



# Production of radioisotopes with the ISOL technique

Thierry.stora@cern.ch

Did you say ? (topics to be covered)

Production

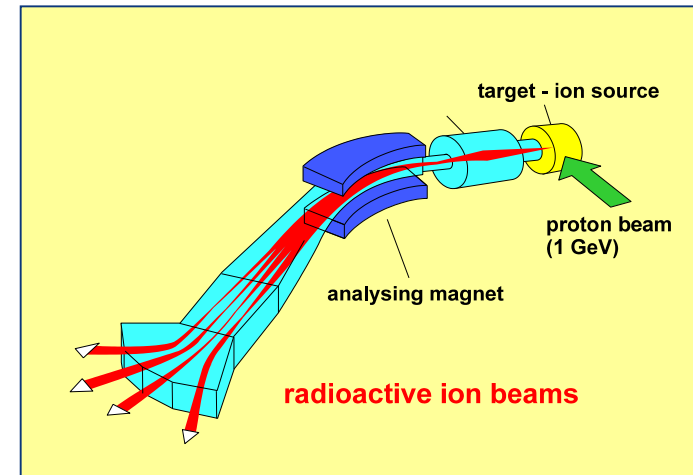


(of medical )

radioisotopes



By the ISOL technique



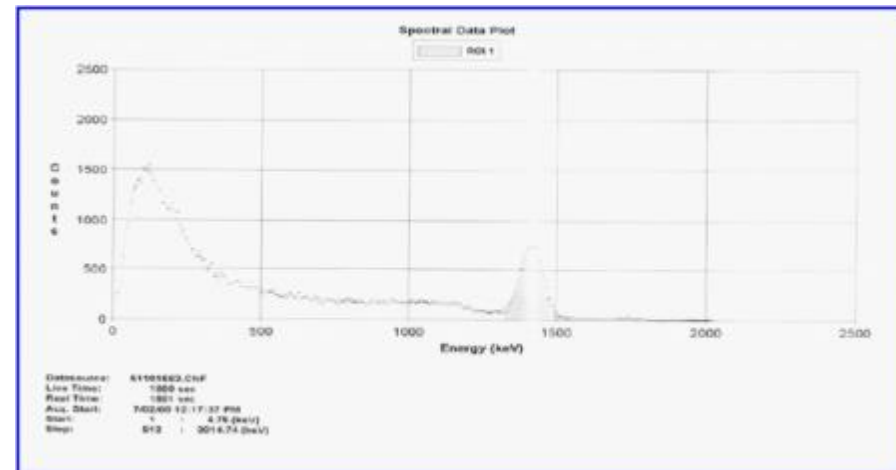
# Radioisotopes in biological organisms

Daily, we “internalize” radiomarkers with rather well defined protocols



Country	France
Source	Évian-les-Bains
Type	still
pH	7.2
Calcium (Ca)	80
Chloride (Cl <sup>-</sup> )	6.8
Bicarbonate (HCO <sub>3</sub> )	360
Magnesium (Mg)	26
Nitrate (NO <sub>3</sub> )	3.7
Potassium (K)	1
Silica (SiO <sub>2</sub> )	15
Sodium (Na)	6.5
Sulfates (SO)	12.6
Website	<a href="http://www.evian.com">http://www.evian.com</a>

All values in milligrams per liter (mg/l)

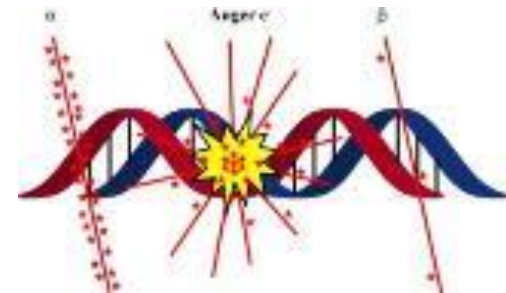
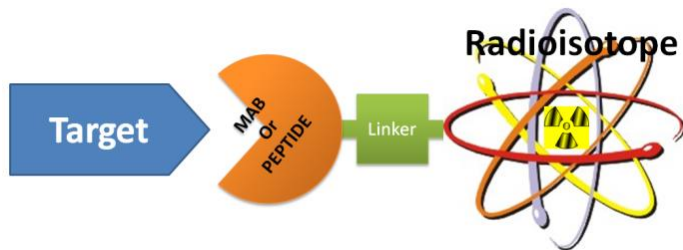
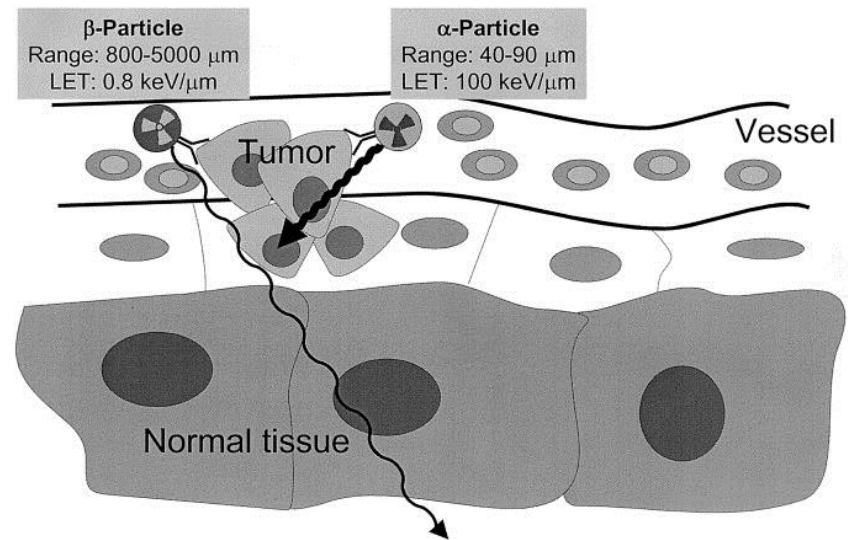


M Goma et al



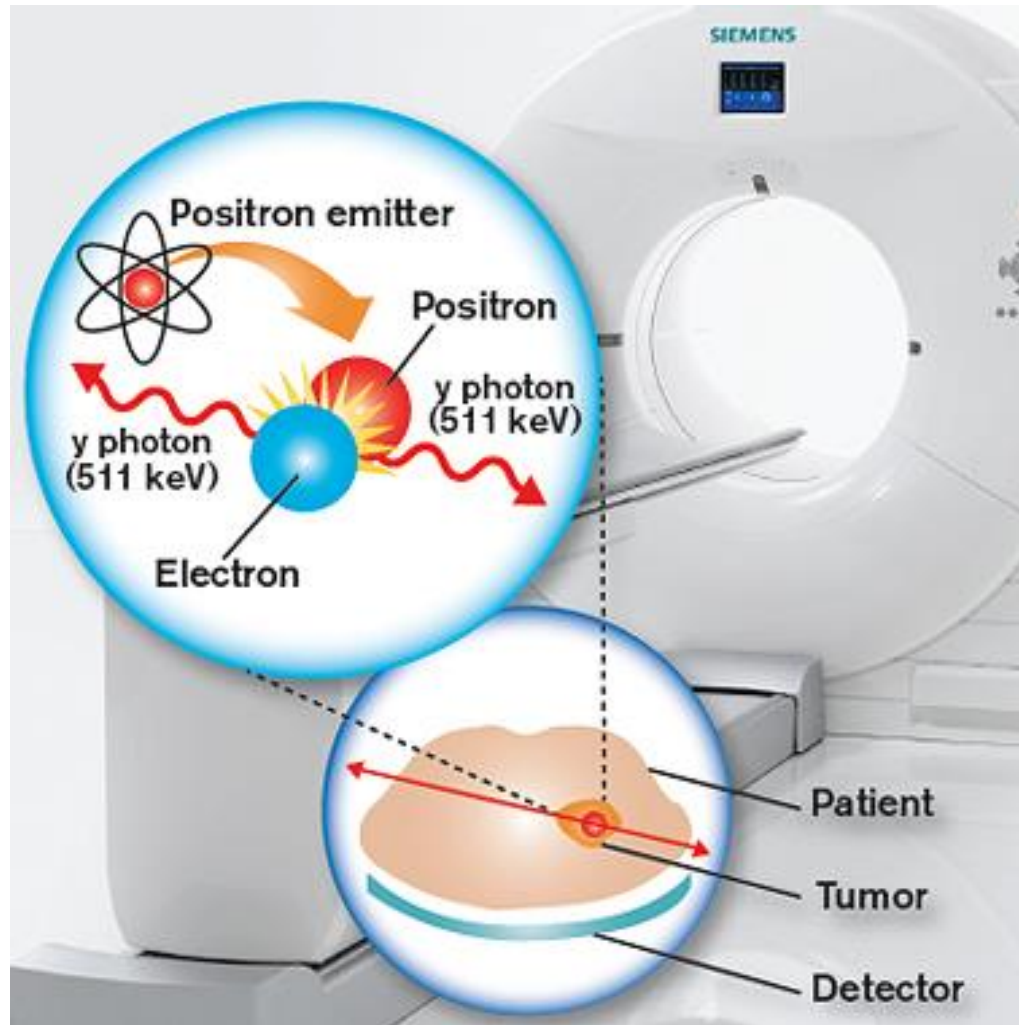
# Targeted internal therapy

This is moving and localising several isotope sources close to the tissue to be treated



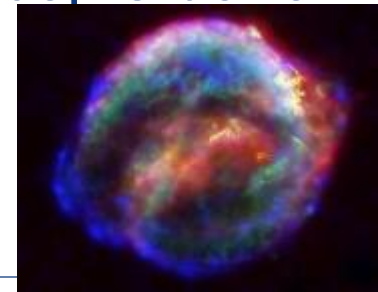
Already seen for imaging (slide # ?)

