

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Ferrara



università di ferrara
DA SEICENTO ANNI GUARDIAMO AVANTI.

Approccio diagnostico-terapeutico al carcinoma differenziato della tiroide

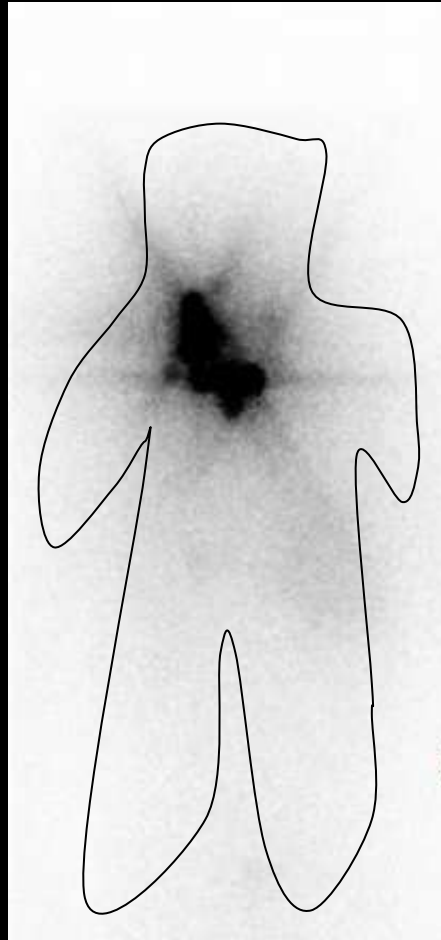
RUOLO DELLA MEDICINA NUCLEARE

Stefano Panareo

UOC Medicina Nucleare - Ferrara

(Direttore. L. Feggi)

STADIAZIONE



^{131}I Iodio whole body scan

Stadiazione post-operatoria

- definisce la prognosi del singolo paziente sottoposto ad intervento chirurgico;
- valuta l'opportunità di ulteriori trattamenti post-operatori, quali la terapia con radioiodio e la soppressione dei livelli di TSH;
- decide la frequenza e le modalità del *follow-up* ;
- fornisce un'accurata sintesi dell'estensione ed aggressività della malattia agli operatori impegnati nella gestione terapeutica del paziente;
- crea dei registri territoriali dei tumori utili alla conduzione di studi epidemiologici e protocolli di intervento.

Cooper DS, Doherty GM, Haugen BR et al. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. The American Thyroid Association Guidelines Task Force.

Thyroid 2006;16(2):1-33

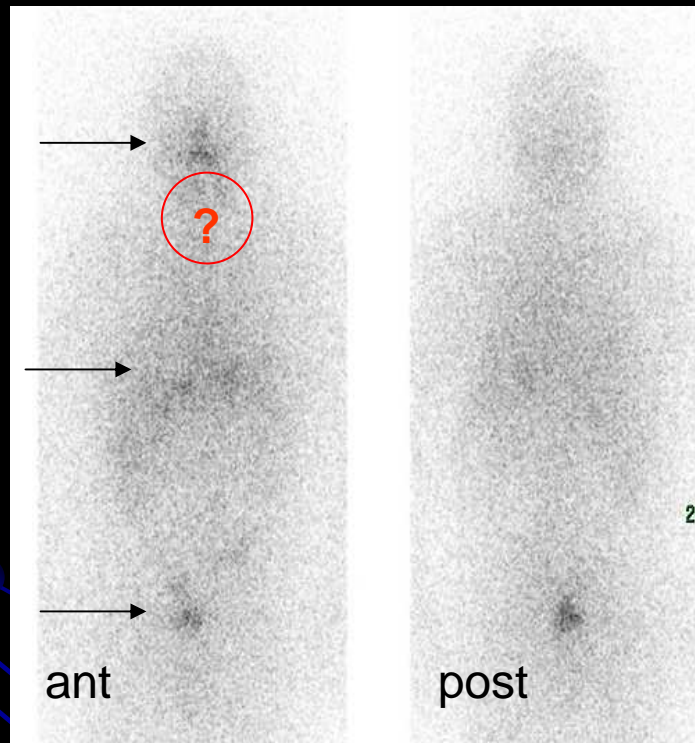
Scintigrafia con ^{131}I Iodio

Fisiologica distribuzione

Cavità
orale

App.
gastro
intestinale

vescica



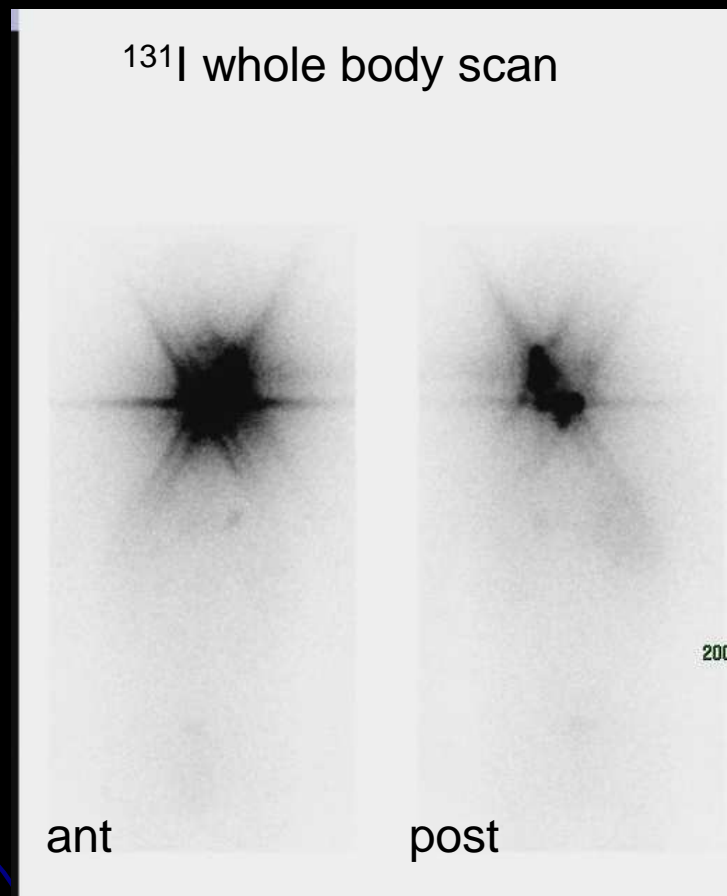
^{131}I whole body scan

NO ALLA RADIOIODIO TERAPIA

carcinoma papillare della tiroide di diametro ≤ 10 mm senza:

1. evidenza di metastasi,
2. invasione capsulare,
3. multifocalità,
4. sottotipi istologici non favorevoli (tall-cell, cellule colonnari, sclerosante diffusa),
5. storia di pregressa esposizione ad alte dosi di radiazioni ionizzanti
6. Apparente assenza di residuo

Scintigrafia con ^{131}I Iodio

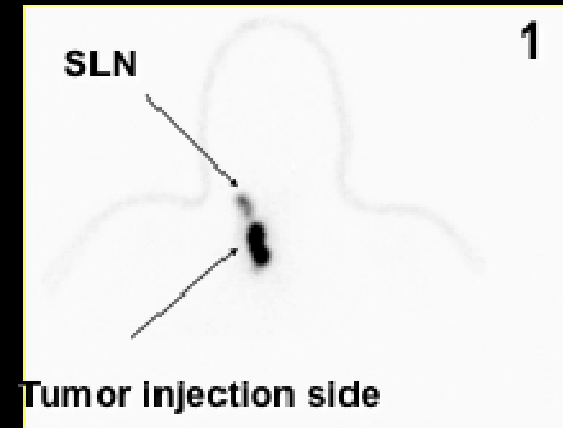


Residuo tiroideo post tiroidectomia – fissa il **12%** della attività (~ 200 MBq) di radioiodio somministrata a scopo diagnostico

Strumenti a disposizione per una accurata stadiazione del CDT

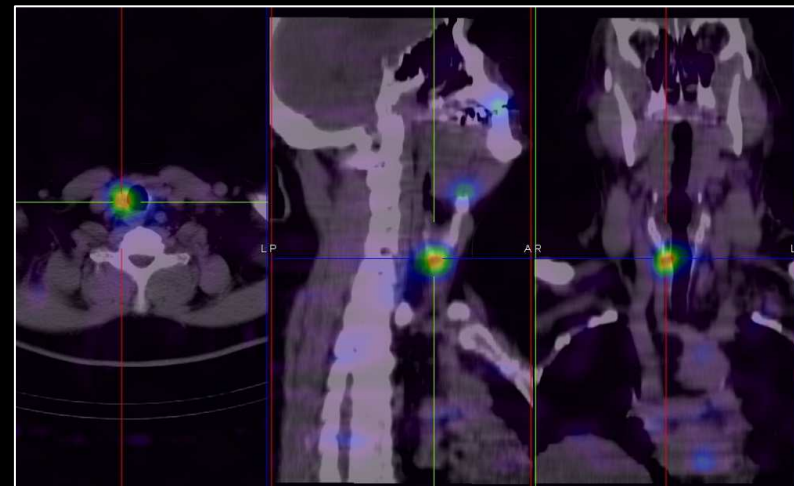
Linfonodo Sentinella

^{99m}Tc nanocoll®



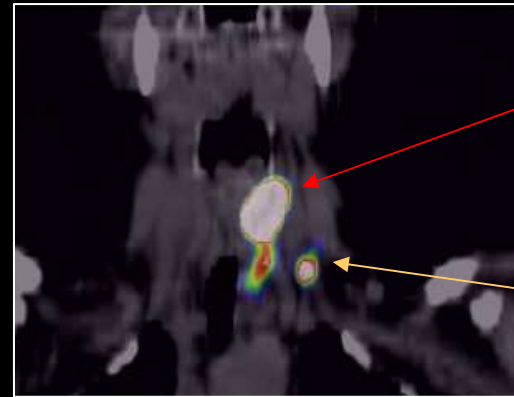
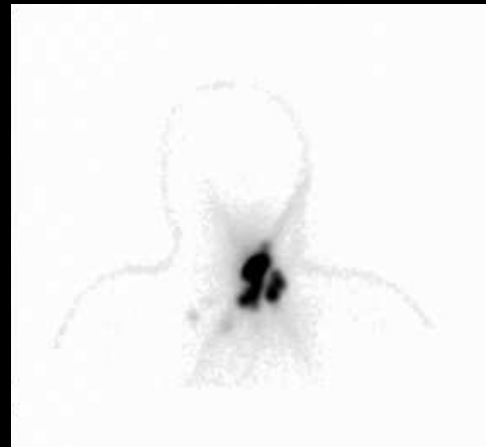
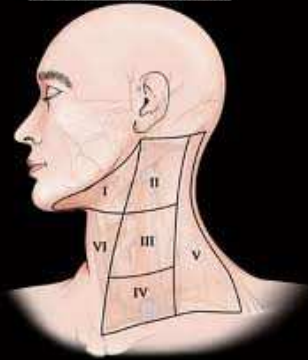
SPECT/CT

¹³¹I-ioduro



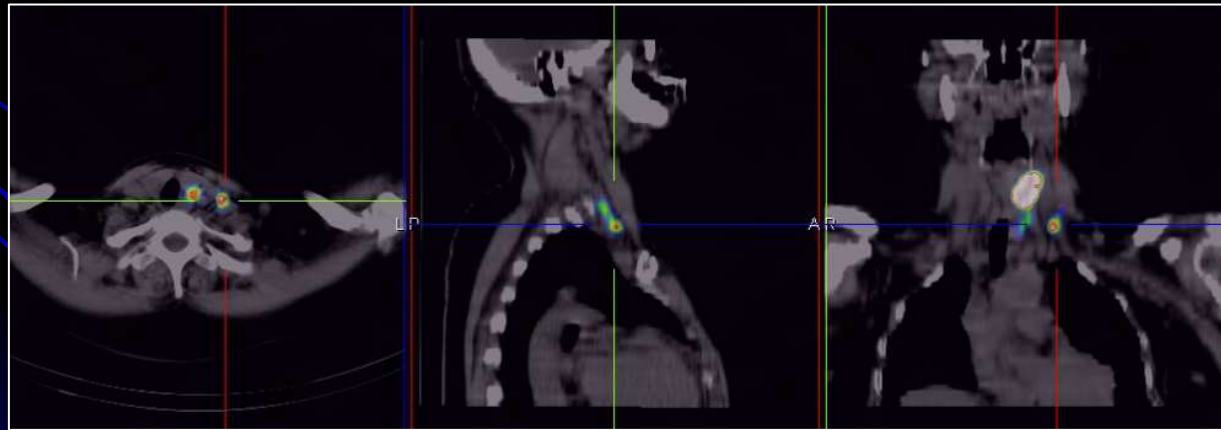
Linfonodo Sentinella: ha senso localizzarlo?

