



## Functional Cancer Staging in Black Africans - An Initial Experience with Whole Body Diffusion MRI

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### Abstract

**Aim:** To report on our initial experience with whole body diffusion weighted MRI (WB-DW-MRI) for cancer staging, using the Metastasis Reporting and Data System for Prostate (MET-RADS-P) criteria and scoring, aiming at finding evidence of visceral/and or bony metastasis in already diagnosed tumor cases involving different types of tumors.

**Methods:** The study involved 34 known oncological patients who were referred for cancer staging with Whole Body Diffusion Weighted MRI (WB-DW-MRI) at our center within the period of the study. WB-DW-MRI was performed on a 1.5T clinical scanner recently installed in our center. Scans were performed using 6 Channel body phase array coils isocenter matrix coil (spine coil) and 16 Channel Head/Neck Coil. Patients were examined in supine position and four stations of axial free breathing Diffusion Weighted Imaging (DWI).

**Results:** Majority of our study population were males, recording a mean age of 60.2 years. The lesions indicated for WB-DW-MRI included prostate cancer, breast cancer, uterine cancer, gastric cancer, Non-Hodgkin lymphoma, Burkitt's lymphoma, rectal cancer and lung cancer. Prostate cancer was the most common lesion (n=25, 73.5%). Visceral and/or bony metastasis was evident in 12 out of the 34 cases reported, majority of which were prostate cancer cases.

**Conclusion:** Whole body diffusion weighted MRI has proven to be effective in assessing visceral, nodal and bony metastasis in various types of malignancies in a black African population. Based on this experience, we reinforce the recommendation that WB-DW-MRI should be integrated into routine clinical practice.

**Keywords:** Whole body diffusion; Diffusion weighted imaging; MRI; Prostate cancer; Breast cancer; Bony and visceral metastasis

### Introduction

With the emergence of validated clinical indications for patients with known or suspected malignancy, the demand for imaging in oncology care is increasing. Imaging modalities such as Positron Emission Tomography (PET), Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Bone Scintigraphy (BS) and ultrasound are employed in establishing early diagnosis and performing appropriate monitoring of patients with regards to visceral and bony metastasis, common in the brain, liver and lungs [1,2]. Also, in an era where novel surgical and interventional techniques are utilized for the management of cancers, proven imaging techniques are needed for accurate tumor staging and precise evaluation of the metastatic burden in order to plan appropriate therapeutic management of patients with malignancy [3-5].

Bone Scintigraphy (BS) and CT scan have been utilized in detection and therapeutic response assessments, but are not very effective in evaluating therapeutic response in bone disease, which is the most common disease site in breast, multiple myeloma and prostate cancer [6]. For instance, BS is limited in the assessment of multiple myeloma when there is an insufficient osteoblastic reaction to the presence of an active disease. Even in the presence of osteoblastic reaction, BS usually provides misleading information when utilized in the assessment of therapeutic effectiveness. Also, increased BS uptake in number and extent of lesions can create confusion between progression and response, in therapy response settings [6]. Whole body imaging tools such as PET-CT and whole body diffusion weighted MRI (WB-DW-MRI) has thus emerged as a viable alternative assessment

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tool.

Positron Emission Tomography-Computed Tomography (PET-CT) is considered the gold standard among whole body imaging modalities, and has been employed in the initial detection, staging and evaluation of most malignancies [7-9]. Although PET-CT measures the metabolic activity of a tumor, covers most of the body, and is used for treatment response and staging, it is sometimes limited by factors such as variability in tracer uptake in lesions, high uptake in normal organs, increased radiation dose, or indeterminate findings due to the size of the lesion (<1 cm). Therefore, there is a growing interest in alternative imaging techniques that achieves accurate lesion detection and do not involve exposure to ionizing radiation, especially in cases of either incomplete response to treatment or a significant risk of disease recurrence, both of which necessitate a longer active surveillance period and an increased number of imaging studies [10,11].

