European Commission

A target system for ion-beam activation of particulate nanomaterials

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Institute for Health and Consumer Protection

Joint Research Centre
www.jrc.ec.europa.eu

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Stimulating innovation
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Outline

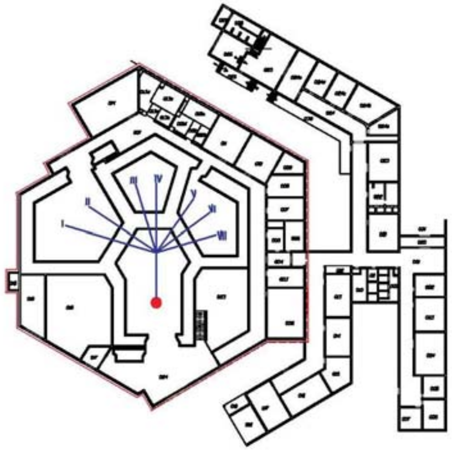
- The MC40 Cyclotron laboratory in Ispra
- Radioactive Nanoparticles: why?
- Radioactive Nanoparticles: how?
- The nano-[48-V]TiO2: a case of study.
- Conclusion and outlooks

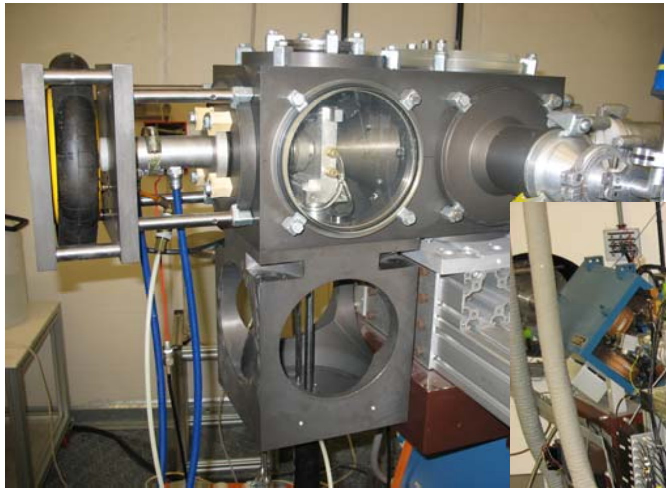
Scanditronix MC40 cyclotron

- Variable energy, multiple particle accelerator
- 6 beam lines ending in three independent irradiation rooms
- Commercial production of [18F]-FDG night-time, available for research day-time mainly for nanoparticles activation and nuclear medicine.

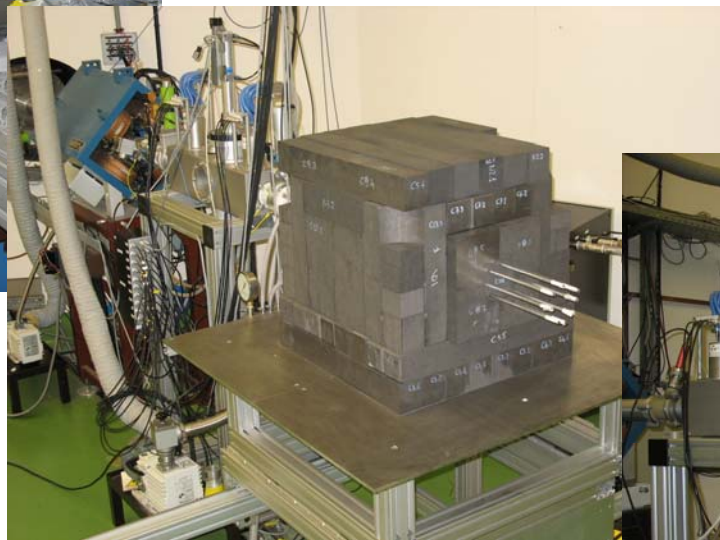
Partic.	Min. Energy (MeV)	Max. Energy (MeV)	Maximum Current (μA)
p	8	39	60
α	8	39	30
$^3He^{2+}$	8	53	30
d	4	19.5	60

The beam lines for NP





General purpose
solid target



Neutron activator

High power solid target
With automatic transfer

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The cyclotron labs & people

Several specific labs:

