



CORSO TEORICO-PRATICO
PER LA GESTIONE OTTIMALE
DEI PAZIENTI AFFETTI DA
LINFOMA MANTELLARE,
LINFOMA FOLLICOLARE E
LEUCEMIA LINFATICA CRONICA

Torino, 21-22-23 maggio 2018

Coordinatore
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Presidio Molinette

Sede
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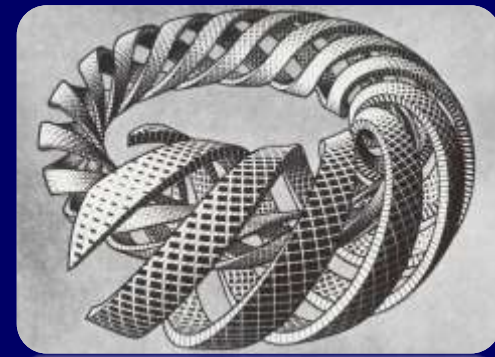
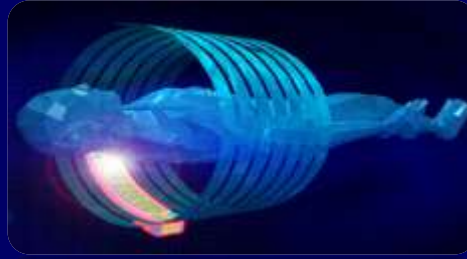
Ruolo dell'imaging nelle malattie linfoproliferative:

Tomografia Computerizzata

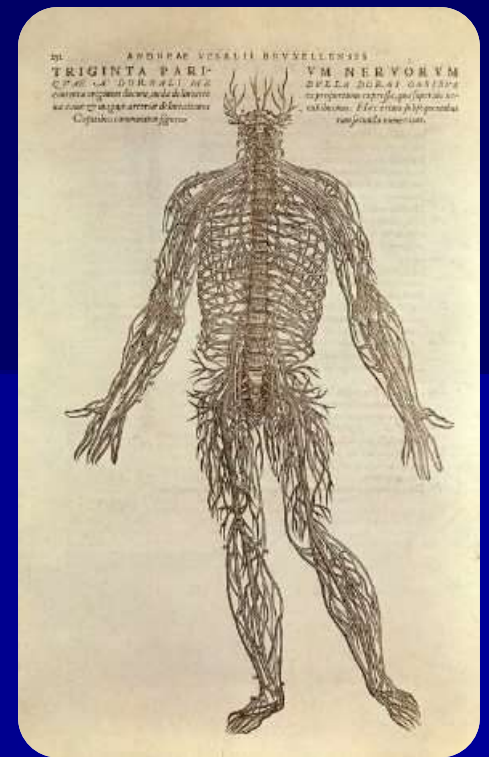
Giorgio Limerutti

Radiagnostica Ospedaliera

Città della Salute e della Scienza Torino
Presidio Molinette



Sin dall'inizio della sua applicazione clinica la TC ha un ruolo centrale nello studio delle malattie linfoproliferative grazie alla possibilità di visualizzare direttamente i linfonodi ingranditi in tutti i distretti corporei



Cosa può valutare la TC?

-LINFONODI:

- Sedi
- Misura (asse corto e lungo)
- Bulky disease (masse > 10 cm)
- N° di stazioni linfonodali coinvolte
- Effetti locali (es idronefrosi)
- Diffusione extranodale contigua

-ORGANI ADDOMINALI

-POLMONI, OSSO, SPAZI EPIDURALI



Diagnosi

Sospetto clinico

Rx torace o TC eseguiti
con altra indicazione

Rilevare e definire l'estensione della malattia



Stadiazione

Fattori prognostici, confronto tra studi diversi,
valutazione iniziale per definire risposta e progressione



Recommendations for Initial Evaluation, Staging, and Response Assessment of Hodgkin and Non-Hodgkin Lymphoma: The Lugano Classification

Bruce D. Cheson, Richard I. Fisher, Sally F. Barrington, Franco Cavalli, Lawrence H. Schwartz, Emanuele Zucca, and T. Andrew Lister

**CT metodica migliore per
misurazione di tutte le
localizzazioni, valutazione
organomegalia e bulky disease**

**CT-PET preferita nei linfomi
avididi FDG**



Table 2. Revised Staging System for Primary Nodal Lymphomas

Stage	Involvement	Extranodal (E) Status
Limited		
I	One node or a group of adjacent nodes	Single extranodal lesions without nodal involvement
II	Two or more nodal groups on the same side of the diaphragm	Stage I or II by nodal extent with limited contiguous extranodal involvement
II bulky*	II as above with “bulky” disease	Not applicable
Advanced		
III	Nodes on both sides of the diaphragm; nodes above the diaphragm with spleen involvement	Not applicable
IV	Additional noncontiguous extralymphatic involvement	Not applicable

NOTE. Extent of disease is determined by positron emission tomography-computed tomography for avid lymphomas and computed tomography for nonavid histologies. Tonsils, Waldeyer's ring, and spleen are considered nodal tissue.

*Whether stage II bulky disease is treated as limited or advanced disease may be determined by histology and a number of prognostic factors.

Stadiazione

Fino a 6 lesioni target misurabili (i 2 ø)

Linfonodi (ø maggiore >1,5 cm, in ≠ sedi)

Masse adenopatiche

Lesioni linfomatose extranodali (>1cm)

**Altre eventuali lesioni oltre alle target
devono essere considerate non
misurabili**

LINFOMI NODALI

FDG PET/CT : sensibilità 94% specificità 100%
CT con contrasto: sensibilità 88% specificità 86%

LINFOMI EXTRANODALI

FDG PET/CT: sensibilità 88% specificità 100%
CT con contrasto: sensibilità 50% specificità 90%

NHL: upstage 31%

HD: upstage 32%, downstage 15%

Radiology 2004;232:823–829.

RadioGraphics 2010;30(1):269–291.

Radiology 2015; 276:323–328

Valutazione risposta con TC

CR: linfonodi ridotti di volume con $\varnothing$ min $< 1,5$ cm

Assenza lesioni extranodali

Assenza di nuove lesioni

Regressione organomegalia

PR: riduzione $\geq 50\%$ della somma del prodotto (SPD)
dei $\varnothing$ perpendicolari delle lesioni target (6 o meno)

Stabilità delle lesioni non target

Assenza di nuove lesioni

SD: No-CR

No-PR

No-PD



Ripresa / Progressione

(dopo CR / in corso di terapia o dopo PR,SD)

Almeno una delle seguenti:

Linfonodo con $\varnothing$ min $> 1,5$ cm

Lesione extranodale > 1 cm

Incremento $\geq 50\%$ PPD di un singolo Inf al nadir

Incremento di 0,5 cm o 1 cm di uno dei $\varnothing$ per
linfonodi ≤ 2 cm o $>$ di 2 cm

Nuova insorgenza o ricomparsa di splenomegalia

Comparsa/sicura progressione di lesioni non target

REVIEW

International Working Group consensus response evaluation criteria in lymphoma (RECIL 2017)

A. Younes^{1*}, P. Hilden², B. Coiffier³, A. Hagenbeek⁴, G. Salles³, W. Wilson⁵, J. F. Seymour⁶, K. Kelly⁷, J. Gribben⁸, M. Pfreunschuh⁹, F. Morschhauser¹⁰, H. Schoder¹¹, A. D. Zelenetz¹, J. Rademaker¹¹, R. Advani¹², N. Valente¹³, C. Fortpied¹⁴, T. E. Witzig¹⁵, L. H. Sehn¹⁶, A. Engert¹⁷, R. I. Fisher¹⁸, P.-L. Zinzani¹⁹, M. Federico²⁰, M. Hutchings²¹, C. Bollard²², M. Trneny²³, Y. A. Elsayed²⁴, K. Tobinai²⁵, J. S. Abramson²⁶, N. Fowler²⁷, A. Goy²⁸, M. Smith²⁹, S. Ansell¹⁵, J. Kuruvilla³⁰, M. Dreyling³¹, C. Thieblemont³², R. F. Little³³, I. Aurer³⁴, M. H. J. Van Oers³⁵, K. Takeshita³⁶, A. Gopal³⁷, S. Rule³⁸, S. de Vos³⁹, I. Kloos⁴⁰, M. S. Kaminski⁴¹, M. Meignan⁴², L. H. Schwartz⁴³, J. P. Leonard⁴⁴, S. J. Schuster⁴⁵ & V. E. Seshan²

**Armonizzare ai criteri RECIST
la valutazione NHL nei trials clinici**

(max 3 lesioni target, singolo diametro, categoria MR)

Table 4. Comparison between RECIST 1.1, Lugano lymphoma classification, and RECIL 2017

	RECIST 1.1	Lugano	RECIL 2017
Number of target lesions	Up to 5	Up to 6	Up to 3
Measurement method	Uni-dimensional: long diameter of non-nodal lesions, short diameter of lymph nodes	Bi-dimensional: perpendicular diameters	Uni-dimensional: long diameter of any target lesion
Incorporates PET results to describe CR	May be considered to confirm CR and/or to declare PD based on detecting new lesions	Yes	Yes
Minor response	No	No	Yes, reduction in sum of long diameters between $\geq 10\%$ and $< 30\%$
Stable disease	-29% to $+20\%$	-50% to $+50\%$	decrease $< 10\%$ to increase $\leq 20\%$
PD	Increase in sum of diameters by 20%	Increase in the sum of products of perpendicular diameters by $> 50\%$, or any single lesion by $> 50\%$	Increase in sum of the longest diameters by 20%. For relapse from CR, at least one lesion should measure 2 cm in the long axis with or without PET activity

CR, complete response; PD, progression of disease; PET, positron emission tomography.

Risposta Finale

TC per la valutazione della risposta finale deve essere riservata a:

- **Linfomi con bassa o variabile avidità per FDG**
- **Se la PET non è disponibile**
- **Per la valutazione della risposta a nuovi farmaci usati in malattie plurirecidivate**



Follow up

La frequenza
variabile dipende
dalla risposta
clinica e dall'im-

aging è
all'istologia,
terapia, dalla
colli di studio

Rout

scans



J

014

Pro



Contro

Legati alla metodica

**Legati alle informazioni fornite
dall' indagine**



Legati alla metodica

- ❖ Velocità di esecuzione
(minimizzazione degli artefatti da movimento)
- ❖ Elevata risoluzione spaziale
(spessore sottile)
- ❖ Larga disponibilità delle apparecchiature
- ❖ Ben accettata dai pz.
- ❖ Dose di radiazioni ionizzanti
- ❖ Uso di m.d.c
(allergia, nefrotossicità)
- ❖ [N° elevato di immagini]

Evoluzione dell'hardware

2002
4 strati

6-8-10-32

2008
64 strati



MONKIUS EATALOTIS



CHIMPUS IMBECILUS



APEIS STUPIDIUS



NEANDERSLOB

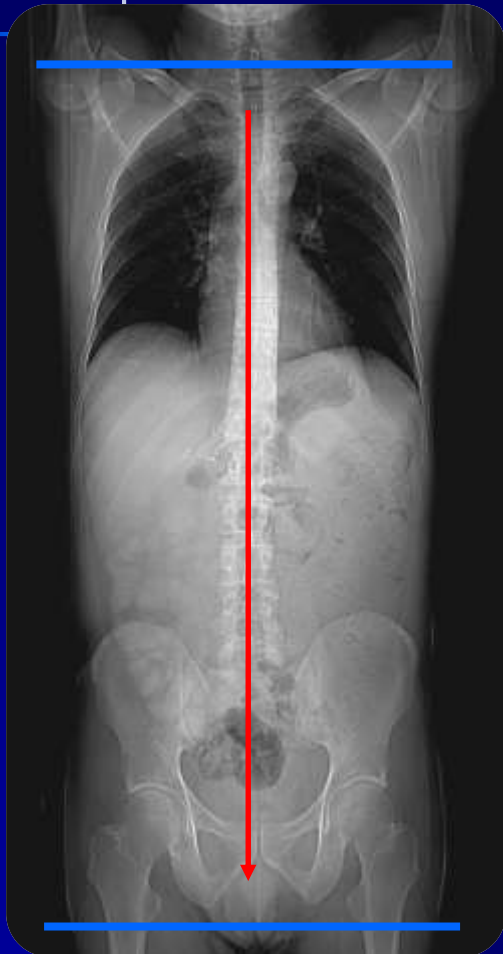


HOMERSAPIEN

HOMERSAPIEN

2015: 256 strati

Velocità di acquisizione



0,3-0,5 sec



< 10 sec

Se: 2
Im: 1+C

Oct 04 2005
12:21:41 PM





European Commission

RADIATION PROTECTION 118

Referral guidelines for imaging



Referral guidelines for imaging

Adapted by experts representing
European radiology and nuclear
medicine

In conjunction with
the UK Royal College of Radiologists

Typical effective doses from diagnostic medical exposures in the 1990s

Diagnostic procedure	Typical effective dose (mSv)	Equivalent No. of chest x-rays	Approximate equivalent period of natural background radiation ⁽¹⁾
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X-ray examinations:

Limbs and joints (except hip)	<0.01	<0.5	<1.5 days
Chest (single PA film)	0.02	1	3 days
Skull	0.07	3.5	11 days
Thoracic spine	0.7	35	4 months
Lumbar spine	1.3	65	7 months
Hip	0.3	15	7 weeks
Pelvis	0.7	35	4 months
Abdomen	1.0	50	6 months
IVU	2.5	125	14 months
Barium swallow	1.5	75	8 months
Barium meal	3	150	16 months
Barium follow through	3	150	16 months
Barium enema	7	350	3.2 years
CT head	2.3	115	1 year
CT chest	8	400	3.6 years
CT abdomen or pelvis	10	500	4.5 years

Dose efficace

Rx torace in PA: 0.01 mSV

uomo	torace: 6,6 mSv addome: 6.9/9.2 mSv TOTALE: 13.5/15.8 mSV
donna	torace: 6,6 mSv addome: 9.3/12 mSv TOTALE: 15.3/18.6 mSV

50.000 esami TC /anno

10-12 mSV ogni TC → 500.000 mSV

5 possibili tumori ogni 100.000 mSV



25 TUMORI INDOTTI DA ESAMI TC



Legati alle informazioni fornite dall' indagine



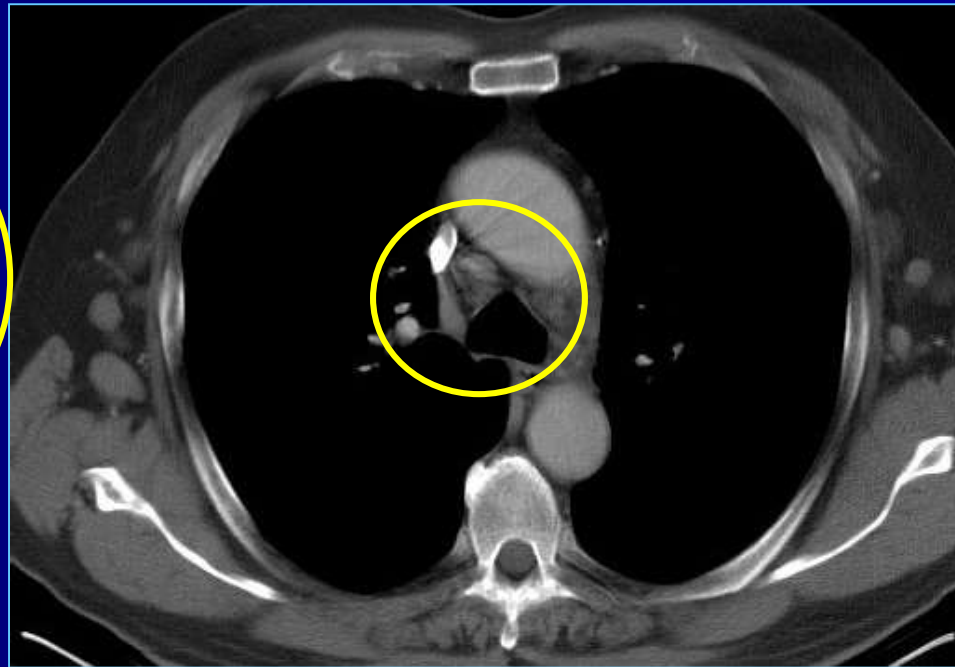
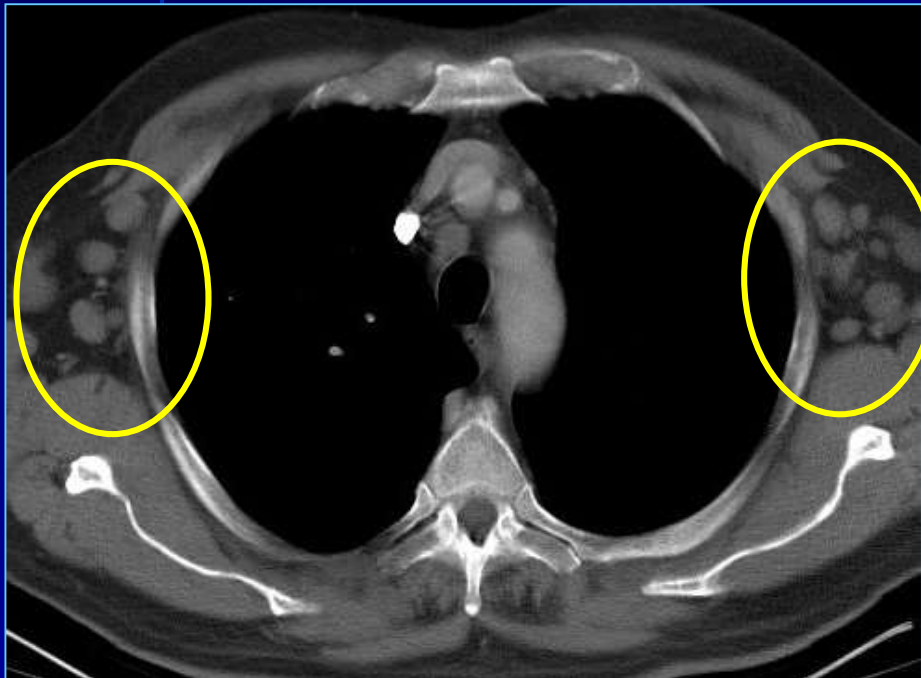
- ❖ Semeiotica consolidata
- ❖ Diagnosi di patologie correlate
- ❖ Diagnosi di anomalie o patologie associate
- ❖ Guida per manovre bioptiche
- ❖ Informazioni unicamente morfologiche
- ❖ Sedi “difficili”
- ❖ Interessamento midollo osseo non documentabile
- ❖ Valutazione reale risposta alla terapia in caso di masse residue

