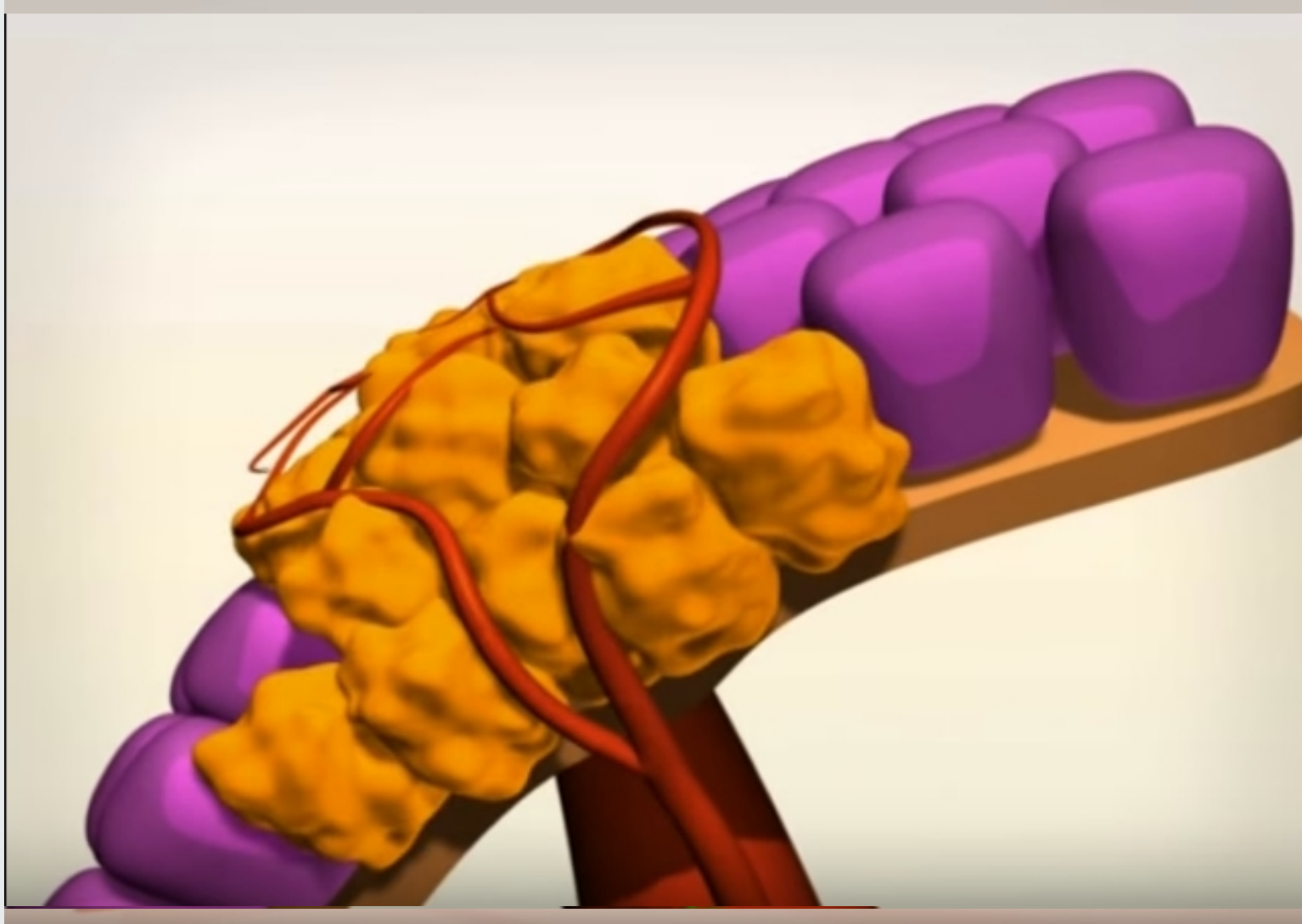


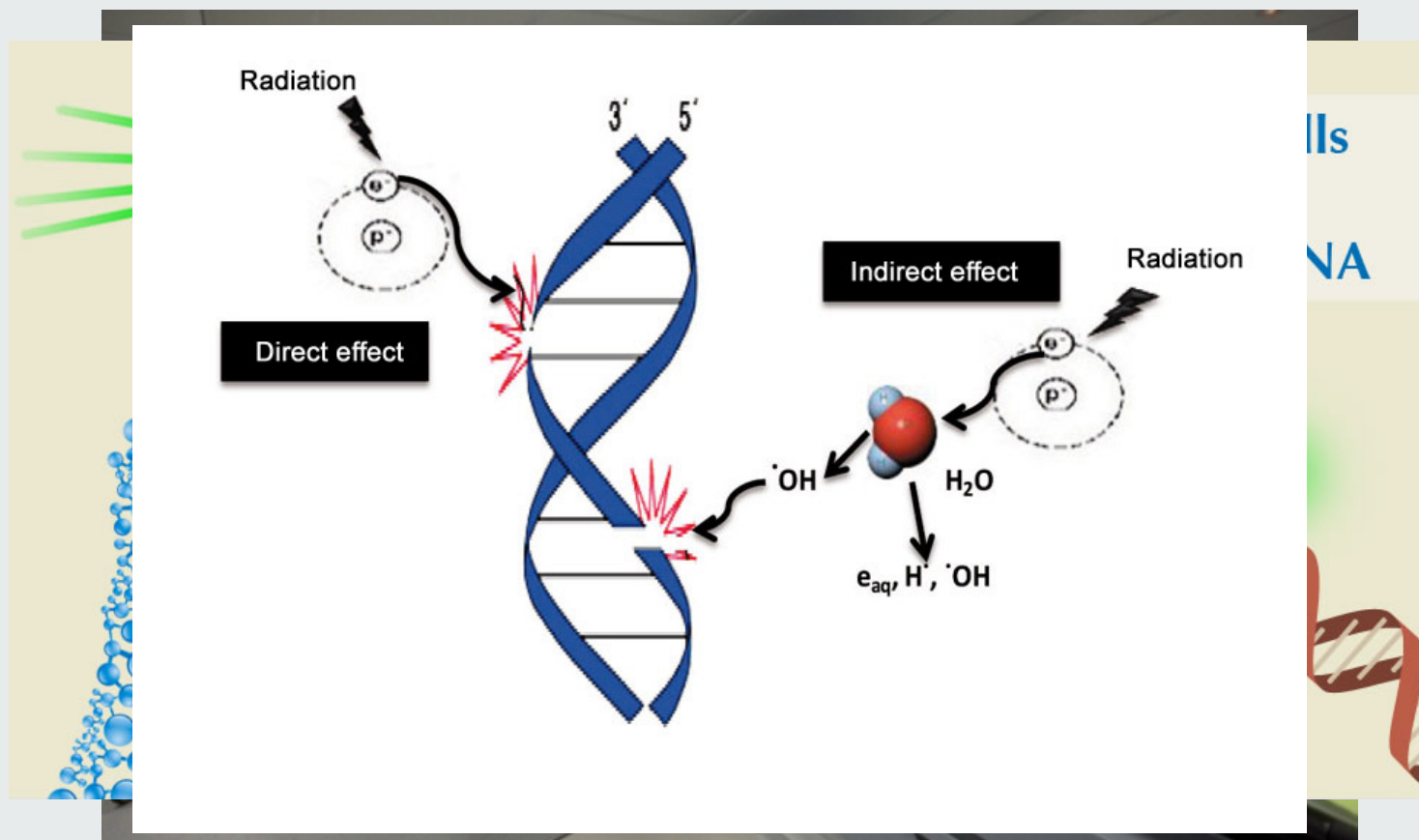
# MEDICIS-Promed: Dos Nanomateriais aos Radiofármacos para o Tratamento do Cancro

**Alice D'Onofrio, S. Chowdhury,  
A.P. Gonçalves, A. Paulo**

*C<sup>2</sup>TN, Instituto Superior Técnico, Universidade de Lisboa,  
Bobadela, Portugal*



Tratamento no qual se utilizam radiações ionizantes para destruir ou impedir que o número das células de tumor aumentem.



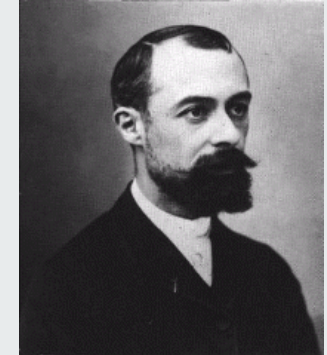
1895

Röntgen descobre os raios X



1896

Becquerel descobre a radioactividade natural do urânio



1898

Pierre e Marie Curie descobrem o Rádio (Ra) e o Polónio (Po)





1931

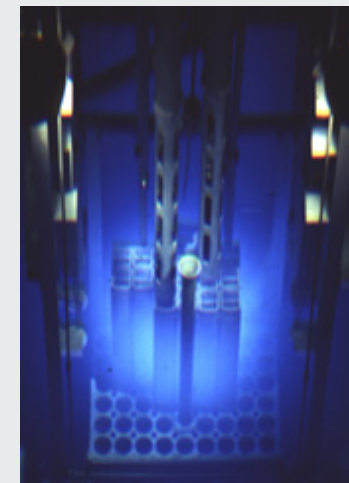
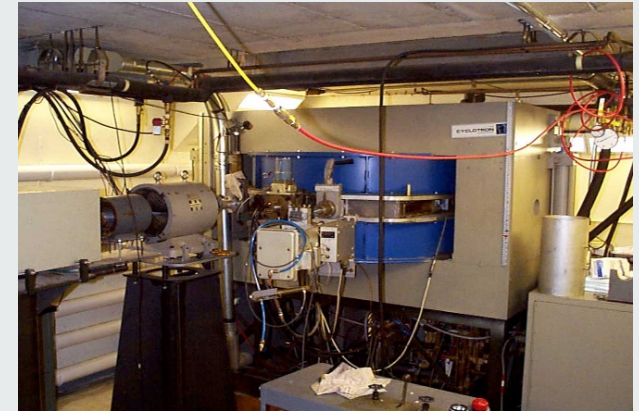
Irene e Frederic Joliot-Curie produzem os primeiros radioisótopos artificiais

