

Wider Horizons for Pharmacists

Radiopharmacy

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Radiopharmacy?



Radiopharmacy!



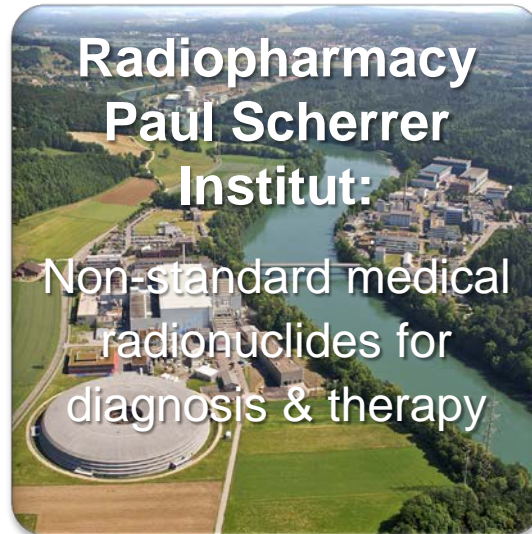
- **Radiopharmacy** (= **Nuclear pharmacy**) is a branch of pharmacy, which deals with the preparation, characterization and quality of **radioactive materials for use in nuclear medicine procedures**
- A **Radiopharmaceutical** (*radiotracer, tracer*) is a radioactive compound for diagnosis and therapy of human diseases.

The Center for Radiopharmaceutical Sciences (CRS)

- ❑ Founded 1997 (PSI-USZ); 2005 (ETH); 2010 new Head
- ❑ Ca. 50 FTE (Prof., PhD, PostDocs, PhD students, staff)



Dept. Chemistry and
Applied Biosciences



Department of
Biology and
Chemistry



Dept. for Nuclear
Medicine

The Radiotracer Principle

- A radioactive tracer is a chemical compound in which one or more atoms have been replaced by a radioisotope. It is applied in minimal amounts, therefore, it has no pharmacologic effect in vivo. It can also be used to explore the mechanism of bio-/chemical reactions by tracing the path that the radioisotope follows from reactant to product



George de Hevesy

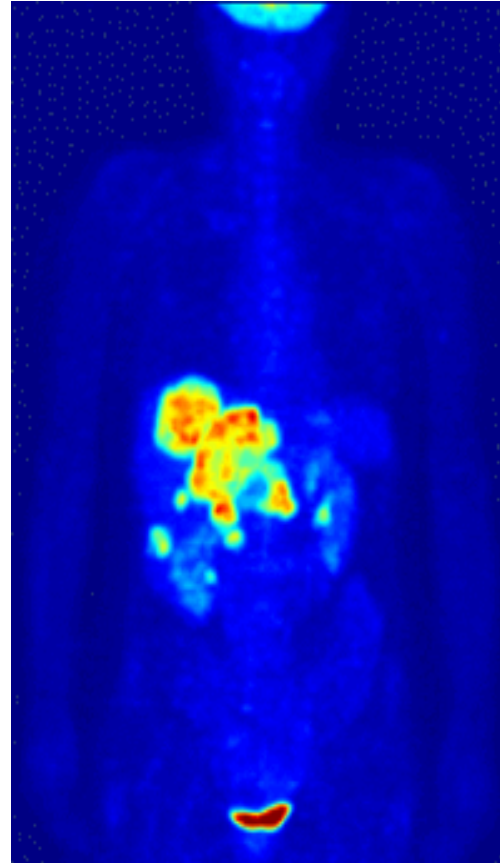
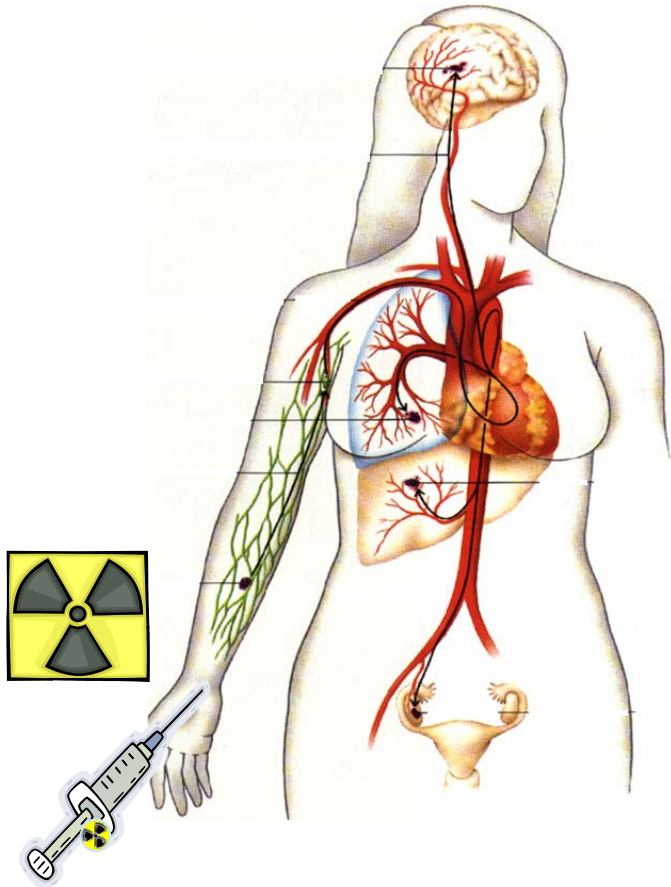
Noble Prize (1943): „...“for his work on the use of isotopes as tracers in the study of chemical processes” “

General Design of a Modern Radiopharmaceuticals


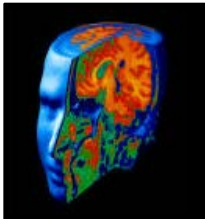
Radioactive part	Non-radioactive part
<p>Radionuclide</p> <p>Defines the physical parameters such as physical half-life (${}^{\text{phy}}T_{1/2}$) and type of radiation for diagnosis or therapy</p>	<p>Chemical and/or biological part</p> <p>Defines the biological parameters such as biological half-life (${}^{\text{biol}}T_{1/2}$) and specificity</p>



Principles of Nuclear Diagnosis



Spectrum of Imaging Techniques

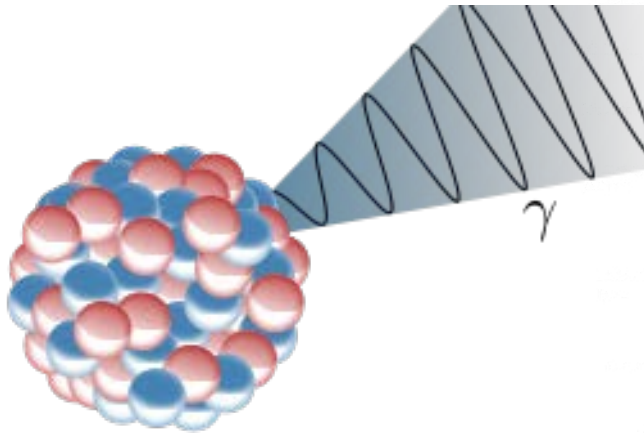
Imaging Method	Spatial resolution	Sensitivity		
Ultrasound	50 μm	10^{-3} Mol		Morphology
CT	50 μm	10^{-3} Mol		
MRI	100 μm	10^{-5} Mol		
Bioluminescent	1-3 mm (depth!)	10^{-8} Mol		Function
Nuclear*	> 5 mm	10^{-9}-10^{-12} Mol		

E.g. 370 MBq of ^{11}C -tracer necessary for a brain scan with $^{11}\text{CPIB}$ corresponds to 100 picogram total mass injected.

