NUKLEARNA MEDICINA

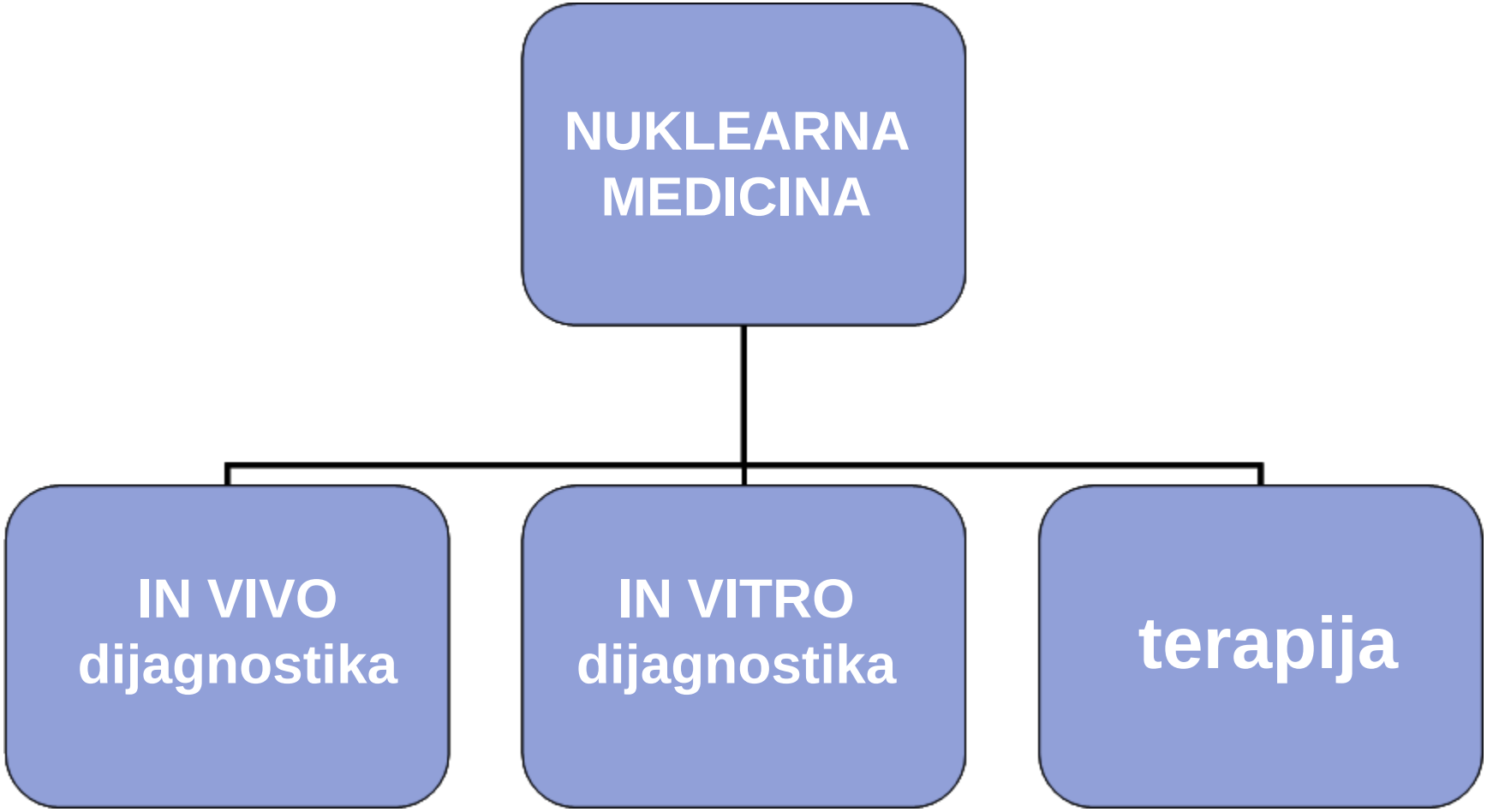
Doc. dr Branislava Radović
Centar za nuklearnu medicinu KCS
tcmapple@gmail.com

NUKLEARNA MEDICINA

- medicinska ispitivanja (dijagnostičke studije) u cilju *otkrivanja* i *lečenja* bolesti upotrebom **radoizotopa**
- Georg Karl von Hevesy rane 1920.
- zasnovana na funkciji (patofiziologija)

funkcionalni imidžing

PODELA NUKLEARNE MEDICINE



dve **glavne** vrste zračenja

- emisija **γ zraka ⇨ gama** kamera
- anihilacija-koincidenta emisija iz jezgara **bogatih p+ ⇨ PET** kamera

element

N protona = atomski (redni) broj (Z)

N (proton + neutron) = maseni broj (A)

$$^{A}_{Z}X \qquad ^{127}_{53}J$$

IZOTOPI *isos topos* **isti** broj **p+**; **različit** broj **n**

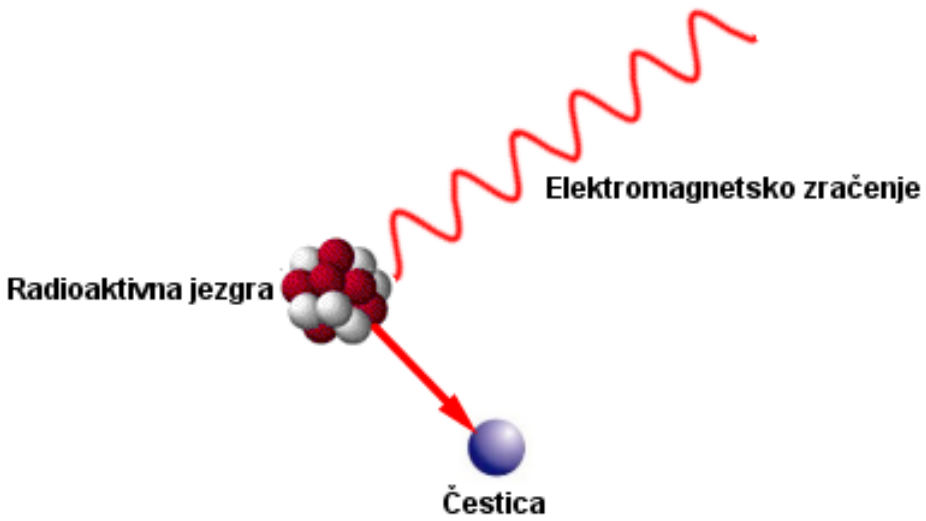
radionuklid radioaktivno jezgro

J^{131}....J^{123}....Tc^{99m}

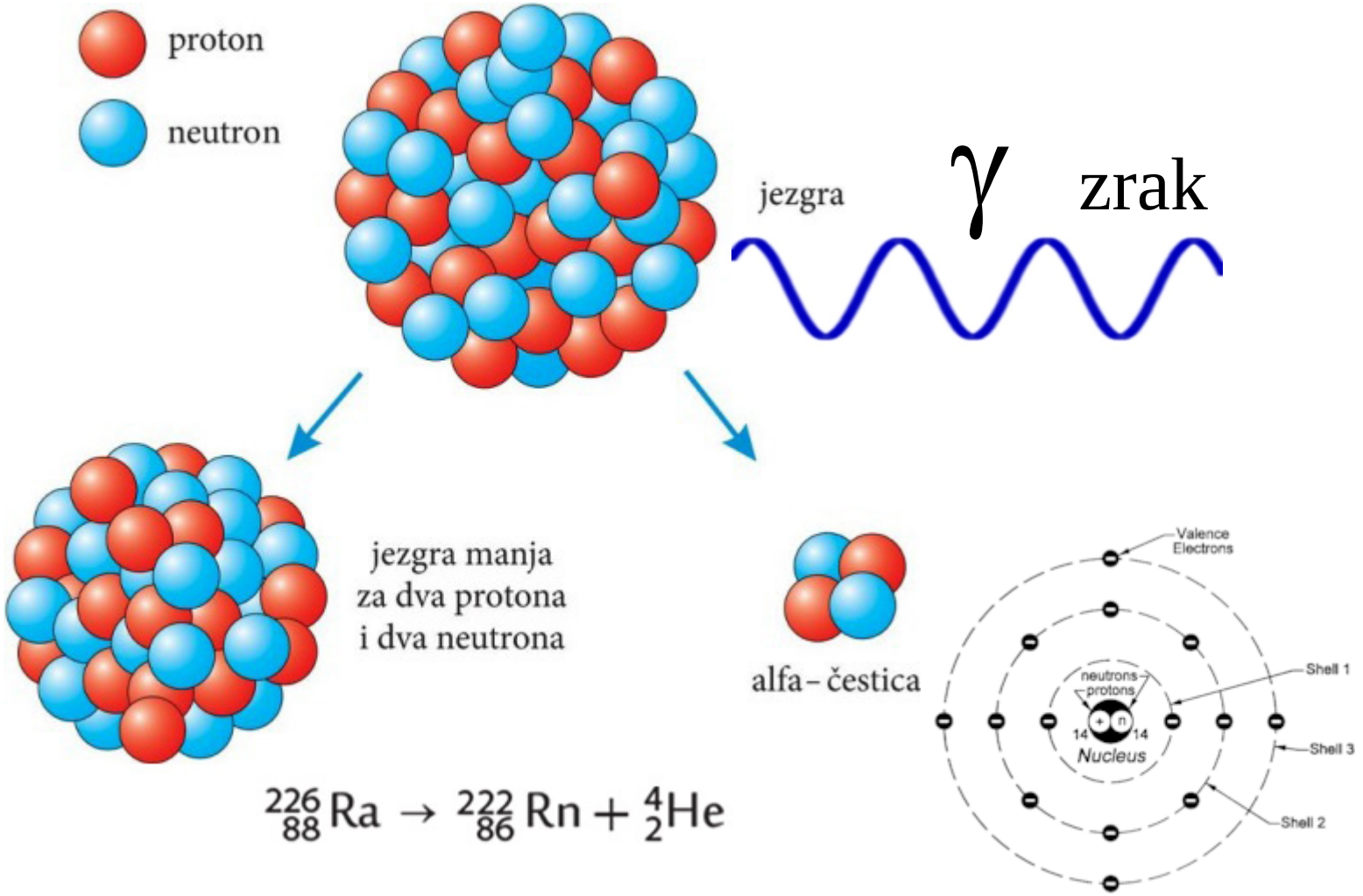
radioaktivnost

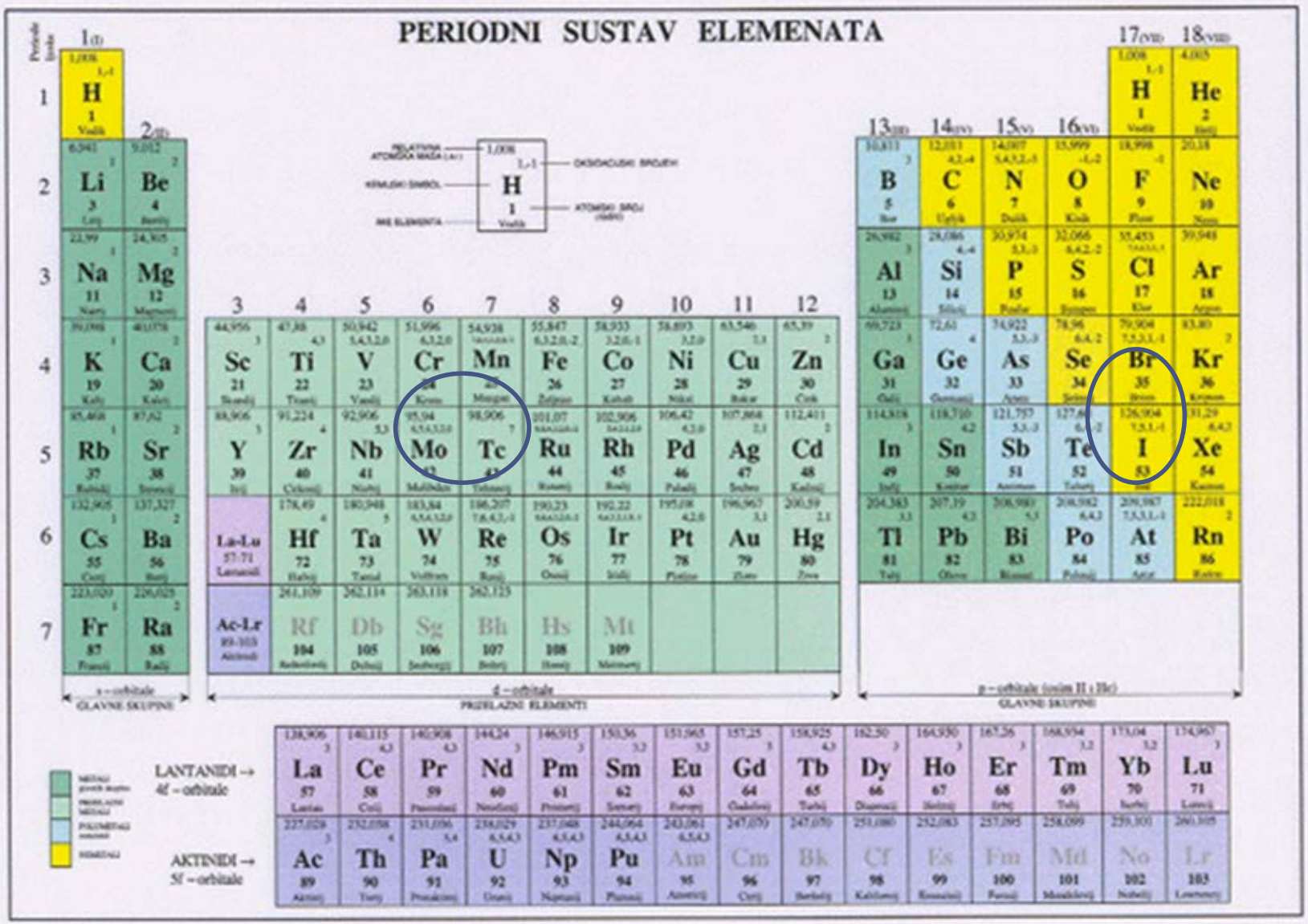
- **radioaktivnost** svojstvo atoma (nestabilni) da im se jezgro spontano menja pri čemu emituju energiju u obliku EM zračenja i/ili čestice.