Aree linfonodali del collo



*Sede di
iniezione
intratumorale*

**Linfonodo
sentinella**



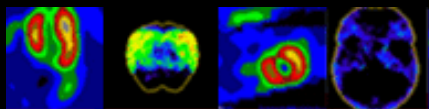
Scintigrafia planare e SPECT/CT con ^{99m}Tc nanocoll® per localizzazione del LNS

Perché rilevare il linfonodo sentinella nel cancro differenziato della tiroide?

- Mappatura precisa del drenaggio linfatico dal tumore favorendo una linfadenectomia selettiva (non necessariamente del compartimento centrale).
- Accurata identificazione dei linfonodi metastatici (anche al di fuori del compartimento centrale).
- Selezione dei pazienti da destinare a dissezione linfonodale completa.
- Corretta identificazione dei pazienti da trattare con radioiodioterapia.

Perché rilevare il linfonodo sentinella nel cancro differenziato della tiroide?

Anche se attualmente non c'è una evidenza diretta che la biopsia del linfonodo sentinella condizioni la prognosi del paziente con cancro differenziato della tiroide, nella nostra esperienza abbiamo osservato che ***a 2 anni dal trattamento chirurgico non è stata osservata ripresa di malattia.***



SNM
2009 Annual Meeting

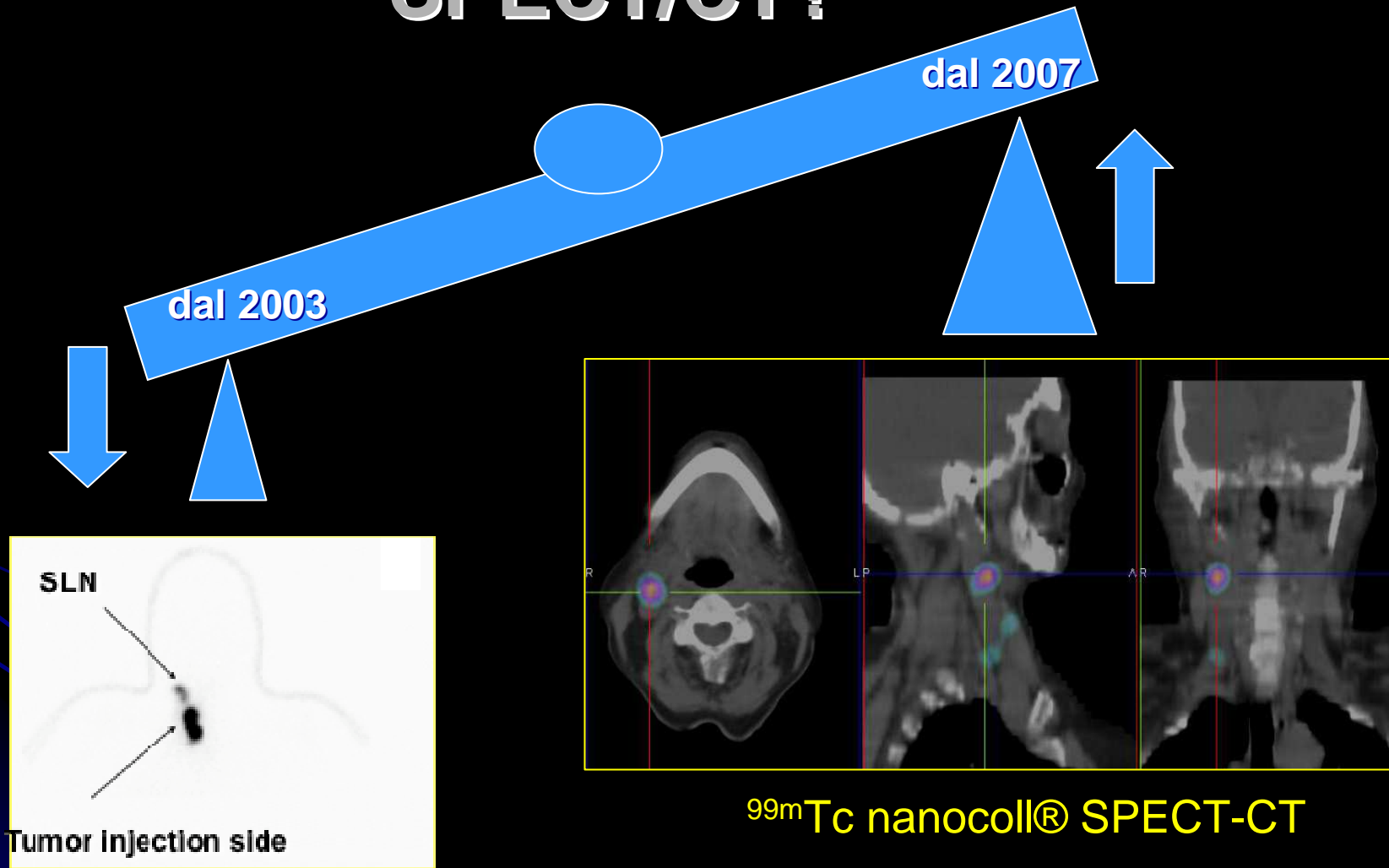
June 13-17, 2009
Toronto, Canada

MIDDLE TERM FOLLOW-UP RESULTS OF SENTINEL LYMPH NODE (SLN) DETECTION IN PAPILLARY THYROID CANCER (PTC)

L. Feggi (1); **S. Panareo** (1); P. Carcoforo (2); N Prandini (1); M. Giganti (1);
C. Cittanti (1); R. Rossi (3); G. Trasforini (3); A. Blotta (4); S. Lanzara (2);
G.C. Pansini (2); E. Degli Uberti (3); A. Liboni (2)

Nostra casistica ad ottobre 2011: 439 pazienti

LNS: acquisizione planare o SPECT/CT?



Planar scintigraphy
 ^{99m}Tc nanocoll®

Nostra esperienza

439 pazienti (dal 2003 al 2011) - 362 femmine, 77 maschi (età media 54 ± 2)

Sede del tumore: 213 (48.5%) lobo destro, 169 (**38.5%**) lobo sinistro, 59 (**13.4%**) istmo-paraistmo

Linfonodo sentinella scintigraficamente identificato nel **99,4%** dei casi.

Sede del LNS: omolaterale alla lesione (**72%**), controlaterale alla lesione (**3,8%**), compartimento centrale (**35%**),

LNS scintigraficamente non visualizzato nel **0.6%** dei casi.

Possibili cause di non visualizzazione del LNS:

- 1. linfonodo metastatico***
- 2. linfonodo mascherato dalla attività tiroidea***
- 3. dimensioni del linfonodo***

Il LNS è stato chirurgicamente identificato nel **99%** dei casi.

Expert Reviews



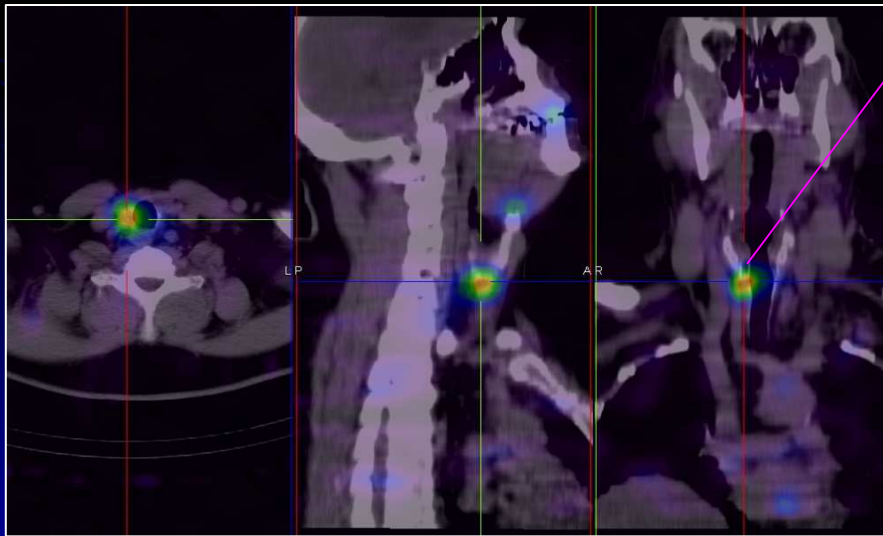
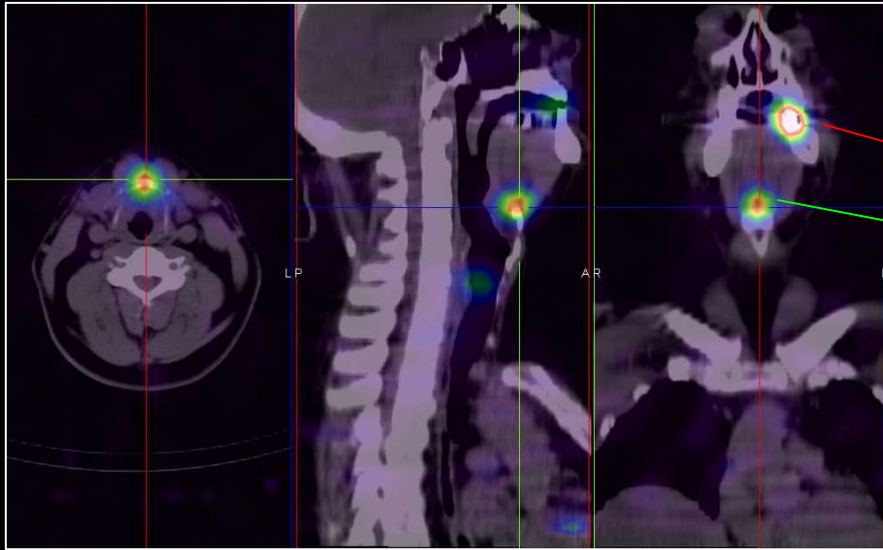
Role of sentinel lymph node biopsy in thyroid cancer

Jong-Lyel Roh and Wayne M Koch,

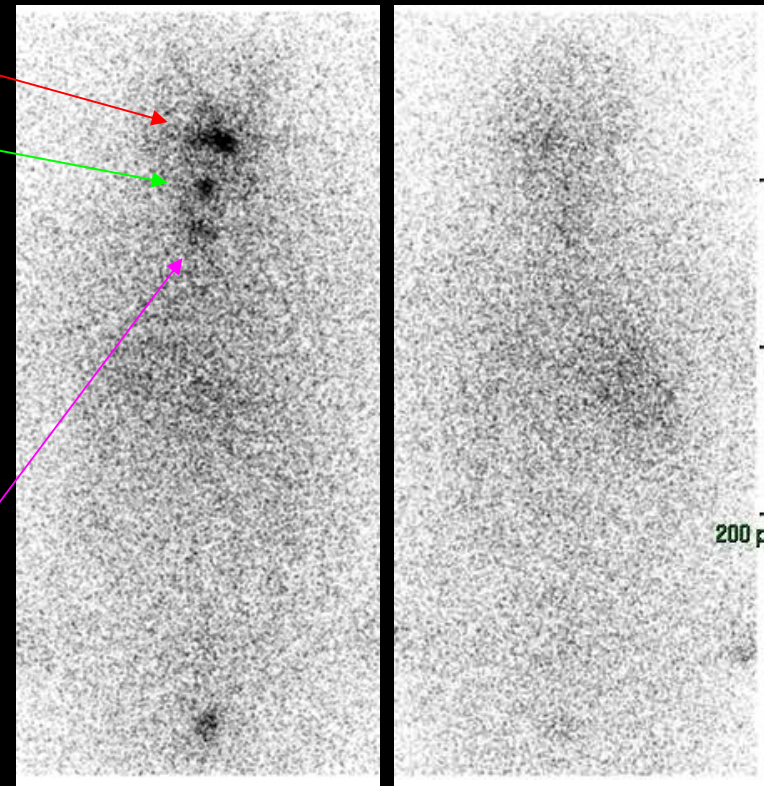
Expert Review of Anticancer Therapy, September 2010, Vol. 10, No. 9, Pages 1429-1437

... The SLNB procedure is safe and feasible, with high accuracy in predicting occult metastases of differentiated thyroid cancer. The sensitivity of the SLNB technique has increased as technical details and complementary immunohistochemical and molecular techniques have been developed. SLNB for thyroid cancer may display practical benefits in accurate nodal staging, the detection of metastatic lymph nodes outside the central neck, and the selection of patients who would benefit from complete neck dissection and optimized ¹³¹I ablation therapy. Currently, however, there is no direct evidence that SLNB is associated with long-term clinical and survival benefits in patients with thyroid cancer. Well-controlled prospective clinical trials will determine the clinical significance of occult metastases and their early detection by SLNB in patients with thyroid cancer.

