

# ISOLTRAP the mass measurement tool of ISOLDE/CERN and its power to enhance the radio isotope production for medical purposes

Andree Welker

09.09.2016

1st MEDICIS-Promed general training



TECHNISCHE  
UNIVERSITÄT  
DRESDEN



Federal Ministry  
of Education  
and Research

# Outline

## Motivation

- **What about masses?**

## Setup

- **Overview of ISOLDE**
- **ISOLTRAP-Tools:**
  - **Multi Reflection Time-of-Flight Separator/Spectrometer (MR-ToF)**
  - **Decay spectroscopy outlet**
  - **Precision Penning-Traps**
  - **Medical perspectives**

# Old tools and new tools



**QUANTUM PHYSICS**  
**WAVEFUNCTION  
 REALITY CHECK**  
*Mathematical tools – or  
 are they for real?*  
**PAGE 278**

**BIOTECHNOLOGY**  
**TROUBLE  
 BREWING**  
*Regulation needed to contain  
 opiate-producing yeasts*  
**PAGES 267 & 281**

**CRYSTALLOGRAPHY**  
**MAPPING OUT  
 DISORDER**  
*The next challenge for  
 structure determination*  
**PAGE 303**

**NATURE.COM/NATURE**  
 21 May 2015 £10  
 Vol 521, No. 7552  
 9 770028 083095  
 2 1 b

# Old tools and new tools



Göbekli Tepe, 10000 BC



**QUANTUM PHYSICS**  
**WAVEFUNCTION  
 REALITY CHECK**  
*Mathematical tools – or  
 are they for real?*  
 PAGE 278

**BIOTECHNOLOGY**  
**TROUBLE  
 BREWING**  
*Regulation needed to contain  
 opiate-producing yeasts*  
 PAGES 267 & 281

**CRYSTALLOGRAPHY**  
**MAPPING OUT  
 DISORDER**  
*The next challenge for  
 structure determination*  
 PAGE 303

**NATURE.COM/NATURE**  
 21 May 2015 £10  
 Vol 521, No. 7552  
 9 770028 083095  
 2 1 b

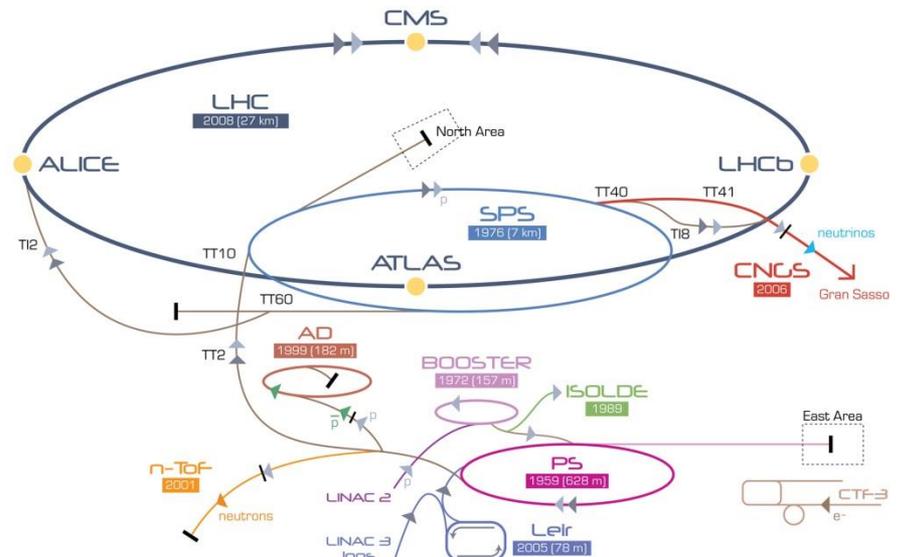
# Old tools and new tools



Göbekli Tepe, 10000 BC



CERN, 2000 AD



**QUANTUM PHYSICS**  
**WAVEFUNCTION REALITY CHECK**  
 Mathematical tools – or are they for real?  
 PAGE 278

**BIOTECHNOLOGY**  
**TROUBLE BREWING**  
 Regulation needed to contain optate-producing yeasts  
 PAGES 267 & 281

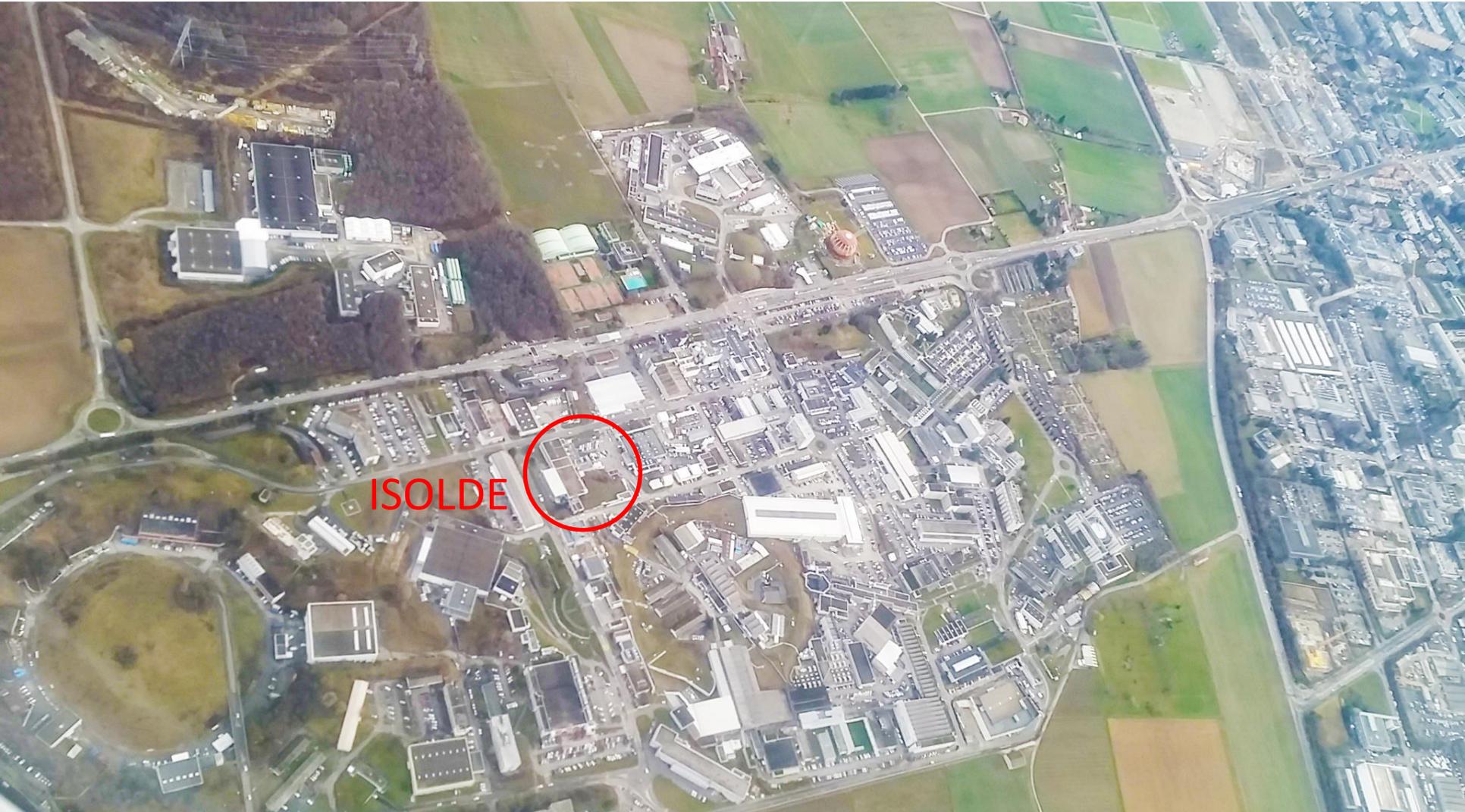
**CRYSTALLOGRAPHY**  
**MAPPING OUT DISORDER**  
 The next challenge for structure determination  
 PAGE 303

NATURE.COM/NATURE  
 21 May 2015 £10  
 Vol 521, No 7552  
 9 770028 083095 2 1 b

