**Role of Advanced MRI in Differentiation between Benign and Malignant Lung Lesions**

M.M.Omar(1), T.S.Essawy(1), M.A.Nasr(1), S.M.Tawfik(1), S.M.Abo Yousef(1)

(1)Chest Diseases and Radiology, Dept., Faculty of Medicine, Benha Univ., Benha, Egypt

**Abstract**

Background: Lung malignancy is the most common cause of death in the developed countries. Male to female ratio is 3:1. Consumption of Tobacco upsurges the rate of evolving lung cancer by 30 folds. Other risk factors include repeated exposure to aspects like carcinogens, asbestos, pulmonary fibrosis and radiotherapy. Aim of Study: The aim of this study is to assess the role of advanced MRI in the differentiation between malignant and benign pulmonary lesions. Patients and Methods: This study was conducted on 32 patients with lung lesions found on CT admitted at Benha University Hospital, chest department during the period from October 2018 to April 2021. They all signed informed consent forms. All the patients were diagnosed by direct chest X-ray and underwent a CT scan. The morphological characteristics of the lesions were evaluated. Patients underwent MRI study followed by pathological assessment. Results: Of the 32 lesions, 22 were malignant and 10 were benign. This study demonstrated that the mean ADC value of benign lesions was 1.74 ±0.27 –3mm2/s and for malignant lesions it was 1.09 ±0.18 -3mm2/s, which was significantly lower than that of the benign lesions (p = 0.02). The mean ADC in the center was 1.29 ±0.37, while in the periphery, it was 1.48 ±0.52. ADC was significantly lower in the center (1.29 ±0.37) than the periphery (1.48 ±0.52) (P = .0.017). The mean ADC in the center and periphery were significantly lower in the malignant lesions (1.09 and 1.26, respectively) than those with benign lesions (1.74 and 1.97, respectively). P values were < 0.001 and 0.005, respectively. ROC analysis was done for the ADC center and periphery for predicting malignancy. It showed significant AUC for ADC center (AUC = 0.964, P < 0.001) and periphery (AUC = 0.859, P = 0.001). The best cutoff points were ≤ 1.29 × 10–3 mm2/s for ADC center and ≤1.54 × 10–3 mm2/s for ADC periphery, at which sensitivity and specificity were 95.5% and 90%, respectively, for ADC center and 86.4% and 80%, respectively, for ADC periphery. Conclusion: Diffusion-weighted MRI and ADC can significantly differentiate between benign and malignant pulmonary masses.

**Key Words:** Diffusion MRI – ADC – Benign – Malignant – Pulmonary lesions.

**1.Introduction**

Lung cancer is the leading cause of cancer related death in adults **(25).**

It usually arises as a solid nodule or mass on chest radiography or computed tomography (CT).

Although many well-known characteristics have been described for nodule differentiation on CT, it remains a challenge for radiologists to differentiate lesions as malignant or benign **(15).**

In recent years, fluorine-18 fluorodeoxyglucose positron emission tomography (PET) has been used for this purpose.

Both CT and PET deliver high doses of radiation. In addition PET has been known to give false-positive results in inflammatory masses **(30) .**

For these reasons, an accurate and safe alternative method is still desirable for the determination of malignant versus benign pulmonary lesions.

Recent advances in fast imaging techniques like echo-planar imaging, makes magnetic resonance imaging (MRI) more suitable for chest applications **(23) .**

There are reports using dynamic contrast MRI of lung masses **(24).**

-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 **(14).**

MRI of the chest using fast acquisition sequences with a high temporal resolution has become feasible with the recent developments in gradient technology and multichannel coils. Experience with thoracic applications of diffusion weighted imaging (DWI) techniques is still growing, and preliminary studies have reported promising results **(17)**.

DWI involves the acquisition of a magnetic resonance signal related to random thermal motion (Brownian motion) or the “diffusion” of water protons in tissue **(27).**

Two main categories of magnetic resonance imaging (MRI) techniques can be used to measure tissue perfusion in vivo.

The first is based on the use of an injected contrast agent that changes the magnetic susceptibility of blood and thereby the MR signal which is repeatedly measured during bolus passage **(13).**

The other category is based on arterial spin labelling (ASL), where arterial blood is magnetically tagged before it enters into the tissue being examined and the amount of labelling that is measured and compared to a control recording obtained without spin labelling **(8).**

In malignant lesions (as they are solid), the extravascular extracellular space is markedly diminished compared with the intracellular space due to an increased number of cells that are compact and numerable, cellular pleomorphism, large cell volume and neoangiogenic vessels disorganized.

This increased microstructural density and organization will in turn cause restriction of the random water molecule movement.