1935

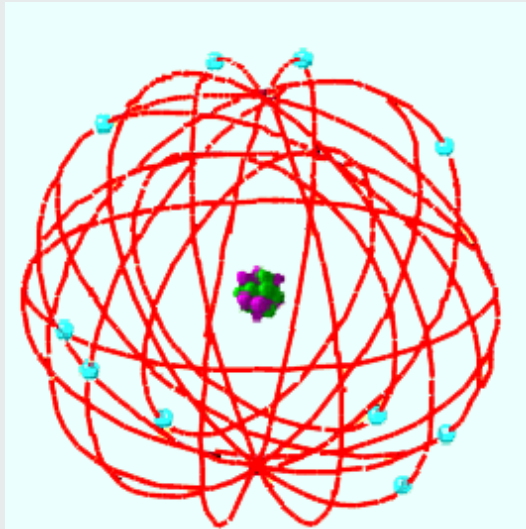
Ernest Lawrence produz o isótopo radioactivo de sódio num ciclotrão

1942

O primeiro reactor nuclear é construído e posto operacional no Oak Ridge National Laboratory

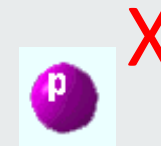


## Átomo/Núcleo

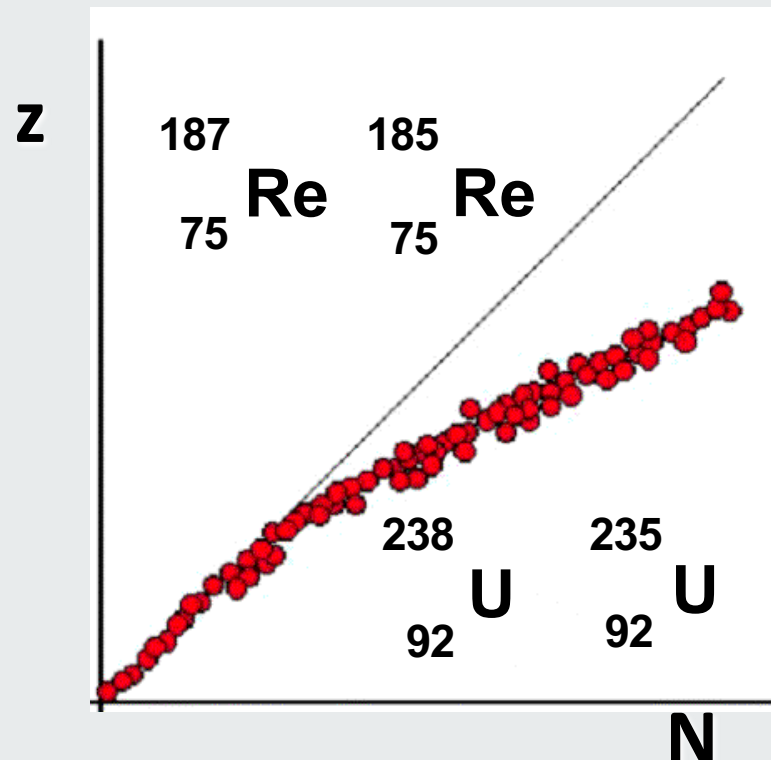


## Isótopos

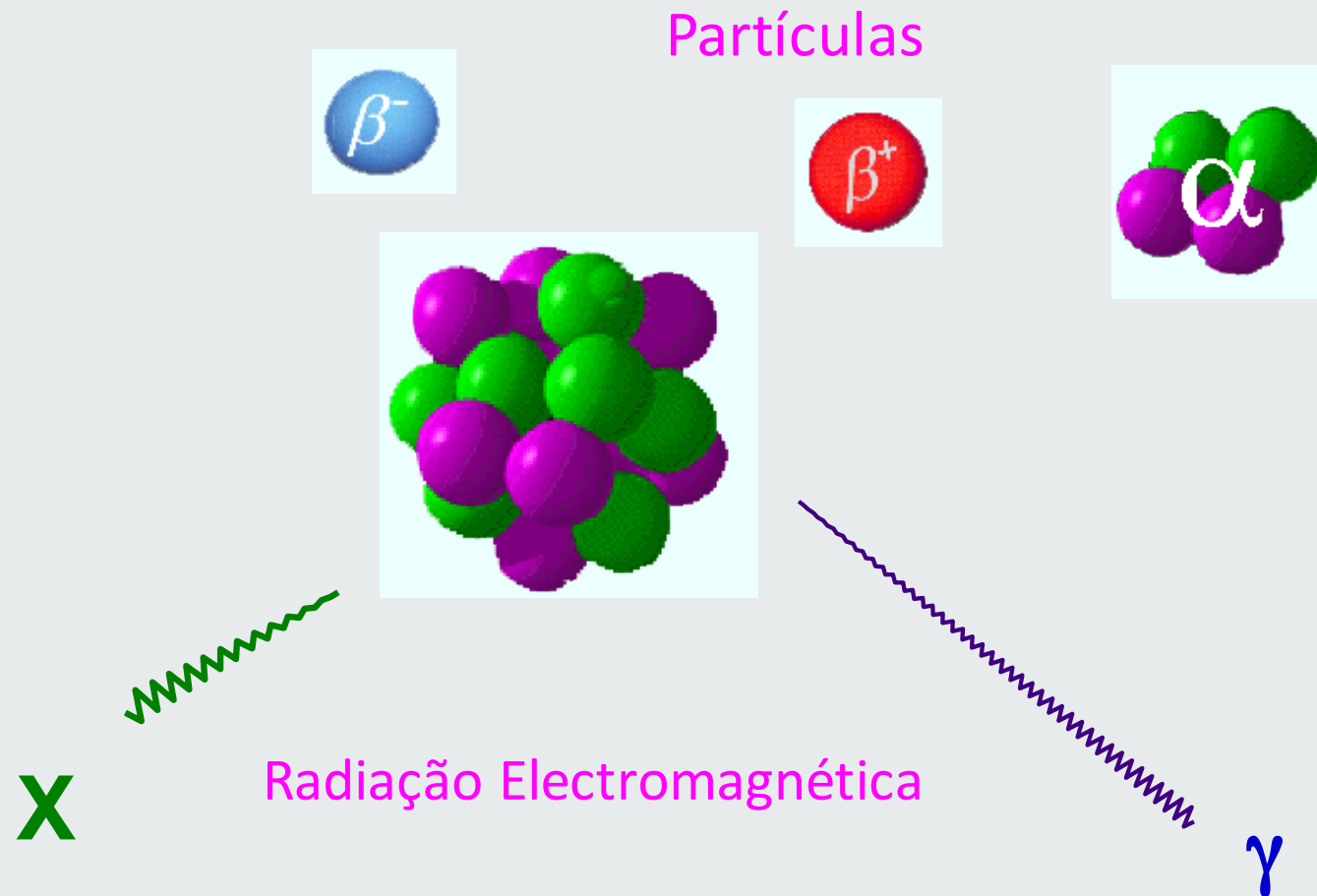
Número de Massa



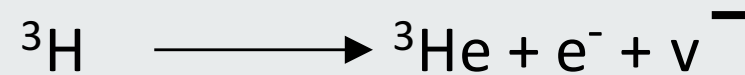
Número Atómico



## TRANSMUTAÇÃO NUCLEAR ESPONTÂNEA



**Decaimento <sup>-</sup>** : núcleos ricos em neutrões



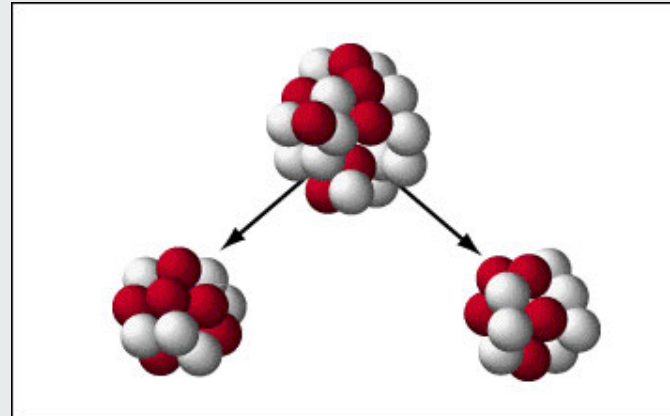
**Decaimento <sup>+</sup>** : núcleos ricos em protões



**Captura Electrónica** : núcleos ricos em protões

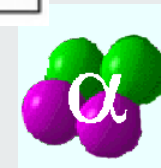
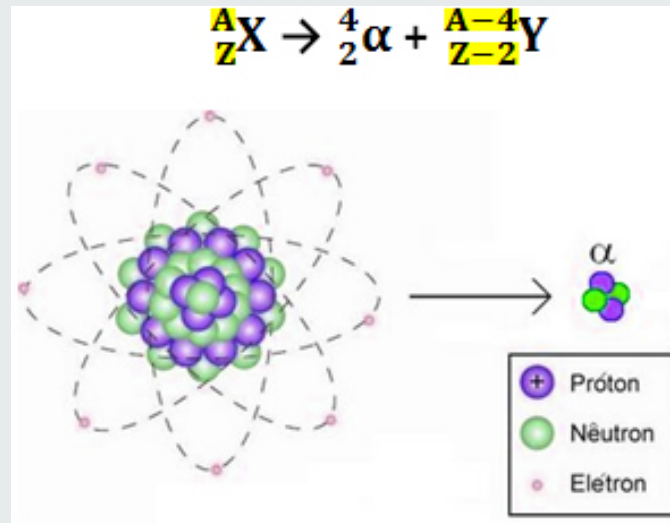


