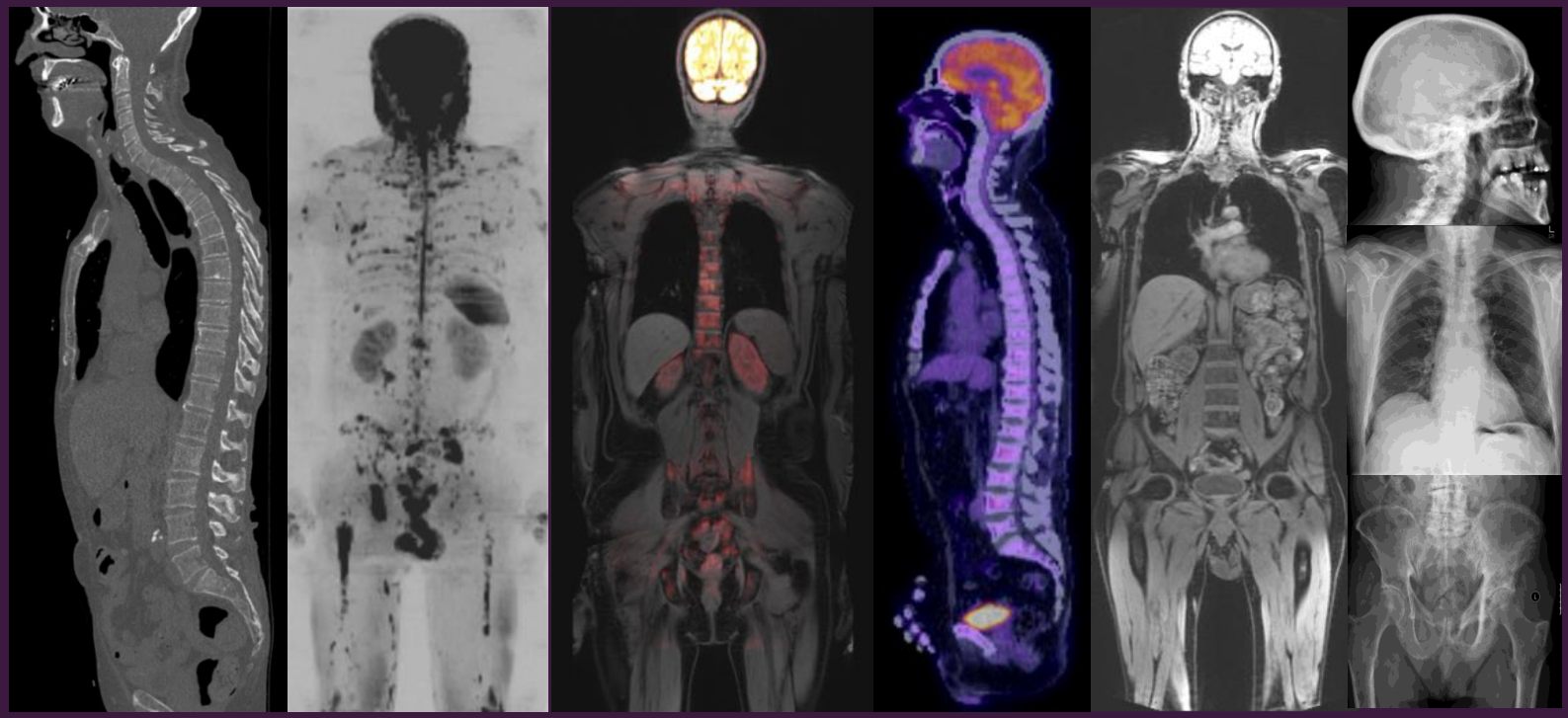
Myeloma : What to do and when



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NHS

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I have no conflicts of interest to declare

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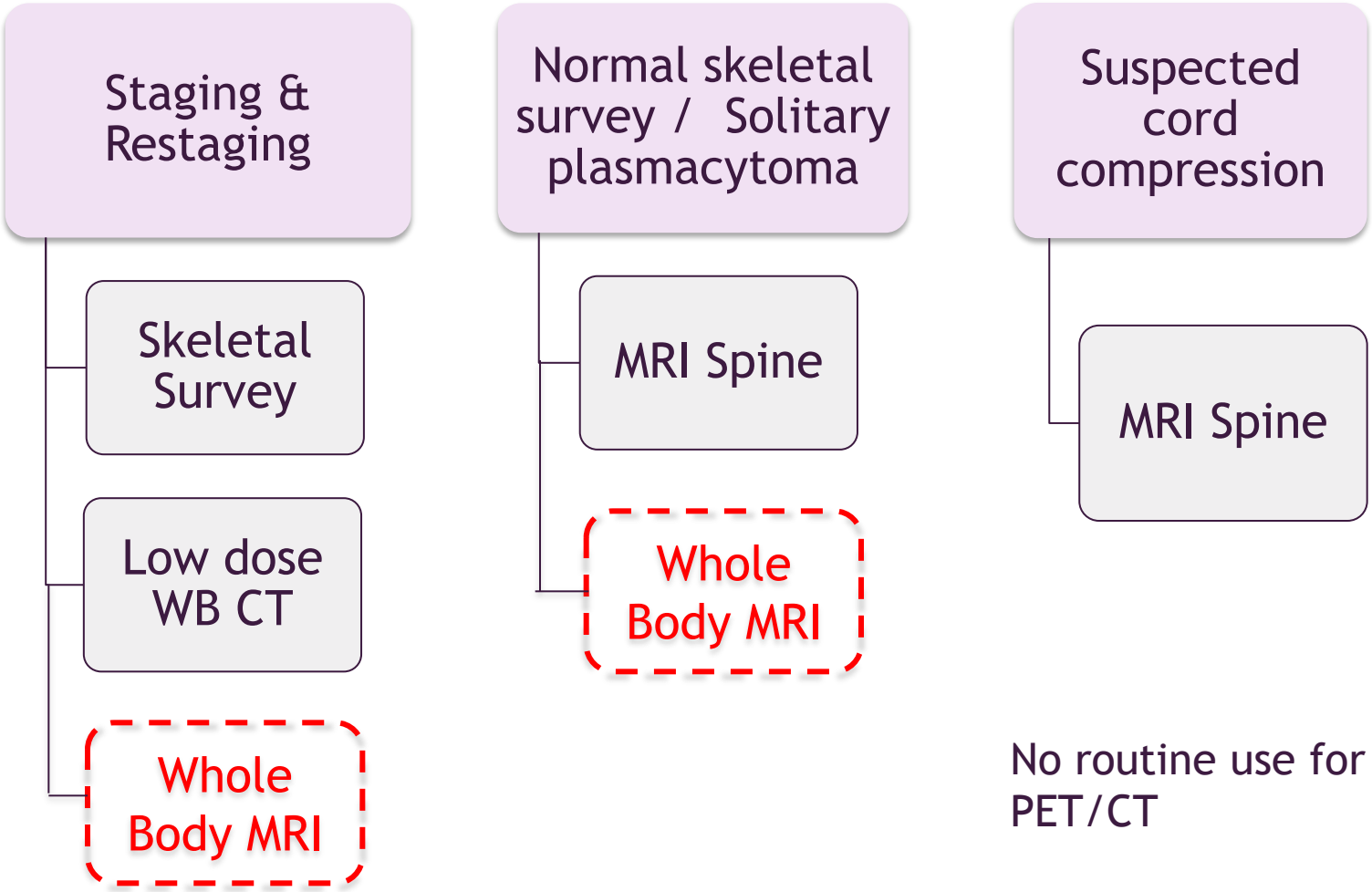
REVIEW

International myeloma working group consensus statement and guidelines regarding the current role of imaging techniques in the diagnosis and monitoring of multiple Myeloma

M Dimopoulos[1], E Terpos[1], RL Comenzo[2], P Tosi[3], M Beksac[4], O Sezer[5], D Siegel[6], H Lokhorst[7], S Kumar[8], SV Rajkumar[8], R Niesvizky[9], LA Moulopoulos[10] and BGM Durie[11] On behalf of the IMWG

Leukemia, 2009



No routine use for FDG PET/CT

Diagnosing myeloma bone involvement

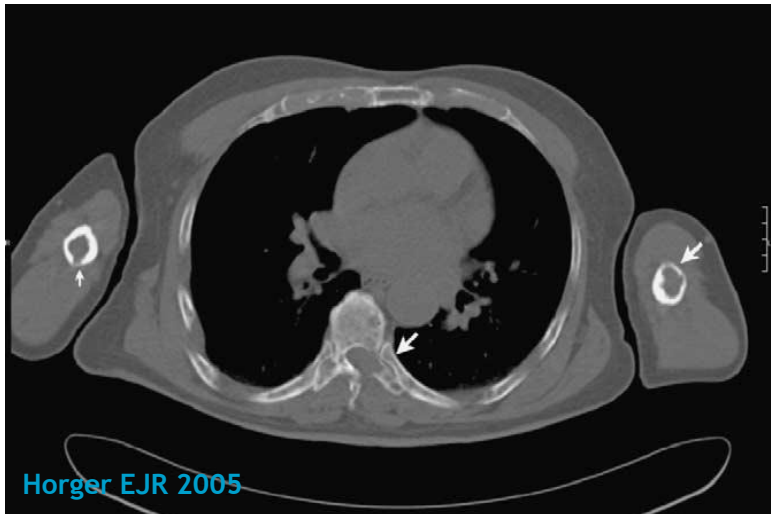
Skeletal survey

+ symptomatic areas

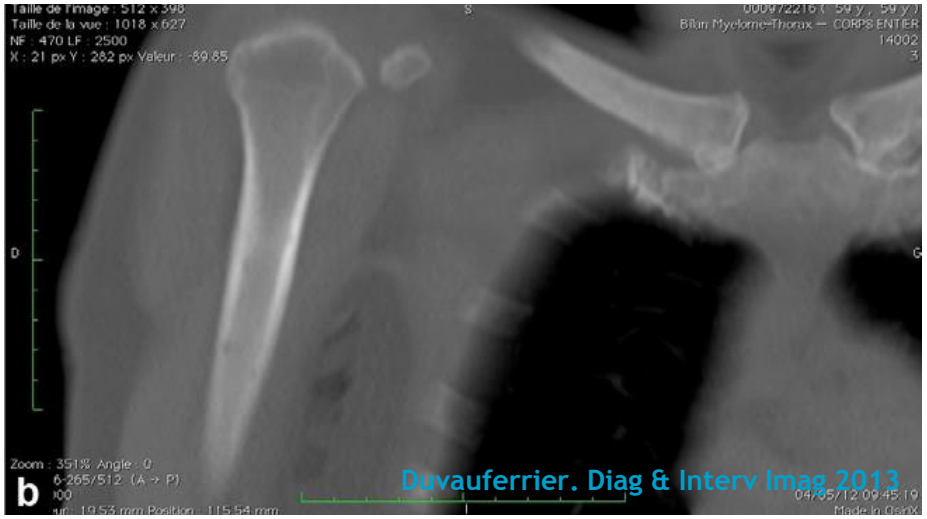
15% non-specific,osteopaenia,vertebral collapse

Low dose WBCT - an alternative to SS?

Lytic lesions



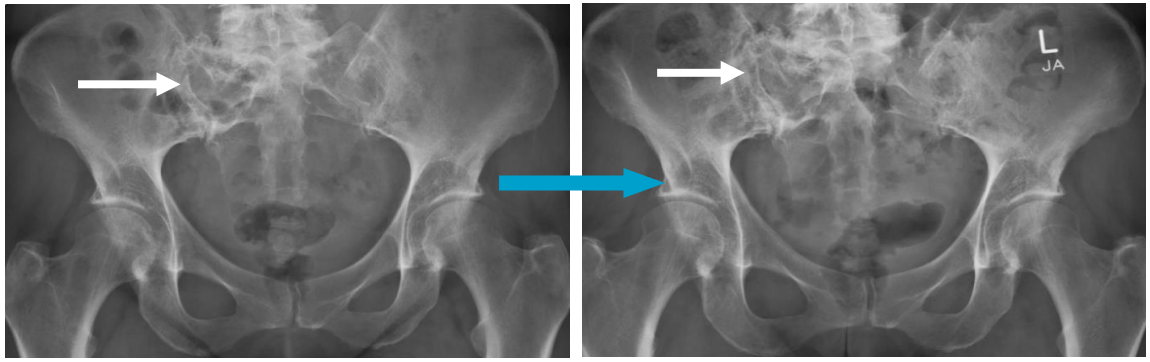
Endosteal scalloping



IMWG: “realistic alternative for patients with painful symptoms or symptomatic patients with no evidence of osteolysis on SS.”

