

Automated microfluidic production of radiopharmaceuticals for theranostics

– Laurent Tanguy, Partnerships manager, PMB-ALCEN



Synopsis

- **Microfluidic Production of Radiopharmaceuticals**
 - Presentation of iMiGiNE systems
 - Microfluidic advantages for radiochemical synthesis
 - Latest results and future developments in preclinical and clinical



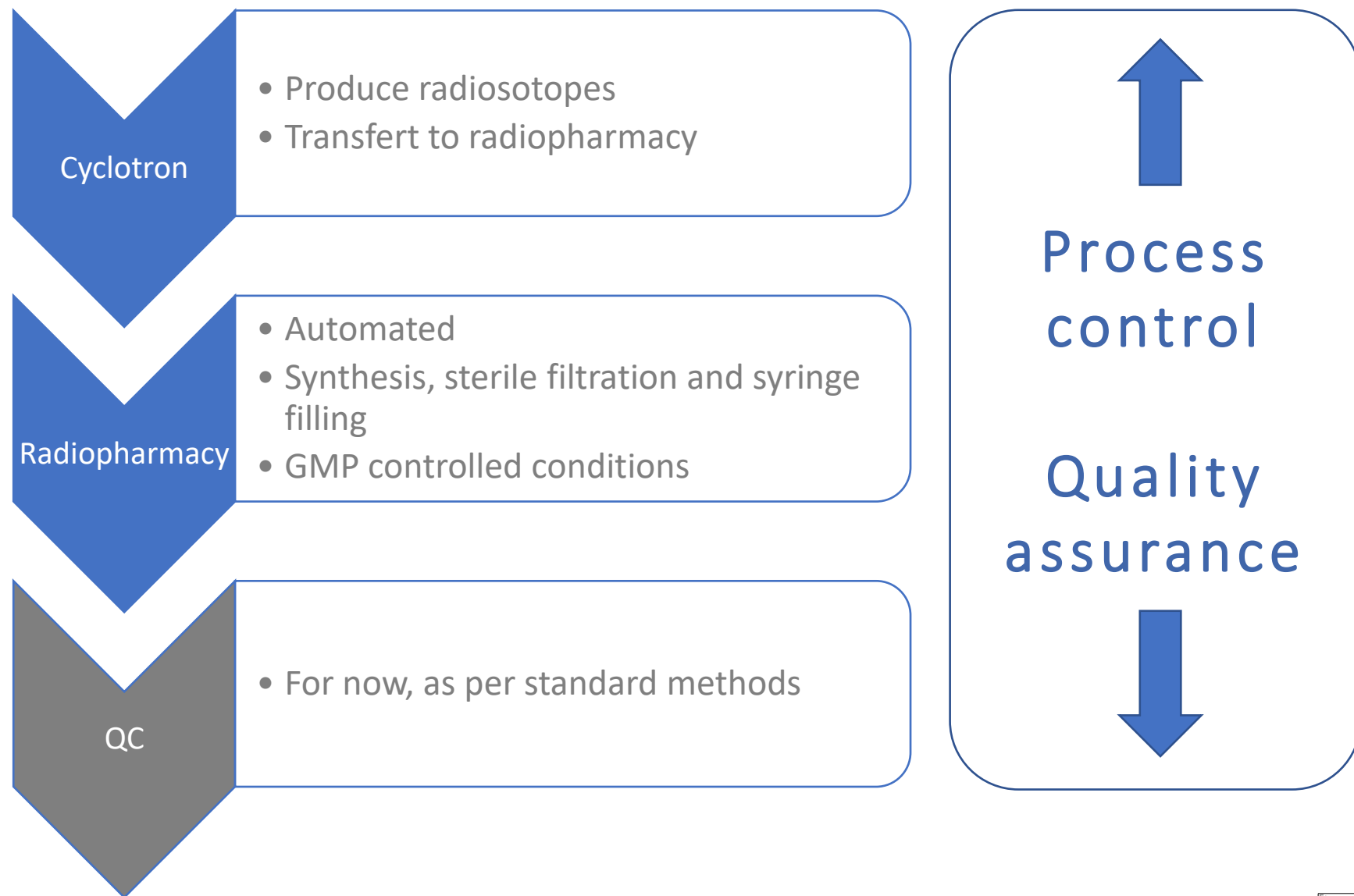
What is iMiGiNE for?

- Precision medicine and personalized medicine means there is a growing need for « a la carte » production of radiopharmaceutical. Actual manufacturing network is not set-up for this.
- Hotcell based lab are too expensive to be installed and operated in every radiopharmacy.

