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Original article

Role of Whole Body Diffusion Magnetic Resonant Imaging in Detection of Metastatic Disease

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Abstract:

Background: whole body diffusion weighted imaging (WB-DWI) has become a standard imaging sequence for the evaluation of patients with cancer. Major advantages of DW MRI imaging include the fact that no ionizing radiation is administered and no injection of isotopes or any contrast medium is necessary, **Aim and Objective:** The aim of the work is to assess the role of WB-DWI in detection of the metastatic diseases in patients with various histopathologic types of malignancies, **patient &Methods:** study was carried out in Radiology department of Benha university hospital, where 30 patients were selected , Included patients underwent WB DWI within 1 week of conventional imaging. **, Results:** There is moderate to good degree of agreement between WB DWI and conventional imaging in the screening of metastasis. However, the use of both evidently increased the accuracy of metastasis detection and increased the possibility of further lesions detections, **Conclusion:** adding WB-DWI to the routine sequence of metastasis screening increased the possibility of further lesions detections that may be beyond the scope of the requested conventional imaging study**.**

Keywords: metastases, whole body diffusion magnetic resonant imaging, conventional imaging.

Abbreviations

- ADC: apparent diffusion coefficient.
- AUC: area under the ROC curve.
- CT: computed tomography.
- DCEMR: dynamic contrast-enhanced MR imaging.
- DWI: diffusion weighted imaging.
- FGG-PET/CT: fluorodeoxyglucose CT scans.
- MRI: magnetic resonance imaging.

- PET- CT: Positron Emission Tomography and Computed Tomography Scans.
- ROC: receiver-operating curve.
- STIR: short tau inversion recovery.
- T: tesla.
- T1W: T1 weighted.
- T2W: T2 weighted.
- TE: time of echo.
- TR: time of repetition.
- TSE: turbo spin echo.
- WB: whole body.

Introduction

Cancer is a potentially curable disease and the combined effects of early detection and adjuvant systemic therapy are likely the key elements that explain the observed reduction in cancer mortality over the last 20 years **(1).**

Diagnostic work-up in the evaluation of oncological patients includes some staging procedures that play key therapeutic and prognostic roles **(2).**

Conventional cross-sectional imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI) have been used as modalities for screening metastases with relatively good sensitivity and specificity**(3).**

Conventional imaging is especially useful in situations where Positron Emission Tomography - Computed Tomography (PET/CT) is not available or is not feasible. However, CT has a disadvantage of exposing patients to radiation, as well as requiring contrast agent administration. Although bone scintigraphy is very sensitive in detecting skeletal metastases, it again requires the administration of radioactive dyes **(3).**

MRI is a very sensitive method for the localized detection of metastatic lesions in viscera and bone, using either T2- or T1-weighted images with fat-suppression and Short time inversion recovery (STIR) methods. **(1).**

Diffusion-weighted MRI (DW MRI) is a quantitative magnetic resonance technique that measures the random (Brownian) motion of water molecules in biological tissues **(2).**

DW MRI uses pulse sequences and techniques that are sensitive to the very small-scale motion of water protons at the microscopic level. Apart from its applications in intracranial pathologic abnormalities, DW MRI of the whole body (WB) has also become a standard imaging sequence for the evaluation of patients with cancer, especially for 1.5-T MRI systems **(3).**

One of the major advantages of DW MRI imaging is that The information obtained can be quantified and displayed as parametric maps, thus enabling spatial heterogeneity of tissues and tumors to be analyzed before and in response to treatment **(4).**

Data obtained is reformatted in multi planar manner as whole body images in coronal planes and inverted as black and white grey scale images 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 **(5).**

Patients and Methods

This is a prospective study, took place at Radiology department of Benha university hospital occur between February 2018 and July 2019. It included 30 patients.. The study was approved by the ethical committee of the Benha university hospital. A written consent and thorough medical history were taken.

Included patients underwent WB DWI within 1 week of conventional imaging to ensure stationary data.

All of patients were subjected to the following procedures:

I-Preparation of the study:

-The previous studies concerning similar objective were reviewed and the protocol of the study was planned in view of them.