Assessing treatment response /restaging
Plain film/CT

Fixed bone defect



Plain film / CT cheap, readily available first line screen for bone involvement.

Limited sensitivity: marrow not visualized
Limited restaging: fixed bone defects

Bone defects can stay stable for years despite changes in disease activity

IMWG: Patients with negative skeletal survey and no other criteria for active disease require MRI spine

MRI spine shows disease in 30-50% of patients with normal SS

Plain film/CT detect cortical destruction

MRI detects marrow disease

Burden and pattern of disease demonstrated on MRI is linked with outcomes

Symptomatic Patients

Number of lesions and diffuse pattern correlate with ↓ survival

Moulopoulos 2005, Lecouvet 1998, Moulopoulos 2012…….

Asymptomatic Patients

Asymptomatic patients with positive MRI or diffuse disease have a shorter time to progression than those with normal MRI

Hillengass 2010, Moulopoulos 1995, Kastritis 2013...

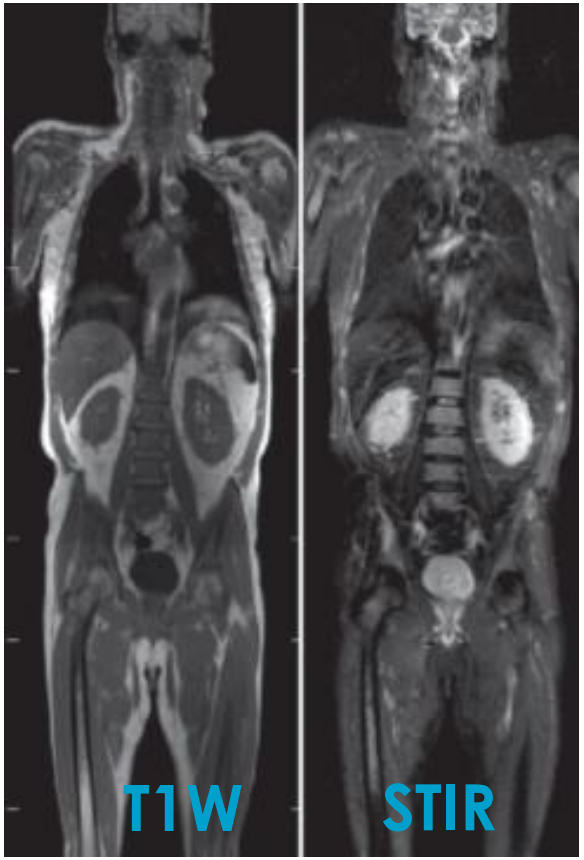
Patients with high risk SMM randomised between lenalidomide + low dose Dex vs observation, treatment gave a sig OS advantage

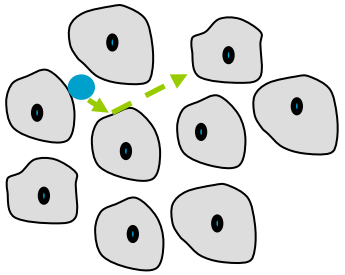
(Mateos 2013)

Whole body MRI in Myeloma

1 in 10 patients with new myeloma diagnosis have lesions limited to the extra axial skeleton.

? Need for whole body imaging.

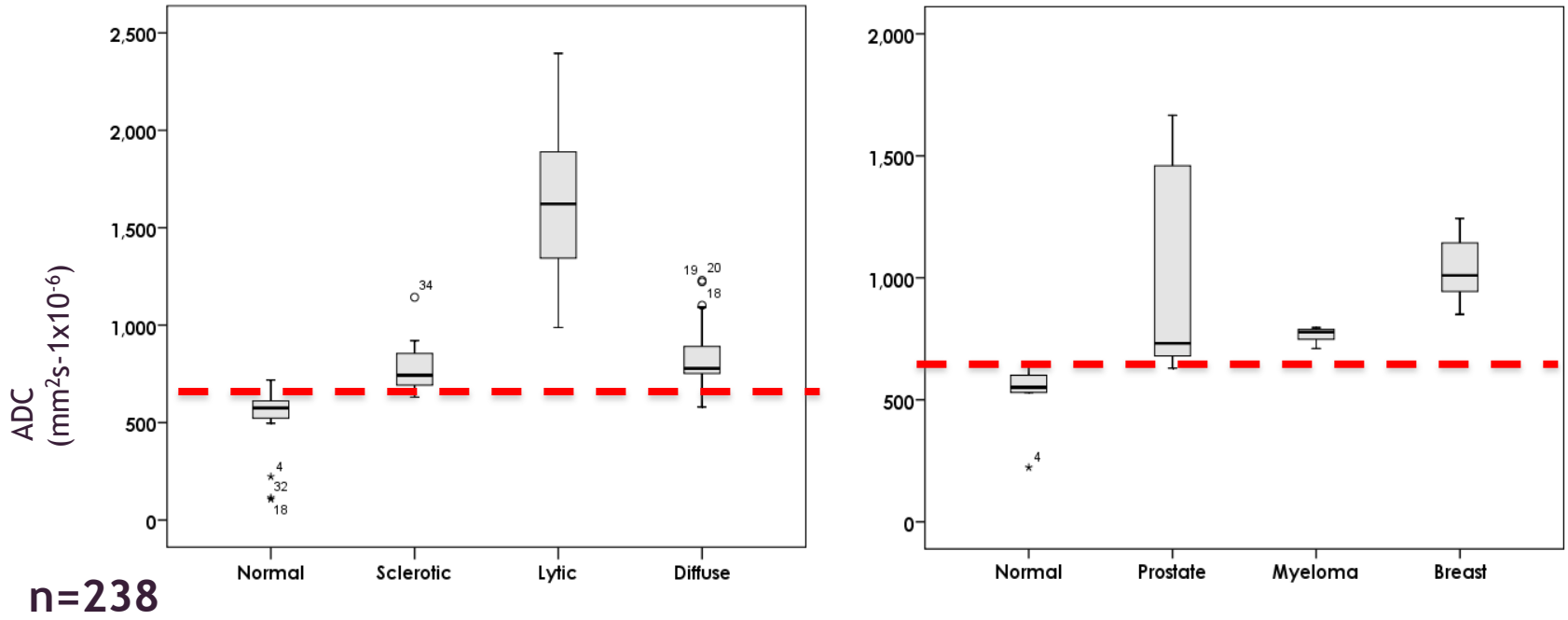




Advantages of WB DW-MRI in bone marrow

Excellent tissue contrast

DW-MRI is quantitative



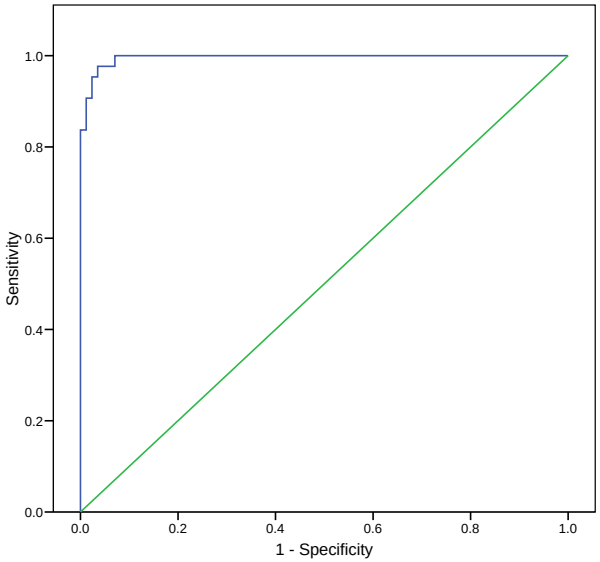
n=238

Significant differences between ADC of all groups of marrow disease (ANOVA F<0.001).

Messiou C et al. Eur Rad 2011

DW-MRI

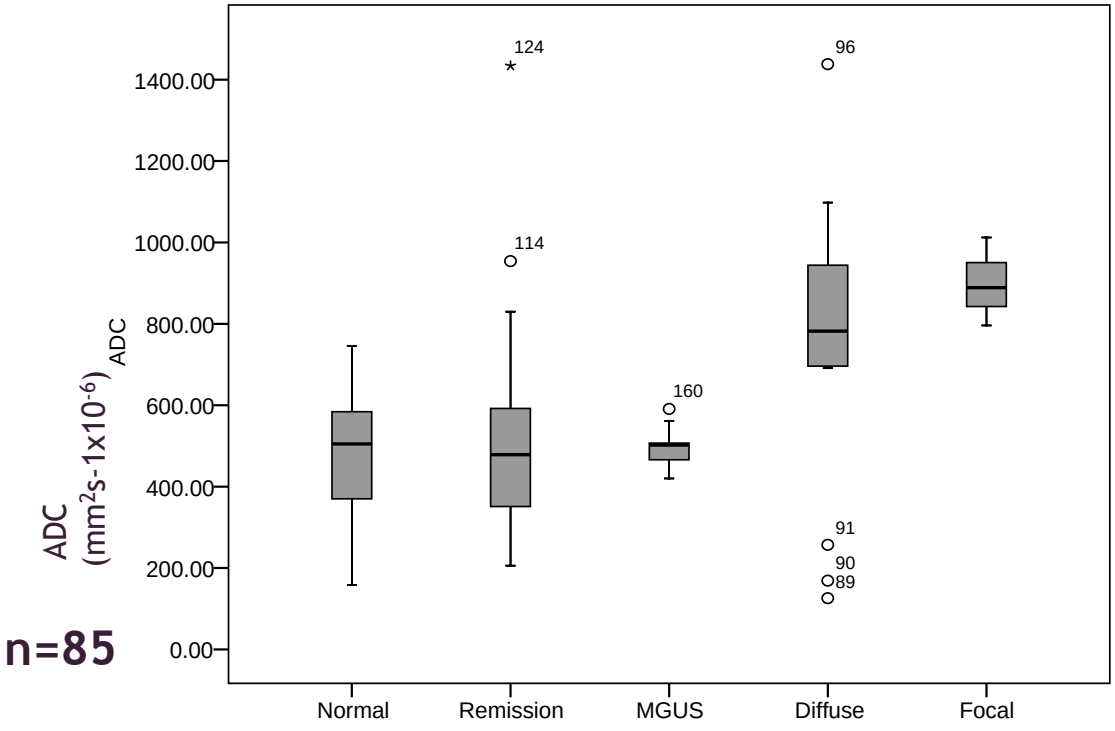
ADC cut off $655x10^{-6}mm^2s^{-1}$ separates normal from abnormal marrow with sensitivity of 90% and specificity of 93%.