Valore aggiunto della SPECT/CT nella stadiazione post-chirurgica del CDT



¹³¹Iodio SPECT /CT



¹³¹Iodio whole body scan

Radioiodine Scintigraphy with SPECT/CT: An Important Diagnostic Tool for Thyroid Cancer Staging and Risk Stratification

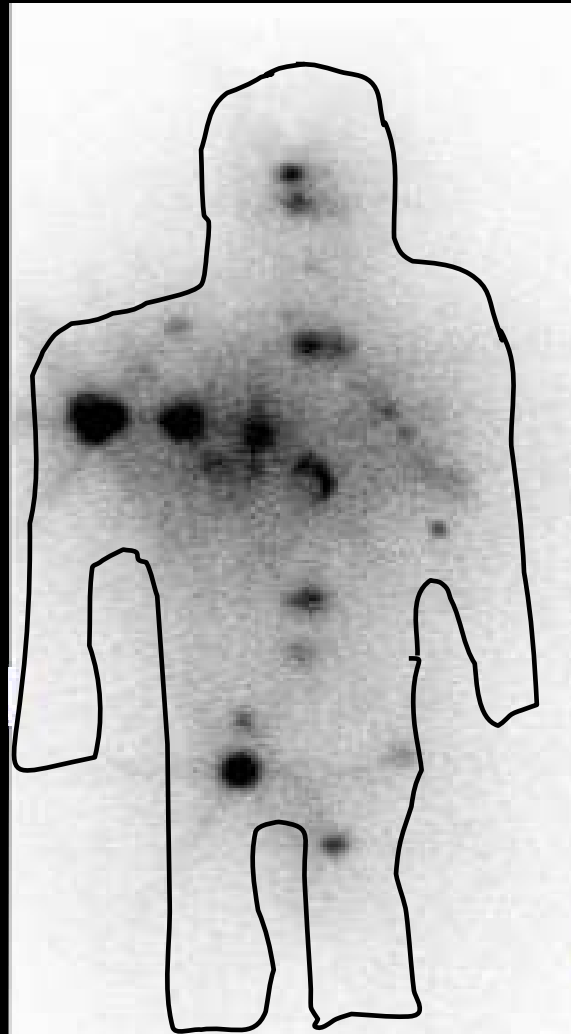
Anca M. Avram, J Nucl Med May 1, 2012 vol. 53 no. 5 754-764

Conclusions: ... used on selected patients with inconclusive planar images ... Proposed changes in management include: deciding whether to give or withhold radioiodine treatment, indicating and guiding the extent of surgery, selecting patients for external-beam radiation therapy, and indicating the need for alternative imaging strategies such as ^{18}F -FDG PET ... change in management has been reported in 11% (65), 23% (45), 24% (42), 25% (38), 36% (66), 41% (39), 47% (41), and 58% (68) of patients in various studies.

SPECT/CT is a powerful diagnostic tool that allows accurate anatomic localization and characterization of radioiodine foci and has substantially improved the interpretation of classic radioiodine scintigraphy. SPECT/CT contributes to completion of staging for patients with thyroid cancer by improved characterization of N and M scores ...



FOLLOW UP



¹³¹Iodio whole body scan

PERSISTENZA O RECIDIVA DI MALATTIA NEL CDT

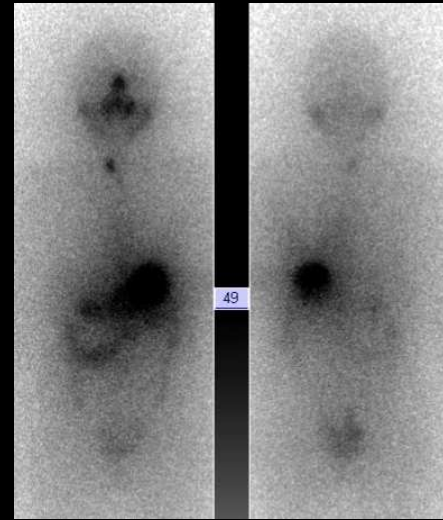
Prevalenza di recidive è del 35% (nei primi 3 anni dalla diagnosi).

Le recidive locali rappresentano circa il 70% (letto tiroideo, linfonodi locoregionale, tessuti molli del collo, vie aeree e digestive superiori - extralinfonodale) con mortalità a 30 anni del 12%.

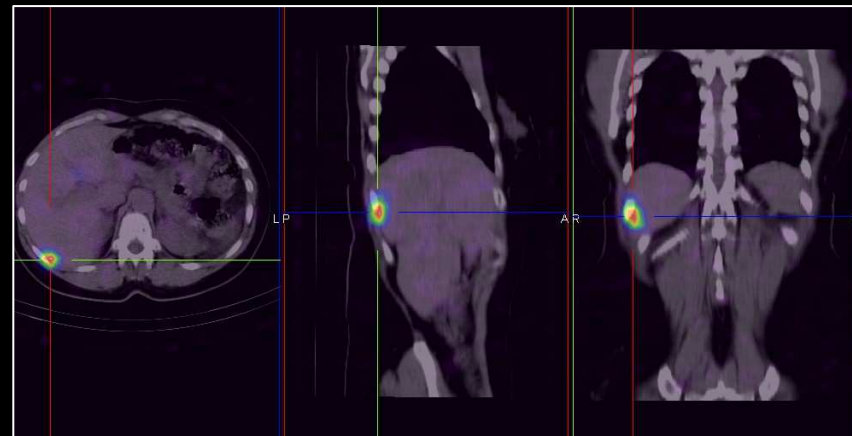
Le recidive a distanza rappresentano il 30% (osso, polmone) con mortalità a 30 anni pari al 43%.

La diagnosi precoce delle recidive aumenta la sopravvivenza del paziente se si tratta di mts operabili e/o iodocaptanti.

^{131}I whole body



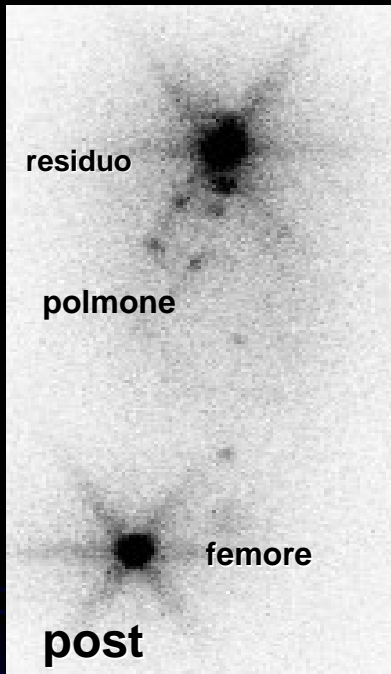
^{131}I SPECT/CT



^{18}F -FDG PET/CT



Valore aggiunto della SPECT/CT



¹³¹Iodio WB scan



¹³¹Iodio SPECT/CT positiva: osso, polmone + residuo tiroideo

Value of (131)I SPECT/CT for the evaluation of differentiated thyroid cancer: a systematic review of the literature.

14 studies involving 1.066 patients

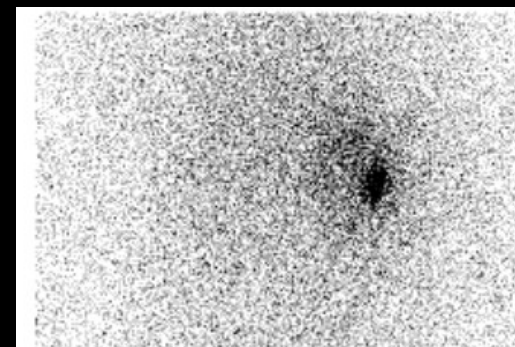
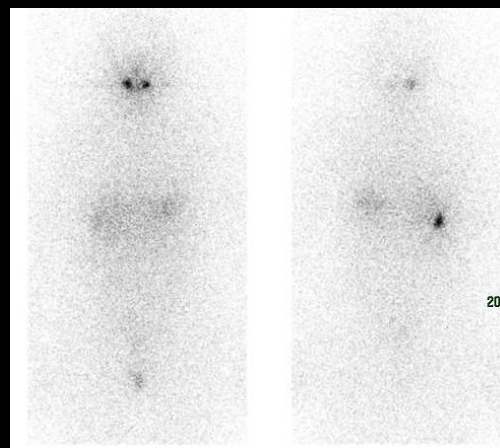
CONCLUSION:

Integrated SPECT/CT is a useful tool for the diagnosis, staging, risk stratification, and follow-up of DTC. The impact of (131)I SPECT/CT on the management of patients with thyroid cancer was increased.

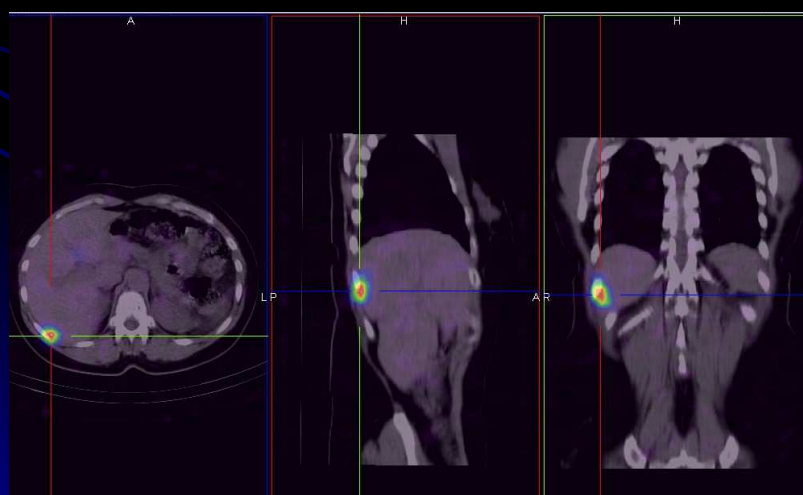
Xue YL et al. EJNMMI 2012

Scintigrafia con ^{131}I Iodio di ristadiazione: MTs ossea

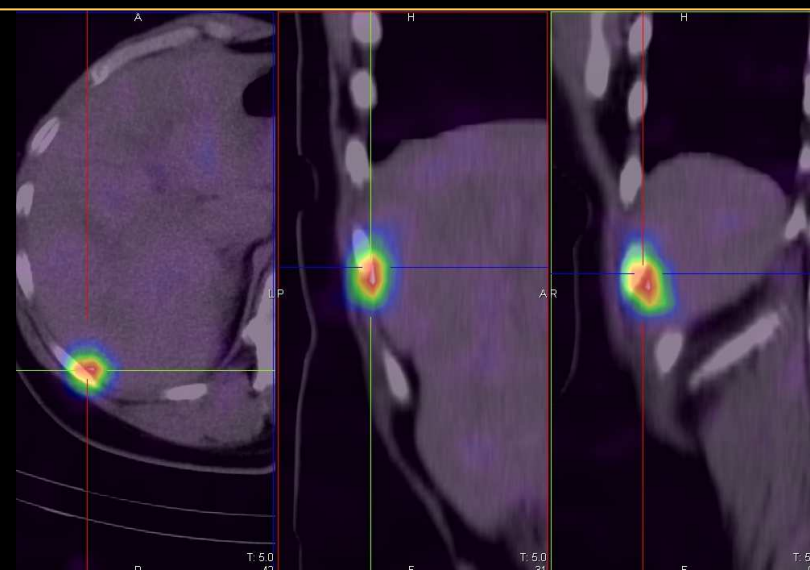
^{131}I Iodio whole body



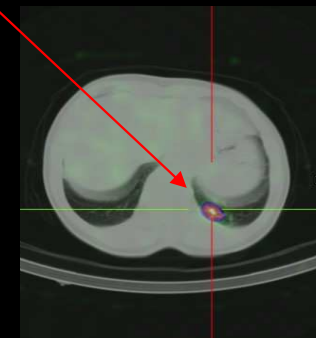
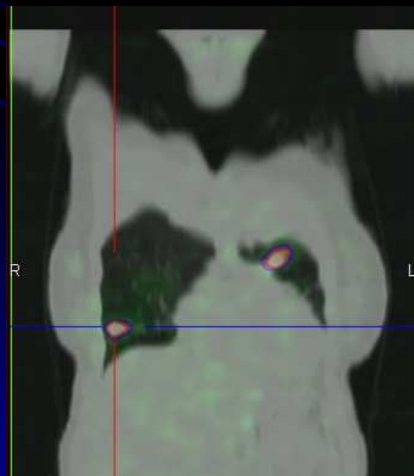
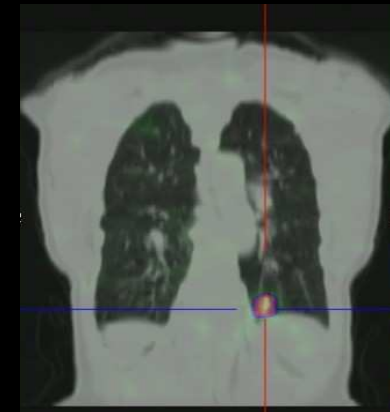
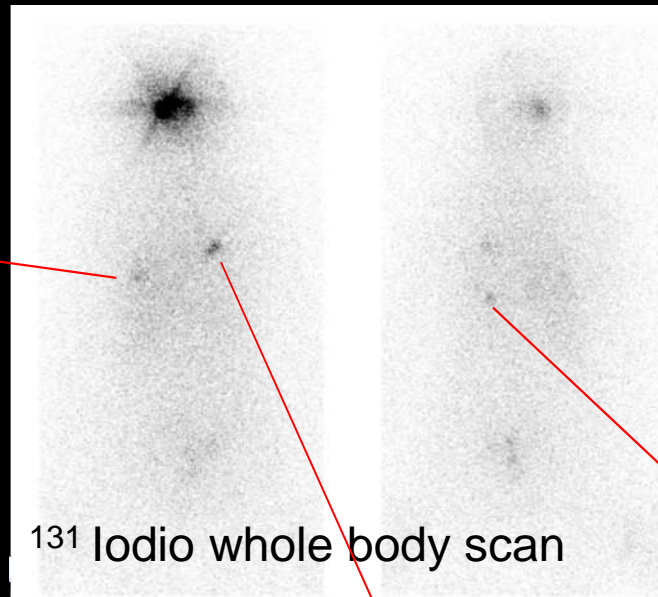
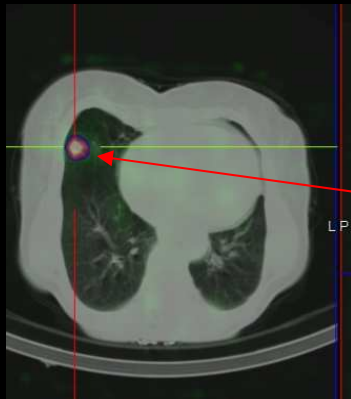
^{131}I Iodio particolare torace