In contrast to that, in cases of inflammation and infection, the extravascular extracellular space is relatively enlarged compared with the intracellular space due to the presence of interstitial edema and inflammatory reaction that increases the extra-cellular space. Thus, the decreased interactions with cell membranes that become way apart can therefore facilitate the random water molecule movement **(3).**

The mediastinal masses have a wide histopathological and radiological spectrum, where the most common in adults are the primary thymic neoplasms, thyroid masses and lymphomas. Anterior mediastinal tumors account for 50% of all mediastinal masses, including thymoma, teratoma, thyroid disease and lymphoma. Masses of the middle mediastinum are most commonly congenital cysts while those arising in the posterior mediastinum are often those of neurogenic tumors origin **(7).**

Diffusion-weighted imaging was proved to be useful beside other modalities in differentiating lymphoma from sarcoidosis in mediastinal and hilar lymphadenopathy. This can be done by detecting the ADC value of the enlarged lymph nodes; the ADC value in the lymphoma was detected to be lower than that in the sarcoidosis group **(10).**

DWI is also recently used to help characterize lung lesions, to detect tumor invasiveness in early-stage lung cancer, to detect tumors in collapsed lungs, and for nodal staging in cases of metastatic lung cancer **(27).**

MRI can feasibly detect and stage lung cancer in recent studies and trials, and this method could be an excellent alternative to CT or PET/CT in the investigation of lung malignancies and other diseases **(12).**

Recent studies concluded that lung cancers can be easily visualized by DWI, as malignant compact lesions are bright in diffusion series and low in ADC map (restricted) and that differentiating central lung cancer from post-obstructive lobar collapse (non restricted) by DWI is feasible. By the same way quantitative analysis of DWI has the ability to differentiate lymph nodes with the reactionary/inflammatory ones having a higher ADC value than metastatic ones  (**10).**

MRI is emerging as a valuable lung imaging modality, together with X-ray and CT.

It offers a unique combination of morphological and functional information in a single examination without any radiation burden to the patient. New users are advised to make themselves familiar with the particular advantages and limitations of the technique and its diagnostic scope to appreciate its potential benefits **(17).**

**2. Aim of the study**

This study was carried out to assess the role of advanced MRI in the differentiation between malignant and benign pulmonary lesions.

**3.Patients and methods**

This study was conducted on 32 patients with lung lesions found on CT admitted at Benha University Hospital, chest department during the period from October 2018 to April 2021.

They all signed informed consent forms. All the patients were diagnosed by direct chest X-ray and underwent a CT scan. The morphological characteristics of the lesions were evaluated. Patients underwent MRI study followed by pathological assessment.

**Inclusion criteria:**

* -Presence of a parenchymal lung Lesion.
* -Ability of patients to lie supine and hold their breath in the MRI unit.

**Exclusion criteria:**

* -Known malignant patient on current administration of chemotherapeutic or radio therapeutic treatment.
* -Implanted pacemaker or defibrillator: Until recently, MRI was contraindicated for all patients with implantable cardiac devices because the fields generated have the potential to damage components and interfere with functioning.
* -Ferromagnetic aneurysm clipsmay move or become dislodged under the force of the magnetic field.
* -A cochlear implant can be damaged or create tissue damage in the presence of an MRI system.
* -The electrodes used in deep brain stimulation may cause injury or suffer damage during MRI.
* -Metallic foreign bodies:  Shrapnel or other metallic objects in the body can be heated and/or moved by the magnetic field.
* -Some varieties of ocular implantspose a risk of damage to the eye due to metallic components.

**All patients were subjected to the following:**

-History and physical examination.

* -Full lab. Investigations (CBC, ESR, Liver function and kidney function tests, PT, PTT, INR).
* -CXR
* -CT chest with contrast.
* -MRI was done in the radiology department (DWI, quantative analysis).
* -Biopsies of lung lesions were done by different methods (FOB, U\S, CT guided) according to the site of the lesion.

**Clinical assessment:**

By history taking, patients were manifested by dyspnea, chest pain, hemoptysis, cough, Fever, weight loss and hoarseness of voice.

**Radiological diagnosis**

First, CT images were evaluated in order to assess the calcification, necrosis and GGO components. CT scans were also evaluated for contour characteristics of the lesions (irregular or smooth).

The range of interval between the CT and MRI examinations was 0-10 days (mean, 5. 6 days).

DWI using a round or elliptical region of interest (ROI).

The ROI was placed centrally, and the size of the ROI was kept as large as possible, covering at least two-thirds of the lesion, yet avoiding the interference from the surrounding lung tissue, necrotic parts and major blood vessels. ADCs were then calculated from the ADC maps that were reconstructed from b = 0 and b = 1000 s/mm² values.

In order to reduce artifacts due to respiratory motion, all patients underwent breathing training before MRI scanning, holding their breath at the end of inspiration after a deep breath.

**MRI technique:**

All MR examinations were performed using 1.5-T (SIEMENS) MRI with a body phased-array coil, and patients were in a supine position. Sequences included conventional T1 and T2-WI, T2 fat sat images, and DWI.

T1-weighted fast spin echo sequence was obtained with the following parameters: TR/TE, 475.3 ms/15 ms; numberof signals acquired, 1; field of view, 36 cm; slice thickness, 6 mm; gap, 1 mm; matrix, 269 × 222; flip angle, 70°.

Respiratory gated T2-weighted fast spin echo sequence was obtained using the following parameters: TR/TE,1250 ms/80 ms; echo train length, 80; number of signals acquired, 1; matrix, 328 × 281; field of view, 36 cm; slice thickness, 6 mm; gap, 1 mm.

Diffusion gradients were applied in the three orthogonal directions, using a single-shot echo planar imaging sequence. DWIs were acquired with b values of 0 and 1000 s/mm2. It had the following parameters: TR/TE, 2027 ms/70 ms; number of averages, 2; matrix, 168 × 168; field of view, 36 cm; slice thickness, 6 mm; gap, 6.6 mm; flip angle, 90°; echo train length, 77.

