Medicis Promed

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MEDICIS-PROduced radioisotope beams for MEDicine

Summer School on PET-aided Hadron therapy @ CNAO

The EU Framework Programme for Research and Innovation

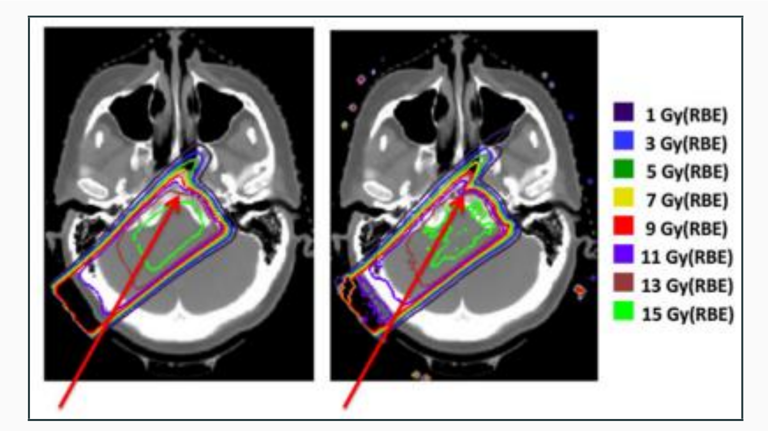
HORIZON 2020

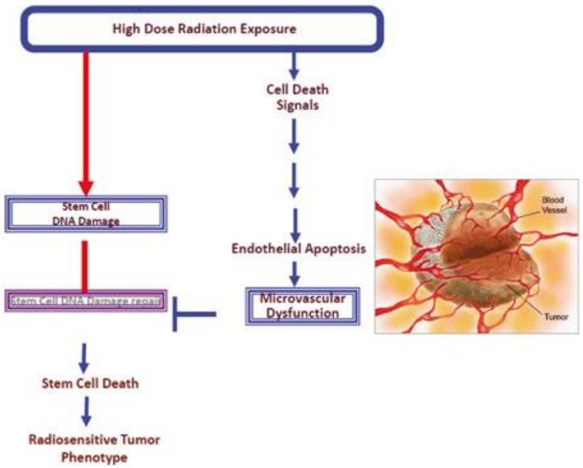
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 642889

How to neutralize cancer tissues

Brute force : Remove or destroy cancer tissue, e.g. by irradiation, and spare healthy tissue

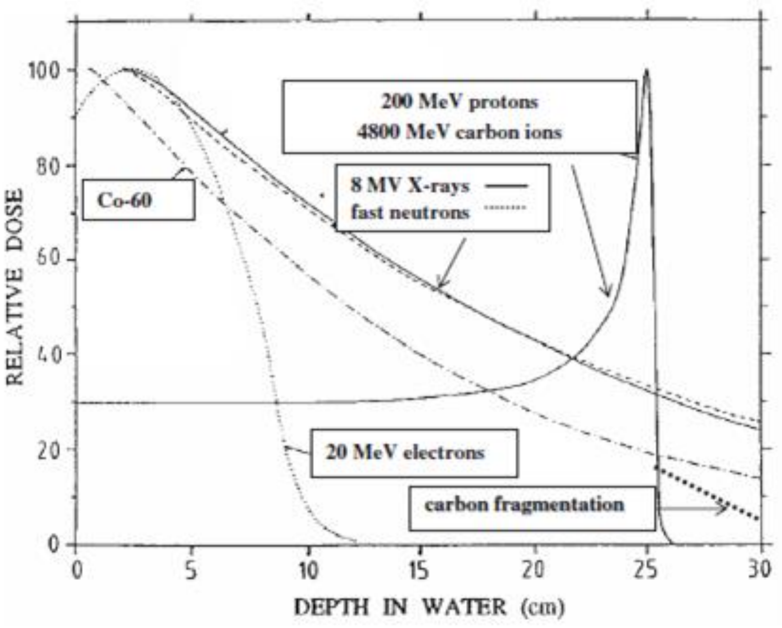
Sometimes, not that simple



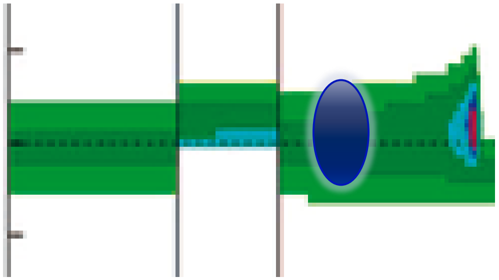


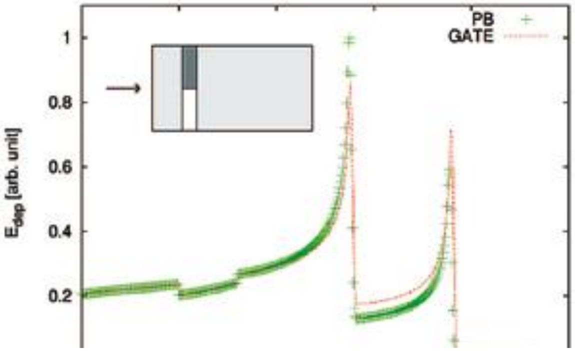
NuPECC Nuclear Physics for Medicine (2014)

Advantage of Ion beams (hadron therapy) : Bragg peak for local dose delivery



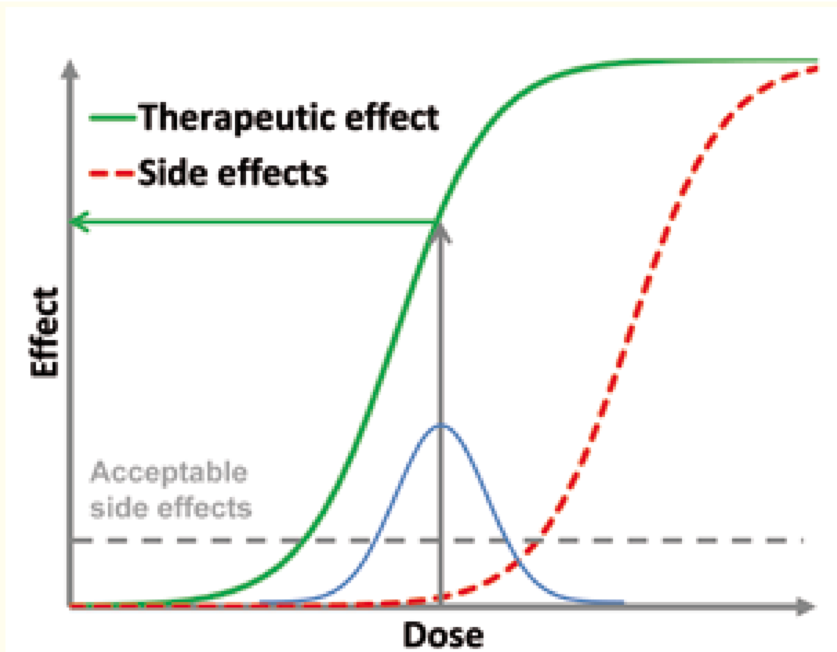
U.Amaldi, G.Kraft,
Rep.Prog.Phys.68,1861(2005)





