The pleura 2.0: Functional imaging and oncology applications

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Learning objectives

1. To introduce the several functional imaging modalities available to study oncological and non-oncological diseases in the thorax.

2. To show the different applications in the evaluation of pleural diseases in general and in Malignant pleural mesothelioma in particular.
Background

Several tumoral characteristics, like metabolism, vasculature or cellularity, can be studied by several imaging methods (Fig. 2 on page 9). The most used widespread and externally validated of them is $^{18}$Fluorodeoxiglucose ($^{18}$FDG) positron emission tomography (PET) - computed tomography (CT) for assessing mainly, but not only, tumor metabolism (Fig. 2 on page 9).

The application of magnetic resonance (MR) based imaging in the thorax, although technically demanding, are gradually more present in the daily clinical practice. Added to the absence of ionizing radiation, one of the major advantages is the possibility of study several neoplastic characteristics at the same time included in one stand-alone protocol (Fig. 2 on page 9). Therefore it allows the integral evaluation of tumoral and non-neoplastic tissues.

1. Anatomy and physiology of the pleura

The pleura (gr. #; side) is a membrane containing a single layer of mesothelial cells. It has two different layers, the parietal and visceral pleura, which are continuous at the hilum and pulmonary ligament (Fig. 3 on page 9). The left and right pleura do not communicate each other and there is a pleural space between the visceral and parietal pleura (1,2).

The visceral pleura is adhered to the lung and lines in fissures whereas the parietal pleura lays lines the inner surface of the chest wall and is separated from the endothoracic fascia by the pleural space (Fig. 3 on page 9).

Ascending thoracic, musculophrenic and intercostal arteries irrigate the parietal pleura whereas the visceral pleura is feeded by bronchial arteries. Bronchial and intercostal veins drain respectively visceral and parietal pleura. Intrapulmonary lymph nodes drain visceral pleura but the parietal layer is drained by intercostal, paraesternal, diaphragmatic and posterior mediastinal lymph nodes (Fig. 3 on page 9)(2).

The pleural space is a virtual cavity which contains a minimal amount of pleural fluid creating negative intrathoracic pressures which helps to maintain inflated the lung during the respiratory cycle (Fig. 4 on page 10). There is a constant equilibrium of production and absorption of pleural fluid, with a mean rate of 0.01 ml/kg/hour, according to the Frank-Starling equation. Also, there is a large reserve of pleural fluid reabsorption ranging from 0.01 to 0.28 ml/kg/hour (Fig. 4 on page 10 ; 1,2).
The parietal pleura is more crucial in the homeostasis of the pleural fluid because in that layer vessels are closer to the pleural surface (10-12 µm) than in the visceral pleura (20-50 µm), and reach higher filtration pressures. Absorption is done by lymphatic stomata located in parietal pleura (1-6 µm) and, in a lesser portion, by venules remaining the rest in the pleural space (Fig. 4 on page 10). A pleural effusion results when there is a disbalance between production and absorption of the pleural fluid. Also, ascitis may migrate from the peritoneum towards the pleural space via diaphragmatic holes (sympathetic pleural effusion)(1,2).

2. Functional techniques for evaluation of pleural diseases

2.1. Diffusion Weighted Imaging (DWI): Technical aspects

In the era of functional imaging DWI by means of the calculation of the Apparent Diffusion Coefficient (ADC) has become a powerful cancer biomarker with prognostic implications. Focusing on the pleura has been related to the evaluation of several oncologic nosologies and its potential pitfalls, with different methods of acquisition and postprocessing (Fig. 5 on page 11)(3).

DWI focuses on the evaluation of brownian motion of water motion in biologic tissues, which has been related to tissue cellularity and architecture. It is based on a modified Single Shot Turbo Spin Echo (SS-TSE) sequence (Stejskal-Tanner) by means of placing several motion probe gradients (MPG) surrounding a 180 degrees pulse of radiofrequency (4-6).

The application in the thorax is technically demanding requiring the application of echo planar imaging (EPI) readout and parallel acquisition strategy (Fig. 5 on page 11). EPI allows the acquisition of the whole k space within one repetition time (TR). The main disadvantage is the presence of geometrical distortion artifact secondary to B0. inhomogeneities. In contrast, parallel technique reduces the acquisition time by means of reducing the echo train length (ETL)(4-6).

