

Preparation of Laser Isotope Separation for the Nuclear Medical Project – MEDICIS

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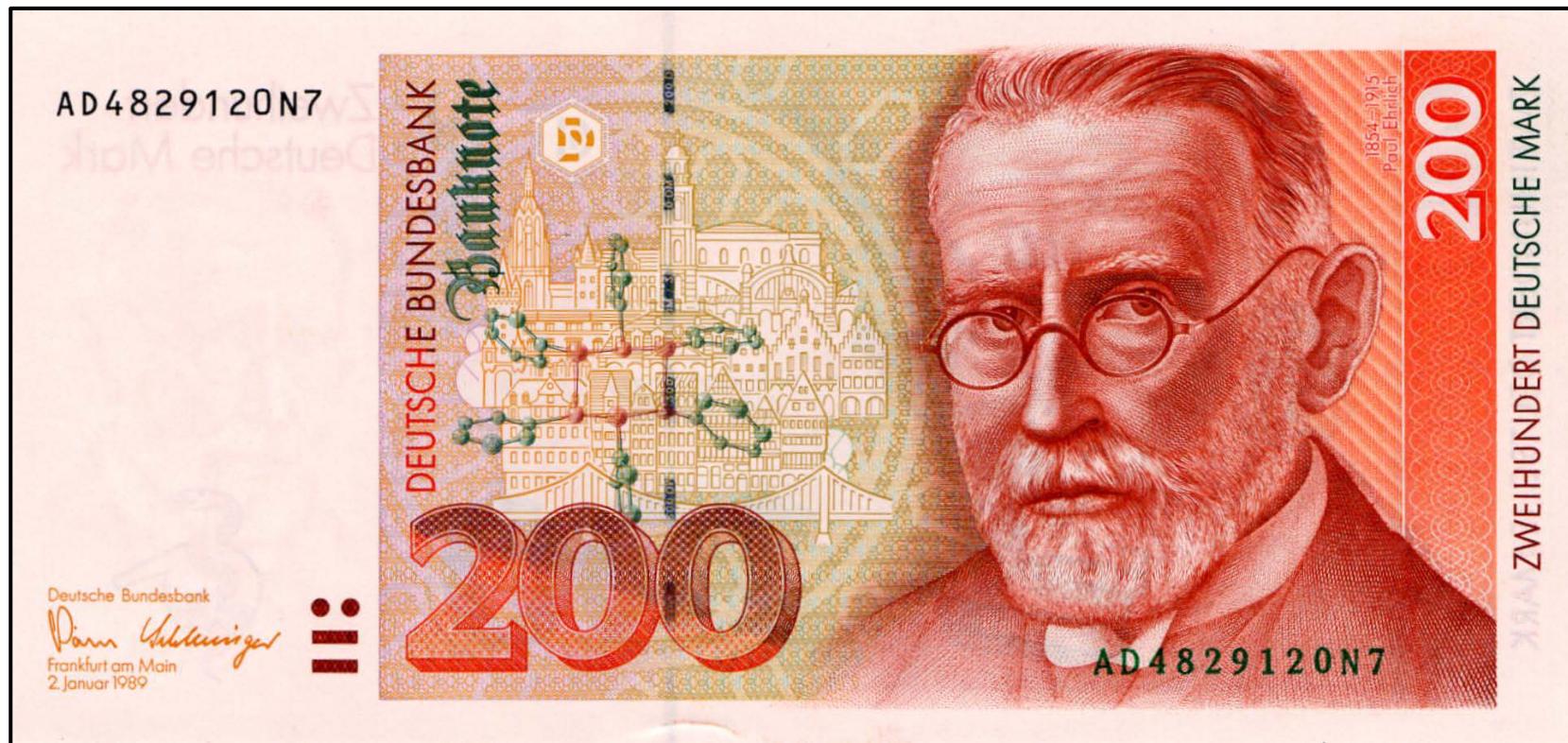
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Striving for the “Magic Bullet” Concept in Medicine

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(Medical) Therapies should lead to death of the targeted organism without damaging the (human) host.

Paul Ehrlich (1854–1915)

Novel radioisotopes for theranostics

Isotope production
Graphene layer protection
Transportation

Functional Imaging

Validation of biological models
Preclinical imaging studies
DNA synthesis markers

Radiotherapy

Personalized cancer treatment
Radioimmunotherapy
Surgery

THERAPY + DIAGNOSTIC = THERANOSTIC

WP 1 :
mass separation
of new medical isotopes

WP 2 :
PET aided ^{11}C hadrontherapy

WP 3 :
theranostic pharmaceuticals
and surgery
for new ovarian cancer
personalized treatment