- promena jezgra ⟹ **radioaktivni raspad**



radioaktivnost




PERIODNI SUSTAV ELEMENATA
1 H 1
2 Li 3 Be 4
3 Na 11 Mg 12
4 K 19 Ca 20
5 Rb 37 Sr 38
6 Cs 55 Ba 56
7 Fr 87 Ra 88
3 Sc 21 Ti 22 V 23 Cr 24 Mn 25 Fe 26 Co 27 Ni 28 Cu 29 Zn 30
4 Y 39 Zr 40 Nb 41 Mo 42 Tc 43 Ru 44 Rh 45 Pd 46 Ag 47 Cd 48
5 La-Lu 57-71 Hf 72 Ta 73 W 74 Re 75 Os 76 Ir 77 Pt 78 Au 79 Hg 80
6 Ac-Lr 89-103 Rf 104 Db 105 Sg 106 Bh 107 Hs 108 Mt 109
13 B 5 Al 13 Ga 31 In 49 Tl 81
14 C 6 Si 14 Ge 32 Sn 50 Pb 82
15 N 7 P 15 As 33 Sb 51 Bi 83
16 O 8 S 16 Se 34 Te 52 Po 84
17 H 1 F 9 Cl 17 Br 35 I 53 At 85
18 He 2 Ne 10 Ar 18 Kr 36 Xe 54 Rn 86
La 57 Ce 58 Pr 59 Nd 60 Pm 61 Sm 62 Eu 63 Gd 64 Tb 65 Dy 66 Ho 67 Er 68 Tm 69 Yb 70 Lu 71
Ac 89 Th 90 Pa 91 U 92 Np 93 Pu 94 Am 95 Cm 96 Bk 97 Cf 98 Es 99 Fm 100 Md 101 No 102 Lr 103
LANTANIDI → 4f – orbitale
AKTINIDI → 5f – orbitale
s – orbitale GLAVNE SKUPINE
d – orbitale PRIJELAZNI ELEMENTI
p – orbitale (osim H i He) GLAVNE SKUPINE

radioaktivni izotopi

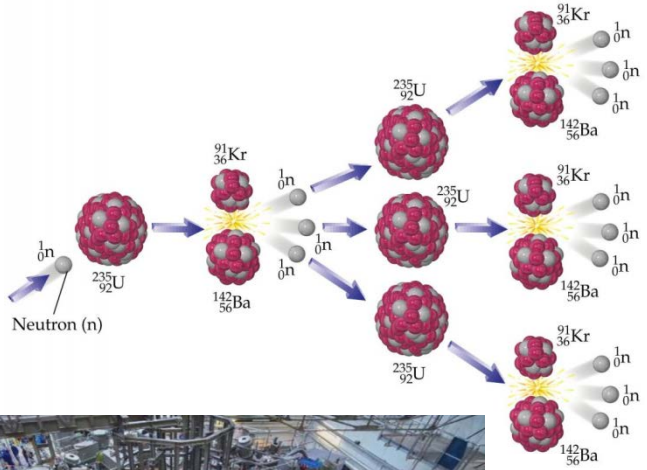
izotopi	T/2	energija (KeV)
I-131	**8.1 d**	364
I-123	**13 h**	159
I-125	**60 d**	35
Tc-99m	**6 h**	140
T1-201	**73 h**	80,135,167
Ga-67	**78 h**	93,184
In-111	**67 h**	173,247,320
P-32	**14.3 d**	695(b)

Mesta produkcije radionuklida

1. nuklearni reaktor

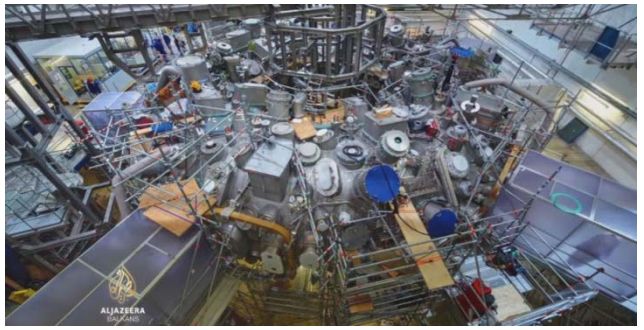
fisija

hemijski element U ^{235} se izlaže fluksu neutrona...β raspad čestice



2. ciklotron

bombardovanje stabilnih atoma naelektrisanim česticama p+, deuteroni, helioni (α čestice)
Tl ^{201} se bombarduje protonima i nastaje Pb ^{201}



3. generator

dugoživući radionuklid (**roditelj**) se raspada spontano u radionuklid kraćeg $T^{1/2}$ (**potomak**)



proizvodnja radioaktivnih izotopa

- **nuklearni reaktor**
  ^{131}I, ^{125}I, ^{99}Mo, ^{133}Xe, ^{32}P, ^{14}C, ^{166}Ho, ^{186}Re

- **ciklotron (akcelerator)**
  ^{201}Tl, ^{67}Ga, ^{123}I, ^{111}In, ^{57}Co
  ^{11}C, ^{13}N, ^{15}O, ^{18}F

- **generator**
  ^{99m}Tc, ^{188}Re

fizičke osobine radionuklida

- **vreme poluraspada $T_{1/2}$**: vreme za koje se početni broj jezgara smanji na polovinu
- **fizičko vreme poluraspada $T_{1/2}$ = *ln2/k***....pokazatelj brzine radioaktivnog raspada
- **biološko vreme poluraspada** brzina eliminacije radionuklida iz organizma
- **efektivno vreme poluraspada**

  fizičko+ biološko vreme poluraspada

fizičke osobine radionuklida

Energija

- osnovna jedinica **eV** (energija 1 e- u električnom polju sa razlikom potencijala od 1 V)
- u nuklearnoj medicini 20-500 keV in vivo
- **optimalna** E oko 150 keV
- **niska** **Xe^{133}** **80 keV, Tl^{201}** **63-81 keV** veće aktivnosti jer se zadržavaju u tkivu, apsorbuju
- **visoka** **J^{131}** **364 keV**

Tc^{99m} **140 keV**

J^{123} **159 keV**

osobine radionuklida

Aktivnost

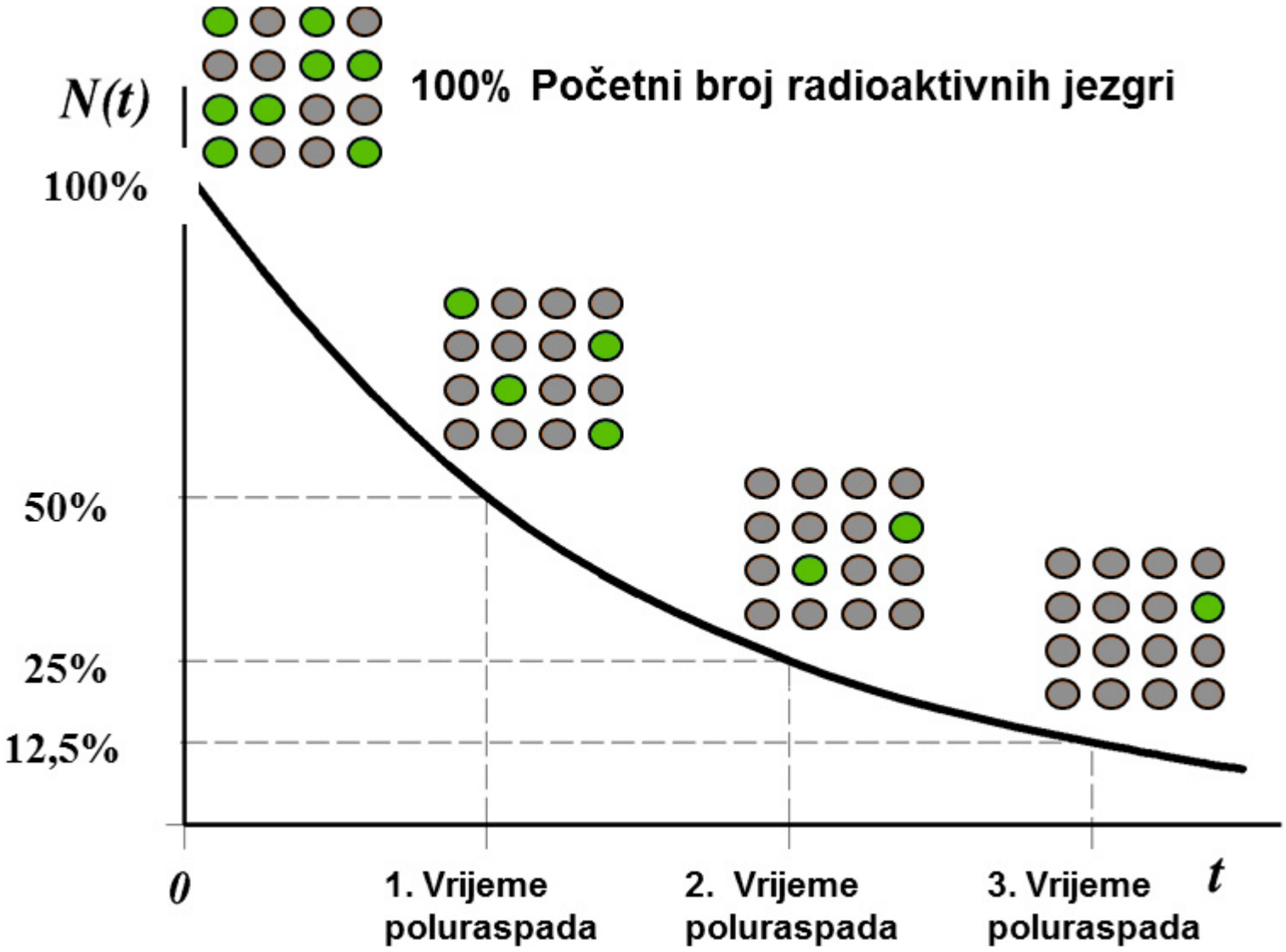
Broj raspada u jedinici vremena

$$1\ \mathcal{B}q = \frac{raspad}{1\ s}$$

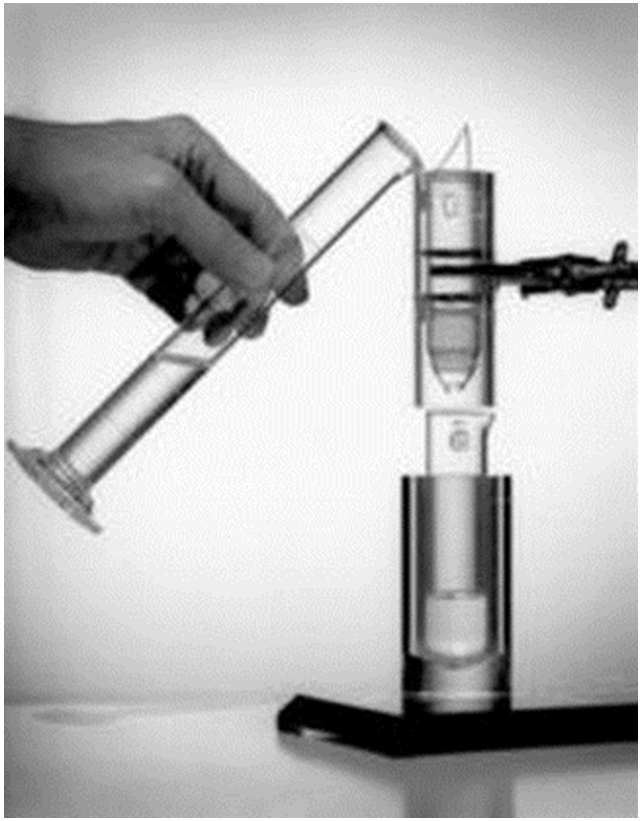
kBq.....MBq....GBq

Ci = $\frac{3{,}7 * 10^{10}}{s}$.....mCi (37x mCi=MBq)

- apsolutna
- relativna


N(t)
100%
100% Početni broj radioaktivnih jezgri
50%
25%
12,5%
0
1. Vrijeme poluraspada
2. Vrijeme poluraspada
3. Vrijeme poluraspada
t

generator





^{99}Mo..... ^{99m}Tc

radiofarmak

- **jedinjenja** i **biološke supstance** obeležena **radionuklidima** koja se koriste u nuklearnoj medicini u cilju otkrivanja različitih bolesti i lečenja
- proizvode se po pravilima **FARMAKOPEJE**
- **ne menjaju fiziološke / patofiziološke procese u organizmu**
  - **^{99m}Tc radiofarmaci**
  - **NE-^{99m}Tc** radiofarmaci
  - biološke supstance

radiofarmaci

- radionuklid + **hemijska supstanca**
- radionuklid + **biološka supstanca**

- ^{99m}Tc MDP (scintigrafija kostiju)
- ^{99m}Tc MAA (scintigrafija pluca)