One of the main problems to deal with this technique is derived from the macroscopic respiratory motion and heart beat which could difficult its acquisition. Respiratory triggering in the chest is usually preferred compared to breath-holding approach (Fig. 5 on page 11). For avoiding pulsation artifacts cardiac triggering may be useful, especially in small lesions and those located near the heart, although it is not used routinely and it is time consuming.

2.2. DWI: monocompartimental and bicompartimental fitting
**Apparent diffusion coefficient (ADC)** represents the exponential signal decay of a single component of water molecules inside one voxel. It may be calculated by using at least two b values, although the more b values included the more accurate is the calculated ADC. It represents the amount of motion of water molecules so the more static the hipointense the voxel is in the ADC map. In fact, a high ADC corresponds to a steeper slope of the exponential curve (Fig. 6 on page 12).

Recently, *intravoxel incoherent motion (IVIM) model* of diffusion signal decay has been shown to better fit than monoexponential analysis specially in the evaluation of several well vascularized organs such as kidney, liver, pancreas or prostate (3-6). ADC curves have rapid attenuation at low b values (b < 100 s/mm$^2$) due to phase dispersion secondary to bulk motion of water molecules in capillaries. By contrast, at higher b values they show a decrease slope secondary to non-Gaussian movement in tissues (cell membranes, inhomogeneous tissular architecture, etc.) (Fig. 6 on page 12). This model is necessary to differentiate pure molecular diffusion from bulk motion of water molecules in randomly oriented capillaries. By these model, we could define three derived parameters:

1. **Real diffusion of tissue H2O molecules (D):** uninfluenced by movement of water molecules within the capillaries.

2. **Perfusion contribution to diffusion signal (f):** fractional volume of flowing water molecules within the capillaries.

3. **Perfusion contribution to signal decay (D*)** of the amount of non-diffusional random movements of water molecules.

IVIM derived parameters are, theoretically, more reliable markers of tissue diffusivity than ADC. A correlation has been described between intravascular tracer and IVIM parameters (blood volume with f and blood flow with D* (Fig. 6 on page 12).

**2.3. Perfusion weighted MRI (DCE-MRI)**

**Tumor angiogenesis** is essential for the development and behavior of solid tumors. Angiogenic factors affect vasculature formation, growth pattern and vascular permeability. Also modulate host response and influence tumor invasion, development of metastases and prognosis (7).
DCE-MRI is a non-invasive functional imaging technique which provides information of tumor physiology and sensitive to blood flow, vascular volume and permeability. It is measurable obtaining potential imaging biomarkers of tumor angiogenesis (8).

Most commonly free breathing, high temporal resolution, 2D or 3D Gradient Echo (GE) sequences acquired during a 5 minutes period of time. They have limited coverage and the use of parallel techniques in it acquisition is mandatory. However, due to difficulties in obtaining a robust and reproducible technique, its implementation in daily clinical practice has been limited. In fact, motion and respiratory artifacts are common problems that require the use of motion correction software (8,9).

The description of the shape of time intensity curves (TIC) are the mainstay of the qualitative analysis of DCE-MRI. Several curve descriptors are used to classify TICs, like:

- **Contrast arrival time**: time when contrast arrive to a pixel
- **Time to peak**: time to a maximum signal intensity
- **Area under the curve (AUC)**: integral of the contrast concentration time curve for a specific time interval

The curve shapes are similar to those physiological parameters obtained from compartmental models, except that does not separate perfusion and permeability. This is the most common approach used in clinical practice.

Quantitative or parametric models are based on the use of compartments, defined as a space where the trace is evenly distributed. There ar two different models described in the literature:

1. **Monocompartmental model (Tofts model)** (Fig. 7 on page 13)
2. **Bicompartimental model** (Fig. 8 on page 14)

K\text{trans} does not measure pure capillary permeability. Its changes with treatment and represents a number of different physiological processes. Lack of standardization of models applied and sequence design have prevented them to be introduced in the clinical setting.

### 2.4. Perfusion computed tomography (PCT)

Another way to evaluate tissue and organ vascularization is by the administration of low molecular weight contrast (<1kDa) and evaluation of its passage by MDCT (}
Fig. 9 on page 15). Because of practically absence of binding to serum proteins, low molecular weight contrast has an extracellular distribution, with passage between intravascular and extravascular/extracellular compartments (brain, kidney and testis). This intercompartmental flow has been related to (1) rate of tissue delivery, (2) vessel surface area and (3) vascular permeability (10,11).