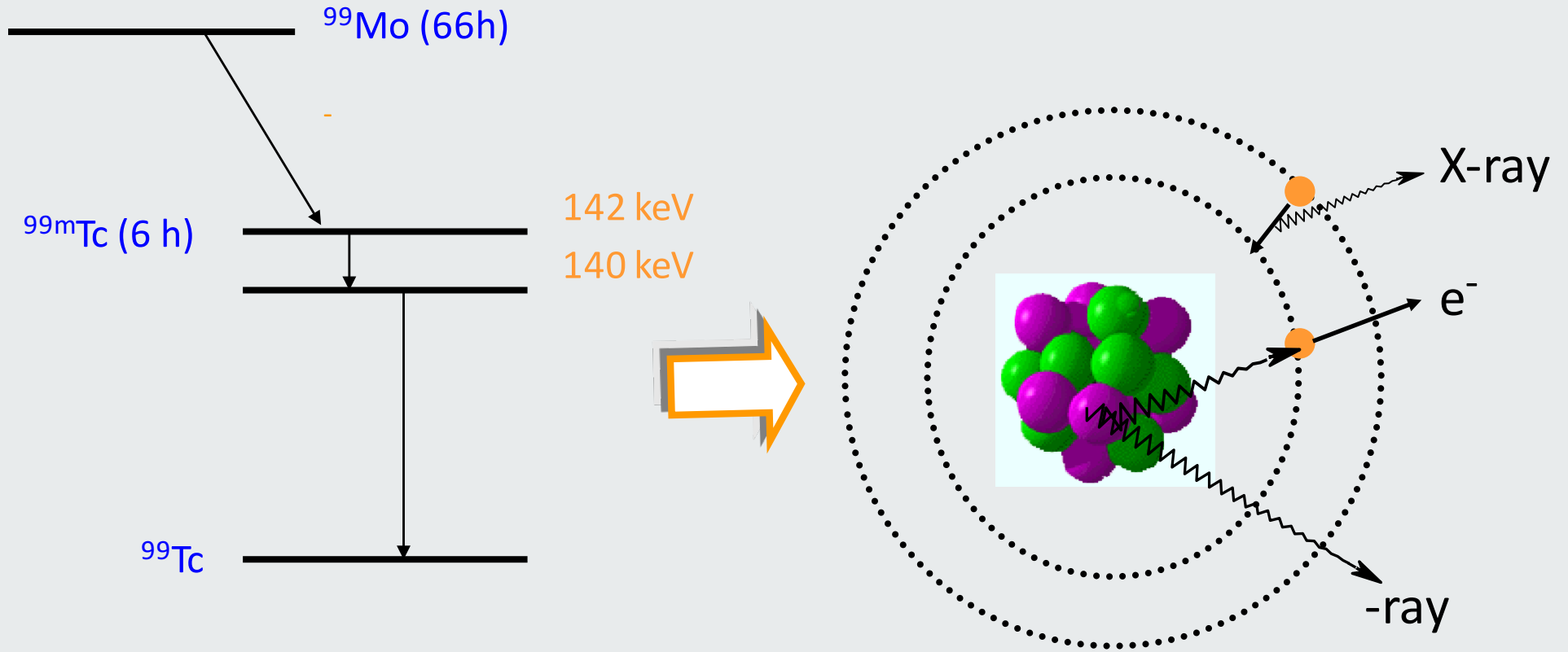
## Fissão Espontânea



+ Energia

## Decaimento





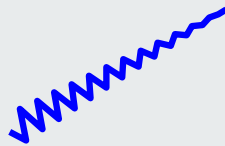


4  
2  $\text{He}^{2+}$

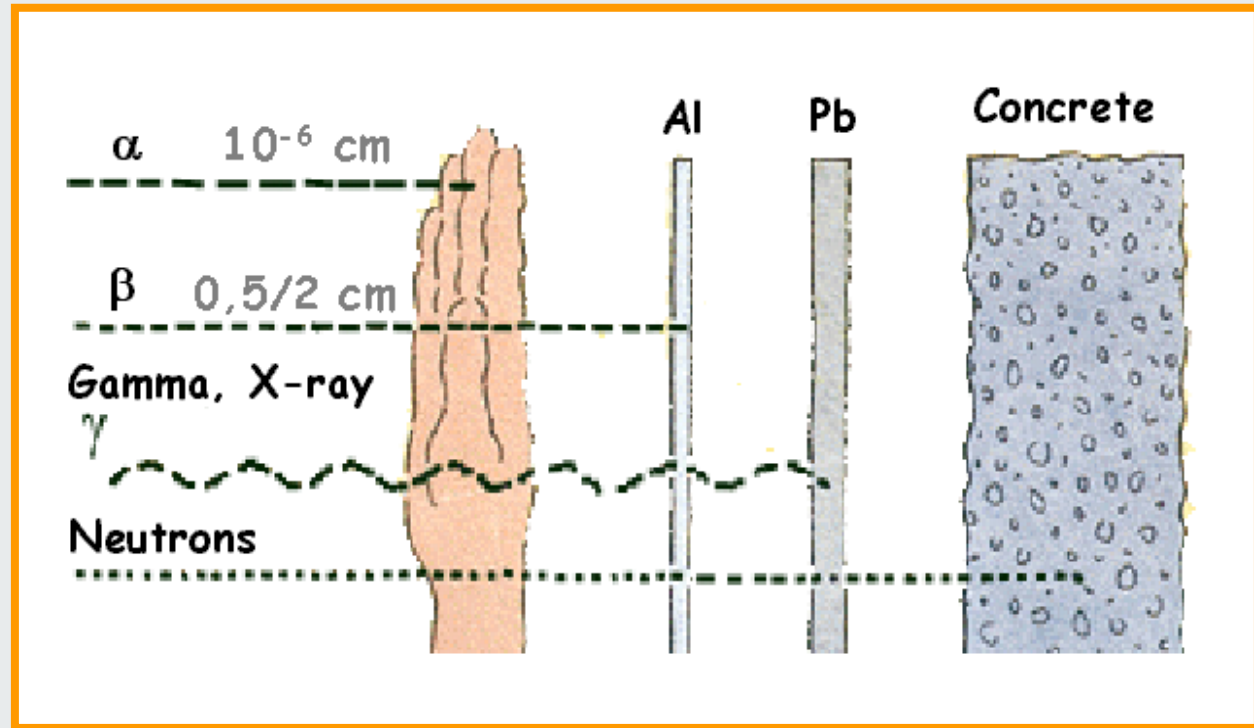


0  
-1  $e^{-}$

$\gamma$



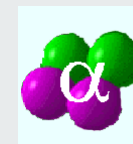
0  
1  $e^{+}$



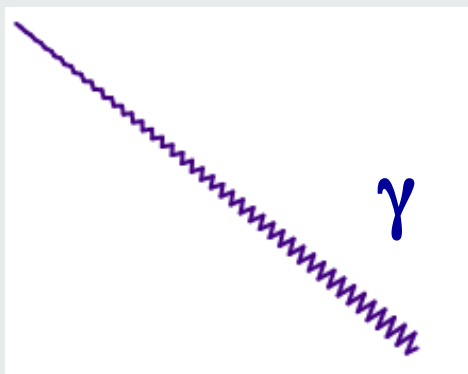


Compostos que contêm um radionuclido e são usados em medicina para aplicações de diagnóstico ou terapêutica

**Terapia com Radionuclidos**

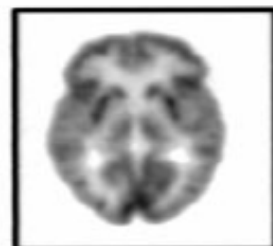
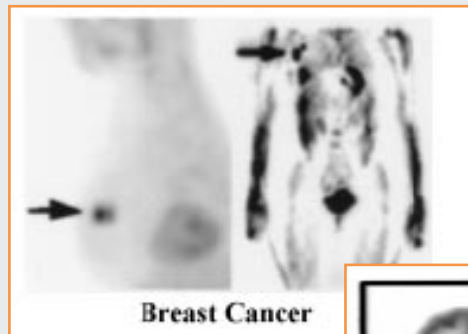
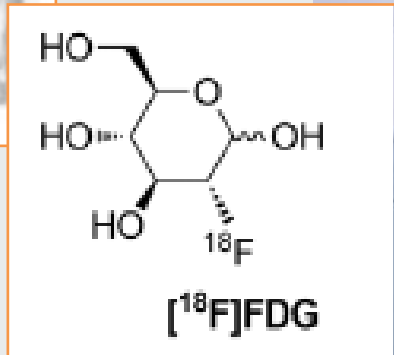
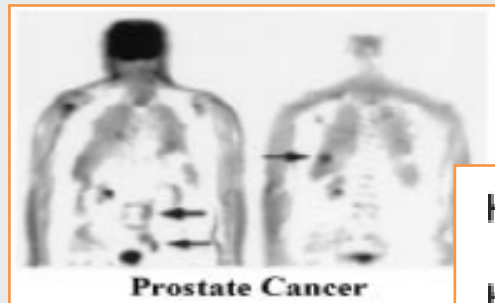


**PET: Positron Emission Tomography**

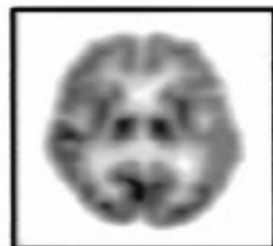


**SPECT: Single Photon Emission Computerized Tomography**

*O radiofármaco é administrado a um paciente e um detector externo detecta os fotões  $\gamma$  emitidos: 50-250 keV (SPECT); 511 keV (PET)*



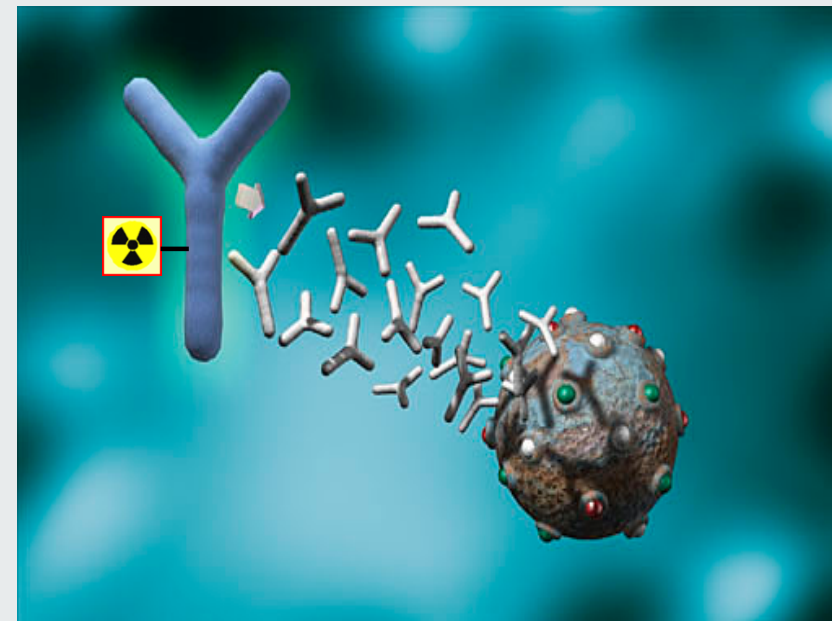
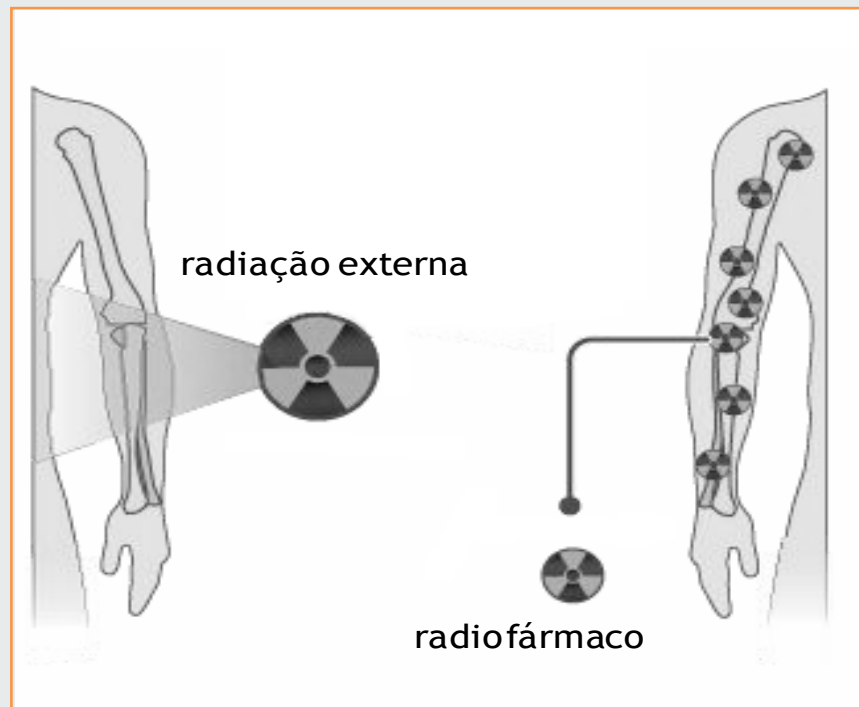
**Normal**



