



Is Whole Body –Diffusion MRI an Alternative to PET-CT! A Review of Literature

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Abstract

WB-DWMRI and PET-CT are the two functional tools available for detection and staging of cancer patients. PET-CT has been the established modality since last two decades however with the improvements in MRI technology it is now possible to perform a whole body functional and anatomical imaging. This article reviews the current literature to determine whether WB–DWMRI can be an alternative imaging to PET-CT for imaging cancer patients. The study reviewed 19 studies from 2009-2016 for all types of regional and metastatic cancers including lymphomas and myelo infiltrative disorders to determine the sensitivity and specificity of both the imaging modalities. The results of these studies are discussed and these showed a comparable sensitivities and specificities. The study concludes that due to inherent advantages of WB-DWMRI i.e. lack of radiation, time saving, no use of contrast and lower cost it can be considered as an alternative imaging tool in the evaluation of such patients.

Introduction

Diffusion Weighted Magnetic Resonance Imaging (DW-MRI) is a useful and attractive technique for evaluation of cancer patients [1]. Recent technological advances have made it a promising technique for staging disease in oncology practice [2]. Till date PET-CT is the established modality for evaluation of oncology patients however it is associated with considerable cost and also adds radiation burden to the patient and also to the medical personal.

The article reviews the current position of body these modalities in staging oncology patients to find the answer to the question of whether WB-DWI MRI is an alternative to PET-CT!

Technique

WB-DW MRI is done on both 1.5T and 3.0T MRI systems with the use of 4-5 station coils without the use of any contrast with images taken from head to mid tibia level and are acquired axially in free breathing state. Diffusion sequences are applied in X,Y and Z axis before and after 180 degree inversion pulse to have a fat saturation image along with diffusion sensitivity b values of 0,400,800mm²/sec. Data obtained is reformatted in multi planar manner as whole body images in coronal planes and inverted as black and white grey scale images (Figure 1a and b) for analysis. ADC values for any region of interest are determined for estimation of tumor cellularity and expressed in units of 10mm²/s -3mm²/s. Another parameter used is lesion to spinal cord ratio determined on high b value image by using ROI technique.

Review of Literature

We searched the Pub med for studies done for correlation and comparison of PET-CT and WB-DWMRI and reviewed the results. 19 studies from current literature were found out which compared the results of both the modalities in patients of cancer for staging and suspected metastasis and also other myeloproliferative disorders (Table 1). All these studies were found to be having a common conclusion that WB- DWMRI can be used as a diagnostic test to diagnose and stage the disease and also to assess treatment response in such patients for which quantities DWMRI can be used as biomarker for early assessment of response to treatment.

Lung Cancer Detection and Staging

Mori “et al”. [3] performed prospectively 18F-FDG PET-CT and DWMRI on 104 patients with pulmonary nodules of which 106 were proven malignant. SUV values and SUV CR values were obtained to determine the nature of lesion on PET-CT and ADC min values are determined on DW

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Table 1: List of studies comparing WB-DWMRI and PET-CT for staging cancer patients.

| No. | Study | Year | No. of Patients | Organ | WB-DWMRI | | PET-CT | | Conclusions |
|-----|-----------------------|------|-----------------|----------------------------|---------------------------|------------------|---------------|------------------|--------------------------------|
| | | | | | Sens (in %age) | Specif (in %age) | Sens (in%age) | Specif (in %age) | |
| 1 | Mori et al. [3] | 2008 | 104 | Lung | 72 | 97 | 70 | 79 | Results of DWI better |
| 2 | Ohba et al. [4] | 2009 | 110 | Lung | 73 | 96 | 72 | 82 | Similar |
| 3 | Takenaka et al. [5] | 2009 | 115 | Lung | 75 | 93.7 | 73 | 95.4 | Similar |
| 4 | Gong et al. [6] | 2015 | 28 | Colorectal | 81.1 | 99.1 | 95.1 | 99.8 | Similar |
| 5 | Ono et al. [7] | 2009 | 25 | Colorectal | 80 | 76.9 | 30 | 100 | DWI Better for nodal detection |
| 6 | Schmidt et al. [8] | 2004 | 33 | Breast | 90 | 86 | 91 | 90 | Similar |
| 7 | Heusner et al. [9] | 2010 | 20 | Breast | 91 | 72 | 94 | 99 | Similar |
| 8 | Pawlyn et al.[10] | 2016 | 17 | Myeloma | WB-DWI Better than PET-CT | | | | |
| 9 | Shen et al. [11] | 2014 | 27 | Meta analysis Prostate CA | 97 | 95 | 91 | 99 | DWI better |
| 10 | Barchetti et al. [12] | 2016 | 154 | Prostate Ca | 99 | 98 | 99 | | Similar |
| 11 | Eschmann et al. [13] | 2007 | 42 | Prostate Ca | 76 | 94 | 96 | 74 | Similar |
| 12 | Lin et al. [14] | 2010 | 15 | Lymphoma | 81 | 100 | 90 | 94 | Similar |
| 13 | Stecco et al. [15] | 2015 | 17 | Lymphoma | 100 | 96 | 96 | 100 | Similar |
| 14 | Gutzeit et al. [16] | 2010 | 36 | Any Metastasis | 97 | 99 | (Scinti)91 | 87 | Better |
| 15 | Fischer et al. [17] | 2011 | 68 | Any Metastasis | 72 | 89 | 74 | 91 | Similar |
| 16 | Li et al. [18] | 2013 | 1067 | Any Metastasis | 89 | 95 | 89 | 97 | Similar |
| 17 | Stecco et al.[19] | 2009 | 29 | Any Malignancy | 89.1 | 98.5 | 100 | | Similar |
| 18 | Choi et al. [20] | 2019 | 236 | Uterine cerv Ca | 86 | 80 | 100 | | Similar |
| 19 | Hassan et al. [21] | 2014 | 6 | Meta analysis Head Neck Ca | 100 | 71 | 68 | 84 | Better |

