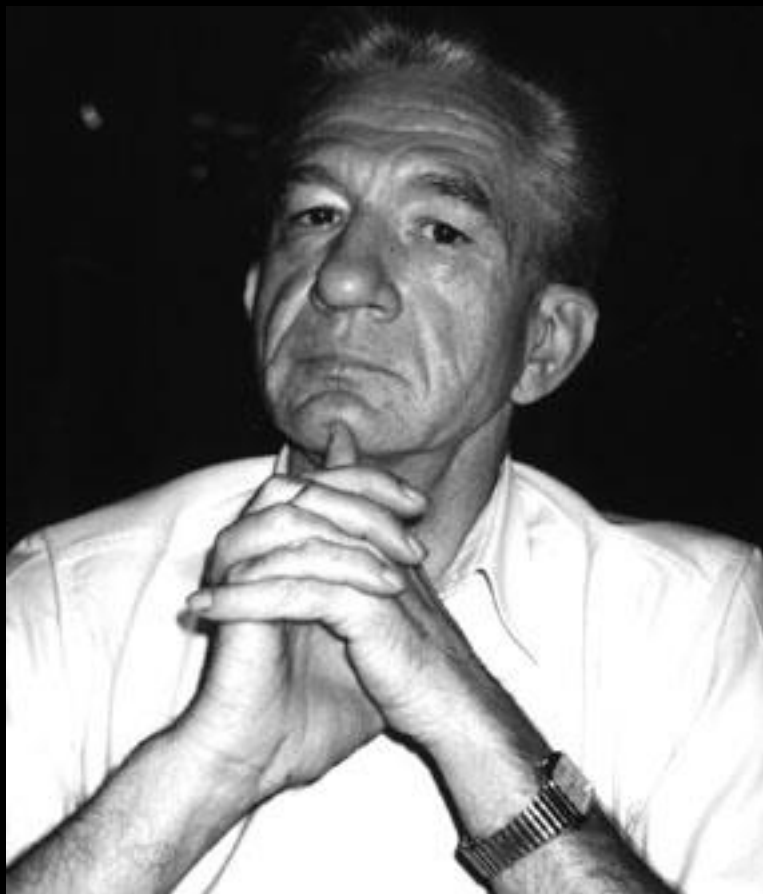


La diagnosi endoscopica precoce del mesotelioma pleurico

CONVEGNO

Venerdì 3 dicembre 2021
8.30 – 17.00

**Evoluzione
dell'approccio
al mesotelioma:
dalla multidisciplinarietà
alla interdisciplinarietà**

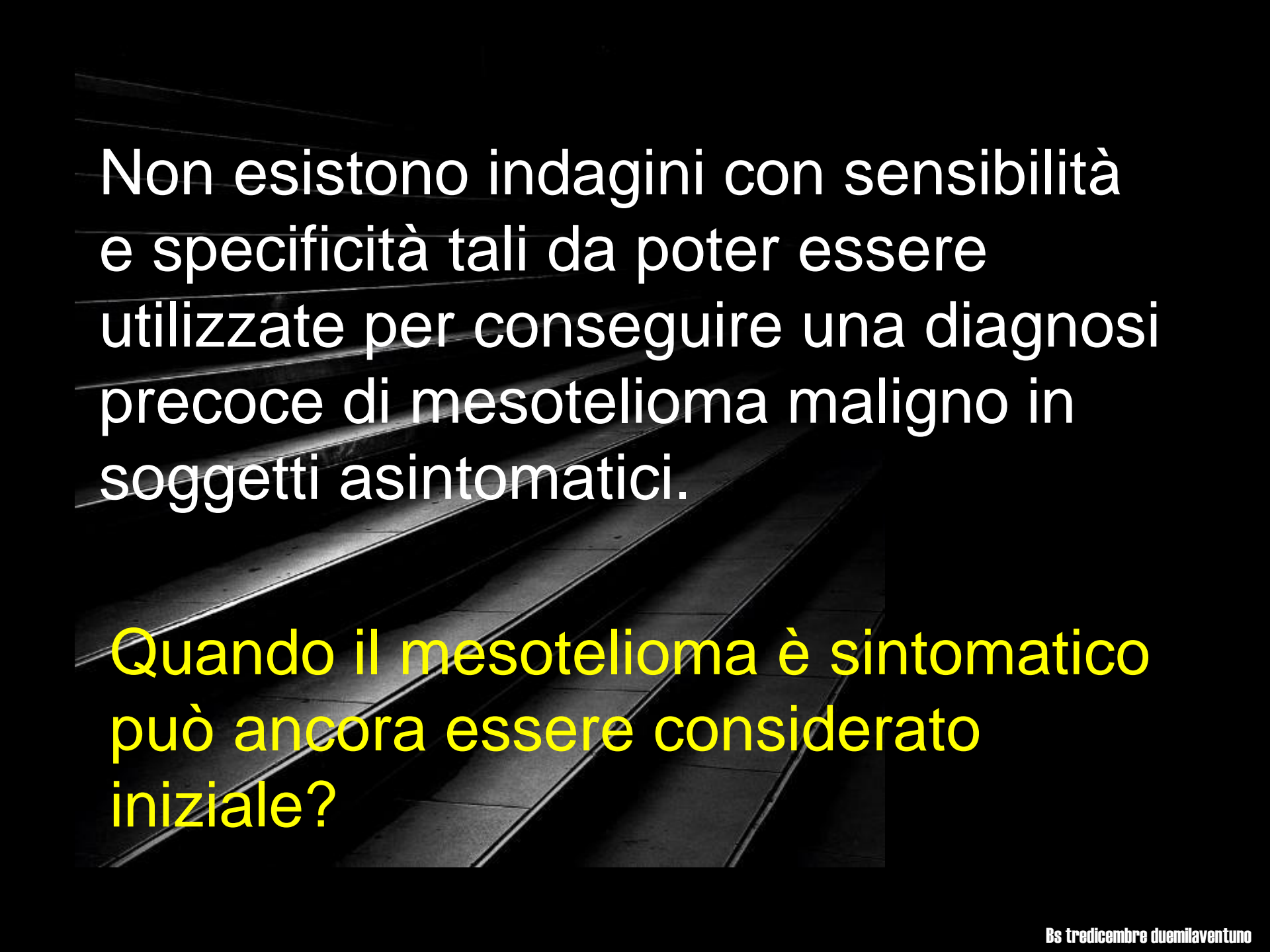


Caro Gian Pietro

il mesotelioma iniziale trattato
ha una sopravvivenza migliore
semplicemente perché
lo si scopre prima
ma lui va avanti lo stesso
per la sua strada


Diagnosticare il MPM iniziale è difficile

- Paucisintomatico o sintomi aspecifici
- Anamnesi a volte muta per esposizione asbesto
- Liquido citologicamente negativo nel 70%
- TC poco significativa negli stadi iniziali
- PET promettente ma quando?
- Marcatori sierici insufficienti (mesotelina?)
- Il versamento può regredire spontaneamente
- Il versamento può regredire con terapia cortisonica
- Talvolta scambiato per tbc
- Alcune biopsie pleuriche parlano di iperplasia mesoteliale (BAP1)
- Poche Pneumologie in Italia fanno toracosopia medica



Non esistono indagini con sensibilità e specificità tali da poter essere utilizzate per conseguire una diagnosi precoce di mesotelioma maligno in soggetti asintomatici.

Quando il mesotelioma è sintomatico può ancora essere considerato iniziale?



*La patologia pleurica
è tanto più grave e a prognosi sfavorevole
quanto meno è sintomatica*

*Pertanto è ragionevole essere
aggressivi nella diagnosi
soprattutto in presenza di
pleuropatie paucisintomatiche*

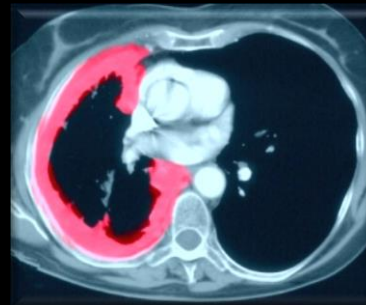
MPM: diagnosi

La diagnosi di mesotelioma non può essere basata sul solo **esame citologico del liquido** (A)

La toracosopia è necessaria per la diagnosi di mesotelioma a meno di controindicazioni legate alle condizioni del pz. o ad impossibilità tecnica (sinfisi pleurica) (A)

Le biopsie transparietali TC ed eco- guidate sono indicate nei pazienti in cui non è possibile una toracosopia (A)

La toracotomia deve essere utilizzata solo in presenza di sinfisi pleurica che impedisca la toracosopia (A)



Numero totale toracoscopie: 3000

Anni 1984 - 2016

- 591 k polmone
- 276 k mammella
- **581 meso epitelioide**
- **63 meso bifasico**
- 48 k rene
- 32 k ovaio
- 98 neo ?
- 15 k stomaco
- 32 linfomi
- 112 pnt
- 151 tbc
- 195 empiema/parapneumoniche
- **806 pleuriti aspecifiche**

Quanti iniziali?

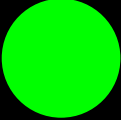

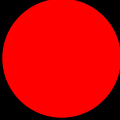














































































Classificazione TNM (Ottava Edizione)	
T1	Il tumore coinvolge la pleura parietale omolaterale oppure la sola pleura viscerale, con o senza coinvolgimento di pleura viscerale, mediastinica o diaframmatica.
T2	Il tumore coinvolge la pleura omolaterale (viscerale o parietale) con almeno uno dei seguenti: <ul style="list-style-type: none"> - Coinvolgimento del muscolo diaframma - Invasione del parenchima polmonare
T3	<ul style="list-style-type: none"> - Il tumore coinvolge la pleura omolaterale (viscerale o parietale) con almeno uno dei seguenti: coinvolgimento della fascia endotoracica - Invasione del grasso mediastinico - Focus solitario di tumore che invade i tessuti molli della parete toracica - Coinvolgimento del pericardio non transmurale
T4	<ul style="list-style-type: none"> - Il tumore coinvolge la pleura omolaterale (viscerale o parietale) con almeno uno dei seguenti: estensione diffusa o multifocale alla parete toracica con o senza erosione costale associata - Estensione diretta al peritoneo attraverso il diaframma - Estensione alla pleura controlaterale - Estensione diretta del tumore agli organi mediastinici (esofago, trachea, cuore, grandi vasi) - Estensione diretta del tumore alle vertebre, forami intervertebrali, midollo spinale - Estensione del tumore alla superficie interna del pericardio (con o senza versamento pericardico)
N	<i>Linfonodi regionali</i>
NX	Linfonodi non valutabili
N1	Metastasi ai linfonodi intratoracici omolaterali (bronco-polmonari, ilari, sottocarinali, paratracheali, aorto-polmonari, paraesofagei, peridiaframmatici, del grasso del cuscinetto pericardico, intercostali e mammari interni)
N2	Metastasi ai linfonodi intratoracici controlaterali; metastasi ai linfonodi omolaterali o controlaterali sovraclaveari.
M	<i>Metastasi a distanza</i>
M0	Assenza di metastasi a distanza
M1	Presenza di metastasi a distanza



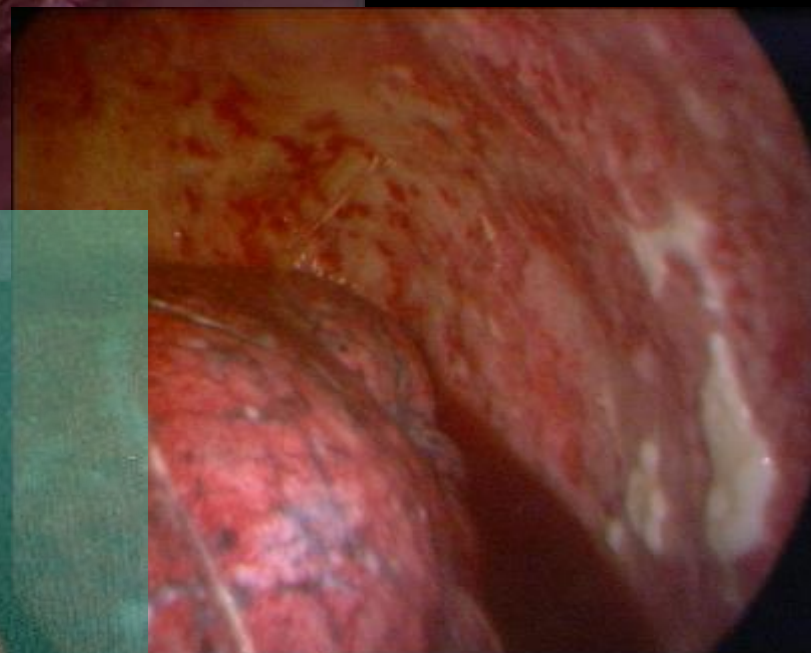
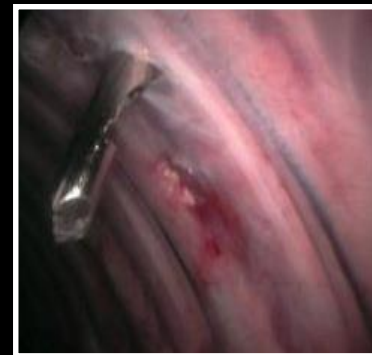
T