Rare-Earth Medical Radioisotopes of MEDICIS Interest

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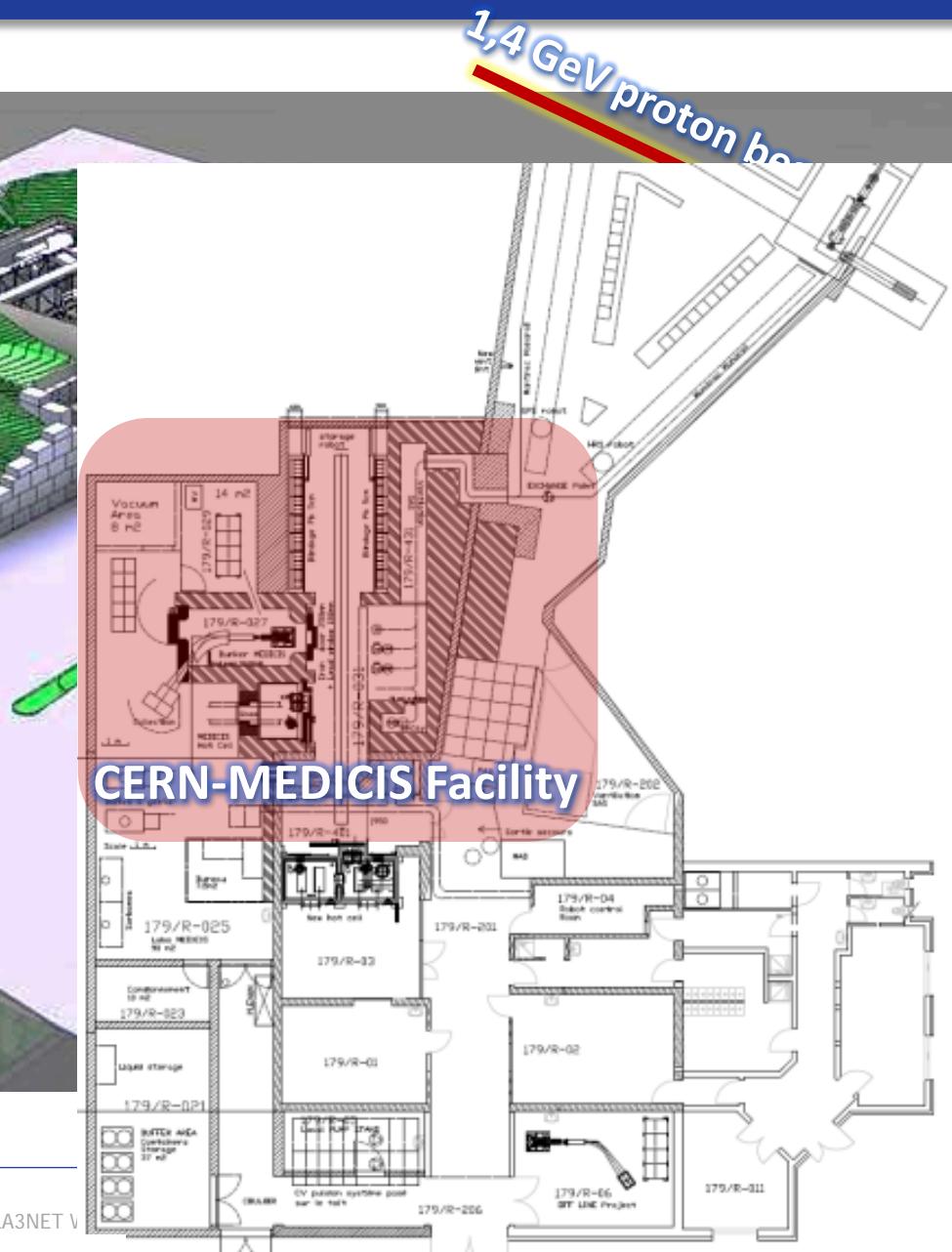
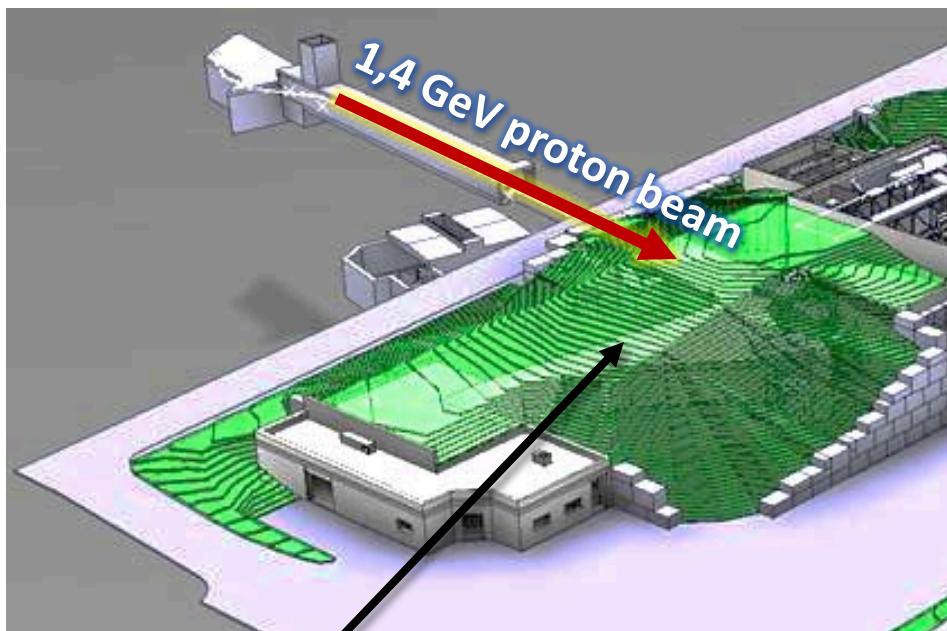
The figure consists of three main parts. The top part is a standard periodic table highlighting several elements in yellow boxes: Lu (Lu 174.967), Yb (Yb 173.04), Tb (Tb 144), Gd (Gd 143), Eu (Eu 142), Sm (Sm 141), Pm (Pm 140), and Nd (Nd 139). The middle part is a detailed view of the lanthanide series from Dy to Tb, with Tb 144 highlighted in a red box. The bottom part shows the full periodic table with various elements highlighted in yellow boxes, including Lu 177, Yb 176, Tb 146, Gd 145, Eu 144, Sm 143, Pm 140, and Nd 140.



Lu 177

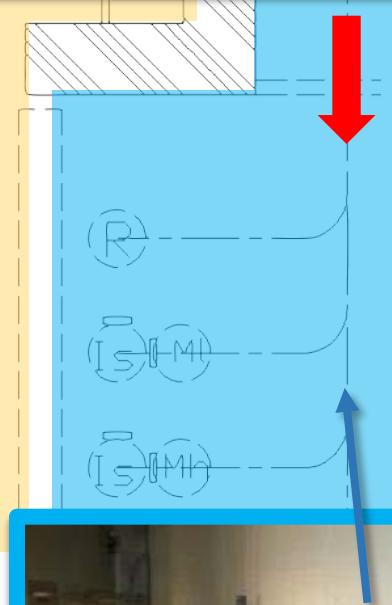
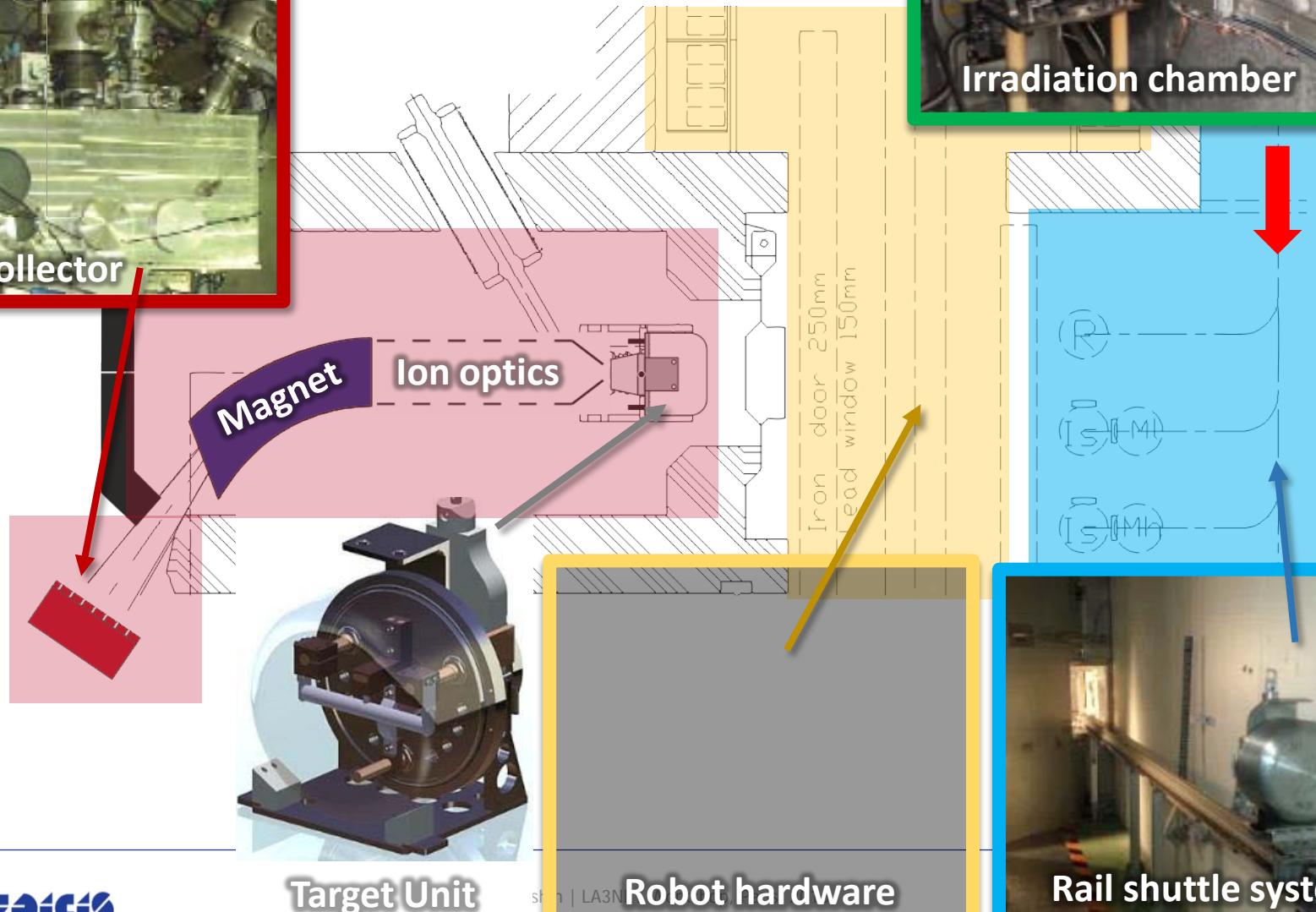
R. M. dos Santos Augusto et al.,
CERN MEDICIS – A New Facility
Appl. Sci. 4, 265-281 (2014)