ADC maps were automatically generated by the software on the basis of the images obtained. ADC was calculated by drawing elliptical regions of interest (ROI) with an average size of 25±5 voxels.

We met further technical limitations as difficult to avoid artifacts, breathing movement and cardiac motion which cause image distortion and difficult interpretation of DWI especially in small sized lesions that may be missed with breathing or motion.

**Assessment of diffusion weighted image:**

Each lesion was evaluated for its size, extent, and relation to adjacent structures. Its signal intensity was evaluated in all pulse sequences T1WI, T2WI and ADC map were compared.

The MRI scanning images are uploaded to the scanner processing station and reviewed by the experienced imaging physician, who focus on the location and morphology of the lesion from the MRI scan routine sequence, measure the lesion area in the high signal area on the DWI image, analyze the benign and malignant nature of the pulmonary lesion, and make a final diagnosis after discussion of the images that are questionable.

**Pathological diagnosis:**

Histopathological analysis was our standard reference. Tissues used for histopathological examination for final diagnosis were taken by: fiberoptic bronchoscope, ultrasound guided or CT guided biopsy.

The pathological diagnostic results were recorded. The number of benign and malignant tumor cases was recorded, and their imaging characteristics were analyzed according to the MRI scan results and diagnostic results.

At the same time, the diagnostic efficacy of MRI for different lung lesions, including sensitivity, specificity, and accuracy, was also analyzed by using the pathological diagnostic results as the gold standard.

This study adopted image blinding reading, and the imaging physician was unaware of the pathological results.

Fig(1)Male patient 52years old with right upper lobe mass, core biopsy revealed non small cell carcinoma.

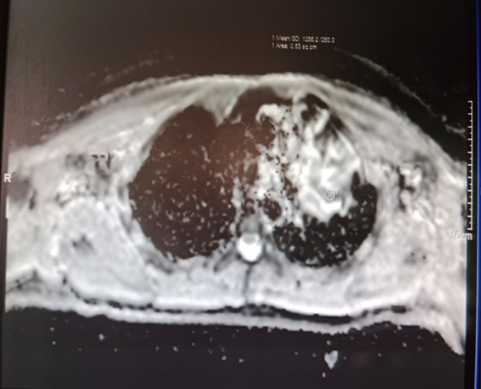
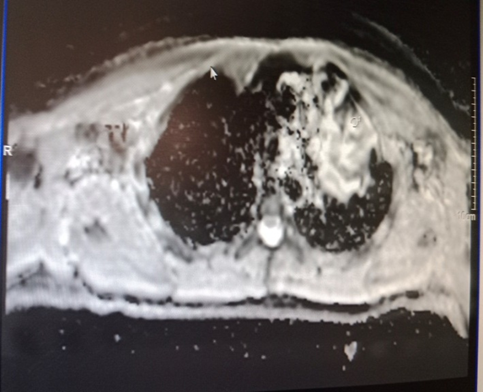
MRI showing an irregular shaped ill defined lesion is seen epicenered on the right lower lobe. Another ledion is seen in the right upper lobe (apical segment) extending to involves the upper part of the hilum. The lower lobe lesion shows intermediate T2 signal. The upper lobe lesion shows central low T2 core and peripheral lobular multilocular cystic part. Right hilar mediastinal lymphadenopathy. The lower lobe lesion ADC measures from lowest ROI is 1.199±192.2×10-3 mm2\sec. The upper lobe lesion ADC measures 1.383±0.0825×10-3 mm2\sec. Slow flow signal in the right pulmonary artery branch.

Fig (2) male patient 41 years old, ultrasound guided biopsy revealed tissue consolidation, non specific inflammatory reaction with reparative changes. Old pneumonic patch negative for tumor tissue.

MRI: well defined lobulated left upper lobe lesion involving the anterior segment with associated lingual collapse. ADC measures from the lowest ROI is 1.218±192.2×10-3 mm2\sec. Some central foci with ADC 1.136±0.9×10-3 mm2\sec.

Likely associated with high cellularity of chronic inflammatory changes. Collapse area ADC 2.01±3.0×10-33 mm2\sec. Non specific inflammation.

The data obtained were tabulated and statistically analyzed.

**4.Results**

This study was conducted on 32 patients with lung lesions found on CT, admitted at Benha University Hospital, Chest Department.

**General characteristics**

The mean age of the studied patients was 58 ±9 years, and males predominated in the study (75%). About two-thirds were smokers (62.5%)**.**

**Biopsy and pathology findings**

Biopsies done were US-guided (31.3%), CT-guided (34.4%), and bronchoscopic biopsy (34.4%). More than two-thirds (68.8%) had malignant lesions, and 68.2% of them were well differentiated. The most frequent benign lesion was nonspecific inflammation (60%), while the most frequent malignant lesion was NSCLC (86.4%). NSCLC types were adenocarcinoma (42.1%), squamous cell carcinoma (31.6%), and other types (26.3%). More than half of those with malignant lesions (54.5%) had metastasis **(Table 1).**