Qualitative evaluation could be done by means of time-density curves and quantitative analysis could be assessed according to the kinetic model used. In that way, several parameters could be defined:

1. **Regional blood flow (BF)**: correspond to the flow rate of blood through the target lesion vasculature and, therefore, the delivery of oxygen and nutrients (Fig. 9 on page 15).
2. **Regional blood volume (BV)**: it is the volume of flowing blood within the target lesion vasculature. It’s related to tissue vascular density (Fig. 9 on page 15).
3. **Permeability surface area (PS)**: product of permeability and total surface area of capillary endothelium volume/mass. Is equivalent to vascular leakage capillaries and neovessels (Fig. 9 on page 15).

Relationship between DCE-MRI and PCT has been evaluated in the literature, being the latter more reproducible (14-24% of variation in tumors). In fact, a more clear relationship between contrast concentration and derived quantitative parameters has been described in PCT rather than DCE-MRI (10).

The main disadvantage of this technique is the radiation dose related to the procedure. A maximum effective dose of 20 mSv for a volume of 4 cm in cranio-caudal orientation should not be exceeded (10).

2.5. 18FDG-Positron Emision Tomography/Computed Tomography (FDG-PET/CT)

It is a hybrid equipment combination of the morphological (CT) and functional information (PET) of physiological and pathological process. PET depicts spatial distribution of positron emissary biomarkers and tumor metabolic activity. A PET radiotracer is a substance that contains a radioisotope for detection and measurement and is combined with a biologically active molecule (carrier) (Fig. 10 on page 16). The carrier determines de distribution in the body and location in a specific metabolic pathway (12).

The data obtained could be analyzed qualitatively, by the detection of areas of increased uptake other than physiologically tracer accumulation, or quantitatively, by means of
standardized uptake value (SUV) (Fig. 10 on page 16). SUV is an index of tumor uptake normalized to injected activity and body distribution (body weight). Usually the maximum SUV (SUVmax) in a region of interest is calculated (13).
### Images for this section:

![Table and diagram](health-time.png)

#### Fig. 2

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**Fig. 3**

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Fig. 4

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**SINGLE SHOT EPI SEQUENCE**

**Recommended sequence**

- Single Shot Spin Echo EPI; 3 orthogonal motion probing gradients
- Phased array Surface Coil; Respiratory triggered
- b-values: 0, 50, 100, 500, 1000 s/mm²
- FOV: 320–400, **Pixel resolution** 2.5x2.5x7 mm³
- **Parallel Imaging** acceleration factor of 2: Spectral Fat Suppression
- **Number of Slices**: 24; **TR**: 5000 ms; **TE**: 53 ms (shortest)

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**Synchronization on chest DWI.** Five different approaches under different strategies of motion compensation of the same DWI sequence are shown, using the same b value (300 s/mm²) at a 3-T magnet, in a patient with **SCLC** (Small Cell Lung Cancer).

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**Fig. 5**

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**Fig. 6**

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Quantitative analysis:

**Monocompartmental model: Tofts model**

- Compartment: space where the tracer is evenly distributed.
- Monocompartmental Model (Tofts):
  - Account the tracer in the vasculature.
  - Measurements directly from signal intensity quantification.
- Increased tumor angiogenesis → associated with a specific time intensity curve pattern (fast wash-in and washout: type III > II).
- Considerable variation between acquisition method and individual examinations → not appropriate for comparison. No clear physiological basis.
- Unlike CT perfusion, the relationship between signal intensity and contrast agent concentration is not linear, making conversion of the signal intensity data far from straightforward.

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**Fig. 7**

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Quantitative analysis:

**Bicompartmental analysis**

- Two different compartments: Blood plasma (P) and extravascular-extracellular (E):
  1. P and E are compartments
  2. E no exchange tracer with environment
  3. Clearance P = Clearance E
  4. Clearance P to the environment = plasma flow

- Leakage of contrast from P to E and vice versa:
  1. $K^{trans}$, transfer rate of blood from P to E
  2. $K^p$: transfer rate of blood from E to P
  3. $V_e$: Volume of E inside the voxel
  4. $V_p$: Volume of P inside the voxel

- $K^{trans}$ does not purely measure capillary permeability. Its change with treatment represent a number of different physiological processes.

- Lack of standardization of the models applied and sequence design have prevented them to be introduced in the clinical setting.

