
CERN

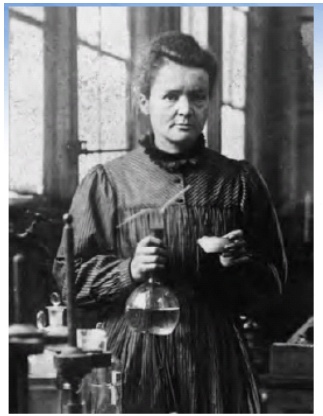
CERN-MEDICIS

Non-conventional radioisotopes for medical research

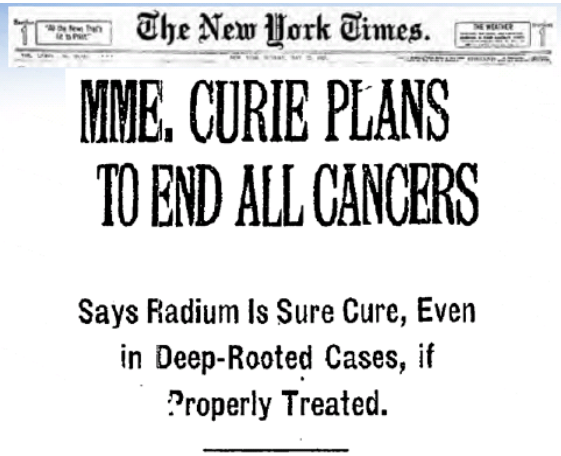
Thierry Stora for the CERN-MEDICIS Collaboration

New radiopharmaceuticals for therapy

Xofigo® and Luthatera® have recently been approved for treatment



Published:
May 12th 1921
© The New York Times



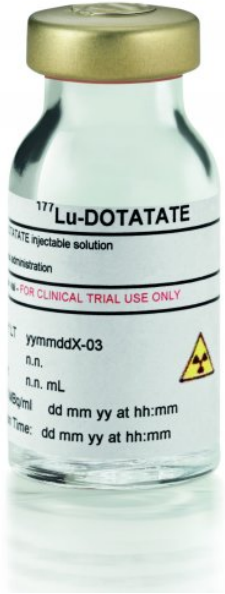
The New York Times.

MME. CURIE PLANS TO END ALL CANCERS

Says Radium Is Sure Cure, Even in Deep-Rooted Cases, if Properly Treated.

1921

2015



2017

Courtesy prof O. Ratib

European Journal of Nuclear Medicine and Molecular Imaging
https://doi.org/10.1007/s00259-018-4015-2

ORIGINAL ARTICLE

Prolonged survival in secondary glioblastoma following local injection of targeted alpha therapy with ^{213}Bi-substance P analogue

Leszek Krolicki[1] · Frank Bruchertseifer[2] · Jolanta Kunikowska[1] · Henryk Koziara[3] · Bartosz Królicki[3] · Maciej Jakuciński[4] · Dariusz Pawlak[5] · Christos Apostolidis[2] · Saed Mirzadeh[6] · Rafał Rola[7] · Adrian Merlo[8] · Alfred Morgenstern[2]

Received: 5 December 2017 / Accepted: 9 April 2018

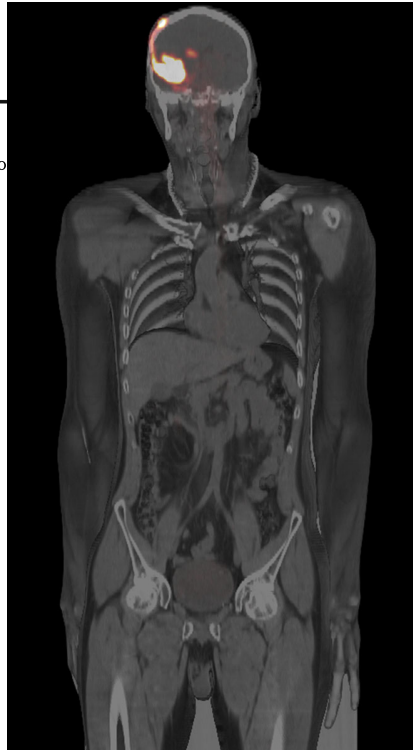
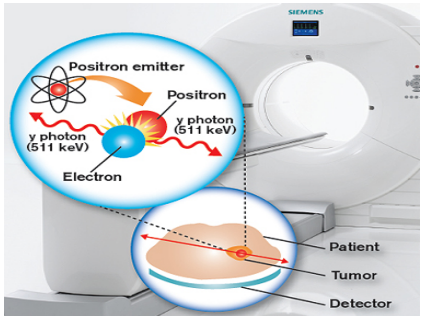
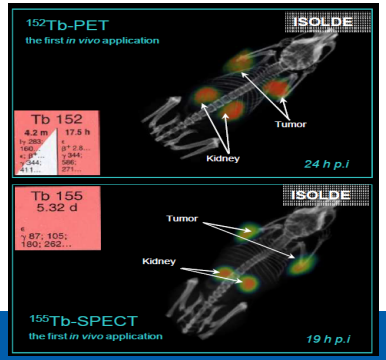