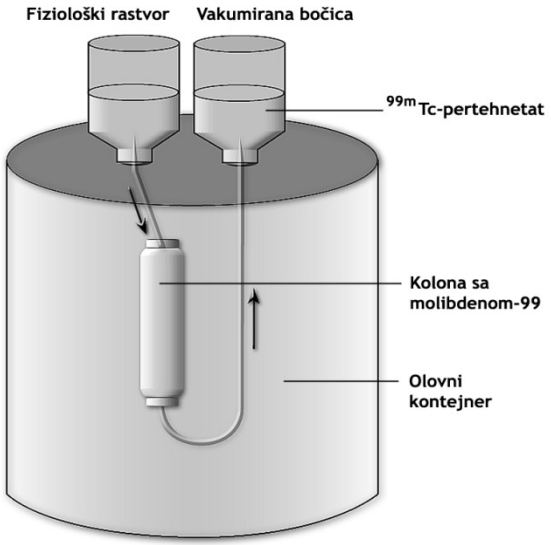
- organ specifični mehanizam

- optimalna energija (100 – 200 KeV)

Tc^{99m} 140 keV

radiofarmaci sa ^{99m}Tc

- dobijanje **$NaTc^{99m}O_4$** natrijumpertehnetata: iz generatora radioaktivnim raspadom **^{99}Mo**



Najveci prinos ^{99m}Tc- posle 23 h

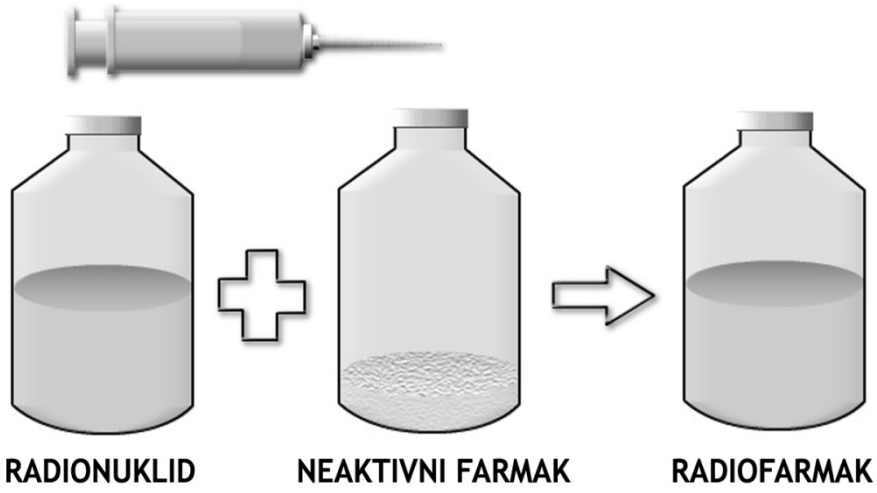
Trajnost – 12 dana

Fizicke osobine ^{99m}Tc: cist γ emiter, T1/2 = 6 h, 140 keV

Primena: scintigrafija tireoideje, pljuvacnih zlezda, procena vaskularizacije, Mckelov-divertkulum

U obliku radiofarmaka: bioloski elementi, koloidi, fosfati, MAA, DTPA, DMSA,

Markiranje (obeležavanje) radiofarmaka



^{99m}Tc **DMSA** **99mTc – DMSA**

radiofarmak

fizičke osobine radiofarmaka	
fizički oblik	**radiofarmak**
gasovi	**^{133}Xe ^{127}Xe ^{81m}Kr**
pravi rastvori	**Na^{131}J ^{99m}Tc DTPA ^{99m}Tc DMSA ^{201}TlCl$_2$**
koloidni rastvori	**^{99m}Tc Sn - koloid ^{99m}Tc S - koloid**
suspenzije	**^{99m}Tc MAA ^{99m}Tc-erotrociti ^{111}In-trombociti**
čvrsti oblik	**obrok obeležen pertehnetatom**

radiofarmak

parametri kvaliteta radiofarka	
radionuklidna čistoća	**procenat radioaktivno obeleženog jedinjenja**
radiohemijska čistoća	**procenat određenog hemijskog oblika**
specifična radioaktivnost	**aktivnost u 1ml radiofarmaka**

radiofarmak

- distribucija radiofarmaka

  - **valenca radionuklida**

    - **^{99m} Tc (III) DMSA**
    - **^{99m} Tc (IV) DMSA (tubule nefrona)**
    - **^{99m} Tc (V) DMSA (C ćelije tireoideje)**

  - **pH radiofarmaka**
  - **veličina molekula**
  - **afinitet za proteine plazme**
  - **rastvorljivost**
    - **liposolibilni ^{99m} Tc MIBI.... ^{99m} Tc HMPAO**
    - **hidrosolubilni (Na ^{99m} Tc O $_4$) --- aktivan transport**

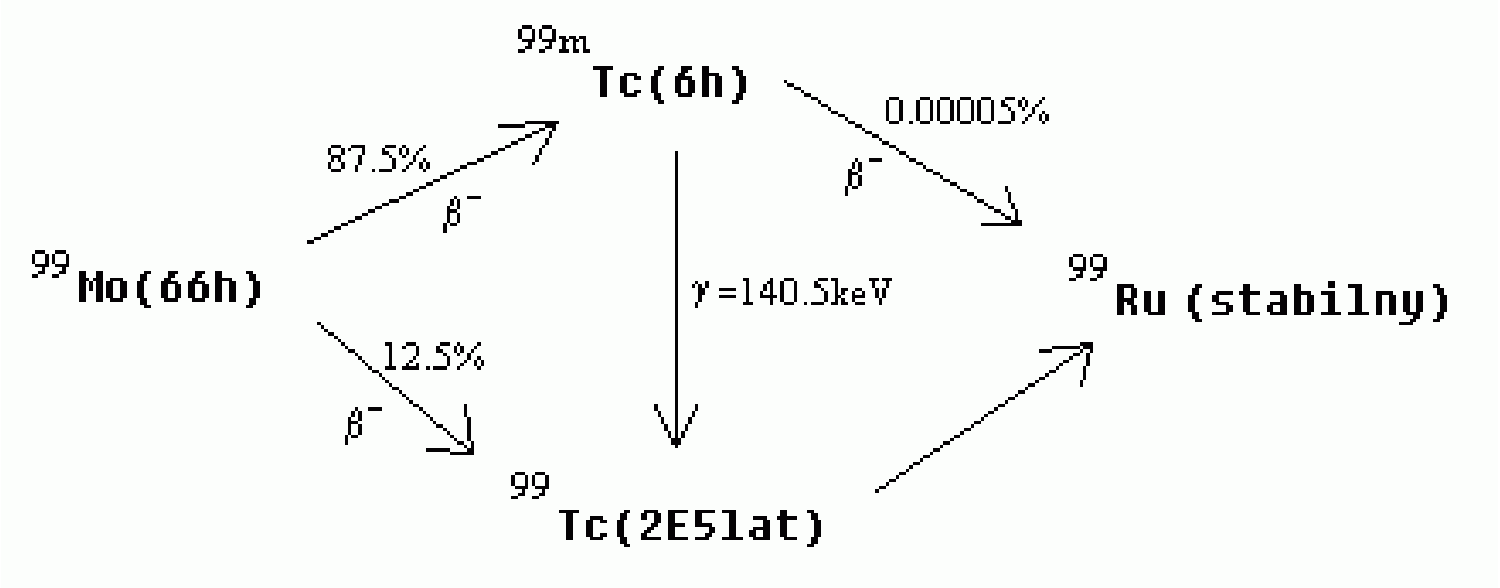
radiofarmak

- **putevi distribucije**
  - **dilucija**
  - **aktivni transport**
  - **pasivi transport....difuzija**
  - **fagocitoza**
  - **sekvestracija**
  - **mikroembolija**

radiofarmak

- **radiofarmaci sa 99m Tc**

molibden - tehnecijumski generator





- generator

- jonoizmenjivačka kolona Al_2O_3
- **adsorbovan ^{99}Mo** u jamicama belog komprimata
- u sistemu vakuma
  - ispiranje fiziološkim rastvorom
  - **ELUICIJA**
- **maksimalni** prinos generatora posle **23 sata**
  - dobijeni rastvor **sterilan apirogen** sa određenom **radionuklidnom i radiohemijskom** čistoćom

radiofarmak

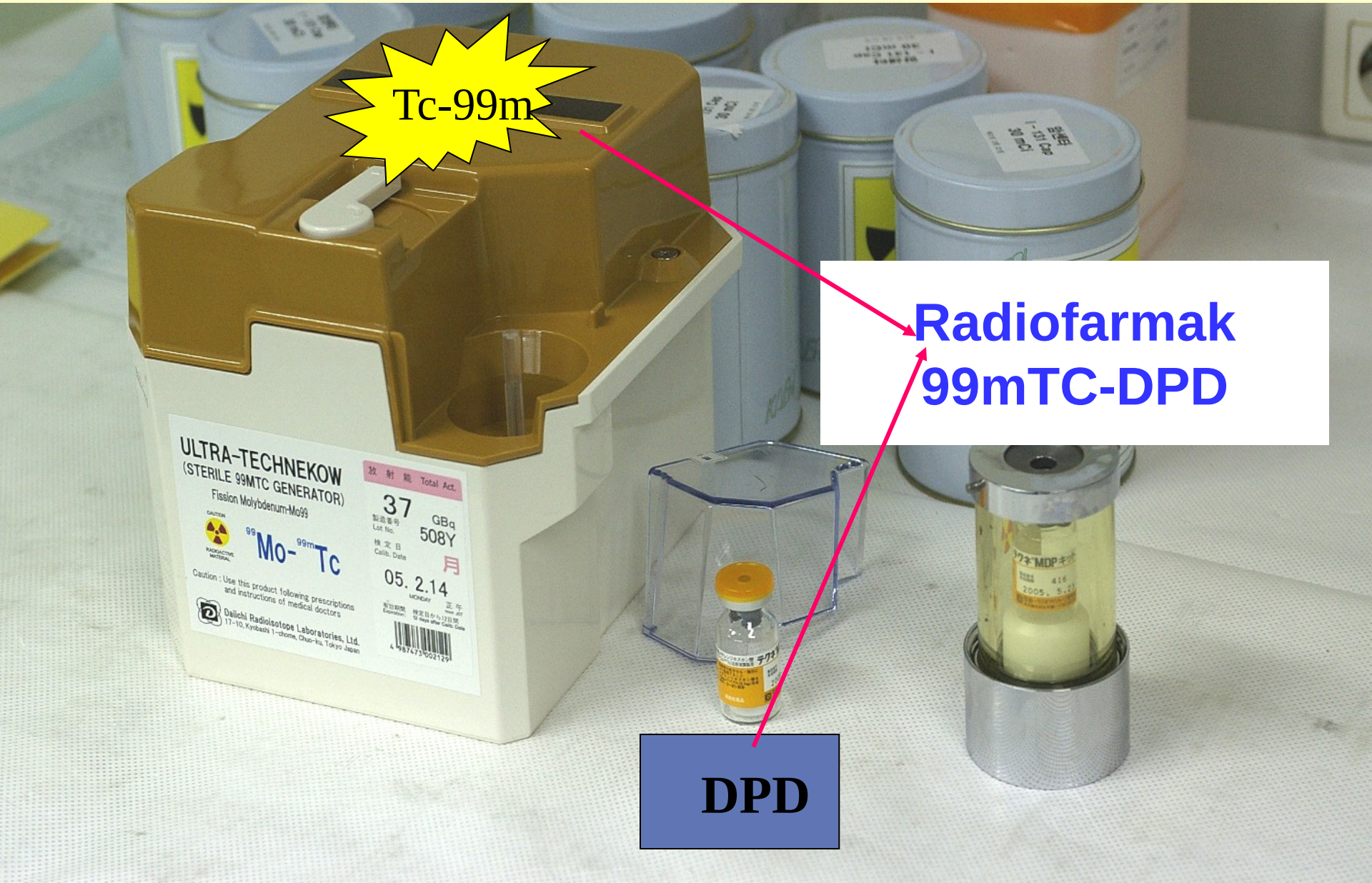
karakteristike ^{99m}Tc
čist **γ** emiter
γ fotoni **140 keV**
kratko T ½ **6 sati**
generatorska proizvodnja
stabilno vezivanje sa ***hladnim*** molekulom



