# Activités et perspectives Nucléaire-santé


Nautilus Pompilius

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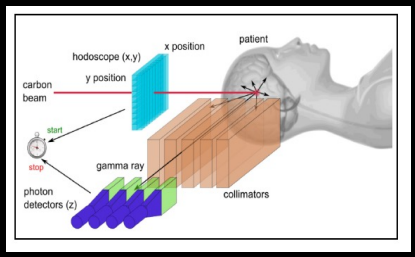
## Diagnosis

*Clinical Exam*
*Medical & Molecular Imaging*
*Contrast Agent*

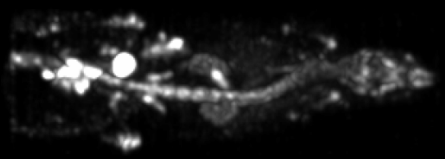
## Therapy

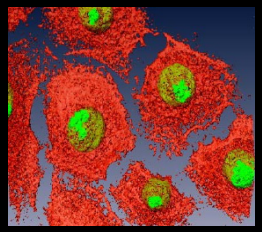
*Radio-Immunotherapy*
*Hadrontherapy*
*Surgery*




## Fundamental Research

*Radiobiology: particle interaction / cell*
*In vitro Imaging*
*Cellular Imaging*
*In vivo Imaging*

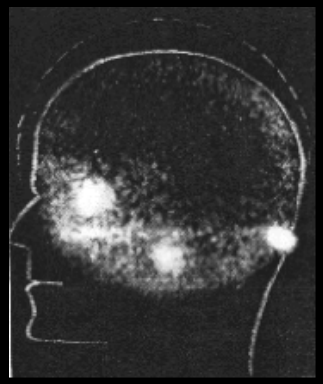




## Bioinformatics

*Modeling & Simulation (Geant4, Gate)*
*Reconstruction Algorithms*

## Nuclear Medicine



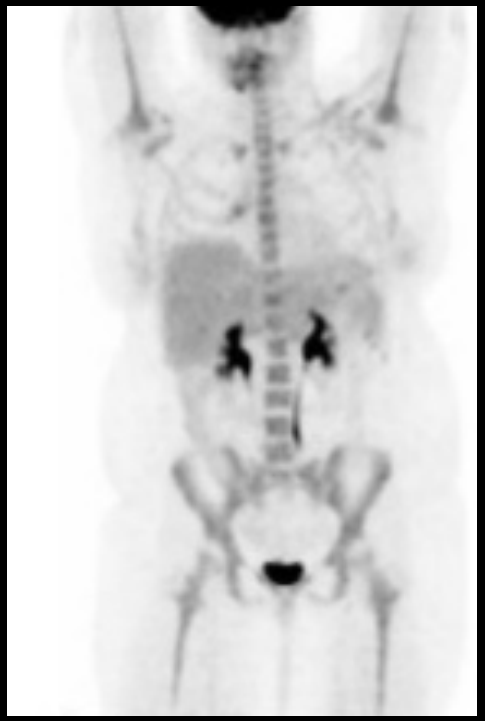
*1963, Hal Anger*
*First clinical study*
*using $^{68}$Ga*

Detector improvement
- *Scintillation crystal (NaI -> LSO)*
- *Photodetector (PMT -> SiPM)*
- *block structure*

Acquisition protocol
- *2D -> 3D, 4D, 5D…*
- *whole-body*
- *Multimodality (PET/CT, PET/MR)*

Radiopharmaceutical
- *1976, FDG*

## Molecular Imaging



*2016, FDG exam*

## Motivations

Molecular Imaging should be Accurate, at an Early stage, Predictive.

Theranostics (Therapy + Diagnosis )
The Right Drug To The Right Patient
For The Right Disease At The Right Time With The Right Dosage

➡ **Personalized medicine**

# What are our imaging expectations ?

## Molecular Imaging should be Accurate

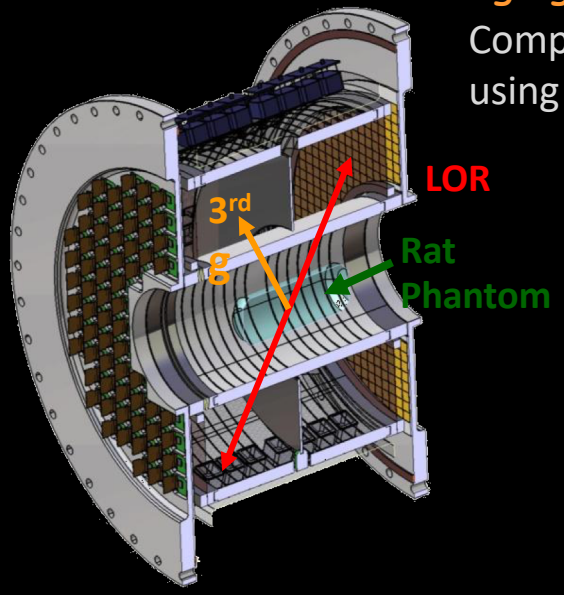
Improve Spatial Resolution & Detection Efficiency of Positron Emission Tomography (PET)

- *Dedicated Readout Electronics*
- *Crystal/photodetectors coupling*
- *Reconstruction Algorithms*

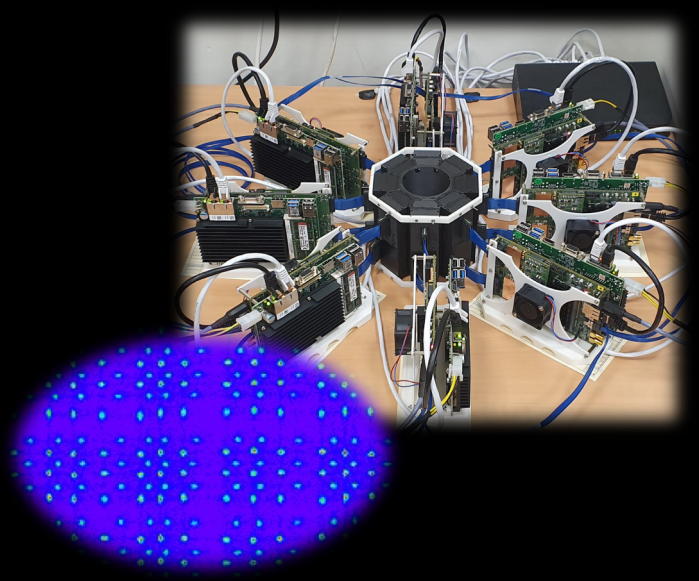
- Innovative Instrumentation (PET 3γ)
- Time Of Flight (TOF)

XEMIS2 and 3-Photon Imaging Project (Subatech)