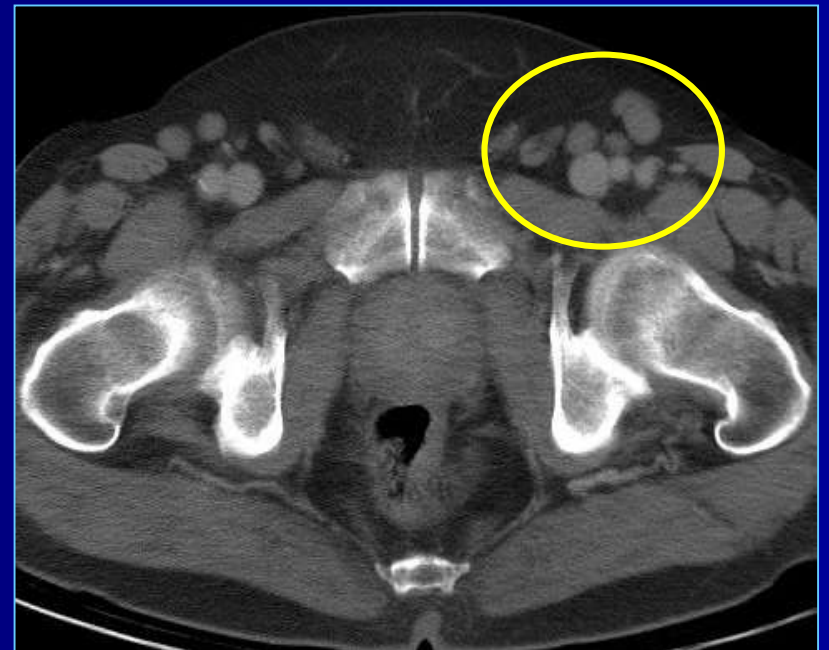
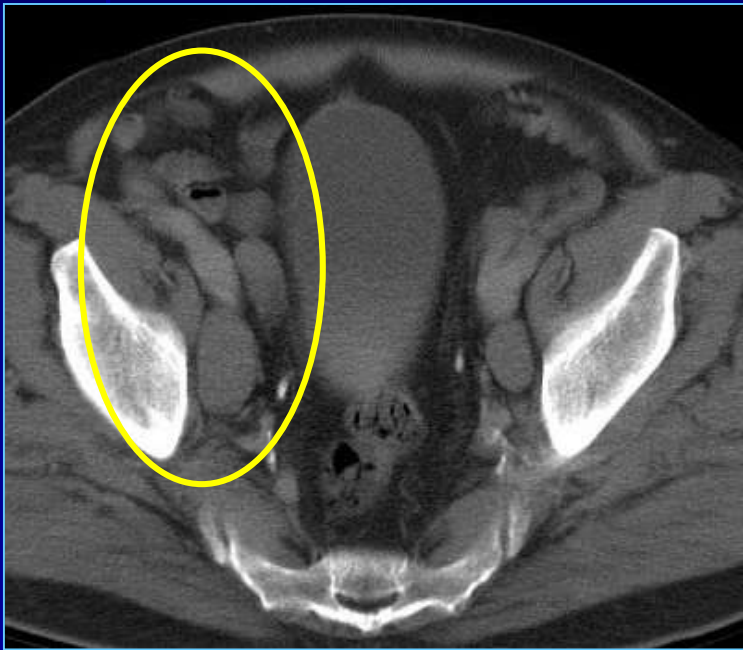
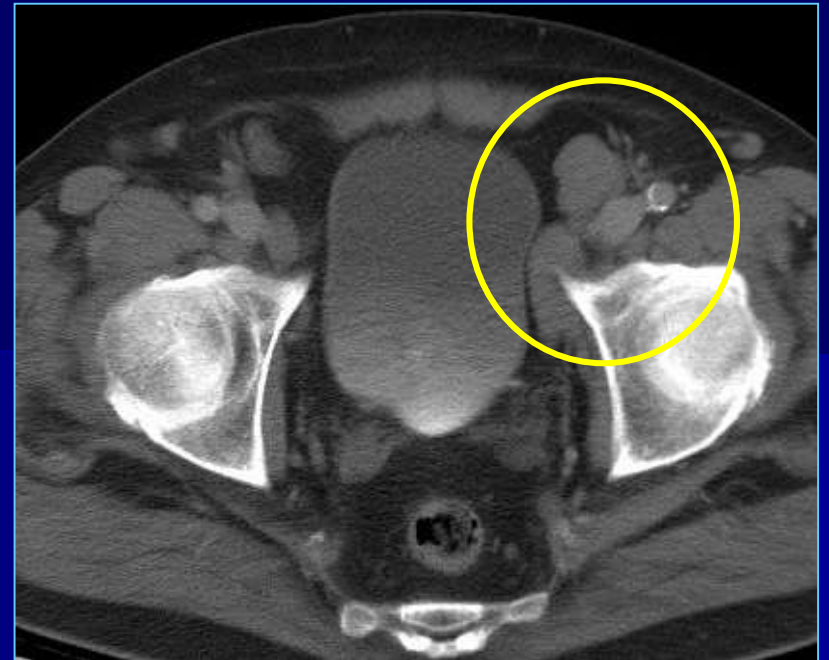
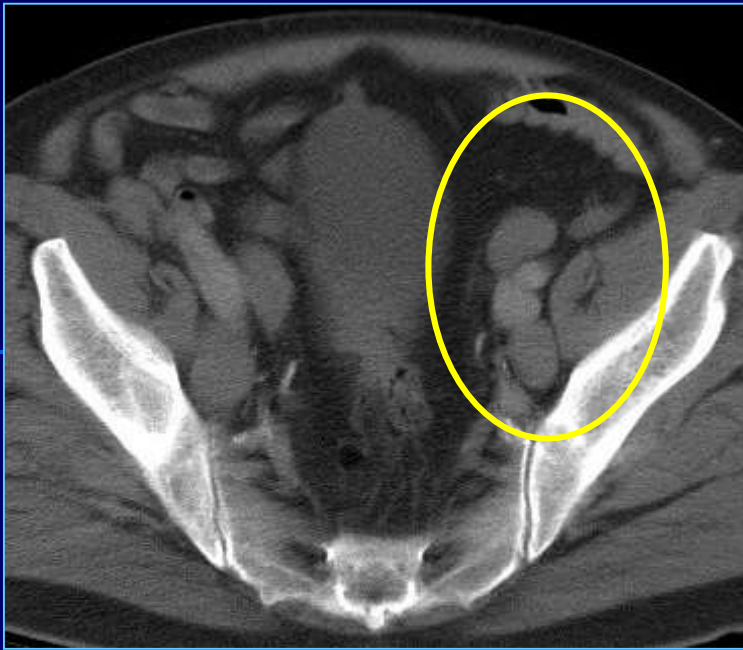
Malattia nodale

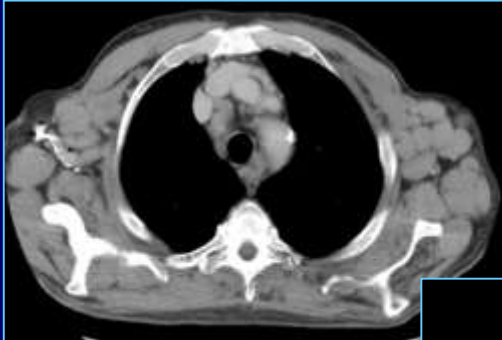
Distribuzione delle adenopatie

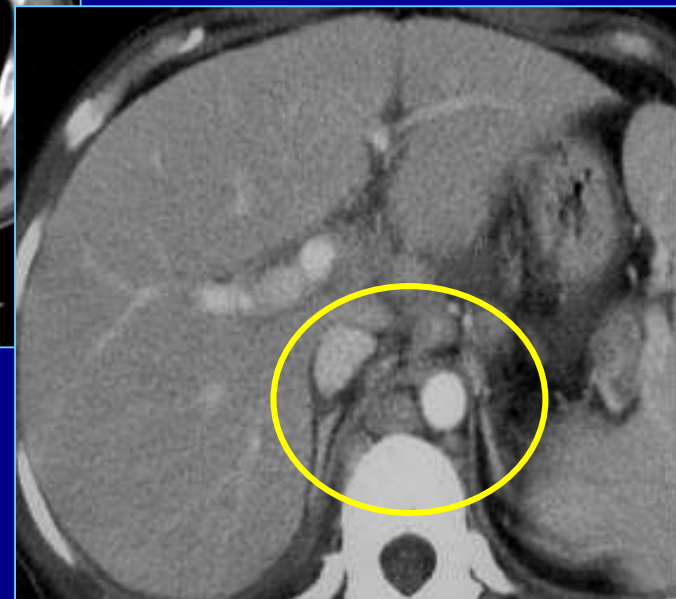
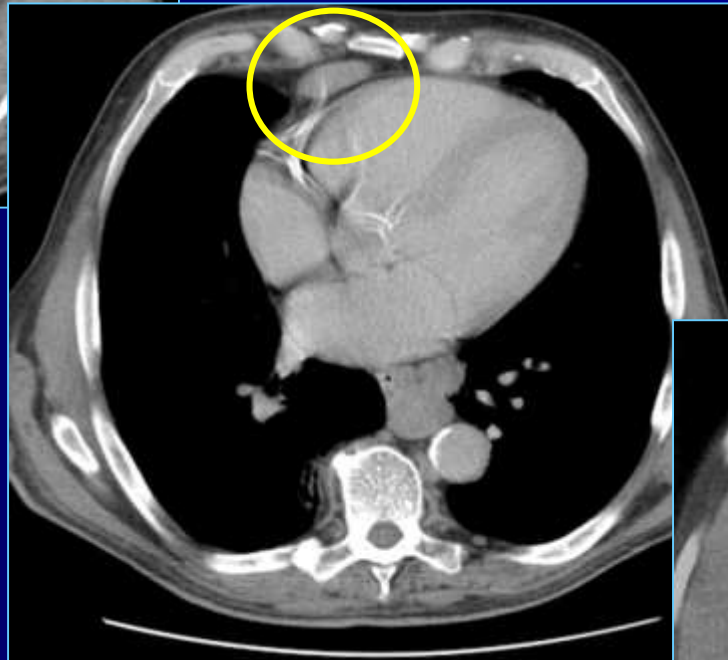
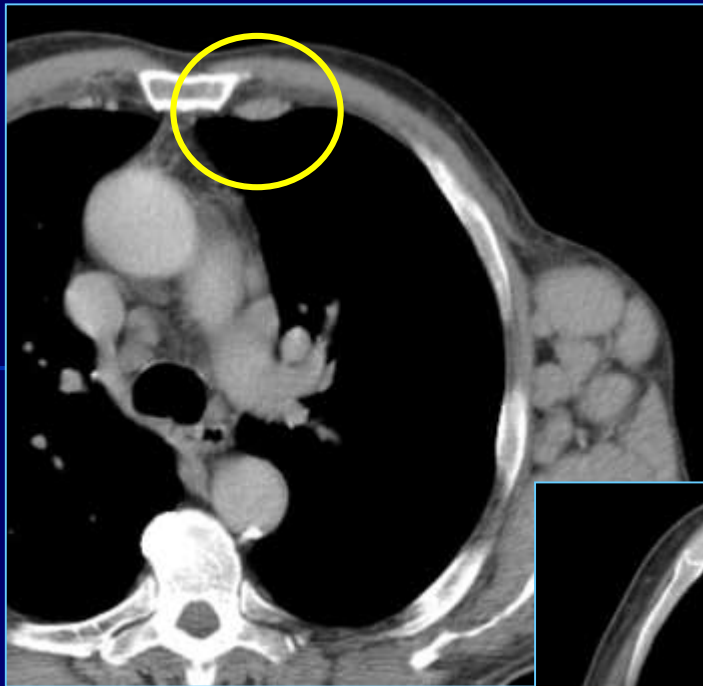
Misurazione dimensioni linfonodi

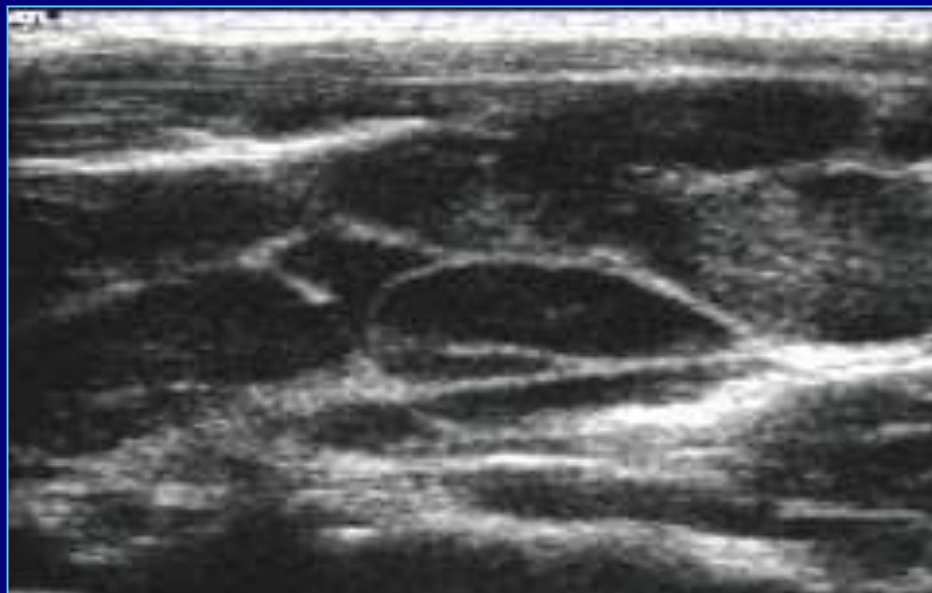
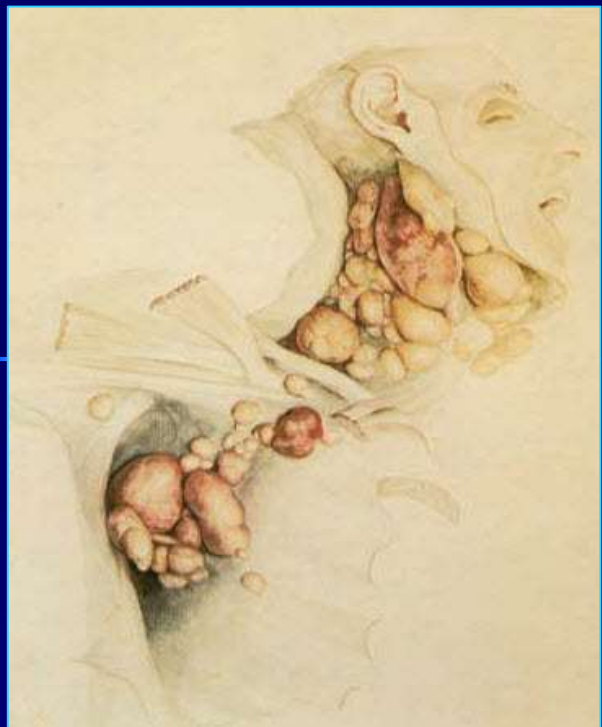
Semeiotica consolidata

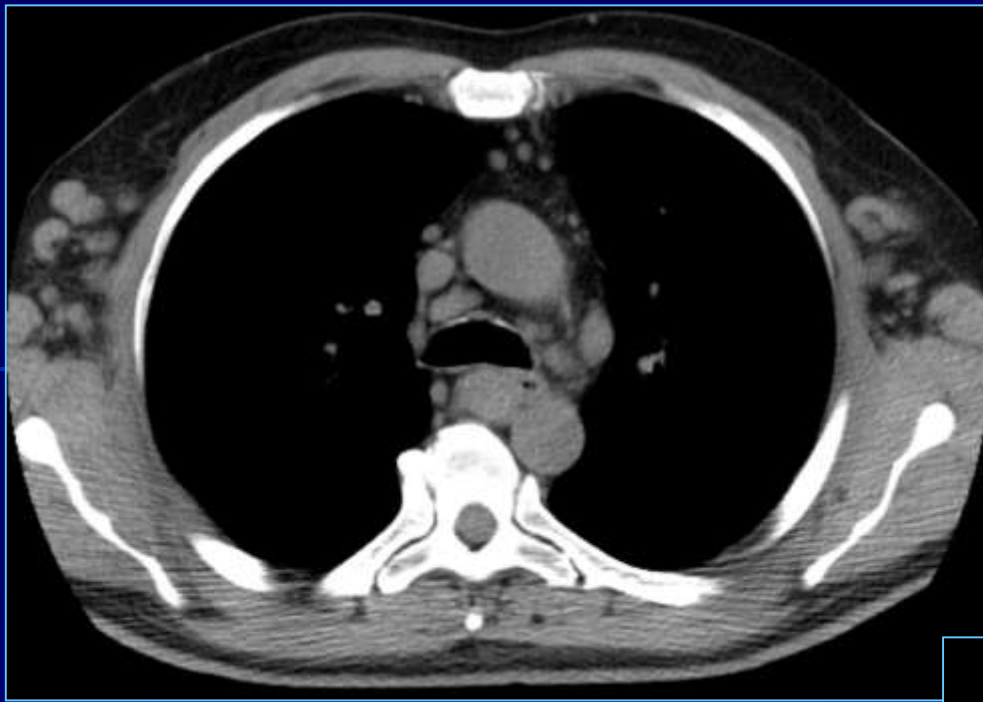










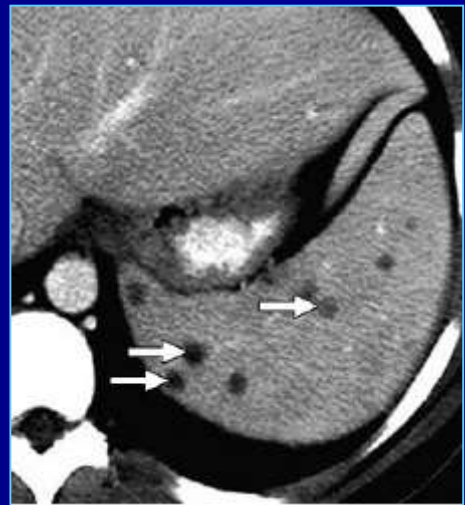
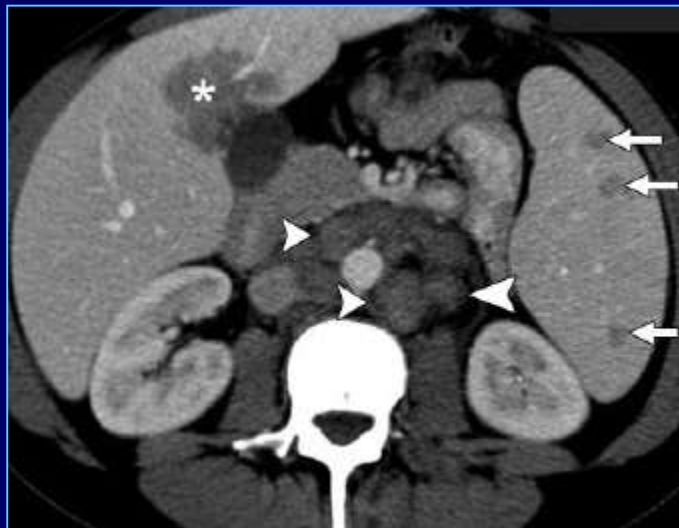
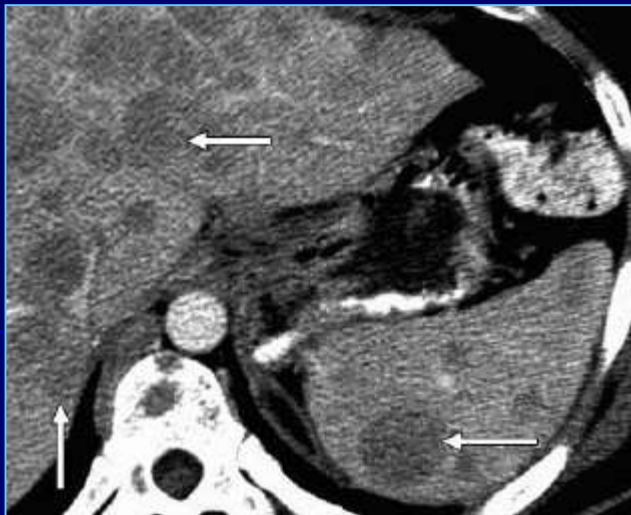