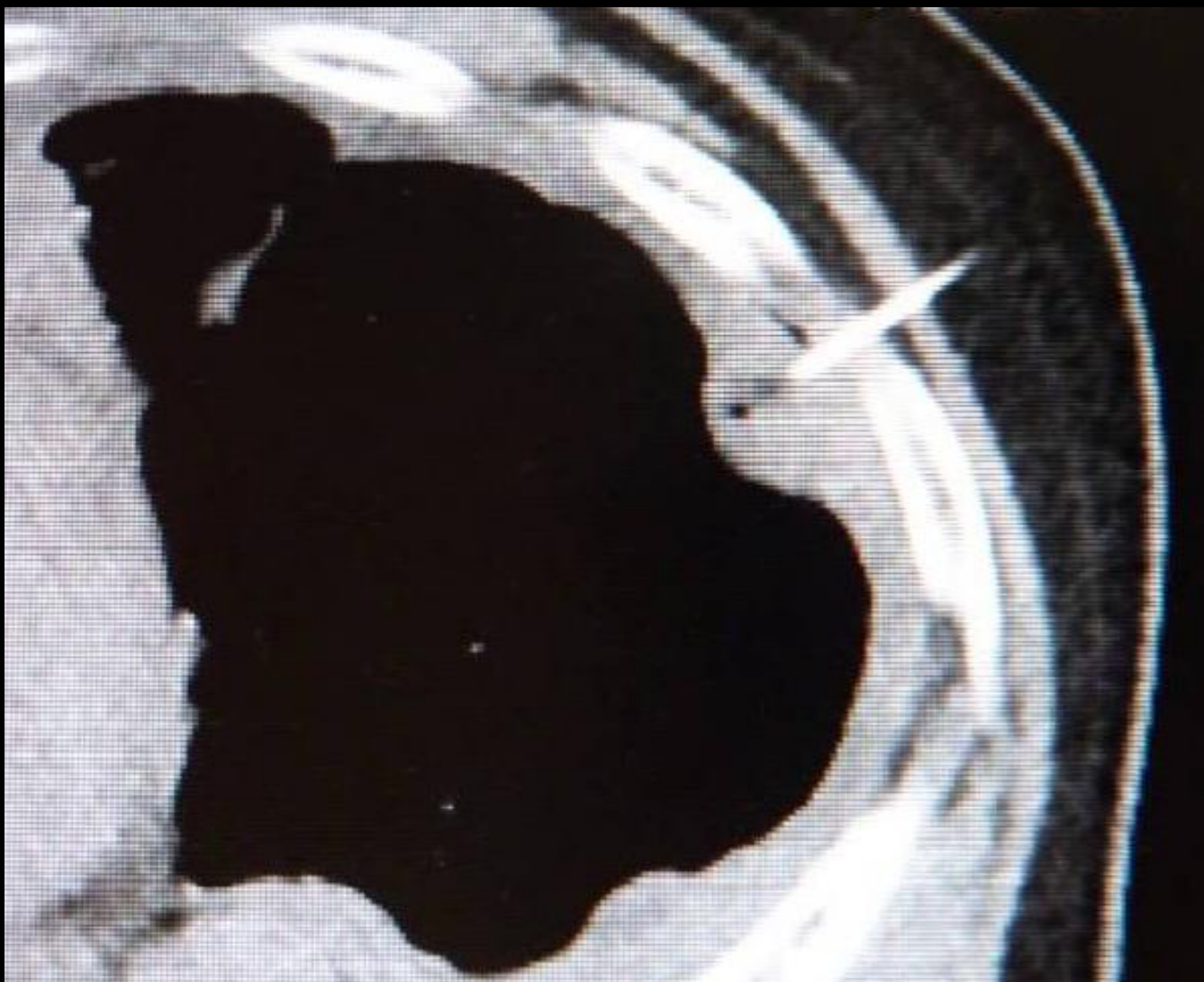


	Butchart	Chahinian	IUCC	IMIG	Sugarbaker	AJCC	AJCC
				T1a		T1a	

  		Clinica - Rx	Toraco	TC	RM - PET	ECO	Chirurgia
pleura parietale							
pleura mediastinica							
diaframma	superficiale						
	muscolo						
	trans						
pleura viscerale	focale						
	confluente						
pericardio	superficiale						
	trans						
fascia endotoracica							
parete toracica							
organi mediastinici							
linfonodi							

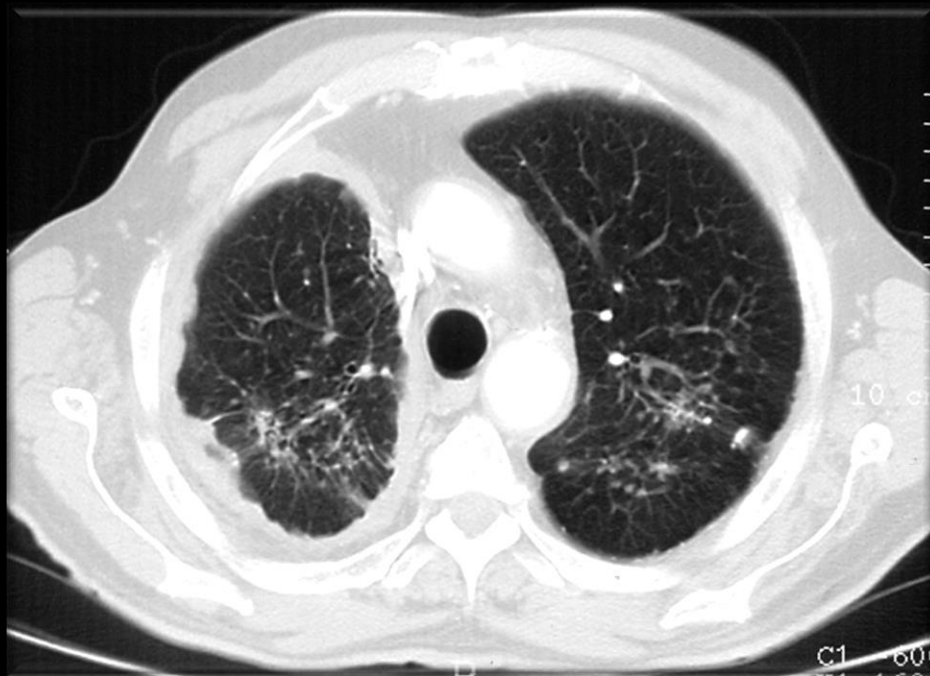
Mesotelioma: ancora valida l'agobiopsia?





Alternative alla biopsia toracoscopica





Mesotelioma

Ruolo dell'ecografia

Pneumologia - Spedali Civili Brescia

07-03-2019 11:04:44

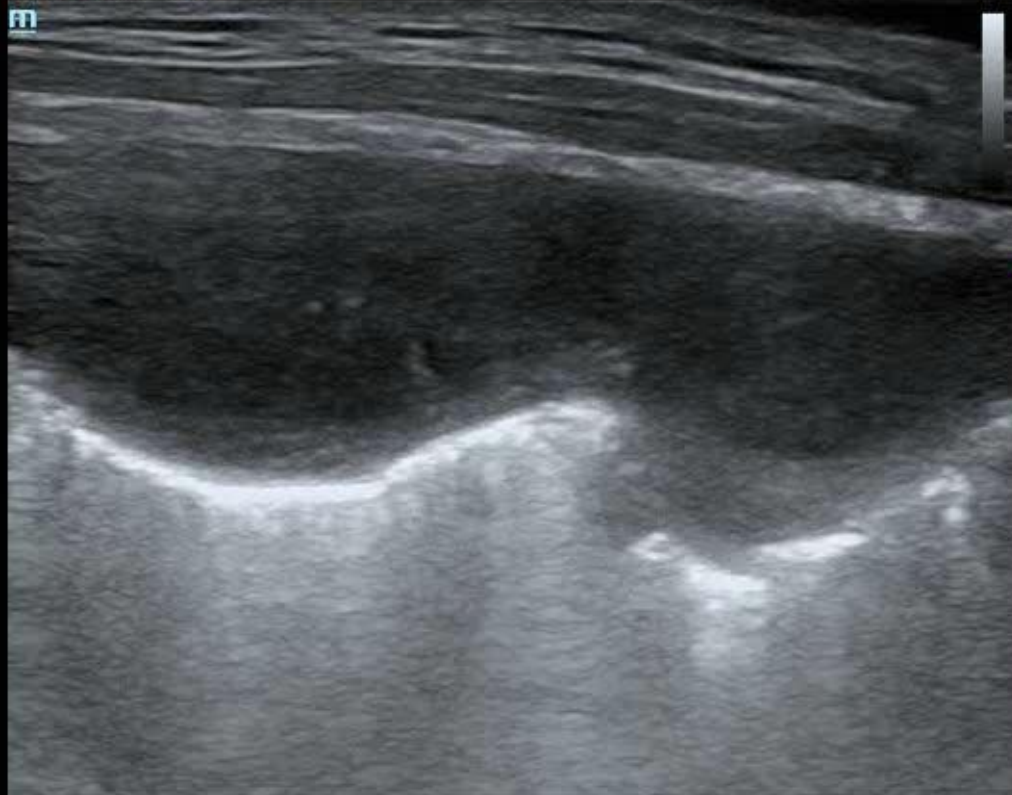
20190307-102934-6EA0

Tiroide

L12-4s

AP 96.6% MI 1.4 TIS 0.5

m



mindray

M9

B

F 6.6~13.5

D 3.0

G 45

FR 62

DR 110

iClear 5

iBeam 1

@saote MyLab Divisione Pneumologia Brescia
BioIspPleurico, 05 GEN 2012 13:39
0:00:00.33
B F 3.5 MHz G 64%
P 10 cm XV
PRC 10-2-B PRS 3
PST 2

POLMONE CA430



Pneumologia - Spedali Civili Brescia

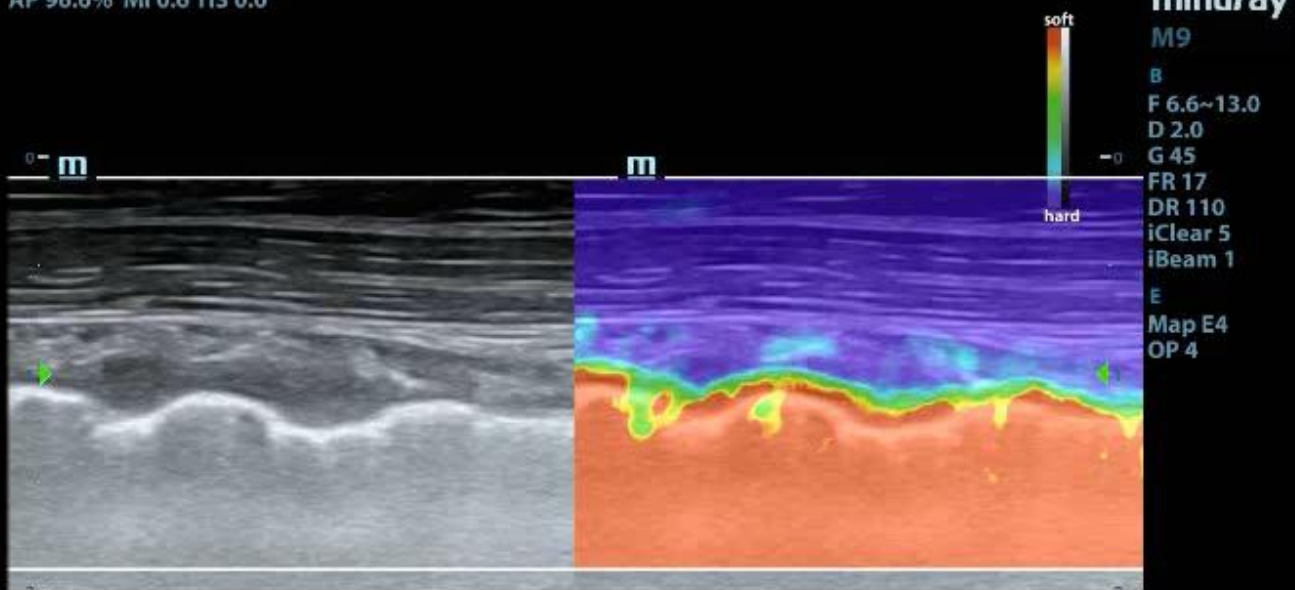
16-07-2019 10:42:51

20190716-100249-6EA0

Tiroide

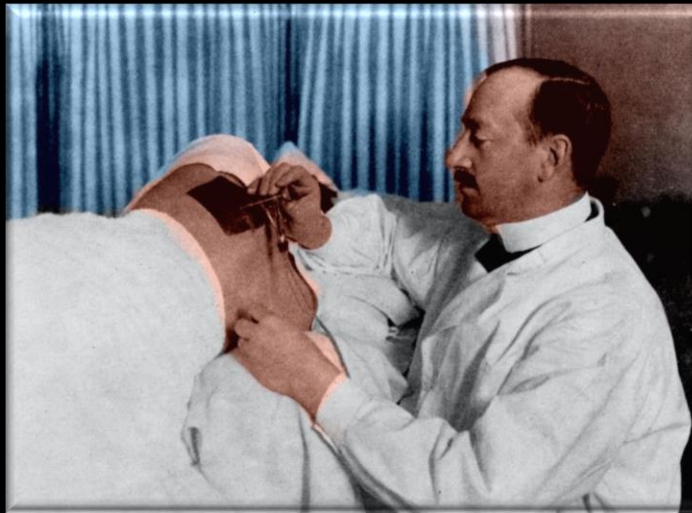
L12-4s

AP 96.6% MI 0.6 TIS 0.0



Toracoscopia nella Pleurite Cronica Aspecifica

- Dopo lungo follow-up, la sensibilità è del 91%
- Di 208 casi di pleurite aspecifica, 31 (15%) avevano una pleurite maligna dopo un follow-up medio di 4.4 mesi.
(4.3% del totale)



La maggior parte dei falsi negativi sono
mesoteliomi (DD con iperplasia mesotelio)

Fenotipizzare il paziente per individuare il rischio di mesotelioma: come?