**Early Alzheimer's**

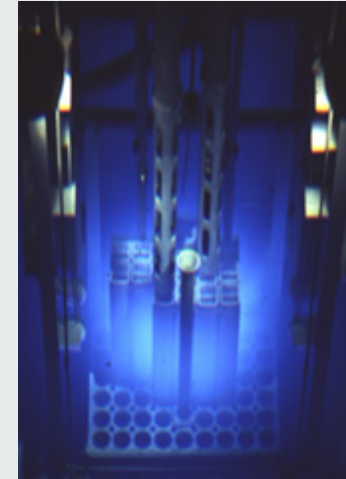


O *radiofármaco* é administrado a um paciente e a radiação ionizante emitida (partículas  $\beta^-$  ou  $\alpha$ ) exercem um efeito antitumoral



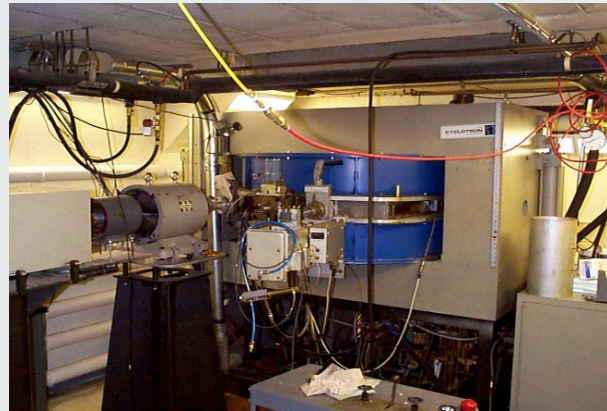
## ❖ Reactores Nucleares

Emissores  $\beta^-$ /  
Ricos em Neutrões



## ❖ Ciclotrão

Emissores  $\beta^+$  ou  $\gamma$ /  
Ricos em Protões



## ❖ Geradores de Radionuclidos

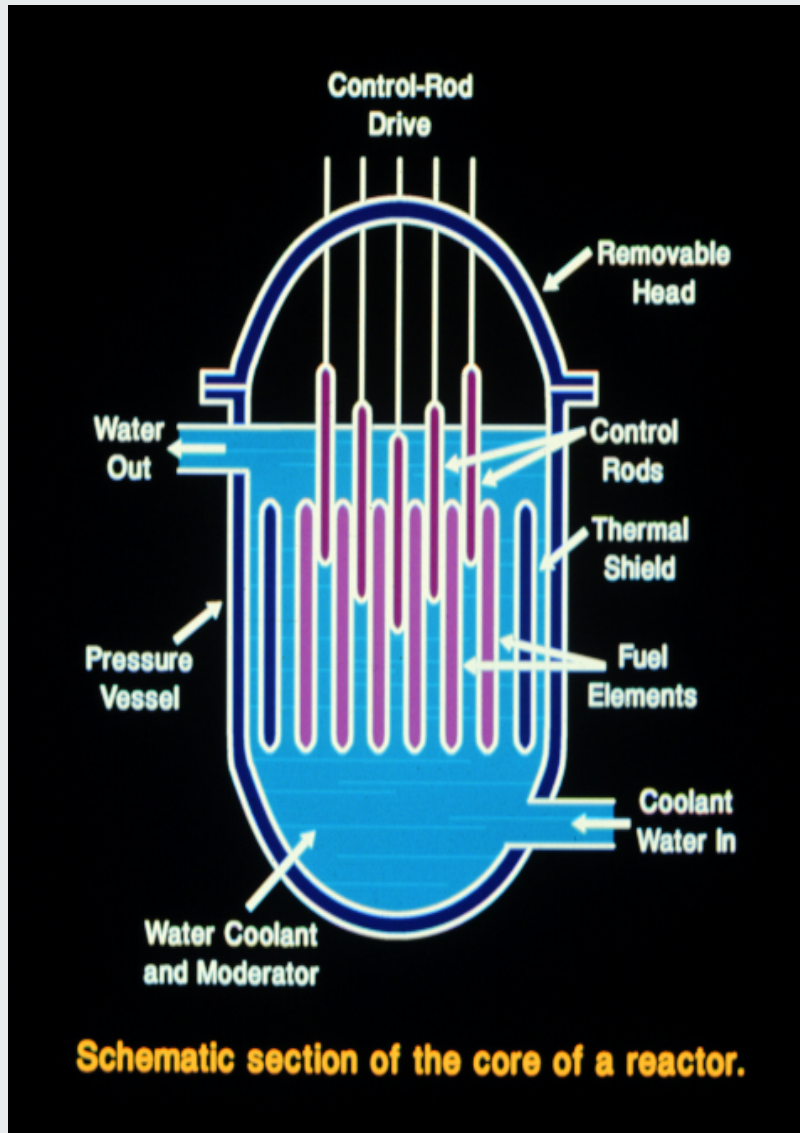
Emissores  $\beta^-$  ou  $\beta^+$ /  
Emissores  $\gamma$



$^{99m}\text{Tc}$  generator



## Núcleo do Reactor: Material Cindível



$^{235}\text{U}$  ou  $^{239}\text{U}$  ou  $^{233}\text{U}$

Cisão induzida em cadeia controlada/  
Barras de Controlo (B, Cd, Hf)

Fonte de Neutrões

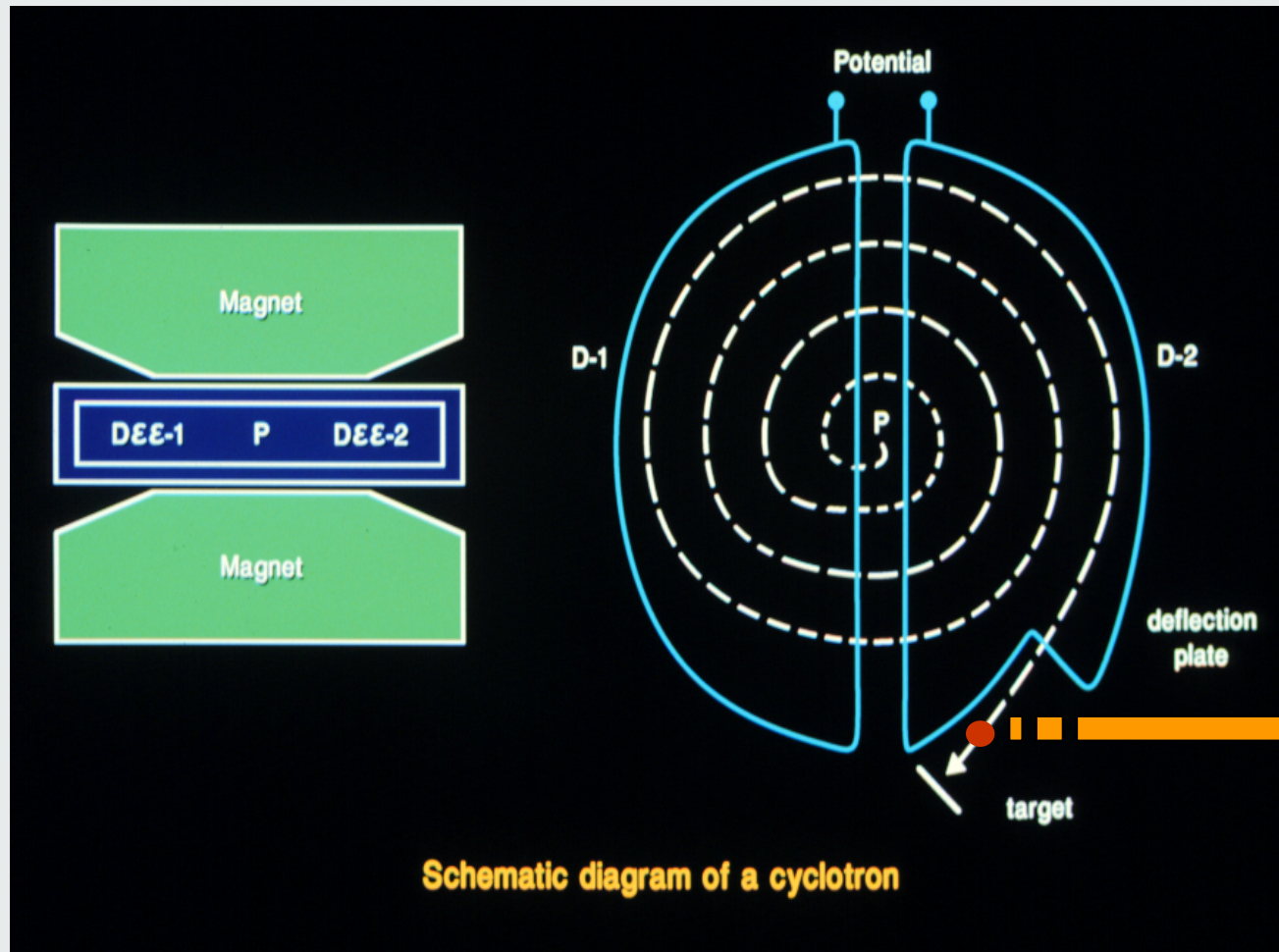
**Neutrões Térmicos:**  $E < 0.4 \text{ eV}$

