Nuovi approcci dell'imaging nel paziente neutropenico febbrile

Rimini, 16 Aprile 2016

tools:

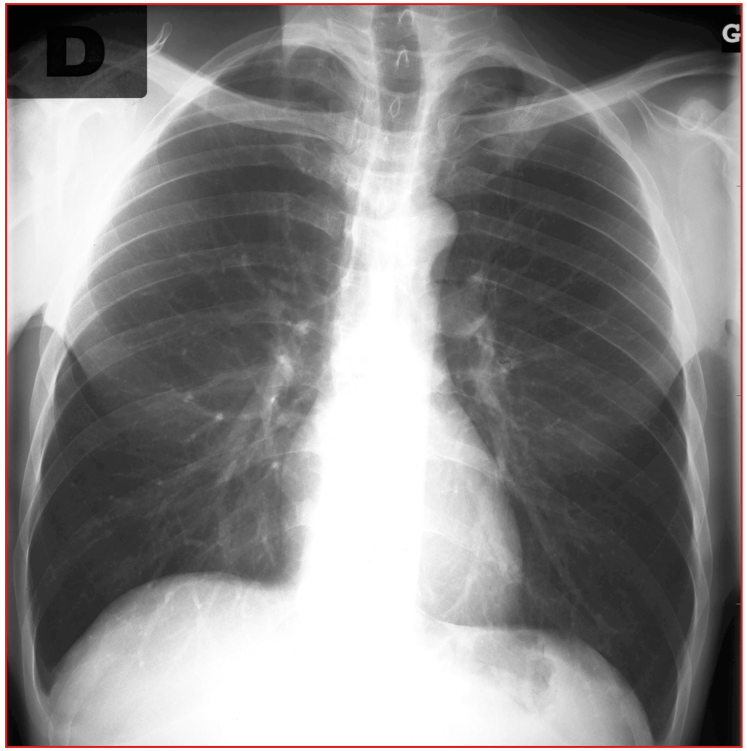
(almost yesterday…)

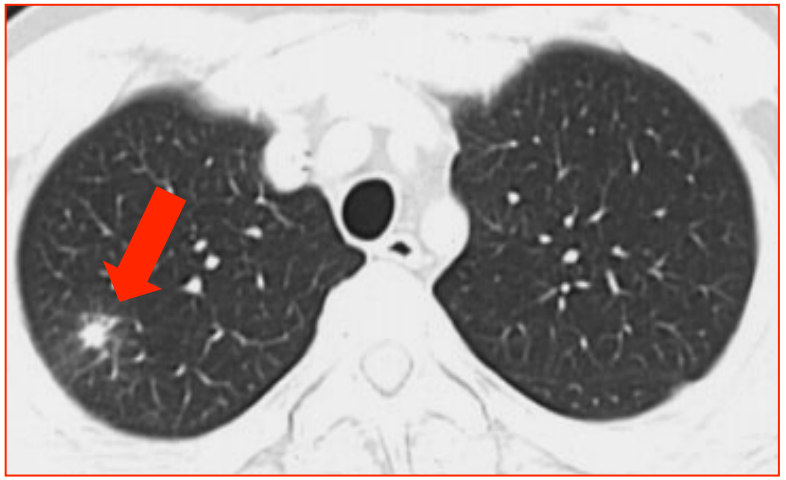
1. Chest radiography (CXR)

2. High Resolution CT (HRCT)

Nuovi approcci dell'imaging nel paziente neutropenico febbrile

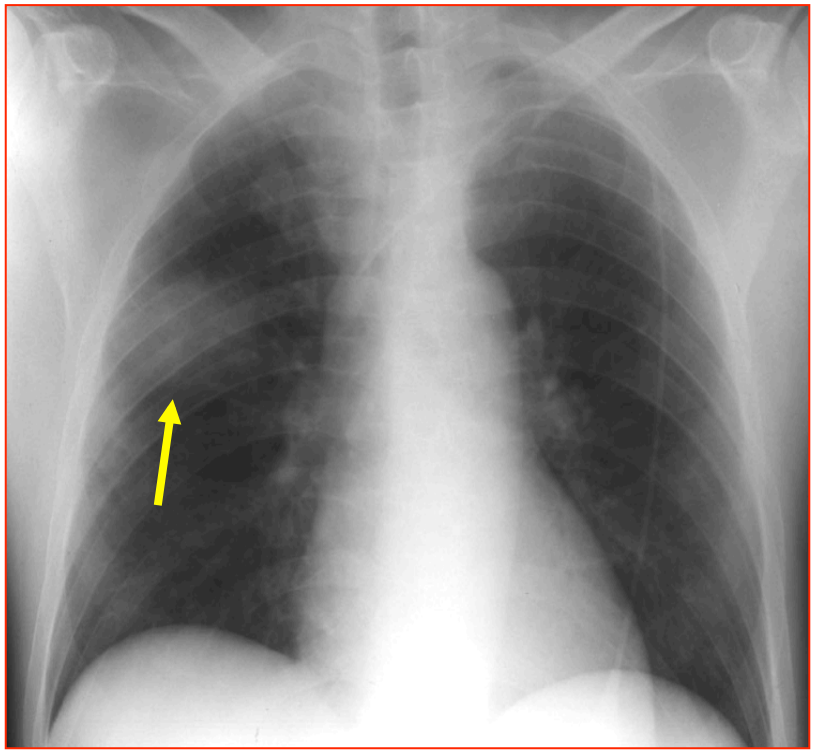
RX – → **HRCT + (60%)**

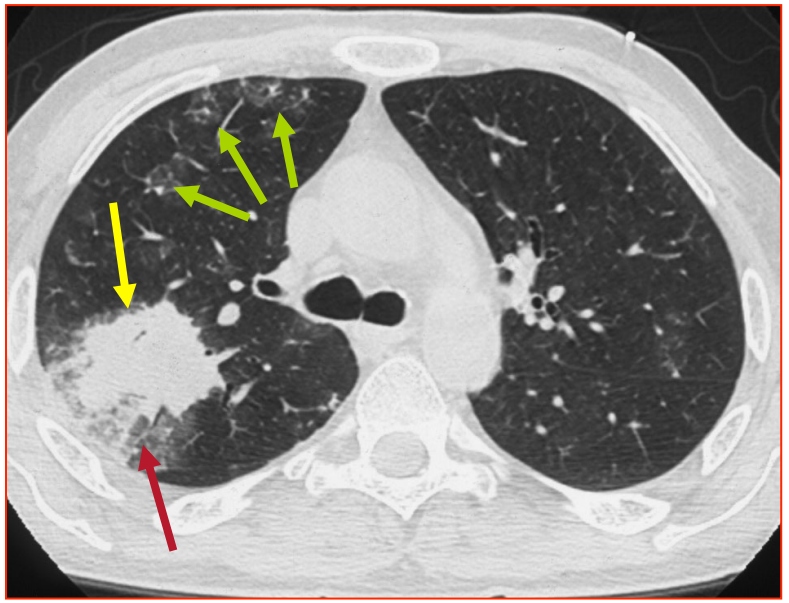




Nuovi approcci dell'imaging nel paziente neutropenico febbrile

RX + → **HRCT: more findings**





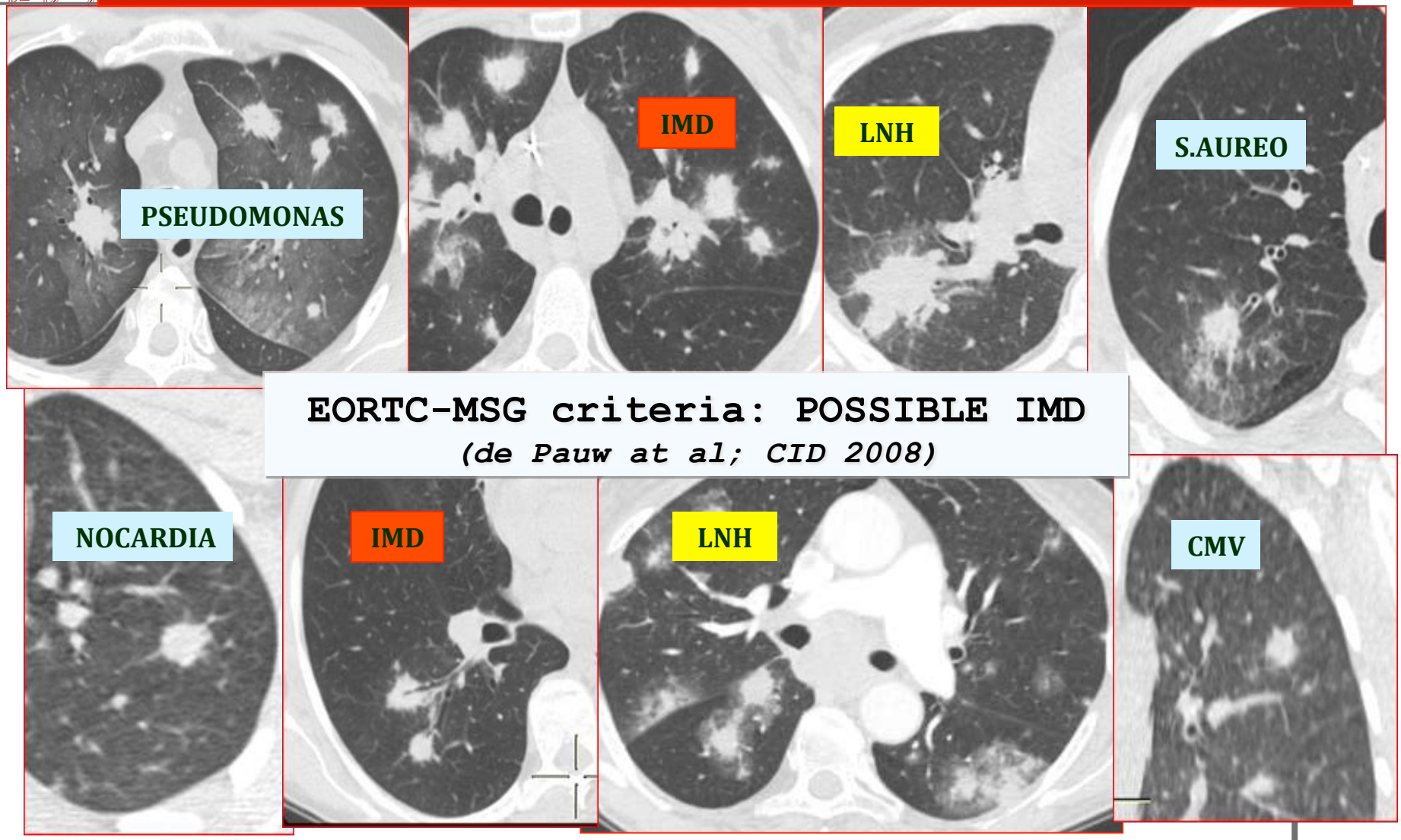
- Nodule
- Halo sign
- Ground-glass

HRCT
patterns & signs

- Ground-glass (gg)
- Consolidation
- Nodule (< o > 1
- Sept
- Tree in bud
- Crazy paving
- Halo sign
- Reversed-ha sign
- Air-crescent sign
- other (adenopaty, pleural effusion…)

NONE PATHOGNOMONIC!

