



18th International Myeloma Workshop

Prospective comparison of contemporary whole body MRI and FDG PET/CT for disease detection and correlation with markers of disease burden in myeloma: Results of the iTIMM trial

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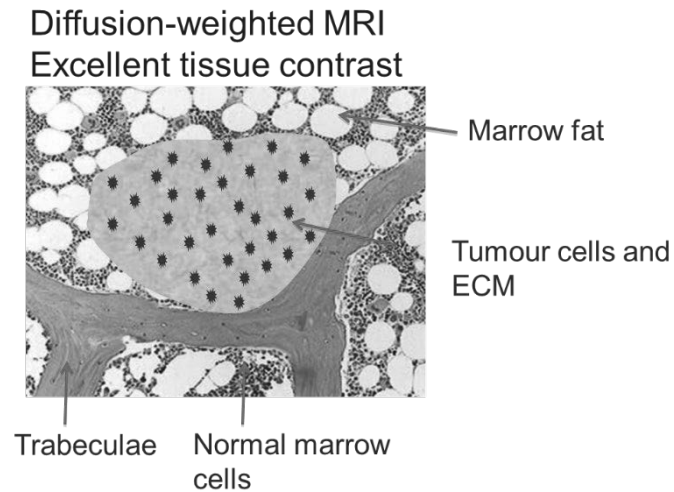
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Abbvie: Consultancy; Amgen: Consultancy, Honoraria; BMS/Celgene: Consultancy, Honoraria, Research Support, Travel Support; Janssen: Consultancy, Honoraria, Travel Support; GSK: Consultancy; Karyopharm: Consultancy; Pfizer: Consultancy; Seattle Genetics: Consultancy; Takeda: Consultancy, Honoraria, Travel Support



Bone marrow disease imaging in multiple myeloma (MM)

- Sensitive and early imaging followed by risk-adapted management can improve patient outcome (IMWG diagnostic criteria 2014)
- Current imaging standards (IMWG imaging guidelines 2019):
 - Whole body MRI (WB MRI)
 - FDG PET/CT
- Development of contemporary MRI including diffusion-weighted protocols
 - Increased sensitivity over 'classical' MRI
 - Excellent soft tissue contrast (EMD)
 - Measuring 'cellularity' of lesions
 - Excellent therapy response assessment

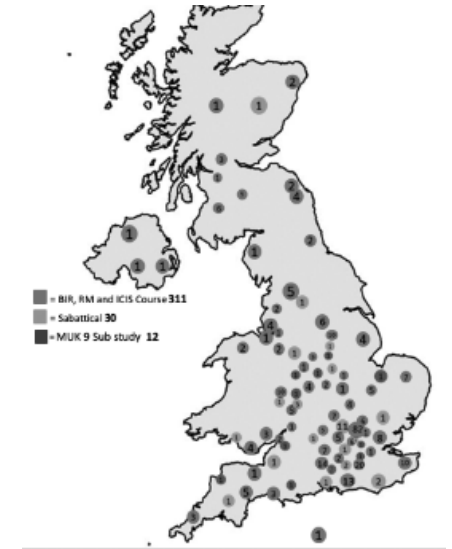
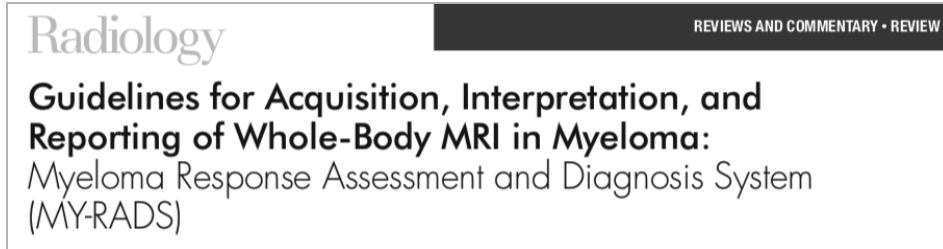


