CT features of pleural mesothelioma in a large patient group: differential diagnosis from others pleural based on results of video-assisted thoracoscopic surgery

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Purpose

Pleural mesothelioma is a rare malignant neoplasm correlated to the asbestos exposition with a poor prognosis of approximately 12 months after the first radiological or histological diagnosis. Chest Computed Tomography represent the first, and maybe the most important, radiological technique which allow the recognition and the diagnosis of a malignant pleural thickening. This ensure its high spatial and contrast resolution combined to good territorial distribution. Unfortunately malignant mesothelioma is a pathology that presents several radiological signs which are common with others pleural diseases that can mime the presence of pleural mesothelioma.

Development of more performing multislice CT-Scanners allow radiologist to reduce scanning time, to reduce movement artifacts and to increase spatial resolution of the exams. Meanwhile fine multiplanar reconstructions allow to recognize exactly the extension of the mesothelioma shown the infiltration of surrounding thoracic and mediastinic structures for a better pre-operative staging and planning.

In our geographic area, the presence of an intense shipbuilding activity causes a progressive increase of pleural mesothelioma incidence during last 10 years. Consequently this cause an increased number of requests for radiological examinations in order to confirm or exclude the presence of malignant pleural mesothelioma.

In this study we reviewed TC imaging of a large selected population of 152 patients coming to our department with the clinical and/or radiological suspect of malignant pleural disease.

The aim of the study was to describe the different features in CT-imaging of different pleural mesothelioma subtypes and different pleural pathology that can mime pleural mesothelioma.
Methods and Materials

During period of 4 years (2006-2010) 209 patients (176 male and 33 female; mean age of 70+-10) were referred to our hospital for suspected pelural mesothelioma based on previous chest x-ray. Including criteria for a CT-imaging confirmation was the presence of a diffuse or focal pleural thickening at the x-ray-imaging, or the presence of pleural mass or massive unilateral pleural effusion. 152 of those patients (132 male and 20 female; mean age 71+-10) underwent a Chest-CT before istological biopsy confirmation that was performed from 1 week to 1 month after CT-scan with a VATS procedure or a CT-guided biopsy.

The CT-images are retrospectivelly evaluated with the purpose of recognise and define the prevalence of different radiological signs and correlate them with final histological diagnosis.

Scanning prothocol:

All patients underwent at least one CT exam before istological confirmation or surgical procedure (when surgical approch was possible).

Chest-CT studies were obtained with two different CT-scanners.

132 patients were examinated with a 64-detectors CT scanner (Aquilion 64; Thoshiba Medical System, Tokyo, Japan) and 20 patients were scanned with a single slice CT scanner (TomoScan AV1, Philips Bothell, USA).

Standard volumetric CT acquisition was performed before and after the injection of non-ionic iodine contrast agent followed by the injection of saline chase. The contrast medium and the saline were injected using a power injector (Stellant CT Injection system; MEDRAD; Pavia Italy) through a 16 gauge IV cannula into an antecubital vein.

Standard volumetrical scan parameters were as follows: FOV 400mm, 1mm slice thickness, recostruction interval 0.5mm, 0.5 sec gantry rotation speed, pitch factor 0.969. The tube voltage was set at 120kV and current set at 150mA with Z-Axis dose modulation enabled.

High resolution volumetrical scan parameters were as follows: FOV 400mm, 1mm slice thikness, recostruction intervall 0.5mm, pitch facton 0.626. The tube voltage was 100-120kV and the current set at 150mA with Z-Axis dose modulation enabled.
Hight resolution volumetrical scans are alwayy performed without contrast medium injection and followed by a standard volumetrical acquisition after the injection of contrast medium.

In the patients that underwer more than one CT-exam we consider the last scan before VATS or CT-guided histological confirmation.

**Image analysis:**

Full volume dataset: (0,5 mm native stack images), were retrospectively reloaded from PACS system (Esaote DICOMed PACS; Esaote, Genova, Italy), to advanced visualization console (Vitrea, version 3.1.1; Vital Images, Plymouth, MN, USA); for images analysis. The images were analyzed by two radiologist with different chest imaging experience (2 and 5 years).

