Utilization of New Imaging Modalities (DW MRI Imaging) in NSCLC Staging and Radiotherapy Planning

MOHAMED A. HASAN, M.D.**; MOSTAFA AL-DALY, M.D.**; MARIAN F. FARID, M.D.* and RIHAM HANY, M. S c.**
The Departments of Radiology* and Radiotherapy**, Faculty of Medicine, Cairo University

Abstract

Background: Lung cancer represents one of the leading causes of cancer mortality worldwide, fourteen percent of all diagnosed cancers are lung cancer. Lung cancer pathology includes both Non-Small-Cell Lung Cancer (NSCLC) accounting for 80-85% of lung cancers, while small-cell lung cancer has been decreasing in frequency over the last few decades. CT scans with the addition of FDG PET is the standard of care for diagnosis of lung cancer; however, there is poor distinction between structures with similar electron densities, making it difficult to differentiate lung cancers from surrounding lung collapse, consolidation or pleural effusion. DW-MRI scan sequences produce image contrast that depends on differences in tissue-water mobility. By performing DWI using different b-values which is a quantitative analysis by which the calculation of Apparent Diffusion Coefficient (ADC) values is possible, and then displaying an ADC map. Restricted water diffusion demonstrates high signal intensity on DWI and lower ADC values on ADC map corresponding with foci of hypercellularity and malignancy.

Aim of the Work: The aim of the work is incorporation of MRI diffusion as one of the functional images in lung cancer staging in addition to lung radiation therapy and its impact on the different target volumes in addition to nodal detection and assessment.

Patients and Methods: This study was carried out at Kasr El-Ainy Center of Clinical Oncology and Nuclear Medicine (NEMROCK) in corporation with the Department of Radiodiagnosis during the period between March 2014 to January 2015. Twenty patients were recruited in the study.

Conclusion: MRI diffusion has the ability to differentiate lung cancer mass from postobstructive collapse or consolidation (even better than PET CT) which affect the Gross Tumor Volume (GTV) at the end, and on the return more sparing of the normal structures.

Key Words: DWI – MRI – NSCLC radiotherapy.

Introduction

“The LUNG cancer represents one of the leading causes of cancer mortality worldwide, accounting for 1.3 million deaths per year”. Lung cancer pathology includes both non-small-cell lung cancer (NSCLC) accounting for 80-85% of lung cancers, while small-cell lung cancer has been decreasing in frequency over the last few decades” [1].

The most significant determinant for lung cancer treatment and survival is the stage of the disease. Surgical resection is the main therapy for localized NSCLC patients with stage IA to IIB and in selected IIIA patients. However, in unresectable stage III patients, concurrent chemoradiation is the treatment of choice, whereas stage IV is treated with palliative treatment [2].

“The 5-year survival rate for all stages of NSCLC combined is only 16%. Only 15% of lung cancers are diagnosed at a localized stage, for which the 5-year survival rate is 52%. The 5-year survival for small cell lung cancer (6%) is lower than that for non-small cell (18%)” [3].

CT scans are important for the assessment of patients with suspected lung cancers; however they are unreliable for detection of metastases of mediastinal lymph nodes. Whereas lymph node more than 1 cm in transverse diameter suggests being malignant lymphadenopathy, other enlarged but histologically benign lymph nodes are often observed in the tumors associated with volume loss or postobstructive pneumonitis. Also, lymph nodes less than 1 cm contain foci of malignant cells, at about 15% depending on the size, histology and location of the primary tumor [4].
FDG-PET is applied for any newly diagnosed suspicious lung lesion. FDG-PET scans are useful for mediastinal lymph node detection as well as visceral and bony metastases [5].

Studies have compared FDG-PET with standard CT scans for mediastinal lymph nodes detection and staging in lung cancer patients. “The overall accuracy, sensitivity, and specificity of PET scans are nearly 70%, 70%, and 80% respectively, compared with 70%, 50%, and 70% respectively, for CT scans for the detection of histologically confirmed mediastinal lymph node (N2 and N3) metastases. Furthermore, FDG-PET scans are considerably superior to CT scans for the detection of N1 disease (42% vs. 13%; \( p=0.017 \)) in patients with potentially operable lung cancers [6].

In addition for being PET-CT scans superior to CT-scans in staging lung cancers, also superior in assessing responses to chemotherapy and/or radiation in patients with these neoplasms [7].