Whole body diffusion weighted MRI (WB-DW-MRI) with its inherent advantages including lack of ionizing radiation, no use of contrast, time saving and relatively lower cost, is a practical technique that may fulfill this role [10,11]. WB-DW-MRI, introduced by Takahara et al. [12] is able to suppress background body signal, thus allowing assessment of metastasis of various malignancies without motion artifact, and Three-Dimensional (3D) images can be obtained using reformatting techniques such as Maximum-Intensity Projection (MIP) and Multi-Planar Reformatted (MPR). Furthermore, the Apparent Diffusion Coefficient (ADC) map obtained from diffusion weighted MRI reflects cellular density, tumor morphology, nuclear-to-cytoplasm ratio and integrity of cell membrane, regardless of cancer type and location [13,14]. WB-DW-MRI has thus emerged as a powerful tool, capable of evaluating both bone and soft tissue disease, and showing both cell viability and tissue cellularity, thus increasing confidence in the detection, characterization and monitoring of treatment response in metastatic lesion [6]. It has proven to be efficacious for overcoming the limitations of CT and BS for detection and therapeutic response assessments in patients with bone marrow tumors [15]. Consequently, WB-DW-MRI is progressively proposed by clinicians as an efficient examination for an expanding range of indications [16]. In this study, we report on our initial experience with WB-DW-MRI for cancer staging in a black African population, providing additional evidence that whole body diffusion weighted MRI has an important role in the staging of different types of tumors and it is a viable alternative to Positron Emission Tomography Computed Tomography (PET-CT) for cancer staging.

## Methods

Within the period of October 2018 to February 2019, 34 known oncological cases were referred from various health facilities for cancer staging with whole body diffusion weighted MRI scan at our center. Ethical approval for the study was obtained from the Committee on Human Research, Publications and Ethics (CHRPE/AP/306118). Also, written informed consent was obtained from the participants before their inclusion into the study.

WB-DW-MRI was performed on a 1.5T clinical scanner (Magnetom Essenza Siemens Healthineers, Erlangen German) recently installed in our center. Scans were performed using 6 Channel body phase array coils together with 16 Channel Head/Neck Coil. Patients were examined in supine position and four stations of axial free breathing DWI with Short Tau inversion Recovery (STIR) fat



**Figure 1:** WB-DW-MR images in an 80-year-old male with a confirmed prostate Ca and extensive bony metastasis involving the whole of the imaged axial skeleton. A) Shows sagittal STIR whole spine, B) shows T1 sagittal whole spine and C) shows whole body MRI diffusion with inverted 3D MIP reconstruction. D) Normal whole body diffusion for a patient with prostate cancer without metastasis.



**Figure 2:** Whole body diffusion for a confirmed prostate cancer on hormone therapy. A) Showing whole spine Sagittal STIR and B) Whole spine sagittal T1 depicting multiple vertebral metastasis. C and D) shows coronal and sagittal inverted MIP whole body diffusion images, depicting subtle diffusion restriction in the affected spine owing to the effect of the hormone therapy.

suppression obtained using the scan parameters as follows Echo Time (TE) 93ms; Repetition Time (TR) 9000 MS; Inversion Time (TI) 160 ms, B values 50 and 900 s/mm<sup>2</sup>, Read out bandwidth 1628 Hz/Pixel, 6 Averages, Field of View (FOV) 400 MM, Slice thickness 5 mm, Image matrix 128 × 128, Voxel size 1.6 mm × 1.6 mm × 5.0 mm. Acquisition time per station 7.30 min. The protocol also included four stations of Coronal T2 Fat Sat free breathing with the following parameters: TR 2000 ms; TE 93ms; Image matrix 256 × 256, Voxel size 1.5 mm × 1.5 mm × 5 mm with SPAIR Fat suppression mode. After the completion of the last acquisition, four stations including Head/Neck, Thorax, Abdomen and Pelvis were then composed inline. No contrast media was administered and total duration of each examination was about 50 min to 55 min.