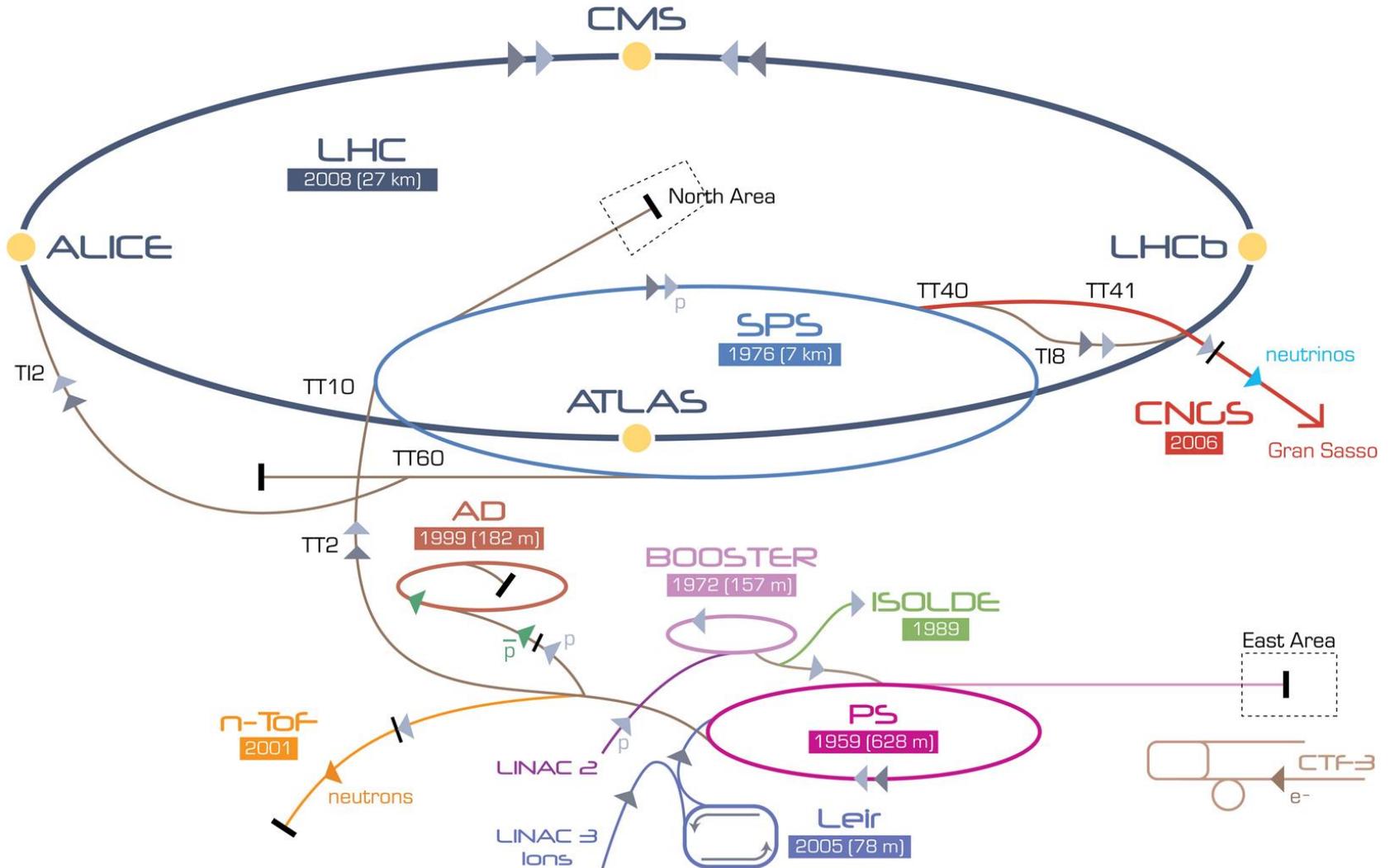
# ISOLTRAP@ISOLDE@CERN



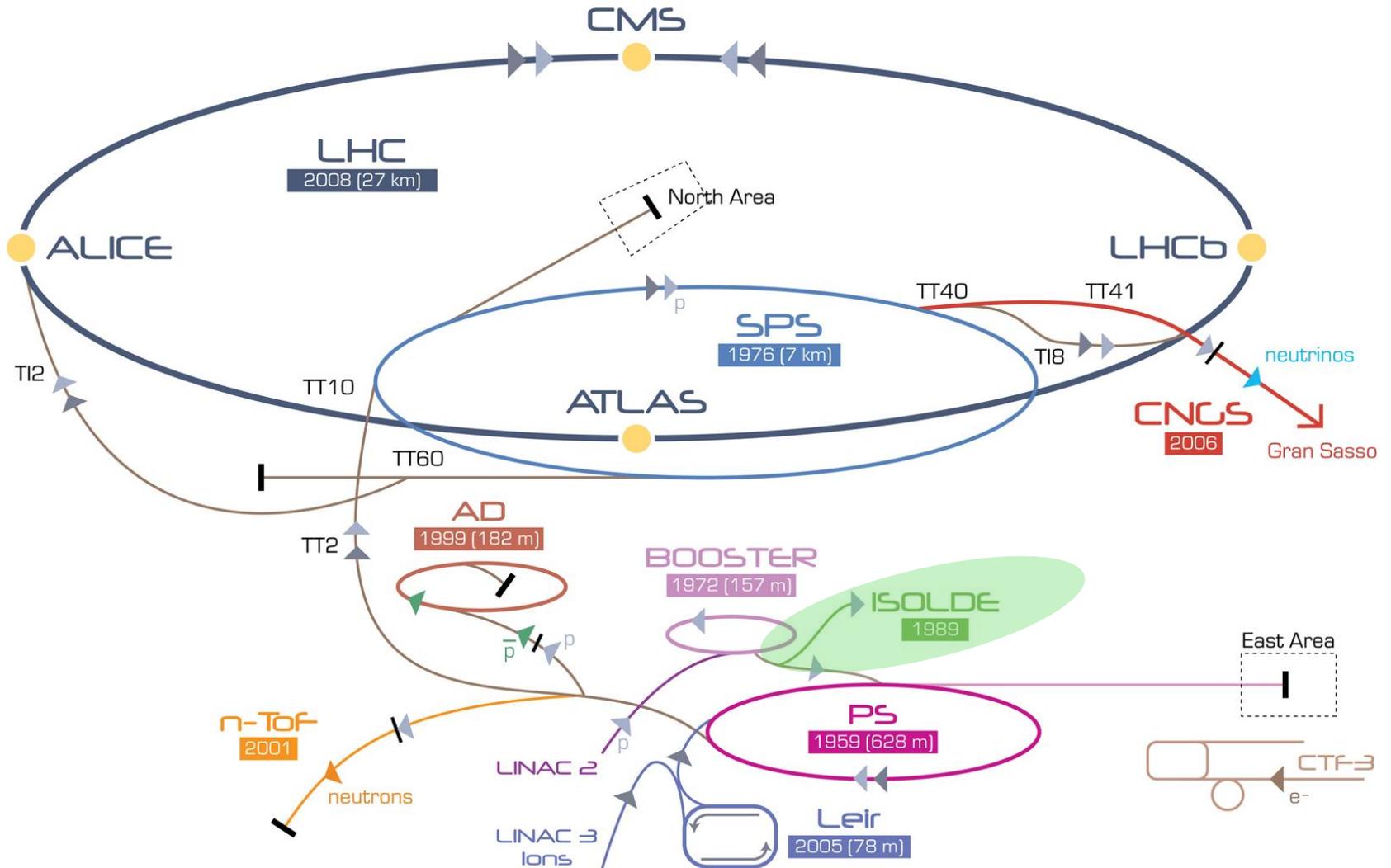
# ISOLTRAP@ISOLDE@CERN



# ISOLTRAP@ISOLDE@CERN



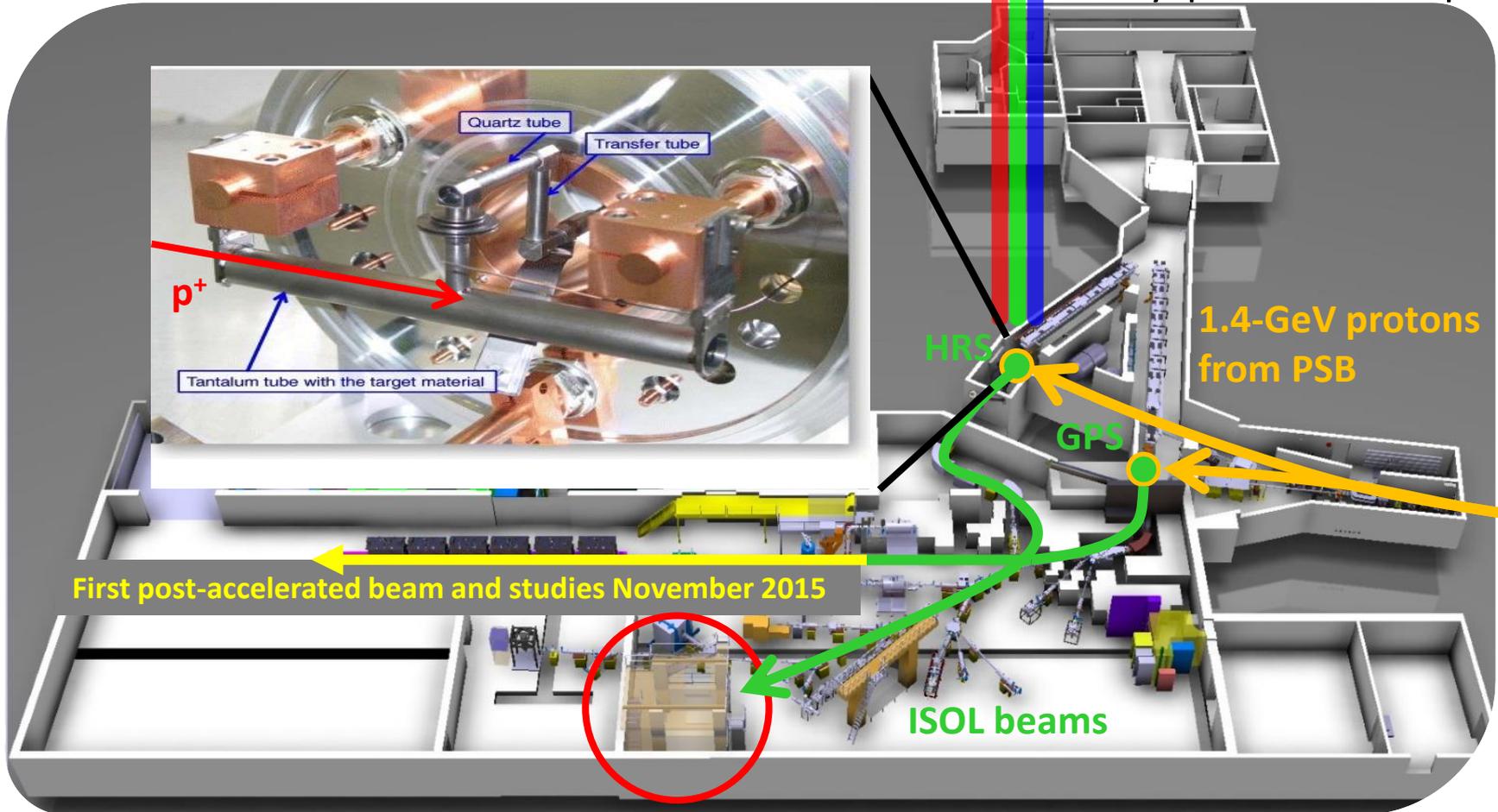
# ISOLTRAP@ISOLDE@CERN



# ISOLTRAP@ISOLDE@CERN



**RILIS** Laser ionization of polonium and dysprosium isotopes

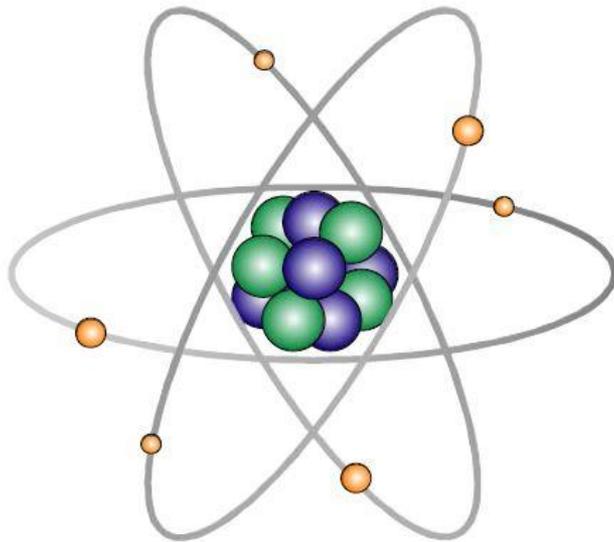


First post-accelerated beam and studies November 2015

**ISOLTRAP**

# Nuclides

Masses determine the atomic and nuclear binding energies reflecting all forces in the atom/nucleus.



$$= N \cdot \text{green sphere} + Z \cdot \text{blue sphere} + Z \cdot \text{orange sphere} - \text{binding energy}$$

$$M_{\text{Atom}} = N \cdot m_{\text{neutron}} + Z \cdot m_{\text{proton}} + Z \cdot m_{\text{electron}} - (B_{\text{atom}} + B_{\text{nucleus}})/c^2$$