# PET scan imaging

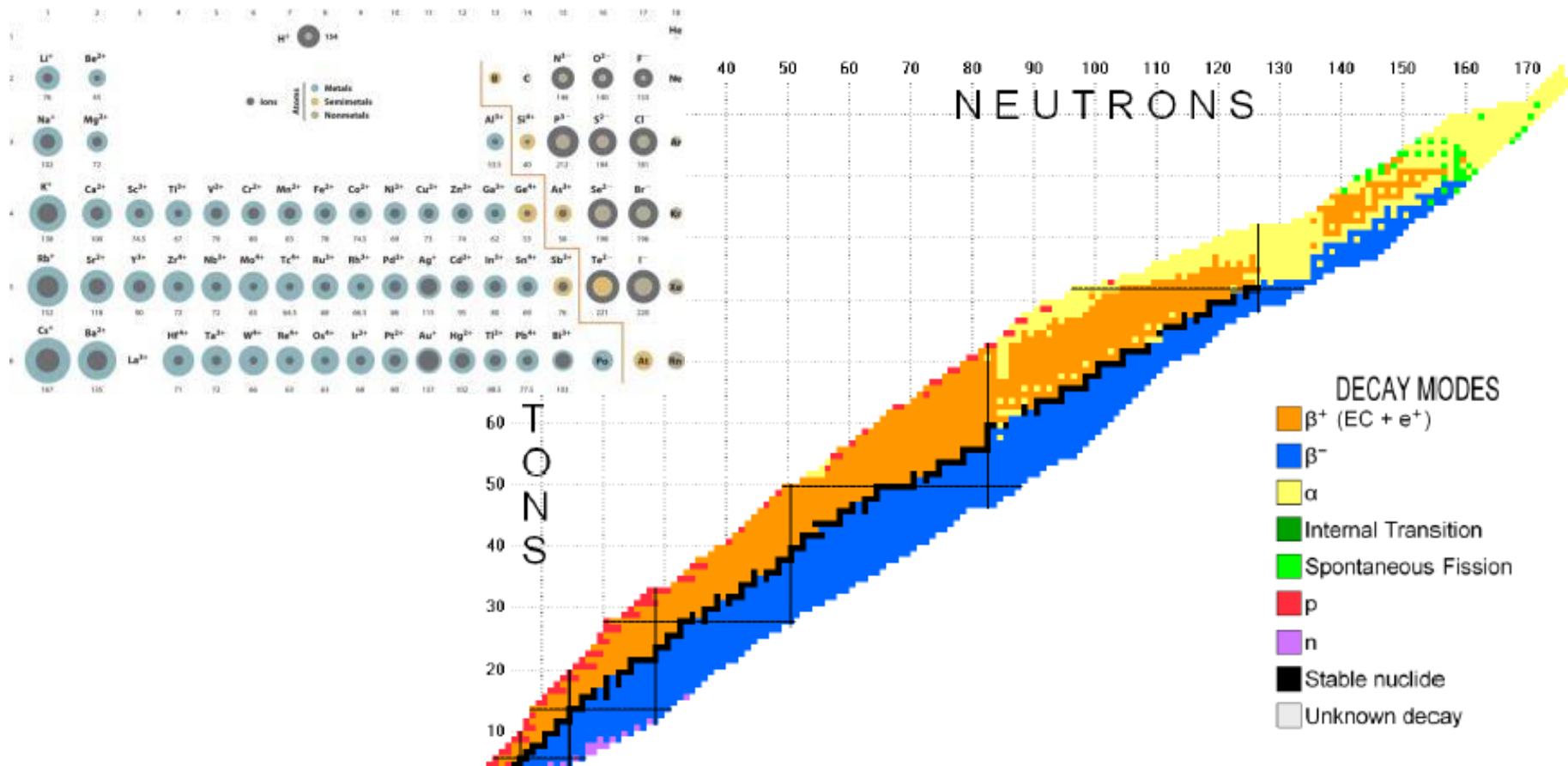


# What accelerator to produce which isotopes ?

- (p,n), (p,2p), (p, $\alpha$ ), (p,X), (p, $\alpha$ n), etc...  $p^+ A/q=1$
  - (d,n), (d,p), etc...  $d^+ A/q=2$
  - ( $^3\text{He}$ ,n), ( $^3\text{He}$ , $\alpha$ ), etc...  $^3\text{He}^{++} A/q=1.5$
  - ( $\alpha$ ,n), ( $\alpha$ ,2n), ( $\alpha$ ,p), etc...  $\alpha^{++} A/q=2$
  - ( $^7\text{Li}$ ,Xn), etc ...  $\text{Li}^{++} \text{Li}^{+++} A/q=3.5, 2.33$
  - (n, $\gamma$ ), (n,2n), (n,p), etc...  $n^0 A/q=\text{infinity}$
- 
- And we need accelerators, facilities, concepts better suited than explosive supernovae



# Which radioisotopes do we need ?

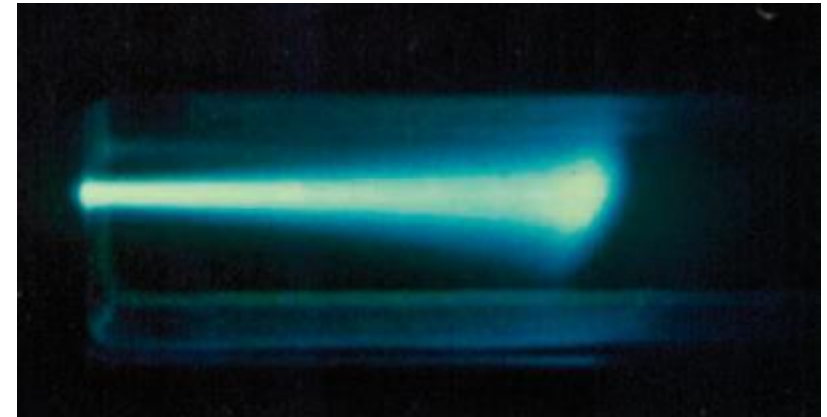
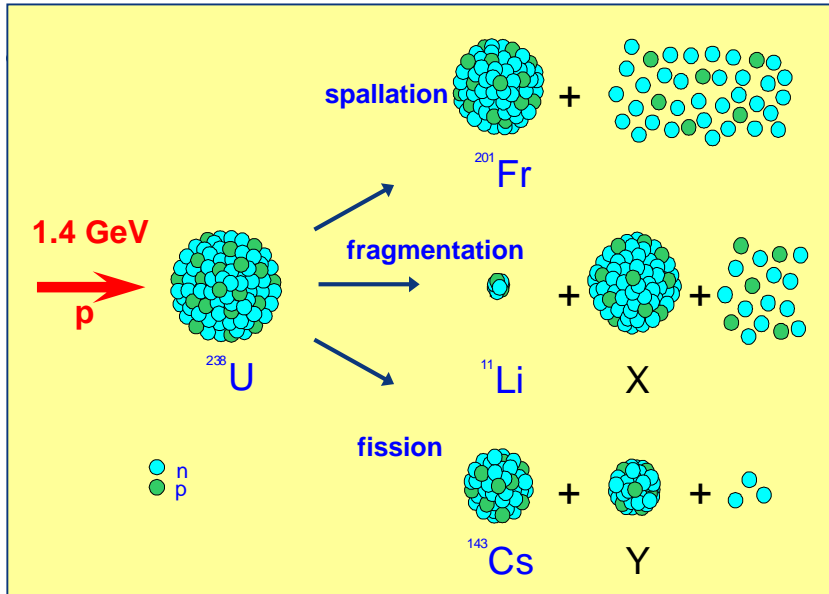


While there are a few “blockbusters” ( $^{99m}\text{Tc}$ ,  $^{18}\text{F}$ ) and some other emerging ( $^{177}\text{Lu}$ ,  $^{223}\text{Ra}$ ) There is room/need for even **better suited new radioisotopes along with their production**

# List of some PET isotopes

Nuclide	Half-life (min)	Decay mode	Maximum energy (MeV)	Mean energy (MeV)	Max. range (mm)	Max. SA (theoretical) (Ci/ $\mu$ mol) <sup>a</sup>
C-11	20.4	100% $\beta^+$	0.96	0.386	4.1	9 220
N-13	9.98	100% $\beta^+$	1.19	0.492	5.4	18 900
O-15	2.03	100% $\beta^+$	1.7	0.735	8.0	91 730
F-18	109.8	97% $\beta^+$	0.69	0.250	2.4	1 710
Cu-62	9.74	99.7% $\beta^+$	2.93	1.314	14.3	19 310
Ga-68	68.0	89% $\beta^+$	1.9	0.829	9.0	2 766
Br-75	96.0	75.5% $\beta^+$	1.74	0.750	8.2	1 960
Rb-82	1.25	95.5% $\beta^+$	3.36	1.5	16.5	150 400
I-122	3.62	75.8% $\beta^+$	3.12	1.4	15.3	51 950
I-124	6019.2	23.3% $\beta^+$	2.13	0.8	10.2	31

# Targets (production, not biological !)

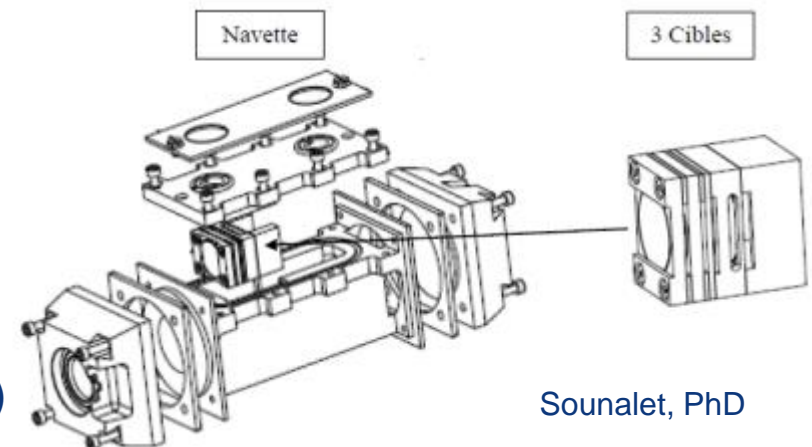


Gas target

IAEA, trs465

(ie  $N_2$  + trace of  $O_2$  for  $^{14}N(p,\alpha)^{11}CO_2$ )

Solid target  
(RbCl for  $^{82}Sr$ ,  $Ga_3Ni_2$  for  $^{68}Ge/Ga$ )



Sounalet, PhD

# From excitation function to production rate

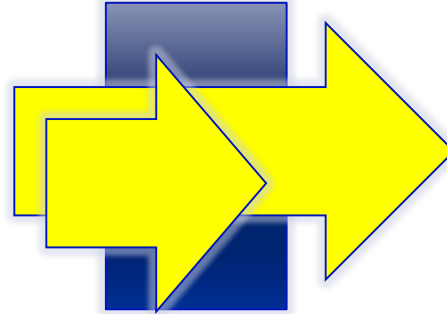
$$I_{[\text{pps}]} \sim \Phi_{[\text{pps}]} \sigma_{[\text{barn}]} N_{[\text{g/cm}^2]}$$

production rate

$10^{10}\text{pps}$      $100\mu\text{A}$  ( $6 \cdot 10^{14}$ )     $1\text{mbarn}$      $1\text{g/cm}^2$  for  $A_{\text{target}}=30\text{g/mol}$

$$R [\text{Bq}] = I\lambda/(1-\lambda) = I \text{ for } 5 T_{1/2} (\lambda=0.606/T_{1/2}) \quad \text{saturation activity}$$

Incident particle  
Beam intensity



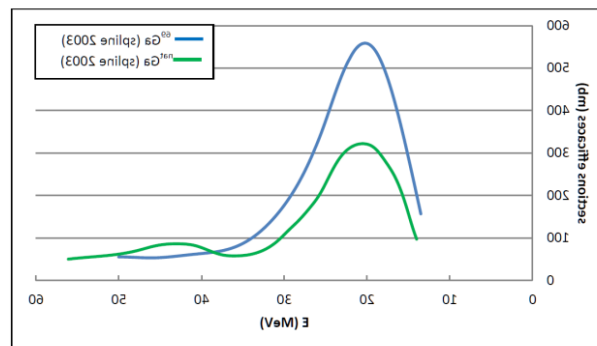
Bragg peak possibly  
in a dump

Target thickness

An individual dose

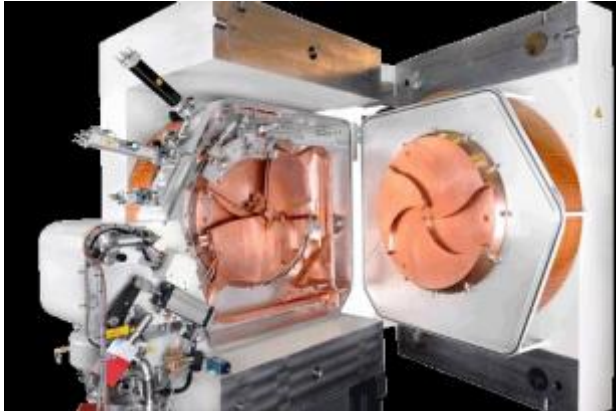
For imaging is  $\sim 100$ 's MBq

For treatment  $\sim 1$  GBq

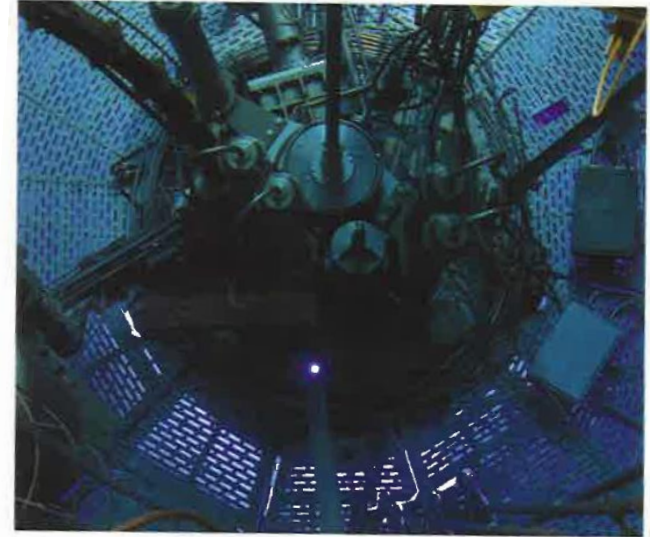


# Some ways to accelerate ions or generate neutrons

The most common methods :



At medical cyclotrons (p/d/ $\alpha$ ,X)  
9-70MeV



At nuclear reactors (n,X)