False-positive PET results are mainly in Granulomatous inflammation, silicosis, and sinus histiocytosis, whereas certain tumors with relatively low proliferative rates as carcinoid, bronchoalveolar or mucoepidermoid carcinomas produce false-negative results [7].

The term “functional MRI” has been adopted to describe any MRI technique capable of demonstrating information in addition to the anatomical images more routinely acquired, e.g. Diffusion-weighted (DW) MRI sequences, Dynamic Contrast Enhanced (DCE) and Magnetic Resonance Spectroscopic Imaging (MRSI) [8].

As a general description, functional MRI is used to define techniques that probe the status of the tumor itself. This functional information as tumor perfusion vascular permeability, extracellular space tortuosity, metabolic status and hypoxia can also be obtained. DWI is applied by using different \( b \) values which is a quantitative analysis, by which the calculation of Apparent Diffusion Coefficient (ADC) values is possible, and then displaying an ADC map. Restricted water diffusion demonstrates high signal intensity on DWI and lower ADC values on ADC map corresponding with foci of hypercellularity and malignancy [9].

CT scans with the addition of FDG PET is the standard of care for diagnosis of lung cancer; however, there is poor distinction between structures with similar electron densities, making it difficult to differentiate lung cancers from surrounding lung collapse, consolidation or effusion. MRI diffusion can enable differentiation of these situations through improved soft-tissue contrast. And also some state its role in the differentiation of malignant or benign Iry lung lesions in addition to mediastinal and hilar lymph nodes [10].

New radiation techniques have provided the means to deliver highly conformal treatments offering the promise of improved sparing of normal tissue and tumor dose escalation. For these techniques to achieve their full potential, there is an increasing need for anatomical and functional imaging to be used at the planning stage and ideally as a verification tool throughout radiotherapy to localize disease with a high level of accuracy. The technique is having an increasing role in contouring the Gross Tumor Volume (GTV) and Organs at Risk (OAR) in radiation therapy Treatment Planning Systems (TPS). MRI-planning scans from diagnostic MRI scanners are currently incorporated into the planning process by being registered to CT data which provides a solid geometric and electron density map for accurate dose calculation on the TPS computer [9].

The role of MRI in diagnosis and staging of lung cancer and its advantages to the other diagnostic tools (CT and PET/CT) is significant. In general, T1-weighted images are considered best for gross structural information (anatomy) and T2-weighted images for biological characteristics that may aid with pathology information. The advanced techniques “functional MRI” are additional sequences [8].

DW-MRI sequences which are one of the functional MRI, produce image contrast that depends on differences in tissue-water mobility. The Apparent Diffusion Coefficient (ADC), in units \( \text{mm}^2/\text{s} \), is the quantitative parameter used for the assessment of water diffusion through tissue. By acquiring at least two images with different \( b \) values (usually \( b=0 \) and \( b=1000\text{mm}^2/\text{s} \)), the ADC can be measured directly [11].

Tumor tissues have disrupted water molecule diffusion and a lower Apparent Diffusion Constant (ADC) leading to a high signal in DW images. A rise in ADC during therapy, indicates a positive response to therapy. The observed increase in water ADC following therapy is directly related to the number of cells killed and is thought to be due to the liberation of water into the extracellular space as a result of cell necrosis [12].

Diffusion-weighted imaging is probably a useful new tool in tumor response. Cohort studies show
its potential in providing evidence of tumor recurrence [13].

The use of MRI to avoid normal tissues in lung-cancer radiotherapy planning is an emerging area of research. Use of MRI in radiotherapy treatment planning is well established for many treatment sites such as brain, prostate and head and neck. The use of MRI for the purposes of radiotherapy treatment planning, monitoring of tumor response over the course of treatment and assessment of relapse following treatment and for radiotherapy contouring has been investigated for over a decade [9].

There have been no definitive contouring studies comparing the delineation of lung cancer on MRI to CT or PET-CT scans. As a diagnostic tool in differentiating benign from malignant nodules, DWI has shown similar accuracy to PET scans [14].

MRI may be used as a prognostic tool for treatment outcomes. Ohno et al., performed post-treatment DCE-MRI scans in 114 patients who had chemoradiotherapy for Stage III NSCLC. Patients were divided into two groups for analysis: 11 month difference in survival was noted between the suggested two groups (those with local control and those with local failure). However this has not been compared to other imaging such as PET scans [15].