- Alpha and beta manipulation labs, Gamma spectrometry
- Nanoparticles characterization (DLS, Z-potenzial, XRD)
- Radiopharmaceutical clean rooms (GMP)
- Rad-chem and bio labs

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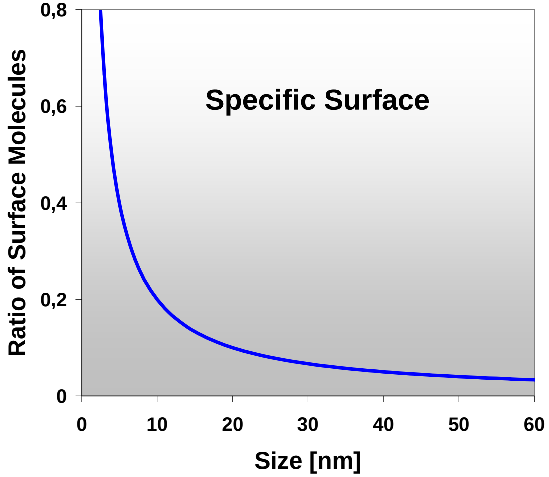
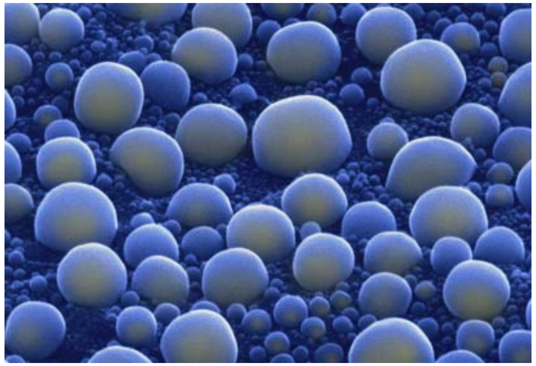
Few words about nano

- Large specific surface
- Chemical reactivity very different compared to bulk material
- Quantum effects lead to special properties (electronic, mechanical, optical ...)
- Matrix dependent properties
- Many forms: fullerenes, nanotubes, nanocarriers, nanoemulsions, encapsulates



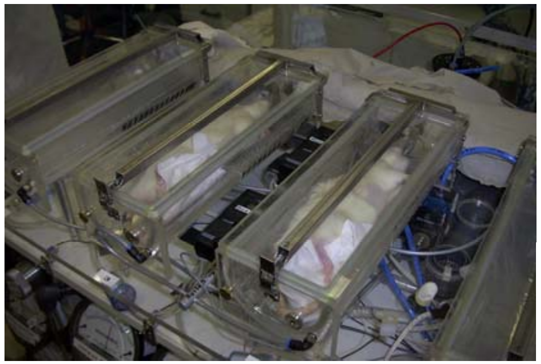


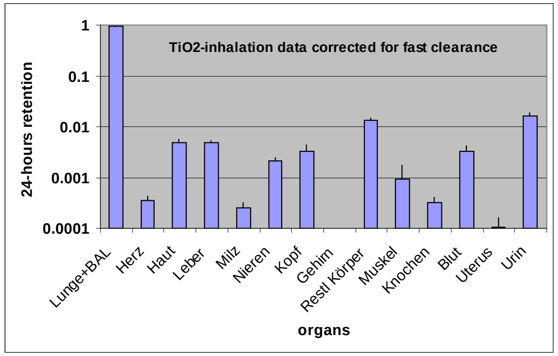
Safety of industrially produced NP, must be assessed

Radiotracers to help toxicologist

- Radiotracer principle
  - Minimum requirements on specimen preparation
  - Imaging option
- High sensitivity
- No NP surface change

In vitro cellular uptake
In vivo biokinetics and biodistribution





Courtesy W. Kreyling et al.

