

IV Congresso Nazionale di Ecocardiografia -Milano 10-12 Marzo 2010

**RUOLO DELLA MEDICINA NUCLEARE NELLA
DIAGNOSTICA DELL'IPERTENSIONE
POLMONARE**

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UOC Medicina Nucleare e PET/TC
AO San Paolo Milano*

PH: Definizione e gravità

Condizione clinica caratterizzata dall' alterazione dei valori pressori nei vasi polmonari con:

*pressione polmonare media a riposo ≥ 25 mmHg
(pressione polmonare durante esercizio ≥ 30 mmHg)*

> 25 mmHg

> 45 mmHg

> 65 mmHg



Lieve

Moderata

Severa



Updated clinical classification of pulmonary hypertension (Dana Point, 2008)

www.escardio.org/guidelines

1 Pulmonary arterial hypertension (PAH)

- 1.1 Idiopathic
- 1.2 Heritable
 - 1.2.1 BMPR2
 - 1.2.2 ALK1, endoglin (with or without hereditary haemorrhagic telangiectasia)
 - 1.2.3 Unknown
- 1.3 Drugs and toxins induced
- 1.4 Associated with (APAH)
 - 1.4.1 **Connective tissue diseases**
 - 1.4.2 HIV infection
 - 1.4.3 Portal hypertension
 - 1.4.4 Congenital heart disease
 - 1.4.5 Schistosomiasis
 - 1.4.6 Chronic haemolytic anaemia
- 1.5 Persistent pulmonary hypertension of the newborn

1' Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis

2 Pulmonary hypertension due to left heart disease

- 2.1 Systolic dysfunction
 - 2.2 Diastolic dysfunction
 - 2.3 Valvular disease
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3 Pulmonary hypertension due to lung diseases and/or hypoxia

- 3.1 Chronic obstructive pulmonary disease
- 3.2 Interstitial lung disease
- 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
- 3.4 Sleep-disordered breathing
- 3.5 Alveolar hypoventilation disorders
- 3.6 Chronic exposure to high altitude
- 3.7 Developmental abnormalities

4 Chronic thromboembolic pulmonary hypertension

5 PH with unclear and/or multifactorial mechanisms

- 5.1 Haematological disorders: **myeloproliferative disorders**, splenectomy.
 - 5.2 Systemic disorders: **sarcoidosis**, pulmonary Langerhans cell histiocytosis, lymphangiomyomatosis, neurofibromatosis, **vasculitis**
 - 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, **thyroid disorders**
 - 5.4 Others: tumoural obstruction, fibrosing mediastinitis, chronic renal failure on dialysis
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Epidemiology

	Prevalence
Group I	20/milion
Group II	60% LVSD, 100% SSMVD, 65% AoS
Group III	20% COPD, 39% ILD
Group IV	0.5-3,8 PE
Group V	Unknown

Legend: LVSD:: Left Ventricular systolic difunction; SSMVD: Severe Symptmatic Mitral valve disease; AoS: Aortic stenosis COPD: Chronic Obstructive Pulmonary disease
ILD: Interstitial Lung Disease

Sintomi

Sintomi	Esordio	Diagnosi
Dispnea da sforzo	60,00%	98,00%
Facile affaticabilità	19,00%	73,00%
Dolore toracico	7,00%	47,00%
Lipotimia – Sincope	12,00%	75,00%
Cardiopalmo	5,00%	33,00%
Edemi arti inferiori	3,00%	37,00%

Haemodynamic definitions of pulmonary hypertension

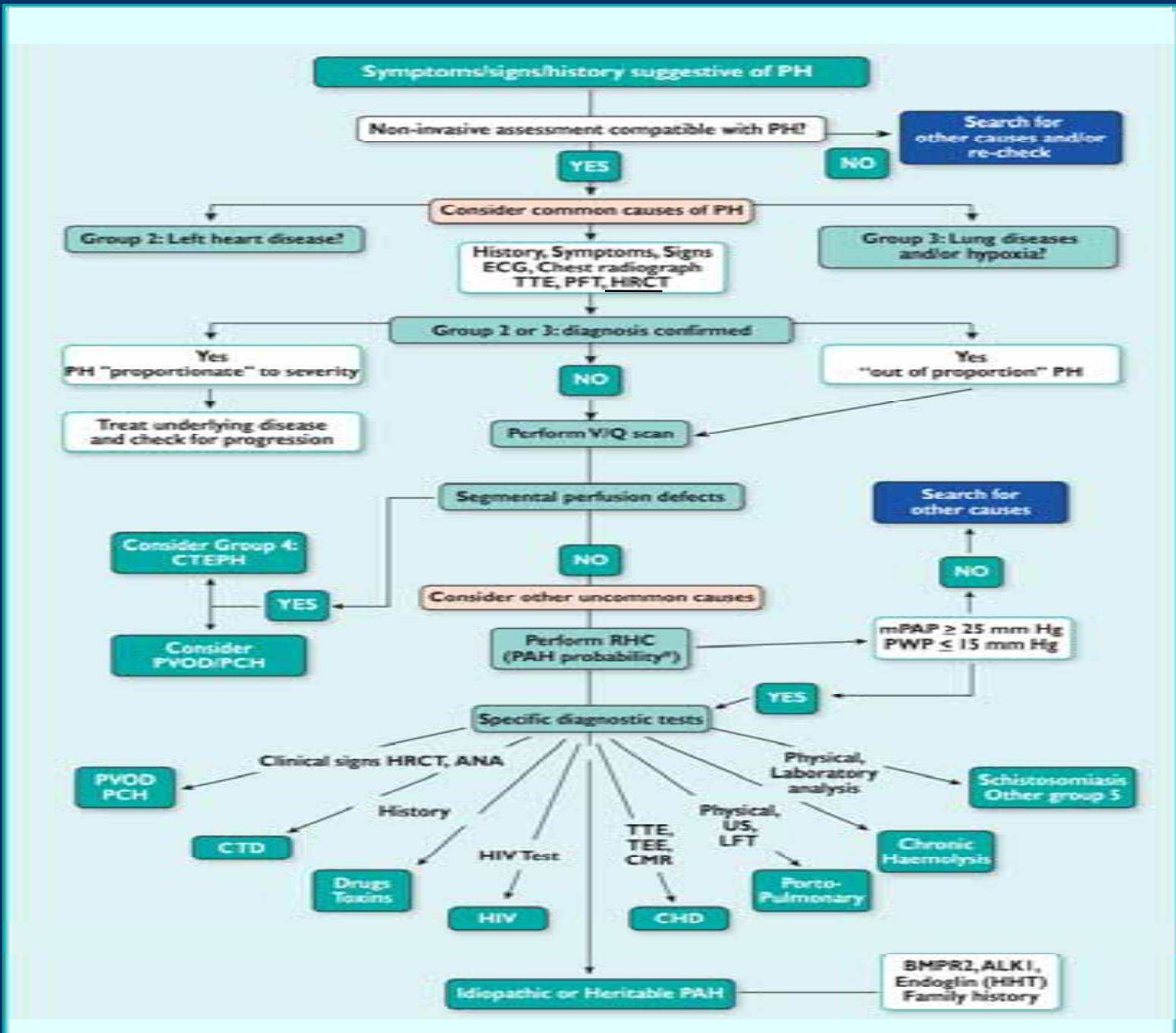
Definition	Characteristics	Clinical group(s)
Pulmonary hypertension (PH)	Mean PAP ≥ 25 mmHg	All
Pre-capillary	PH Mean PAP ≥ 25 mmHg PWP ≤ 15 mmHg CO normal or reduced	1. Pulmonary arterial hypertension 3. PH due to lung diseases 4. Chronic thromboembolic PH 5. PH with unclear and/or multifactorial
Post-capillary PH	Mean PAP ≥ 25 mmHg PWP ≥ 15 mmHg CO normal or reduced	2. PH due to left heart disease
Passive TPG	TPG ≤ 12 mmHg	
Reactive (out of proportion)	TPG ≥ 12 mmHg	