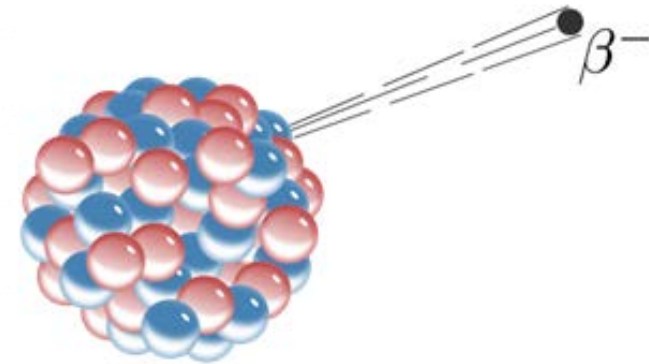
Radiopharmaceuticals are also Role Models for «Theragnostics»

Diagnosis and Therapy with one and the same method

Diagnostic
isotopes



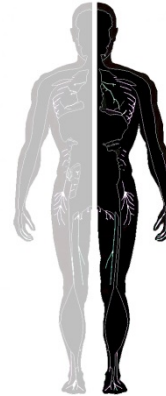
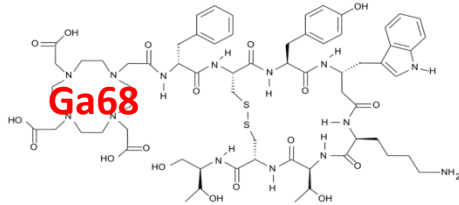
Therapeutic
isotope



«Theragnosis» of Neuroendocrine Tumors

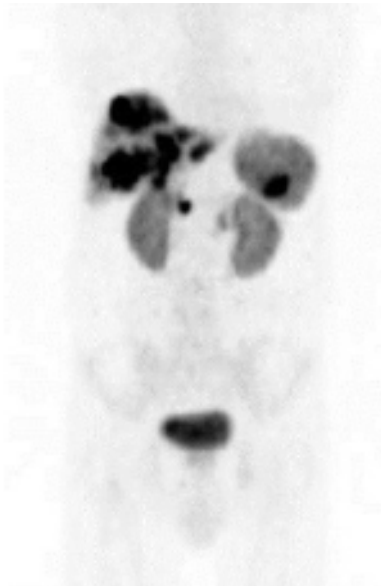
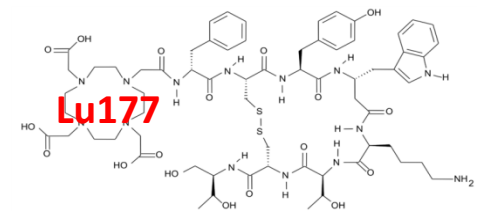
Diagnostics

68 Gallium – DOTATATE

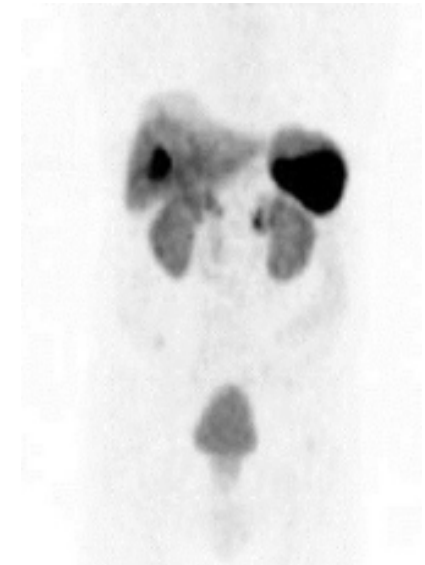
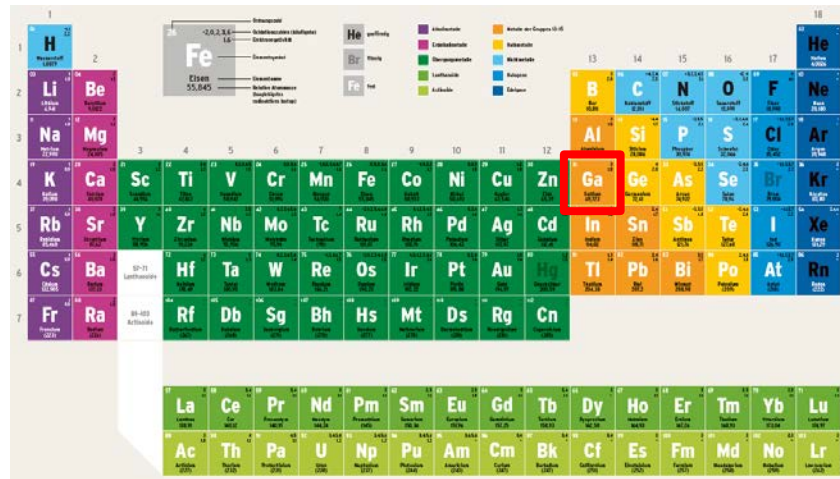


Therapy

177 Lutetium – DOTATATE



PET/CT pre therapy

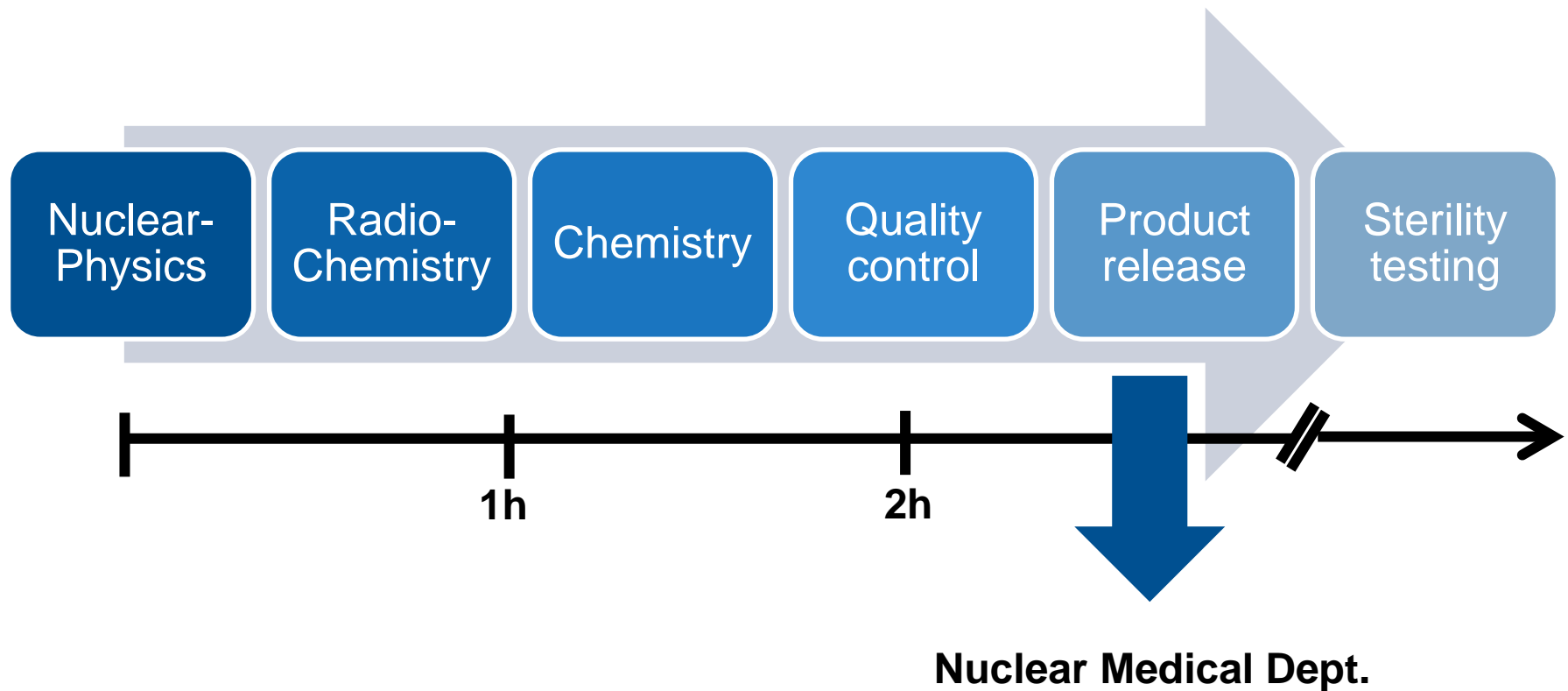


PEI/CT post therapy

Baum RP et al. THERANOSTICS: From Molecular Imaging Using Ga-68 Labeled Tracers and PET/CT to Personalized

