

**3<sup>th</sup> GLOBAL MEETING**  
**WG & Core Group meeting of the COST Action CA19114**  
**Network for Optimized Astatine Labeled Radiopharmaceuticals**

**Date:** October 1<sup>st</sup> – October 4<sup>th</sup>, 2024

*Nantes, France*

**Place:**



**THE 3RD AND FINAL MEETING OF COST NOAR, THE EUROPEAN NETWORK DEDICATED TO ASTATINE-211 ([astatine-net.eu](http://astatine-net.eu))**

**Core Group and Working Groups Leaders:**

Jean-François Gestin  
Emma Aneheim  
Antero J. Abrunhosa  
Marek Pruszyński  
Penelope Bouziotis  
Andreas Tue Ingemann Jensen  
Dana Niculae  
Emilija Janevik  
Laurent Navarro  
Sture Lindegren  
François Guérard  
Stig Palm

**Complete list  
of participants:**

**Participants:**

|            |            |
|------------|------------|
| Allard     | Mathilde   |
| Aneheim    | Emma       |
| Angot      | Christophe |
| Antero     | Abrunhosa  |
| Apostolova | Paulina    |
| Back       | Tom        |
| Bajrami    | Ismet      |
| Balkin     | Ethan      |
| Bilodeau   | Denis      |
| Bitlis     | Arcan      |
| Blaseg     | Udo        |
| BODERE     | Françoise  |
| Bonnet     | Jean       |
| BOURGEOIS  | Mickaël    |

|                 |                   |
|-----------------|-------------------|
| Bouziotis       | Penelope          |
| Calais          | Jeremie           |
| Carsten         | Kramer            |
| Cazzola         | Emiliano          |
| Cecile          | Bourdeau          |
| Chaize          | Clara             |
| Chérel          | Michel            |
| Chouin          | Nicolas           |
| Cui             | Tongjiang         |
| Custodio        | Camille           |
| Damas           | Liliana           |
| De France       | Gilles            |
| De Schepper     | Stijn             |
| Do Carmo        | Sergio            |
| Domingos        | Carla             |
| Donnard         | Jerome            |
| Duval           | Samuel            |
| Edwards         | Richard           |
| Ekinci          | Deniz             |
| Ellinor         | Hansson           |
| Elvas           | Filipe            |
| Eve             | Dave              |
| Eychenne        | Romain            |
| Fanier          | Sylvain           |
| Feng            | Yutian            |
| Fouinneteau     | Romain            |
| Fujioka         | Sunao             |
| Fysikopoulos    | Lefteris          |
| Gabriel         | Bahuaud           |
| Galland         | Nicolas           |
| Garcia-Arguello | Segundo Francisco |
| Gaschet         | Joelle            |
| Gauché          | François          |
| Gaugler         | Marie-Helene      |
| Gautier         | Gaëlle            |
| Gazzola         | Sophie            |
| Gestin          | Jean-François     |
| Gkikas          | Antonis           |
| Gonnot          | Amandine          |
| Gourni          | Eleni             |
| Guérard         | Francois          |
| Guillet         | Sébastien         |
| Gülaldi         | Nedim C.M.        |
| Gülaldi         | Demet             |
| Haddad          | Ferid             |

|                 |              |
|-----------------|--------------|
| Happel          | Steffen      |
| Harousseau      | Jean-Luc     |
| Harray          | Jerome       |
| Heinrich        | Tobias       |
| Herth           | Matthias     |
| Heuze Vourc'h   | Nathalie     |
| Hoehne          | Aileen       |
| Hrynychak       | Ivanna       |
| Hsiaoju         | Lee          |
| Huynh           | Truc (Sally) |
| Ingemann-Jensen | Andreas      |
| Issac           | Delphine     |
| Ivanovska       | Emilija      |
| Jalilian        | Amirreza     |
| Jan Jensen      | Holger       |
| JANIAK          | Tomasz       |
| Jankovic        | Drina        |
| Jashari         | Armend       |
| Jean-Luc        | Lefaucheur   |
| Johnson         | Dave         |
| Kabayama        | Kazuya       |
| Koers           | Lucas        |
| Kolenc          | Petra        |
| Kumlin          | Joel         |
| Le Gal          | Julien       |
| Le Saec         | Patricia     |
| Leidermark      | Erik         |
| Lethimonnier    | Franck       |
| Li              | Yawen        |
| Li              | Feize        |
| Ligeour         | Mathilde     |
| Lindegren       | Syure        |
| Liu             | Yang         |
| Lonnroth        | Milton       |
| Loussouarn      | Anthony      |
| Lugat           | Alexandre    |
| Mahboob         | Gharibi      |
| Maingueneau     | Clémence     |
| Marshall        | Graham       |
| Martin-Gauthier | Joelle       |
| Metello         | Luis F.      |
| Mikolajczak     | Renata       |
| Mirković        | Marija       |
| Mo Kang         | Choong       |
| Moffitt         | Gregory      |