Prevalenza di EP in soggetti non selezionati con sospetto clinico di EP

Studio	Numero di pazienti	% di EP
Wells 2001	930	9.5
Perrier 2000	1034	27.6
Wells 1998	1239	17
Van Beek 1997	487	39
PISAPED 1996	890	39
PIOPED 1990	887	33
PIOPED 1990	755	28

Embolia polmonare

- La diagnosi di EP rimane uno dei più difficili problemi nella pratica clinica, rappresentando la diagnosi più comunemente mancata che ha come conseguenza la morte
 - La sola valutazione clinica non permette quasi mai di fare una diagnosi di certezza anche se non può essere elusa.
 - La sequenza diagnostica deve tenere conto della condizione clinica del Paziente e delle risorse disponibili
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Diagnostic criterion	Clinical probability of PE		
	Low	Intermediate	High
Exclusion of pulmonary embolism			
Normal pulmonary angiogram	+	+	+
D-dimer			
Negative result, highly sensitive assay	+	+	-
Negative result, moderately sensitive assay	+	-	-
V/Q scan			
Normal lung scan	+	+	+
Non-diagnostic lung scan ^a	+	-	-
Non-diagnostic lung scan ^a and negative proximal CUS	+	+	±
Chest CT angiography			
Normal SDCT and negative proximal CUS	+	+	±
Normal multidetector CT alone	+	+	±
Confirmation of pulmonary embolism			
Pulmonary angiogram showing PE	+	+	+
High-probability V/Q scan	±	+	+
CUS showing a proximal DVT	+	+	+
Chest CT angiography			
Single or multidetector helical CT scan showing PE (at least segmental)	±	+	+
Single or multidetector helical CT scan showing subsegmental PE	±	±	±

Principio di ottimizzazione (D.L. Vo 26/5/2000, n.187)

- Art 4:
- Tutte le esposizioni mediche per scopi radiologici (...) devono essere mantenute al livello più basso ragionevolmente ottenibile e compatibile con il raggiungimento dell'informazione diagnostica richiesta

<http://www.doseinfo-radar.com/RADARDoseRiskCalc.html>

- Chest X-Ray (AP-LL): 0.24 mSv
 - Lung scan: 1.22 mSv
 - Lung TC (for PE): 8 mSv
 - Myocardial perfusion: 7.87 mSv
 - Natural Background: 2 mSv/y
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Group 4, CTEPH: Incidenza e Patogenesi

- Non sono state identificate mutazioni genetiche specifiche nello sviluppo della CTEPH.
 - La prevalenza varia dallo 0,5 - 3.8% nei Pazienti che sopravvivono ad un episodio di TEP acuta.
 - In alcune casistiche fino al 50% dei Pazienti affetti da CTEPH non aveva mai sofferto di un episodio di TEP clinicamente manifesto.
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Group 4: CTPEH Patogenesi

- Queste lesioni possono essere completamente “occludenti” il lume vascolare.
 - Nelle aree “non-occluse” è spesso presente un'arteriopatia polmonare indistinguibile da quella delle PAH, comprese le lesioni “plessiformi”
 - Le lesioni più significative sono costituite da trombi organizzati strettamente adesi alla tonaca media delle arterie polmonari con sostituzione della intima “normale”.
 - In genere tende a svilupparsi un circolo collaterale con funzioni almeno inizialmente “vicarianti” che proviene dalle aa. Bronchiali, costali, diaframmatiche e dalle coronarie, nel tentativo di riperfondere le aree “a valle”.
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Lesioni PPH

- Ipertrofia della media
 - Modificazioni fibrotiche e proliferativa dell'intima
 - Ispessimento dell'avventizia con infiltrati infiammatori peri-avventiziali
 - Lesioni “plessiformi” con dilatazione aneurismatiche dei piccoli vasi
 - Trombosi.
 - Vene di norma indenni
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Group 4, CTEPH: Patologia

- La mancata risoluzione di fenomeni embolici acuti può condurre ad una ostruzione cronica dei vasi polmonari
 - Anormalità della cascata della coagulazione, nelle cellule endoteliali o nelle piastrine od in tutte queste componenti possono portare alla creazione di un ambiente “trombofilico” che può favorire od aggravare la tendenza alla trombosi
 - Molto spesso non si riesce a stabilire se e quanto le une siano conseguenze delle altre.
 - Molto spesso nell'esame istologico dei trombi rimossi sono anche presenti infiltrati infiammatori
 - LLA Ab sono stati rinvenuti nel 10-15% dei Pazienti
 - Nel 39% dei Pazienti sarebbero inoltre elevati i livelli di F.VIII
 - Non sono state identificate anormalità nella fibrinolisi
 - Le lesioni della parete vascolare presenti nelle zone non ostruite, virtualmente identiche a quelle presente nella PAH, potrebbero automantenere il processo causando shear-stress e rilascio di mediatori chimici dell'infiammazione
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PH: class 4: Secondary to pulmonary embolism

- Valutazione della presenza di difetti di perfusione
- Loro correlazione con il quadro morfologico



**Diagnosis and Management of Pulmonary
Arterial Hypertension: ACCP Evidence-Based
Clinical Practice Guidelines**

*Lewis J. Rubin, MD, FCCP
(CHEST 2004; 126:4S–6S)*

In patients with PAH, ventilation-perfusion scanning should be performed to rule out chronic thromboembolic pulmonary hypertension (CTEPH); a normal scan effectively excludes a diagnosis of CTEPH.