generator


Saline
Charge
Collect

priprema radiofarmaka



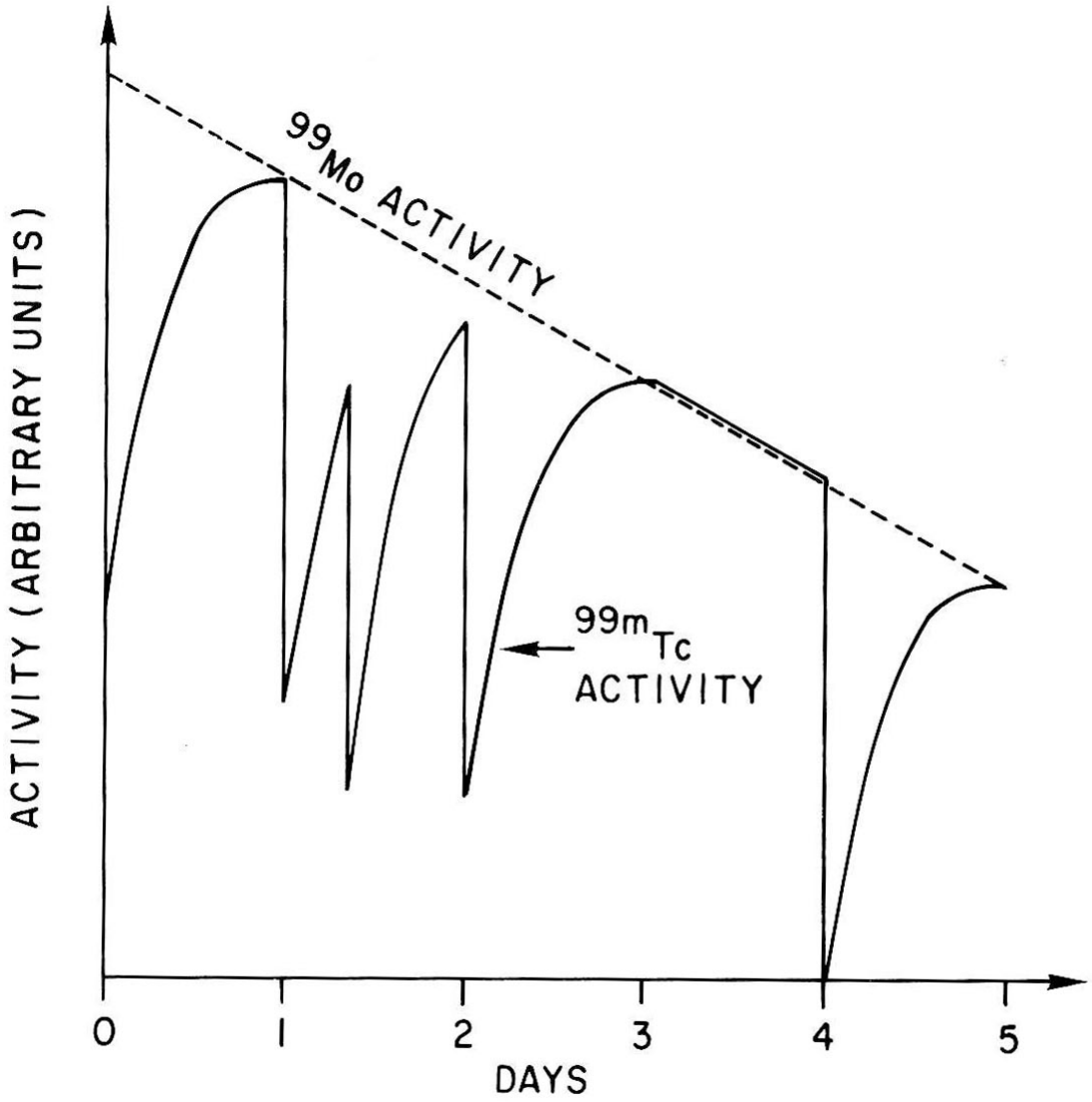


Fig. 7-6. Buildup and decay of ^{99m}Tc generator eluted on days 0, 1, 1.4, 2, and 4.

radifarmaci sa drugim radionuklidima		
^{123} **J**	**γ** 159 keV T ½ 13h	gama kamera ciklotronski proizvod
^{131} **J**	**γ** 364 keV T ½ 8 dana **β** čestica	gama kamera terapija bolesti štitaste žlezde
^{125} **J**	**γ** 30 keV T ½ 60 dana brojači radioaktivnosti	Obeležavanje monoklonskih antitela
^{111} **In**	**γ** 173...247...320 keV T ½ 67 dana	Obeležavanje eritrocita
^{67} **Ga**	**γ** 93...184 keV T ½ 78h	
^{201} **Tl**	**γ** 80...135..167 keV T ½ 73h	Sličan K+ aktivni transport u miocite
^{51} **Cr**	EC, **γ 320 keV** **T ½ 27,8d**	Obeležavanje Er i gubitak proteina preko GIT

Some Radioactive Isotopes Useful in Medical Imaging

Isotope		Mode of Decay	Half-life	Use in Medical Imaging
$^{11}_{6}C$	Carbon-11	β^+, γ	20.3 m	Brain scan to trace glucose metabolism
$^{18}_{9}F$	Fluorine-18	β^+, γ	109 m	Brain scan to trace glucose metabolism
$^{32}_{15}P$	Phosphorus-32	β	14.3 d	Detect eye tumors
$^{51}_{24}Cr$	Chromium-51	E.C., γ	27.7 d	Diagnose albinism, image the spleen and gastrointestinal tract
$^{59}_{26}Fe$	Iron-59	β, γ	44.5 d	Bone marrow function, diagnose anemias
$^{67}_{31}Ga$	Gallium-67	E.C., γ	78.3 h	Whole-body scan for tumors
$^{75}_{34}Se$	Selenium-75	E.C., γ	118 d	Pancreas scan
$^{81m}_{36}Kr$	Krypton-81m	γ	13.3 s	Lung ventilation scan
$^{81}_{38}Sr$	Strontium-81	β	22.2 m	Scan for bone diseases, including cancer
$^{99m}_{43}Tc$	Technetium-99m	γ	6.01 h	Brain, liver, kidney, bone scans; diagnosis of damaged heart muscle
$^{131}_{53}I$	Iodine-131	β, γ	8.04 d	Diagnosis of thyroid malfunction
$^{197}_{80}Hg$	Mercury-197	E.C., γ	64.1 h	Kidney scan
$^{201}_{81}Tl$	Thallium-201	E.C., γ	3.05 d	Heart scan and exercise stress test

Radioaktivni izotopi za terapiju bola kod koštanih metastaza

Table 1 - Radioactive isotopes used for metastatic bone pain management.

ISOTOPE	EMISSION	MEAN HALF-LIFE	MEAN.β ENERGY	SOFT TISSUE PENETRATION
Phosphorus (^{32}P)	β	14.4 days	695 KeV	8 mm.
Strontium (^{89}Sr)	β	50.5 days	583 KeV	2.4 mm.
Samarium (^{153}Sm)	β and γ	4 46.3 hours	233 KeV	3.1 mm.
Renium (^{186}Re)	β and γ	3.8 days	349 Kev	1.1 mm.
Tin (^{117}Sn)	β and γ	13.6 days	135 KeV	0.3 mm.

Table 7-1
Some Reactor-produced Radionuclides Used in Nuclear Medicine and Radiotracer Kinetics

Radionuclide	Decay Mode	Production Reaction	Natural Abundance of Target Isotope (%)	σ_c (b)*
^{14}C	β^-	$^{14}N(n,p)^{14}C$	99.6	1.81
^{24}Na	(β^-,γ)	$^{23}Na(n,\gamma)^{24}Na$	100	0.53
^{32}P	β^-	$^{31}P(n,\gamma)^{32}P$	100	0.19
		$^{32}S(n,p)^{32}P$	95.0	—
^{35}S	β^-	$^{35}Cl(n,p)^{35}S$	75.5	—
^{42}K	(β^-,γ)	$^{41}K(n,\gamma)^{42}K$	6.8	1.2
^{51}Cr	(EC,γ)	$^{50}Cr(n,\gamma)^{51}Cr$	4.3	17
^{59}Fe	(β^-,γ)	$^{58}Fe(n,\gamma)^{59}Fe$	0.3	1.1
^{75}Se	(EC,γ)	$^{74}Se(n,\gamma)^{75}Se$	0.9	30
^{125}I	(EC,γ)	$^{124}Xe(n,\gamma)^{125}Xe \xrightarrow{EC} {}^{125}I$	0.1	110
^{131}I	(β^-,γ)	$^{130}Te(n,\gamma)^{131}Te \xrightarrow{\beta^-} {}^{131}I$	34.5	0.24

*Thermal neutron capture cross-section, in barns, for (n,γ) reactions (see Section D.1). Values from ref. 1.

Table 7-2
Some Cyclotron-produced Radionuclides Used in Nuclear Medicine

Product	Decay Mode	Common Production Reaction	Natural Abundance of Target Isotope (%)
^{11}C	β^+	$^{10}B(d,n)^{11}C$	19.7
		$^{11}B(p,n)^{11}C$	80.3
^{13}N	β^+	$^{12}C(d,n)^{13}N$	98.9
^{15}O	β^+	$^{14}N(d,n)^{15}O$	99.6
^{18}F	β^+,EC	$^{20}Ne(d,\alpha)^{18}F$	90.9
^{22}Na	β^+,EC	$^{23}Na(p,2n)^{22}Na$	100
^{43}K	(β^-,γ)	$^{40}Ar(\alpha,p)^{43}K$	99.6
^{67}Ga	(EC,γ)	$^{68}Zn(p,2n)^{67}Ga$	18.6
^{111}In	(EC,γ)	$^{109}Ag(\alpha,2n)^{111}In$	48.7
		$^{111}Cd(p,n)^{111}In$	12.8
^{123}I	(EC,γ)	$^{122}Te(d,n)^{123}I$	2.5
		$^{124}Te(p,3n)^{123}I$	4.6
^{201}Tl	(EC,γ)	$^{201}Hg(d,2n)^{201}Tl$	13.2

instrumentacija

- jonizacioni detektori
- scintilacioni brojači
- gama kamera
- jednofotonska emisiona tomografija
  SPECT
- Pozitronska emisiona tomografija
  PET
- digitalni računari

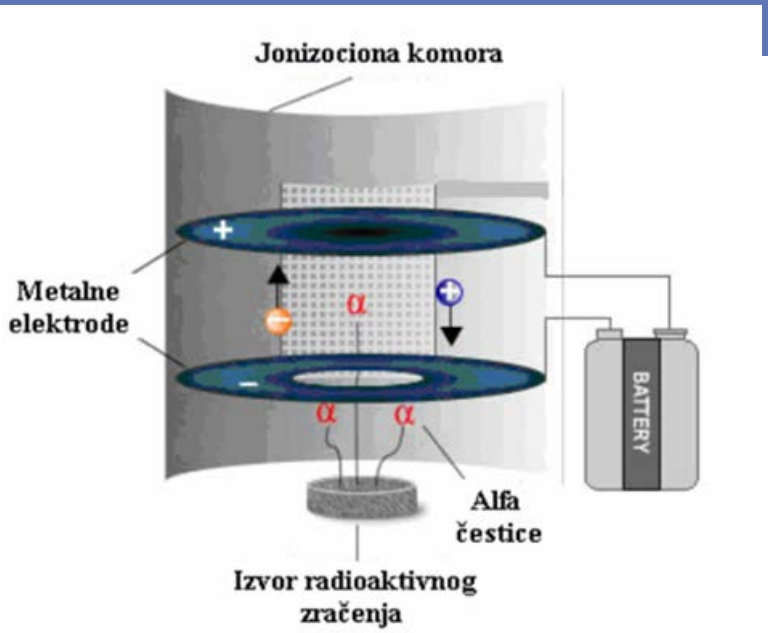
instrumentacija

fizički detektori zračenja	
vrsta	**primena**
Jonizacioni detektori • jonizaciona komora • proporcionalni brojač • Gajger-Milerov brojač	• dozekalibrator, lični dozimetar • gasna hromatografija • merenje zračenja u spoljnoj sredini
Scintilacioni detektori • In vivo brojač • In vitro brojač • Gama kamera • PET kamera	• merenje aktivnosti u organizmu • merenje aktivnosti koncentracije jedinjenja u telesnim tečnostima • planarna scintigrafija •Tomografska scintigrafija sa pozitronskim emiterima

instrumentacija

Jonizacioni detektor

- jonizacija vazduha ili gasa pod dejstvom upadnih radioaktivnih čestica
- opseg promene napona
  - Komora meri kumulativnu dozu zračenja; E upadnog zračenja je proporcionalna amplitudi strujnog impulsa: **Kalibrator doza** (za nuklearnu medicinu)
  - Monitor zračenja registruje ekspozicionu aktivnost radionuklida u laboratoriji
  - Lični dozimetar
  - Gajger Milerov brojač danas samo za merenje zračenja u spoljnoj sredini