Compton imaging
using liquid xenon telescope



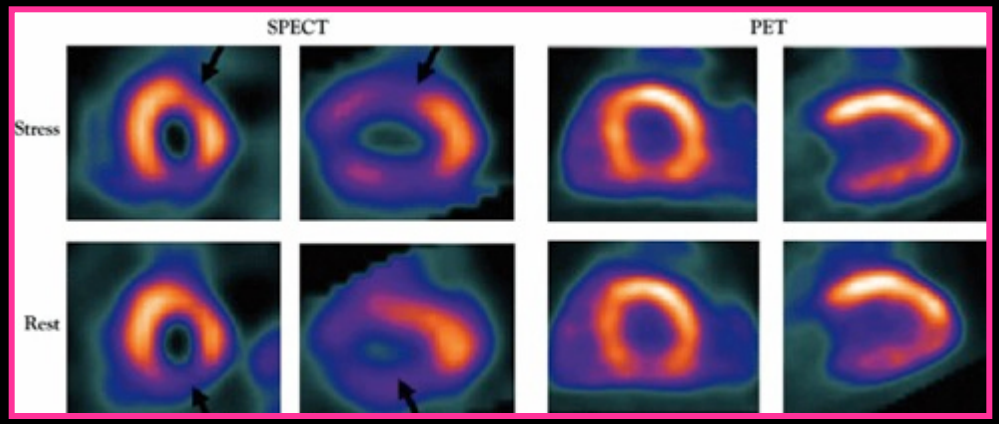

digiPET Project (IPHC)



# What are our imaging expectations ?

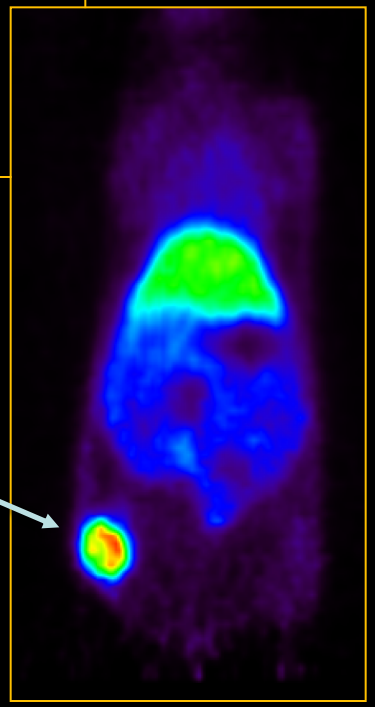
## Molecular Imaging should be at an Early stage

Development of new radiolabeled molecules for PET & SPECT
- Research and Production Sites (ARRONAX, Subatech, IPHC, GANIL)
- Innovative Radionuclide for Nuclear Medicine
  - Generator: Sr-82/Rb-82, Ge-68/Ga-68,
  - Theranostics: Cu-64/67, Sc-44/47
  - Long Half-life: Zr-89
- Research in Radiochemistry
- Target development




*Tc-99m / Rb-82*

*Arronax -> generator Sr-82/Rb-82*




*X-Cu-64*

*IPHC*

*Jiao tong University, Shanghai*

# Isotope for Therapy

## $^{225}$Ac – PSMA-617 : *imaging phase*

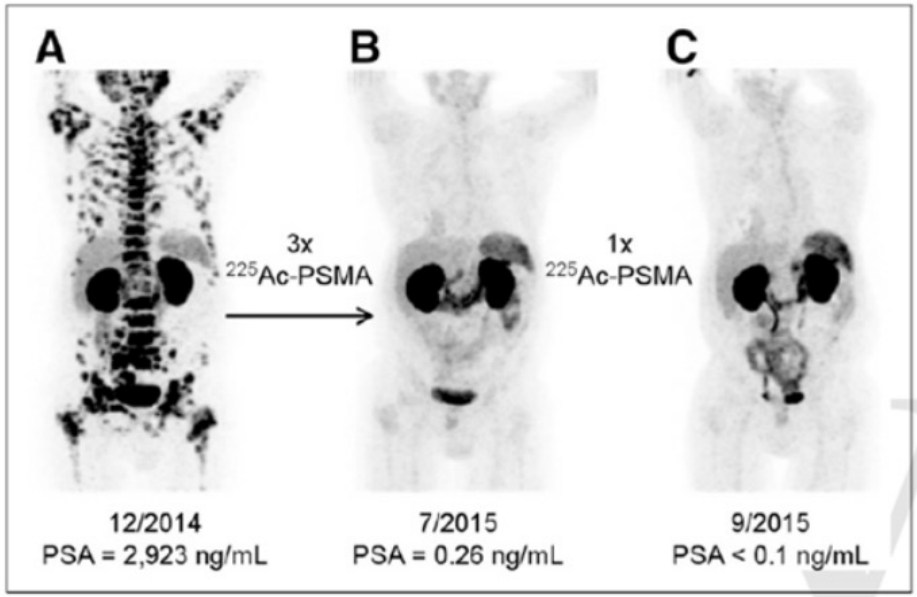



FIGURE 1. $^{68}$Ga-PSMA-11 PET/CT scans of patient A. Pretherapeutic tumor spread (A), restaging 2 mo after third cycle of $^{225}$Ac-PSMA-617(B), and restaging 2 mo after one additional consolidation therapy (C).

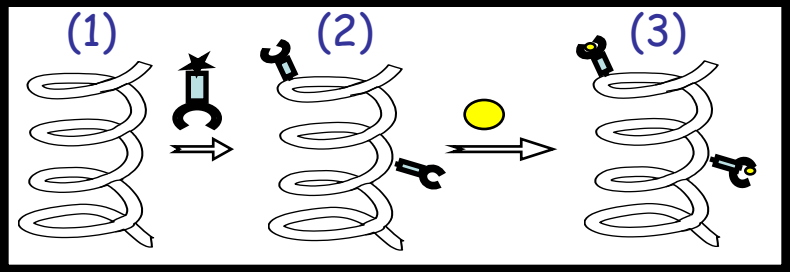
*Kratochwil et al. J Nucl Med 2016*

Theranostics couple:

*Ga-68 / Lu-177*

*Ga-68 / Ac-225*

# Isotope for Therapy

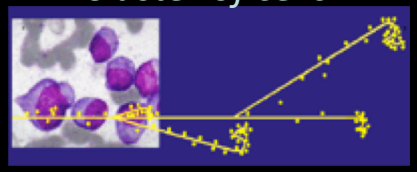



Principle of Radio-Immunotherapy:

- (1) Specific recognition of cancer cells (eg monoclonal Ab's, Ab-fragments, peptides)
+ (2) Chelate/Linker (derivatives of DTPA, DOTA)
+ (3) Effective killing