^{131}I Iodio SPECT/CT

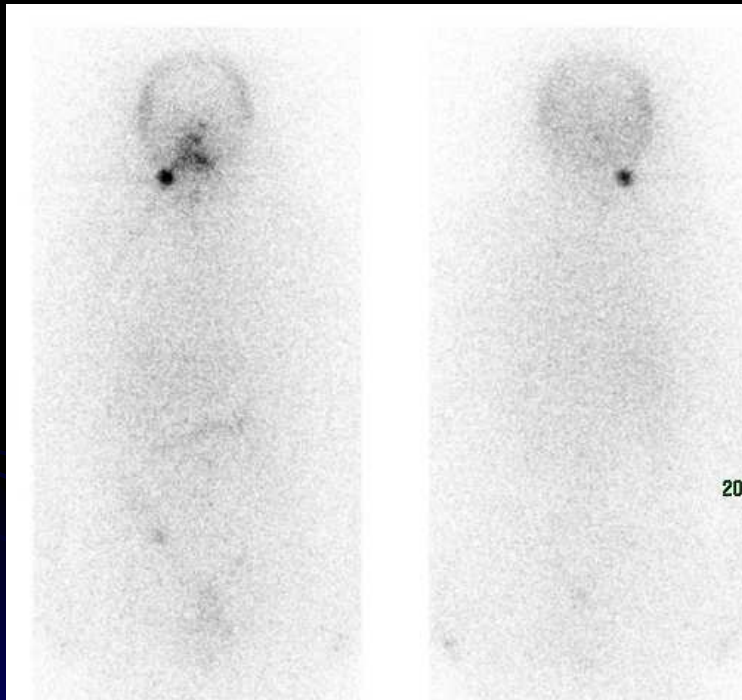


Scintigrafia con ^{131}I Iodio di ristadiiazione: MTs polmone

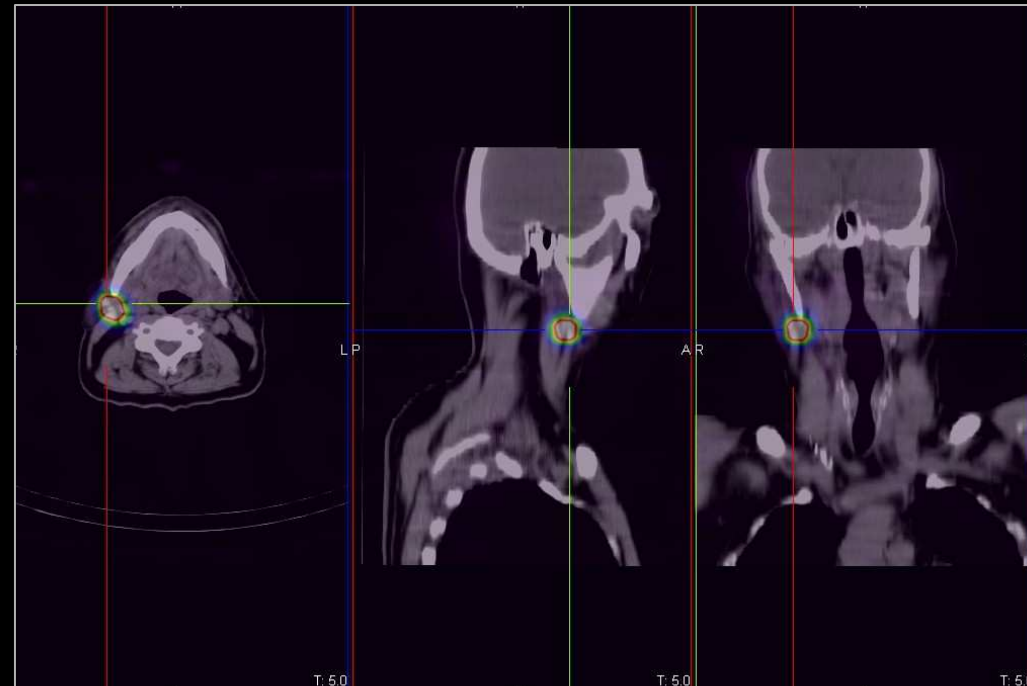


^{131}I Iodio SPECT /CT

Scintigrafia con ^{131}I di ristadiiazione: MTs linfonodali



^{131}I whole body



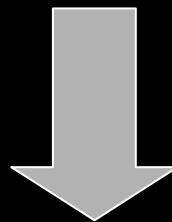
^{131}I SPECT/CT

Metastasi di un linfonodo retromandibolare a destra

Tg elevata e ¹³¹Iodio scan negativo: cosa fare?

È opportuno:

1. eseguire una *ristadiazione completa* ed accurata per mezzo di ecografia del collo, TC (senza mezzo di contrasto) o RMN del torace e - se indicato - dell'addome e del cranio, e RX dello scheletro.
2. in caso di completa negatività o di dubbia interpretazione di tali indagini, è suggerito lo studio scintigrafico con **¹⁸F-FDG PET**, *on-* o *off-L-T4*, o con *traccianti di cellularità* (*^{99m}Tc-MIBI*).



***assente captazione di ¹³¹Iodio e FDG PET
positiva ha significato prognostico sfavorevole***

PET/CT

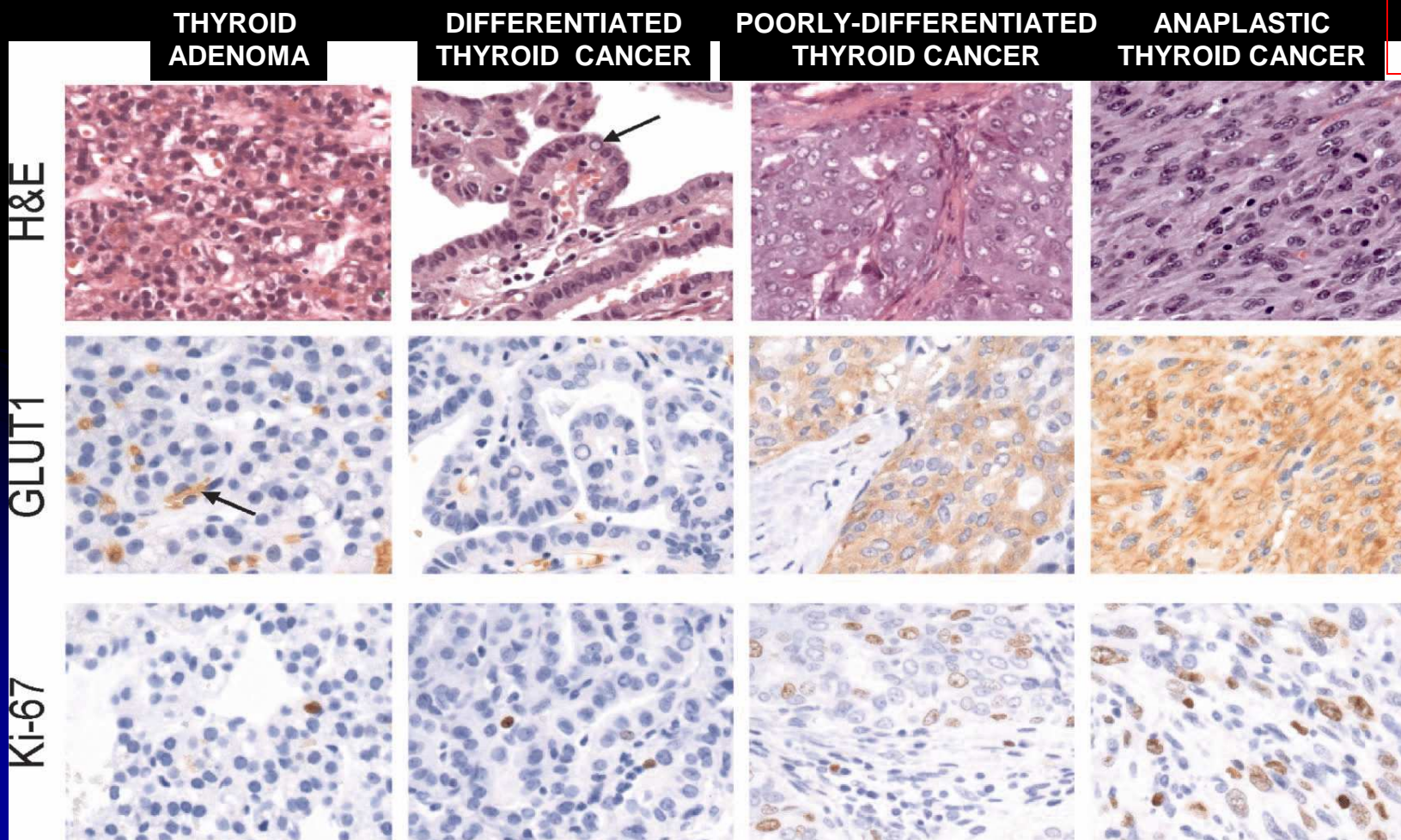
- **^{18}F -FDG PET e PET/CT nel tumore differenziato della tiroideo**
- ^{18}F -FDG PET and PET/CT nel tumore scarsamente differenziato e anaplastico
- Incidentaloma tiroideo rilevato da ^{18}F -FDG PET
- **^{124}I -Iodine PET nel cancro della tiroide**