## Metastasis reporting and data system for prostate (MET-RADS-P)

Despite the wider applicability of Whole Body MRI (WB-MRI), especially in assessing bone and soft tissue metastases, its use has been limited by inconsistencies in how the procedure is performed and interpreted. There was therefore the need for a standardized approach that ensures uniformity in acquisition, interpretation and reporting. This led to the formulation of Metastasis Reporting and Data System (MET-RADS-P), which provides the field of WB-MRI with minimum standards of image acquisition, interpretation and reporting [16,17].

MET-RADS-P criteria were employed in assessing bone metastasis in this study. It enables assessment of 14 predefined regions of the

**Table 1:** Clinical findings in the oncological patients.

Case	Age (years)	Evidence of visceral/ and or bony metastasis	Bones/tissues involved
Prostate cancer	53	none	
Prostate cancer	80	yes	Pelvic bone, lumbosacral spine
Prostate cancer	64	none	
Prostate cancer	74	none	
Prostate cancer	60	yes	Spine, pelvic regions, lymph nodes
Prostate cancer	68	none	
Prostate cancer	67	yes	lungs, axillary nodes
Prostate cancer	60	yes	pelvic lymph node, pelvic bone
Prostate cancer	56	none	
Prostate cancer	62	none	
Prostate cancer	60	none	
Prostate cancer	70	yes	pelvic lymph node
Prostate cancer	66	none	
Prostate cancer	55	none	
Prostate cancer	55	none	
Prostate cancer	73	none	
Prostate cancer	65	none	
Prostate cancer	68	none	
Prostate cancer	75	yes	Spine, ribs, lymph nodes
Prostate cancer	74	none	
Prostate cancer	64	none	
Prostate cancer	72	none	
Prostate cancer	60	none	
Prostate cancer	72	none	
Prostate cancer	75	yes	Spine, ribs, lymph nodes
Breast cancer	56	yes	Thorax, pelvis, lumbosacral spine, dorsal spine, cervical spine, liver Lymph node, multiple bony metastasis
Breast cancer	68	yes	Lungs, liver
			Liver, sternum, lymph nodes
Uterine cancer	62	yes	Lymph node, neck, vertebral
Uterine cancer	56	yes	Lymph nodes, abdominal
Burkitt lymphoma	8	yes	Lungs
Non-Hodgkin's lymphoma	10	yes	Spine, ribs, lymph nodes
Gastric cancer	35	yes	Lungs
Rectal cancer	29	yes	Spine, ribs, lymph nodes
Lung cancer	80	none	

body including seven skeletal regions, primary disease, visceral, five nodal and other sites at baseline and follow-up assessment, making use

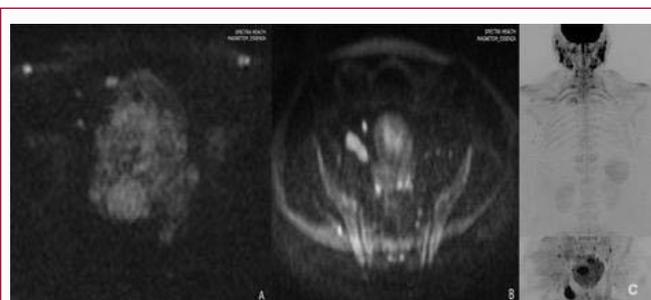
of a 1.5 cm diameter threshold for all measured lesions. Each region was assigned a response assessment on a scale of 1-5 (1, indicating a higher likelihood of a patient responding, up to 5, indicating a higher likelihood of disease progression). In addition, MET-RADS-P utilizes a scoring system that allowed accounting for heterogeneity of responses in different regions. The final response assessment involved assessing the status of the bones, primary disease, viscera and nodes separately [16,17]. In assessing soft tissue metastases, RECIST criteria as described by Eisenhauer et al. [18] were employed.