instrumentacija

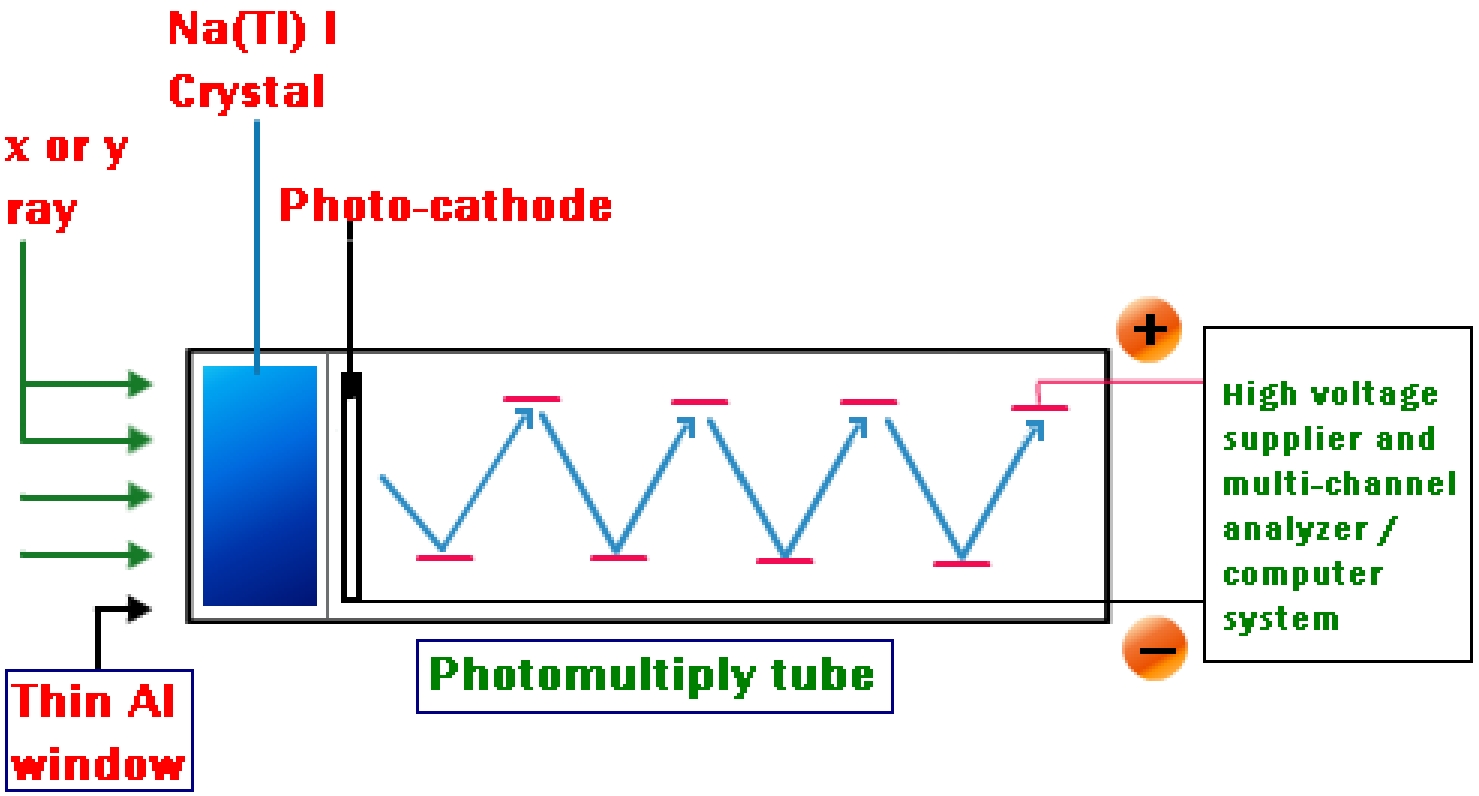


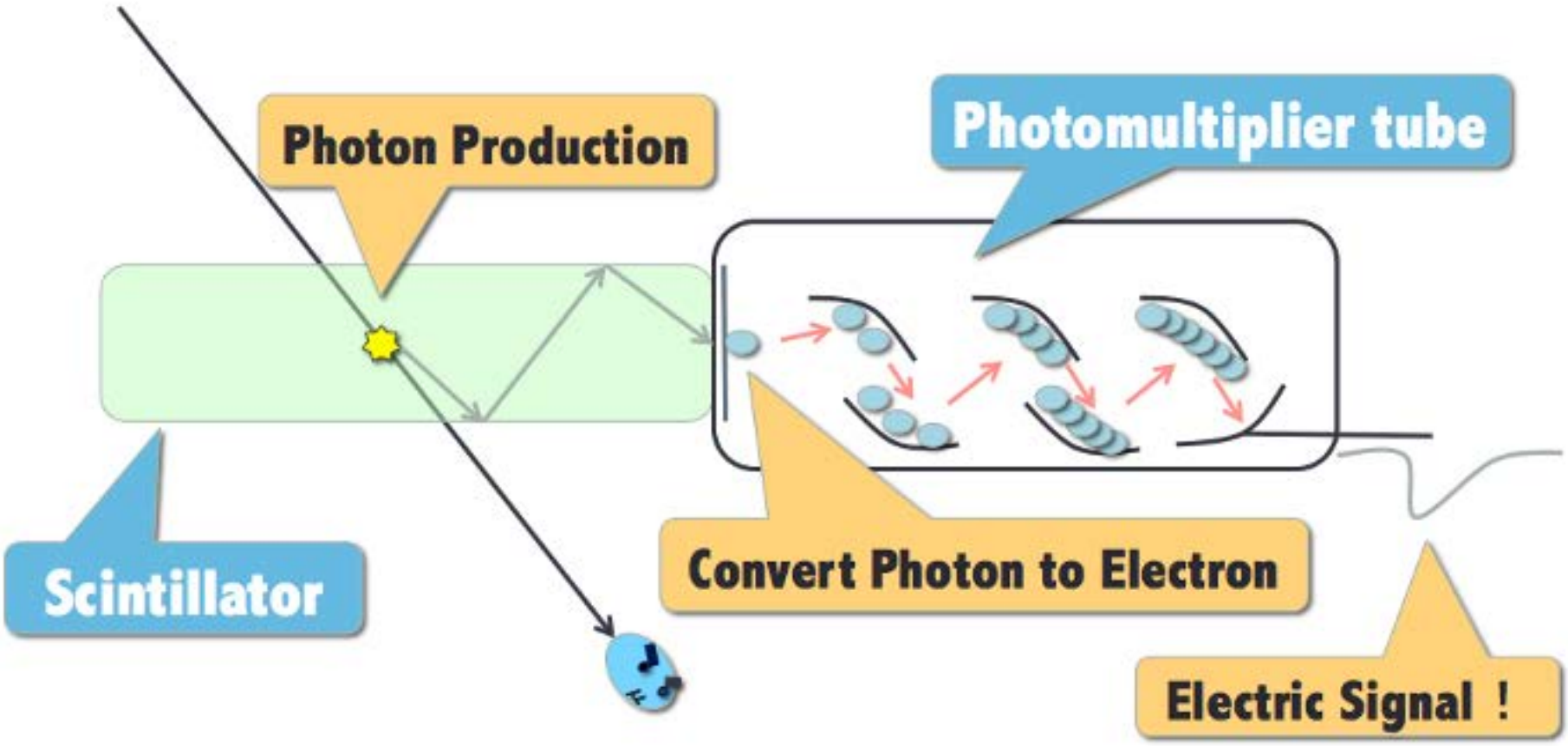
scintilacioni detektori

- kolimator
- kristal
- fotomultiplikator
- linearni pojačivač
- amplitudni analizator
- merač brzine brojanja (skaler)
- merač srednje brzine brojanja (rejtmetar)

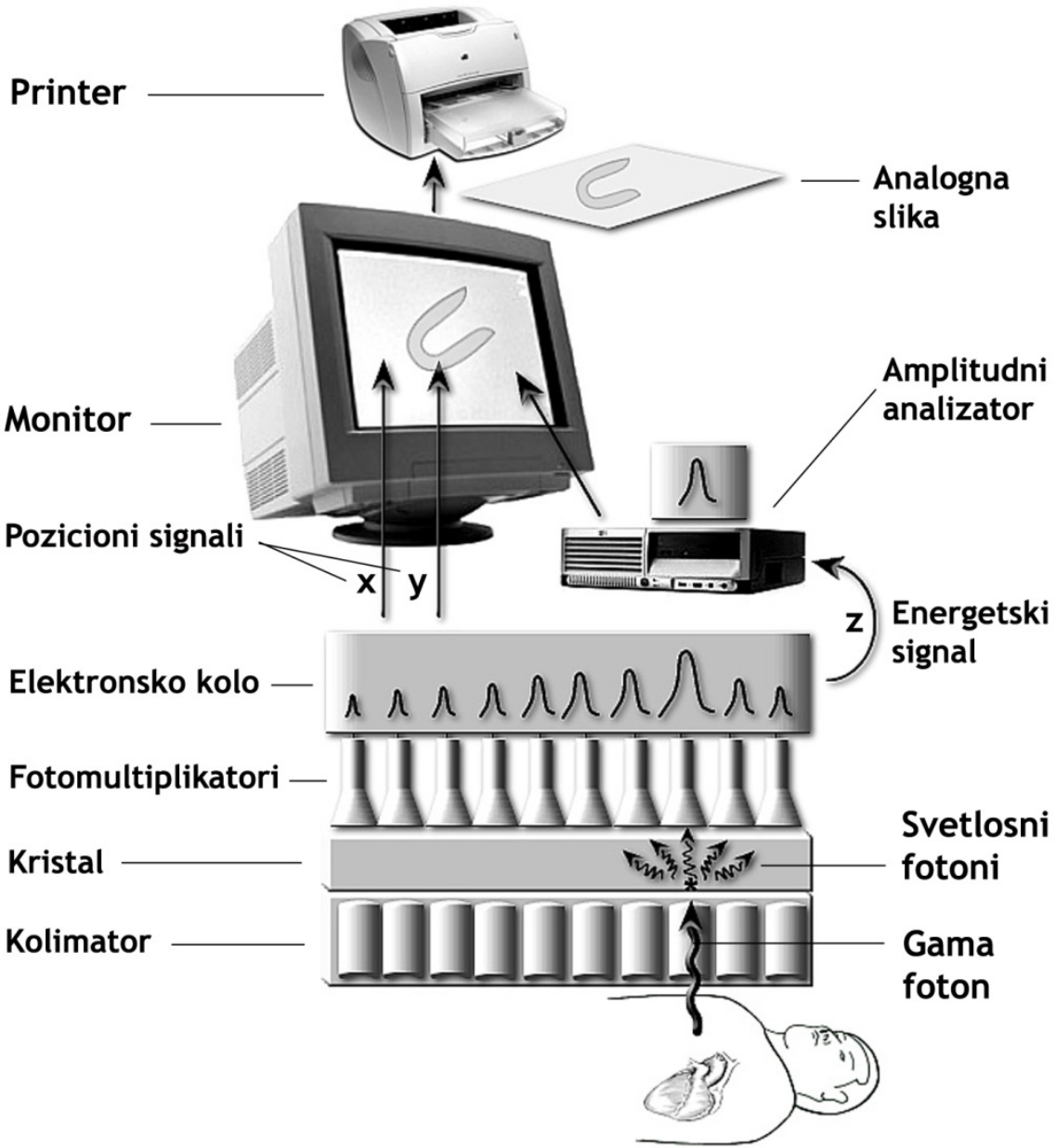
- brojač za in vitro
- tečni scintilacioni brojači

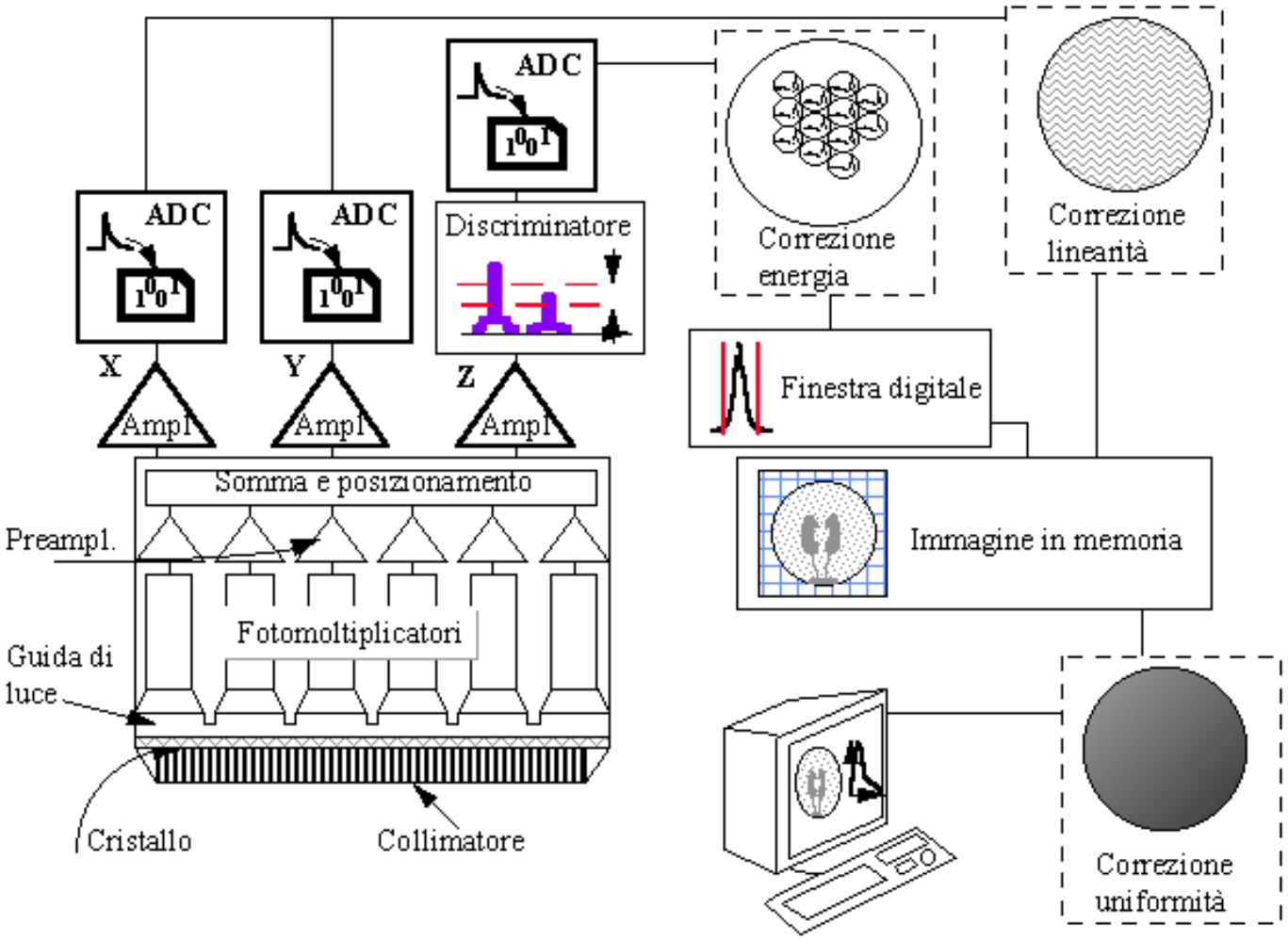
Scintillation Counter




Photon Production
Photomultiplier tube
Scintillator
Convert Photon to Electron
Electric Signal !