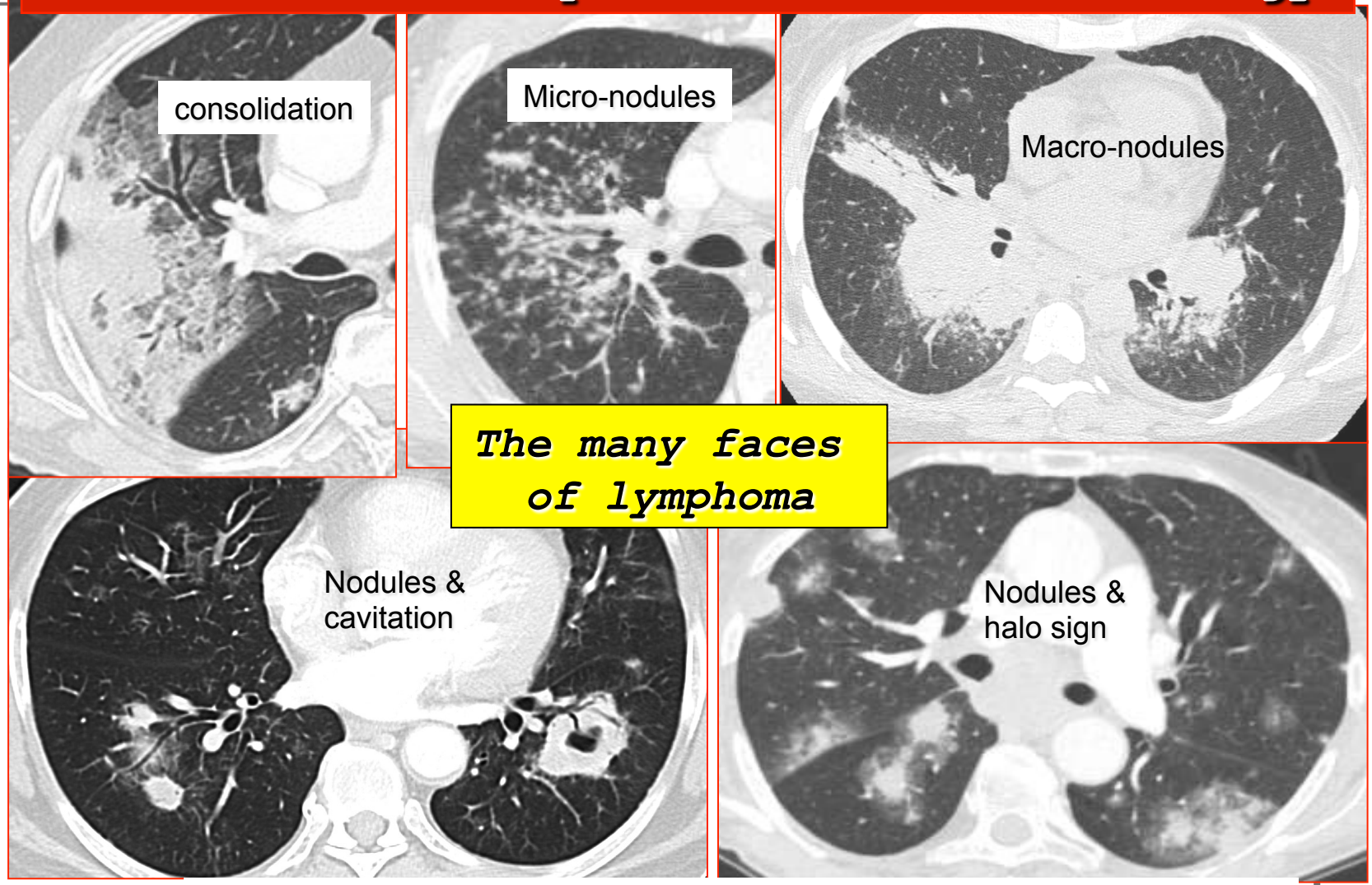
HRCT: same pattern x different etiologies



EORTC-MSG criteria: POSSIBLE IMD

(de Pauw at al; CID 2008)

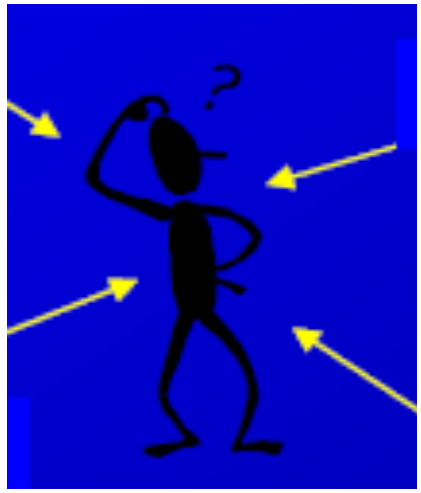
HRCT: different patterns x same etiology



Bae, Radiol Clin North Am 2008 - Lee, Clin Radiol 2009 - Chung, 2011

Nuovi approcci dell'imaging nel paziente neutropenico febbrile

- Clinical course of the disease
- Patient's immune status
- Therapy / prophylaxis



affect the radiologic appearance

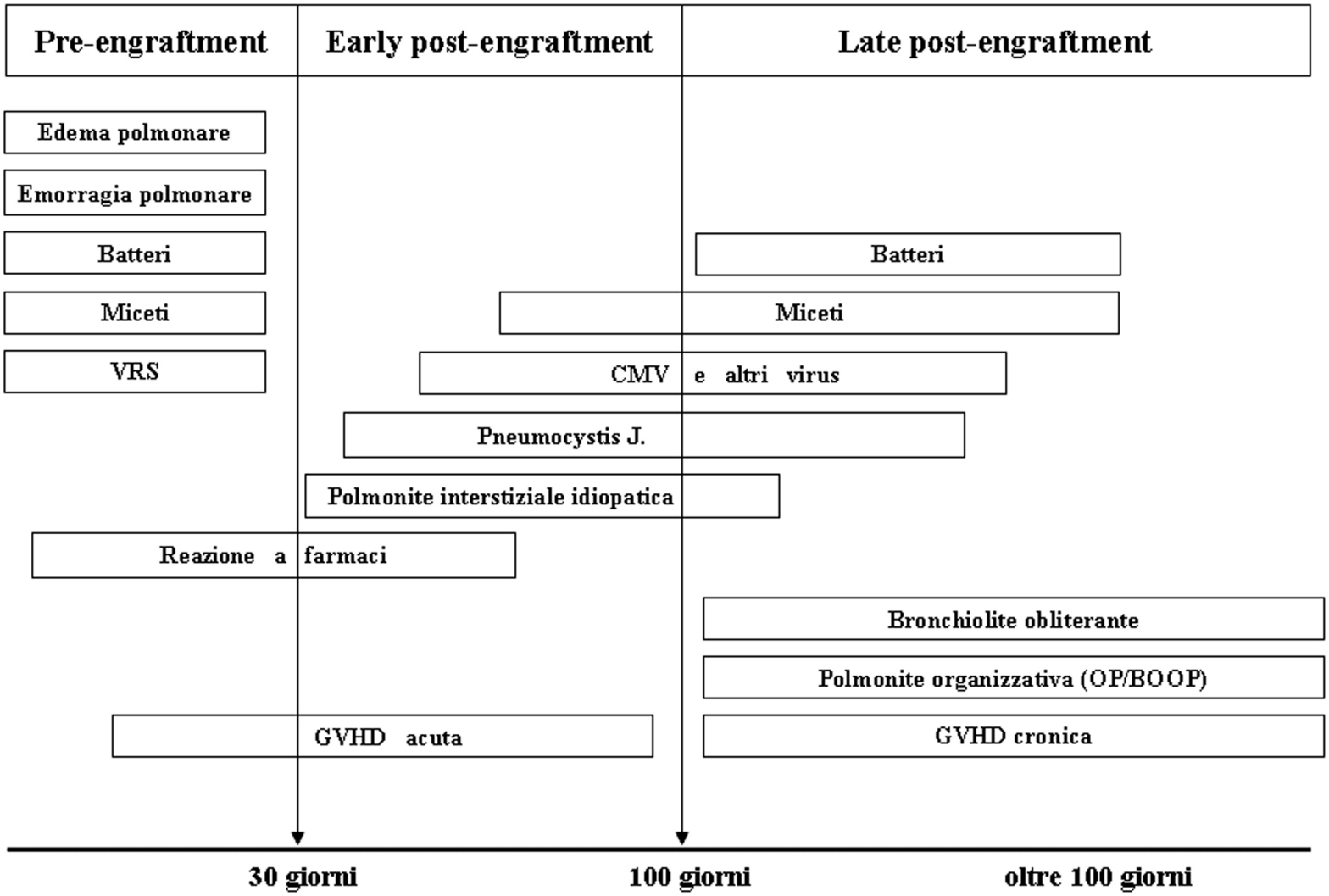
&

afflict the radiologist

DIAGNOSI DESCRITTIVE

INTERVALLO TEMPORALE da TMO

(diverso grado e tipo di deficit immunitario)



Tanaka, Jpn J Radiol 2011

…today tools…

1. Chest RX
2. High Resolution CT (HRCT)
3. CT Pulmonary Angiography(CTPA)

CT Pulmonary Angiography (CTPA)

Stefan Sonnet[1]
Carlos Hernando Buitrago-Téllez[1]
Michael Tamm[2]
Susanne Christen[3]
Wolfgang Steinbrich[1]

AJR:185, March 2005

Direct Detection of Angioinvasive Pulmonary Aspergillosis in Immunosuppressed Patients: Preliminary Results with High-Resolution 16-MDCT Angiography

CONCLUSION. High-resolution MDCT angiography has been shown to be a feasible technique to depict directly vessel occlusion in the setting of suspected fungal infections especially for early diagnosis of angioinvasive pulmonary aspergillosis in immunosuppressed patients.