$$\delta m/m < 10^{-10}$$

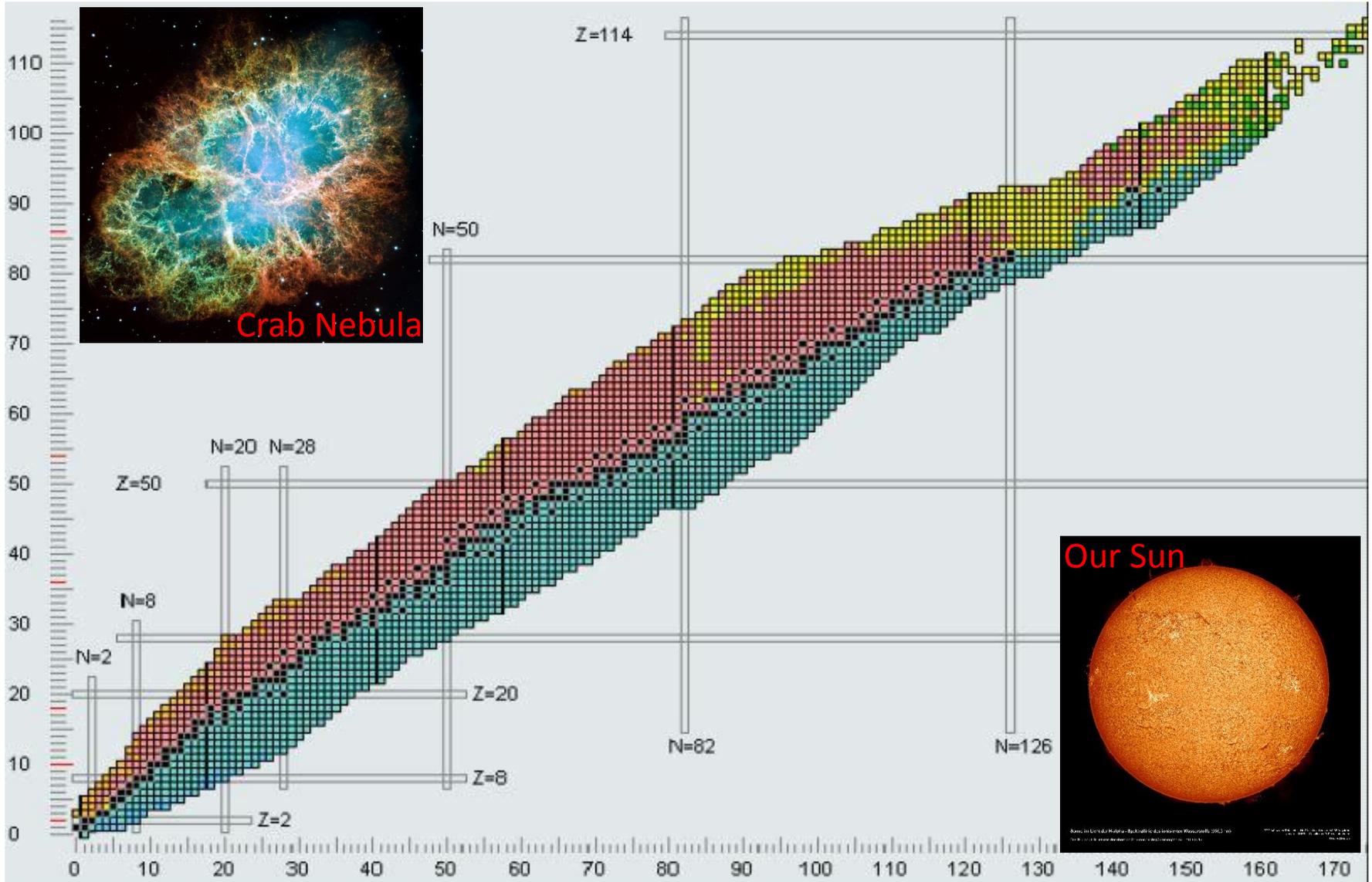
$$\delta m/m = 10^{-6} - 10^{-8}$$

K.Blaum

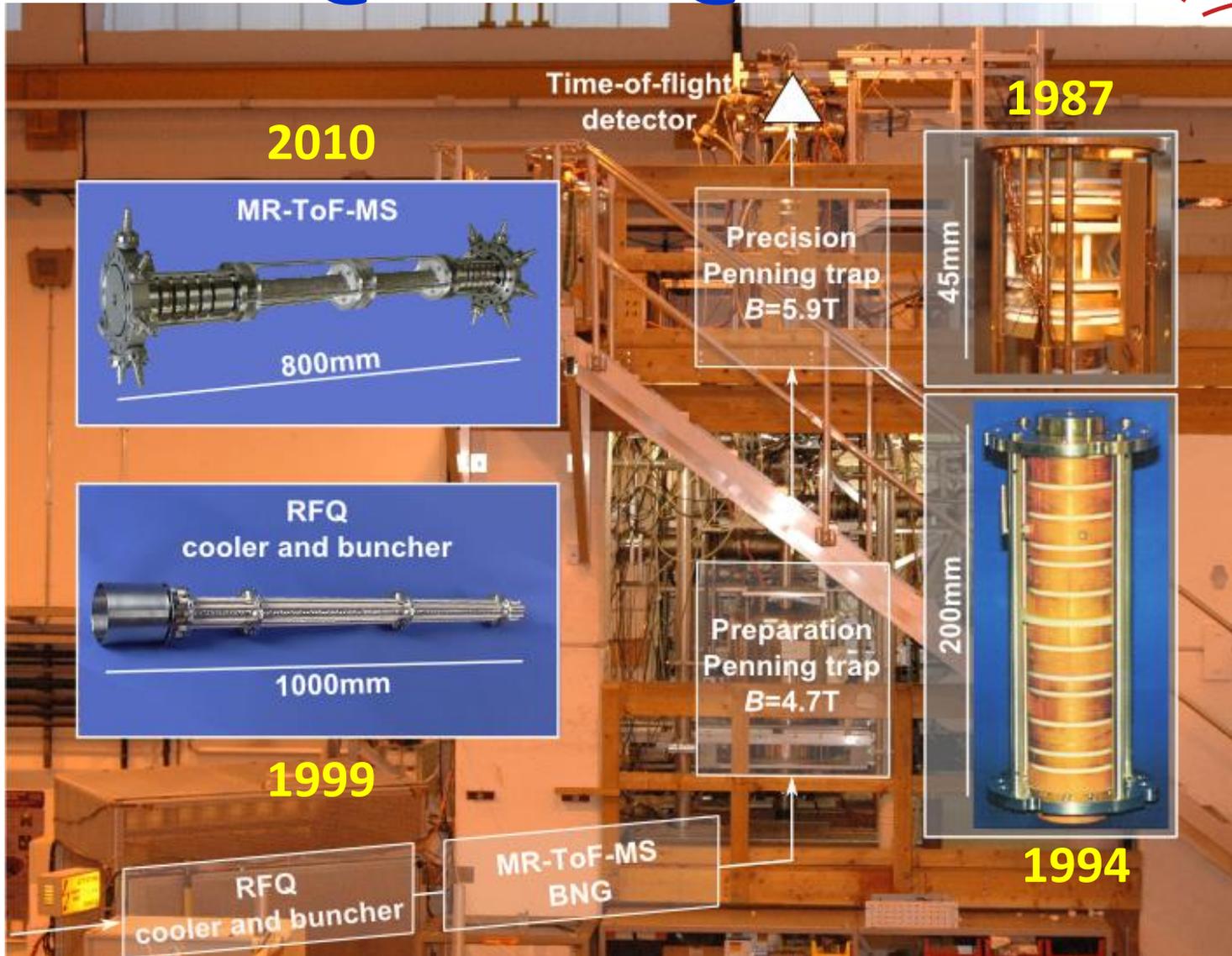
# Table of Nuclides

Masses help to understand:

- Evolution of Universe
- Shell structure of Nuclides
- Possible Neutrino masses
- CKM matrix element calculation

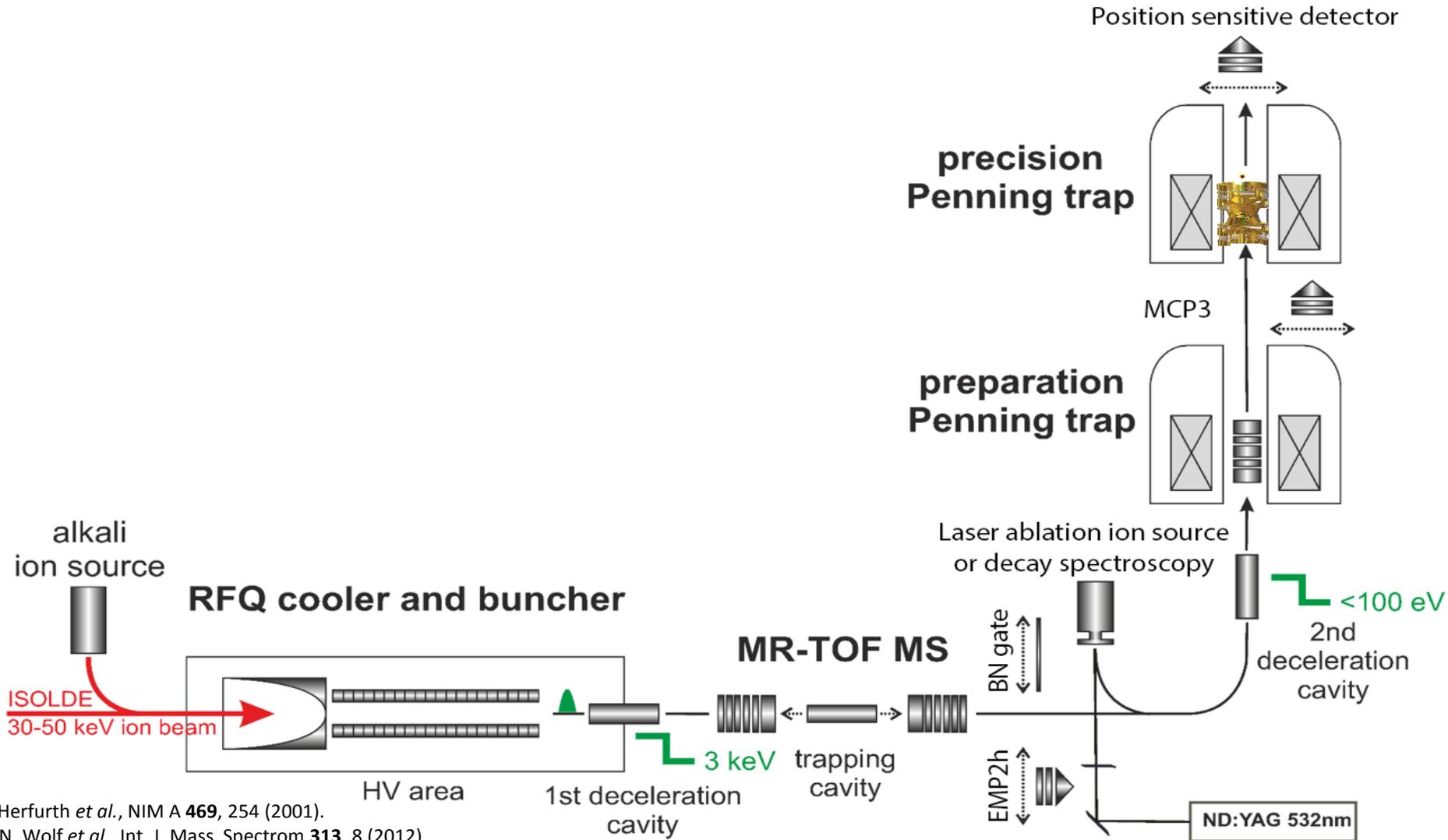


# ISOLTRAP@ISOLDE@CERN



M. Mukherjee *et al.*, Eur. Phys. J. A **35**, 1 (2008). S. Kreim *et al.*, Nucl. Instrum. Methods B **317**, 492 (2013).

# Tools of ISOLTRAP



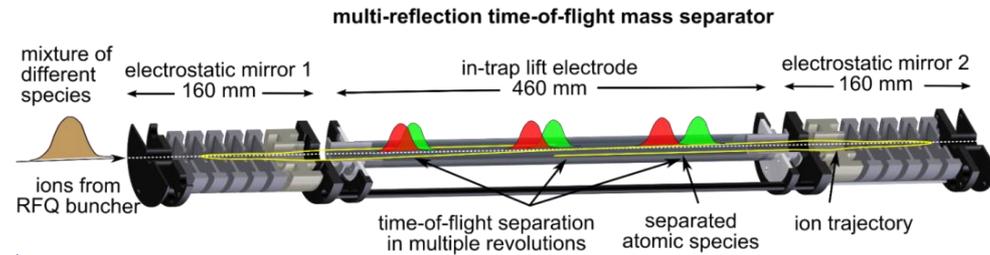
F. Herfurth *et al.*, NIM A **469**, 254 (2001).

R. N. Wolf *et al.*, Int. J. Mass Spectrom **313**, 8 (2012).

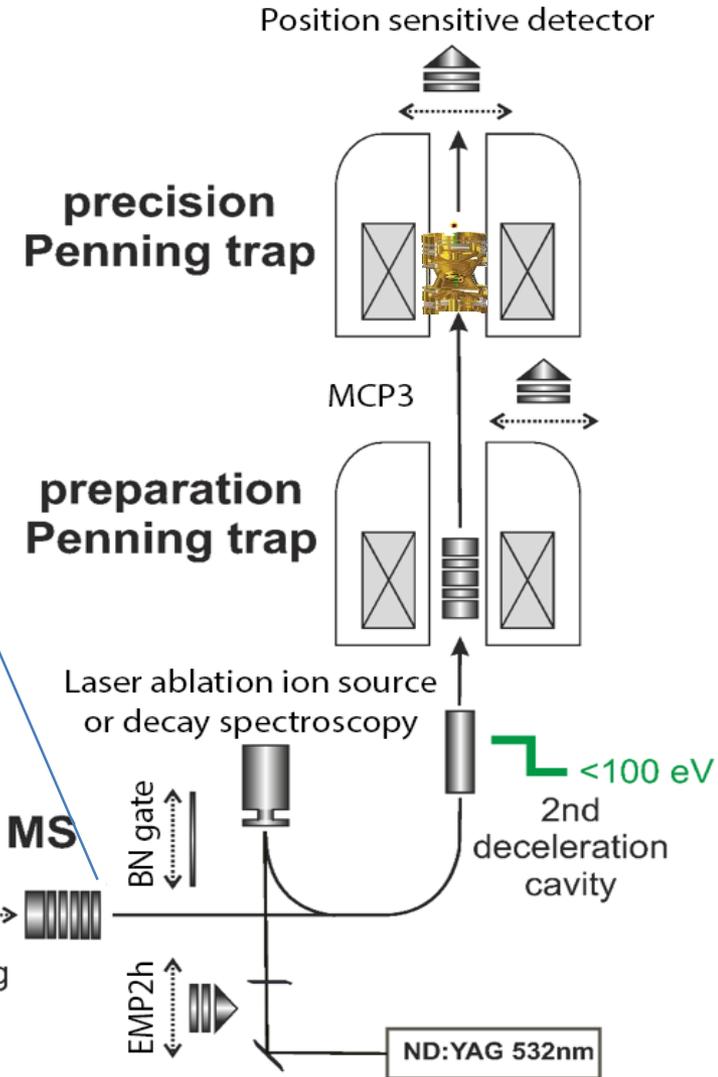
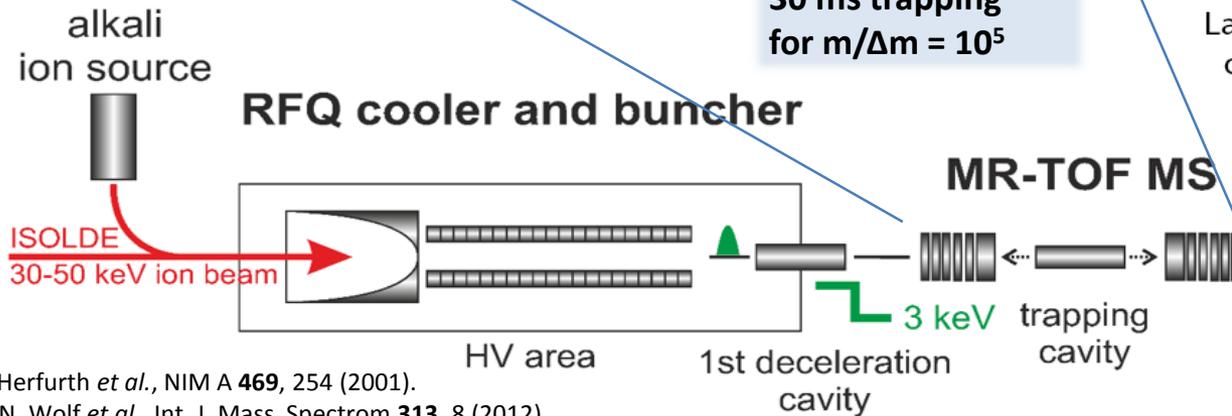
G. Savard *et al.*, Phys. Lett. A **158**, 247 (1991).