Fig. 3 Whole body PET/CT scan shows biodistribution 30 min after intralesional injection of 10 MBq ^{68}Ga-DOTA-SP analogue: the signal detected in the body outside the brain is very faint or negligible in liver, kidney, spleen and bone marrow. The cleaved linear peptidic vector is excreted into the bladder and can show a weak signal corresponding to <5% of injected activity

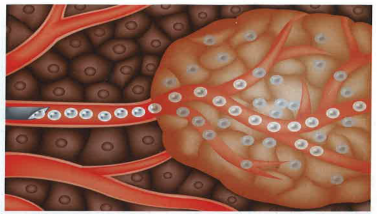
New concept of THERAnostics pairs

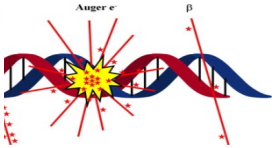
Diagnostics





THERAPY



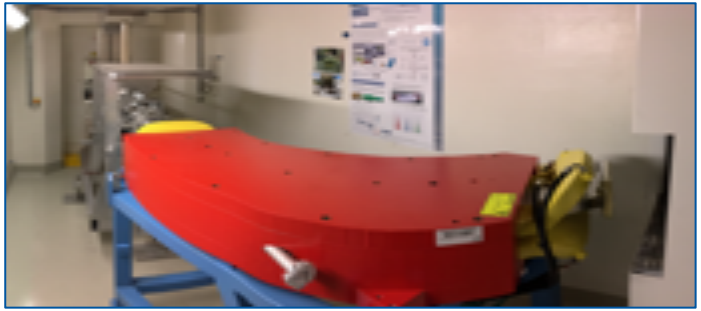


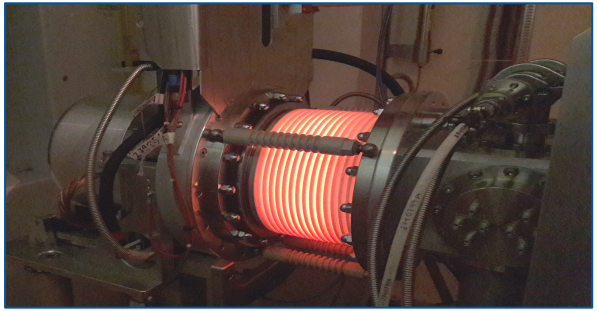
CERN-MEDICIS : A new facility

September 2013

October 2014

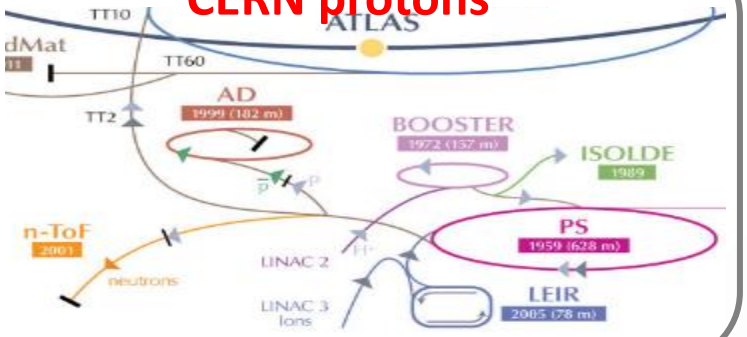
Today:



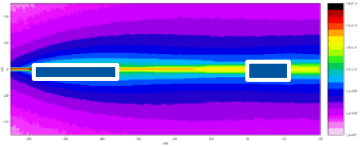


Principle of isotope production

CERN protons



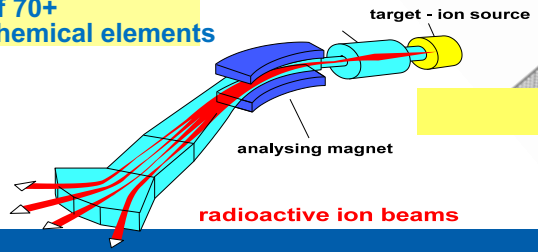
MEDICIS Target Irradiation

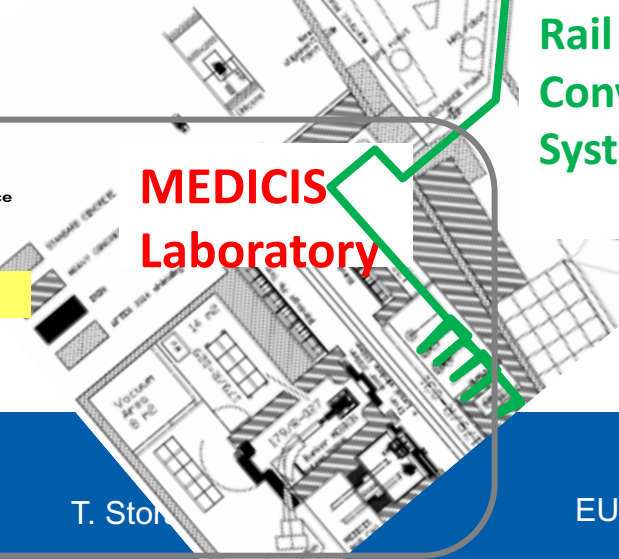


Rail Conveyor System

MEDICIS Laboratory

1000+ isotopes of 70+ chemical elements





Safety clearance and facility permit

CERN-MEDICIS Safety file demonstrative part

PS-CSAP 41st meeting

B. Conde Fernandez on behalf of the
CERN-MEDICIS project and all the contributors

CERN | EN ENGINEERING DEPARTMENT

Safety file demonstrative part timeline

Tentative planning – slide presented > 2 years ago

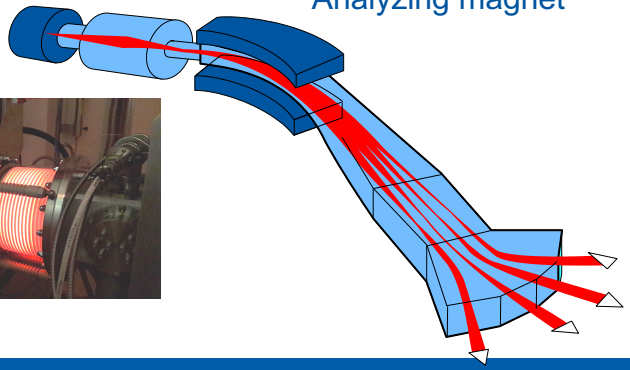
Phase	Action	Date
PHASE I	Commissioning: without beam (*)	2016
PHASE II	Commissioning with beam and light targets to gain operational experience	2017
PHASE II B	Isotope production with light targets	Mid 2017
PHASE III	Extending to heavy targets up to Tantalum	End 2017
PHASE IV	Collection of short lived alpha emitters (e.g. 149Tb)	2018
PHASE IV B	Operation with lasers	2018
PHASE V	Operation with uranium targets/possible proton beam upgrade	2019

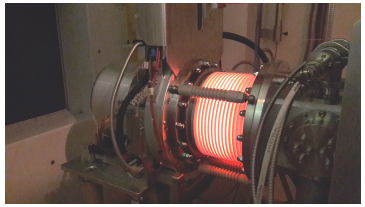
* Preferable but may be hard to achieve

Recent update

1st isotopes produced in ISOLDE HRS beam dump and separated in the lab during commissioning Dec 2017