**Table (1)** Biopsy and pathology findings of the studied patients

|  |  |  |
| --- | --- | --- |
|  |  | **n (%)** |
| **Type of biopsy** | US-guided | 10 (31.3) |
|  | CT guided | 11 (34.4) |
|  | Bronchoscopic biopsy | 11 (34.4) |
| **Type of lesion** | Benign | 10 (31.3) |
|  | Malignant | 22 (68.8) |
| **Differentiation\*** | Well differentiated | 15 (68.2) |
|  | Poorly differentiated | 7 (31.8) |
| **Type of benign lesion\*\*** | Bronchial cyst | 1 (10.0) |
|  | Non-specific Inflammation | 6 (60.0) |
|  | Old pneumonic patch | 1 (10.0) |
|  | Pyogenic abscess | 2 (20.0) |
| **Type of malignant lesions\*** | SCLC | 3 (13.6) |
|  | NSCLC | 19 (86.4) |
| **Type of NSCLC\*\*\*** | Adenocarcinoma | 8 (42.1) |
|  | SQCC | 6 (31.6) |
|  | Other types | 5 (26.3) |
| **Metastases\*** | Present | 12 (54.5) |

\* Percentages were calculated based on total 22 patients with malignant lesions

\*\* Percentages were calculated based on total 10 patients with benign lesions

\*\*\* Percentages were calculated based on total 19 patients with NSCLC

**MRI findings**

More than two-thirds showed irregular morphology (68.8%). About one-third (62.5%) showed intermediate to low T2. The mean ADC in the center was 1.29 ±0.37, while in the periphery, it was 1.48 ±0.52. According to MRI, 87.5% of the patients had malignant lesions **(Table 2).**

**Table (2)** MRI findings of the studied patients

|  |  |  |  |
| --- | --- | --- | --- |
| **MRI findings** |  |  |  |
| **Morphology** | Regular | n (%) | 10 (31.3) |
|  | Irregular | n (%) | 22 (68.8) |
| **T2** | Intermediate to low | n (%) | 20 (62.5) |
|  | Intermediate to high | n (%) | 12 (37.5) |
| **MRI diagnosis** | Benign | n (%) | 4 (12.5) |
|  | Malignant | n (%) | 28 (87.5) |

**ADC in the center and periphery of the lesion**

ADC was significantly lower in the center (1.29 ±0.37) than the periphery (1.48 ±0.52) (P = .0.017) **(Table 3).**

**Table (3)** ADC in the center and periphery of the lesion

|  |  |  |  |
| --- | --- | --- | --- |
| **ADC** |  | **Mean ±SD**  **(× 10–3 mm2/s)** | **P-value** |
| **Center** |  | 1.29 ±0.37 | 0.017\* |
| **Periphery** |  | 1.48 ±0.52 |  |

Paired t-test was sued \*Significant

**General characteristics according to lesion type**

The mean age was significantly higher in those with malignant lesions (61 ±8) than those with benign lesions (52 ±8) (P = 0.009). Also, smoking was significantly higher in those with malignant lesions (77.3%) than those without (30%) (P = 0.01). No gender difference was noted (P = 0.186) **(Table 4).**

**Table (4)** General characteristics according to lesion type

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Benign**  **(n = 10)** | **Malignant**  **(n = 22)** | **P-value** |
| **Age (years)** | Mean ±SD | 52 ±8 | 61 ±8 | 0.009\* |
| **Sex** | Males n (%) | 6 (60.0) | 18 (81.8) | 0.186 |
|  | Females n (%) | 4 (40.0) | 4 (18.2) |  |
| **Smoking** | n (%) | 3 (30.0) | 17 (77.3) | 0.01 |

Independent t-test was used was age. Chi-square test was used for sex and smoking  
\* Significant

**ROC analysis for ADC center and periphery for predicting malignancy**

ROC analysis was done for the ADC center and periphery for predicting malignancy. It showed significant AUC for ADC center (AUC = 0.964, P < 0.001) and periphery (AUC = 0.859, P = 0.001). The best cutoff points were ≤ 1.29 for ADC center and ≤1.54 for ADC periphery, at which sensitivity and specificity were 95.5% and 90%, respectively, for ADC center and 86.4% and 80%, respectively, for ADC periphery**.**

**MRI findings according to lesion type**

Irregular morphology was significantly higher in those with malignant lesions (100%) than those with benign lesions (0%) (P < 0.001). Also, intermediate to low T2 was significantly higher in those with malignant lesions (90.9%) than those with benign lesions (0%) (P < 0.001). The mean ADC in the center and periphery were significantly lower in the malignant lesions (1.09 and 1.26, respectively) than those with benign lesions (1.74 and 1.97, respectively). P values were < 0.001 and 0.005, respectively (Table 4).

**Table (5)** MRI findings according to lesion type

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  | **Benign**  **(n = 10)** | **Malignant**  **(n = 22)** | **P-value** |
| **MRI morphology** | **Regular** | n (%) | 10 (100.0) | 0 (0.0) | <0.001\* |
|  | **Irregular** | n (%) | 0 (0.0) | 22 (100.0) |  |
| **T2** | **Intermediate to low** | n (%) | 0 (0.0) | 20 (90.9) | <0.001\* |
|  | **Intermediate to high** | n (%) | 10 (100.0) | 2 (9.1) |  |
| **ADC (center)** | **Mean ±SD** |  | 1.74 ±0.27 | 1.09 ±0.18 | < 0.001\* |
| **ADC (periphery)** | **Mean ±SD** |  | 1.97 ±0.6 | 1.26 ±0.29 | 0.005\* |