ROC curve

Messiou et al Eu Rad 2011

DW-MRI



n=85

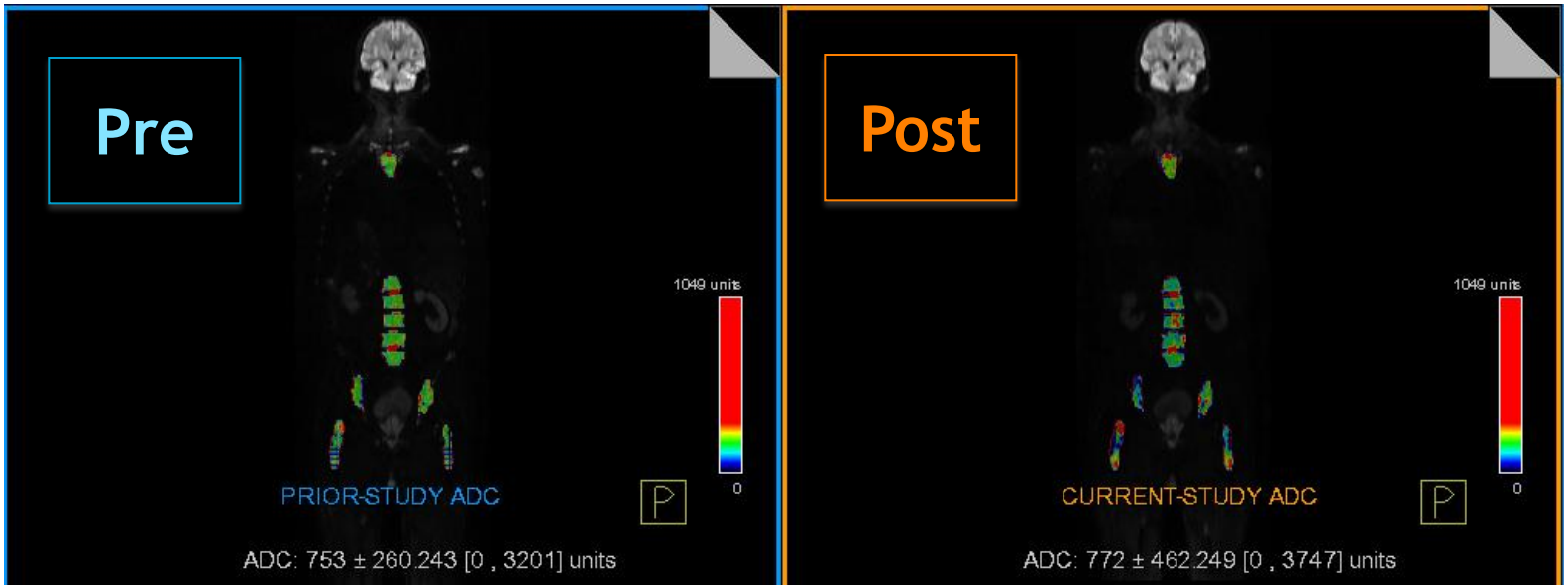
Significant Differences (F<0.001)
MGUS vs Active (diffuse/focal)
Remisson vs Active

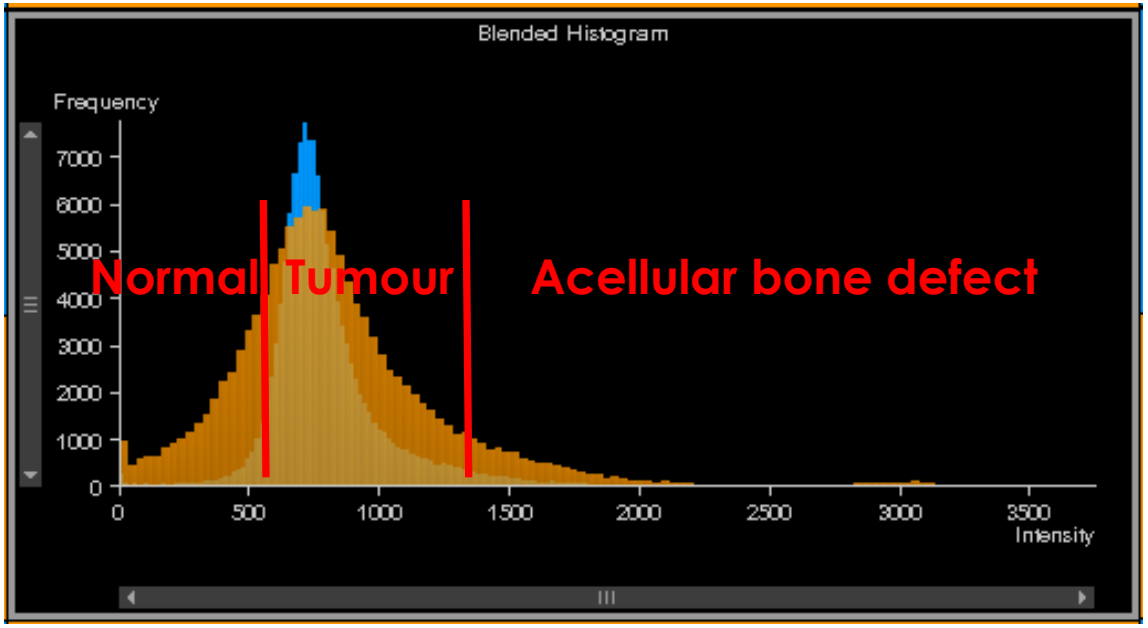
No Sig Difference
MGUS vs Normal age matched

1)Messiou C et al. Eur Rad 2011
2)Messiou C et al. Eur Rad 2011

Significant difference in ADC of MGUS vs multiple myeloma confirmed by Dutoit et al and also showed no sig difference between ADC of MGUS and SMM. Eur Rad 2014

Quantifying treatment response on DWI

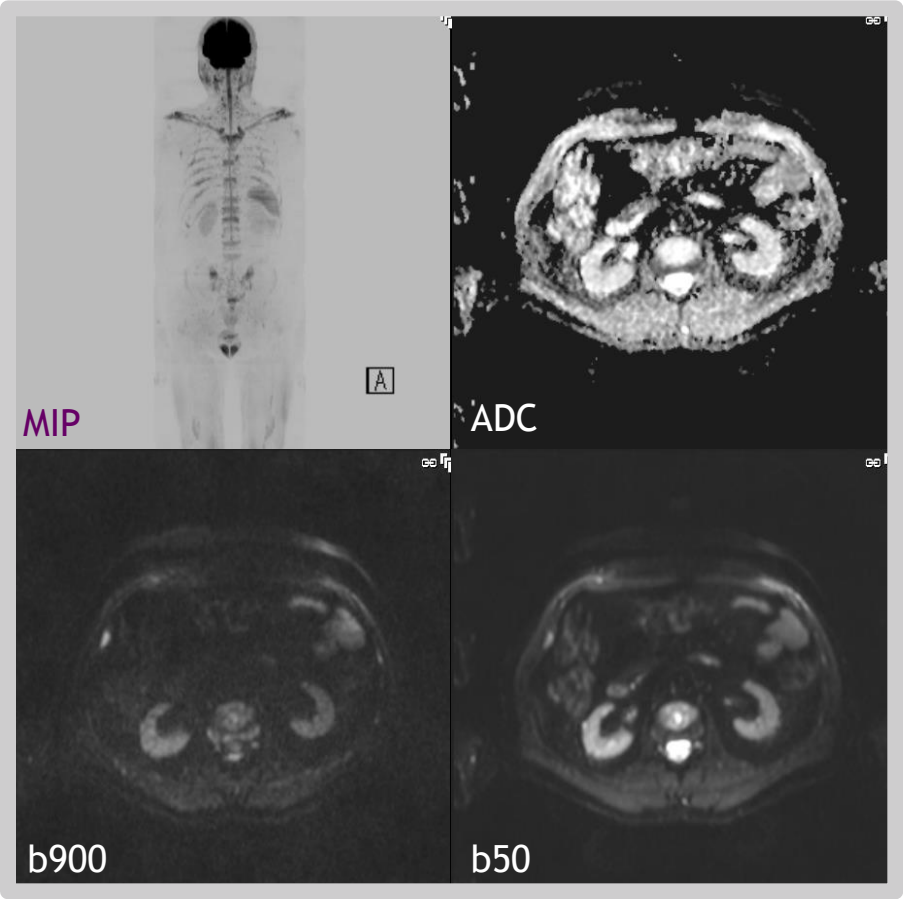




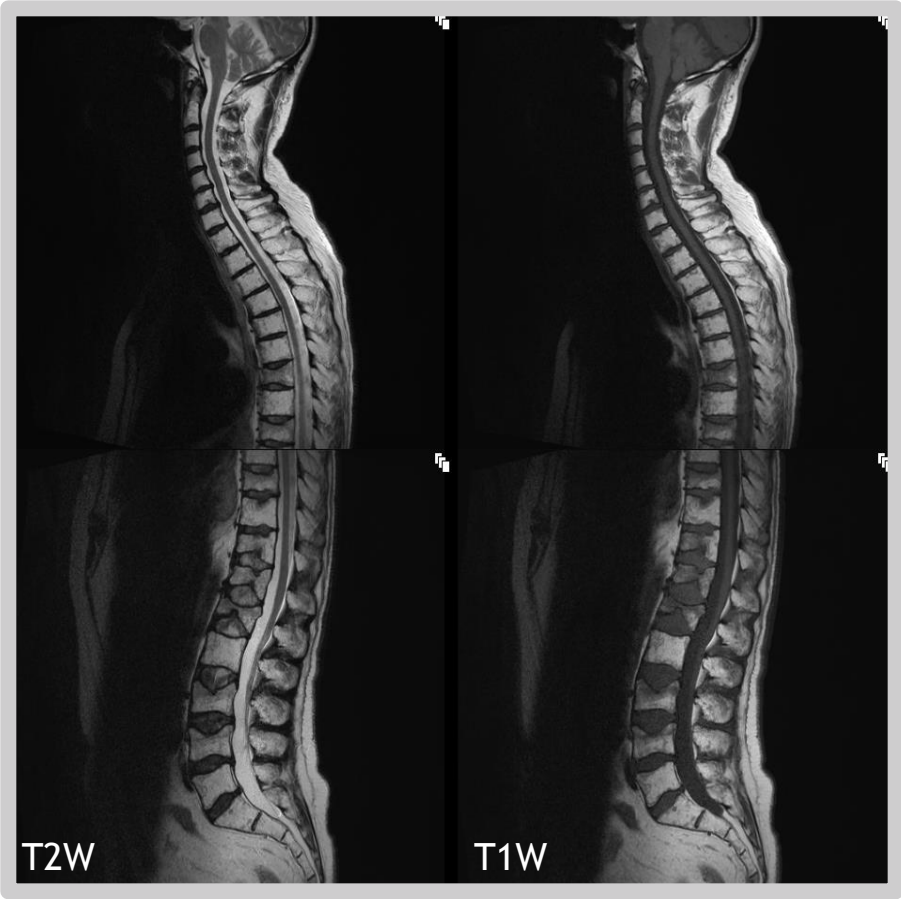
Messiou C et al
Cancer Biomarkers
2010 & ISMRM 2010.