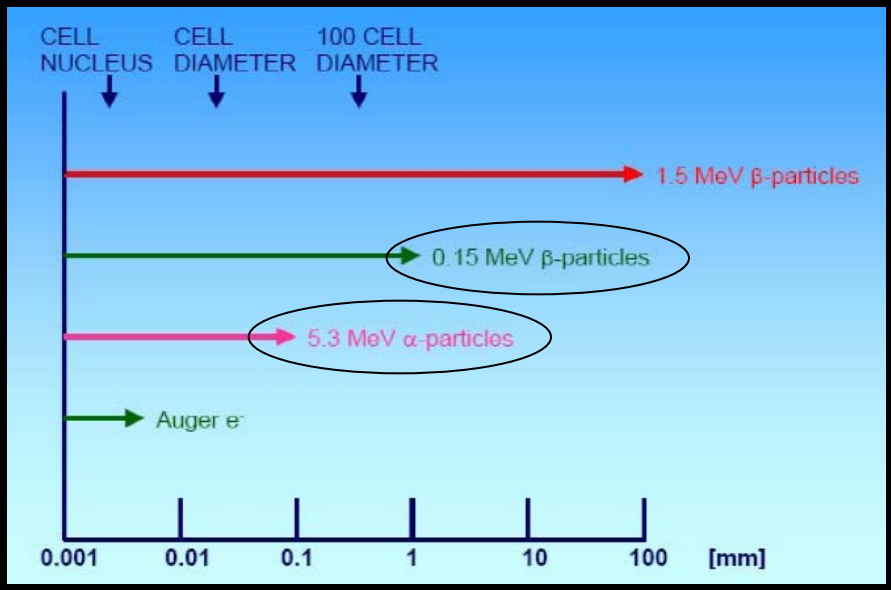
β-: Cu-67, Sc-47

*Cluster of cells*



α: At-211

*Individual cell*



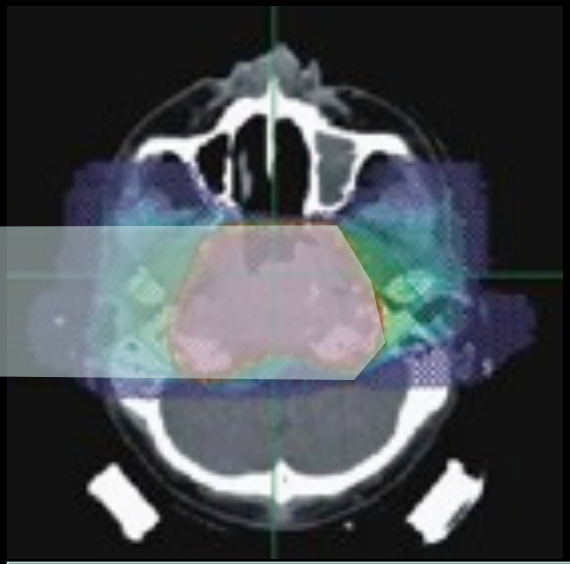

Applications for Alpha-Immunotherapy:

- Monocellular cancers (eg Leukemia)
- Micrometastatic disease
- Minimal residual disease after chemotherapy
- Residual tumor tissue after tumor resection

# Hadrontherapy

*Detector for*
*dose control*
*dose measurement*
*imaging system*

*Detector for*
*beam monitoring*



Treatment planning Optimisation

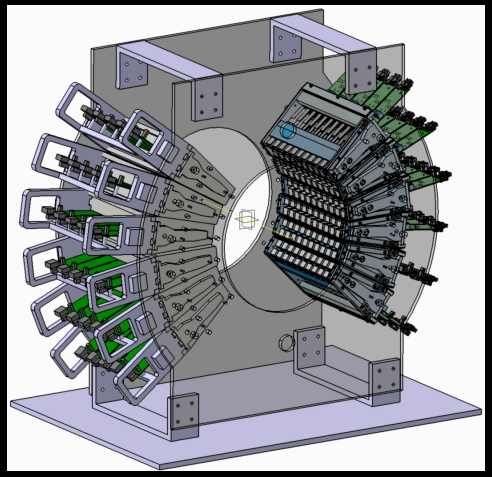
Modelisation

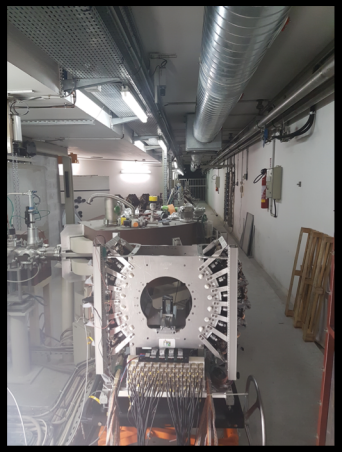
Input from « fundamental research »
*Radiobiology*
*Radiochemistry (DNA and cell damages)*
cross section for secondary particles

# Hadrontherapy

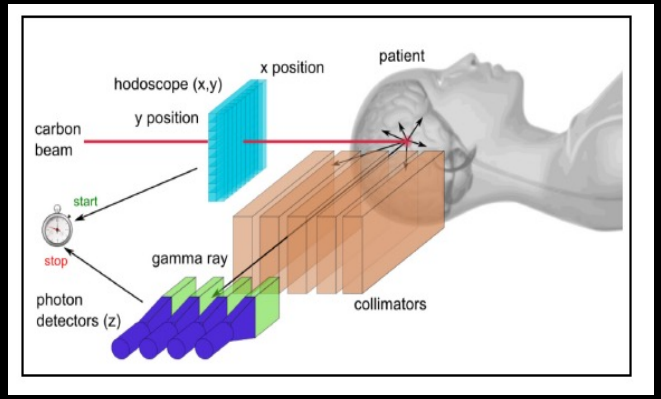
*Imaging systems, quality control in a clinical environment*