Komponente i princip rada gama kamere




ADC
ADC
ADC
Discriminatore
Correzione energia
Correzione linearità
X
Y
Z
Ampl
Ampl
Ampl
Finestra digitale
Somma e posizionamento
Preampl.
Immagine in memoria
Fotomoltiplicatori
Guida di luce
Cristallo
Collimatore
Correzione uniformità

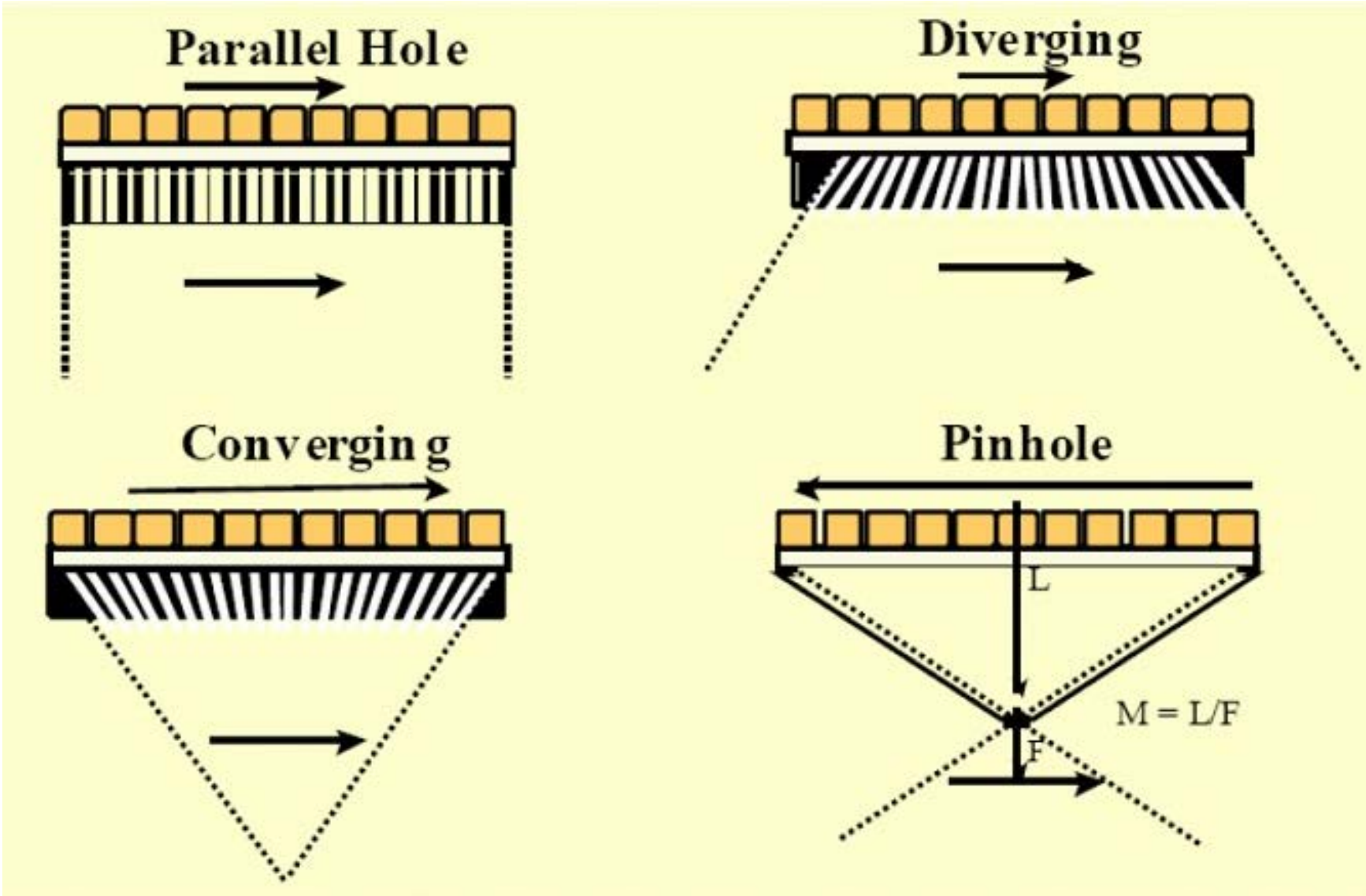


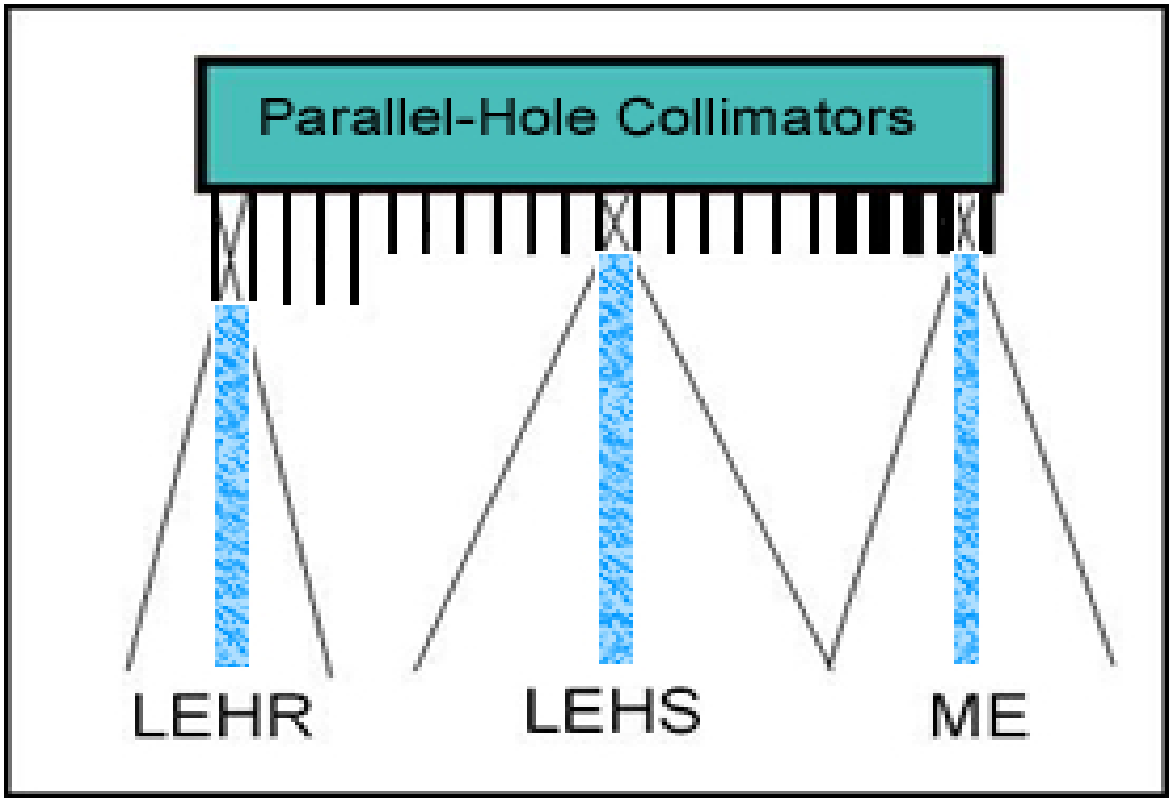
Hal Anger



Gama kamera

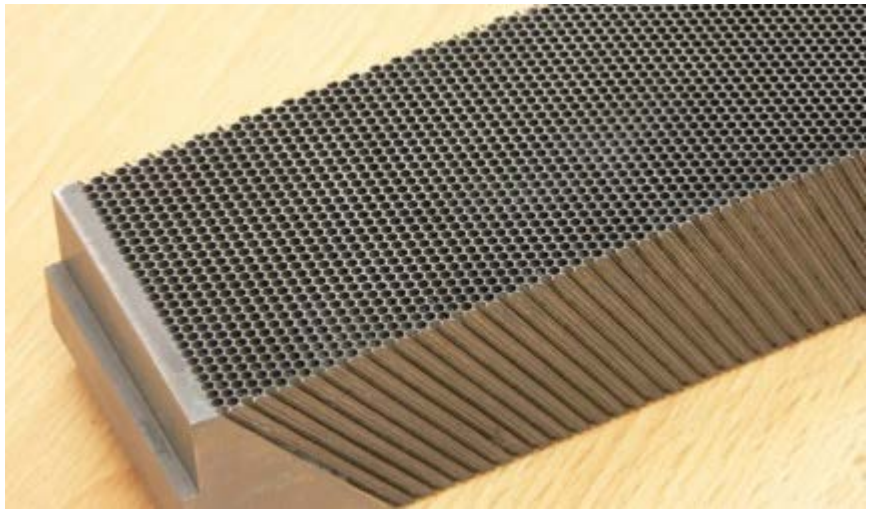


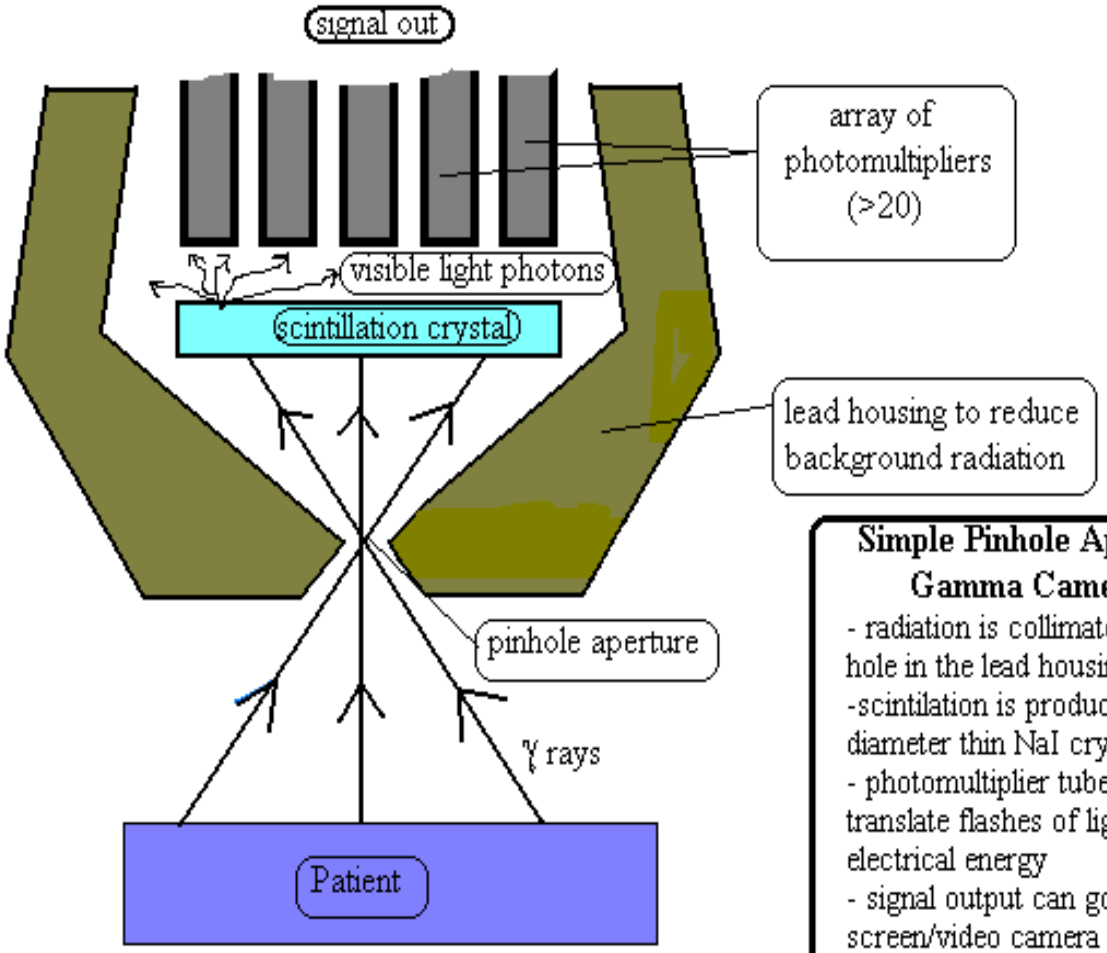

Parallel Hole
Diverging
Converging
Pinhole
L
M = L/F
F

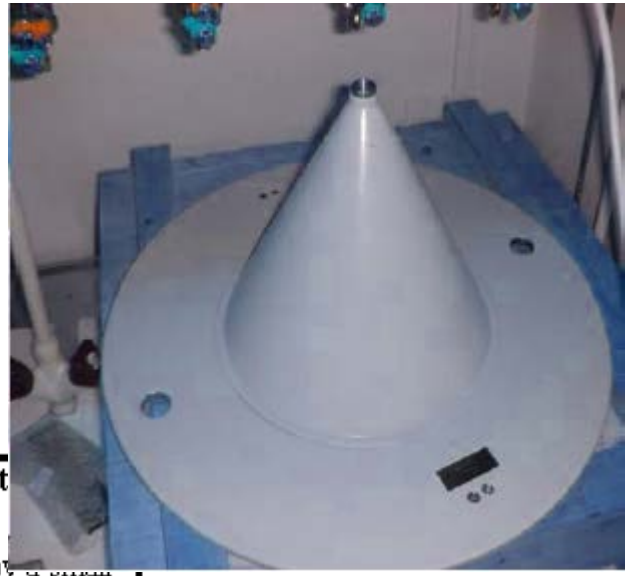




ristal

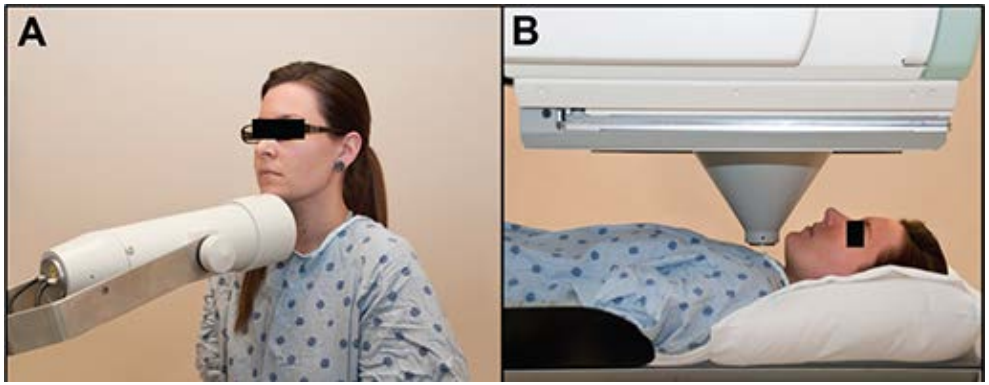




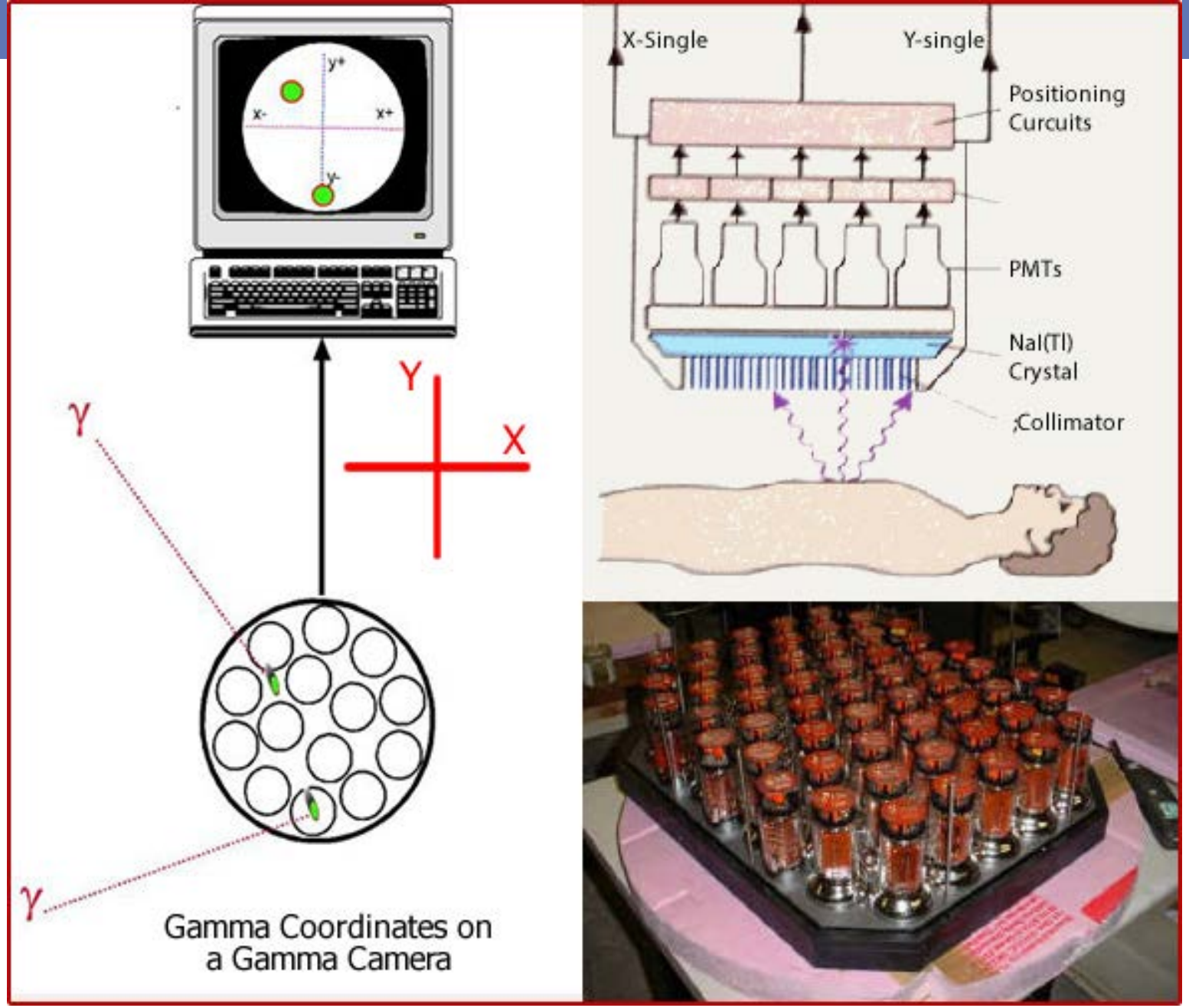


Simple Pinhole Apert
Gamma Camera

- radiation is collimated by a [illegible] hole in the lead housing