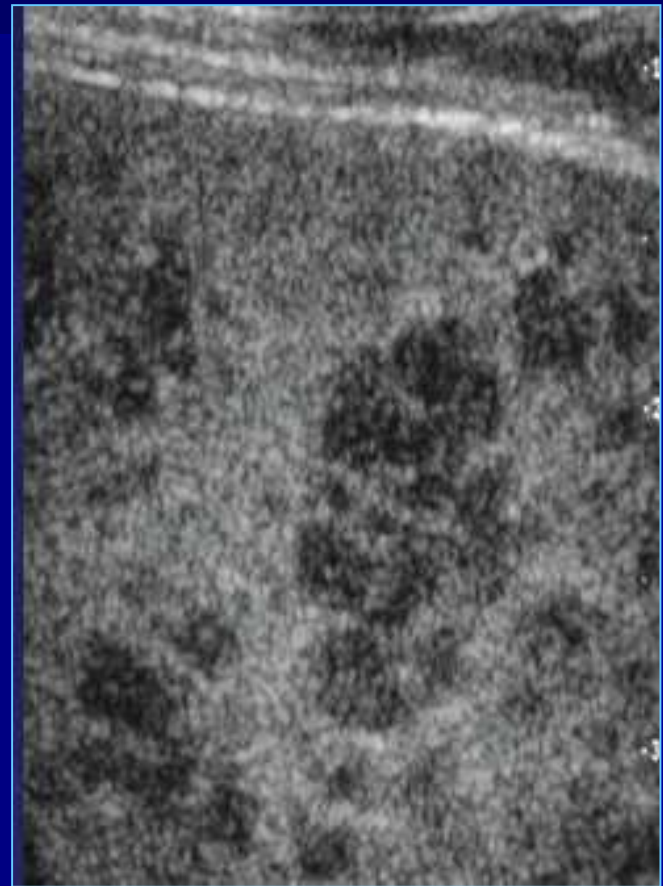
Malattia extranodale

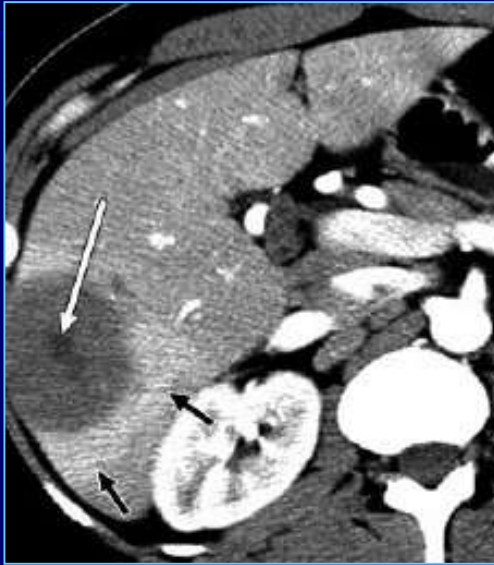
La TC può sospettare la diagnosi

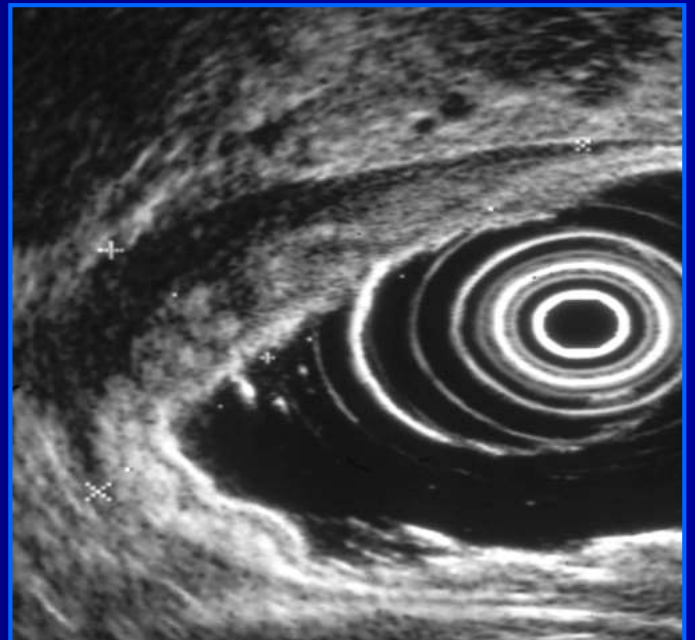
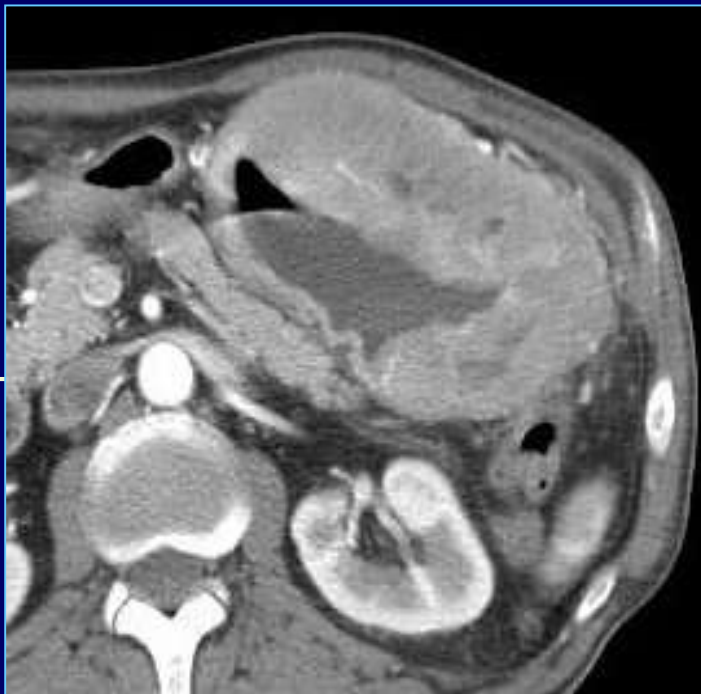
**Ottimo riconoscimento
di alterazioni morfologiche di
organi solidi e cavi**

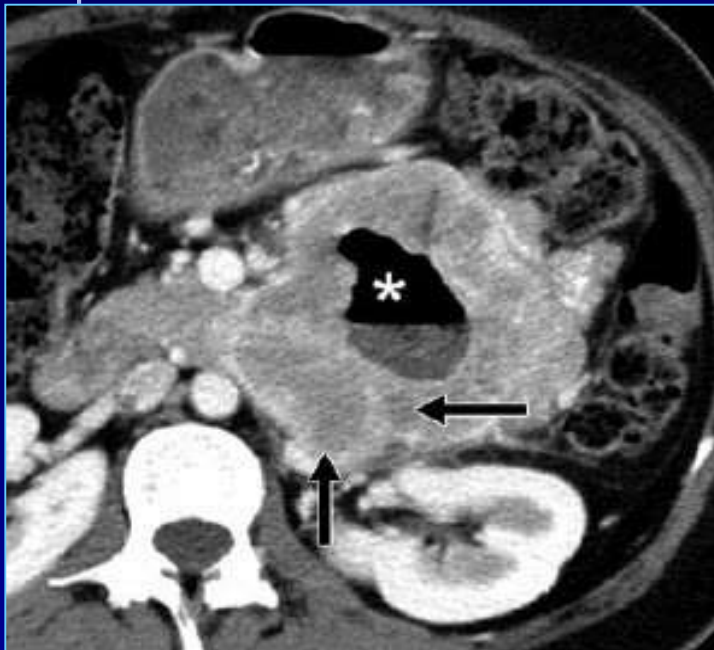
**Tutti gli organi o apparati possono
esser sede di LINFOMA**

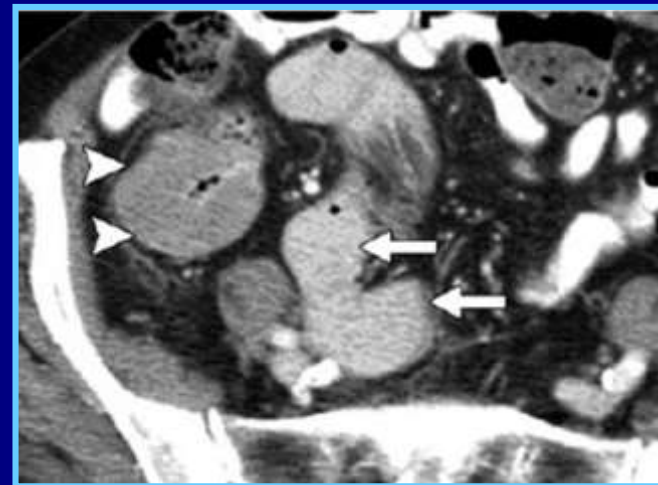
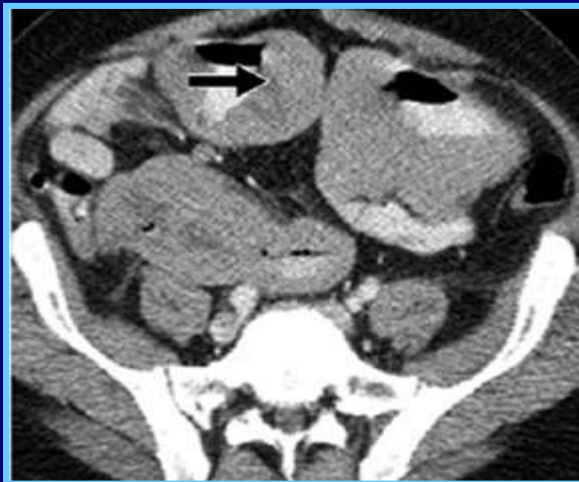
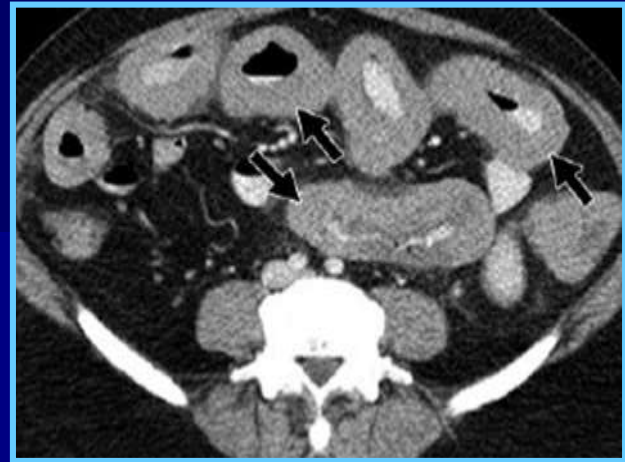
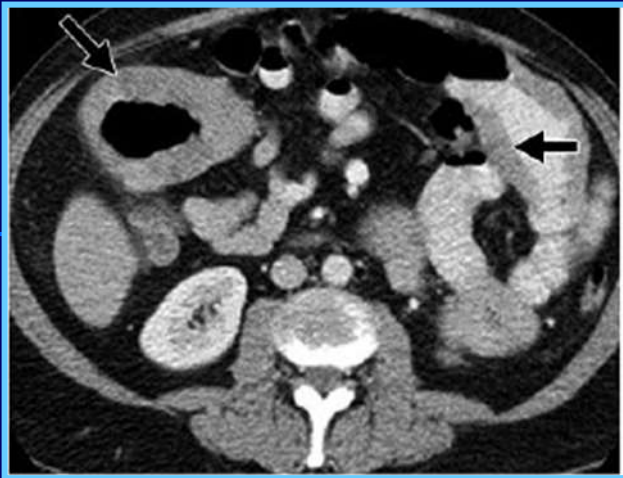


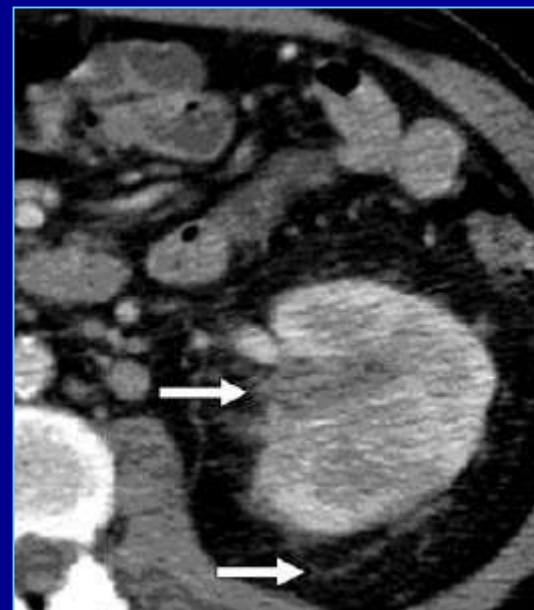


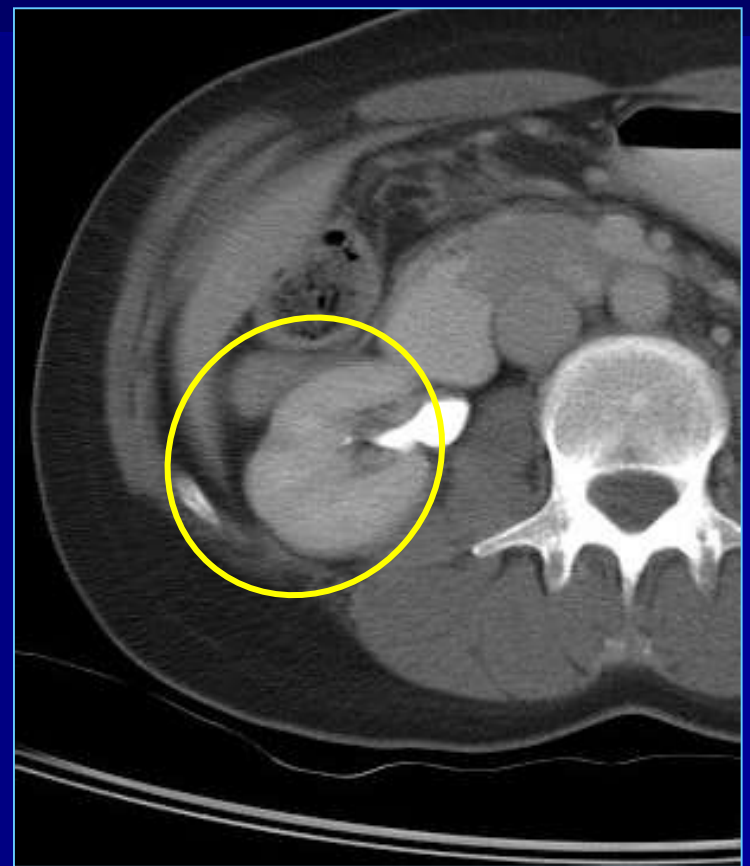
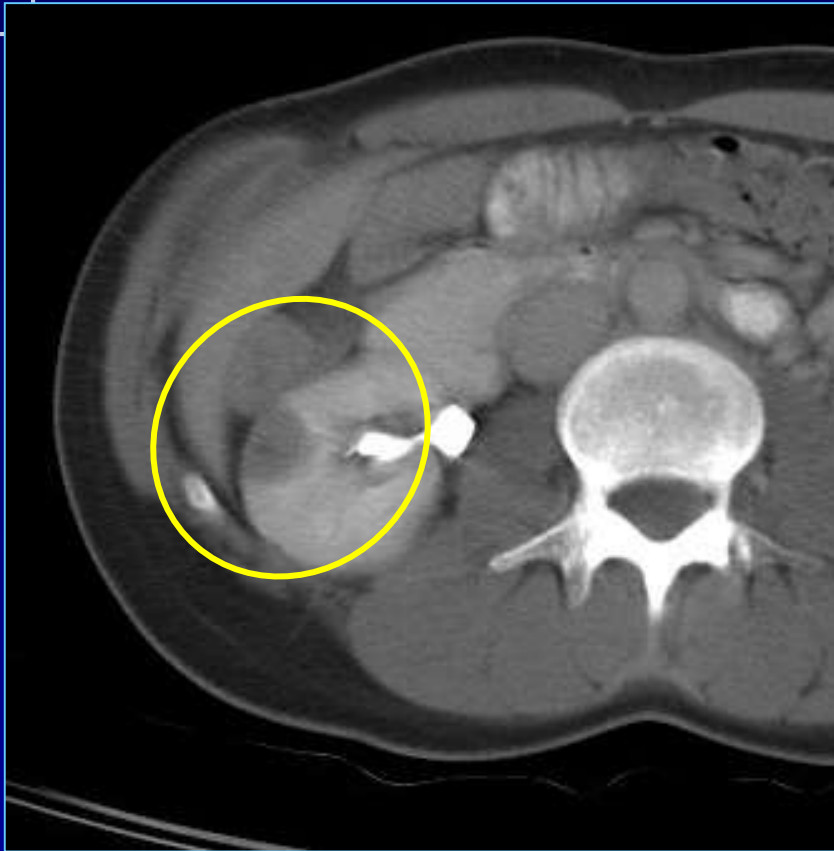












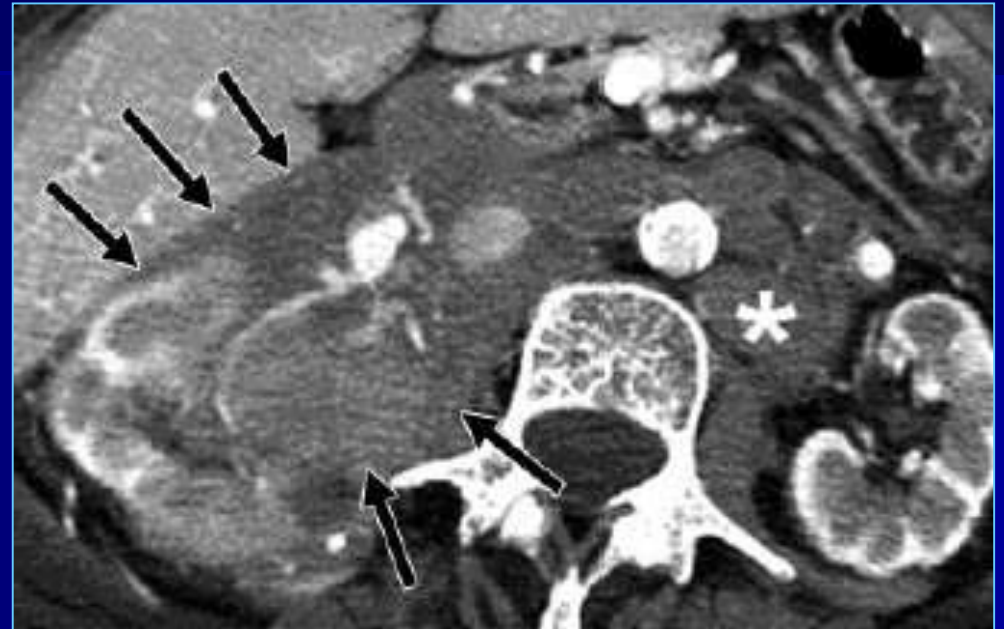
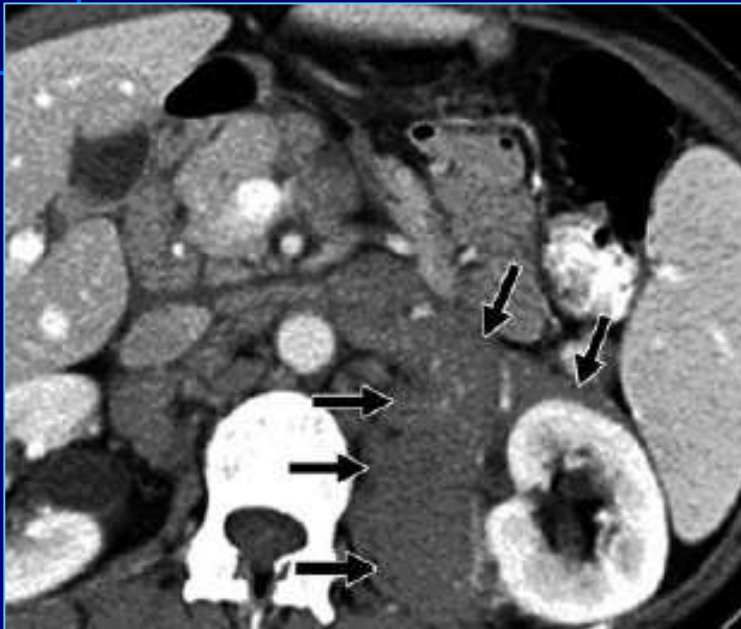