-The procedure of the examination was explained to the patients.

-The patients were prepared for the MRI study; every patient changed to MR gown and removed any clothing with any metal before the examination.

-No patients underwent MRI contrast study.

II- IMAGING (WB DWI protocol design):

- All examinations were performed on closed superconductive 1.5 T magnet (MAGNETOM Aera, Siemens Healthcare. Germany). Q body coil was used, with the patient positioned feet first on an extended anatomical coverage table based on “rolling-table “technology.
- The used sequences were: T1-weighted Turbo Spin Echo (TSE) and T2 –weighted Short Tau Inversion Recovery (STIR) in axial and coronal orientation to encompass all anatomical districts from the head to at least the distal thigh.
- Total examination time was about 25 to 30 min for DWIBS .All data were acquired during free breathing .No contrast agent applied.

III- WBDW Image Interpretation:

A metastatic lesion was considered as any lesion that was bright on DW images at a high b-value (b 800). The presence or absence of lesions was recorded and their locations, sizes and further characterization of the lesions as either benign or malignant.

Statistical analysis was performed using MedCalc_ version 17.9.7 (MedCalc Software bib, Ostend, Belgium). Normally distributed numerical variables were presented as mean + SD. Categorical variables were presented as number (%), and data were classified on the basis of the presence or absence of metastasis in the given regions or organs at both WB DWI and conventional imaging. The sensitivity, specificity, and accuracy of WB DWI and the conventional imaging modalities were calculated separately then collectively. The agreement between both modalities in lesion detection was also calculated Cohen kappa values as following: value of k: <0.20: poor, 0.21-0.40: fair, 0.41-0.60: moderate, 0.61-0.80: good and 0.81-1.00 : very good agreement. Receiver-operating characteristic (ROC) curve analysis was used to examine the diagnostic performance of the studied methods in metastatic lesions detection. The DeLong method was used to compare the area under various ROC curves (AUC).

Results:

- The mean age of the whole study group was 46.7 ±12.4 years, ranging from 25 to 73 years 73.3% of study population were females while 26.7% were males.**(Table 1)**
- The distribution of cases with respect to the type of primary malignancy revealed The highest percent were in patients with breast cancer (40%), all of them were females , 23.33% for Colon/ rectal cancer . **(Table 2)**
- There was good agreement between DWI and conventional imaging in the diagnosis of hepatic metastasis with 91.7% accuracy of the Conventional imaging and 87.5% accuracy of the DWI while the accuracy will be increased to be 96.4% when they used together. **(Table 3)**
- There is good agreement between DWI and conventional imaging in the diagnosis of pulmonary metastasis with 96.3% accuracy of the Conventional imaging and 77.8% accuracy of the DWI while no more detection accuracy was obtained when they used together. **(Table 4)**

- There was moderate agreement between DWI and conventional imaging in the diagnosis of skeletal metastasis with 85.7% accuracy of the Conventional imaging and DWI while the accuracy will be increased to be 92.9% when they used together. **(Table5)**
- there was good agreement between DWI and conventional imaging in the diagnosis of lymph nodes metastasis with 92.6% accuracy of the Conventional imaging and 81.4% accuracy of the DWI while the accuracy will be the same as conventional imaging (92.6%) when they both used together. **(Table 6)**

Table (1): Sex distribution of the patients.

Sex	Number	Percentage
Females	**22**	**73.3%**
Males	**8**	**26.7%**

Table (2): The distribution of cases with respect to the type of primary malignancy.

Diagnosis	n	percentage
Breast cancer	**12**	**40%**
Ovarian carcinoma	**3**	**10%**
Cervical carcinoma / lymphoma	**2**	**6.67%**
Colon/ rectal cancer	**7**	**23.33%**
Gastric carcinoma	**3**	**10%**
Pancreatic carcinoma	**3**	**10%**

Table (3): diagnostic performance of DWI, conventional imaging, and both for liver metastases detection.