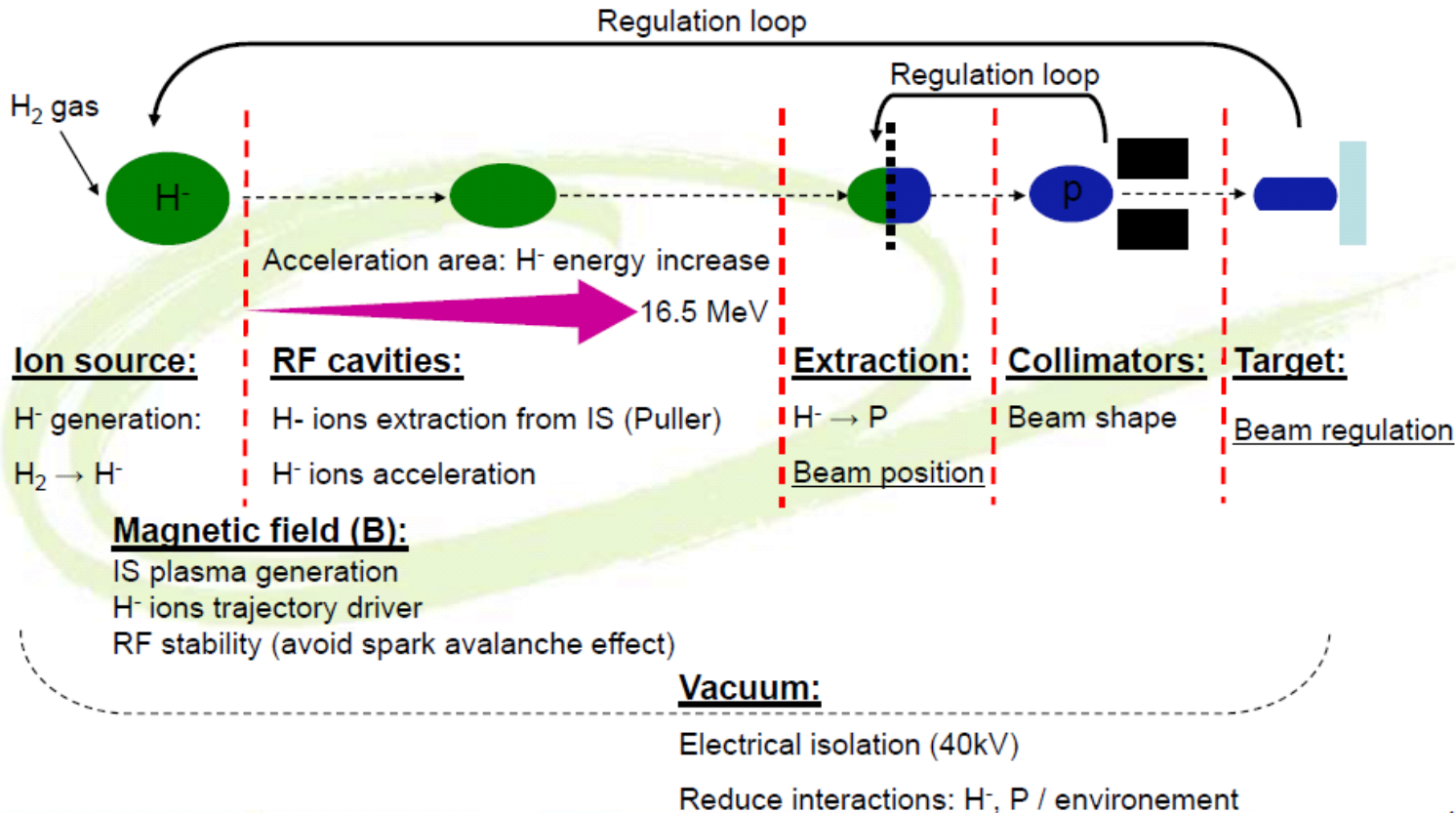
More prospective : compact Linacs,  
Heavy ion cyclotrons, high energy p drivers



© AccSys Technology, Inc.

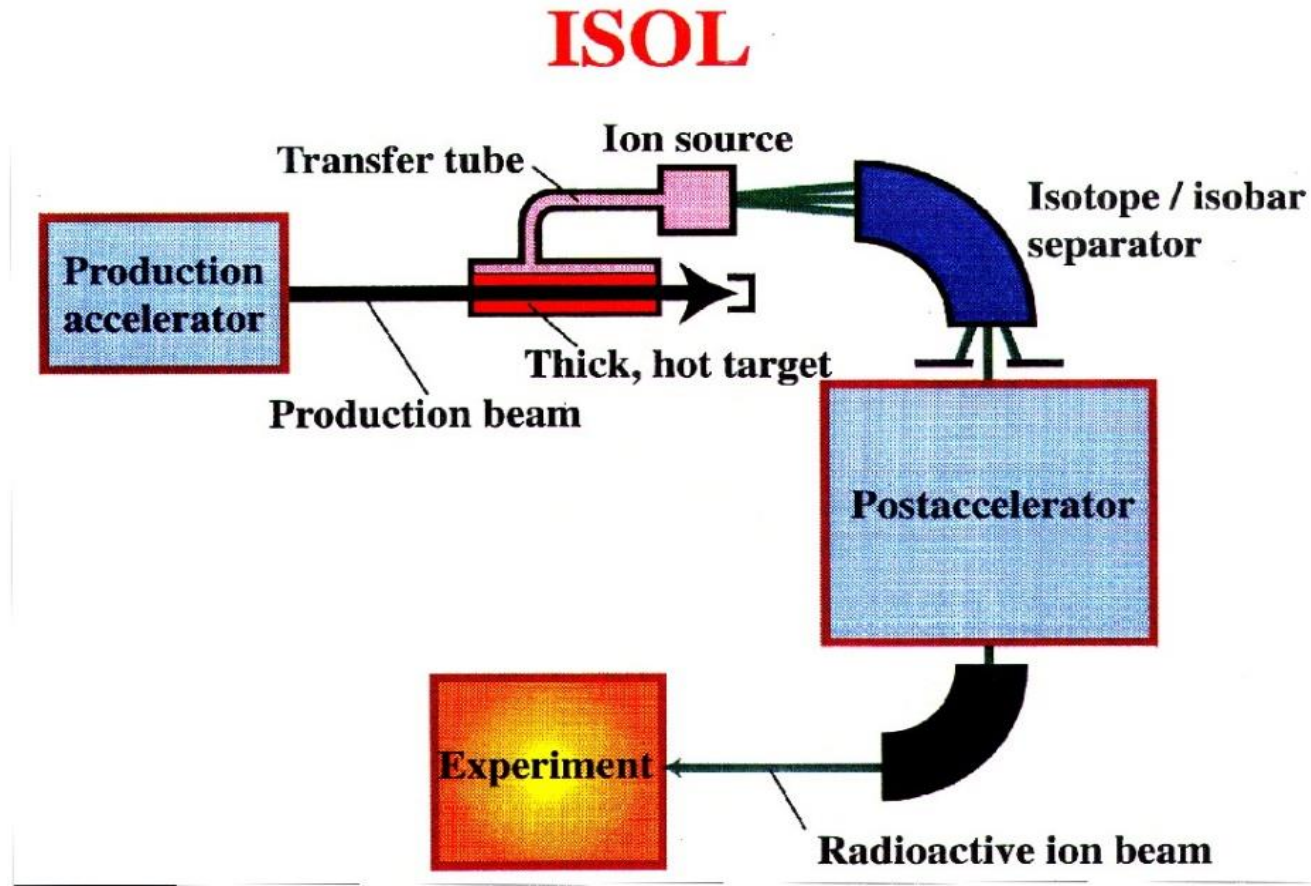
# Principle of beam regulation, diagnostics

## Proton beam generation principle:

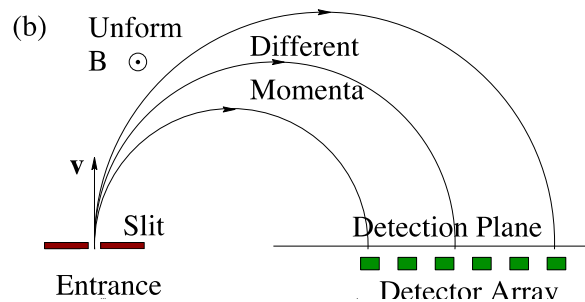
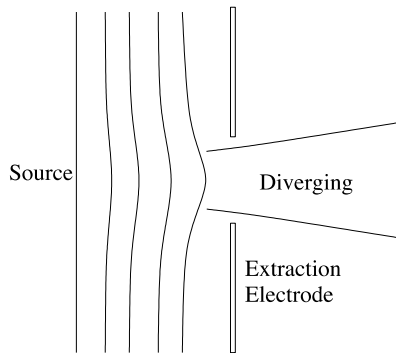