WB DWI

Functional DWI: 20 mins

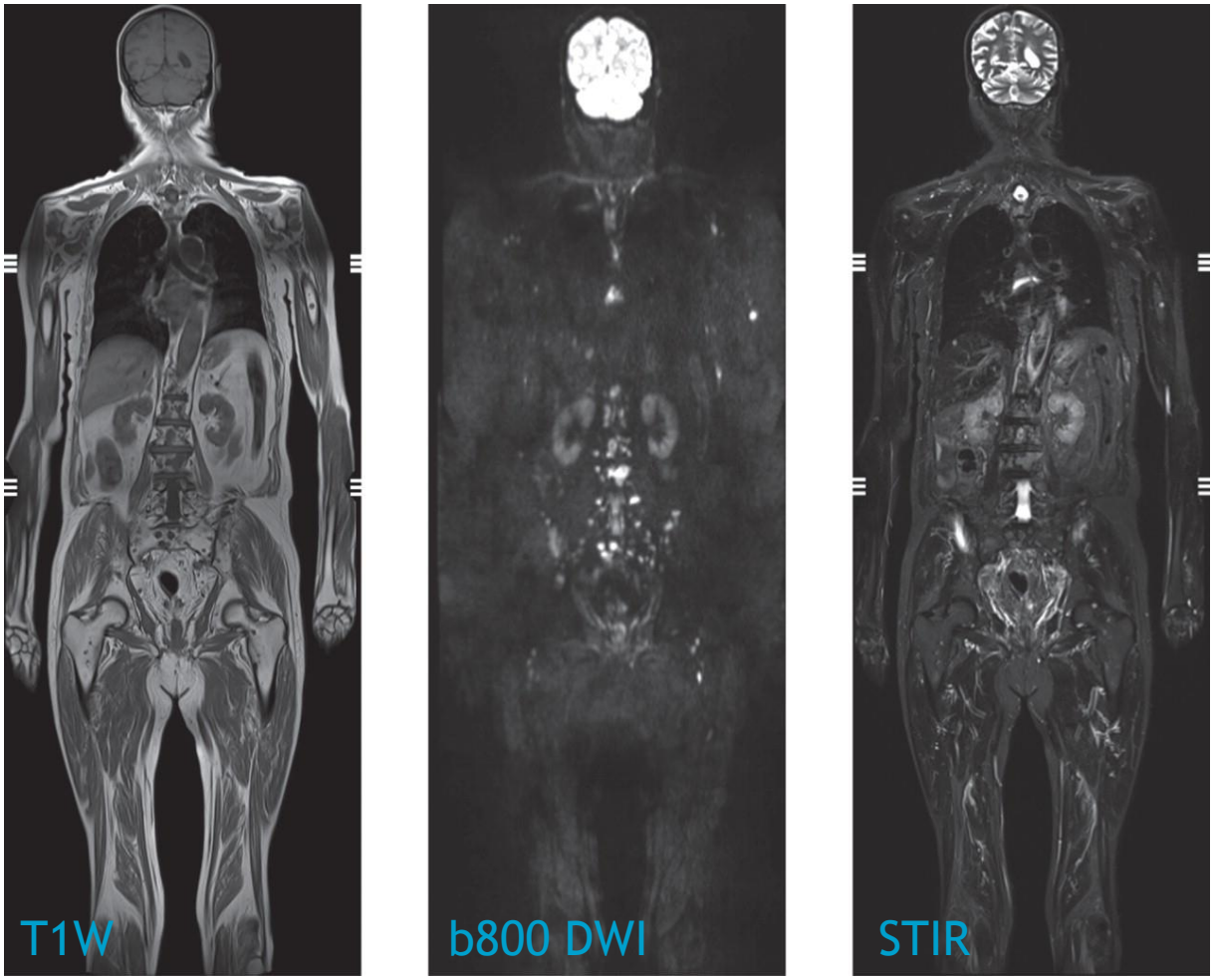


Anatomical imaging



WB DWI + Anatomical Images + Patient Prep = 40 mins scanner time

DW-MRI – increased sensitivity

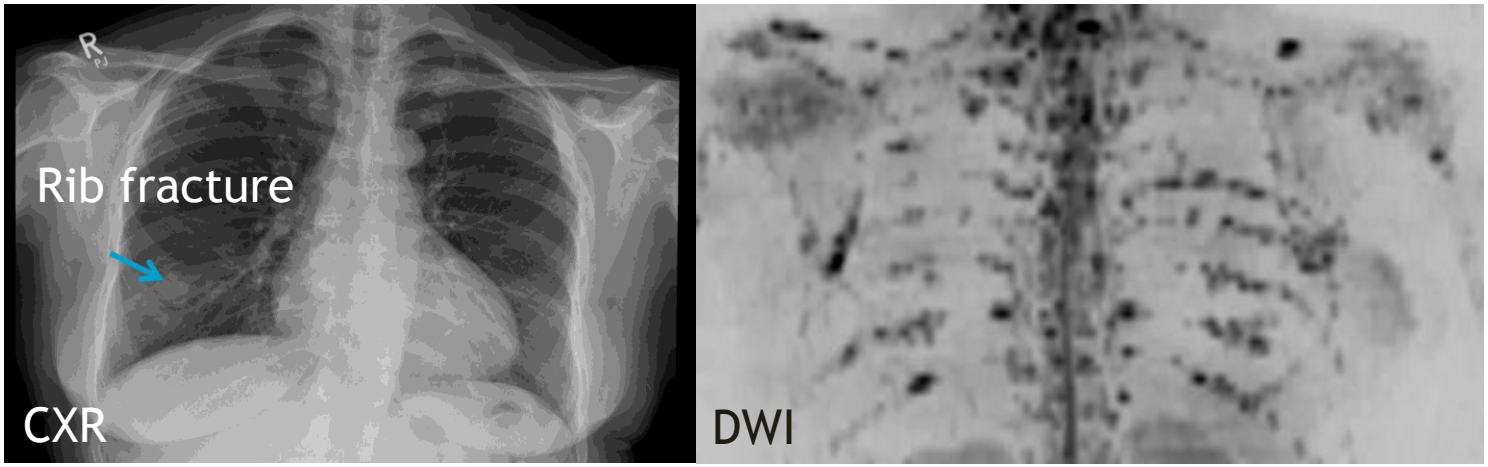


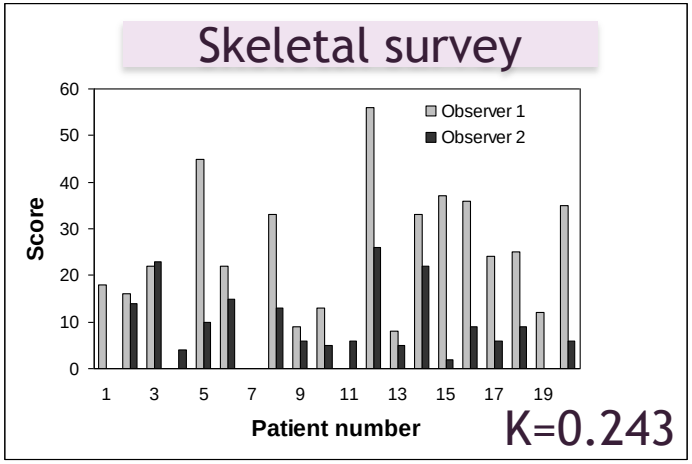
Lesion conspicuity DWI>STIR or T1W MRI

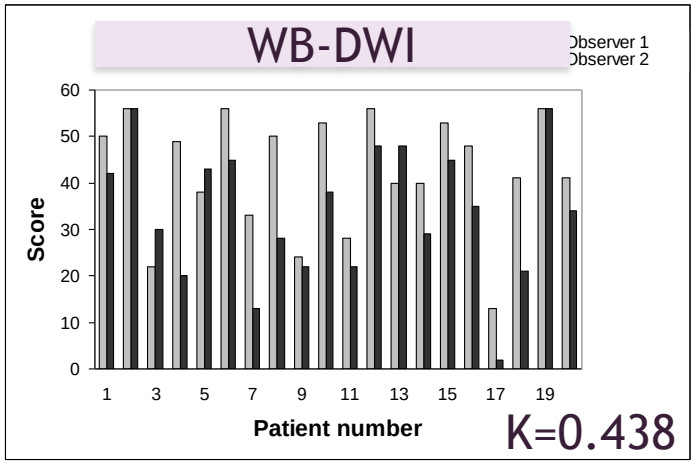
Pearce et al. BJR 2012

Skeletal Survey vs WB-DWI

20 patients. Observer scores higher on DWI than SS (p<0.05)







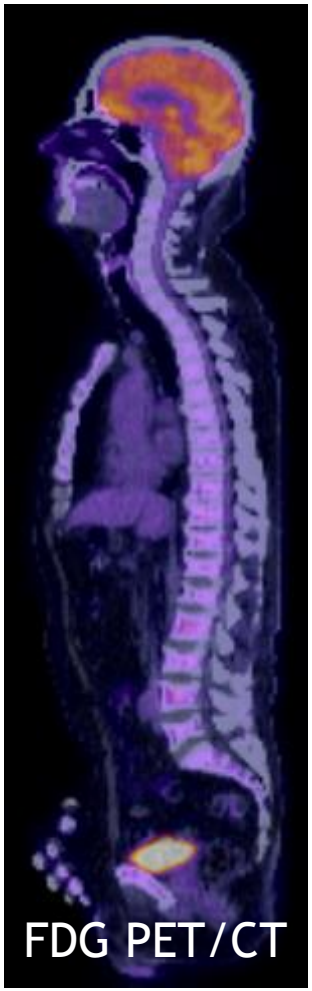
Interobserver Agreement

Giles et al ISMRM 2014

Case 1 - Detection

46 year old man. ? Asymptomatic myeloma

Normal



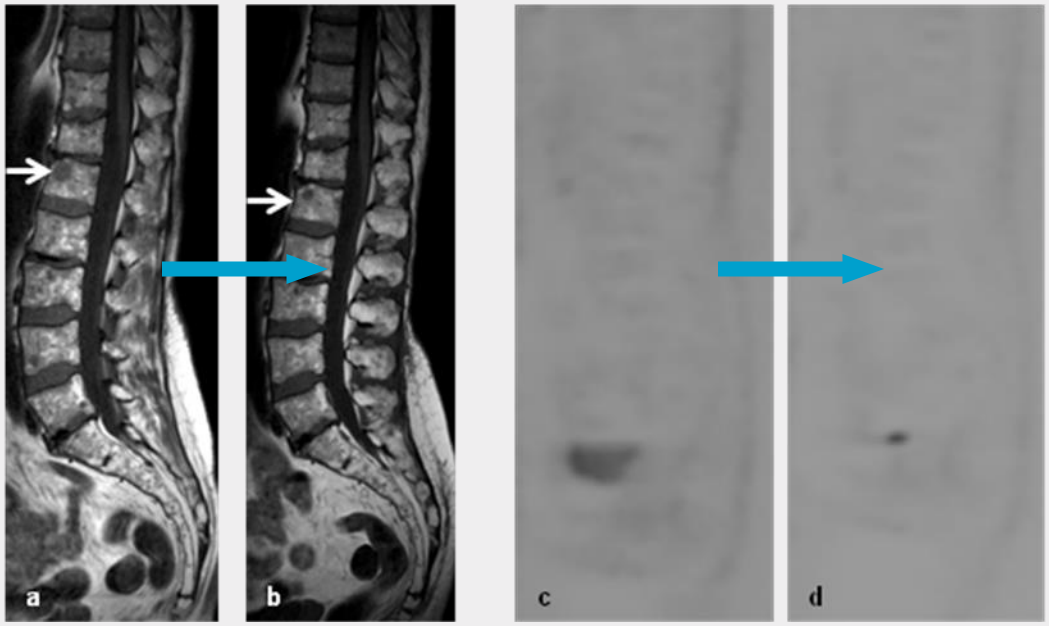
Borderline

Diffuse Marrow Infiltration

FDG PET vs MRI

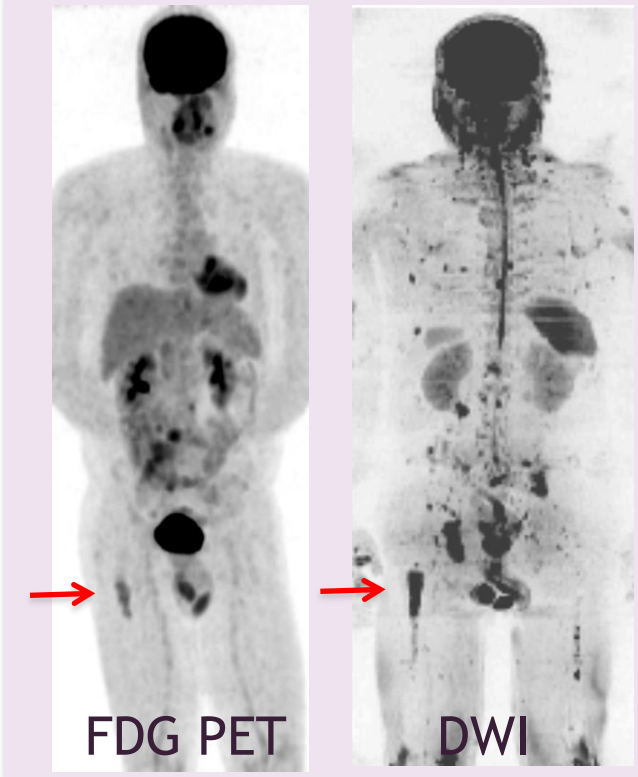
Studies comparing FDG PET/CT and conventional MRI have shown that FDG is inferior for detection of diffuse and small volume disease.