Needs simulation tools, e.g Monte Carlo

Advantage of Ion beams (hadron therapy)

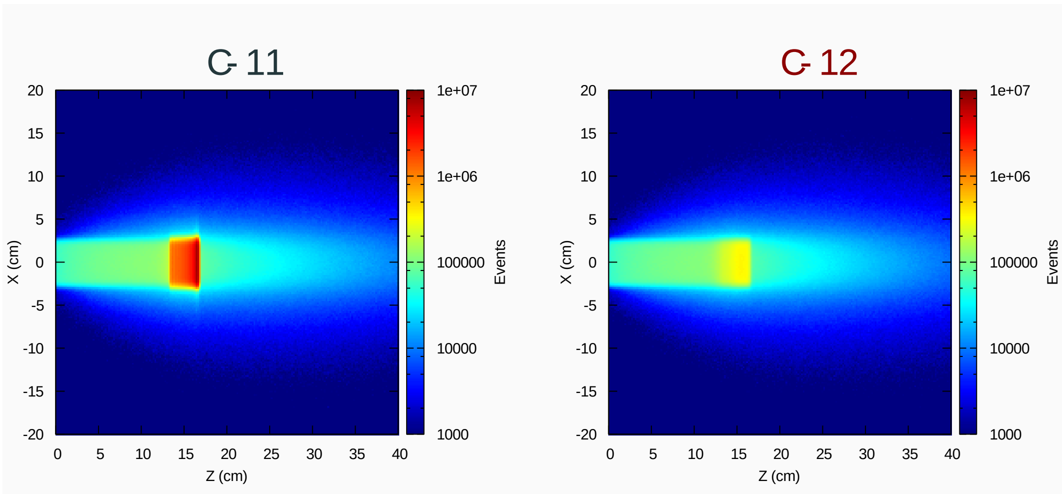


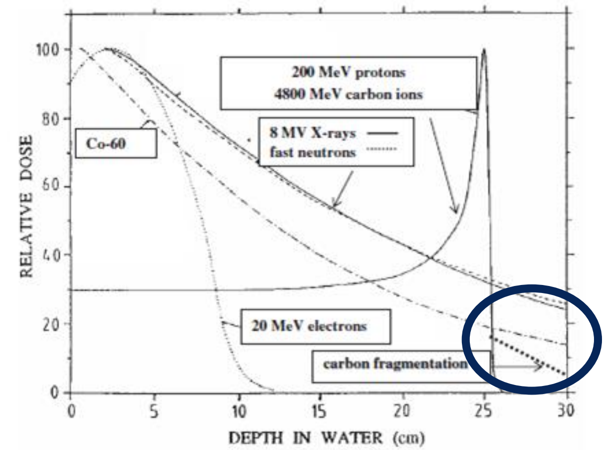
Here again,
Sometime not so simple Relative Biological Effectiveness (RBE) links to physical dose

From NuPECC 2014

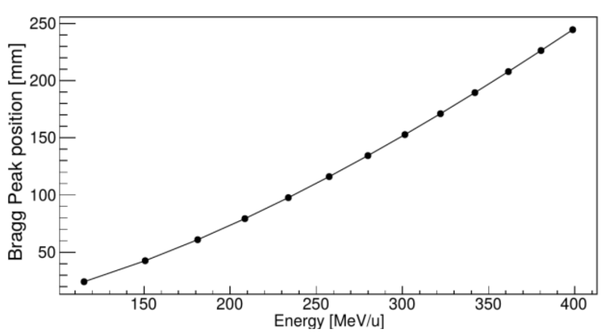
PET Ion beams for Hadron therapy

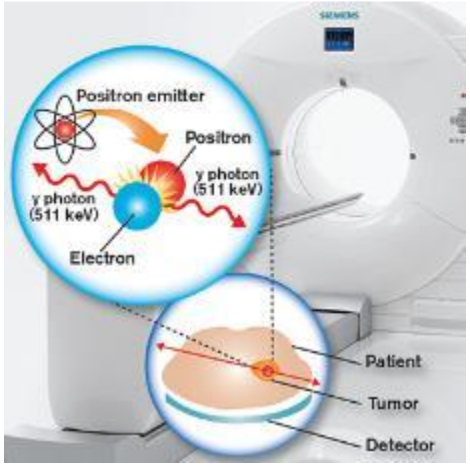
Comparison of in-beam PET with fragment 12C (11C, 15O) and direct 11C use





Simulations by R. Augusto et al. : 10x stronger signal !!

