CURICULUM VITAE

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Current position

1. Head, Department of Nuclear Medicine and Molecular Imaging Faculty of Medicine, Universitas Padjadjaran
2. Country Principle of Asian School of Nuclear Medicine
3. Vice Dean of Asian School of Nuclear Medicine
4. Editorial Board Asia Oceania Journal of Nuclear Medicine

Education :

1. 1984 : Medical Doctor	: Faculty of Medicine, Universitas Padjadjaran
2. 1996 : NM Specialist	: MDS-IDI
3. 2007 : Master of Health Law	: Faculty of Law, Soegiyapranata University
4. 2014 : PhD	: Faculty of Medicine, Universitas Padjadjaran
5. 2014 : Fellow ANMB	: Asian Nuclear Medicine Board

Training / Workshop:

1. Post Graduate Training Course on Nuclear Medicine, ANSTO-RPAH Sydney, Australia 1985 - 1986.
2. Training Course on Nuclear Medicine Data Processing, Nagoya Cancer Centre, Japan, April 1986.
3. Regional Train-the Trainers Course on Data Processing in Radioimmunoassay, IAEA-BATAN, Jakarta Indonesia, July1987.
4. Interregional Training Course on Nuclear Medicine, IAEA-CIAMS, Moscow-USSR, September – November 1987.
5. The National Course on the Application of Nuclear Technique in Medicine, BATAN-ANSTO-RSHS, Bandung 1988.
6. Training on SPECT Camera, Rossville Hospital, San Jose, USA, 1988.
7. Regional Training Course on the Use of Computer in Nuclear Medicine, IAEA-ANSTO, Sydney Australia, 1990.
8. Training Course on Nuclear Medicine, Dept. of Nuclear Medicine, St. German en Laye Hospital, Paris, France, 1994.
9. Fellowship on Nuclear Medicine, IAEA-St. Bartholomew's Hospital, London UK, 1995 - 1996.
10. RCA Training Course on Application of Positron Emission Tomography (PET) in Clinical Practice for Nuclear Medicine Physicians. IAEA-Cardiovascular Institute Fu Wai Hospital. Beijing, China, 2000.
11. RCA Training Workshop on Scintimammography, Sentinel Lymph Node Detection and Intra-Operative Surgical Probe Technology, IAEA-NORI, Islamabad, Pakistan, 2001.
12. RCA) Training Course on Myocardial Perfusion Scintigraphy for Nuclear Medicine Physicians. IAEA-NIRS Chiba, Japan, 2003.
13. RCA) Training Course on Interventional Nuclear Medicine. IAEA-New Delhi, India, 2003
14. IAEA/RCA Project Planning Meeting on "Tumor Imaging Using Radioisotopes" Chiba, Japan, April 2005
15. Research Ethics & Good Clinical Practice Training, Bandung 2011
16. Workshop on Quality Control of Nuclear Medicine Instruments, IAEA-BATAN Bandung, Indonesia, April 1985.
17. Workshop on Radio-aerosol Inhalation Lung Imaging in Developing Countries, IAEA-BARC Bombay, India 1987.
18. Workshop on Liver Imaging, IAEA-Seoul Catholic Hospital, Seoul, Korea, 1989.
19. RCA Training Workshop on Scintimammography, Sentinel Lymph Node Detection and Intra-Operative Surgical Probe Technology, IAEA-NORI, Islamabad, Pakistan, 2001
20. ANSN-IAEA Regional Workshop on Medical Emergency Preparedness and Response, Jakarta 2011

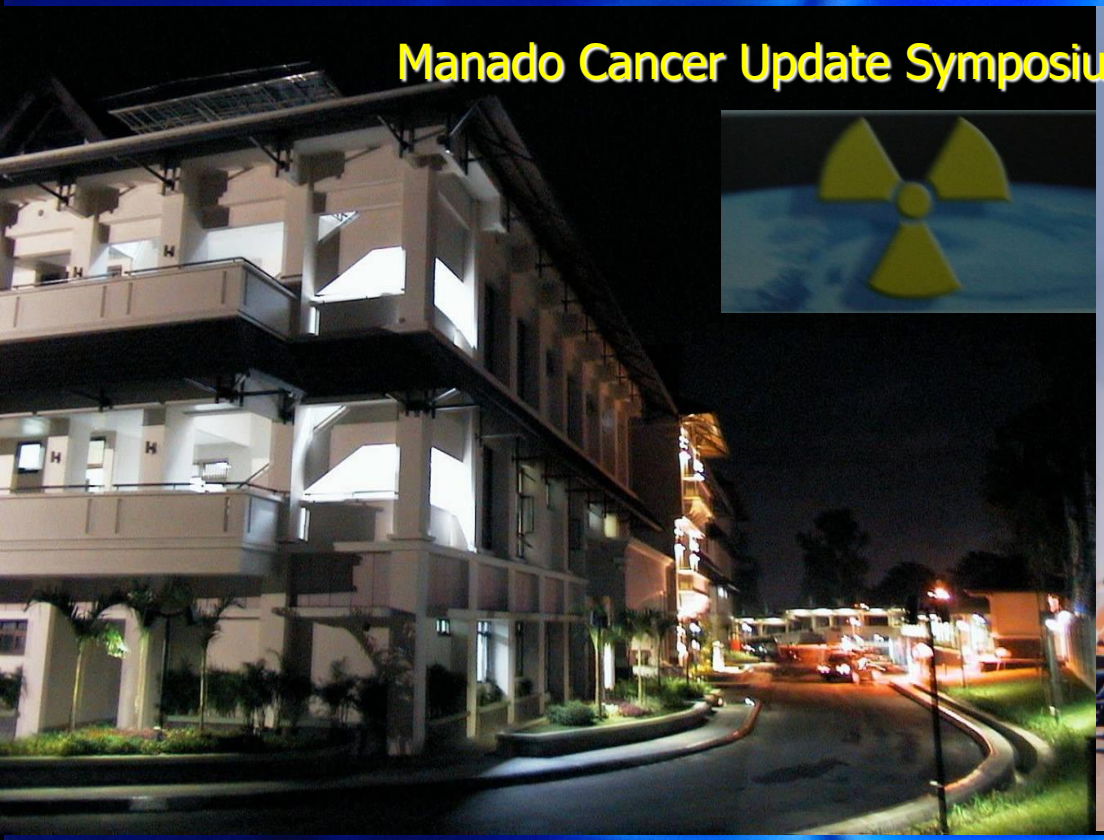
Publications: 131

Organization:

1. Indonesian Medical Association (IDI)
2. Indonesian Society of Nuclear Medicine and Biology (PKBNI)
3. Indonesia Society of Nuclear Medicine (PKNI)
4. Asia Oceania Federation of Nuclear Medicine and Biology (AOFNMB)
5. World Federation of Nuclear Medicine and Biology (WFNMB)
6. Asia Regional Community Council of Nuclear Medicine (ARCCNM)
7. Society of Nuclear Medicine and Molecular Imaging
8. World Association of Radiopharmaceutical and Molecular Therapy

The Role of Nuclear Medicine in Cancer Management

Manado Cancer Update Symposium, 27 January 2018



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OUTLINE

Nuclear medicine
Diagnostic in malignancy
Radionuclide Therapy in malignancy

ATOMIC BOM ATOM HIROSHIMA – NAGASAKI

CHERNOBYL

FUKUSHIMA (TSUNAMI)

Definition :

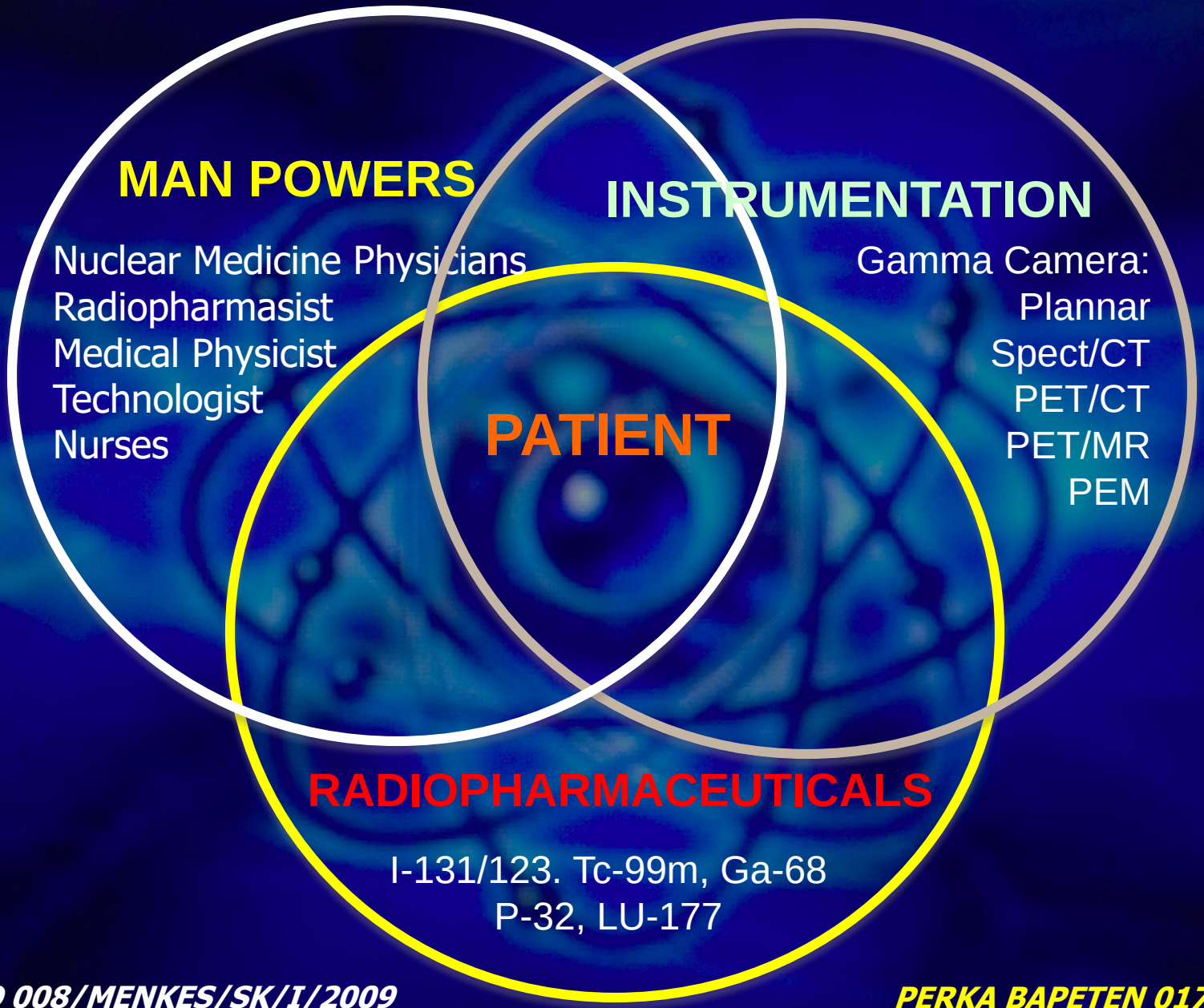
Nuclear Medicine is defined as a medical specialty which uses the nuclear properties of matter to investigate physiology and anatomy, diagnosis diseases, and to treat with unsealed sources of radionuclide.