# General layout of isotope mass separation « online »

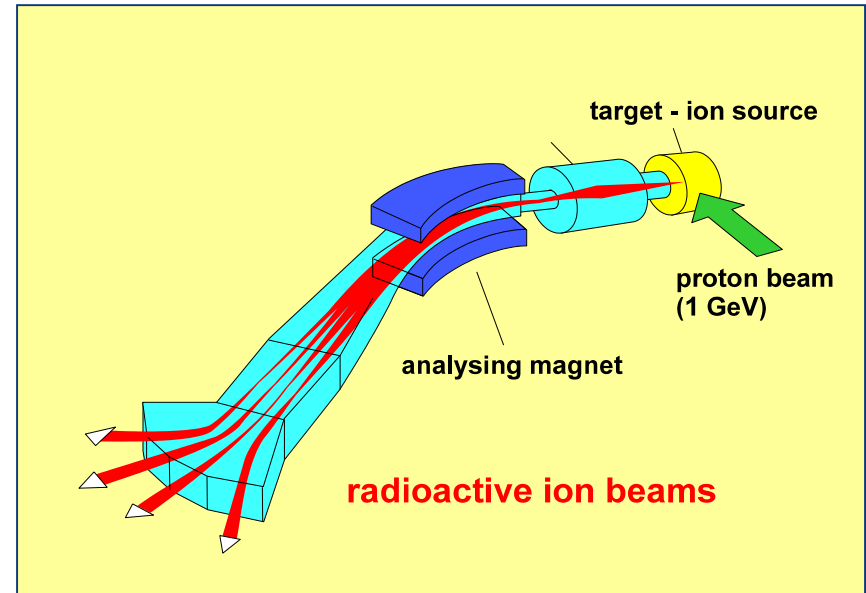
(ISOL) Isotope mass Separation OnLine



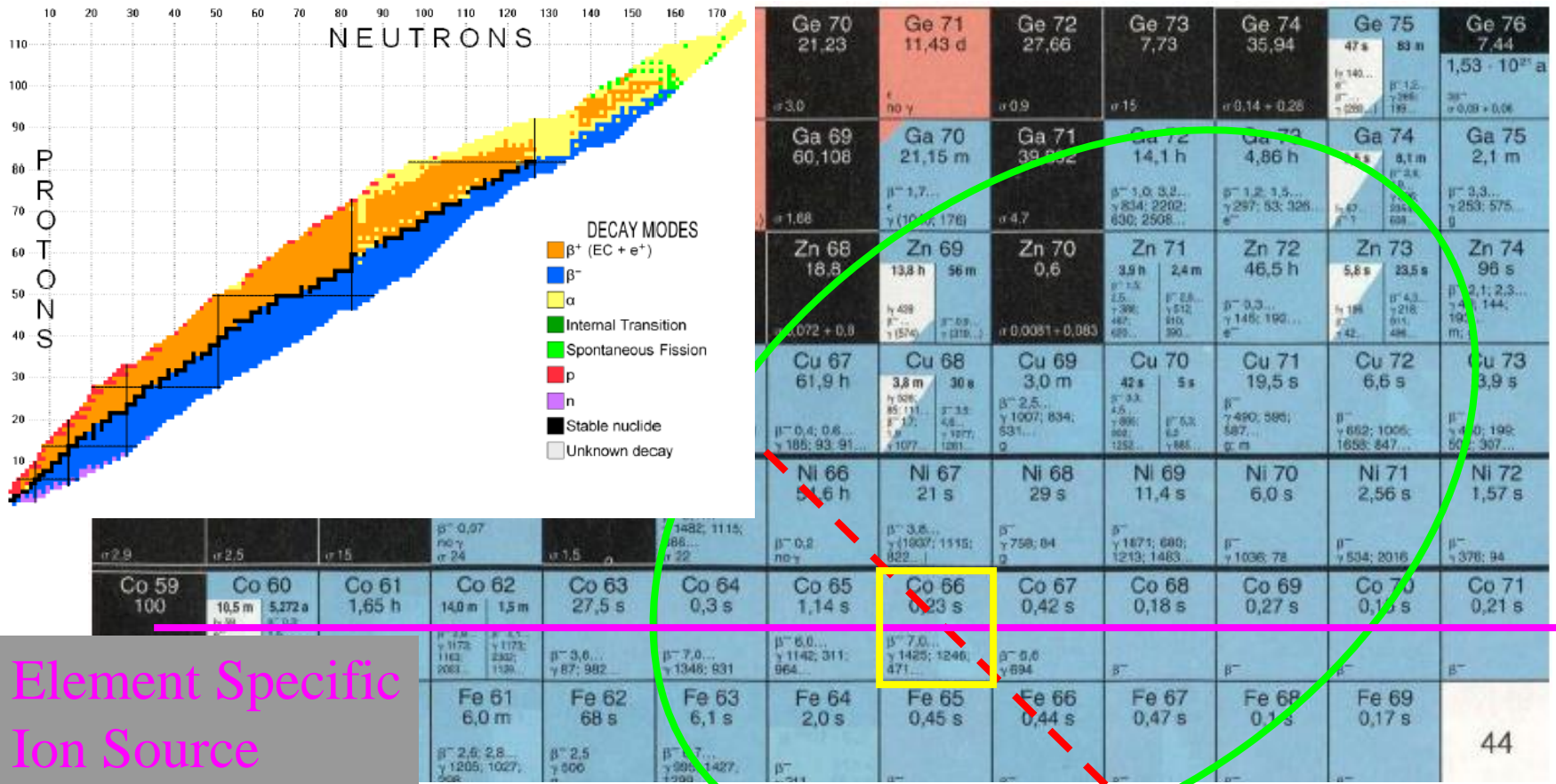
# Principle of mass selection : The Lorentz force



$$m \frac{d\mathbf{v}}{dt} = q(\mathbf{v} \wedge \mathbf{B})$$



# The "ISOL" principle

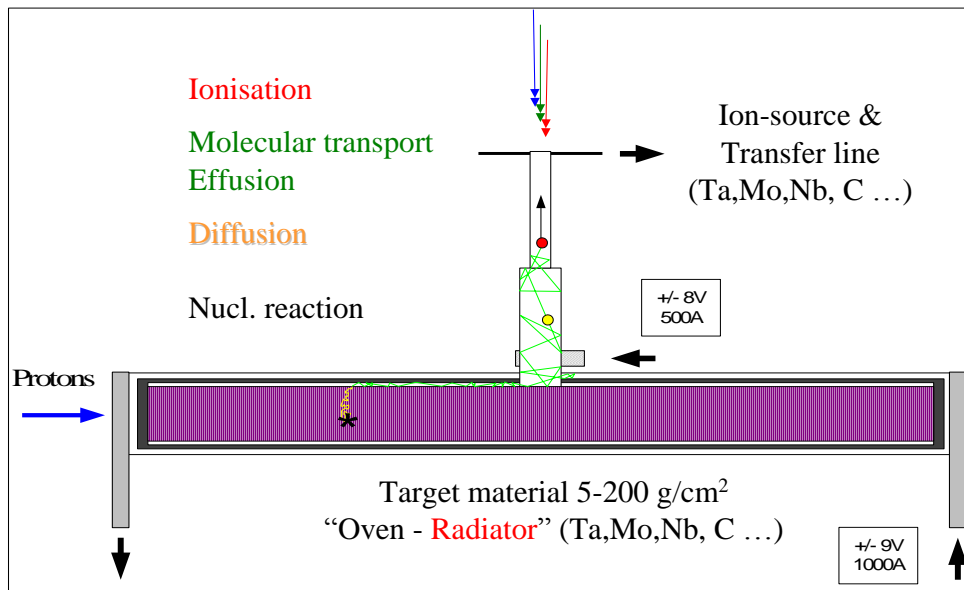


Element Specific Ion Source

Target material

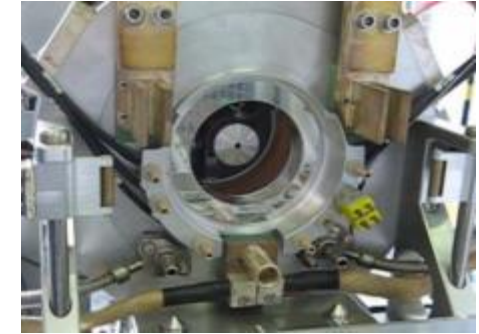
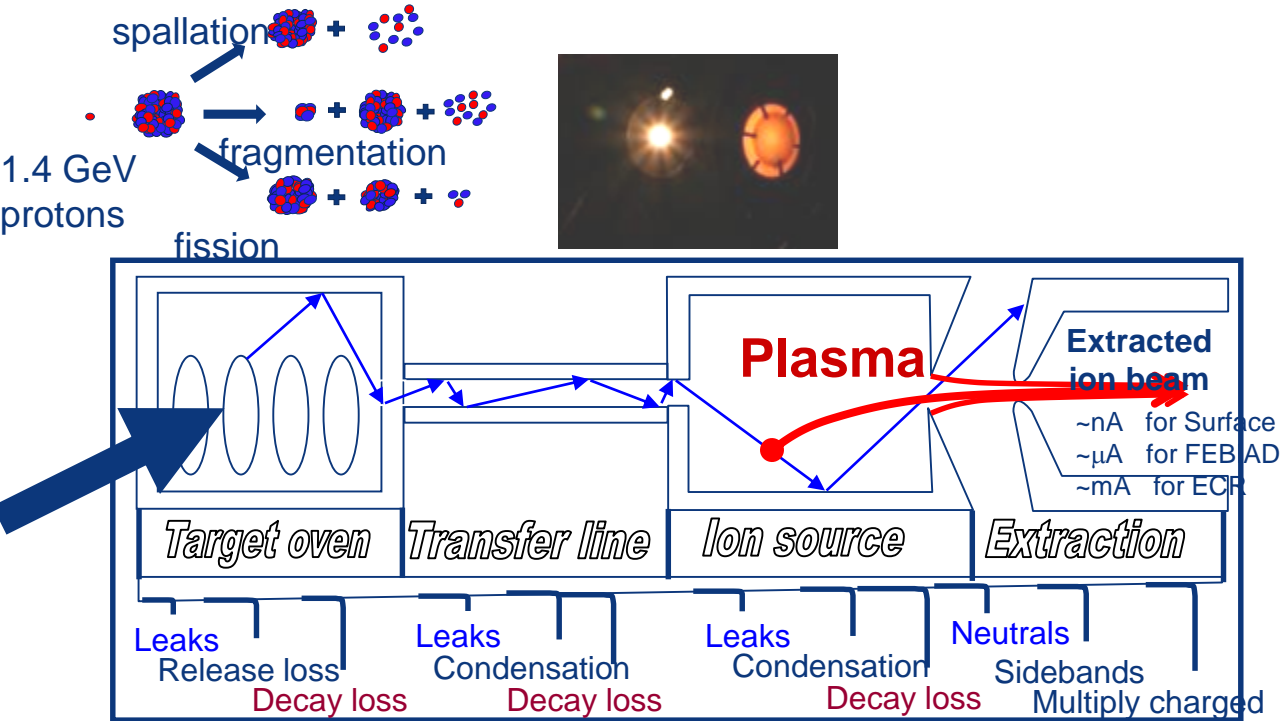
Mass Separation  
( $B\rho \sim A^{1/2}$ )

# The Release of isotopes from the target and their ionization



Isotope  
mass Separation  
On  
Line

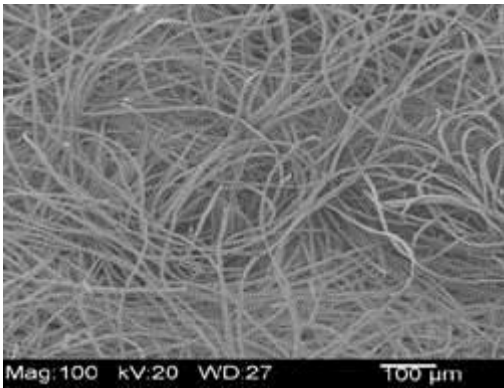
# Principles of radioactive beam production



Primary beam  
(MeV/u-GeV/u)

There is an overall efficiency  
For these extraction processes

# ISOL TARGETS



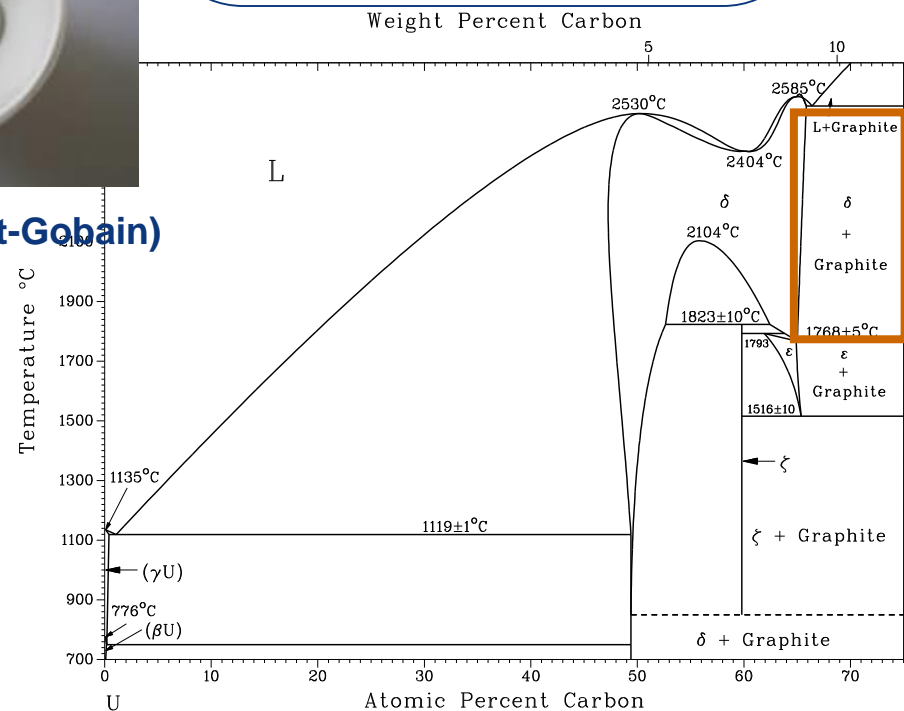
HfO<sub>2</sub> felts from Z. Zirconia



SiC pressed pellets (Saint-Gobain)

## Target materials:

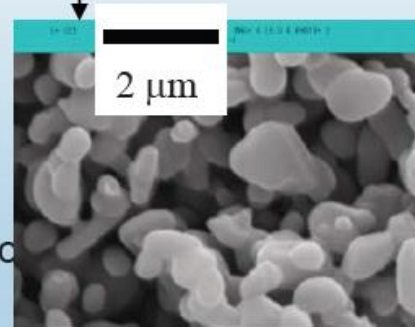
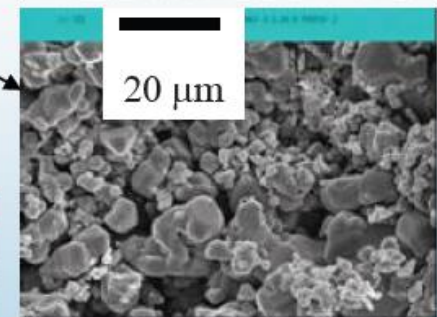
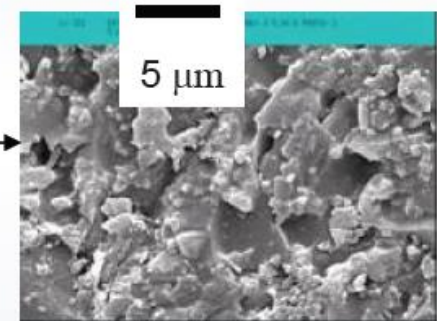
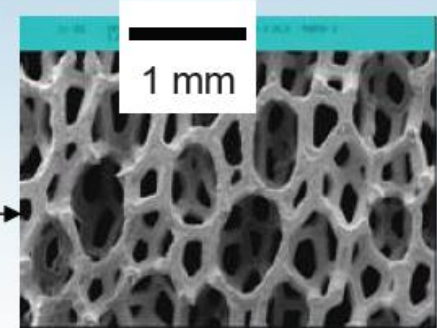
- Refractory ceramics:  
Oxides and carbides  
(UC<sub>2</sub>, SiC, Al<sub>2</sub>O<sub>3</sub>, HfO<sub>2</sub>);
- Solid metals (Ta, Nb, Mo);
- Molten metals (Pb).