Table 2. Summary of CT features in the malignant spectrum of pulmonary lymphoproliferative disorders

Malignant spectrum	CT features
Primary malignant 1. MALT lymphoma	Nodules or consolidation Multiple/bilateral (>70%) Peribronchovascular
<i>The British Journal of Radiology, 85 (2012), 848–864</i>	
REVIEW ARTICLE	
The radiological spectrum of pulmonary lymphoproliferative disease	
¹ S S HARE, MBBS, FRCR, ¹ C A SOUZA, MD, PhD, ² G BAIN, MRCP, FRCR, ¹ J M SEELY, MDCM, FRCPC, ³ M M GOMES, MD, PhD and ² M QUIGLEY, MRCS, FRCR	
¹ Department of Radiology, The Ottawa Hospital, Ottawa, ON, Canada, ² Department of Radiology, North West London Hospitals NHS Trust, London, UK, and ³ Department of Pathology and Laboratory Medicine, The Ottawa Hospital, Ottawa, ON, Canada	
2. Post-transplantation lymphoproliferative disorder	Lymphadenopathy Nodules: single>multiple Usually well defined “Halo sign” Peribronchovascular/subpleural Lymphadenopathy (30–60%)

MALATTIE LINFOPROLIFERATIVE POLMONARI MALIGNI

PRIMITIVE

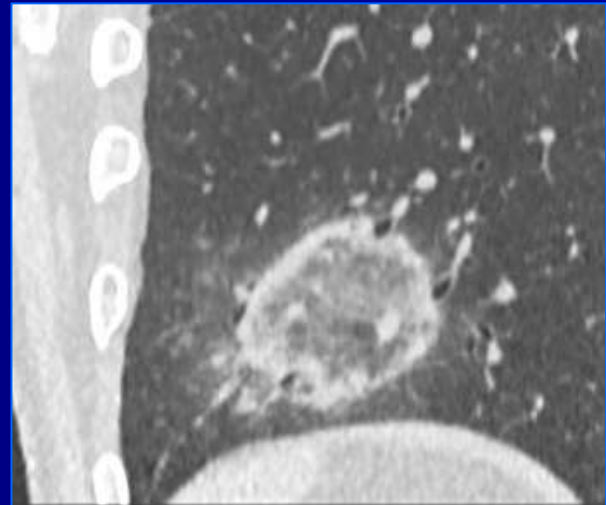
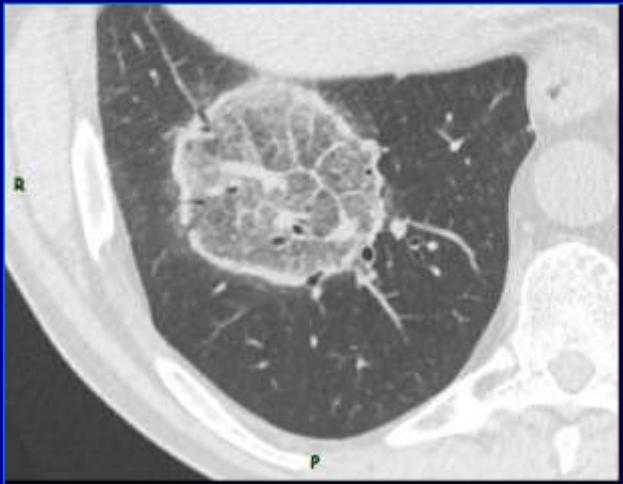
0,5-1% neoplasie polmonari maligne
< 1% NHL (3-4% linfomi extranodali)

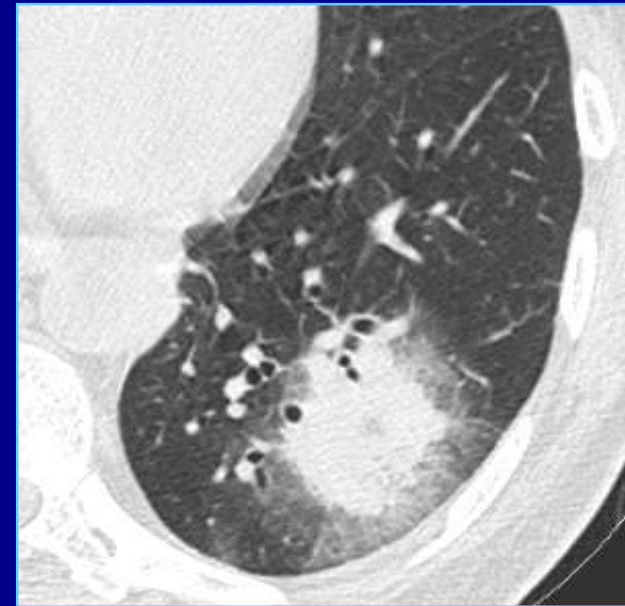
- Linfomi marginali extranodali del MALT (BALT)
- Linfomi diffusi a larghe cellule (DLBCL)
- Granulomatosi linfomatoide (LYG)
- Plasmocitoma polmonare
- Linfomi AIDS correlati (DLCBCL, Burkitt, PEL)
- Disordini linfoproliferativi post trapianto (PTLD)
- Linfoma intravascolare

SECONDARIE

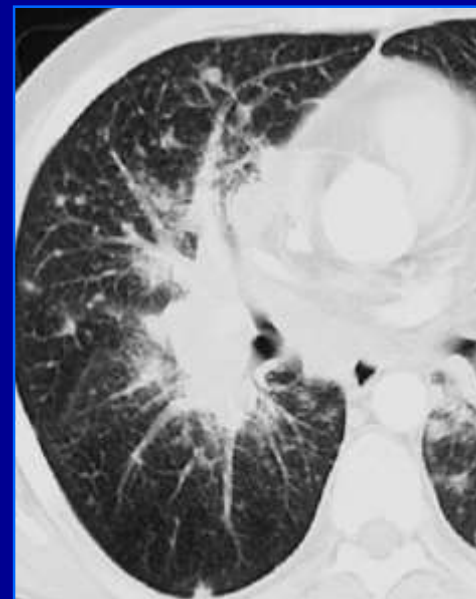
- NHL (24%)
- HL (38%)

*Eur Resp J 2002; 20:750-762
Eur Resp J 2016; 47:1244-1260
Br J Radiol 2012;85 :848-864
RadioGraphics 2016; 36:53-70*



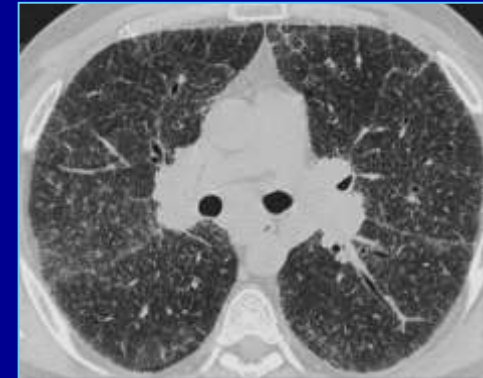


AJR 2011; 197:W69–W75
CHEST 2012; 141(5):1260–1266
Br J Radiol 2005;78 : 862–865



DD LINFOMI MALT POLMONARI

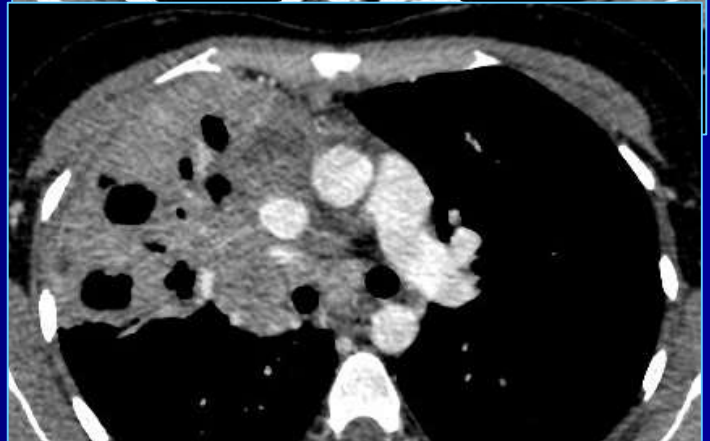
- OP
- COP
- Ca bronchiolo-alveolare
- Granulomatosi con poliangioite
- Infezioni
- Metastasi
- Sarcoidosi

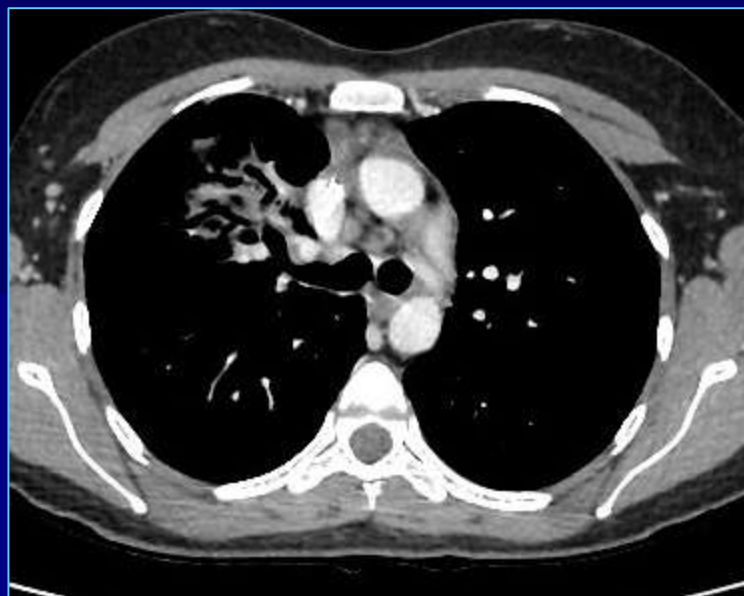


BIOPSIA

*Radiographics 2016;36: 53-70
Eur Respir J 2002; 20: 750-762*

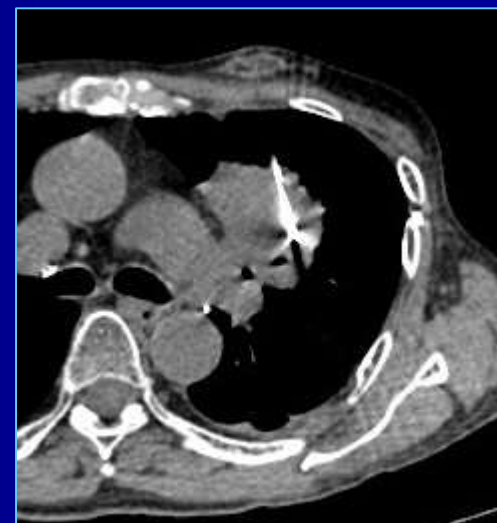
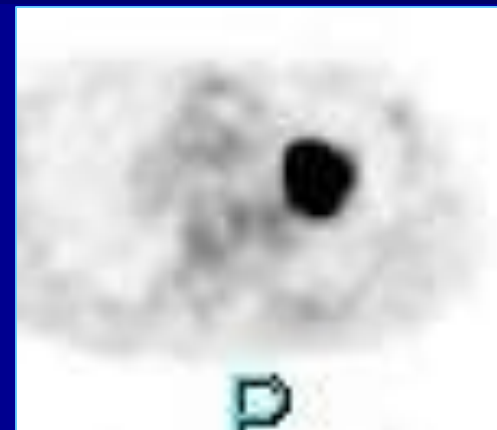
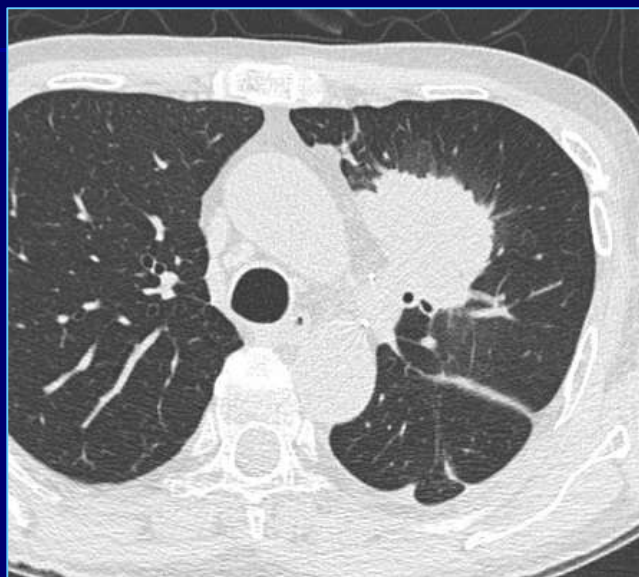
HL
Femmina 36 aa





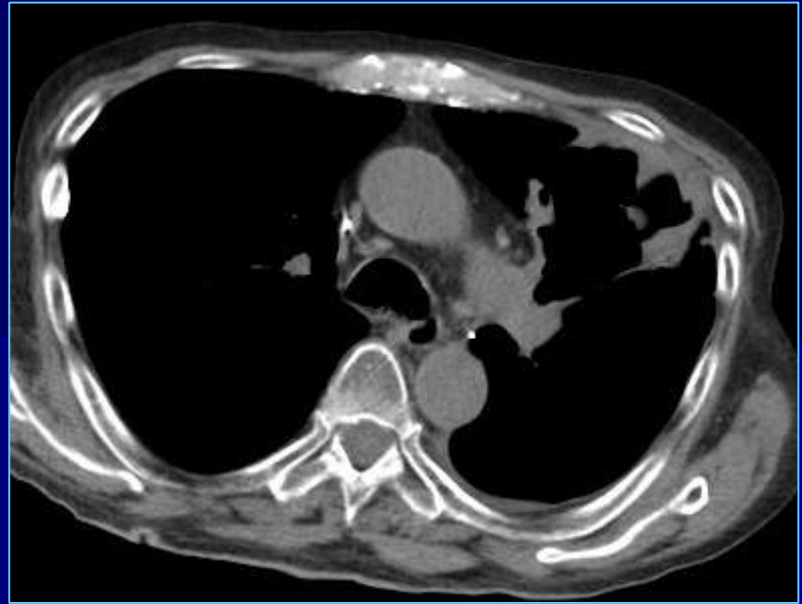
Maschio 67 aa trapianto polmonare luglio 2016

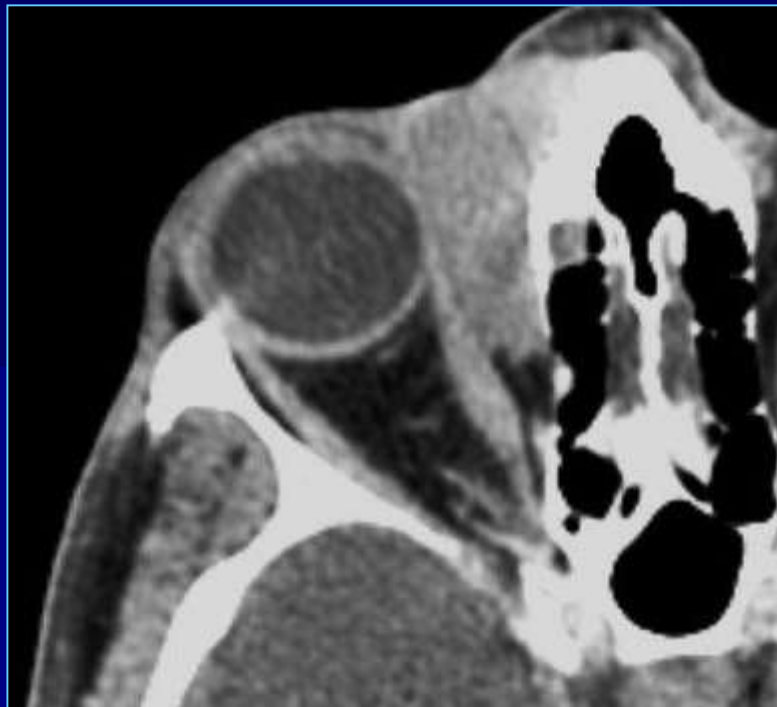
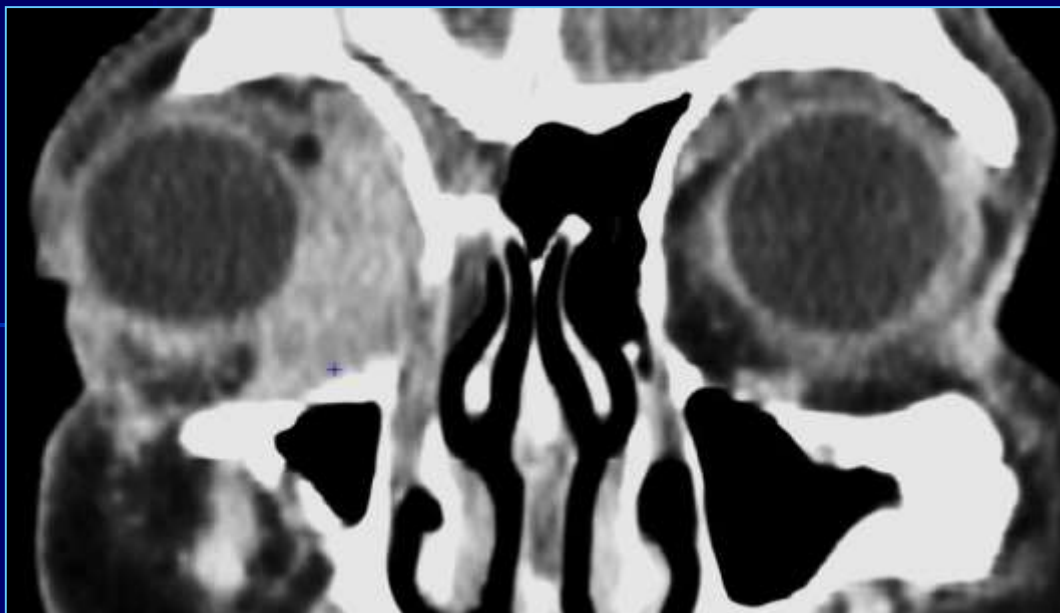