## Results

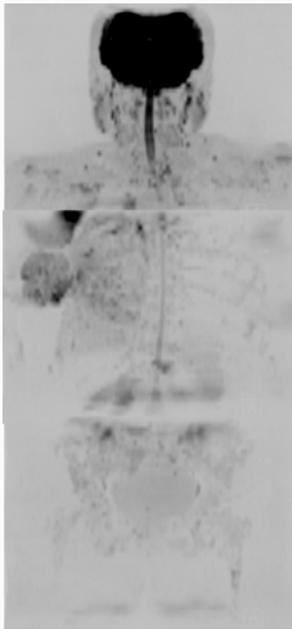
Thirty-four known oncological patients with a mean age of 60.2 years underwent whole body diffusion weighted MRI scan at our center within the period of the study. The lesions indicated for WB-DW-MRI included prostate cancer, breast cancer, uterine cancer, gastric cancer, non-Hodgkins lymphoma, Burkitt's lymphoma, rectal cancer and lung cancer. Prostate cancer was the most common lesion, representing 25 out of the 34 cases. Visceral and/or bony metastasis was evident in 12 out of the 34 cases reported. The distribution is shown in Table 1.

## Discussion

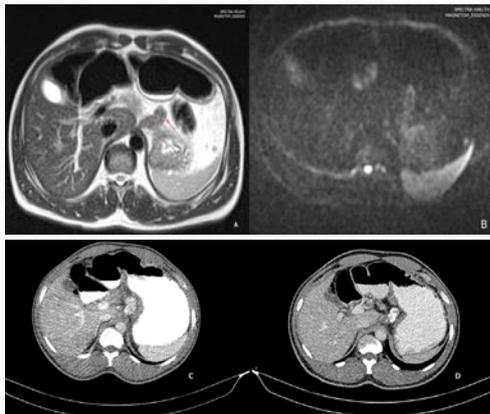
Whole Body Diffusion Weighted MRI (WB-DW-MRI) is an attractive modality for tumor detection and oncological staging owing to lack of radiation, high spatial resolution and soft tissue contrast [10,11,19]. The utilization of Whole Body MRI (WB-MRI) has been hindered in the past due to limitations such as limited availability and forbidding acquisition times [16]. However, recent technological advancements incorporating multi-channel whole body scanners, has led to high sensitivity in the detection of organ metastases, especially for tumors frequently metastasizing to the bone, liver or the brain [20,21]. In addition, the use of Diffusion Weighted Imaging (DWI) has transformed WB-MRI, providing functional information which enables "at-a-glance" assessment of the whole body, thus improving readers' performance and reducing interpretation time [19,22]. The rationale for the use of WB-DW-MRI in oncology is to enable tumor detection and precise staging, which are crucial for assessing prognosis and planning effective treatment. This study to the best of our knowledge is the first to report on whole body diffusion weighted MRI cancer staging in oncological patients of black African origin. The main focus of the procedure was to find evidence of visceral/ and or bony metastasis in already diagnosed tumor cases involving the prostate, gastric, uterine, rectum, lung and breast as well as stage



**Figure 3:** A) WB-DW-MR images in a 67-year-old male with an advanced cancer of the prostate showing diffuse involvement of the gland with significant restriction in the diffusion scan. B) Diffusion scan of the pelvis showed metastatic pelvic and left para-rectal lymph nodes. C) Whole body diffusion with inverted coronal MIP showing a large metastatic in the right inferior ramus of the pelvic bone as well as diffuse pelvic gland involvement and metastatic pelvic lymphadenopathy.



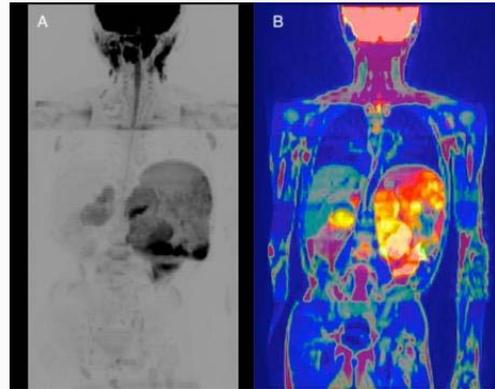
**Figure 4:** Whole body diffusion inverted MIP imaging for a known breast cancer patient showing a multiple bony metastasis as well as depicting the primary right breast cancer and a large ipsilateral axillary lymph node metastasis. Additional liver and lung metastasis were also noted.