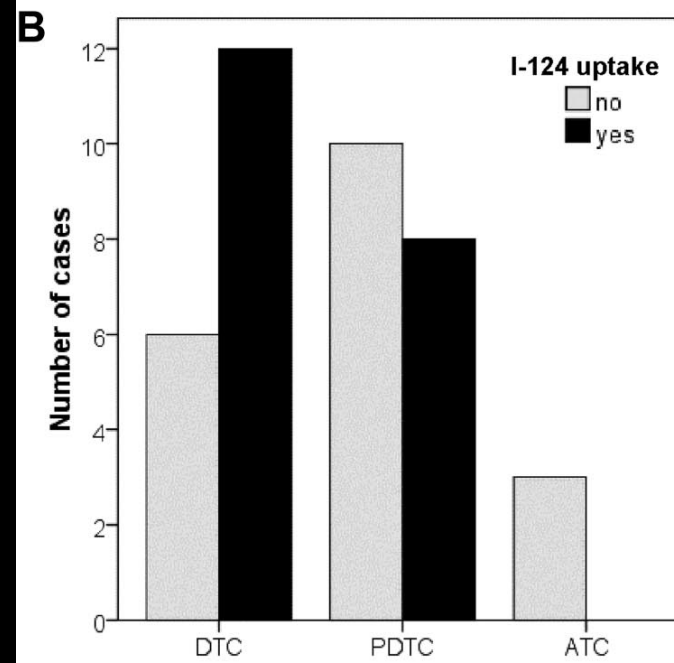
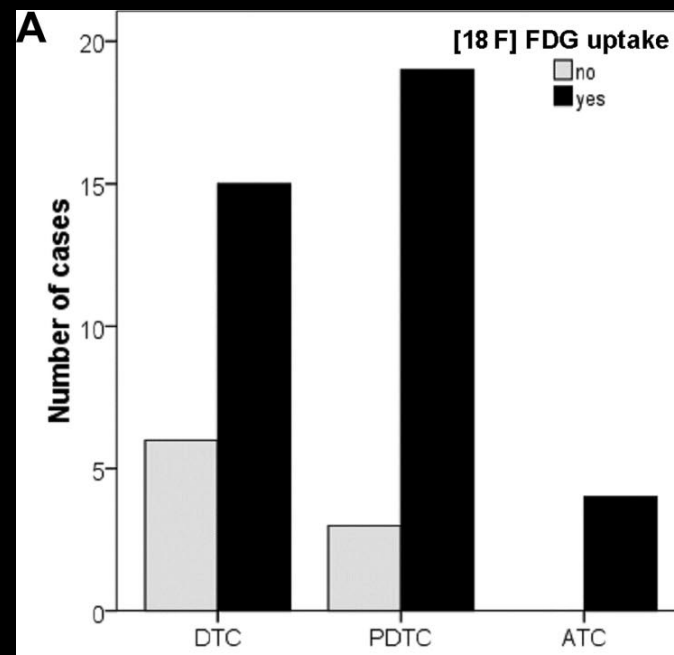
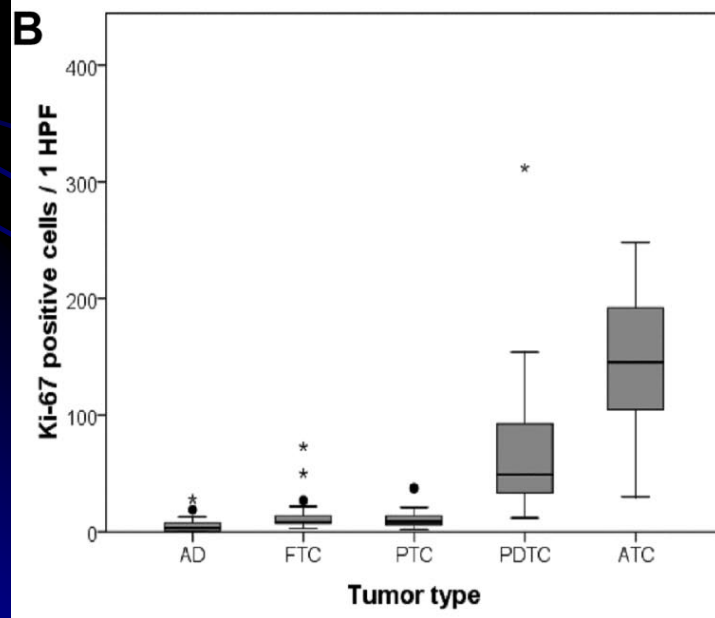
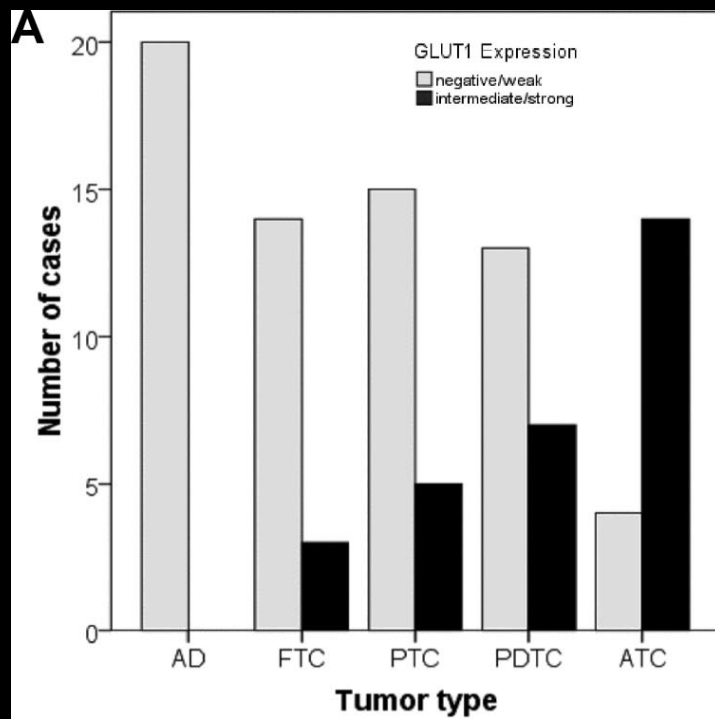
Glucose Transporter 1 Expression, Tumor Proliferation, and Iodine/Glucose Uptake in Thyroid Cancer With Emphasis on Poorly Differentiated Thyroid Carcinoma

Florian Grabellus, MD,* James Nagarajah, MD,† Andreas Bockisch, MD,† Kurt Werner Schmid, MD,* and Sien-Yi Sheu, MD*

(Clin Nucl Med 2012;37: 121–127)

2012





^{18}F -FDG PET and PET/CT in differentiated thyroid carcinoma (DTC)



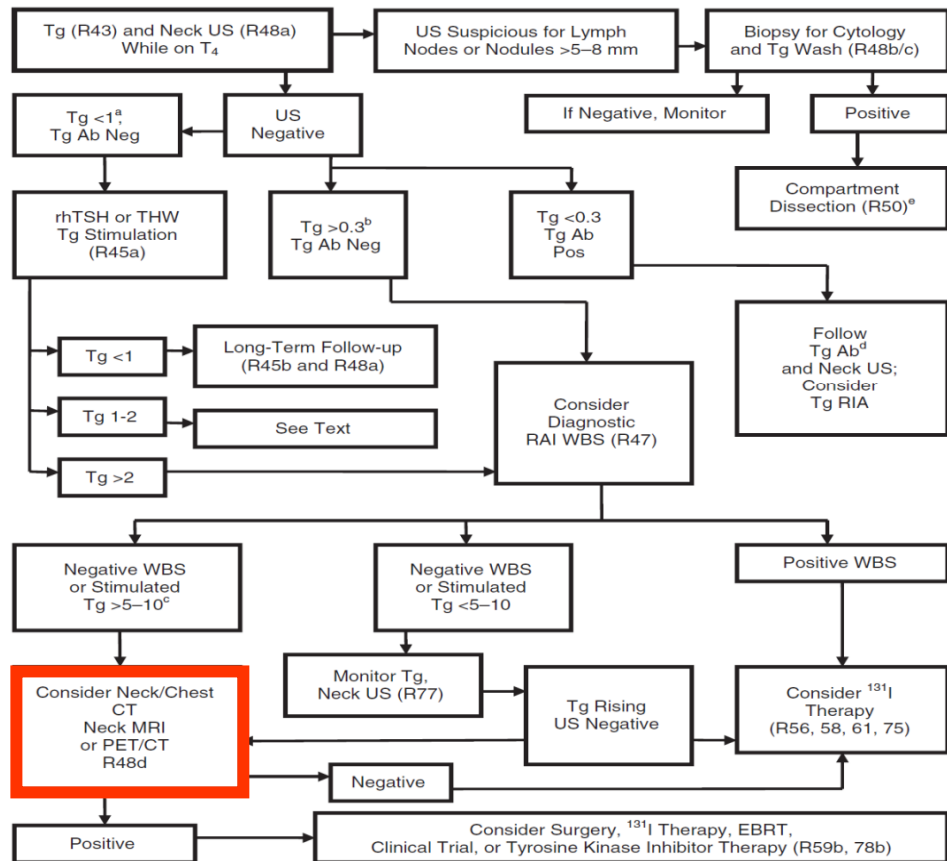
ATA guidelines. Thyroid 2009

Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer

The American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer

David S. Cooper, M.D.¹ (Chair)*, Gerard M. Doherty, M.D.,² Bryan R. Haugen, M.D.,³ Richard T. Kloos, M.D.,⁴ Stephanie L. Lee, M.D., Ph.D.,⁵ Susan J. Mandel, M.D., M.P.H.,⁶ Ernest L. Mazzaferri, M.D.,⁷ Bryan McIver, M.D., Ph.D.,⁸ Furio Pacini, M.D.,⁹ Martin Schlumberger, M.D.,¹⁰ Steven I. Sherman, M.D.,¹¹ David L. Steward, M.D.,¹² and R. Michael Tuttle, M.D.¹³

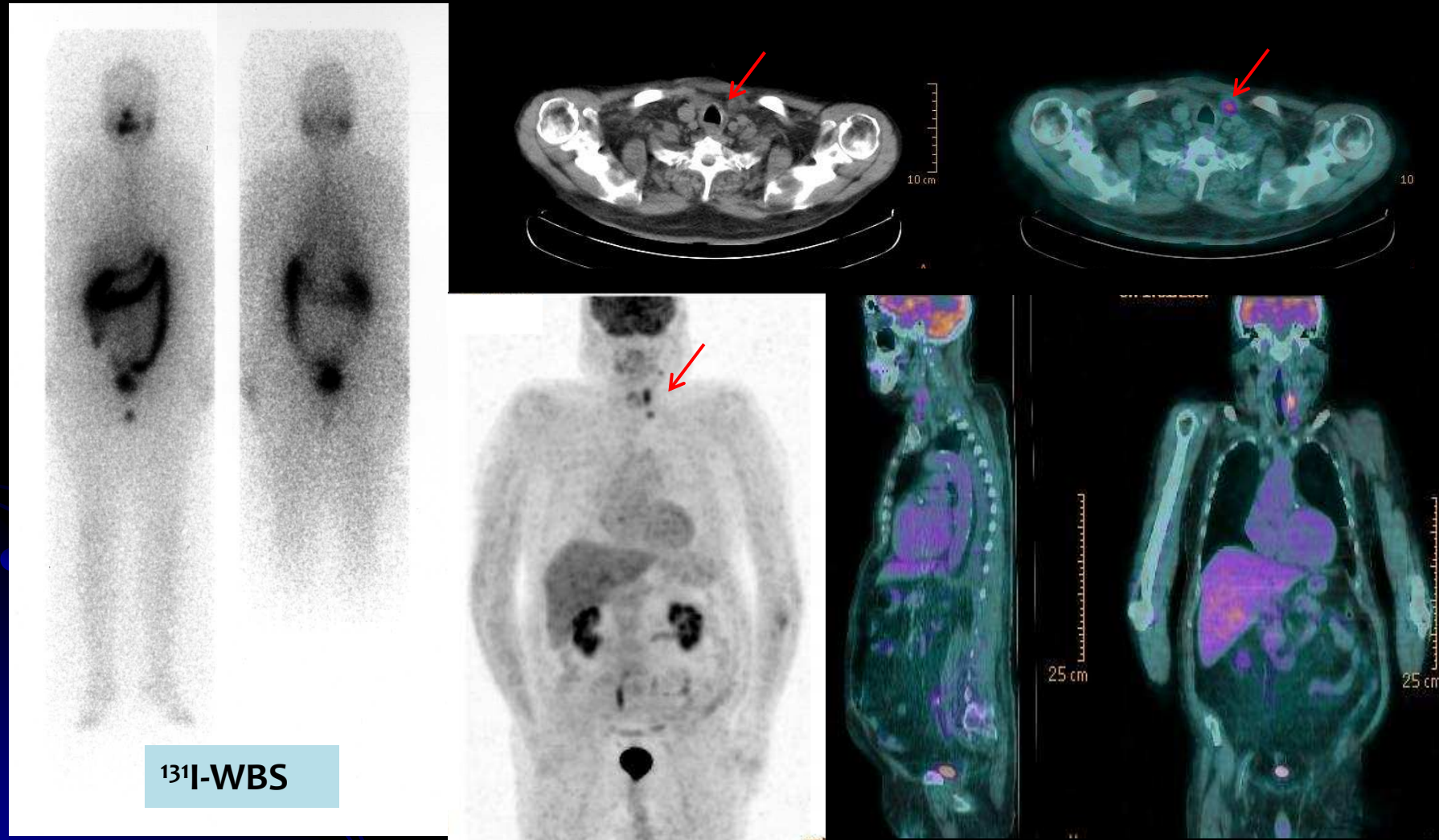
ALGORITHM for MANAGEMENT of DTC SIX to TWELVE MONTHS after REMNANT ABLATION



➤ Currently, the most valuable role of ^{18}F -FDG PET/CT exists in the work-up of patients with DTC post thyroidectomy who present with increasing Tg levels and a negative ^{131}I whole-body scan

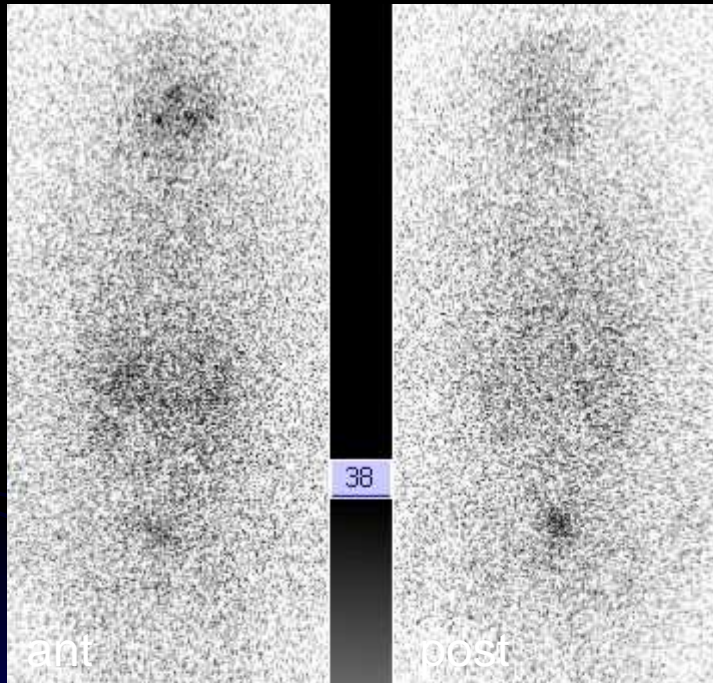
➤ If no disease sites are identified or Tg levels are elevated out of proportion to minor disease found on conventional imaging, ^{18}F -FDG PET/CT should be performed.