(IAEA/WHO, 1988).

PELAYANAN KEDOKTERAN NUKLIR

PELAYANAN KEDOKTERAN NUKLIR ADALAH PELAYANAN PENUNJANG DAN/ATAU TERAPI YANG MEMANFAATKAN SUMBER RADIASI TERBUKA DARI DISINTEGRASI INTI RADIONUKLIDA YANG MELIPUTI PELAYANAN DIAGNOTIK IN-VIVO DAN IN-VITRO MELALUI PEMANTAUAN PROSES FISIOLOGI, METABOLISME DAN TERAPI RADIASI INTERNAL

KEPMENKES NO 008/MENKES/SK/I/2009



KMK NO 008/MENKES/SK/I/2009

PERKA BAPETEN 017/2012

Nuclear Medicine

- Cerebrovascular disease
- Alzheimer' s disease
- Schizophrenia, Epilepsy
- Neurotransmitter study

- **Sciintimammography**
- **Sentinel node detection**

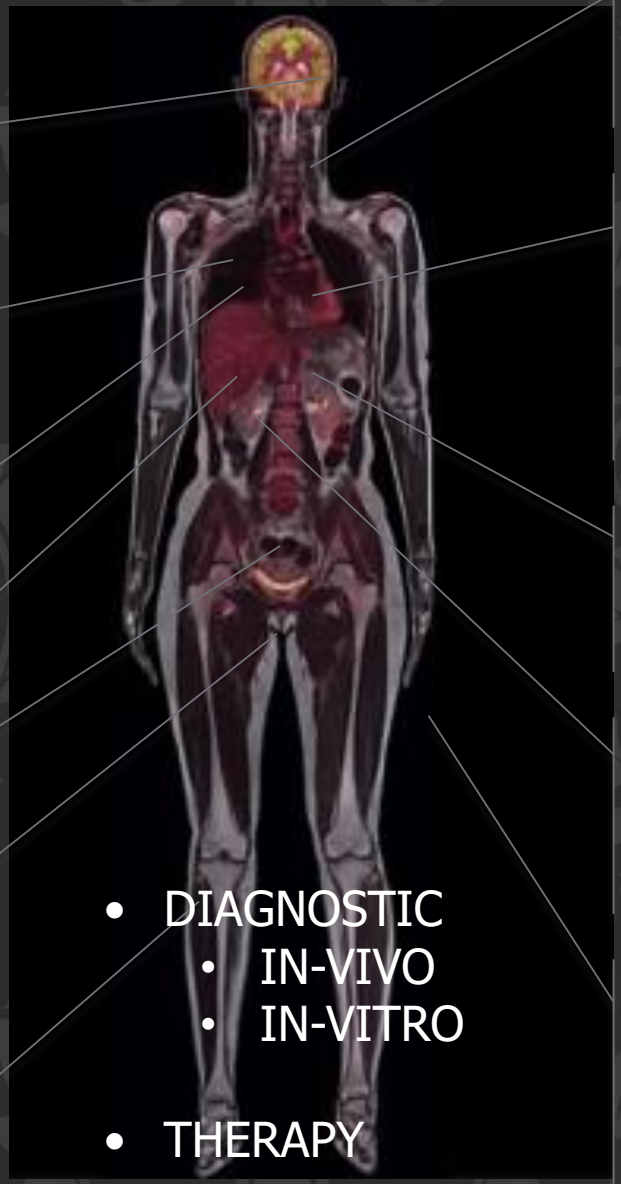
- V/Q Scan --→ PE
- Regional lung function

- Hepatobiliary scan

- Cystography

- Testicular scan

- Flebography
- Venography
- Lymphoscintigraphy



- DIAGNOSTIC
  - IN-VIVO
  - IN-VITRO
- THERAPY

- **Thyroid Scan**
- Thyroid Uptake
- Neonatal hypothyroidis

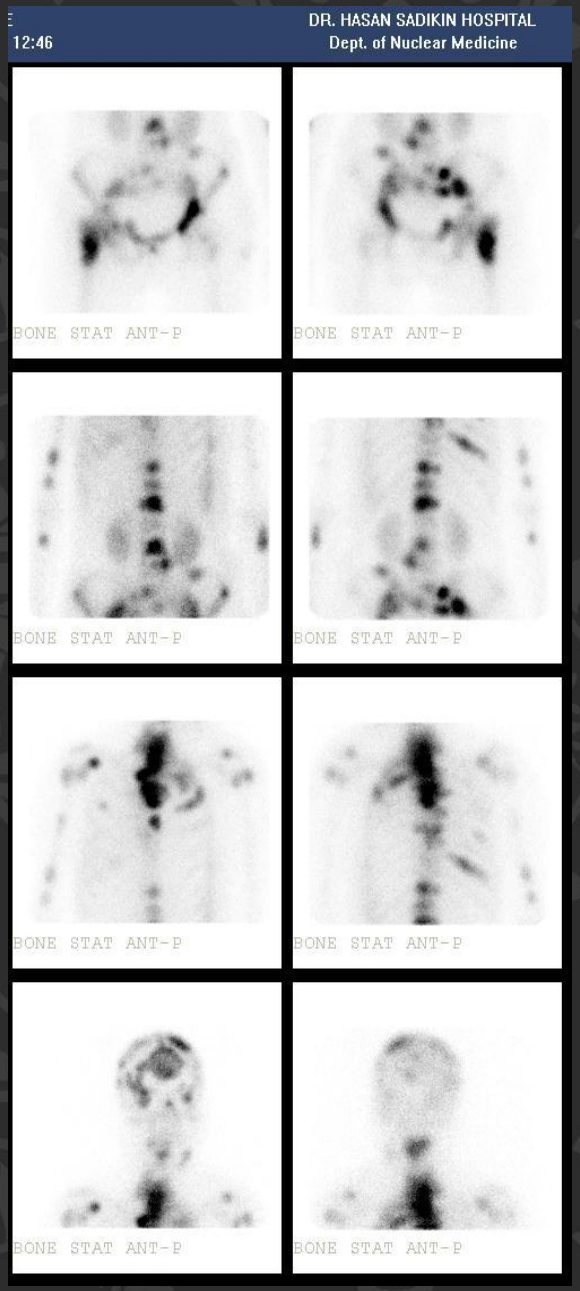
- Myocardial Perfusion Study,
- Viability Study ➔ risk stratification
- Neuroreceptor imaging
- Prevention of restenosis
- Cardiac function

- Oesophageal transit time
- Gastric emptying time
- Gatro-oesophageal reflux

- Renography
- GFR
- ERPF
- Renal scan

Whole body scanning

- **Bone scan**
- **PET**
- Infection scan



Bone Scintigraphy Tc-99m MDP

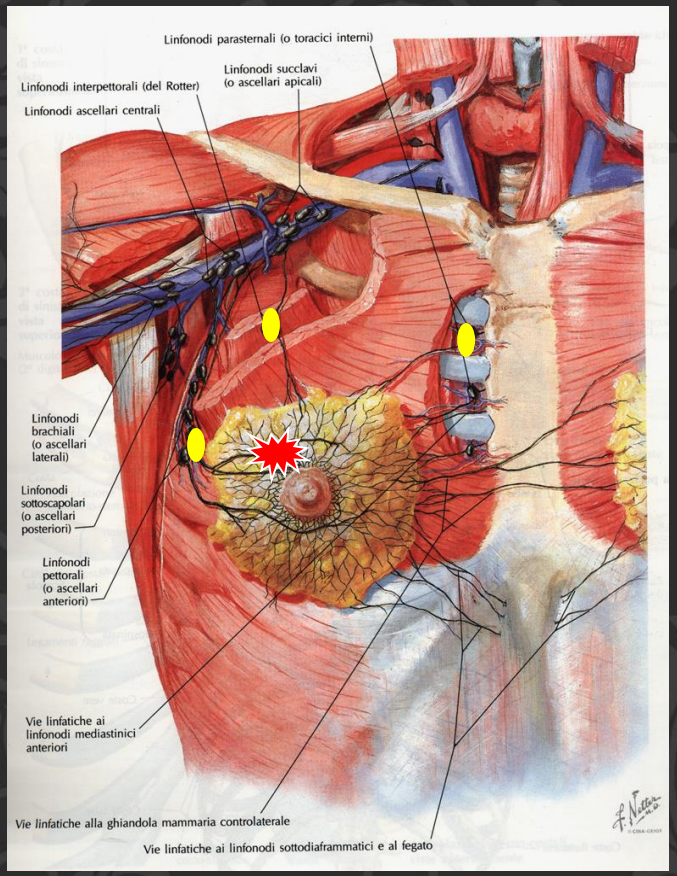
Indications of bone scintigraphy :

- Early detection of bone metastases ➔ staging
- Therapy monitoring

- Bone is the predilection site of metastases : carcinoma of the lung, breast, prostate, kidney, and thyroid

- Increased accumulation of phosphonates at the site of increased osteoblastic activity
  ➔ labeled phosphonate will be seen as hot spots