M. König *et al.*, Int. J. Mass Spectrom. **142**, 95 (1995).

# Tools of ISOLTRAP



Beam purification:  
30 ms trapping  
for  $m/\Delta m = 10^5$



F. Herfurth *et al.*, NIM A **469**, 254 (2001).

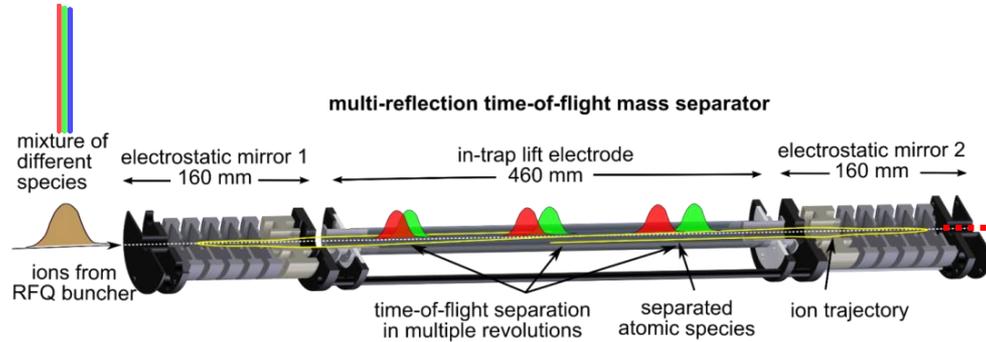
R. N. Wolf *et al.*, Int. J. Mass Spectrom **313**, 8 (2012).

G. Savard *et al.*, Phys. Lett. A **158**, 247 (1991).

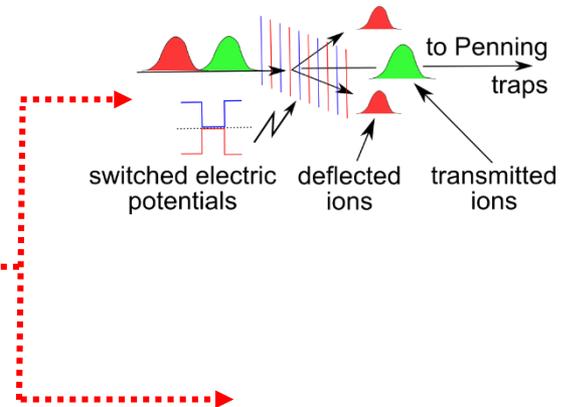
M. König *et al.*, Int. J. Mass Spectrom. **142**, 95 (1995).

# Tools of ISOLTRAP

RILIS

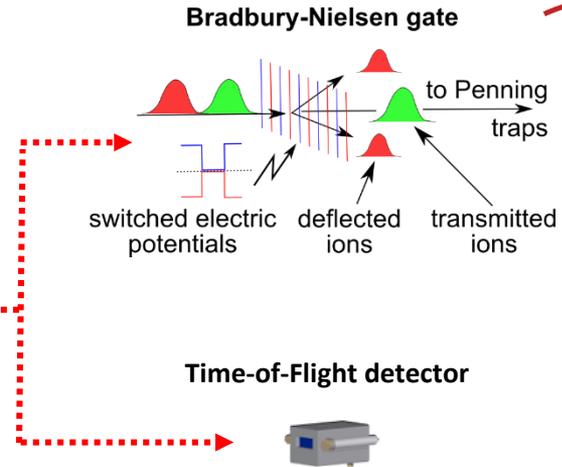
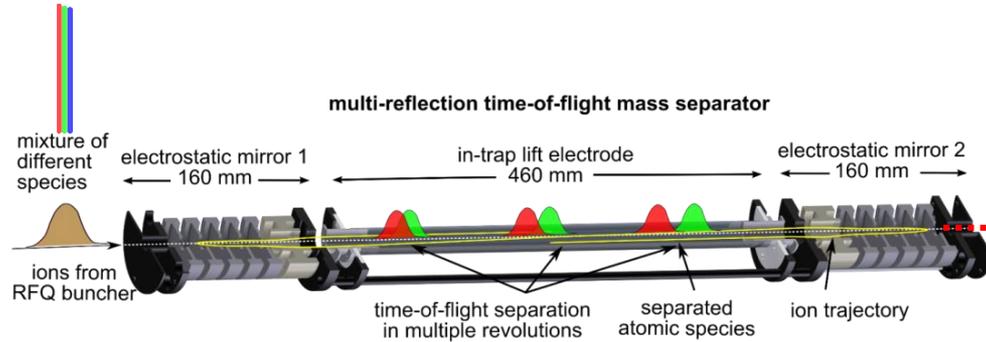


Bradbury-Nielsen gate



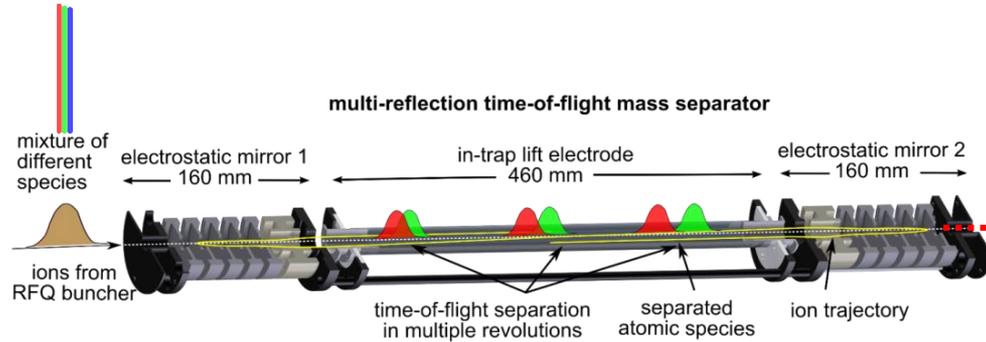
# Tools of ISOLTRAP

RILIS

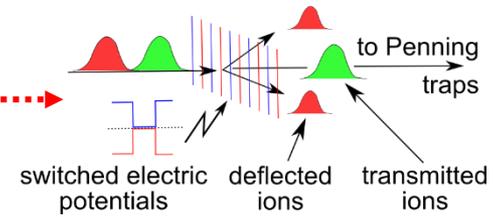


# Tools of ISOLTRAP

RILIS



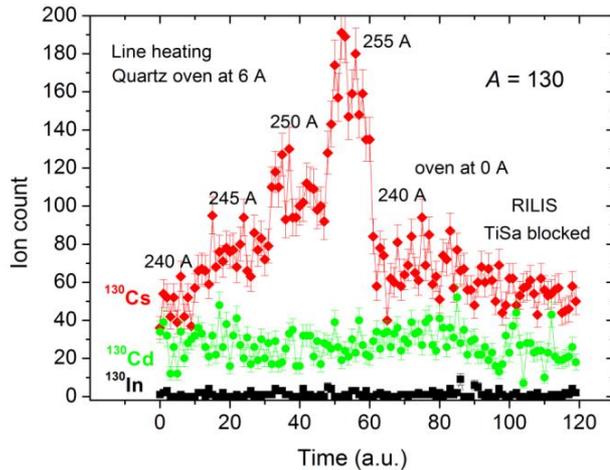
Bradbury-Nielsen gate



Time-of-Flight detector

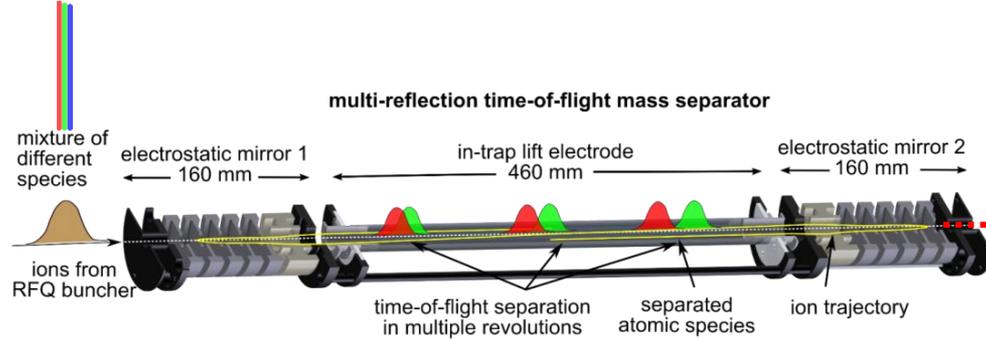


## Yield studies

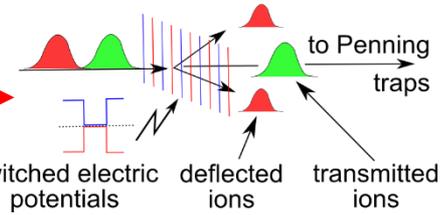


# Tools of ISOLTRAP

RILIS



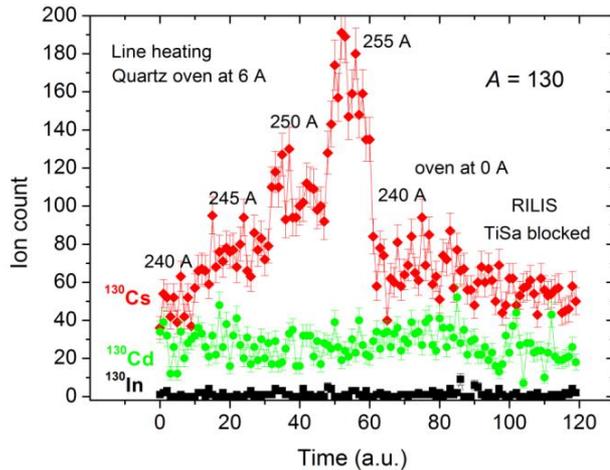
Bradbury-Nielsen gate



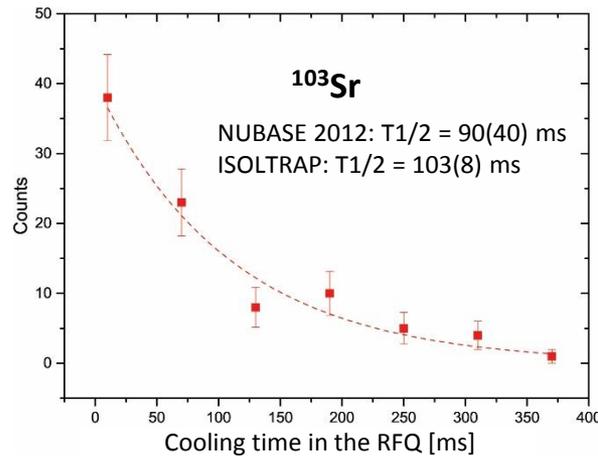
Time-of-Flight detector



## Yield studies



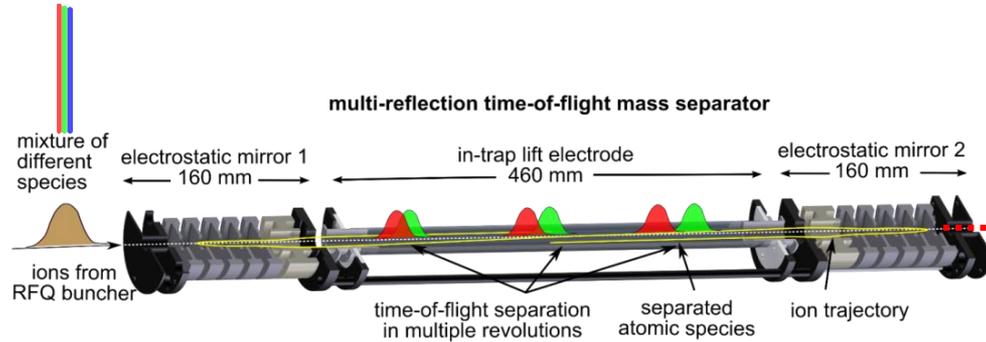
## Half-life or release studies



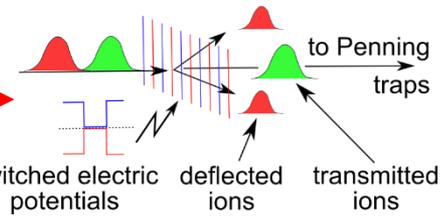
R. Wolf et al., Nucl. Instr. Meth. B, in press (2016)