Independent t-test was used for ADC. Chi-square test was used for categoricaldata \* Significant

**ADC center and periphery in adenocarcinoma and squamous cell carcinoma**

The mean ADC (center) was significantly lower in those with squamous cell carcinoma (1.05 ±0.15) than those with adenocarcinoma (1.22 ±0.13) (P = 0.045), while no significant difference was noted regarding ADC (periphery) (P = 0.741) **(Table 5).**

**Table (6)** ADC center and periphery in adenocarcinoma and squamous cell carcinoma

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **ADC** |  | **Adenocarcinoma** | **SQ C C** | **P-value** |
| **Center** | Mean ±SD | 1.22 ±0.13 | 1.05 ±0.15 | 0.045\* |
| **Periphery** | Mean ±SD | 1.41 ±0.26 | 1.36 ±0.18 | 0.741 |

Independent t-test was used \* Significant

**5.Discussion**

Computed Tomography (CT) and Positron Emission Tomography (PET) are two common non-invasive methods used to examine pulmonary nodules or masses with high diagnostic accuracy, but these two methods have increased radiation exposure and the sensitivity of PET-CT is low in nodules smaller than 20mm, so another non-invasive method is required in the differential diagnosis of lung masses to avoid unnecessary biopsies that cause many risks and complications**(KONO et al., 2007)** **(18).**

MRI is a powerful tool for research and specific clinical applications, although Computed Tomography (CT) remains the gold standard for imaging of lung pathomorphology in cancer patients. The advantages of MRI over CT are not only limited to the lack of ionizing radiation but also combines excellent soft tissue contrast and functional information, it allows for multiple and repeated measurements and can be used to assess motion and perfusion of thoracic organs**(BIEDERERA et al., 2008)** **(5).**

Diffusion weighted MRI detects the random motion of water molecules in the biological tissues; this is called "Brownian motion" and helps in characterization of tissue microstructural changes. Water diffusion is changed in various disease processes reflecting physiological and morphological tissue criteria such as cell density and tissue viability. This can be quantified by Apparent Diffusion Coefficient (ADC) value **(ALNAGHY et al., 2018) (4)**.

ADC relates to the molecular transitional movement of water molecules. Decrease ADC values correlates with increased tumor cellularity which tends to restrict water diffusion **(THOENY et al., 2007**) **(26).**

Although DWI has been used to differentiate malignant and benign lesions in several other locations, there are few studies about the intrathoracic lesion characterization **(Koyama et al., 2010).** **(19)**.

The clinical application of pulmonary (MRI) was limited due to physical motion artifacts and technical limitations. However, with the development of technology in recent years, MRI has become a clinically feasible method for specific pulmonary problems **(WAN et al., 2017)** **(29)**.

This study included 32 patients with pulmonary masses, including 10 benign lesions and 22 malignant lesions.

The mean age of the studied patients was 58 ±9 years age range 41-74 years. , and males predominated in the study 24 males (75%) and 8 females (25%) (**Table 4**).

The mean age was significantly higher in those with malignant lesions (61 ±8) than those with benign lesions (52 ±8) (P = 0.009). No gender difference was noted (P = 0.186) **(Table 4).**

About two-thirds were smokers 20 patients (62.5%). Also, smoking was significantly higher in those with malignant lesions (77.3%) than those without (30%) (P = 0.01).

This result was in agreement with**(Danson et al., 2016)** **(7)**.

Also in agreement with **(HEBA ALLAH et al., 2019) (11)** in which there was statistically significance difference in smoking index between benign and malignant groups (p-value <0.001)

The most frequent presenting symptom was cough (93.8%), followed by dyspnea (90.6%), chest pain (50.0%), toxic symptoms (31.3%), and hemoptysis (18.8%).

No significant differences were noted between those with benign and malignant lesions regarding cough (P = 0.534), dyspnea (P = 0.224), hemoptysis (P = 1.0), chest pain (P = 1.0), and toxic symptoms (P = 0.918)**.**

The final diagnosis of the lesions was confirmed by histopathological examination. Biopsies done were US-guided in 10 patients (31.3%), CT-guided in 11 patients (34.4%), and bronchoscopic biopsy in 11 of them (34.4%).

Of the 32 lesions, 22 were malignant (68.8%) and 10 were benign (31.3%) **(Table 1).**

The malignant lesions consisted of 19 (86.4) non-small cell lung cancers (NSCLCs) and 3 (13.6) small cell lung cancers (SCLCs) and 15 (68.2%) of them were well differentiated and 7 (31.8%) of them were poorly differentiated.

NSCLC subtypes were adenocarcinoma 8 (42.1%), squamous cell carcinoma 6 (31.6%), and other types 5 (26.3%). More than half of those with malignant lesions 12 (54.5%) had metastasis **(Table 1).**

The most frequent benign lesion was nonspecific inflammation 6 (60%) then pyogenic abscess 2 (20%), followed by bronchial cyst 1 (10%) and Old pneumonic patch 1 (10%).

As regard MRI findings more than two-thirds showed irregular morphology 22 (68.8%). **(Table 2).**

Irregular morphology was significantly higher in those with malignant lesions (100%) than those with benign lesions (0%) (P < 0.001).