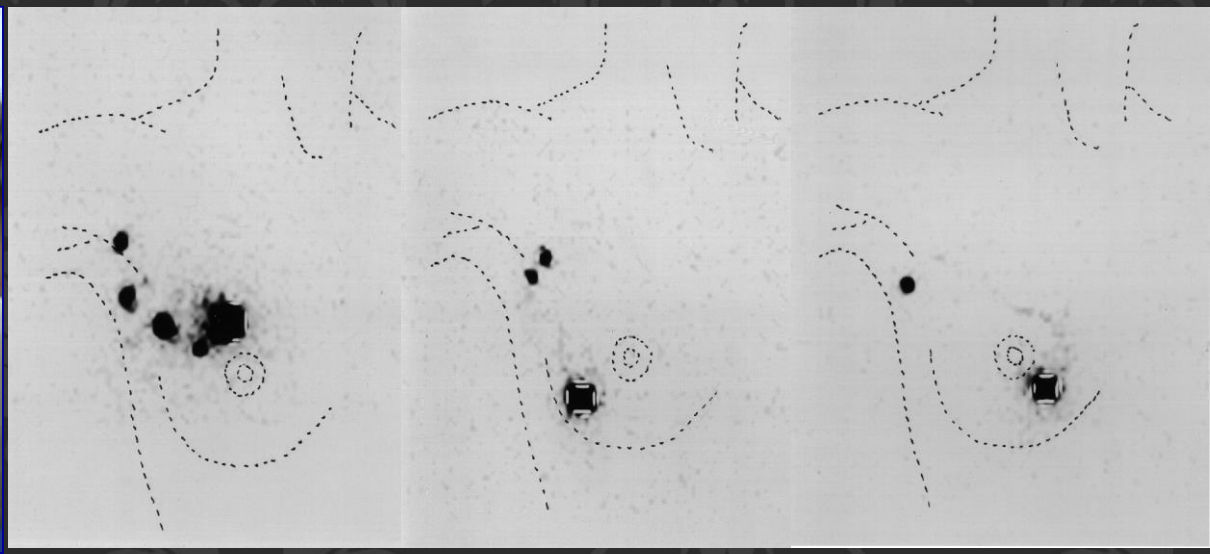
SENTINEL NODE LYMPHOSCINTI GRAPHY

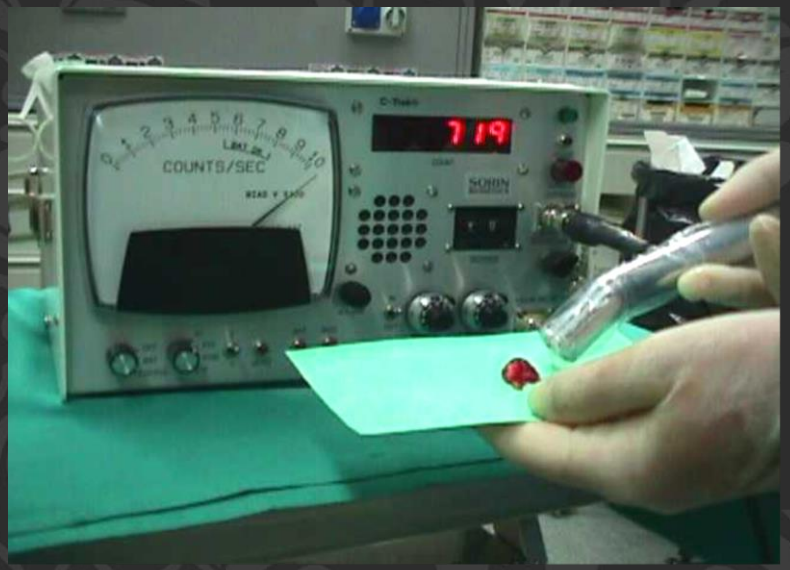


Basic consideration of sentinel node staging of the axilla

- Axillary node dissection for staging early breast cancer is a high morbidity procedure (arm lymphedema, pain, limited motion and paresthesia);
- Approx. 60% women with early breast cancer have no tumor found on routine staging axillary dissection;
- Compared with axillary dissection, sentinel node shows micrometastases more frequently.

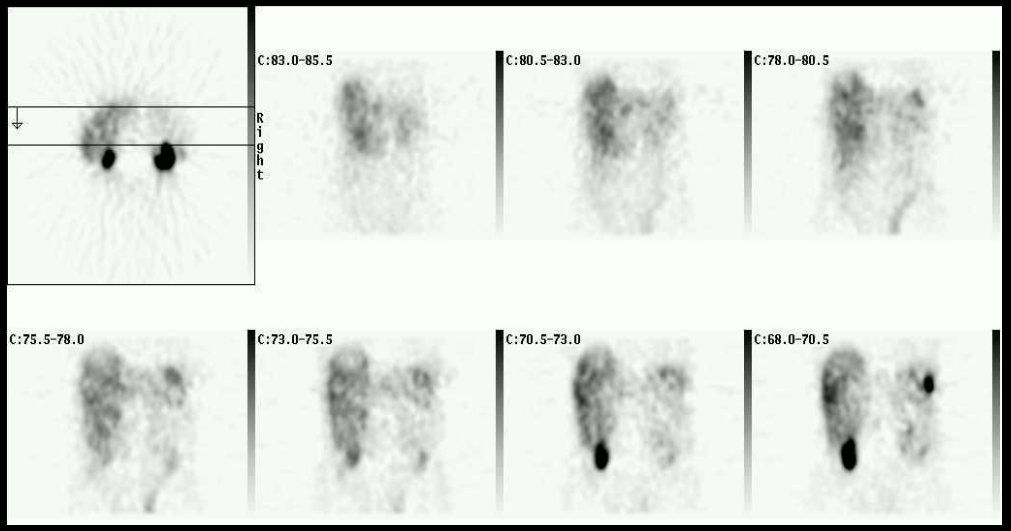
(Alazraki et al., 2001)



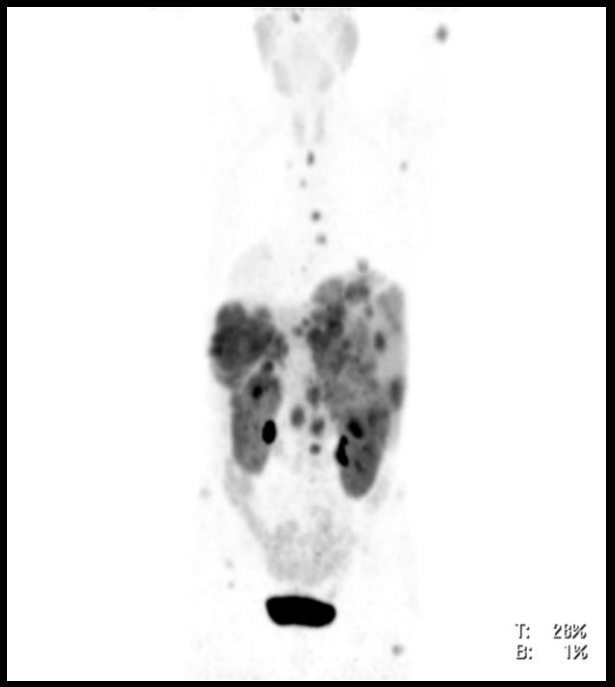


The axillary dissection is probably unnecessary for the patients in whom the SN is negative !

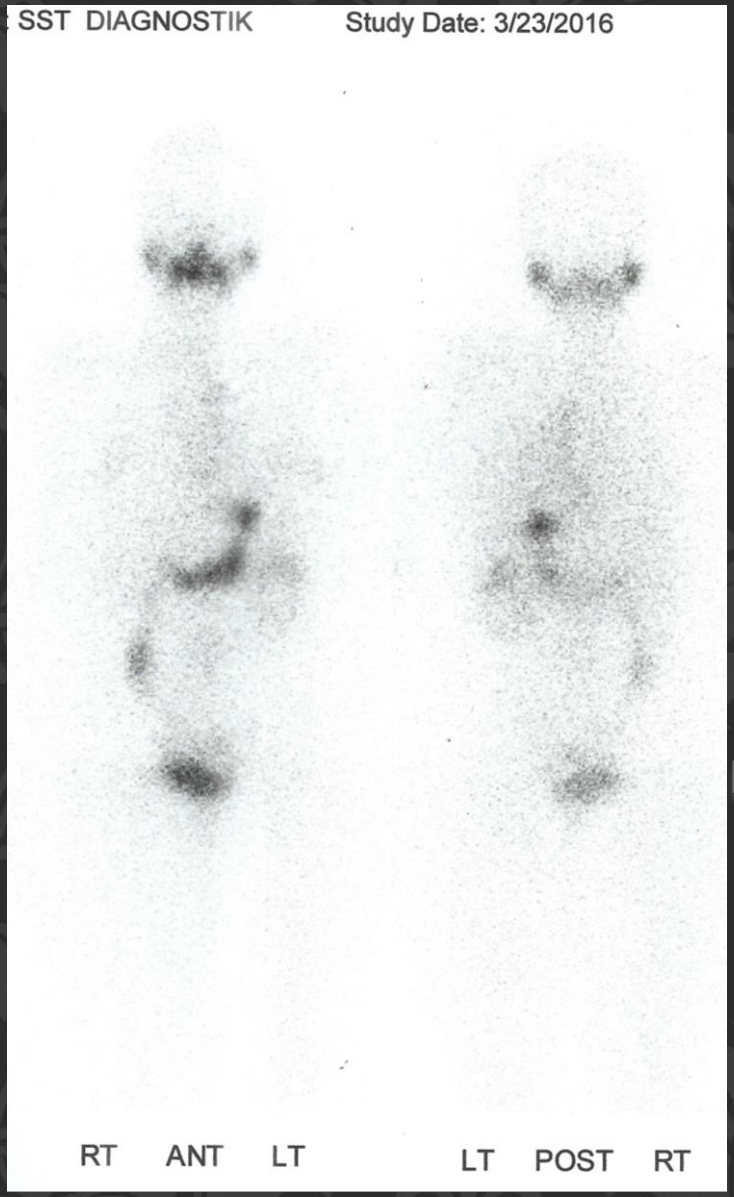
Female With Metastatic NET

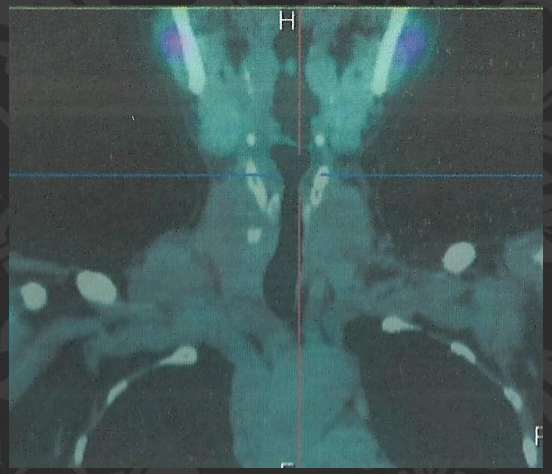


^{111}In-Octreotide



^{68}Ga-Octreotate

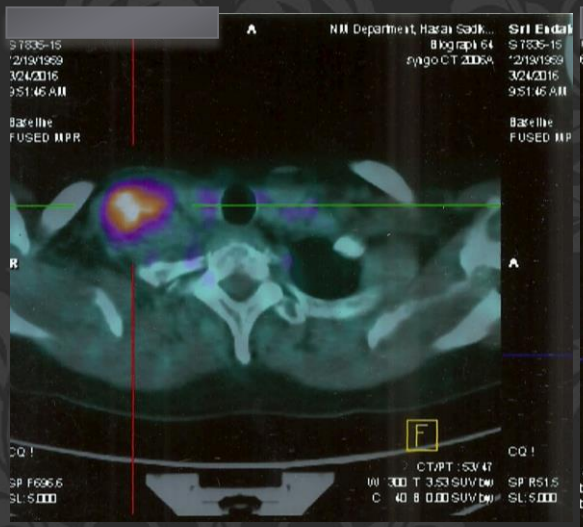




F 56 yrs papillary thyroid ca

Post Total Thyroidectomy and ^{131}I ablation (100 mCi)