Inverse grey scale
b 900



Bone marrow disease imaging in multiple myeloma (MM)

Standardization of MRI - International MY-RADS consensus criteria (2019)



- Acquisition, reporting, response assessment
- ‘Open source’ scanner protocols for all major manufacturers

Health economic evaluation whole-body MRI

UK NICE 2016: at diagnosis net benefit for whole-body MRI & CT, but not PET/CT

Despite lack of data on comparative sensitivity (cost/need to add other imaging) → MRI/CT recommended

However, deficit in prospective comparison of contemporary WB MRI and FDG PET/CT

→ Define optimal imaging modality



The iTIMM trial

(Imageguided Theranostics in Multiple Myeloma; clinicaltrials.gov: NCT02403102)

Prospective, single-centre observational study for patients with symptomatic MM planned for high-dose therapy and ASCT

Aims

- To compare contemporary WB MRI and FDG PET/CT for detection of bone marrow disease
- To correlate imaging with markers of disease burden and molecular markers of biology
- To correlate imaging at baseline and minimal residual disease on WB MRI post ASCT with outcome

Methods

- WB MRI and PET/CT at baseline (pre-therapy)
- Clinical data collection including tumour genetics
- Scans double reported in blinded fashion for focal and diffuse disease by 2 reporting radiologists and 2 nuclear medicine physicians (all >10 years experience)
- Paired methods used to compare burden and patterns of disease on WB MRI vs. FDG PET/CT.

Recruitment

- May 2015 to March 2018 at Royal Marsden Hospital, London, UK
- 60 patients (35 male; median 60 years) with matched WB MRI and PET/CT