DTC post-thyroidectomy with increasing serum Tg and negative ^{131}I -WBS



Relapse in the thyroid bed detected by ^{18}F -FDG PET/CT

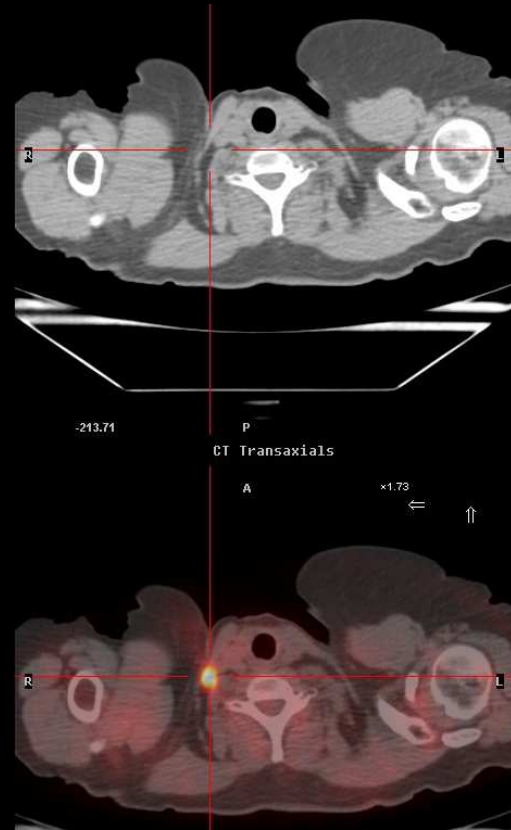
^{131}I scan negativa ^{18}F -FDG PET /CT positiva



^{131}I whole body scan

Tg 5,4 ng/ml

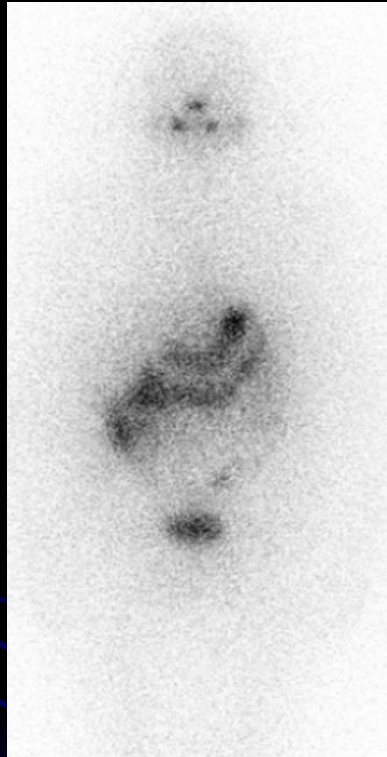
Linfonodo paratracheale



^{18}F -FDG PET/CT
SUV max 12.8



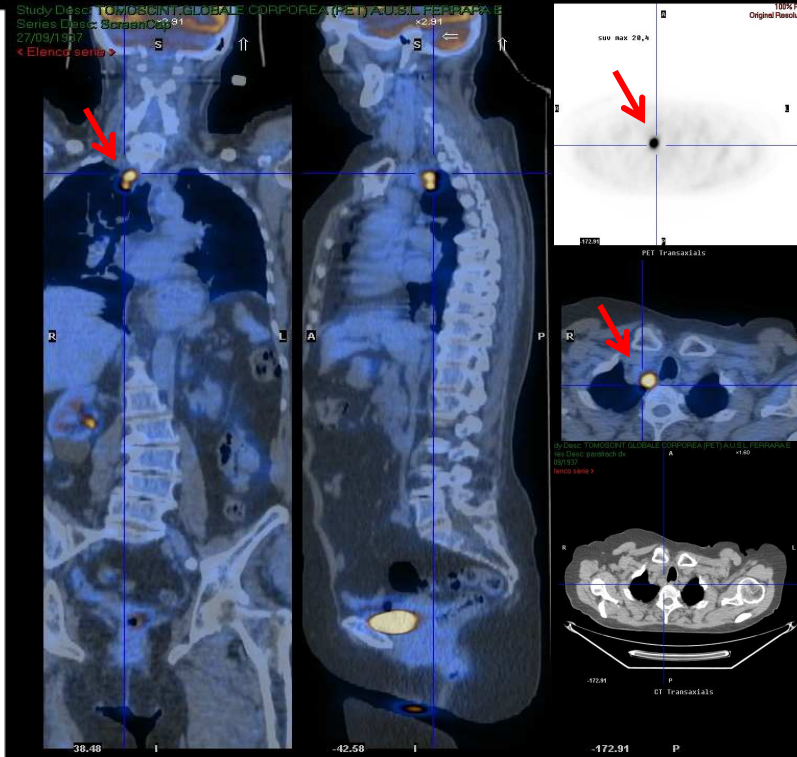
DTC post-thyroidectomy with increasing serum Tg and negative ^{131}I -WBS



^{131}I -WBS



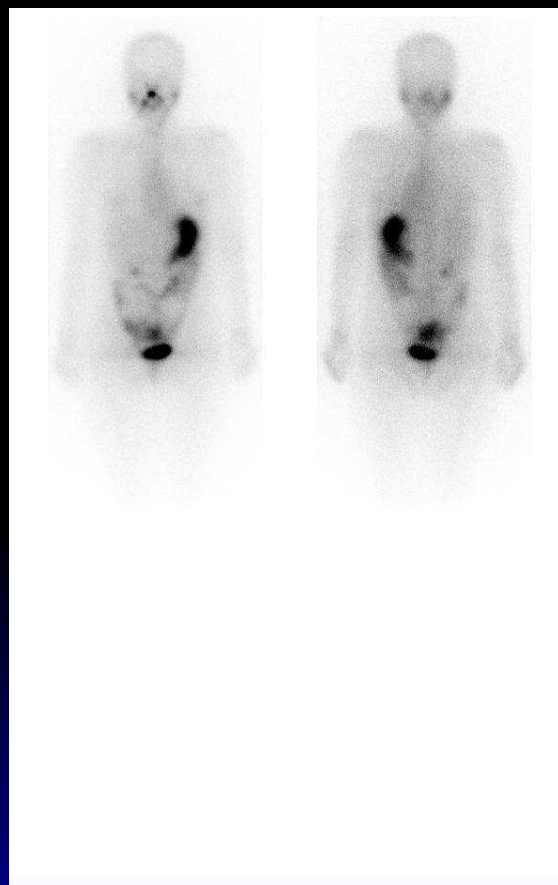
^{18}F -FDG PET/CT



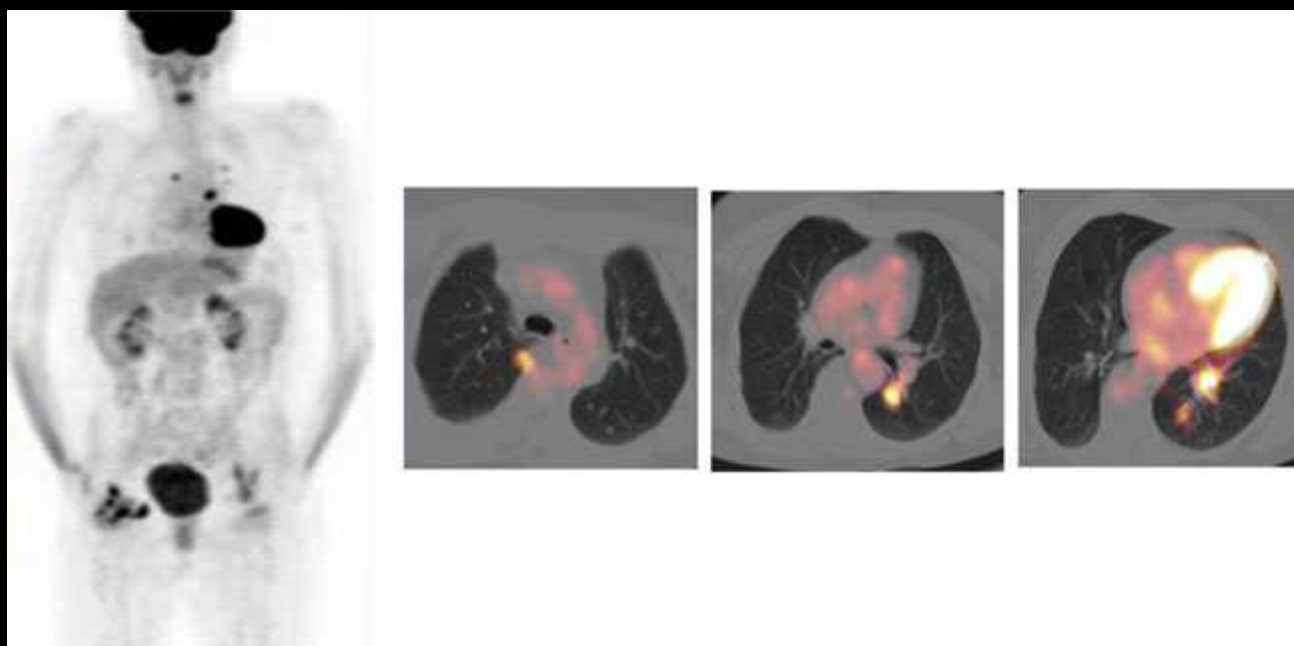
SUV max 20.4

Lymph nodal metastases in the thorax detected by ^{18}F -FDG PET/CT

DTC post-thyroidectomy with increasing serum Tg and negative ^{131}I -WBS



^{131}I -WBS



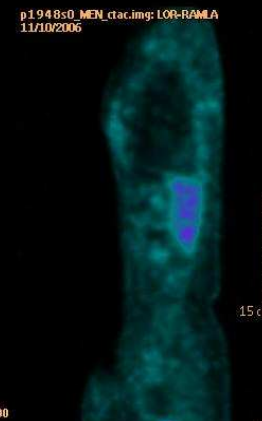
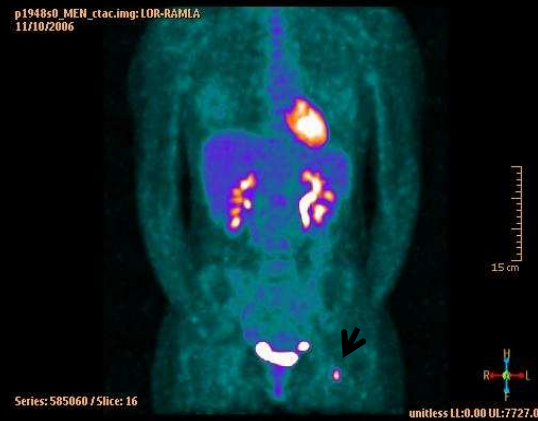
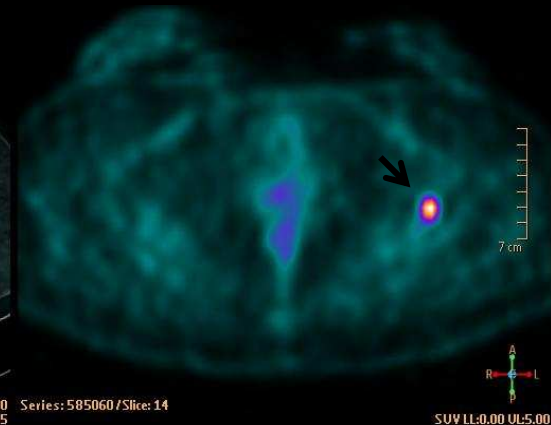
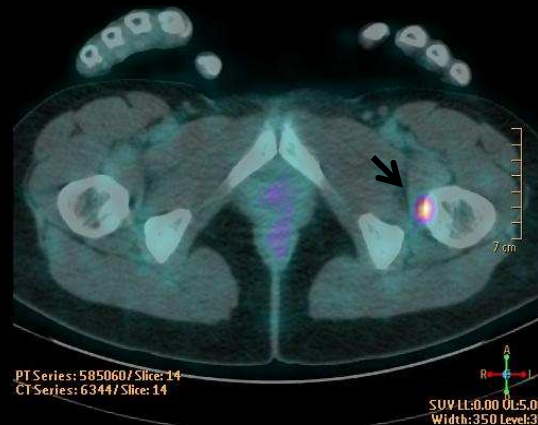
^{18}F -FDG PET/CT