	Conventional imaging	DWI	Both
True positive	**9**	**9**	**10**
False negative	**1**	**1**	**0**
True negative	**13**	**12**	**13**
False positive	**1**	**2**	**1**
Sensitivity	**90%**	**90%**	**100%**
Specificity	**92.9%**	**85.7%**	**92.9%**
Accuracy	**91.7%**	**87.5%**	**98.5%**
AUC	**91.4%**	**87.9%**	**96.4%**

Table (4): Diagnostic performance of DWI, conventional imaging, and both for pulmonary metastases detection.

	Conventional imaging	DWI	Both
True positive	13	9	9
False negative	0	1	4
True negative	13	12	12
False positive	1	2	2
Sensitivity	100%	69.2%	100%
Specificity	92.9%	85.7%	92.9%
Accuracy	96.3%	77.8%	96.3%
AUC	96.4%	77.4%	96.4%

Table (5): Diagnostic performance of DWI, conventional imaging, and both for skeletal metastases detection.

	Conventional imaging	DWI	Both
True positive	6	7	7
False negative	1	0	0
True negative	6	5	6
False positive	1	2	1
Sensitivity	85.7%	100%	100%
Specificity	85.7%	71.4%	85.7%
Accuracy	85.7%	85.7%	92.9%
AUC	٨٥.٧%	85.7%	92.9%

Table (6): Diagnostic performance of DWI, conventional imaging, and both for lymph nodes metastases detection.

	Conventional imaging	DWI	Both
True positive	8	7	8
False negative	1	2	1
True negative	17	15	17
False positive	1	3	1
Sensitivity	88.9%	77.8%	88.9%
Specificity	94.4%	83.3%	94.4%
Accuracy	92.6%	81.4%	92.6%
AUC	9١.٧%	80.6%	91.7%

Discussion

The second leading cause of death in developed countries is cancer. In developing countries, it is also, among the three leading causes of death for adults, and is responsible for 12.5% of all deaths worldwide ***(6).***

A number of imaging options are available in clinical practice for the workup of patients with malignancies. An ideal diagnostic imaging test should be easily available, accurate, comprehensive, cost-effective, time saving, and safe ***(3).***

In the absence of PET/CT, the clinicians usually rely on conventional cross-sectional imaging such as CT and MRI for staging of these malignancies ***(7).***

Unlike CT and scintigraphy, MRI does not expose the patient to radioactivity. However, conventional MRI is usually time-consuming and invariably requires some sort of contrast agent administration ***(3).***

Therefore, there is a need for an imaging method that achieves global tumor assessment and accurate lesion detection without an increase in radiation dose. To address these challenges, developments in whole-body MRI (WB-MRI) technology have resulted in whole-body coverage using anatomic T1- or T2-weighted imaging at 1.5T ***(8).***

Therefore, the aim of this study was to assess the efficacy of WB DWI in detection of the metastatic diseases and compare it to the conventional imaging modalities that were performed on patients with a heterogeneous group of malignancies.

Our study was a prospective study. That comprised 30 patients 22 females and 8 males (26.7%). The mean age was 46.7 ±12.4 years, ranging from 25 to 73 years. The highest percent of the diagnosed primary tumors were patients with breast cancer (12 patients), all of them were females. The other primaries were female genital tract tumors (5 patients), and GIT tumors, which had equal sex distribution (8 males and 8 females).

For simplifying our findings, we classified the metastatic lesions into hepatic, pulmonary, skeletal and lymph nodes metastasis.

Regarding to hepatic metastases, there was very good agreement between the findings of WB DWI and those of conventional, with $\kappa = 0.83$. The sensitivity, specificity, and accuracy for conventional imaging plus DWI reported by Colagrande et al were 92.1%, 72.5%, and 89.2%, respectively, whereas our study showed a mean sensitivity, specificity, and accuracy of 100%, 92.9%, and 98.5%, respectively ***(9).***

The study of Paruthikunnan et al also showed similar research methodology to ours. Yet, they did not consider gathering the use of both conventional imaging methods along with DWI for the detection of lesions, so the sensitivity was lower (83.3%), but the specificity of their study was comparable to ours (93.3 %) ***(3).***

On evaluating pulmonary metastases, the WB DWI sensitivity and accuracy of were significantly lower than that of conventional imaging (69.2% & 77.8% compared to 100% & 96.3% respectively). Most lesions smaller than 1 cm were not detected at WB DWI .Lesions at air-tissue interfaces were more likely to get obscured at DWI. The specificity of WB DWI was comparatively better (85.7% compared to 92.6%).