**Neutrões Epitérmicos:**  $0,4 \text{ eV} < E < 100 \text{ keV}$

**Neutrões Rápidos:**  $E > 100 \text{ keV}$



Alvo irradiado com partículas carregadas, com trajectória circular e aceleradas por acção de um campo electromagnético



Schematic diagram of a cyclotron







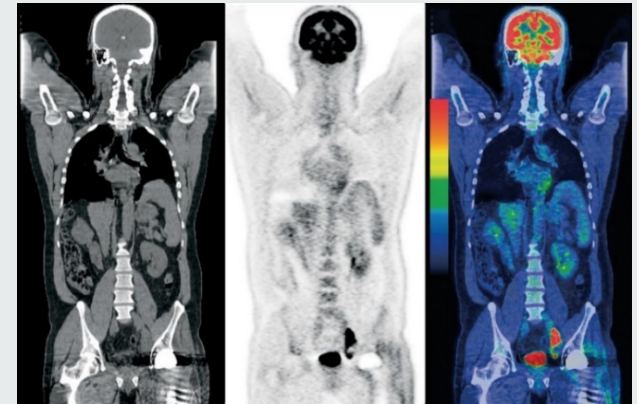
Um projecto **Marie Curie Innovative Training Network (ITN)** coordenado pelo CERN no programa Horizon 2020

Treino de **15 jovens investigadores (ESR)**

Rede de especialistas em **física, química, materiais, engenharia, radioquímica e medicina.**

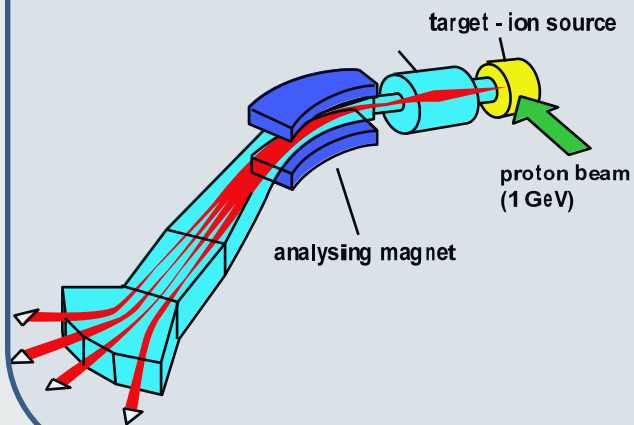


Imagiologia Molecular  
Medicina Personalizada



Terapia com  
Hadrões

Produção de  
Radioisótopos



Transporte



Radiofármacos





Semana de Treino no National Graphene Institute em Manchester  
com o vencedor do premio Nobel Kostya Novoselov, Sept. 2016

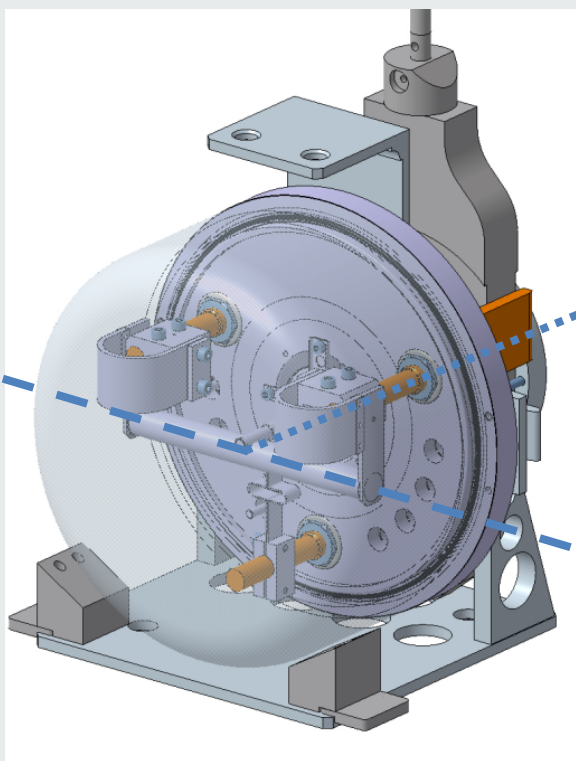


MEDICIS, em obras no  
CERN, Genebra.

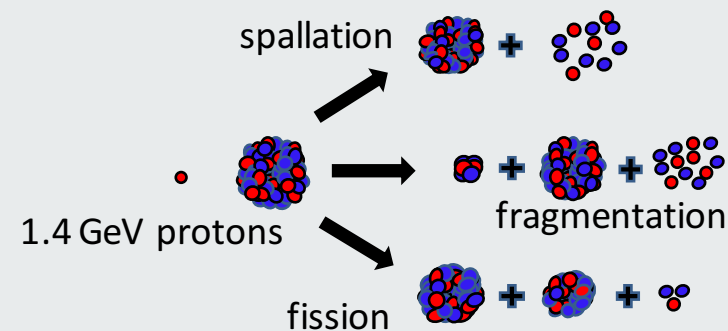


Unidade de Alvo

Feixe de Protões com Alta Energia



Radioisótopos



## Materiais do Alvo:

- Cerâmicos Refractários: Óxidos e carbonetos ( $UC_2$ , SiC,  $Al_2O_3$ ,  $HfO_2$ );
- Metais Refractários (Ta, Nb, Mo);
- Metais Fundidos (Pb).

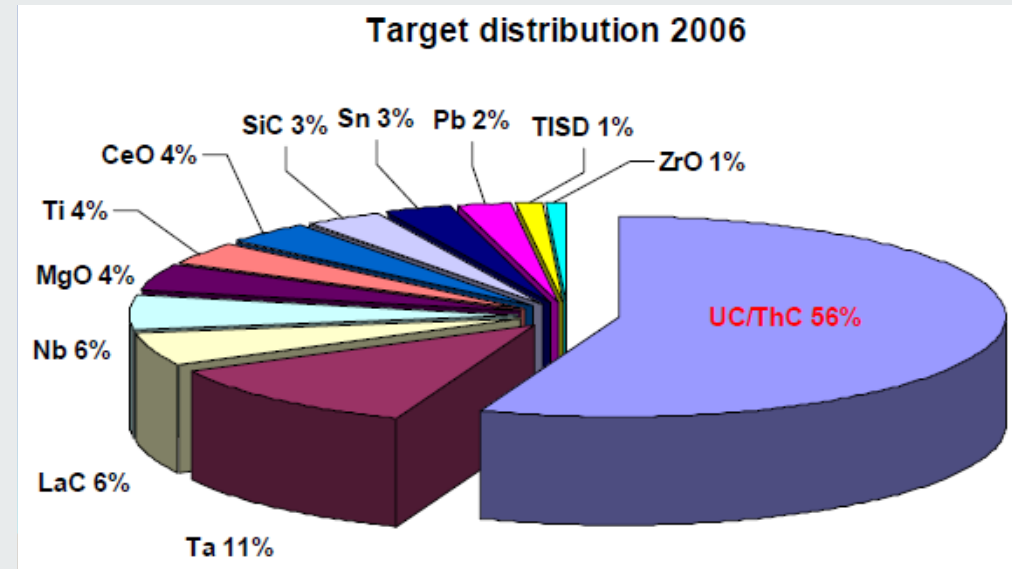


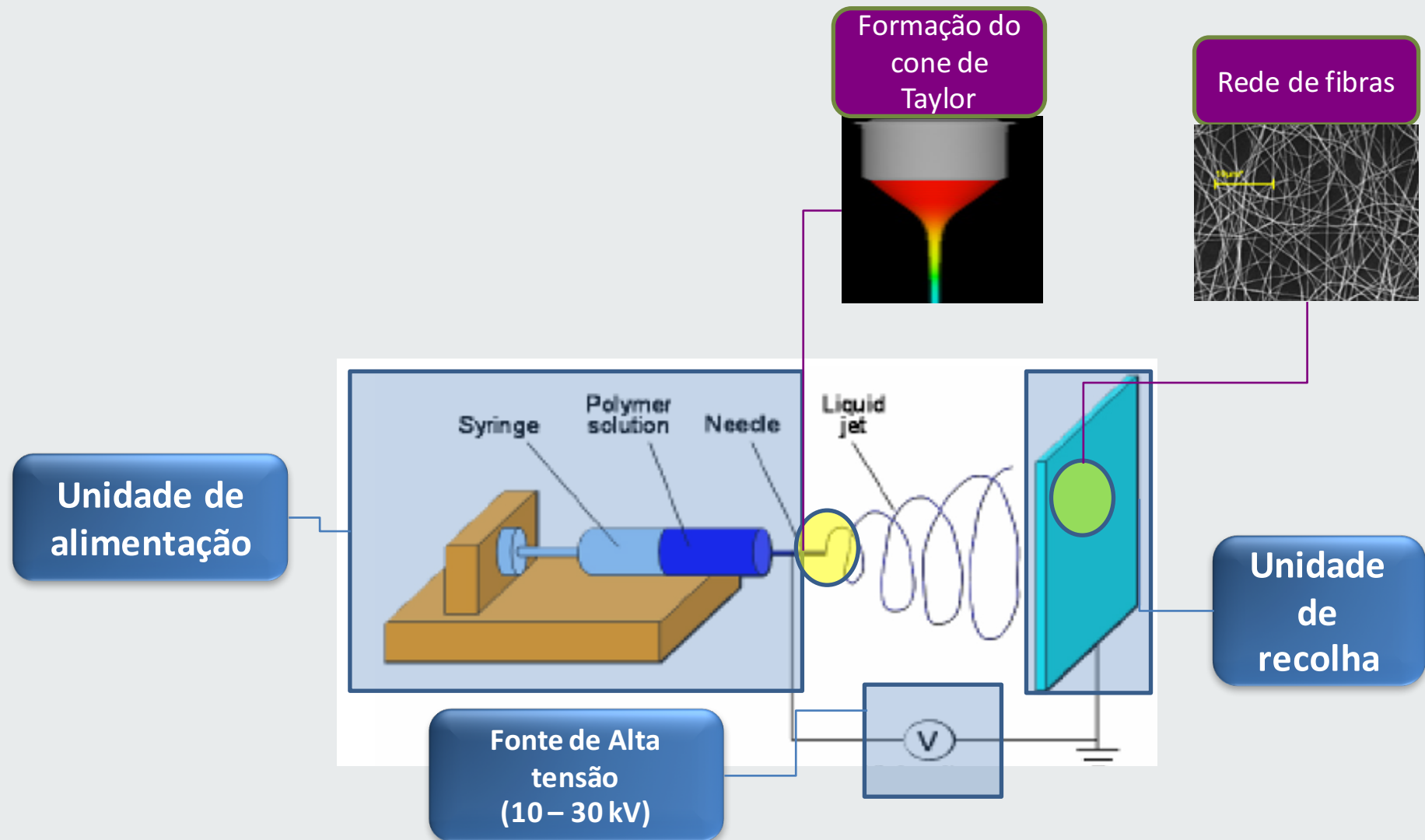
Alvo de carboneto de urânio ( $UC_x$ )