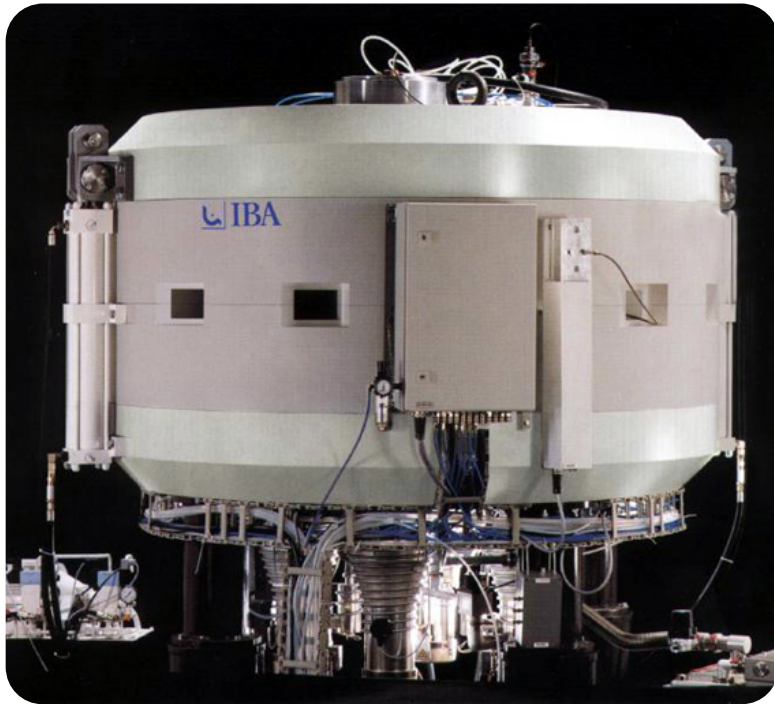
Radionuclide Therapy. Theragnostics. 2012

Preparation of Radiopharmaceuticals: *Daily* a multidisciplinary endeavor



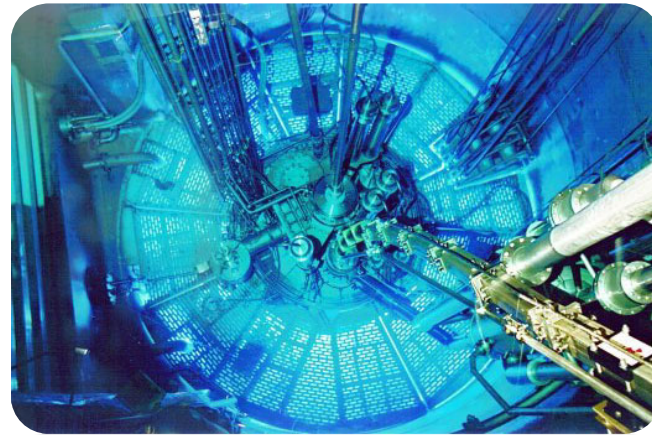
Radionuclide Production

Cyclotron



E.g.: C-11, N-13, O-15
F-18, Cu-64, In-111, I-123

Reactor: Neutron bombardment



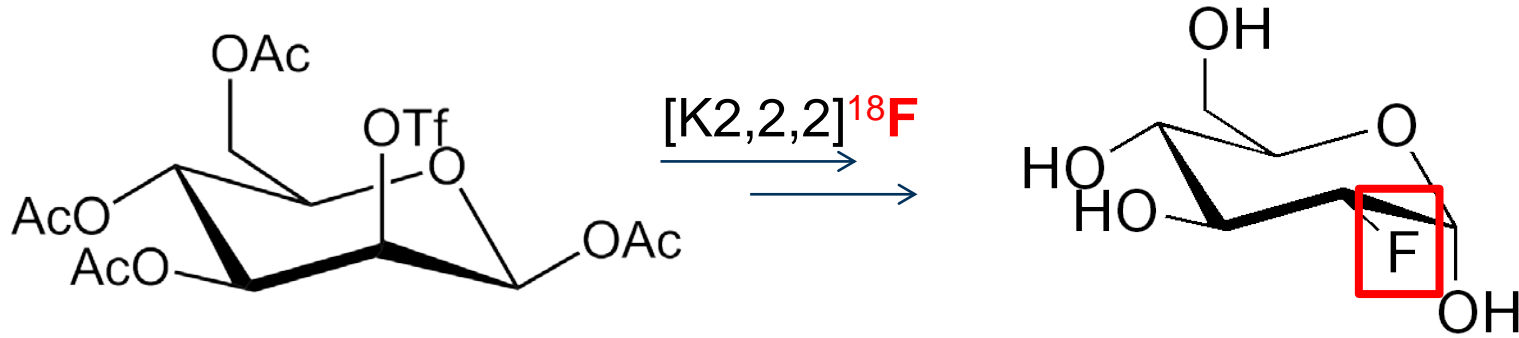
E.g.:
I-131
Sm-153
Ho-166
Lu-177
W-188

On-site generators

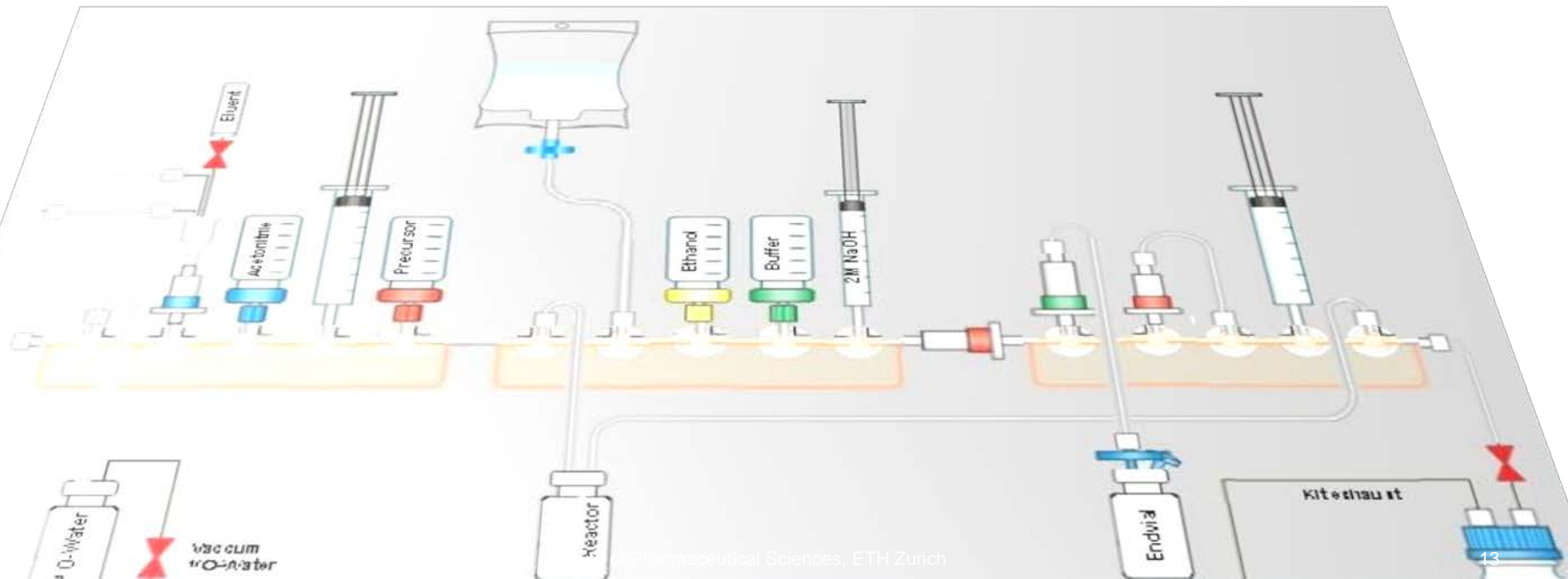


E.g.:
Ga-68
Tc-99m
Re-188

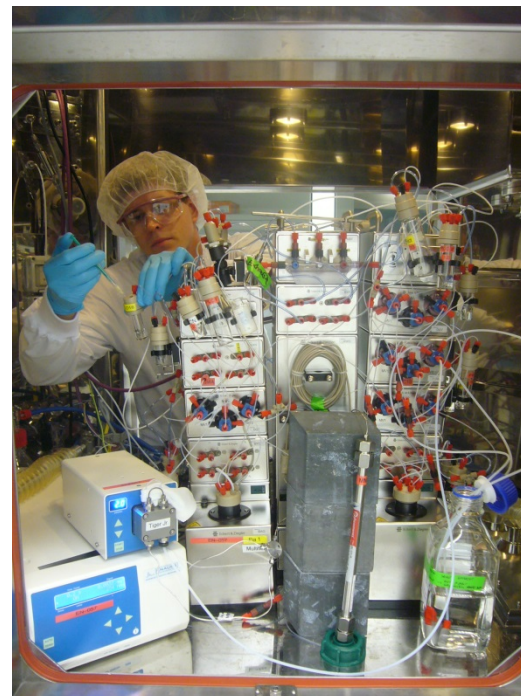
Radiosynthesis of [^{18}F]-2-Fluorodesoxy-glucose (FDG)