**(Table 2).**

About one-third 20 cases (62.5%) showed intermediate to low T2, while 12 cases (37.5) showed intermediate to high T2 **(Table 2).**

Also, intermediate to low T2 was significantly higher in those with malignant lesions (90.9%) than those with benign lesions (0%) (P < 0.001). **(Table 2).**

The associations between ADC value and histopathological parameters were analyzed in 22 malignant and 10 benign lesions, with statistically significance (p<0.001), this was in agreement with **(Zhang et al., 2018)** **(31).**

And also was in agreement with**(HEBA ALLAH et al., 2019)** **(11).**

By working out the ADC value, a lot of studies and researches showed that ADC values of various malignant lesions upsetting various organs in the body like the hepatic, renal, prostatic and uterine tumors were lower than those of benign lesions or normal tissues and showed high signal intensity (restricted pattern) on the DWI. Therefore, the ADC values were anticipated to reflect the histopathological tissue features by a non-invasive technique, not demanding for ionizing radiation**(LIU et al., 2010) (20)**

**ADC values**: this study demonstrated that the mean ADC value of benign lesions was 1.74 ±0.27 –3mm2/s and for malignant lesions it was 1.09 ±0.18 -3mm2/s, which was significantly lower than that of the benign lesions (p = 0.02) . This result was in agreement with the results of **(Liu et al., 2010) (20),** **(Gumustas et al., 2011)** **(9)** and (**Nasr et al., 2016)** **(22).**

The mean ADC in the center was 1.29 ±0.37, while in the periphery, it was 1.48 ±0.52.

ADC was significantly lower in the center (1.29 ±0.37) than the periphery (1.48 ±0.52) (P = .0.017) **(Table 3).**

The mean ADC in the center and periphery were significantly lower in the malignant lesions (1.09 and 1.26, respectively) than those with benign lesions (1.74 and 1.97, respectively). P values were < 0.001 and 0.005, respectively **(Table 5).**

This result was in agreement with **(HEBA ALLAH et al., 2019) (11)** study which demonstrated that the mean ADC value of benign lesions was 1.9±0.2 X10–3mm2/s and for malignant lesions it was 1.04± 0.4 X10–3mm2/s, which was significantly lower than that of the benign lesions. There was statistically significant difference when comparing different pathological lesions with the mean ADC value (p-value >0.001)

Also in agreement with **(Alnaghy et al.,2018)** **(4)** who demonstrated that the mean ADC value of benign lesions was 1.7 ± 0.72 × 10–3 mm2/s, and for malignant lesions it was 1.09 ± 0.0.19 × 10–3 mm2/s, which was significantly lower than the benign lesions with p value equal to 0.01.

In this study ROC analysis was done for the ADC center and periphery for predicting malignancy. It showed significant AUC for ADC center (AUC = 0.964, P < 0.001) and periphery (AUC = 0.859, P = 0.001).

The best cutoff points were ≤ 1.29 × 10–3 mm2/s for ADC center and ≤1.54 × 10–3 mm2/s for ADC periphery, at which sensitivity and specificity were 95.5% and 90%, respectively, for ADC center and 86.4% and 80%, respectively, for ADC periphery**.**

In different results; (**Abdel Razek et al., 2009) (2)** reported cut off ADC value (1.56 X 10–3mm2/s) with sensitivity and specificity 96% and 94% respectively.

While in **(Gumustas et al., 2012) (9)** study, although the mean ADC of the malignant lesions (1.5 x10-3 mm2/sec) was lower than of the benign group (1.9 x10-3 mm2/sec), the difference was not statistically significant (p < 0.675).

**(Gumustas et al., 2012)** **(9)** reported cutoff ADC value (1.39 X 10–3mm2/s) with sensitivity and specificity of 95% and 87% respectively.

**(Liu et al., 2010) (20)** reported different cut off values of the ADC (1.4 X 10–3mm2/s).

**(Mori et al., 2008) (21)** also found a significant difference between malignant and benign lesions by using an ADC cut-off value of 1.1x10-3 mm²/sec.

While in (**Alnaghy et al., 2018)** **(4**) ROC analysis, an ADC cut-off value of 1.4 × 10–3 mm2/s was considered the threshold value, and the sensitivity and specificity were 93.8% and 75%, respectively and the area under the ROC curve was 0.84**.**

**(HEBA ALLAH et al., 2019) (11)** reported that the area under the ROC (Receiving Operator Charachterstic) Curve was 0.98.

A cut off value (1.6 X 10–3mm2/s) was considered to be the threshold.

When an ADC value of 1.6 X 10–3mm2/s or more, the lesion was considered to be benign and a value below the threshold was considered to be malignant, the sensitivity was (100%) and specificity was (90%), positive predictive value (96.8%) and negative predictive value (100%).

Our results were conflicted with the results of **(Uto et al.2009)** **(28),** who reported that there was no significant difference between lung cancer and benign lesions based on the ADC value.

Histopathologically, tumor cellularity of SCLC is high, and these tumor cells have very large nuclei and almost no cytoplasm.

These features were expected to restrict the tissue diffusion and reduce ADC values. SCLC is differentiated from other forms of lung cancer by its aggressive clinical course, widespread metastasis and its sensitivity to chemotherapy and radiation therapy. Treatment for SCLC and NSCLC are not the same.

Surgery is the treatment of choice for patient with NSCLC while chemotherapy and radiotherapy is the standard for SCLC. So; it is important and of clinical significance to distinguish between both types **(CAKMAK et al., 2016).(6).**

In this study, although ADCs were lower in the SCLC than in NSCLC subgroup, the difference was not statistically significant (p-value=0.1061).