Zamagni Haematologica 2007, Shorrt AJR 2009, Dimopoulos Leukemia 2009



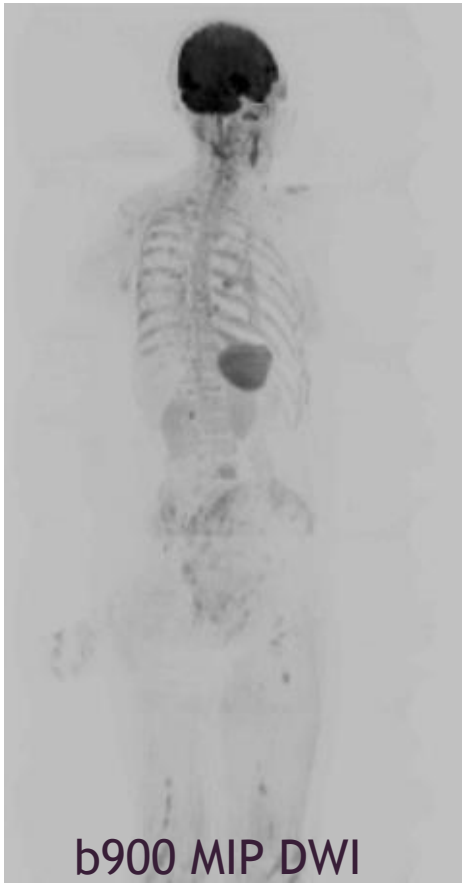
T1W MRI
Sen 68%, Spec 83%

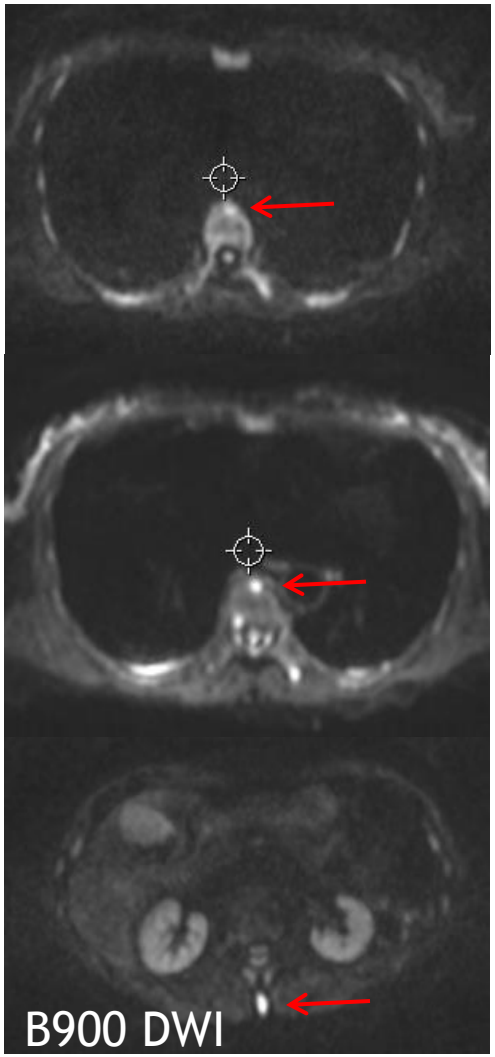
FDG PET
Sen 59%, Spec 75%



Case 2 - Detection

72 year old woman. Poor trephine ? Solitary site ? Radiotherapy

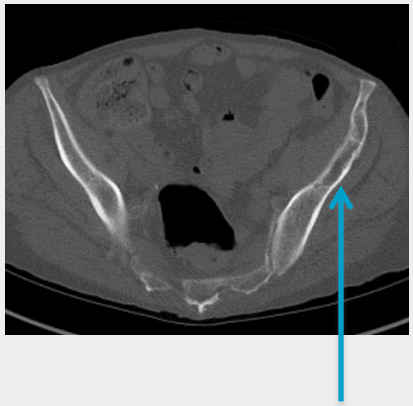




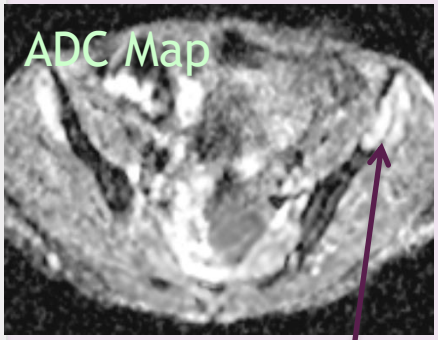
Case 3 - Restaging

63 year old. Hx of myeloma. Rising paraproteins.

Low Dose WB CT



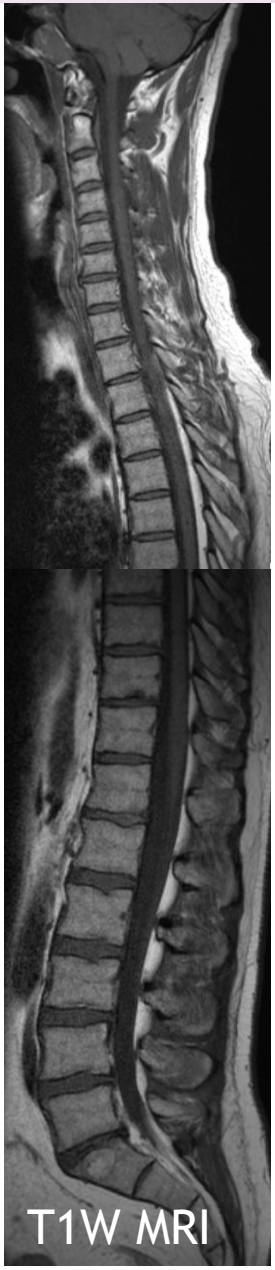
Bone defect.
? significance



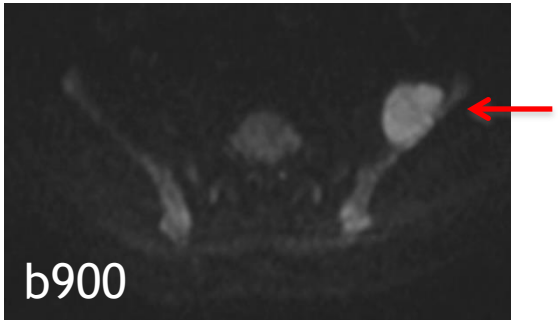
Very High ADC
Acellular bone defect.

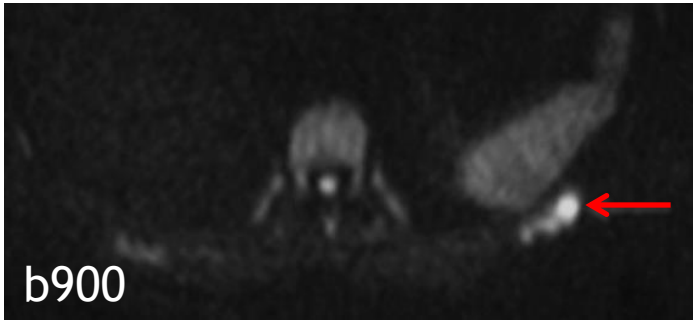
WB - DWI

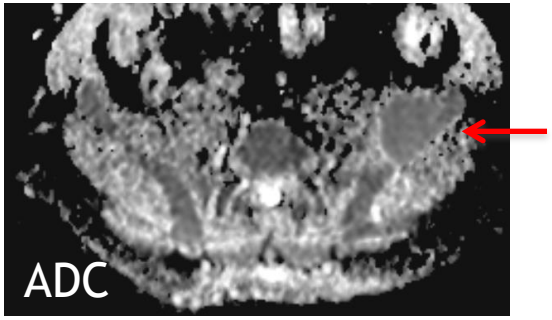
Case 4 - Restaging

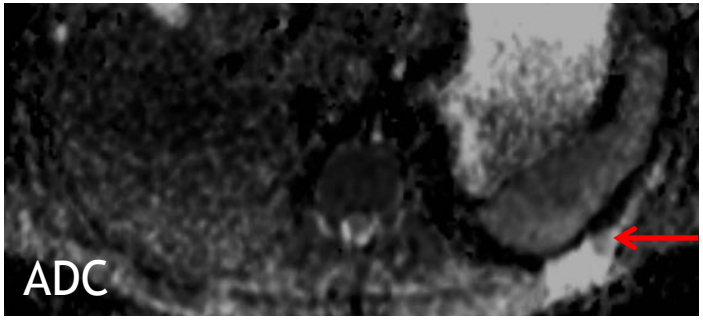


54 year old woman. Hx of solitary rib plasmacytoma





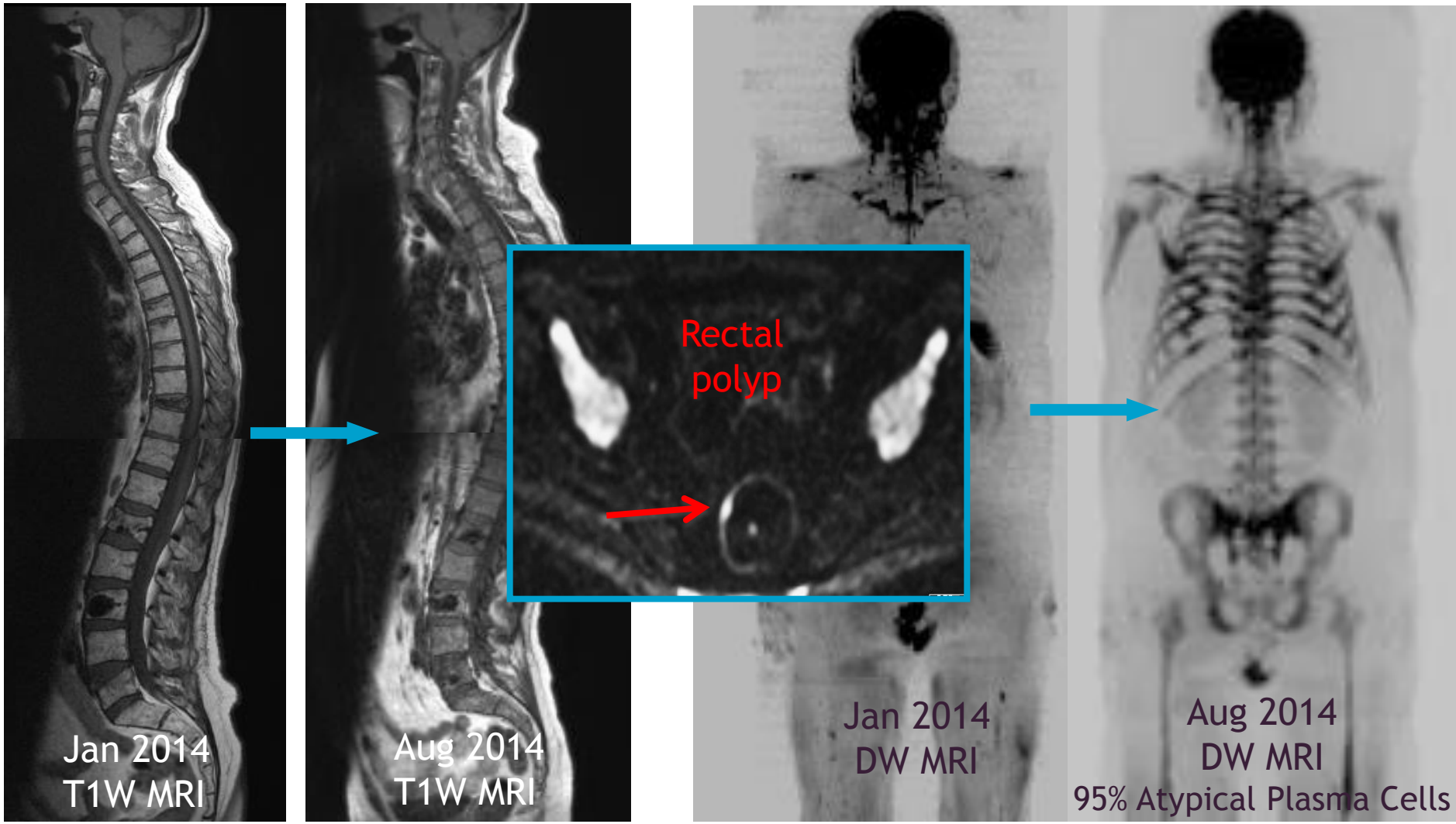




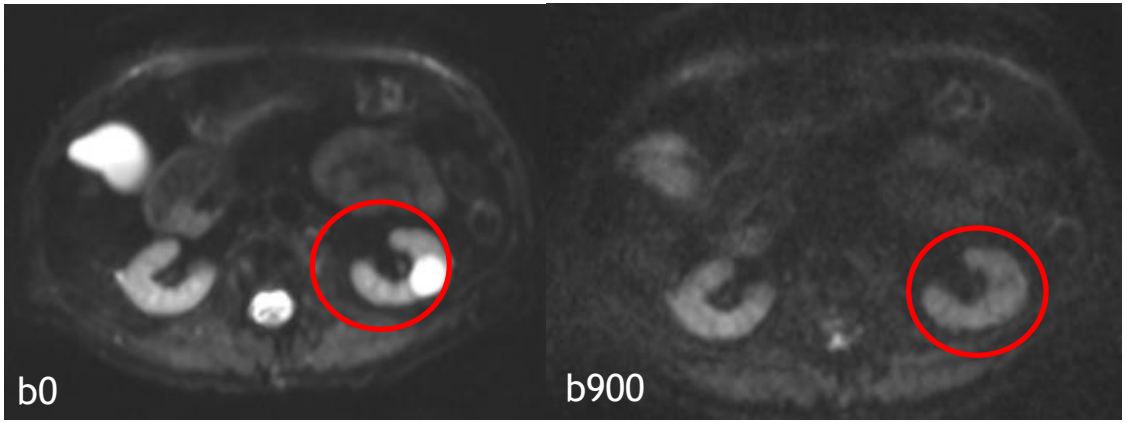
Differentiation of active and inactive sites