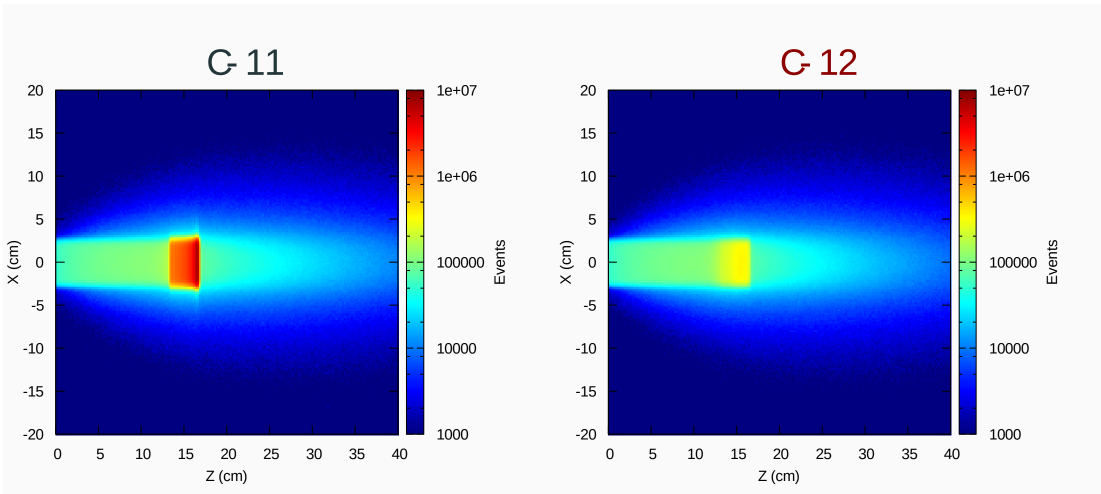


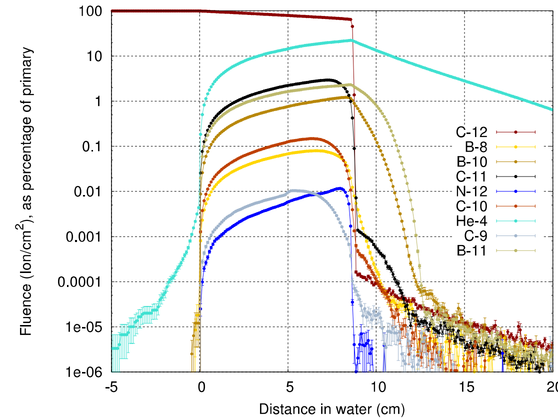


KyungDon Choi, “ESR-9 of MEDICIS-Promed”, CNAO: Personalized 11Carbon PET aided hadron therapy

Experimental studies have been performed at HIMAC, NIRS

PET Ion beams for Hadron therapy





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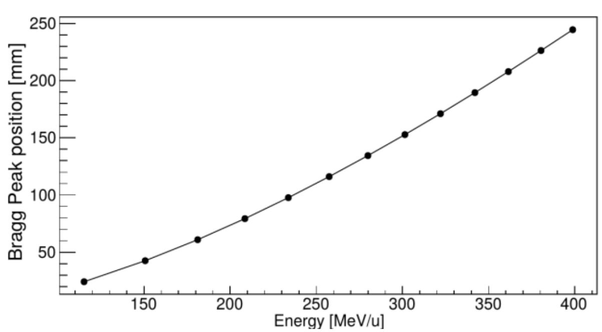

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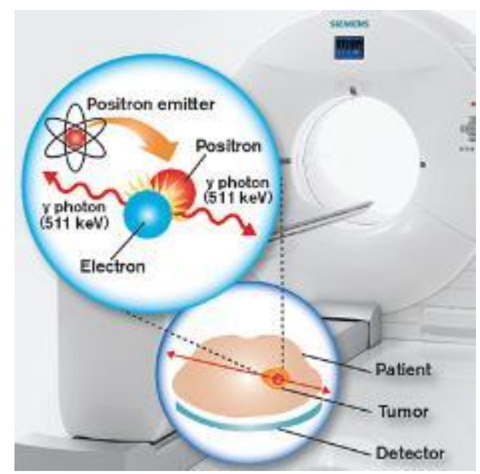
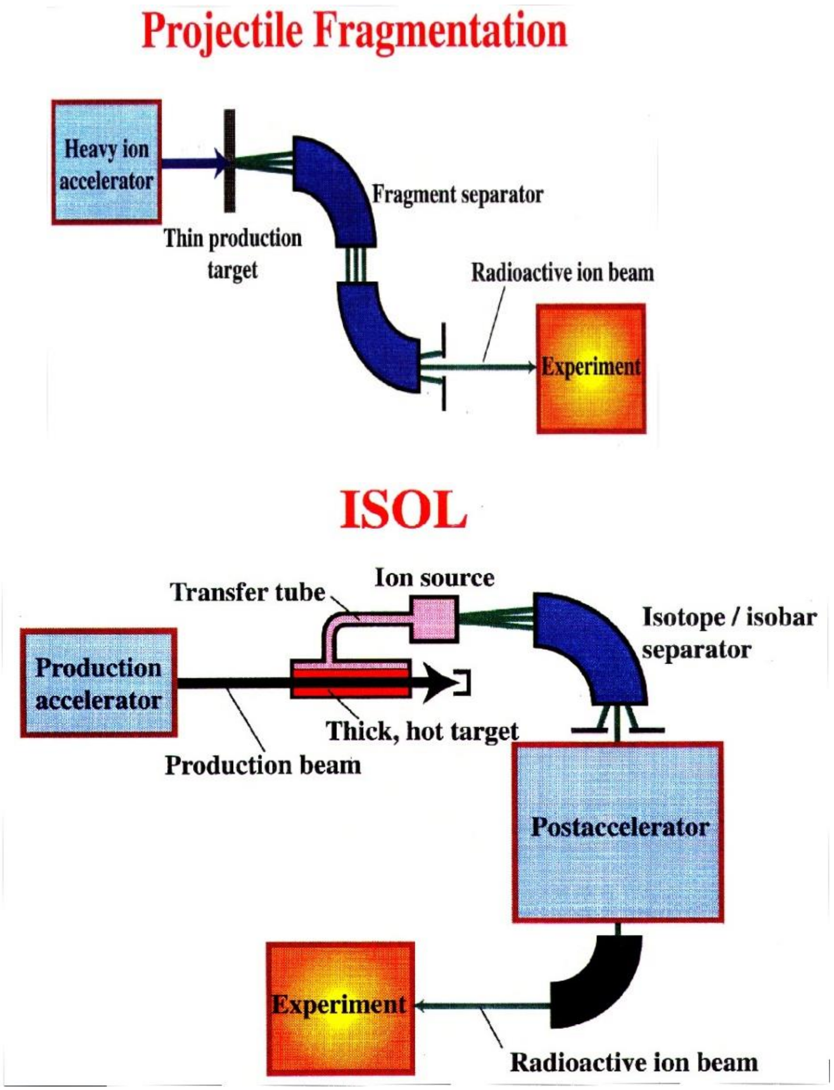
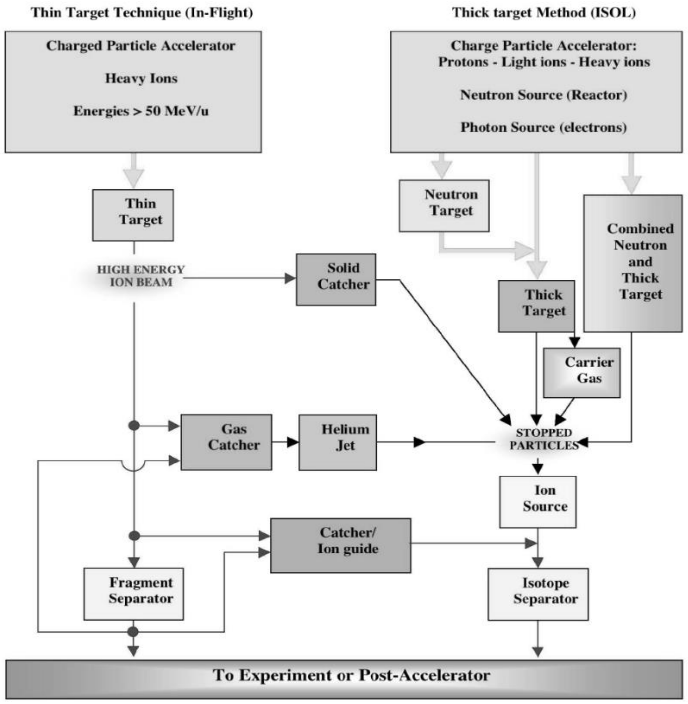