# Tools of ISOLTRAP

RILIS



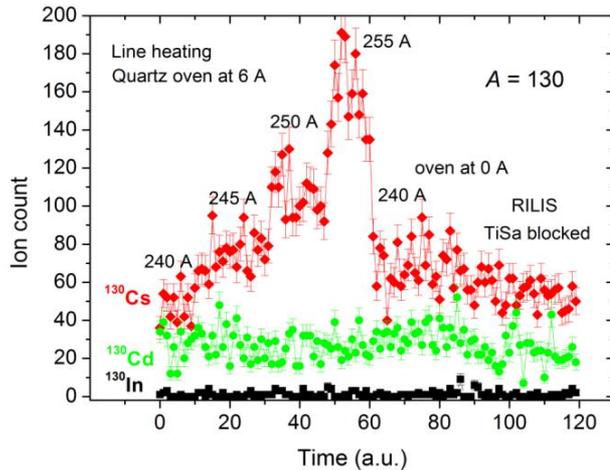
Bradbury-Nielsen gate



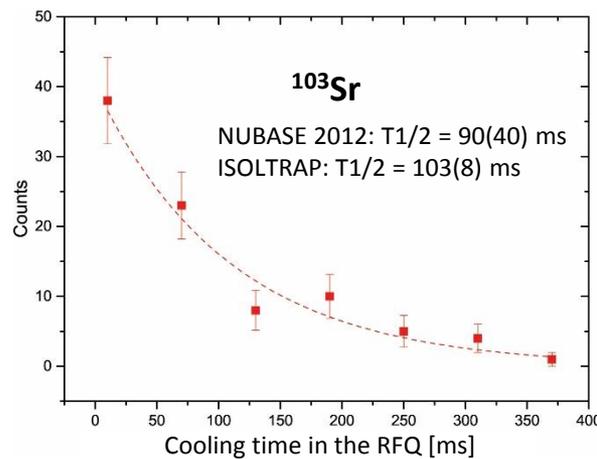
Time-of-Flight detector



## Yield studies

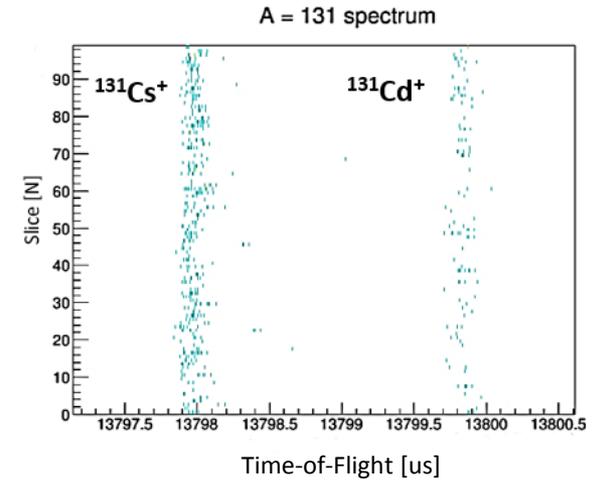


## Half-life or release studies



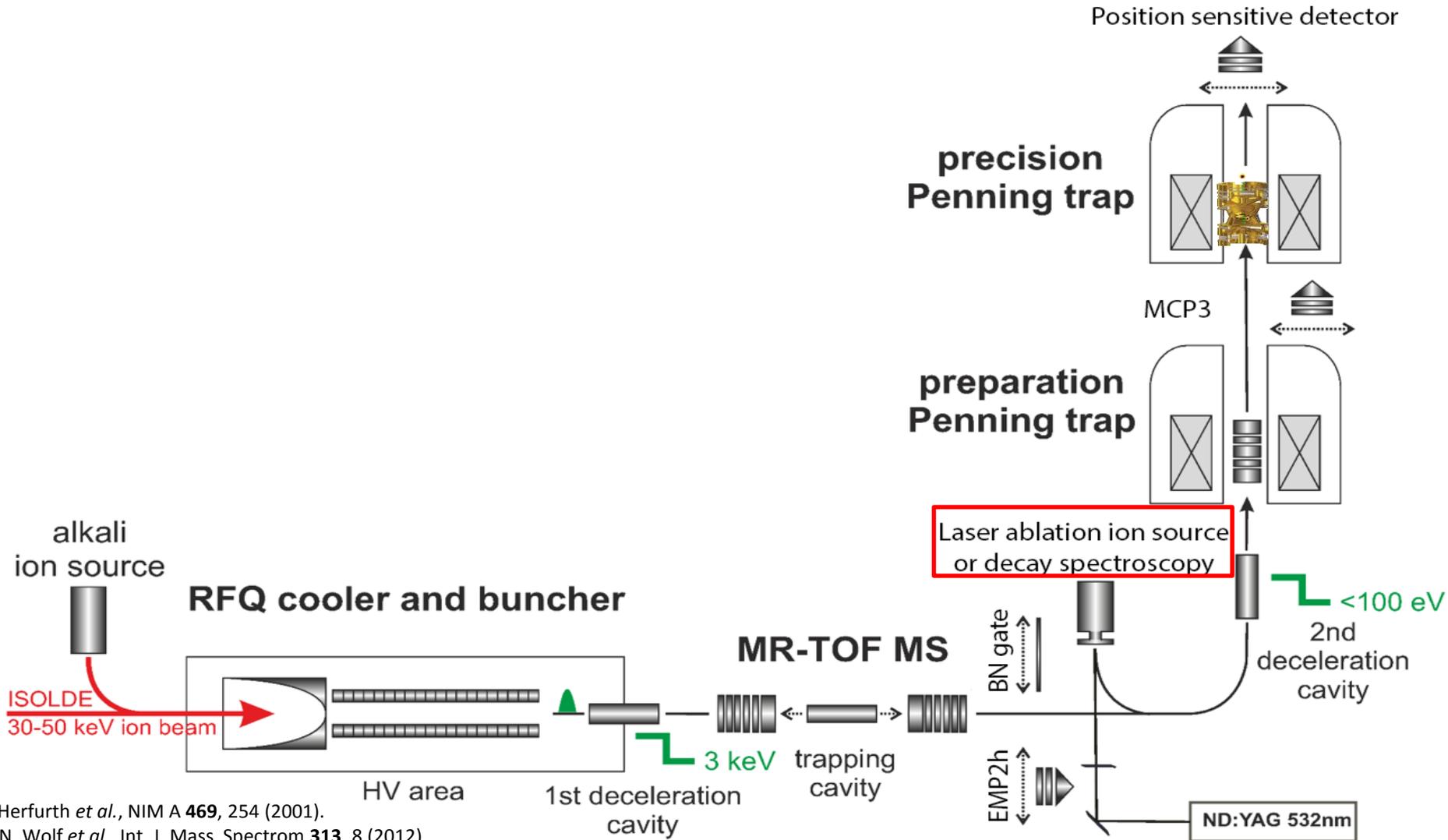
R. Wolf et al., Nucl. Instr. Meth. B, in press (2016)

## Mass measurements



D. Atanasov et al, Phys. Rev. Lett. 115, 232501 (2015)

# Tools of ISOLTRAP

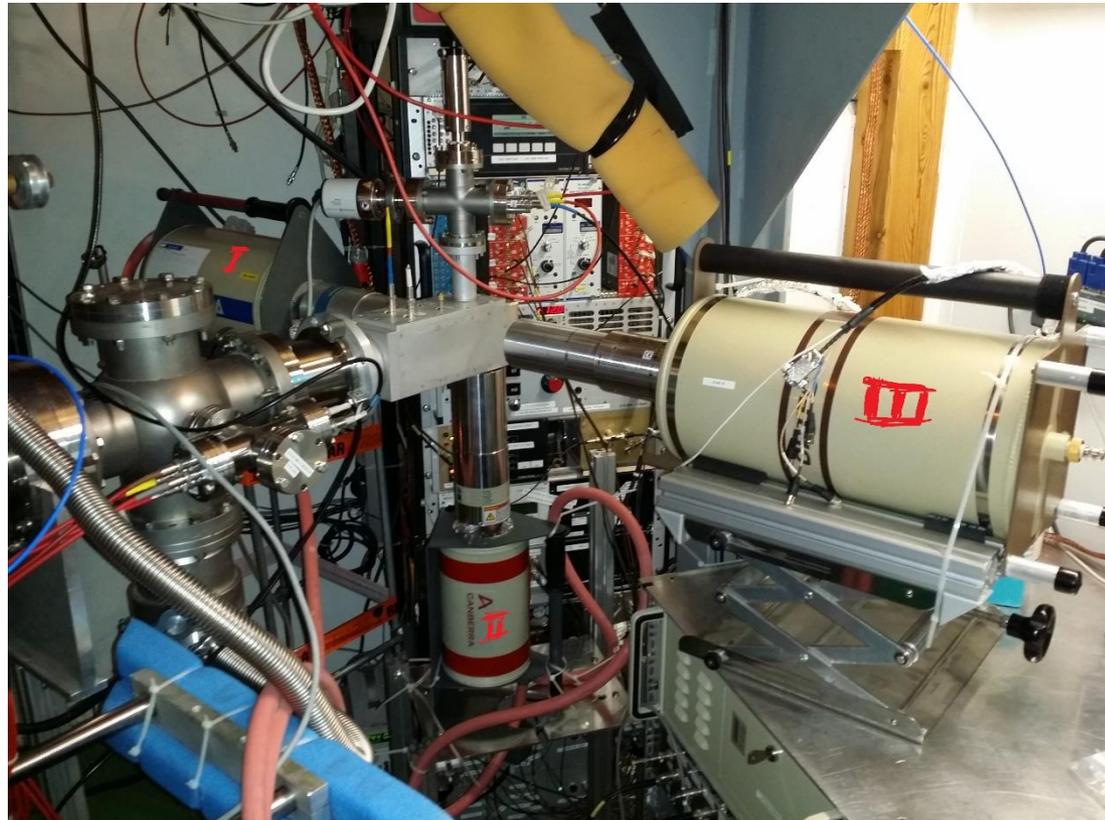


F. Herfurth *et al.*, NIM A **469**, 254 (2001).  
 R. N. Wolf *et al.*, Int. J. Mass Spectrom **313**, 8 (2012).  
 G. Savard *et al.*, Phys. Lett. A **158**, 247 (1991).  
 M. König *et al.*, Int. J. Mass Spectrom. **142**, 95 (1995).

