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Differentiation of malignant and benign lung lesions with diffusion-weighted MR imaging

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ABSTRACT

Rrecent development of diffusion weighted imaging (DWI), is a MRI sequence make it possible image and evaluate the lesion in the lung. The aim of the present study was to differentiate benign and malignant lung lesions. A retrospective study conducted at the MRI units of oncology teaching hospital of medical city, Baghdad-Iraq in the period from March 2017 until January 2018, 33consecutive patients (18 males, 15 females) with variable lung lesions found on MRI. Mean age was 60.8 ± 14.5 years, with 18 males and 15 females, 75% of the lung lesions were malignant, DWI – MRI show 91.7% SN, 100% SP, 100% PPV, and 81.8% NPV for diagnosis of malignant lung lesions, ADC value were significantly lower in malignant lesions compared to benign lesion (1.08 ± 0.41 vs. 1.99 ± 0.42, p <0.001). ADV have excellent ability (AUC = 0.938) to discriminate malignant lesions with optimal cut point of ≤1.4. DWI – MRI both qualitatively and quantitatively (using the ADC value) is useful in the diagnosis and distinguish type of lung lesions.

1. INTRODUCTION

The lungs are the functional units of respiration and are key to survival. They contain 1500 miles of airways, 300-500 million alveoli and have a combined surface area of 70 square meters (half a tennis court) [1]. Lung cancer is the most common cause of cancer in men, and the sixth most frequent cancer in women worldwide. It is the leading cause of cancer mortality worldwide in both men and women accounts for approximately 20% of all cancer deaths [2]. The lung is an extremely common site for metastasis. Large autopsy series of patients with extra thoracic malignancies reveal pulmonary metastases in 20%–54% of patients [3]. Systemic diseases may involve the thoracic structures and it is, therefore, critical for radiologists to be familiar with various patterns of abnormalities associated with them [4]. Recent advances in fast imaging techniques like echo-planar imaging, makes magnetic resonance imaging (MRI) more suitable for chest applications there are reports using dynamic contrast MRI of lung masses [5]. Diffusion-weighted MRI (DW MRI) is a functional imaging technique dependent on the inhibitory effect of cell membranes to the random motion of water molecules (Brownian motion) to generate image contrast by applying two equally sized but opposite diffusion sensitizing gradients, characterized by their b-values [6]. As tumors have greater cellularity than normal tissue, they demonstrate higher signal intensity (that is, restricted diffusion on MRI, reflected in the low mean apparent diffusion coefficient value (ADC). This has the potential to provide both qualitative and quantitative information to aid tumor assessment [7]. Diffusion-weighted magnetic resonance imaging (DWI), initially used in the central nervous system, has been increasingly applied in other body areas, such as the mediastinum, pancreas, and liver [8]. Diffusion weighted imaging has a wide use on oncologic patients for the purpose of diagnosis. In addition, it used in the distinction of acute cerebral infarction and epidermoid or arachnoid cysts [9]. Benefits of DWI MRI: has the following advantages: 1- patients do not have to fast before examination; 2- there is no radiation exposure; 3- less time is required for the examination (30 minutes in DWI versus 90 minutes in FDG-PET); and 4- the cost is considerably less ($100 for DWI versus $700 for FDG-PET in Japan).5- DWI findings have been reported to have prognostic value in the detection of lung cancer [10]. Although MRI routinely used to evaluate cerebral and skeletal metastases, it not commonly used for follow-up diagnosis or evaluations of metastatic disease in patients with extra pulmonary malignancies. Because metastases can affect different anatomic organs, patients may benefit from multiples examinations with CT, MRI, sonography, scintigraphy, and PET. Although 6-mm or greater-diameter pulmonary metastatic nodules may readily identified with whole-body MRI, smaller nodules (< 6 mm) detected with less sensitivity [11]. The aim of the present study was to differentiate benign and malignant lung lesions.