MRI to determine the same. After using an optimal cut off PET-CT showed a sensitivity of 70% while it was 72% with ADC min Similarly Specificities were 79% and 97% respectively. Authors concluded that DWI can be used to distinguish between malignant and benign lung nodules as the results of DWI were better than PET-CT Ohba “et al”. [4] also studied 110 patients of NSCLC and showed similar results of both DWI and PET-CT in Differentiating malignant from benign nodules with sensitivity and specificity of 73%, 96% and 72% and 82%. However authors also suggested that DWI may not be able to predict the aggressiveness of NSCLC.

However, Kanuchi “et al”. [5] in their study showed that DWI had a sensitivity of 90% in predicting tumor aggressiveness in patients of NSCLC with specificity of 81%. They also included the parameter of lesion to spinal cord ratio along with ADC min to categories the nature of lesion. Takenaka “et al”. [5]. Compared the results of staging of lung cancer patients with both the modalities in 115 patients of NSCLC. Results determined were on both per site and per-patient basis and found that the results of WB-DWMRI and PET-CT were similar. However when DWMRI was combined with routine MRI the specificity improved on per site basis.

Colorectal Cancer

Gong “et al”. [6] studied and compared WB-DWMRI and PET-CT in 29 patients of Gastro intestinal malignancies which included predominantly patients of colorectal cancer. They showed a sensitivity and specificity of WB –DWMRI 81.1% and 99.1% while of PET-CT 95.1% and 99.8% with a similar overall accuracy of 98.9% and 95.9%. The sensitivity of PET-CT was higher due to detection of small lung metastasis less than 6mm while two patients of liver metastasis and brain metastasis were missed bt PET-CT. The study concluded

that WB-DWMRI is reliable in detecting gastro intestinal tumor recurrence and metastasis and offers same diagnostic performance as PET-CT and without radiation. The quantitative value of ADC also provides extra information to determine metastasis.

Ono “et al”. [7] compared primary and metastatic lymph node detection in patients with colorectal cancer.

A total of 25 patients of proven colorectal cancer were studied by both PET-CT and WB-DWMRI. Out of the surgically proven patients 23(85.2%) were true positive on both PET-CT and WB-DWMRI. PET-CT however detected only 3/10 patients with nodal metastasis (30% sensitivity) while DWMRI detected 8/10 patients (80% sensitivity). Ohio suggested that DWMRI was better to PET-CT in nodal detection while inferior to it in primary colorectal cancer detection.

Breast Cancer

Schmidt “et al”. [8]. Studied 33 patients with recurrent breast cancer and compared the diagnostic accuracy of WB-MRI and FDG-PET-CT for the detection of tumor recurrence. WB-MRI and PET-CT were both useful for the detection of tumor recurrence. WB-MRI was highly sensitive to detect distant metastatic disease. PET-CT was more sensitive in detecting lymph node involvement. Overall sensitivity was 91% for PET-CT and 90% for WB-MRI. Overall specificity was 90% for FDG-PET-CT and 86% for WB-MR. Heusner “et al”. [9]. Concluded in their study of 20 patients of breast cancer that WB-DWMRI had a sensitivity of 91% compared to 94% of PET-CT for staging of breast cancer but had a low specificity of 72% while PET-CT had a specificity of 99% hence may not be suitable for staging the disease.