MRI scans can be used to evaluate changes in lung tumors and normal tissue response during a course of radiotherapy. Yankelevitz et al., performed 0.6T MRI scans before, during and after radiotherapy in 10 patients. All patients showed increased signal intensity in normal lung tissue during radiotherapy but without clinical evidence of radiation pneumonitis. MRI has the potential to allow adaptive radiotherapy planning in response to changes during treatment [16].

Aim of work:

The aim of the work is incorporation of MRI diffusion as one of the functional images in lung radiation therapy and its impact on the different target volumes in addition to nodal detection and assessment.

Patients and Methods

This study was carried out at Kasr El-Ainy Center of Clinical Oncology and Nuclear Medicine (NEMROCK) in corporation with the Department of Radiodiagnosis at Kasr Al-Ainy during the period between March 2014 to January 2014. Twenty patients were recruited in the study.

Eligibility criteria:

Patients included in our study met the following criteria:

- Patients with newly diagnosed NSCLC.
  A- Early stage amenable for radiotherapy.
  B- Locally advanced stage IIIA and selected cases of stage IIIB; pathologically proven as NSCLC.
- Patients must be ≥ 18 years of age.

Exclusion criteria:

Patients were excluded from our study in case of:

- Contraindications to MRI e.g. metallic pace maker or metallic prosthesis.
- Claustrophobic patients.
- Severe pulmonary or heart disease or being respiratory distressed.
- Renal impairment.
- Prior radiotherapy to the lung, mediastinum or any thoracic structure before enrolment.
- Pregnant women.

Radiotherapy planning technique:

- Preparation:
  All patients were subjected to the following work up:
  - History taking.
  - General and local examination including weight, performance status and nutritional status.
  - Laboratory work-up: Blood picture, kidney function tests, liver function tests.
  - Canula insertion for the IV contrast.

- Patients setup:
  All patients lie in the supine flat treatment position. The patient is instructed to breathe normally. The normal treatment position is ‘arms up, elbows flexed’ so that arms do not block the laser beam markings and the tattoos on the sides of the patient. This is the same position applied in both the CT and MRI.

- Image acquisition:
  A- CT scan:
  - The patients underwent a planning Computed Tomography (CT) scan with contrast.
Utilization of New Imaging Modalities (DW MRI Imaging) in NSCLC Staging

- The slice thickness is 5mm would be considered standard.
- The patients are imaged from the cricoid to midway between xiphoid process.
- The laser beam is used to define CT reference at the xiphoid process anteriorly and mid-separation laterally, "marked with radio-opaque marks" during imaging and then skin tattos were applied for reproducibility of the treatment position.
- The data from this scan are then transferred to the planning systems (Eclipse Version 8.6).

B- MRI scan:
- MR imaging was performed with a 1.5 Tesla magnet (Gyrosan Entra, Philips medical systems, Netherland).
- Cases were imaged in the same position (arms up, elbows flexed) with applying respiratory triggering upon the chest and pulse oximetry (PPU) upon the big toe for better imaging techniques without much artifacts and image haziness.
- Also we have applied the same references that were applied in the CT, using surface markers enhancing by MRI (for better fusion of the MR images with the CT images).
- T1 axial and coronal, T2 axial and coronal, T2 SPAIR and DWI with \( b \)-values of 0,500 and 1000mm\(^2\)/s were obtained in each patient using respiratory triggering which is in the expiratory phase (the same as the CT scan respiratory phase). Other parameters were as follows: Repetition time/echo time, 2,450ms/50.8-67.4ms; field of view, 40-48cm; matrix, 128 X 128; gap, 0mm.
- The slice thickness is 5mm to correspond with the CT images.
- The MRI data from this scan were then imported to the radiotherapy planning systems (Eclipse Version 8.6).