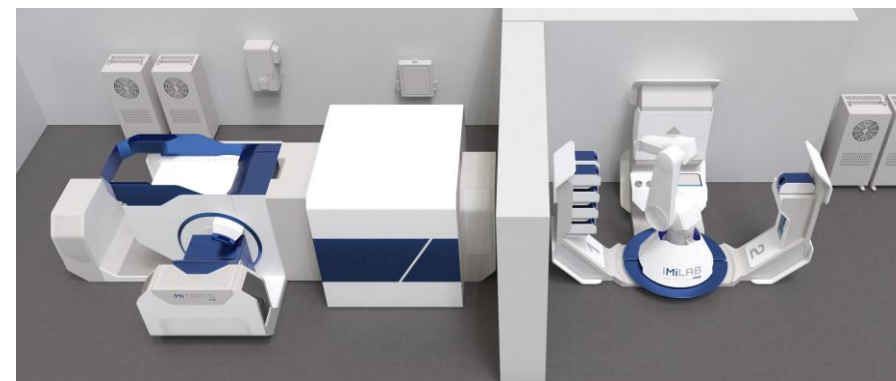
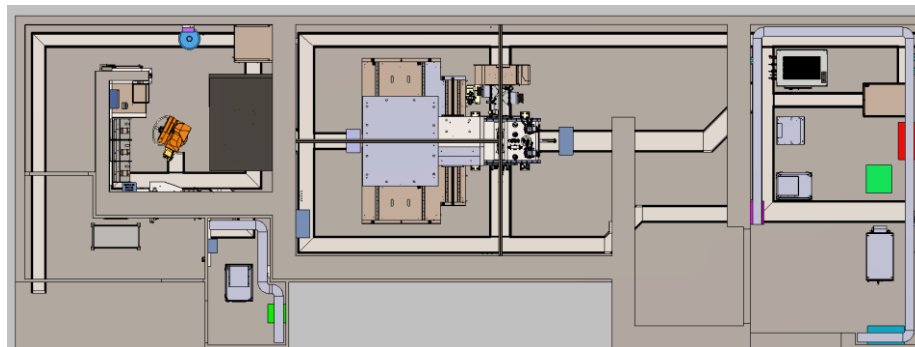
Allow production on site, on demand of
various radiopharmaceuticals



An automated radiopharmacy



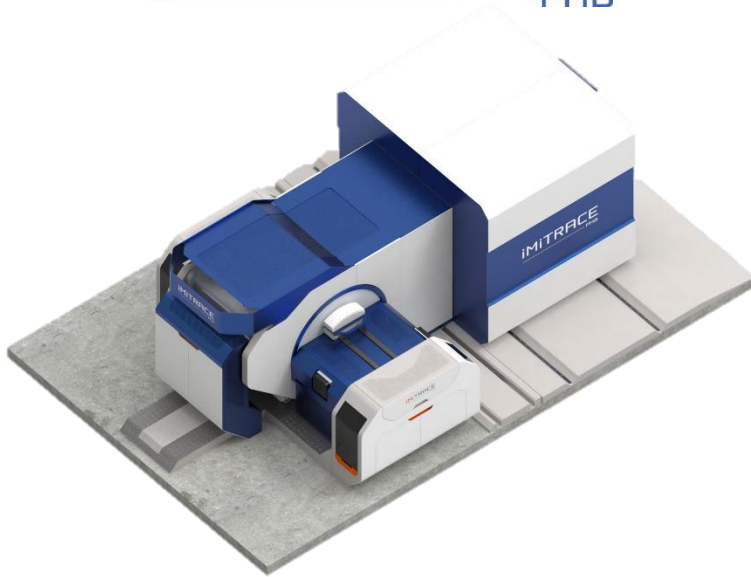
Installed closed to PEC/CT camera



- Requires ~100m² whatever the number of produced radiopharmaceuticals
- Manufacturing of radiopharmaceuticals « à la carte »
- Access to short half-life radioisotopes (¹¹C, ¹³N, ¹⁵O)

iMiGiNE – the different systems

iMiTRACE PMB



Cyclotron 12 MeV

- ^{18}F , ^{11}C , ^{13}N , ^{68}Ga
- Single doses or small batches
- Easy to maintain