Case 5 - Surveillance

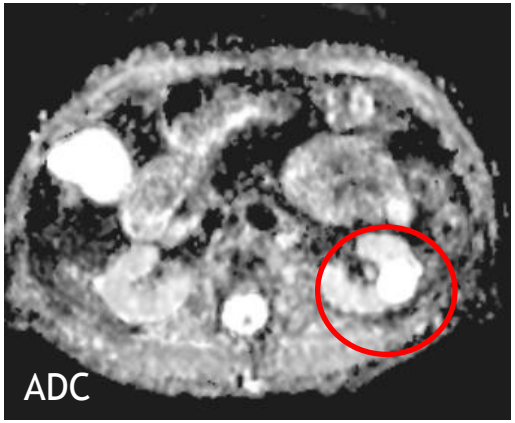
53 year old man. Non secretory myeloma. On surveillance



WB DW-MRI - Incidentalomas



? Renal lesion



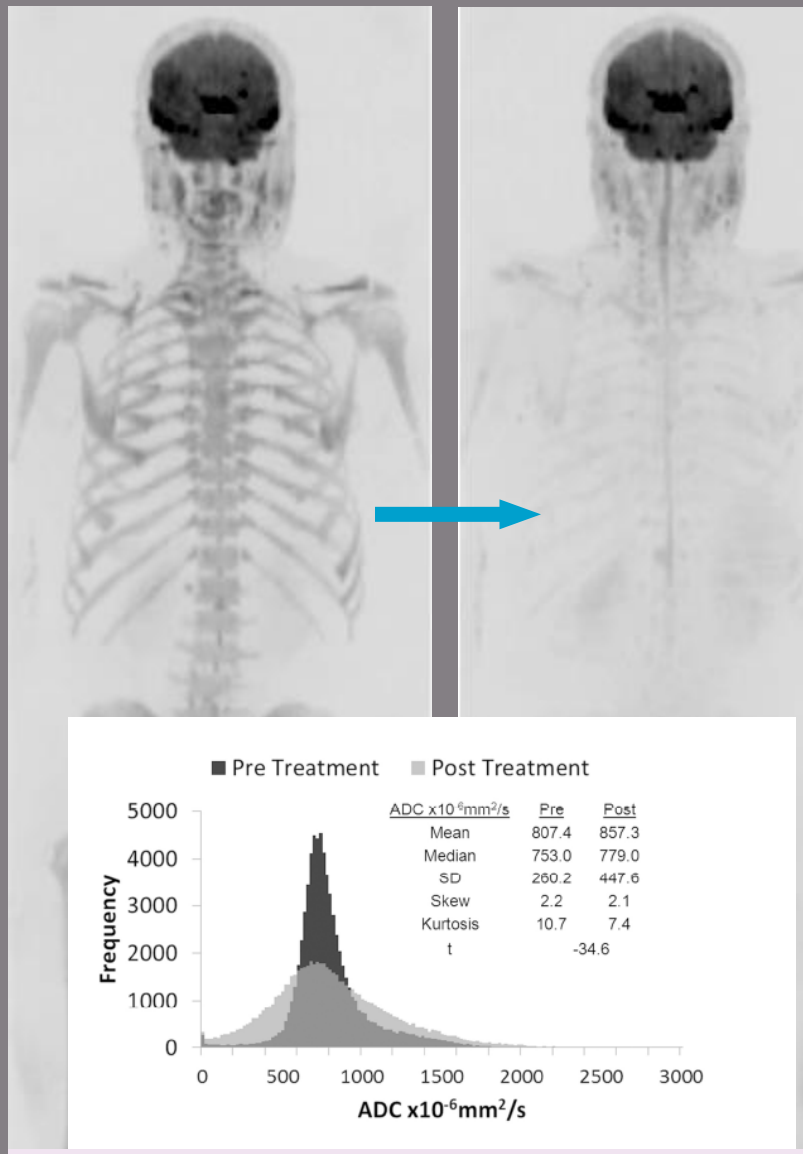
Renal cyst

WB DW-MRI 100 prostate cancer patients.

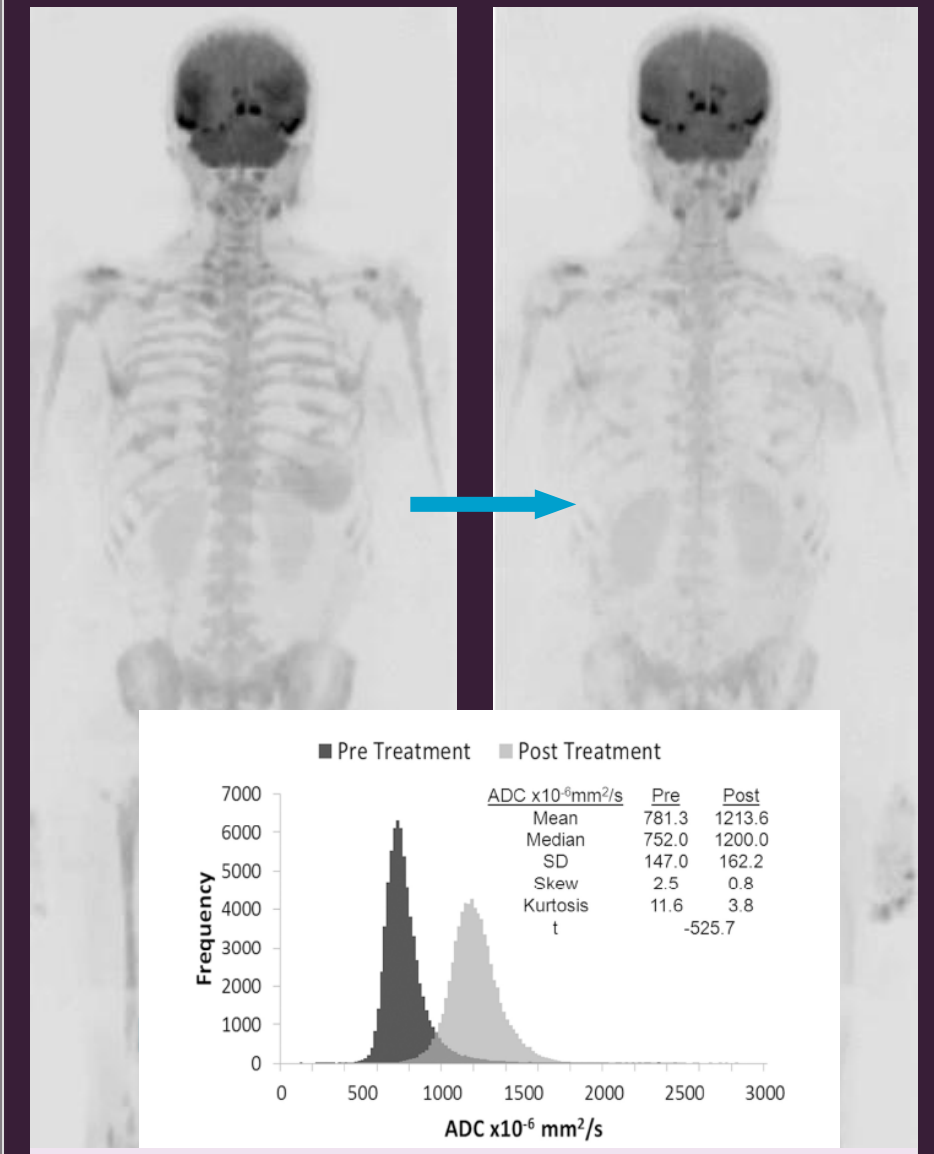
25 incidentalomas:

9 hepatic haemangiomas, 9 cystic renal lesions, 3 solid renal masses, 3 adrenal tumours, 4 aneurysms, 2 thyroid enlargement.
Lecouvet et al. European Urology 2012

Case 6 and 7 – Assessing Response



Case 7



Case 8

Quantifying treatment response on WB-DWI

Prospective study

26 patients (21 responders, 5 non responders)

2 Observers

WB-DWI baseline and 13 weeks after treatment

Semi quantitative vs quantitative assessment of response.

Gold standard – IMWG response criteria

Giles et al. Radiology 2014

Quantifying treatment response on WB-DWI

Reproducibility of WB-DWI ADC measurements

Normal volunteers : 3.8% cv

Patients : 2.8% cv

Giles et al Radiology 2014.

Quantifying treatment response on WB DWI

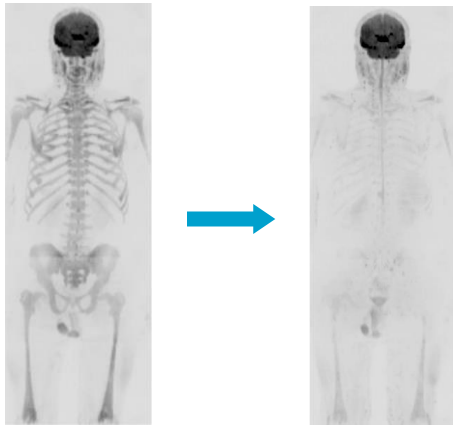
Semi-quantitative assessment vs quantitative

Semi-quantitative

Sensitivity 86%
Specificity 80%

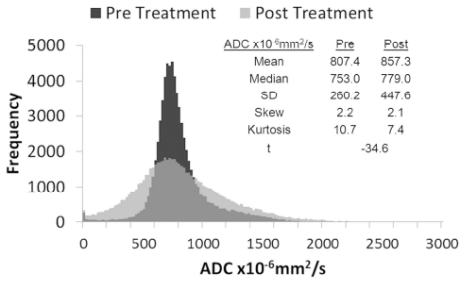
No significant difference between observer scores

Complete agreement



Quantitative ADC histogram

Sensitivity 90%
Specificity 100%



Giles et al Radiology 2014.

Pre and Post Autograft Imaging

- Pre autograft PET-FL identified an inferior prognosis group defined as low risk by GEP.

  Bartel et al. Blood 2009,114: 2068-2076.

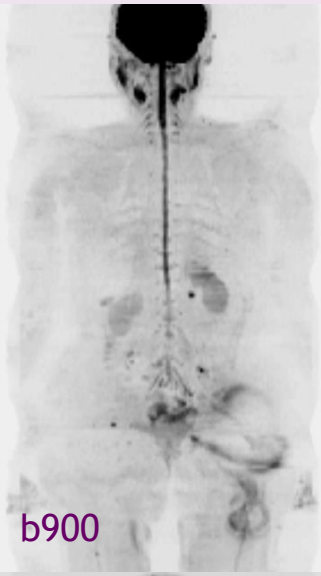
- Persistent uptake after autotransplantation also a reliable predictor of poor prognosis.