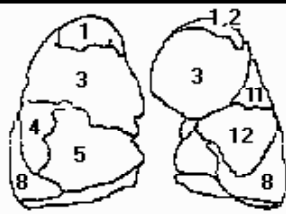
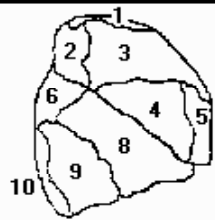
benefit: substantial; strength of recommendation: B

- Valutazione della presenza di difetti di perfusione
 - Scintigrafia polmonare di perfusione
 - ^{99m}Tc -MAA
 - Facile esecuzione
 - Basso costo
 - Utile nel follow-up dei Pazienti con TEP acuta
 - Necessario studio basale
 - SPECT
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Correlazione con il quadro morfologico

- Studio basale (pre-dimissione)
- Specificità (metodiche ibride)
- Disponibilità





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LAT DX

ANTERIORE

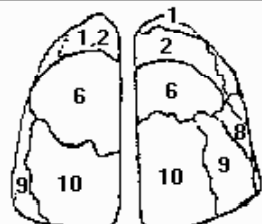
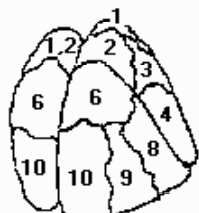
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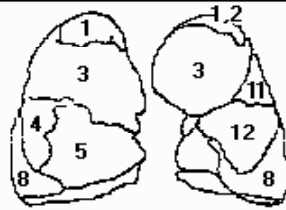
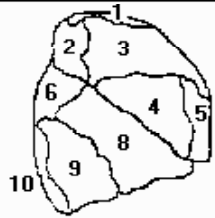
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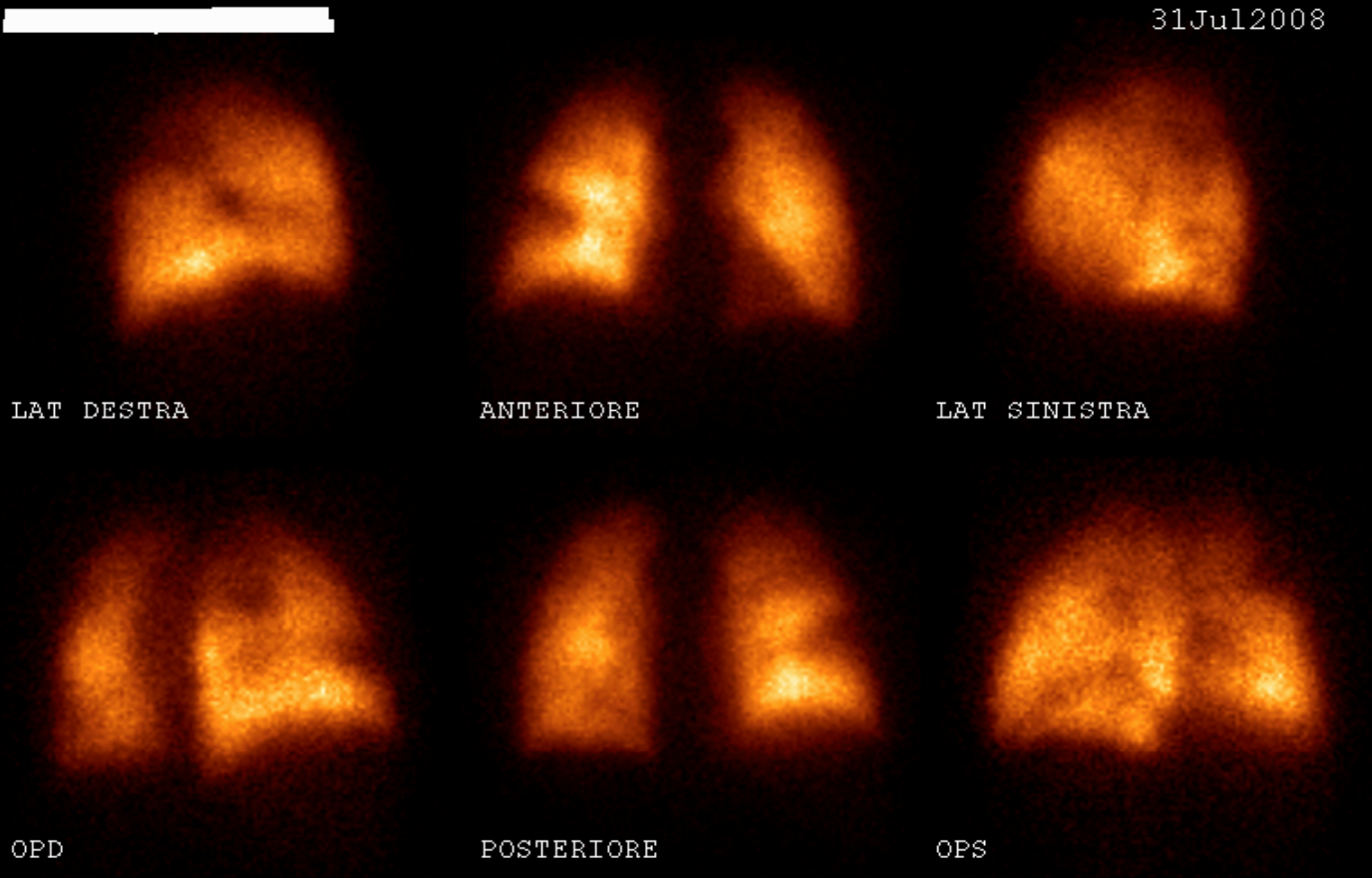
O. POST SIN

- 1. Apical
- 2. Posterior
- 3. Anterior
- 4. Lateral
- 5. Medial
- 6. Superior
- 7. Medial Basal
- 8. Anterior Basal
- 9. Lateral Basal
- 10. Posterior Basal
- 11. Lingual Superior
- 12. Lingual Inferior

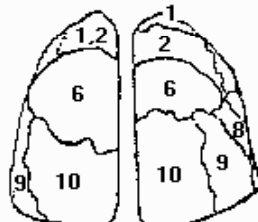
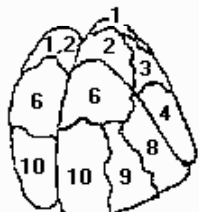


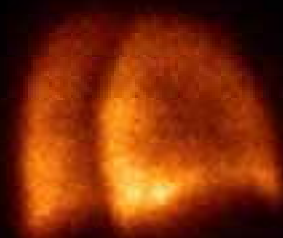


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- 1. Apical
- 2. Posterior
- 3. Anterior
- 4. Lateral
- 5. Medial
- 6. Superior
- 7. Medial Basal
- 8. Anterior Basal
- 9. Lateral Basal
- 10. Posterior Basal
- 11. Lingual Superior
- 12. Lingual Inferior

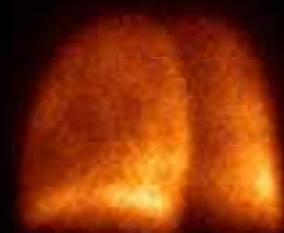




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LAT DS
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LAT SIN
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OPS
03/10/10 10:15:43

Valutazione della attività delle malattie infiammatorie croniche



- * Class I (connective tissue diseases)
- * Class V (myeloproliferative disorders, Thyroid disorders, sarcoidosis, vasculitis)



Kalkanis D

[18F]-fluorodeoxyglucose positron emission tomography combined with computed tomography detection of asymptomatic late pulmonary toxicity in patients with non-Hodgkin lymphoma treated with rituximab-containing chemotherapy.