# Decay spectroscopy

## Mass/spectroscopy:

- Setup with Ge-detectors I-II-III (decay-station):



# Decay spectroscopy

## Mass/spectroscopy:

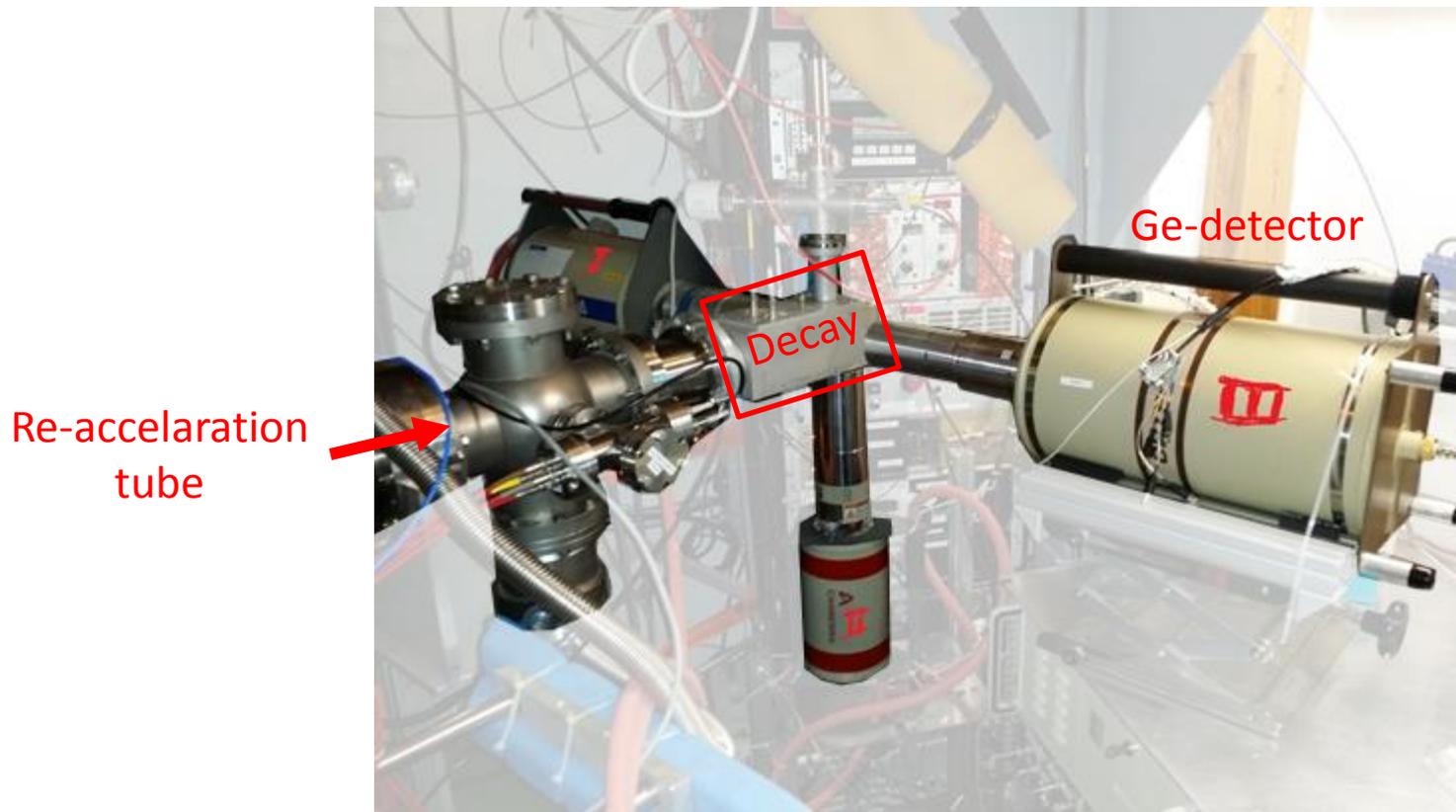
- Setup with Ge-detectors I-II-III (decay-station):



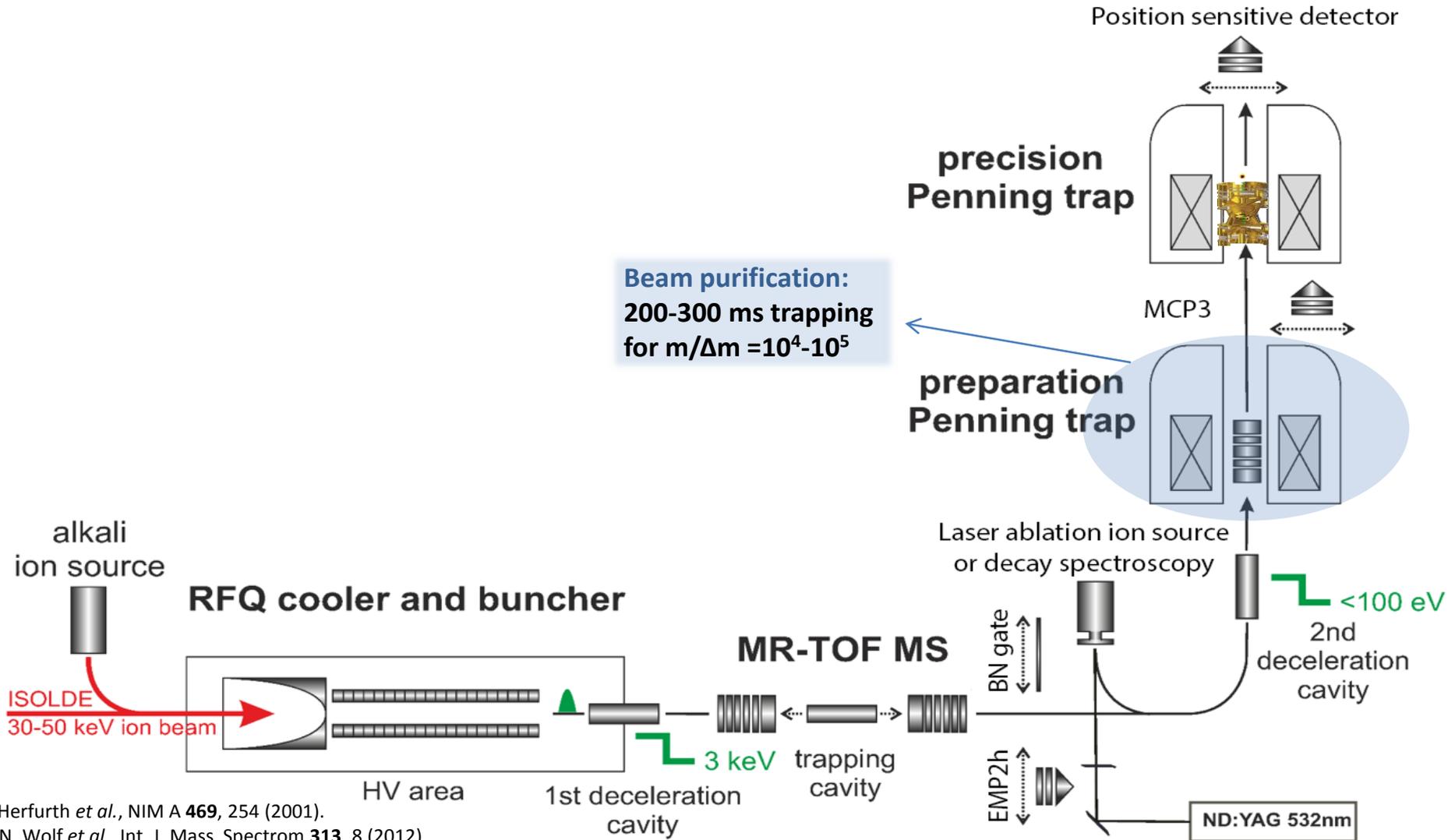
# Decay spectroscopy

## Mass/spectroscopy:

- Setup with Ge-detectors I-II-III (decay-station):



# Tools of ISOLTRAP



F. Herfurth *et al.*, NIM A **469**, 254 (2001).

R. N. Wolf *et al.*, Int. J. Mass Spectrom **313**, 8 (2012).

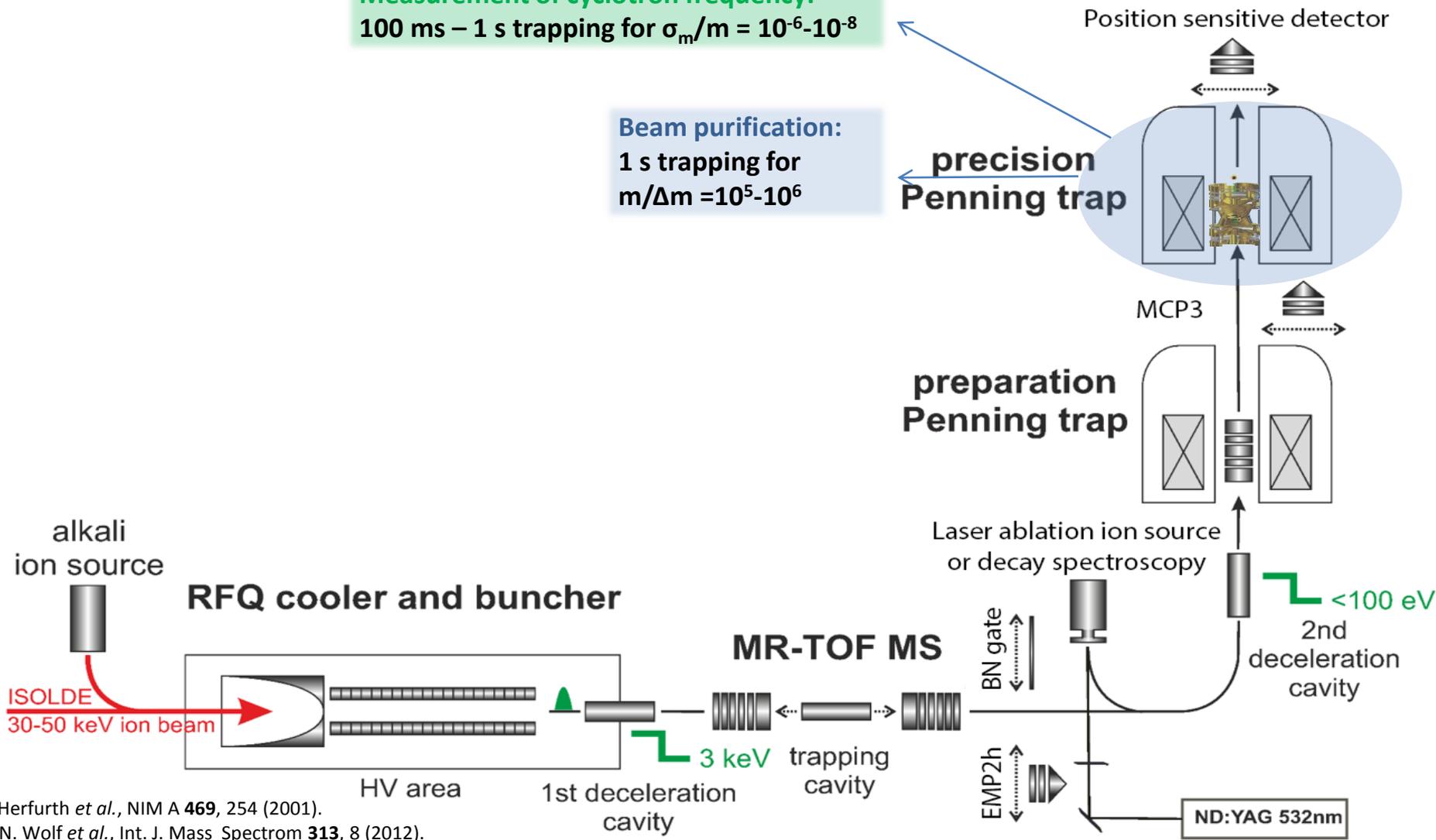
G. Savard *et al.*, Phys. Lett. A **158**, 247 (1991).

M. König *et al.*, Int. J. Mass Spectrom. **142**, 95 (1995).

# Tools of ISOLTRAP

Measurement of cyclotron frequency:  
100 ms – 1 s trapping for  $\sigma_m/m = 10^{-6}-10^{-8}$

Beam purification:  
1 s trapping for  $m/\Delta m = 10^5-10^6$



F. Herfurth *et al.*, NIM A **469**, 254 (2001).  
 R. N. Wolf *et al.*, Int. J. Mass Spectrom **313**, 8 (2012).  
 G. Savard *et al.*, Phys. Lett. A **158**, 247 (1991).  
 M. König *et al.*, Int. J. Mass Spectrom. **142**, 95 (1995).

