UNIVERSITÀ CATTOLICA del Sacro Cuore

Terapia con ^{131}I del Carcinoma Tiroideo

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Sommario

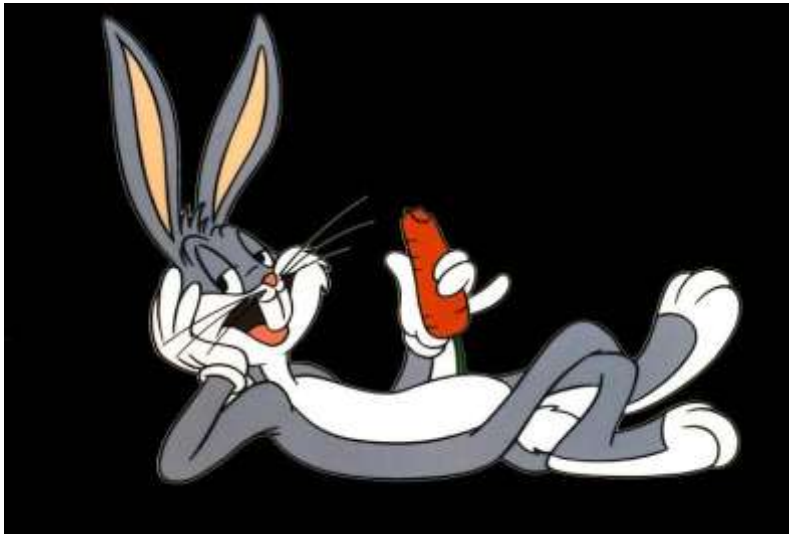
- Scoperta ed iniziale uso del radioiodio
- Attuale uso diagnostico del radioiodio
- Terapia ablativa e delle metastasi con ^{131}I

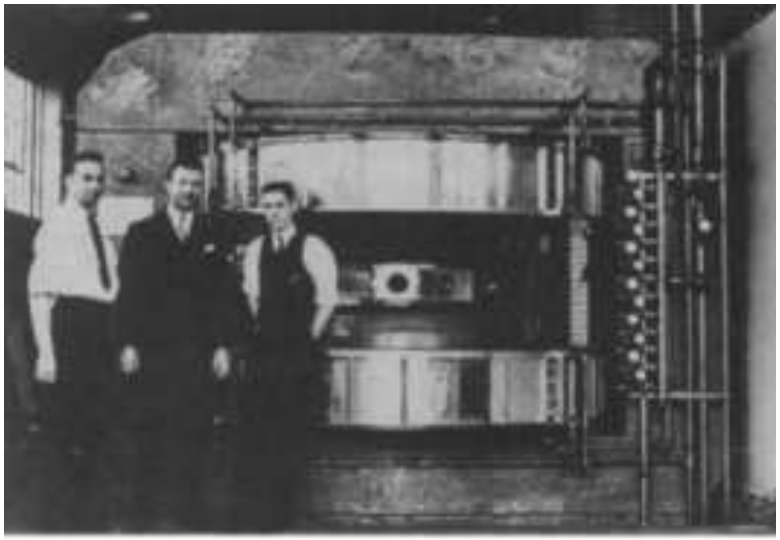
- ✓ Enrico Fermi scopre 14 nuovi elementi radioattivi
- ✓ L'11°della lista con "*iodine-intense effect, period about 30 minutes*"
- ✓ Era lo ^{128}I ($T\frac{1}{2}$ 25 min.), primo isotopo dello iodio ad essere prodotto

Fermi E. Nature 1934; 133:757
Radiocativity induced by neutron bombardment

- ✓ Nel 1938 è dimostrato per la prima volta accumulo di radioiodio in tiroide

- ✓ A Boston, nello stesso anno è avviata la costruzione del primo ciclotrone per uso medico con produzione di ^{130}I



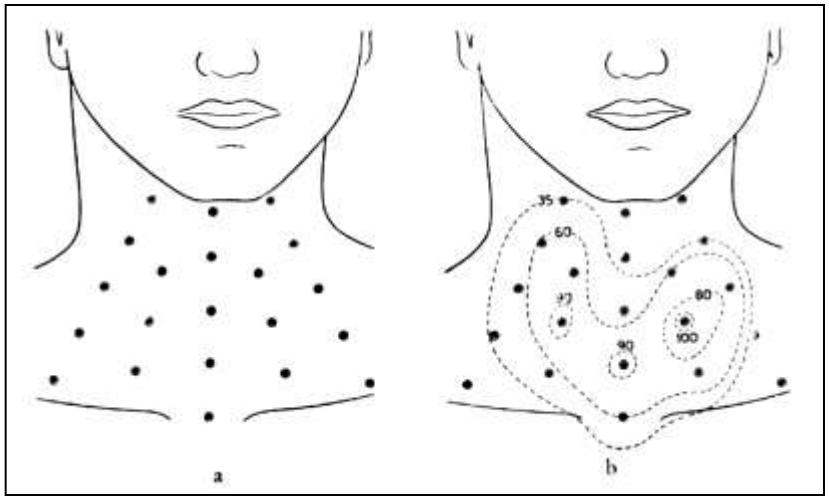


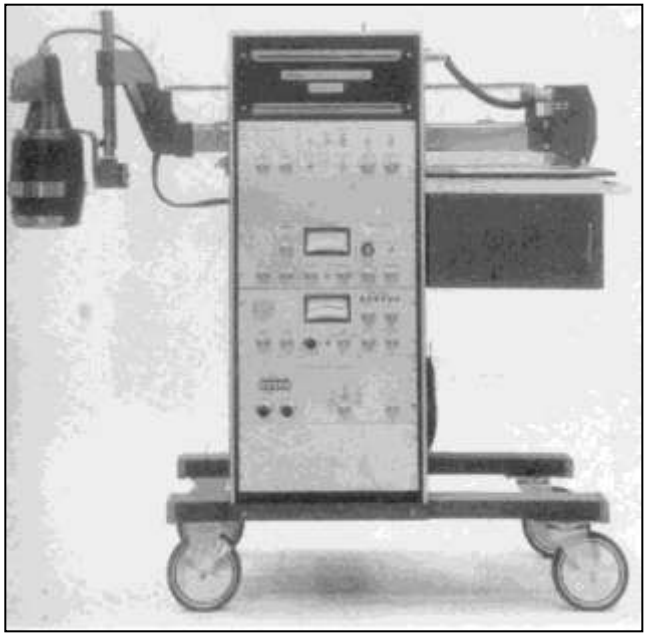
Hertz S, et al. Proc Soc Exp Biol Med 38:510-513,1938

- ✓ Il 21 Gennaio 1941 al MIT viene trattato il primo paziente ipertiroideo con circa 1 mCi di ^{130}I
- ✓ Nel 1946 il Reattore di Oak Ridge inizia a produrre ^{131}I ed in quegli anni si recupera e si purifica lo ^{131}I dalle urine di pazienti già trattati
- ✓ Nel 1951 il ^{131}I-ioduro di sodio diviene il primo radiofarmaco approvato da FDA per uso clinico

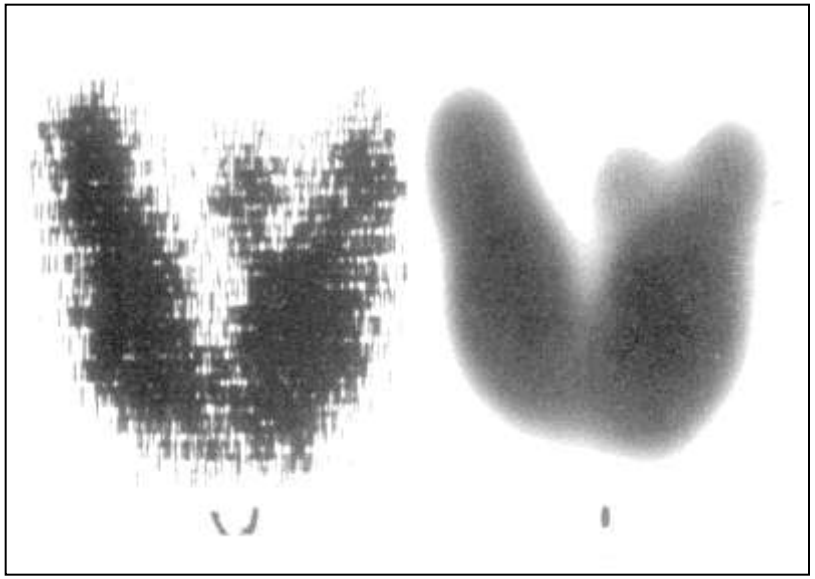
Hamilton JG, et al. Am J Physiol 127:557-572,1939