**Figure 5:** Whole body diffusion images in a 35-year-old male with metastatic gastric Ca and unclear persistent celiac lymphadenopathy whose size was maintained from primary CT and for all follow up examinations for a year. MRI diffusion did not suggest metastatic involvement. A) Axial T2 scan showing 2 celiac lymph nodes in contact with each other. B) Shows axial diffusion MRI with the lymph nodes showing no restriction on the diffusion. C) and D) showing contrast enhanced portal venous CT scan taken a year apart depicting unchanged appearance of the non metastatic partially calcified celiac lymph nodes (C taken in 2017 and D taken in 2018).

lymphomas.

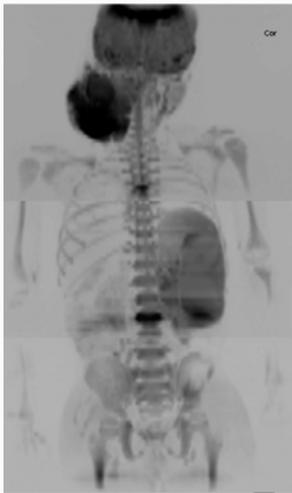
Majority of the cancer staging with WB-DW-MRI in this study involved prostate cancer patients, and metastases were evident in 6 out of the 25 cases (Figure 1-3). In most of these cases of prostate cancer, there was an early spread to bones and regional nodes. A meta analysis from 27 studies have shown that, on per patient basis, WB-DW-MRI is superior to PET-CT and Bone Scintigraphy (BS) in the detection and staging of prostate cancer [23]. The presence of metastasis in prostate cancer imaging in this study was crucial for the patients, assisting in defining the advanced disease state and the absence or presence of metastasis outside the true pelvis was highly



**Figure 6:** Eight-year-old male with confirmed non-Hodgkins Lymphoma. A) Shows whole body diffusion with an inverted MIP showing splenomegaly with multiple lesions in the spleen and the liver hilum. B) Whole body diffusion with fusion imaging depicting the lesion in bright colors.

prognostic, thus affecting subsequent therapy choices. Also, the use of MET-RADS-P reporting template enabled us to characterize the metastatic bone disease response into 5 categories (1 Response: highly likely; 2 Response: likely; 3 stable; 4 progression: likely; 5 progression: highly likely), which was considered helpful compared to the limited clinically groups of progression and no-progression, eventually overcoming the limitations of BS and CT scans. In the reported prostate cancer cases, WB-DW-MRI was successful in establishing metastasis to the pelvic bone, pelvic lymph node and lumbosacral spine as depicted in Figure 1-3.

Extensive metastasis was recorded in the breast cancer cases reported in this study. The bone is recognized as the most common metastatic site in breast cancer cases, with axial and proximal appendicular skeleton been the most affected sites [24]. In the current study, WB-DW-MRI for the breast cancer case established metastasis involving the lung, liver and axial skeleton (vertebral, pelvis and ribs) (Figure 4). The main focus of performing WB-DW-MRI in this advanced case was to assess clinical response, evaluate post-therapeutic changes and complications, and search for hypercellular lesions for the purpose of disease staging. Moreover, it is essential to establish an early diagnosis and adopt appropriate monitoring strategies in breast cancer cases, as research has shown that about 10% of the patients will have secondary neoplastic involvement of multiple organs [25]. Schmidt et al. [26] in their study of breast cancer patients compared the diagnostic accuracy of WB-MRI and PET-CT for the detection of tumor recurrence. WB-MRI was found to be highly sensitive in detecting distant metastatic disease, as confirmed in our study, while PET-CT was more sensitive in detecting lymph node involvement. Also, a meta-analysis conducted by Yang et al. [27] which involved 145 studies in various types of malignancies, including breast cancer, showed that WB-MRI and PET-CT have comparable diagnostic performance, and were found to be superior to CT and BS in terms of specificity and sensitivity to detect bone metastases. The current study demonstrates that WB-DW-MRI showed high specificity and sensitivity in detecting both visceral and bony metastases as depicted in Figure 4, thus serving as a “one-time” approach to staging the advanced case of breast cancer. This was in line with the recommendation by the UK’s National Institute for Health and Care Excellence that the progression of bone metastasis in patients with advanced breast cancer must be evaluated by MRI rather than PET-CT or BS [28].