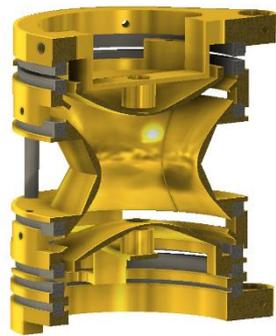
# Tools of ISOLTRAP: Penning trap

Eigen motions:

Penning trap:  
Storage of ions by the superposition  
of electric and magnetic fields

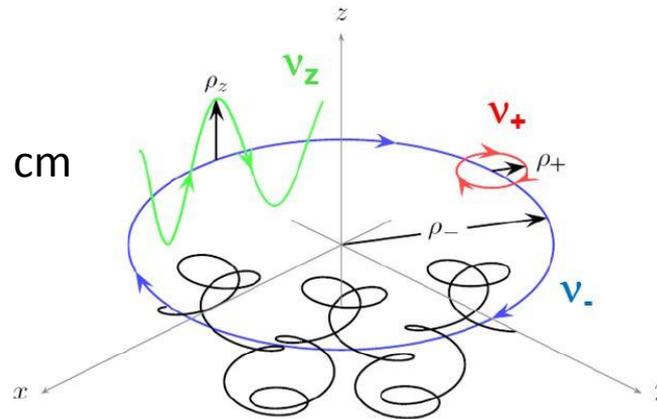


Three harmonic oscillators:



2,5 cm

Hyperbolic Penning trap



$$\omega_c = \sqrt{\omega_+^2 + \omega_-^2 + \omega_z^2}$$



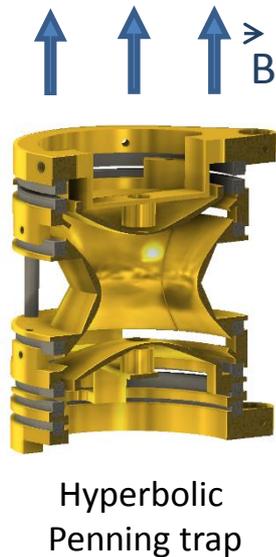
$$v_c = \frac{qB}{2\pi m}$$

Brown & Gabrielse, Rev. Mod. Phys. 58, 233 (1986).  
Gräff *et al.*, Z. Physik A - Atoms and Nuclei 297, 35 (1980).  
S. George *et al.*, Phys. Rev. Lett. 98, 162501 (2007).

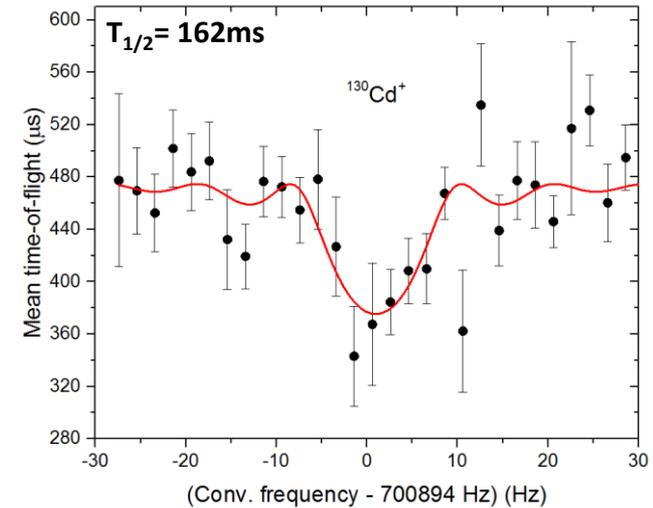
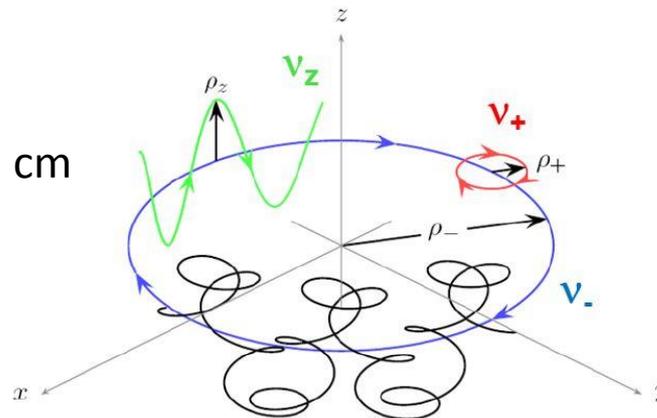
# Tools of ISOLTRAP: Penning trap

Eigen motions:

Penning trap:  
Storage of ions by the superposition  
of electric and magnetic fields



Three harmonic oscillators:



$$\omega_c = \sqrt{\omega_+^2 + \omega_-^2 + \omega_z^2}$$

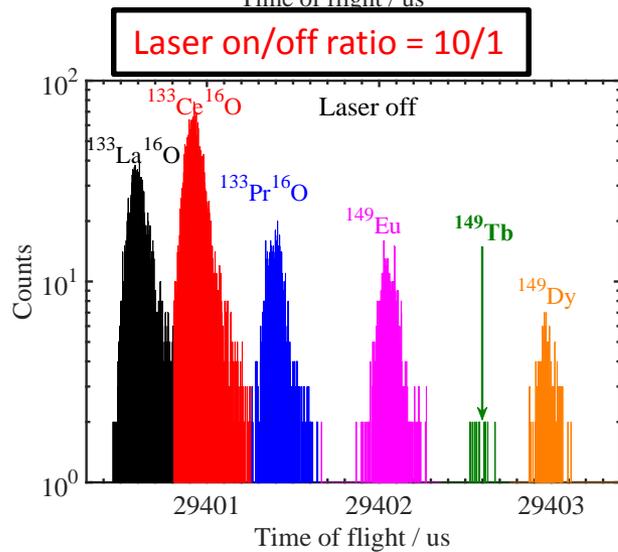
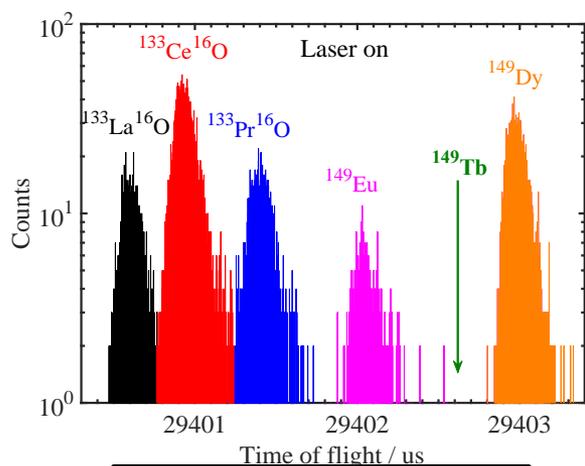


$$v_c = \frac{qB}{2\pi m}$$

Brown & Gabrielse, Rev. Mod. Phys. 58, 233 (1986).  
Gräff *et al.*, Z. Physik A - Atoms and Nuclei 297, 35 (1980).  
S. George *et al.*, Phys. Rev. Lett. 98, 162501 (2007).

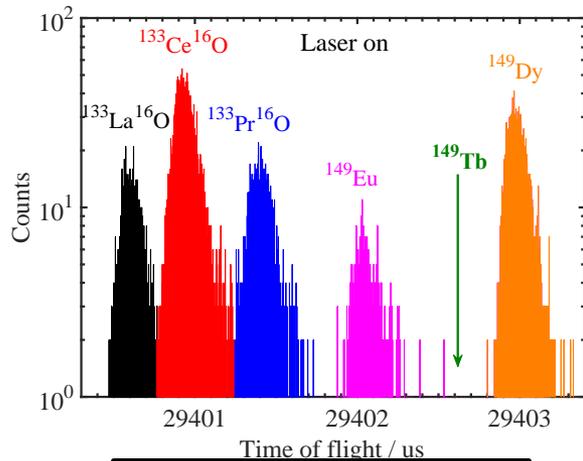
# Dy-beam time

## Collection example for A=149:

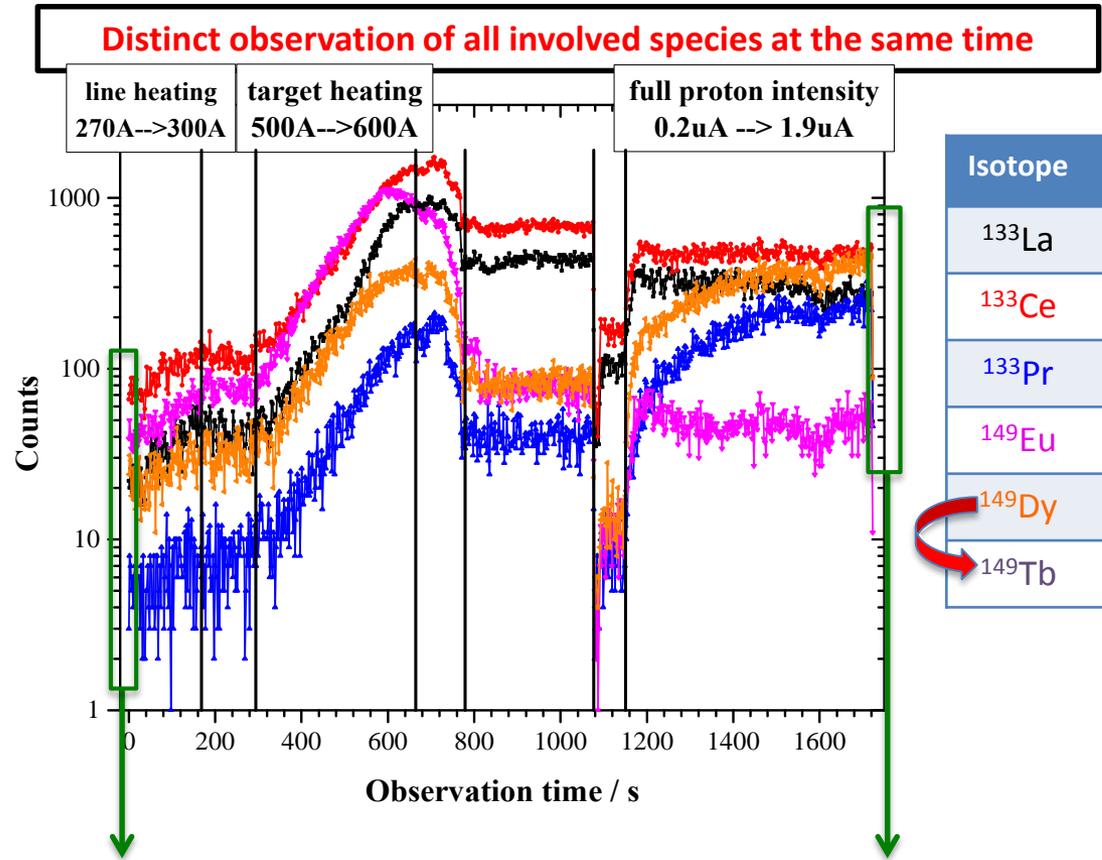
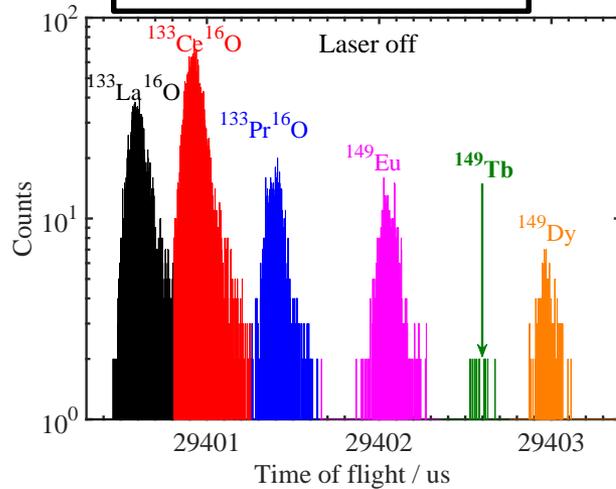


# Dy-beam time

Collection example for A=149:



Laser on/off ratio = 10/1



Isotope	Half life
<sup>133</sup> La	3.912h
<sup>133</sup> Ce	97m
<sup>133</sup> Pr	6.5m
<sup>149</sup> Eu	93.1d
<sup>149</sup> Dy	4.2m
<sup>149</sup> Tb	4.118h

Before optimization: 6.3/1      After optimization: 2.3/1  
**contaminants / <sup>149</sup>Dy → almost factor 3 improvement!**

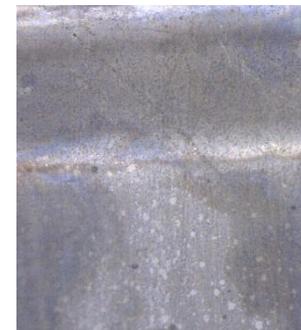
# Dy-beam time

## Collection example for A=149:

Foil holder for deposition of ion beam



Foils are gold plated with zinc.