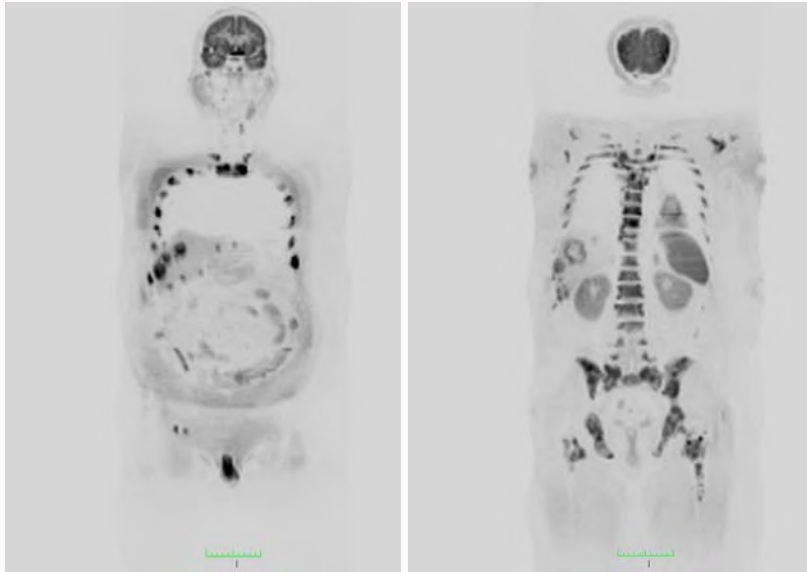


Figure 1a and b: WB-DWMRI MIP images of the whole body with inverted MIP format showing multiple areas of focal restricted ADC in liver and in the skeletal system consistent with metastasis in patient with bronchogenic carcinoma.

Multiple Myeloma

Whole body screening MRI is recommended for evaluation of any patient with plasmacytoma, asymptomatic myeloma for staging and lesion detection. Pawlyn “et al”. [10] evaluated 17 patients using WB-DWMRI and PET-CT for detection and quantification of lesions and showed that DWMRI detected far more statistically significant active diffuse disease than PET-CT. This is a important finding in the setting of new international myeloma working group consensus would lead to greater number of patients meeting criteria for active disease requirement. WB-DWMRI also outperformed PET-CT in assessment of iliac bone infiltration for good trephine results in such patients. In their study diffuse disease was seen in 37% (51/138) regions on WB-DWMRI compared to only 7% (10/140) on FDG PET-CT. Most of the regions reported with diffuse disease on DWMRI were reported as no disease on PET-CT. Overall 3/17 patients were reported as disease free on PET-CT had active diffuse disease on DWMRI.

Prostate Carcinoma

Prostate cancer is the most common cancer in males. Detection of disease is a challenge as is its staging. Most of the time there is early spread to regional nodes and bones. Shen “et al”. [11], did a meta analysis from 27 studies comparing PET-CT and DWMRI along with Bone Scan (BS) in detection and staging of prostate cancer. Their meta analysis showed on a per-patient basis, the pooled sensitivities by using choline PET-CT, MRI, and BS were 0.91, 0.97, 0.79 respectively. The pooled specificities for detection of bone metastases using choline PET-CT, MRI, and BS, were 0.99, 0.95 and 0.82 respectively. This meta-analysis indicated that MRI was better than choline PET-CT and BS on a per-patient basis. Barchetti “et al”. [12] studied 152 males with recurrent prostate cancer after radical prostatectomy and showed a sensitivity and specificity of 99% and 98% with choline FDG PET-CT in evaluation of recurrent disease in such patients. Eschmann “et al”. [13] also compared both the modalities in 42 patients with prostate cancer and found high accuracy with similar results with the WB-DWMRI and PET-CT.

Lymphoma and Myeloproliferative Disorders

Staging of lymphoma is a important perspective before starting treatment of such patients. In routine clinical practice contrast enhanced CT is the commonly used modality because of its availability. WB-DWMRI becomes a attractive alternative due to lack of radiation and non use of contrast. Lin “et al”. [14] evaluated 17 patients of Diffuse large B cell lymphoma and compared results with PET-CT and showed 81% and 100% sensitivity of DWMRI in staging of disease. Stecco “et al”. [15] evaluated 17 patients with primary abdominal lymphomas and showed comparable results of DWMRI and PET-CT with sensitivity and specificity of 100%, 96% and 96% and 100% respectively. WB-DW-MRI was true-positive for 75 (100%) of the lymphomatous node groups and true-negative for 79 (96%) of the no metastatic node groups, while 18FFDG-PET-CT was true-positive for 71 (94%) of the lymphomatous node groups and true-negative for 83 (100%) of the non lymphomatous node groups. The study suggested like those of Abdulqadhr “et al”. [22] a role for WB-DW-MRI, combined with 18FFDG-PET-CT, in initial staging and provided that there is agreement between the two techniques as a standalone follow-up imaging technique. This would not only be safer for patients, but also improve cost-effectiveness and total examination time, both important limitations of 18F-FDG PET-CT, in the long term.