1949



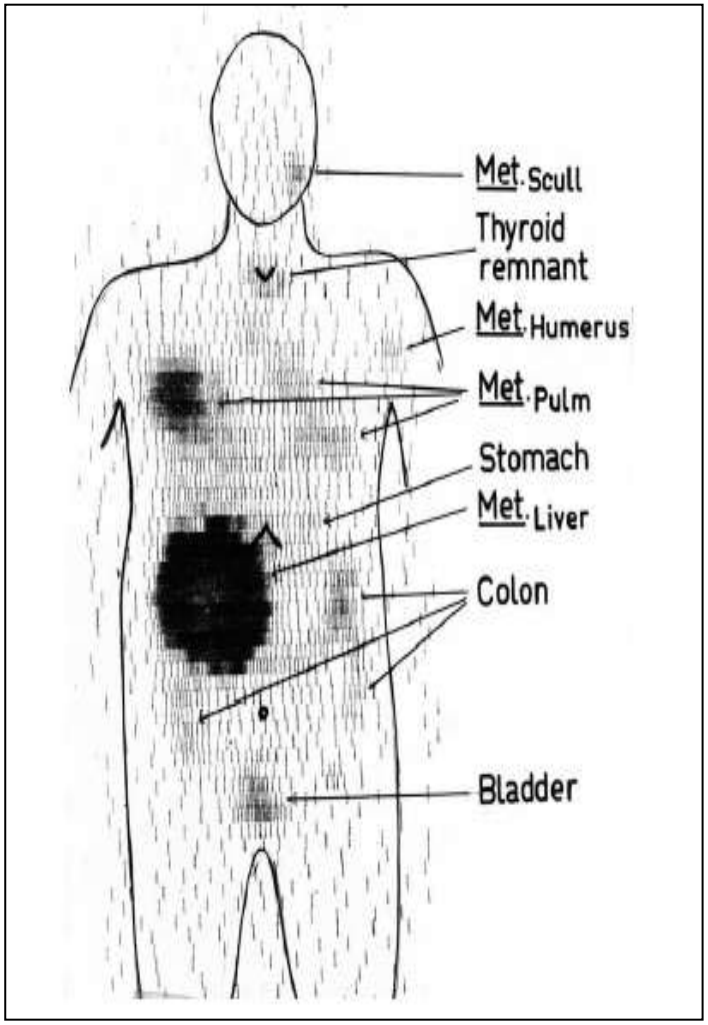


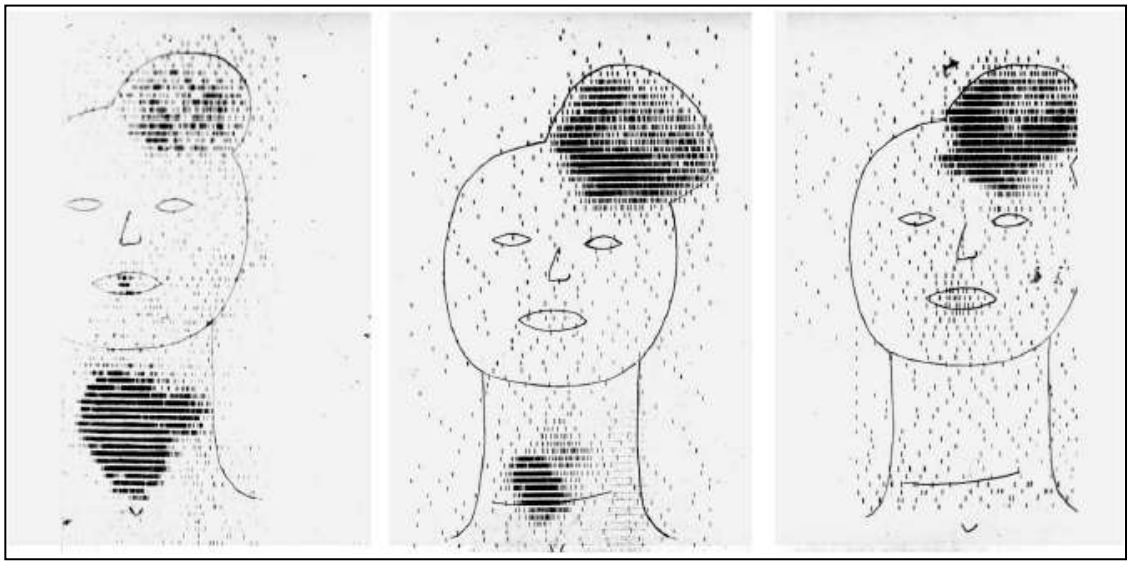
1958

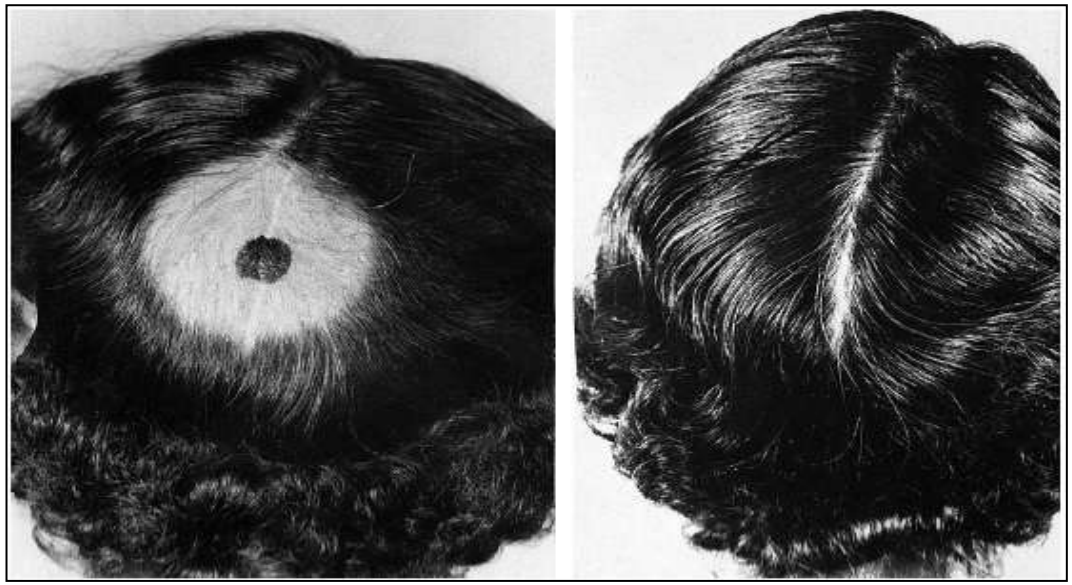


Misure di uptake tiroideo con contatore Geiger

Primi studi di scintigrafia corporea globale per CDT







Sommario

- Scoperta ed iniziale uso del radioiodio
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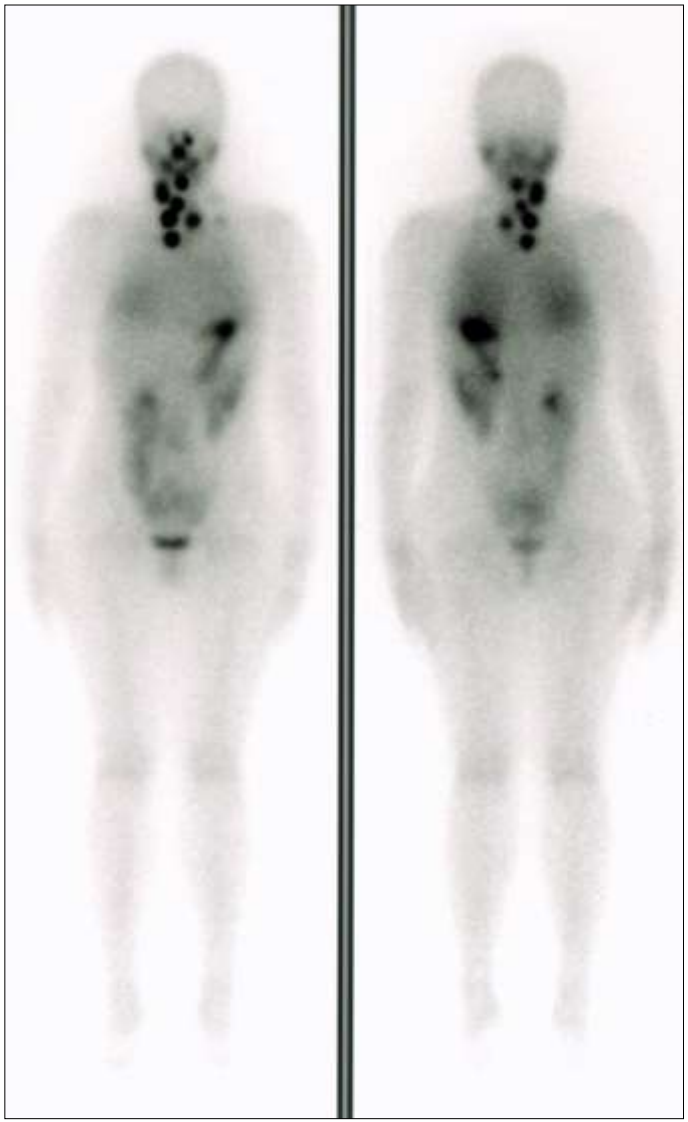
- Terapia ablativa e delle metastasi con ^{131}I

Indicazioni storiche a ^{131}I DxWBS



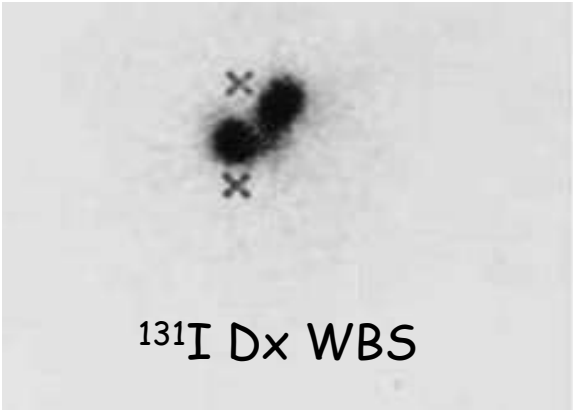
- Studio del residuo tiroideo dopo chirurgia
- Diagnosi di metastasi funzionanti
- Indicazione a ^{131}I terapia
- Risposta a ^{131}I terapia
- Follow-up a breve e lungo termine

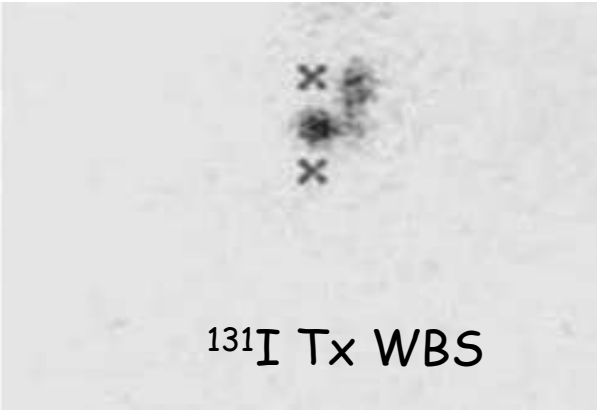
Elevata accuratezza diagnostica della Tg

A Consensus Report of the Role of Serum Thyroglobulin as a Monitoring Method for Low-Risk Patients with Papillary Thyroid Carcinoma

E. L. MAZZAFERRI, R. J. ROBBINS, C. A. SPENCER, L. E. BRAVERMAN, F. PACINI, L. WARTOFSKY, B. R. HAUGEN, S. I. SHERMAN, D. S. COOPER, G. D. BRAUNSTEIN, S. LEE, T. F. DAVIES, B. M. ARAFAH, P. W. LADENSON, AND A. PINCHERA

Thyroid Stunning

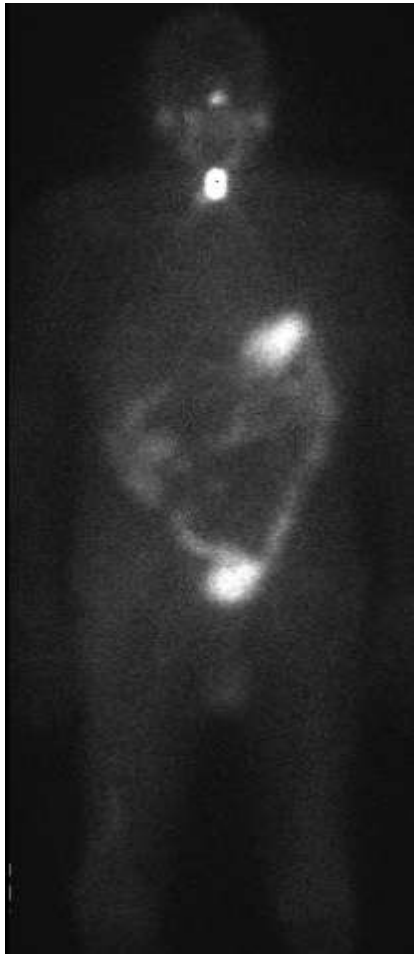


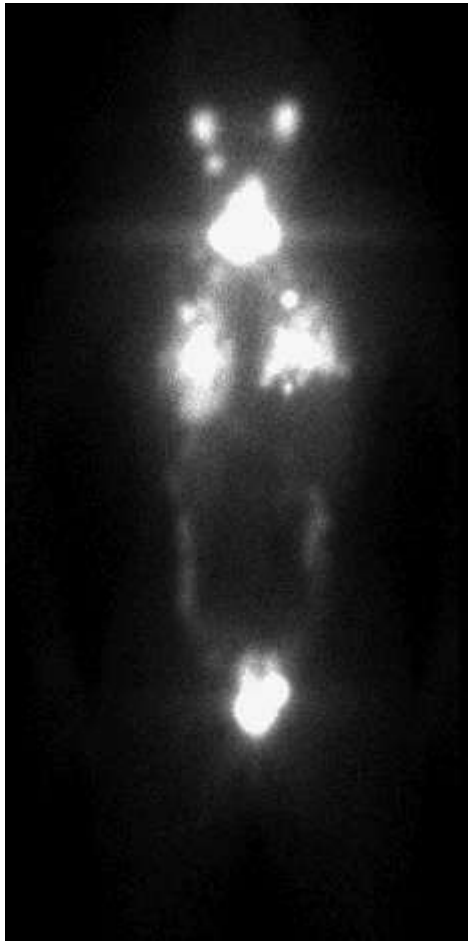


Robbins et al , JCEM 86:619,2001

Superiorità diagnostica del Tx WBS

Dx WBS
5 mCi





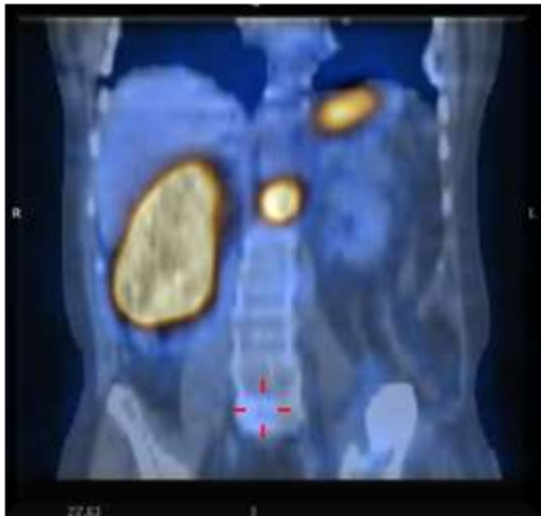
Tx WBS
100 mCI

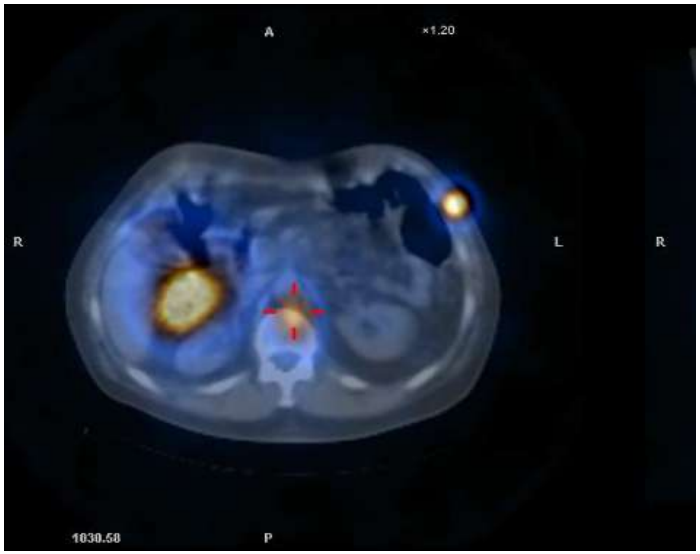
^{131}I DxWBS nel FUP dei casi ad alto rischio