Labelling for nanotox

INDUSTRIALLY AVAILABLE NPs

- Use commercially available samples
  - Relevant NPs from OECD lists
  - No in-house synthesis
  - No sample modification
- Follow std protocol for re-suspension and stabilization

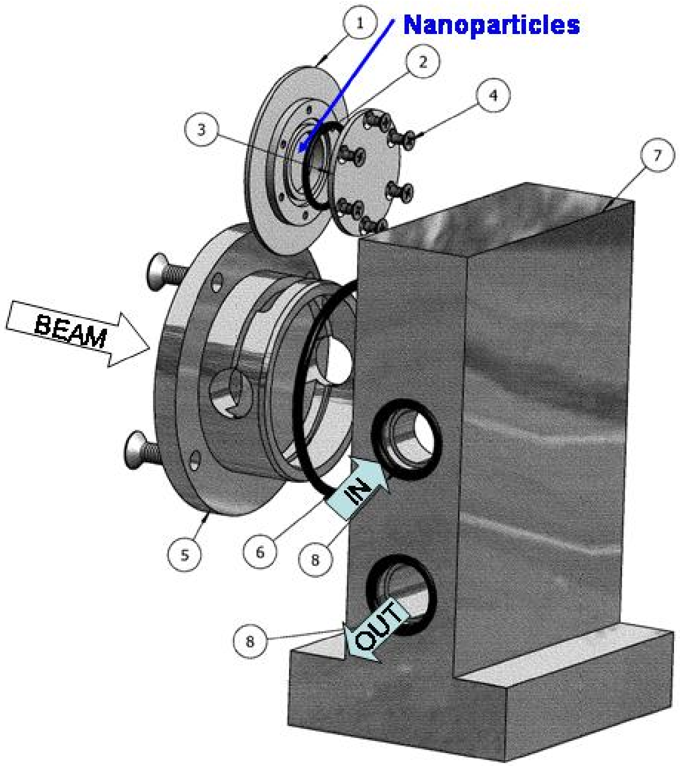
NO DAMAGE

- Radiation damage
  - From primary protons
  - From recoiling labels
- Thermal damage
  - Avoid agglomeration
  - Avoid crystal phase changes
  - Efficient cooling

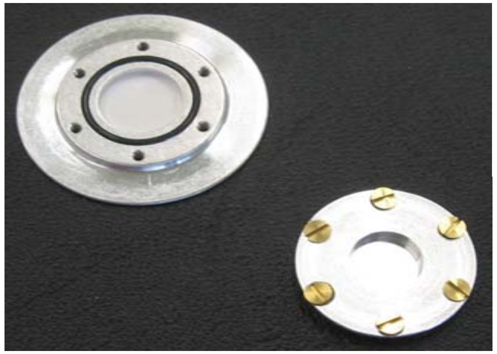
YIELD

- Enough material
- Selection of the proper irradiation energy
- Maximize the beam current

Thin Target design for NPs



- 300 µm entrance window
- 400 µm "target thickness"
- typical payload 20-30 mg
- front and rear side cooling
  - water cooling
  - refrigerated He



Optimize beam properties

- Choose the entrance energy in order to maximize the desired reaction cross section (simulations)
- As wide and as uniform as possible beam profile (collimators)

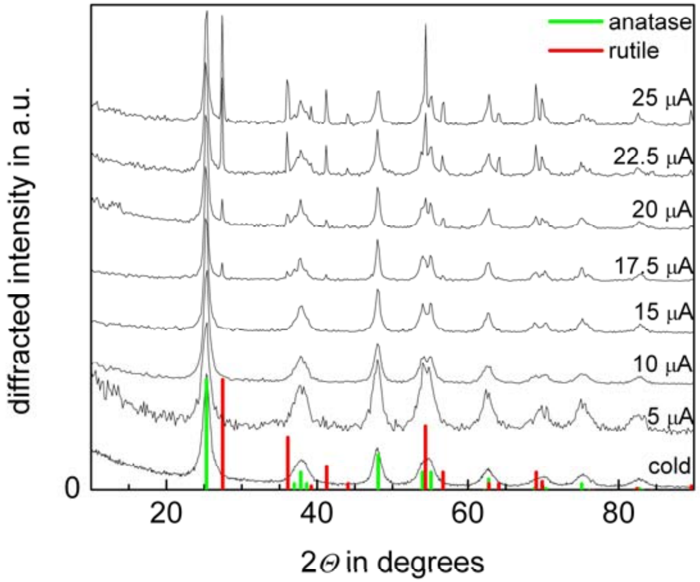
- The most difficult part is to select the maximum current.
  - Temperature profile inside the capsule depends on energy deposition (beam current, dE/dx, target thickness and **thermal conductivity**)
  - Thermal conductivity at the nanoscale is unknown and needs to be estimated experimentally.

→ TiO_2 is a suitable thermometer!