C- ADC maps:
- A senior radiologist with MRI experience evaluated the CT, MRI data and fusion images.
- DW reconstructed images with \( b \)-value=0,500 and 1000 evaluated.
- These DW images were inspected for the presence of high signal intensity (restricted diffusion). In the evaluation of diffusion images, cases in which the tumor showed obvious hyperintensity compared with the Post Obstructive Collapse (POC) were considered distinguishable.
- Matched ADC maps were applied using a Phillips Advantage windows workstation.
- After image reconstruction, for any visually suspicious lung lesion (excluding necrosis which is easily detected by ADC) either seen on CT scan or MRI (DWI or T2 images), a two-dimensional (2D) round or elliptical Region of Interest (ROI) was drawn on this solid area including questionable areas of consolidation or collapse. The procedure was repeated three times and the mean ADC value was obtained.
- Lung lesions or lymph nodes with an ADC value that was equal or less than the Optimal Cut-off Value (OCV) of the ADC value denoting highly cellular tissues, were defined as positive for malignancy which was 1.4mm\(^2\)/sec.

**Image fusion:**

*Items for better D W-MRI/CT fusion:*
- We placed the body surfaces markers (one anteriorly and two laterals) on the patients as image match point when they underwent a planning CT scan and the MRI scanning.
- We used the same thickness (5mm) and FOV (40cm) for CT and MRI scans.
- All patients underwent MRI scanning in the same position and respiratory phase at the end of expiration to the CT scan which was also performed at the end of expiration corresponding to the MRI respiratory phase.
- We fused the DWI scans with CT images manually by matching the outer body contour, and the lungs and the heart anatomical positions.
- We fused the T2 and the DW images for better visual correlation.

Similar to FDG/PET scan, DW images can not show anatomic structures clearly as its spatial resolution is limited, while CT and the T2 images can show anatomic structures clearly because of high spatial resolution. We have fused the two images using treatment planning system.

*Target volume delineation:*
The target volumes were defined to the planning system on all CT cuts and the dose limiting normal tissues according to the International Commission on Radiation Units (ICRU).

**Statistical methods:**
Data management and analysis will be performed using Statistical Package for Social Sciences
Numerical data were summarized using means and standard deviations or medians and ranges. Categorical data were summarized as percentages.

Comparisons between 2 numerical measurements were done using the Wilcoxon signed rank nonparametric test. Comparisons between categorical measurements were performed by the McNemar’s test. All p-values are two-sided. p-values <0.05 were considered significant.

Results

The study was carried out at Kasr Al-Ainy Center of Clinical Oncology and Nuclear Medicine (NEMROCK) in corporation with the Radiodiagnostic Department at Kasr Al-Ainy during the period between March 2014 to January 2014.

A total of 20 patients were included in the study. During the imaging process of both the CT and MRI no adverse reaction was observed and complete data sets of both imaging modalities were achieved for all patients. Disturbing artifacts related to respiratory motion or severe field inhomogeneities limiting the MR image quality were not identified. In average, MRI was performed 2 days (range 0-2 days) following the CT.

Patients characteristics (Table 1).

Characteristics of lung tumor:
- Site (Table 2).
- Pathology and grade (Table 3).
- T-stage of the tumor (Table 4).
- N stage of the tumor (Table 5).
- TNM staging according to CT and MRI diffusion (Table 6).

Application of MRI diffusion has lead to change in TNM staging of six patients which in return affected staging of these patients in which 50% of them were upstaged in their disease and 50% were downstaged in it mainly due to change in the nodal staging as 3 patients were upstaged in the nodal status while 3 patient were downstaged in the nodal status and one of them developed also decrease in the tumor stage after exclusion of the collapse being changed from T3 to T2 lesion.

Nodal status:

Nodal status according to both CT and MRI changes in six patients, which may affect the operability of the patient and also possibility of radiation therapy or the need of chemotherapy for down-staging of the patients tumor stage. Three patients were upstaged after application of MRI diffusion in the form of: Two patients changed from N1 to N2 and on patient changed from N2 to N3, while another three patients were downstaged in the form of: Two of them changed from N3 to N2, and lastly one patient changed from N2 to N0.

Statistics of the volumes of the 20 cases:

The different volumes were studied to detect the means, medians, standard deviations, minimum and maximum values (Table 7).

Sixteen patients developed decrease in the volume of the GTV 1ry on the MRI Diffusion when compared to that on the CT scan, while 3 patients developed increase in it and one patient had equal volumes.