A similar study on the detection of pulmonary nodules with DWI was performed by Regier et al. showed high sensitivity of 97% for nodules larger than 10 mm, 86% sensitivity for nodules 6–9 mm, and a low sensitivity of 43.8% for nodules 5 mm or smaller ***(10).***

Liu et al. also compared the diagnostic accuracy of CT versus WB DWI for assessing pulmonary metastases in cases of renal cell carcinoma and showed a sensitivity of 100% for nodules larger than 10 mm, which reduced to 61.5% for nodules 5 mm or smaller ***(11).***

Our study shows very poor sensitivity of lesion detection on DWI, Furthermore, all lesions detected in our study were larger than 1 cm, which corroborated the findings of previous studies that lesions smaller than 1 cm are poorly detected by DWI. This is also similar to a great extent to the results of the study of Paruthikunnan et al who elucidated lower sensitivity of DWI as shown by our study ***(3).***

Regarding to skeletal metastases, the sensitivity of WB DWI (100%) was higher than that of the conventional imaging (85.7%), while specificity was lower (71.4% compared to 85.7%), finally accuracy was the same (85.7%). When using both methods together, we achieved higher accuracy (92.9%). The higher specificity of the DWI may be attributed to that part of the patients was imaged by CT, which is known for its low sensitivity in detection of bones metastasis.

Our sensitivity and specificity were comparable to the previously published literature which incorporated T1-weighted or STIR-based WB imaging along with DWI ***(12).***

while higher than that published by Paruthikunnan et al because they used WB DWI as a single-step screening modality only and did not combine its results with the results of conventional imaging **(3).**

Koh et al suggested that increased marrow cellularity and hence, abnormal heterogeneous marrow signal may be due to smoking, anemia, osteoporotic changes or hematopoietic growth factor therapies **(13).**

In our study, the assessment of lymph node metastases revealed that the sensitivity (77.8%) specificity (83.3%), and accuracy (81.4%) of WB DWI was inferior to that of conventional imaging (88.9%, 94.4% and 92.6 % respectively). Previous studies had results that are similar to ours **(14).**

Though all the lymph nodes that were considered in our study did not have histopathologic correlation, they were followed up on imaging or clinically to monitor for growth in size for a period of 1 year and were later labeled as benign or malignant. Whether ADC-based quantitative analysis with our protocol of DWI would have further improved the diagnostic accuracy needs to be further evaluated.

Our study concluded moderate to good degree of agreement between WB DWI and conventional imaging in the screening of metastasis. And ensured that use of both evidently increased the accuracy of metastasis detection and increased the possibility of further lesions detections that were beyond the scope of the requested conventional imaging study.

The main limitation of this study was the small number of the patient sample ,lack of comparison with FDG PET/CT, owing to the lack of a PET scanner in our hospital. Also, it was not possible to obtain histopathologic confirmation of all metastatic lesions for some patients with multiple metastases. However, this limitation was partly offset by following up the patients for 6 months to look for interval progression of the lesions and assess the PET scan exam done by some patients.

Because it was not possible to get histopathologic confirmation for all lymph nodes detected at multiple locations for all patients, we used a size criterion of 10 mm as a cutoff for metastatic lymphadenopathy. This might have caused us to miss small metastatic deposits in lymph nodes, despite follow-up.

Whether the quantitative analysis by ADC would help to improve the performance of WB DWI should be evaluated in future studies using multiple b values to improve the accuracy of ADC calculation. Finally, there were no subcutaneous or muscular deposits in our study population; hence, the detection accuracy of lesions could not be assessed.

Conclusion

There is moderate to good degree of agreement between WB DWI and conventional imaging in the screening of metastasis. However, the use of both evidently increased the accuracy of metastasis detection and increased the possibility of further lesions detections that may be beyond the scope of the requested conventional imaging study.

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