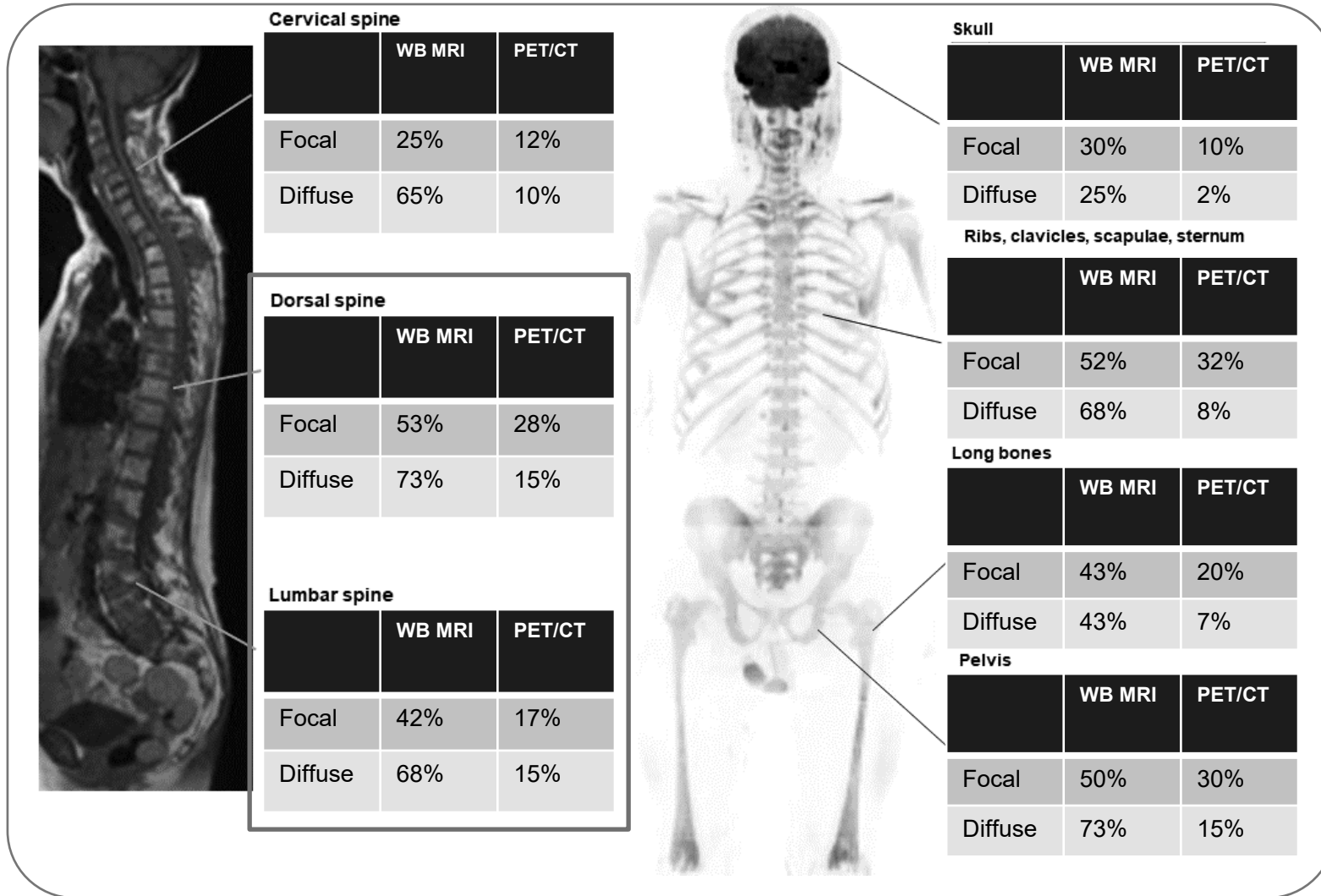


Patients

		Overall	
		N	%
Patients with paired baseline WB-DWI & PET/CT		60	100
Sex			
	Female	25	41.7
	Male	35	58.3
Age (years), mean (SD)		60.2 (8.8)	
ISS Stage I/II/III			
	I	27	45
	II	20	33.3
	III	6	10
	Unknown	7	11.7
Laboratory markers		N	Med (P25-P75)
	Beta2-microglobulin	53	2.8 (2.4-4.1)
	Albumin	54	36.0 (32.0-39.0)
	Plts	56	231.0 (190.5-274.0)
	Hb	56	115.5 (102.0-132.5)
	Calcium	54	2.3 (2.2-2.4)
	LDH	38	164.5 (142.0-210.0)
	Creatinine	56	77.5 (67.0-87.5)
Tumour Assessments & Genetics		N	%
	t(4;14)	3	5
	t(14;16)	3	5
	t(14;20)	1	1.7
	del(1p)	3	5
	gain(1q)	17	28.3
	del 17p	1	1.7
Any above high risk marker		20	33.3



Results: comparison WB MRI vs PET/CT



Focal lesions – example regions

		FDG PET/CT		
		No lesion	1-4	> 4
WB-MRI	No lesion	42	2	1
	1-4	10	3	1
	≥ 5	8	8	2

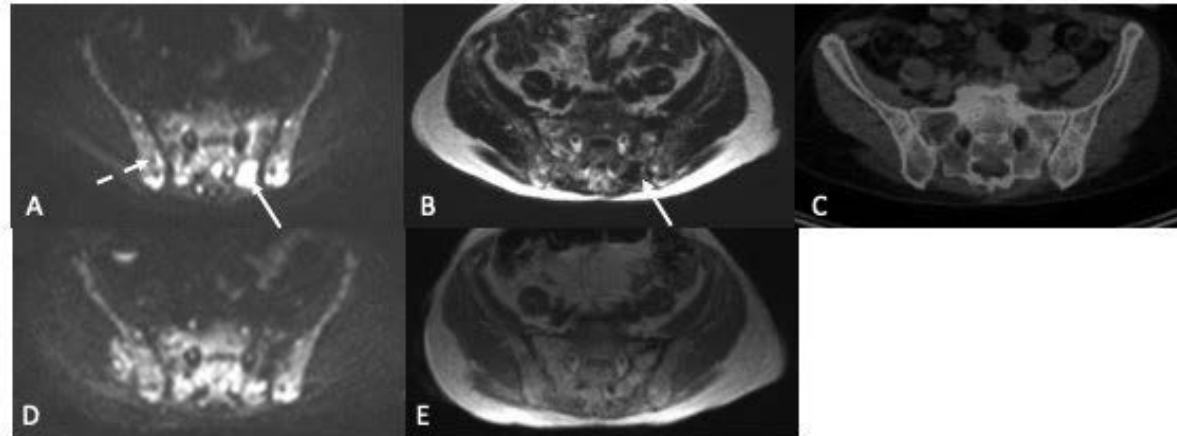
		FDG PET/CT		
		No lesion	1-4	> 4
WB-MRI	No lesion	42	2	0
	1-4	10	3	2
	≥ 5	7	3	0