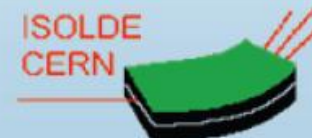
Actinide target (UC<sub>2</sub>)

# Case Study: Silicon carbide

Sample description	Bulk density (g/cm <sup>3</sup> )	Average total porosity (%)	Average grain size (μm)
DUOCEL FOAM 25-30%	0.8-1.0	70-75	-
CVD R & H (Chemical vapor deposition)	3.21	0	5
SiC Poco Graphite (POCO SiC Conversion)	2.6	21	-
SiC Starfire (CIP + Infiltration)	2.4	20	0.3
			0.7
SiC 3% Starfire	1.8-1.9	40	4
SiC SG Saint-Gobain (CIP)	1.4	56	4.4
	1.2	62	0.6



G. Arnau  
TS-MME CERN



# Diffusion in target matrices

- Arrhenius Equation:  $D = D_0 \cdot e^{\left(-\frac{Ea}{RT}\right)}$
- Assumptions:

Fick's second law  
diffusion equation  
(spherical particles)\*:

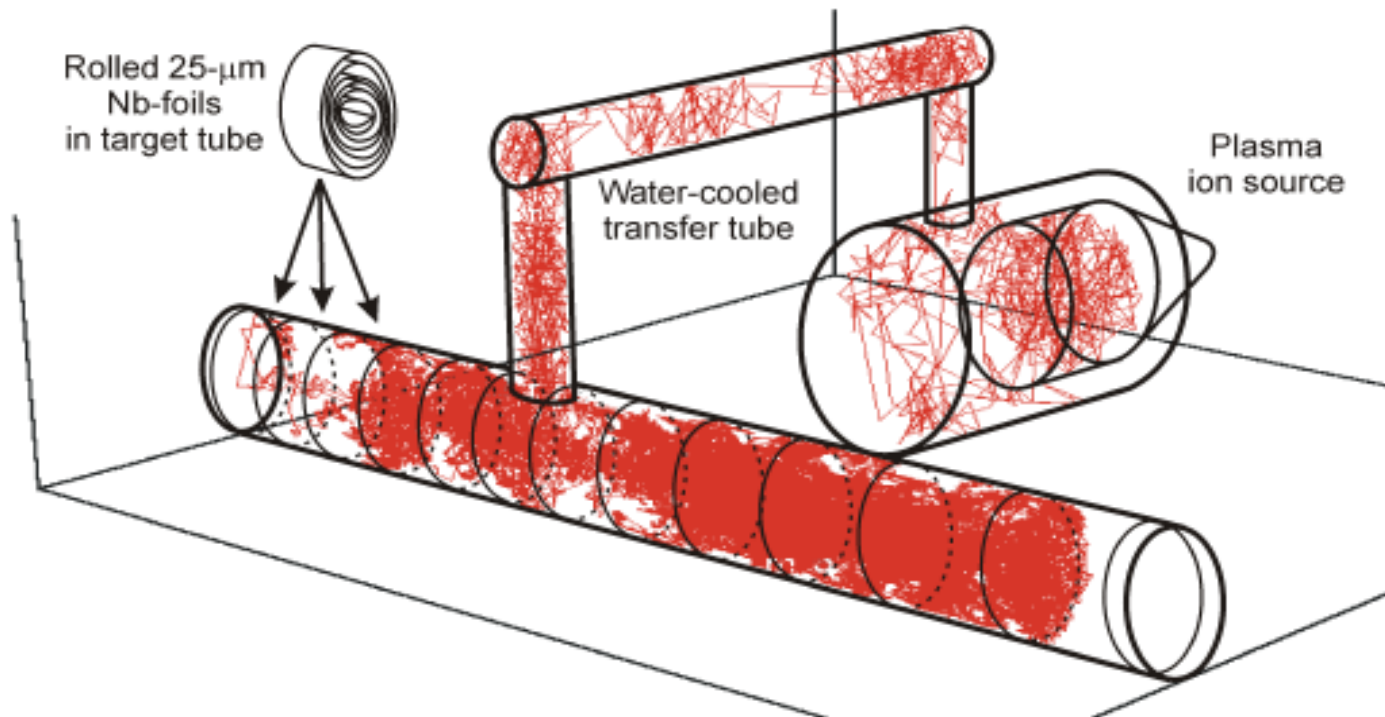
$$F(t) = \frac{6}{\pi^2} \sum_{k=1}^{\infty} \frac{1}{k^2} e^{-k^2 \mu_s t}$$

t = heating time

$\mu_s$  = diffusion parameter

$$\mu_s = \frac{\pi^2 D}{r^2}$$

# The isotopes need to find their way to the ion source

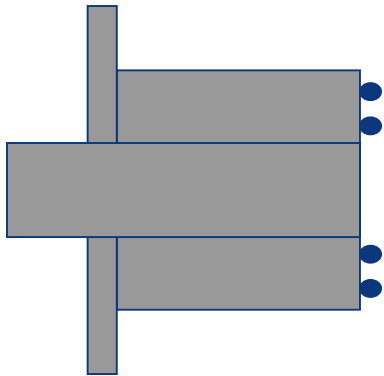


Monte Carlo numerical simulation of isotope trajectory  
(RIBO code)

# THE “FEBIAD” ION SOURCE

## Forced Electron Beam Induced Arc Discharge

- Electrons emitted from a hot cathode ( $\sim 2000^{\circ}\text{C}$ )

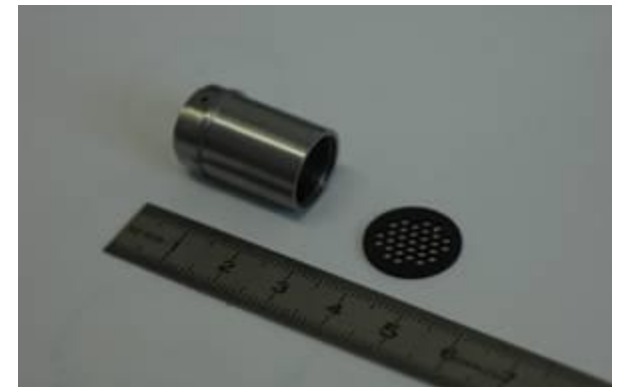
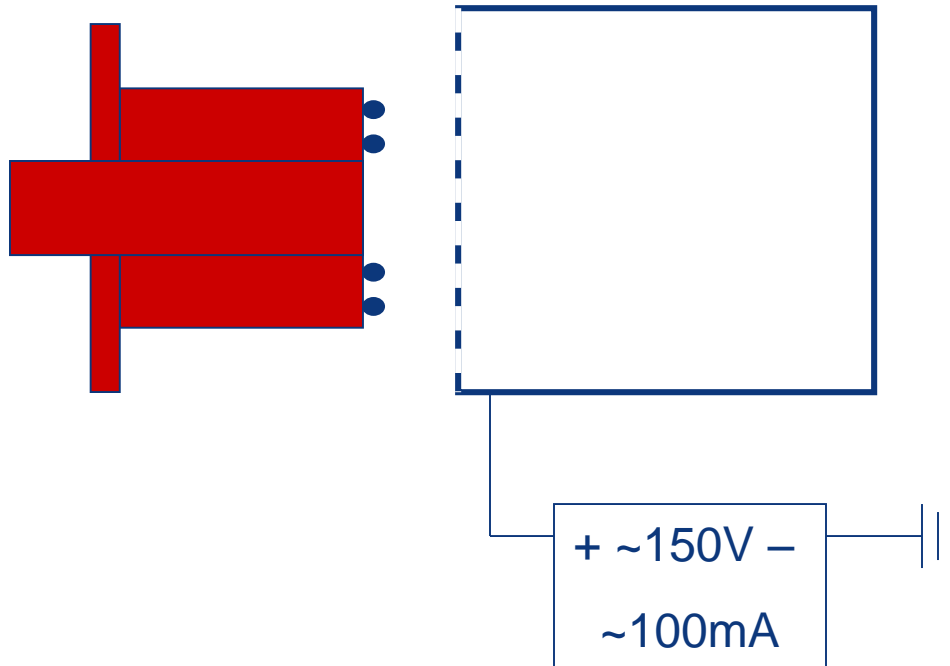


Courtesy L. Penescu/R. Catherall, “Marie Curie” Conference, Manchester 10-12 April 2006

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## Forced Electron Beam Induced Arc Discharge

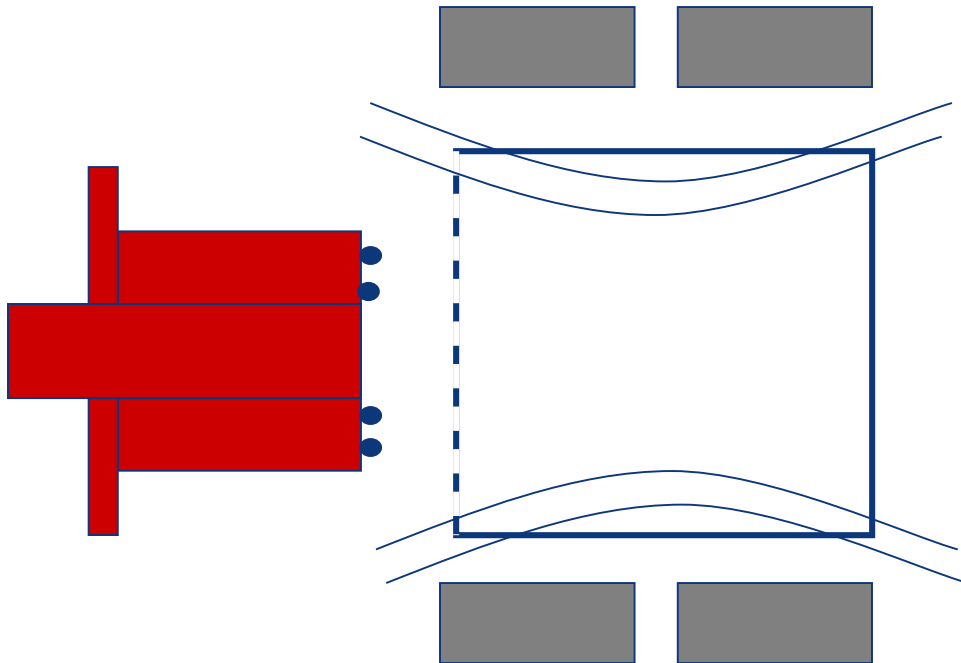
- Electrons emitted from a hot cathode ( $\sim 2000^{\circ}\text{C}$ )
- Electrons accelerated by a grid ( $\sim 150\text{V}$ )



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## Forced Electron Beam Induced Arc Discharge