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**Fig. 8**

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Fig. 9

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Fig. 10

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Malignant pleural mesothelioma (MPM)

*Malignant pleural mesothelioma* is a rare, locally aggressive and potentially lethal neoplasm originating from the mesothelial cells of pleura, pericardium or peritoneum. The described prevalence in the USA is of 2000 - 3000 new cases/year and has been related to asbestos exposure (40-80%; incidence of MPM of 10%) (14).

Three types have been described: *epithelioid* (55-65%), *sarcomatoid* (10-15%) and *biphasic or mixed type* (20-35%; at least 10% of both epithelioid or sarcomatoid) (Fig. 11 on page 26). Due to its asymmetric morphology, by means of coalescence of pleural nodes and plaques, non-spherical and non-compact growth, it is difficult to stage and follow up (Fig. 11 on page 26). In fact, adequate assessment of resectability is capital for treatment selection and survival rate (14).

*18FDG-PET/CT*, by using a threshold **SUV of 2.2**, has excellent performance in differentiating benign versus malignant pleural lesions, giving an adequate guidance for target lesion biopsy (Fig. 12 on page 26). The typical appearance is of a moderate to high radiotracer uptake involving areas of thickened pleura. It depends on histologic subtype, being less metabolically active those epithelials compared to sarcomatoid or mixed subtype (3).

Based on dual phase PET/CT, early and advanced disease could be differentiated based on the patterns and kinetics of *18FDG* uptake. Hybrid *18FDG-PET/CT* systems have been reported great utility in delineating chest wall invasion, differentiation of tumoral tissue from lung atelectasis and in the detection of suspected extratoracic metastasis (15). Despite rises are higher in MPM than in normal lung and in stages IV than in less extended disease, fair accuracy is seen in the detection of lymph node metastasis (15).

Although CT is the primary technique for diagnosis and staging MPM, frequently **chest MR** is been used in the initial evaluation as a problem solving modality. The most frequent manifestation of MPM is a pleural effusion, focal or diffuse pleural plaques with/without interlobar fissure extension, affection of mediastinal pleura and growth gradient from the diaphragm to the apex. In advanced stages, loss of volume of one hemithorax could be seen ("shrinking lung sign"). The pleural plaques are iso-hyperintense on T1 weighted images (T1WI) and moderately hyperintense on T2 weighted imaging (T2WI) (1,2).
Infiltration of adjacent structures favours malignancy, although some infections (actinomycosis, nocardiosis, tuberculosis) could present this feature (empyema necessitatis), being in those situations focal rather than multifocal (Fig. 13 on page 27)(16).

By using a threshold ADC value of $1.56 \times 10^{-3}$ mm$^2$/s, DWI has been shown similar sensitivity and specificity than $^{18}$FDGPET/CT for differentiating benign vs malignant pleural diseases (Fig. 12 on page 26). Also it allows the reduction of false positives results seen with $^{18}$FDGPET/CT (inflammatory pleuritis, talc pleurodesis and tuberculous plaques, etc.)(17,18). DWI shows diffuse hyperintense focal spots at high b values with corresponding low ADC indicating restrictive tissue diffusivity ("pleural pointilism sign") (Fig. 14 on page 28)(19). Significant differences have been described in the ADC between different MPM subtypes (epithelial vs sarcomatoid type; $1.31\pm0.15 \times 10^{-3}$ mm$^2$/s vs $0.99\pm0.07 \times 10^{-3}$ mm$^2$/s; p<0.005, respectively). There is a wide overlapping with mixed subtype (15).

Although bicomartmental analysis of DWI (IntraVoxel Incoherent Motion; IVIM) is feasible in the thorax, there is sparse data regarding the evaluation of chest malignancies. Its utility has been described in order to yield the differentiation of central lung tumoral masses from postobstructive pneumonitis (20). There is no report in the literature regarding the evaluation of pleural lesions (Fig. 16 on page 30). This fitting takes into consideration the fast initial loss of signal due to microvascular perfusion (perfusion fraction; f) and separates from the true diffusivity (D) being, theoretically, more tissue specific (6).

Adding DCE derived parameters (Cpeak > 1.5; initial slope (IS) > 6 arbitrary units per second [au/s]) differentiation of benign vs malignant pleural lesions is improved by means of reduction of false negatives of DWI (intratumoral necrosis and inflammation) (Fig. 12 on page 26; Fig. 15 on page 29). Also has better performace than CT in the differentiation of mediastinal, transdiaphragmatic, chest wall invasion and fissural extension of MPM (Fig. 15 on page 29)(17,18).