Any Metastasis

Gutzeit “et al”. [16] evaluated 37 patients with suspected bone metastasis and compared WB-DWMRI with bone scintigraphy and found a higher sensitivity of former of 97% with specificity of 99% while bone scintigraphy had sensitivity of 91% and 87% respectively. Fischer “et al”. [17] also showed in 68 patients higher detection rate of WB-DWMRI combined with routine T2WI whole body MRI images in detection of bony metastasis. The high performance of whole-body MRI can in large part be ascribed to the emerging technique of WB DW-MRI. Li “et al”. [18]. Showed WB DW-MRI in comparison to PET/ CT had similar sensitivity (89.7% versus 89.5%) and specificity

(95.4% versus 97.5%) for disease detection. A number of morphologic criteria for bone disease progression and response were described. Progression criteria include new focal/diffuse area(s) of metastatic infiltration within normal marrow, increase in number/size of focal lesions, evolution of focal lesions to a diffuse neoplastic pattern, appearance of or increases in soft tissue associated with bone disease.

Stecco "et al". [19] prospectively compared WB-DWMRI with FDG PET-CT for staging 29 patients with malignancies to stage and detect metastasis and showed an 89.1% sensitivity and 98.5% specificity on region based detection of metastatic lesions using PET-CT as a reference standard and suggested a high predictive value of DWI as a diagnostic tool.

Uterine Cervical Cancer

Choi "et al". [20]. Retrospectively evaluated 236 patients of uterine cervical cancer with both WB-DWMRI and FDG PET-CT and the latter findings were used as standard of reference. Using ADC min value of 0.64 in nodes DWMRI showed a sensitivity of 86% and specificity of 80% in nodal metastasis detection also showed in 33 patients an inverse correlation of ADC min DWMRI and SUV max on PET-CT in Evaluation of uterine cervical cancer patients.

Head and Neck Cancer

Hassan "et al". [21] did a metaanalysis of 6 studies in a search of 20 years of patients with Head and Neck Small Cell Carcinomas (HNSCC) and evaluated 329 patients with clinically N0 stage of nodal disease. Their results showed 100% sensitivity and 71% specificity of DWMRI in nodal detection while PET-CT showed a sensitivity and specificity of 68% and 84%. The evidence given in the study suggested that DWI was more sensitive than PET-CT in preoperative evaluation of C N0 disease in patients with HNSCC. PET-CT had a low sensitivity and a positive test would not help the clinician in the management of a patient with clinically N0 disease and therefore should not be routinely used in neck nodal status workups. The low sensitivity of PET-CT resulting in false negative results may be due to tumor necrosis FDG is not a cancer specific agent and its uptake is based on the metabolic rate of the cancer cell.

Conclusion

Review of the current literature in the present study highlights the role of the WB-DWMRI as a functional and anatomical tool to diagnose and stage different types of cancer patients. All most all the studies have suggested comparable sensitivity and specificity of both the modalities in detection of metastasis with PET-CT have a slight edge in diagnosing small lung metastasis and sub cm nodal metastasis. On the other hand DWMRI had a slight edge in detecting Liver, brain and bony metastasis. The meta analysis done by Shen "et al". [11] showed that DWMRI had highest pool sensitivity for detection of bony metastasis in prostate 0.97 followed by choline PET-CT 0.91 and SPECT bone scan was 0.71. For bone marrow assessment DW MRI is considered to be the best as is sensitive to bone marrow cell density, the relative proportions of fat and marrow and tumor infiltrating cells, water content and bone marrow perfusion. The information obtained can be quantified easily by ADC values and can be used as robust parameter in assessing treatment response of such patients. The strength of DWI MRI is also clearly established in imaging of myeloma patients where whole body MR imaging is being recommended by Myeloma working group guidance [25]. For evaluation of lymphoma patients the evaluated studies in this paper

shows comparable accurate results of both modalities. Since normal nodes in the body also have high cellularity and show reduced ADC it is important to Determine ADC min values with cut off threshold value to detect metastasis in nodes which are sub cm in size as was shown in the studies discussed. However it would be more prudent to have a combined DWI MRI and PET-CT base line study in the first work up of such patients and then to follow up such patients with WB DW MRI as a standalone technique. This would not only cut down radiation dose in these patients but also be more convenient, time saving and more importantly be cost effective [22]. Further in monitoring of disease the use WB-DWMRI can also quantify the tumor cellularity by use of ADC values and also obviates the phenomenon of pseudo flare phenomenon seen of the plain MRI T1W images.

To conclude review of the literature clearly shows that WB-DWMRI has a. important role in detection and staging of different type of cancer patients and can be a viable alternative to PET-CT. However one also needs to be aware of inherent pitfalls in the technique DW-MRI like the false negatives in the presence of tumor necrosis, cystic metastasis and imaging areas near to the heart.

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