Higher sensitivity of WB MRI to detect focal and diffuse disease in all bone marrow areas

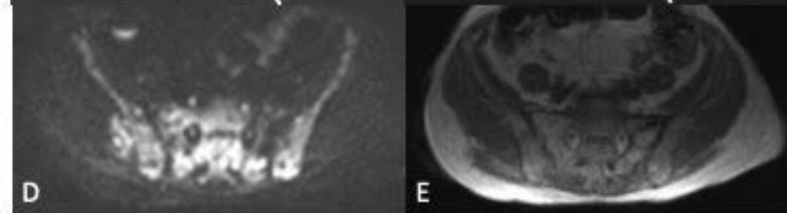


Example patient – focal disease

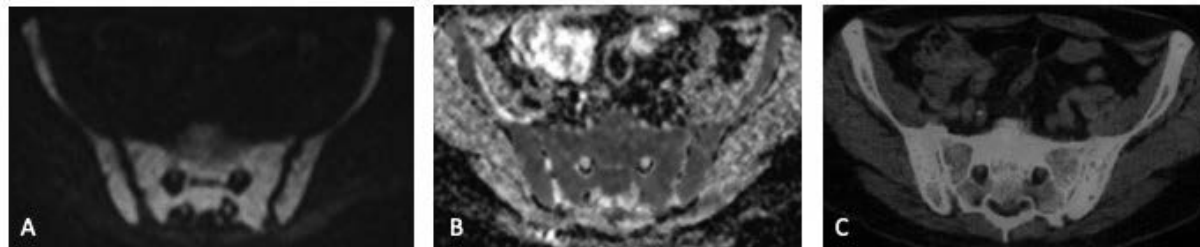
Pre-treatment



Post-treatment



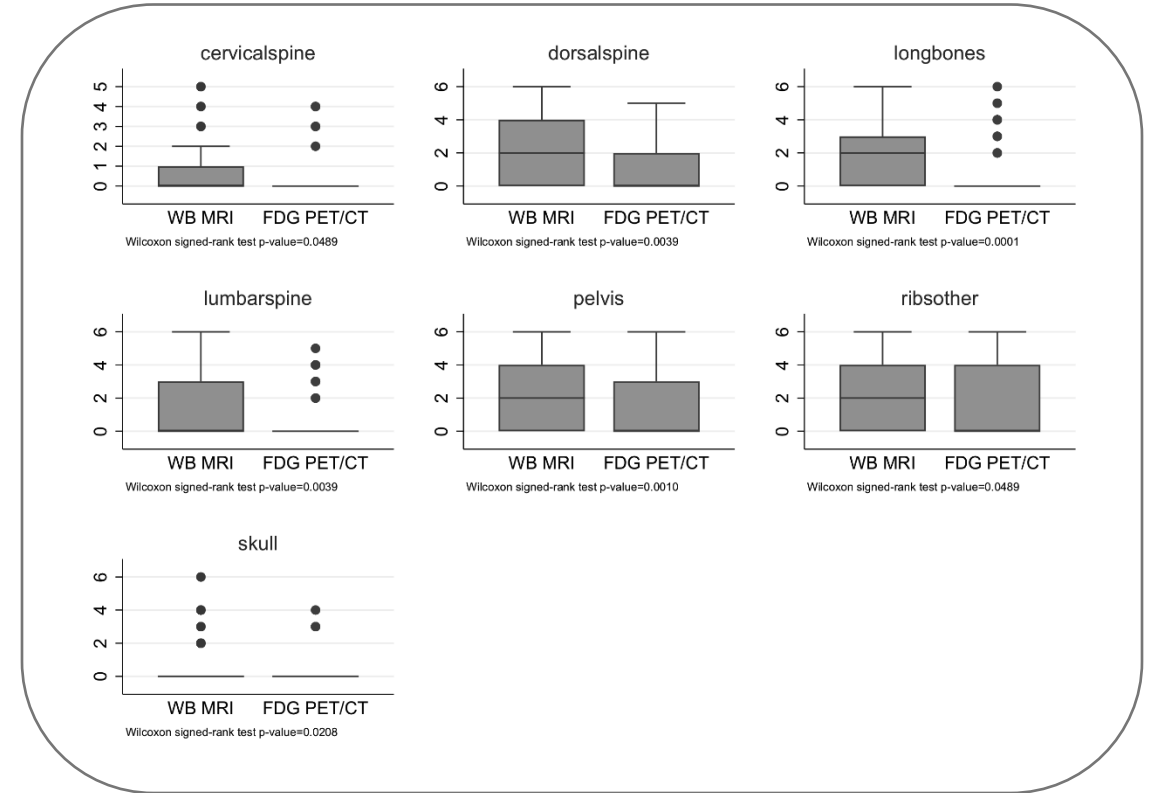
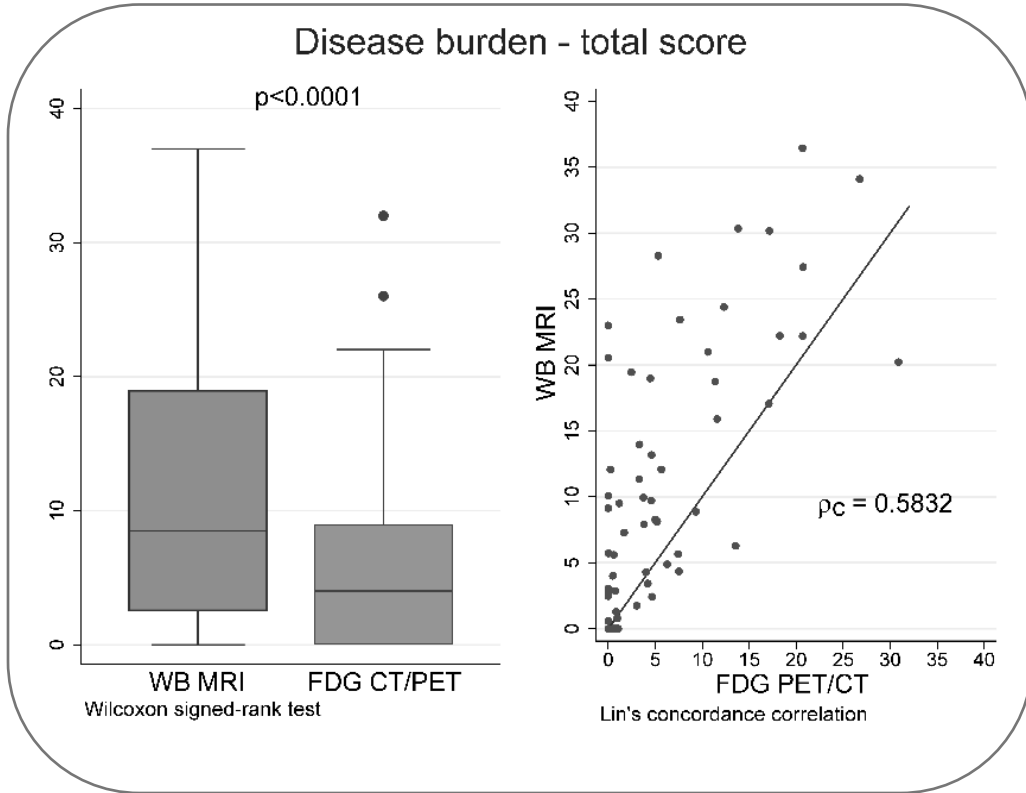
Example patient – diffuse disease