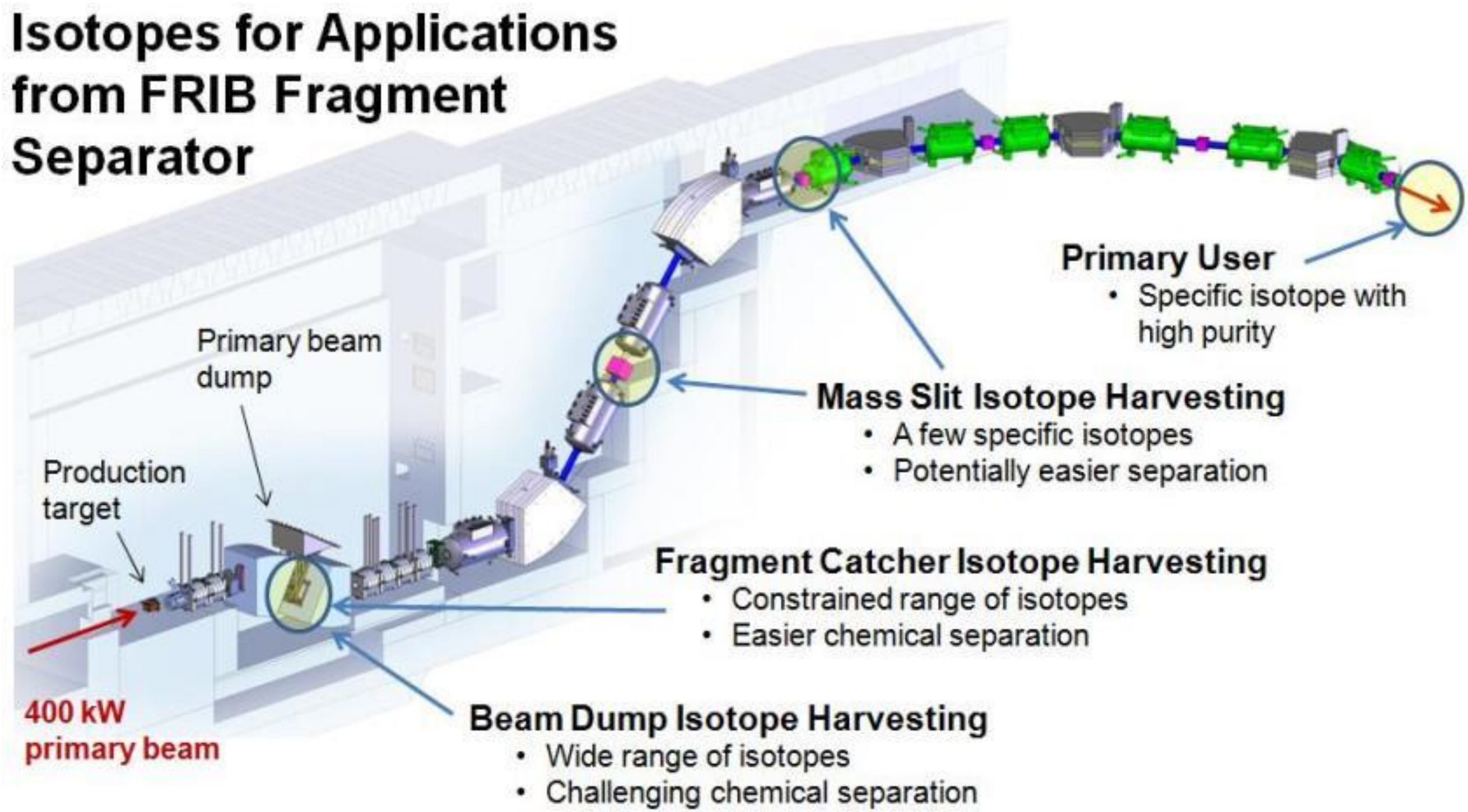
Experimental studies have been performed at HIMAC, NIRS

The main ingredients :An accelerator for isotope production + isotope acceleration/separation



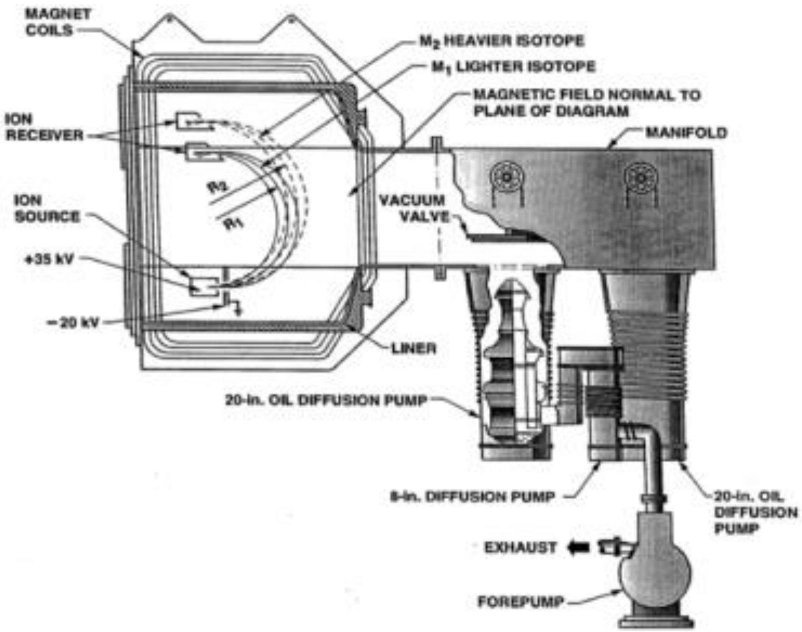


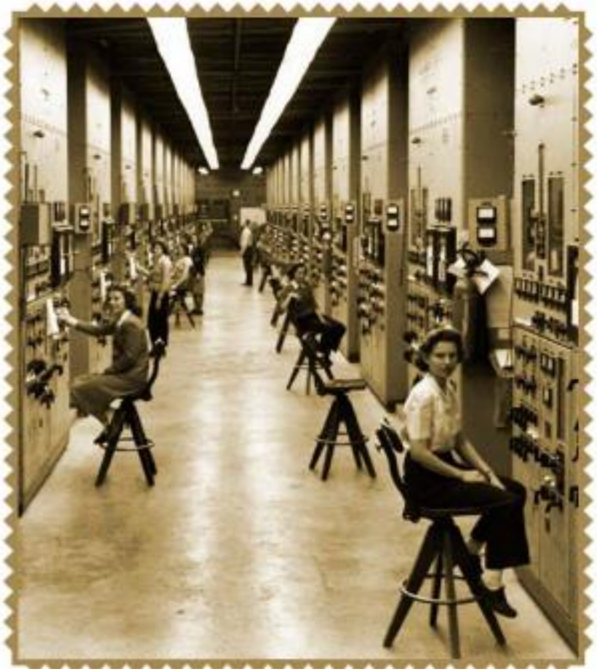
A large fragment separator :
FRIB under construction at MSU (USA)