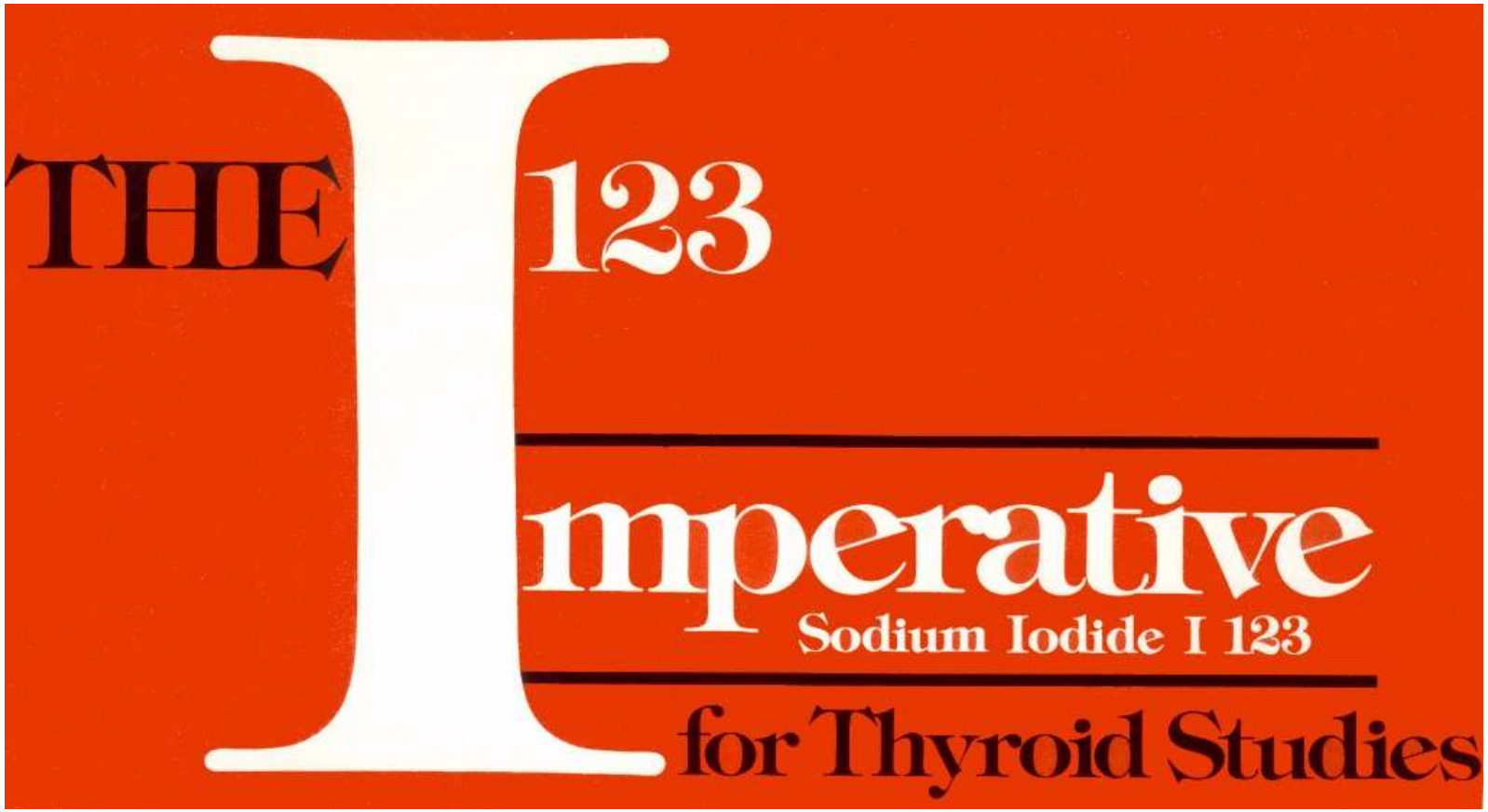
^{131}I DxWBS
baseline

^{131}I DxWBS
in corso di FUP

^{131}IDxWBS SPECT/TC

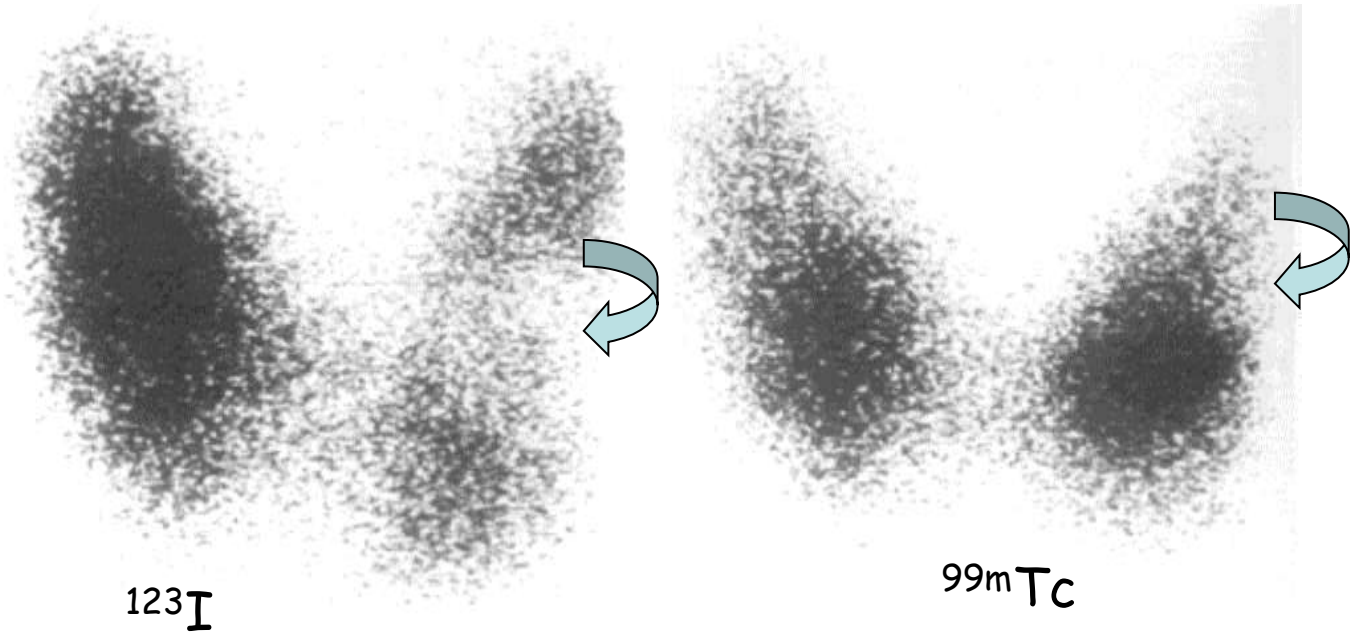






$$^{127}I(p,5n)^{123}Xe \xrightarrow{\beta^+} {}^{123}I$$

Iodio-123 per scintigrafia tiroidea

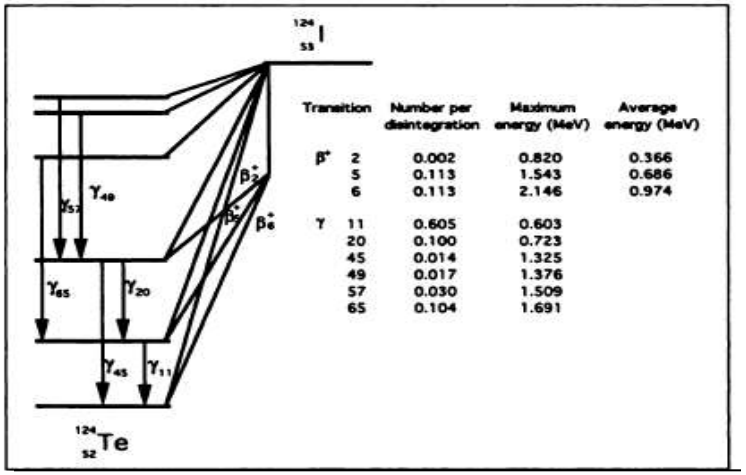


Routine reimaging of 99mTc hot nodules with radioiodine for cancer detection does not appear to be necessary

J Nucl Med 1990;31:393

Iodio-124

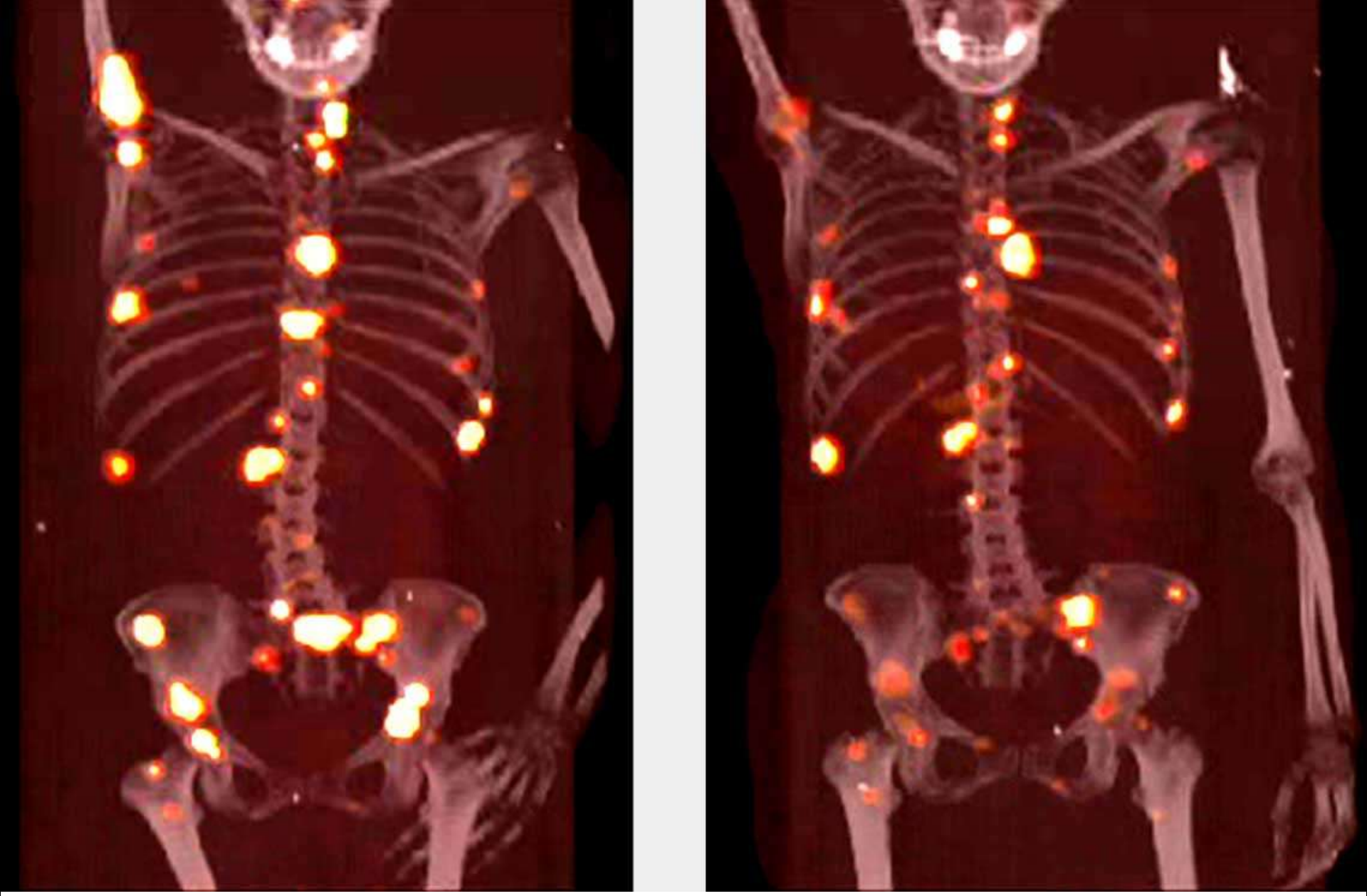
- *Schema di decadimento* : complesso
  - 25 transizioni CE
  - 6 " positroniche
  - 97 " gamma



Transition		Number per disintegration	Maximum energy (MeV)	Average energy (MeV)
β^+	2	0.002	0.820	0.366
	5	0.113	1.543	0.686
	6	0.113	2.146	0.974
γ	11	0.605	0.603	
	20	0.100	0.723	
	45	0.014	1.325	
	49	0.017	1.376	
	57	0.030	1.509	
	65	0.104	1.691	

- *Emivita fisica* : 4,2 gg.
- *Disponibilità* : recente
- *Produzione* : ottimizzata
- *Uso e attività* : dosimetria e diagnosi, 74 MBq ^{124}I
- *Dose efficace* : 7.0 mSv
  11.0 mSv (185 MBq ^{131}I)
  340 mSv (5.550 MBq ^{131}I)

Brianzoni E , Macerata 2009



^{124}I WB: metastatic spread

^{124}I PET/TC per diagnostica e dosimetria

Diagnostica

- Risultati analoghi al ^{131}I TxWBS
- Complementare alla PET/TC con ^{18}F-FDG
- La TC permette identifica lesioni non-iodocaptanti

Dosimetria

- Attività massima sicura (met. di Benua)
- Dose alla lesione (met. di Maxon)

  - elevato rapporto lesione/fondo
  - preciso calcolo dei volumi

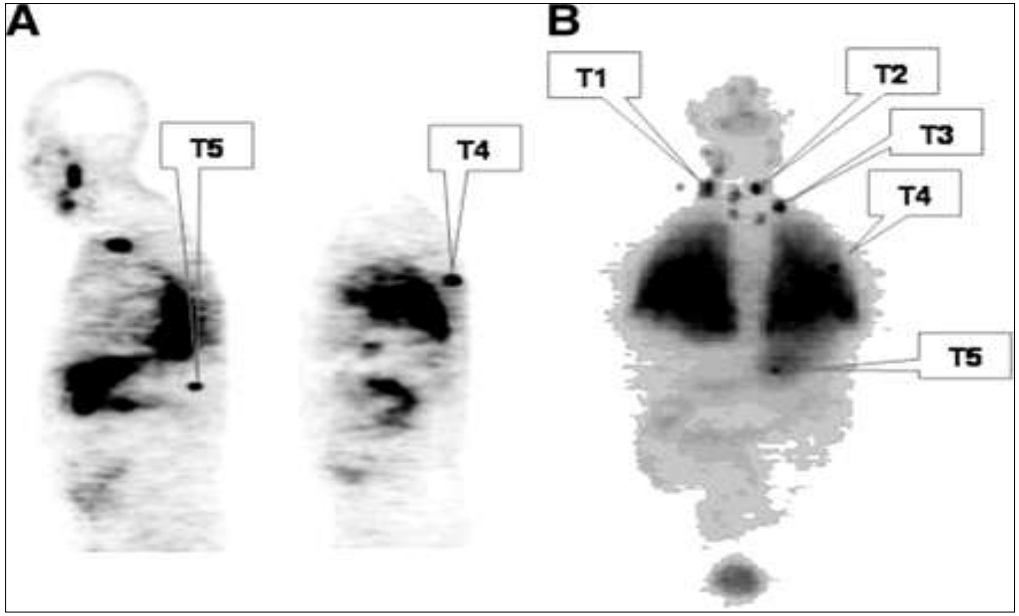


TABLE 4
Mean, Minimum, and Maximum Absorbed Dose in Individual Tumors of Patient 16

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).