- Negative ^{131}I- scan
- Tg : 18.5 ng/dL
- Anti-Tg : > 3000 U/mL



Mediastinal Staging of Non-small Cell Lung Cancer

	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)	Prevalence (%)
CT	57	82	83	56	28
PET	84	89	93	79	32
Blind TBNA	76	96	71	100	70
EUS-FNA	88	91	77	98	69
Mediastinoscopy	81	100	91	100	37

P. De Leyn et al. EJCTS 2007;32: 1-8

Monitoring Response to Therapy

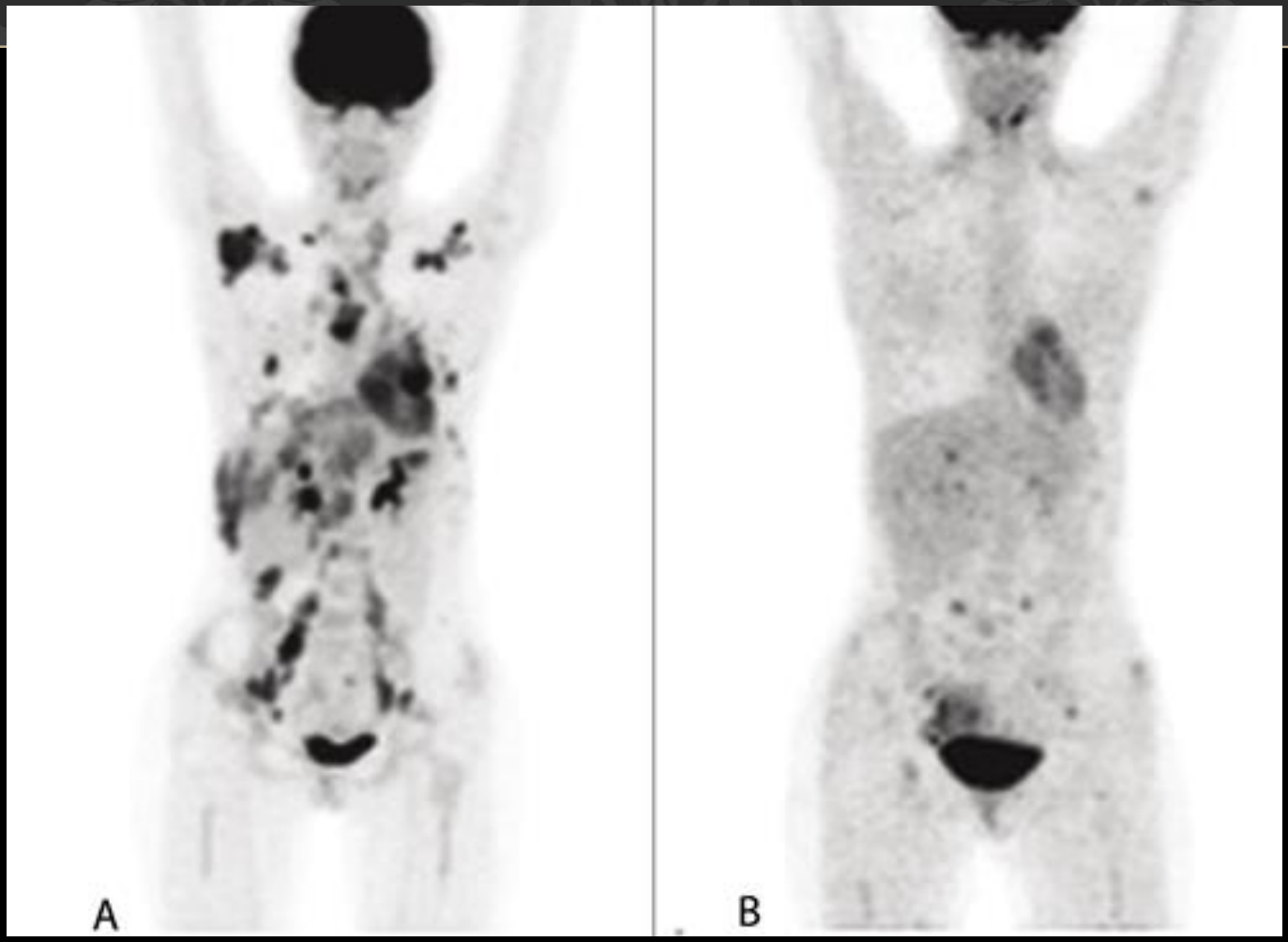
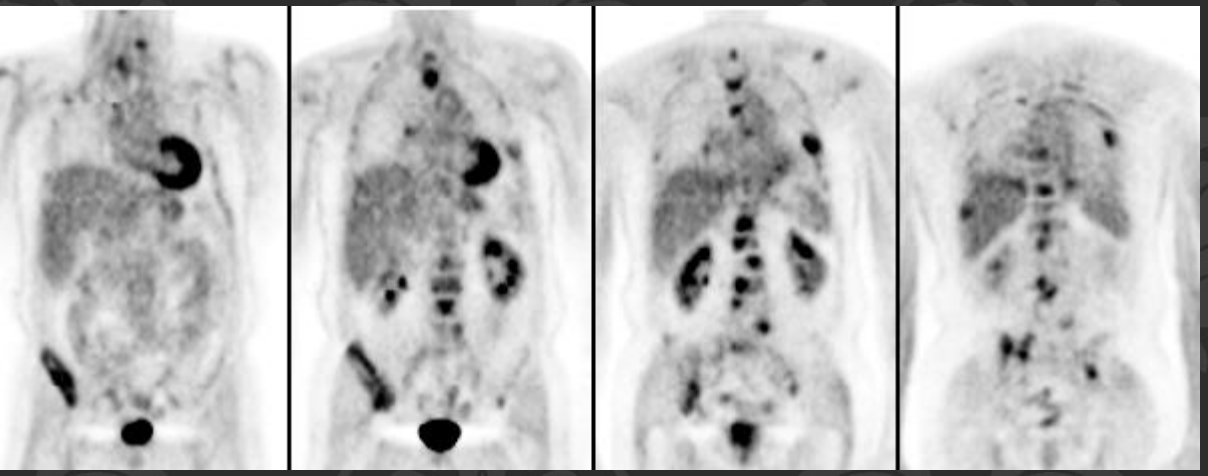
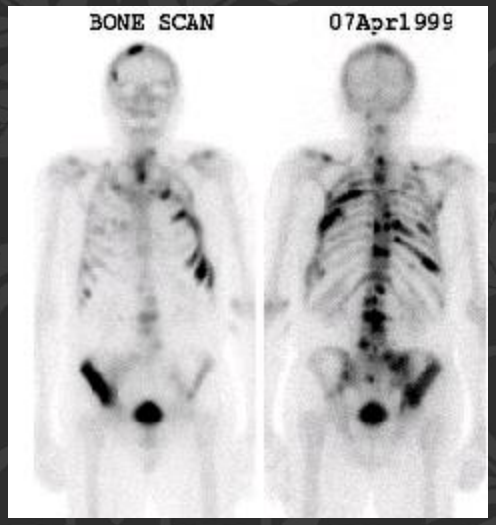


Fig. 4. Treatment of non-Hodgkin's lymphoma with radio-immunotherapy (i.e. Y-90-ibritumomab tiuxetan (Zevalin)). A. FDG- PET/CT before treatment: extensive metastases. B. FDG-PET/CT after two administrations of radio-immunotherapy (Zevalin): no evidence of disease activity. (Images courtesy of G Mariani, Pisa University Medical School, Italy.)

FDG-PET 4/7/99 PSA= 75 ng/ml



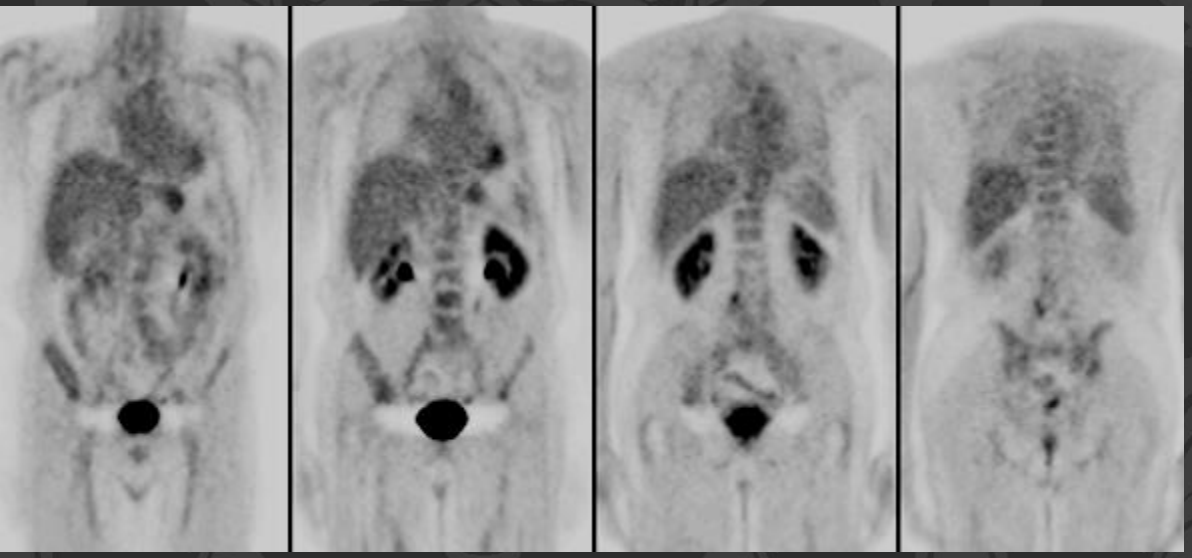
ANTERIOR CORONAL VIEWS POSTERIOR



ANT. POST.