## PET approach





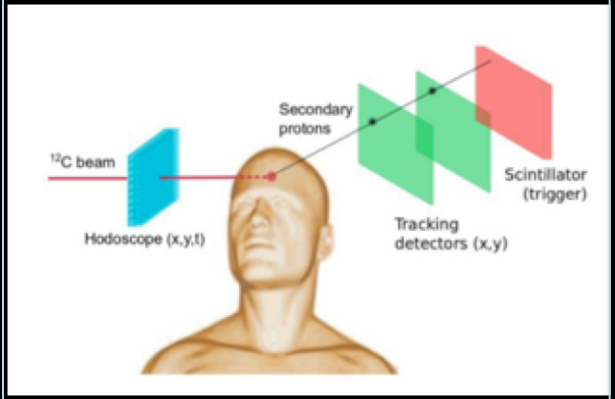
## γ-prompt approach



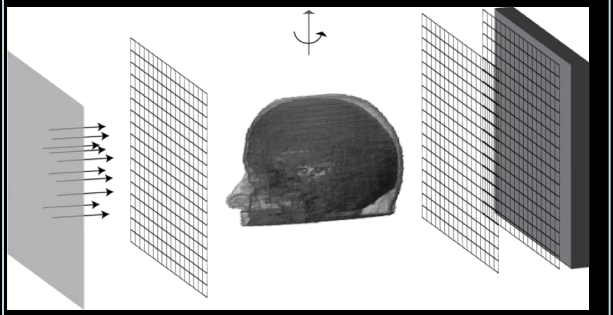

*Hodoscope*

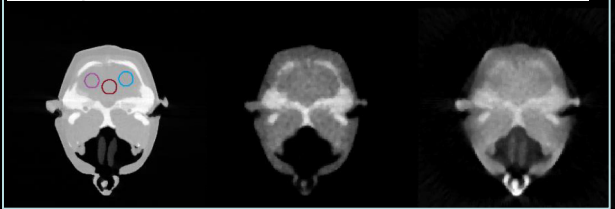
*Compton camera*

## IVI approach




## pCT approach



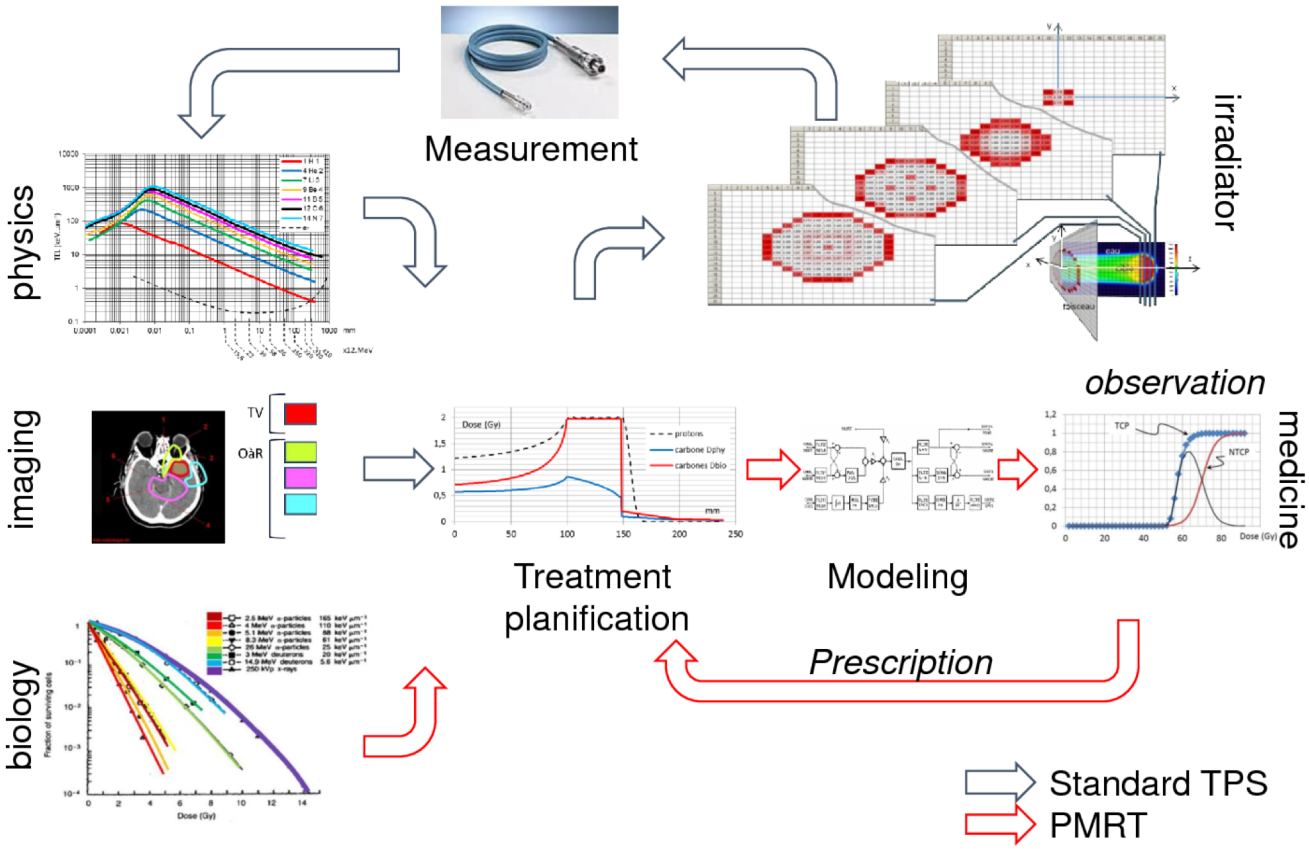


# Hadrontherapy

*Modelisation in a clinical context*

## PMRT Plateforme de Modélisation en RadioThérapie

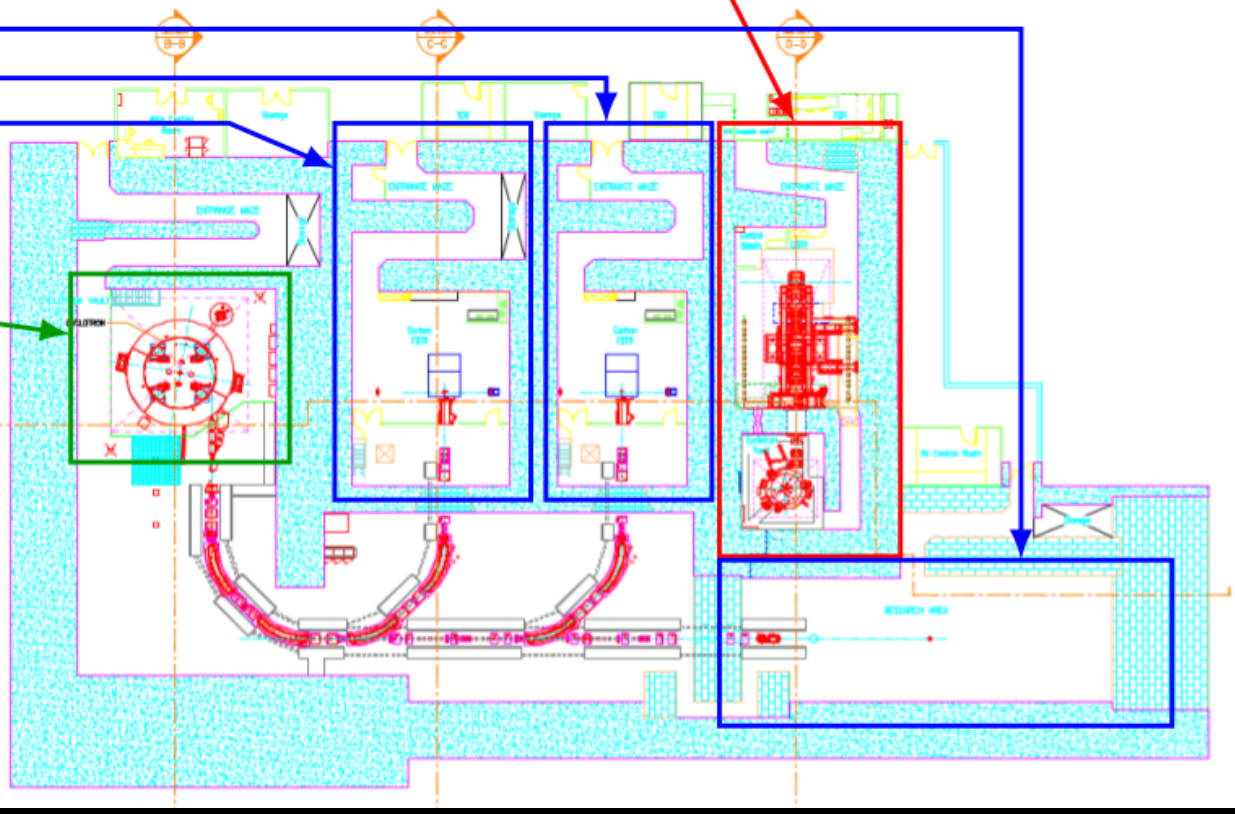
How to take into account the medical feed-back to predict the future of the patient?