Analyzing magnet





149/152/155/161Terbium ions collected in metal foils

Large Collaboration with regional and European Institutes

TÉCNICO LISBOA

SCIENCE AND TECHNOLOGY

CTN receives the 1st batch of innovative radioisotopes for medical applications

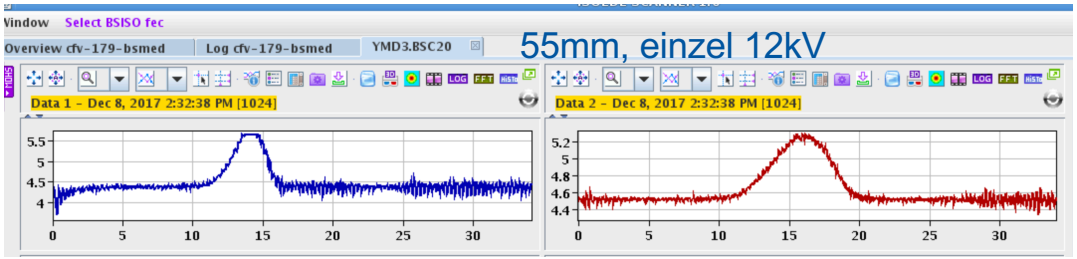
le dauphiné libéré

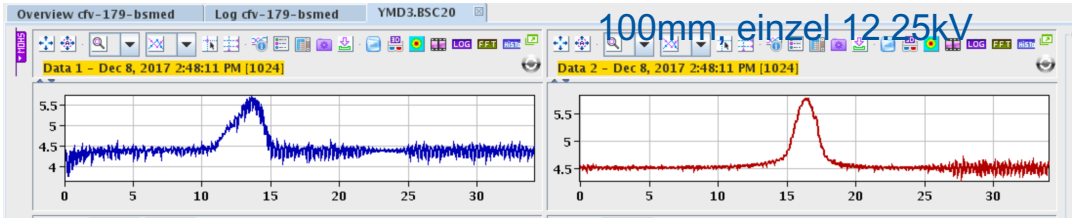
BELLEGARDE & PAYS DE GEX

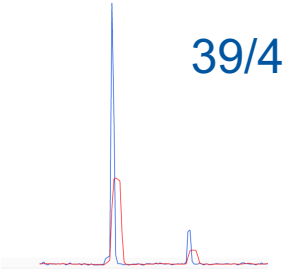
GENEVOIS LE SAVOIR DES PHYSICIENS AU SERVICE DE LA MÉDECINE DE DEMAIN

La lutte anti-cancer se prépare au Cern

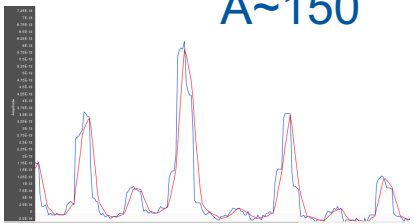
Beam profile : in BI Box





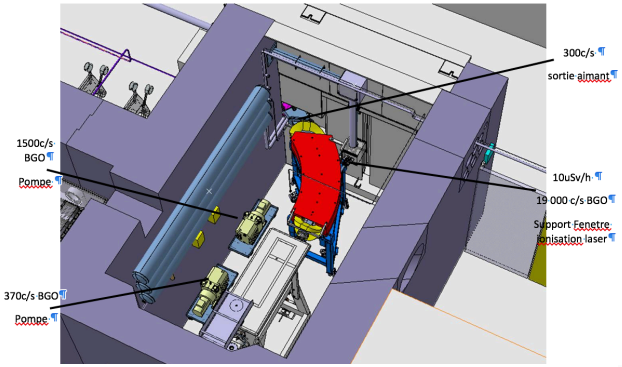


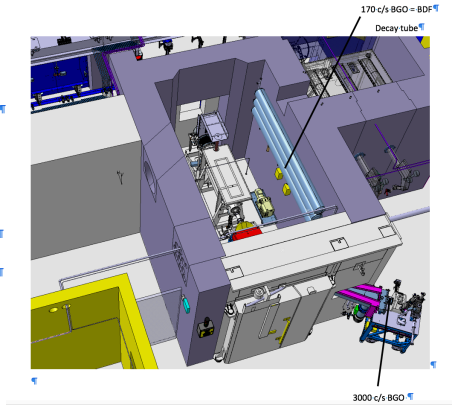
39/41K potassium beams

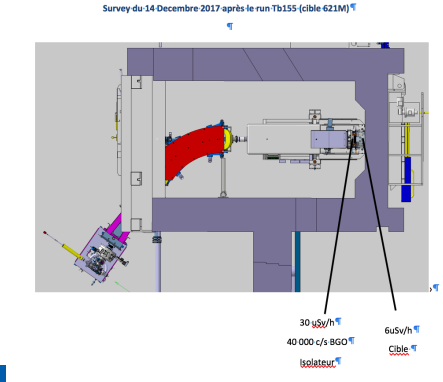


A~150 beams

RP : survey after separator operation







1st MEDICIS Collaboration Board Meeting

Wednesday 21 Feb 2018, 09:00 → 17:00 Europe/Zurich

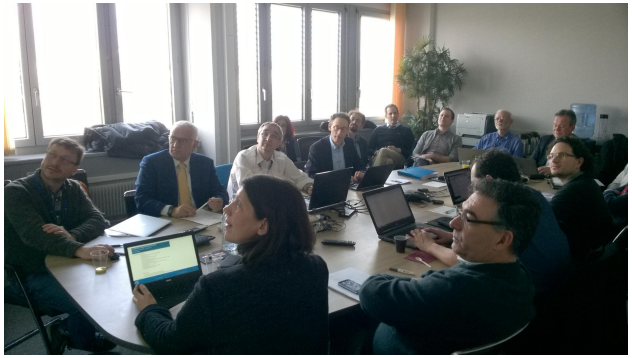
4-3-001 (CERN)

Description **Liste de participants**:

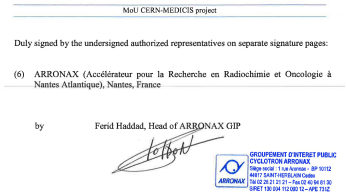
- Thierry Stora (CERN)
- Frédérick Bordry (CERN's Director for Accelerators and Technology)
- Simone Gilardoni (CERN)
- Thomas Elia Cocolios (KULeuven)
- Prof. Oyen Wim (ICR – Institute of Cancer Research, UK)
- Nick van Dermeulen (PSI)
- Antonio Paulo (Instituto Superior Técnico, Portugal)
- Dr. Michel Forni (Hôpital de La Tour, Geneva)
- Prof. Ismael Martel Bravo (FABRIS - Fundación Andaluza Beturia para la Investigación en Salud, Spain).
- Prof. Ferid Haddad (Arronax, France)
- Prof. Klaus Wendt (University of Mainz, Germany)
- Prof. Martin Walter (Head of Nuclear Medicine and Molecular Imaging, Geneva Hospital)
- Gerda Neyens (CERN)
- David Viertl (Lausanne University Hospital Center)
- Dante Gregorio (CERN)
- Tor Bjørnstad (IFE – Institute for Energy Technology, Norway)
- Frank Bruchertseifer (European Commission)

Via remote-connection:

- *Prof. Susanta Lahiri (SINP - The Saha Institute of Nuclear Physics, India)*
- *Dr Martyn Sené (Deputy CEO for the National Physical Laboratory - NPL)*
- *Prof. John Prior Head of Nuclear Medicine and Molecular Imaging, Lausanne University Hospital Center)*



Memorandum of Understanding for the CERN-MEDICIS project at CERN



MoU CERN-MEDICIS project

Duly signed by the undersigned authorized representatives on separate signature pages:

(6) ARRONAX (Accélérateur pour la Recherche en Radiochimie et Oncologie à Nantes Atlantique), Nantes, France

by Ferid Haddad, Head of ARRONAX GIP

GROUPEMENT D'INTERET PUBLIC CYCLOTRON ARRONAX

From the board to a drafted schedule

Number	Date	Institute	Principal investigator	Email	Title
MED001	16-Feb-18	CHUV	Francesco Cicone, MD	francesco.cicone@chuv.ch	Theranostics of 149Tb-labelled antibodies against cancer
MED002	18-Feb-18	PSI	nick van der Meulen, Dr, Cristina Mueller, Dr	nick.vandermeulen@psi.ch	Development of 149Tb and 152Tb production from ISOL targets and its subsequent preclinical and clinical evaluation
MED003	19-Feb-18	HUG	Martin Walter, MD	martin.walter@hcuge.ch	A Terbium-155 labeled nanoparticle platform for imaging-guided drug development
MED004	19-Feb-18	C2TN	Antonio Paulo, Dr	apaulo@tecnico.ulisboa.pt	Clickable Terbium Complexes for Radioimmuno-Imaging & Therapy
MED005	19-Feb-18	C2TN	Lurdes Gano, Dr	lgano@ctn.tecnico.ulisboa.pt	155/161Tb-labeled peptides towards the estrogen receptor for breast cancer theranostics
MED006	19-Feb-18	KULeuven	Thomas Cocolios, Prof	thomas.elias.cocolios@cern.ch	MEDICIS-Promed Contest
MED007	19-Feb-18	KULeuven	Simon Stegemann	simon.stegemann@kuleuven.be	Carbon release study from BN
MED008	19-Feb-18	NPL	Christopher Cawthorne, Dr,Steve Archibald, Prof	C.cawthorne@hull.ac.uk; s.j.archibald@hull.ac.uk	Development of CXCR4-targeted agents for molecular radiotherapy with 67Cu
MED009	19-Feb-18	FABIS (hospital Juan Ramon Jimenez, Huelva)	Carlos Saldago, Dr	josesanchez.oncort@gmail.com	Estudio de Teragnósis con isótopos radiactivos de Terbium en tumores de pulmón
MED010	19-Feb-18	Arronax	Roberto Formento	roberto.formento@cern.ch	Laser ionization yield enhancement of external targets radionuclides production at CERN-MEDICIS
MED011	19-Feb-18	Arronax	Roberto Formento	roberto.formento@cern.ch	Very high specific activity Er-169 production at MEDICIS from external ILL target
MED012	19-Feb-18	Arronax	Roberto Formento	roberto.formento@cern.ch	Large production of Scandium and Terbium at very high specific activity for theranostics applications: combining cyclotron production with off-line mass separation
MED013	20-Feb-18	UNIGE/HUG	Renaud Jollivet Prof/Magda Kowalska Dr		provisional : tests of isotope polarization