This was in agreement with **(CAKMAK et al., 2016)** (**6)**and also was in agreement with **(11)** who found that there was no significance between ADC values of SCLC & NSCLC.

When comparing the mean ADC value of NSCLC and SCLC showed that ADC value of SCLC was lower than that of NSCLC (1.12±0.45 X 10–3 vs. 0.80±0.12 X 10–3) with no significant difference (p-value=0.106) **(HEBA ALLAH et al., 2019)** **(11).**

This result was also in agreement with **(Gumustas et al., 2012)(9)** study which reported that although the ADC value of the SCLCs was lower than the ADC value of the NSCLCs, the difference was not statistically significant (p < 0.464).

However, this was not in agreement with the results of **(Abdel Razek et al., 2012)** **(3)**as they found that there were significantly lower ADC values for SCLC when comparing with NSCLC groups in a similar patient population.

**(Koyama et al., 2010) (19)** also found that there were no significant differences between subtypes of lung cancers.

**(Liu et al., 2010) (20**) also found that the ADC values for the SCLC were significantly lower than the NSCLC group he reported that the mean ADC value of small cell lung cancer was 1.06 × 10–3 mm2/s, which was lower than the mean ADC value of non-small cell lung cancer (p-value= 0.007).

In our study, the mean ADC (center) was significantly lower in those with squamous cell carcinoma (1.05 ±0.15) than those with adenocarcinoma (1.22 ±0.13) (P = 0.045), while no significant difference was noted regarding ADC (periphery) (P = 0.741) **(Table 6).**

ROC analysis was done for the ADC center for differentiating adenocarcinoma from squamous cell carcinoma. It showed significant AUC of 0.823 (P = 0.045).

The best cutoff point was > 1.035, at which sensitivity and specificity were 87.5% and 66.7%, respectively**.**

Whilein **(11)** study, the highest ADC value was that of adenocarcinoma (1.440±0.107 X 10–3 mm/s) and the lowest ADC value was that of large cell carcinomas (0.750±0.300 X 10–3mm/s).

In **(9)**  study, results of significantly lower ADCs in poorly-differentiated adenocarcinomas compared medium-well- differentiated cancer types were reported.

**6.Conclusions**

Diffusion MR imaging offers functional imaging of lung cancer due to its ability to probe the micro-structure of the tumors, which is complementary to the routine anatomic MR imaging of the chest. The potential value of diffusion MR imaging is in its detection and characterization of lung cancer.