Isotope mass separation with long-lived isotopes*

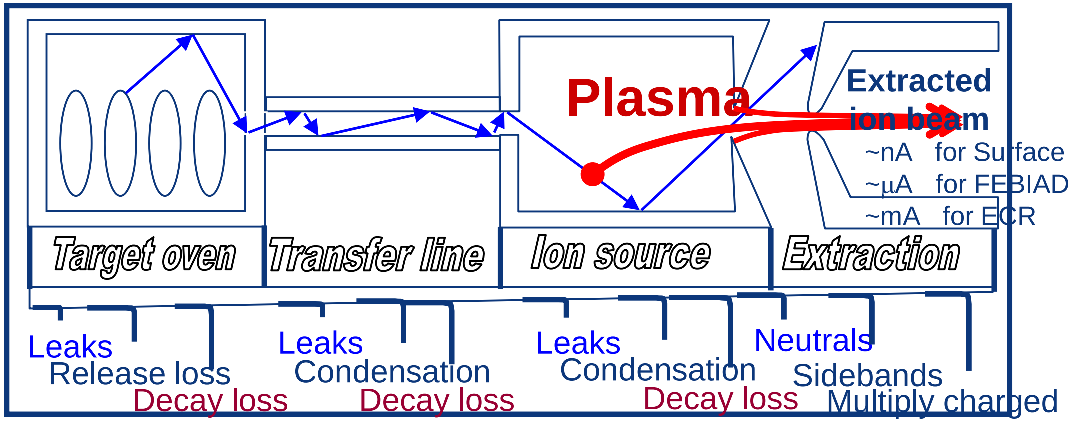
The Calutron (E. Lawrence) used during 2nd world-war





* are 11Carbon or 15Oxygen PET isotopes long-lived ?

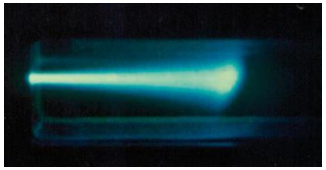
Losses in radioactive beam production



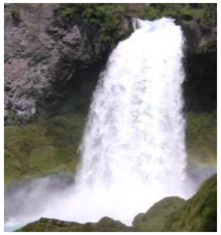
Make sure you collect a large fraction and fast, before it is decayed !

H. Ravn and W. Brian
"On-line mass separators.
" Treatise on heavy ion science. Springer US, 1989. 363-439.

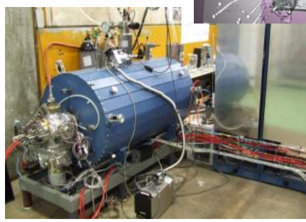
Accelerator components and concepts are required

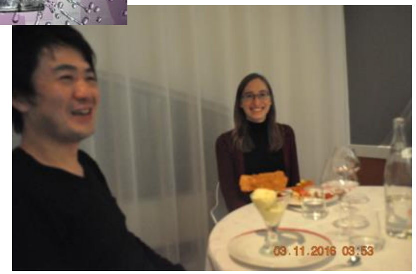


Gas target
(N_2 $^{14}N(p,\alpha)^{11}CO_2$)

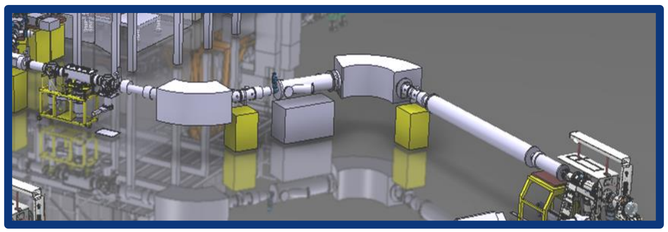


^{11}C isotope production
S. Segemann ESR11



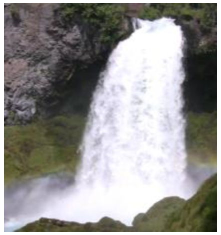


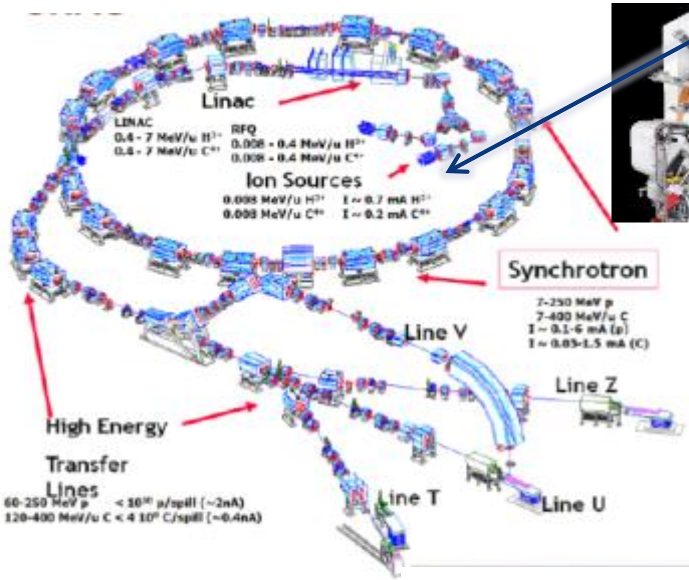
Ion Source,
J. Pitters, ESR3

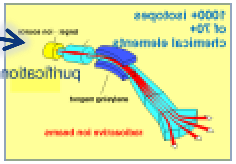


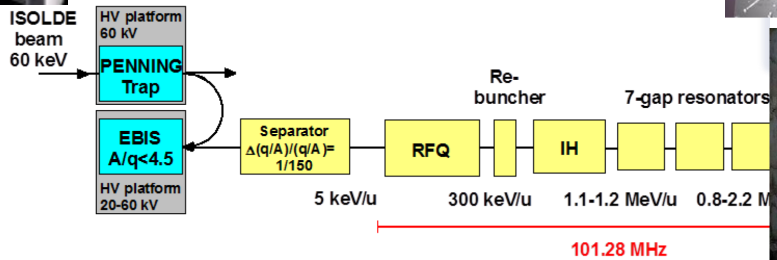
Break-up and trapping,
A. Ringvall-Moberg, ESR1