Differentiating the collapse:

Mean ADC value of the tumor versus ADC value of the collapse:

In our study, the malignant lesions that were proved pathologically had mean ADC equals 0.98 ± 0.22 X10 X10 -3 mm 2/sec and the ADC min. and max. were 1.31 X 10 -3 mm/sec respectively, while that of the collapse or consolidation had a mean value 1.99±0.22 X 10 -3 mm/sec with the min. and max. values as 1.53 and 2.3 X 10 -3 mm/sec respectively. This differences showed statistical significance (p=<0.001).

Differentiation of lung collapse and/or consolidation because of utilizing MRI diffusion weighted images was found in 14 cases out of the 20 cases in the study, while 7 cases only were detected by CT. This difference was statistical significance (p= 0.016).

Table (1): Patients characterization.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Variable</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Males</td>
<td>17</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>Females</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>Age</td>
<td>&lt;60</td>
<td>17</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>&gt;60</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>Smoking h/o</td>
<td>Yes</td>
<td>15</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>5</td>
<td>25</td>
</tr>
</tbody>
</table>
Table (2): Site: The different site of tumor.

<table>
<thead>
<tr>
<th>Site</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>LT lower lobe</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>LT upper lobe</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td>RT lower lobe</td>
<td>5</td>
<td>25</td>
</tr>
<tr>
<td>RT middle lobe</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Rt upper and middle lobes</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Rt upper lobe</td>
<td>5</td>
<td>25</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>20</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

Table (3): Pathology and grade.

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma</td>
<td>12</td>
</tr>
<tr>
<td>Squamous</td>
<td>5</td>
</tr>
<tr>
<td>Large</td>
<td>1</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>1</td>
</tr>
<tr>
<td>Adenosquamous</td>
<td>1</td>
</tr>
</tbody>
</table>

Grades

<table>
<thead>
<tr>
<th>Grades</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>7</td>
</tr>
<tr>
<td>III</td>
<td>13</td>
</tr>
</tbody>
</table>

Table (4): T-stage of the tumor.

<table>
<thead>
<tr>
<th>T-stage</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>T&lt;=5cm</td>
<td>6</td>
<td>30</td>
</tr>
<tr>
<td>T5-7cm</td>
<td>6</td>
<td>30</td>
</tr>
<tr>
<td>T&gt;7cm</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>20</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

Table (5): N-stage of the tumor (CT based).

<table>
<thead>
<tr>
<th>N-stage</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>N1</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>N2</td>
<td>12</td>
<td>60</td>
</tr>
<tr>
<td>N3</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>20</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

Table (6): TNM staging according to CT and MRI diffusion.

<table>
<thead>
<tr>
<th>No in CT</th>
<th>NO in DW-MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1N1</td>
<td>1</td>
</tr>
<tr>
<td>T1N2</td>
<td>0</td>
</tr>
<tr>
<td>T2N0</td>
<td>1</td>
</tr>
<tr>
<td>T2N1</td>
<td>2</td>
</tr>
<tr>
<td>T2N2</td>
<td>6</td>
</tr>
<tr>
<td>T2N3</td>
<td>2</td>
</tr>
<tr>
<td>T3N0</td>
<td>0</td>
</tr>
<tr>
<td>T3N1</td>
<td>1</td>
</tr>
<tr>
<td>T3N2</td>
<td>4</td>
</tr>
<tr>
<td>T3N3</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>20</strong></td>
</tr>
</tbody>
</table>

Table (7): The difference between the tumor gross volume by CT and MRI diffusion.

<table>
<thead>
<tr>
<th>Volume</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>Mini.</th>
<th>Maxi.</th>
</tr>
</thead>
<tbody>
<tr>
<td>GTV 1ry CT</td>
<td>360.4</td>
<td>196.6</td>
<td>336.5</td>
<td>20.1</td>
<td>857</td>
</tr>
<tr>
<td>GTV 1ry MRI</td>
<td>320.4</td>
<td>178.2</td>
<td>318.7</td>
<td>11.2</td>
<td>840.6</td>
</tr>
<tr>
<td>GTV LN CT</td>
<td>89.1</td>
<td>74.7</td>
<td>74.9</td>
<td>0.0</td>
<td>255.5</td>
</tr>
<tr>
<td>GTV LN MRI</td>
<td>82.7</td>
<td>82.2</td>
<td>48.6</td>
<td>0.0</td>
<td>260.2</td>
</tr>
<tr>
<td>GTV CT total</td>
<td>445.3</td>
<td>386.7</td>
<td>70.9</td>
<td>218.7</td>
<td>1038.1</td>
</tr>
<tr>
<td>GTV MRI diff total</td>
<td>391.8</td>
<td>231</td>
<td>353.8</td>
<td>64.3</td>
<td>1040.3</td>
</tr>
</tbody>
</table>