Titania ST01: a case of study

Thermally induced crystal phase change
Sintering and crystal growth

- Starting material is pure anatase, 3 nm diameter
- From annealing studying:
  - Sintering starting at 250 C
  - Anatase to rutile starting at 700 C



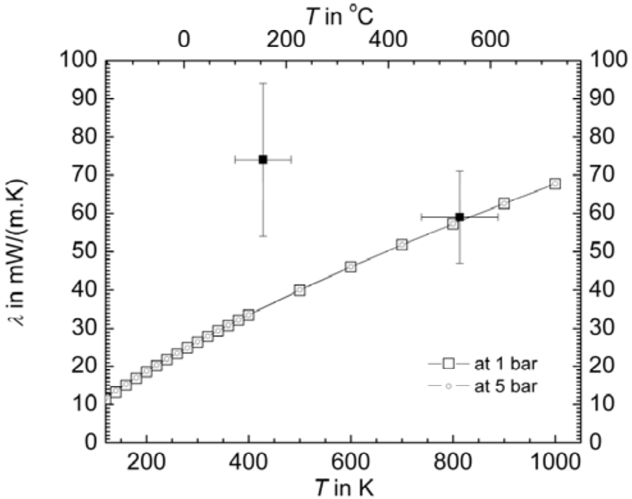
XRD spectra can identify both critical temperatures

- Series of irradiations with increasing beam current
- Estimation of the thermal conductivity

Not far away from air

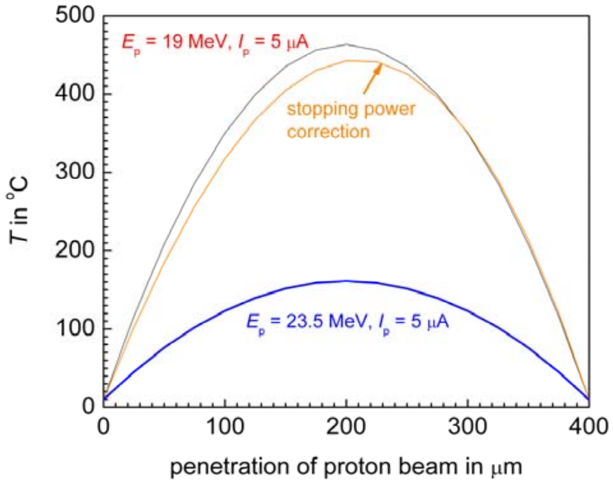
For dry TiO_2 the estimated thermal conductivity is not too far away from the one of air.

- This is good! It makes the results valid in general.



Parabolic shape of the temperature profile

- Very high temperature in the middle of the sample
- The max value can be used to define the max beam current