Leuk Lymphoma. 2009 Jun;50(6):904-11.

Department of Radiology, Division of Nuclear Medicine, Jackson Memorial Hospital and Sylvester Comprehensive Cancer Center, University of Miami School of Medicine, Miami, FL 33136, USA.

Rituximab is a chimeric anti-CD20 monoclonal antibody widely used in the treatment of B-cell non-Hodgkin lymphomas (NHL). Most adverse effects are due to infusion-related reactions, and severe respiratory complications are rare. We retrospectively reviewed clinical data and serial imaging studies of five patients with NHL treated with rituximab-containing chemotherapy who developed new pulmonary abnormalities on routine follow-up FDG-PET/CT imaging. **None of the patients had pulmonary lymphoma or other pulmonary disease before therapy and all remained asymptomatic during follow-up.** New pulmonary interstitial FDG-uptake was detected on follow-up **FDG-PET/CT between 1 and 3 months post-treatment, preceded computed tomography abnormalities** in one case, and persisted for several months. FDG uptake was linear, subpleural with maximum Standardized uptake value (SUV) from 2.0 to 5.84. Rituximab-containing chemotherapy for NHL may be associated with asymptomatic late pulmonary toxicity characterised by a distinct FDG uptake pattern. Awareness of this finding is important and should not be confused with lymphoma

Groves AM, Win T, Screatton NJ, Berovic M, Endozo R, Booth H, Kayani I, Menezes LJ, Dickson JC, Ell PJ.

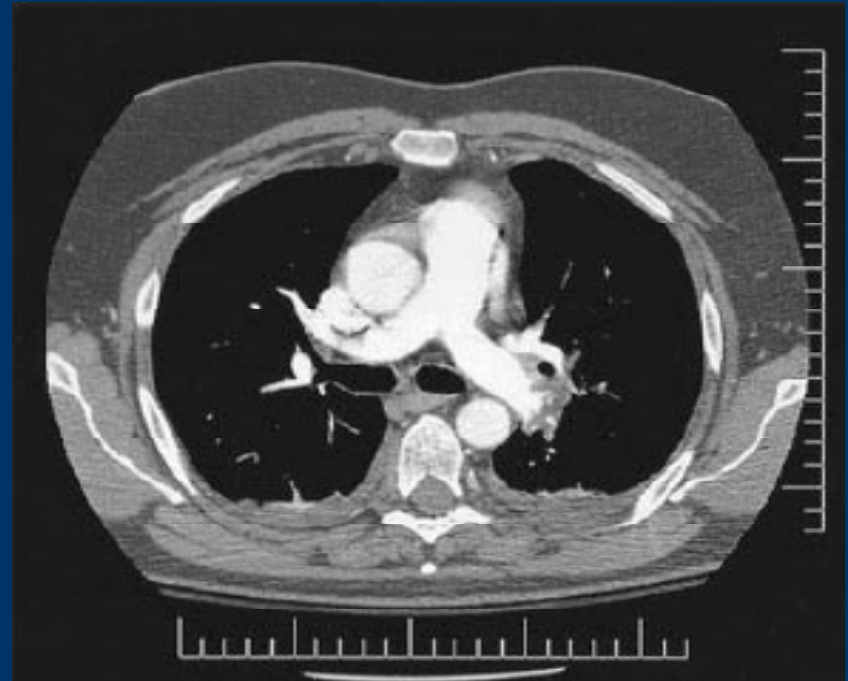
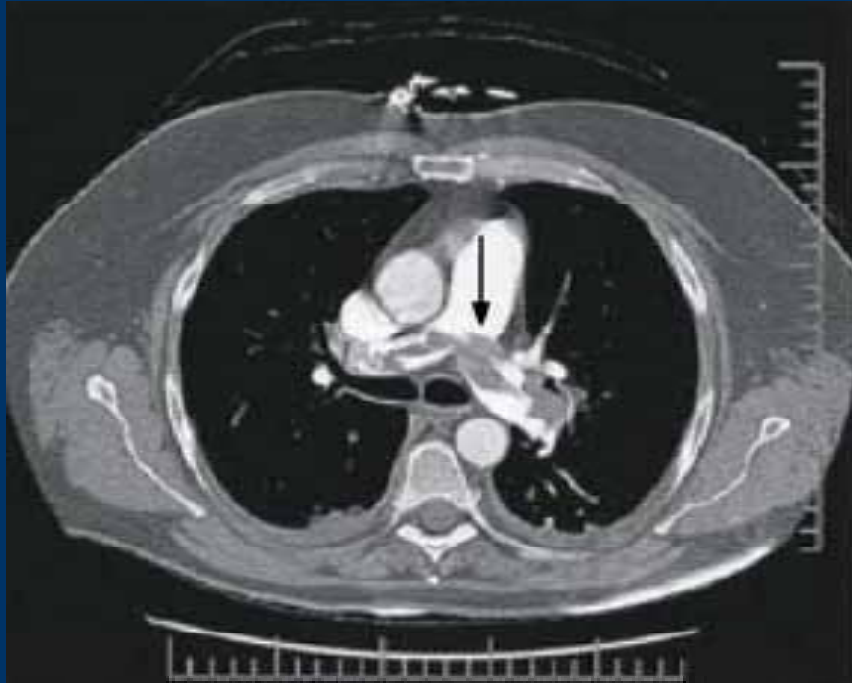
Idiopathic pulmonary fibrosis and diffuse parenchymal lung disease: implications from initial experience with ^{18}F -FDG PET/CT.