TITLE

Authors (Name, affiliation, contact of the Principal Investigator):

Max 2 pages from Introduction to References and Funding

Introduction & background: (state of the art and goal/motivation for the project)

Project description : (detailed description of the project, translational, pre-clinical, imaging, treatment, new method)

Materials and Methods : (planned experiments, where, licences for radioisotopes/animals, timeline)

References and Funding: (literature, funding of project, other projects/grants linked)

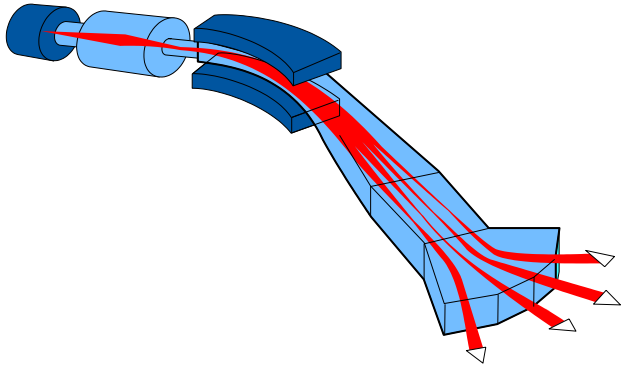
Isotope requests : (which isotope, activity, number of deliveries over period, purity grade)

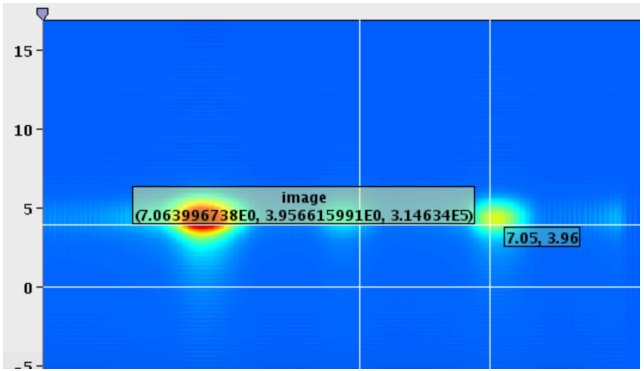
Number	Institute	Principal investigator	Title	Isotope	Activity	Week	Shipping
MED001	CHUV	Francesco Cicone, MD	Theranostics of 149Tb-labelled antibodies against cancer	149Tb or 155Tb	90MBq	25	foil : CERN-->PSI-->CHUV
MED002	PSI	nick van der Meulen, Dr, Cristina Mueller, Dr	Development of 149Tb and 152Tb production from ISOL targets and its subsequent preclinical and clinical evaluation	152Tb	100MBq	23,25	foil : CERN-->PSI
MED003	HUG	Martin Walter, MD	A Terbium-155 labeled nanoparticle platform for imaging-guided drug development	155Tb	200MBq	21	foil : CERN-->NPL-->HUG
MED004	C2TN	Antonio Paulo, Dr	Clickable Terbium Complexes for Radioimmuno-Imaging & Therapy	155Tb	100MBq	20	foil : CERN-->IST
MED005	C2TN	Lurdes Gano, Dr	155/161Tb-labeled peptides towards the estrogen receptor for breast cancer theranostics	155Tb	100MBq	19	foil : CERN-->IST
MED006	KULeuven	Thomas Cocolios, Prof	MEDICIS-Promed Contest			week 21 ?	
MED007	KULeuven	Simon Stegemann	Carbon release study from BN	11C*		26?	no
MED011	Arronax	Roberto Formento	Very high specific activity Er-169 production at MEDICIS from external ILL target	169Er	5MBq	18	168Er target : ILL-->RISO-->CERN

CERN-MEDICIS

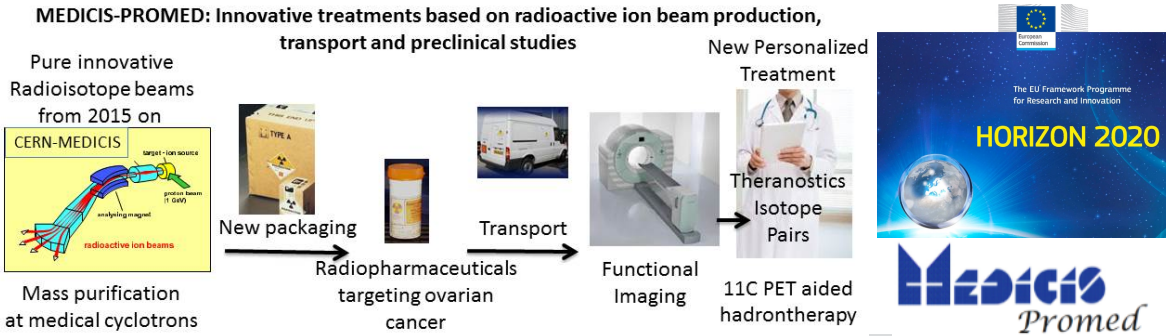
Irradiation for experiment MED004/MED005 on Ta646M target started 18th May
Finished 22nd May; 2.7e18poT (5e18 poT max defined)