ARCHADE aims to create a European Centre for Research and Development in Hadrontherapy dedicated to basic and applied research.
But also to conduct a collaborative research program to develop and validate a cyclotron prototype.

- Hadrontherapy center :
  - Protontherapy treatments
    - Proteus One (S2C2)
    - Protons at 250 MeV
  - Research in carbon-therapy
    - Physics
    - Biology
    - Clinical testing

- Supraconducting Cyclotron C400
  - $^{12}C$ at 400 MeV/u
  - Protons at 250 MeV
  - All light nuclei with A/Z=2



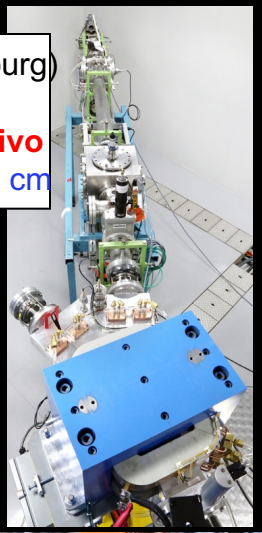
# Hadrontherapy

*Preclinical infrastructures*

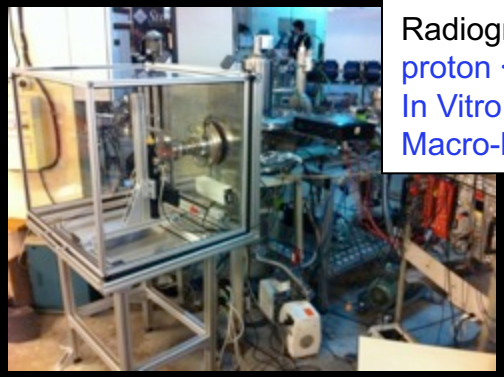
Development of complementary irradiation platforms
- different particles and energies
- in vivo and in vitro experiments
from cell (micro-beam) to tumor irradiation

AIFIRA (Bordeaux)
proton,$\alpha$ < 3MeV
In Vitro
**Micro-beam < 2$\mu$m**

PAVIRMA (Clermont)
**X, neutron** < 2,5MeV
In Vitro



PRECy (Strasbourg)
Proton < 25MeV
In Vitro and **In Vivo**
Macro-beam < 2 cm

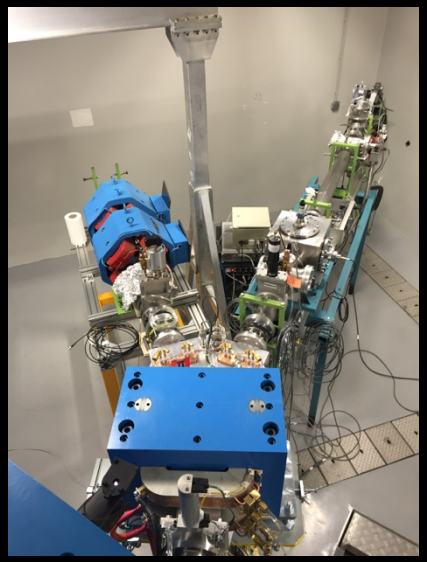


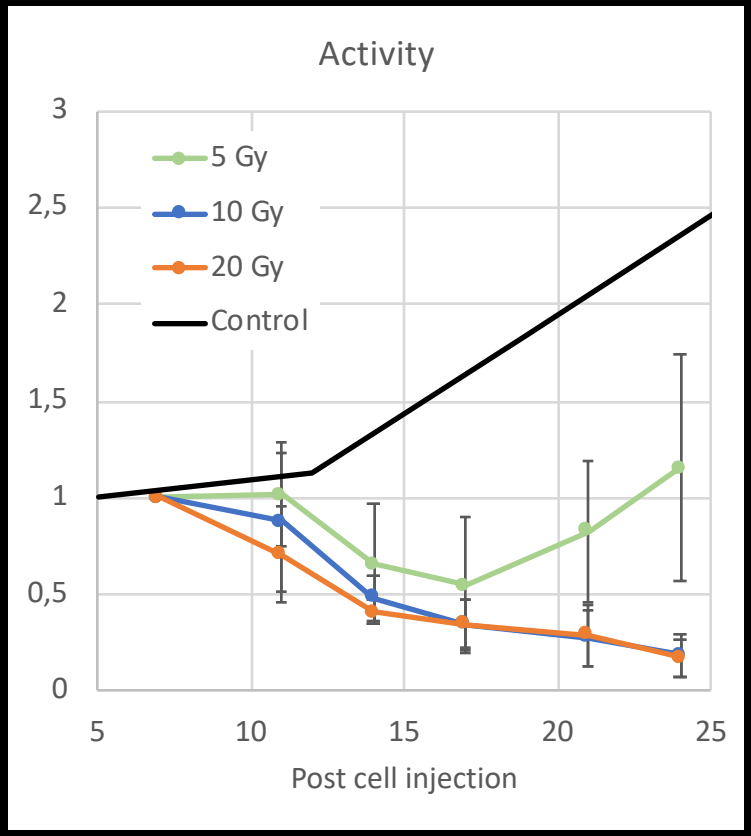
Radiograph (Lyon)
proton < 3,5MeV
In Vitro
Macro-beam < 2 cm