Possible acceleration schemes : efficiencies matter









"A la Isolde"

Directly in the ECRIS

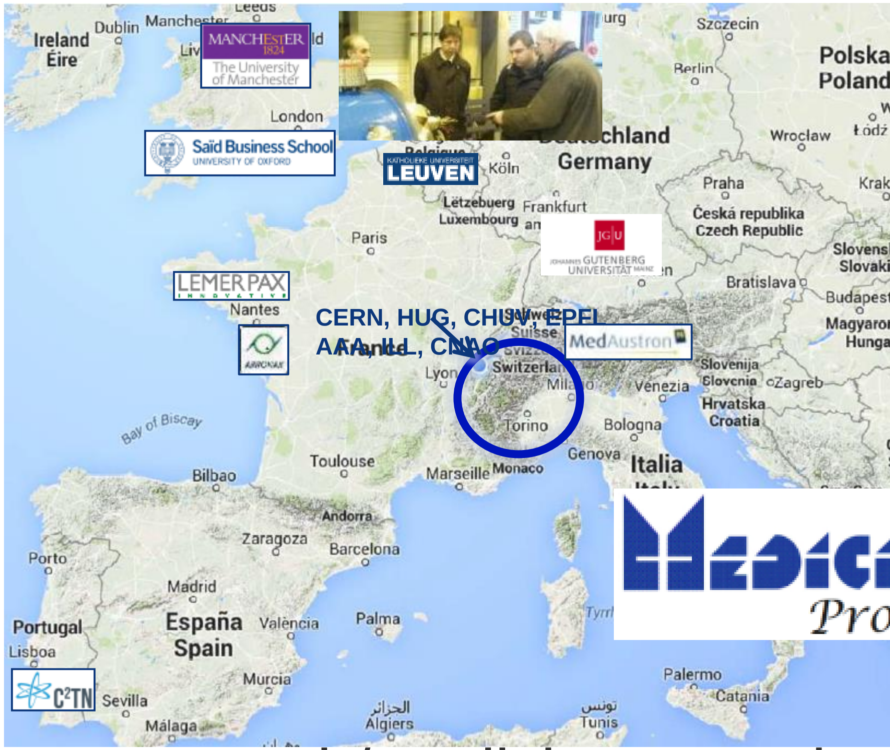
Ion. eff.	Trap & EBIS	Linac	Synchrotron

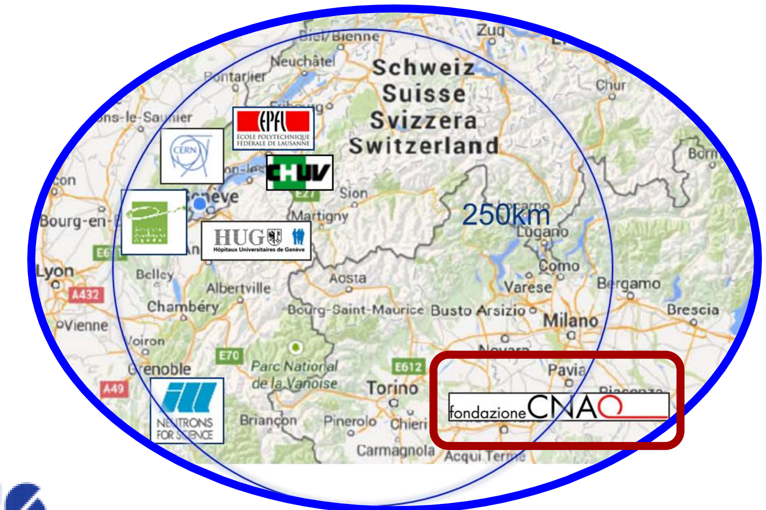
$$0 \xrightarrow{5\%} 1^{+} \xrightarrow{45\%\ \&\ 30\%} 4^{+}/6^{+} \xrightarrow{90\%} \text{Injection} \xrightarrow{60\%} \text{Ejection}$$

Main parameters for ^{11}C production.

Method	Cyclotron		Target	Reaction	In target production [pps]	Trap charging time (ms)	Injector [p/injection cycle]	Injector repetition rate [Hz]
	E [MeV]	I[μA]						
PET production (production batch)	22	150	N_2 (≲1 atm)	$^{14}N(p,\alpha)^{11}C$	3×10^{10}	741	1.5×10^{8}	1.3
REX-ISOLDE (ISOL)	70	1200	NaF:LiF eutectic	$^{19}F(p,2\alpha n)^{11}C$	4×10^{11}	56	1.5×10^{8}	18

- T.M. Mendonca et al., CERN-ACC-2014-0
S. Hojo, et al. NIMB 240, 75 (2005).
- R. Augusto et al NIMB, 376, 374 (2016)