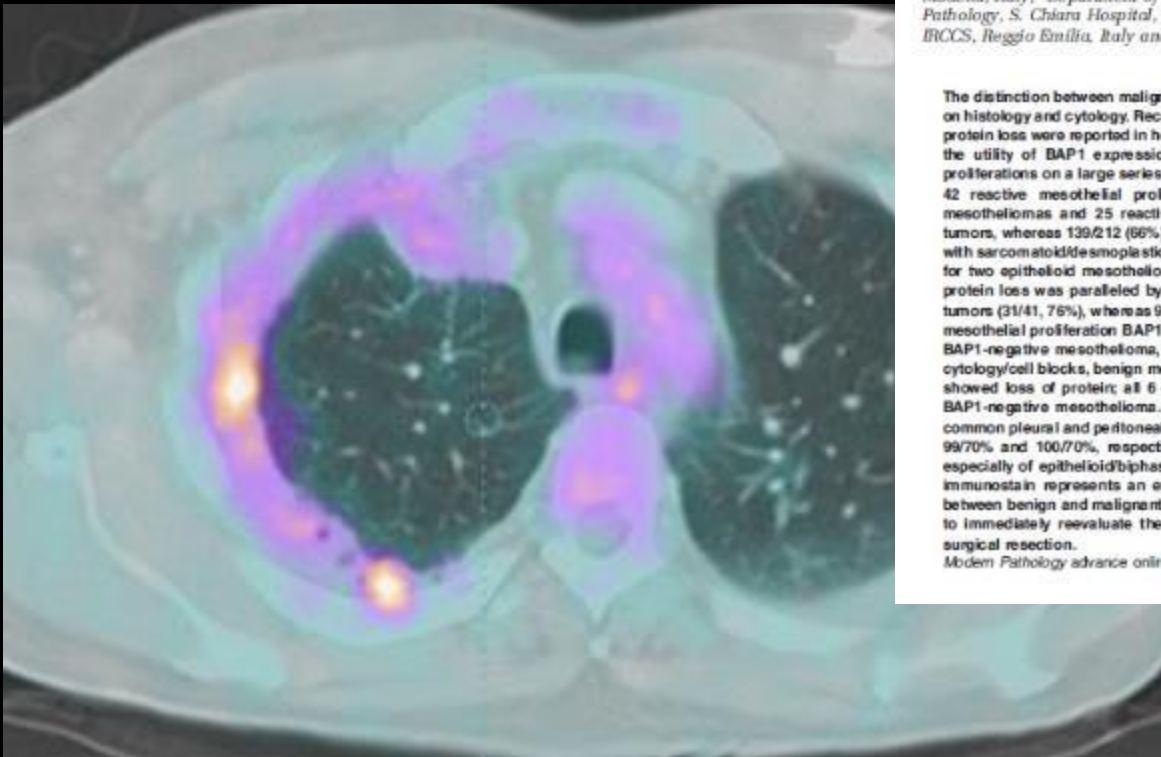
BAP1 (BRCA1-associated protein 1) is a highly specific marker for differentiating mesothelioma from reactive mesothelial proliferations

Marta Cigognetti¹, Silvia Lonardi¹, Simona Fisogni¹, Piera Balzarini¹, Vilma Pellegrini¹, Andrea Tironi¹, Luisa Bercich¹, Mattia Bugatti¹, Giulio Rossi², Bruno Murri³, Mattia Barbareschi⁴, Silvia Giuliani⁴, Alberto Cavazza⁵, Gianpietro Marchetti⁶, William Vermi¹ and Fabio Facchetti¹

¹Department of Molecular and Translational Medicine, Section of Pathology, University of Brescia, Spedali Civili, Brescia, Italy; ²Department of Pathology, Azienda Ospedaliero-Universitaria Policlinico of Modena, Modena, Italy; ³Department of Pathology, Ospedale Dell'Angelo, Venezia-Mestre, Italy; ⁴Unit of Surgical Pathology, S. Chiara Hospital, Trento, Italy; ⁵Department of Pathology, Azienda Arcispedale S. Maria Nuova, Reggio Emilia, Italy and ⁶Department of Pneumology, Spedali Civili, Brescia, Italy

The distinction between malignant mesothelioma and reactive mesothelial proliferation can be challenging both on histology and cytology. Recently, variants of the *BRCA1-associated protein 1 (BAP1)* gene resulting in nuclear protein loss were reported in hereditary and sporadic mesothelioma. Using immunohistochemistry, we evaluated the utility of BAP1 expression in the differential diagnosis between mesothelioma and other mesothelial proliferations on a large series of biopsies that included 212 mesotheliomas, 12 benign mesothelial tumors, and 42 reactive mesothelial proliferations. BAP1 stain was also performed in 70 cytological samples (45 mesotheliomas and 25 reactive mesothelial proliferations). BAP1 was expressed in all benign mesothelial tumors, whereas 139/212 (66%) mesotheliomas were BAP1 negative, especially in epithelioid/biphasic compared with sarcomatoid/desmoplastic subtypes (69% vs 15%). BAP1 loss was homogeneous in neoplastic cells except for two epithelioid mesotheliomas showing tumor heterogeneity. By fluorescence *in situ* hybridization, BAP1 protein loss was paralleled by homozygous deletion of the *BAP1* locus in the vast majority of BAP1-negative tumors (31/41, 76%), whereas 9/10 BAP1-positive mesotheliomas were normal. In biopsies interpreted as reactive mesothelial proliferation BAP1 loss was 100% predictive of malignancy, as all 6 cases subsequently developed BAP1-negative mesothelioma, whereas only 3/36 (8%) BAP1-positive cases progressed to mesothelioma. On cytology/cell blocks, benign mesothelial cells were invariably positive for BAP1, whereas 64% of mesotheliomas showed loss of protein; all 6 cases showing BAP1 negativity were associated with histological diagnosis of BAP1-negative mesothelioma. BAP1 stain also showed utility in the differential of mesothelioma from most common pleural and peritoneal mimickers, such as lung and ovary carcinomas, with specificity and sensitivity of 99/70% and 100/70%, respectively. Our results show that BAP1 protein is frequently lost in mesothelioma, especially of epithelioid/biphasic subtype and is commonly associated with homozygous *BAP1* deletion. BAP1 immunostain represents an excellent biomarker with an unprecedented specificity (100%) in the distinction between benign and malignant mesothelial proliferations. Finding BAP1 loss in mesothelial cells should prompt to immediately reevaluate the patient; moreover, it might be useful in mapping tumor extent and planning surgical resection.

Modern Pathology advance online publication, 29 May 2015; doi:10.1038/modpathol.2015.65

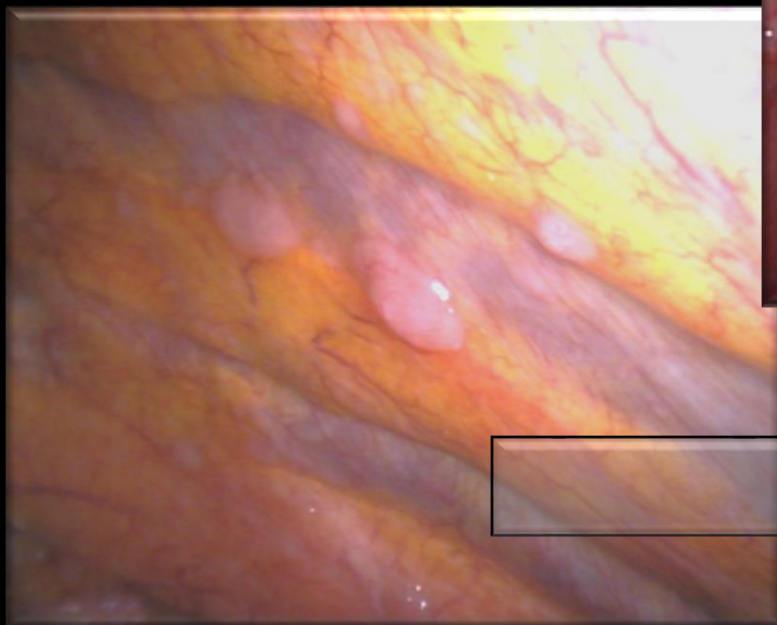
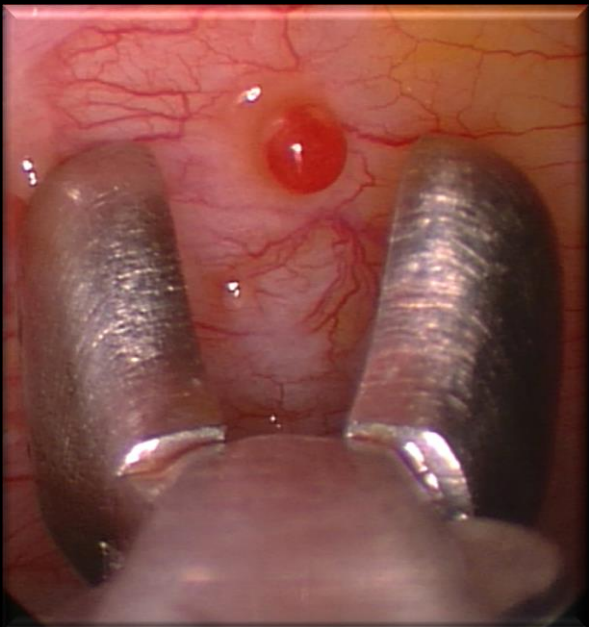


PCA

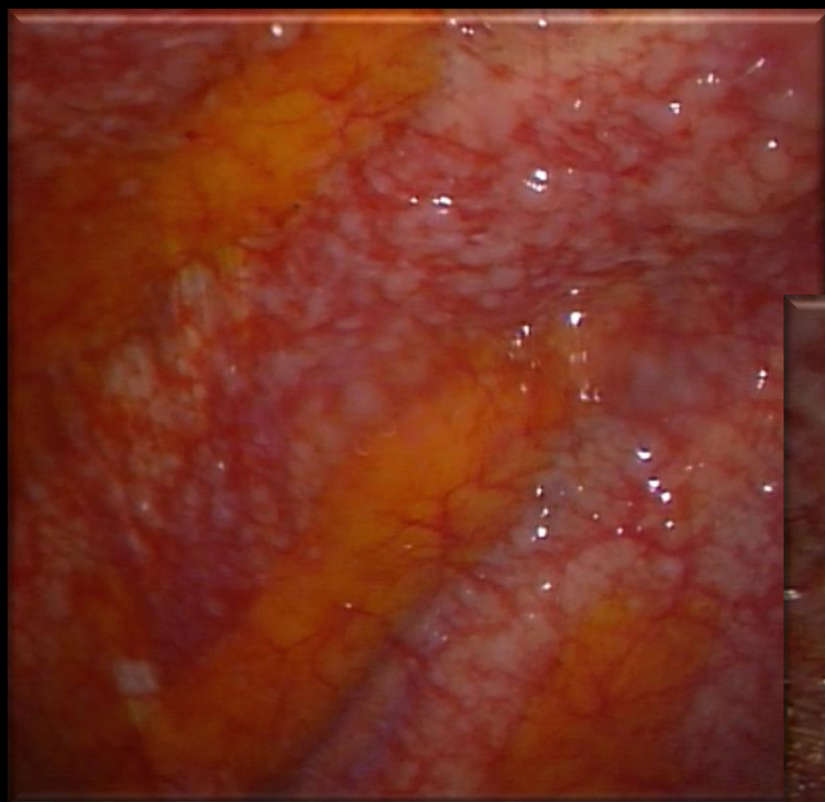
MESO

Dopo un anno

Falsi negativi 12%

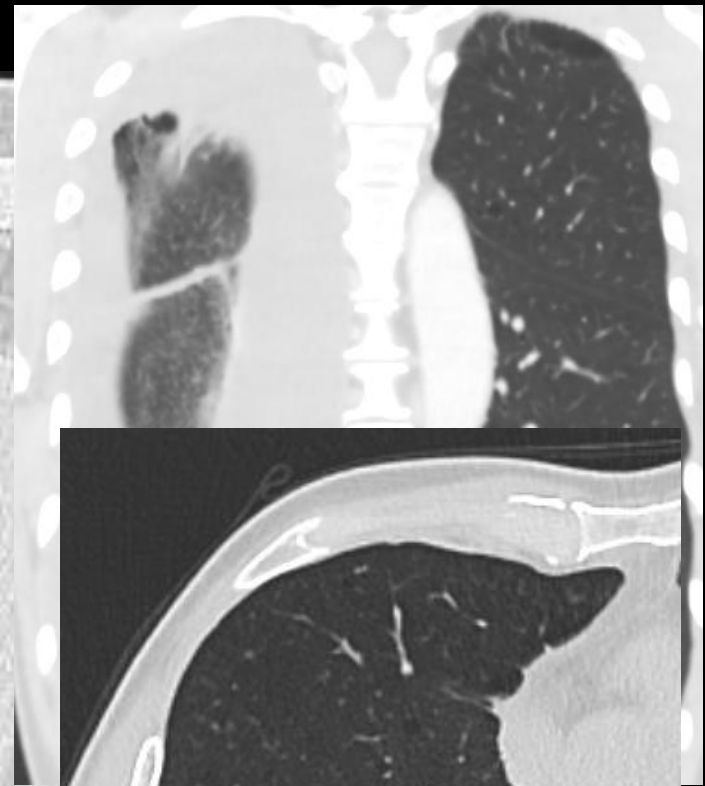
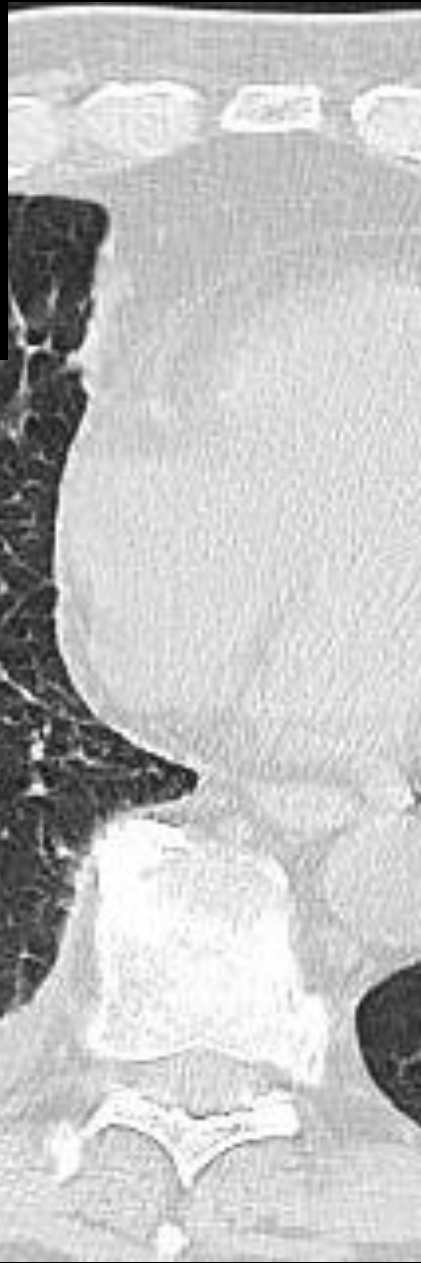