Herceptin followed by Taxol

FDG-PET 7/9/99 PSA=8.6 ng/ml



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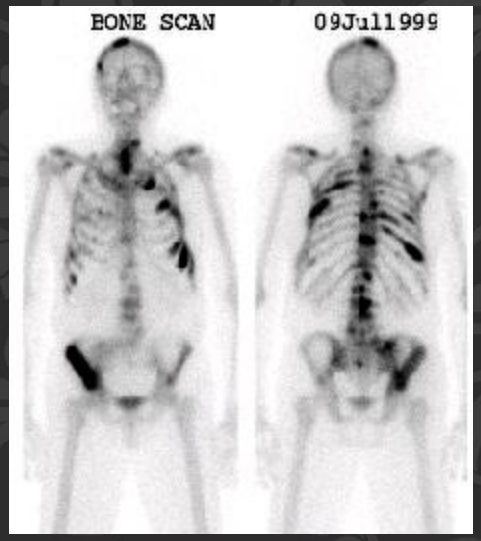
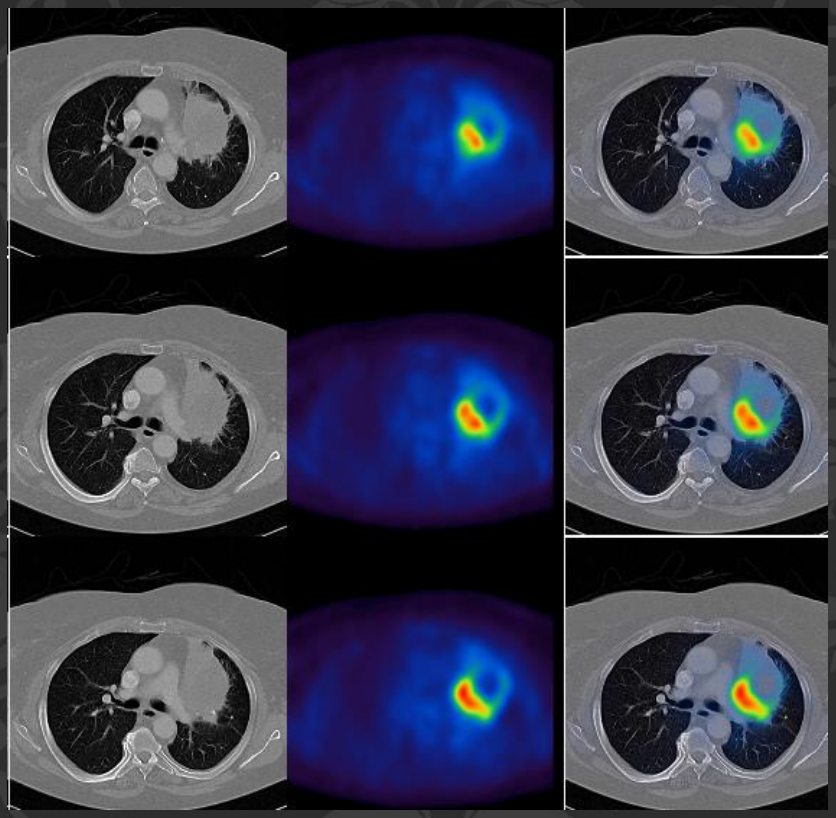
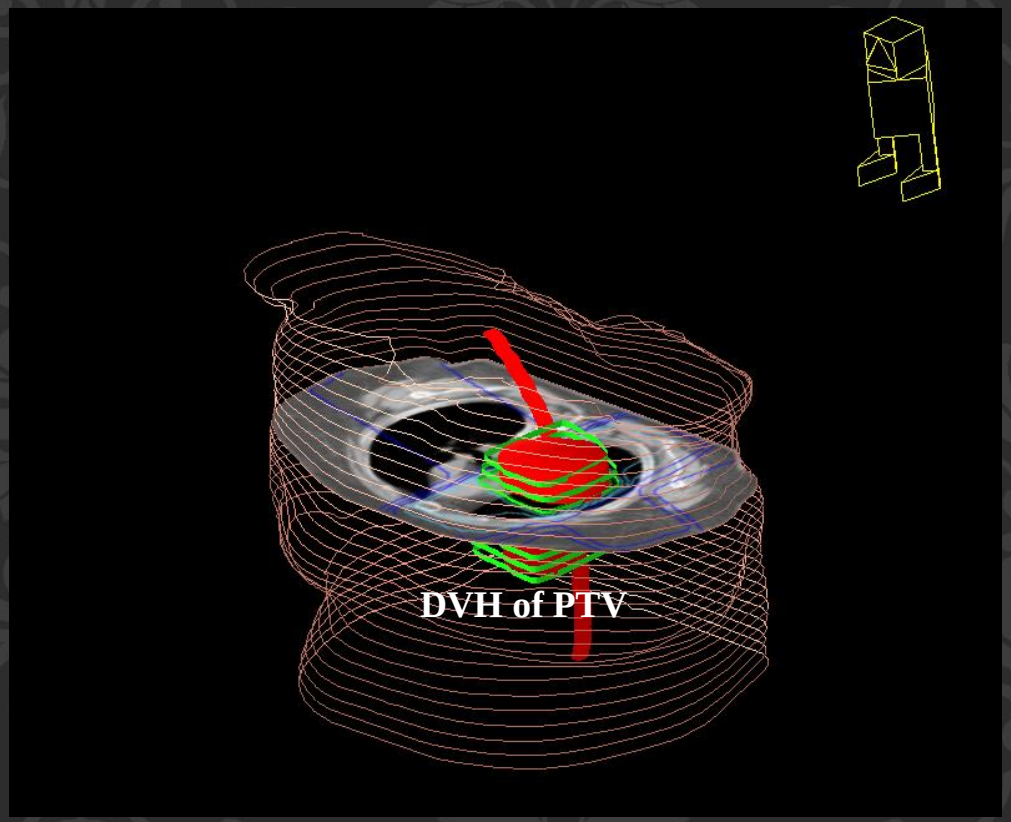


ANT. POST.

Molecular Radiation Treatment Planning (MRTP)





Functionally inoperable lung cancer
Metabolic radiation treatment planning (MRTP)
Extensive atelectasis

Baum RP et al. SNM 2000

RADIONUCLIDE TREATMENT

Internal Radiation Therapy

DIFFERENTIATED THYROID CARCINOMAS (DTC)

The initial treatment recommended :

- Total thyroidectomy
- Radioiodine ablation (^{131}I),
- TSH suppression therapy with levothyroxine

Optional - External beam radio therapy (EBRT)
- Chemotherapy

The goals ^{131}I ablation in clinical practice:

1. to destroy occult small DTC foci,
2. decreasing the long-term risk of recurrent disease;
3. to eliminate any remaining healthy thyroid tissue,

Preventive radioablation with I-131 (RAI) following total thyroidectomy remains controversial in very low and low risks well-differentiated thyroid cancer (DTC).

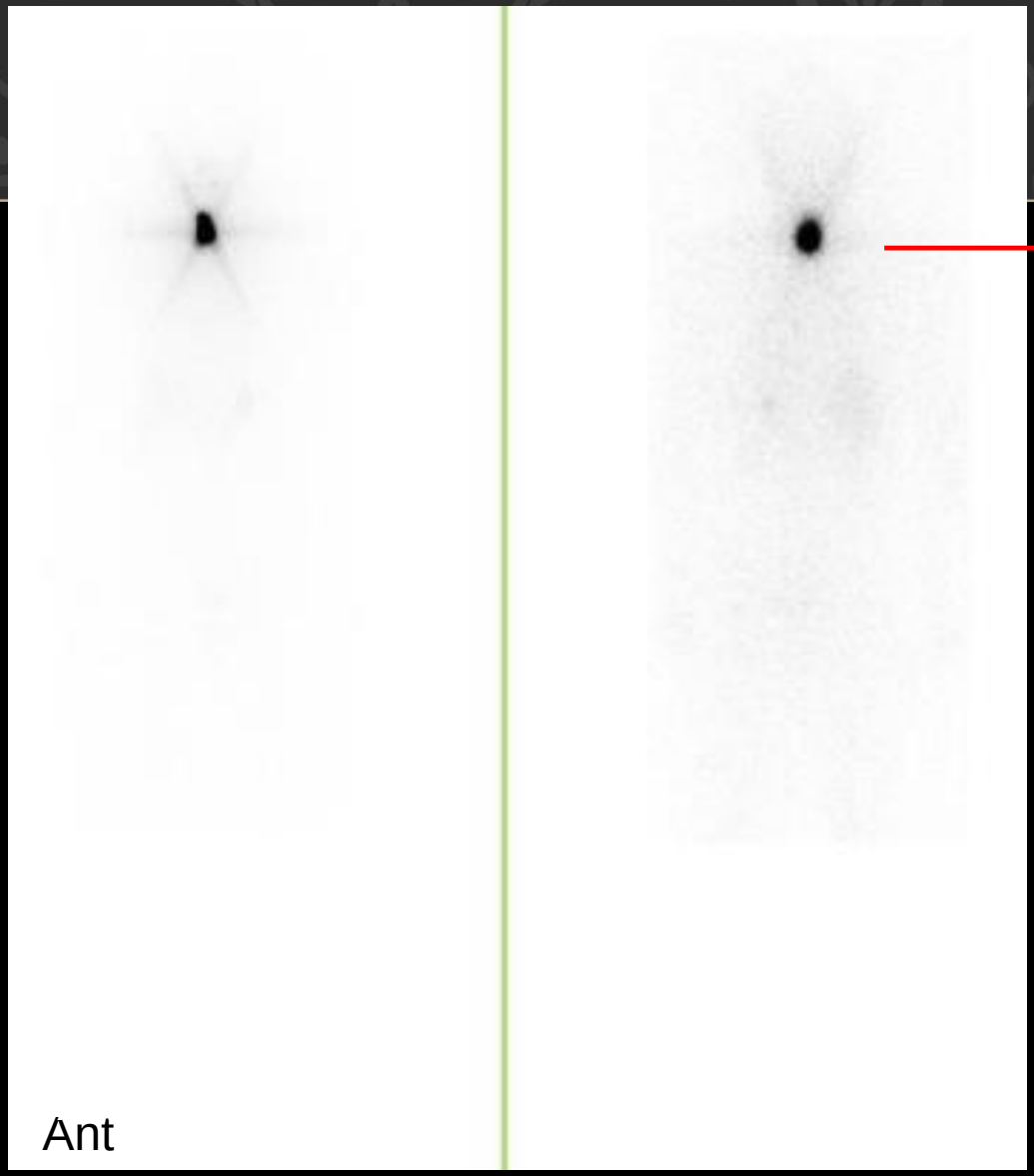
In the views of a number of physicians, there is no survival or recurrence benefit in using RAI in very low and low risk groups.

Excision of DTC by the most highly skilled surgeons can obviate the need for ^{131}I ablation at least in patients with a low risk of mortality and tumor recurrence.