2. Method

This retrospective study was conducted at the MRI unit of oncology teaching hospital of medical city complex in Baghdad/Iraq, in the period from March 2017 till January 2018, 33consecutive patients (18 males, 15 females), the patient referred to us from respiratory outpatient clinic and cardiothoracic surgery outpatient clinic and from other centers within the medical city complex, already diagnosed by biopsy, surgery, bronchoscopy or by clinical and laboratory findings, with 33 lung lesions found on CT were included in this retrospective study according to our entry criteria. Inclusion criteria: (A) presence of a solid pulmonary lesion. (B) lesion size >10 mm in diameter in view of the limited planar resolution of DWI; (C) presence of a specific proven diagnosis of the lesion either histopathologically or by using clinical, radiological and laboratory data or based on at least 6 months radiological follow-up; (D) absence of any contraindications for MRI; and (E) ability of patients to lie still and hold their breath approximately 26 seconds in the MRI.

2.1 Exclusion criteria

(A) Patients who had contraindications for MRI. (B) those don’t have definitive diagnosis by either hisopathologically or by clinical and laboratory investigations as sputum smear. (C) Children below 15 years because of non-availability of anesthetist. Examination technique: No anesthesia was required for MRI study; MRI examination was done using 1.5-tesla MRI machine (Magnetom Area, Siemens medical system, Germany) using phased array body coil, FOV (26-28cm).

2.2 Image analysis and interpretation

First, CT images evaluated in order to assess the calcification, necrosis and GGO components. CT scans also evaluated for contour characteristics of the lesions (irregular or smooth) and concomitant interstitial findings recorded. Those findings compared with the DWI findings. Then, the lesion visualized once more on the conventional T1-W and T2-W MRI in terms of location, size and content of cystic-necrotic parts. These conventional images only used for the lesion identification and not for the analysis. Afterwards, signal intensity (SI) of the lesion was measured for each b value (0, 500 and 800 s/mm2) on DWI using a round region of interest (ROI). Diffusion-weighted images (DWI) interpreted referring to T1- and T2-weighted images. The lesion identified as mass of hyperintensity or hypointensity on DWI.

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2.3 Statistical Analysis

Statistical analysis performed using SPSS 20.0.0. The data presented as mean ± standard deviation or as numbers and percentages. The categorical data compared by applying Chi-Square test; Independent unpaired student t-test was used to analyze the differences in the values of ADC at different pathological regions. Binary logistic regression analysis used to calculate the odd ratio (OR) and their 95% confidence intervals, when the outcome can be categorized into 2 binary level. Cohen's kappa analysis of agreement was used to assess the possible agreement (or disagreement) and it's magnitude for similarity between 2 discrete variables. Receiver operator curve used to see the validity of different parameters in separating active cases from control (negative cases) and area under the curve i.e. AUC and its p value prescribe this validity (if AUC ≥ 0.9 mean excellent test, 0.8 – 0.89 means good test, 0.7 – 0.79 fair test otherwise unacceptable). A probability (P) value of less than 0.05 considered statistically significant.

3. Results

The method of diagnosis of each lesions, in which fibrosis (of old TB lesions) confirmed by clinical and radiological methods, the rest of data illustrated in table 1. There is significant assessment of DWI-MRI of the lung lesions as in table 2. As table 3 there is positive predictive value and validity of DWI – MRI in diagnosis of malignant lung lesions 91.7% sensitivity and 100% specificity and 93.9% accuracy. Also in current study the mean and SD of types of lung lesions show in table 4. The predictor of malignant lung lesions appear in table 5. Figure 1 show the ROC of ADC for diagnosis of malignant lung lesions and Figure 2 show ADC value according to lung lesions type.