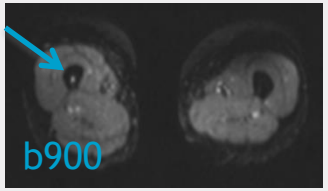
- 23% of patients in clinical CR had persistent FDG-FL.

  Zamagni et al. Blood 2011,118: 5989-5995.

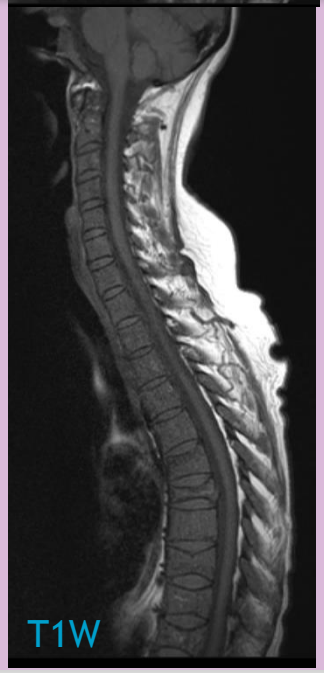
Case 8 – Pre and post autograft

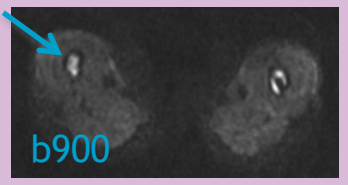
3 months post autograft





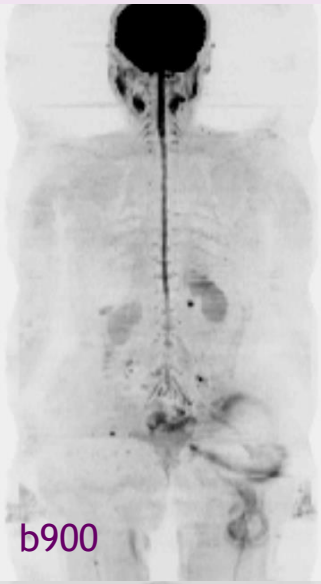
Pre autograft

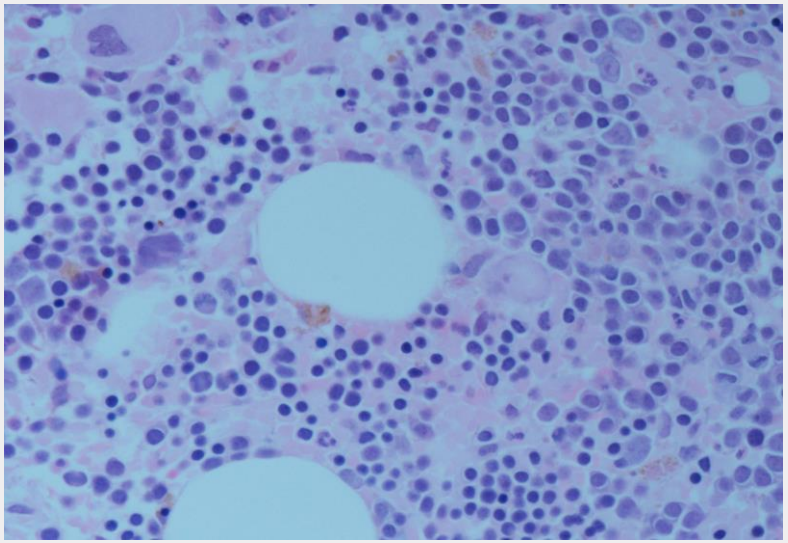




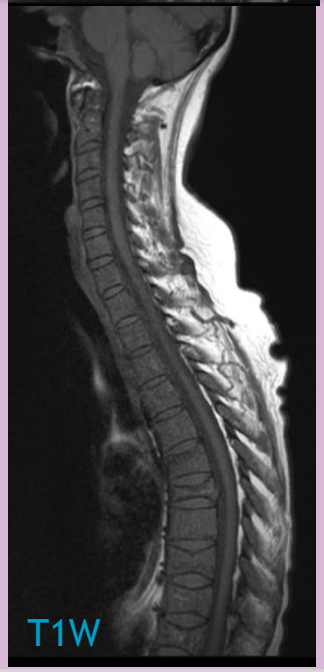
Why does T1 signal remain stable?

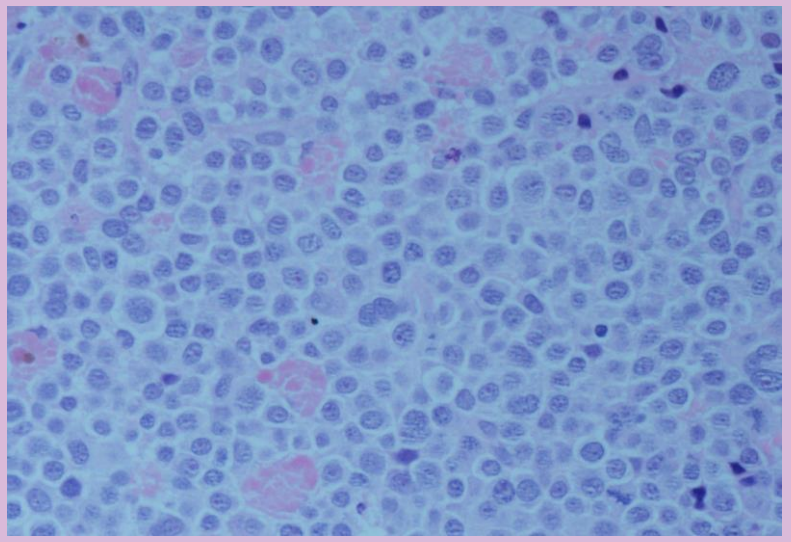
3 months post autograft





Pre autograft

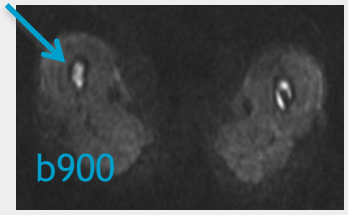




Histology courtesy of Dr S O'Connor

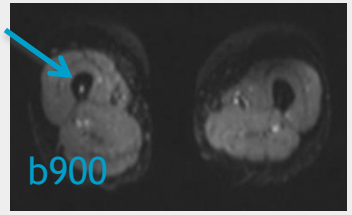
The significance of post autograft abnormal signal ?