## ALTAS TEMPERATURAS!!!!

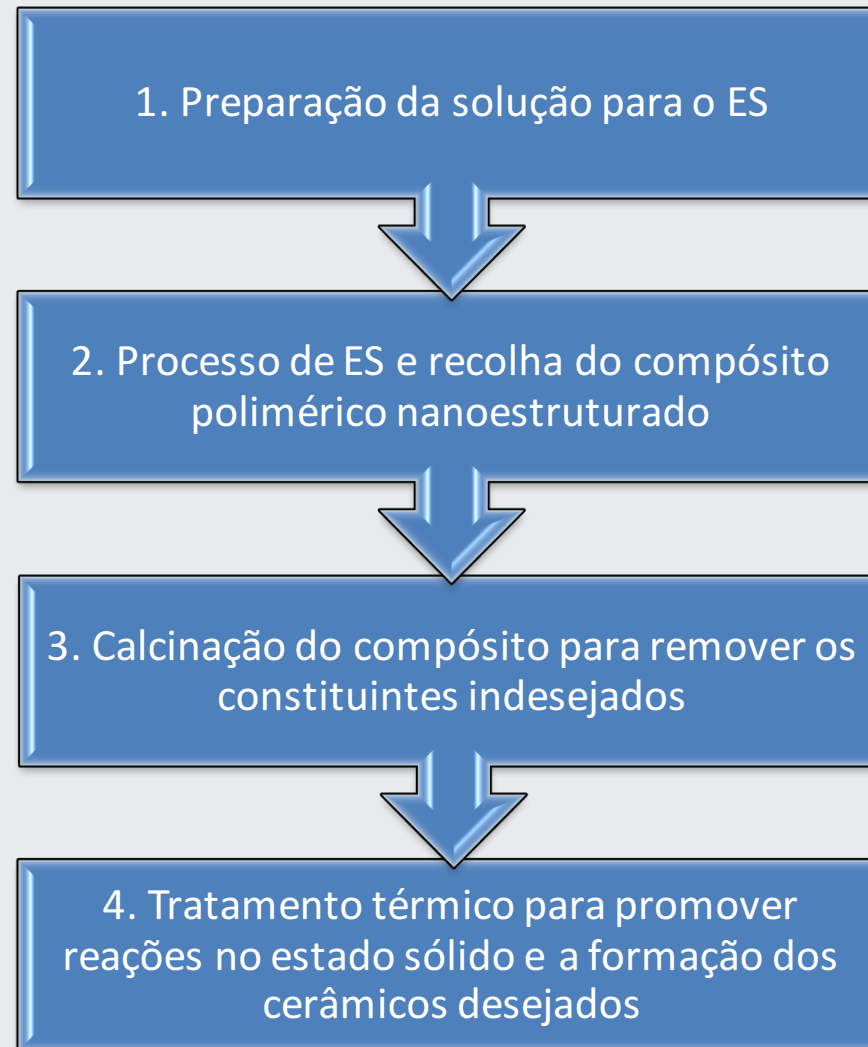
- Estabilidade química
- Estabilidade térmica
  - Fusão
  - Vaporização
  - Sublimação
- Aumentar a difusão!
- Aumentar a efusão!
- Novos alvos!!
  - Alvos refractários nanoestruturados!!!





<http://www.flow3d.com>  
<http://www.news.vcu.edu>

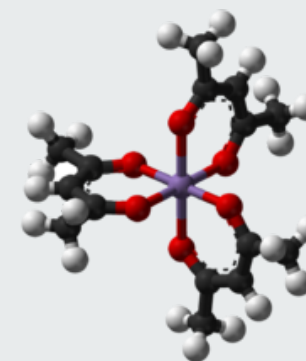
J.-S. Park, *Adv. Nat. Sci.: Nanosci. Nanotechnol.* 1 (2010) 043002





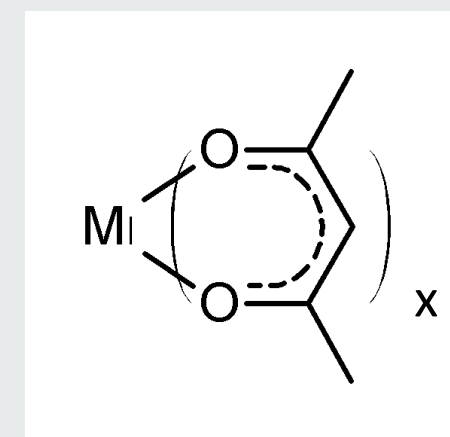
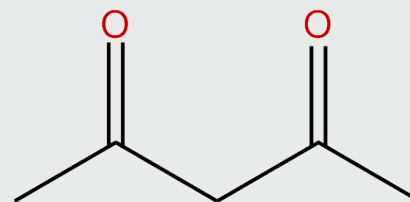
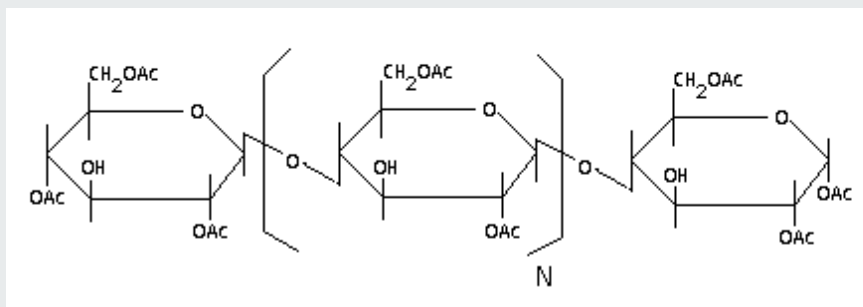
## •PREPARAÇÃO

### Solução de partida

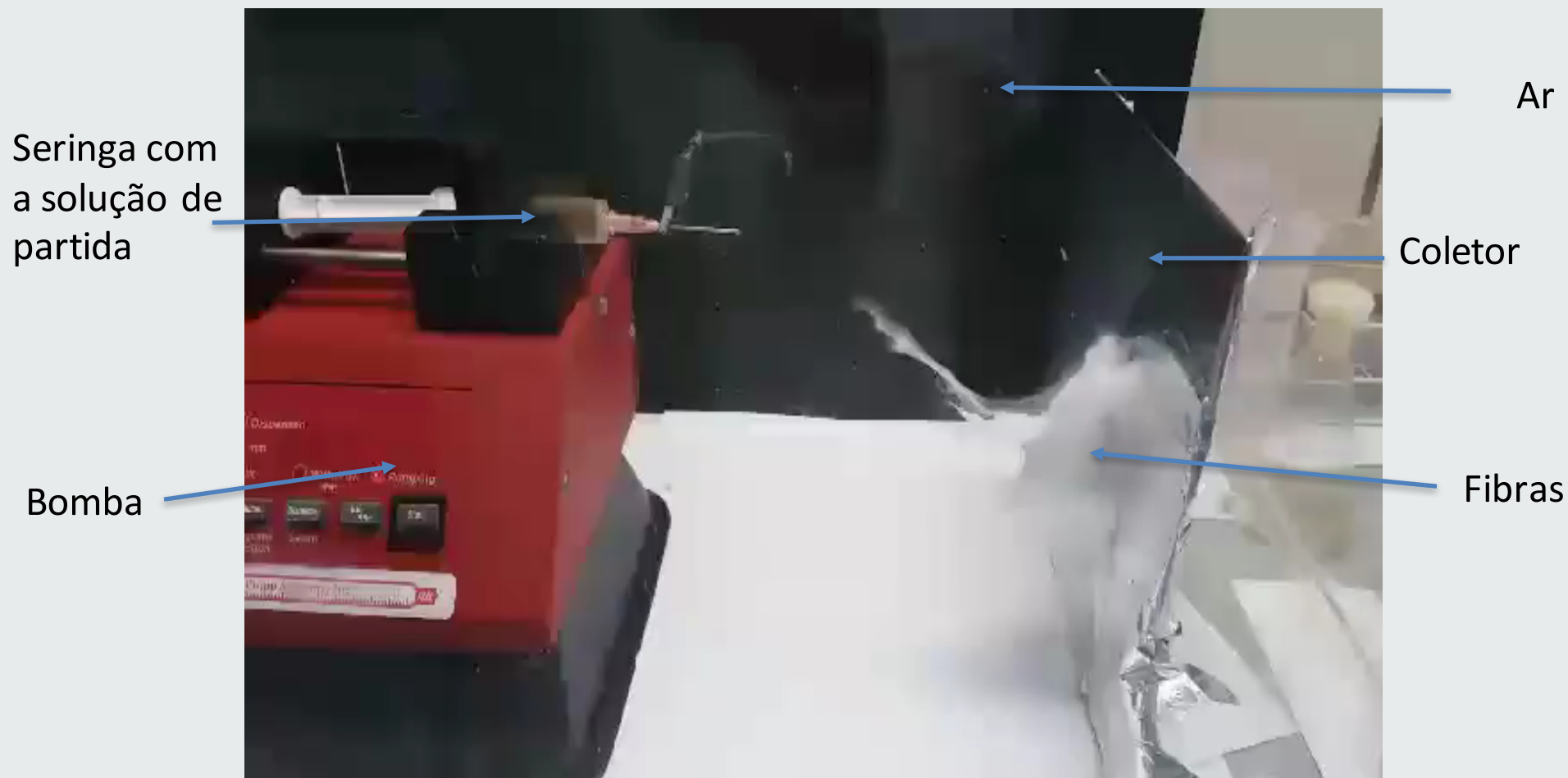


Acetato de celulose + 2,4-pentanedione +

Ln acetilacetato, acetato ou oxalato  
(Ln = Y, Eu, Er, Yb)