TABLE 1. RECOMMENDATIONS FOR TREATMENT WITH RADIOACTIVE IODINE FOR DIFFERENTIATED THYROID CARCINOMA

	<45 years	*>45 years*	*RAI (+/–)*
Very low risk	Microcarcinoma: unifocal or multicentric Tumor <4cm confined to the thyroid Stage I [T0–T2 (s,m), N0, M0]; MACIS <6	Microcarcinoma: unifocal or multicentric Stage I [T0–T2 (s,m) N0 M0]; MACIS <6	No
Low risk	Tumor <4cm with or without microscopic central compartment lymph node metastases Stage I [T0–T2 (s,m), N0–N1a, M0]; MACIS <6	Tumor <4cm confined to the thyroid (no LN involvement) Stage II [T2, N0, M0]; MACIS <6	No
Moderate risk	Tumor >4cm Macroscopic (>1cm) central compartment or lateral lymph node metastasis Poor histologic type (hurthle cell, insular, sclerosing, tall cell, etc.) Minimal extrathyroidal extension (i.e. sternothyroid muscle or perithyroid soft tissue) Minimally (i.e. *micro*scopic) invasive follicular ca <4 cm Stage I [T1–T3, N1b, M0]	Histologic subtype conferring increased risk (hurthle cell, insular, sclerosing, tall cell, etc.) Minimally (i.e. *micro*scopic) invasive follicular ca <4 cm	Selective cases
High risk	Distant metastasis Extension to muscle, invasion of prevertebral fascia, subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve Tumor encases carotid artery or mediastinal vessels Stage I [T4a–T4b] Stage II	Tumor >4cm Extension to muscle, invasion of subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve Invasion of prevertebral fascia or encases carotid artery or mediastinal vessels Central or lateral compartment lymph node metastasis Distant metastasis *Macro*scopic invasive follicular carcinoma or >4cm Stage III Stage IV	Yes

Sacks et al, THYROID;Volume 20, Number 11, 2010



Female;41 y.o; T1N0M0; papillary

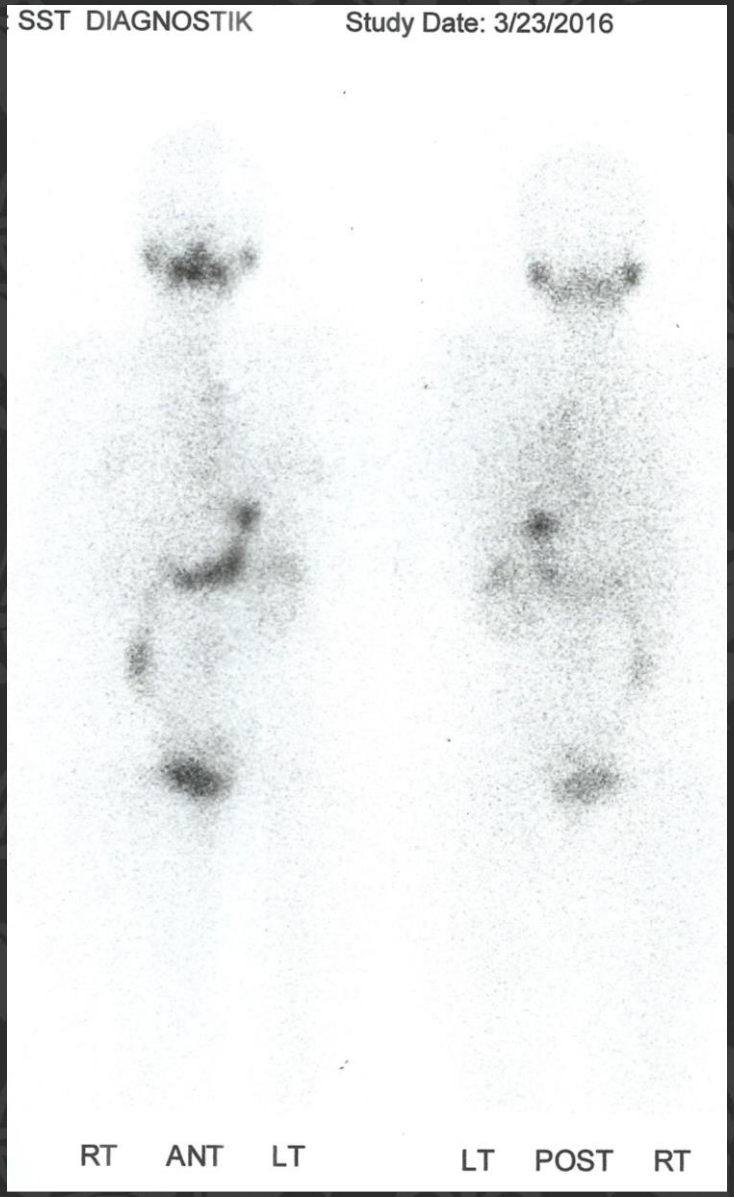
Uptake of I-131→ thyroid remnant

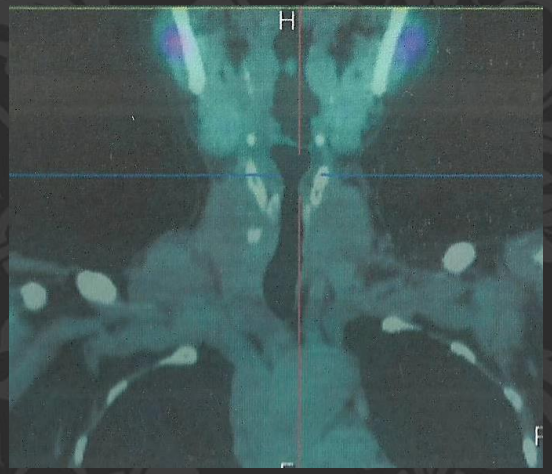
"Preventive" radiothyroablation

In patients in whom all tumor was believed to have been removed by surgery alone, a preventive I-131 ablation was used to eliminate the remnant.

Nemec et al; 1979

Whole Body Scan post therapy





F 56 yrs papillary thyroid ca

Post Total Thyroidectomy and ^{131}I ablation (100 mCi)

- Negative ^{131}I- scan
- Tg : 18.5 ng/dL
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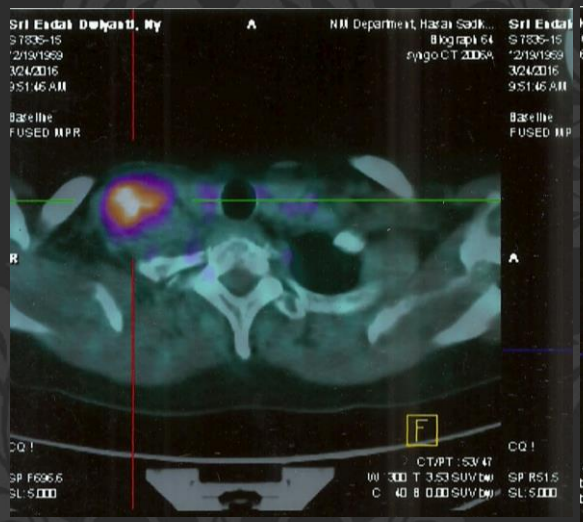


FROM TRIAL AND ERROR MEDICINE TO PERSONALIZE MEDICINE

Breaking the cycle of trial and error medicine

The right treatment, for the right patient, at the right time, at the right dose.

Personalized Medicine to Personalized Health Care

Targeted Radionuclide Therapy

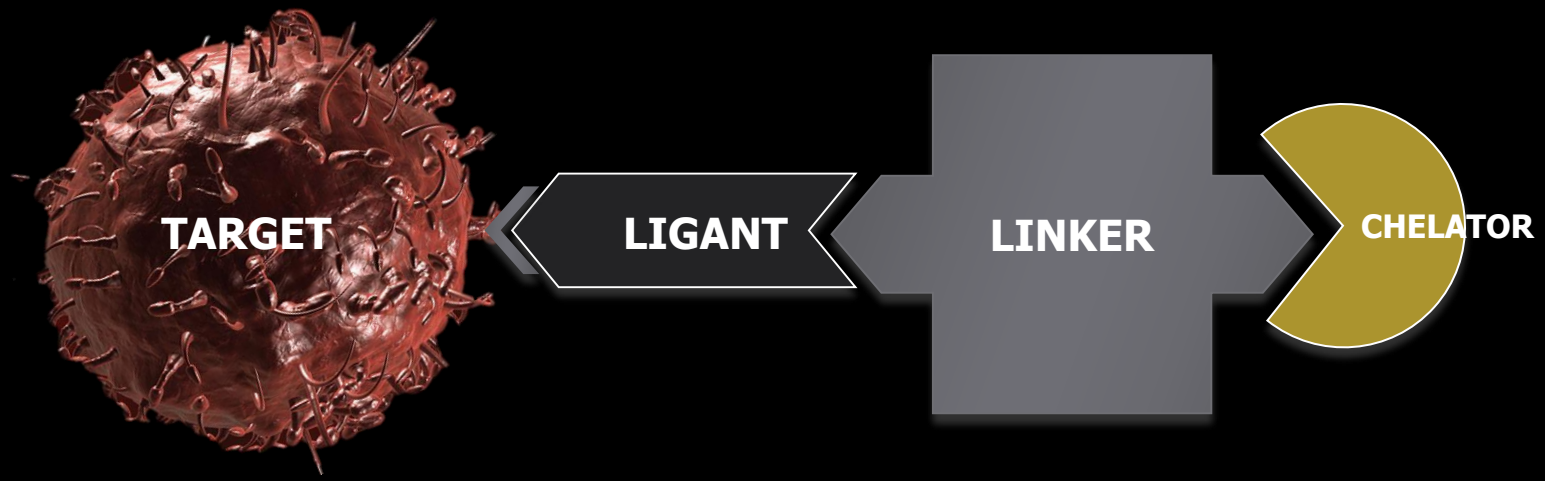
THERANOSTIC

"THERANOSTICS"

- The combination of a *diagnostic* tool that helps to define the right *therapeutic* tool for a specific disease (the pillars of medicine)
- Easy to apply and to understand in Nuclear Medicine, because of an easy switch of the radionuclide from diagnostic to therapy on the same vector
- The most prominent and oldest application is radioiodine
- The concept of Personalized Medicine appeared.