CERN-MEDICIS Facility: MEDical Isotopes Collected from ISOLDE 6



MEDICIS Off-line Mass Separator

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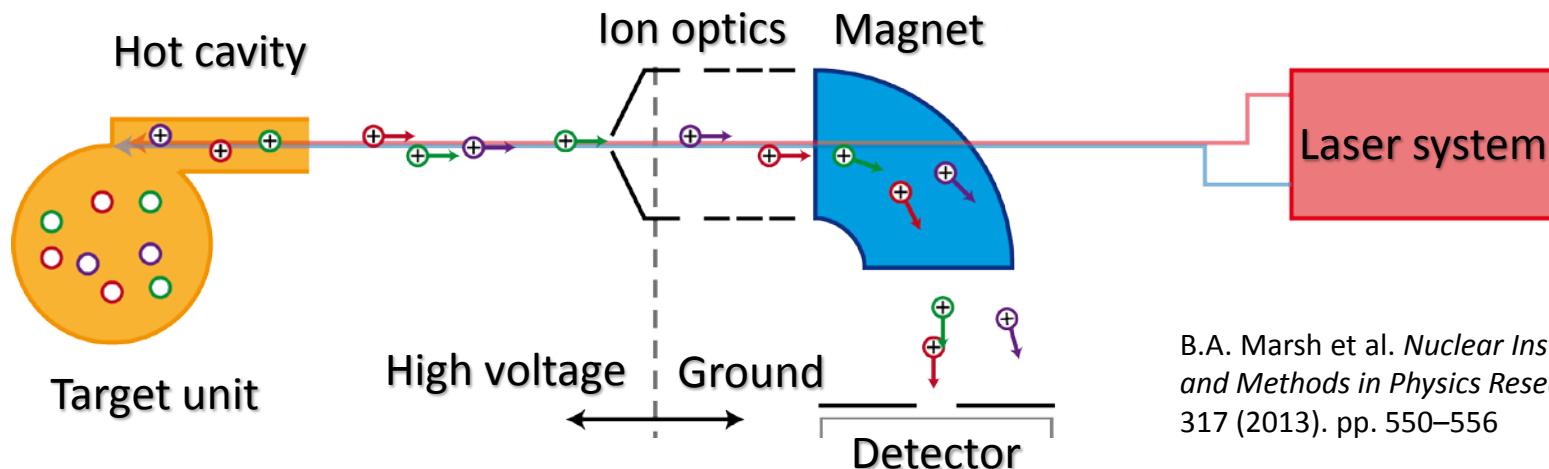


Resonance Ionization Laser Ion Source

Auto-ionizing state
Relevance of using the RILIS technology:

- Elemental selective ionization;
- **Most efficient ionization process;**
- **Highest purity of ion beam production**
by preeminent suppression of isobaric contamination.

Ground state



B.A. Marsh et al. *Nuclear Instruments and Methods in Physics Research B*, 317 (2013). pp. 550–556

Ta 176	Ta 178	Ta 179	Ta 180	Ta 181
56.6	125 m	2.45 h	> 10 ¹⁵ a	99.988
2.00	332...	no	σ = 560	σ = 0.012 + 20
g	β<0.7	β<0.7	σ = 560	σ = 10 ⁻⁶
σ = 930	g	g	g	g
g	4.0 s	27.28	8.15 h	35.08
τ = 23	4.0 s	25 d	18.7 s	35.08
Hf 176	Hf 178	Hf 179	Hf 180	Hf 180
5.2	4.0 s	4.0 s	5.5 h	35.08
2.3	332...	454;	443; 215;	443; 215;
Lu 175	Lu 176	Lu 178	Lu 179	Lu 179
77.41	2.3	7 m	4.6 h	4.6 h
3.3	3.3	3.3	2.14	2.14
1.3	1.3	1.3	0.43	0.43
σ = 16 + 6	σ = 0.5...	σ = 2.14	σ = 1.3	σ = 1.3
Yb 174	Yb 175	Yb 176	Yb 178	Yb 178
31.83	4.2 d	12 s	74 m	74 m
σ = 63	γ = 396; 283;	γ = 293	γ = 390; 190;	γ = 390; 190;
σ = 0.00002	114...	390; 190;	98...	98...
Tm 173	Tm 174	Tm 175	Tm 176	Tm 176
8.2 h	2.29 s	15.2 m	1.9 s	1.9 s
β = 0.9; 1.3...	β = 1.2...	β = 0.9; 1.9...	β = 2.0; 2.8...	β = 2.0; 2.8...
γ = 399; 461...	γ = 366;	γ = 515; 941;	γ = 190; 1069;	γ = 190; 1069;
152	992; 273;	364...	382...	382...
	177...		g	g

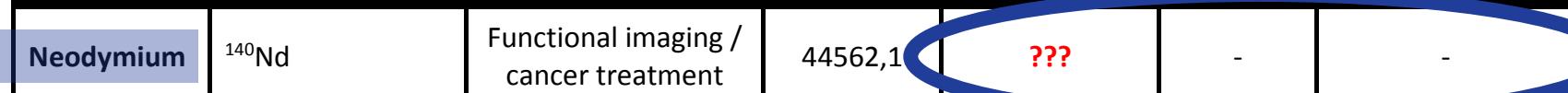
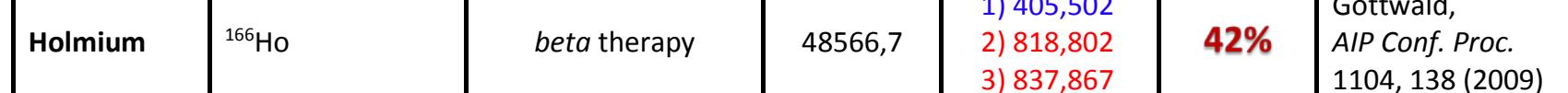
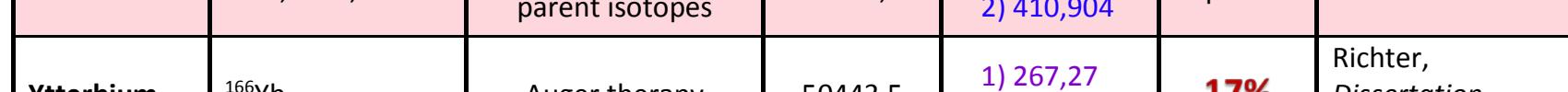
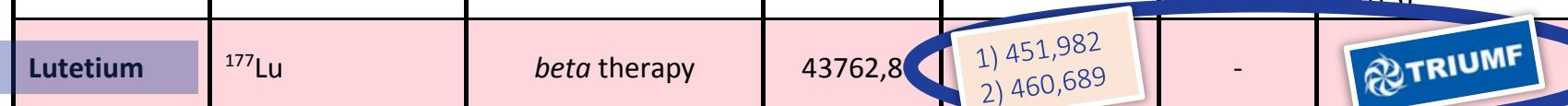
Application Experience of the Laser Ionization Methods