**Initial staging and treatment selection**

**Stagging system:**
Fig. 17

References: MR Unit, RESSALTA - Córdoba/ES

Treatment:
**Fig. 19**

**References:** MR Unit, RESSALTA - Córdoba/ES

**Follow up method:**
High elevated uptake of $^{18}$FDG uptake in MPM has been linked with unfavourable prognosis, with shortening of the cumulative survival rate (Fig. 17 on page 31; Fig. 18 on page 32; Fig. 19 on page 33; Fig. 20 on page 34).

$SUV_{\text{max}}$ has been described as a prognostic marker as long as histologic subtype, metastasis nodal status, presence of distant metastasis and elevated tumor growth markers (Fig. 22 on page 36; Fig. 23 on page 37). Consequently, overall survival is lower in patients with high $SUV_{\text{max}}$, elevated $SUV_{\text{mean}}$, $SUV_{\text{peak}}$ and total glycolitic volume (15).

Regarding histologic subtype, rising of PET derived parameters in epithelioid MPM has been related with poorer overall survival. $^{18}$FDG-PET/CT has an important role in the radiotherapy planning, in order to achieve higher doses on avid $^{18}$FDG uptake regions in patients without extrapleural pneumonectomy (EPP) (Fig. 24 on page 38) (15).
4. Metastatic pleural disease

Metastatic pleural disease is the most common cause of malignant pleural thickening (21). The most frequent origin is metastatic lung cancer (40%) following by breast (20%), lymphoproliferative disorders (10%), gastric and ovarian neoplasms (5%) (Fig. 25 on page 39). Lymphoma usually presents as a recurrent disease of contiguous extension whereas sarcomas rarely metastasize unless surgical intervention of lung nodule (seeding metastasis). Drop metastases are usually seen in invasive thymoma and thymic carcinoma (21).

In both DCE-MRI and DWI, metastatic pleura will manifest as multiple nodules or plaques with significant gadolinium uptake and restriction in DWI sequences in a patient with a known primary tumor (Fig. 25 on page 39). In the same way, $^{18}$FDG-PET/CT will show significant radiotracer uptake indicating metabolically active tumoral cells (Fig. 26 on page 40).

5. Solitary fibrous tumour of the pleura (SFTP)

STFP is a rare (less than 5% of pleural tumors), slow growing tumor of the pleura which arises from the mesenchimal cells of the visceral pleura (80%) (Fig. 27 on page 41)(22-24). Although usually asymptomatic, the onset and type of symptoms is usually related to tumor size, being frequently observed in lesions over 16 cm. Due to intratumoral expression of insulin like growth factor II (ILGF-II) they also could present with hypoglycemia in up to 4% of the patients (23).

It represents a smooth lobulated and well-defined mass which abuts the diaphragm mimicking an elevation of it in chest X ray. Tumoral mobility has been described secondary to the presence of a pleural stalk connecting the lesion to the pleura (Fig. 27 on page 41).

Non-malignant SFTP constitutes a well-known pitfall of MPM mesothelioma in $^{18}$FDG-PET/CT as it demonstrates significant radiotracer uptake (false positive) (22-24).

6. Benign pleural plaques

Pleural plaque is a thickening of the parietal or visceral pleura. They are associated to benign entities such as exposure to asbestos, previous pleural tuberculosis or talc
(dense). Some of them may calcify. They are the most common manifestation of asbestos exposure (latency period 20-30 years) (21).

They are composed of dense hyaline collagen within mesotelial layers of the parietal pleura. MR better detect pleural thickening, extrapleural fat hypertrophy and effusions. Contrarily, CT better depicts pleural calcification. $^{18}$FDG-PET/CT usually has false positives in the characterization of benign pleural plaques due to chronic inflammation. Some examples of these false positives are: pleural TBC, benign inflammatory pleuritis, benign asbestos related pleural plaques and parapneumonic effusion (Fig. 28 on page 42)(21,25).

**DWI and DCE MRI** could adequately depict the benign nature of those lesions, reducing the false positives of $^{18}$FDG-PET/CT (Fig. 28 on page 42). A non-restrictive pleural plaque (Fig. 29 on page 43), that is hipointense on high b values and hiperintense on ADC maps, and non-enhanced or slowly enhanced lesion on DCE-MR (Fig. 30 on page 44) should go along with a pleural plaque of benign origin (21,25).