Isotope separation for experiment MED011 from external 168/169Er source





Overview of MEDICIS-Promed



MEDICIS_PROMED training network

Coordination Dr. T. Stora, CERN — Medical coordination : PhD, MD J. Prior, CHUV

"Timely Innovations"

WP3 : theranostic pharmaceuticals/surgery for new ovarian cancer personalized treatment

Terbium isotope theranostic pairs
Biological targets for ovarian cancers

- **AAA (FR) lead- radiopharmaceuticals - ESR6**
- IST (PT)/dna targetting - ESR8
- CERN MEDICIS (EU)/molecular break-up - ESR1
- *HUG (CH)/surgery - ESRCH3*
- *CHUV(CH)/preclinical tests - ESRCH2*

"Timely Innovations"

WP 1 : mass separation of new medical isotopes

- Graphene — **JOGU (DE) lead - laser purification - ESR5**
- CERN-MEDICIS — UNI MANCHESTER (UK)/adv material- ESR4
- Ti:Sa Ion sources — CERN MEDICIS (EU)/ production safety - ESR2
- Lemer-Pax (FR) /transport - ESR10
- α-isot. Transp. — IST (PT)/nanofibers - ESR7

WP 2 : Pet aided 11C hadrontherapy

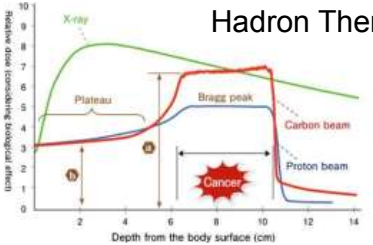
- **CNAO (IT) lead - 11C hadrontherapy - ESR9**
- KUL (BE) - mass sep 11C - ESR11
- CERN MEDICIS (EU) - 11C acceler. - ESR3
- *HUG (CH) - imaging tests -ESRCH1*
- *EPFL (CH) - biochemical synthesis - ESRCH4*
- *Medaustron (AT) - hadrontherapy*

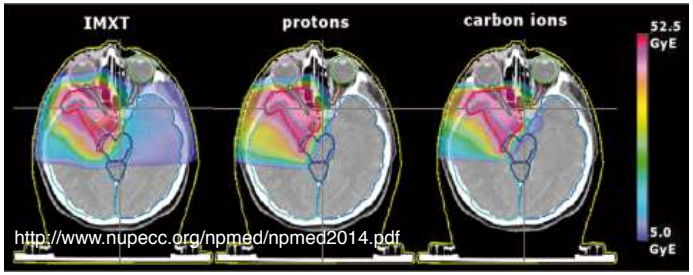
"Timely Innovations"