Mannose

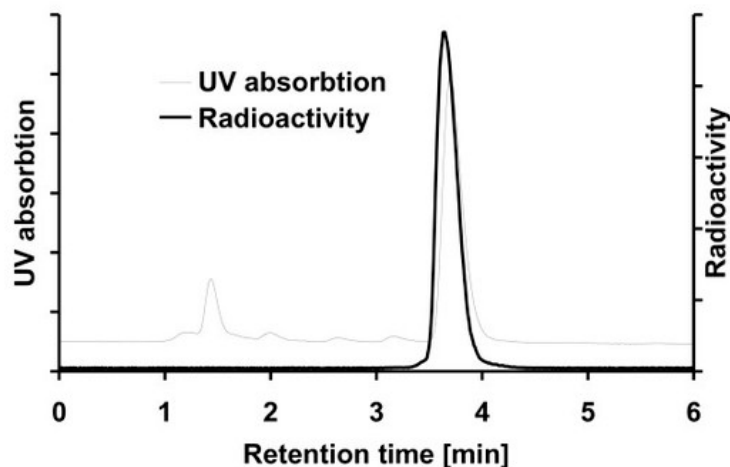
[^{18}F]-2-Fluorodesoxy-glucose (FDG)

Synthesis of Radiopharmaceuticals according to GMP



Quality Control of Radiopharmaceuticals

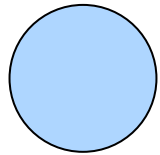
- Isotope purity & Radionuclide identity
- Dosage of radioactivity
- Radiochemical purity
- Chemical purity
- Sterility
- Apyrogenicity
- Visible purity
- pH



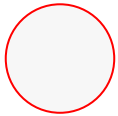
Important β^+ Emitters in Radiopharmacy

Radionuclide	$T_{1/2}$	Mean β^+ energy (keV)	Resolution (mm)
^{11}C	20 min	386	1.1
^{15}O	2 min	735	1.5
^{18}F	110 min	250	0.7
^{64}Cu	12.7 h	278	0.7
^{68}Ga	1.1 h	830	2.4
^{76}Br	16.3 h	1180	3.2
^{124}I	4.17 d	820	2.3
^{89}Zr	3.27 d	396	1.1

From *decentralized* to *centralized* production: Logistic & Commercial Challenges for Radiopharmacies



= optimal radius for ^{44}Sc ($T_{1/2} = 3.9$ h)



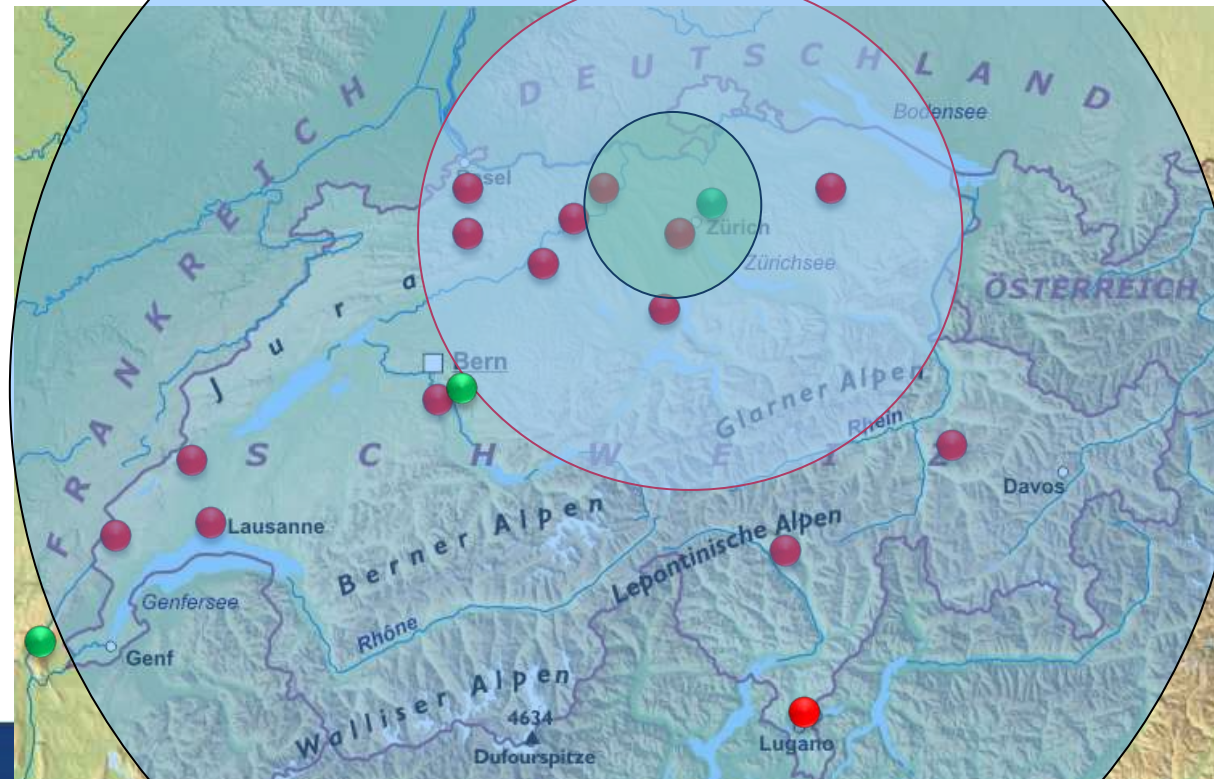
= optimal radius for ^{18}F ($T_{1/2} = 110$ min)



= optimal radius for ^{68}Ga ($T_{1/2} = 68$ min)