7. Pleural effusions

Pleural effusions are secondary to an imbalance of the normal homeostasis of pleural liquid production and absorption. Different differential diagnosis and management regarding the type of pleural effusion: exudative versus trasudative (26,27). That's why is so important to accurately assess the type of pleural effusion.

*Exudative pleural* effusions are secondary to an increase in capillary permeability. They are seen in malignancy, infection or thromboembolic disease. Contrarily, *transudative pleural effusions* are due to rise in hydrostatic pressure or decrease of oncotic pressure.

A **DWI threshold value** (ADC: $3.38-3.6 \times 10^{-3}$ mm$^2$/s) has been described in order to differentiate between them, with 71% and 63% of sensitivity and specificity, respectively (Fig. 31 on page 45) (26-29).
Exudative pleural effusions: increase in capillary permeability → malignancy, infection or thromboembolic disease.

Transudative pleural effusions: rise in hydrostatic pressure or decrease of oncotic pressure.

**DWI threshold value** (ADC: 3.38-3.6 x 10⁻³ mm²/s) could differentiate between them with 71% and 63% of sensitivity and specificity, respectively.

**Fig. 31**

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Fig. 11

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**Fig. 12**

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Infiltration of adjacent structures favors malignancy but some infections (actinomycosis, tuberculosis or nocardiosis), can also invade chest wall (empyema necessitatis). The pattern of benign chest wall invasion is focal rather than multifocal.

Fig. 13

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• Note the presence of multiple hyperintense pleural spots on high b value DWI images → **pleural pointillism**

• Significant **differences in ADC** between different MPM subtypes (epithelial vs sarcomatoid type = $1.31\pm0.15 \times 10^{-3} \text{ mm}^2/\text{s}$ vs $0.99\pm0.07 \times 10^{-3} \text{ mm}^2/\text{s}$; $p=0.005$).

• There is some overlapping with biphasic MPM.

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**Fig. 14**

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**Fig. 15**

*Dynamic contrast enhanced MRI (DCE-MRI) showing a hипervascular pleural plaques, with acute initial slope and maintained enhancement compared to paravertebral muscle (TIC type II), suggesting malignant origin.*

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Fig. 16

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Fig. 17

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Fig. 18

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Fig. 19

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### MPM: Treatment selection and follow up

| Surgical treatment (Sx) | EPP (complete resection) | 1. Epithelial histology
| | P/D (lung sparing) | 2. Early stage disease (I;II)
| | | 3. NO
| | | 4. Adequate functional state
| Poor prognostic factors* → P/D | |
| Unresectable disease → Debulking: ↓ symptoms & ↑ pulmonary reserve |

#### Chemotherapy (ChT)

- **1st line** Cisplatin + Pemetrexed (Cp+P)
- **2nd line** Gemcitabine and Vinorelbine ± Cisplatin (G/V ± Cp)

*Combination ChT:* - improved median survival time (12.1 vs 9.3 months; p=0.02)
- longer median time to disease progression (5.7 vs 3.9 months; p=0.001)

#### Radiotherapy (RT)

- **Prophylactic radiation:** not supported
- **Palliation:** risk contralateral lung toxicity
- **IMRT:** Adjuvant therapy post-surgery: 45Gy in 25 fractions in multiple beams
  - Inclusion of preoperative pleural surface, ipsilateral lymph nodes, retrocrural space & deep margin thoracotomy
  (IMRT: **Intensity – modulated radiation therapy**)

#### Targeted therapy

- Erlotinib/Gefitinib: low results (↓ mutations of EGF)
- Vatalanib/Sorafenib: VEGF tyrosine kinase inhibitors; promising results

**MPM expression:** - Epidermal Growth Factor (EGF)
- Vascular endothelial growth factor (VEGF): independent prognostic factor in MPM
- Platelet-derived growth factor (PDGF)
- Transforming growth factor 8 (TGF-8)

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**Fig. 20**

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### MPM: Treatment selection and follow up

| WHO RECIST 1.0 | Up to 5 measurable lesions |
| RECIST 1.1 | Up to 5 lesions per organ (up to 10) |
| Mesothelioma specific modified RECIST | Up to 2 lesions per organ (up to 5) |
| | Tumor thickness at 2 positions at 3 separate CT sections; ≤ 6 target lesions |