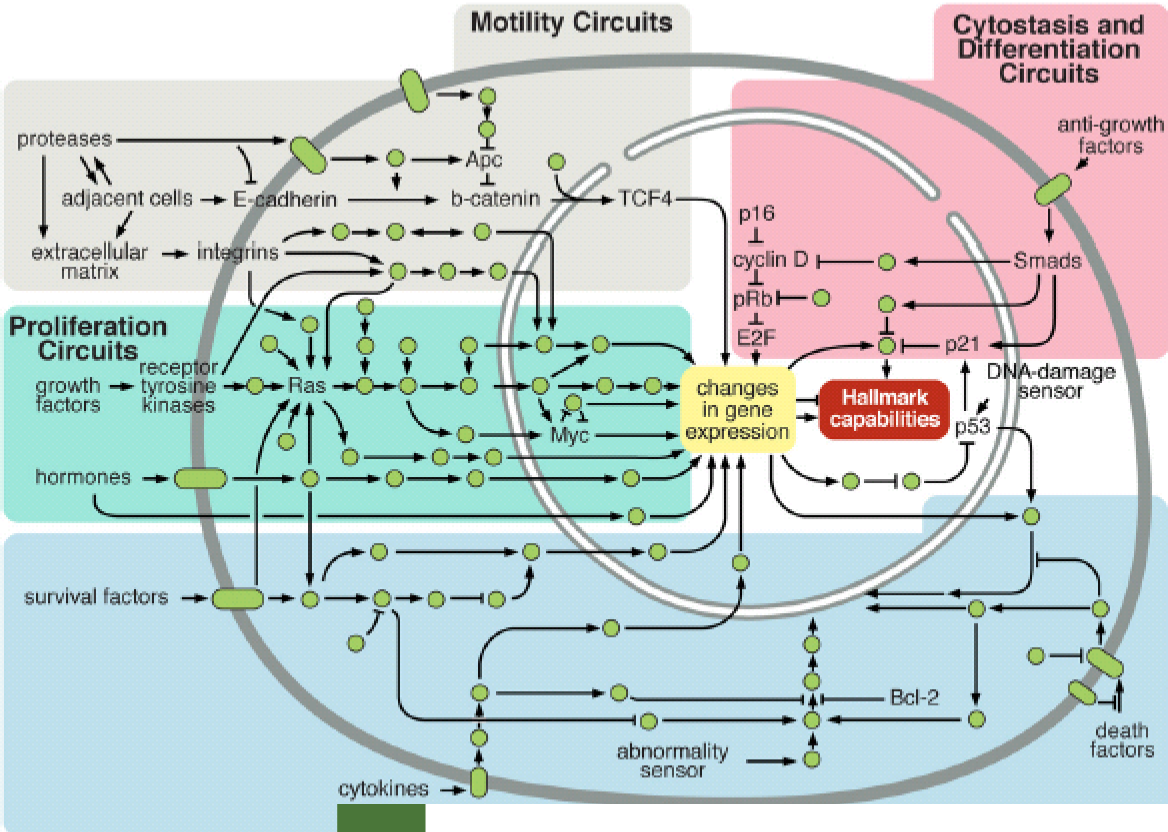
www.cern.ch/medicis-promed

I wish you a very successful summer school hosted by CNAO!!!

"Noah, tell me again who's your project sponsor?"

RESERVE

Cancer regulation pathways: « it's simple »



Disruptions of Negative-Feedback Mechanisms that Attenuate Proliferative Signaling

Yet another example involves the mTOR kinase, a coordinator of cell growth and metabolism that lies both upstream and downstream of the PI3K pathway. In the circuitry of some cancer cells, mTOR activation results, via negative feedback, in the inhibition of PI3K signaling. Thus, when mTOR is pharmacologically inhibited in such cancer cells (such as by the drug rapamycin), the associated loss of negative feedback results in increased activity of PI3K and its effector Akt/PKB, thereby blunting the antiproliferative effects of mTOR inhibition (Sudarsanam and Johnson, 2010; O'Reilly et al., 2006). It is likely that compromised negative-feedback loops in this and other signaling pathways will prove to be widespread among human cancer cells and serve as an important means by which these cells can achieve proliferative independence. Moreover, disruption of such self-attenuating signaling may contribute to the development of adaptive resistance toward drugs targeting mitogenic signaling.

Cell

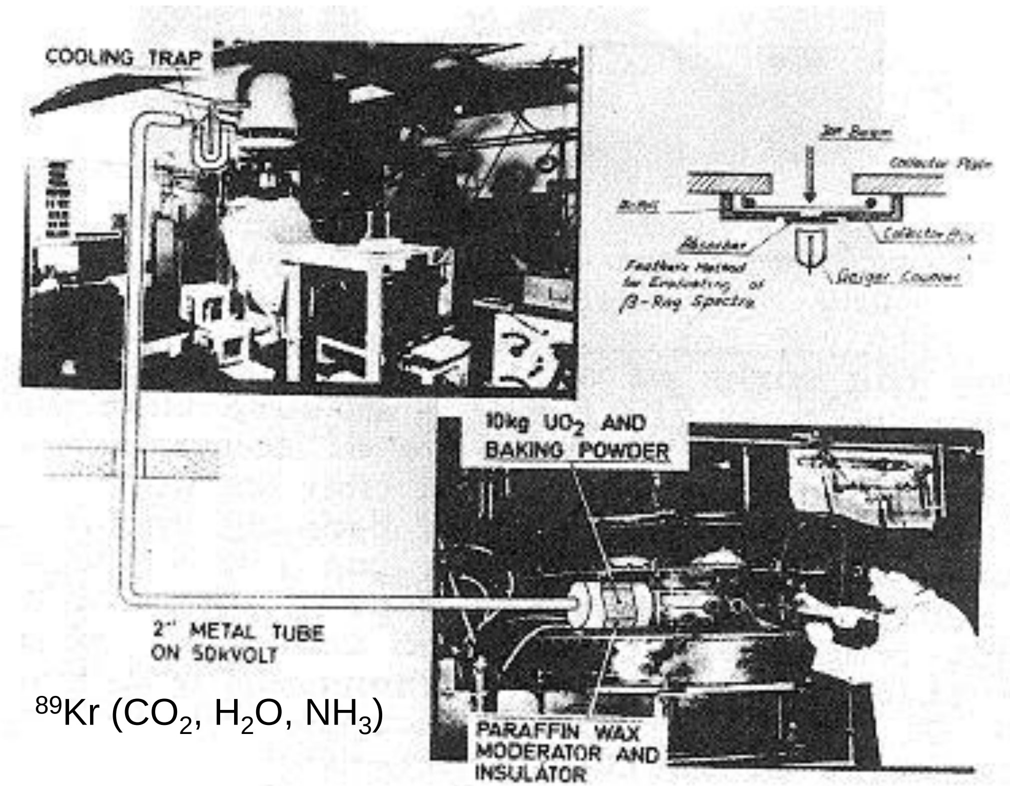
Leading Edge
Review

Hallmarks of Cancer: The Next Generation

Douglas Hanahan[1,2,*] and Robert A. Weinberg[3,*]
[1]The Swiss Institute for Experimental Cancer Research (ISREC), School of Life Sciences, EPFL, Lausanne CH-1015, Switzerland
[2]The Department of Biochemistry & Biophysics, UCSF, San Francisco, CA 94158, USA
[3]Whitehead Institute for Biomedical Research, Ludwig/MIT Center for Molecular Oncology, and MIT Department of Biology, Cambridge, MA 02142, USA
*Correspondence: dh@epfl.ch (D.H.), weinberg@wi.mit.edu (R.A.W.)

ISOLDE "0"

O.Kofoed-Hansen
K.O. Nielsen
Dan. Mat.Fys.Medd. 26, no. 7 (1951)



^{89}Kr (CO_2, H_2O, NH_3)

10 MeV deuterons
d-to-n converter (Be)
n moderator (wax)
UO_2 (10 kg)
Baking powder

CERN 76-13, 3rd conf. nuclei far from stability

ISOL Beam intensities

RIB intensity $[s^{-1}\ \mu A^{-1}]$

Proton beam Intensity $[s^{-1}\ \mu A^{-1}]$

Avogadro Numb.