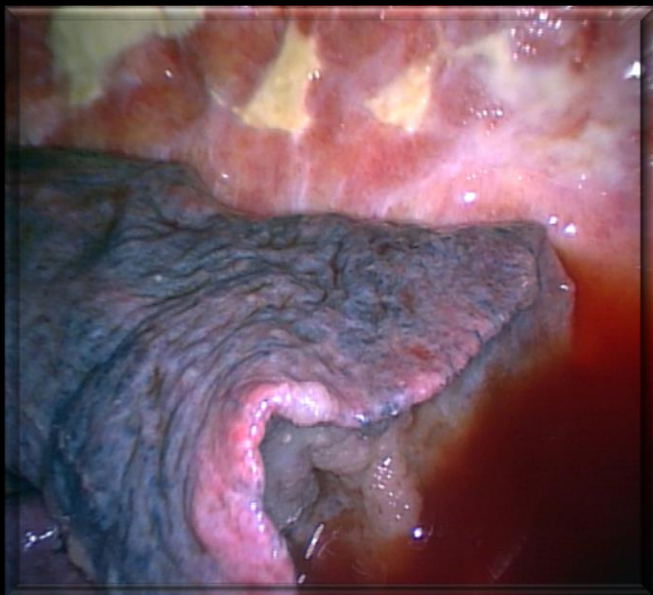
Otto mesi



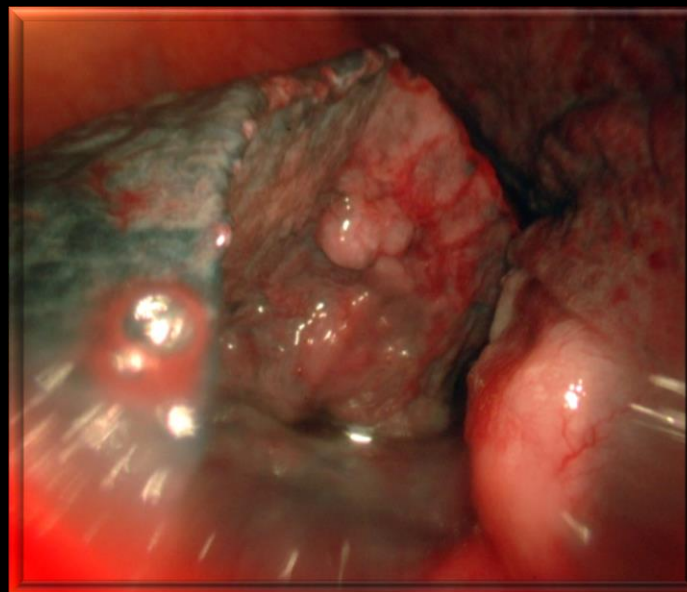
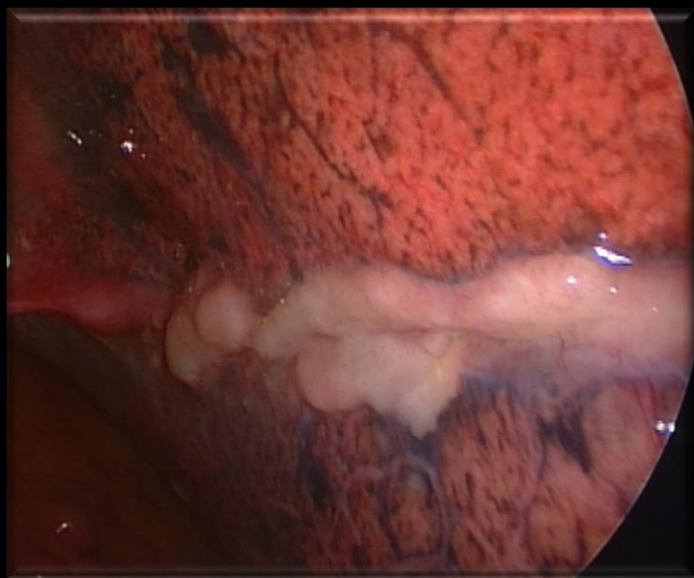
Dopo un anno







Invasione scissura



Come ridurre il numero delle Pleuriti Croniche Aspecifiche



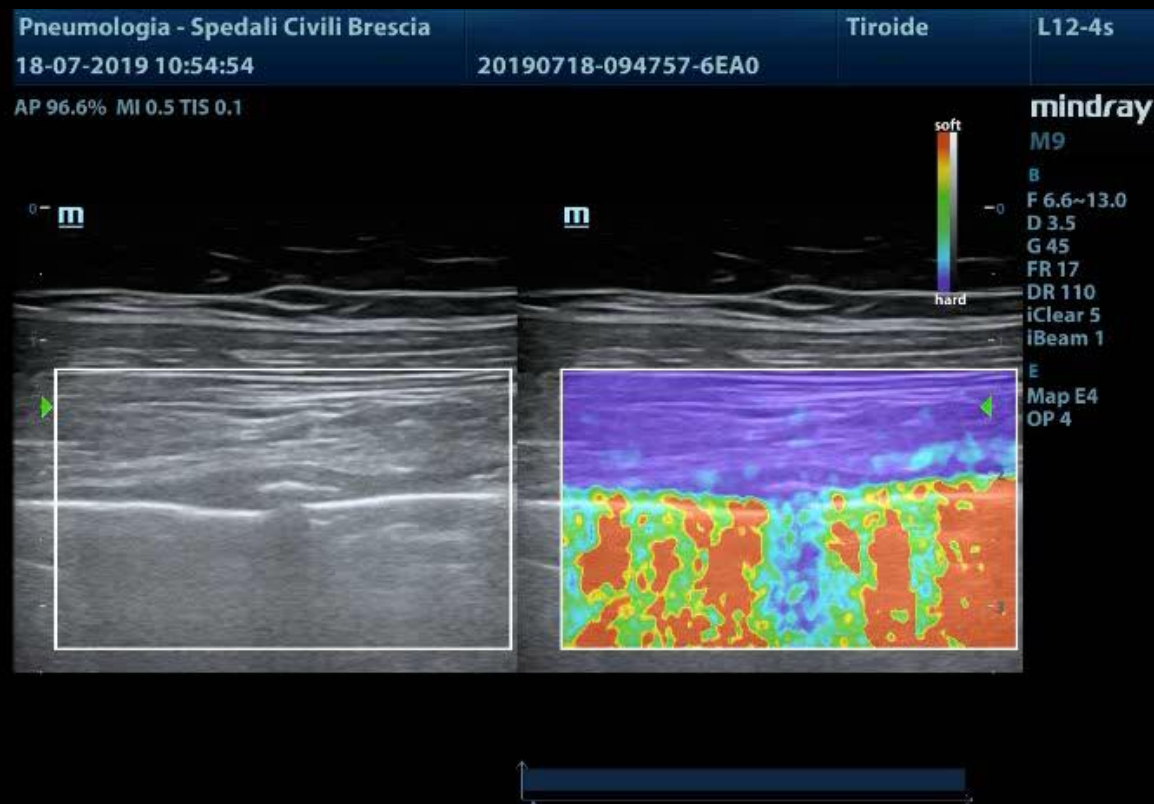
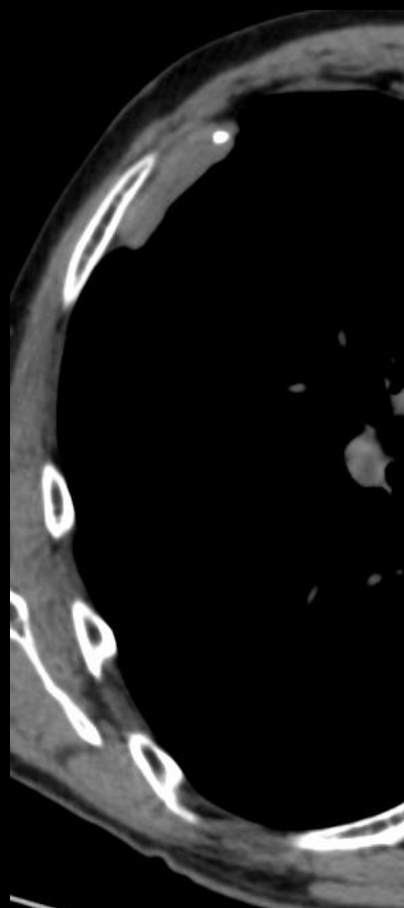
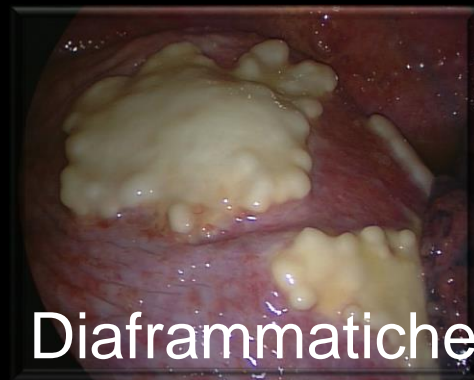
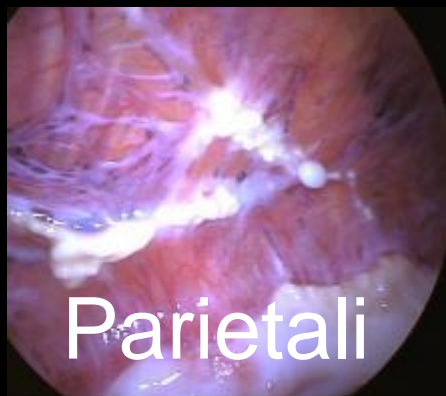
- Prelievi numerosi (10/15)
- Prelievi in più zone
- Prelievi più profondi
- Prelievi più grandi
- Biopsia su biopsia
- Ampia toilette prima delle biopsie
- Ripetere toracosopia
- Ricorso alla toracotomia?



PCA: quando stare attenti!



- In esposti all' asbesto
- Coesistenza di placche
- Istologia: iperplasia "atipica"
- Persistenza febricola
- **Persistenza dolore**
- Imaging in peggioramento



Accuracy of Pleural Biopsy Using Thoracoscopy for the Diagnosis of Histologic Subtype in Patients With Malignant Pleural Mesothelioma

CONCLUSIONS. Pleural biopsy performed using thoracoscopy is considered to be the cornerstone of the diagnosis and pleural staging of MPM. However, this procedure appears to be less efficient in diagnosing the histologic subtype as either epithelial or biphasic. *Cancer* 2007;110:2248–52. © 2007 American Cancer Society.

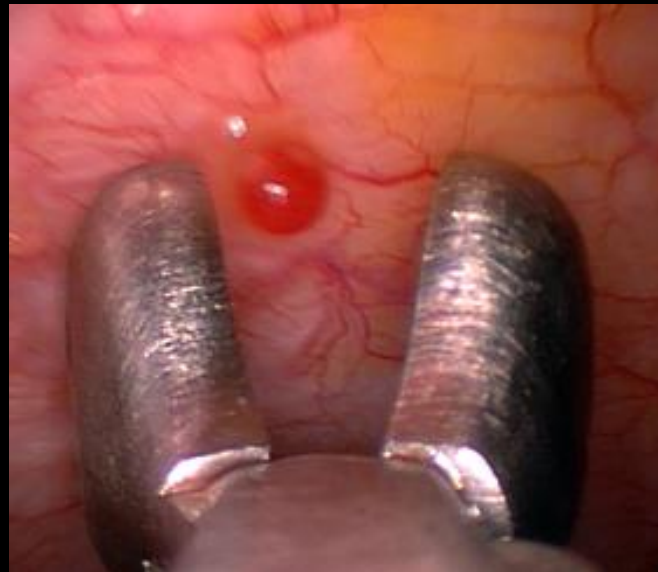
Laurent Greillier, MD^{1,2}
Arnaud Cavailles, MD¹
Anne Fraticelli, MD^{1,2}
Arnaud Scherpereel, MD³
Fabrice Barlesi, MD¹
Gianfranco Tassi, MD⁴
Pascal Thomas, MD¹
Philippe Astoul, MD^{1,2}

¹ Division of Thoracic Oncology, Federation of Pulmonary Diseases and Thoracic Surgery, University of the Mediterranean Sea, Ste-Marguerite Hospital, Marseille, France.

² UPRES 3287, School of Medicine La Timone, University of the Mediterranean Sea, Marseille, France.

³ Department of Pulmonary and Thoracic Oncology, Calmette Hospital, University of Lille II, Lille, France.

⁴ Pulmonology Unit, Civil Hospital, Brescia, Italy.



Reproducibility of Malignant Pleural Mesothelioma Histopathologic Subtyping

Luka Brcic, MD, PhD; Gregor Vlacic, MD; Franz Quehenberger, PhD; Izidor Kocj, MD

Context.—Malignant pleural mesothelioma (MPM) is a rare tumor with poor prognosis. Several studies have analyzed potential prognostic markers, but histologic type remains the single most important prognostic factor. Histologic subtypes of epithelioid MPM seem to have prognostic and therapeutic implications. Interobserver agreement in histologic pattern classification should be high.

Objective.—To assess interobserver and intraobserver reproducibility in histologic differentiation between the main types of MPMs, and in further subtyping of epithelioid-type mesotheliomas.

Design.—One representative hematoxylin-eosin-stained slide was selected from the archive for each of 200 patients with MPM. They were reviewed independently by 3 pathologists and classified according to the current World Health Organization classification of pleural tumors. After the first round of evaluations, a consensus meeting was

organized where problems were addressed and representative images for each histologic category were selected. Two months later, cases were reevaluated by all 3 pathologists.

Results.—After the first round, overall interobserver agreement for histologic subtyping of mesothelioma was fair (κ , 0.34). The agreement was increased to substantial (κ , 0.63) in the second round. Improvement was found in interobserver agreement for all types of MPM, and for most epithelioid subtypes.

Conclusions.—Moderate to substantial agreement in histologic typing and subtyping of MPM can be achieved. However, training with additional clarification of diagnostic criteria, their strict application, and help from consensus-based illustrative images is needed.