Lung metastases detected by ^{18}F -FDG PET/CT

DTC post-thyroidectomy with increasing serum Tg and negative ^{131}I -WBS



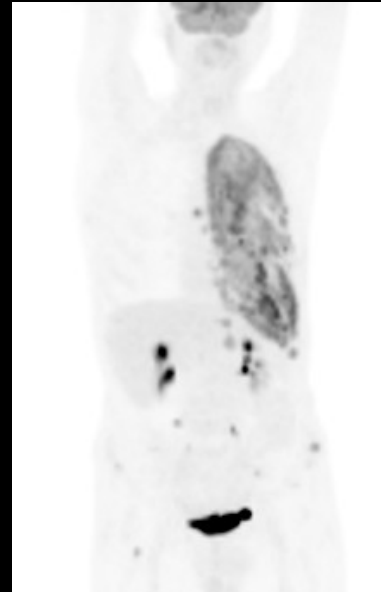
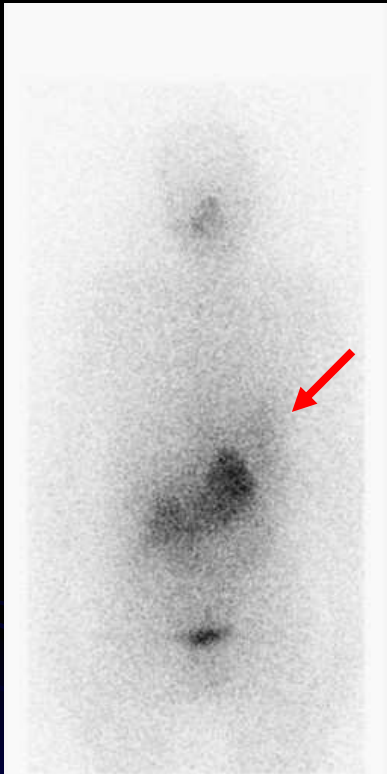
^{131}I -WBS



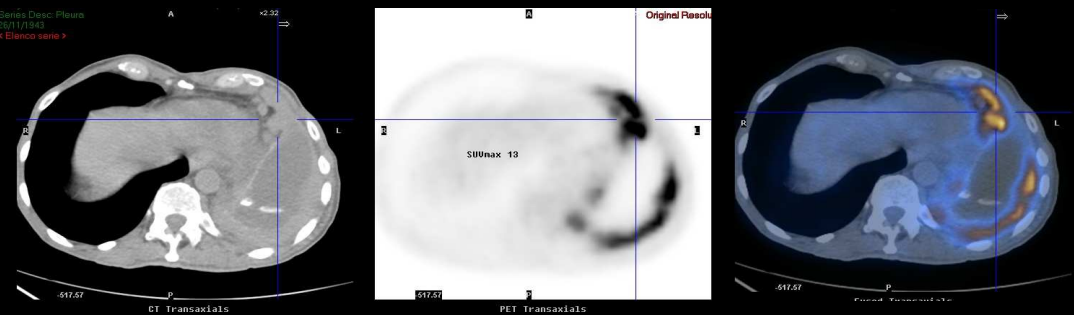
^{18}F -FDG PET/CT

Bone metastasis detected by ^{18}F -FDG PET/CT

Interesting case

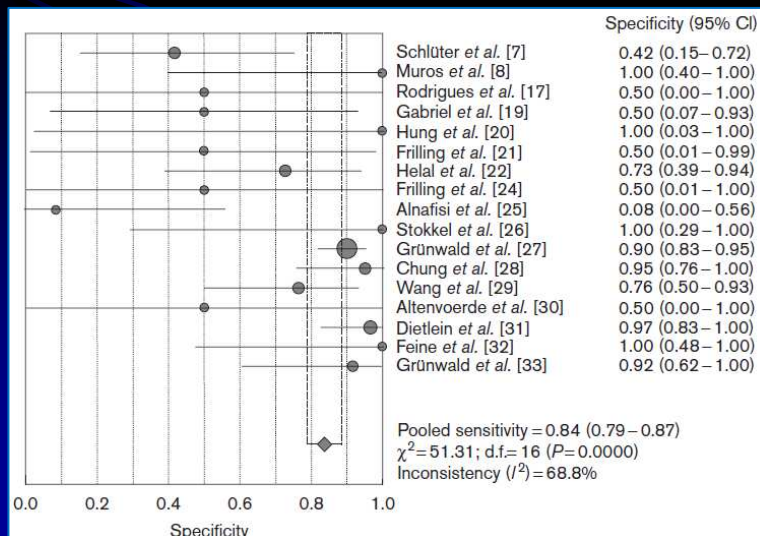
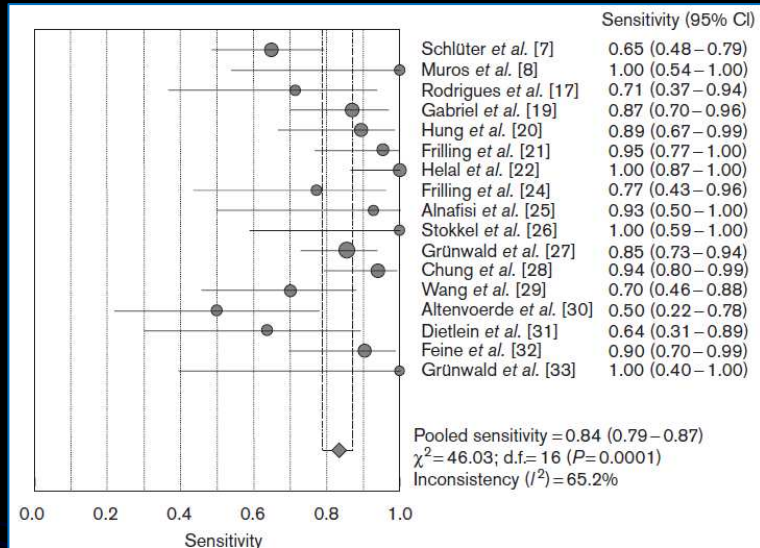


^{131}I whole body planar and SPECT/CT, Tg 0.3 ng/dl



^{18}F -FDG PET/CT – left lung (pleural) uptake
SUV max 13

Diagnostic performance of ^{18}F -FDG PET in DTC post-thyroidectomy



Original article

Nuclear
Medicine
Communications

Value of ^{18}F -FDG-PET/PET-CT in differentiated thyroid carcinoma with radioiodine-negative whole-body scan: a meta-analysis

Meng-Jie Dong, Zhen-Feng Liu, Kui Zhao, Ling-Xiang Ruan, Guo-Lin Wang, Shu-Ye Yang, Fang Sun and Xu-Guang Luo

Nuclear Medicine Communications 2009, 30:639-650

Results In total, 17 studies with 571 patients who had recurrent or metastatic DTC and a radioiodine-negative whole-body scan were collected, and the overall patient-based sensitivity and specificity of FDG-PET were 0.835 [95% confidence interval (CI): 0.791-0.873] and 0.843 (95% CI: 0.791-0.886), respectively. Of these studies, six included lesion-based data, totaling 237 lesions, and the pooled lesion-based sensitivity and specificity were 0.916 (95% CI: 0.863-0.953) and 0.775 (95% CI: 0.660-0.865), respectively.

Should ^{18}F -FDG PET/CT be performed under TSH stimulation?



The sensitivity of ^{18}F -FDG-PET scanning may be marginally improved with TSH stimulation (especially in patients with low Tg values), but the clinical benefit of identifying these additional small foci is yet to be proven

ATA guidelines. Thyroid 2009

- Experimental evidence suggests that glucose uptake in thyroid cells should be increased after TSH stimulation
- Clinical evidence is emerging that the performance of ^{18}F -FDG PET is also improved after TSH stimulation (either by hormone withdrawal or rhTSH administration) in patients with DTC

Abraham & Schöder. Semin Nucl Med 2011

Should ^{18}F -FDG PET/CT be performed under TSH stimulation?

European Journal of Endocrinology (2010) 163 177–183

ISSN 0804-4643

REVIEW

The role of TSH for ^{18}F -FDG-PET in the diagnosis of recurrence and metastases of differentiated thyroid carcinoma with elevated thyroglobulin and negative scan: a meta-analysis

Chao Ma^{*}, Jiawei Xie^{1,*}, Yanhui Lou^{1,*}, Yanyan Gao², Shuyao Zuo and Xufu Wang

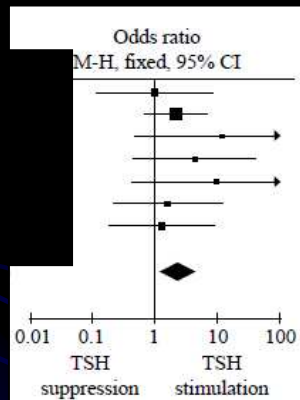


Figure 2 The comparison of PET true-positive patients during TSH stimulation (under rhTSH or thyroid hormone withdrawal) and suppression. 'Events', PET true-positive patients.

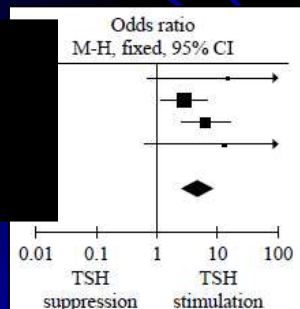


Figure 3 The comparison of PET sensitivity for the number of the detected lesions observed during TSH stimulation (under rhTSH or thyroid hormone withdrawal) and suppression. 'Events', the number of the PET-detected lesions.

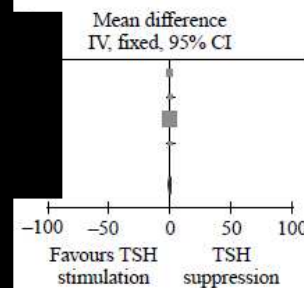
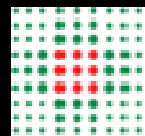


Figure 4 The comparison of the mean SUV_{max} of the PET-detected lesions observed during TSH stimulation (under rhTSH or thyroid hormone withdrawal) and suppression. 'Mean', the mean SUV_{max} of the PET-detected lesions'.

The results obtained from the seven prospective controlled clinical trials suggest that TSH stimulation done under thyroid hormone withdrawal or rhTSH slightly and significantly improves the diagnostic performance of PET for the detection of Tg-positive and radioiodine-negative metastases of DTC. Therefore, TSH stimulation may be recommended for DTC patients undergoing PET scanning in these circumstances. However, the clinical significance remains uncertain due to the small sample sizes, short durations of follow-up, and the absence of systematic histological verification of all the PET-detected lesions in the included trials.



Recombinant Thyrotropin Stimulation improves ^{18}F -FDG PET/CT sensitivity in patients with Recurrent Differentiated Thyroid Cancer

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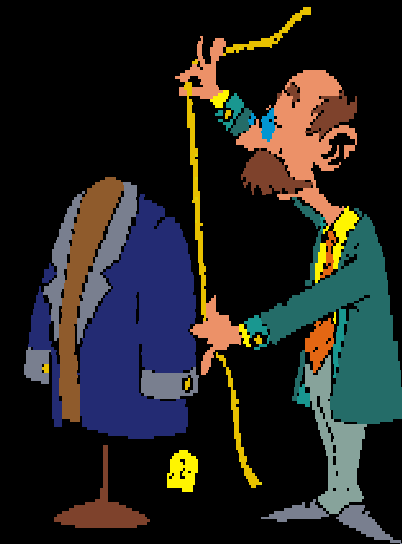
Should ^{18}F -FDG PET/CT be performed only when Tg is > 10 ng/ml?