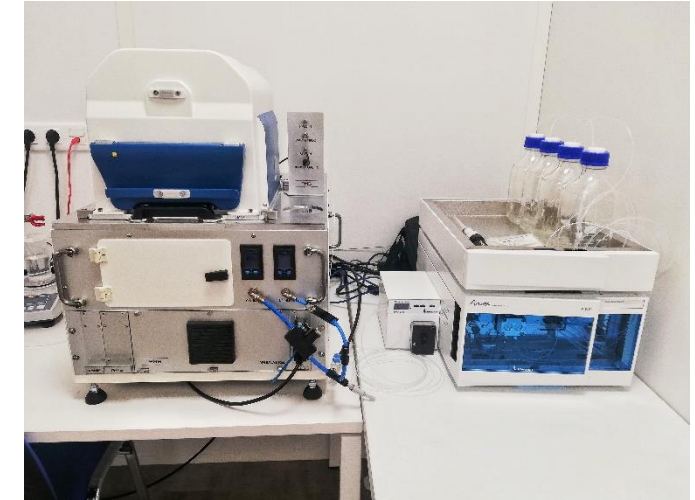
iMiLAB PMB



Radiopharmacy

- Entirely automatized
- Single doses or small batches
- Various tracers

iMiDEV PMB



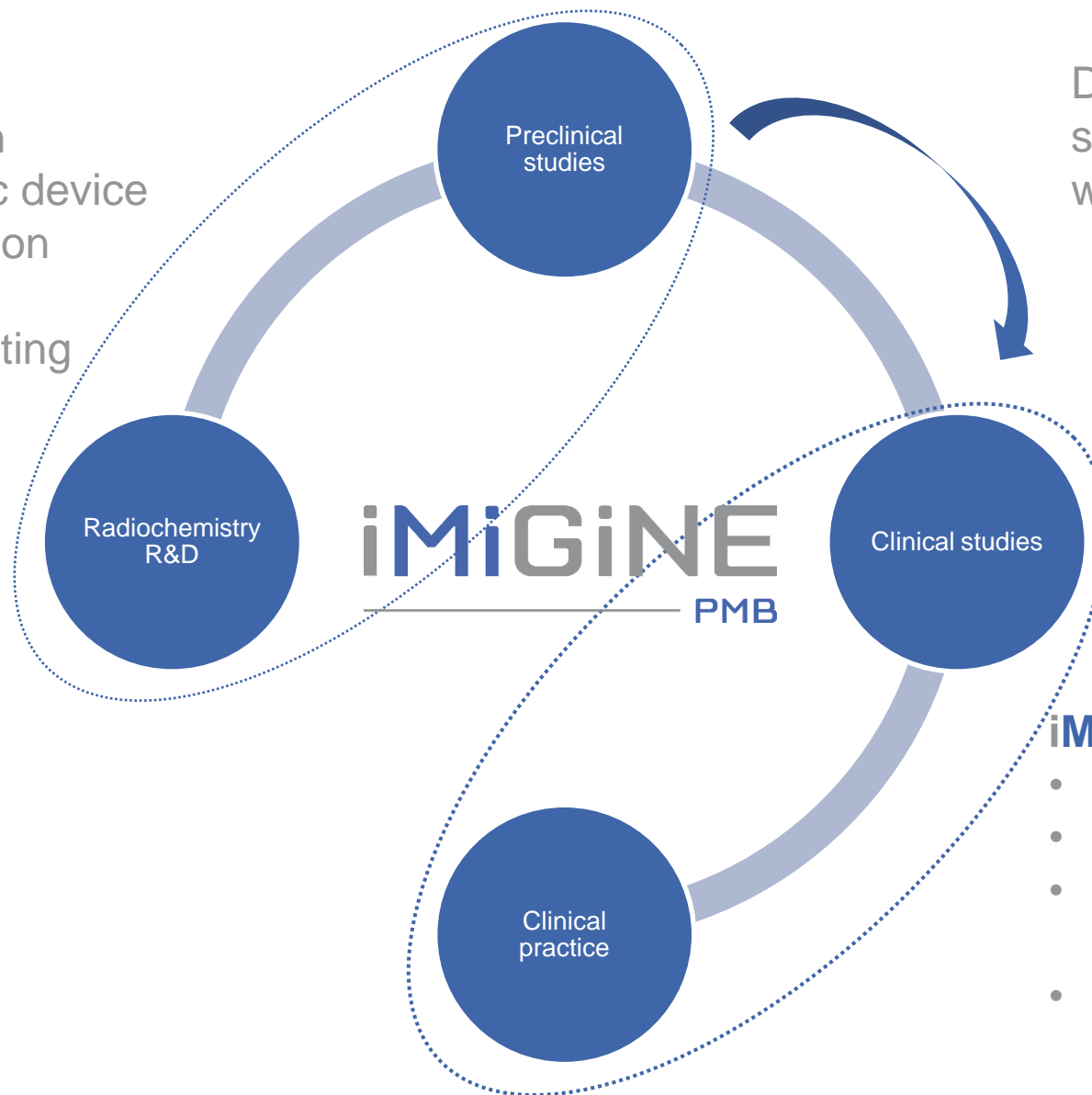
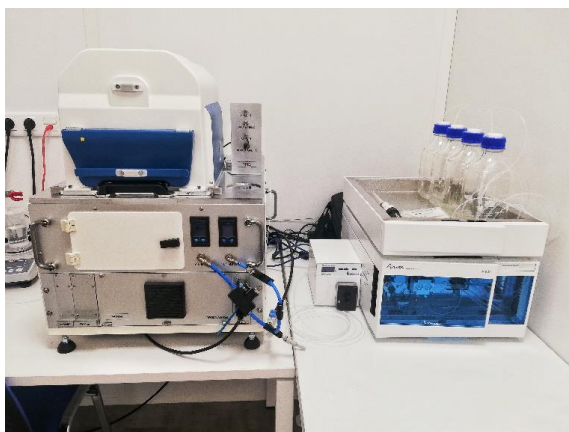
Radiosynthesis module by microfluidics