# Dy-beam time



Dy 150 7.2 m ε; β <sup>+</sup> ... α 4.23 γ 397	Dy 151 17 m ε; α 4.07 γ 386; 49; 546; 176... σ <sub>n</sub>	Dy 152 2.4 h ε α 3.63 γ 257	Dy 153 6.29 h ε; β <sup>+</sup> ... α 3.46... γ 81; 214; 100; 254	Dy 154 3.0 · 10 <sup>6</sup> a α 2.87	Dy 155 10.0 h ε β <sup>+</sup> 0.9; 1.1... γ 227...	Dy 156 0.056 σ <sub>n</sub> 33 σ <sub>n</sub> , α < 0.009	Dy 157 8.1 h ε γ 326...	Dy 158 0.095 σ <sub>n</sub> 33 σ <sub>n</sub> , α < 0.006	Dy 159 144.4 d ε γ 58; β <sup>-</sup> σ <sub>n</sub> 8000	Dy 160 2.329 σ <sub>n</sub> 60 σ <sub>n</sub> , α < 0.0003	Dy 161 18.889 σ <sub>n</sub> 600 σ <sub>n</sub> , α < 1E-6	Dy 162 25.475 σ <sub>n</sub> 170	Dy 163 24.896 σ <sub>n</sub> 120 σ <sub>n</sub> , α < 2E-5
Tb 149 4.2 m ε α 3.97... β <sup>+</sup> 1.8... γ 796; 165...	Tb 150 4.1 h ε; β <sup>+</sup> 3.1; h 49; 25 s α 3.41; γ 232; 287; 496...	Tb 151 3.67 h ε; β <sup>+</sup> 3.1; h 49; 25 s α 3.41; γ 232; 287; 496...	Tb 152 4.2 m 4.1 h ε; β <sup>+</sup> 2.8... α 3.44; γ 344; 566; 271	Tb 153 2.34 d ε β <sup>+</sup> 2.12; 170; γ 212; 83...	Tb 154 23 h 9.0 h 21 h ε β <sup>+</sup> 1.1; 1.2; γ 248; 347; 1420; 946; 1274	Tb 155 5.32 d ε γ 87; 105; 180; 262...	Tb 156 5.4 h ε β <sup>+</sup> 7 γ 58 h 58 e <sup>-</sup>	Tb 157 99 a ε γ (54)	Tb 158 10.5 s 180 a ε β <sup>-</sup> 0.9 γ 944; 962; 80	Tb 159 100 σ <sub>n</sub> 23.2	Tb 160 72.3 d β <sup>-</sup> 0.6; 1.7... γ 879; 299; 966... σ <sub>n</sub> 570	Tb 161 6.90 d β <sup>-</sup> 0.5; 0.6... γ 26; 49; 75... e <sup>-</sup>	Tb 162 7.76 m β <sup>-</sup> 1.4; 2.4... γ 260; 808; 888...
Gd 148 74.6 a α 3.183 σ <sub>n</sub> 14000	Gd 149 9.28 d ε; α 3.016 γ 150; 299; 347...	Gd 150 1.8 · 10 <sup>6</sup> a α 2.72	Gd 151 120 d ε; α 2.60 γ 154; 243; 175...	Gd 152 0.20 1.1 · 10 <sup>12</sup> a α 2.14; σ 700 σ <sub>n</sub> , α < 0.007	Gd 153 239.47 d ε γ 97; 103; 70... σ <sub>n</sub> 20000 σ <sub>n</sub> , α 0.03	Gd 154 2.18 σ <sub>n</sub> 60	Gd 155 14.80 σ <sub>n</sub> 61000 σ <sub>n</sub> , α 0.00008	Gd 156 20.47 σ <sub>n</sub> ~ 2.0	Gd 157 15.65 σ <sub>n</sub> 254000 σ <sub>n</sub> , α < 0.05	Gd 158 24.84 σ <sub>n</sub> 2.3	Gd 159 18.48 h β <sup>-</sup> 1.0... γ 364; 58...	Gd 160 21.86 σ <sub>n</sub> 1.5	Gd 161 3.66 m β <sup>-</sup> 1.6; 1.7... γ 361; 315; 102... σ <sub>n</sub> 20000

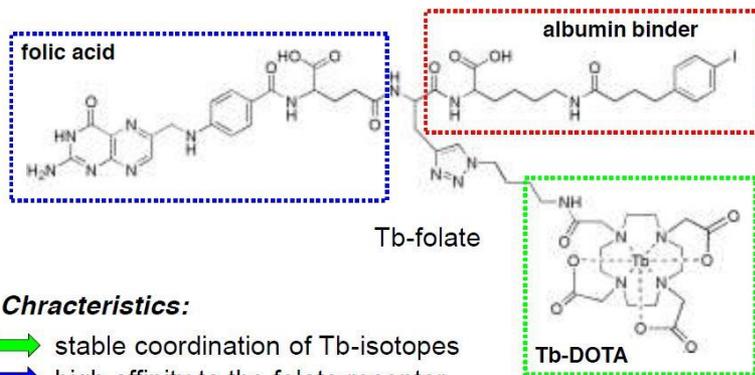


Müller *et al.*, J. Nucl. Med. 54: 124 (2013).

Andree Welker for ISOLTRAP, 1st MEDICIS-Promed general training, Manchester, 09.09.2016

# Dy-beam time

## Tumor Targeting Agent for Tb-Coordination Chemical Structure with 3 Functionalities

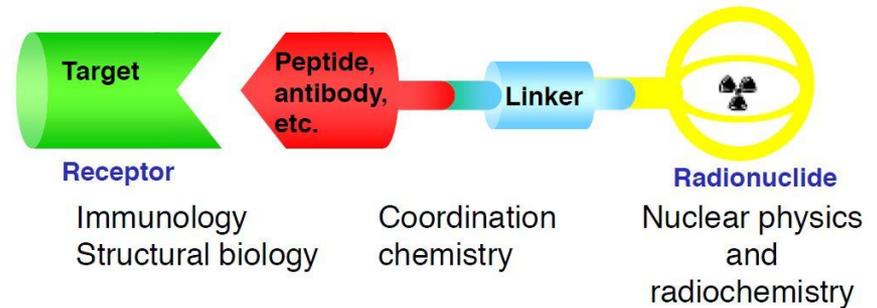


**Characteristics:**

- stable coordination of Tb-isotopes
- high affinity to the folate receptor
- prolonged blood circulation time

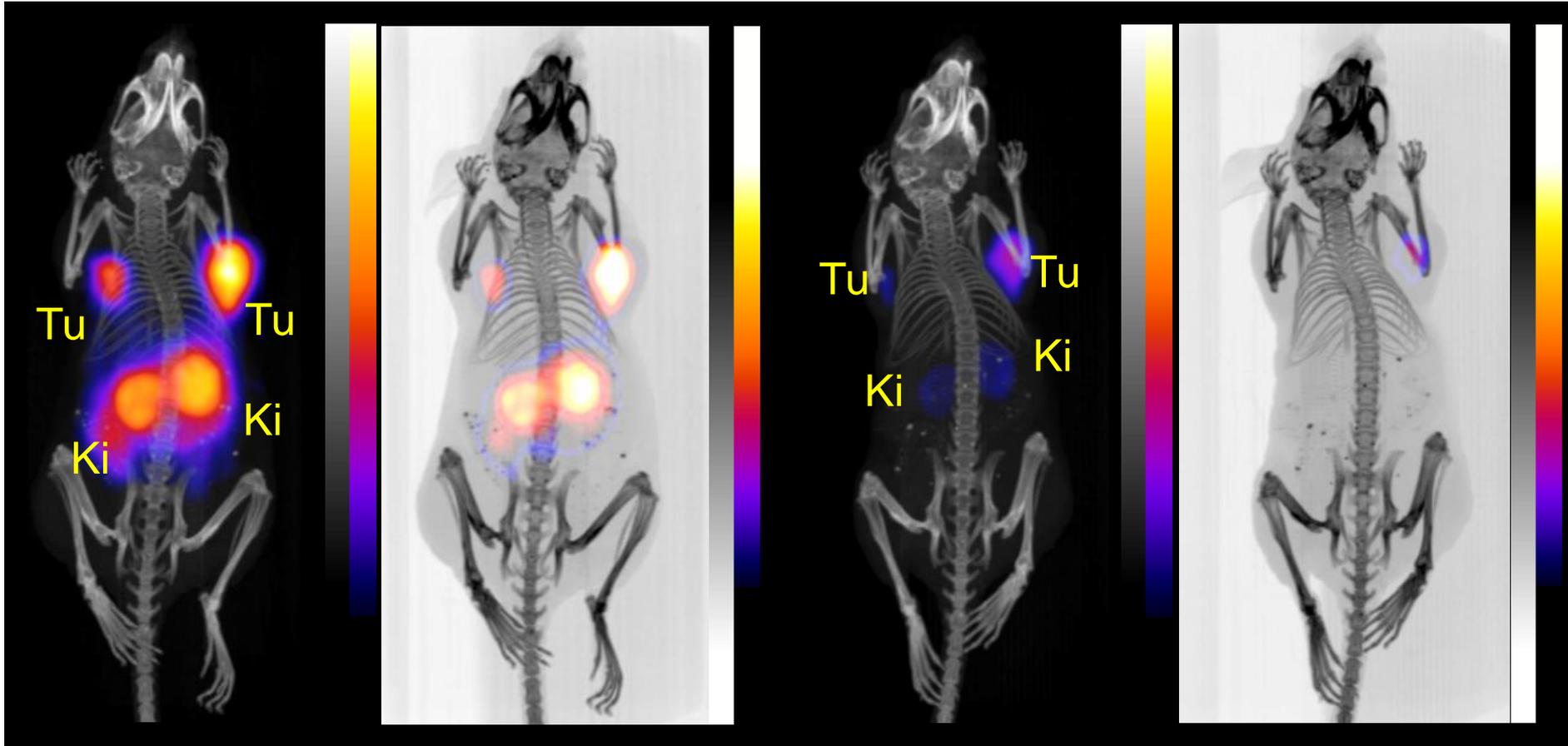
*C. Müller et al., J Nucl Med 2012;53:1951.*

## Multidisciplinary collaboration to fight cancer



# Dy-beam time

Müller et al., submitted to Eur J Nucl Med Mol Imaging Research, Nov 2015



PET/CT 5 h after Injection of  $^{152}\text{Tb}$ -DOTANOC

PET/CT 22 h after Injection of  $^{152}\text{Tb}$ -DOTANOC



# Acknowledgments



N. Althubiti, P. Ascher, **D. Atanasov**, D. Beck, K. Blaum, T. Cocolios, S. Eliseev, S. George, F. Herfurth, A. Herlert, D. Kisler, M. Kowalska, Yu. A. Litvinov, D. Lunney, **V. Manea**, E. Minaya-Ramirez, **M. Mougeot**, D. Neidherr, M. Rosenbusch, H. Schmidt-Böcking, L. Schweikhard, **F. Wienholtz**, M. Wang, **A. Welker**, R. Wolf, K. Zuber

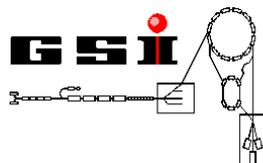
Thank you very much for your attention!



ERNST MORITZ ARNDT  
UNIVERSITÄT GREIFSWALD

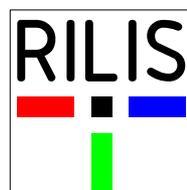


Federal Ministry  
of Education  
and Research



Grants No.:  
05P12HGCI1  
05P12HGFNE  
05P15ODCIA

ISOLDE Target  
and Technical Group



<http://isoltrap.web.cern.ch>