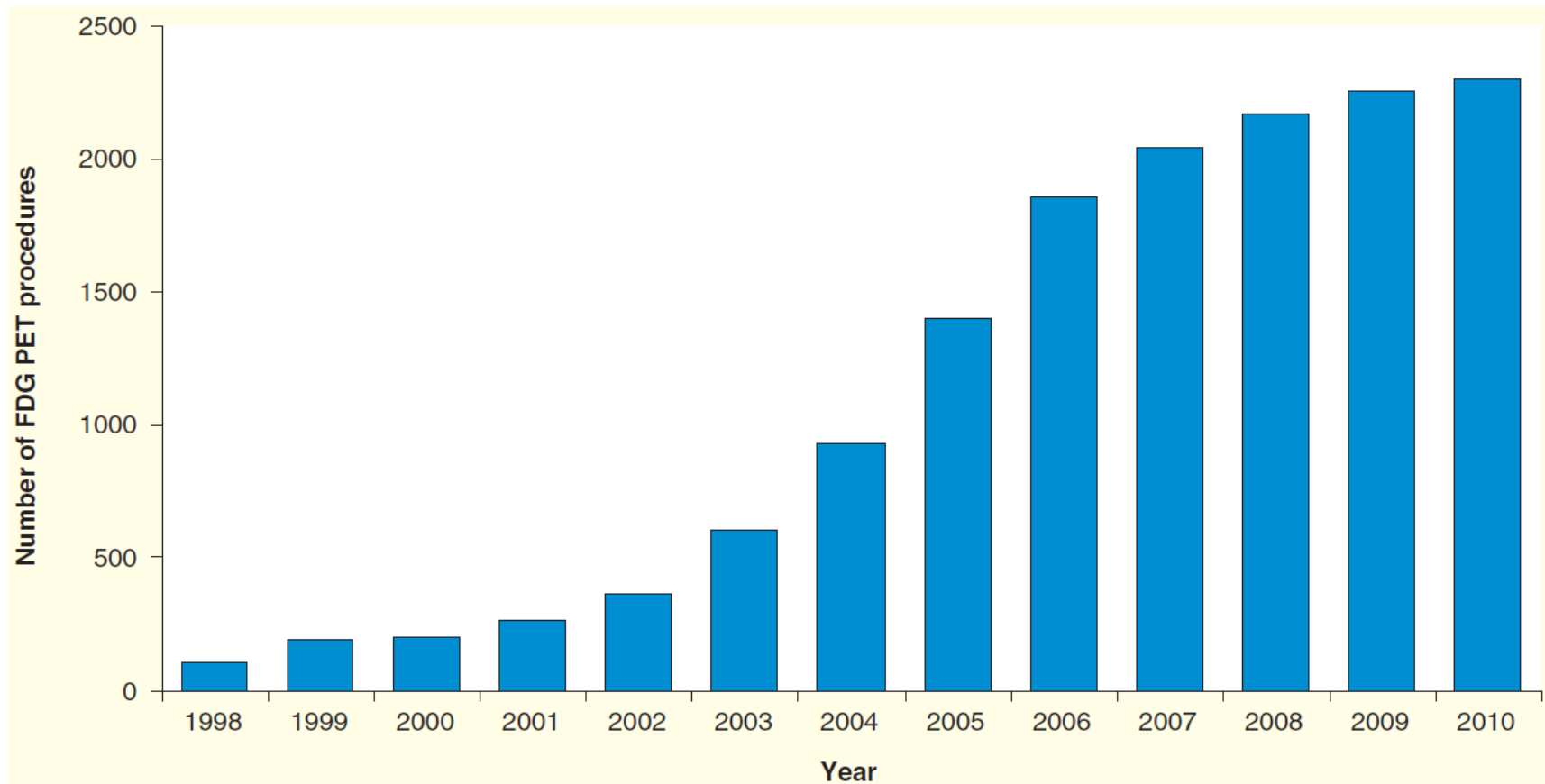
● Nucl. Med. Dept.

● Rad. Pharm. with cyclotron

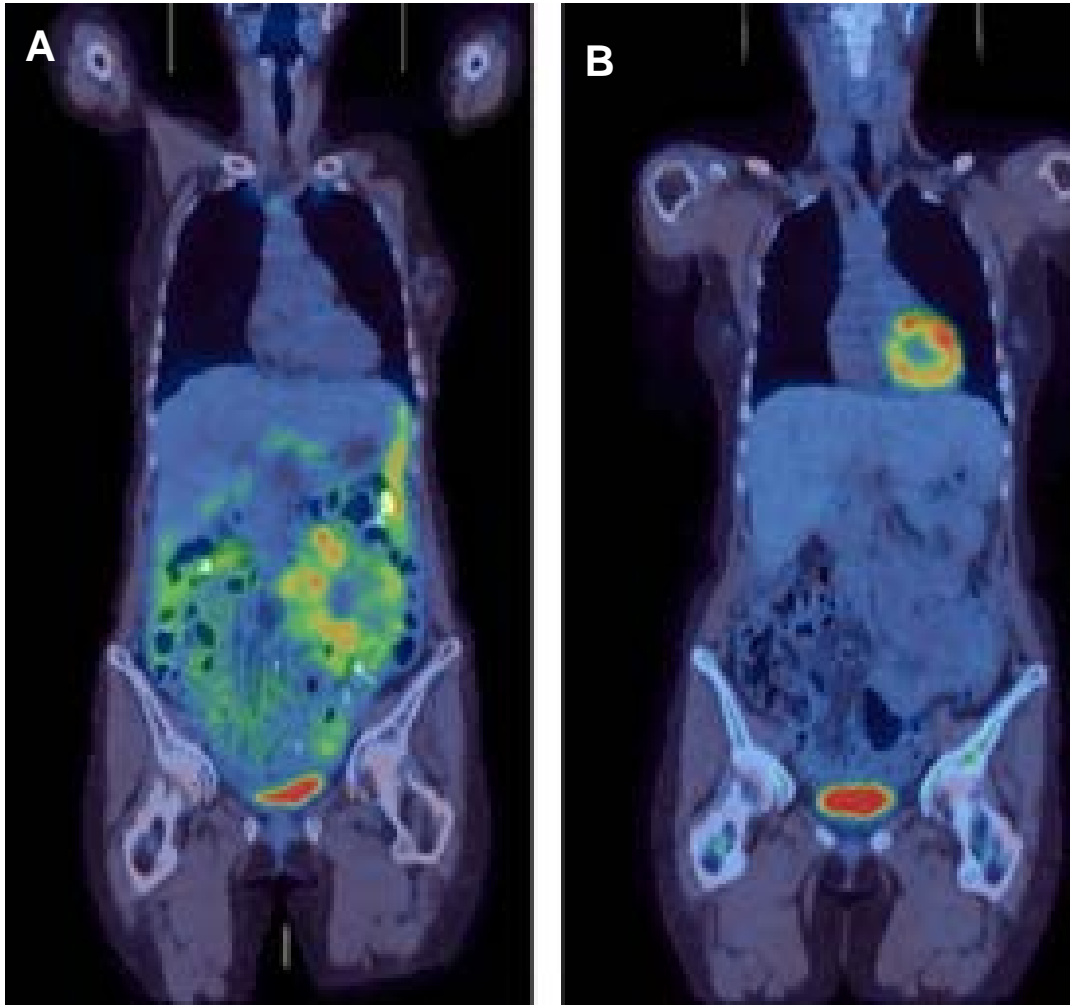


[¹⁸F]-FDG: The Working Horse in Nuclear Medicine

- Number of [¹⁸F]-FDG scans in the USA(x1000)



Combination of Functional and Morphological Imaging (PET/CT) Changed the Patient Care in Medicine

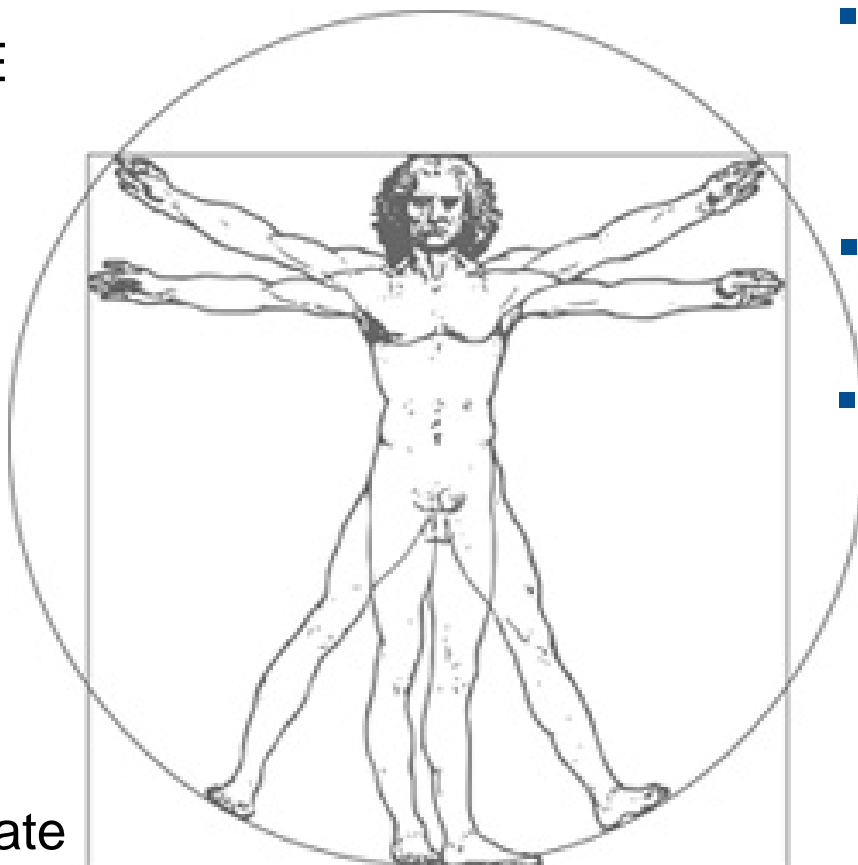


[¹⁸F]-FDG/CT:

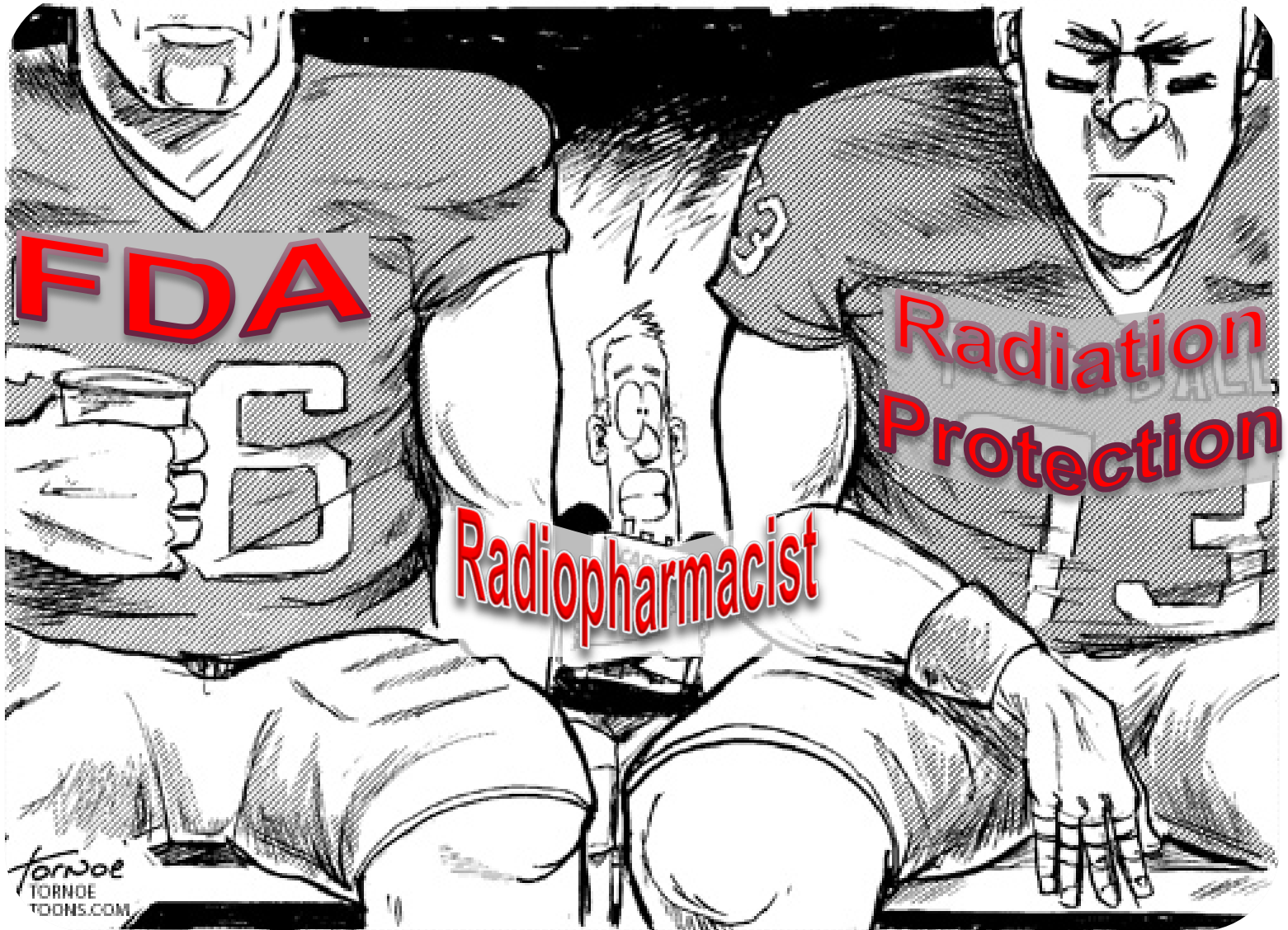
(A) At staging, patient with diffuse large B-cell lymphoma
(B) Interim scanning after 2 cycles of chemotherapy showed complete response.

Clinically Approved Radiotracer Daily Produced

- ^{68}Ga -DOTATATE
- ^{177}Lu -DOTATATE
- ^{90}Y -Zevalin
- Na^{18}F
- ^{18}F -FDG
- ^{18}F -Choline
- ^{18}F -DOPA
- ^{18}F -FET
- ^{11}F -Flutametamol
- ^{15}O - H_2O
- ^{13}N - NH_3
- $^{99\text{m}}\text{Tc}$ -Pertechnetate
- $^{99\text{m}}\text{Tc}$ -MDP



- $^{99\text{m}}\text{Tc}$ -Nanocol
- $^{99\text{m}}\text{Tc}$ -MAG3
 - $^{223}\text{RaCl}_2$
- $^{99\text{m}}\text{Tc}$ -HMPAO
- $^{99\text{m}}\text{Tc}$ -EDC
- ^{153}Sm -EDTMP
 - Na^{131}I
- ^{131}I -MIBG
- ^{131}I -Bexxar
- ^{18}F -MISO
 - ...



There are Master and Post Graduate Courses in Radiopharmacy

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Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich
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College
LONDON

Radiopharmaceutics & PET Radiochemistry | MSc, PG Dip and PG Cert | Part Time, Full Time | Admissions status: Open

Overview Details Structure Entry requirements Applying, fees & funding Further information

Printer friendly version

The training provided by the Radiopharmaceutics & PET Radiochemistry MSc programme will equip you to work as a radiopharmaceutical scientist in a PET diagnostic and therapeutic radiopharmaceuticals to nuclear medicine centres or to study for a PhD.

KEY BENEFITS

- The only MSc level course in PET Radiochemistry subject worldwide.
- Includes a one-week work experience placement in a hospital, PET centre or industrial cyclotron centre.
- Multidisciplinary programme open to graduates in various science disciplines: chemists, bio-scientists, physicists, pharmacists.
- Located in the heart of London.

KEY FACTS

Programme leader/s
Professor Philip Blower
Awarding institution
King's College London
Pathways
Two paths of study are offered: 1. PET Radiochemistry (modules 1, 2, 3a, 4a and 5), suitable for those interested in a research career in the field or work in a PET radiochemistry centre; 2. Radiopharmaceutical Science (modules 1, 2, 3b, 4b and 5) to suit those interested in a career in hospital radiopharmacy. Certificate and diploma pathways are available. Credit value (UK/ECTS equivalent) UK 180/ECTS 90
Duration
One year FT, two years PT, September to September.
Location
St Thomas' and Waterloo campuses.
Research projects and work placements may be at other locations.
Student destinations
Expected destinations are the NHS and commercial nuclear medicine services, the pharmaceutical industry or PhD research.
Year of entry 2014
Offered by
School of



«Radiopharmaceutical Chemistry» is a mandatory part of the ETH Bachelor Pharmacy curriculum (2 ECT)

Swiss Federal Institute of Technology Zurich. The institute is devoted to cutting-edge prototypes for tomorrow's diagnostics and therapeutics. Teaching in pharmaceutical science enables graduates to assume positions of responsibility in all areas of the pharmaceutical industry.



Pharmaceutical Biology
Prof. Karl-Heinz Altmann



Pharmaceutical Chemistry
Prof. Jonathan Hall



Pharmacogenomics
Prof. Michael Datmar



Pharmacology
Prof. Hanns Ulrich Zeilhofer



Radiopharmaceutical Sciences
Prof. Roger Schibli
Prof. Simon Ametamey
PD Dr. Stefanie Krämer (Biopharmacy)

Accreditation of Courses by the European Soc. Nuclear Medicine

POSTGRADUATE CERTIFICATE COURSE IN RADIOPHARMACEUTICAL CHEMISTRY/RADIOPHARMACY

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Radiochem/Radiopharm

Postgraduate Certificate Course in Radiopharmaceutical Chemistry/Radiopharmacy

The ETH Zurich as one of the world's leading universities for technology and natural sciences offers a unique postgraduate program in Radiopharmacy. This comprehensive training enables **natural scientists and pharmacists** to assume **responsibility for both production and quality control of radiopharmaceuticals**. The program is held in cooperation with the universities of Ljubljana (Slovenia) and Leipzig (Germany) and provides essential knowledge in

- radiopharmaceutical chemistry,
- drug legislation,
- quality control,
- pharmaceutical technology,
- pharmacology
- nuclear medicine.