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1	H		No	- excitation scheme exists		2	He
3	Li	4	Be			5	B
11	Na	12	Mg	91	Pa	6	C
19	K	20	Ca	21	Sc	7	N
37	Rb	38	Sr	39	Y	8	O
55	Cs	56	Ba	22	Ti	9	F
87	Fr	88	Ra	23	V	10	Ne
				24	Cr	11	
				25	Mn	12	
				26	Fe	13	
				27	Co	14	Al
				28	Ni	15	Si
				29	Cu	16	P
				30	Zn	17	S
				31	Ga	18	Cl
				32	Ge	19	Ar
				33		20	
				34	As	21	
				35	Se	22	
				36	Br	23	
				37	Kr	24	
				38		25	
				39		26	
				40		27	
				41		28	
				42		29	
				43		30	
				44		31	
				45		32	
				46		33	
				47		34	
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				111		83	
				112		84	
				113		85	
				114		86	
				115		87	
				116		88	
				117		89	
				118		90	

Lanthanides for the MEDICIS-PROMED Project

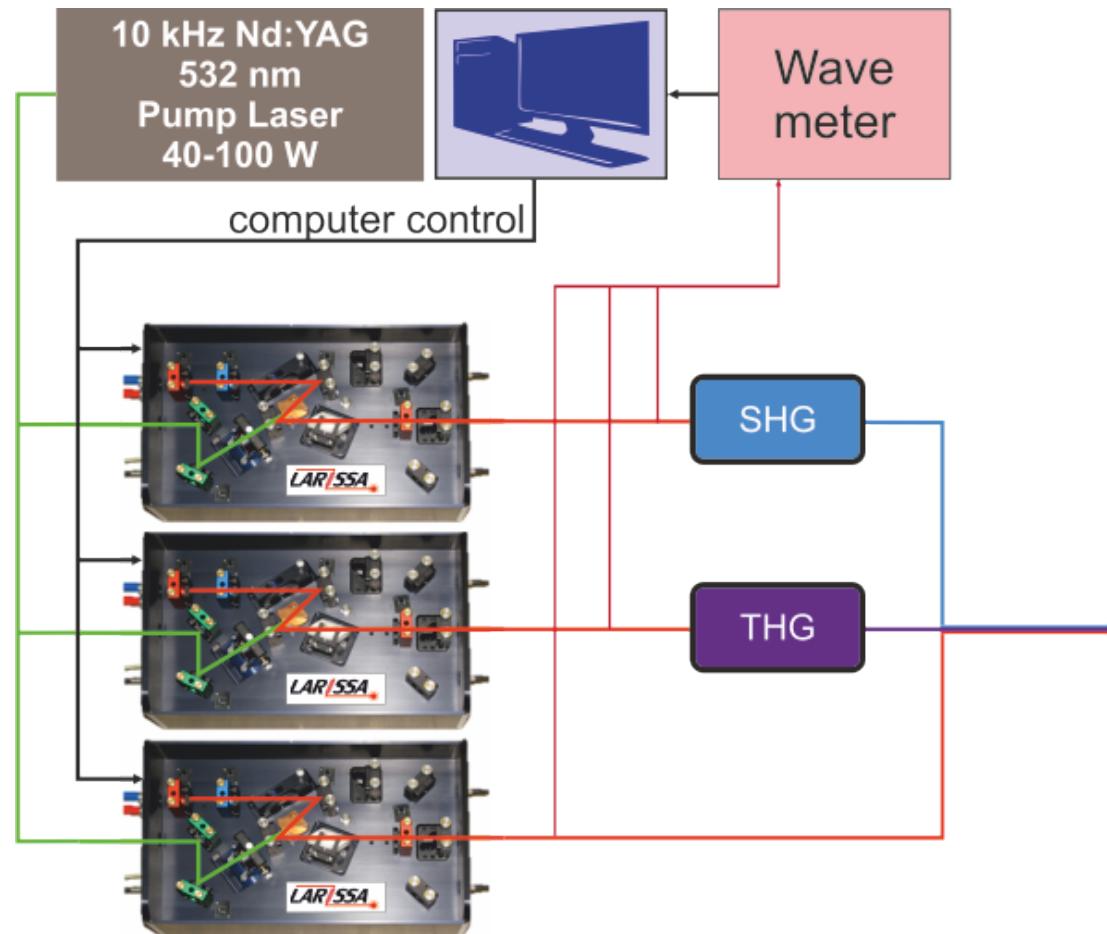
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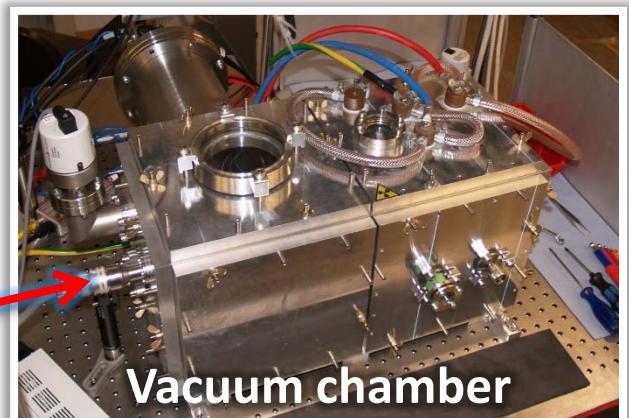
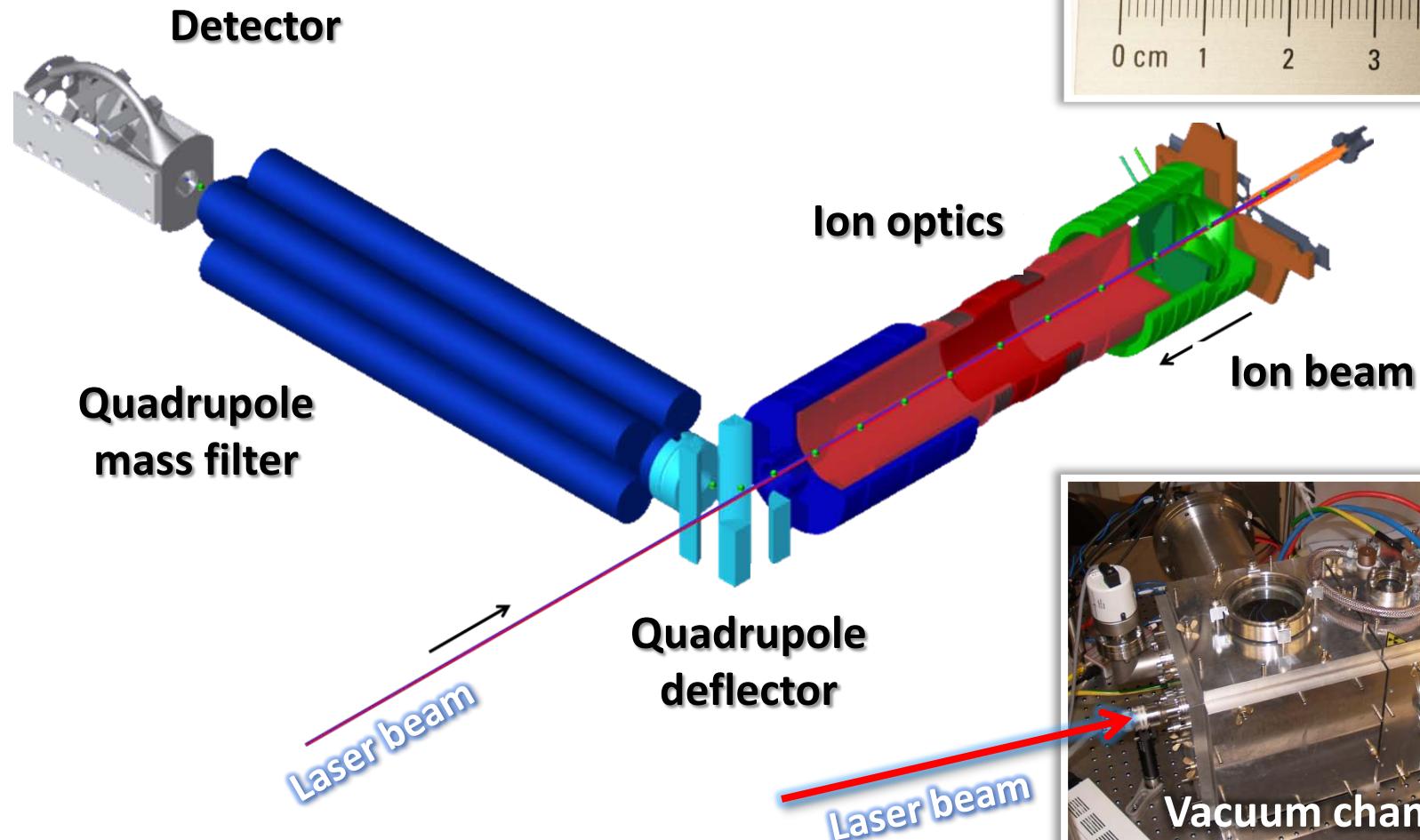
Name	Desired radioisotopes	Medical application	Ionization potential, cm ⁻¹	Ti:Sa laser excitation scheme, nm	Ionization efficiency	References
Neodymium	¹⁴⁰ Nd	Functional imaging / cancer treatment	44562,1	??? 	-	-
Samarium	¹⁵³ Sm	<i>beta</i> therapy	45519,5	1) 436,415 2) 885,55 3) 881,80	n/a	Sonnenschein, <i>Dissertation</i> (2014)
Terbium	¹⁴⁹ Tb, ¹⁵² Tb, ¹⁵⁵ Tb, ¹⁵⁶ Tb, ¹⁶¹ Tb	Functional imaging / cancer treatment	47294,7	1) 432,00 2) 795,41 3) <864	n/a	Gottwald, <i>AIP Conf. Proc.</i> 1104, 138 (2009)
Dysprosium	¹⁵² Dy, ¹⁵⁵ Dy	Parent isotopes, sources	47900,5	1) 418,80 2) 786,058 3) 837,616	25% 	Studer, <i>Diplomarbeit</i> , (2015)
Holmium	¹⁶⁶ Ho	<i>beta</i> therapy	48566,7	1) 405,502 2) 818,802 3) 837,867	42% 	Gottwald, <i>AIP Conf. Proc.</i> 1104, 138 (2009)
Erbium	¹⁶³ Er, ¹⁶⁵ Er, ¹⁶⁷ Er	Auger therapy / parent isotopes	49261,9	1) 400,910 2) 410,904	In process	-
Ytterbium	¹⁶⁶ Yb	Auger therapy	50443,5	1) 267,27 2) 736,67	17% 	Richter, <i>Dissertation</i> (2015)
Lutetium	¹⁷⁷ Lu	<i>beta</i> therapy	43762,8	1) 451,982 2) 460,689	- 	TRIUMF 