Refering on pleural disease literature 20 CT signs most correlated with the presence of malignant mesothelioma were considered and evaluated for each patient. [21,28,29,30,31,36,37]

In particular we considered:

1) Pleural focal or diffuse thickening > 2mm
2) Pleural focal thickening > 1cm
3) Diffuse irregular pleural thickening
4) Nodular solid pleural thickening
5) Global circonferrential thickening with encasement
6) Mediastinic pleural thickening
7) Presence of pleural plaque <1cm thick and with smooth surflace
8) Presence of pleural calcium deposit into the pleural plaque
9) Presence of pleural calcium deposit into pleural thickening or pleural mass
10) Presence of unilateral pleuric effusion
11) Presence of pleuric mass with major diameter of at least 3cm
12) Contrast enhancement after the injection of iodine contrast medium
13) Scissural pleuric involvement
14) Loss of volume of involved emithorax
15) Thoracic wall involvement with muscular infiltration
16) Diaphragm involvement with muscular infiltration
17) Mediastinal neoplastic infiltration
18) Ribs neoplastic infiltration
19) Vertebral neoplastic infiltration
20) Presence of mediastinal lymph nodes > 1cm
Results

We have divided our patients (n=209) by the final histological results. We divided patients into two groups: Mesothelioma affected patients (n=109) and others non-mesothelioma affected patients (n=100) including benign and malignant pleural diseases.

We also divided the mesothelioma affected group into three different histological subtypes as Epithelioid Mesothelioma (n=92), Sarcomatoid Mesothelioma (n=4) and Biphasic Mesothelioma (n=13).

TABLE 1 on page 11

<table>
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<tr>
<th></th>
<th>Mesothelioma</th>
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<td>70,7</td>
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</tbody>
</table>

Fig.: Our patients dataset: We have divided our patients (n=209) by the final histological results. We divided patients into two groups: Mesothelioma affected patients (n=109) and others non-mesothelioma affected patients (n=100) including benign and malignant pleural diseases.

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Other patients (n=100) present several pleural disease with different pleural histological diagnosis. In particular there was n=2 Colic adenocarcinoma metastasis; n=2 undifferentiated renal cell carcinoma metastasis; n=5 lung adenocarcinoma; n=1 bronchial alveolar cancer; n=1 chondromatosis amartoma; n=1 aspergilliosis; n=1 small cells lung carcinoma; n=2 neuroendocrine carcinoma; n=1 undifferentiated lung cell carcinoma; n=7 squamous cell lung carcinoma; n=1 retro-mediastinal cysts; n=1 elastofibromas; n=20 chronic pleuritis; n=1 fibrosarcomas; n=1 pleural malignant fibrous tumor; n=1 mycobacterial granulomatous flogosis; n=1 focal lymphocytes thickening; n=2 fibrosis; n=1 silicosis; n=2 Hodgkin lymphomas; n=2 breast adenocarcinoma metastasis;
n=1 fibroblastic fibro-hemorrhagic pleuritis. In others 43 cases the biopsy was negative for any pluralical pathology.

**CT-Images analysis:**

As described 152 patients of 209 underwent a CT-scan before the VATS-biopsy. 80 of those were mesothelioma affected confirmed by the histological results, while 72 of those are non-mesothelioma affected.

The distribution of the 20 selected CT-features was as followed:

Some CT-features are significantly correlated with histological mesothelioma diagnosis.

In particular we recognise that irregular pluralal thickening was present in n=31 patients (36,90%), multiple or single nodular pleural thickening was present in n=24 patients (28,57%), Mediastinic pleural thickening was present in n=44 patients (52,38%) and focal or diffuse pleural thickening more than 1cm was present in n=32 patients (38,1%).

Those 4 CT-parameters were correlated to the malignancy of the pleural lesion (P<0.05).

Contrariwise Irregular pleuric thickening, nodular thickening mediaticnic pleura thickening and pleural thickening > 1cm are recognisable only in 9,33%, 1,33%, 8% and 5,33% of others plural patohtologies and don’t reach statistic significativity (P>0.05)

Pleural thickening enhancement after the intravenous injection of iodine contrast medium was present in 30 patients with histolocical diagnosis of malignant mosothelioma (35,71%) (P<0.05) and in 3 patients with other plural pathologies (4%) (P>0.05).

The presence of circonferrential pleural thickening with lung parenchima encasement, that is considered in the literature as the most specific radiological sign for the malignant mesothelioma diagnosis in our study was present only in 14% of patients with histological diagnosis of mesothelioma. (P>0.05)

Other CT-signs results aspecific for the diagnosis of mesothelioma. Expecially unilateral pleural effusion that was present in 80,95% of mesothelioma group and 72% of other pluralar disease group.

**TABLE 2** on page
Fig.: 152 patients underwent a CT-scan before the VATS-biopsy. 80 of those were mesothelioma affected confirmed by the histological results, while 72 of those are non-mesothelioma affected. The distribution of the major 20 selected CT-features was as followed:

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We have also search for a correlation between pleural CT-signs and the three different mesothelioma histological sub-types: Epithelioid Mesothelioma (n=92), Sarcomatoid Mesothelioma (n=4) and Biphasic Mesothelioma (n=13).
Epithelioid Mesothelioma presents an higher frequency of mediastinic pleural thickening (n=40; 57,14%) such as mediastinal infiltration (n=8; 11,43%) in comparision to sarcomatoid and biphasic mesotheliomas (n=4; 28,57%9) and (n=1; 7,14%).