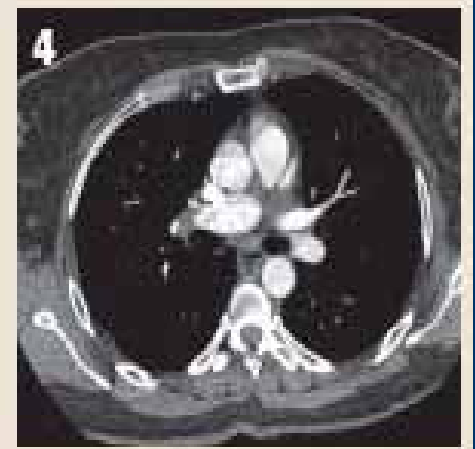
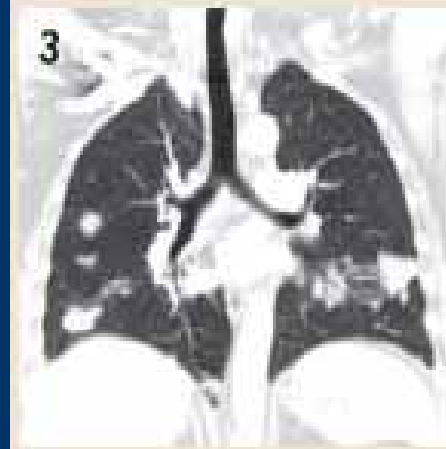
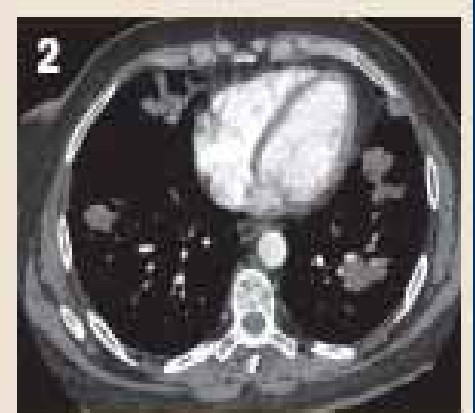
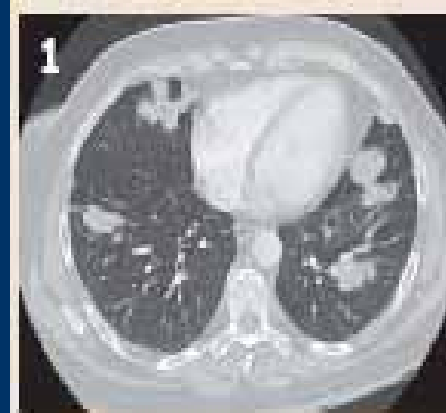
2009 Apr;50(4):538-45. Epub 2009 MJ Nucl Med.ar 16.

Institute of Nuclear Medicine, University College
London, London, United Kingdom

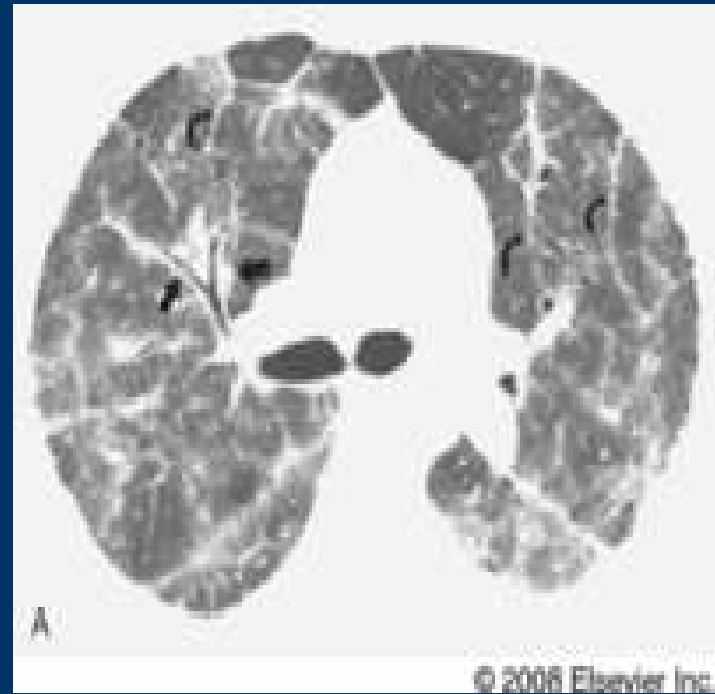
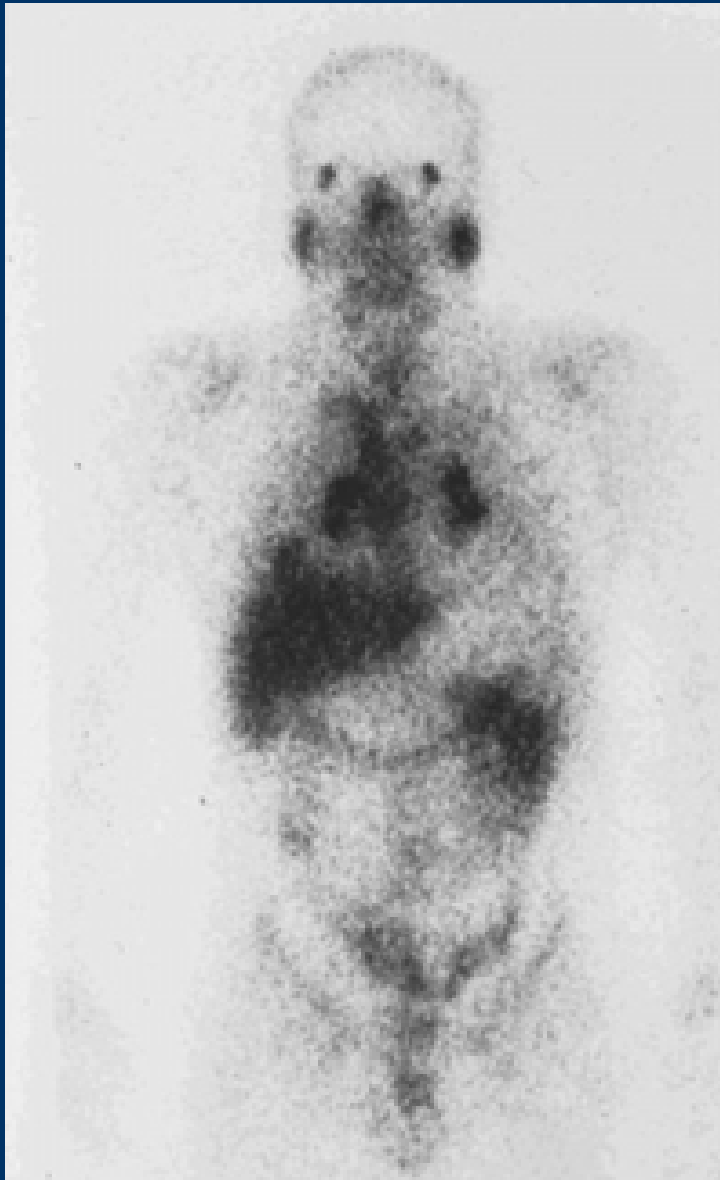
The purpose of this study was to evaluate integrated (18)F-FDG PET/CT in patients with idiopathic pulmonary fibrosis (IPF) and diffuse parenchymal lung disease (DPLD).