Sgouros G et al. J Nucl Med 2004 ;45:1366

Sommario

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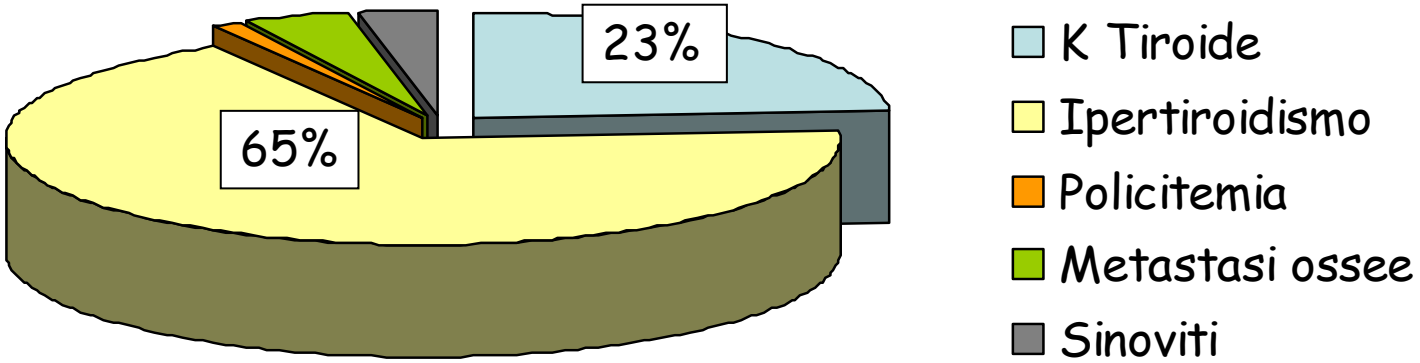
Trattamenti di MN nel Mondo (1991-1996)

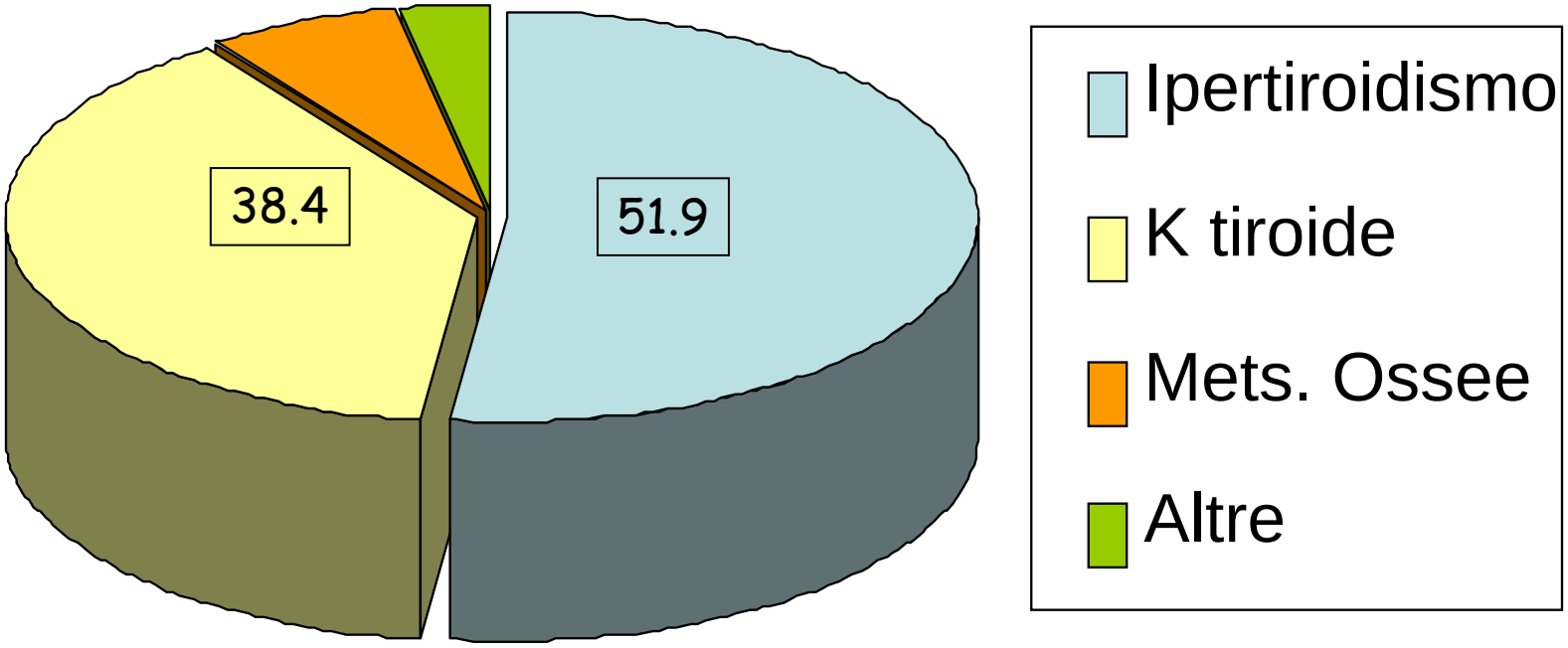
- ✓ 380.000 trattamenti con radiofarmaci
- ✓ ~ il 90% eseguito utilizzando ^{131}I
- ✓ ~ 78.000/anno per carcinoma tiroideo



Ref. UNSCEAR 2000Volume I: SOURCES Annex D: Medical radiation exposures **http://www.unscear.org/unscear/en/publications/2000_1.html**

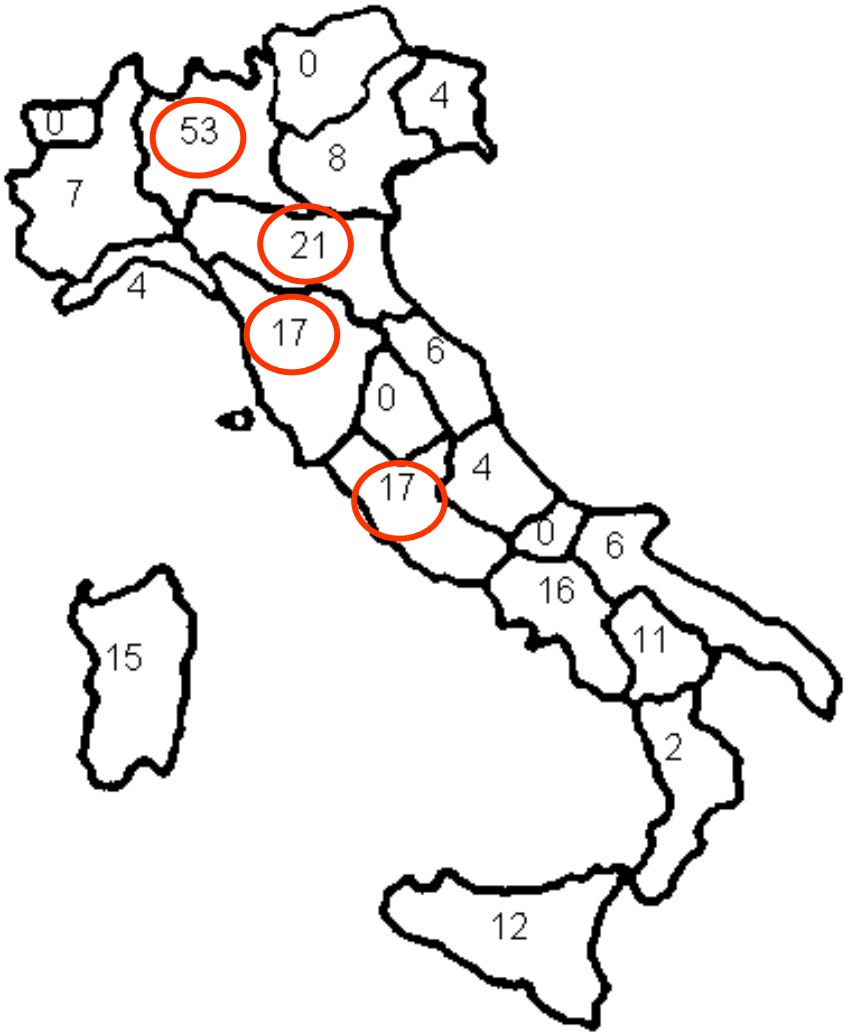
Trattamenti di MN in Italia (2002)

- ✓ 14.956 trattamenti con radiofarmaci
- ✓ Il 90.3 % eseguito utilizzando 131I
- ✓ ~ 5.000 per carcinoma tiroideo



Notiziario AIMN, n.3 2005

Posti letto in degenza protetta in Italia (2002)