- scintilation is produced in the large diameter thin NaI crystal
- photomultiplier tubes change translate flashes of light into electrical energy
- signal output can go to a TV screen/video camera etc.






y+
x-
x+
y-
Y
X
γ
γ
Gamma Coordinates on
a Gamma Camera
X-Single
Y-single
Positioning
Curcuits
PMTs
NaI(Tl)
Crystal
;Collimator

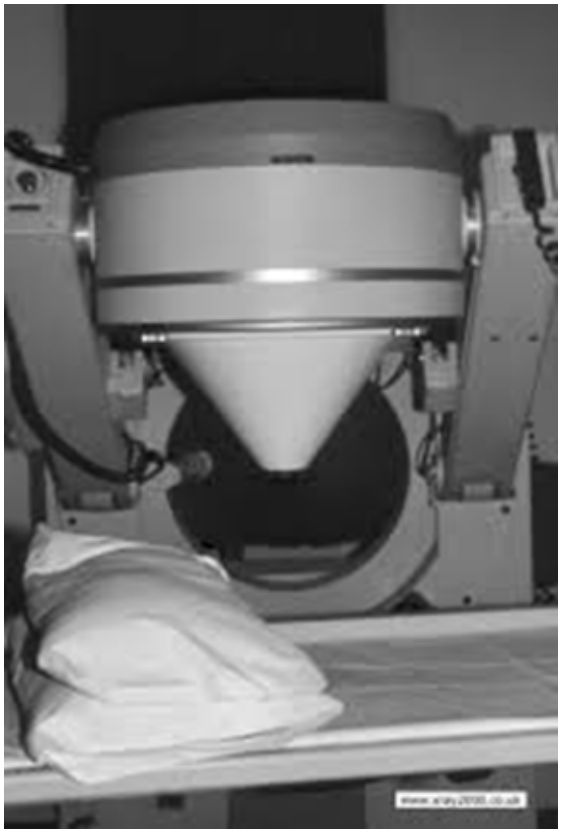






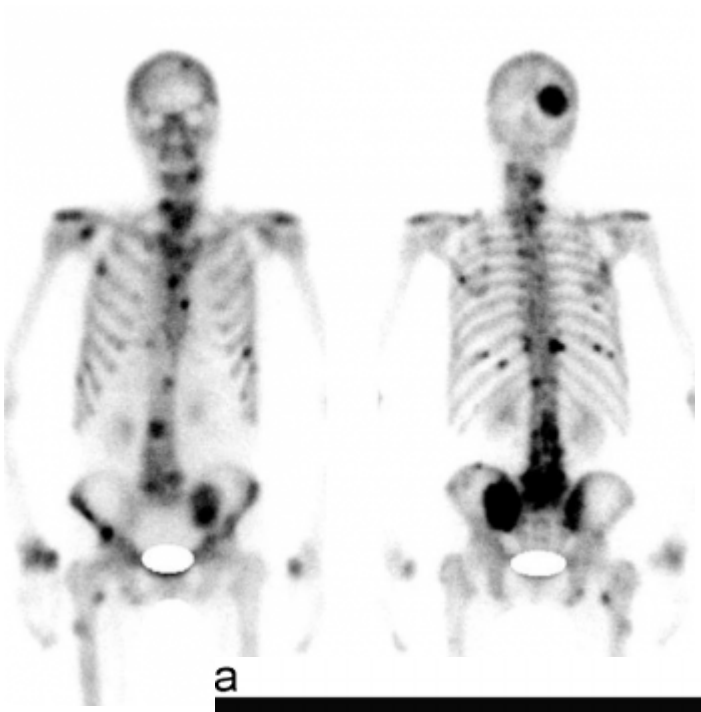

Symbia

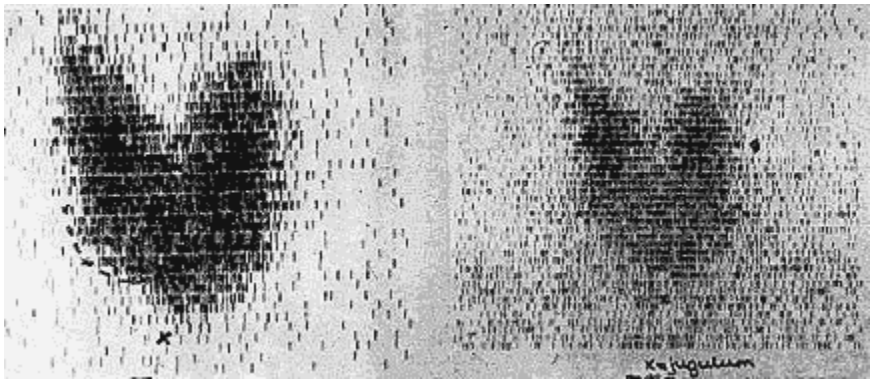




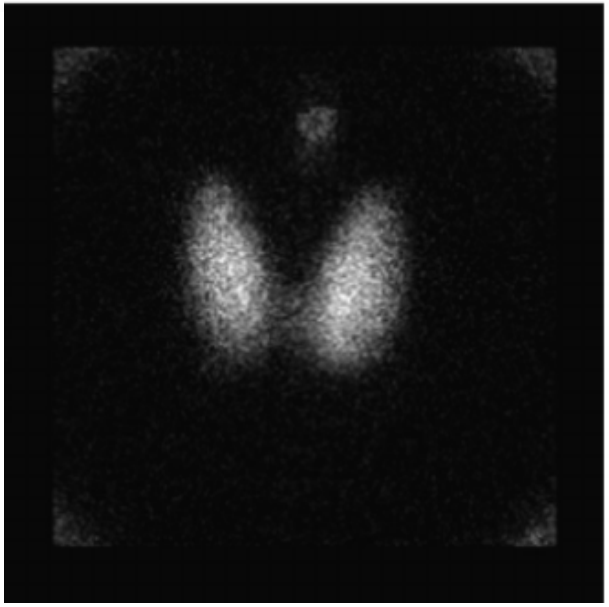
scintigram

- **scintigrafija** je postupak dobijanja slike distribucije radioaktivnosti u ciljnom organu
- slika se zove **scintigram**
  - **statička**
  - **dinamska**
  - **planarna**
  - **tomografska**
    - **gama emiteri SPECT**
    - **pozitronski emiteri PET**