Arronax (Nantes)
**Proton,$\alpha$ < 70 MeV**
In Vitro
Macro-beam < 5 cm

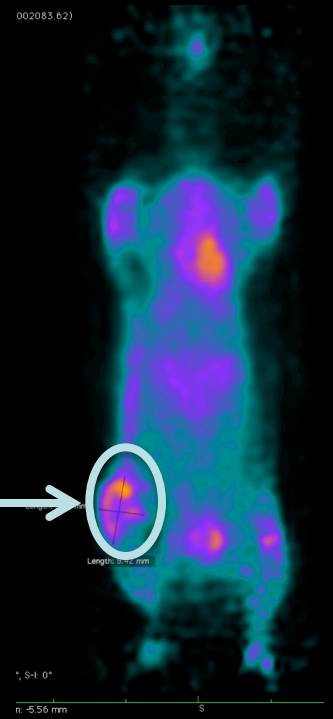

GANIL (Caen)
**$^{12}$C < 95 MeV/n**
In Vitro
Macro-beam < 5 cm

# Example: merging Hadrontherapy and Imaging





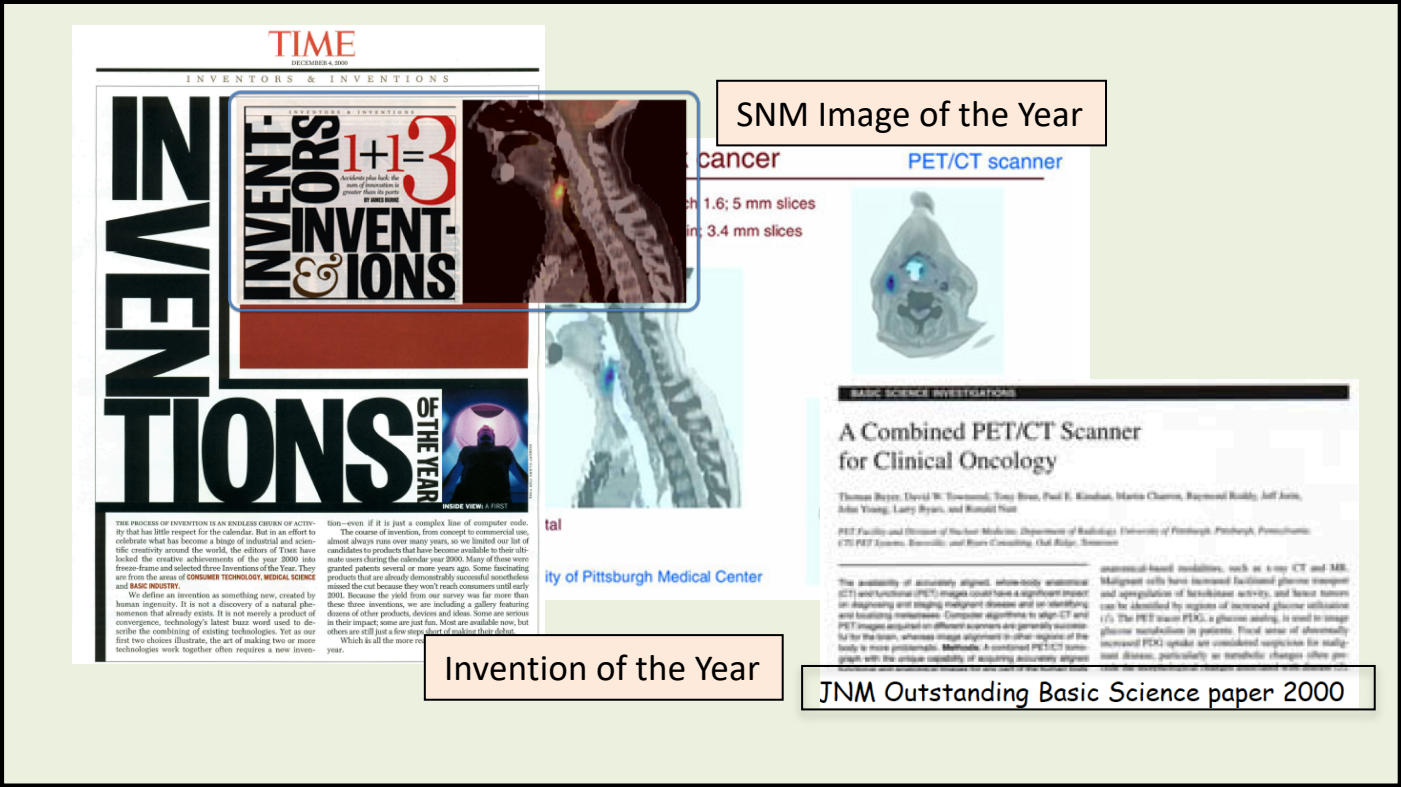

**Longitudinal studies**
*metabolism*
*Cell proliferation*
*Apoptosis*



*rpPET project, IPHC*

# Perspectives…

## Almost 20 years ago…



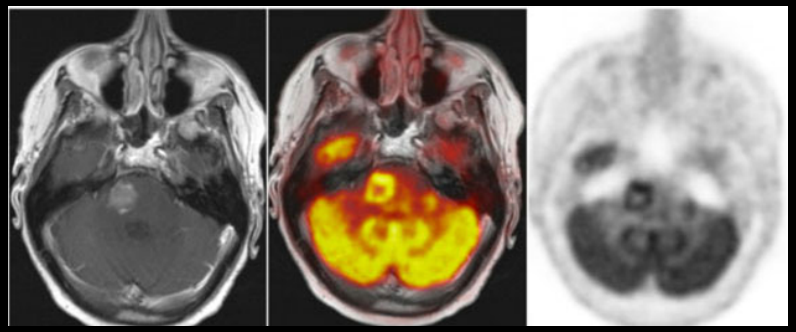

PET/CT is a technical evolution that has led to a **medical revolution**

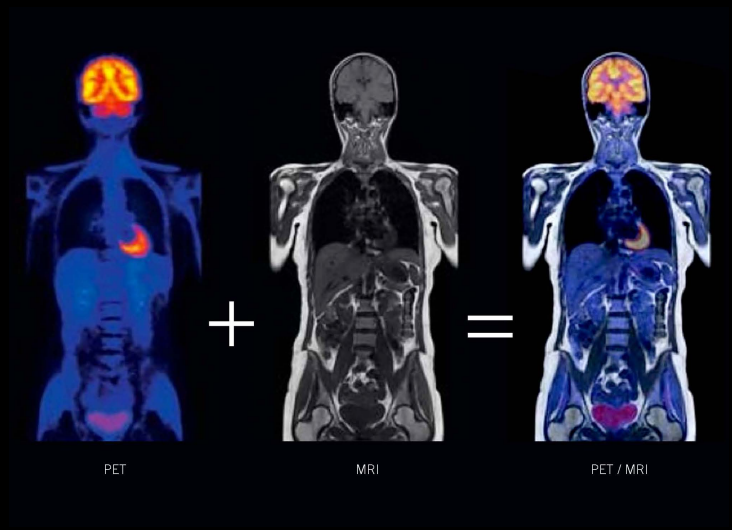
(Johannes Czernin, UCLA, 2003)

## MRI compatibility

PET/CT is a technical evolution that has led to a medical revolution
(Johannes Czernin)

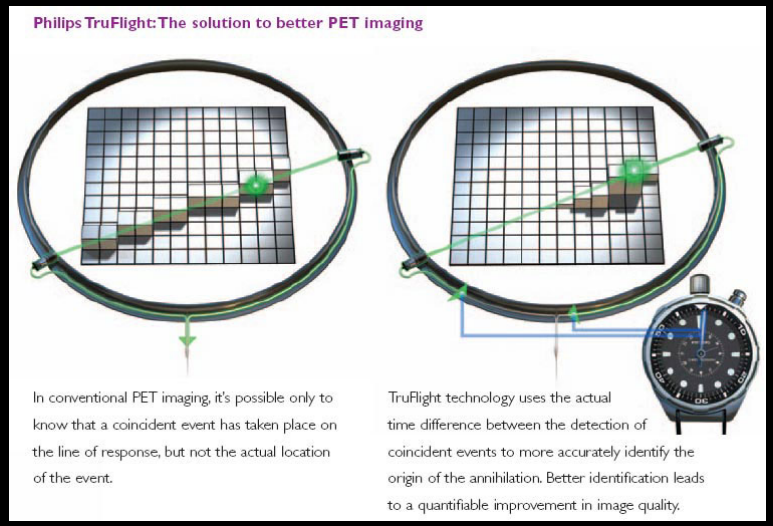
PET/MRI is a medical evolution based on a technical revolution (Thomas Beyer)






PET/CT or PET/MR, use of multi-parameters approaches ?
AI can help ?