Diffusion+ Effusion Efficiency

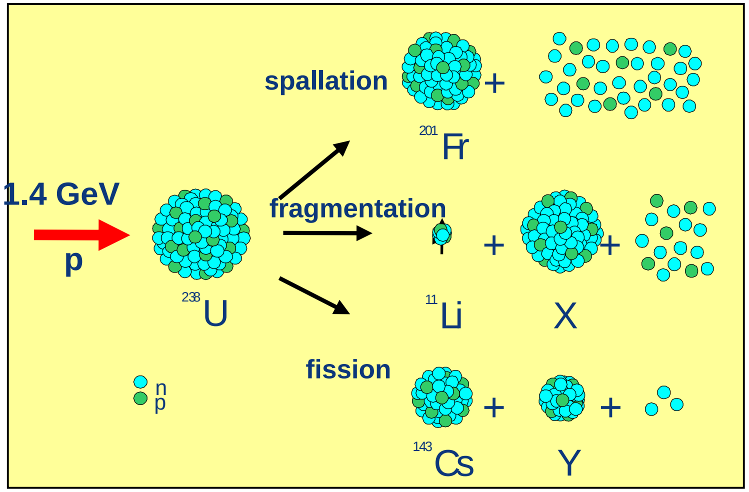
$$I = \int \sigma(E)\ \Phi(E, x)\ \rho(x)\ N/A\ dx\ \varepsilon_{diff+eff}\ \varepsilon_{ion}$$

Cross section $[cm^2]$

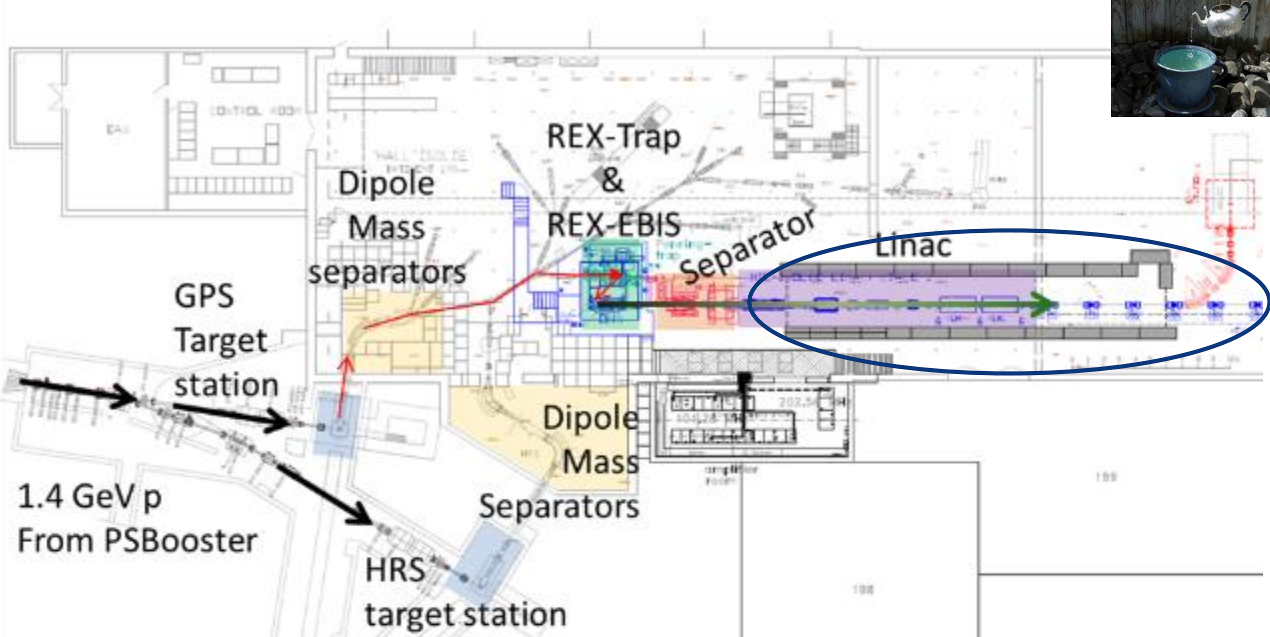
Target density $[g\ cm^{-3}]$

Target Atomic Mass [g]

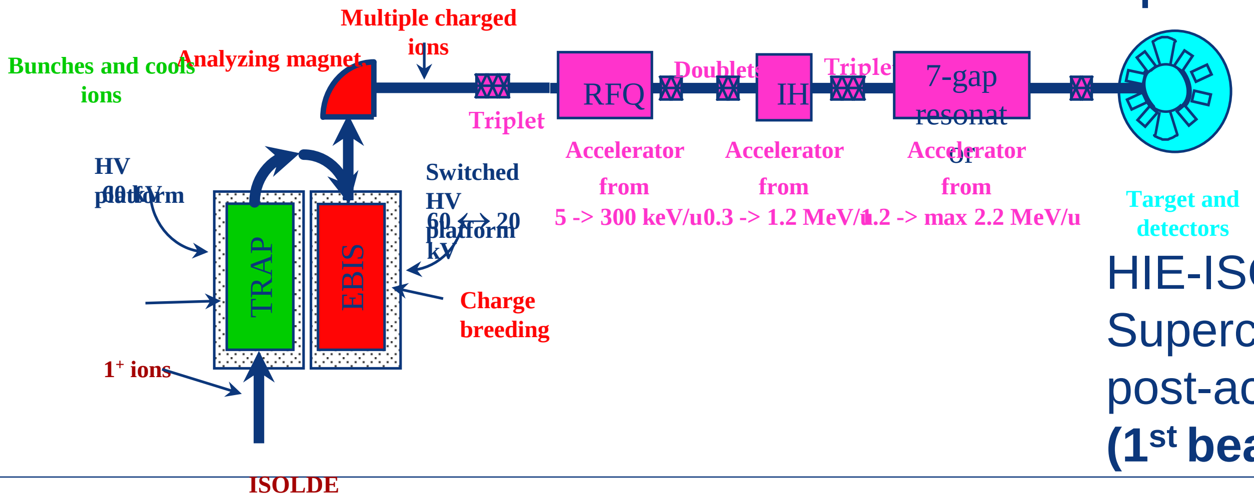
Ionization Efficiency



Isotope mass separation and post acceleration



REX-ISOLDE radioactive ion beam post-accelerator



HIE-ISOLDE:
Superconducting
post-accelerator
(1st beam in 2015)

A dedicated mass separation facility for medical applications