MAJOR ARTICLE

Stanzani et al. Clin Infect Dis 2012;54(5):610-6.

Computed Tomographic Pulmonary Angiography for Diagnosis of Invasive Mold Diseases in Patients With Hematological Malignancies

Marta Stanzani,[1] Giuseppe Battista,[2] Claudia Sassi,[2] Russell E. Lewis,[3,4] Giulia Tolomelli,[1] Cristina Clissa,[1] Rayka Femia,[2] Alberto Bazzocchi,[2] Fabio Tumietto,[5] Pierluigi Viale,[5] Simone Ambretti,[6] Michele Baccarani,[1] and Nicola Vianelli[1]

EDITORIAL COMMENTARY

Herbrecht R, Roedlich MN. Clin Infect Dis 2012;54(5):617-20.

Earlier Diagnosis of Angioinvasive Pulmonary Mold Disease: Is Computed Tomography Pulmonary Angiography a New Step?

Raoul Herbrecht[1] and Marie-Noëlle Roedlich[2]
[1]Department of Oncology and Hematology, [2]Department of Radic

aspergillosis [12]. The vascular occlusion sign probably deserves a place among the criteria defining invasive mold disease.

MAJOR ARTICLE

Clinical Infectious Diseases® 2015;60(11):1603–10

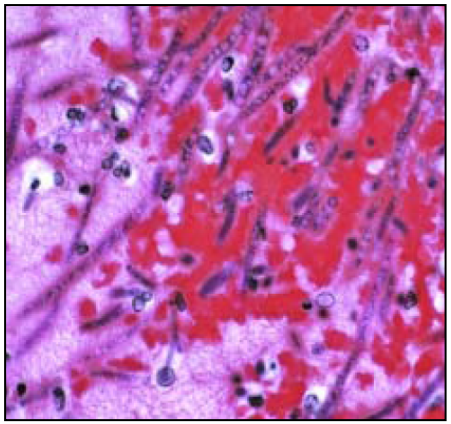
High Resolution Computed Tomography Angiography Improves the Radiographic Diagnosis of Invasive Mold Disease in Patients With Hematological Malignancies

Marta Stanzani,[1] Claudia Sassi,[2] Russell E. Lewis,[3] Giulia Tolomelli,[1] Alberto Bazzocchi,[4] Michele Cavo,[1] Nicola Vianelli,[1] and Giuseppe Battista[2]

*CTPA **improves the sensitivity**, and possibly the **specificity** of HRCT diagnosis of invasive mold diseases in the high-risk patients with hematological malignancies.*

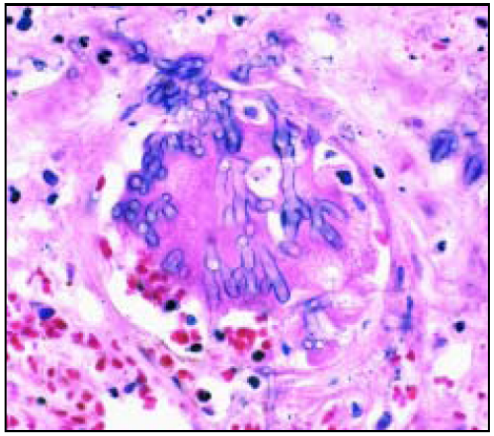
Nuovi approcci dell'imaging nel paziente neutropenico febbrile

Emorragia alveolare



Host-Dependent Patterns of Tissue Injury in Invasive Pulmonary Aspergillosis

Theodouli Stergiopoulou, MD,[1] Joseph Meletiadis, PhD,[1] Emmanuel Roilides, MD, PhD,[1,2] David E. Kleiner, MD,[3] R. Schaufele, MS, MLA,[1] Maureen Roden, MSN,[1] Susan Harrington, PhD,[4] Luqman Dad, MA,[1] Brahm Segal, MD,[5] and Thomas J. Walsh, MD[1]



Infarto emorragico

neutrophils, hyphae elongate and invade lung parenchyma and pulmonary blood vessels. The result is thrombosis of blood vessels, hemorrhagic infarction, and intra-alveolar hemorrhage. Perhaps the thrombosis of blood vessels can also be induced by the ability of *Aspergillus* to stimulate endothelial cells to become prothrombotic by expressing thromboplas-

Am J Clin Pathol 2007;127:349-355

Methods:

Hematologic febrile neutropenic patient

STEP 1

Chest HRCT

dense, well-circumscribed lesion(s):

- ✓ Ø >10 mm (> 12-15mm if subpleural)
- ✓ with or without a *halo sign*
- ✓ WITHOUT *cavitation/air crescent sign*

YES

NO

STEP 2

CTPA

Follow-up

Stanzani et al. *Clin Infect Dis* 2015

Methods:

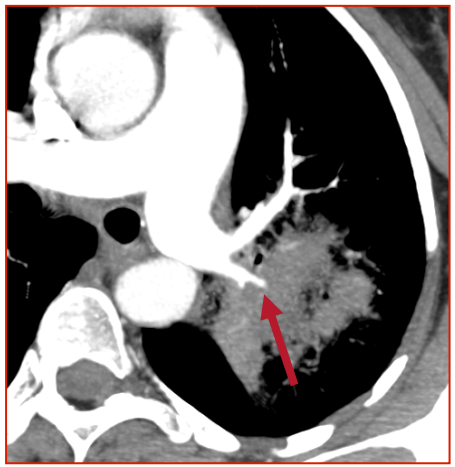
Step 2: Pulmonary Angio-CT (CTPA)

- I.v. administration of 70-75 mL of jodinated CM; flow rate: 3.5-4 mL/sec
- Chest scan: dedicated start-delay for pulmonary angiography

CONTRAINDICATIONS:

- *allergy to jodinated CM*
- *renal failure*

Step 3: post-processing



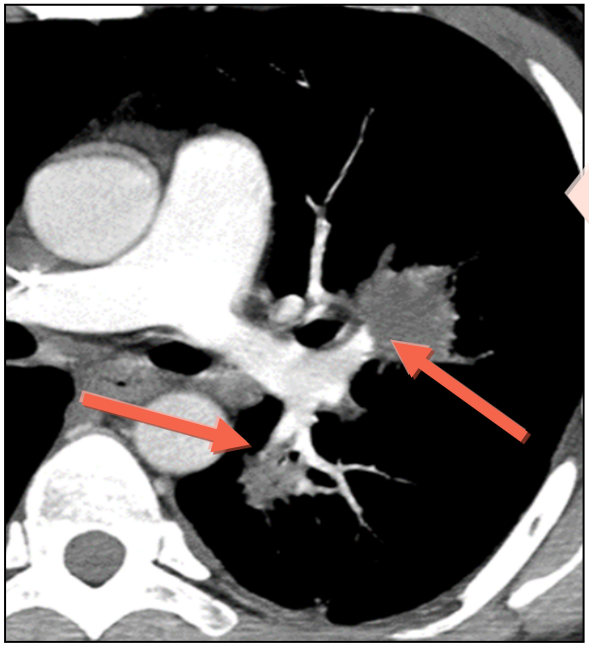
DON'T DISTURB! Radiologist at work

✓the radiologist performs 2D MPR and MIP multiplanar reformatted images using a dedicated workstation.