# Almost 20 years ago…time of flight (TTV03)




## The 10ps challenge: a step towards reconstructionless TOF-PET

The 10ps challenge:
- a spur on the development of fast timing
- an opportunity to get together
- an incentive to raise funding
- a way to shed light on nuclear instrumentation for medical imaging

One unique challenge launched for 5 to 10 years and operated by an international organisation with rules issued by the community based on the measurement of CTR combined to sensitivity

Several milestones and prices:
- 3 years after the launch of the challenge: 1M€ expected for the Flash Gordon prices delivered for the achievement of 3 important milestones
- until the end of the challenge: 1M€ expected for the Leonard McCoy price for the first team meeting successfully the specifications of the challenge


*P Lecoq, C Morel, J Nuyts*

# Dedicated imaging systems…

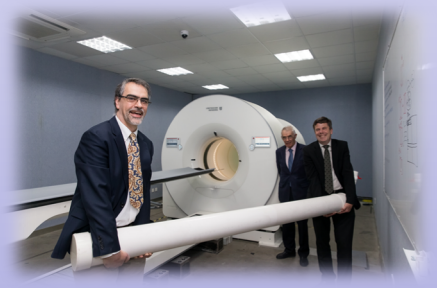
*Whole body imaging*

THE STATE OF THE ART (FEATURED ARTICLE OF THE MONTH)

## Total-Body PET: Maximizing Sensitivity to Create New Opportunities for Clinical Research and Patient Care

Simon R. Cherry[1,2], Terry Jones[2], Joel S. Karp[3], Jinyi Qi[1], William W. Moses[4], and Ramsey D. Badawi[1,2]

*[1]Department of Biomedical Engineering, University of California, Davis, California; [2]Department of Radiology, University of California Davis Medical Center, Sacramento, California; [3]Department of Radiology, University of Pennsylvania, Philadelphia, Pennsylvania; and [4]Lawrence Berkeley National Laboratory, Berkeley, California*



*https://explorer.ucdavis.edu*

# Dedicated imaging systems…

*Brain imaging*



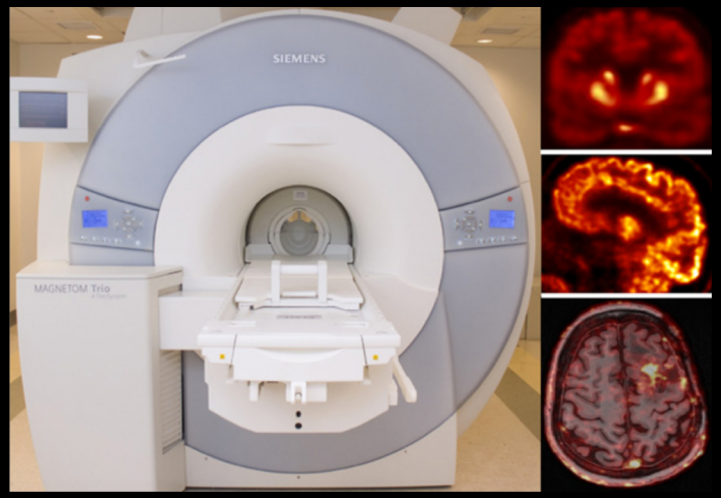
THE STATE OF THE ART

## Development of Dedicated Brain PET Imaging Devices: Recent Advances and Future Perspectives

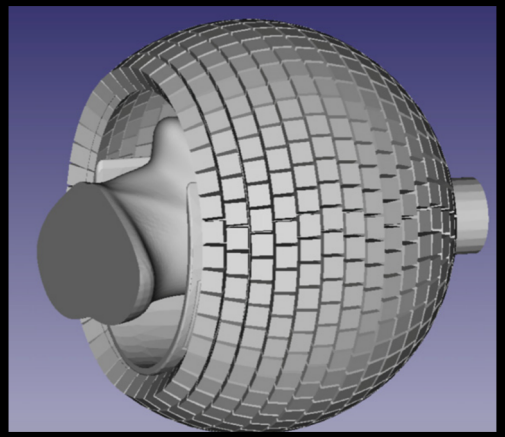
Ciprian Catana

*Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital and Harvard Medical School, Charlestown, Massachusetts*