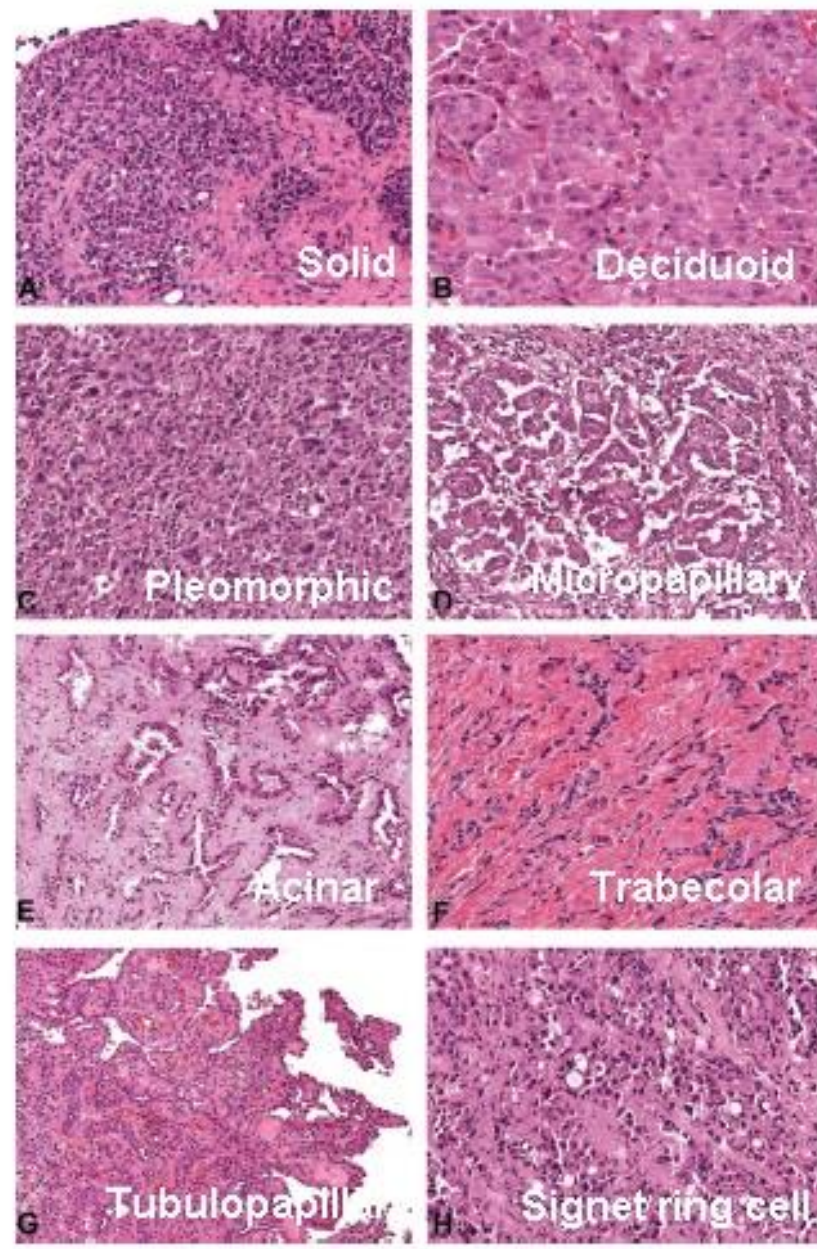
(Arch Pathol Lab Med. doi: 10.5858/arpa.2017-0295-0A)

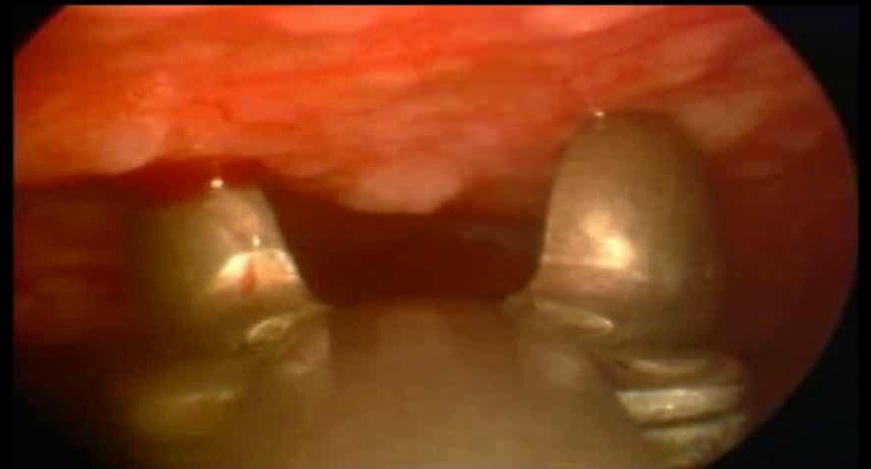
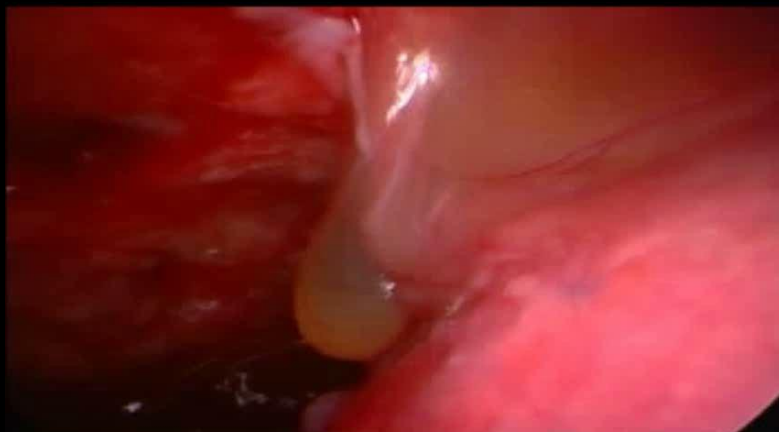
deciduoid, and pleomorphic.¹¹ The prognostic significance of different histologic patterns of epithelioid mesotheliomas has been analyzed in a few studies, which suggest poorer survival for individuals with the pleomorphic pattern.^{12–14} In contrast, the myxoid/microcystic pattern was shown to be a favorable prognostic marker.¹⁵ Furthermore, Kadota et al¹³

CONCLUSIONS

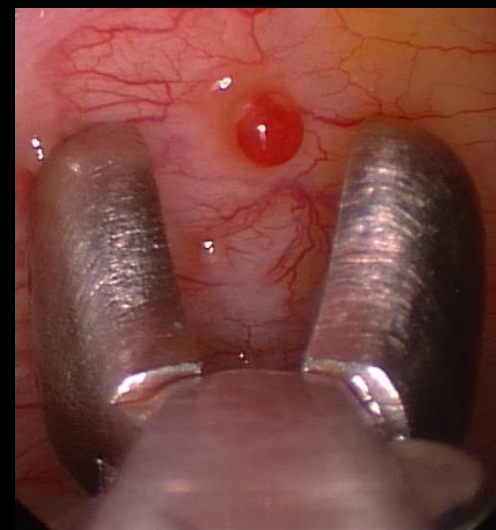
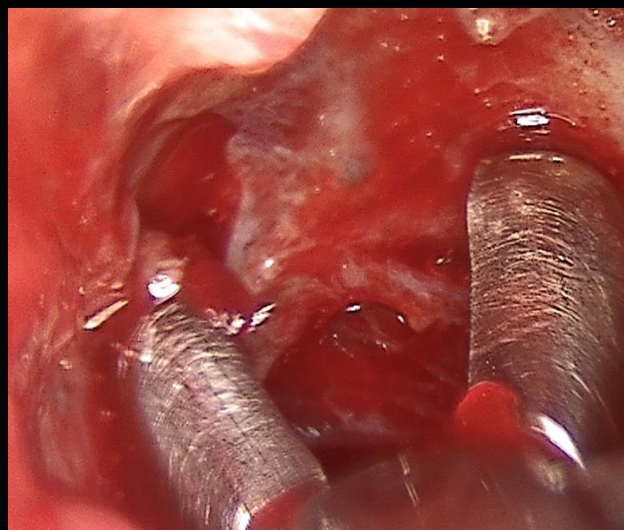
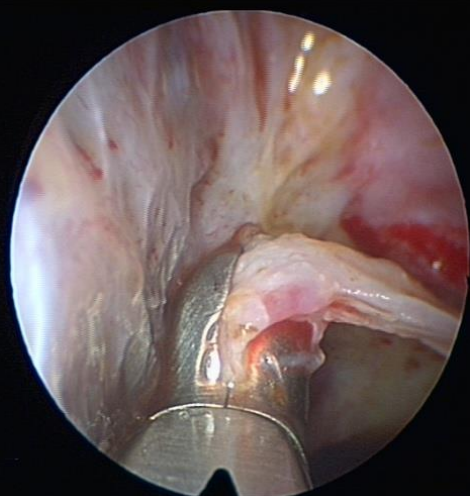
Our study demonstrated that moderate to substantial agreement in histologic typing and subtyping of MPM can be achieved. Size of the sample seems to be an important limiting factor in achieving this agreement. Furthermore,