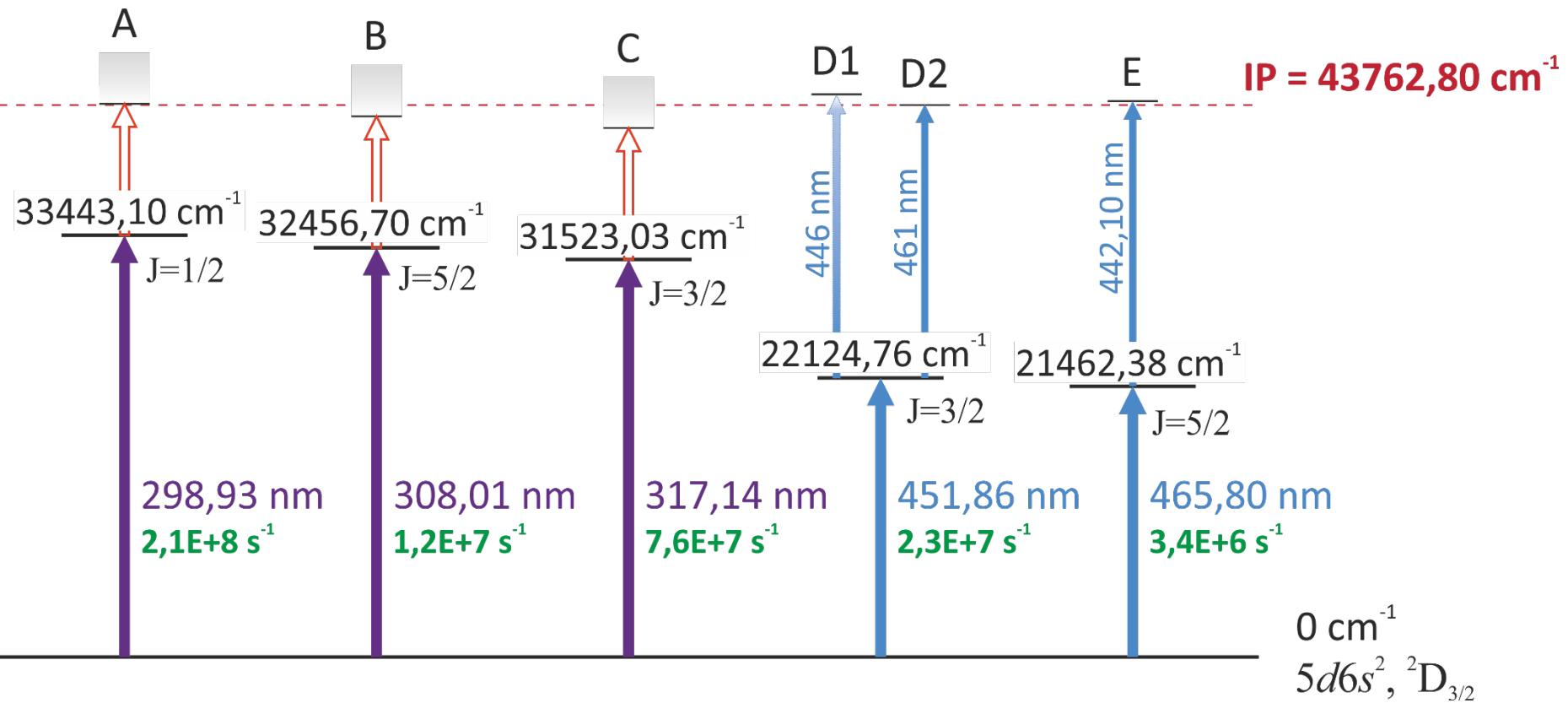


Ti:Sapphire solid-state laser

- Line width: 5 GHz
- Pulse length: 30-50 ns
- High reliability
- High spectral stability
- Constant output power: up to 5 W
- Work range:
 - fundamental: 690-960 nm
 - doubled: 350-480 nm (SHG)
 - tripled: 233-320 nm (THG)
 - quadrupled: 205-232 nm