85% myeloma infiltration on bone marrow biopsy (histopathology)
Representative of overall marrow



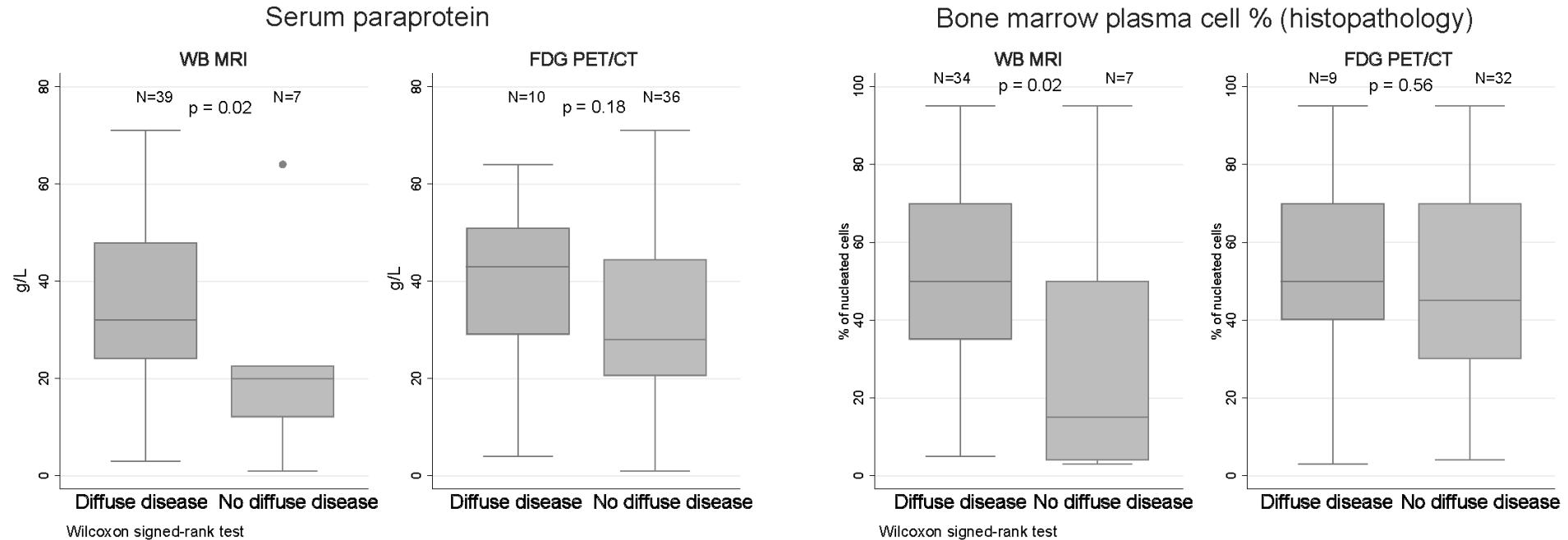
Results: comparison WB MRI vs PET/CT (2)