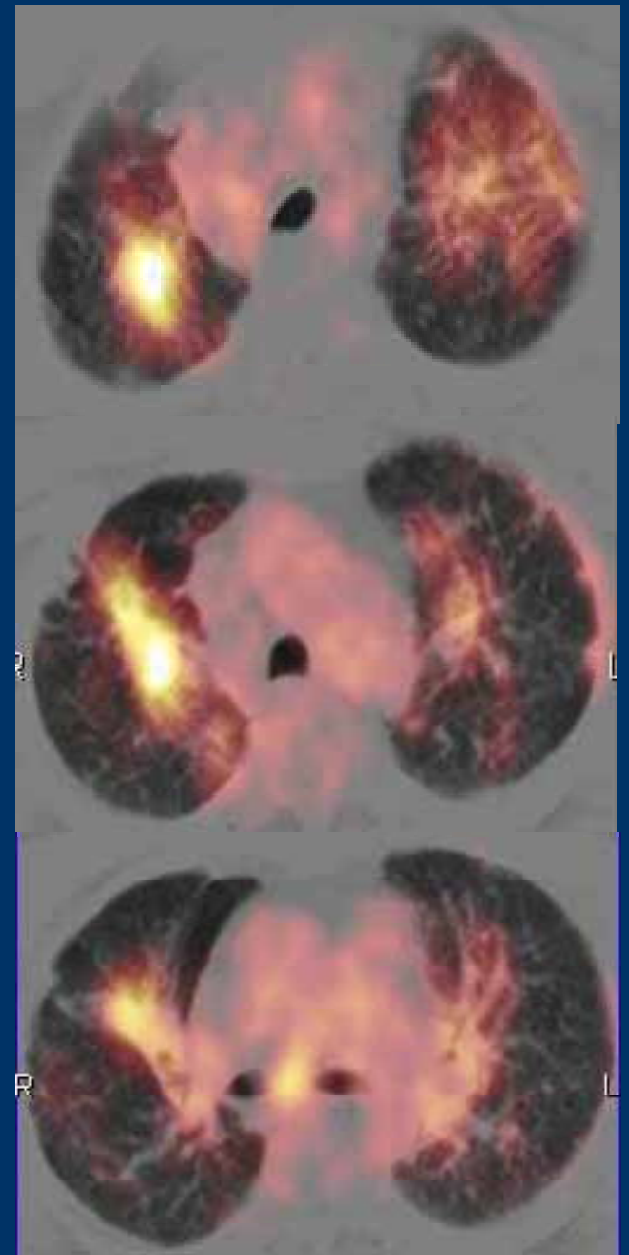
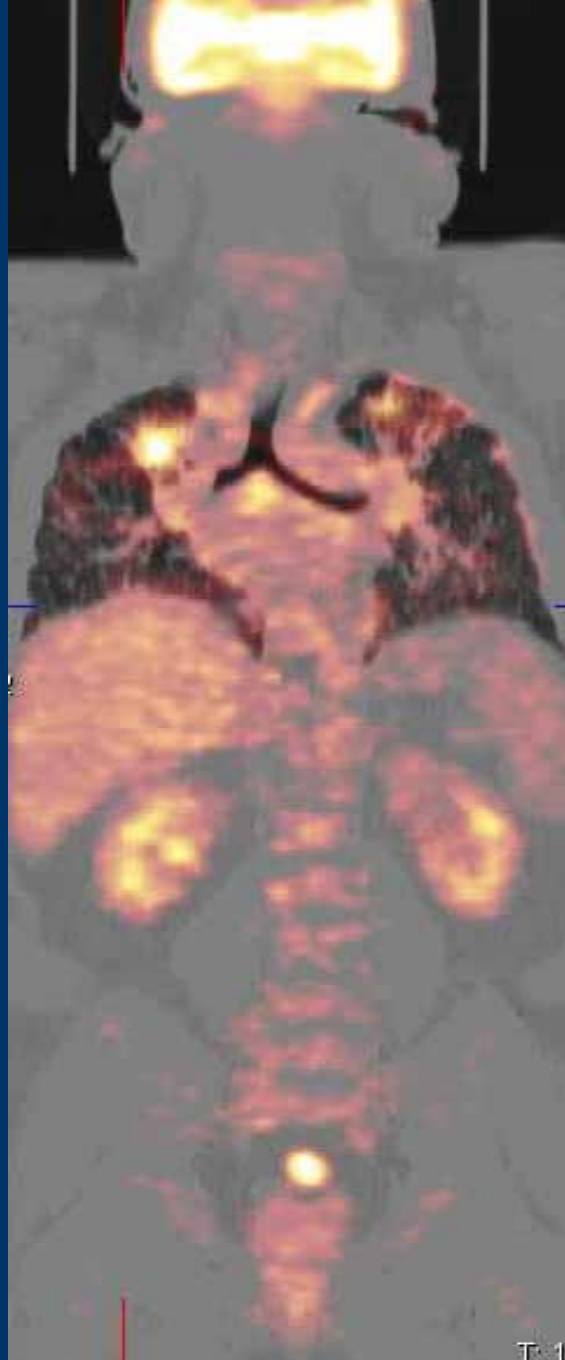
METHODS: Thirty-six consecutive patients (31 men and 5 women; mean age \pm SD, 68.7 \pm 9.4 y) with IPF (n = 18) or other forms of DPLD (n = 18) were recruited for PET/CT and high-resolution CT (HRCT), acquired on the same instrument. The maximal pulmonary (18)F-FDG metabolism was measured as a standardized uptake value (SUV(max)). At this site, the predominant lung parenchyma HRCT pattern was defined for each patient: ground-glass or reticulation/honeycombing. Patients underwent a global health assessment and pulmonary function tests. **RESULTS:** Raised pulmonary (18)F-FDG metabolism in 36 of 36 patients was observed. The parenchymal pattern on HRCT at the site of maximal (18)F-FDG metabolism was predominantly ground-glass (7/36), reticulation/honeycombing (26/36), and mixed (3/36). The mean SUV(max) in patients with ground-glass and mixed patterns was 2.0 \pm 0.4, and in reticulation/honeycombing it was 3.0 \pm 1.0 (Mann-Whitney U test, P = 0.007). The mean SUV(max) in patients with IPF was 2.9 \pm 1.1, and in other DPLD it was 2.7 \pm 0.9 (Mann-Whitney U test, P = 0.862). The mean mediastinal lymph node SUV(max) (2.7 \pm 1.3) correlated with pulmonary SUV(max) (r = 0.63, P < 0.001). Pulmonary (18)F-FDG uptake correlated with the global health score (r = 0.50, P = 0.004), forced vital capacity (r = 0.41, P = 0.014), and transfer factor (r = 0.37, P = 0.042). **CONCLUSION:** Increased pulmonary (18)F-FDG metabolism in all patients with IPF and other forms of DPLD was observed. Pulmonary (18)F-FDG uptake predicts measurements of health and lung physiology in these patients. (18)F-FDG metabolism was higher when the site of maximal uptake corresponded to areas of reticulation/honeycomb on HRCT than to those with ground-glass patterns.



