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Learning objectives

The first-line exams in detection of pleural malignant mesothelioma (MPM) remain computed tomography (CT) and biopsy, but recently other imaging modalities, such as magnetic resonance imaging (MRI) and whole body integrated system positron emission tomography (PET)/ computed tomography (CT) with fluorine 18 fluorodeoxyglucose (FDG) have achieved a high grade of accuracy in the staging and for a better characterization of the disease, concerning about the extension and the contours.

Even if PET/CT can be considered "the gold standard" in the staging of MPM, recently MR imaging with supply of diffusion-weighted sequences (DW) and dynamic contrast material-enhanced sequences (DCE), is acquiring a real importance. The purpose of our study was to examine the role of DW imaging in MR in the evaluation of MPM compared to PET/CT, which is considered as the reference standard (RS), before starting previous multimodal treatment. We also intended to verify the concordance between DWI in MR and PET/CT.
Background

MPM is an aggressive neoplasm of mesothelial cell origin that arises mainly from the pleura [1]. The tumor can invade both visceral and parietal pleura and frequently extends to adjacent structures, such as the chest wall, mediastinum, and diaphragm [1]. Lymph node spread and/or metastases to distant organs, such as the lungs, liver, kidneys, adrenal glands, and brain, can occur [1]. The overall survival in MPM is related to the extent of the primary tumor [1]. The majority of MPM cases are associated with asbestos exposure; although MPM was once uncommon, its incidence is increasing worldwide as a result of widespread exposure to asbestos [1,2]. MPM has a very poor prognosis; the median survival after diagnosis ranges between 4 and 18 months [3,4,5]. The major histologic subtypes are epithelial, sarcomatoid and mixed [6]. Imaging plays an important role in the diagnosis and staging of MPM, because biopsy and video-assisted thoracoscopic surgery carry the risk of tumor seeding [7]. A large group of noninvasive imaging modalities such as ultrasonography, CT, PET/CT with FDG and MR is currently used [8].

CT is widely used as the primary imaging modality for the diagnosis, staging and monitoring of therapeutic response in MPM. Typical findings include nodular pleural thickening, unilateral pleural effusion, and tumor invasion of adjacent structures [6].

In the majority of MPM patients, pleural thickening is present as circumferential (rind-like) pleural involvement with multiple nodules [9]. Other most common CT findings are involvement of the interlobar fissures, volume reduction of the chest and homolateral mediastinal shift [10].

CT tends to underestimate early chest invasion, direct mediastinal invasion, and peritoneal involvement and has well-known limitations in the evaluation of lymph node metastases [6]. Contrast-enhanced CT can evaluate the microvasculature of tumors, while its disadvantages, such as high radiation exposure, and side effects from iodinated contrast media, limit its use in both research and clinical settings [6].

Integrated FDG PET/CT is considered the standard technique for the staging of MPM, because it combines metabolic and anatomic information, with a reported sensitivity, specificity, and accuracy in stage IV disease of 93%, 67%, and 83%, respectively [11]. In accordance with low specificity of FDG PET/CT (uptake can be seen in benign inflammatory lesions as well), occasionally the accurate staging of MPM is difficult [12]. Usually FDG PET/CT allows to detect pleural thickenings having moderate and high 18 F-FDG uptake; this value can also be depicted as standardized uptake values (SUV). Gerbaudo et al. describe different patterns of FDG uptake in MPM, which can be present as focal, linear, mixed or encasing distributions of the tracer [12]. Although PET/CT is able to valuate the extension of the pleural disease and to discover distant metastases better than other imaging modalities, it is not particularly accurate in the recognition of lymph nodal MPM metastases.
MR imaging has several advantages over FDG PET/CT. It has better soft-tissue contrast and higher intrinsic flow sensitivity and does not use ionizing radiation [13].