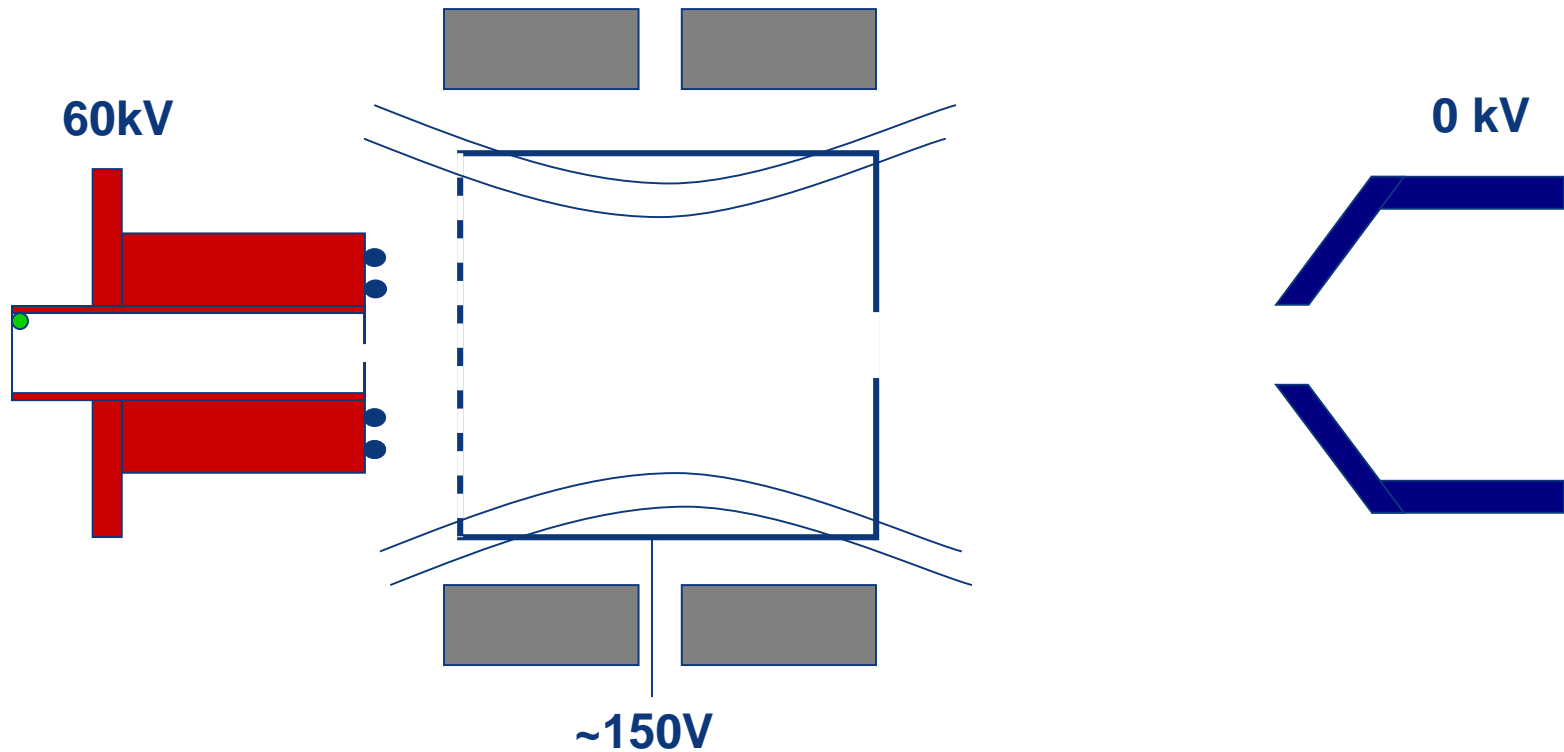
- Electrons emitted from a hot cathode ( $\sim 2000^{\circ}\text{C}$ )
- Electrons accelerated by a grid ( $\sim 150\text{V}$ )
- Electron's path is increased by a magnetic field



# THE “FEBIAD” ION SOURCE

## Forced Electron Beam Induced Arc Discharge

- Electrons emitted from a hot cathode ( $\sim 2000^{\circ}\text{C}$ )
- Electrons accelerated by a grid ( $\sim 150\text{V}$ )
- Electron's path is increased by a magnetic field
- Atoms enter from a hole in the cathode
- Atoms ionized in the plasma volume and extracted (60 kV)

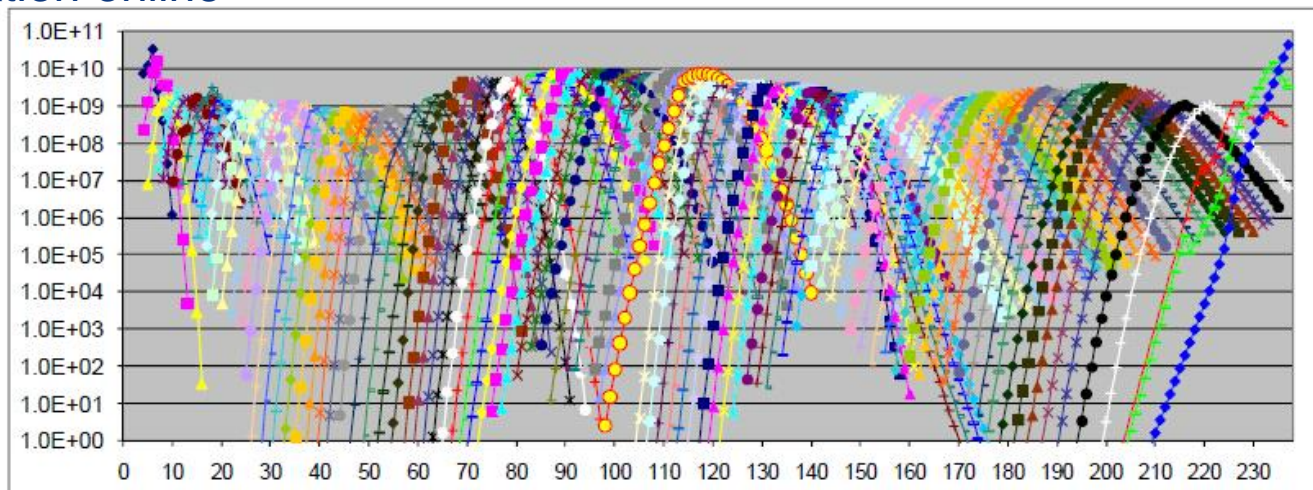


# The « ISOL » filter

Isotope mass separation online

In-target production rate

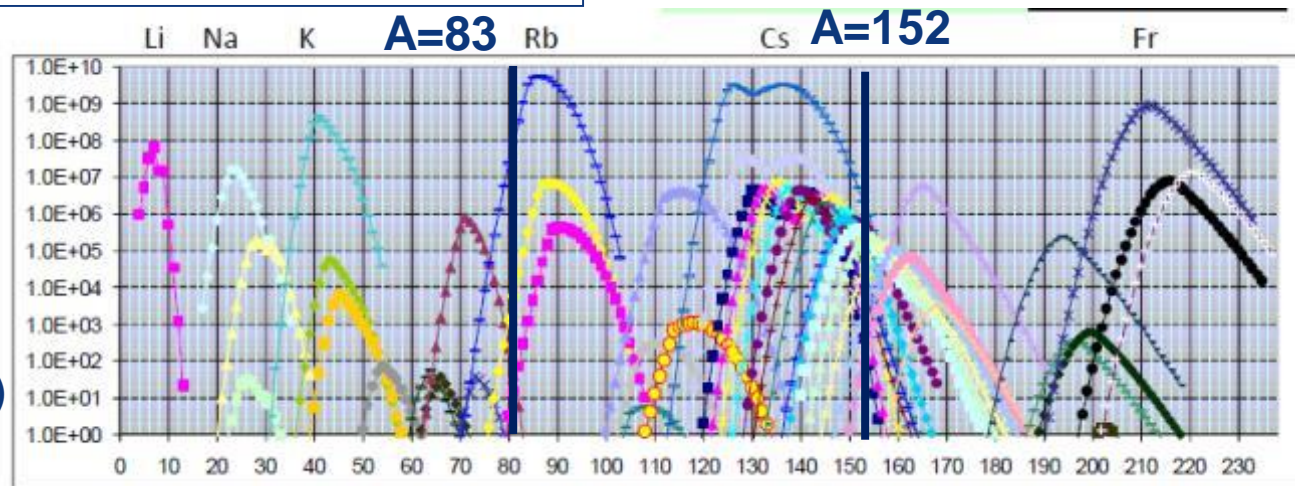
1000+ isotopes  
(for 73+ elements)  
“online”



$$I_{[\text{pps}]} \sim \Phi_{[\text{pps}]} \sigma_{[\text{barn}]} N_{[\text{g/cm}^2]} \varepsilon [\%]$$

**Intensity  
Purity**

Beam production rate  
(Mass separation filter)



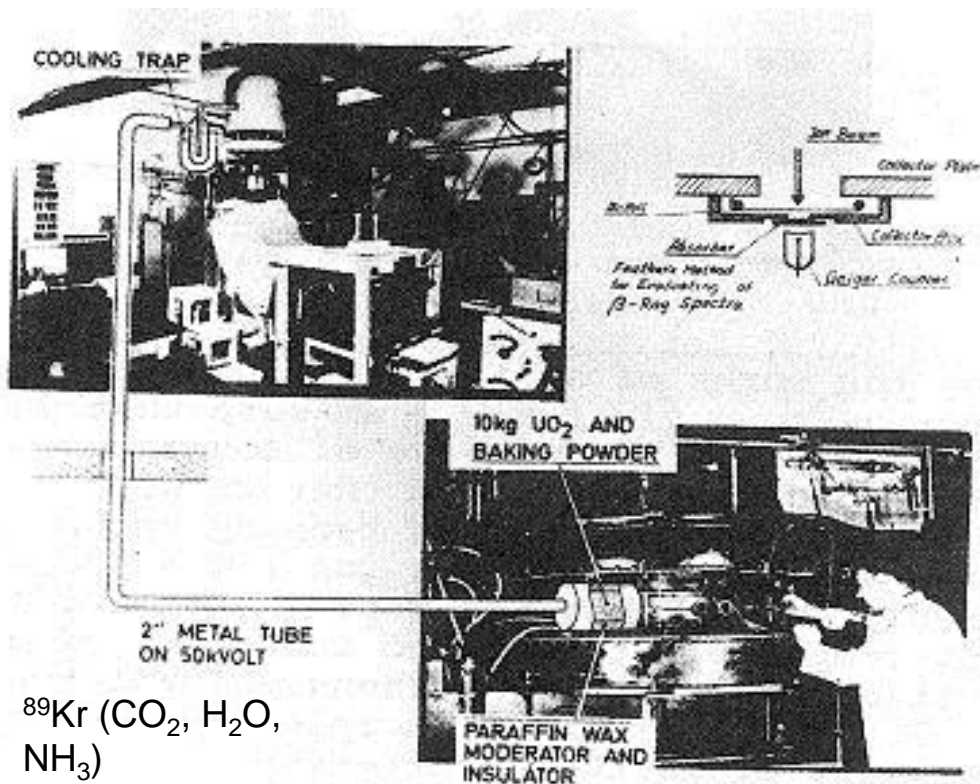
# THE BIRTH OF ON-LINE ISOTOPE SEPARATION

## ISOLDE "0"

**O.Kofoed-Hansen**

**K.O. Nielsen**

*Dan. Mat.Fys.Medd. 26, no. 7 (1951)*

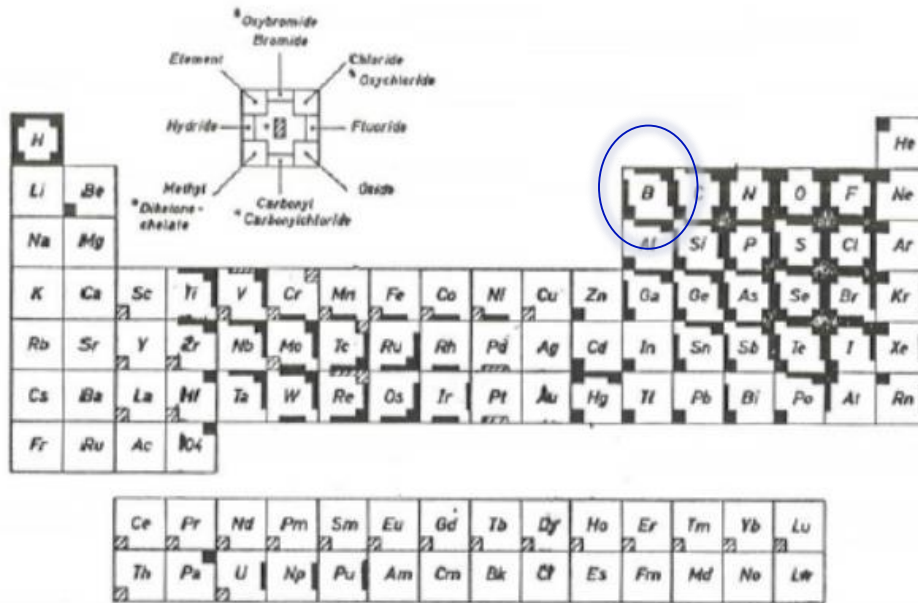


10 MeV deuterons  
d-to-n converter (Be)  
n moderator (wax)  
UO<sub>2</sub> (10 kg)  
Baking powder

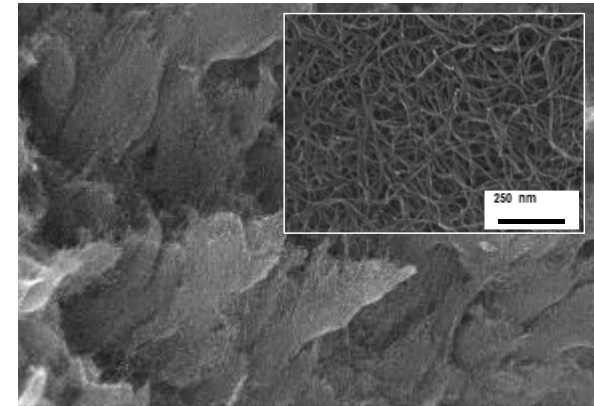
From CERN 76-13, 3<sup>rd</sup> conf. nuclei far from stability