- Single doses or small batch
- Open system to set-up synthesis into the microfluidic cassette

Transition from R&D to clinic

iMiDEV

- Intuitive process design
- Easy to use microfluidic device
- Low reagent consumption
- Low initial investment
- Easy installation in existing premises



Direct transfer of the synthesis developed with iMiDEV to iMiLAB

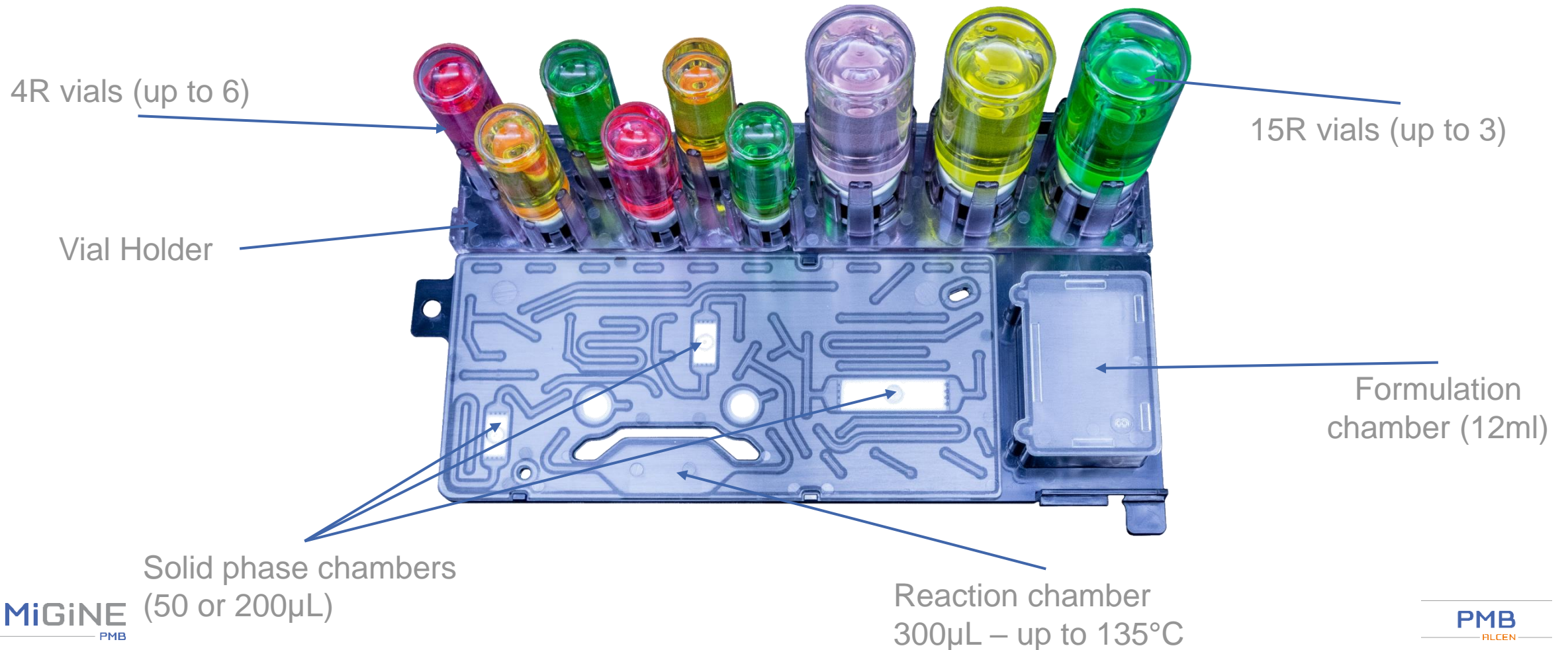


iMiLAB

- Multi tracers
- On site, compact
- Automated, ensure maximal reproducibility from site to site
- Attention paid to details for maximum SRA