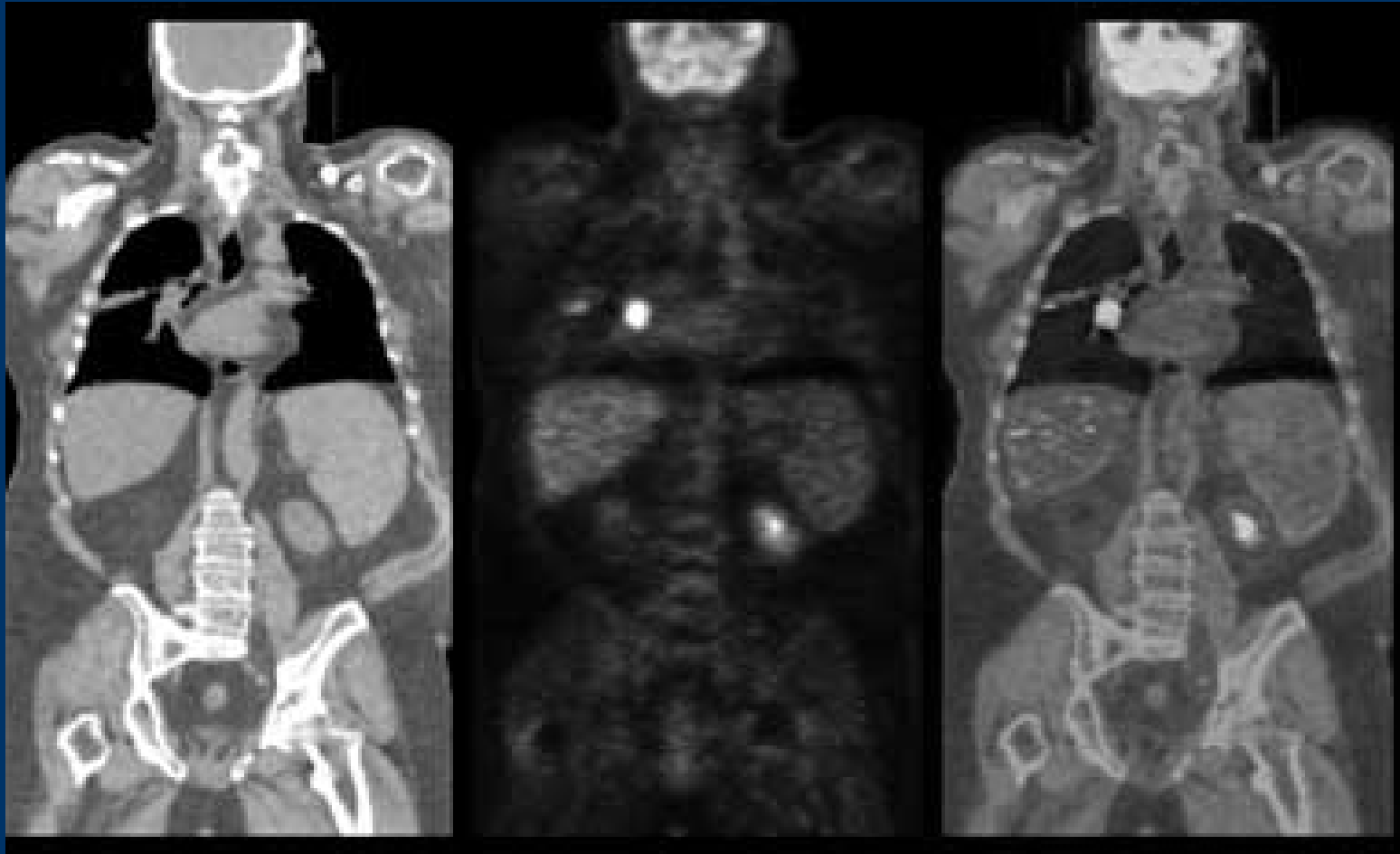




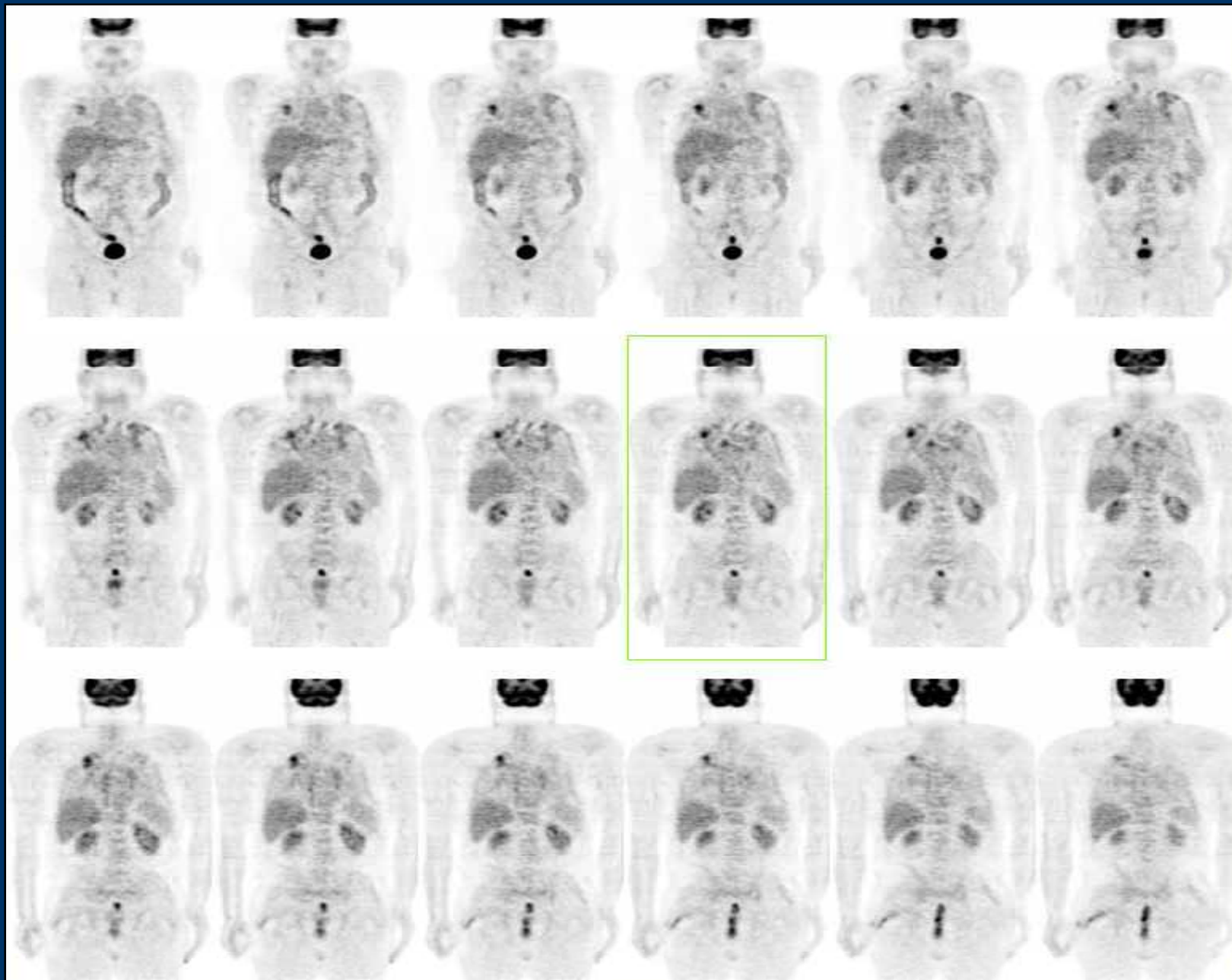




Courtesy Prof.L.Giovanella – EOC-IOSI Bellinzona-Lugano -CH



Courtesy Prof.L.Giovanella – EOC-IOSI Bellinzona-Lugano -CH



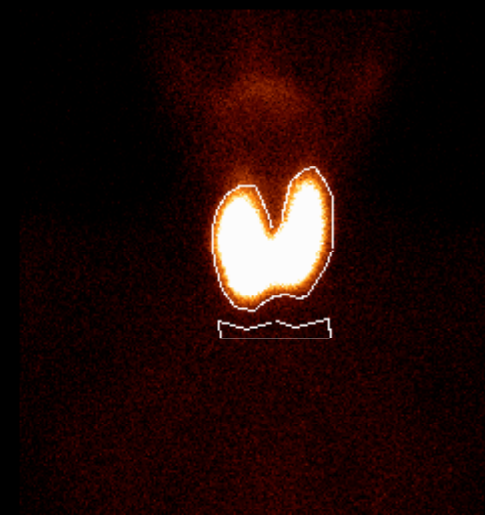
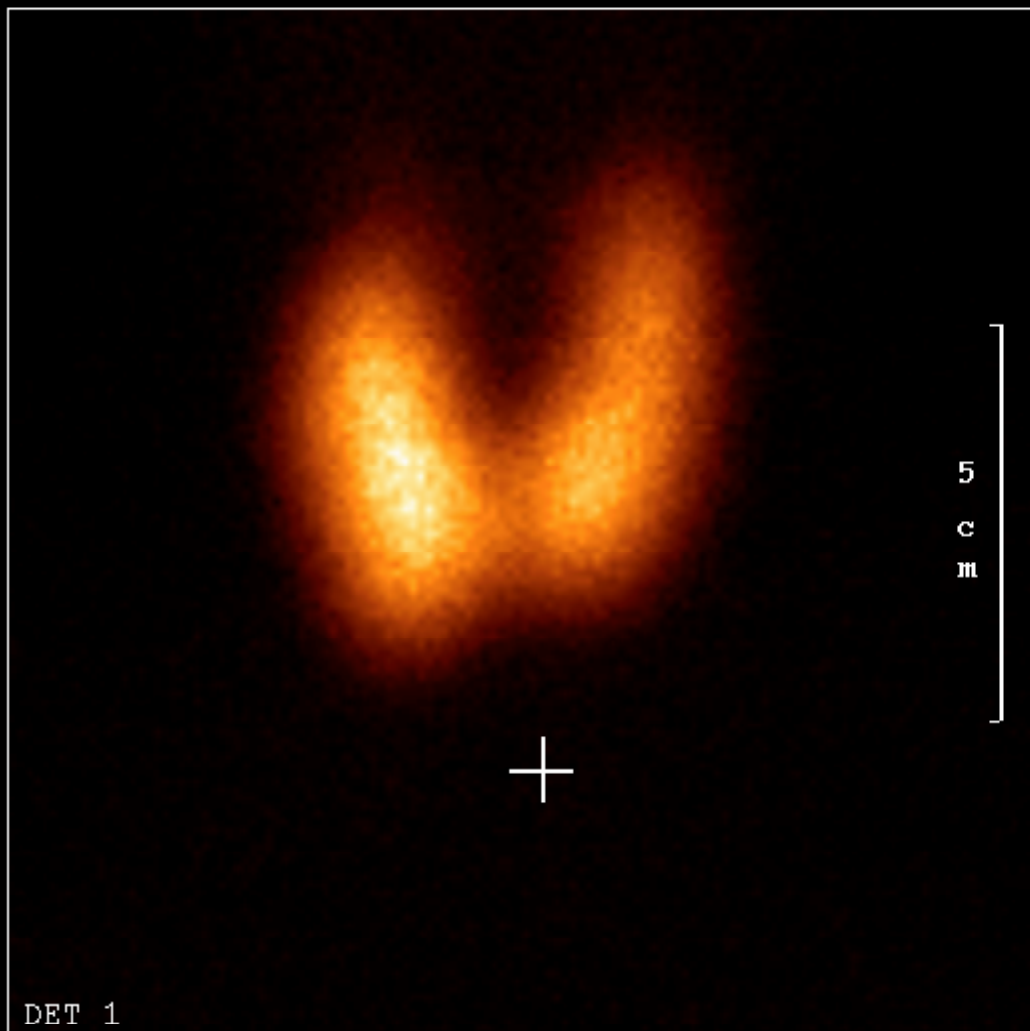
Courtesy Prof.L.Giovanella – EOC-IOSI Bellinzona-Lugano -CH

Quantificazione della funzione ventricolare destra

- Angiocardioscintigrafia di primo passaggio
- MUGA (angiocardioscintigrafia all'equilibrio)
- Hanno ormai un valore storico

Valutazione dell'innervazione simpatica del ventricolo destro e del metabolismo degli acidi grassi





THYROID UPTAKE : 21.17 %

Area 35.4 (sqcm) Mass 68.8 g

Patient Name :

Patient ID : 60607

Exam Date : 21Jul2008

THYROID UPTAKE

Azienda Ospedaliera SAN.PAOLO
Polo Universitario
Milano

Conclusioni



CTEPH

- La scintigrafia polmonare di perfusione ha un alto valore predittivo negativo
 - Un risultato positivo richiede di essere confrontato con il quadro morfologico rispettivo
 - Necessario uno studio basale in fase sub-acuta
 - E' utile lo studio SPECT
 - Il costo e la dose al Paziente sono molto contenuti
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Patologie interstiziali

- Le malattie del tessuto connettivo, le malattie linfoproliferative, le vasculiti e la sarcoidosi possono essere valutate attraverso PET/TC
 - Esistono studi che mostrano l'utilità del 18FDG PET/TC nella valutazione di attività di malattia.
 - Il 67Ga-citrato ha ridotto il suo spazio di impiego
 - Considerare sempre l'ipertiroidismo nella valutazione delle ipertensioni polmonari soprattutto nell'anziano
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Grazie per la vostra attenzione