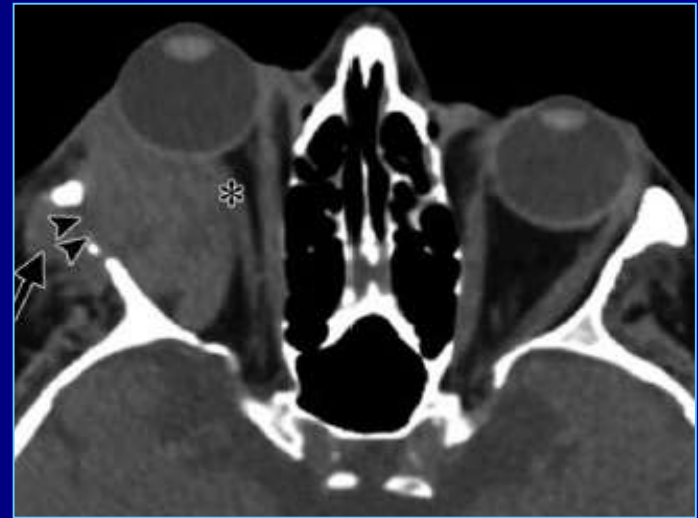


Luglio 2017
PTLD: Linfoma Diffuso a grandi
cellule B

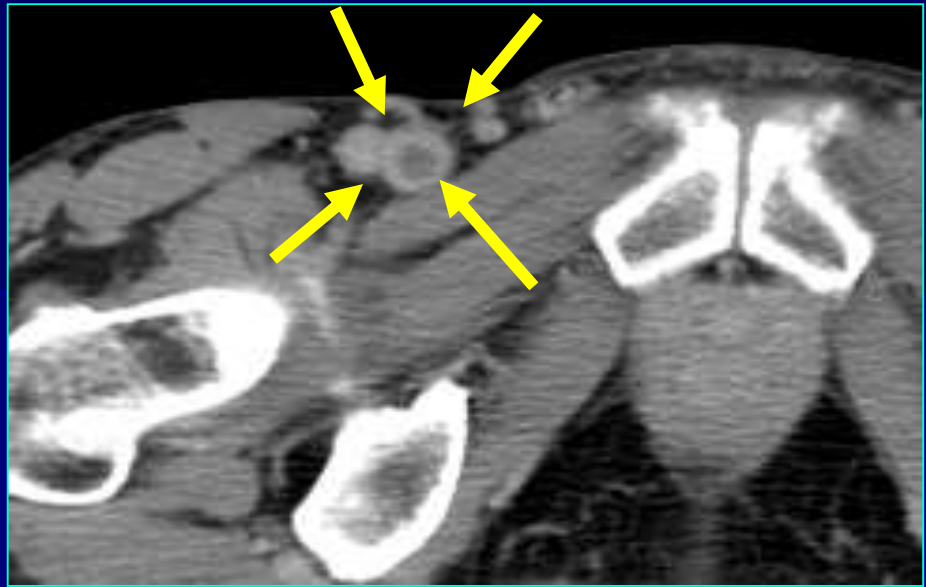
Controllo 6/10/2017



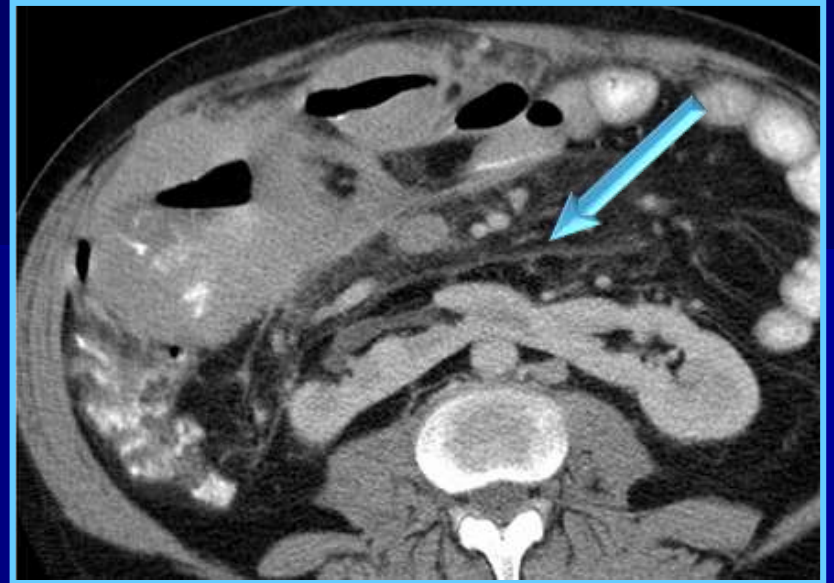
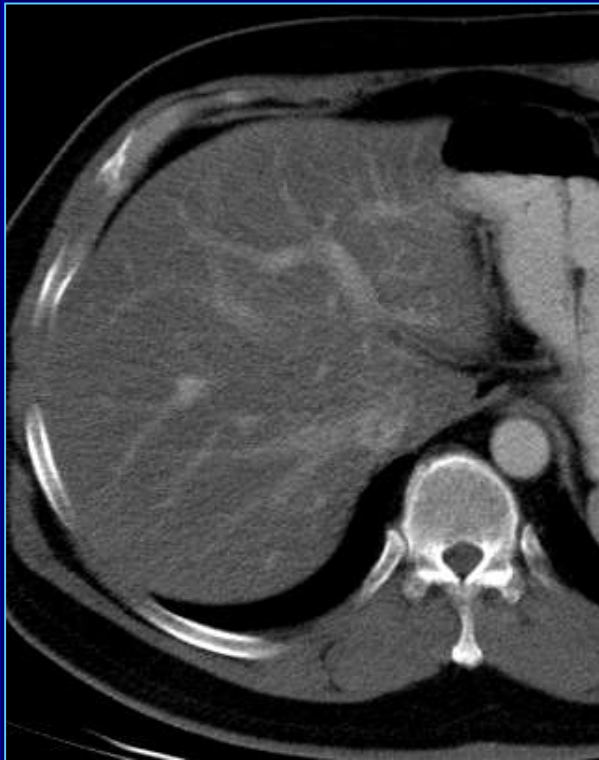




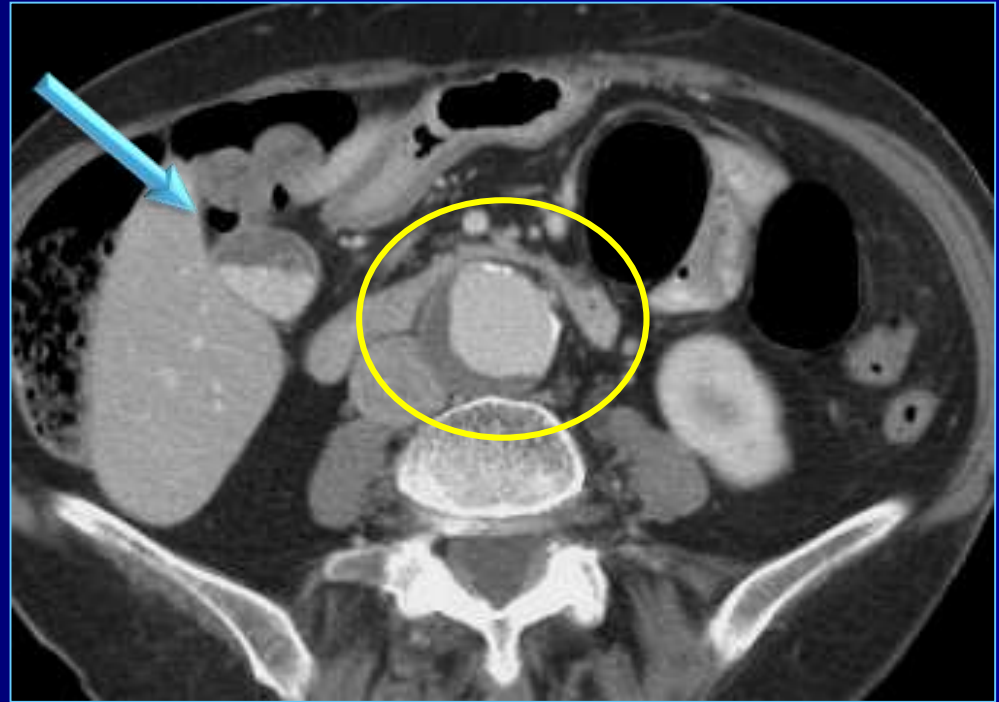
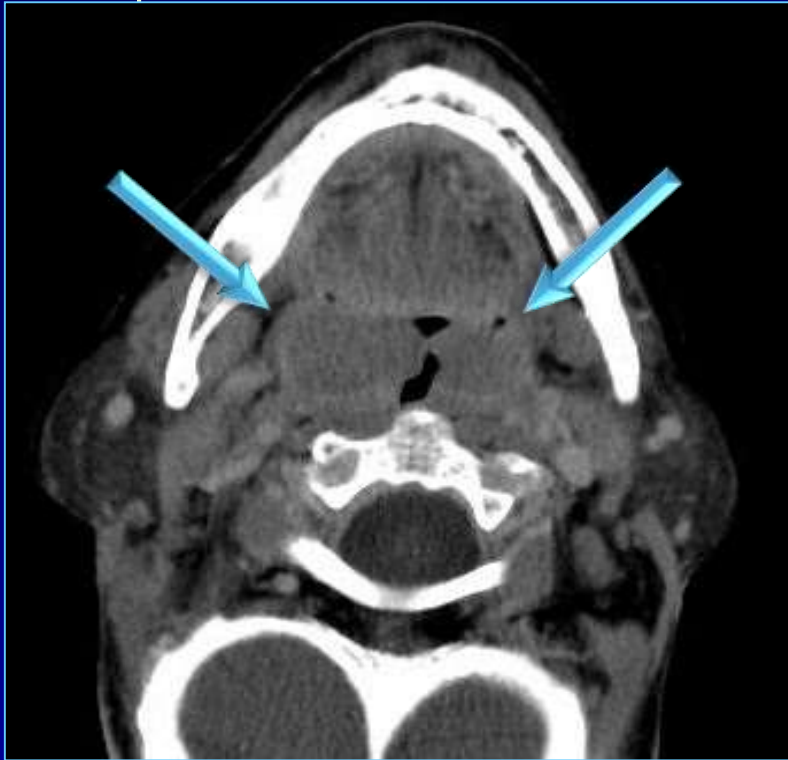
Patologie correlate



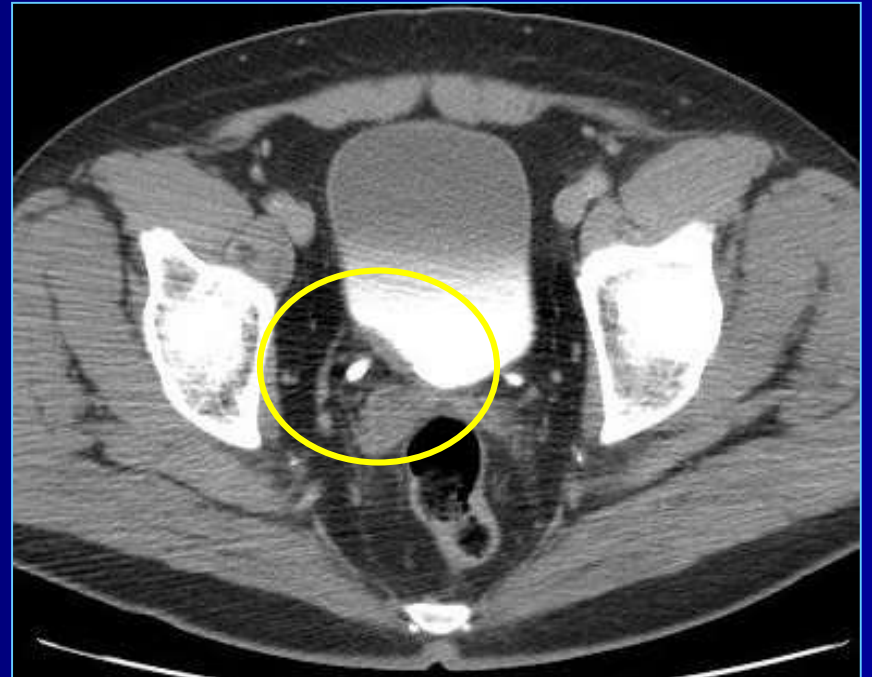
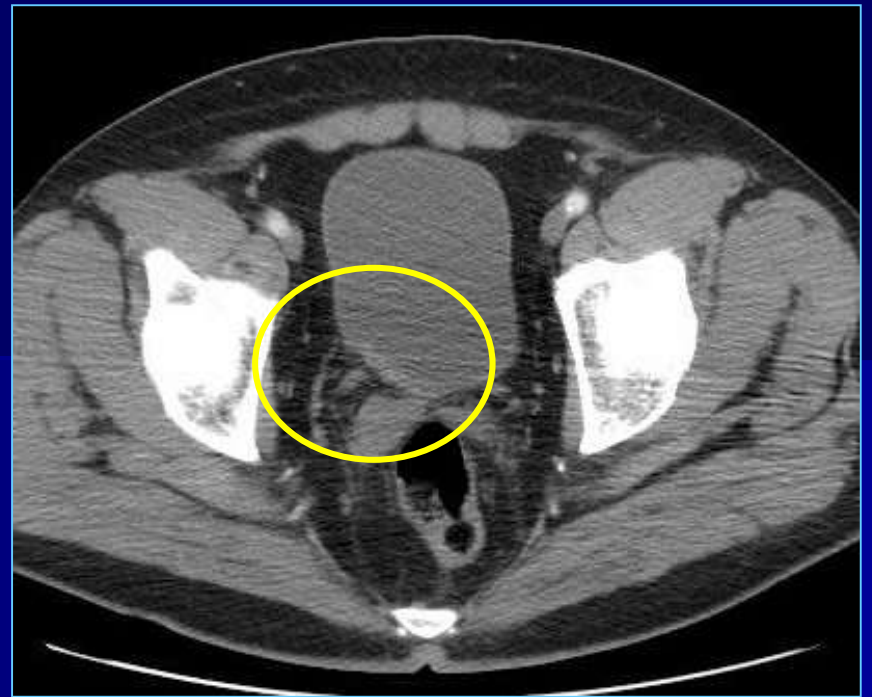
Anomalie associate



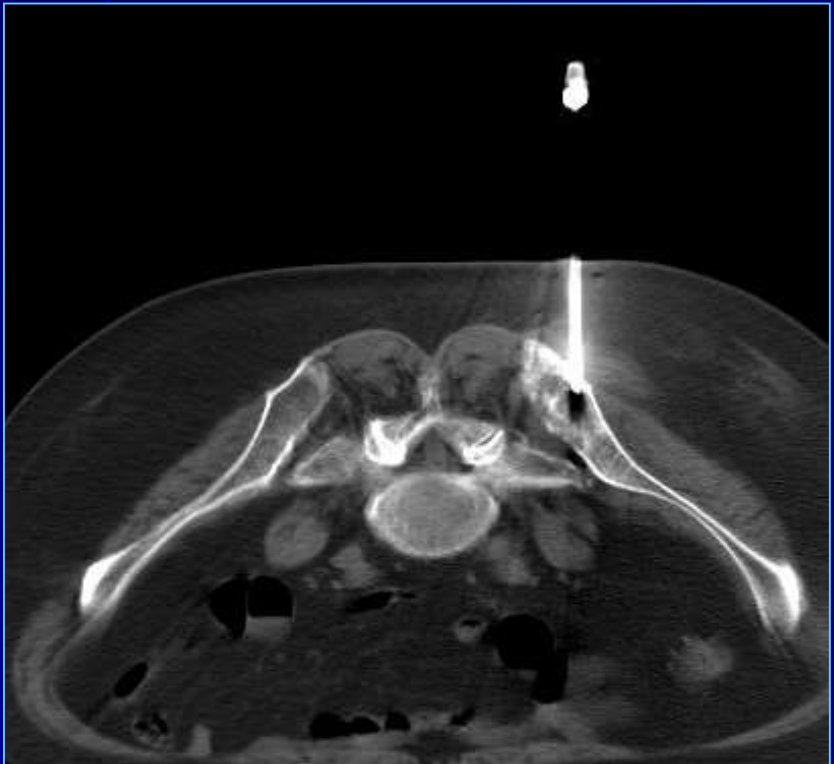
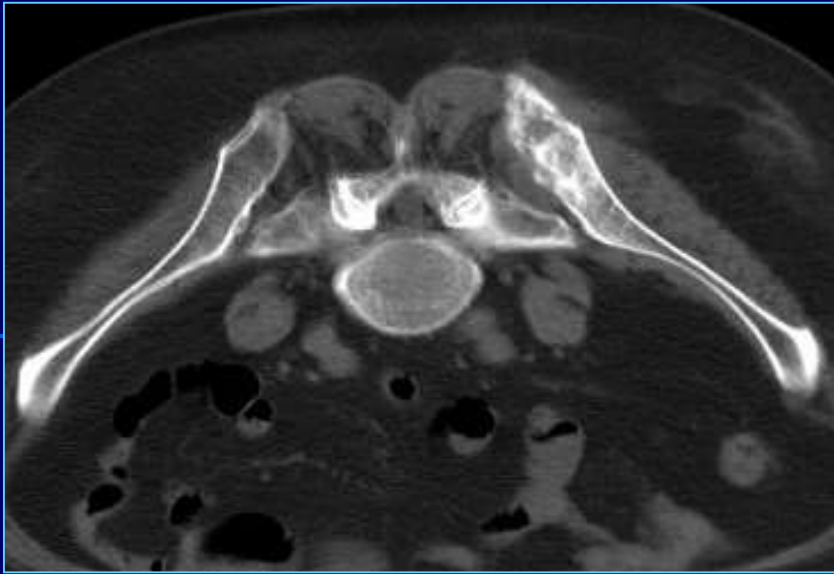
Patologie associate