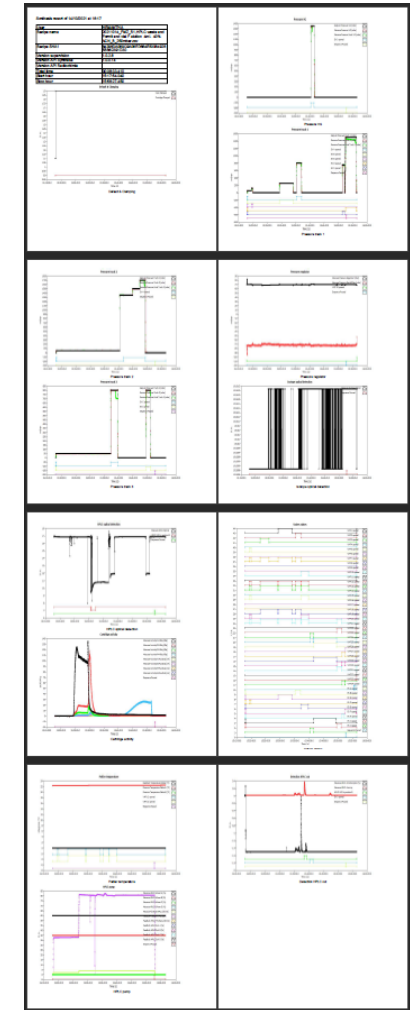
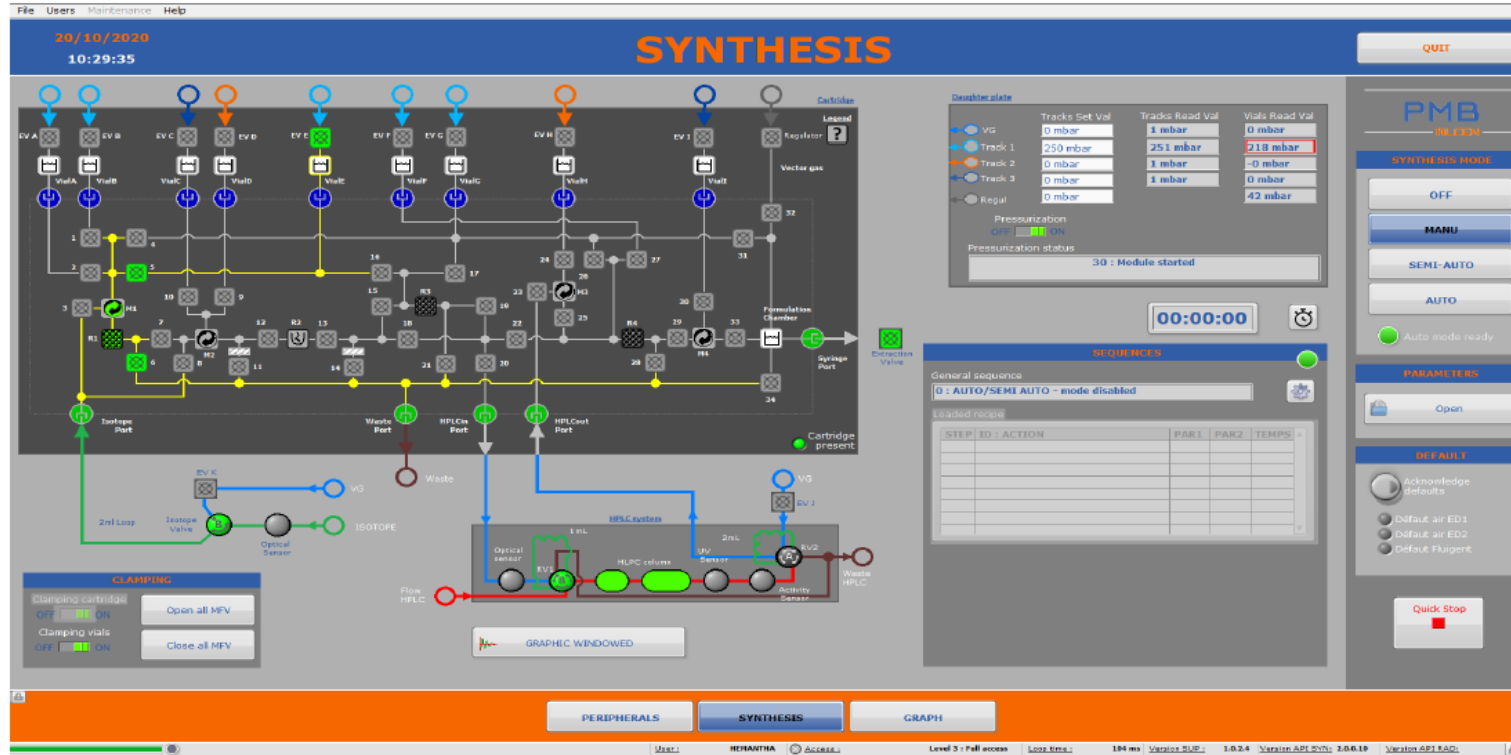
Microfluidic cassette

- Only one fully integrated and unique cassette for all tracers and both systems



HMI – Overview

- Both system uses the same dedicated intuitive HMI
 - Automated or manual recipe can be executed
 - Reports are generated containing all important data for traceability