Stanzani et al. *Clin Infect Dis* 2015

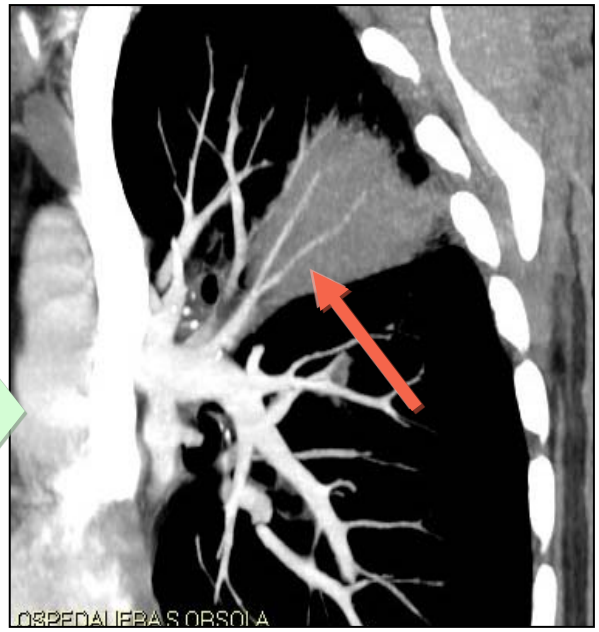
CTPA & *occluded vessel sign*

ANGIO-INVASIONE



PRESENTE

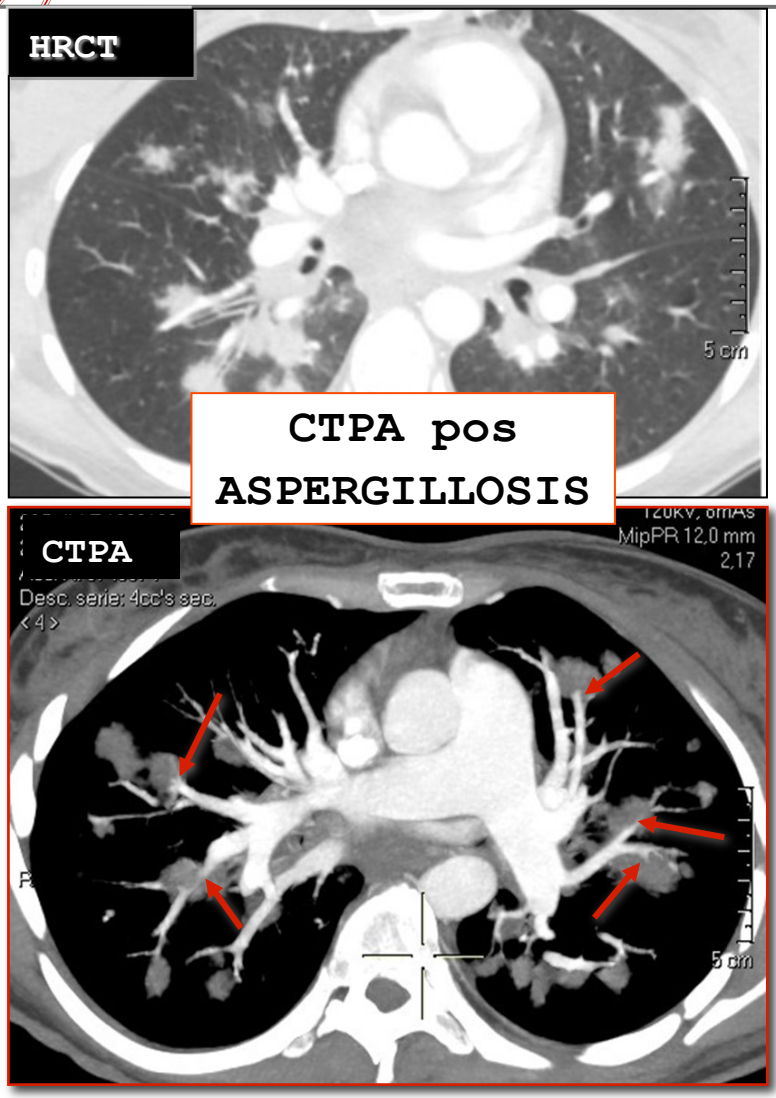
ASSENTE

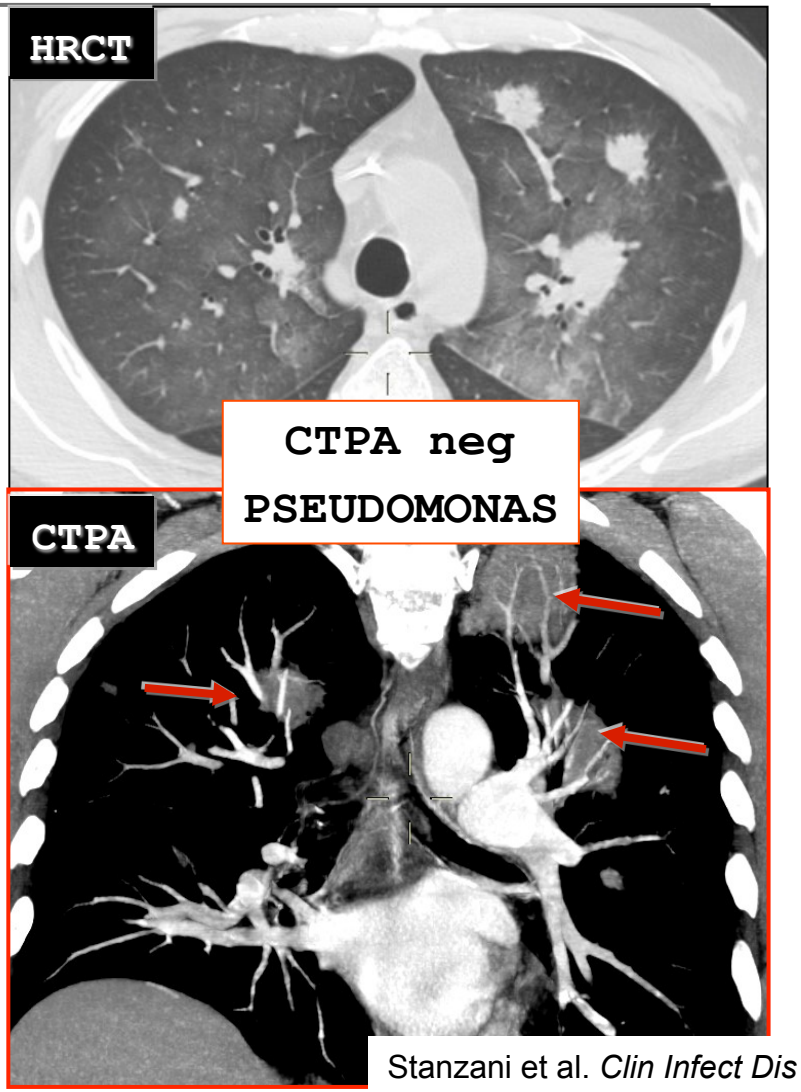


OCCLUSO	Vaso tributario:	NON-OCCLUSO
1. amputato, irregolare	1. vaso afferente	1. continuo, irregolare
2. Assenza	2. vasi interni	2. Presenza

Stanzani et al. *Clin Infect Dis* 2015

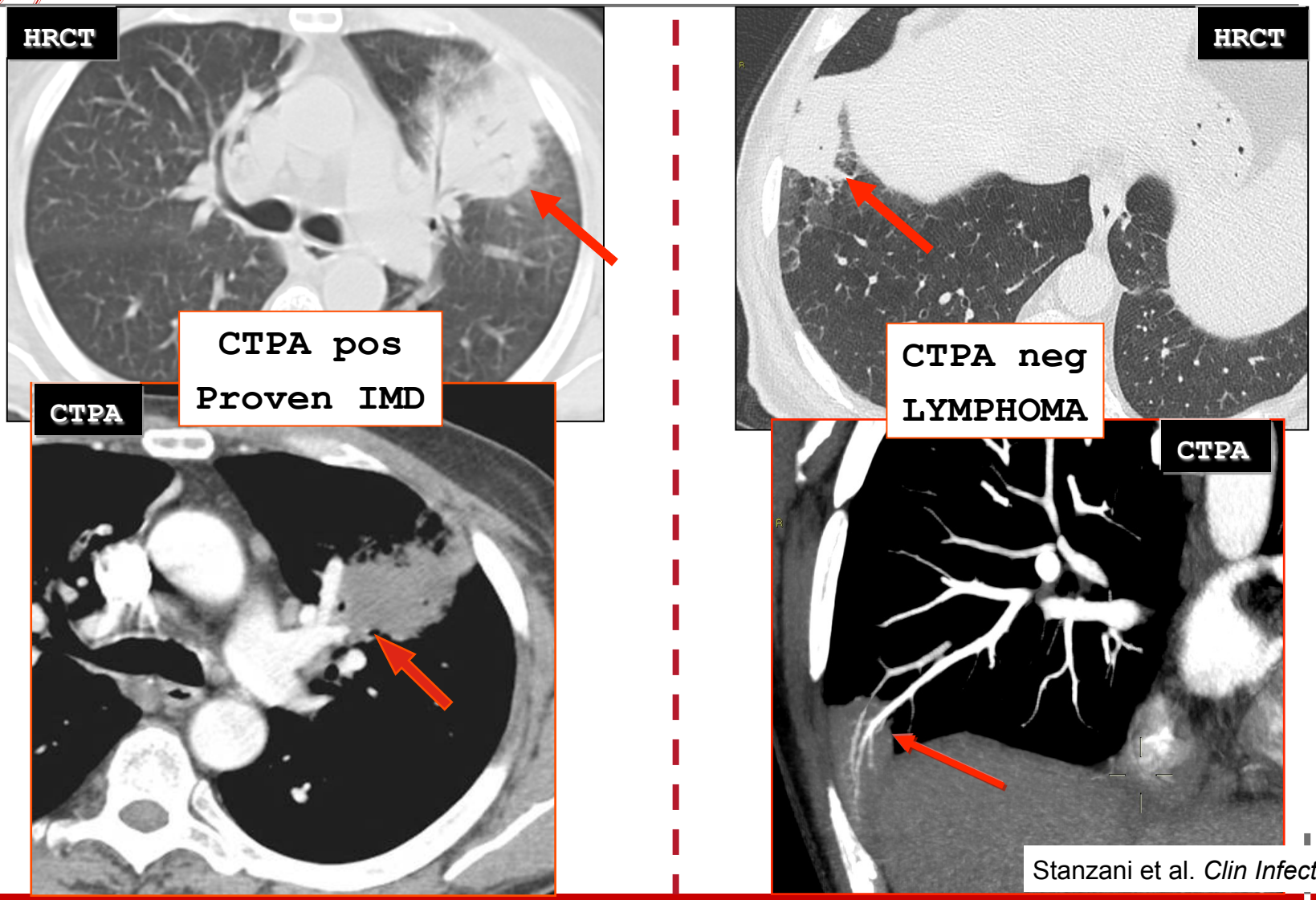
CTPA discriminates IMD from NO-IMD diseases