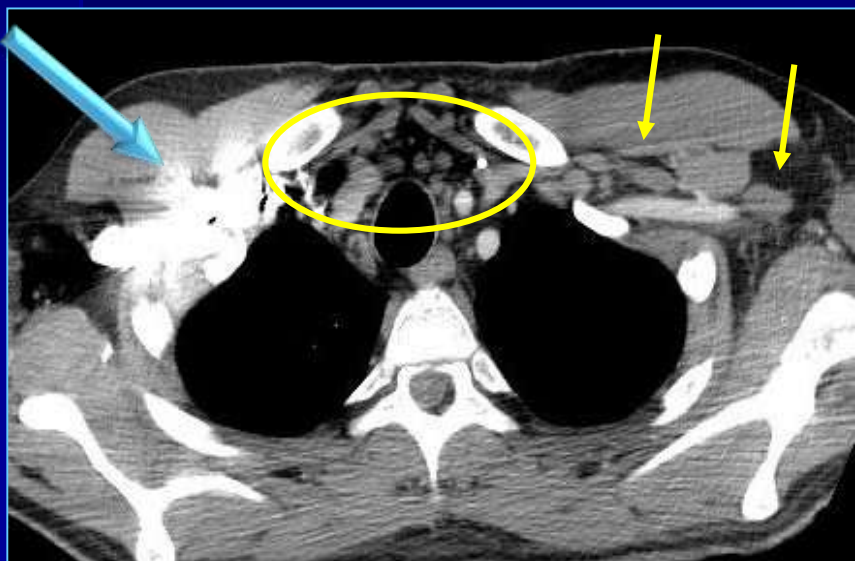
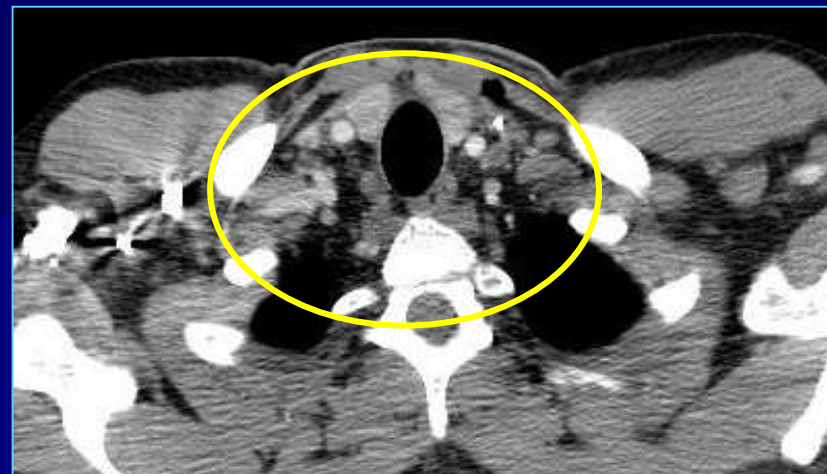
Patologie associate

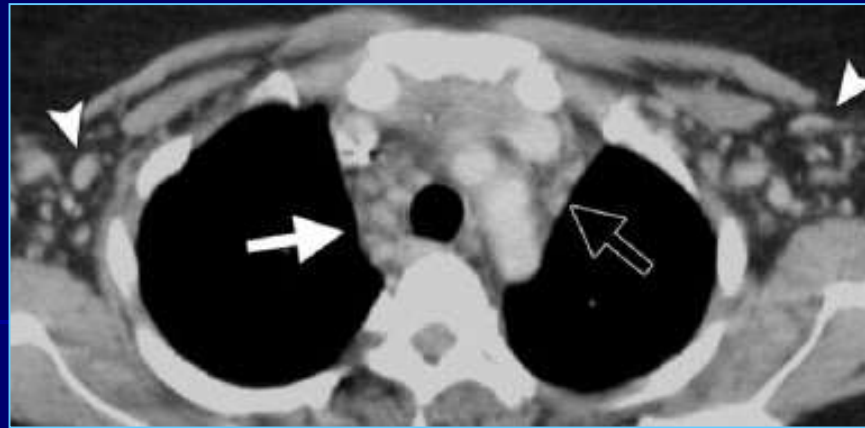


Guida manovre biottiche



Sedi difficili e Criteri solo dimensionali





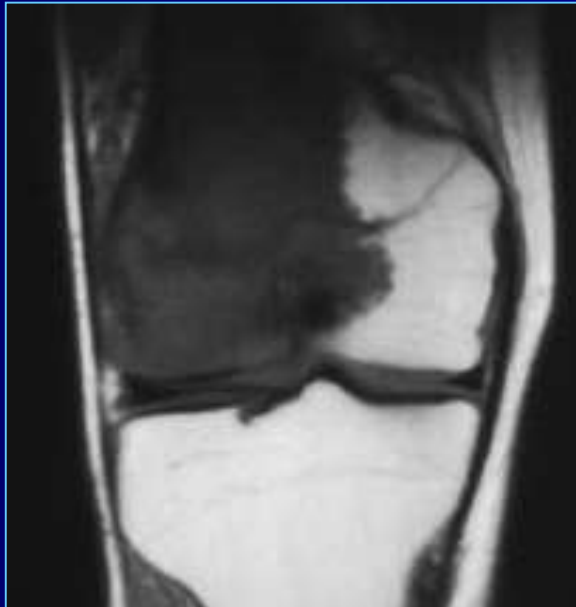
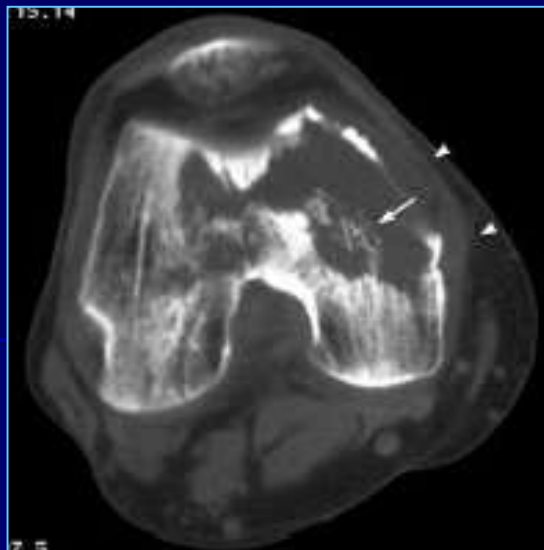
Castelman

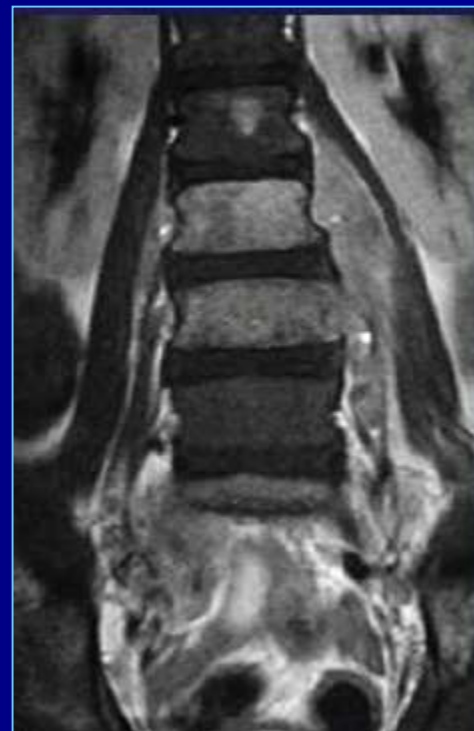
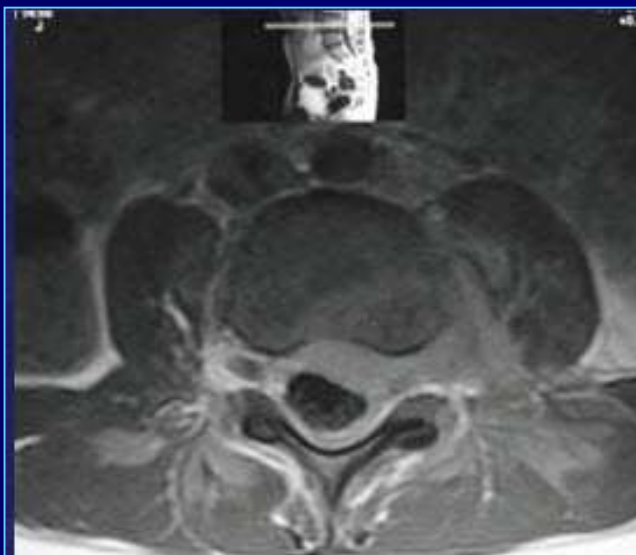
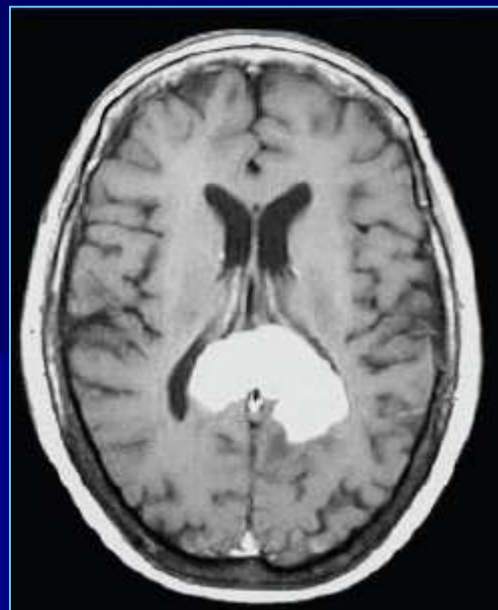
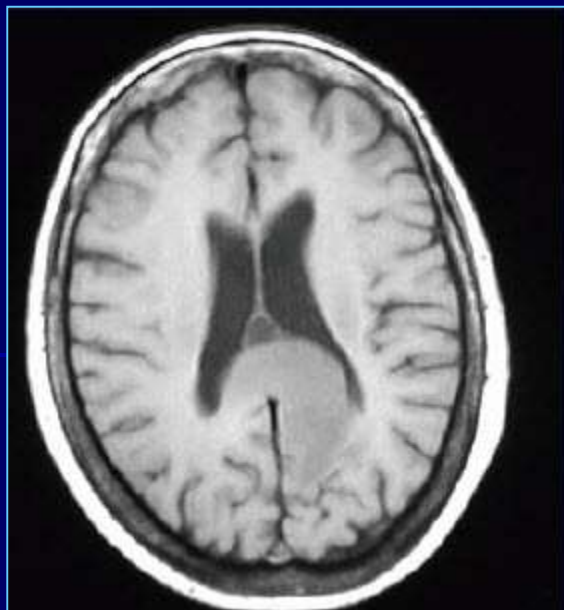


Problemi

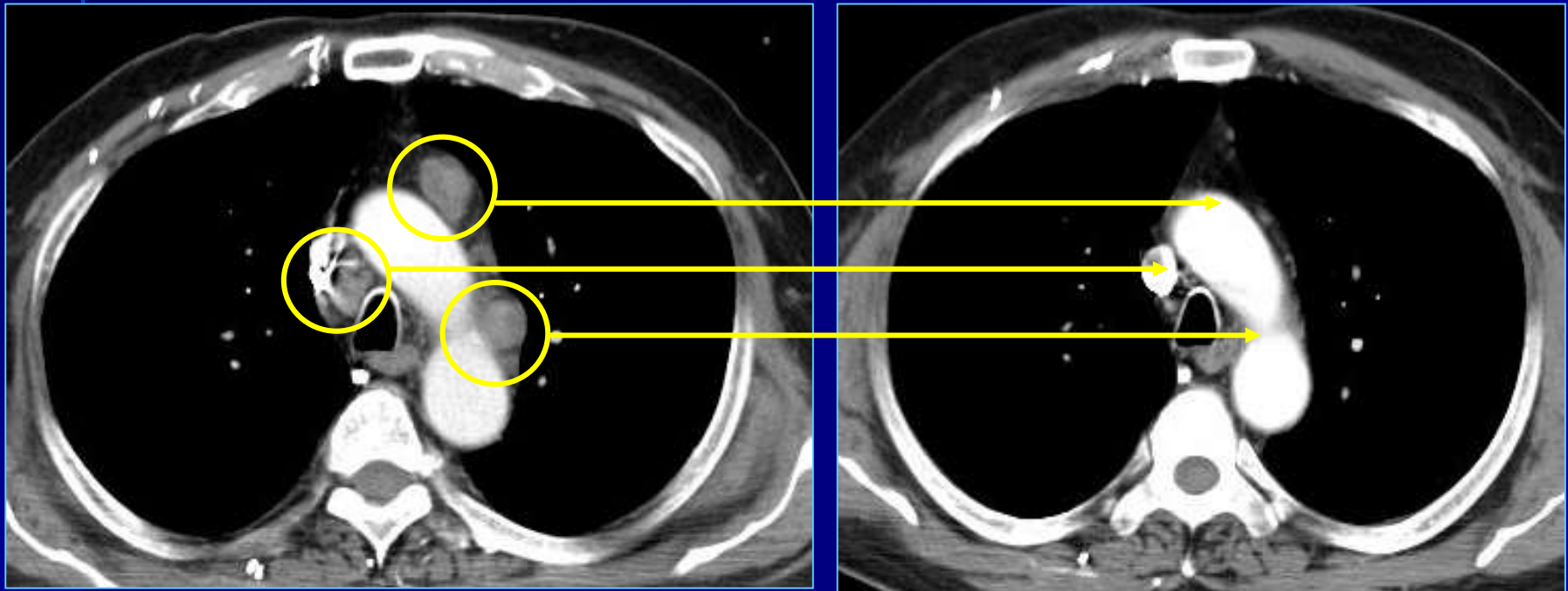


**Linfomi con linfonodi non ingranditi
o con lesioni in sedi non comuni
(muscoli, cute, osso, snc)**

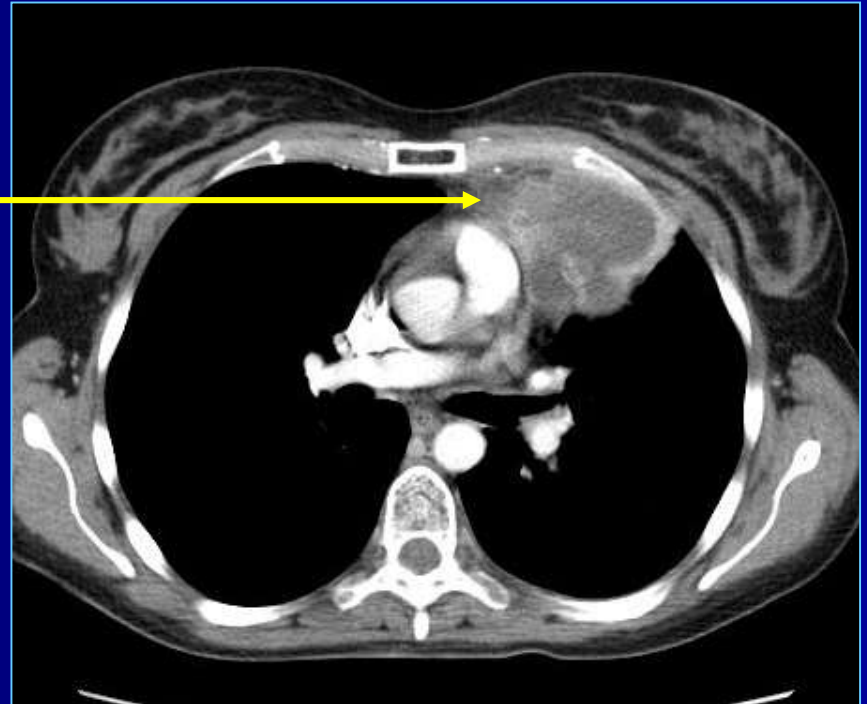
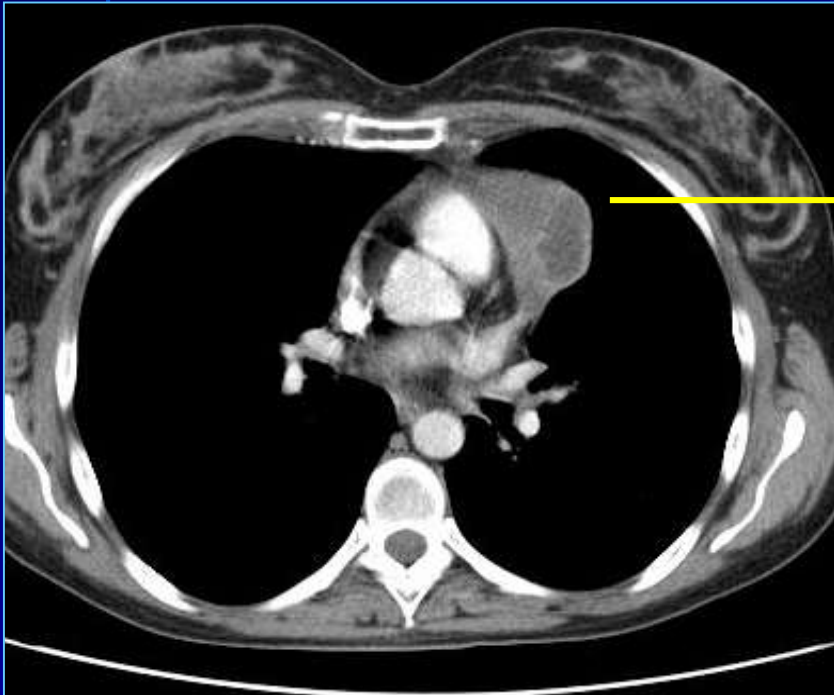


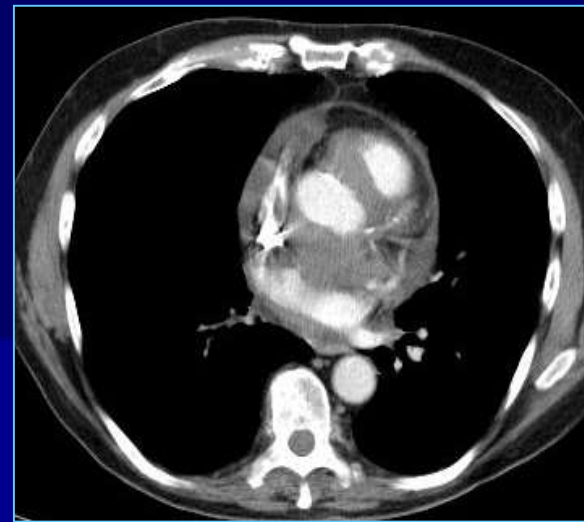
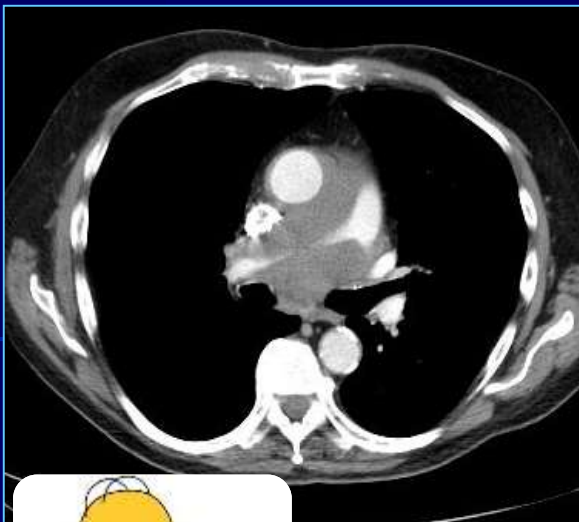