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Microfluidics & radiochemistry

- **Expectations and promises are very high**
 - Improved reaction speed and selectivity
 - Improved yield and radiochemical purity
 - Reduction of consumption of reagents
 - Integrated and closed system
 - Improved specific activity
 - Smaller footprint
- **Better, simpler and more targeted production of radiotracers for patients**

Microfluidics & radiochemistry

- **Microfluidics in radiochemistry**

- Used since beginning of 2000
- Applied to various tracers based on ^{18}F , ^{68}Ga mainly but also ^{11}C
- Applied to many different synthesis ways and strategies

- **Several companies and universities have developed advanced solutions**

- For example: GE Healthcare, Trasis, Advion
- Most solutions are either lab prototypes or dedicated to one or few radiotracers.

- **There is a lack of an integrated, developed, commercially available solutions to perform directly microfluidic synthesis of radiotracers**

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PMB partners

- They trust us in France and Europe



**Installation
Sept. 2019**

Goals:
 ^{18}F , ^{68}Ga

**Mars-Avril
2020**

^{18}F -radiochemistry
 $[^{18}\text{F}]\text{NaF}$

**Août-Septembre
2020**

^{68}Ga -radiochemistry
 $[^{68}\text{Ga}]\text{Ga-Citrate}$

**Janvier-Mars
2021**

^{68}Ga -radiochemistry
 $[^{68}\text{Ga}]\text{Ga-PSMA-11}$

**Avril
2021**

Ovdiichuk *et al.*
Lab Chip 2021

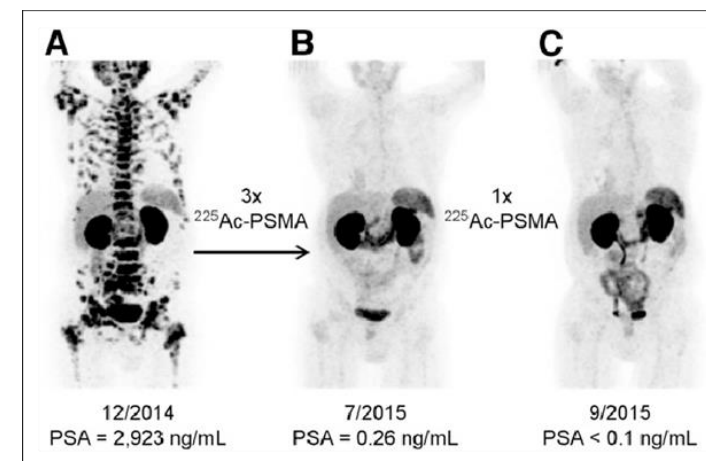
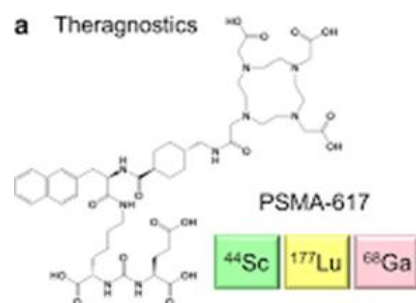
**Juin
2021**

ESRS'21
Ovdiichuk *et al. Nucl. Med. Biol.* 2021
Marquage dans R2
 $[^{18}\text{F}]\text{FTAG}$

**Novembre
2021**

Optimisation
 $[^{68}\text{Ga}]\text{Ga-PSMA-11}$

- $[^{68}\text{Ga}]\text{Ga-PSMA11}$:
 - Diagnostic molecule for prostate cancer with PET imaging
 - Companion diagnostic molecule for internal radiotherapeutical approaches



Conventional kit (TRASIS)