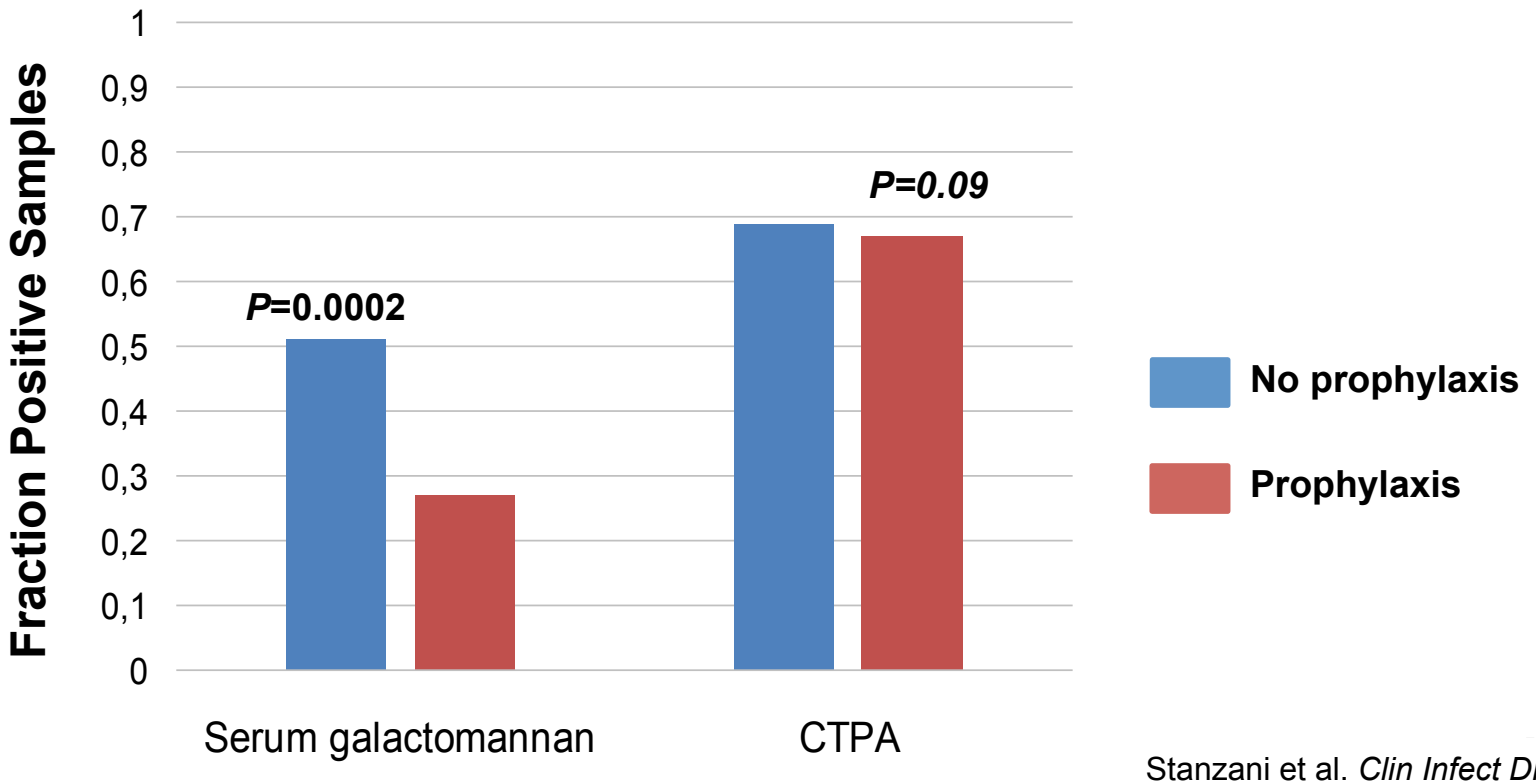
Stanzani et al. *Clin Infect Dis* 2015

CTPA discriminates IMD from lymphoma



Stanzani et al. *Clin Infect Dis* 2015

CTPA *vs* GM-test: impact of mold-active prophylaxis on sample positivity

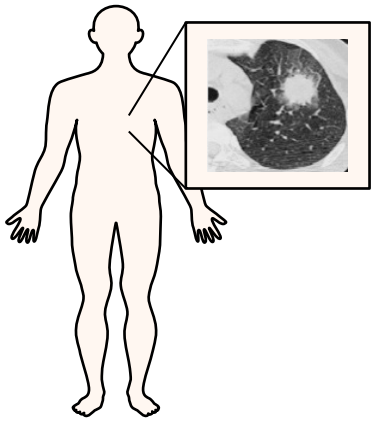


Stanzani et al. *Clin Infect Dis* 2015

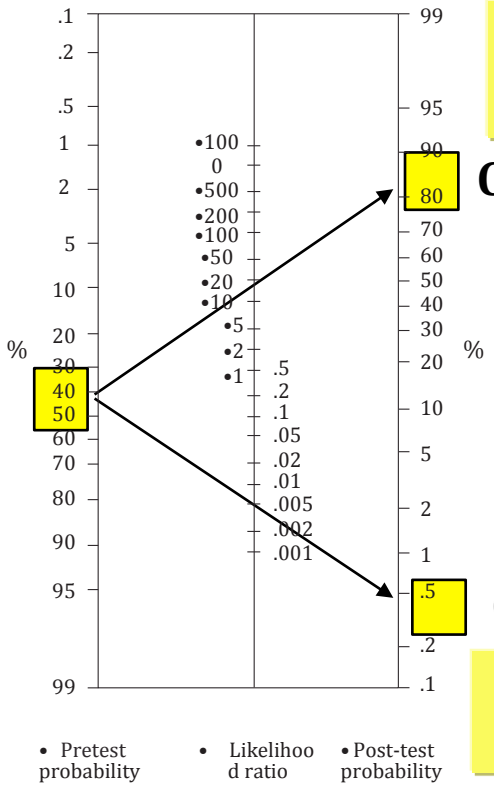
CTPA & clinical management
of febrile neutropenic pts.

- **Proven, probable, highly possible mold**
- Current study: **+ LR 8.86; - LR 0.02**

- **High-risk**
- **hematology patient**



- **40-50% pre-test**
- **Probability**
- **(i.e. EORTC *possible* cases)**



UPGRADE
possible IFI to "probable IFI"

CTPA pos. (probability >80%)

CTPA "probably deserves a place among criteria defining IMD"

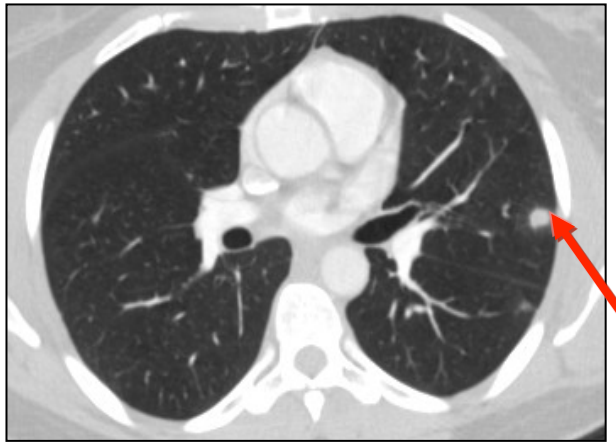
Herbrecht, CID 2012;54(5):617-20

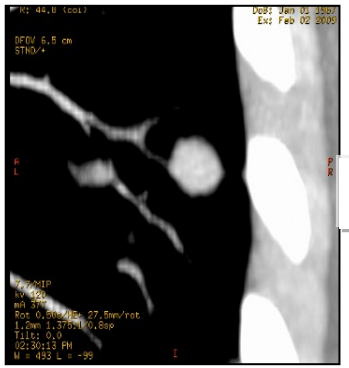
CTPA neg. (probability < 1%)

DOWNGRADE
possible IFI to "probably NO-IFI"

Stanzani et al. *Clin Infect Dis* 2015

CTPA technical limits & *unreadable* cases





10 mm

Small (<12mm) peripheral lesions

Sonnet S et al. AJR 2005;184:746-751; Stanzani et al. *Clin Infect Dis* 2015

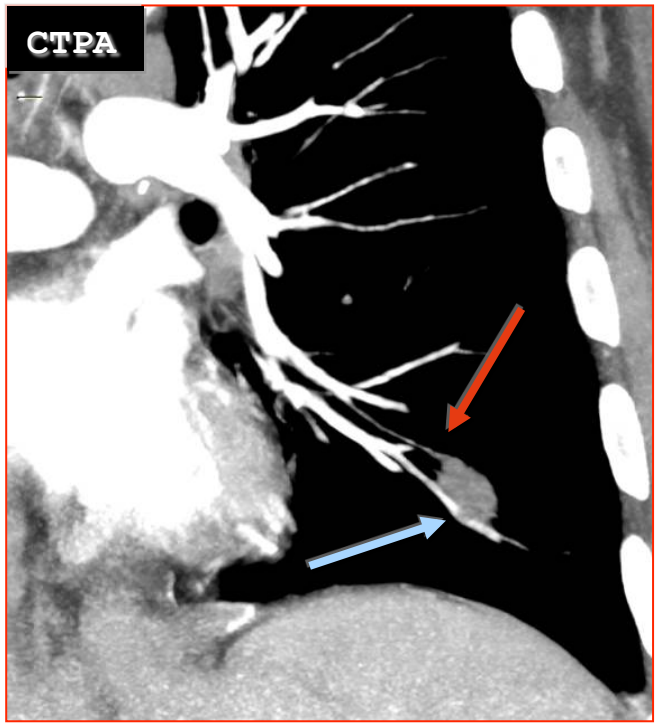
CTPA need training

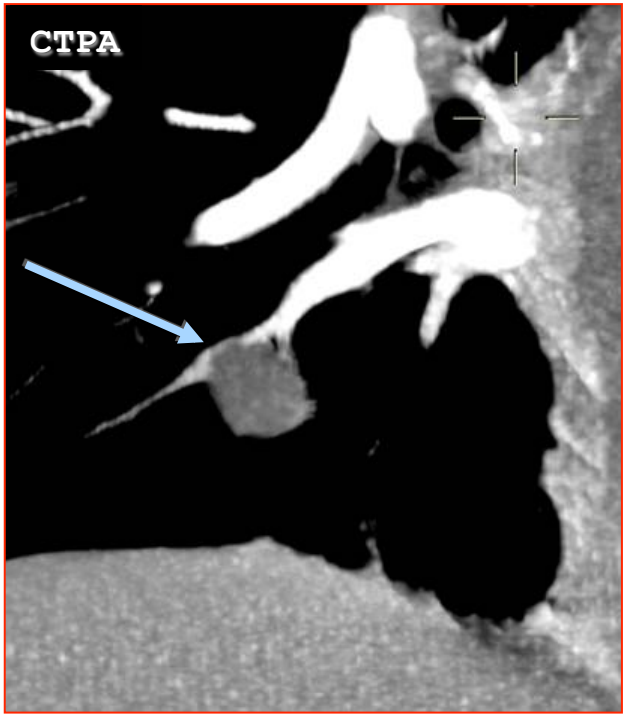
- Technical execution
- Post-processing MPR reconstructions
- Partial vessel occlusion

ARTERIA
VENA

- B.A., 44 ys, M
- Lymphoma; relapse
- Prophilaxis: fluconazole
- Serum GM pos

Probable IMD



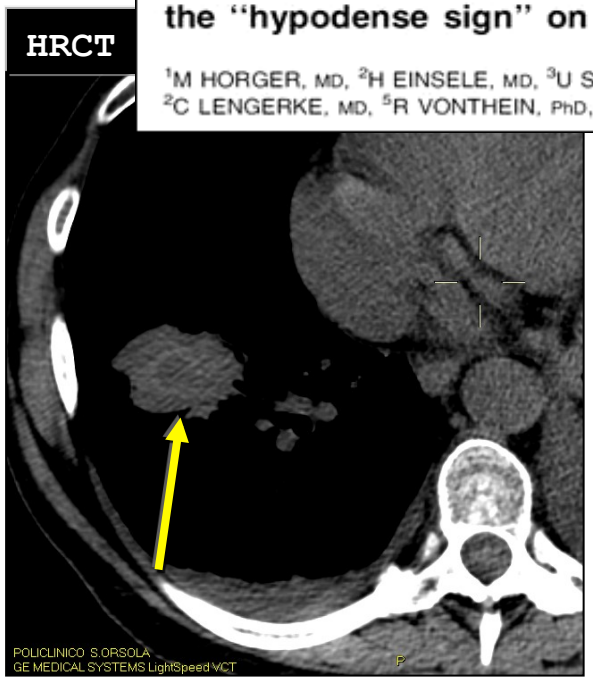


Il *segno* nel cassetto

The British Journal of Radiology, 78 (2005), 697–703 © 2005 The British Institute of Radiology
DOI: 10.1259/bjr/49174919

Invasive pulmonary aspergillosis: frequency and meaning of the "hypodense sign" on unenhanced CT