THERANOSTIC PAIRS
THE KEY-LOCK PRINCIPLE

"See and Treat Concept"



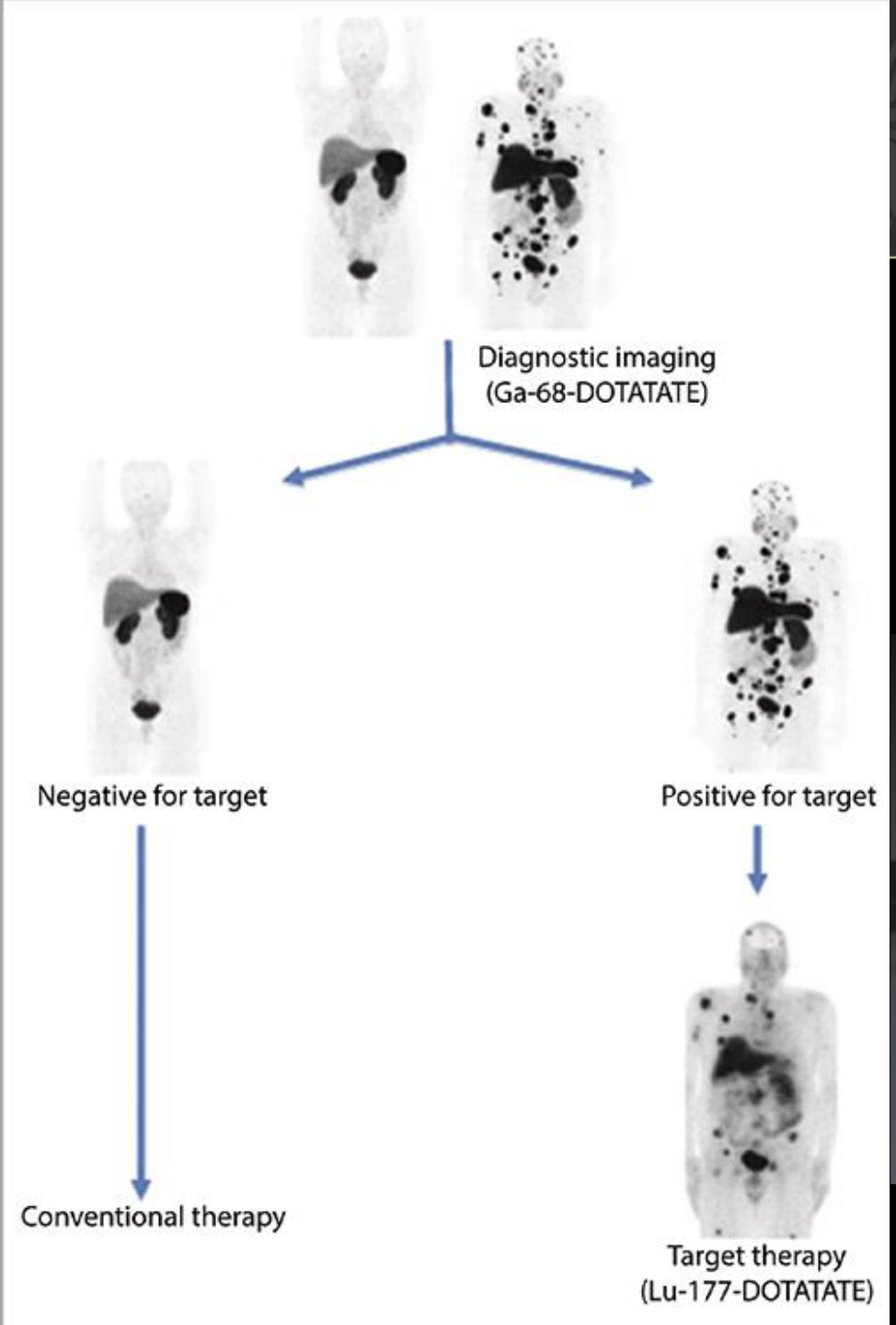
- Antigent
- Transporters
- Enzyme
- Inhibitor

- Antibodies
- Peptides
- Amino acids

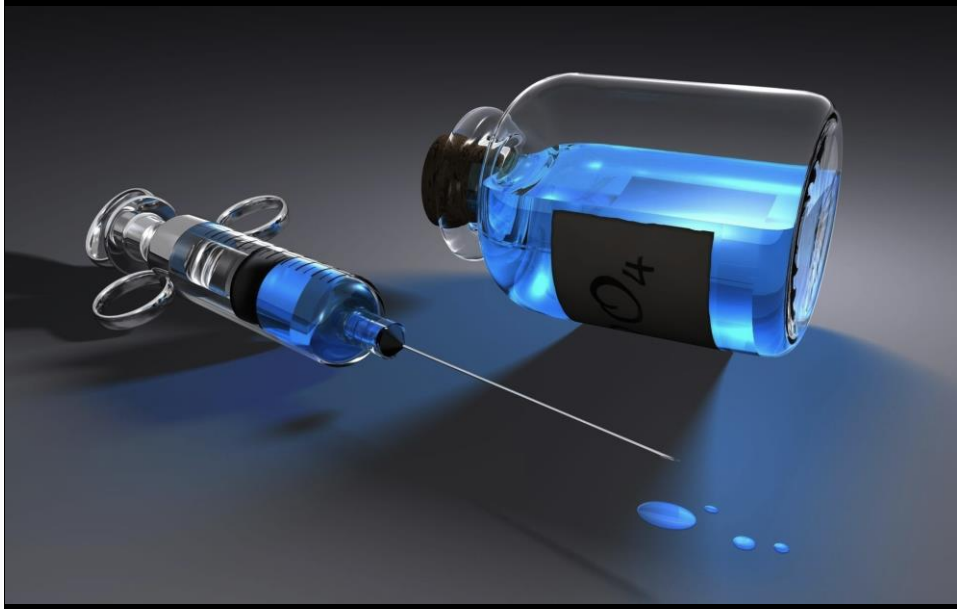
Reporting Unit
- ^{68}Ga, ^{99m}Tc, ^{111}In,

Cytotoxic Unit
- ^{90}Y, ^{177}Lu, $^{186,\ 188}Re$

TARGETED RADIONUCLIDE THERAPY

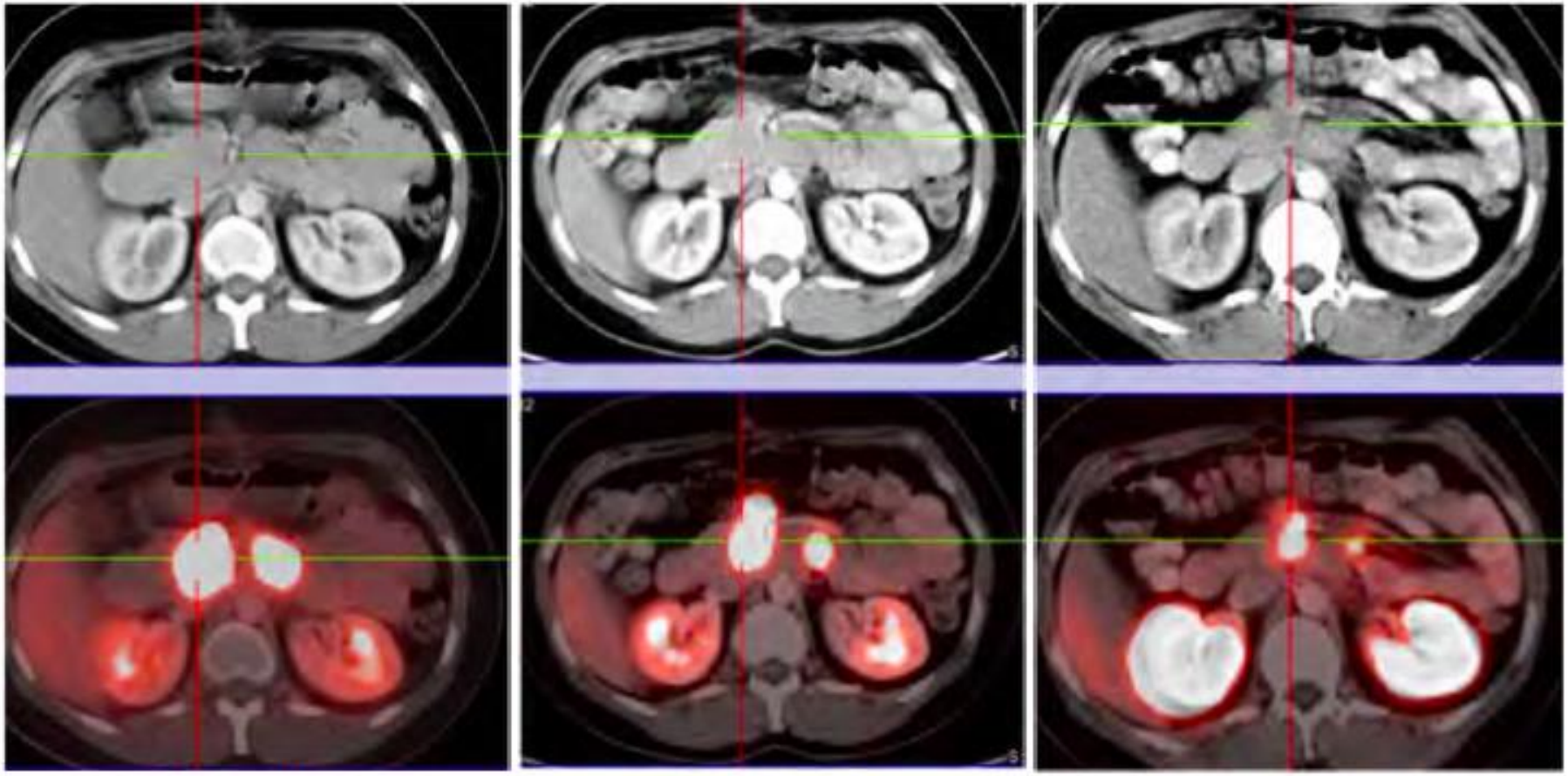


Targeted radionuclide therapy demonstrating how theranostic systems combine diagnostic imaging (Ga-68-DOTATATE PET/CT) to detect the presence of a molecular target (somatostatin receptors) in each patient. A patient who is found to be positive for a molecular target is selected for therapeutic intervention, in this case Lu-177-DOTATATE.



M Sathekge . *CME*Health & Medical Publishing Group 2014

Sequential PRRT (Y-90 DOTA-TATE) of Inoperable Pancreatic NET



Before PRRT-1
6 GBq Y-90
SUV 29.4

Jan. 2007

Before PRRT-2
4.5 GBq Y-90
SUV 25.4

May 2007

5-mo after PRRT-2
pre Op.
SUV 12.5

Oct. 2007

PSMA THERANOSTICS FOR PROSTATE CA.

^{68}Ga-PSMA PET/CT Imaging

^{177}Lu-PSMA Therapy

Prostate Cancer

- The second most common cancer worldwide in male and the fourth most common cancer overall
- 5-year survival rate :
  - localised 100 %
  - distant metastases 31 %
- Deaths are due to advanced disease, which results from any combination of lymphatic, blood, or contiguous local spread.

Prostate Cancer

- Early diagnosis is important to identify functional abnormalities which precede morphological changes
- Molecular imaging may contribute to the reduction of morbidity and mortality
- Over 90% investigations are performed with PET ^{18}F-FDG, but non specific
- ^{18}F-FDG fails in diagnosis of slowly growing tumours
- Specific imaging agents providing information on the molecular and cellular background would allow improvement in patient management and outcome.