4. Discussion

The advent of DWI led to advance in the amount of information that obtained from the microscopic motion of water protons that cannot be obtained from conventional MR imaging [12]. Various applications of DWI for the diagnosis of different types of solid tumors been investigated. DWI can give useful quantitative information and qualitative information as diagnostic tool for benign and malignant tissues [13]. In the current study patient age was 60.8 ± 14.5 years, with (1.2 to 1) male to female ratio, our finding was in agreement with in which mean patients age was 58.37 years with 38 men and 24 women (1.6:1) [12] also in agreement with in which mean age was 57 years with 22 men and 9 women (2.4:1), [14] and in agreement with mean age of 64.8 years and 11 men with 17 women (0.65:1), [15] will some studied the patient higher age [16] the majorities presented with similar age group and gender which reflect the age and gender distribution of lung cancer (since the majorities of these studies examined lung cancer). In the current study lung adenocarcinoma were diagnosed using FNA, bronchoscope or CT guided biopsy, while squamous carcinoma assessed mostly using FNA and bronchoscope, on the other hand benign lesions like fibrosis of old TB lesions where mostly diagnosed based on clinical and radiological findings. Many techniques developed to enhance the process of differential diagnosis for the physicians based on tissue histopathology, which include FNS (fine transthoracic needle aspiration) and bronchoscopy. However, for patients with peripheral tumors the sensitivity is low, even the introduction of fluoroscopic and CT – guided FNA, the SN only increase to 70% and remain low for patients with tumor size less than 2 cm. [17]. Transthoracic FNA offered better sensitivity than bronchoscopy in the patients with peripheral tumor especially in those that are not candidate for surgical procedure [18]. The advantage of these techniques came from their invasive nature that includes bleeding, pneumothorax, nasal discomfort, sore throat and mild hemoptysis, with rate of complication between 0.08 to 6.8 percent [19]. In the current study ADC value was found to be significantly lower in malignant lesions compared to benign lesions (1.08 ± 0.41 vs. 1.99 ± 0.42) x 10-3 mm2/s, in which ADC had an odd ratio of 0.018 to predict malignant lung lesions, after performing ROC analysis the optimal cut was ≤1.4 x 10-3 mm2/s with sensitivity (SN) = 91.7% and 100% specificity (SP).

Reported similar findings with ADC being significantly (p=0.001) lower in malignant compared to benign lung lesions with similar cut point of ADC ≤1.4 x 10-3 mm2/s, however both the SN and SP was slightly lower (83.3% vs. 74.1%) [1] other studies reported slightly higher cut point like ≤ 1.7 x 10-3 mm2/swith SN = 0.87 and SP = 0.74 [20] in another study it was ≤1.6 x 10-3 mm2/swith SN = 67% and SP = 99% [16] while other study revealed slightly lower ADC value ≤1.2 x 10-3 mm2/swith SN = 73% and SP = 96% [21]. Reported in their meta-analysis the pooled SN = 0.80 and SP = 0.93 with pooled AUC = 0.91, which is similar to the results presented by the current study [22]. DWI can be used to differentiate malignant from benign lesions on the basis of tissue cellularity [23] according to apparent diffusion coefficient (ADC) cutoff values less than 1.1–1.4 × 10−3 mm2/s) had sensitivity and specificity of 70–83% and 74–97% for pulmonary malignancy [24]. In the current study metastatic lung lesion had higher ADC value (1.100 ± 0.200) compared to adenocarcinoma and squamous carcinoma (but it was no statistically significant), which was in agreement with [16] this higher ADC value can be attributed to ADC value of lymph nodes might increase with motion artifact caused by heart beats and the beats in the great vessels in the hilum and mediastinum. In their study which included 250 patients, reported a two time higher cut point of 2.5 x 10 -3 mm2/s with AUC = 0.86 (i.e. good test), they also reported mean ADC for metastatic tumor lesions of 1.1±0.9x 10 -3 mm2/s, 2.5±0.8x 10 -3 mm2/s for non-metastatic lesions [25]. In the current study patient with fibrosis of old TB lesions had an ADC value 1.817 ± 0.117, patients with adenocarcinoma had an ADC with 0.938 ± 0.141 which not statistically significant than squamous cell carcinoma with ADC 0.929 ± 0.189, it was in agreement with in which there was no significant difference between adeno and squamous cell carcinoma, also they reported inverse relationship between ADC value and cell differentiation in which cells with poorly differentiation had the lowest value [20] in addition other studies reported similar findings [26]. One of the requirements to lower respiratory motion through DWI procedure of the lung is Breath-holding, but it will limits the acquisition time leading to affecting both the spatial resolution and the signal-to-noise ratio (SNR). In the current study, in order to reduce such error, a single-shot echo-planar imaging sequence with a relatively high b value and free breathing was used for DWI, since thinner slices, higher SNR and increased anatomical coverage are offered by free breathing, compared with breath-hold DWI [27]. The advantage of DWI: no exposure to ionizing radiation, noninvasive procedure, and does not cause patient discomfort, also its ability to accurately detect malignant tissue from benign lesion, with the disadvantage of weak ability to differentiate subtypes of cancer even with the use of ADC). In addition, other advantages do not require fasting of the patients, low time for examination (especially compared to PET) and less cost.