Because of the excellent contrast resolution, MR is superior to CT both in the differentiation of malignant from benign pleural disease and in the assessment of chest wall and diaphragmatic involvement of MPM. [14]. MPM has intermediate or slightly high signal intensity on T1-weighted images (T1-WI) and moderately high signal intensity on T2-weighted images (T2-WI) [15,16,17]. MPM signal is enhanced with the use of gadolinium-based contrast material (Gd-CM) [15,16,17]. MRI findings in MPM include diffuse pleural thickening, pleural effusion, and involvement of adjacent structures. Pleural effusion is frequently observed as focal areas of very high signal intensity on T2-WI [16].

MRI is superior to CT in the differentiation of malignant from benign pleural disease. High signal intensity in relation to adjacent musculature on T2-WI and/or significant contrast enhancement on T1-WI is suggestive of malignant disease [6]. MRI has a high sensitivity and specificity in the detection of pleural malignancy [18]. In addition, contrast-enhanced T1 fat-suppressed sequences are the most sensitive techniques for detecting enhancement of interlobar fissures and tumor invasion of the adjacent structures [19].

DWI has the potential to reveal tissue characteristics based on the diffusivity of water molecules within the tissue. With this technique, signal loss can be quantitatively assessed with the apparent diffusion coefficient (ADC), which depends on the restriction of water molecules diffusion by cell membranes and macromolecules, indirectly providing information about tissue cellularity and also obtaining an ADC map [20,21].

Furthermore, Coolen et al., in a prospective study presented in 2012, reported two radiologic parameters, namely the "shrinking lung" sign (i.e., volume loss of the affected lung) and the newly introduced sign of pointillism (i.e., speckled hyperintensities on diffusion-weighted images, acquired with a high b-value most likely caused by small multifocal deposits of tumors), in patients suspected of having MPM [22]. [Fig. 1,2]
Fig. 1: Figure 1: the upper axial images (right hemithorax) show marginal-costal and pleural thickenings in DWI (b=1000, on the left) and in E-THRIVE sequences after the administration of contrast material (on the right) at the cranial limit of the aortic arch; the lower axial images (right hemithorax) represent marginal-costal and mediastinal pleural thickenings in PET (on the left) and in PET/CT (on the right) at the same level.

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Fig. 2: Figure 2: the upper axial images show apical anterior and posterior marginal-costal and mediastinal pleural thickenings in DWI (b=1000, on the left) and in E-THRIVE sequences after the administration of contrast material (on the right) in the left hemithorax; the lower axial images represent the same anterior and posterior marginal-costal and mediastinal pleural thickenings in ADC map (on the left) and in PET (on the right).

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Findings and procedure details

In our experience it was decided patients, after a CT and histology-based diagnosis of MPM, to perform both multiparametric MR with DWI imaging and PET/CT exams to have a comparison of effectiveness between them.

So the patients previously underwent PET/CT and then MR. Magnetic resonance examination consisted of a standardized protocol, which included multiplanar imaging sequences for the study of chest, such as gradient recalled echo (GRE) T1-weighted sequences, SINGLE SHOT (SS) T2-sequences, SENSE BTFE 2D (Balanced Turbo Field Echo) sequences, DWI sequences and then E-THRIVE sequences before and after intravenous administration of contrast material (Multihance 0,2 ml/kg). Suspicious lesions were detected by radiologists with an experience of over 5 years in reading pleura MRI.

From May 2011 to October 2013, 18 patients (17 males and 1 female; mean age at diagnosis 66,7 years) underwent both DW-MRI and PET-CT for the evaluation of pleural involvement in MPM. Pleural involvement, evaluated both in MRI and in PET/CT, consisted of marginal-costal, diaphragmatic, mediastinal and spread pleural thickenings. Further, for each patient, three different anatomic levels on the axial plane (cranial limit of aortic arch, mitral valve and costodiaphragmatic recess) were considered. [Fig. 3, 4, 5]

The MR exam was performed in a 1,5 T scanner with a sense XL TORSO coil consisting of flexible sixteen channels anterior and posterior sections.