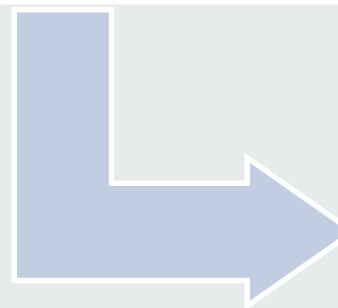
## A Electrofiação



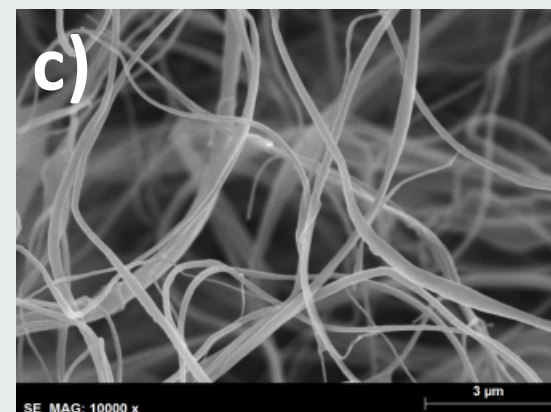
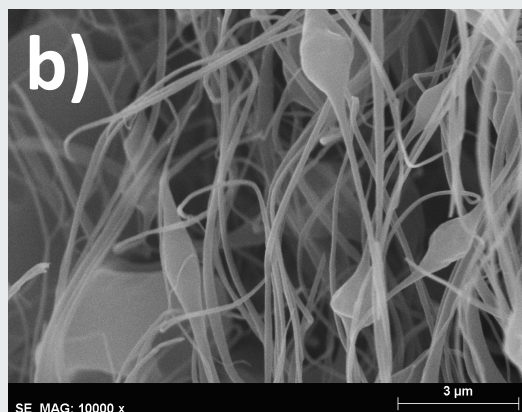
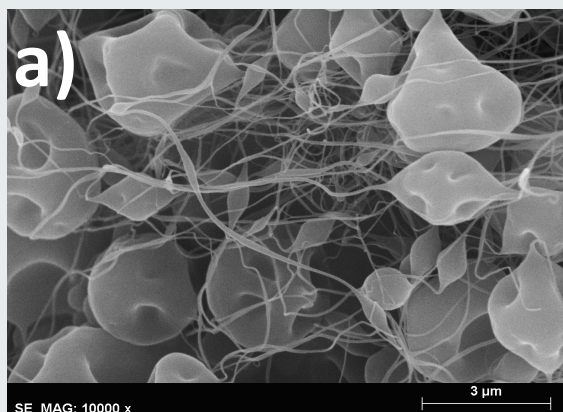
## • RESULTADOS

Massa (%) ↓ Amostra →	Facilidade de formação das fibras		
	Y(acac) <sub>3</sub>	Y(Ac) <sub>3</sub>	Y <sub>2</sub> (Ox) <sub>3</sub>
10	Não	Não	Não
15	Sim	Sim	Sim
20	Sim	Sim	Sim

Formação das fibras desfavorecida para concentrações mássicas de acetato de celulose (AC) de 10%

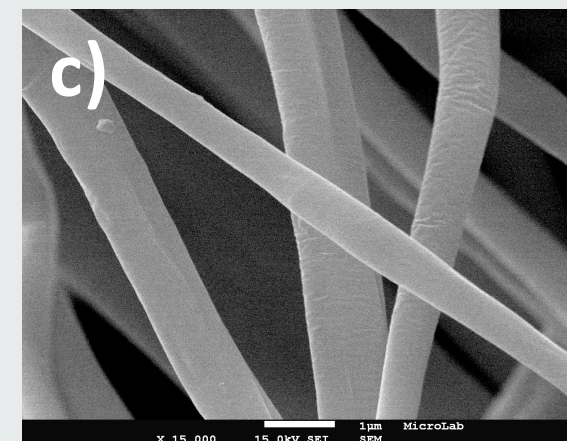
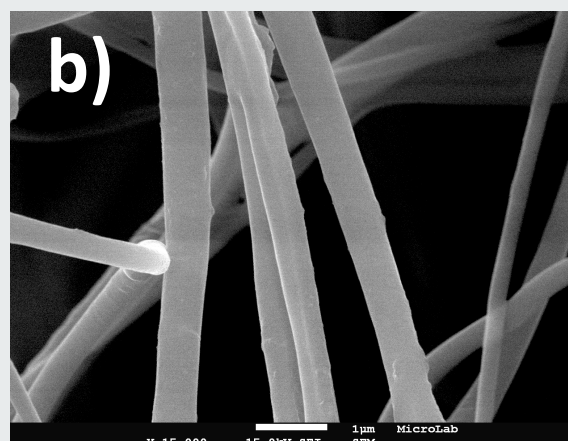
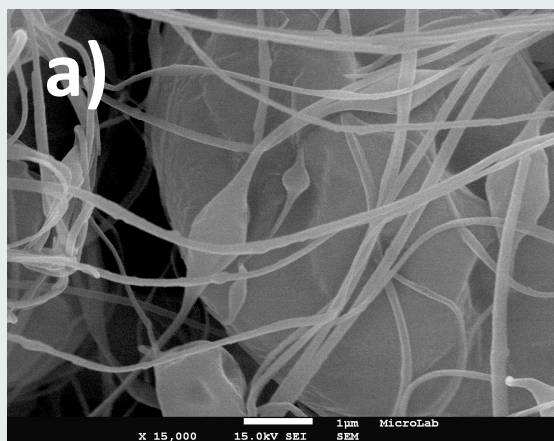


Fibras de boa qualidade para concentrações de 20% de AC



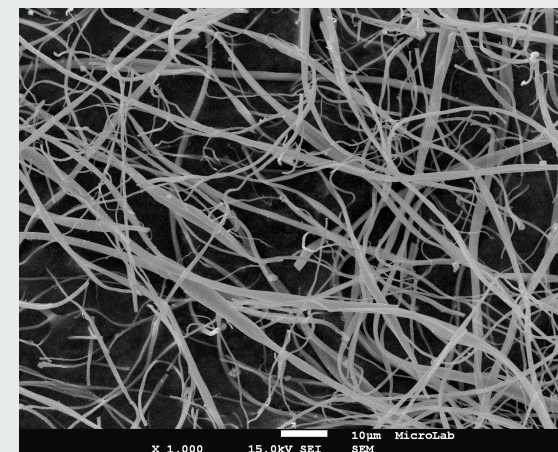
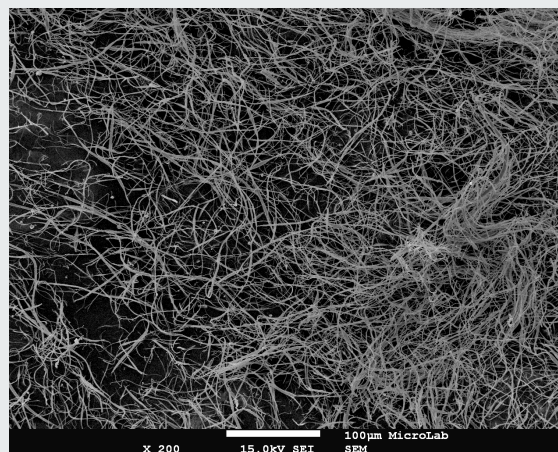
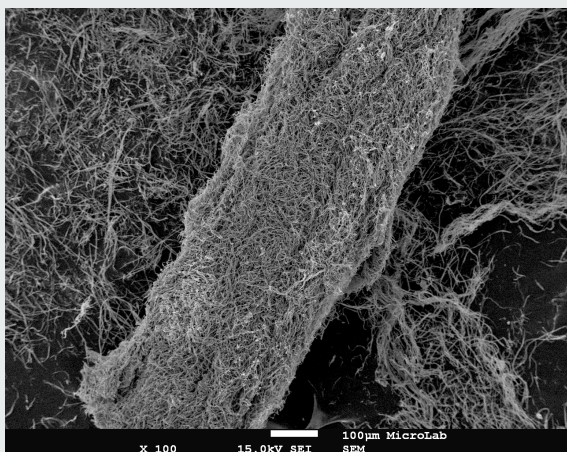
Micrografias electrónicas de varrimento de fibras preparadas com o precursor Y-acac e uma percentagem de massa de acetato de celulose a) 10, b) 15 e c) 20%.

Amostra ↓ Massa (%) →	Facilidade de formação das fibras		
	U(ac) <sub>2</sub>	U(acac) <sub>2</sub>	U(formate) <sub>2</sub>
10	Não	Não	Não
12.5	Sim	Sim	Sim
15	Sim	Sim	Sim

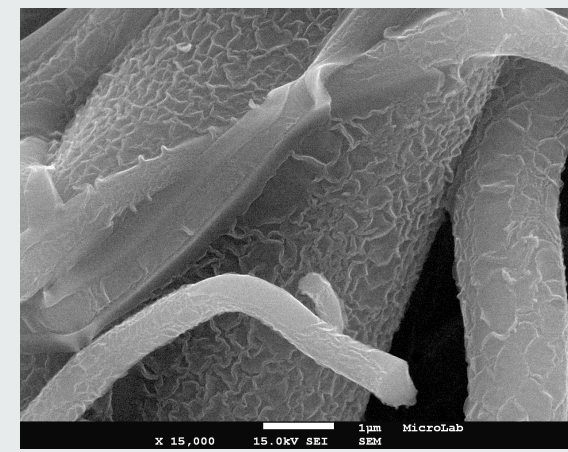
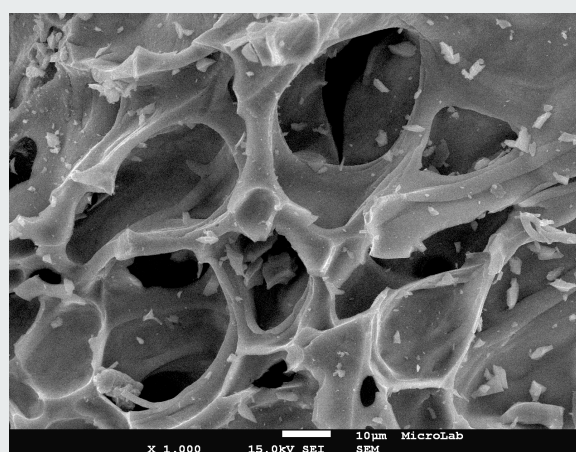
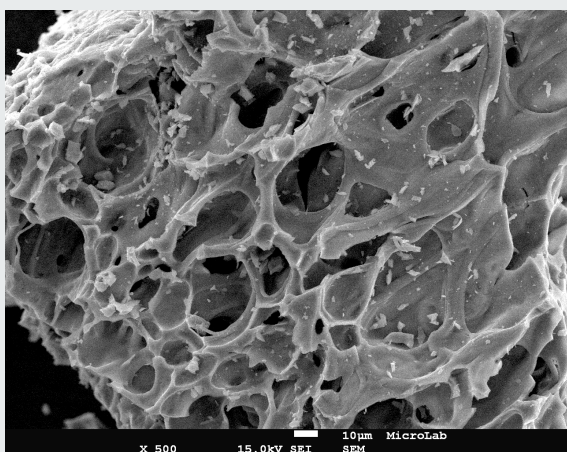


Micrografias electrónicas de varrimento de fibras preparadas com o precursor acetato de urânio e uma percentagem de massa de acetato de celulose a) 10, b) 12.5 e c) 15%.