Graduates will achieve the ETH degree "**Certificate of Advanced Studies (CAS) in Radiopharmaceutical Chemistry / Radiopharmacy**". The course contents follow the guidelines of the **European Association of Nuclear Medicine EANM**, which recognises the program as theoretical part of the **SPAC** in **Radiopharmacy**.

[> register now for Module III, Aug/Sept 2014, Leipzig, Ger](#)

ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

UNIVERSITÄT LEIPZIG

University of Ljubljana
Faculty of Pharmacy

CAS RADIOPHARMACY
Radiopharmaceutical Chemistry

European Training Program 2013/2014
Recognized by European Association of Nuclear Medicine (EANM)

ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

former participants



Prof. T. Gmeiner Stopar



Prof. M. Schulz-Siegmund

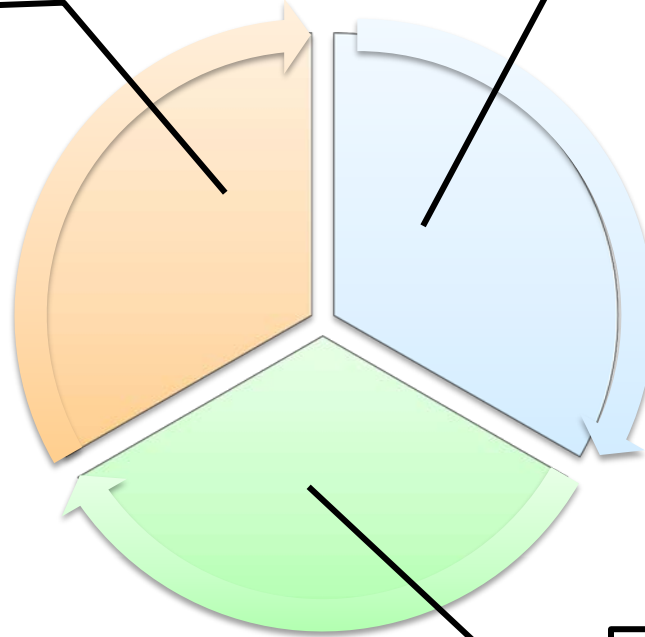
Post-Graduate Course in Radiopharmacy in Europe

Completed a nationally acceptable course on radiation safety.

University postgraduate diploma courses (three modules à 2 weeks)

Open for pharmacists, chemists, biochemists and biologists (min. Master level)

Completed a two-year period of experience in a radiopharmacy



Content of the Post Graduate Course

Block 1: Pharmacy (Uni. Ljubljana)

- Pharmaceutical Technology
- Implications of GMP
- Sterile Manufacture
- Pharmaceutical microbiology
- Parenteral Products
- Formulation and Packaging
- Pharmaceutical Analysis
- Pharmacopoeia monographs
- Quality Control Procedures
Stability and Shelf Life
- Biopharmacy (Pharmacokinetics,
membrane transport,
biodistribution, metabolism)
-

Radiopharmaceutical chemistry

- Physics of radioactivity
- Production of radionuclides in
nuclear reactor and cyclotron
- Targetry, nuclear chemistry,
generators
- PET - radiopharmaceuticals (^{18}F ,
 ^{11}C , ^{13}N , ^{15}O)
Synthesis of labelled compounds
- Bioconjugation chemistry
- Radionuclides in analytics,
autoradiography
- $^{99\text{m}}\text{Tc}$ -radiopharmaceuticals
- Animal models
- ...

Content of the Post Graduate Course & Conditions for EANM Certificate

Block 3: Clinical Radiopharmacy

Practical Components (2 years)

- Working in a sterile environment
- Design and application of a quality assurance program
- Use of safe radiation practices,
- Use, maintenance and calibration of equipment used in radiopharmacies
- Procurement of Radiopharmaceuticals
- Radiopharmaceutical preparation
- Quality control of radiopharmaceuticals
- Supply of radiopharmaceuticals
- ...

The screenshot shows the website of the European Association of Nuclear Medicine (EANM) Radiopharmacy Committee. The page is titled 'Specialisation in Radiopharmacy' and lists the following topics:

- » European specialisation
- » Status of the certificates
- » Mechanism for award of the certificate
- » Radiopharmacy courses
- » Appendix I
- » Block 1: Pharmacy
- » Block 2: Radiopharmaceutical chemistry
- » Block 3: Associated topics
- » Appendix II
- » Appendix III
- » Appendix IV

The page also includes a sidebar with navigation links: Members, Education >, Reporting Schemes, Communication, Specialisation, Guidelines & Activities >, Links, Reports, National Advisors, and IMPDs.

The main content area contains the following text:

European specialisation certificate in radiopharmacy
The Radiopharmacy Committee of the European Association of Nuclear Medicine (EANM) has established a European post-graduate specialisation certificate in Radiopharmacy. A certificate after successful attendance may be awarded to participants, who, in the view of the EANM Radiopharmacy Board, are suitably qualified, in that they have

1. Acquired a university postgraduate diploma through attendance at appropriate courses teaching the theoretical components of the radiopharmacy syllabus (listed in Appendix I)
2. Completed a two-year period of experience in a radiopharmacy department during which they have completed the practical components of the syllabus (listed in Appendix II), if there is uncertainty if the 2 year on the job experience is adequate, the candidate should contact the committee chairman; a board member will be assigned, who will find a solution together with the candidate.
3. Completed a nationally acceptable course on radiation safety

Status of the certificate
Award of this certificate means that in the view of the EANM, the individual has acquired the knowledge and practical experience needed for them to assume responsibility for the design and quality control of radiopharmaceuticals. At the present time, this is the hope of the Association that it will, in time, be possible to state as the appropriate qualification for those

Radiopharmacists are national and international organized in Societies



SOCIETY OF Radiopharmaceutical Sciences

The Society of Radiopharmaceutical Sciences (SRS) is at the heart of all nuclear imaging, radiopharmaceuticals, and can be used in vivo to trace (follow) a particular physiological process.

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WELCOME TO THE WEBSITE OF THE SOCIETY OF RADIOPHARMACEUTICAL SCIENCES

Our primary goal for this website is to make it accessible to non-members. Some content is accessible to members only. Access to the site through the authentication area at the top right of the site requires an e-mail address and password are required.

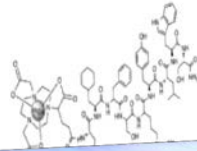
Non-members are invited to browse all but the authentication area. For more information about the SRS, including the 15th International Symposium on Radiopharmaceutical Chemistry (WTTC15), the 2nd International Symposium on Radiopharmaceuticals in Chemistry and Medicine (TECHM2), and the 10th International Symposium on Radiopharmaceuticals (ISRP10), please visit the website.



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Action to Plan
Jubilant Dose
wide pricing
sustainable
February 2012
**97th Canadian
Information**



Canadian Association of Radiopharmacists **VirRAD Community**

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Forums
18F-FCH automated preparation
Have your say on the future of the VirRAD platform
A replacement for ITLC?