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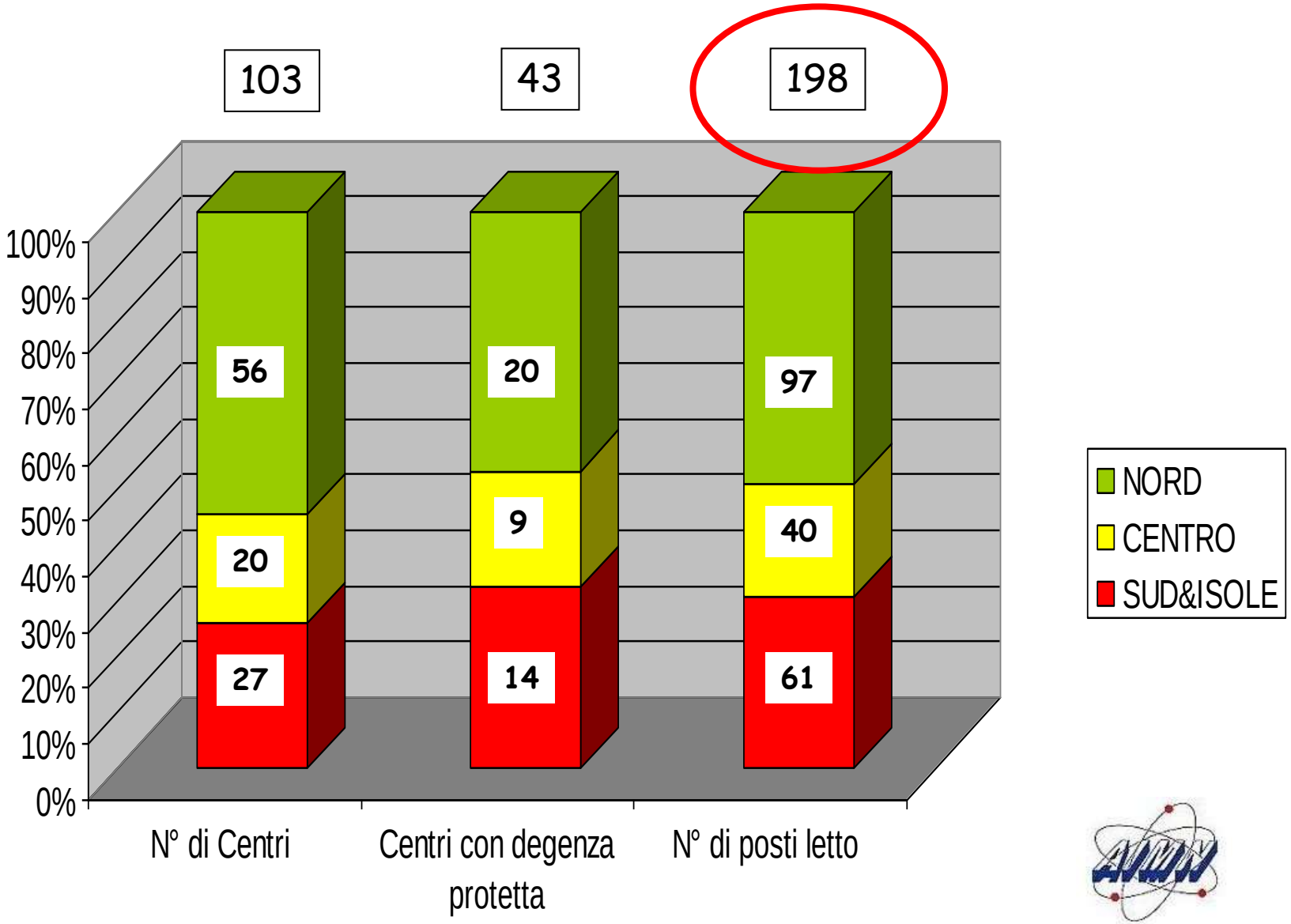
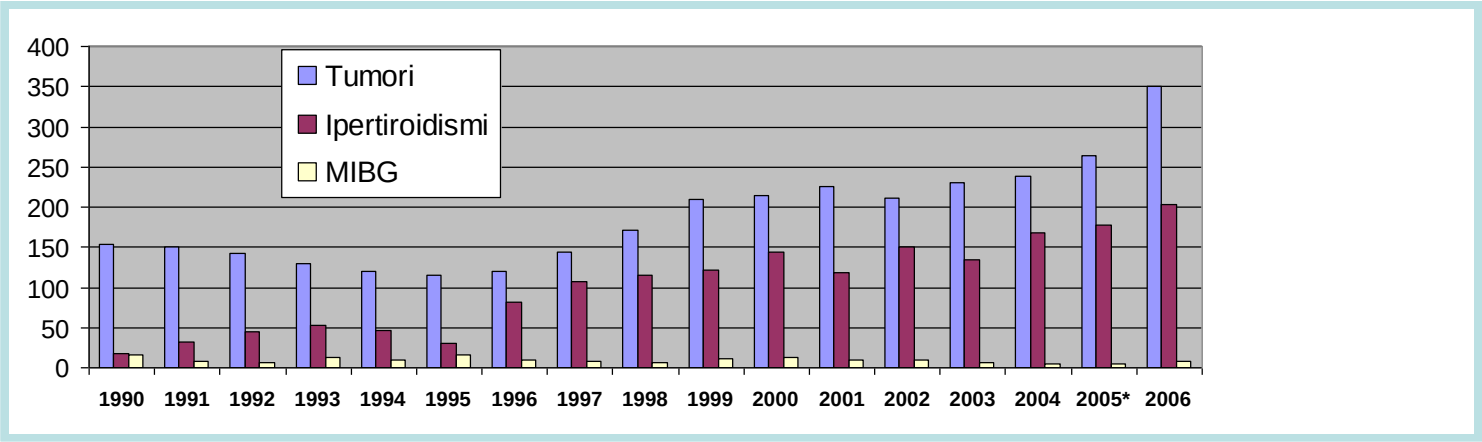
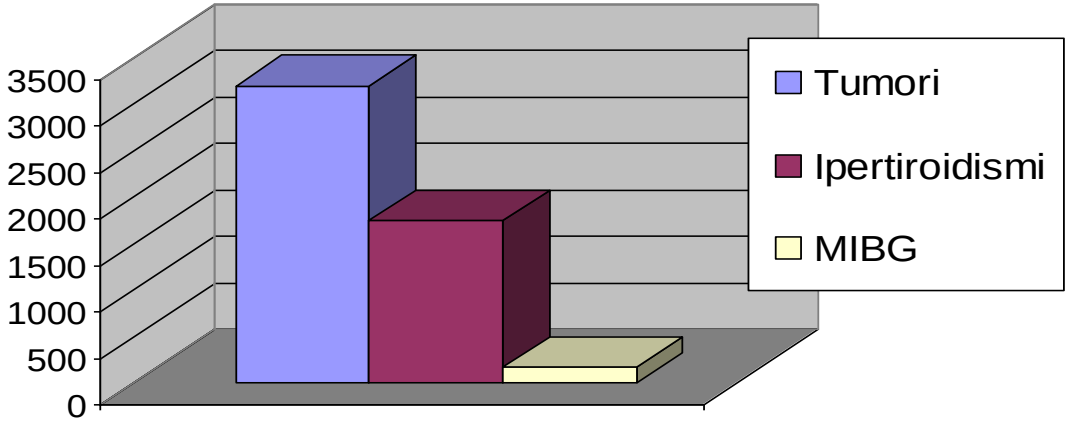
Posti letto in degenza protetta in Italia (2002)



Terapie con ^{131}I UCSC – Roma, 1990-2006





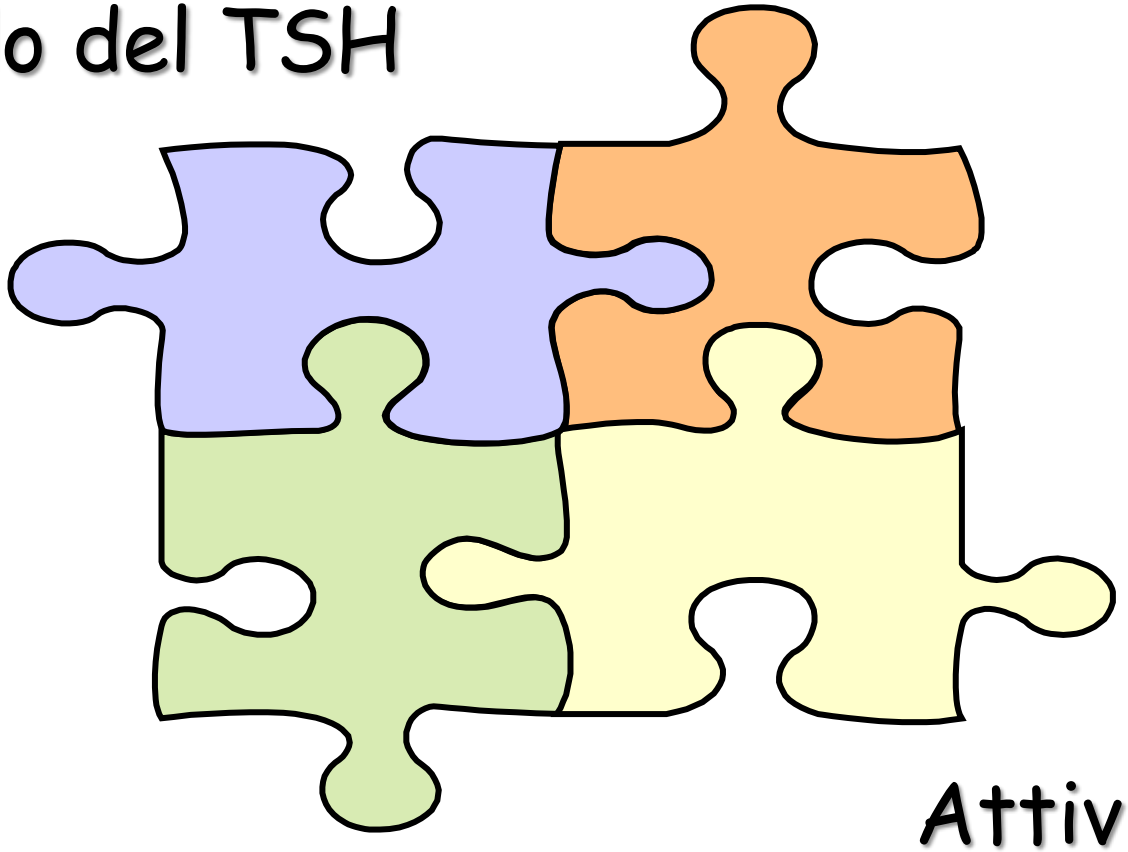
Trattamento con ^{131}I del CDT

- Trattamento ablativo
- Terapia delle recidive loco-regionali
- Terapia delle metastasi a distanza