**6.References**

1. A.Abdel Razek, A.Fathy, T.Abdel Gawad Correlation of apparent diffusion coefficient value with prognostic parameters of lung cancer. J Comput Assist Tomogr.vol.35,pp.248–252,2011.
2. A.ABDEL RAZEK, A.ELMORSY, M.ELSHAFEY. Assessment of mediastinal tumors with diffusion weighted single shot echo planar MR imaging. J. Mag. Reson. Imaging.vol.30,pp.535-40,2009.
3. A.ABDEL RAZEK. Diagnostic magnetic resonanance imagimg of chest tumours. Cancer Imaging.vol.12,pp.452-63, 2012.
4. E.ALNAGHY, M.EL-NAHAS, A.SADEK. Role of diffusion-weighted magnetic resonance imaging in the differentiation of benign and malignant pulmonary lesions. Polish Journal of Radiology.vol. 83,pp.585-94, 2018.
5. J.BIEDERERA, C.HINTZE and FABEL M.: MRI Of pulmonary Nodules: Technique and Diagnostic Value, Cancer Imaging.vol. 8,pp.125-30, 2008.
6. V.CAKMAK, F.UFUK, and KARABULUT N.: Diffusion-Weighted MRI of Pulmonary Lesions: Comparison of Apparent Diffusion Coefficient and Lesion-to-Spinal Cord Signal Intensity Ratio in Lesion Characterization, J. Magn. Reson. Imaging.vol.45,pp.144-180,2016.
7. J.DANSON, C.H.ROWLAND, R.ROWE. The relationship between smoking and quality of life in ad-vanced lung cancer patients: A prospective longitudinal study Support Care Cancer.vol. 24,pp.1507-16, 2016.
8. A.Detre, John; Rao, Hengyi. (May 2012). ["Applications of arterial spin labeled MRI in the brain"](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3326188). Journal of Magnetic Resonance Imaging.vol.**35** (5),pp. 1026– 1037,2017..
9. S.GUMUSTAS, N.INAN and SARISOY H.: Malignant versus benign mediastinal lesions: Quantitative assessment with diffusion weighted MR imaging. Eur. Radiol.vol.21,pp.2255-60, 2011.
10. N.Gümüştaş ,  [Inan](https://pubmed.ncbi.nlm.nih.gov/?term=Inan+N&cauthor_id=24003535), [Gür Akansel](https://pubmed.ncbi.nlm.nih.gov/?term=Akansel+G&cauthor_id=24003535), [I Başyïğït](https://pubmed.ncbi.nlm.nih.gov/?term=Ba%C5%9Fy%C3%AF%C4%9F%C3%AFt+I&cauthor_id=24003535), [E Cïftçi](https://pubmed.ncbi.nlm.nih.gov/?term=C%C3%AFft%C3%A7i+E&cauthor_id=24003535) Differentiation of lymphoma versus sarcoidosis in the setting of mediastinal-hilar lymphadenopathy: assessment with diffusion-weighted MR imaging sarcoidosis Vasc Diffuse Lung Dis .vol.30(1),pp.52-9,2013.
11. H.HEBA ALLAH AMIN. DINA MOGHAZY MOHAMED., OMNIA A. GAD. Role of Diffusion Weighted Magnetic Resonance Imaging in Characterization of Pulmonary Masses. Med. J. Cairo Univ.vol. 87,pp. 4825-4833, 2019.
12. B.Hochhegger, J.Ley-Zaporozhan, E. Marchiori. Magnetic resonance imaging findings in acute pulmonary embolism. Br J Radiol.vol.84,pp.282–287, 2011.
13. S. A.Huettel, A. W.Song, G. McCarthy, Functional Magnetic Resonance Imaging Massachusetts: Sinauer , .vol.79,pp.155-180,2009.
14. N.Inan, F .Kilinc, T.Sarisoy. Diffusion weighted MR imaging in the differential diagnosis of haemangiomas and metastases of the liver. Radiol Oncol.vol.**44,pp.** 24-9,2010.
15. YJ.Jeong, KS.Lee, SY.Jeong. Solitary pulmonary nodule: characterization with combined wash-in and washout features at dynamic multidetector row CT. Radiology.vol.**237,pp.**675-83,2005.
16. YJ.Jeong, KS.Lee, SY.Jeong. Solitary pulmonary nodule: characterization with combined wash-in and washout features at dynamic multidetector row CT. Radiology **.vol.237,pp.** 675-83,2005.
17. Jurgen Biederer, S.Mirsadraee, M.Beer.MRI of the lung –Current applications and future perspectives. Insights into imaging.vol.3 (4),pp.373-386, 2012.
18. R.KONO, K.FUJIMOTO and TERASAKI H.: Dynamic MRI of solitary Pulmonary Nodules: Comparison of Enhancement Patterns of Malignant and Benign Small Peripheral Lung Lesions, Am. J. Reontgenol.vol.188,pp. 26- 36, 2007.
19. H.Koyama, Y.Ohno, N.Aoyama. Comparison of STIR turbo SE imaging and diffusion-weighted imaging of the lung: capability for detection and subtype classification of pulmonary adenocarcinomas. Eur Radiol.vol.**20**,pp.790–800,2010.
20. H.LIU, Y.LIU, T.YU and N.YE. Usefulness of diffusion weighted Magnetic Resonance Imaging in evaluation of pulmonary lesions, Eur. Radiol.vol.20,pp.807-15, 2010.
21. T .Mori, H.Nomori, K.Ikeda. Diffusion-weighted magnetic resonance imaging for diagnosing malignant pulmonary nodules/masses: comparison with positron emission tomography. J Thorac Oncol.vol.3,pp.358–364,2008.
22. A.NASR, H.ELSHAHAT, H.SAFWAT.Diffusion weighted MRI of mediastinal masses: Can measurement of ADC value help in the differentiation between benign and malignant lesions. The Egyptian Journal of Radiology and Nuclear Medicine.vol.47,pp.119-25, 2016.
23. J. Podobnik, I. Kocijancic, V .Kovac. MRI in evaluation of asbestos related thoracic diseases – preliminary results. Radiol Oncol.vol.**44,pp.** 92-6, 2010.
24. JF.Schaefer, , J .Vollmar, F.Schick, R. Vonthein, MD.Seemann, H .Aebert. Solitary pulmonary nodules: dynamic contrast-enhanced MR imaging perfusion differences in malignant and benign lesions. Radiology.vol.**232,pp.**544-53,2004.
25. RL.Siegel, KD.Miller, A.Jemal Cancer statistics, CA Cancer J Clin .vol.15,pp. 67-80,2017.
26. H.C. THOENY and F.De KEYZER.Extracranial appli-cations of diffusion weighted magnetic resonance imaging, Eur. Radiol.vol.27,pp.1385-93, 2007.
27. B.Türkbey, O.Aras, Karabulut, Nevzat, A.T.Turgut. Diffusion-weighted MRI for detecting and monitoring cancer: A review of current applications in body imaging. Turkish Society of Radiology .vol.50,pp.500-800,2012.
28. T.Uto, Y. Takehara, Y.Nakamura. Higher sensitivity and specificity for diffusion-weighted imaging of malignant lung lesions without apparent diffusion coefficient quantification. Radiology.vol. 252,pp.247-254,2009.
29. Q.WAN, Y.DENG, J.ZHOU . Intravoxel incoherent motion diffusion-weighted MR imaging in assessing and characterizing solitary pulmonary lesions. Scientific. Report.vol.7,pp.43-257, 2017.
30. CA.Yi, KS.Lee, B-T.Kim. Tissue characterization of solitary pulmonary nodule: comparative study between helical dynamic CT and integrated PET/CT. J Nucl Med.vol.47,pp.443–450,2006.
31. F.ZHANG, Z.ZHOU, D.TANG. Diffusion-weighted MRI in solitary pulmonary lesions: Associations between apparent diffusion coefficient and multiple histopatholog-ical parameters. Sci. Rep.vol.8 (1),pp.112-248, 2018.