Pleura MRI scanning protocol contemplates:

- Achieva 1,5 T MRI, Philips Healthcare;
- 18 gauge (G) cannula placed in a distal arm vein;
- GD BOPTA (Multihance, Bracco) 0,2 ml/kg; perfusion velocity 2 ml/sec;
- A single scout including the chest;
- Sequences of our protocol:

<table>
<thead>
<tr>
<th>TR (msec)</th>
<th>TE (msec)</th>
<th>Slice thickness (mm)</th>
<th>b values in DWI (s/mm²)</th>
<th>NSA</th>
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</thead>
<tbody>
<tr>
<td>GRE T1-HR IP axial, sagittal and coronal.</td>
<td>Shortest 4,61</td>
<td>5</td>
<td>2</td>
<td></td>
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<tr>
<td>Sequence</td>
<td>Description</td>
<td>Shortest</td>
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<tr>
<td>S4SSh</td>
<td>T2 axial, sagittal and coronal.</td>
<td>Shortest</td>
<td>80, 5, 2</td>
<td>1</td>
</tr>
<tr>
<td>SENSE</td>
<td>BTFE 2D axial, sagittal and coronal.</td>
<td>Shortest</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>DWI 3b RT</td>
<td>axial.</td>
<td>Shortest</td>
<td>5, 0, 100, 750</td>
<td>2</td>
</tr>
<tr>
<td>E-THRIVE</td>
<td>dynamic axial, sagittal and coronal.</td>
<td>Shortest</td>
<td>2,5x2,5x2</td>
<td>1</td>
</tr>
</tbody>
</table>
**Fig. 1:** Figure 1: the upper axial images (right hemithorax) show marginal-costal and pleural thickenings in DWI (b=1000, on the left) and in E-THRIVE sequences after the administration of contrast material (on the right) at the cranial limit of the aortic arch; the lower axial images (right hemithorax) represent marginal-costal and mediastinal pleural thickenings in PET (on the left) and in PET/CT (on the right) at the same level.

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**Fig. 2:** Figure 2: the upper axial images show apical anterior and posterior marginal-costal and mediastinal pleural thickenings in DWI (b=1000, on the left) and in E-THRIVE sequences after the administration of contrast material (on the right) in the left hemithorax; the lower axial images represent the same anterior and posterior marginal-costal and mediastinal pleural thickenings in ADC map (on the left) and in PET (on the right).

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Fig. 3: Figure 3: the axial upper images show mediastinal, marginal-costal and diaphragmatic pleural thickenings at the level of mitral valve in DWI (b=1000, on the left) and in E-THRIVE sequences after the administration of contrast material (on the right) in the right hemithorax; the lower axial images represent the same pleural thickenings in PET (on the left) and in PET/CT (on the right) at the same level.

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Fig. 4: Figure 4: the upper axial images show pleural thickenings at the level of anterior and posterior costodiaphragmatic recess in DWI (b=1000, on the left) and in E-THRIVE sequences after the administration of contrast material (on the right) in the right hemithorax; the lower axial images represent the same pleural thickenings in PET (on the left) and in PET/CT (on the right) at the same level.

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Fig. 5: Figure 5: the axial upper images show mediastinal and marginal-costal pleural thickenings in E-THRIVE sequences (on the left) and in DWI (b=1000, on the right) in the left hemithorax; the axial lower images represent the same pleural thickenings in ADC map (on the left) and in PET (on the right). Additionally in all pictures it is possible to detect a basal posterior loculated pleural effusion and a pericardial nodular thickening localized in the left hemithorax.

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Conclusion

Diagnostic performance of DW-MRI was compared for each level to PET/CT as the RS and the results of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were respectively 98%, 92%, 88% and 90% for DW-MRI respect to PET-CT. Concordance between DW-MRI and PET/CT was also evaluated for each level of pleural involvement with Cohen K coefficient analysis and it was optimal (k 0.88 for upper level, 0.82 for middle level and 0.88 for lower level).

In our study a high concordance between DW-MRI and PET-CT was found. In diagnostic centres, in which PET-CT is not available, MRI with DW sequences could be considered as a valid alternative for chest evaluation in patients with MPM.
Personal information

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References