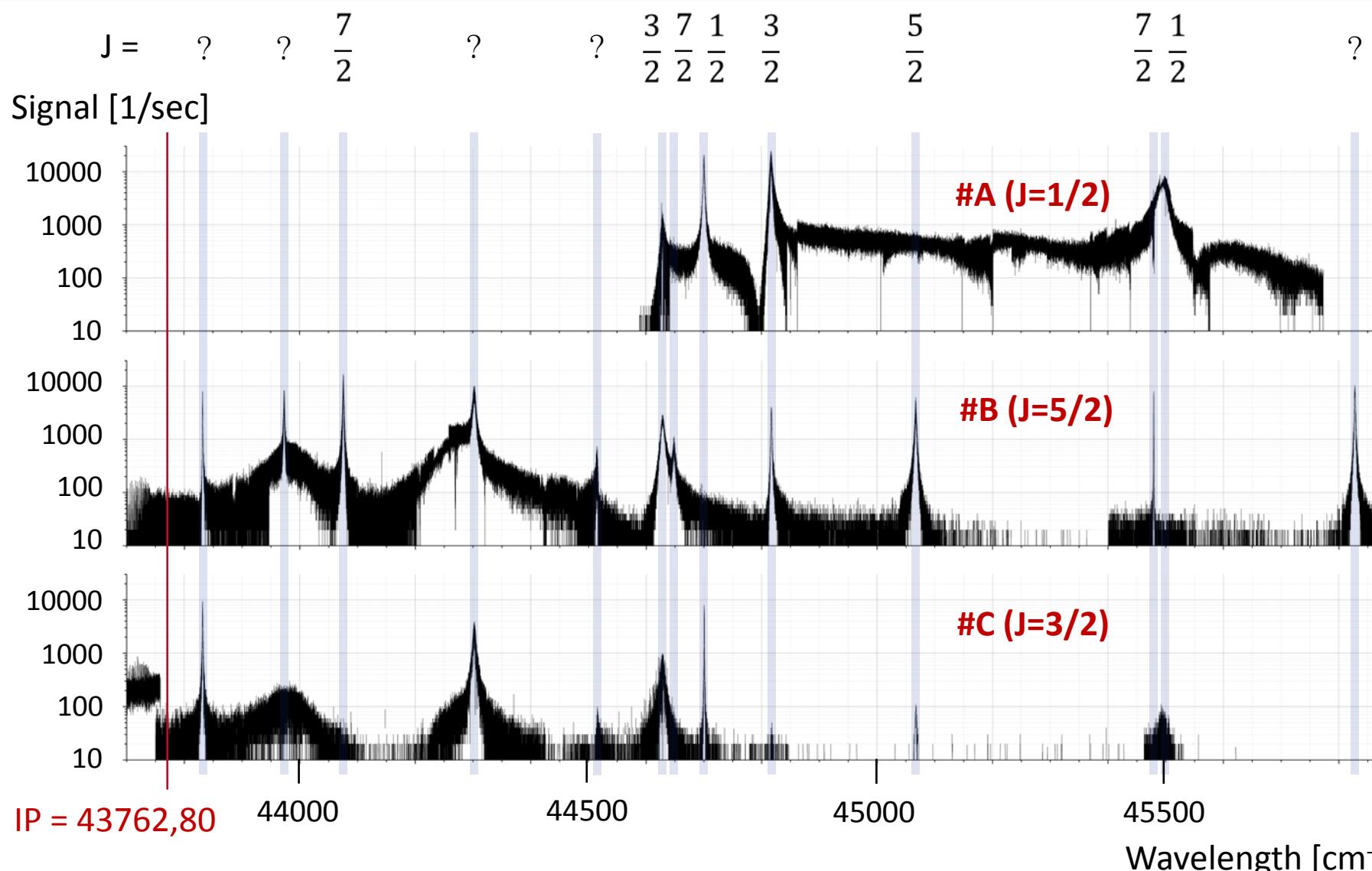
D: Bekov G.I. (1981); Miller C.M. (1982); Li R., TRIUMPH (2016)

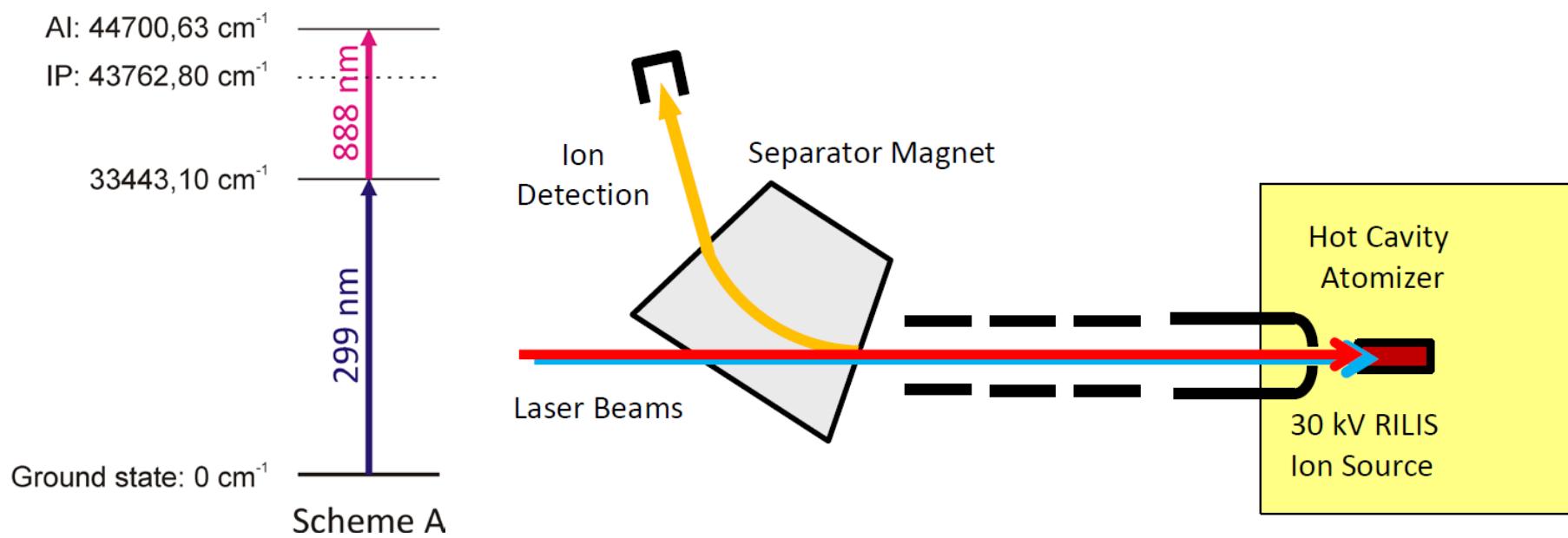
D2: Krustev T.B. (1993);

E: Xu C.B. (1993)