Fig. (1): Male patient 56 years old presented with NSCLC. Axial CT (A) Image showing delineation of the GTV total on the CT scan (cyan colour), (B) The delineation of the GTV total on the DW-MRI (red contouring) showing preserved lung tissue.
Fig. (2): Male patient 50 years old with NSCLC. CT images used for contouring of critical organs. Heart (yellow contour), oesophagus (blue contour), spinal cord (purple contour), RT lung (cyan contour) and LT lung (orange contour).

Fig. (3): Male patient 53 years old with NSCLC (A) The CT contouring of the GTV lower lobe lung lesion (Red contour), (B) The ADC values in differentiating the lung lesion and the nearby consolidation/collapse.

Fig. (4): Male patient 56 years old with lung cancer and nodal enlargement: Shows level 6 LN station positive in both the CT scan but on the ADC image, the mean value 2.01 indicating non malignant spread to it (?? inflammatory).
Fig. (5): Male patient 56 years old with lung cancer and nodal enlargement showing (A) Coronal T2 MRI with partial lung collapse above the lung lesion pointed by the yellow arrow in the T2 image; (B) Shows the DWI with the hyperintense lung lesion in addition to the positive mediastinal lymph nodes. (C) The mean ADC value was 1.076 with a deeper colour than that of the collapse with a mean value 2.535. (D) The ADC image one cut above (C) Showing the collapse only with a mean value 2.26 and a pale colour.

Fig. (6): Male patient 48 years old. The images show the apical lung lesion in the CT scan (A), DWI (B) And the ADC images. (C,D) With the corresponding ADC values of the lung lesion and the surrounding lung collapse.
Our study is a prospective pilot study included 20 of NSCLC patients aiming at incorporation of MRI diffusion as a functional image in the lung radiation therapy. The majority of patients were males (85%) due to higher percentage of males smoking compared to females. Approximately 30% of patients with NSCLC have unresectable, locally advanced disease at diagnosis. The standard treatment of unresectable LA-NSCLC is definitive concurrent chemotherapy and radiotherapy with a dose not less than the biological equivalent of 60 Gy in 2.0 Gy fractions.

Unfortunately, failure of locoregional treatment remains a major problem in locally advanced NSCLC, despite of advances in radiation technology [17].

Treatment related severe toxicities can be fatal. Radiation pneumonitis attributed death occurred in up to 10% of patients treated with concurrent chemoradiation (66 Gy in 33 fractions) and up to 4.3% of patients treated with radiation alone [18].

The patients were pathologically proved to be lung cancer, NSCLC subtype. Adenocarcinoma was the most predominant type in our patients representing 60%. Although through the 1960s, the predominant type of NSCLC was squamous cell carcinoma. In 2002, Giovino stated that adenocarcinoma represents 40% of NSCLC, while squamous cell carcinoma represents 30% and large cell represents 10% [19].

The recent era of applying functional and molecular imaging in diagnosis, treatment and assessment of response, resulted in great change in term of practice and treatment guidelines of different types of cancers [20].

18F-FDG PET is proved to have a dominant role in lung radiotherapy in primary lesion definition, proper localization of involved lymph nodes and differentiation of nearby collapse or consolidation within atelectatic lungs as the exact knowledge of the tumor extension is of crucial importance [21].

Diffusion-Weighted MRI (DWI) is another rapidly evolving functional imaging modality that can be used to evaluate oncologic and nononcologic lesions throughout the body [22].

Tumor tissues are generally more cellular compared with the native tissues from which they originate, and thus they show high signal (restricted diffusion) on diffusion-weighted MR imaging. Fusion images created by the addition of DW-MRI to a conventional T1-or T2-weighted image can improve the detection of small nodes throughout the body [23].

Evidence indicates the superiority of DWI in comparison with PET-CT in both sensitivity and specificity. Usuda et al., conducted a study revealed that the sensitivity and accuracy of DWI was significantly higher than that of FDG-PET in pulmonary nodules and masses and nodal assessment. The advantages of DWI can be explained not only by giving fewer false-positive results but also by giving fewer false-negative results [24].