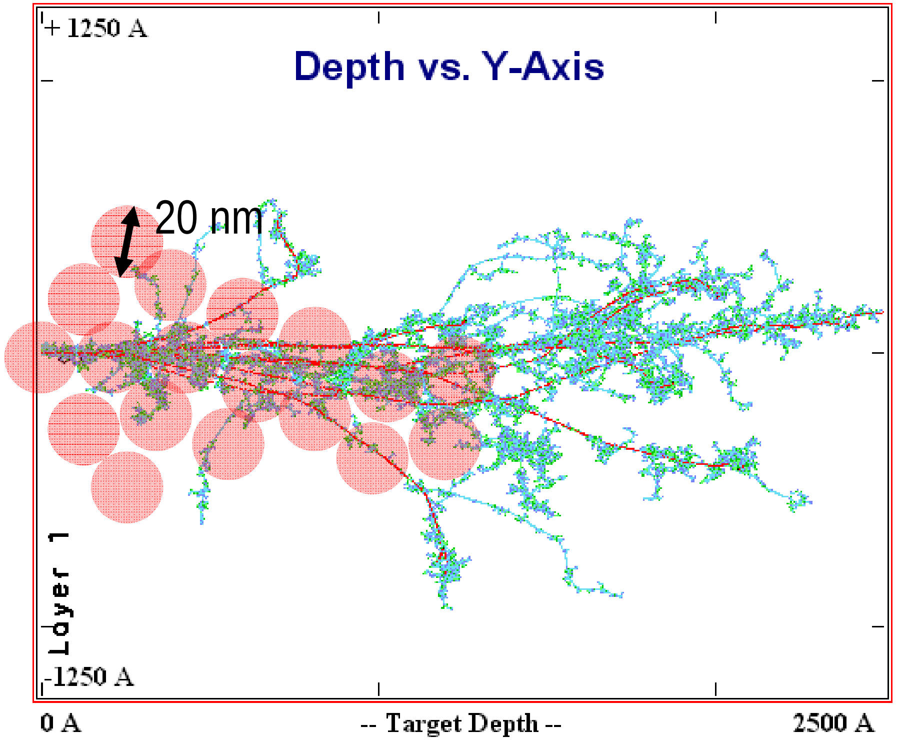


$$\eta = \frac{I_p \Delta E_p}{\pi r_p^2 d} \qquad T_{\max} = T_0 + \frac{\eta d^2}{8\lambda}$$

Labelling route

Recoil implantation

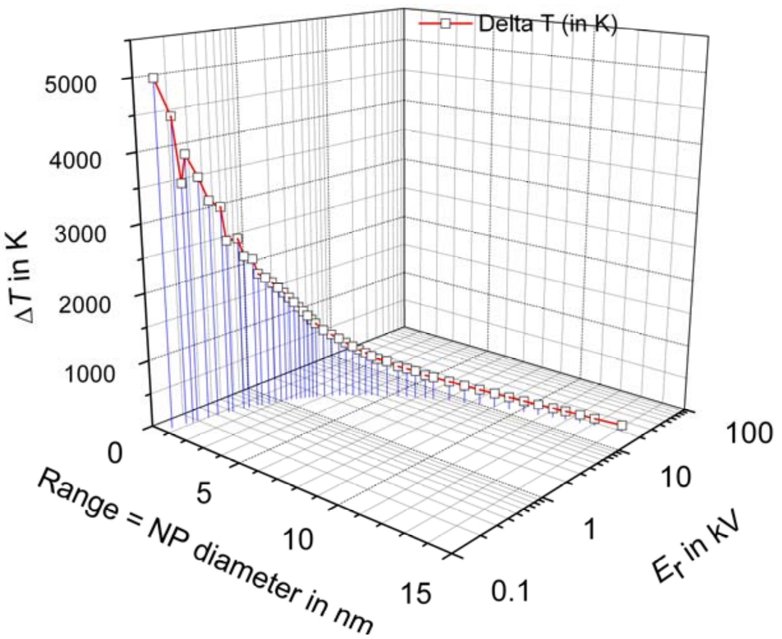
- Primary projectiles induce nuclear reactions
- Conservation of E, **p** implies the recoiling atom (label) to move from its original lattice position
- Recoiling labels can travel several NP-diameters before stopping and possibly be implanted somewhere else



Thermal effects on a single NP

What happens to the "last" NP?

- Recoiling label deposits large amount of energy when stopping
  - "Last" in track and "labelled" NP can be the most affected by the thermal effects
- Heat dissipation through crystal lattice vibration
  - Corresponding temperature increase depends on number of atoms (size of the NP)



- Extremely small NP can evaporate due to the implantation
  - Experimental verification now under investigation

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Radiation damage

Dose goal: 100 microA * h to get enough specific activity in [^{48}V]TiO_2

Two main components: primary protons and recoiling labels

Simulation results: Reference figures for TiO_2 after 100 microAh	
Primary DPA	6.7 E-3
Recoiling DPA	1.1 E-3
Extra DPA (last NP)	2.3 E-3

- Simulation results are negligible.
- Just started a systematic experimental campaign using positron annihilation spectroscopy

The NP Shopping list

- Several different types of NPs have been successfully labelled:
  - Metallic: [198-Au]Au, [110-Ag]Ag, [105-Ag]Ag
  - Oxides: [48-V]TiO2, [7-Be]SiO2, [57-Co]SiO2, [141-Ce]CeO2, [65-Zn]ZnO, [57-Co]Fe3O4
  - Carbon structure: [7-Be]CNT (single and multi wall), [7-Be]C-black, [7-Be]Nanodiamonds

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Conclusions and outlooks

- In the last years, a comprehensive knowledge in NP activation has been developed at the JRC Cyclotron laboratory
- All aspects of NP activation have been deeply studied and are now under control
- Several different types of NP are routinely activated and delivered to European labs for bio-testing

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Thank you
for your attention