5. Conclusion

DWI – MRI both qualitatively and quantitatively (using the ADC value) is useful in the diagnosis and distinguish type of lung lesions.

6. References

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Table 1: methods of diagnosis of lung lesions

	Surgery	**FNA**	**Biopsy + CT guided**	**Bronchoscopy**	**Clinical + Radiological**

Fibrosis	**-**	**-**	**-**	**-**	**6 (42.9%)**
Pneumonia	**1 (20.0%)**	**-**	**-**	**-**	**1 (7.1%)**
Lung adenocarcinoma	**1 (20.0%)**	**3 (42.9%)**	**2 (66.7%)**	**2 (50.0%)**	**-**
Lung squamous carcinoma	**1 (20.0%)**	**4 (57.1%)**	**-**	**2 (50.0%)**	**-**
Lung Metastasis	**-**	**-**	**-**	**-**	**6 (42.9%)**
Small cell lung cancer	**-**	**-**	**1 (33.3%)**	**-**	**-**
Rheumatoid nodules	**-**	**-**	**-**	**-**	**1 (7.1%)**
Non Hodgkin lymphoma	**1 (20.0%)**	**-**	**-**	**-**	**-**
Pleural giant cell tumor	**1 (20.0%)**	**-**	**-**	**-**	**-**
Total	**5**	**7**	**3**	**4**	**14**

Table 2: assessment of DWI-MRI of the lung lesions

	Benign	**Malignant**	**p-value**
Number	**9**	**24**	
Restricted	**0 (0.0%)**	**22 (91.7%)**	**<0.001**
Not restricted	**9 (100.0%)**	**2 (8.3%)**	

Table 3: predictive value and validity of DWI – MRI in diagnosis of malignant lung lesions

Modality	**AUC**	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**+LH**	**-LH**	**Accuracy**
DWI-MRI	**0.960**	**91.7%**	**100%**	**100%**	**81.8%**	**-**	**0.08**	**93.94%**
AUC: area under the curve, PPV: positive predictive value, NPV: negative predictive value, LH: likelihood ratio								

Table 4: mean ADC value according to type of lung lesions

	Number	**Mean ADC value**
Fibrosis	6	1.817±0.117
Pneumonia	2	2.200 ± 0.849
Lung adenocarcinoma	8	0.938 ± 0.141
Lung squamous carcinoma	7	0.929 ± 0.189
Lung Metastasis	6	1.100 ± 0.200

Table 5: predictor of malignant lung lesions

	OR (95%CI)	**p-value**
Age	1.009 (0.957 – 1.063)	0.751
Gender	1.750 (0.373 – 8.204)	0.478
Smoking	1.477 (0.317 – 6.895)	0.620
Diameter of lesion	1.500 (0.284 – 7.934)	0.633
ADC	0.018 (0.001 – 0.267)	0.004
Duration of compliance	0.797 (0.571 – 1.112)	0.181