Spectra of 2nd Resonant Excitation Step in Lutetium

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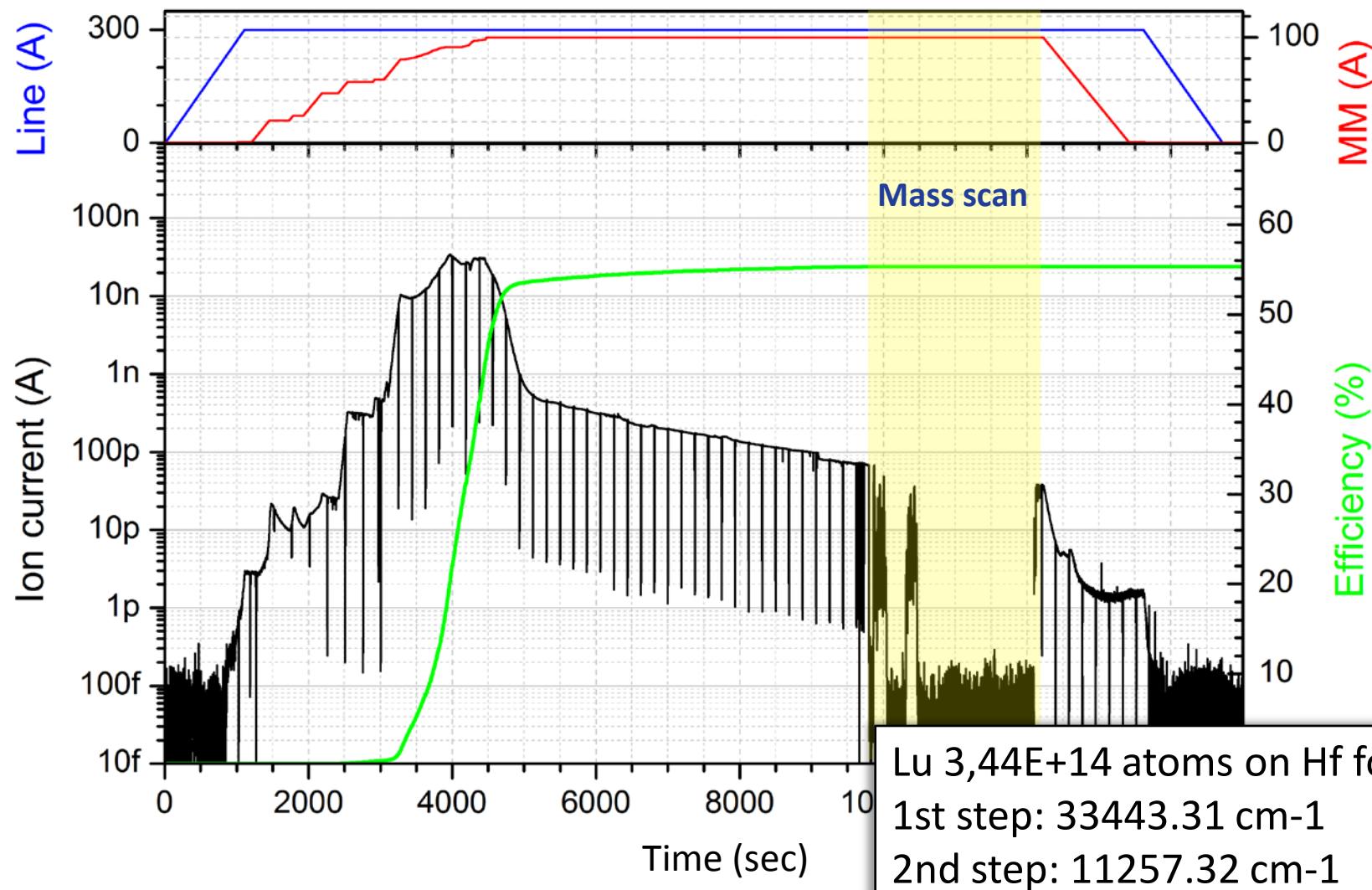


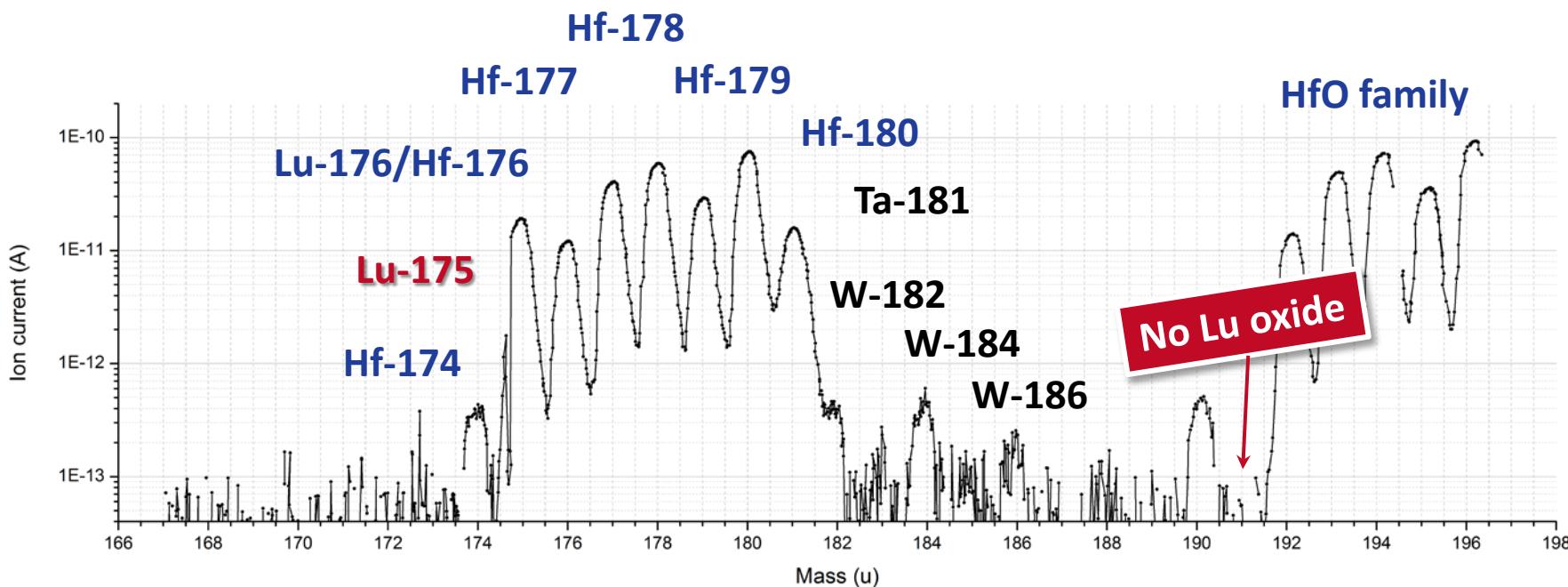


- Has been performed on the **RISIKO Mass Separator**;
- A sample with **3,44E+14 atoms** was prepared from the lutetium standard solution;
- As a support and a reducing agent, the **hafnium foil** was used;
- **Separately heated** sample reservoir («mass marker» + atomizer).

Lutetium Ionization Efficiency Measurement | Example

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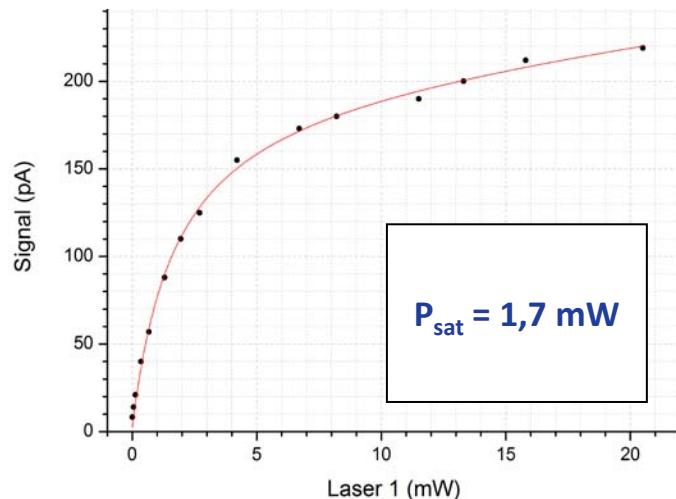




- Isotopes of work materials were observed (Lu, Hf, Ta, W, ...)
- Their oxides also were seen except lutetium oxide, what prove efficient reduction by hafnium;
- Strong dependence of Lu signal on lasers; vice versa, lasers do not affect on other elements.