#### Targeted Lesions

- **Complete response (CR):** Disappearance all target lesions
- **Partial response (PR):** ≥ 30% decrease in the sum of the longest diameters of target lesions
- **Progressive disease (PD):** ≥ 20% increase in the sum of the longest diameter of target lesions compared with the smallest sum of longest diameter recorded or new lesions
- **Stable disease (SD):** No neither PR nor PD

#### Non targeted lesions

- **CR:** Disappearance of all non targeted lesions
- **Incomplete response; SD:** Persistence 1/more target lesions or persistent tumoral markers
- **PD:** 1/more new lesions

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**Fig. 21**

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Patient with Pancoast tumor. Dynamic contrast enhanced CT pre and post-chemoradiation therapy showing a significant functional change in neoplastic behavior during follow up (decrease in blood flow, blood volume and surface permeability), compatible with response, and comparison with $^{18}$FDG-PET/CT, which also shows a complete response. Notice that on CT tumor shows a similar appearance before and after treatment.

**Fig. 22**

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Fig. 23

73 year-old patient with advanced stage epithelioid mesothelioma located in left lower lobe with metastases in left adrenal gland and right major trochanter. After chemotherapy (Pemetrexed + carboplatin) showed reduction of the radiotracer uptake in the primary tumor, consistent with partial metabolic response, but other de novo metastatic lesions appeared in left pleura and sixth rib.

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Fused $^{18}$FDG-PET/CT (left) and non-fused PET (right) of a patient with malignant pleural mesothelioma showing, initially (April 2011) several nodules with significant radiotracer uptake, in keeping with the known diagnosis, the major of them is located on right mediastinal pleura (SUVmax: 7.67; yellow arrow). Left subcarinal (SUVmax: 2.35) and right paratracheal (SUVmax: 2.5) metastatic lymph nodes (blue arrows; stage N3).

Note with the subsequent surveillance (Sept 2011 & April 2013) the progression of the pleural disease (green arrows) with invasion of right pectoral muscle on the last follow up (SUVmax: 8.7) and metastatic lymphadenopaties present in previous studies (right paratracheal, SUVmax: 8.4; red arrows) and in other nodal stations (right supraclavicular, paraesophageal, retrocrural, red arrows).

Fig. 24

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Fig. 25

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Fig. 26

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Fig. 27

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Fig. 28

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Pitfalls: Tuberculous (TBC) and non - TBC pleuritis

The pleural plaque is hyperintense on ADC map revealing the absence of restriction and favoring the in keeping diagnosis of **benign pleural plaque** related to **old healed granulomatous disease** (red arrow). On DWI while increasing the applied b values a progressive signal decay of the pleural plaque is noted. On high b values (b = 900 s/mm²; White arrow), it shows absence of signal.

**Fig. 29**

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DCE-MRI shows a low grade and progressive enhancement of the apical pleural plaque, with slow initial slope and progressive enhancement compared to paravertebral muscle, confirming a benign origin.

Fig. 30

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Fig. 31

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Conclusion

1. ALTHOUGH CT CONSTITUTES THE PRIMARY IMAGING MODALITY FOR THE EVALUATION OF PLEURAL DISEASES, FUNCTIONAL TECHNIQUES SUCH AS $^{18}$FDG-PET/CT AND MRI ARE GAINING INCREASING IMPORTANCE.

2. FUNCTIONAL TECHNIQUES PRODUCE VALUABLE INFORMATION REGARDING DIAGNOSIS AND STAGING OF MALIGNANT PLEURAL MESOTHELIOMA AND MAY HELP IN MONITORING THERAPEUTIC RESPONSE AND IN THE DETECTION OF RECURRENTNESS.

3. MRI FUNCTIONAL TECHNIQUES HAVE THE ABILITY TO DIFERENTIATE BENIGN VS MALIGNANT PLEURAL LESIONS. FUNCTIONAL MRI CAN BE USED AS A SECOND LINE TEST IN ORDER TO CLARIFY POTENTIAL PITFALLS OF $^{18}$FDG-PET/CT OR AS AN ALTERNATIVE TO THIS TECHNIQUE.

4. MRI CAN ANALYZE MULTIPLE TUMOR CHARACTERISTICS USING MORPHOLOGICAL AND FUNCTIONAL (DWI AND DCE-MRI) SEQUENCES IN A STAND-ALONE PROTOCOL.
References

Bibliography


Personal Information

I hope you have enjoy the exhibit.

See you next ESTI. Enjoy!!!

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