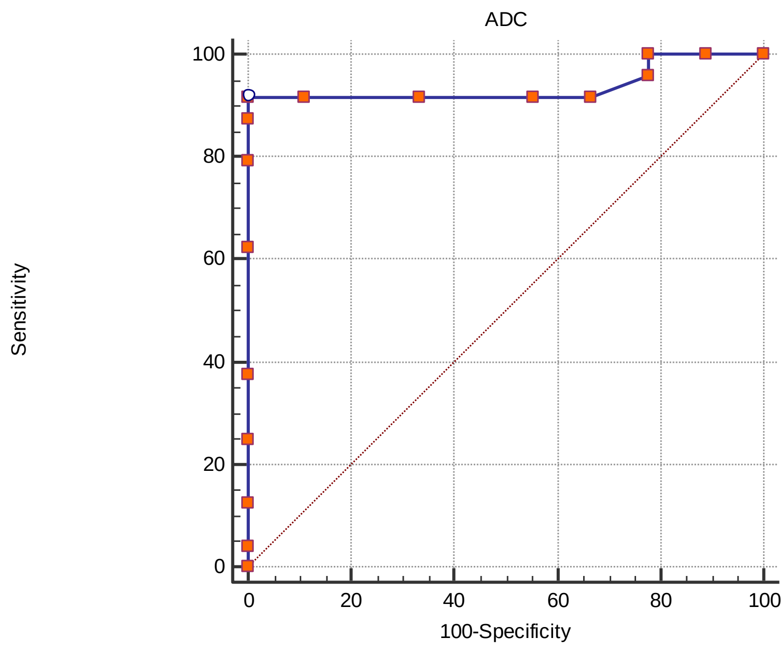

Figure 1: ROC of ADC for diagnosis of malignant lung lesions

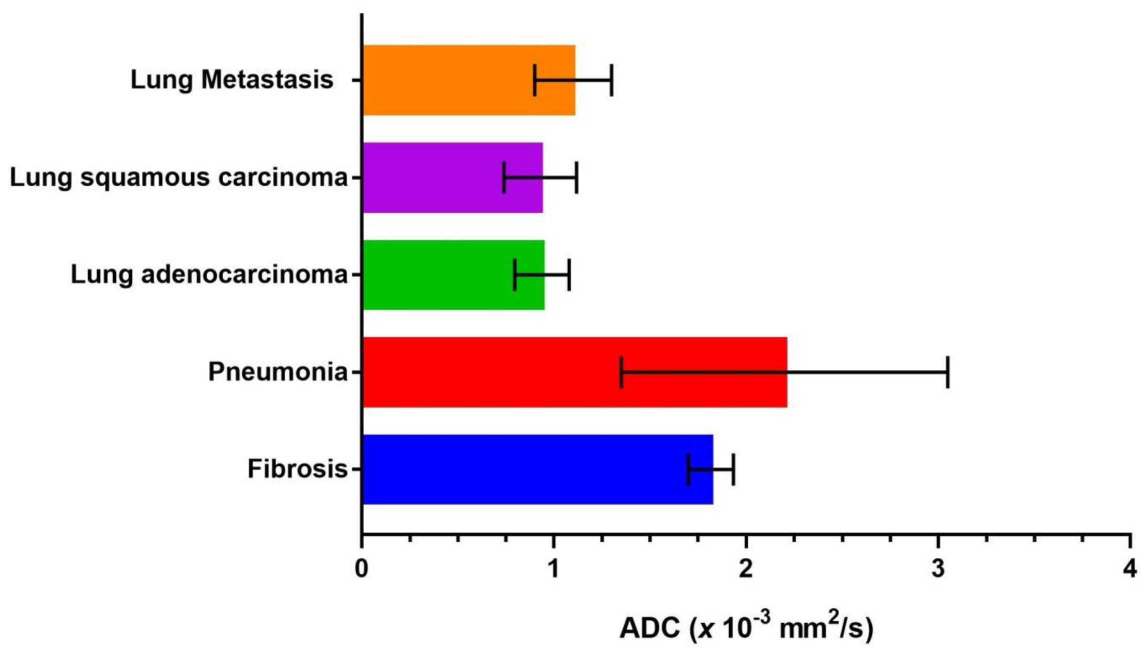

Figure 2: ADC value according to lung lesions type