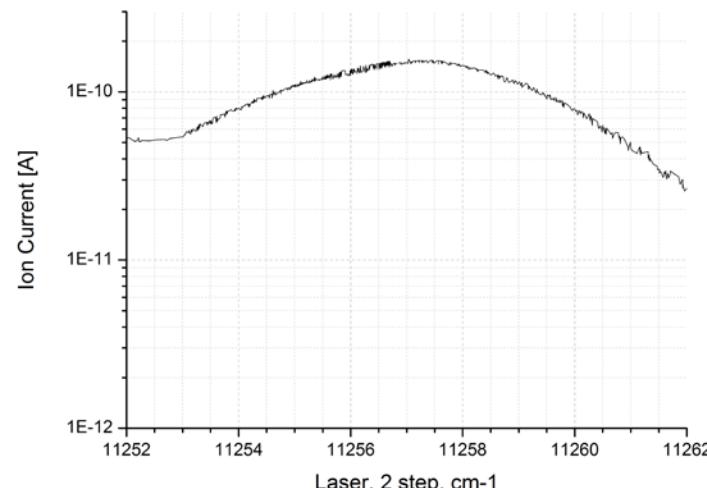
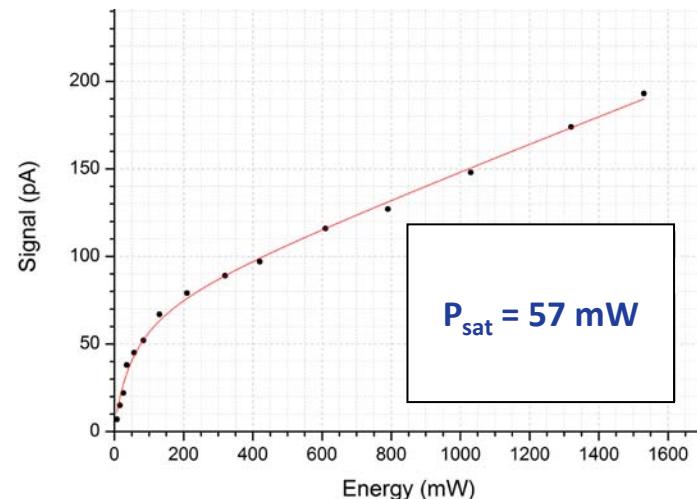
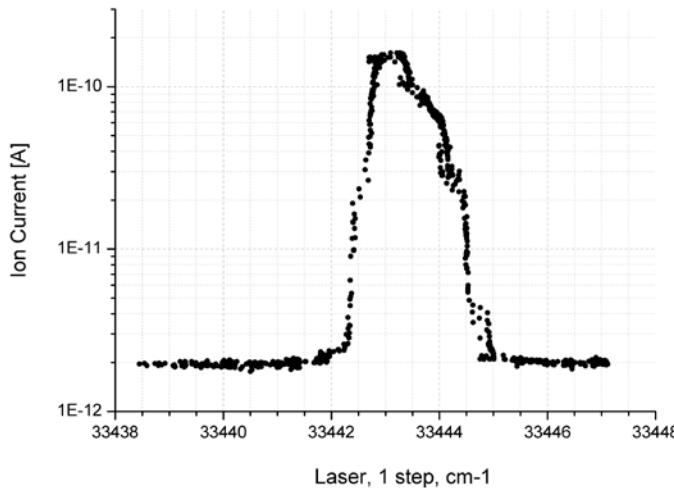
Laser 1 ($33443,31 \text{ cm}^{-1}$)

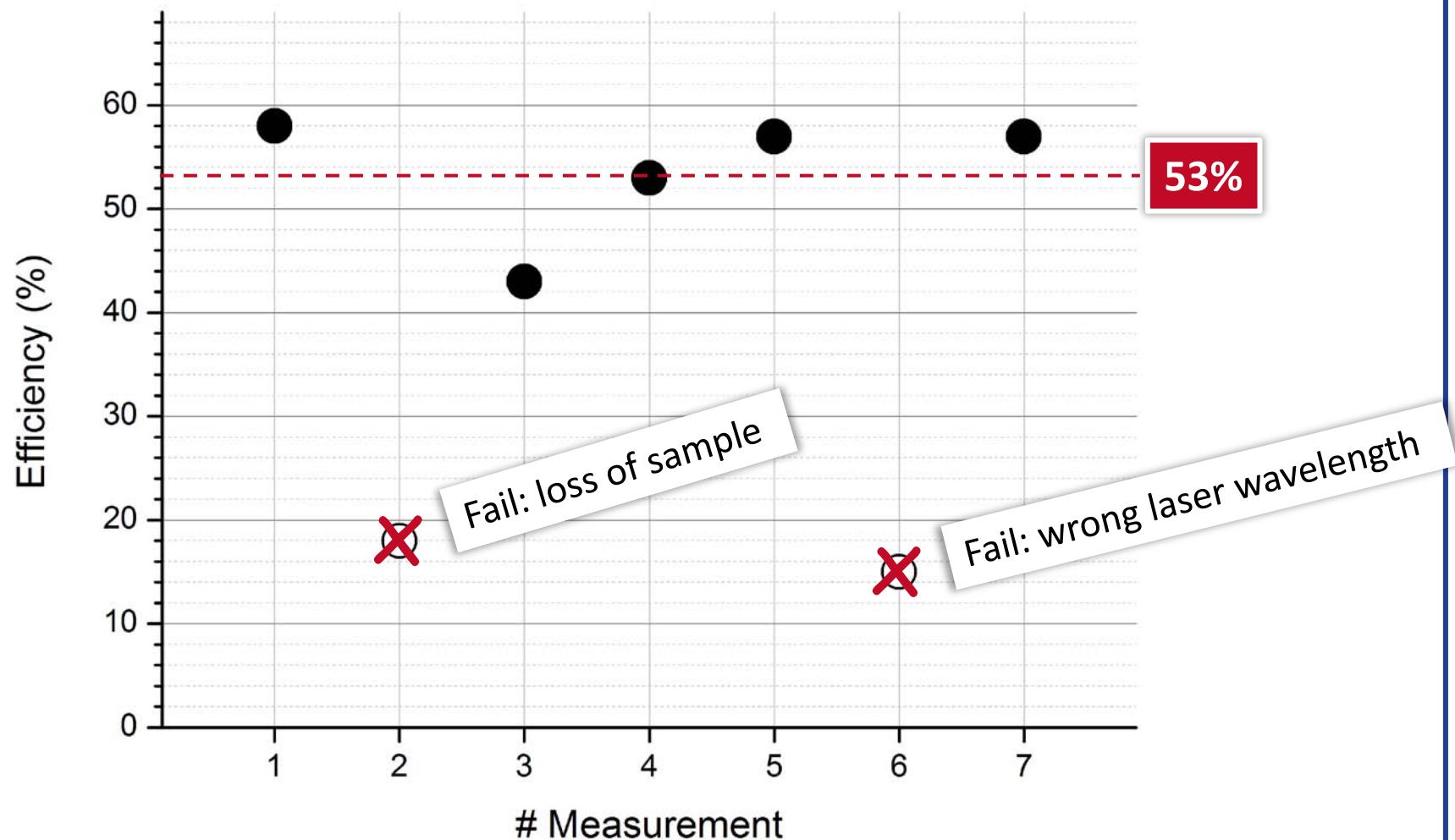
Saturation curve



Laser 2 ($11257,32 \text{ cm}^{-1}$)

Laser frequency





Goal of Work Package 1:

- Providing of highly purified mono-isobaric ion beam production via elemental selective laser ionization



- Characterization of a 2- or 3- steps laser excitation scheme for **Nd** isotopes;
- Accomplishment of efficiency measurement for **Tb** isotopes;
- Demonstration of the highly selective and efficient laser ionization for purification processes on RISIKO, ISOLDE and MEDICIS mass separators.

Acknowledgment



This research project has been supported by a Marie Skłodowska-Curie Innovative Training Network Fellowship of the European Commission's Horizon 2020 Programme under contract number 642889 MEDICIS-PROMED.

Conclusion

- MEDICIS Innovative Training Network started in April 2015;
- CERN-MEDICIS facility under construction;
- Resonant 2-step excitation schemes in lutetium studied;
- Lutetium ionization efficiency measurement was performed with preliminary **53%** efficiency;
- Further MEDICIS elements of interest: Nd, Tb, ...



Questions?



Thank you for your attention!

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under contract number 642889 MEDICIS-PROMED.*

Scheme #A | 1st laser: 33443.31 cm⁻¹ | 2nd laser: 11257.32 cm⁻¹