# Case studies : 1<sup>st</sup> Boron $^8\text{BF}_2^+$ from carbon nanotubes

$^8\text{BF}_2^+$  (T1/2 880ms) produced from multiwall carbon nanotube target (fast diffusion) and  $\text{SF}_6$  reactive gaz injection (volatile  $\text{BF}_3$  molecule)



MWCNT



C. Seiffert, Production of radioactive molecular beams for CERN-ISOLDE.

PhD thesis TU Darmstadt, CERN (2015)

# Isotope mass separation added value

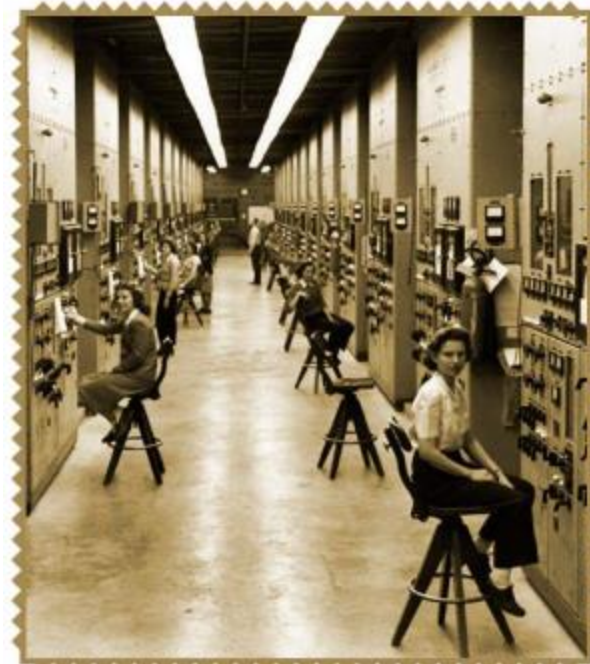
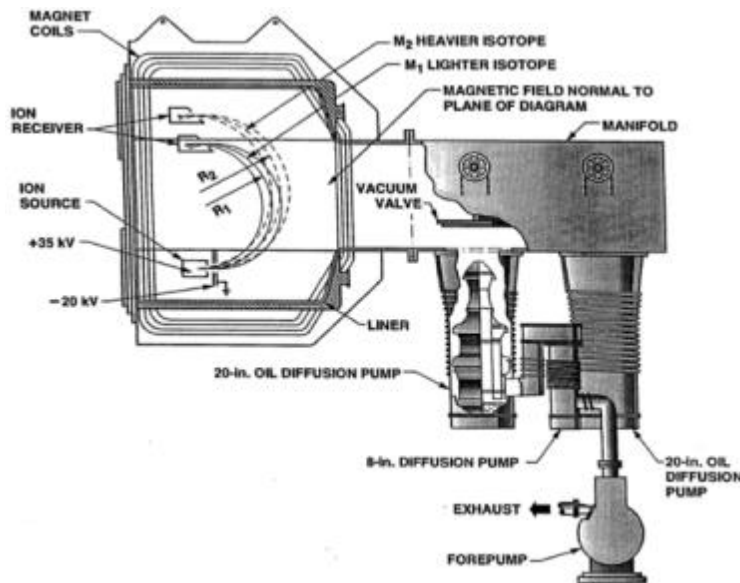
Non carrier added radioisotope fraction (high specific activity)

Efficiencies to be developed

Can this process be applied in large scale ?

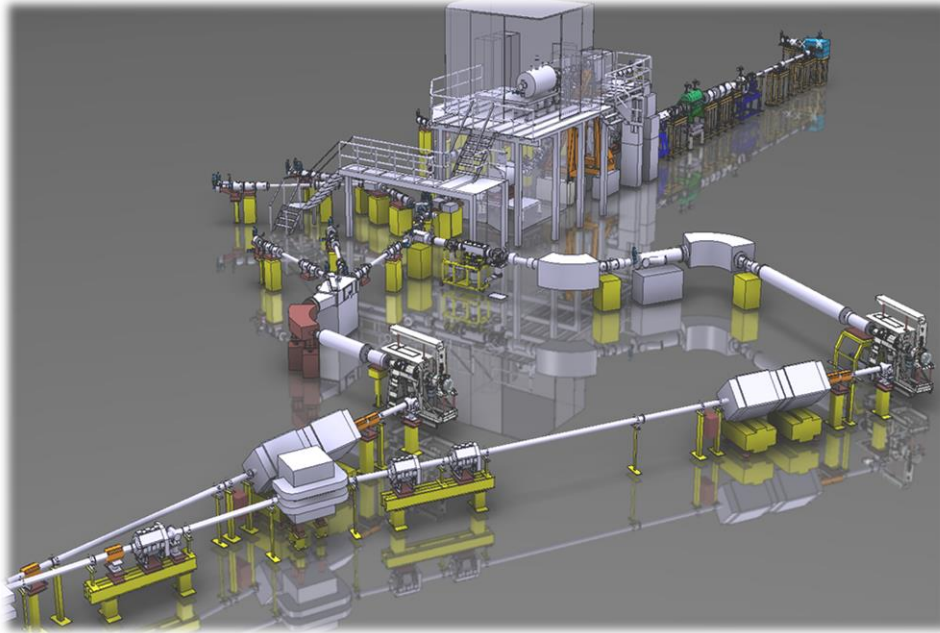
A first terrifying use:  $^{235}$  uranium enrichment of “Little Boy”

And later a much more positive application :  
isotope enrichment for medical isotope production



The Calutron (E. Lawrence)

# And today



CERN ISOLDE

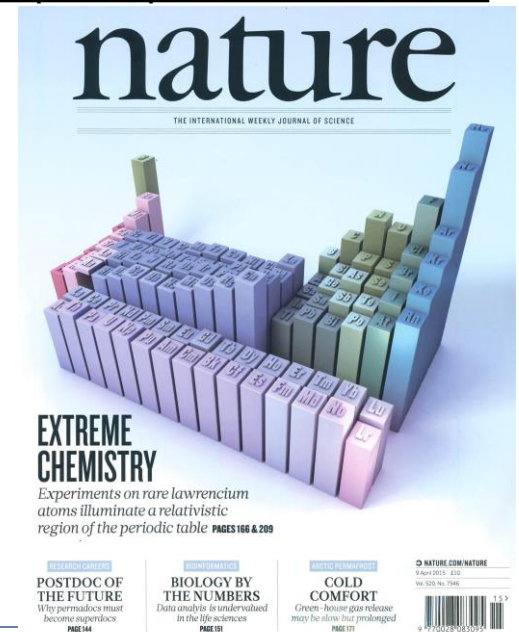
## LETTER

doi:10.1038/nature14342

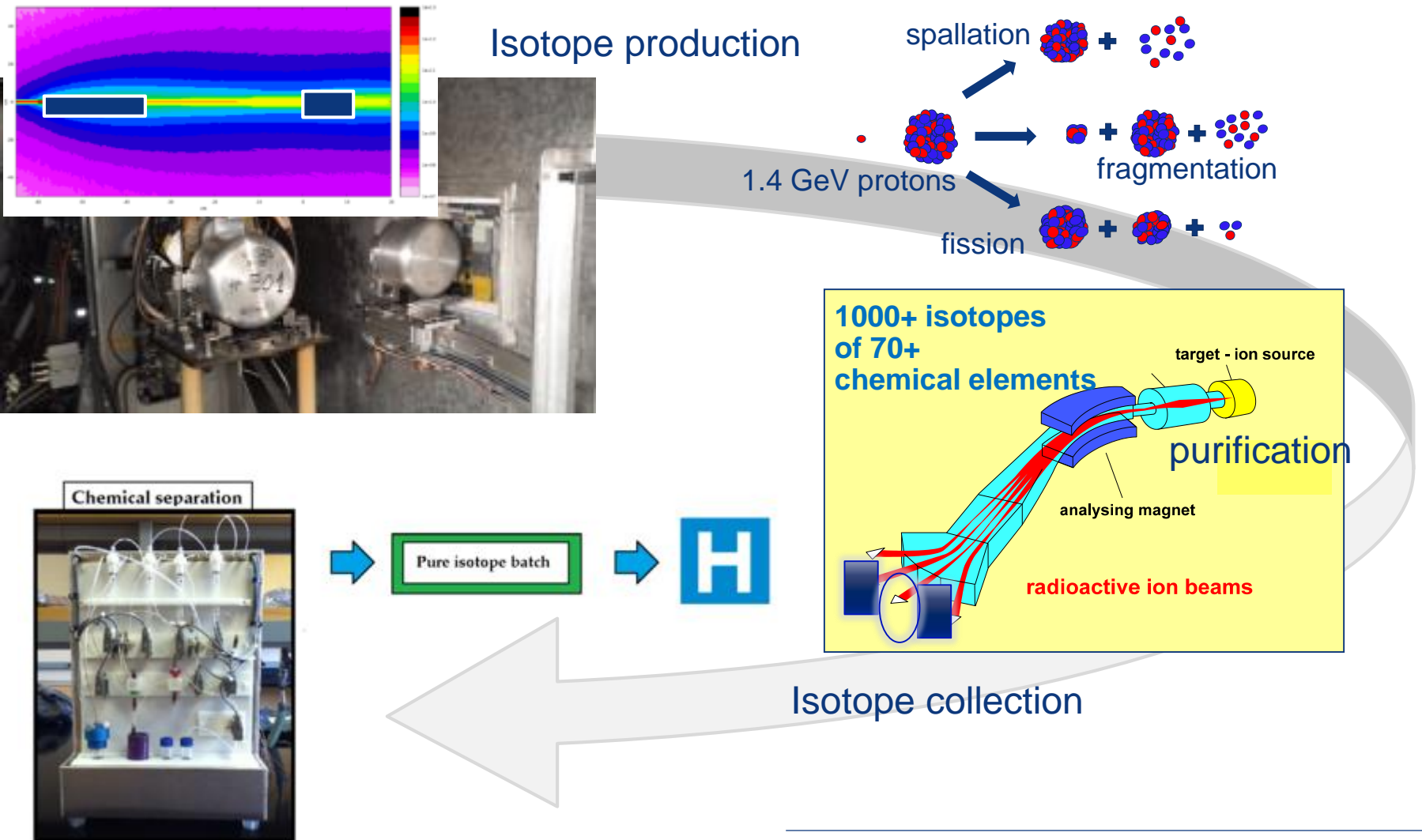
### Measurement of the first ionization potential of lawrencium, element 103

T. K. Sato<sup>1</sup>, M. Asai<sup>1</sup>, A. Borschevsky<sup>2,3</sup>, T. Stora<sup>4</sup>, N. Sato<sup>1</sup>, Y. Kaneya<sup>1,5</sup>, K. Tsukada<sup>1</sup>, Ch. E. Düllmann<sup>3,6,7</sup>, K. Eberhardt<sup>3,7</sup>, E. Eliav<sup>8</sup>, S. Ichikawa<sup>1,9</sup>, U. Kaldor<sup>9</sup>, J. V. Kratz<sup>7</sup>, S. Miyashita<sup>10</sup>, Y. Nagame<sup>11</sup>, K. Ooe<sup>11</sup>, A. Osa<sup>11</sup>, D. Renisch<sup>7</sup>, J. Runke<sup>7</sup>, M. Schädel<sup>7</sup>, P. Thörle-Pospiech<sup>12</sup>, A. Toyoshima<sup>13</sup> & N. Trautmann<sup>7</sup>