Efficacia del Trattamento

Dieta ipoiodica

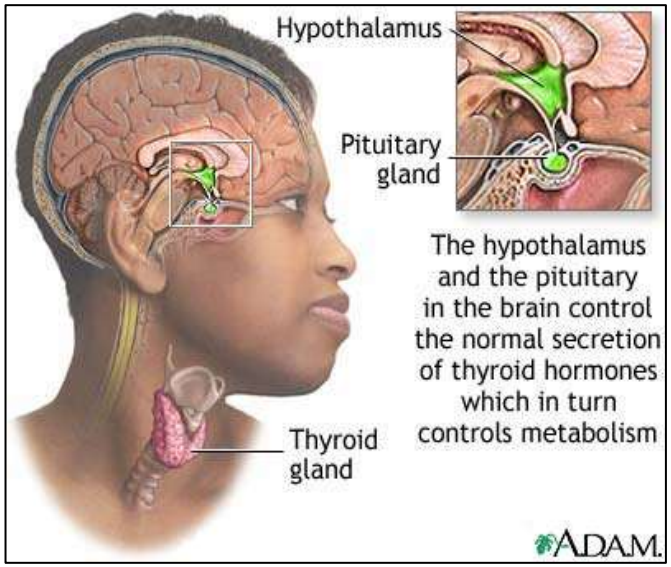
Stimolo del TSH

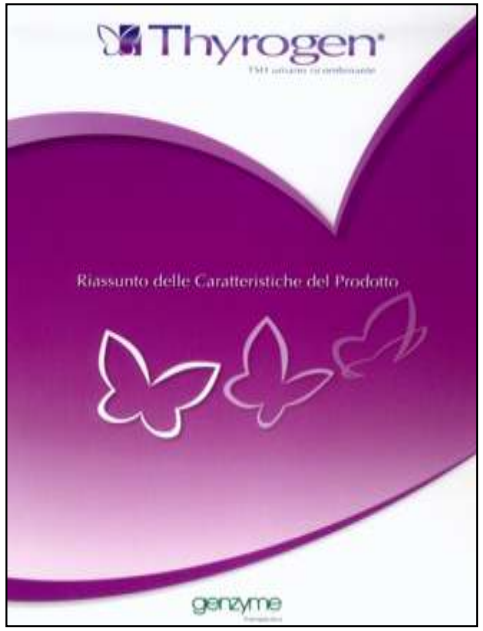


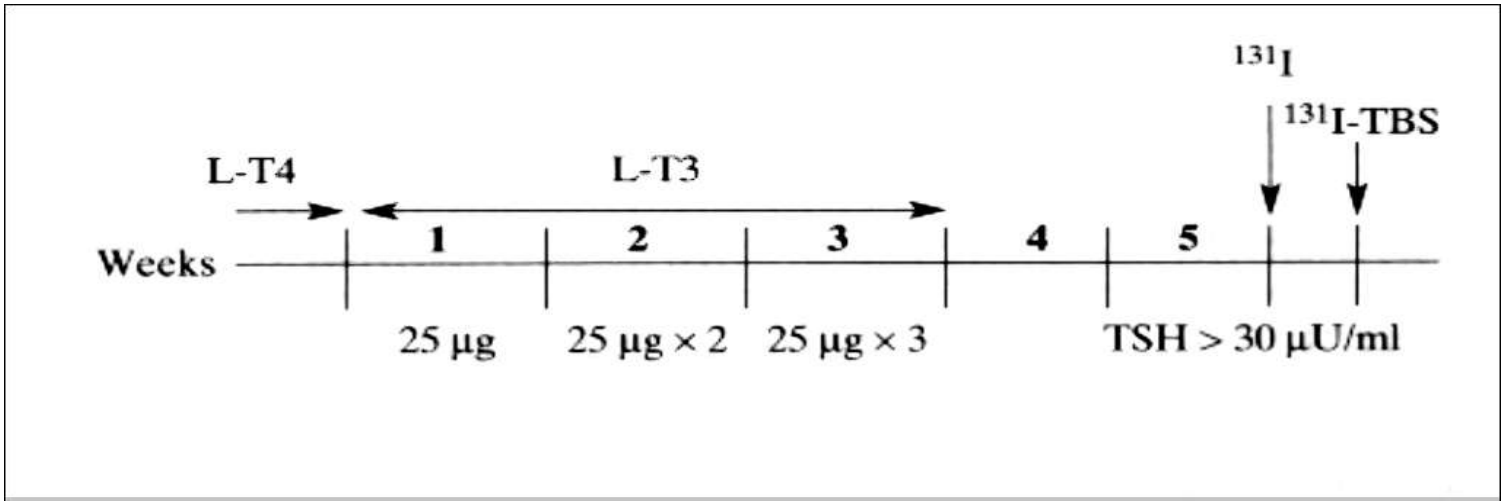
Attività di ^{131}I

Interferenze farmacologiche

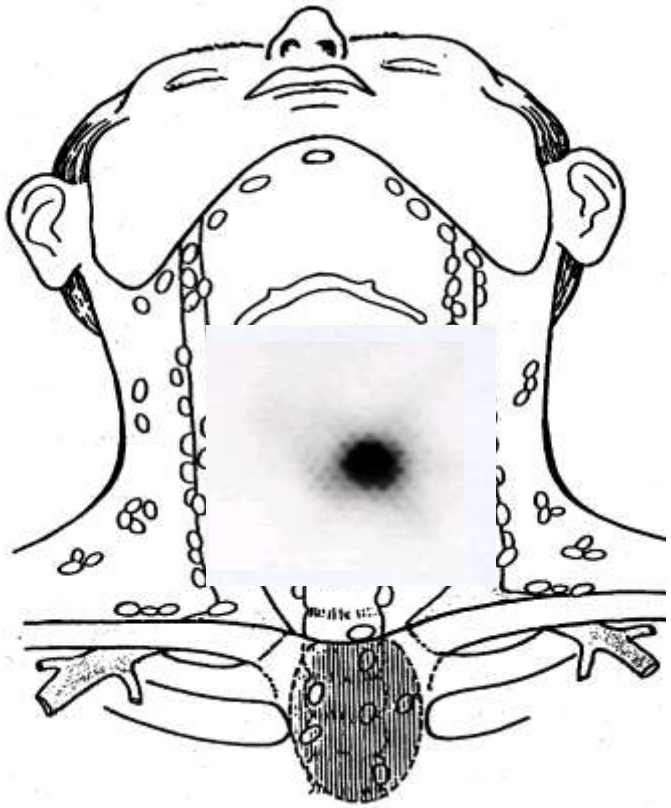
Stimolazione Endogena o Esogena del TSH



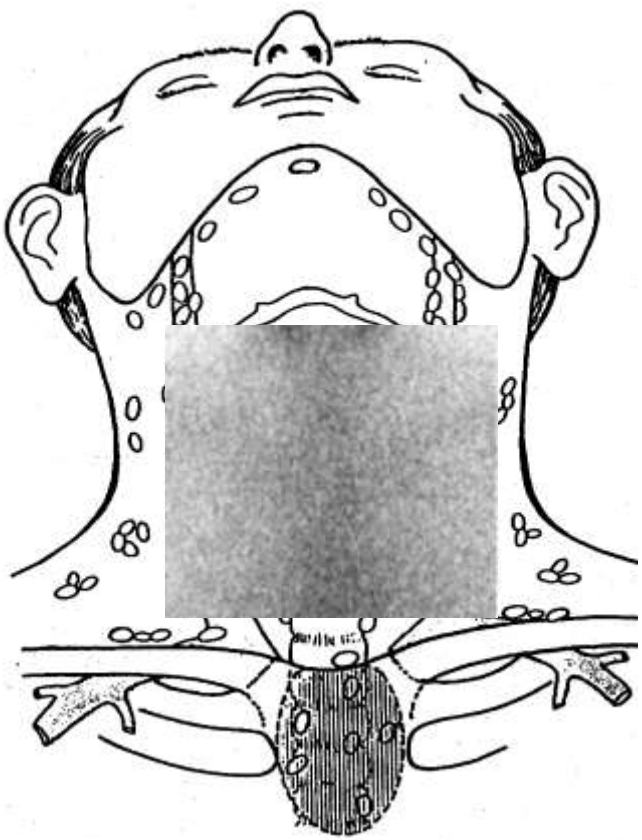




Trattamento Ablativo



Prima di ablazione con ^{131}I



Dopo ablazione con ^{131}I

Vantaggi teorici

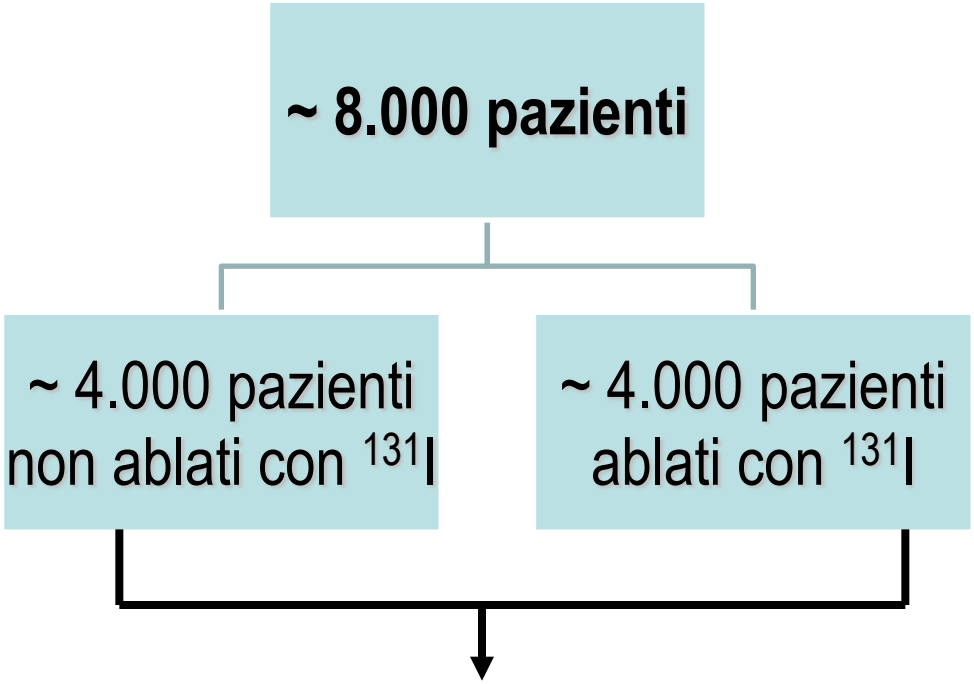
- Semplificare il follow-up (Tg,WBS)
- Eseguire un ^{131}I TxWBS
- Trattare la possibile multifocalità

Quali reali vantaggi clinici ?

- Riduzione di recidive
- Riduzione della mortalità

- Assenza di trial clinici randomizzati
- Soltanto studi retrospettivi

Studio randomizzato per dimostrare un aumento di sopravvivenza dopo ablazione con ^{131}I



riduzione di mortalità del 10% dopo 25 anni dal trattamento ablativo con ^{131}I

Wong et al 1990; Clinic Endocrinol Metab North Am 19:741

" *Bearing these concepts in mind, each physicians who treats thyroid cancer must decide from incomplete knowledge whether to use ^{131}I as a radioactive eraser. To ablate or not to ablate is a question that will haunt us for some time to come"*

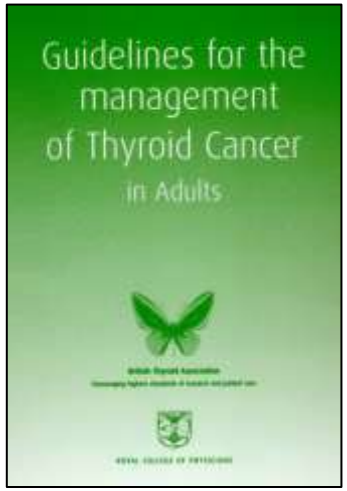
J.C.Sisson , J Nucl Med 1983 ; 24:743

Trattamento Ablativo con ^{131}I

Impiego
Estensivo

Uso
Selettivo

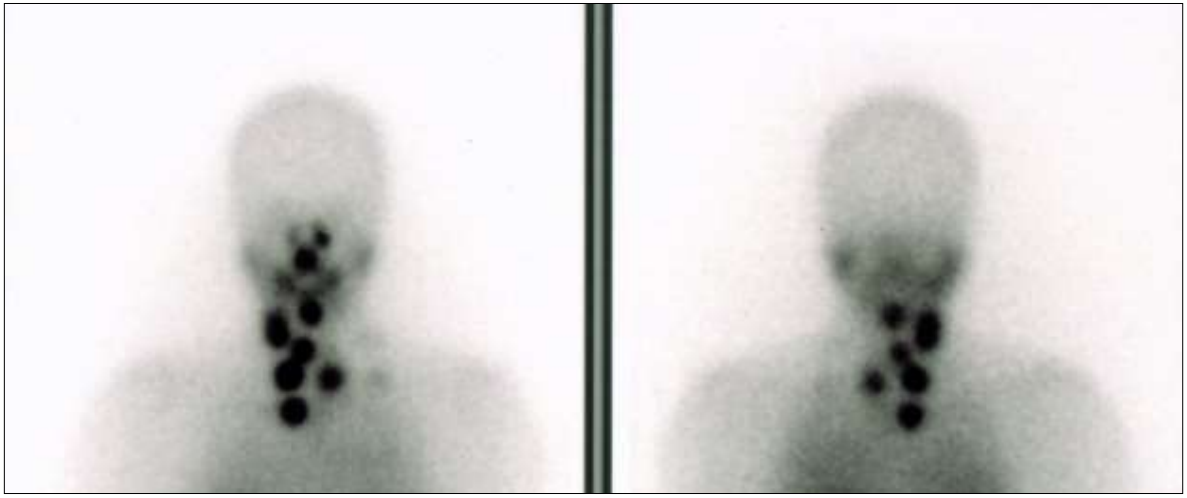
No indication (low risk of relapse or cancer-specific mortality)	**Probable indication** (use high or low activity (3.7 or 1.1 GBq (100 or 30 mCi))	**Definite indication** (use high activity (≥3.7 GBq (100 mCi)) after thyroid hormone withdrawal)
Complete surgery Favorable histology Unifocal T ≤1 cm, N0, M0 No extrathyroidal extension	Less than total thyroidectomy or No lymph node dissection or Age <18 years or T1 >1 cm and T2, N0 M0 Or unfavorable histology: Papillary: tall-cell, columnar-cell, diffuse sclerosing Follicular: widely invasive or poorly differentiated	Distant metastases or Incomplete tumor resection or Complete tumor resection but high risk for recurrence or mortality: tumor extension beyond the thyroid capsule (T3 or T4) or lymph node involvement

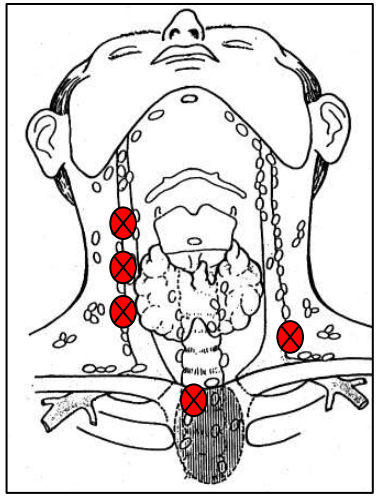


Take Home Message

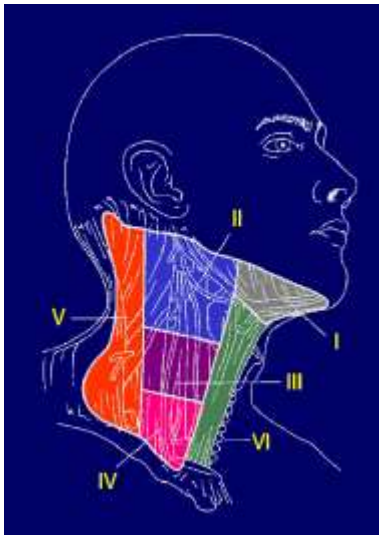
- ✓ L'indicazione va posta su base individuale e la maggior parte dei pazienti a basso rischio non necessita di trattamento ablativo di principio.
- ✓ Una corretta indicazione al trattamento è quella posta per pazienti a rischio di recidiva o di mortalità tumore-specifica.
- ✓ Anche se non eseguito subito dopo la chirurgia, il trattamento può essere somministrato alcuni mesi più tardi in pazienti con persistenti elevati valori di Tg