[1]M HORGER, MD, [2]H EINSELE, MD, [3]U SCHUMACHER, MD, [4]M WEHRMANN, MD, [2]H HEBART, MD, [2]C LENGERKE, MD, [5]R VONTHEIN, PhD, [1]C D CLAUSSEN, MD and [1]C PFANNENBERG, MD



HRCT & Hypodense Sign:

- specificità 100%
- sensibilità 30%

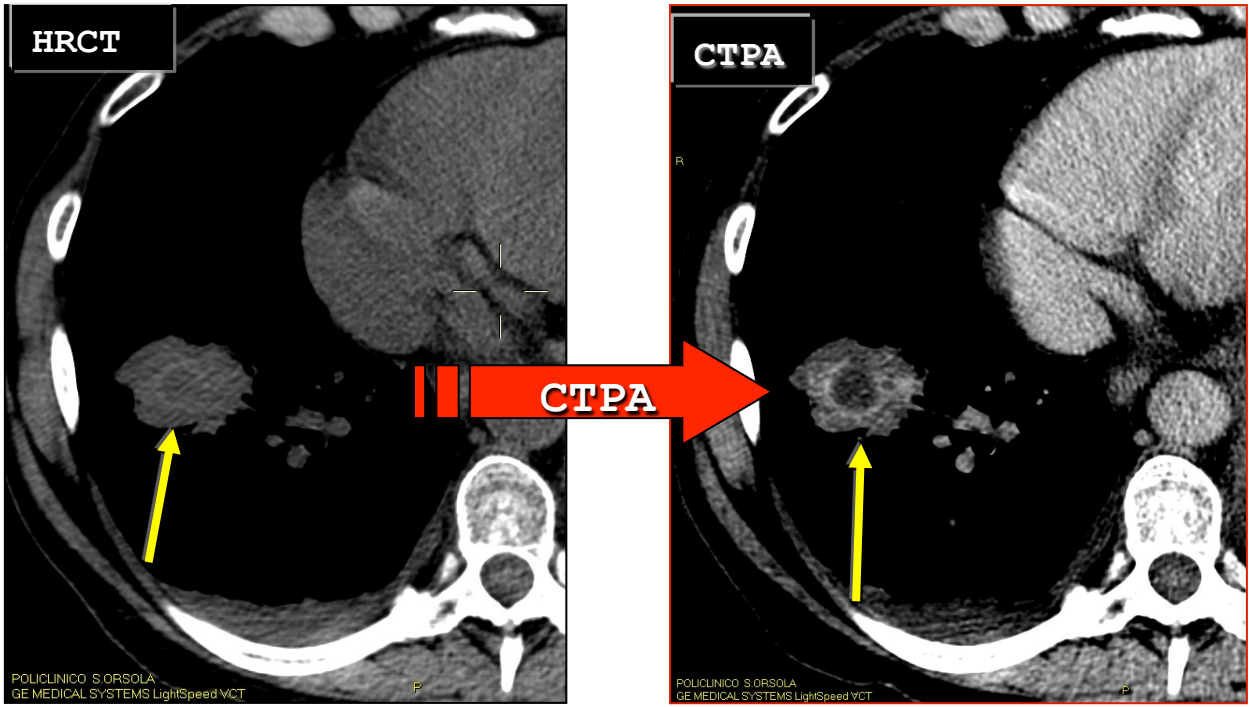
CTPA & Hypodense Sign

in patients who receive iv CM, the sensitivity of hypodense sign *improves* from 30.2% to 80%

- **Hypodense sign**

- **54 ys, F**
- **AML; resistance**
- **Profilaxis: fluconazole**
- **Serum GM pos**

ASPERGILLUS NIGER



Sassi et al, submitted

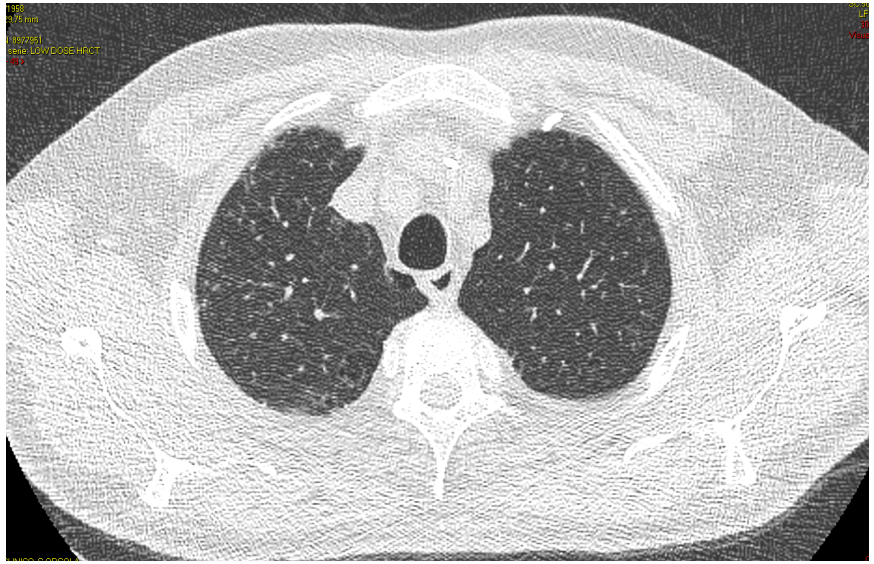
CTPA disadvantages:

- **Technical limits**
  (small and/or peripheral
  - ✓Training
  - ✓Hypodense sign
- **Iodinated CM sommini**
  - ✓No adverse reactions
  - ✓No renal failure
- **Additional radiation**
  - ✓LOW-DOSE protocol

Sonnet S et al. AJR 2005;184:746-751; Stanzani et al. *Clin Infect Dis* 2015

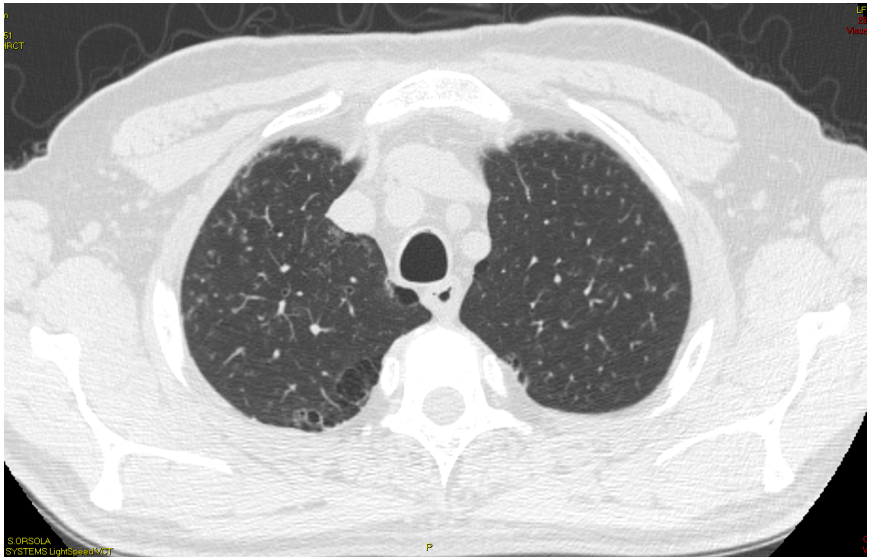
Bologna: LOW-DOSE CT (LDCT)