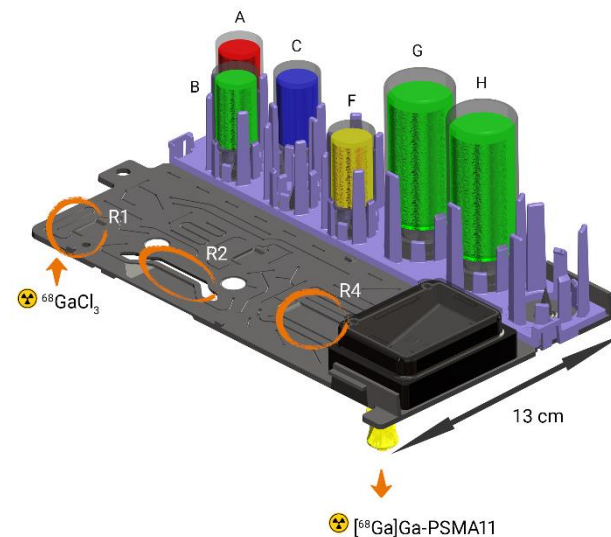
Activity
concentration
and elution

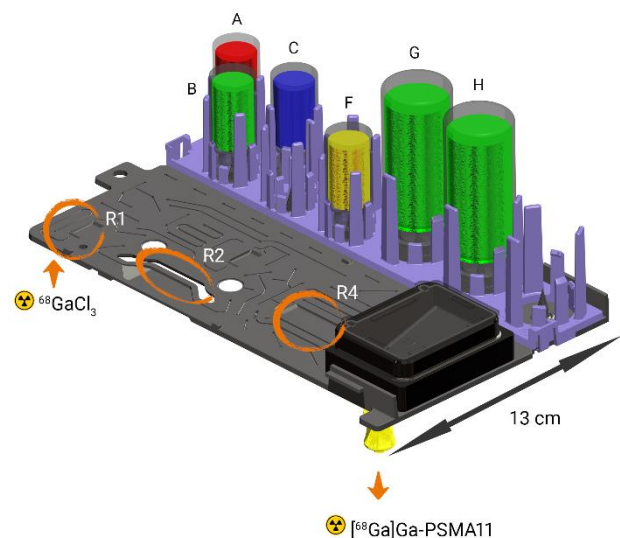
Control of
mix with
precursor

Filling of
reaction
chamber
(300 μL) and
synthesis

Formulation
in C18

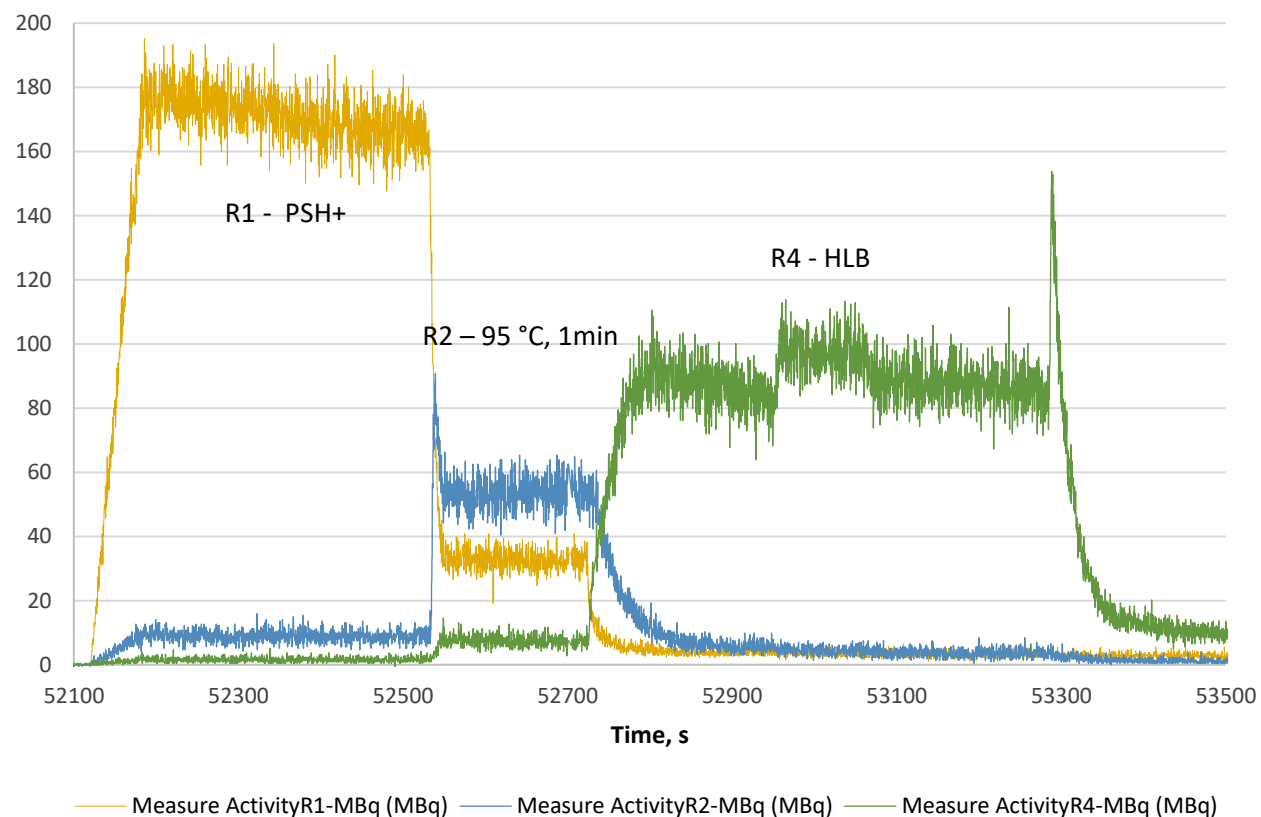
Microfluidic cassette





- **Vial A** : elution solution
- **Vial B** : NaCl 0,9% for rinsing R1
- **Vial C** : PSMA11 in NaAc
- **Vial F** : EtOH for formulation
- **Vial G** : NaCl 0,9% for rinsing R2
- **Vial H** : NaCl 0,9% for formulation