Recidive loco-regionali



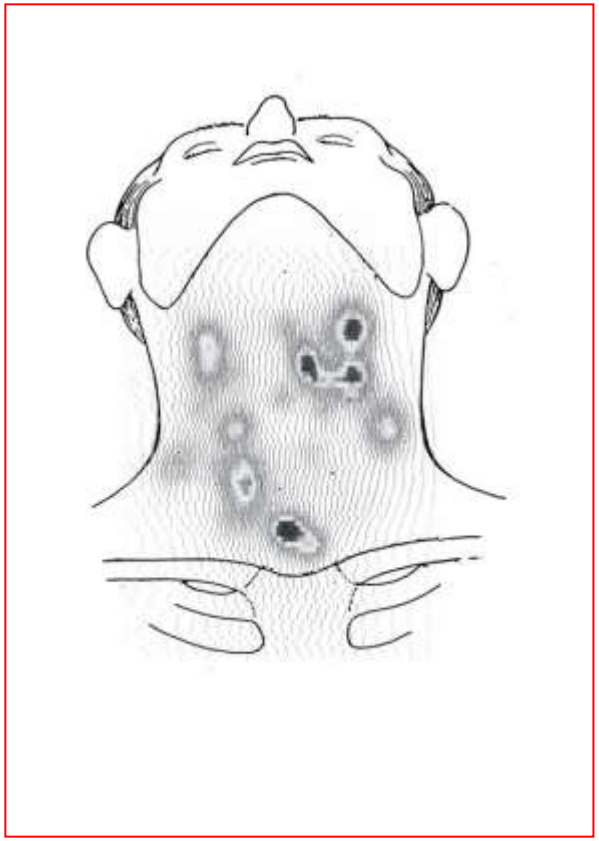


80 – 120 Gy	80% di risposta completa
< 30 – 40 Gy	risposta di fatto assente



Chirurgia Radioguidata

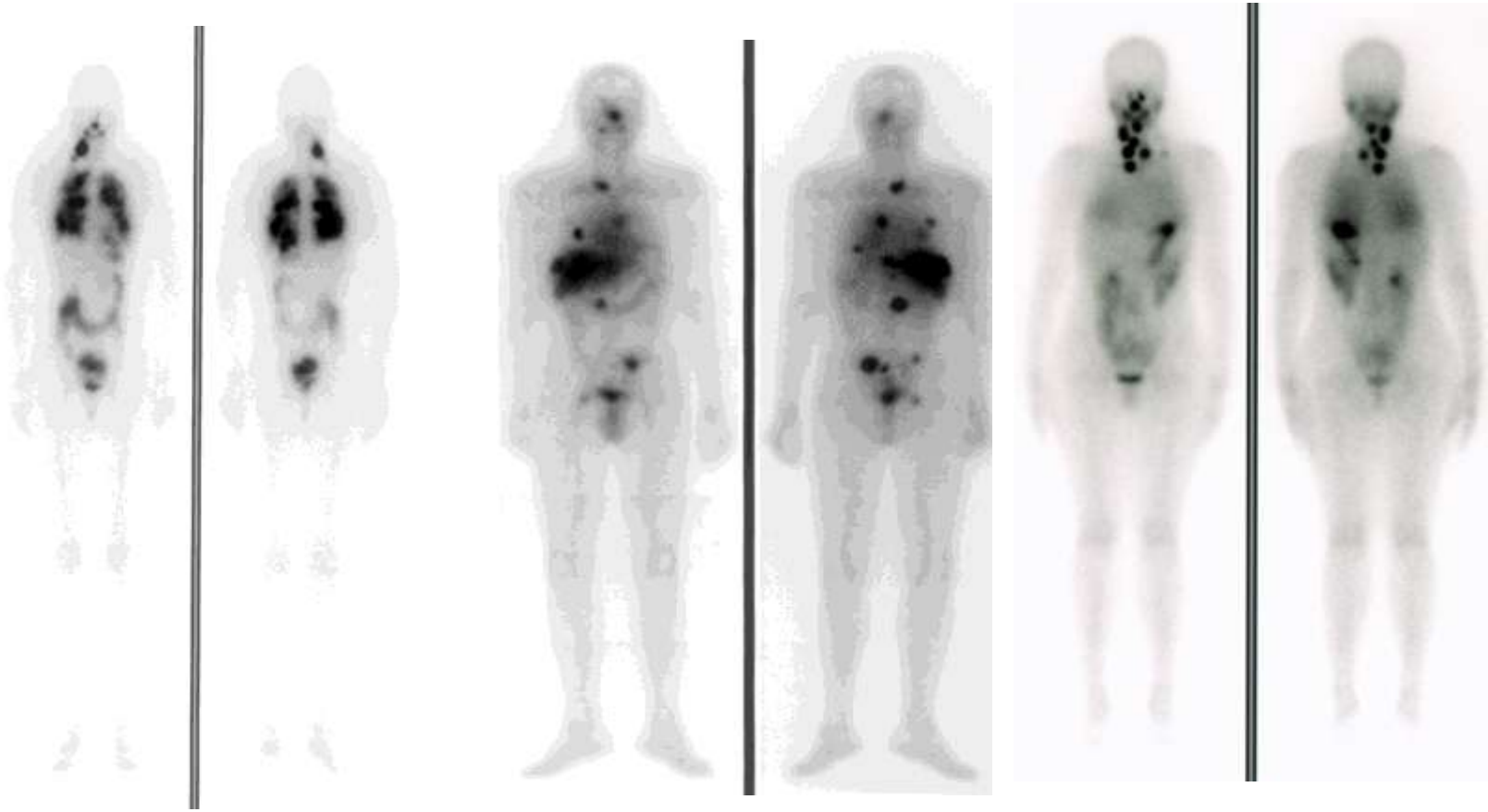
Sonda per chirurgia RG



^{131}I WBS pre-chirurgia

^{131}I WBS post-chirurgia

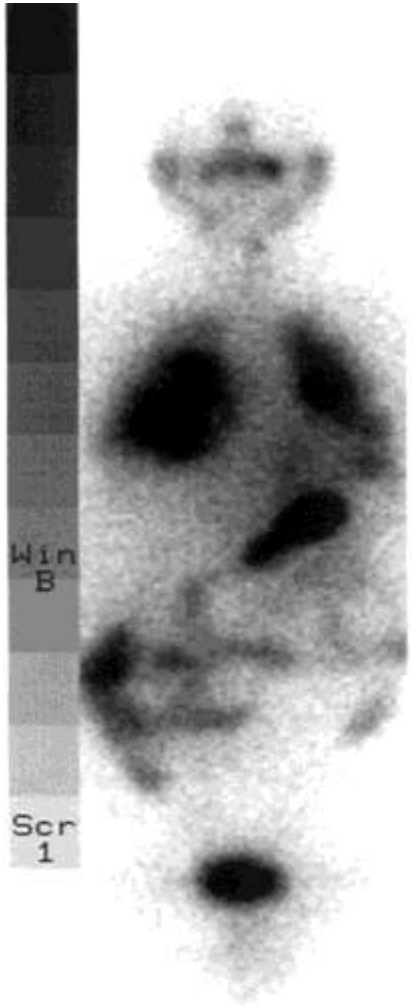
Metastasi a Distanza



Principali schemi di trattamento

Beierwaltes (1978)	150-175 mCi per metastasi linfonodali 175-200 mCi per metastasi polmonari 200 mCi per metastasi ossee
Schlumberger et al. (1996) Hindiè et al. (2003)	100 mCi ogni 3-6 mesi fino ad ottenere un TxWBS negativo
Brown et al.(1984)	150 mCi ogni 3-4 mesi
Petrich et al (2001)	100 mCi, con TxWBS positivo vengono somministrati subito altri 200 mCi
Menzel et al (1996)	300 mCi ad intervalli di 3 mesi

Metastasi polmonari iodocaptanti



pattern diffuso

pattern focale

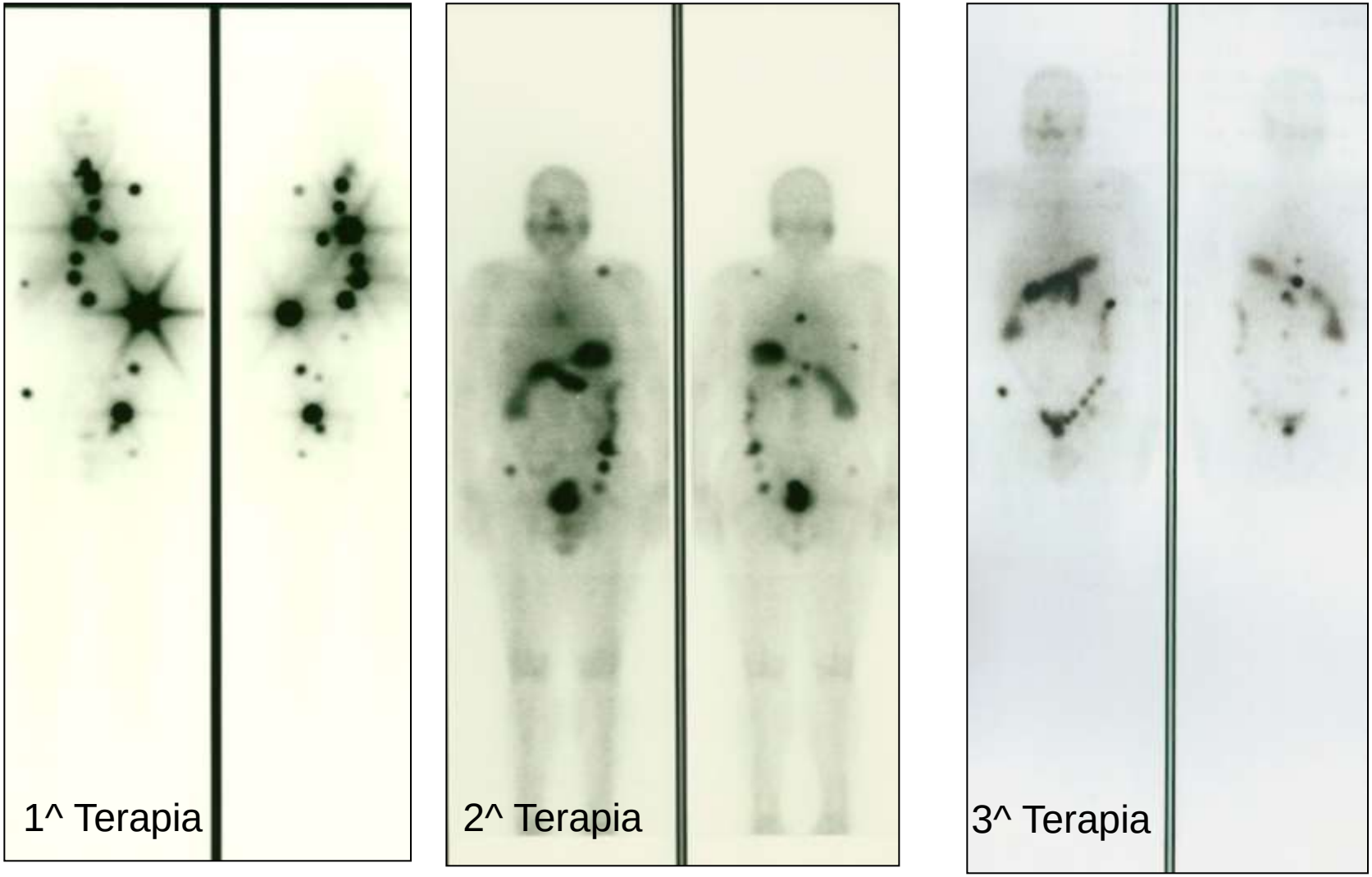
Metastasi polmonari non-iodocaptanti

Outcome *vs.* Pattern Scintigrafico/Radiologico

N. pazienti	^{131}I-WBS	Sopravvivenza a 10 anni	Remissione completa
42 (31%)	^{131}I + Rx -	96 %	78 %
54 (40%)	^{131}I + Rx +	36 %	3.7%
38 (29%)	^{131}I - Rx +	11 %	0.0%

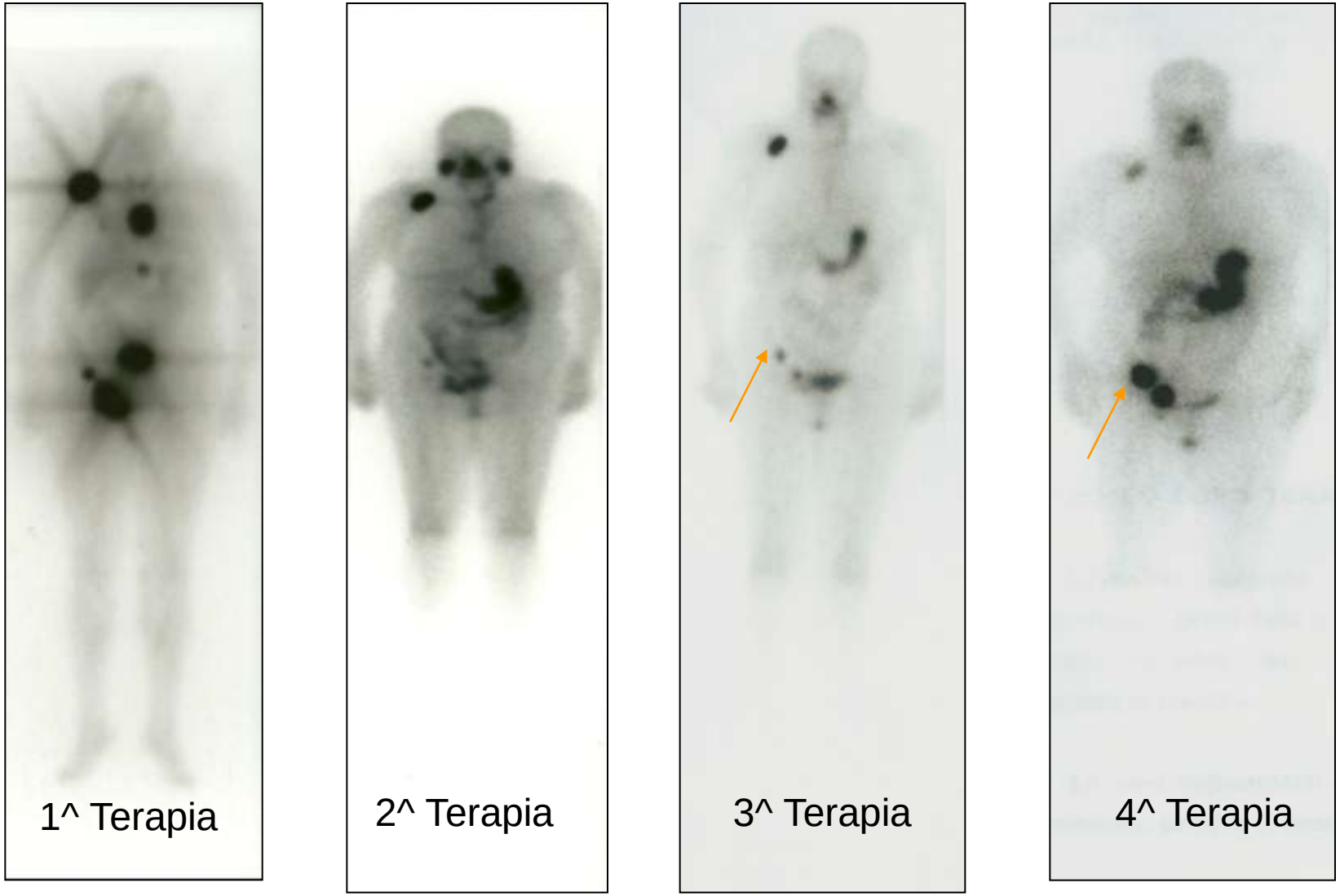
Casara D et al. J Nucl Med 1993

Metastasi scheletriche



V.C., maschio, anni 70 , mts. ossee, attività cumulativa 600 mCi

Metastasi scheletriche



E.P., femmina, anni 73, mts. ossee, attività cumulativa 750 mCi

Risposta al Trattamento

SEDE di mts. & N° pazienti	RISPOSTA COMPLETA	RISPOSTA PARZIALE	ASSENZA DI RISPOSTA
Linfonodi 85 pts	**68.2 %**	**18.8%**	**12.5%**
Polmone 292 pts.	**45.9%**	**27.7%**	**24.5%**
Scheletro 233 pts.	**6.8%**	**35.6%**	**54.2%**