Author	Year	$IP_1/eV$	method
E. Eliav <sup>14</sup>	1995	4.887	DCB+FSCC <sup>a</sup>
W. Liu <sup>29</sup>	1998	5.28	RECP+CASSCF+ACPF+ $\Delta_{SO}$ <sup>b</sup>
X. Cao <sup>30</sup>	2003	4.80	RECP+CASSCF+ACPF+ $\Delta_{SO}$ <sup>b</sup>
A. Borschevsky <sup>17</sup>	2007	4.893	DCB+FSCC <sup>a</sup>
V. A. Dzuba <sup>18</sup>	2014	4.934	CI+all-order <sup>c</sup>
This work		4.963(15)	DC CCSD(T)+Breit+Lamb shift <sup>d</sup>
This work		4.96 <sup>+0.08</sup> <sub>-0.07</sub>	Experimental



# CERN-MEDICIS : Isotope production in the dump and mass separation in the lab

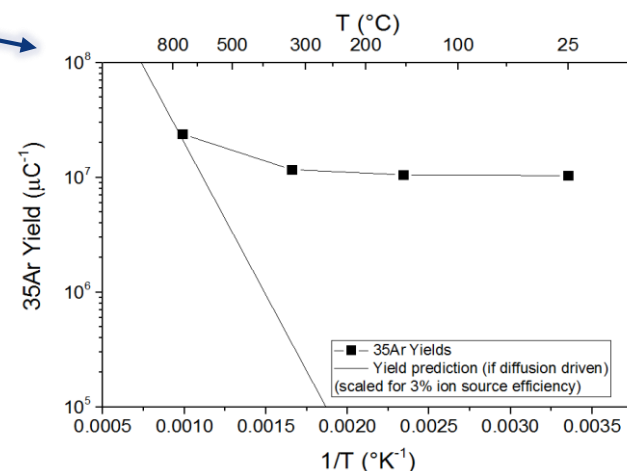
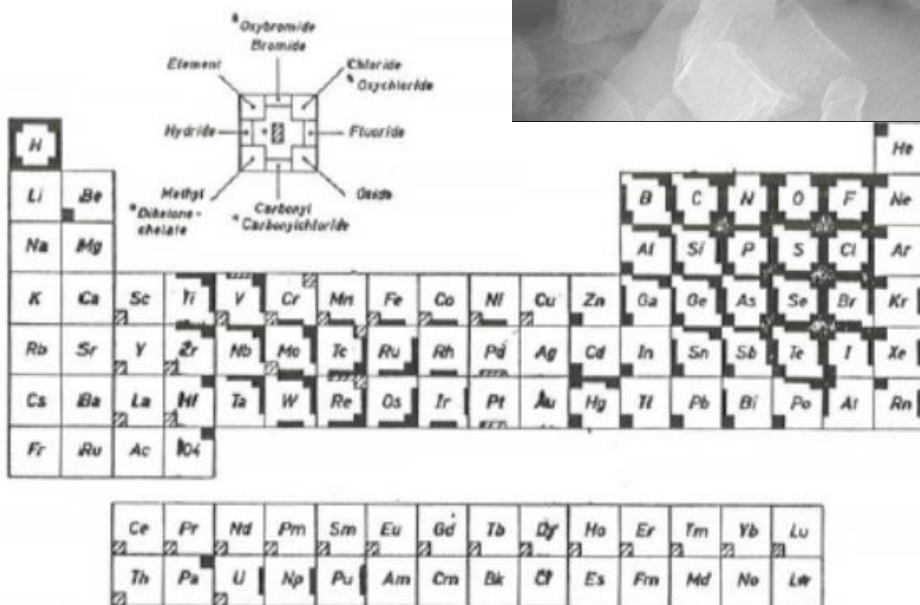
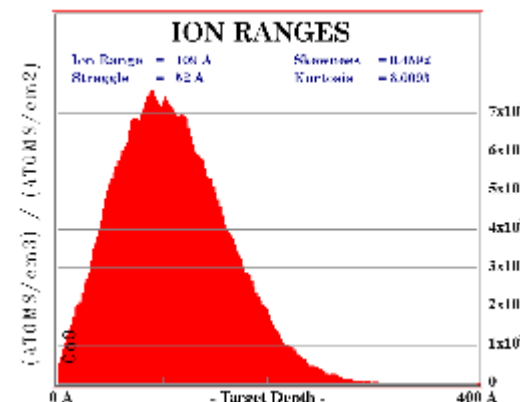
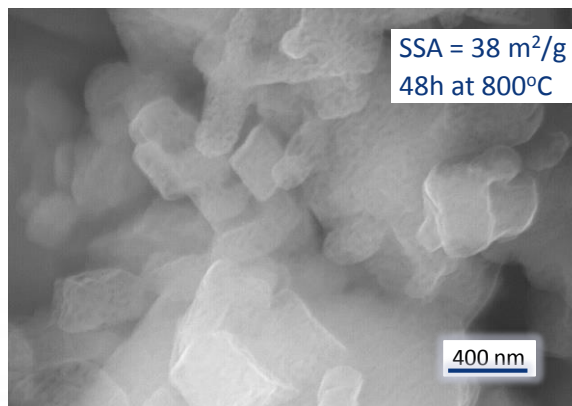


- Merci, Questions ?

- RESERVE

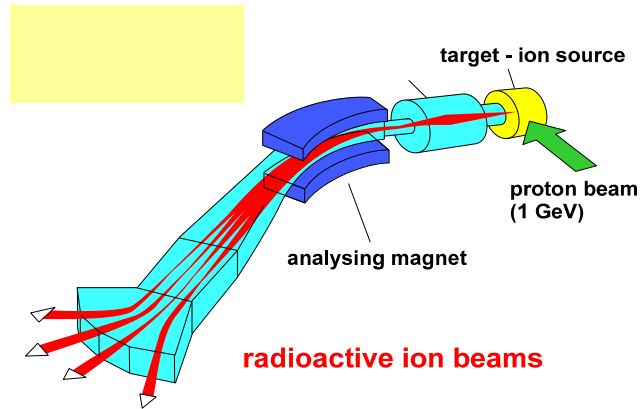
# Case studies : $^{35}\text{Ar}$ + from cold nanostructured targets

Fast release of  $^{35}\text{Ar}$  from cold nanostructured CaO targets:  
Recoil into nanomaterial

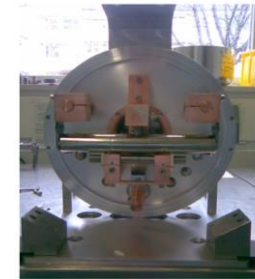


J. P. Ramos et al., submitted (2015)

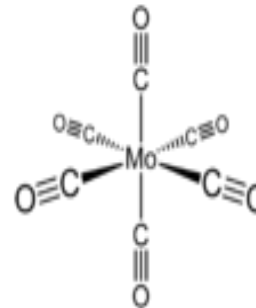
# R&D towards Mo-99/Tc-99m mass separation at CERN-MEDICIS



- Method similar to that found in a neutron spallation facility (SNS, ESS, JSNS, ISIS, etc)



- $^{238}\text{U}$  is fissioned by fast neutrons to produce Mo
- Requires the use of  $\mu\text{m}$  thick  $^{238}\text{U}$  metallic foil target for fission recoil
- However Mo is a refractory element, it cannot be released in atomic form.
- Our plan: react it with CO gas. Forms a complex which is volatile.



Formation of  $\text{Mo}(\text{CO})_6$  complex already achieved

*J. Even, et al Radiochim Acta 2014*

# R&D towards Mo-99/Tc-99m mass separation at CERN-MEDICIS

- $\text{Mo}(\text{CO})_6$  not very stable – can easily oxidize and dissociate at high temperature
- Requires the use of  $\mu\text{m}$  thick  $^{238}\text{U}$  metallic foil target for fission recoil out (25 micron  $^{\text{nat}}\text{U}$  foils) at low temperature
- Grow graphene:  
does not stop recoil isotopes, reduce oxidation and taylor  $\text{Mo}(\text{CO})_6$  adsorption



K.S. Novoselov and AH Castro Neto. "Two-dimensional crystals-based heterostructures: materials with tailored properties." *Physica Scripta* 2012.T146 (2012): 014006.  
D. Prasai, et al. "Graphene: corrosion-inhibiting coating." *ACS nano* 6.2 (2012): 1102-1108.

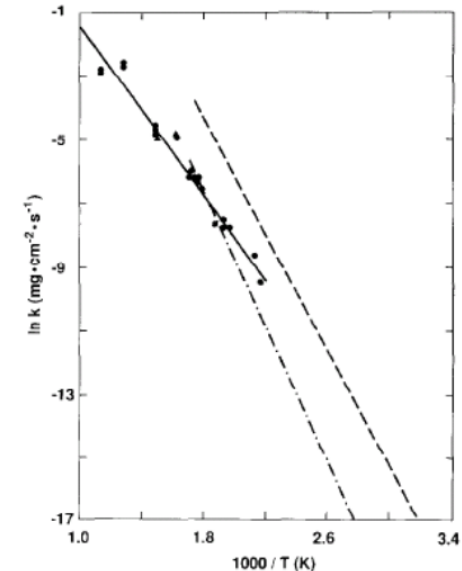
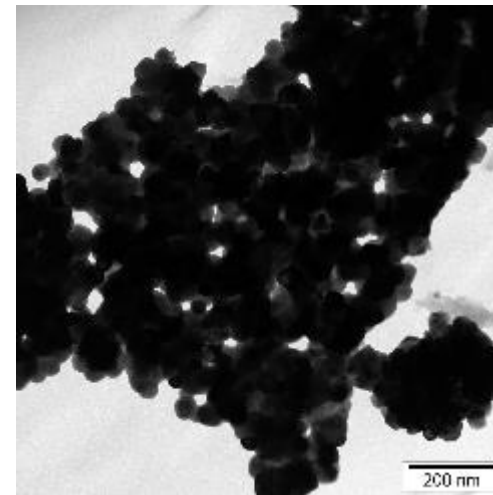
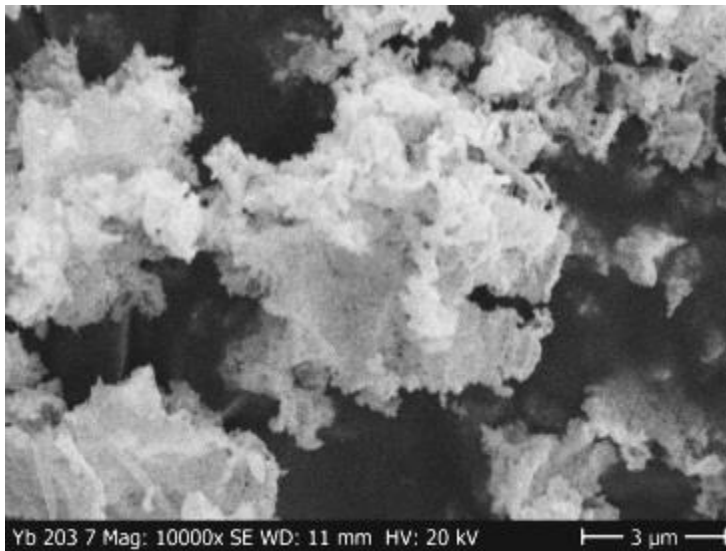


Fig. 4. Comparison of Ar-25%  $\text{O}_2$  oxidation rates (circles) with dry-air oxidation rates from eqs. (6) (dashed line) and (7) (dot-dashed line) and from ref. [16] (triangles).

P.J. Hayward et al., *J. Nucl. Mat* 187, (1992)

# R&D towards Mo-99/Tc-99m mass separation at CERN-MEDICIS

- Alternative target materials : towards submicron uranium-based materials
- Work has started as with lanthanide precursors via electrospinning



*M. S. Henriques, et al. "Preparation of Yb<sub>2</sub>O<sub>3</sub> submicron-and nano-materials via electrospinning." Ceramics International 41(9), 10795 (2015).*