1. Activity trapping
2. Elution and mix with precursor followed by 1' heating at 95°C
3. SPE / formulation : accrochage du [^{68}Ga]Ga-PSMA-11 brut sur C18/HLB suivi par rinçage & élution du produit final avec 10% EtOH/NaCl_{0,9%}



- **Performed synthesis in iMiDEV have already demonstrated**
 - **Faster reaction time**
 - Increased **radiochemical purity** and **incorporation yield**
 - Adaptability to different classical PET radioisotopes (^{68}Ga , ^{11}C , ^{18}F)
 - **Fully automated** synthesis of various radiotracers
 - **European Pharmacopeia conform production of radiotracers**
 - Comparable diagnostic performances with standardly produced tracers

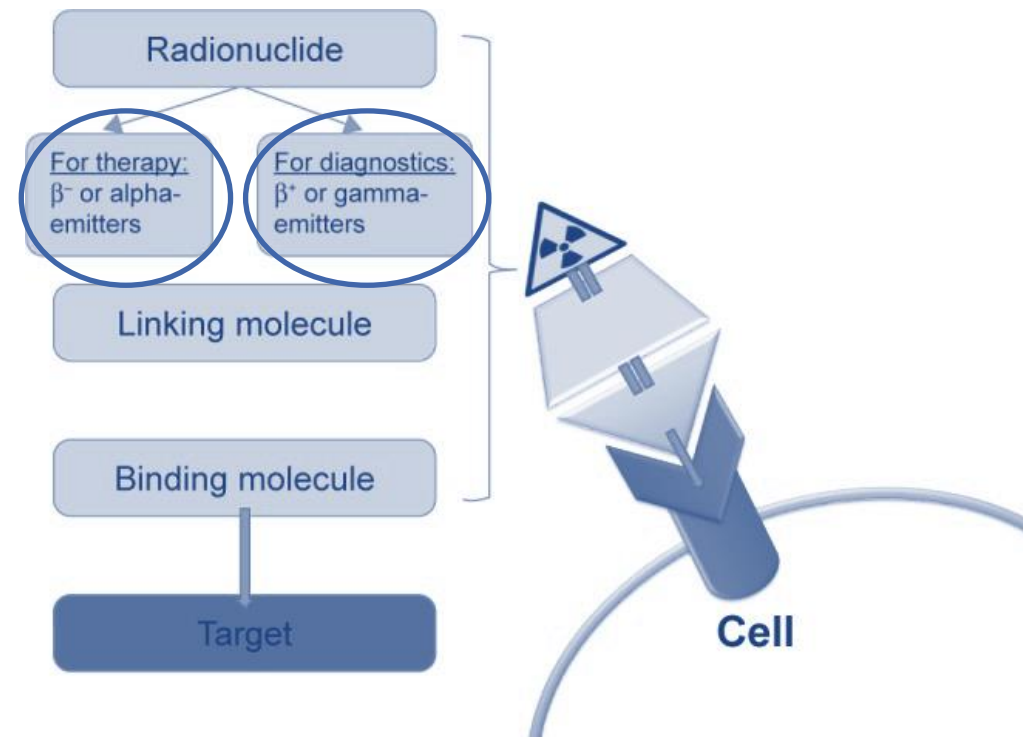
What's next?

■ For diagnostic

- Increase the radiotracers library and especially for F18 based tracers
- Finalize ^{68}Ga -PSMA and other ^{68}Ga - peptide synthesis (FAPI, DOTATOC, DOTATATE)

■ For therapy

- Show performance of the cassette with molecules and radioisotopes suitable for therapy



Yordanova A, Eppard E, Kürpig S, Bundschuh RA, Schönberger S, Gonzalez-Carmona M, Feldmann G, Ahmadzadehfar H, Essler M. Theranostics in nuclear medicine practice. *Onco Targets Ther.* 2017;10:4821-4828

One cassette for diagnostic and therapeutic molecules in preclinical and clinical

AMIDEX Project granted with C2VN/CERIMED



First granted collaborative project between C2VN/CERIMED and PMB :

MiRTxGlio

Microfluidic radiosynthesis for theranostics of glioblastoma
multiform

PMB

ALCEN



Thanks for your attention!

Special thanks to:

- **Olga Ovdiichuk** at Nancyclotep
- **Hemantha Mallapura** at Karolinska Institute
- **PMB's team**

For further info, please check:

O.Ovdiichuk et al, Lab Chip, 2021,21, 2272-2282

Future presentations at ISRS 2022

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Thank you for your attention