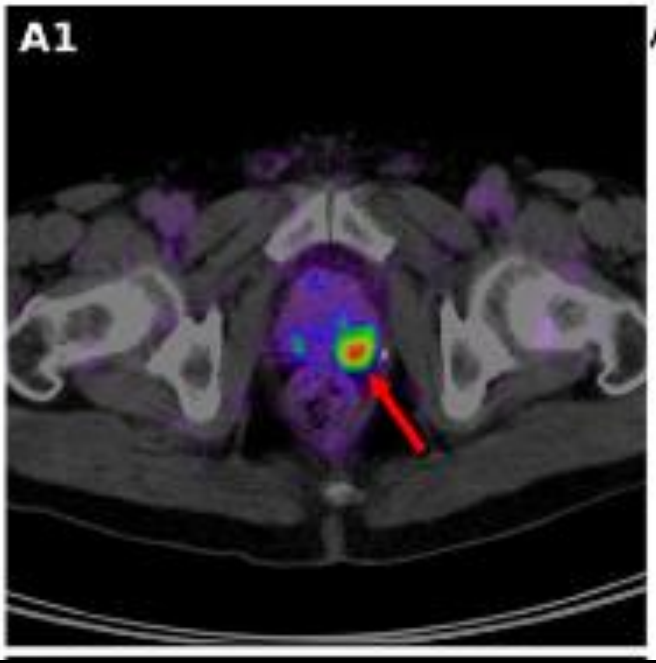
PROSTATE-SPECIFIC MEMBRANE ANTIGEN (PSMA)

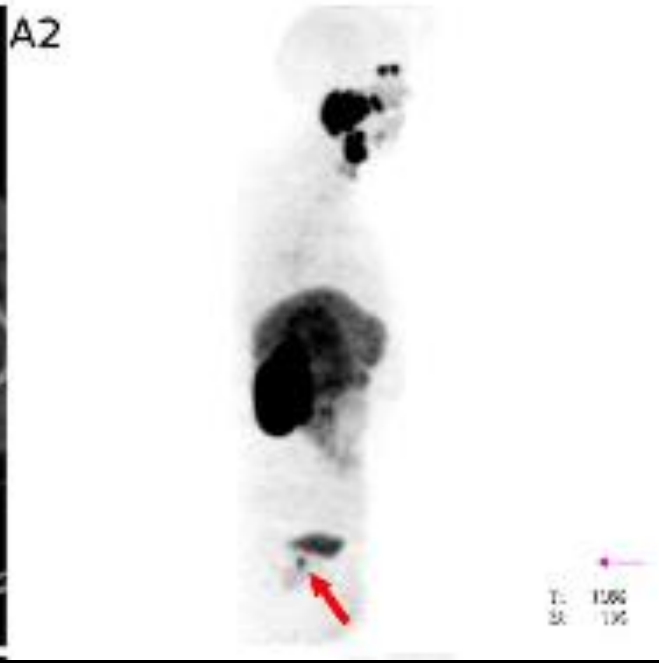
- a cell membrane glycoprotein,
- expressed at higher levels in prostate cancer compared to other tissues.
- provides a promising target for specific imaging and therapy due to its transmembrane location and internalization after ligand binding
- very low levels in normal prostate
- A potentially effective therapeutic strategy

[^{68}GA]GALLIUM- PSMA

- Identifies tumor cells expressing PSMA antigen with excellent sensitivity & specificity, thereby detecting lesions remaining unidentified by conventional methods.
- Excellent contrast and a high detection rate even when the level of PSA is low.
- A potentially valuable marker in the treatment of patients with prostate cancer.
- Promising potential for restaging in recurrence/ biochemical failure after definitive treatment of prostate cancer.
- Marker of patient response to anti-androgen drugs.

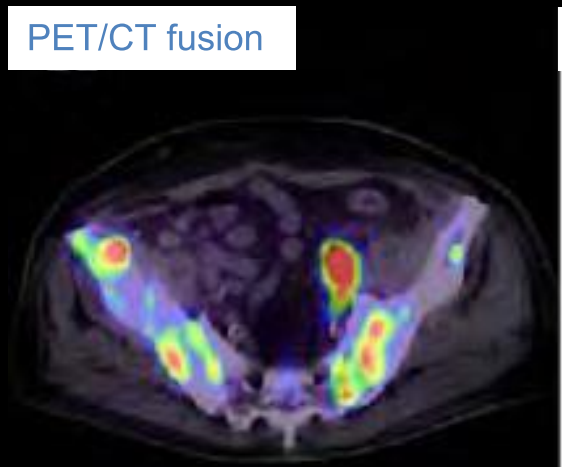
Eur J Nucl Med Mol Imaging (2012) 39:1085–1086

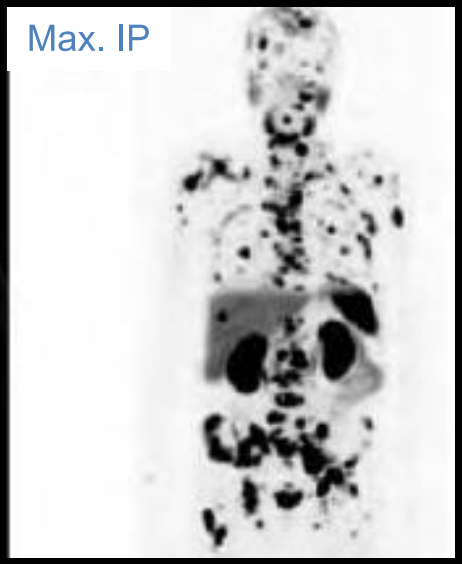




The 67-year-old patient had undergone previous radiotherapy of the prostate due to carcinoma and had received androgen therapy since 2002. The patient presented with a continuous increase of PSA values (from 1 ng/ml in 2002 to 7.4 ng/ml in May 2011)

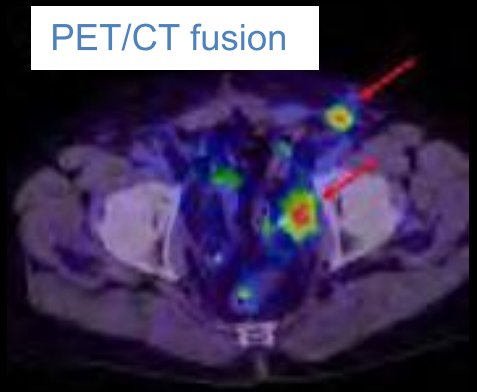
^{68}Ga-PSMA PET/CT





^{68}Ga-PSMA PET/CT

Patient representative for disseminated lymph node and bone metastases of prostate cancer.



^{68}Ga-PSMA PET/CT

Patient with low PSA level (0.01 ng/ml) and lymph node metastases.
Minimal PSA elevation despite visible tumor lesions suggests dedifferentiation of prostate cancer metastases.

At PSA levels < 2.2 ng/ml, lesions suspicious for cancer were observed in 60 % of the patients.
At PSA levels > 2.2 ng/ml, lesions were detected in all patients.

A. Afshar-Oromieh et al. EJNM MI 2012

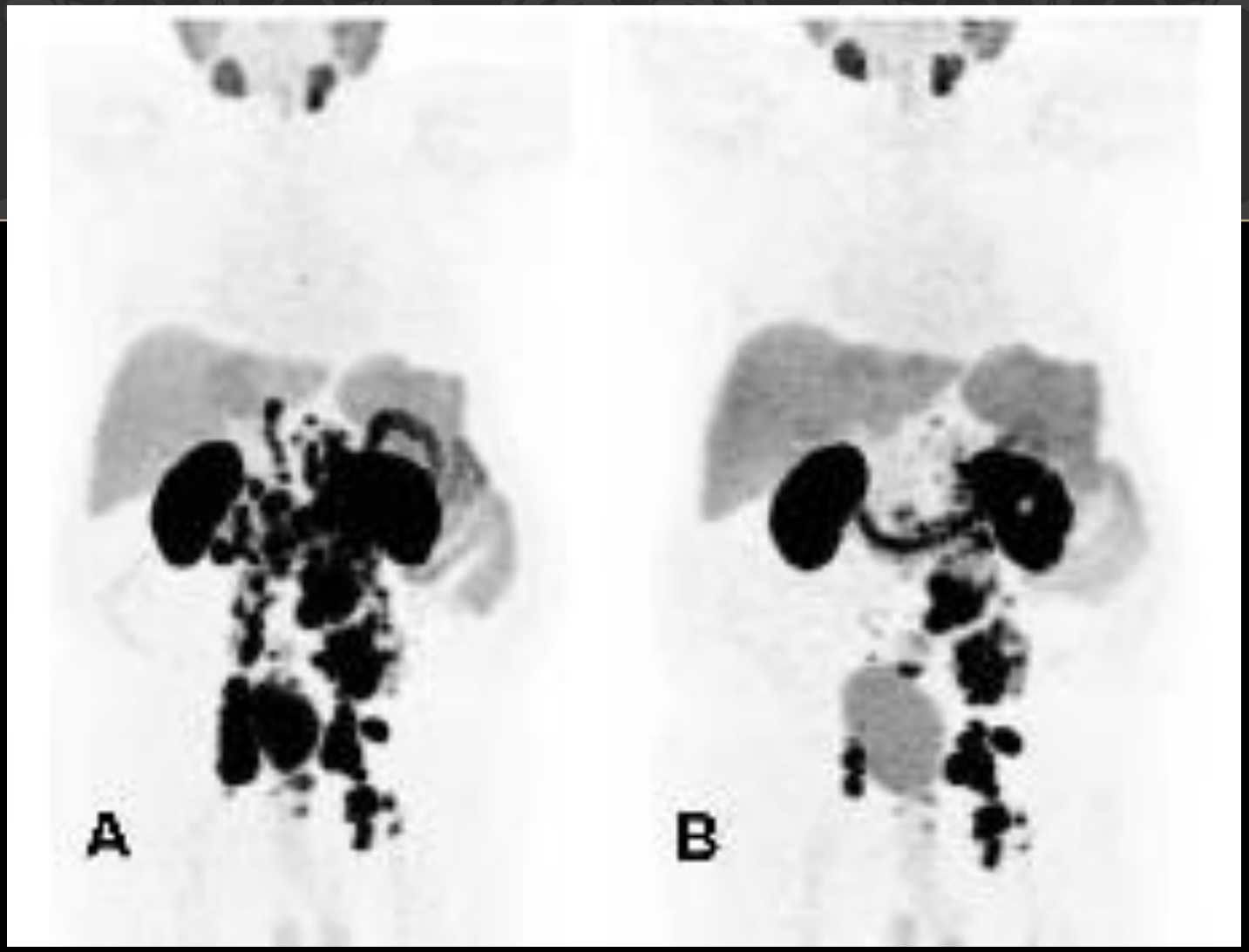


Fig 1. A 74-year old patient with hormone and chemo-refractory prostate cancer underwent PSMA PET/CT. (A) : which showed diffuse abdominal and iliacal lymph node metastases. The patient underwent RLT with 5.7 GBq 177Lu-PSMA. The PSA level was at the time of the therapy 790 ng/ml. (B): A partial response 7 weeks after RLT with 63% PSA decline at this time, the PSA level was 293 ng/ml

Concluding Remarks

The Role of Nuclear Medicine in Cancer Management

- **Diagnostic**
- **Staging**
- **Monitoring response therapy**
- Molecular Radiation Treatment Planning (MRTP)
- Therapy

Molecular Nuclear Medicine and THERANOSTICS are definitely part of Personalized Medicine.

Targeted radionuclide therapy has unique promise for personalized treatment of cancer

The Role of Nuclear Medicine in Cancer Management

Manado Cancer Update Symposium, 27 January 2018

THANK YOU

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