Risposta alla terapia

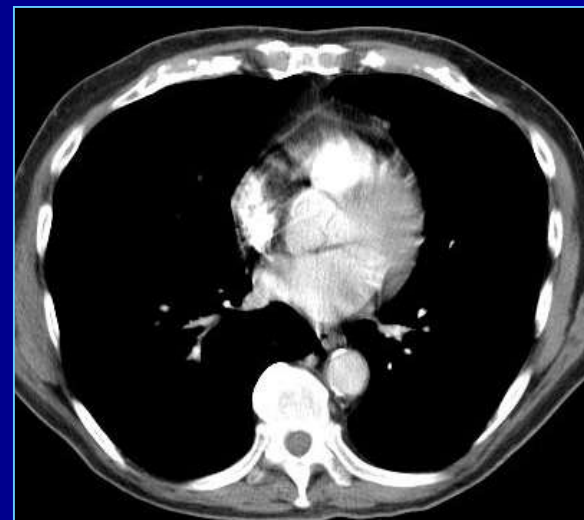
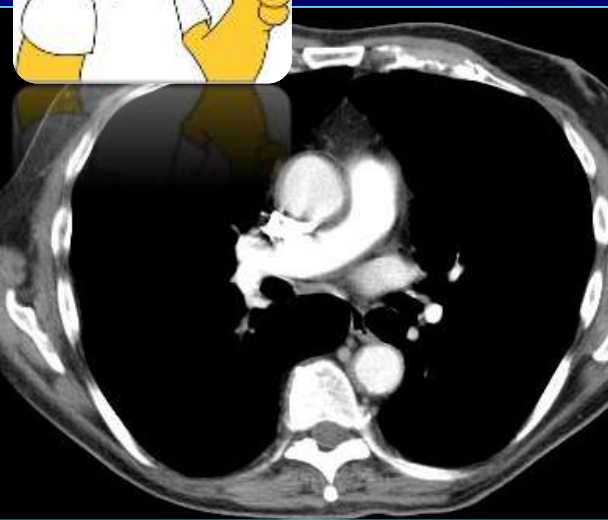


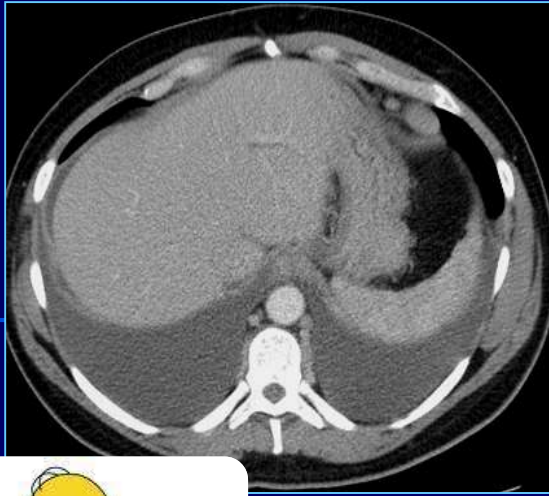
Risposta alla terapia



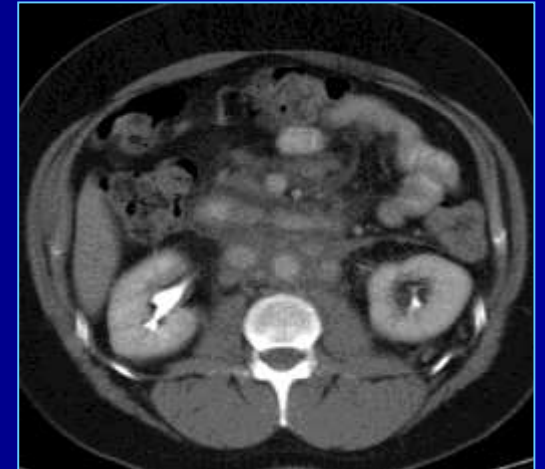
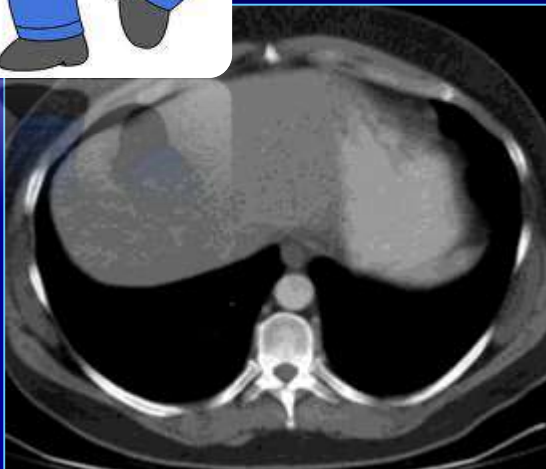


Risposta alla terapia

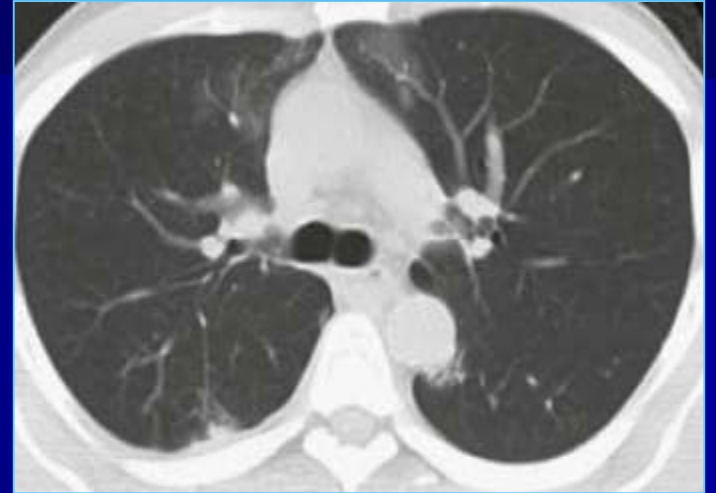




Risposta alla terapia

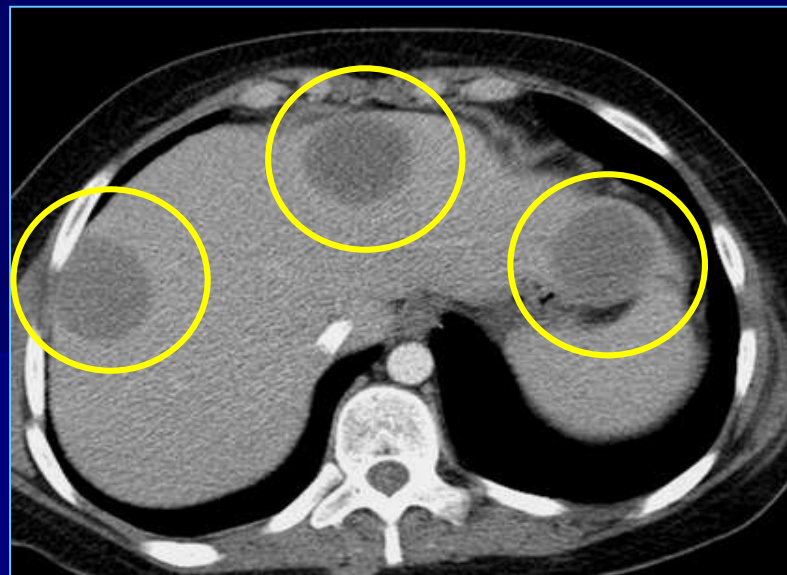
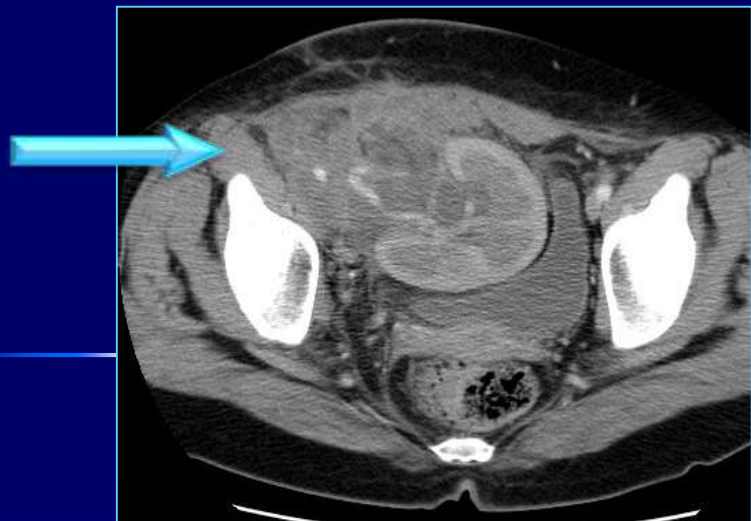


Esiti terapia

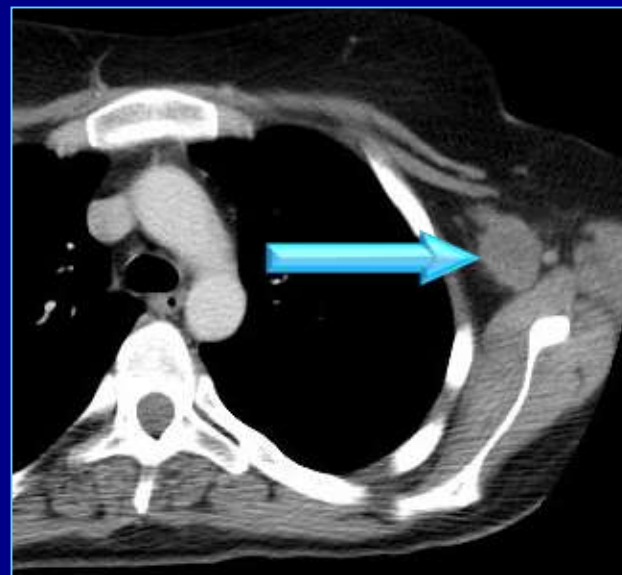
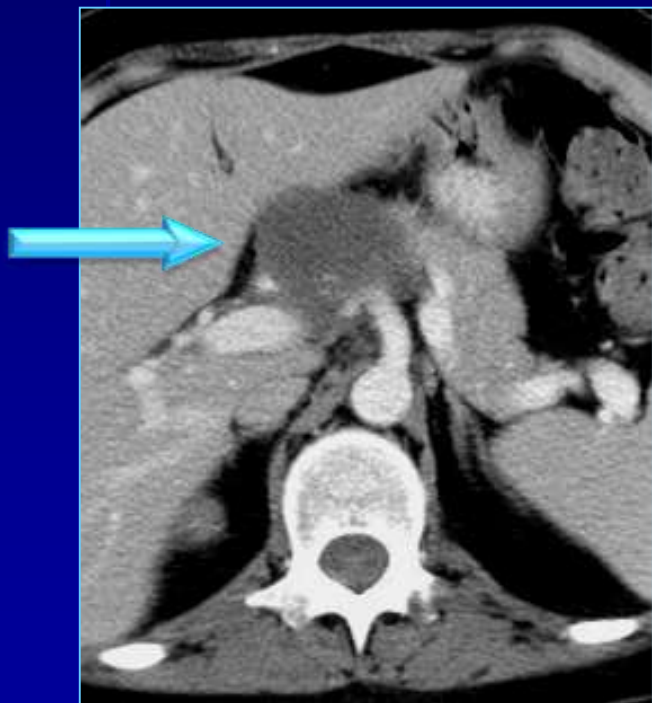




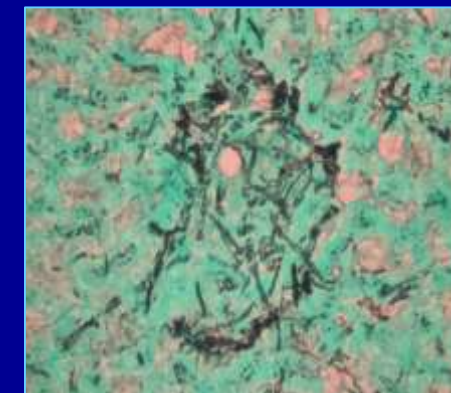
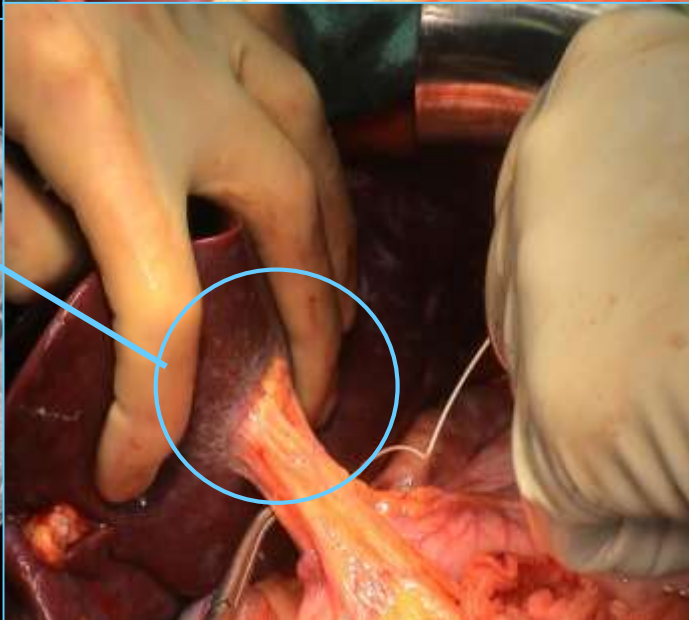
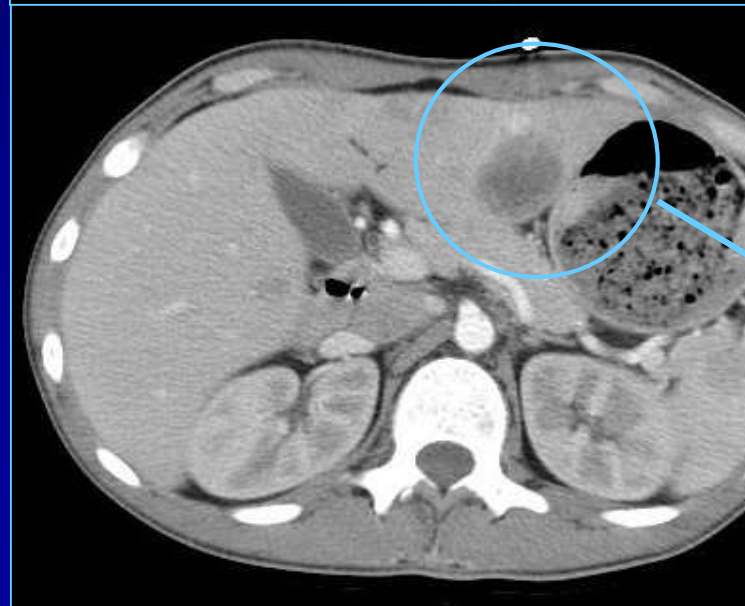
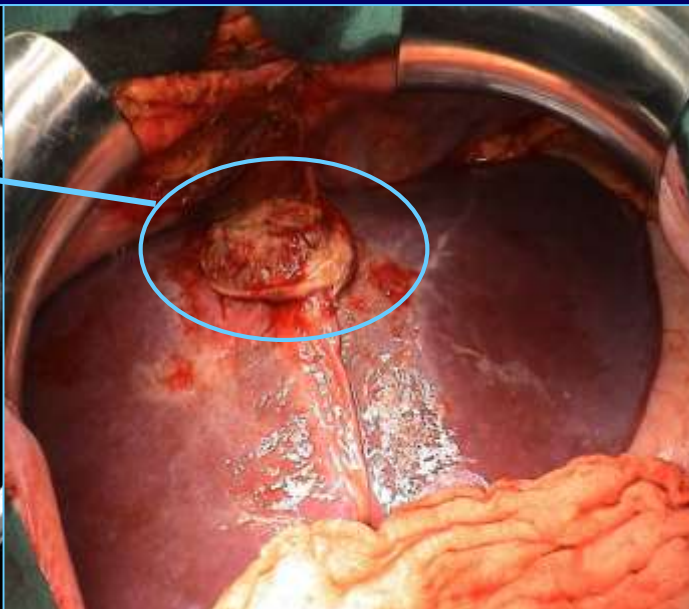
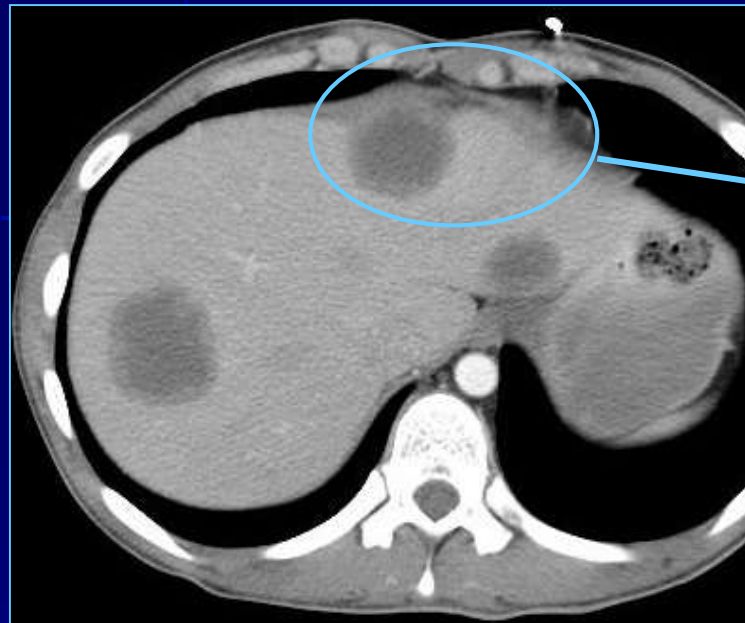
REAL LIFE STORIES



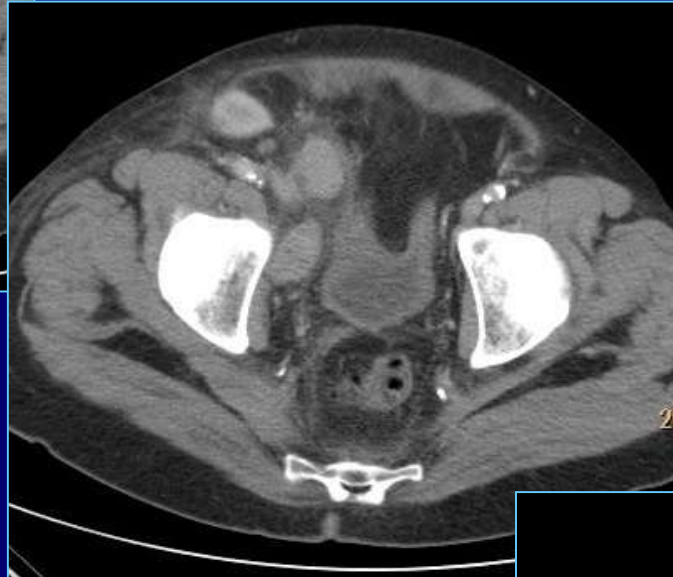
Caso 1



Caso 2



Caso 3



Transplantation Proceedings, 47, 2245–2247 (2015)