LOW dose



CTDI: 2.13 mGy
DLP: 71.10 mGy

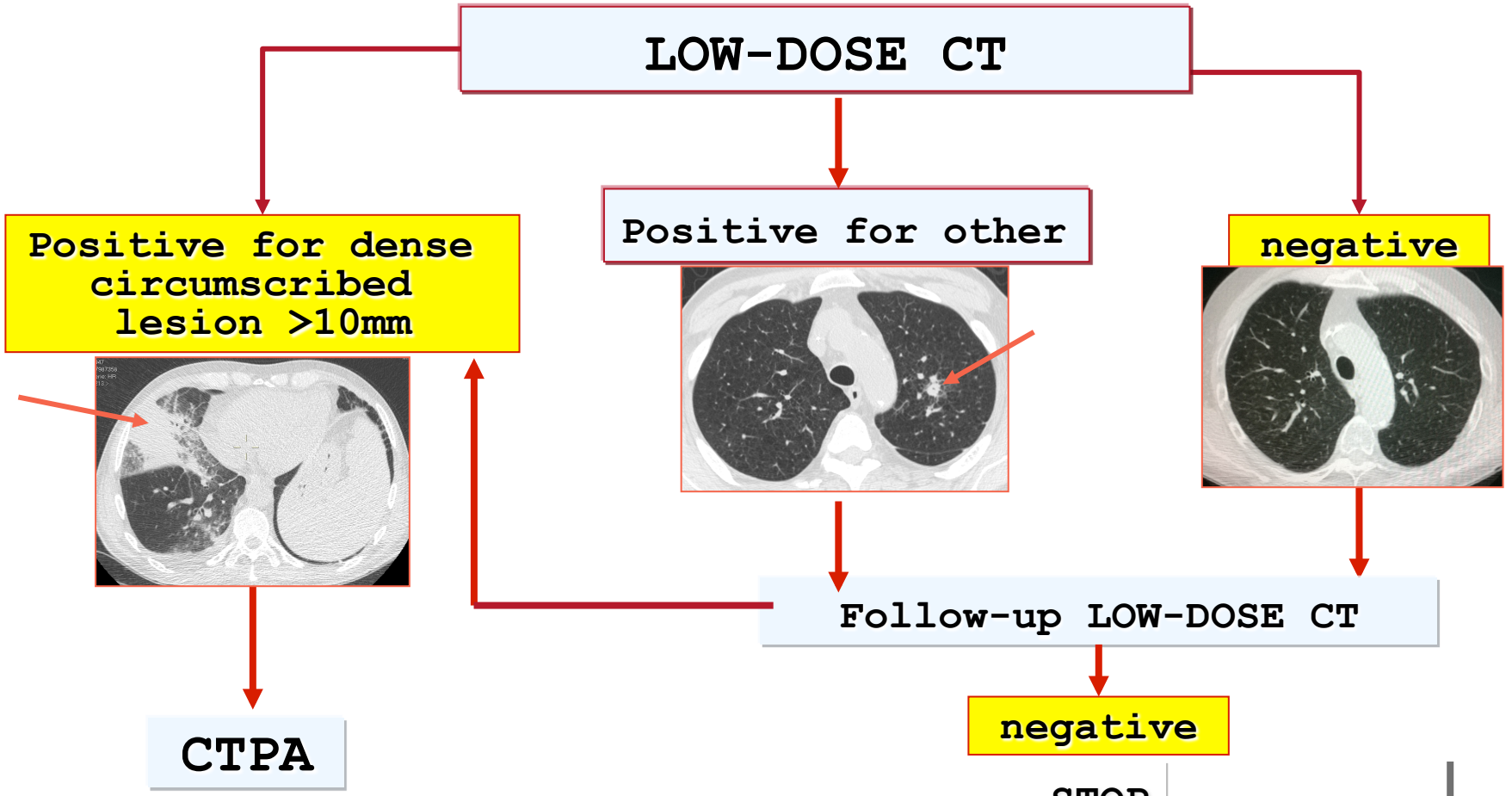
STANDARD dose



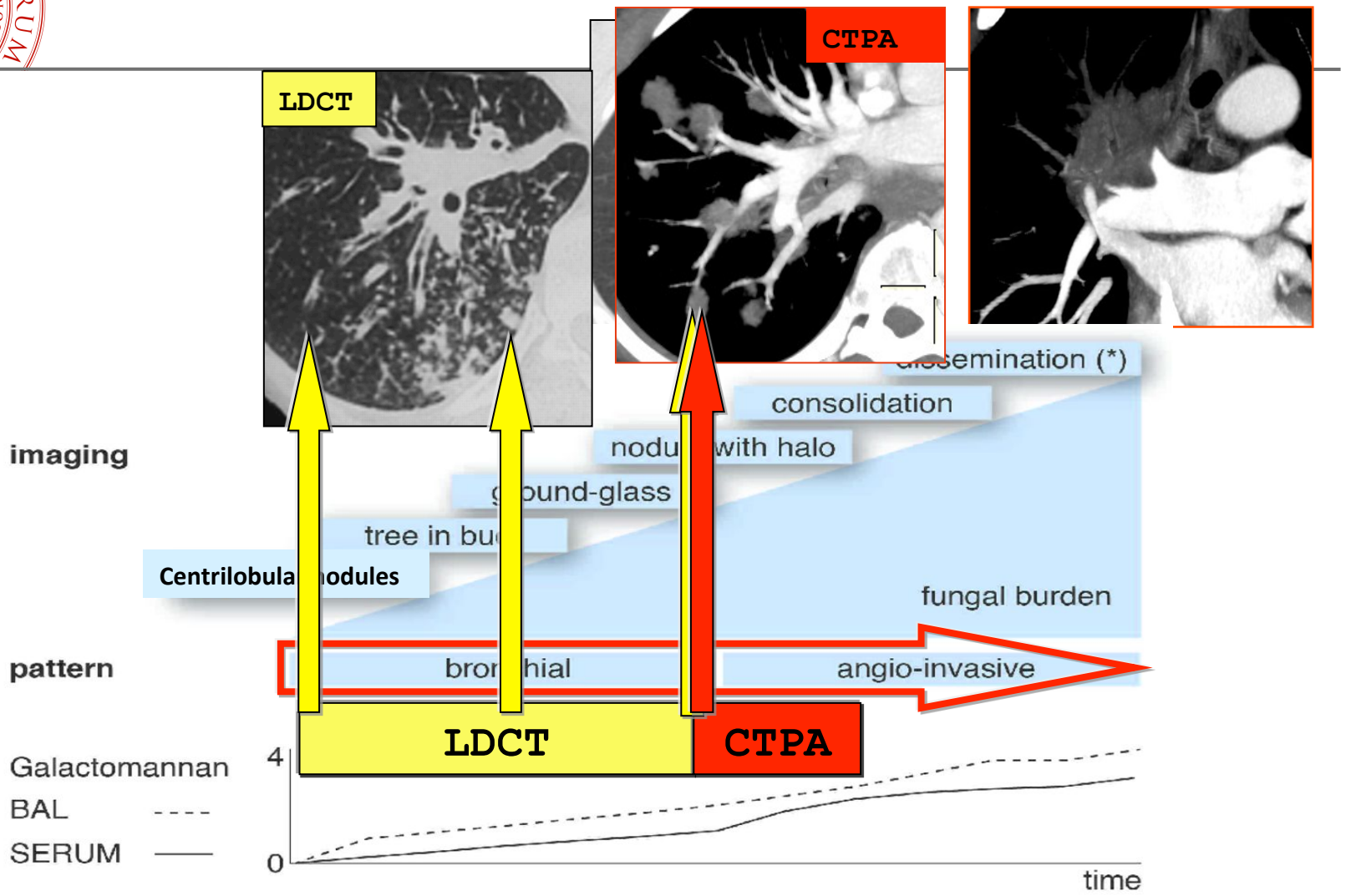
CTDI: 6.14 mGy
DLP: 227.80 mGy

Nuovi approcci dell'imaging nel paziente neutropenico febbrile

Bologna: low-dose CT in febrile neutropenic pts.



The clinical & radiological evolution of IMD
in neutropenic pts.



* lesions evolve to air crescent and cavity when neutrophils recover
BAL: bronchoalveolar lavage.

Modificata da M.Nucci et al.Haematologica 2013;98:1657-1660

The role of diagnostic imaging in the management of febrile neutropenic pts.

is changing:

- **Screening: LDCT**
  Low-dose CT should replace chest-XR in high risk pts
- **Characterization: CTPA**

Tomorrow tools……

1. Low-dose CT (LDCT)

2. CT Pulmonary Angiography(CTPA)

Thank you!

Acknowledgment

Bologna
IFI working group

- Marta Stanzani [1]
- Nicola Vianelli [1]
- Claudia Sassi [2]
- Giuseppe Battista [2]
- Russell E. Lewis [3]
- Riccardo Ragionieri[1]

[1]*Institute of Hematology "Lorenzo e Ariosto Seràgnoli", Department of Hematology and Oncology, S.Orsola-Malpighi Hospital, University of Bologna, Italy*

[2]*Department of Experimental, Diagnostic and Specialty Medicine (DIMES), Division of Radiology, S.Orsola-Malpighi Hospital, University of Bologna, Italy*

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CASO 1

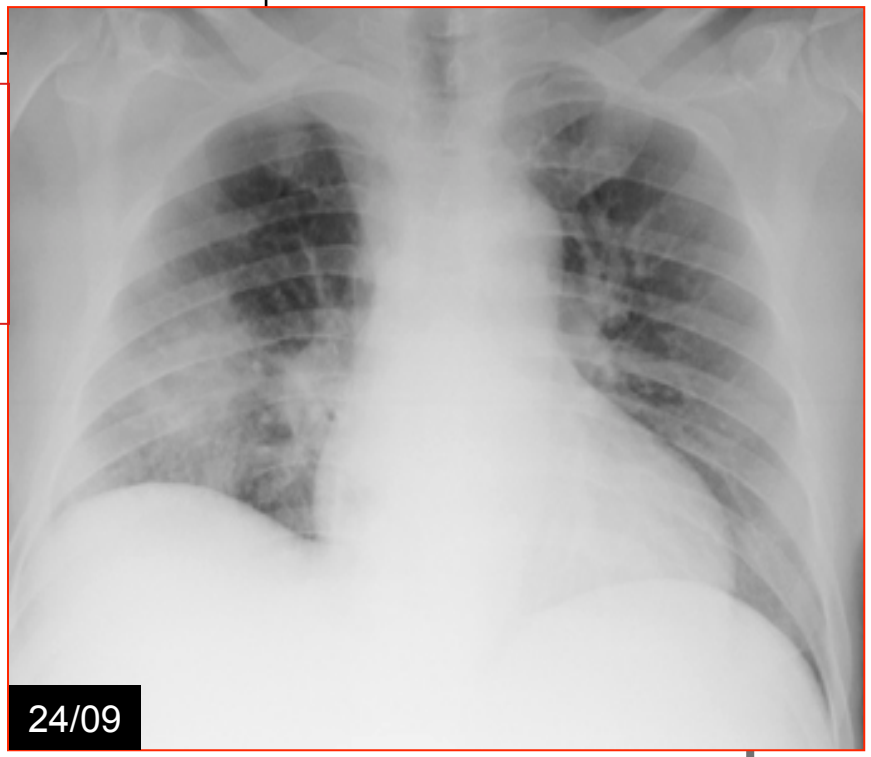
CASO CLINICO n.1

- M – 66 aa
- 1995 = Leucemia a cellule capellute / 1996 = RC
- 1999 / 2001 / 2004 / 2007 = I-II-III-IV relapse-RC
- 2007 = apicectomia polmone dx (BAC)
- 08/2008 = V relapse (Rituximab)

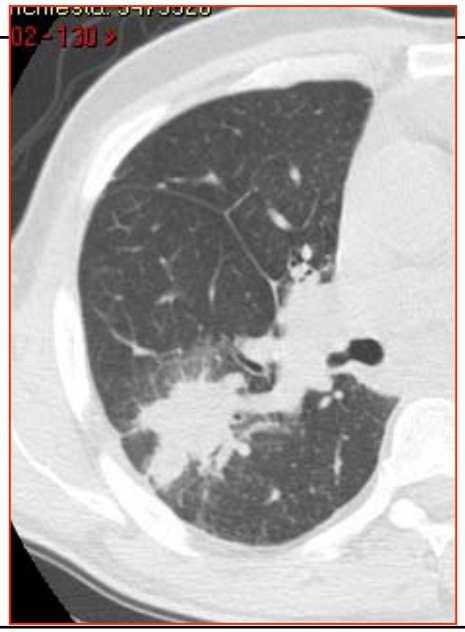
- ricovero in altro ospedale per CT: pancitopenia, febbre:
- TC “focolaio bp base dx”
- Terapia antibiotica 1° linea – 2° linea

- BAL (15/09) = negativo per cellule neoplastiche, microrganismi PAS- positivi e bacilli alcol-acido resistenti

EMATOLOGIA SERAGNOLI



- *"Addensamento parenchimale nodulare con sfumato GG periferico, al segmento … Gli aspetti della lesione sono compatibili con IFI …"*