Higher disease burden scores with WB MRI for all anatomical areas



Results: imaging disease burden and biology

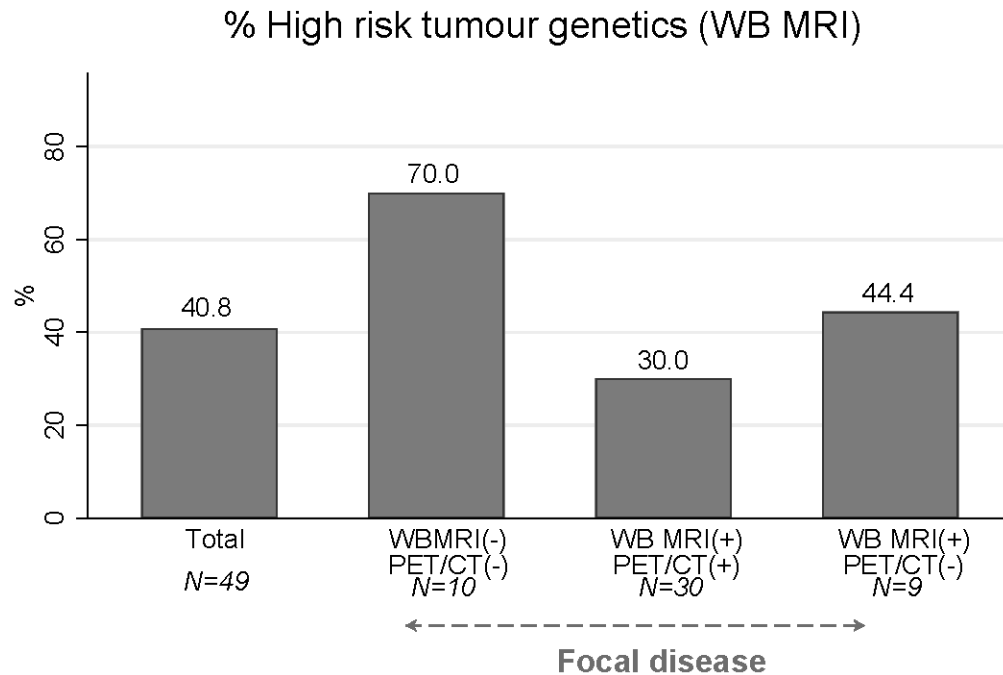


First time correlation between imaging quantitation and surrogate (paraprotein) or direct (BM) disease

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Results: imaging disease burden and biology



	Diffuse disease		No diffuse disease		p-value
	N	%	N	%	
Total Number	49	100	11	100	
ISS Stage I/II/III					
I	18	36.7	9	81.8	0.071
II	18	36.7	2	18.2	
III	6	12.2	0	0	
Unknown	7	14.3	0	0	
Laboratory markers	N	Med (P25-P75)	N	Med (P25-P75)	
Beta2-microglobulin	43	3.0 (2.4-4.5)	10	2.6 (2.4-2.8)	0.083
Albumin	43	36.0 (29.0-39.0)	11	37.0 (36.0-44.0)	0.083
Plts	45	231.0 (194.0-279.0)	11	207.0 (186.0-269.0)	0.49
Hb	45	113.0 (100.0-126.0)	11	132.0 (124.0-146.0)	0.0031
Calcium	43	2.3 (2.2-2.4)	11	2.3 (2.3-2.5)	0.255
LDH	29	172.0 (141.0-219.0)	9	155.0 (150.0-168.0)	0.583
Creatinine	45	75.0 (67.0-87.0)	11	83.0 (68.0-95.0)	0.279

Diffuse disease on WB MRI without focal disease associated with high risk genetics



Summary/Outlook

- Contemporary WB MRI as per MY-RADS criteria significantly more sensitive to detect focal and diffuse disease than FDG PET/CT
- Detection of diffuse disease on WB MRI associated with higher disease burden and high-risk molecular profiles
- Results propose WB MRI as a gold standard for tumour imaging in myeloma
- Direct disease quantitation and correlation of phenotype with myeloma biology supports development of radiomic biomarkers
- Analysis of iTIMM ongoing: imaging MRD after ASCT and outcome
- NIHR real-world trial investigating machine assisted diagnosis to open