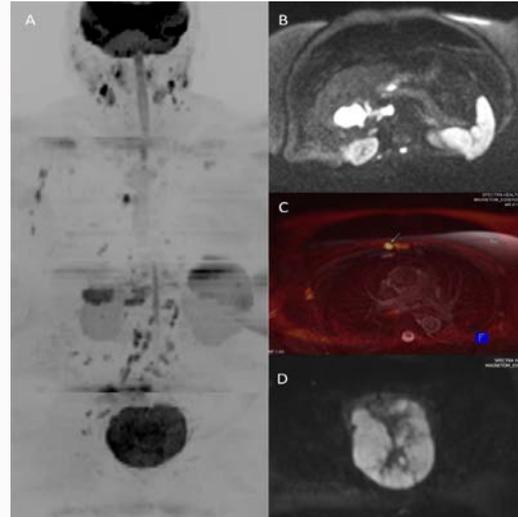
**Figure 7:** Whole body diffusion imaging for a confirmed Burkitt's lymphoma with paraparesis showing large lesions involving the right submandibular region, lymphomatous involvement of the spleen and lesions involving the spine.

WB-DW-MRI also proved useful in the staging of cases involving gastric cancer (Figure 5), uterine cancer (Figure 5), Non-Hodgkin's lymphoma (Figure 6) and Burkitt's lymphoma (Figure 7 and 8). In all these cases, WB-DW-MRI enabled overall assessment of the disease by providing accurate information on nodal and distant metastasis (Table 1), thus rendering crucial information for assessing prognosis, risk stratification and planning effective treatment. Worthy of note was the presence of lung metastasis in both gastric cancer (Figure 5) and uterine cancer (Figure 8) and hepatic metastasis in uterine cancer (Table 1). This demonstrates the utility of WB-DW-MRI in the detection of secondary visceral involvement, and this may even be detected before they appear in other sequences [2].

In summary, WB-DW-MRI allows more accurate tumor detection of both visceral and bony metastasis, as evident in the cases presented in this study. Bony metastases as shown in this study are detectable in patients with advanced stages of prostate, breast and uterine tumors. WB-MRI with diffusion imaging provide clear categorization of the treatment response of bone metastases due to the calculation of the ADC value, as against BS and PET/CT which are able to identify only disease progression [29,30]. Various studies have thus demonstrated its superiority to BS for the detection of bone metastasis, and was better than PET-CT on a per-patient basis [23,31]. However, several studies comparing the diagnostic accuracy of WB-DW-MRI and PET-CT have reported no significant difference, with some concluding that they are complementary techniques [23,27,32]. Moreover, in the performance of WB-DW-MRI, one needs to be aware of inherent pitfalls such as false negatives in the presence of cystic metastasis, tumor necrosis and imaging areas close to the heart [33].

## Conclusion

Whole body diffusion weighted MRI is a proven technology in cancer staging. It is currently the preferred imaging modality for multiple myeloma and bony metastasis, and it compares very well with PET-CT for all other indications as shown in several studies. In breast and prostate cancer cases, which constituted majority of the reported cases in this study, WB-DW-MRI proved useful in assessing visceral, nodal and bony metastasis. Based on our experience with



**Figure 8:** WB-DW-MR images in a 57-year-old woman who had tumor debulking and chemoradiation for a uterine/cervical/vaginal vault cancer. Findings showed a large malignant residual vaginal vault tumor showing strong restriction in the diffusion scan A and D, metastatic retroperitoneal lymph nodes, A liver metastases, A and B, and right sternal metastasis A and C.

WB-DW-MRI for cancer staging in a black African population, we reinforce the recommendation that it should be integrated into routine clinical practice.

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