Tanti mesoteliomi epitelioidi con prognosi diverse



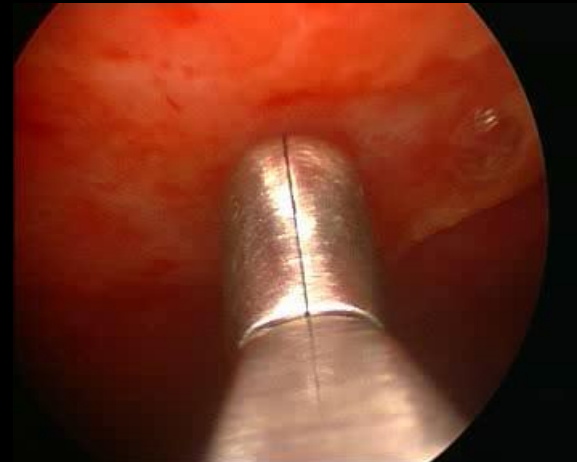


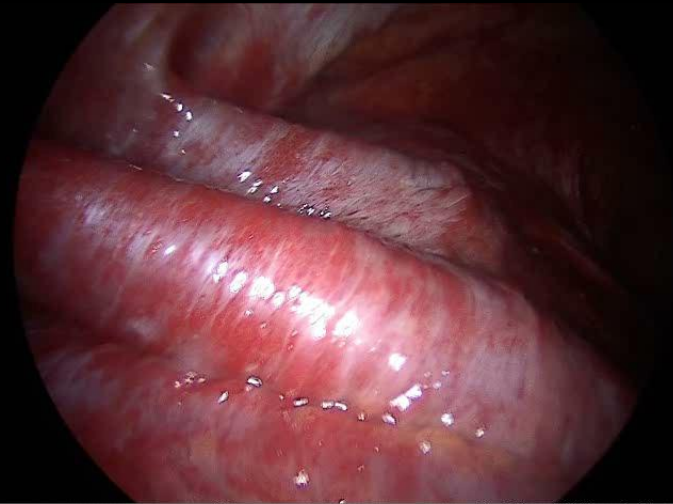
La Biopsia nel mesotelioma



Biopsia
a strascico

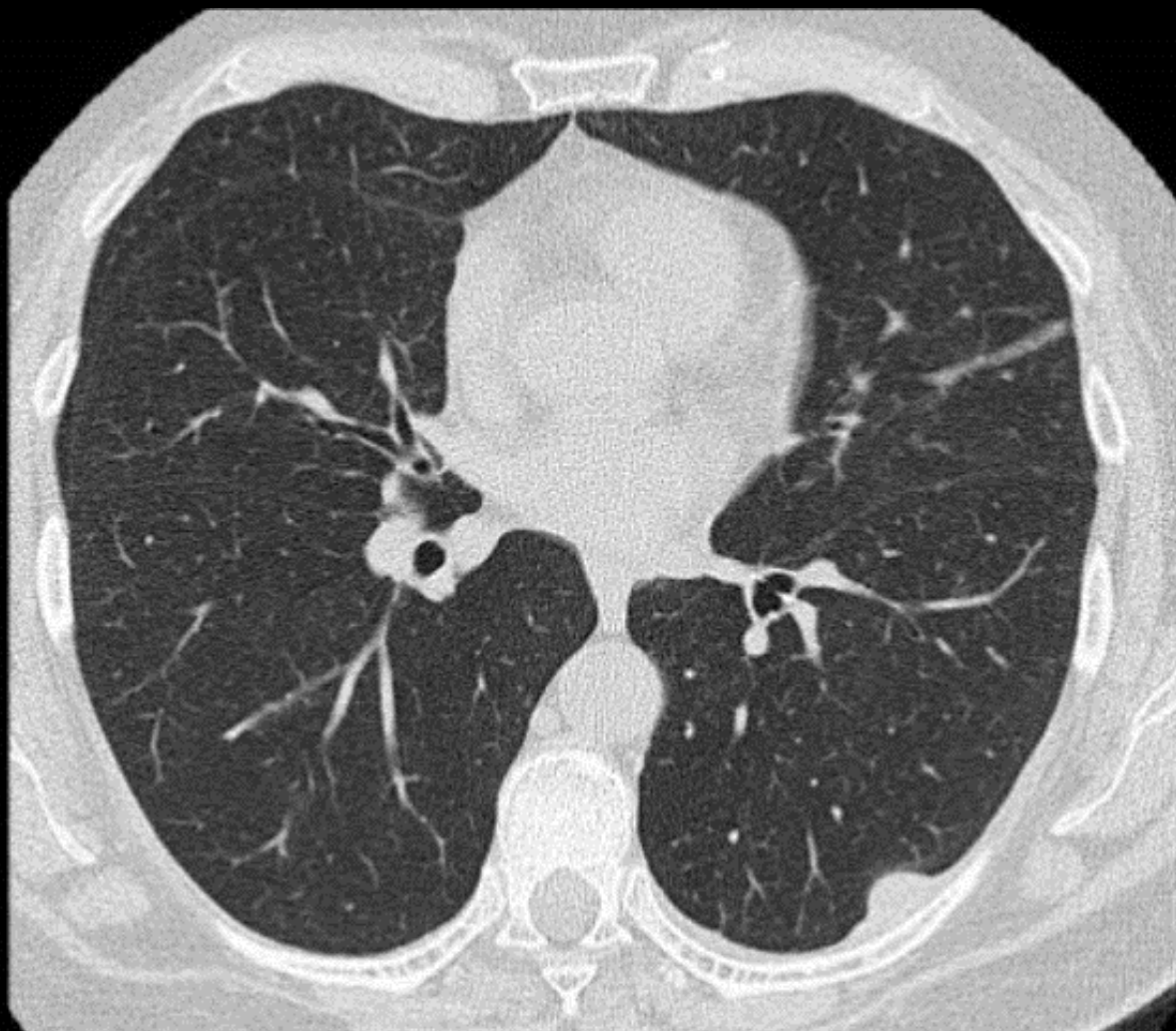
Biopsia
su biopsia

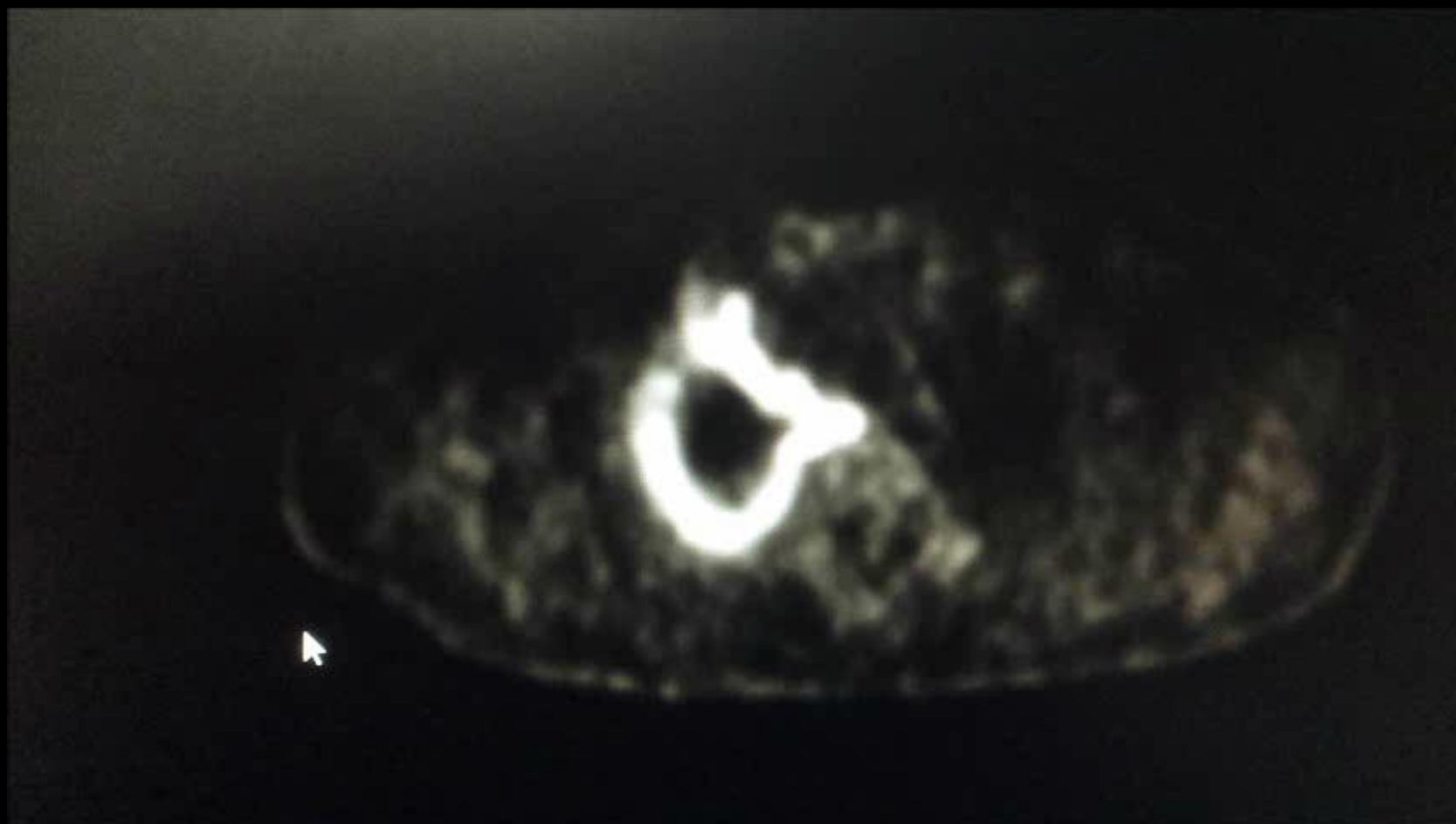




x1.0 2 mm 2 REC 00:00:00 (3min) (3%)

Mesotelioma iniziale?





The role of endobronchial ultrasound-guided fine needle aspiration in the diagnosis of pleural mesothelioma

M. R. Ghigna*, A. Crutu†, V. Florea†, S. Soummer-Feuillet† and P. Baldeyrou†

*Department of Pathology, †Department of Thoracic and Vascular Surgery, Marie Lannelongue Surgical Centre, Le Plessis-Robinson, France

Accepted for publication 19 March 2015

M. R. Ghigna, A. Crutu, V. Florea, S. Soummer-Feuillet and P. Baldeyrou

The role of endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of pleural mesothelioma

Objective: The aims of the present study were to investigate the role of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in the diagnosis of malignant pleural mesothelioma (MPM), and to identify specific clinical settings in which this procedure can be recommended.

Methods: We retrospectively reviewed the clinical and pathological files of patients having undergone EBUS-TBNA from February 2011 to October 2014 to investigate thoracic lesions. Among 736 patients, we identified four of them with a diagnosis of MPM achieved primarily through EBUS-TBNA. The diagnosis was made on formalin-fixed paraffin-embedded cell blocks, by checking the expression of mesothelial and carcinoma-specific markers.

Results: In all patients, the collected tissue was adequate, and the histological analysis in association with immunohistochemistry led us to the diagnosis of malignant pleural mesothelioma. In three patients, the diagnosis of mesothelioma was clinically suspected, as patients presented with diffuse pleural thickening. In two patients, videothoracoscopy was not possible owing to the 'dry' presentation of the pleural disease and the site of thickening. In this setting, EBUS-TBNA was considered, as a multidisciplinary consensus meeting, as the most adequate available method to obtain a histological diagnosis.

Conclusion: EBUS-TBNA may be a valuable diagnostic technique in selected clinical settings. More specifically 'dry' mesothelioma accessible by surgery or by computed tomography/ultrasonography is an indication to perform EBUS-TBNA.

CAS CLINIQUE

Échoendoscopie bronchique pour le diagnostic de mésothéliome pleural malin



Endobronchial ultrasound in the diagnosis of malignant pleural mesothelioma

J. Guinde^a, S. Laroumagne^a, E. Kaspi^{b,c}, S. Martinez^a,
R. Tazi-Mezalek^a, P. Astoul^{a,c}, H. Dutau^{a,*}

^a Service d'oncologie thoracique, maladie de la plèvre et pneumologie interventionnelle, hôpital Nord, chemin des Bourrely, 13000 Marseille, France

^b Service de biologie cellulaire, hôpital La Timone, 13000 Marseille, France

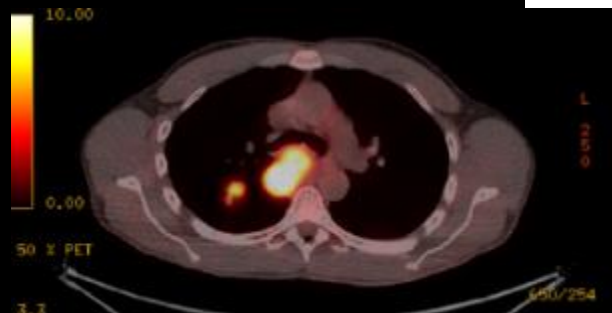
^c Université d'Aix-Marseille, 13000 Marseille, France

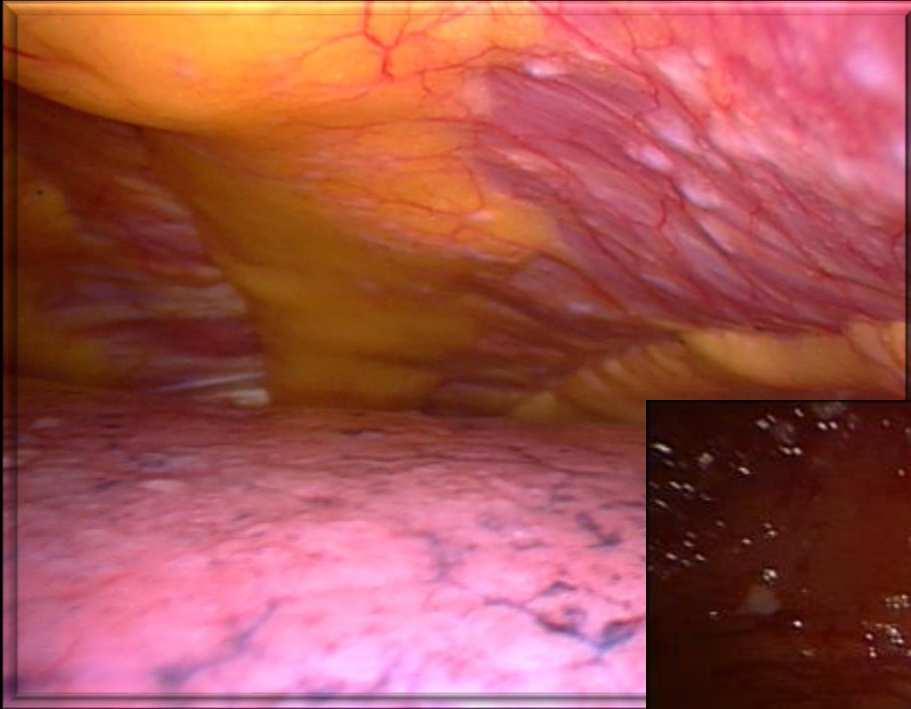
Reçu le 27 juillet 2014 ; accepté le 29 décembre 2014

Disponible sur Internet le 9 juin 2015

N1

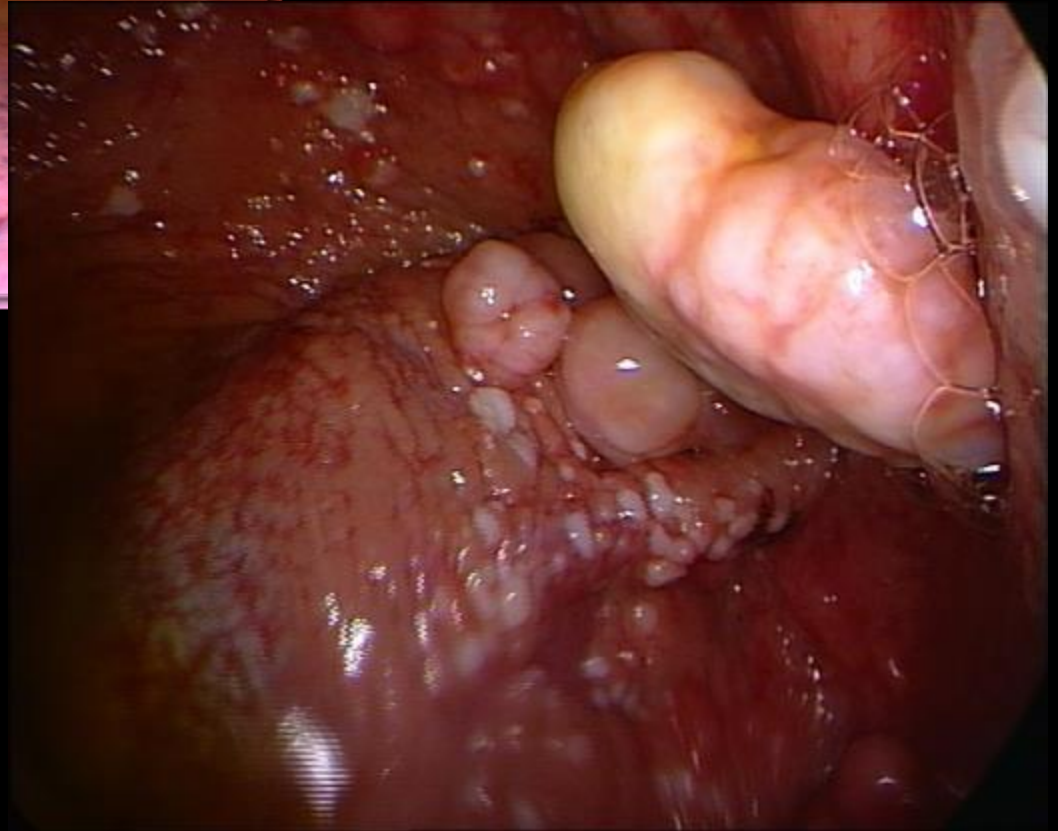
- Ilari
- Sottocarenali
- Paratracheali
- Ao-polmonari
- Paraesofagei
- Peridiaframmatici
- Pericardici
- Intercostali
- Mammari