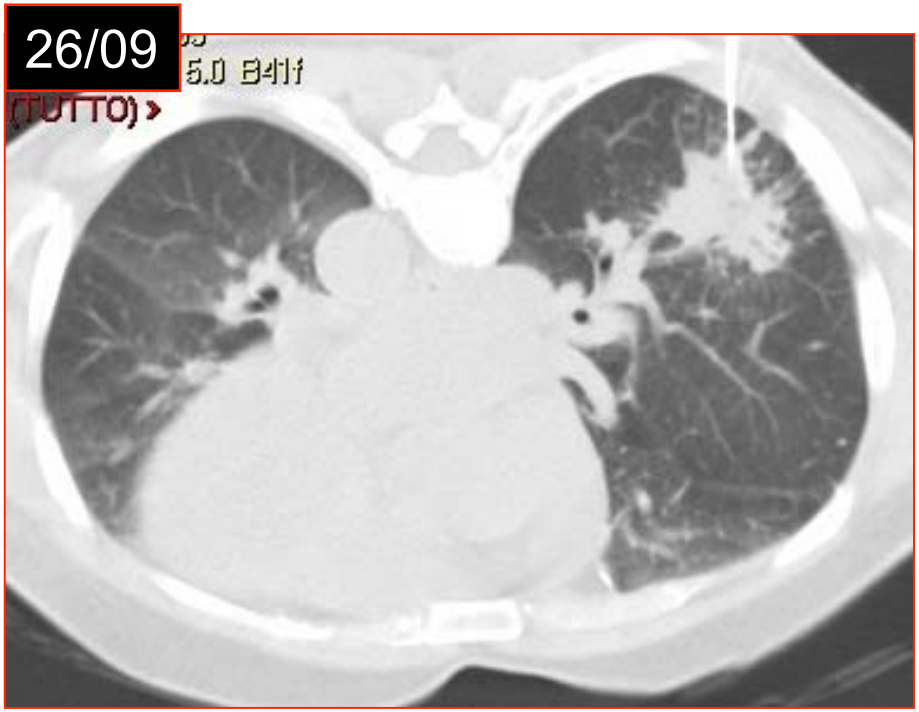


25/09

CTPA

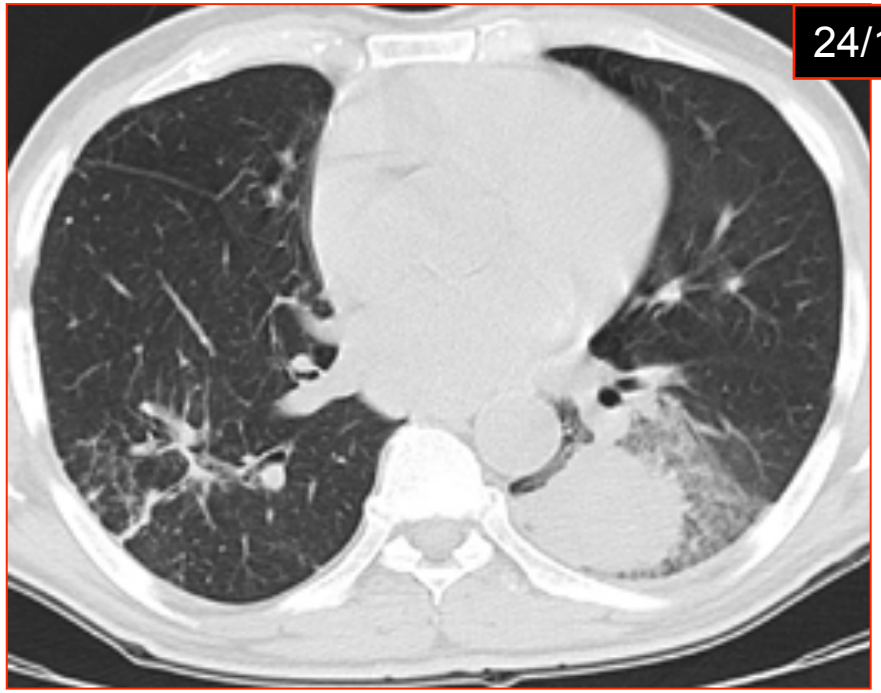
- *"… tuttavia lo studio angio-TC non documenta occlusione vascolare, non avvalorando l'ipotesi segnalata. Considerata la discordanza dei dati, anche in rapporto agli elementi clinico-laboratoristici (GM -, pregresso BAC), si consiglia approfondimento diagnostico mediante biopsia".*

- **Istologico:** ***"localizzazione polmonare di linfoma di derivazione dai linfociti B periferici, tipo Hairy Cell Leukemia"***



- **Episodio di emoftoe.**
- **Controllo a 3 h:** ***"circoscritti fenomeni di ingorgo endobronchiale a probabile natura ematica in sede perifocale …"***
- **Controllo 1/10: riduzione degli aspetti segnalati.**
- **3/10 dimissione**

- **Dal 13/10 terapia salvataggio con IFN-Alfa 1.5 MUI**
- **24/10 = iperpiressia (39.5), con brivido e dolore toracico posteriore sx / neutrofili 200 totali**



- ***TC "… addensamento al lobo inferiore sx, in regione posteriore".***

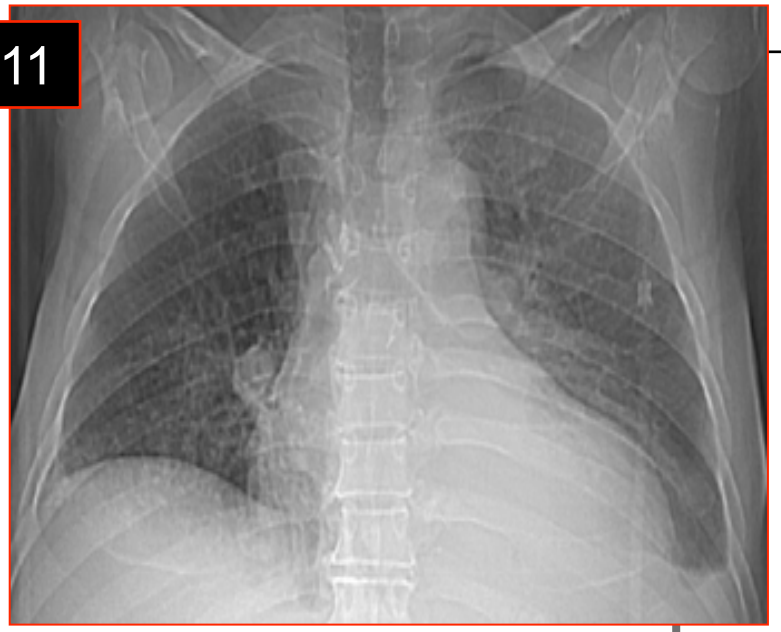
- **Interpretazione clinica (?)** ***"verosimile localizzazione secondaria alla base del polmone sx"***

- 25/10 = ricovero (altra sede) / + terapia antibiotica
- 29/10 BAL = negativo per cellule neoplastiche, microrganismi PAS positivi e alcol-acido resistenti
- Persiste febbricola

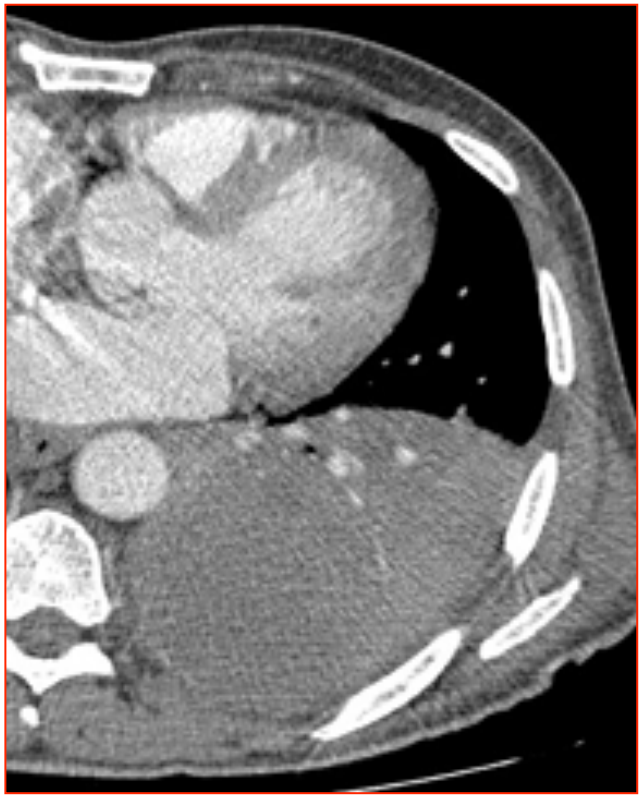
31/10

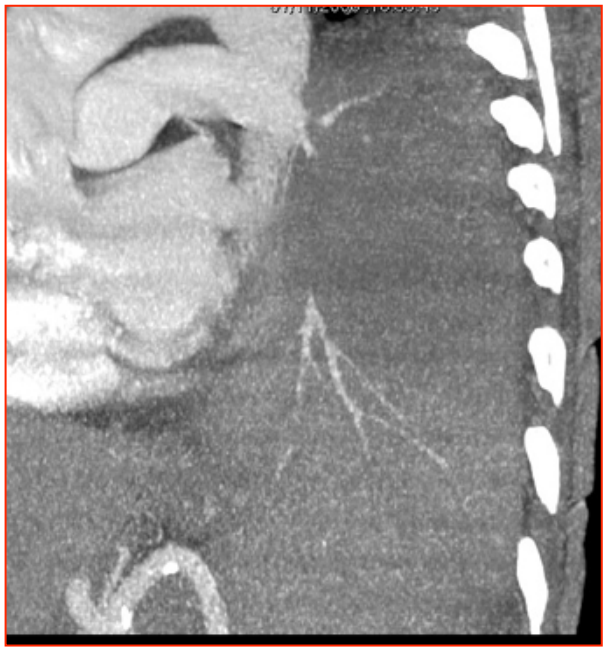
- TC: *"Aumento volumetrico della lesione segnalata nel segmento postero-basale del LIS; all'interno della massa sembra di intravedere un'area centrale piuttosto ipodensa di incerta natura".*

- **1/11 = + G-CFS**
- **4/11 BAL (negativo) + agoaspirato (“…aggregati di ife fungine frammentate da miceti verosimilmente del *genere Aspergillus. Non cellule con caratteri citologici di malignità”.***
- **+ Voriconazolo**
- **5/11 = TC *“Aumento volumetrico della lesione … inoltre, epatizzazione del parenchima sottostante la lesione … versamento pleurico sx”.***
- **6/11 = EMATOLOGIA SERAGNOLI**



7/11 CTPA





- **CTPA: Presenza di ampio addensamento senza bronocogramma aereo con segni di angioinvasione e hypodense sign, riferibile ad IFI.**
- **Inizia terapia con voriconaziolo.**