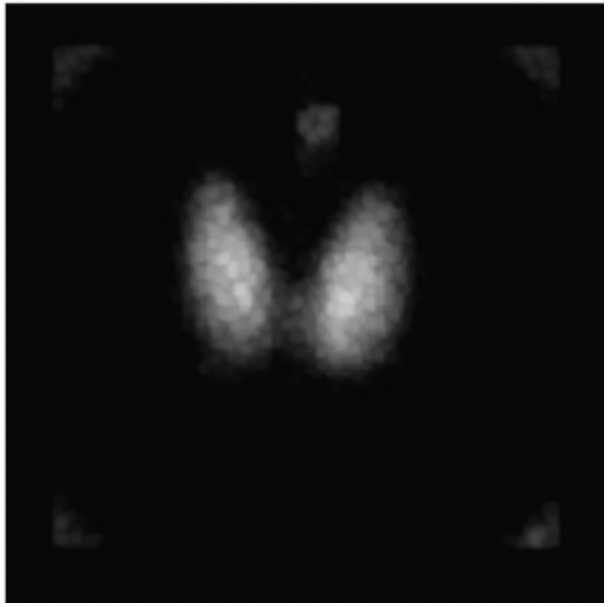


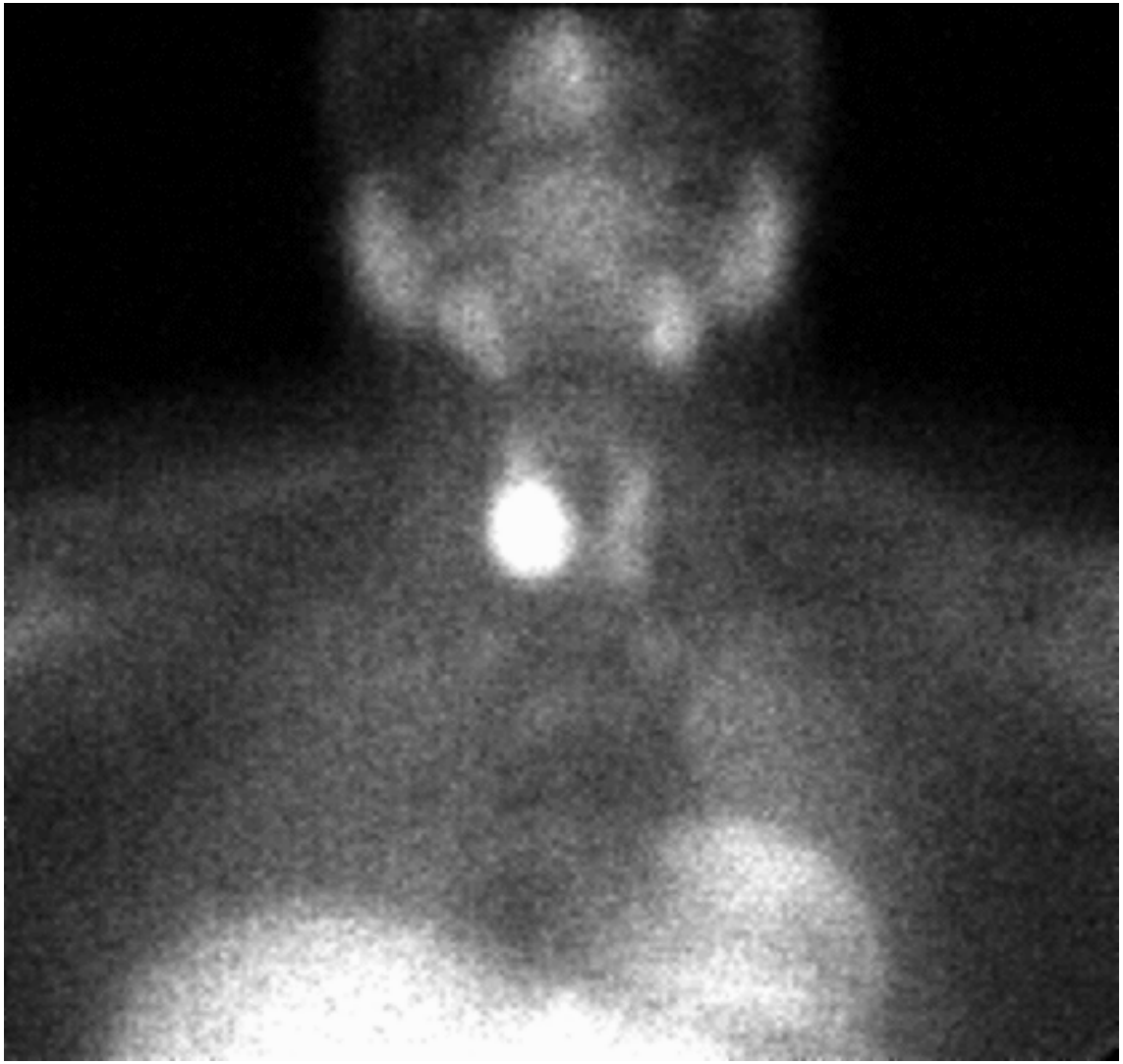


a



b





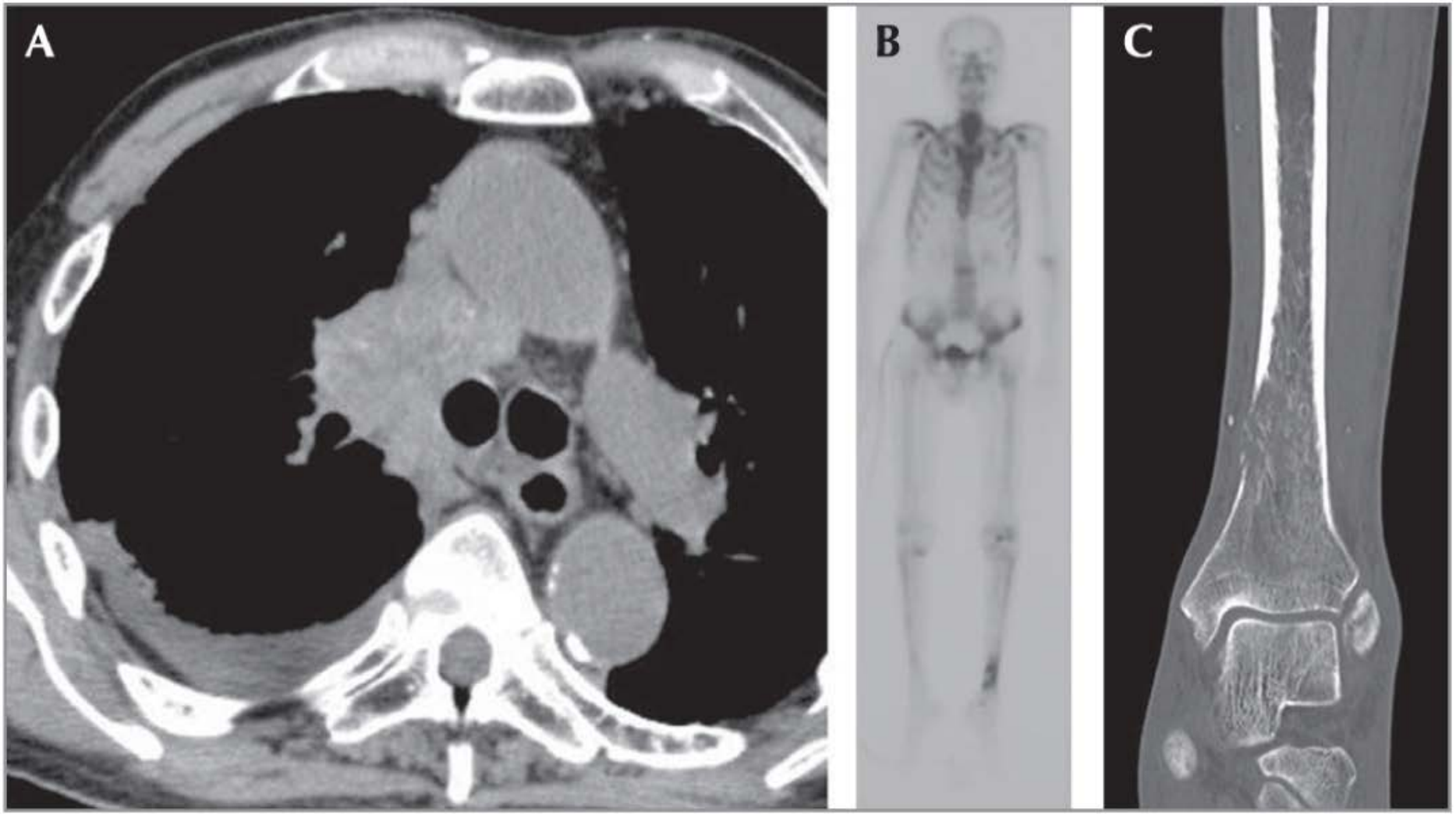
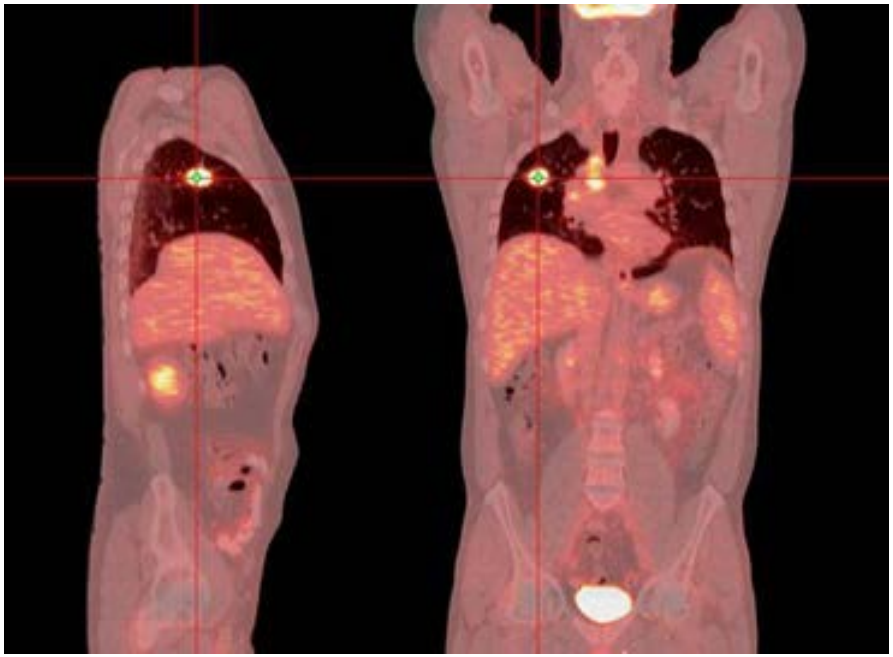
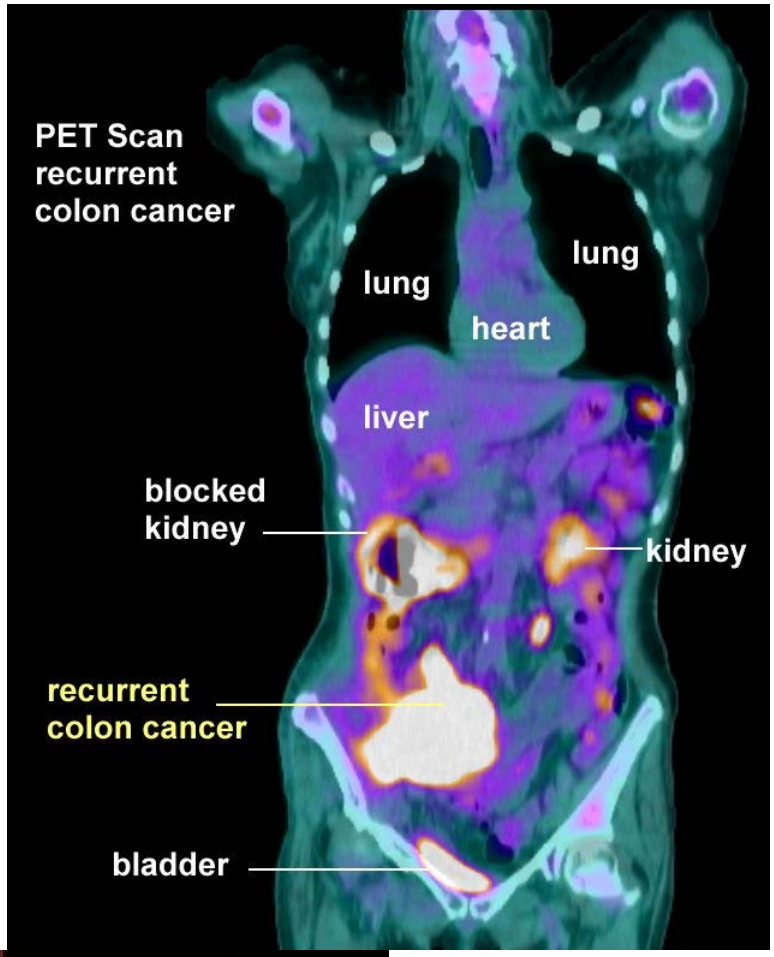
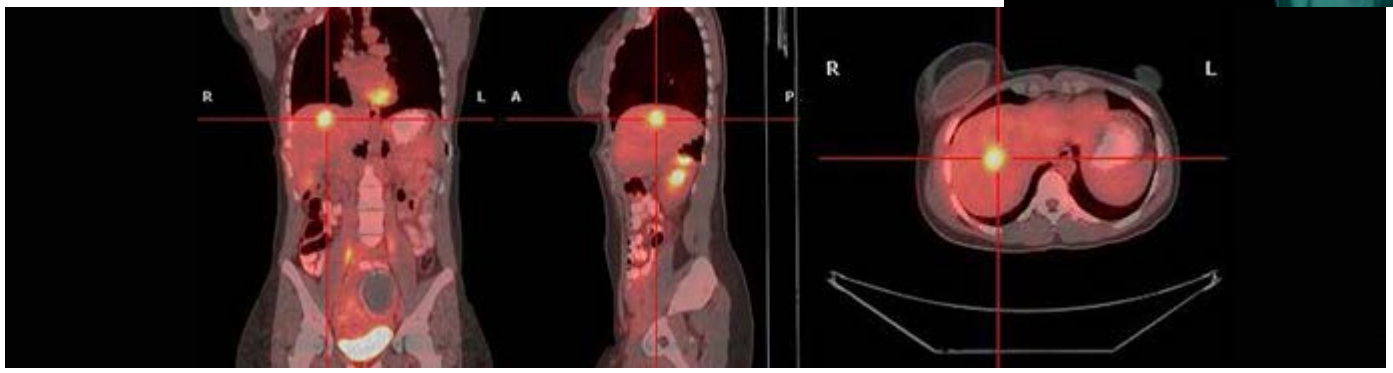


Figure 1. Chest CT scan showed a mass with ipsilateral hilar and mediastinal lymph node swelling and pleural fluid (A). 99Tc-MDP bone scintigram (B) and CT scan (C) showed solitary tibia metastasis.




PET Scan
recurrent
colon cancer
lung
lung
heart
liver
blocked
kidney
kidney
recurrent
colon cancer
bladder


R
L
A
P
R
L

Florbetapir 18 Month
Follow up Study