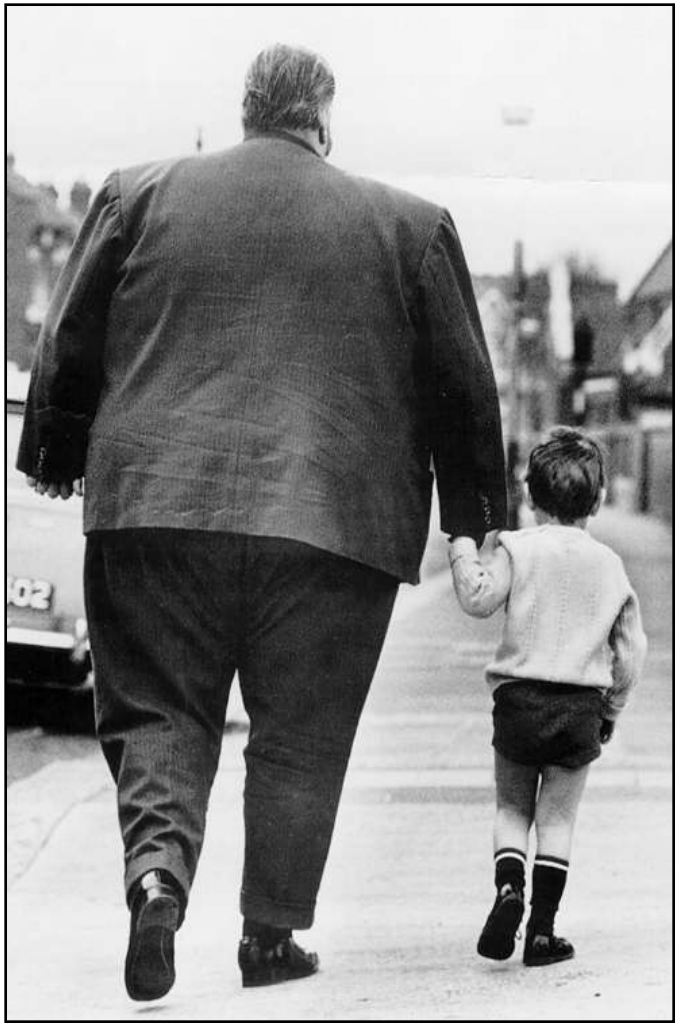
Maxon III HR et al. End Metab North Am 19:685-718,1990

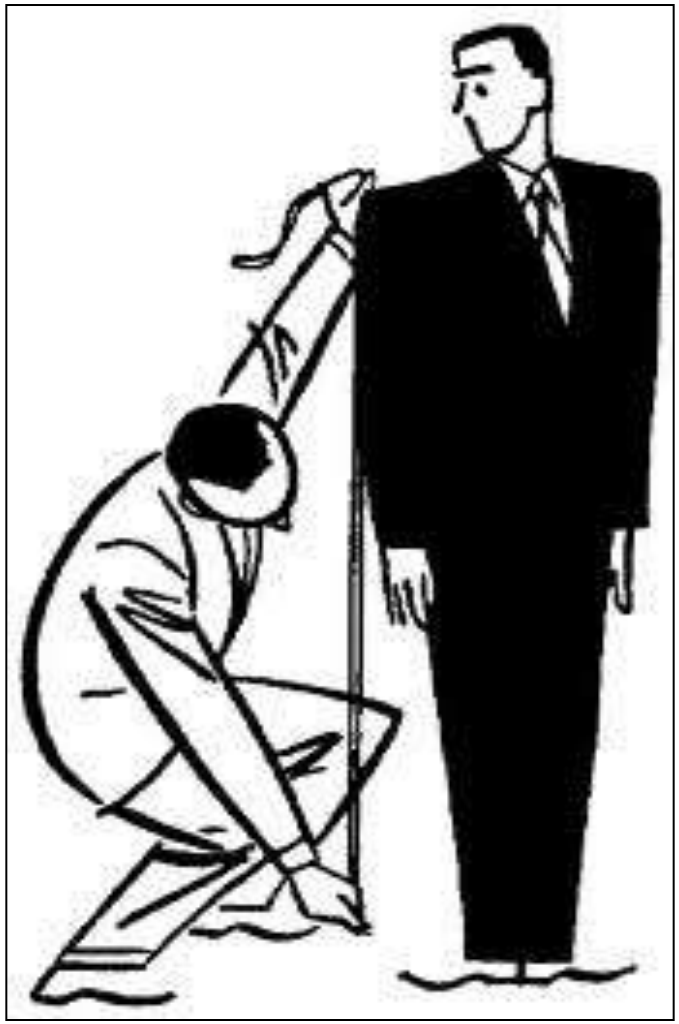
Tassi di Sopravvivenza a 10 anni

SEDE DI METASTASI	TASSI DI REMISSIONE	SOPRAVVIVENZA A 10 ANNI
Metastasi Polmonari e Scheletriche	7 %	13%
Metastasi Polmonari	50%	61 %
Metastasi Scheletriche	10 %	21%

Schlumberger M. et al. J Nucl Med 1996; 37:598

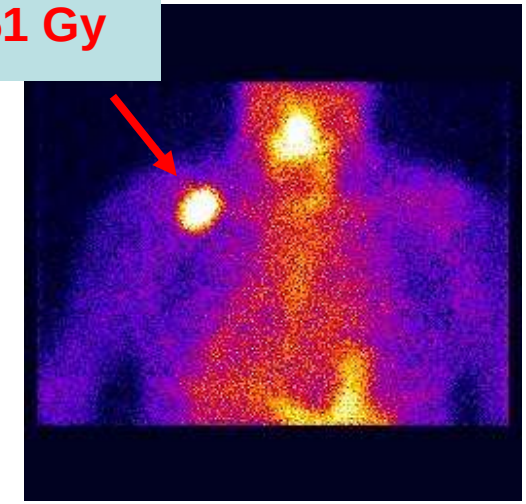
Ottimizzare meglio il trattamento

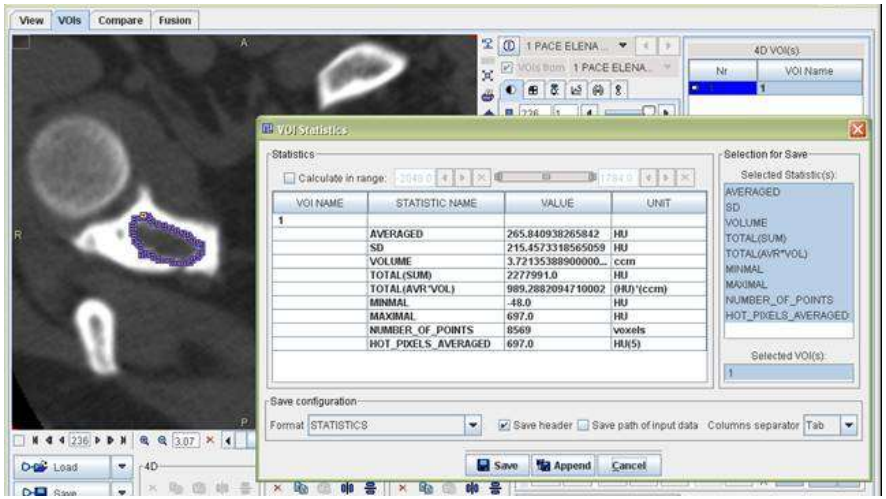




Dosimetria previsionale e terapeutica

51 Gy



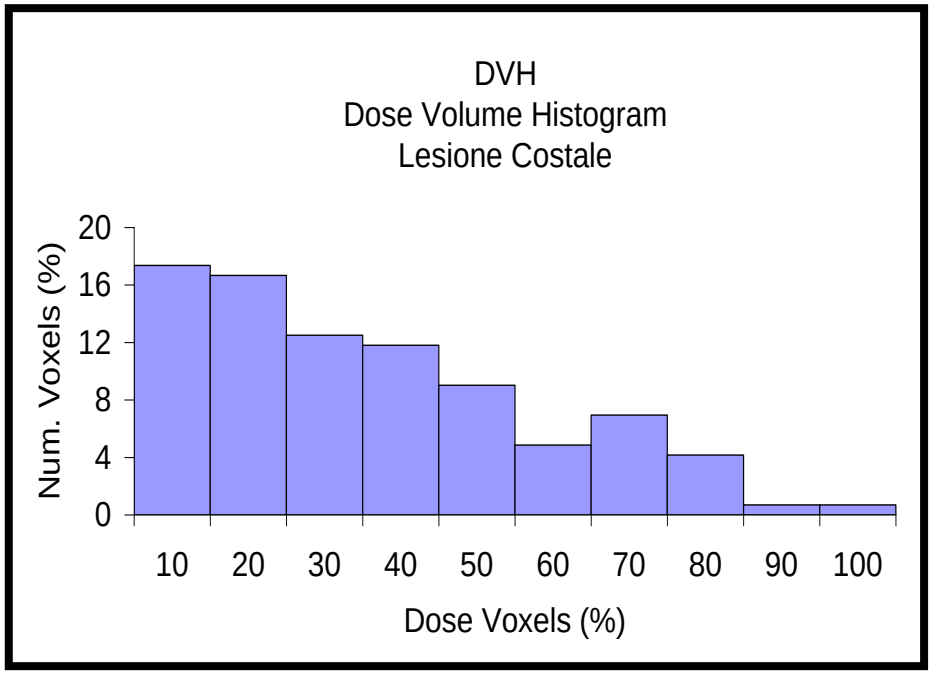


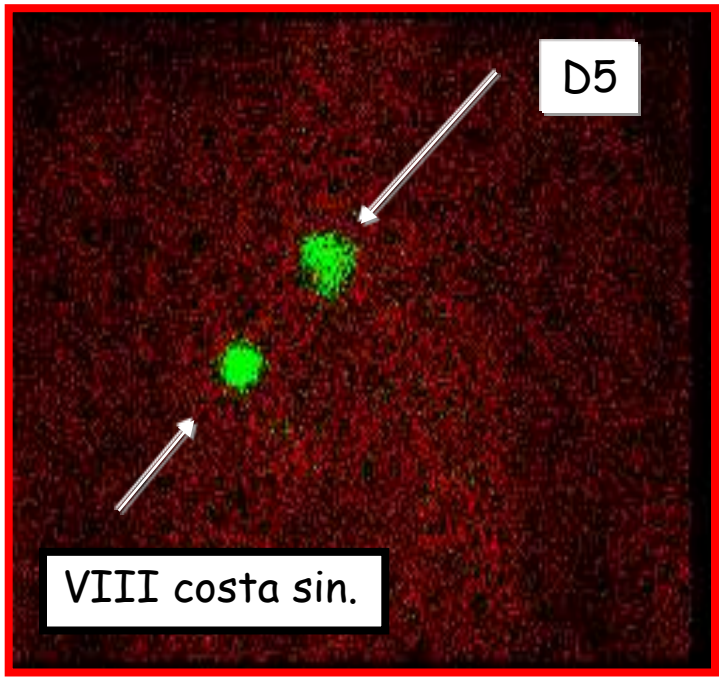
Dosimetria	Attività (GBq) **(per 2 Gy Sangue)**	Attività (GBq) **(2 Gy Dose Midollo)**	Attività (GBq) **(80 Gy Lesione)**
Previsionale	**21.0**	**29.4**	**7.6**

Terapeutica	**20.9**	**28.9**	**11.1**

C2- P004
Policlinico Gemelli - Roma

Dosimetria previsionale





Dose < 15 Gy in entrambe le lesioni

Paziente candidato ad asportazione chirurgica della lesione costale ed a EBRT della lesione vertebrale

Vi ringrazio per l'attenzione