*Helmet-PET*



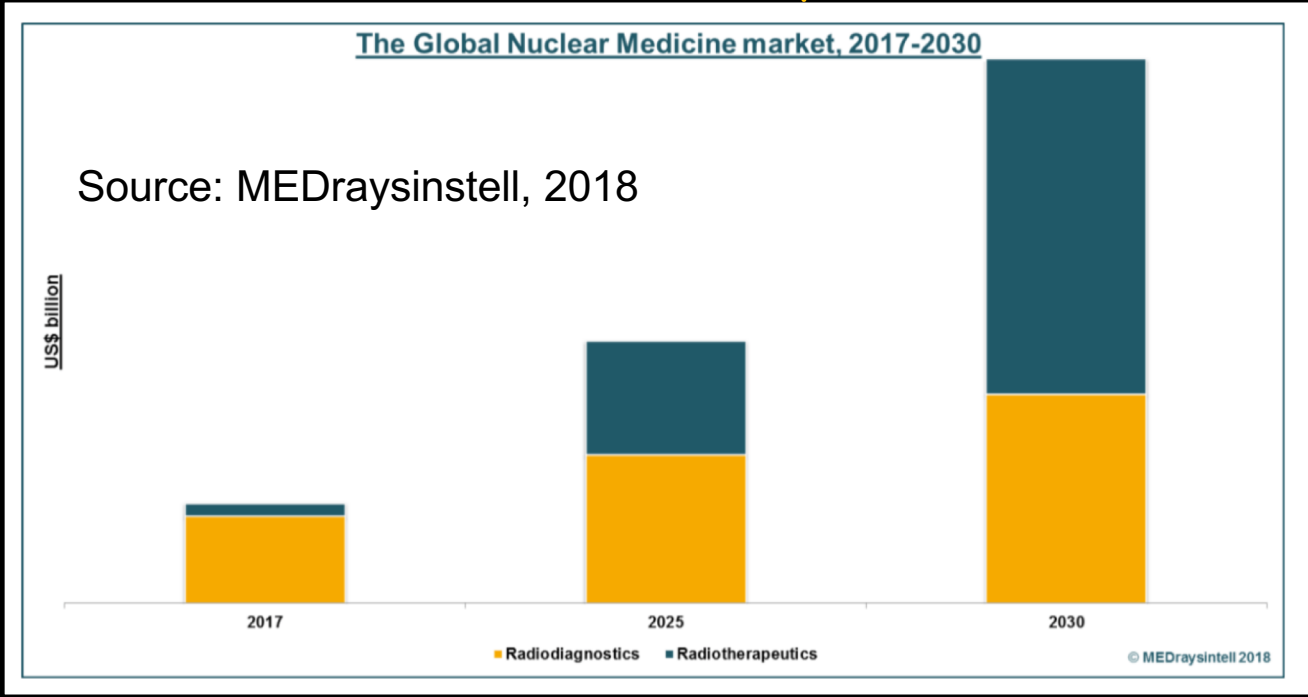

*BrainPET*

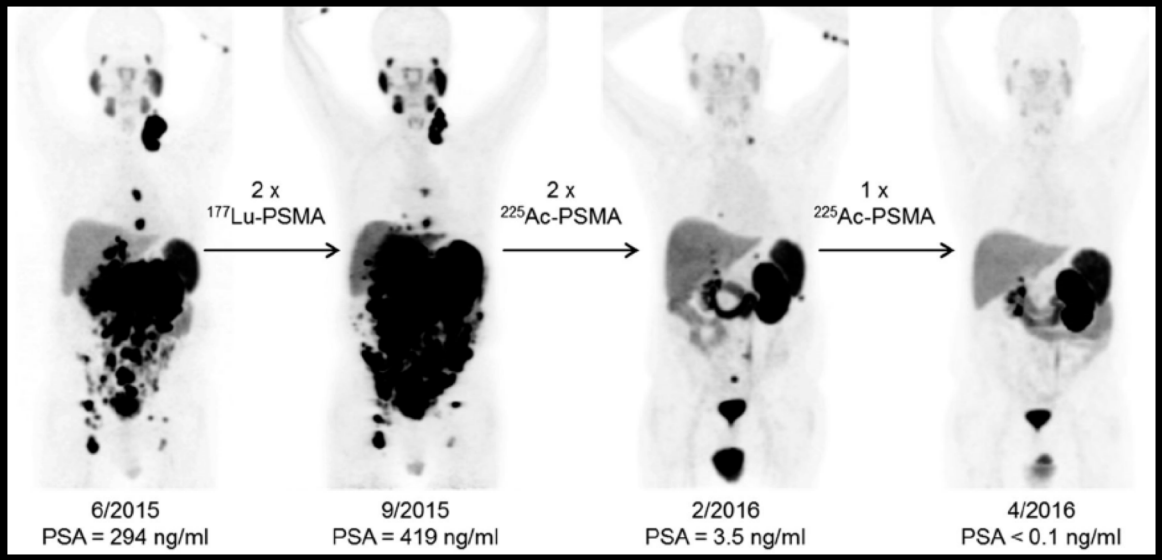


*Possible geometry*

# Targeted therapy and companion test

## Use of metalic isotopes




Source: Kratochwil et al, JNM 2016

# Artificial Intelligence…

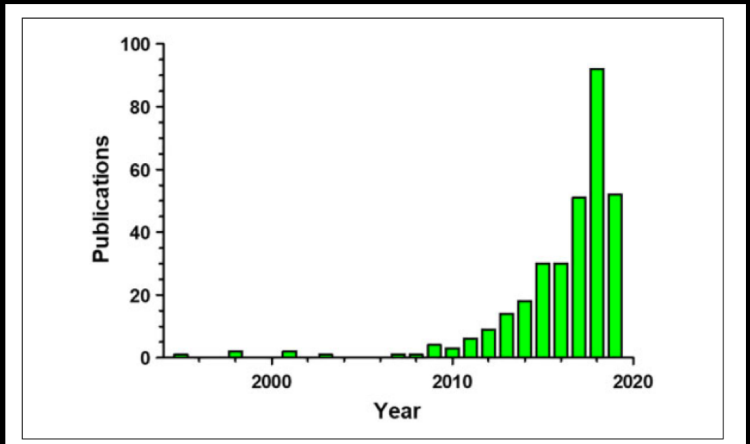
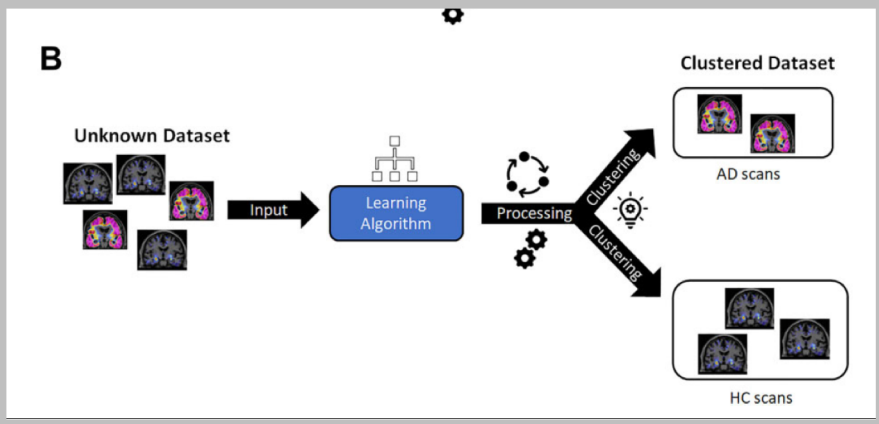
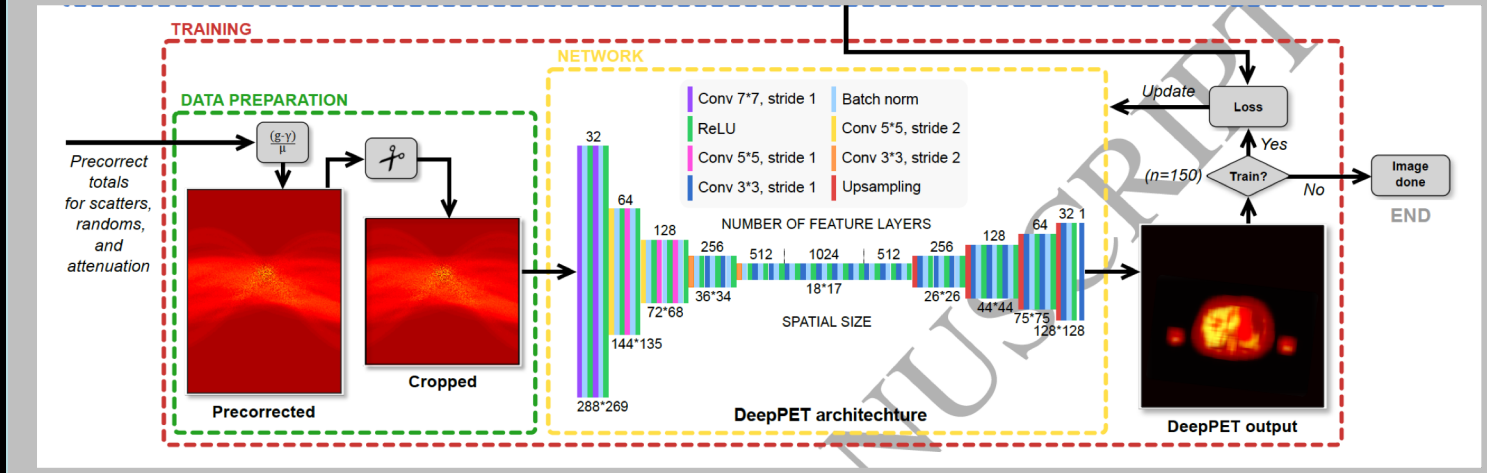



**Figure 1.** Number of publications in PubMed per year (from January 1995 to April 2019) using the keywords "deep learning" or "machine learning" and "PET".

*From Duffy et al, Molecular Imaging, 2019*




*From Duffy et al, Molecular Imaging, 2019*




*From Häggström et al, Medical Image Analysis, 2019*