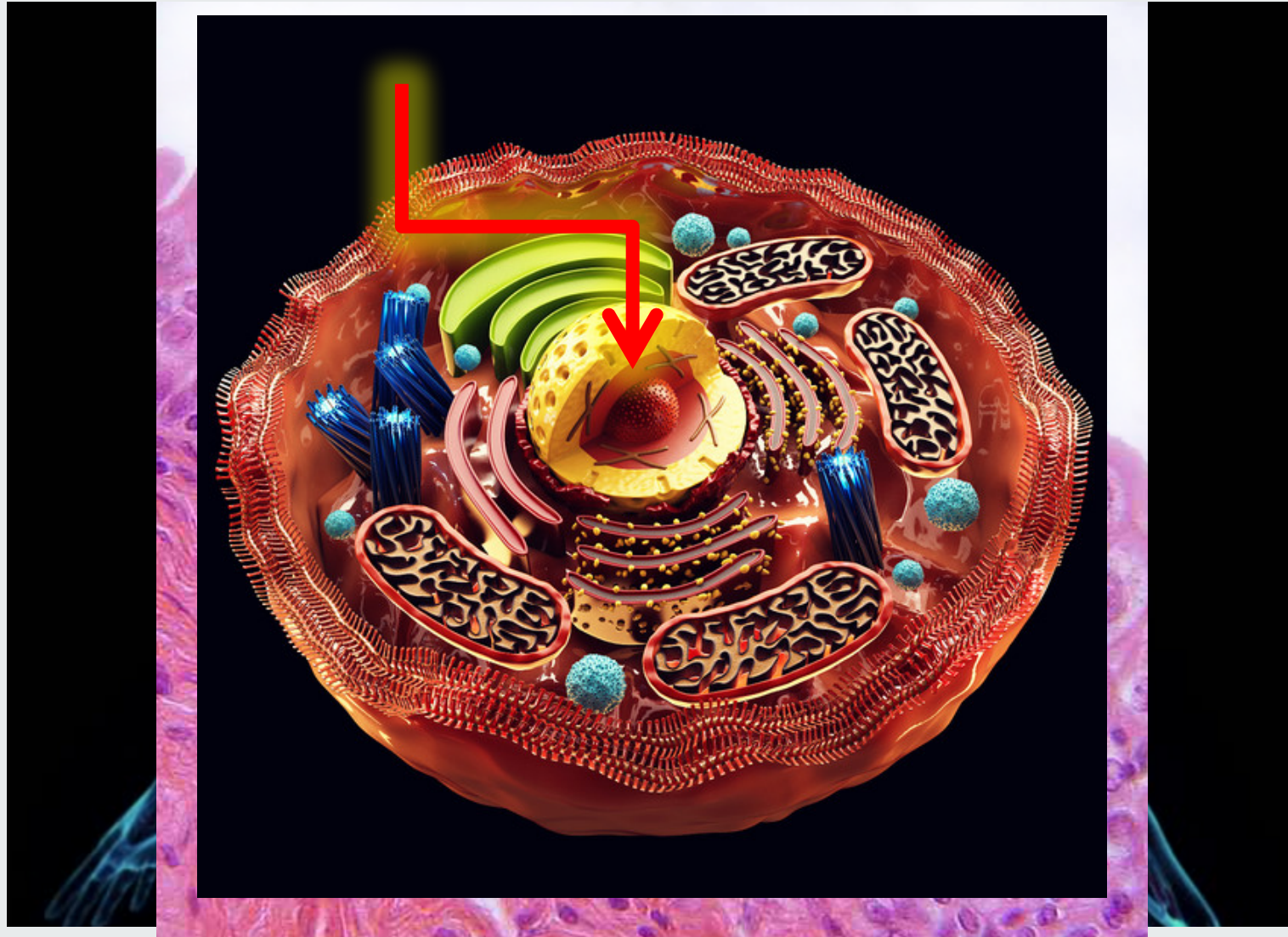


Micrografias electrónicas de varrimento de fibras obtidas com o precursor acetato de urânio e 15% massa de acetato de celulose aquecidas lentamente (1°C/min) a 600°C.



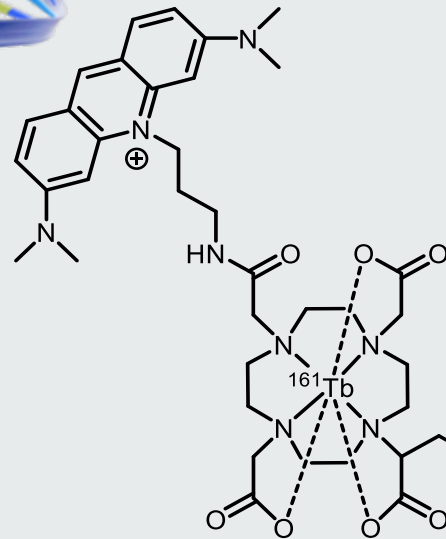
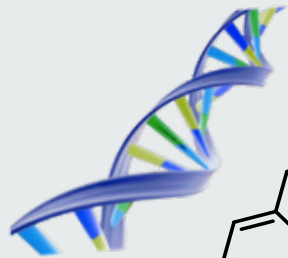
Micrografias electrónicas de varrimento de fibras obtidas com o precursor acetato de urânio e 15% massa de acetato de celulose aquecidas rapidamente (>100°C/min) a 600°C.





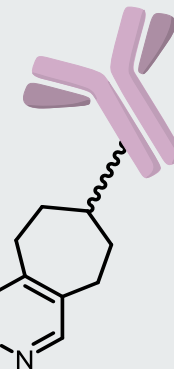
- Radioimunoterapia (RIT) dirigida ao ADN

**ACRIDINE ORANGE**  
Aumento da eficácia



**QUELANTE DOTA**  
Estabiliza o Radiometal

**RADIOISÓTOPO**  
Diagnóstico/Terapia



**ANTICORPO MONOCLONAL**  
Aumento da seletividade para as células tumorais





**$^{149}\text{Tb}$**   
 $\alpha$  e  $\beta^+$   
 $t_{1/2}$  4.12 h

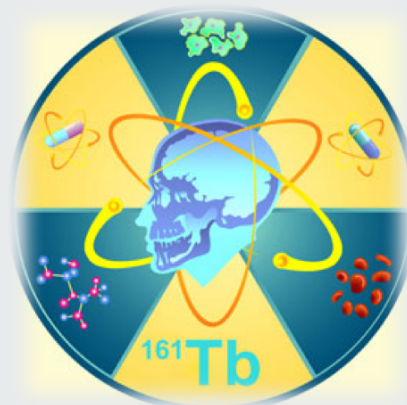
$\text{Tb } 149$	$\text{Tb } 152$	$\text{Tb } 155$	$\text{Tb } 161$
4.2 m	4.2 m	5.32 d	6.90 d
4.1 h	17.5 h		
$e^-$	$e^-$	$e^-$	$e^-$
$\beta^+$	$\beta^+$	$\beta^+$	$\beta^-$
$\alpha$ 3.99	$\alpha$ 3.97	$\gamma$ 87;	$\beta^-$ 0.5; 0.6...
$\beta^+$ 1.8	$\beta^+$ 2.8...	105;...	$\gamma$ 26; 49; 75...
$\gamma$ 796;	$\gamma$ 344;	180, 262	
$\gamma$ 352;	586;		
165...	411...		

**$^{161}\text{Tb}$**   
 $\beta^-$  e Auger  
 $t_{1/2}$  6.89 d

**$^{152}\text{Tb}$**   
 $\beta^+$   
 $t_{1/2}$  17.5 h

**$^{155}\text{Tb}$**   
 EC  
 $t_{1/2}$  5.32 d

➔ Uma química, duas terapias e duas modalidades terapêuticas!

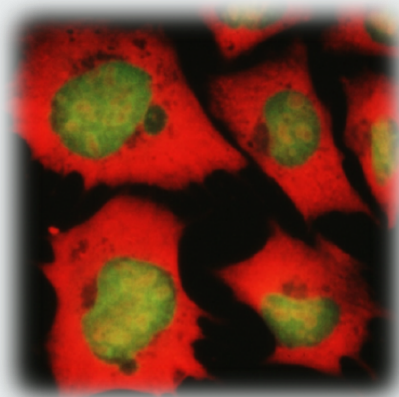


Meia-vida de 6.91 dias.

Emissor de partículas  $\beta^-$  de baixa energia e curta penetração.



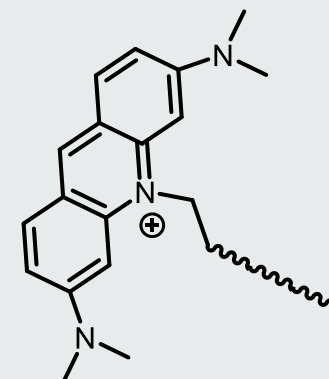
**MUITO PROMISSOR PARA O TRATAMENTO DE  
TUMORES PEQUENOS E METÁSTASES!**



Emissão de 2.24 eletrões Auger por decaimento  
Percurso nos tecidos inferior ao diametro de uma célula



**A ACUMULAÇÃO NO NÚCLEO DAS CÉLULAS E  
CRUCIAL PARA O EFEITO TERAPÊUTICO**



O sítio na internet

<http://medicis-promed.web.cern.ch>

Encontra-nos na rede social



**Contacta-nos!**

*Este projecto foi apoiado pela Marie Skłodowska-Curie Innovative Training Network Fellowship do programa Europeu Horizonte 2020, com o número de contrato 642889 MEDICIS-PROMED.*