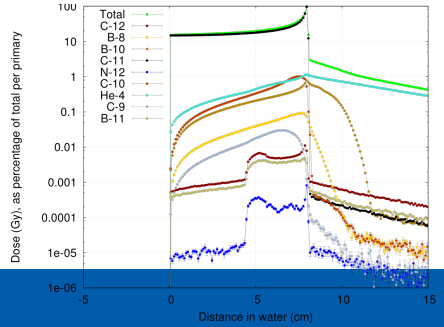
Medaustron animal models

^{11}C Beams for combined PET/Hadron therapy

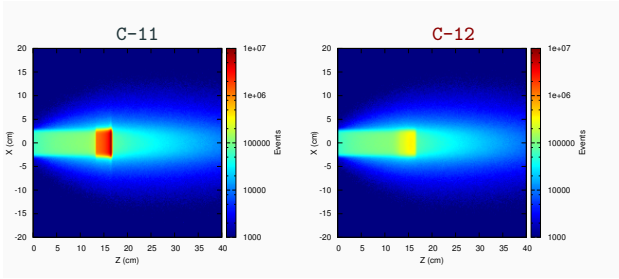
Hadron Therapy

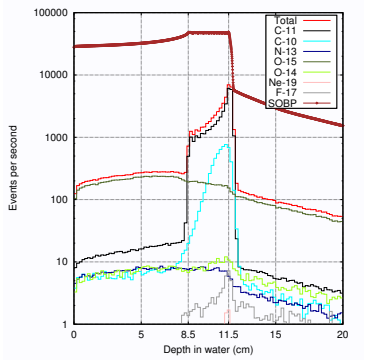






Comparison of
in-beam PET with fragment 12C (11C, 15O)
and direct 11C use





R. Augusto et al.

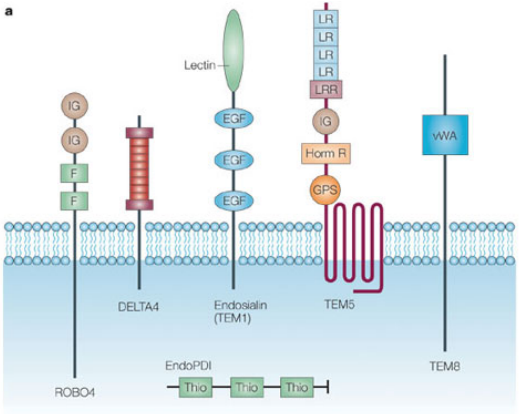
The Target : Tumor Endotelial Marker-1 (TEM1)

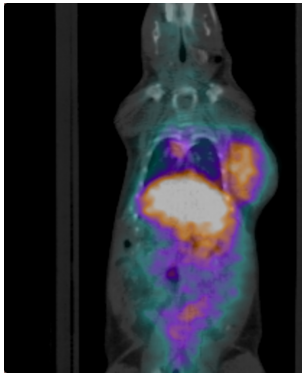
Overexpressed by:

Tumor Vessels

Tumor cells

Host microenvironment (fibroblasts, pericytes)





Morab 0004 (Clinical phase 2)

scFv78-Fc (78Fc)

full IgG anti-TEM1

Cicone F et al.

Towards High Isotope Separation Efficiencies

MEDICIS Promed

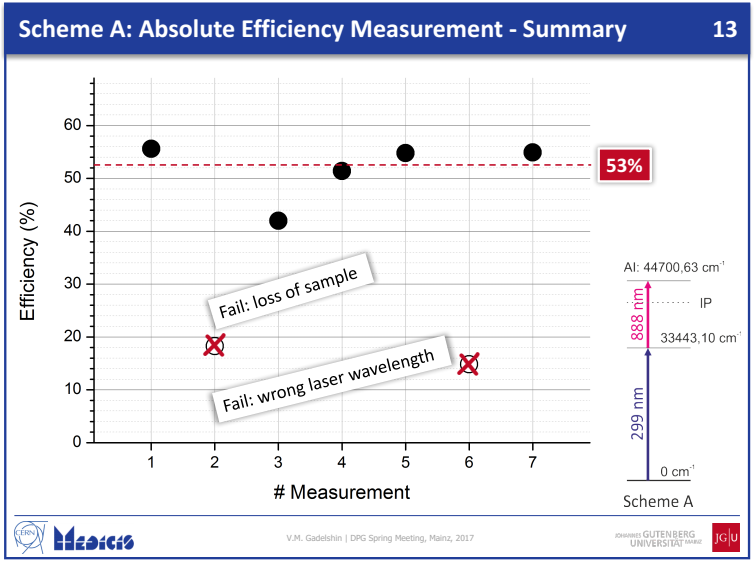
JOHANNES GUTENBERG UNIVERSITÄT MAINZ

Laser Resonance Photoionization Spectroscopy on Lutetium within the MEDICIS project

V. Gadelshin[1], R. Heinke[1], T. Kieck[1], B. Marsh[2], P. Naubereit[1], S. Rothe[2], T. Stora[2], D. Studer[1], and K. Wendt[1]

[1]Institute of Physics, University of Mainz, Germany
[2]EN Department, CERN

LARISSA



Thank you

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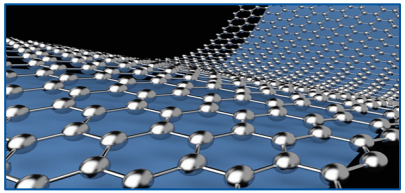
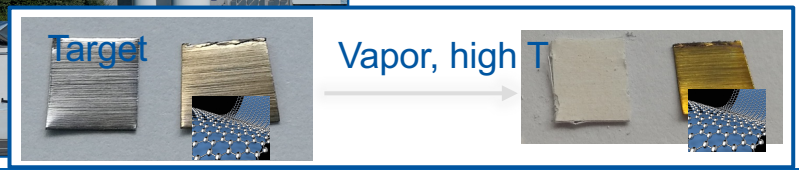
(soon : https://medicis.cern)

Training in Manchester
with prof. Kostya Novozelov





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