➤ The current ATA guidelines suggest that this only be done when Tg levels are 10 ng/mL, but in reality, no clear cut-off can be established

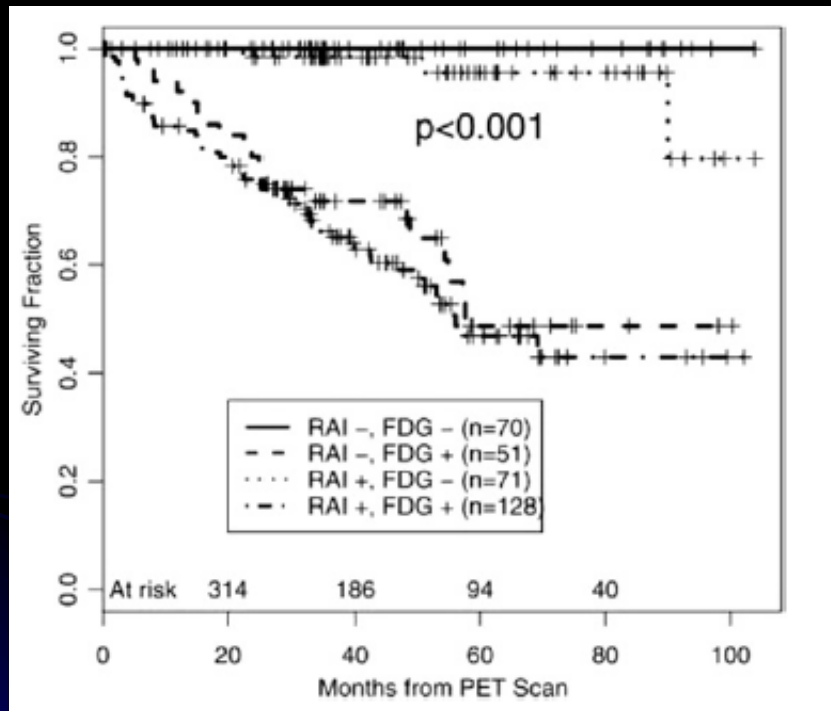
➤ Although the proportion of true positive ^{18}F -FDG PET scans and findings increase with increasing Tg levels, true-positive findings have been reported in 10%-20% of patients even when Tg levels are <10 ng/mL

➤ In daily practice, the decision regarding when to perform ^{18}F -FDG PET/CT should be individualized for each patient, considering not only Tg levels and ^{131}I -WBS findings, but also individual risk on the basis of clinical and histopathologic features

➤ Depending on the clinical setting, ^{18}F -FDG PET/CT findings may change patient management in 20-40% of cases



Prognostic role of ^{18}F -FDG PET in DTC



➤ The outcome is worse for patients with positive ^{18}F -FDG PET scan, regardless of findings on ^{131}I -WBS

➤ Greater SUV and greater number of ^{18}F -FDG-positive lesions conferred a worse prognosis

➤ In multivariate analysis, only age and ^{18}F -FDG PET findings (^{18}F -FDG-positivity, number of ^{18}F -FDG-positive lesions and SUV) are strong predictors of survival

^{18}F -FDG PET and PET/CT in differentiated thyroid cancer

Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer

The American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer



Current additional clinical uses of ^{18}F FDG-PET or PET/CT in DTC may include:

- prognostic tool for identifying which patients with known distant metastases are at highest risk for disease-specific mortality
- selection tool to identify those patients unlikely to respond to additional radioactive iodine therapy
- measurement of post-treatment response following external beam irradiation, surgical resection, embolization, or systemic therapy

Low-risk patients are very unlikely to require ^{18}F -FDG PET scan as part of initial staging or follow-up. To date, ^{18}F -FDG PET/CT is not recommended for preoperative assessment

¹²⁴I-PET and PET/CT in thyroid cancer

Eur J Nucl Med Mol Imaging (2011) 38 (Suppl 1):S48–S56
DOI 10.1007/s00259-011-1773-5

REVIEW ARTICLE

Clinical applications of ¹²⁴I-PET/CT in patients with differentiated thyroid cancer

Lutz S. Freudenberg • Walter Jentzen •
Alexander Stahl • Andreas Bockisch •
Sandra J. Rosenbaum-Krumme

➤ ¹²⁴I has a half-life of 4.2 days and a relatively complex decay scheme, producing positrons of relatively high energies (1532 keV and 2146 keV), as well as several high-energy gamma and X-rays

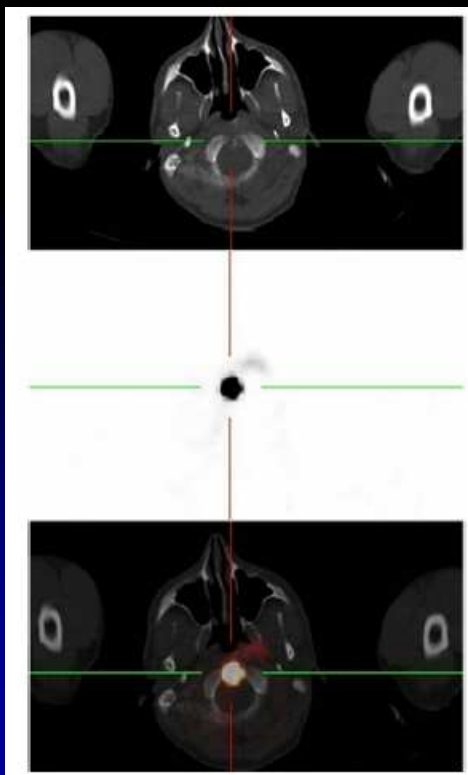
➤ Despite the high abundance of high-energy gamma photons images of satisfactory quality can be acquired and quantitation of tracer uptake can be performed

Two aspects deserve special mention about the applications of ¹²⁴I-PET and PET/CT in DTC:

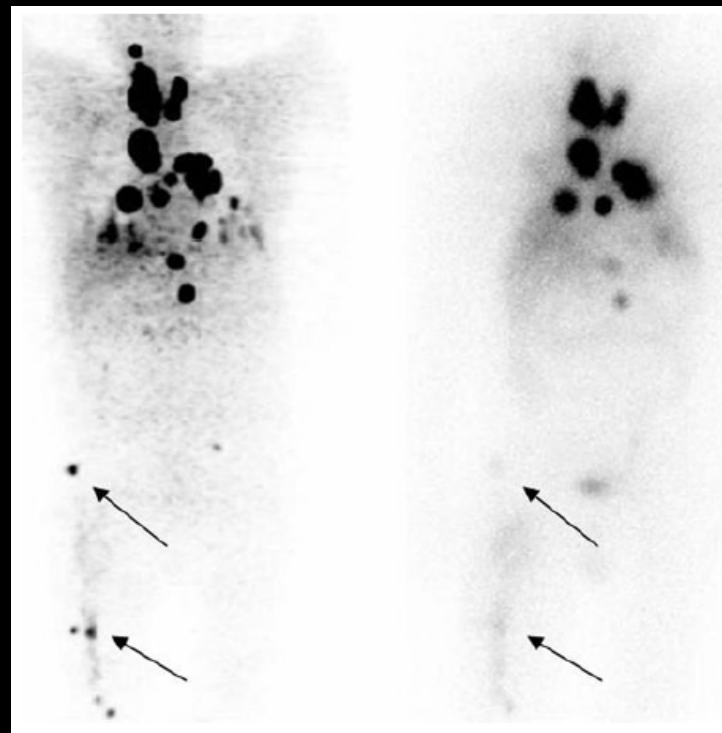
- **staging of recurrent or residual disease**
- **pretherapy dosimetry**

^{124}I -PET in DTC: staging of recurrent or residual disease

- Used in combination ^{124}I -PET and CT allow foci of highly specific ^{124}I uptake to be localized with a low radiation dose, which is important in pre-therapy diagnostics
- ^{124}I -PET provides images of higher spatial resolution and lesion contrast than either planar imaging or SPECT with ^{131}I , resulting in better lesion detection but the impact of improved lesion detection compared to ^{131}I in patients with documented or reasonably suspected metastatic disease remains to be proven



^{124}I -PET



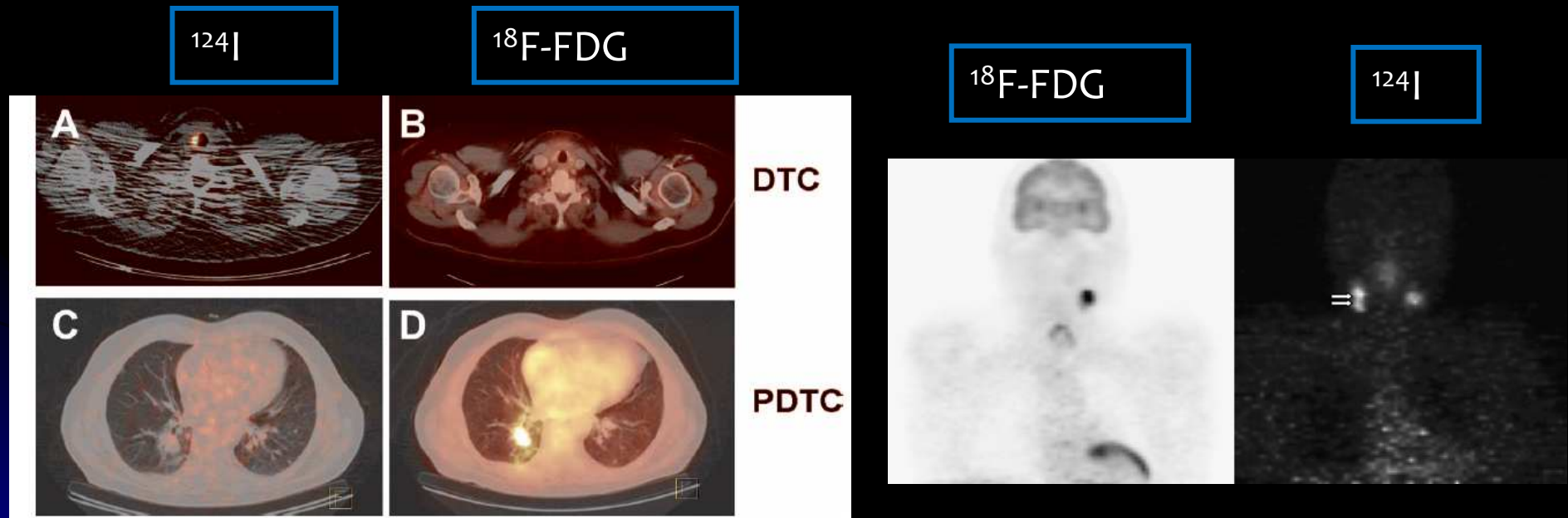
^{131}I -WBS

Abraham & Schöder.
Semin Nucl Med 2011

Freudenberg L et al.
EJNMMI 2011

^{124}I -PET in DTC: staging of recurrent or residual disease

- The combination of ^{18}F -FDG and ^{124}I PET/CT allows to detect non-iodine-avid lesions and to discriminate from simultaneously occurring iodine-positive lesions

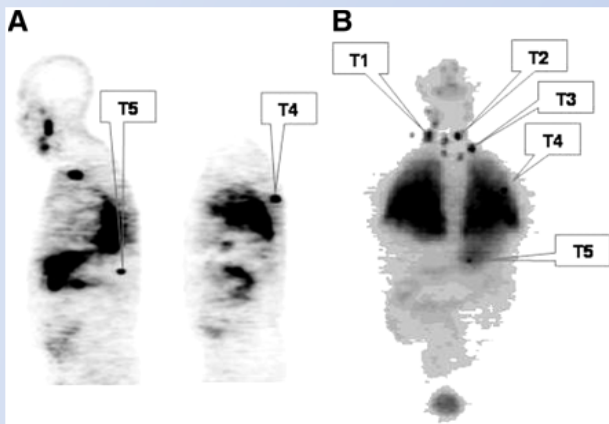


Grabellus F et al. Clin Nucl Med 2012

Freudenberg L et al. EJNMMI 2008

^{124}I -PET in DTC: pretherapy dosimetry and emerging indications

- The pretherapy dosimetry by using ^{124}I -PET may result in a significant alteration in the therapeutic procedure compared to standard therapy with fixed therapeutic activities
- ^{124}I -PET dosimetry is a useful procedure especially in advanced DTC and allows the administration of safer and more effective radioiodine activities



Tumor no.	Absorbed dose* (Gy)		
	Mean	Minimum	Maximum
1	100	5.0	720
2	270	9.8	1,700
3	170	17	760
4	350	37	1,000
5	100	5.5	880

*Administered activity = 15 GBq (400 mCi).

- An emerging indication is response assessment of patients who undergo targeted therapies aimed at achieving reestablishment of iodine uptake through inhibition of molecular tumor pathways

Conclusions

- The role of ^{18}F -FDG PET/CT in DTC is well established, particularly in patients presenting with elevated Tg levels and negative radioactive iodine WBS
- Iodine-124 may serve a role in obtaining lesional dosimetry for better and more rationale planning of treatment with Iodine-131

Other radiopharmaceutical: ^{68}Ga -DOTANOC/ ^{111}In pentetretotide → SSt analogues detection → therapeutic role ($^{90}\text{Y}/^{177}\text{Lu}$ [DOTA]0-Tyr3octreotate o DOTATATE)

TERAPIA

RADIOMETABOLICA



CHIRURGIA RADIOGUIDATA

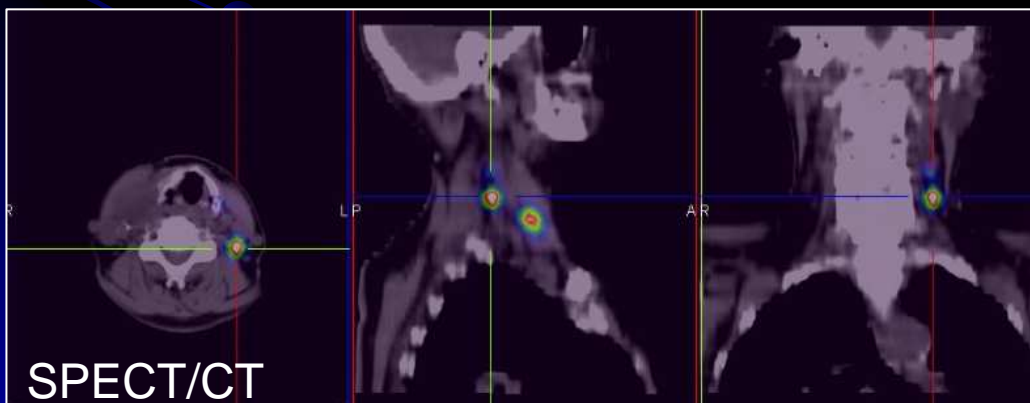




CHIRURGIA RADIOGUIDATA



Chirurgia mini invasiva
Ridotta ospedalizzazione
Ridotte complicanze post chirurgiche





Grazie per l'attenzione