There's also a relevant difference between the histotipes in therms of Scissural pleuric thickening that was more frequent in epithelioid types (n=19; 27,14%) than biphasic or sarcomatoid type (n=1; 7,14%). Also mediastinal node involvment is more frequent in epithelioid hystotipe present in n=33 patients (47,14%) in comparasion to sarcomatoid ones (n=3; 21,42%).

In sarcomatoid and biphasic is very frequent one or more than one pleural mass with maximal axial diameter more than 3cm (28,57%) in comparasion to the epithelioid types that have more frequently pleuric circonferential thickening expression (n=12 17,14%).

Other frequent expression of the sarcomatoid mesothelioma was thoracic wall involvement (n=4; 28,57%), emotorax loss of volume (n=4; 28,57%) and ribs neoplastic infiltration with bone erosion (n=3; 21,42%). Meanwhile in the epithelioids histotypes those expressions are less frequent (n=9; 12,85% - n=11; 15,71% - n=6; 8,57%)

TABLE 3 on page 11
Fig.: Epithelioid Mesothelioma (n=92), Sarcomatoid Mesothelioma (n=4) and Biphasic Mesothelioma (n=13). This table show the distribution of selected CT-features in Epithelioid Mesotheliomas and in Sarcomatoid and biphasic mesotheliomas.

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**Fig. 0:** 68 yo patient with Epithelioid Mesothelioma present massive pleuric effusion on the left emithorax with pleural thickening

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Fig. 0: 70 yo patient. Coronal reconstruction. Massive left pleural effusion with irregular pleuric mass.

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Fig. 0: 71 yo Patient with epithelioid mesothelioma. Diffuse pleurar thickening that involve scissural pleura and right emithorax loss of volume.

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Fig. 0: 76 yo patient with epithelioid mesothelioma. Circumferential pleural thickening with scissural involvement and basal pleural effusion

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Fig. 0: 69 yo patient with mesothelioma. Pleuric focal mass pattern.

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Fig. 0: 70 yo patient with mesothelioma. Nodular pleural thickening with mediastinic nodular pleural involvement.

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Fig. 0: 72 yo patient with mesothelioma. Nodular pleural thickening with mediastinic pleural involvement.

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**Fig. 0:** 78 yo patient with mesothelioma. Irregular thickening and loss of emithorax volume

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**Fig. 0:** 67 yo patient with mesothelioma. Scissural pleural thickening.

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**Fig. 0:** 73 yo patient with mesothelioma. Mediastinal invasion.

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**Fig. 0:** 70 yo patient with sarcomatoid mesothelioma. Pleural mass with thoracic wall involvement and ribs erosion.

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Fig. 0: 70 yo patient with mesothelioma. Diffuse pleural thickening

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Fig. 0: 75 yo patient with mesothelioma with diffuse pleural thickening and loss of volume

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Fig. 0: 68 yo patient with pleuric chronic fibrosis

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Fig. 0: 67 yo patient with pleuric emphyema

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Fig. 0: 67 yo patient with pleuric emphyema

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Fig. 0: 70 yo patient with lung adenocarcinomas metastasis

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Conclusion

Chest-CT is an irreplaceable technique for the diagnosis of pleural mesothelioma.

New multislice scanners allow shorter acquisition time with less movement artifacts and an increasing spatial and contrast resolution. With multidetector CT-scanner, thanks to the isotropic voxel multiplanar reconstructions, now it is possible to perform better evaluations of the infiltration of proximal structures and tissues like mediastinum, thorax, diaphragm and nodes. In our geographic area, with an history of high exposition population, we forecast a progressive increase of the incidence of malignant mesothelioma in our population during next 10 years. So will be important to know different morphological presentation patterns of this pathology and the expression of those signs in different histotypes. Is also important to determinate sensibility and specificity of different radiological signs to correctly guide the diagnostic ...percorso... and to provide to the surgeons accurate pre-operative informations about infiltration and diffusion of the mesothelioma through thorax and mediastinic structures.

In our study CT-scanning result essential for diagnosis, characterization, staging and prognosis evaluation of the malignant mesothelioma.

Specific radiological signs was the presence of an focal irregular thickening more than 1cm, nodular thickening, circonferential pleural thickening and pleural intrascissural involvement.

Other signs, in our experience, must considered less predictive and specific for mesothelioma diagnosis because are common with others pleuric neoplastic and non-neoplastic diseases.

In particular the presence of mediastinal nodes, unilateral pleural effusion, and pleural enhancement must be considered non specific sings and force us to continue the diagnostic process with TC-guided biopsy or with Video Assiste Thoracoscopic Biopsy (VATS).

Histological assessment must be always performed as final reference to reach correct characterization of the lesion before surgical treatment.
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