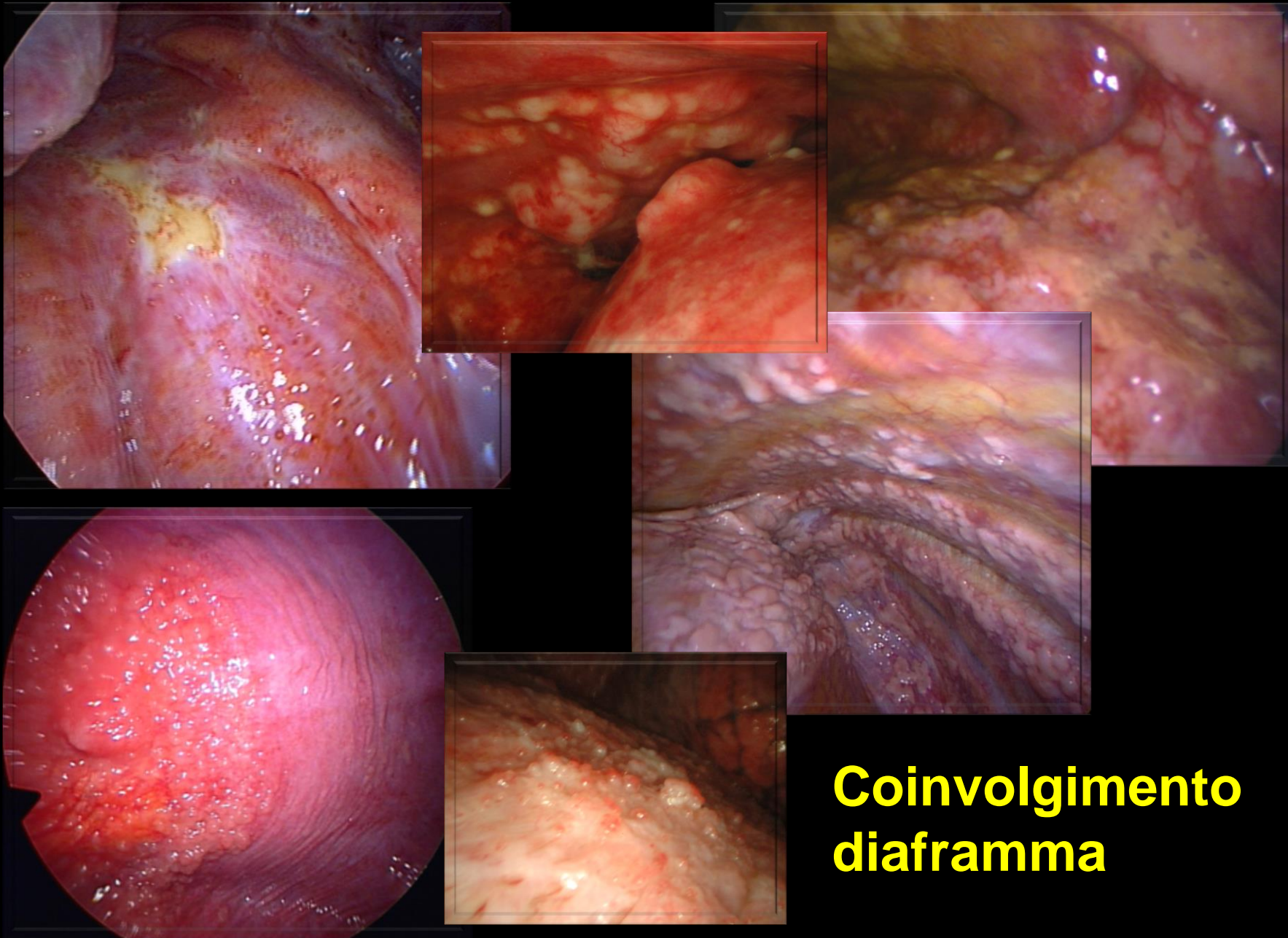




Tutti e due stadio 1?

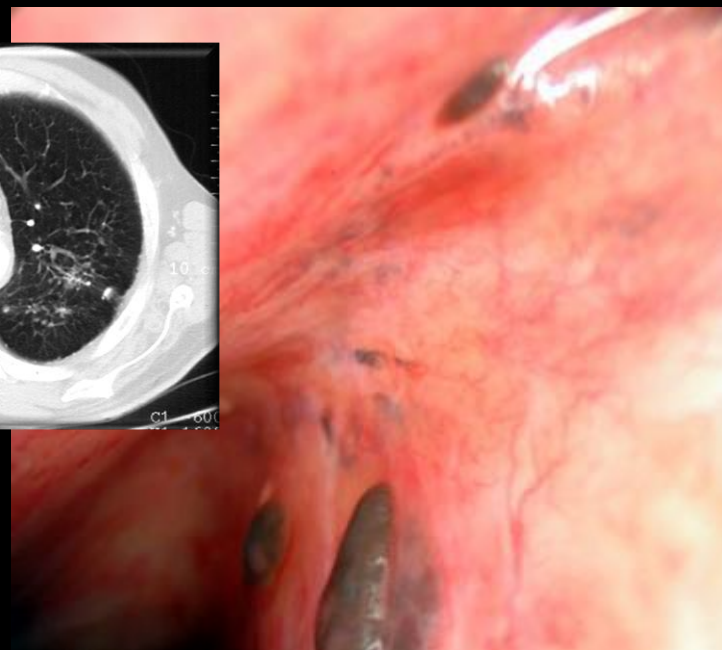
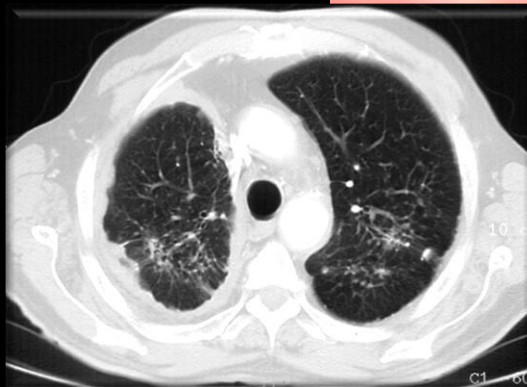
Prognosi
uguale?

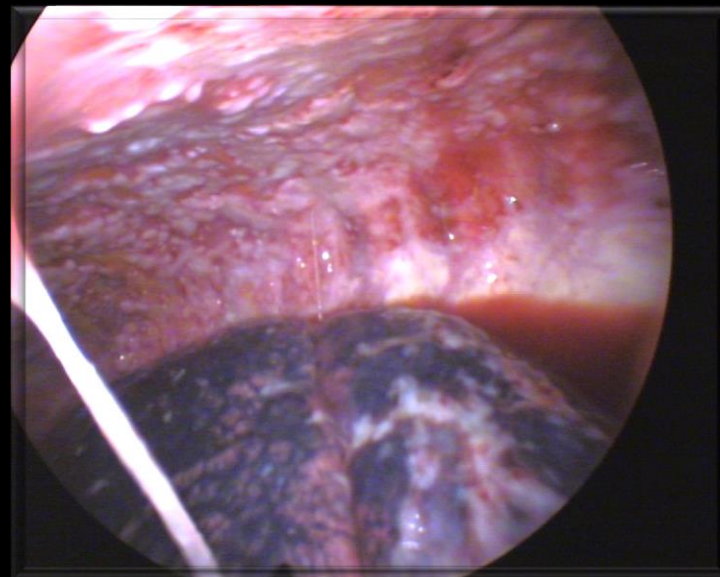




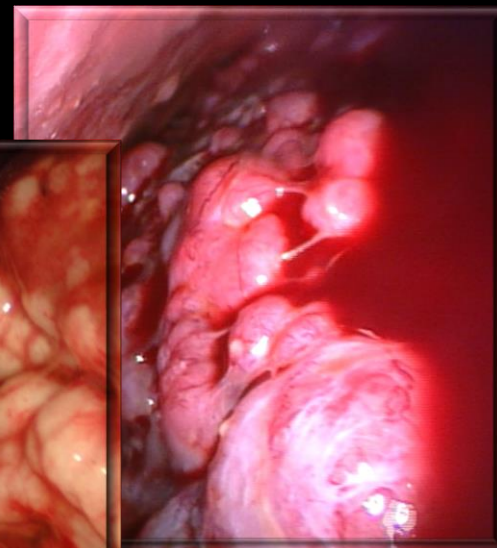
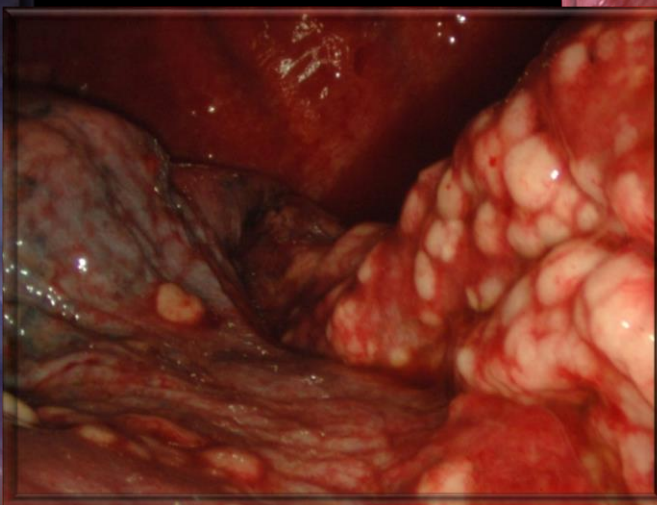
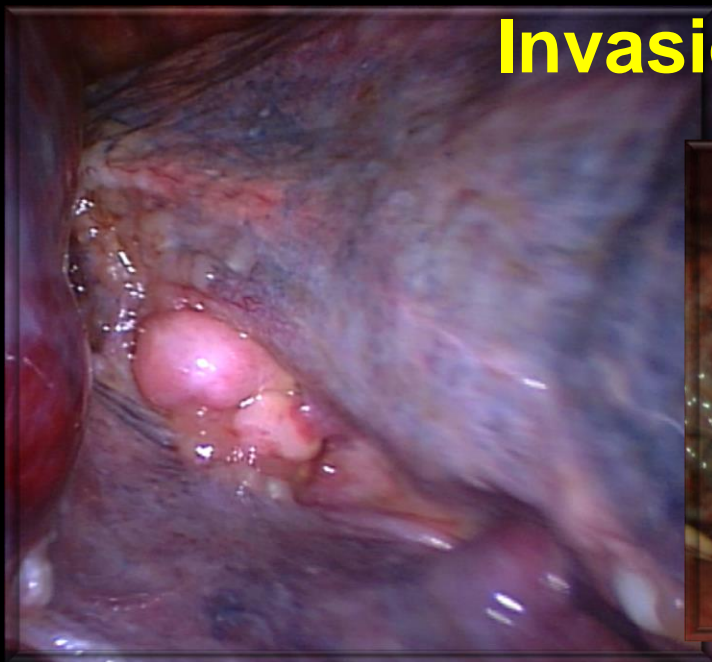
**Coinvolgimento
diaframma**

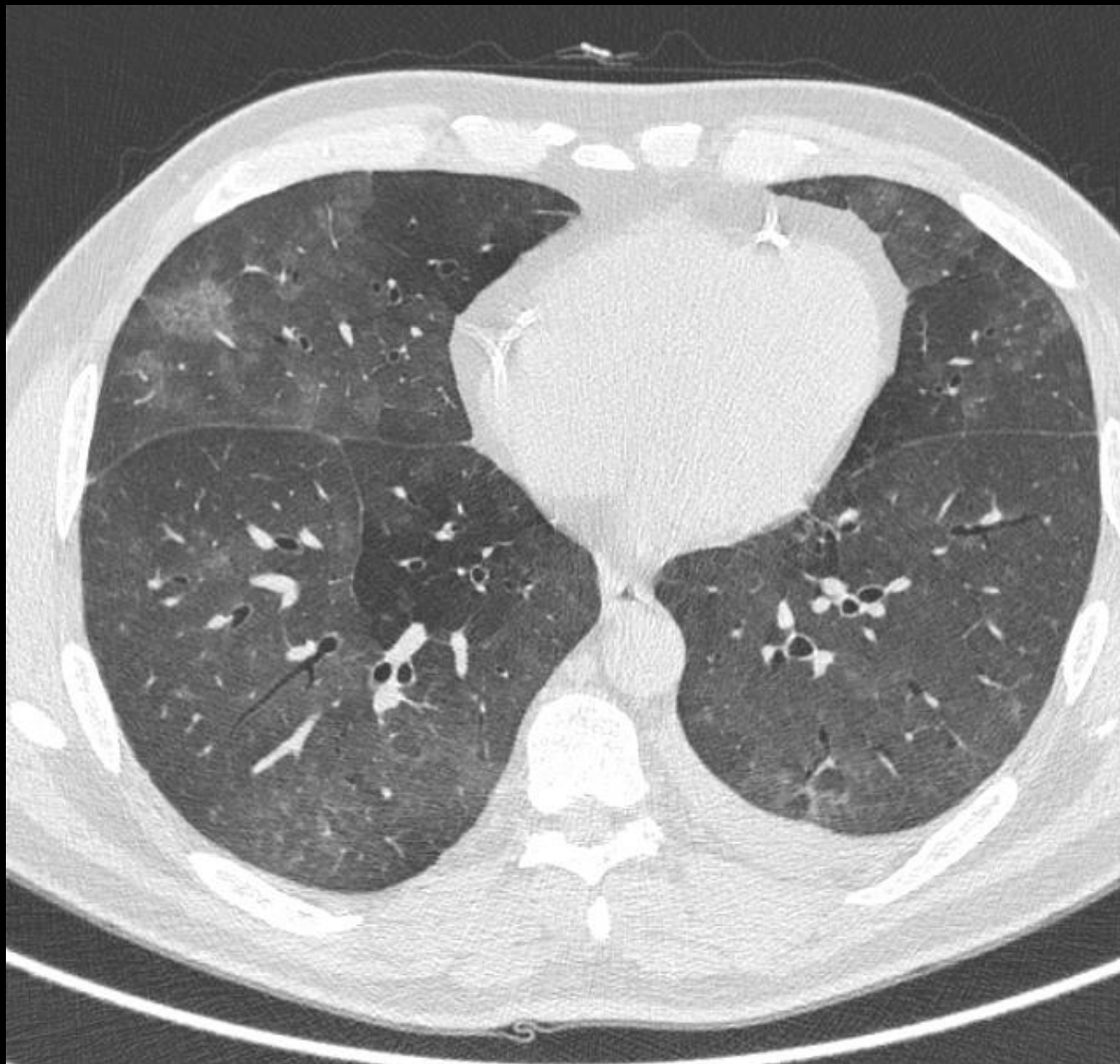
**Quale stadio
per la
retrazione
dell' emitorace?**