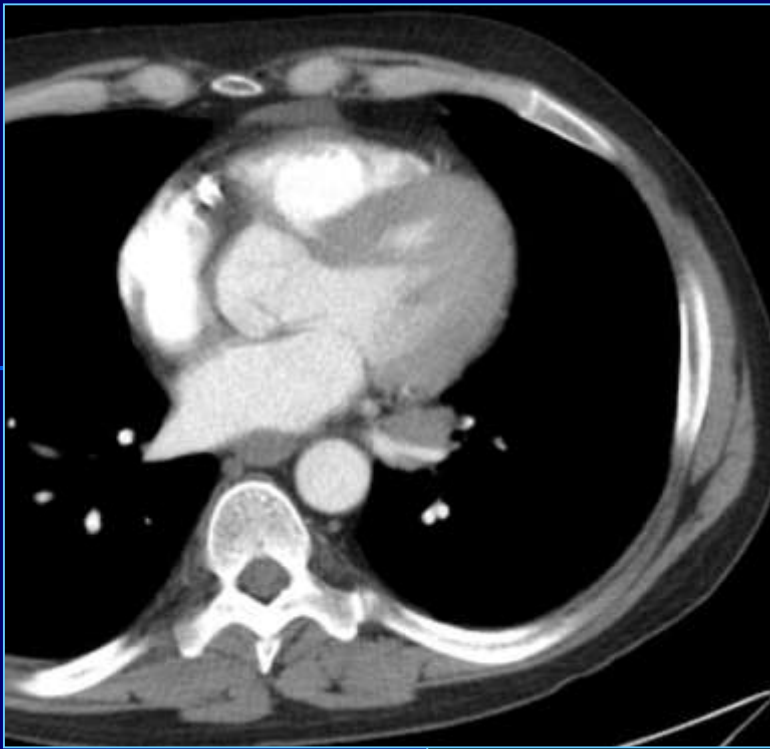


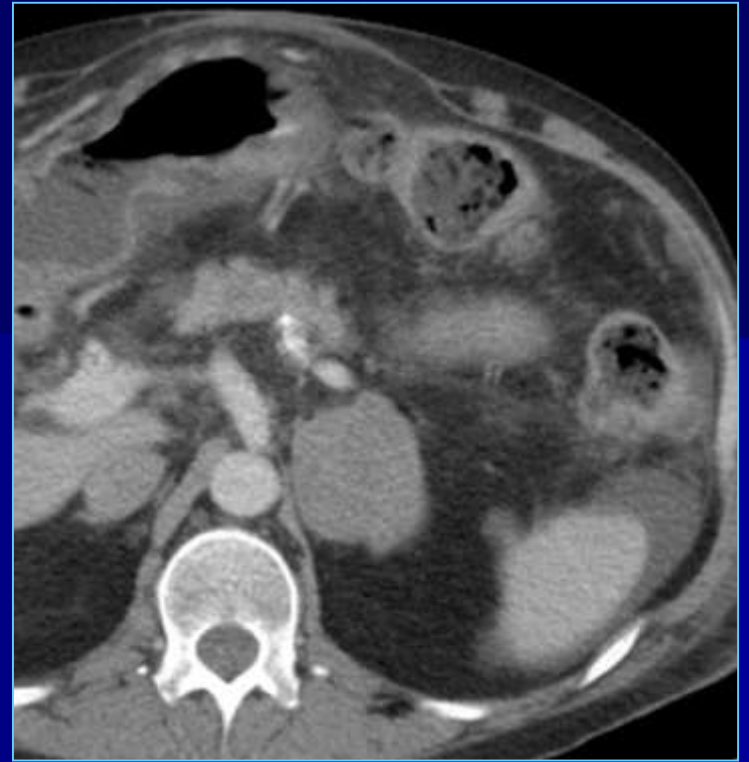
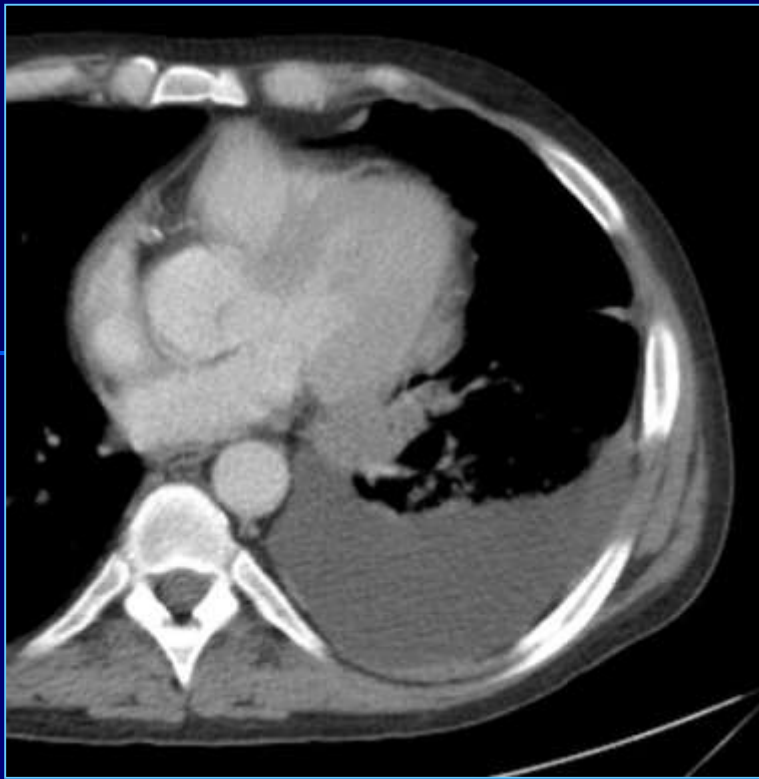
Cat-Scratch Disease: Case Report and Review of the Literature

M. Gai^{a,*}, G. d'Onofrio^b, M.C. di Vico^a, A. Ranghino^a, A. Nappo^a, D. Diena^a, D. Novero^c, G. Limerutti^d, M. Messina^a, and L. Biancone^a

^aNephrology, Dialysis, and Transplantation Unit, University of Torino–AOU Città della Salute e della Scienza di Torino, Molinette, Italy; ^bNephrology and Dialysis Unit, “Magna Graecia” University of Catanzaro, Catanzaro, Italy; ^cAnatomic Pathology 2 Unit, University of Torino–AOU Città della Salute e della Scienza di Torino, Molinette, Italy; and ^dRadiology Unit, AOUI Città della Salute e della Scienza di Torino, Molinette, Italy

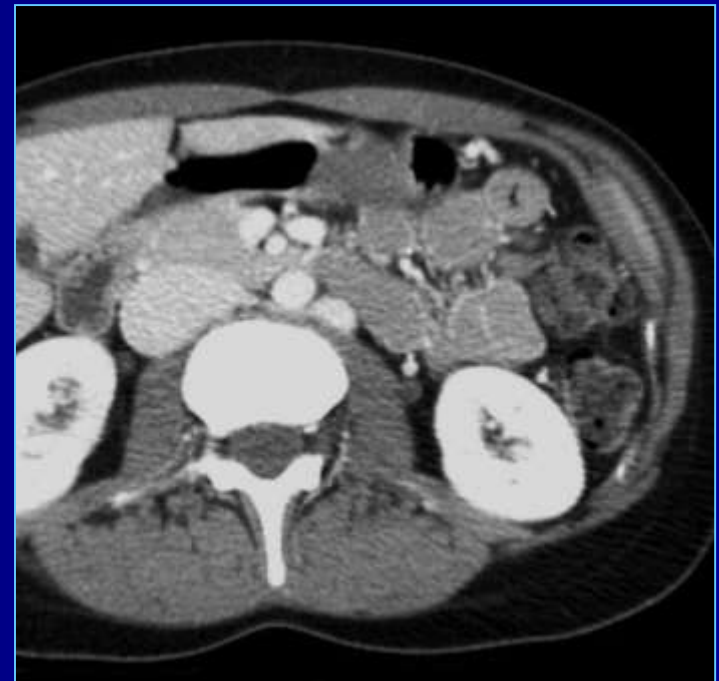
Caso 4

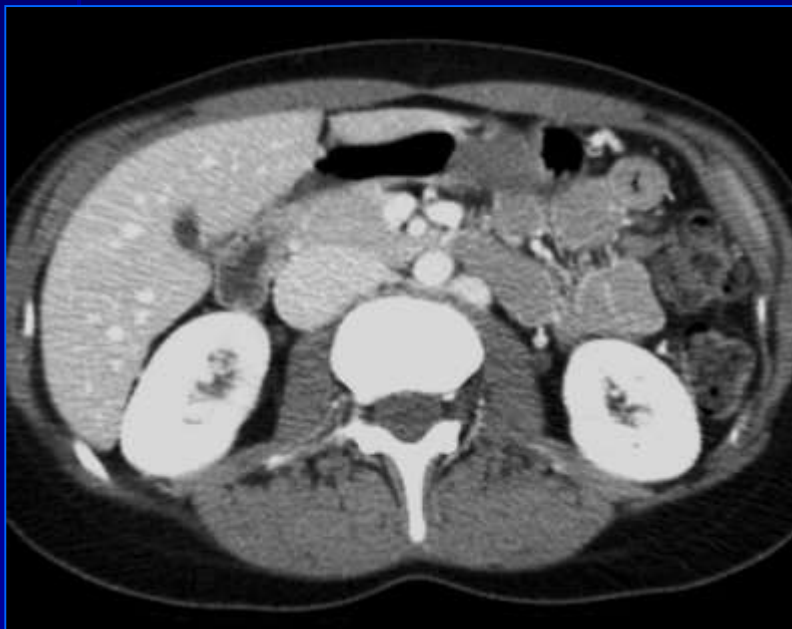
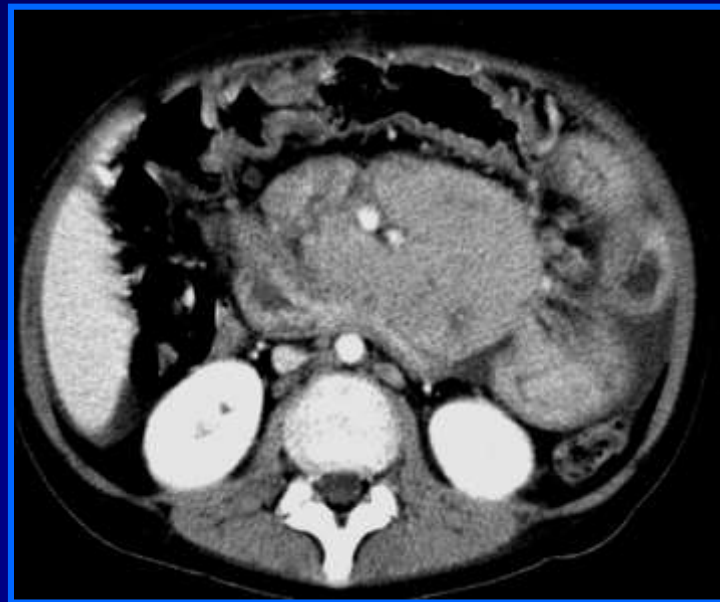


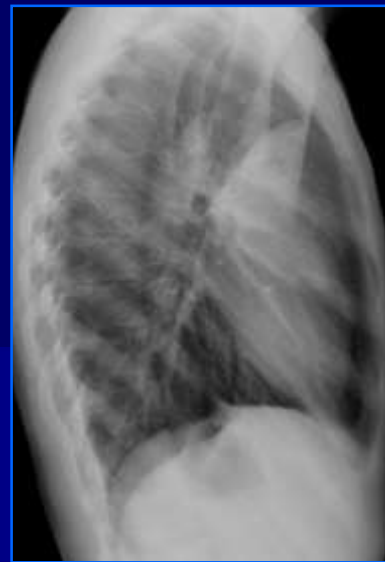




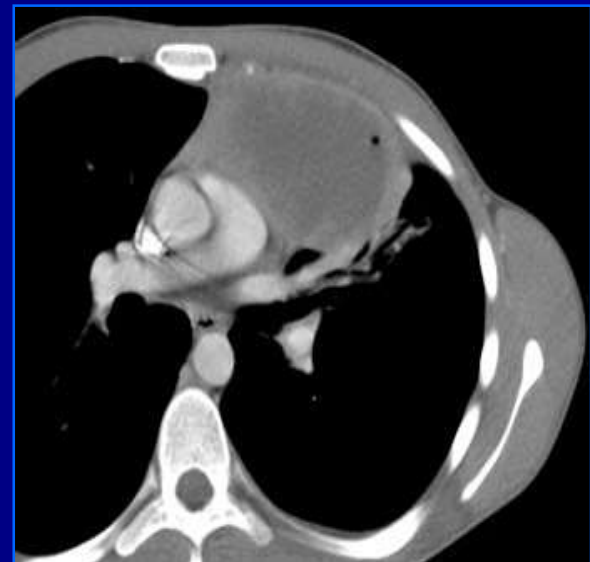
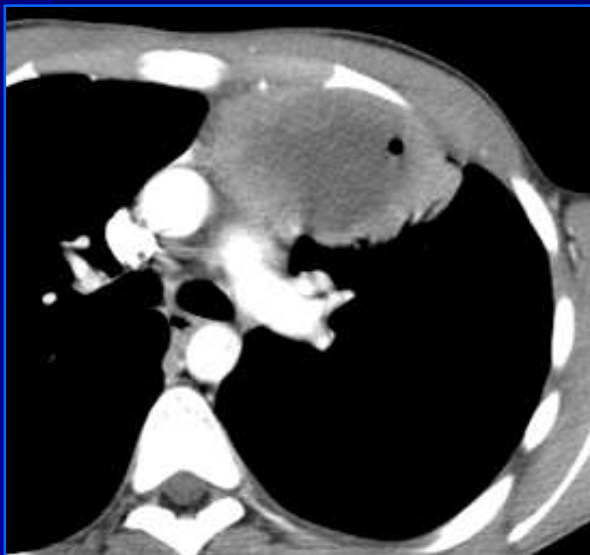
**Caso
5**

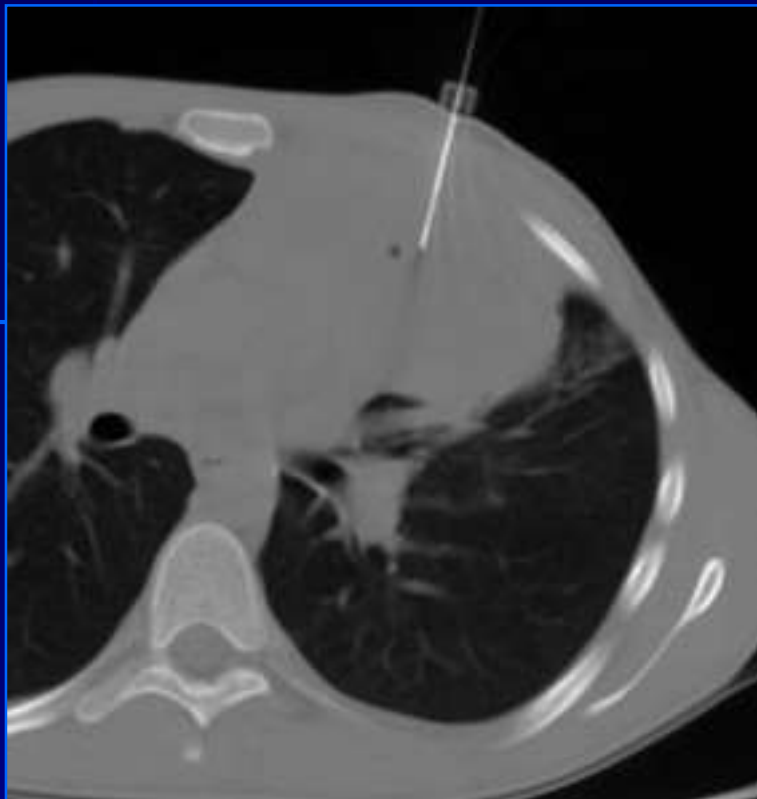


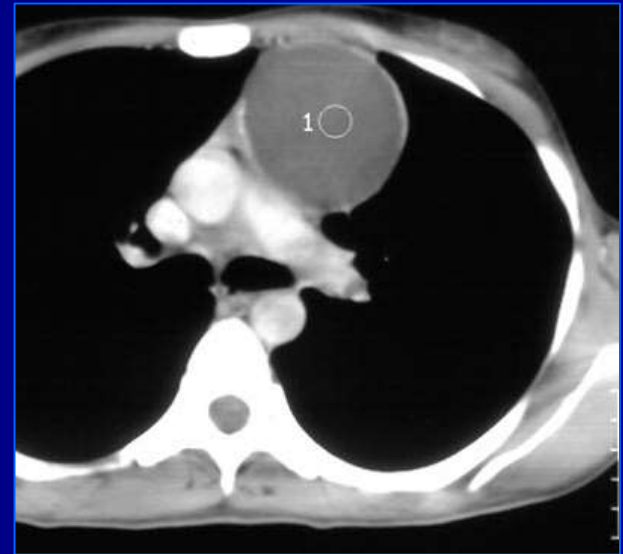
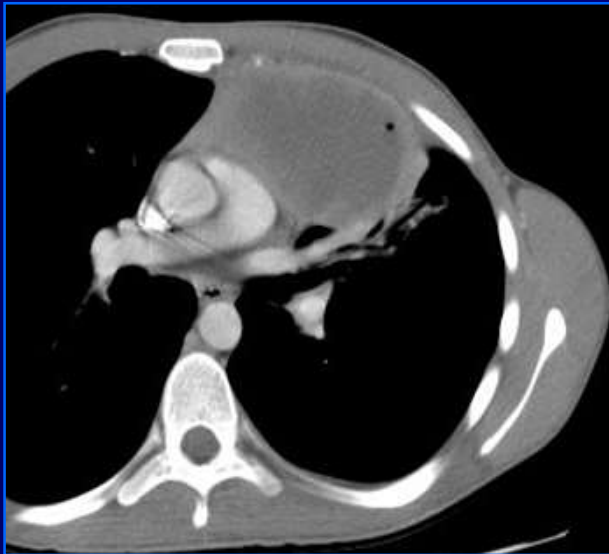
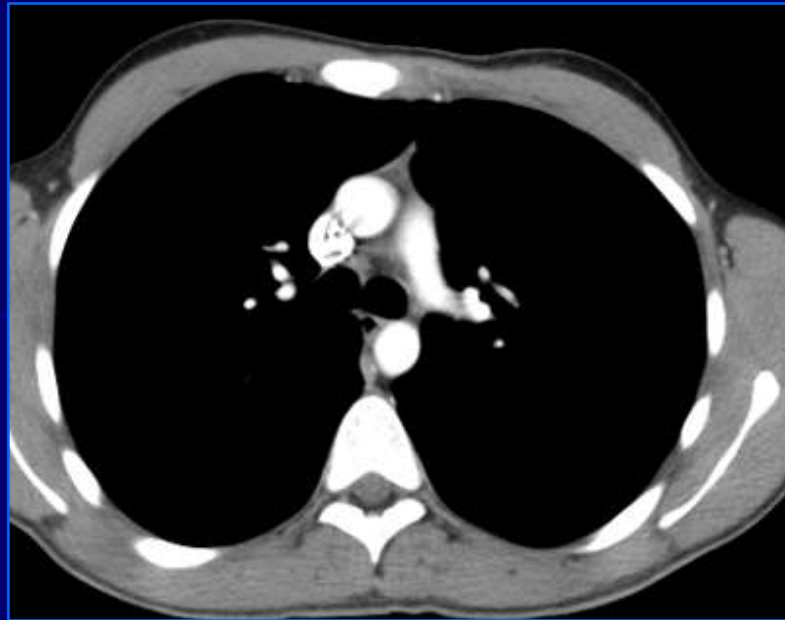




Caso 6







TAKE HOME POINT

Ruolo tomografia computerizzata

**Riconoscimento, bilancio estensione, risposta terapia
con pro e contro**

Elevata esposizione a radiazioni ionizzanti

Sempre maggiore ruolo PET

(esecuzione contemporanea delle indagini?)

GRAZIE PER L'ATTENZIONE