Events
Upcoming event: 16th European Symposium on Radiopharmacy and Radiopharmaceuticals, April 26-29th, 2012, Nantes, France
Deadline for Abstracts: December 5, 2011
.....more

Dear Friends,
Welcome to VirRAD - your WWW link to the Global Radiopharmacy Community.
I hope you find system helpful and informative. Please don't hesitate to contact us with any comments and questions.
Kind Regards, Steve Mather

Summary & Conclusion

- Radiopharmacy and radiopharmaceutical preparation is multi-disciplinary endeavor
- There is a clear trend from decentralized to centralized radiopharmaceutical production with qualified personnel in qualified environment due to increasing regulations
- Pharmaceutical, (radio)chemical and radiophysical/ radiation protection know-how is essential
- Education of radiopharmacists is necessary at the University level (master or higher) to cope with complexity
- International standards have to be achieved to shape the future of radiopharmacy

Acknowledgment

- President of Scientific Committee (Prof. Dr. Borut Božič)
- Prof. Irena Mlinarič-Raščan
- Prof. Prof. T. Gmeiner Stopar

- Dr. Angela Küng & Regular Furegati (ETH)

University of Ljubljana
Faculty of *Pharmacy*



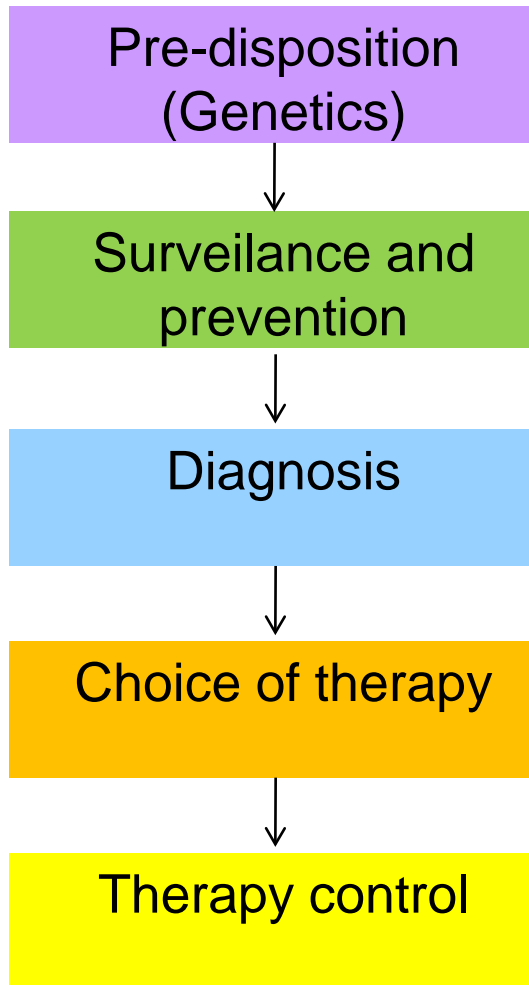
EAFP

**EUROPEAN ASSOCIATION OF
FACULTIES OF PHARMACY**



Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Radiotracer and radiopharmaceuticals play an important role in personalized medicine



■ Diagnosis & Therapy control

- Protein expression (receptors, enzymes)
- Protein function (transport, metabolism)
- Assessment of biological function (e.g. blood flow)

■ Drug development

- Efficiency
- Pharmacokinetics

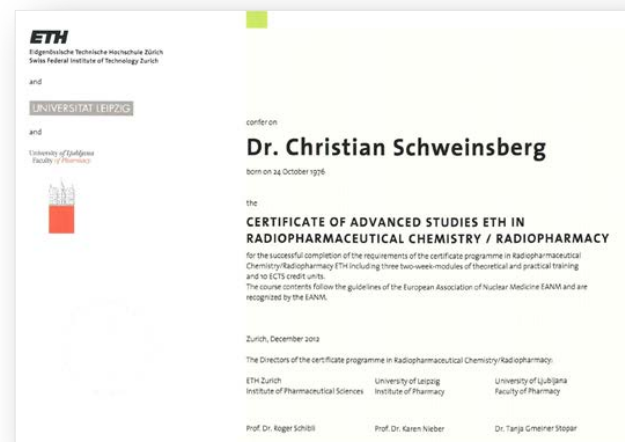
■ Therapy

- Optimize therapy of specific cancer

Examinations and certificates 2011/12

	Module	Module II	Module III
participants	28	26	21
examinees	26	22	20
examination centers	7	6	10
success rate	100 %	100 %	100 %
graduates of CAS	6	2	9

17 graduates at present cycle



Financial aspects

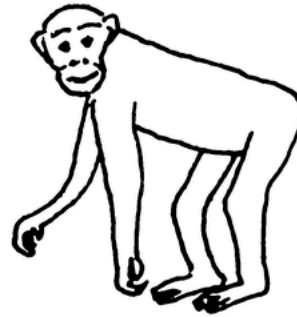
Costs for entire CAS program

Study fees payable to ETH “Schulgeld”	CHF 17'400.-
Advisory board meeting	CHF 3'500.-
Promotion (Advertisement, Flyers, Mailing, Website)	CHF 6'000.-
ETH visit of partner university during course	CHF 2'000.-
total	CHF 28'900.-

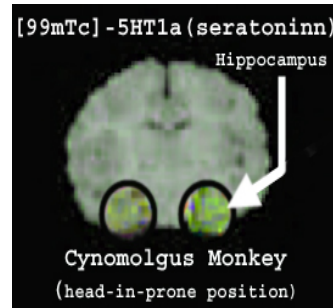
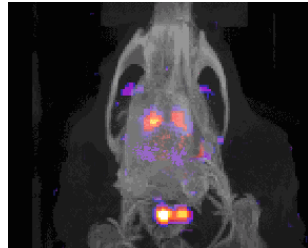
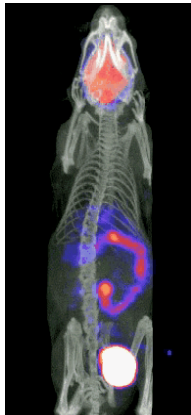
(occurring biannually, based on 30 participants)

Imaging from Mice-to-Men

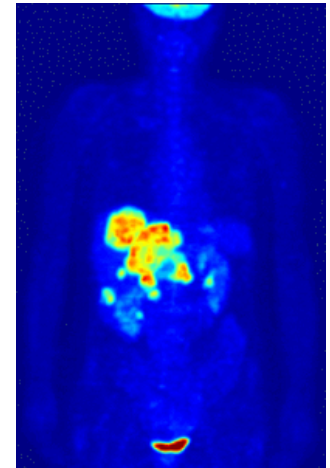
Imaging across the scale



Pre-clinical



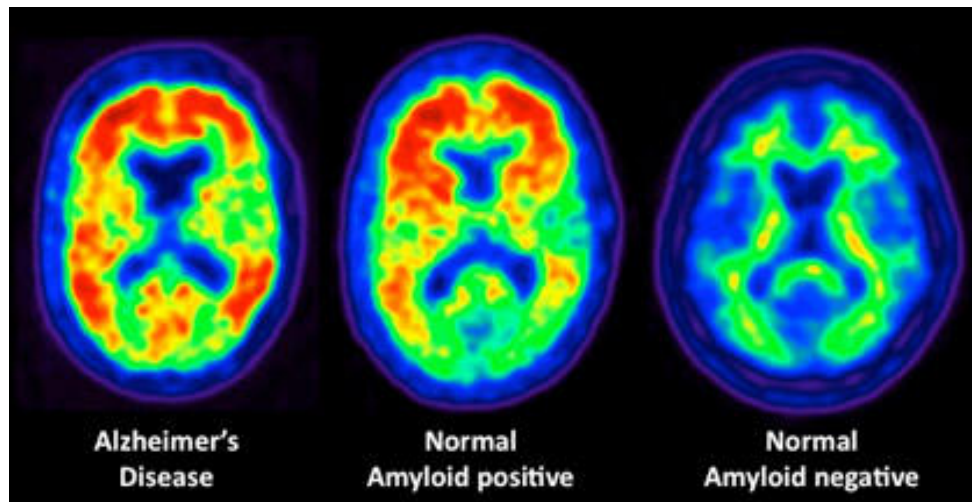
Clinical



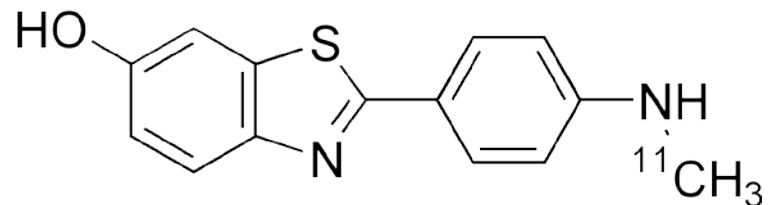
Radiopharmaceuticals are ideal for non-invasive imaging



Hieronymus Bosch Entfernung
des Wahnsinnssteines



Detection of beta-amyloid plaques, the pathologic hallmarks of Alzheimer's disease in brain tissue via ^{11}C -PIB



(Pittsburgh compound B)