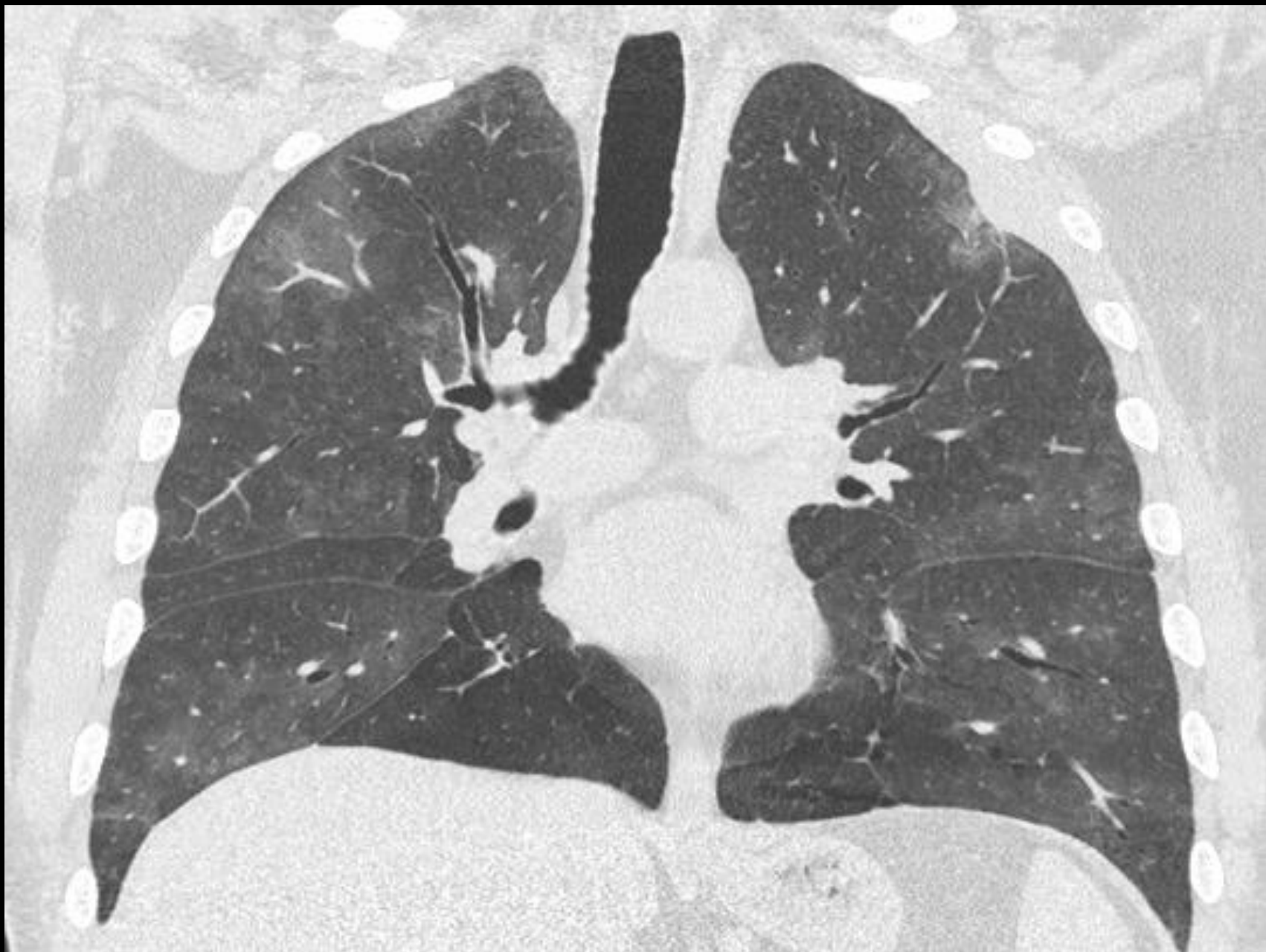


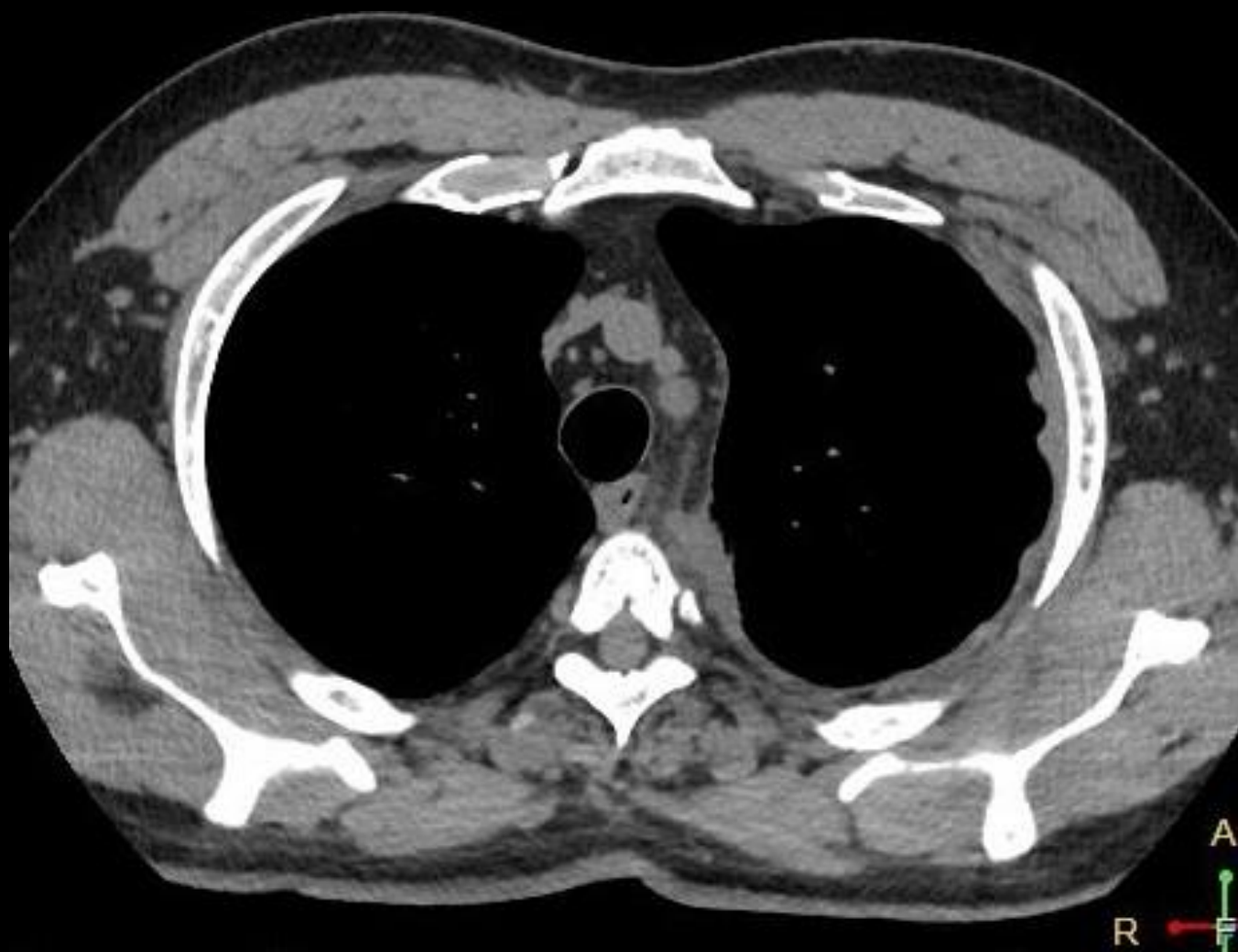
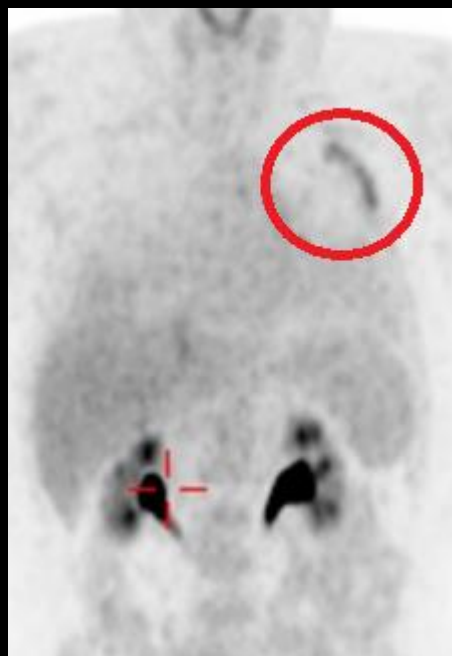


Invasione viscerale









Pneumologia - Spedali Civili Brescia

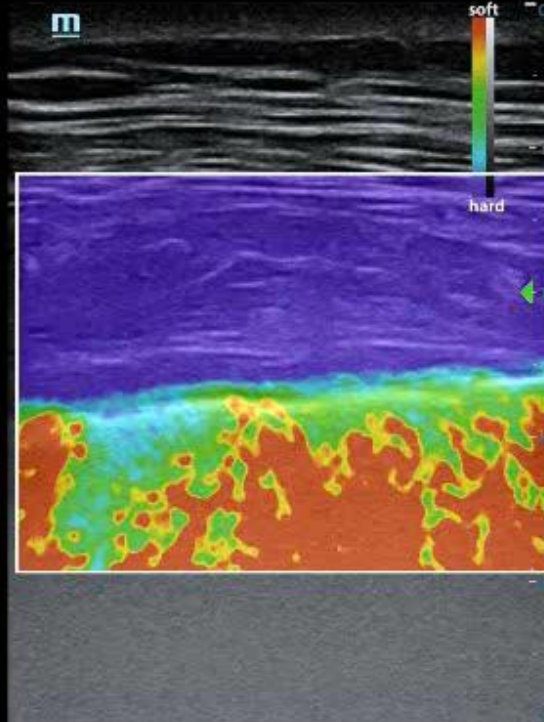
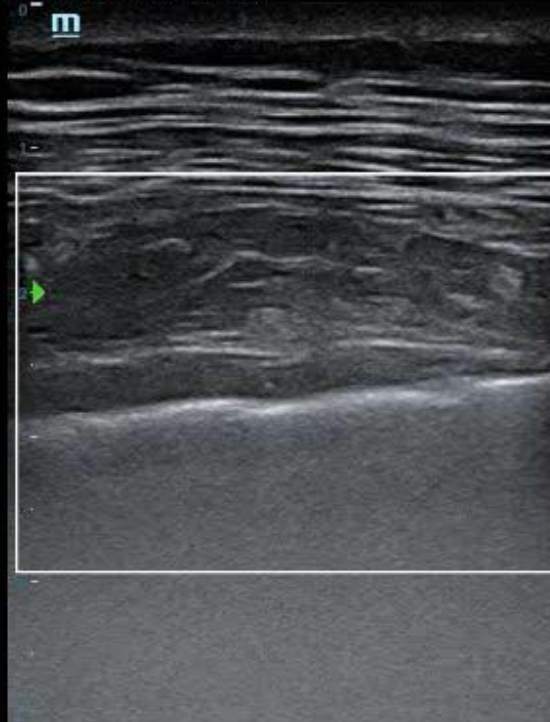
05-07-2021 17:59:18

20210705-134202-6EA0

Superfic.

L12-4s

AP 96.6% MI 1.4 TIS 0.4



mindray

M9

B

F H10.0

D 5.0

G 51

FR 23

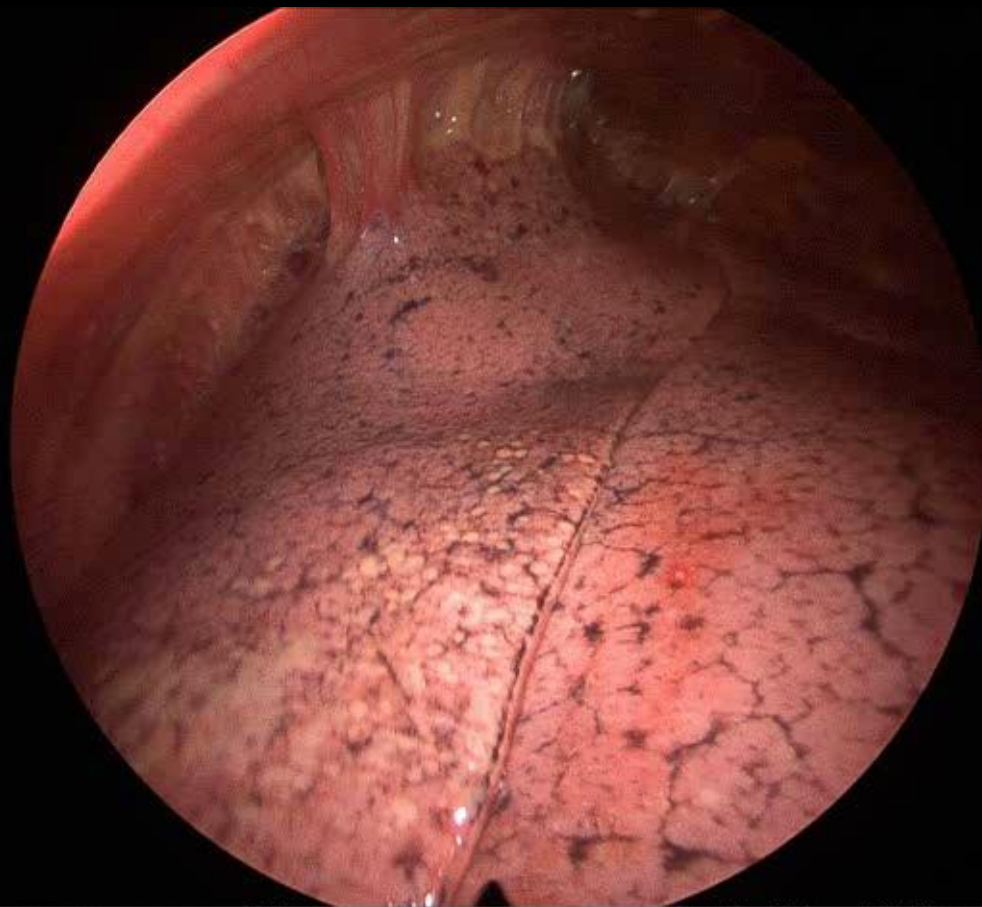
DR 110

iClear 5

E

Map E4

OP 4



x1.0 6 4 • REC 00:00:00 (32min) (30%)



Domande che da sempre mi faccio sul mesotelioma.

Quando essere aggressivi nel sospetto mesotelioma?

Quando il mesotelioma finisce di essere iniziale?

Decorticare comunque una PCA/Mesotelioma in situ?

Endoscopicamente cosa non ho visto?

Trovarlo precocemente allunga la sopravvivenza?

E non fare nulla?