False negative diagnosis with 18F-FDG PET/CT caused by concurrent lymphadenitis is well known for N staging in patients with NSCLC. It confirmed that DW-MRI has the potential to be a reliable
alternative non-invasive imaging method for the preoperative staging of mediastinal and hilar lymph node in patients with NSCLC, in place of 18FFDG PET/CT for the N staging, especially in hospitals in which MRI examinations can be done and 18FFDG PET/CT examinations are not accessible [28].

CT chest is almost uniformly used to evaluate hilar and mediastinal lymph nodes. The overall accuracy of mediastinal CT scanning was only 80%, resulted in the poor reliability of CT scanning in mediastinal lymph node evaluation [26]. Also lymph node size is the only criterion used to diagnose nodal metastases by CT scan, with nodes greater than 1cm in short-axis diameter considered abnormal [27]. However, lymph node size is not a reliable parameter for the evaluation of nodal metastatic disease in patients with NSCLC as significant lymph node enlargement occurs in the absence of metastatic involvement, 37% of 2-to 4-cm lymph nodes are tumor free and non enlarged nodes may contain tumor deposits, particularly adenocarcinoma [28].

In our study, patients were categorized according to the site of the tumor, tumors present in both lower lung lobes represent 40%, while those present in the upper lobes represent 45% and the rest were in the right middle lobe or RT upper and middle lobes. While out of the 20 patients, 30% of the lung tumors were extending from the hilum to the chest wall, 30% were exclusively central lesions and 40% were peripherally located. Nodal staging among our 20 patients were different in the two modalities, in which on the planning CT scans, 5% had no lymph nodes metastasis, 20% had N1, 50% of the cases were N2 staging and 25% of them were N3. While on the MR diffusion images, 10% had no lymph nodes metastasis, 5% were N1, 65% were N2 stage and 20% were N3.

Application of DW-MRI lead to change in the TNM staging of six patients (6/20) when compared to the CT scans. The change was mainly due to change in the lymph nodal status and to a lesser extent due to decrease in the maximum diameter of the 1ry tumor after avoiding the collapse; in which 3 patients (50%) of them were upstaged in their disease in the form of: 2 patients changed from N1 to N2 and one patient changed from N2 to N3, while another 3 patients (50%) were downstaged in the form of: 2 of them changed from N3 to N2, and lastly one patient changed from N2 to N0. Also one patient changed in the tumor stage from T3 to T2 after exclusion of the collapse.

Due to the great importance of the mediastinal lymph nodes on staging, prognosis and treatment, radiologically positive lymph nodes globally among the 20 patients were observed, in which there were 10 upper mediastinal lymph nodes (up to level 4) on the CT scans versus 8 on the MRI diffusion while 15 positive lymph nodes on the CT in the lower mediastinum (from level 5 down to level 9) versus 16 on the MRI diffusion.

Using the CT images for localizing level 4 (paratracheal) station, 10 cases were found to be positive versus 8 cases in MRI diffusion indicating that 2 cases will receive overtreatment in view of the MR diffusion images criteria when depending on the CT scan alone. This difference was present although statistical analysis in the form of kappa resulted in good measure of agreement for being diagnostic tools among the two modalities. Also regarding level 6 station (para-aortic), 7 cases were diagnosed on CT images while 4 cases only were positive on MR images and hence, statistical analysis didn't show agreement between the two modalities. However, regarding level 7 (subcarinal) station, only 14 cases were diagnosed by CT, while in MR images, it was detected in 15 patients with a good kappa measure of agreement between them. Also, ipsilateral hilar lymph nodes were detected in 16 cases on CT images, while it was detected in 17 cases on MR images with also a good agreement between them. So, the use of MRI diffusion resulted in change in the tumor staging and subsequently affecting the treatment and the radiotherapy decision.