Diffuse



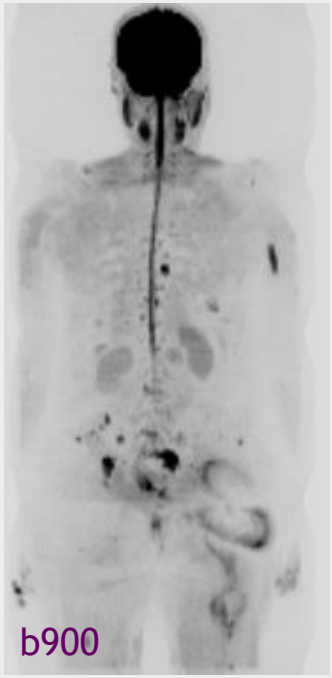
Pre autograft

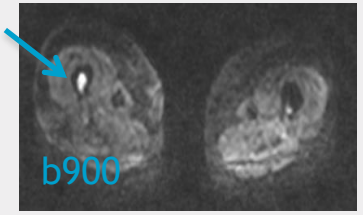
Small volume residual



3 months post autograft

Multifocal

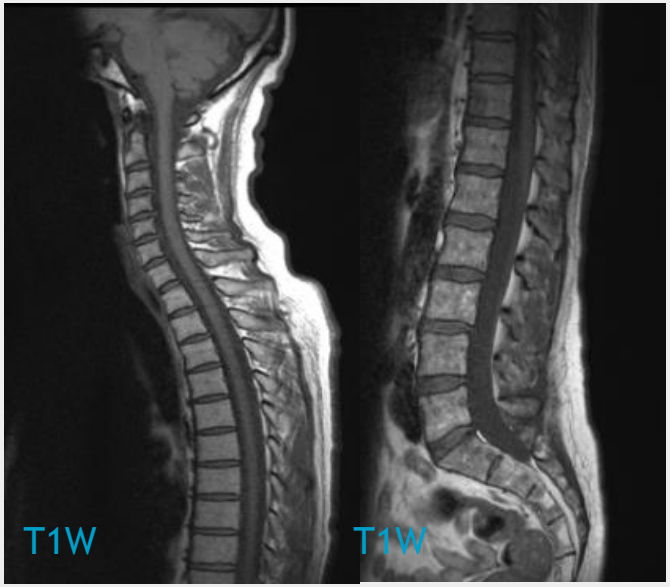


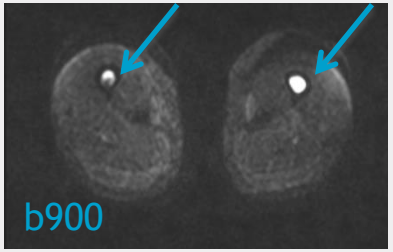


8 months post autograft

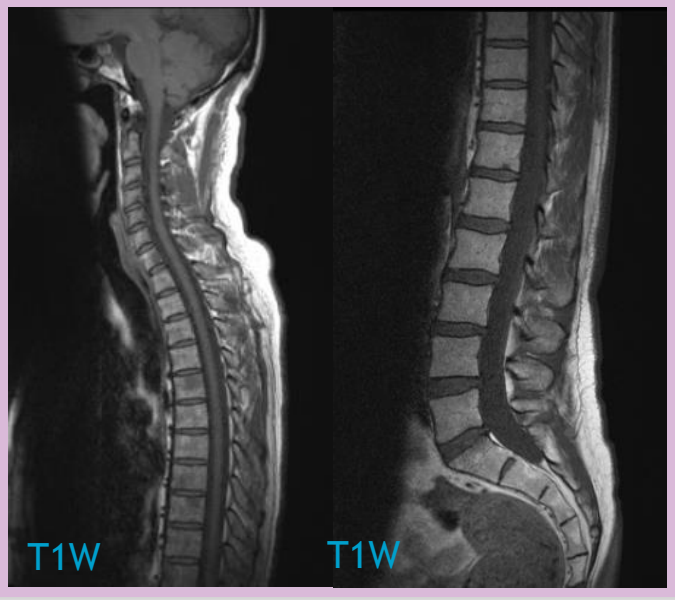
Case 9 –Post autograft

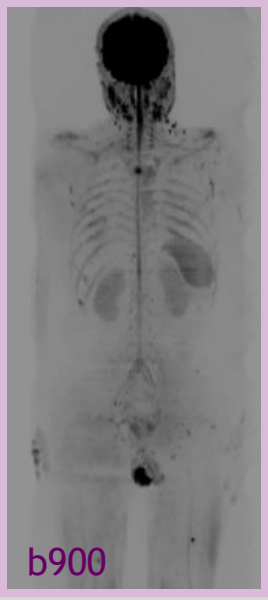
8 months post autograft

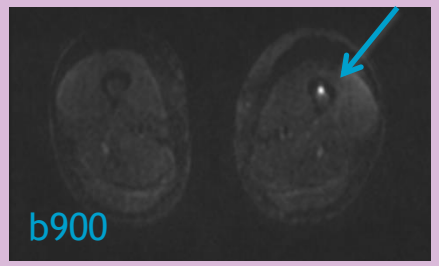




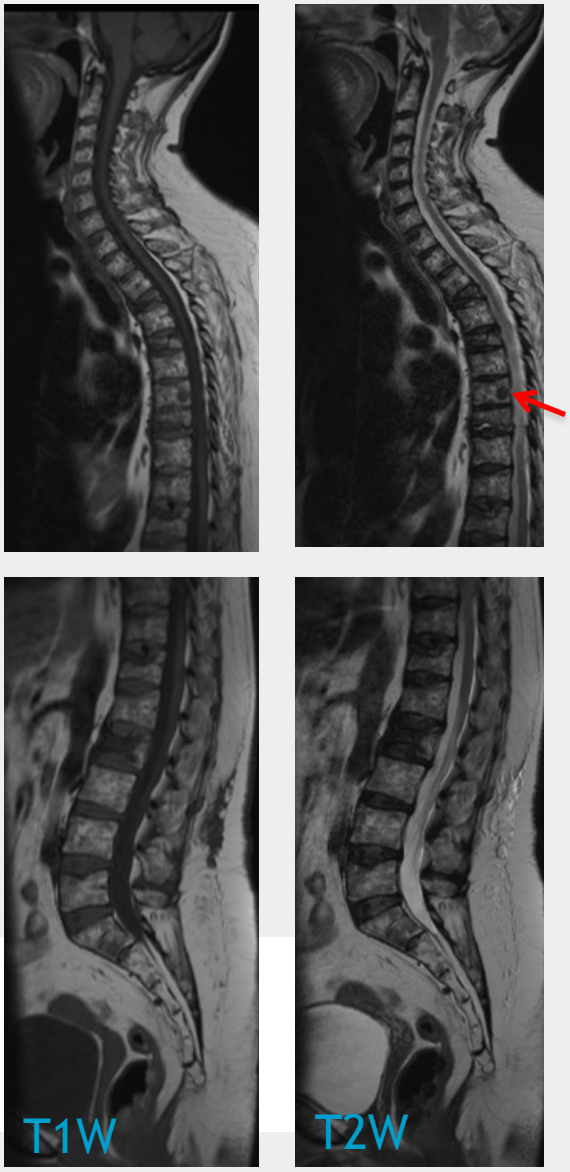
3 months post autograft

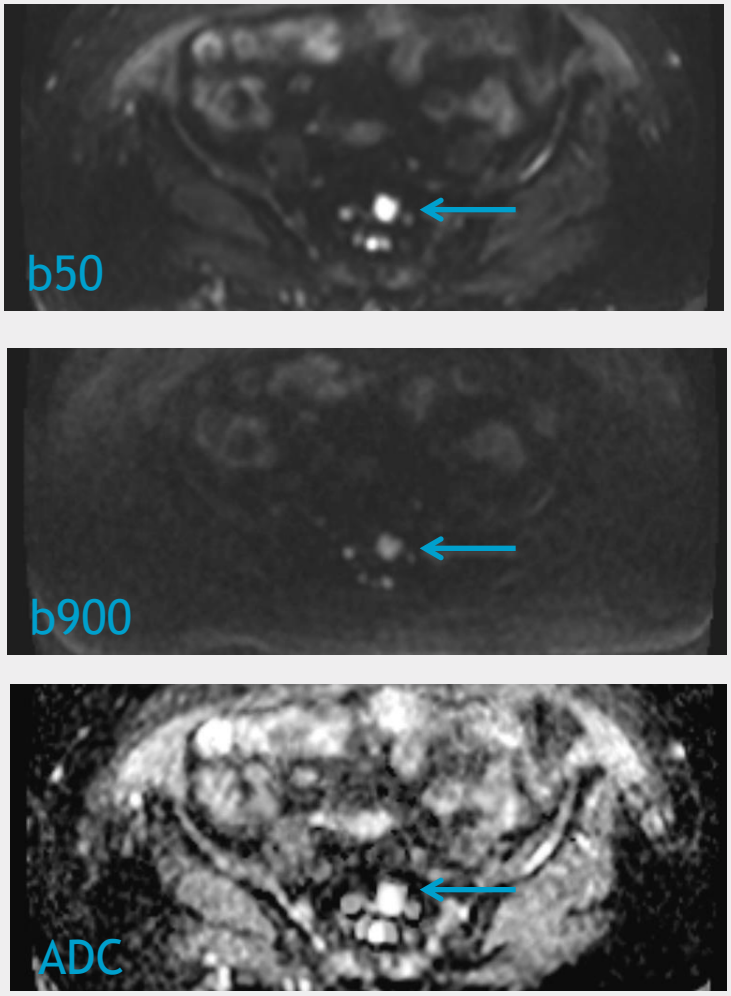






Case 10 –Post autograft





iTIMM

Image Guided Theranostics in Multiple Myeloma

Prospective Observational Study

To compare the relationship of WB-DWI prior to induction, post induction, 3 months post autograft and outcomes.

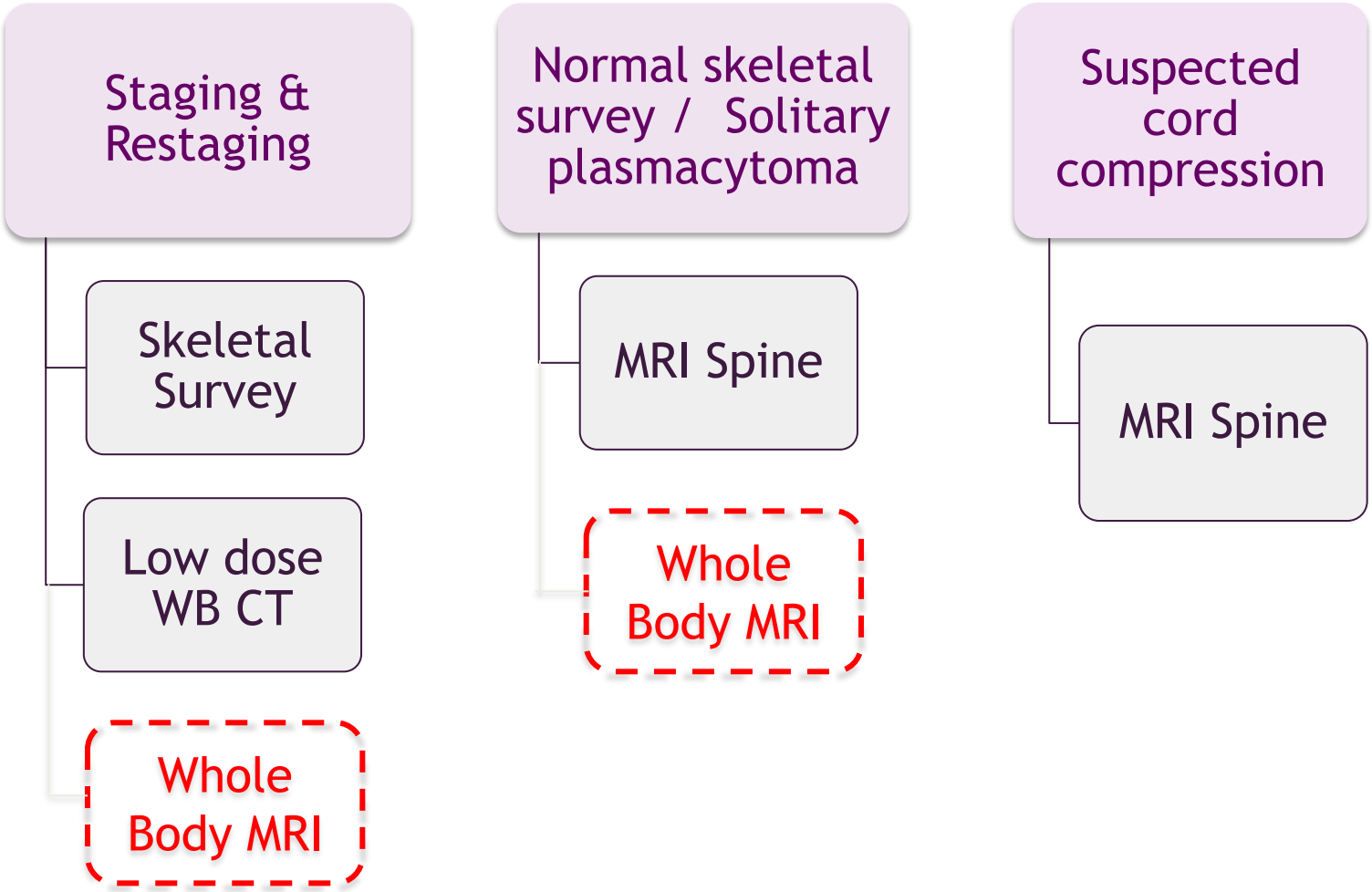
WB-DWI vs FDG PET/CT at baseline

REVIEW

International myeloma working group consensus statement and guidelines regarding the current role of imaging techniques in the diagnosis and monitoring of multiple Myeloma

M Dimopoulos[1], E Terpos[1], RL Comenzo[2], P Tosi[3], M Beksac[4], O Sezer[5], D Siegel[6], H Lokhorst[7], S Kumar[8], SV Rajkumar[8], R Niesvizky[9], LA Moulopoulos[10] and BGM Durie[11] On behalf of the IMWG

Leukemia, 2009



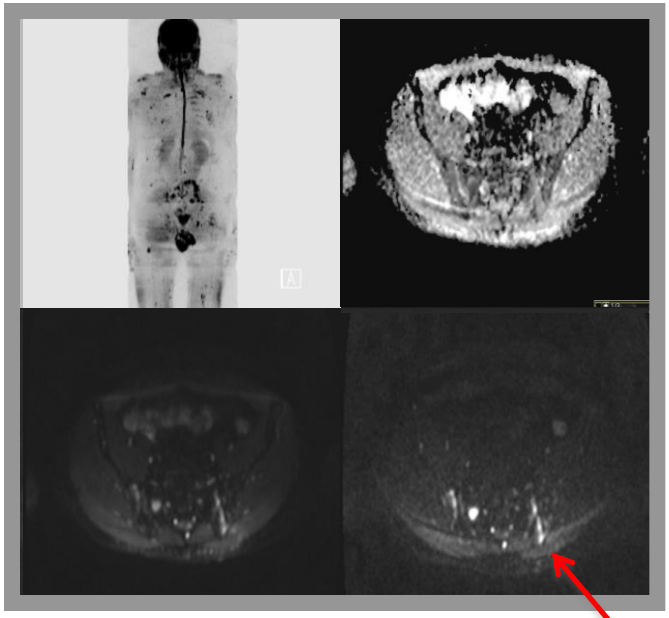
Whole Body MRI

No ionising radiation, No iv contrast, No sampling errors

Quantitative
Burden and Response
Diffuse and Focal

Whole body coverage
Detect extramedullary disease

Mechanical complications
Benign vs malignant
Threat to cord

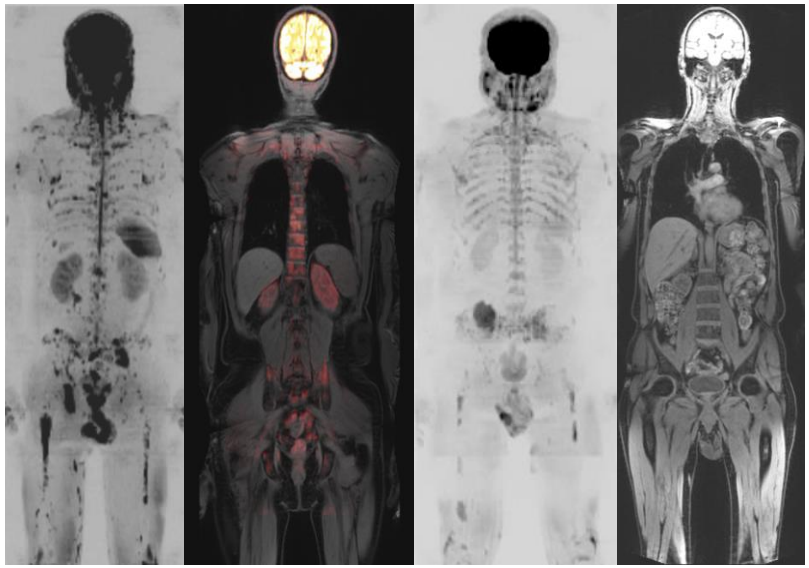


Fracture Risk

Increased sensitivity for diffuse infiltration

Guide Bx
Is trephine representative?

The Future of WB DW-MRI



WB DW-MRI : A new gold standard?

But does it help us and at what cost?

WB DW-MRI vs FDG PET/CT as a prognostic and predictive biomarker

Clinical trials incorporating imaging as a decision making tool

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