Distinguishing a single station N2 disease from a multiple station N2 disease is crucial as Mario and Brock stated that patients with single N2 zone positivity have a significantly higher survival rate than patients with multiple N2 zones and have a prognosis similar to patients with multiple positive N1 lymph nodes [29]. Seven patients out of the 20 cases had one mediastinal LN in the DWMRI in which 6 of them (86%) had subcarinal LN versus three patients only on the planning CT scan had one mediastinal lymph node and 67% of them were the subcarinal lymph node. This is coinciding with Rusch [30] who stated that among the primary lung tumors that had only a single involved N2 station, the most common site of lymph node metastases was level 4R for right upper-lobe tumors, levels 5/6 for left upper-lobe tumors and level 7 for middle and lower-lobe tumors. On the DW MRI, the ADC value can be considered as a useful parameter to differentiate between the lung cancer and accompanying or nearby post-obstructive consolidation or collapse. In our study, the malignant lesions that were proved pathologically, had mean ADC equals $0.98 \pm 0.22 \times 10^{-3}$ mm$^2$/sec and the ADC min. and
max. were 0.34 and $1.31 \times 10^{-3}$ mm$^2$/sec respectively, while that of the collapse or consolidation had a mean value $1.99 \pm 0.22 \times 10^{-3}$ mm$^2$/sec with the min. and max. values as 1.53 and $2.3 \times 10^{-3}$ mm$^2$/sec respectively. This difference was statistically significant ($p=0.0001$). This coincides with [28] in which lesions were differentiated by using optimal cutoff values for ADC ($1.44 \times 10^{-3}$ mm$^2$/sec) in which lesions below the OCV were considered malignant, while lesions more than it were considered benign.

Yang et al., conducted a study applied on cases with NSCLC aiming at differentiation of central lung cancer from atelectasis comparing the diffusion weighted MRI and PET/CT on 38 patients. PET/CT imaging indicated that tumor masses had more FDG uptake than the atelectasis in all 38 patients, making them easily distinguishable. In contrast, the T1W MR images did not allow differentiation of tumor and atelectasis in any of the 38 patients. Conventional T2W images allowed differentiation of lung cancer and atelectasis in 76% of cases [29,38]. DW-MR images allowed easy differentiation of tumor and atelectasis in all 38 patients, and the tumor had higher signal intensity in all cases. In addition, ADC maps clearly showed that the central lung carcinoma had lower mean ADC [31].

Saraiya et al., conducted a study upon six patients with LA-NSCLC evaluating the ability of diffusion-weighted MRI (DW-MRI) to differentiate atelectasis from active tumor to improve radiation therapy targeting and comparing it to PET/CT based delineation for radiation therapy planning. Patients had undergone DW-MRI and PET/CT prior to radiochemotherapy.

Primary Tumor (PT) and Atelectasis (A) were contoured on ADC maps and PET/CT images. Results of this pilot RTOG study demonstrate that both DW-MRI and PET/CT show significant differences between PT and A [32].

In our study, differentiation of lung collapse and/or consolidation because of utilizing MR diffusion weighted images was found in 14 cases out of the 20 cases in the study while 7 cases only were detected by CT showing statistical significance ($p=0.016$). This is coinciding with [31,32].

**Conclusion:**

So we can conclude that the addition of MRI diffusion sequences to the investigation scheme added a lot to the diagnosis and adequately has the ability of detected the exact tumor volume sparing the normal lung tissue in radiotherapy planning.

Accordingly whole body MR-DWI could be an alternative diagnostic tool image to the standard PET CT as a metastatic work up whenever indicated.

**References**


نتائج استخدام الرنين المغناطيسي عن طريق الانتشار على تقييم أورام الرئة وتخطيط العلاج الإشعاعي

الهدف من الدراسة: الهدف الرئيسي للموضوع هو تقييم دور الرنين المغناطيسي عن طريق الانتشار والعلاج الإشعاعي في تقييم درجات أورام الرئة وإختيار أحمض مختلطة للعلاج الإشعاعي مع إمكانية تشخيص الثانويات في الغدد الليفافية.

الاستنتاج: تدمج الرنين المغناطيسي بخصائص الانتشار في الخطة التشخيصية يستخدم التمييز الفضائي بين النسيج والالتهاب والغدة الرئة مما أدى إلى إعادة تشخيص أورام حسب الحجم وثانيئات الغدد الليفافية.

الاستنتاجات: وقعت أثناء استخدام الرنين المغناطيسي عن طريق الانتشار قدرة على التعرف على الخلايا بين الرئة والالتهاب والغدة الرئة مما أدى إلى اختيار موضوع وحجم نسب للإشارة.