|                |           |
|----------------|-----------|
| Moreau         | Aur lie   |
| Navarro        | Laurent   |
| Neumaier       | Bernd     |
| Niculae        | Dana      |
| Ohnuki         | Kazunobu  |
| Paillard       | Alexandra |
| Palm           | Stig      |
| Palmer         | Max       |
| Paulo          | Antonio   |
| PILATIS        | EIRINAIOS |
| Prezeau        | Tony      |
| Prince         | Deidre    |
| PRUSZYNSKI     | MAREK     |
| Radovi         | Magdalena |
| Rajkova a      | Zvezdana  |
| Reymond        | Adrien    |
| Rivi re        | Karine    |
| Rousseau       | Caroline  |
| Royer          | Anne      |
| Santos         | Sofia     |
| Sarah          | Chaib     |
| Scutnaire      | Bruno     |
| Seeman         | Johanna   |
| Senturk        | Murat     |
| Sergi-Lindell  | Francesco |
| Sevenois       | Matthijs  |
| Sora           | Fallaha   |
| Sosabowski     | Jane      |
| Spahiu         | Fakir     |
| Stankovi       | Aljo a    |
| Szucs          | Zoltan    |
| Tabacaru       | Gabriel   |
| Takamatsu      | Masayuki  |
| Taki           | Kazuya    |
| Tereshatov     | Evgeny    |
| Thonon         | David     |
| Ukon           | Naoyuki   |
| Valeix         | Richard   |
| Viana          | Alice     |
| Vranjes-Djuric | Sanja     |
| Washiyama      | Kohshin   |
| Watabe         | Tadashi   |
| Wheldon        | Carl      |
| Wilbur         | Scott     |

|            |           |
|------------|-----------|
| Yokell     | Daniel    |
| Young      | Jennifer  |
| Zahi       | Ilyes     |
| Zalutsky   | Michael   |
| Zhuo       | Weibin    |
| Zimmermann | Richard   |
| Zirn       | Loïc      |
| Zyuzin     | Alexander |

**Responsible minutes:** Emilija Janevik  
Laurent Navarro

**MEETING PROGRAM**

**Tuesday, October 1<sup>st</sup>, 2024 / Nantes**

17.00 **Registration**

18.00 **Welcome address**

**Speakers:** Jean-François Gestin (Action Chair) and Emma Aneheim (Action Vice Chair)

Opening greeting from the Acting Chair and Action Vice Chair:

Welcome to all attendees, and thank you for your interest and support. Acting Chair and Action Vice Chair expressed their gratitude to the core team, working group leaders, MC members, and industry partners for their collaboration over the past four years, starting from the time of the pandemic, as well as to COST Office for their support and funding of the project.

The Acting Chair introduced **Dr Jérémie Calais** as the invited lecturer for the opening of the 3th Global meeting

18.15 **Invited lecture: "PSMA-targeted Lu177 Therapy :From research to standard-of-care"**

**Dr Jérémie Calais** - Pluvicto™ from clinical research to Market Authorization

Associate Professor, Department of Molecular and Medical Pharmacology  
Director, UCLA Theranostics Program  
Director, Clinical Research Program  
Ahmanson Translational Theranostics Division  
University of California, Los Angeles

**PSMA-targeted THERANOSTICS in PROSTATE CANCER**

**<sup>68</sup>Ga-PSMA-11 PET/CT History**

**From Clinical Research to Standard of Care**

**Lutetium-177-PSMA-617**  
FDA approved since 2022

**Gallium-68-PSMA-11 PET**  
FDA approved since 2020

**PSMA**  
Prostate Specific Membrane Antigen

Santor et al. *N Engl J Med.* 2021

C Arnold. *Nature Medicine* 2022

**Since December 2020**

**Gallium Ga 68 PSMA 11** Injection, for intravenous use  
Initial U.S. Approval: 2020

**INDICATIONS AND USAGE:**  
Ga 68 PSMA-11 Injection is a radioactive diagnostic agent indicated for positive emission tomography (PET) of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer.

• with suspected metastasis who are candidates for curative definitive therapy  
• with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level (1).

UCSF UCLA

**Since October 2021**

**CMS.gov**  
Centers for Medicare & Medicaid Services

**Medicare**

TABLE 1. Summary of PSMA PET/CT Indications for Coverage Under Medicare Part B

| ICD-10 Code | ICD-10 Description           | ICD-10 Category | ICD-10 Subcategory           |
|-------------|------------------------------|-----------------|------------------------------|
| C61.91      | Prostate cancer, unspecified | Neoplasms       | Prostate cancer              |
| C61.92      | Prostate cancer, metastatic  | Neoplasms       | Prostate cancer              |
| Z43.01      | Encounter for PSA blood test | Encounter for   | Encounter for PSA blood test |
| Z43.02      | Encounter for PSA blood test | Encounter for   | Encounter for PSA blood test |

**Since January 2022**

**Prostate Cancer**  
Version 3.2022 – January 10, 2022

**"front-line imaging tool"**  
NCCN INDICATIONS

Bone and soft tissue imaging is indicated to look for regional and distant metastases for:

- Initial staging**  
Unfavorable/intermediate Risk  
High Risk  
Very high risk
- PSA persistence/recurrence**  
after RP  
after RT
- Progressing mHSPC or mCRPC**

**BEYOND VISION – ALPHA VS BETA**

**Increase the Radiation Dose Delivery to Tumor ?**

Beta decay:  ${}^A_Z X \rightarrow {}^A_{Z+1} Y + {}^0_{-1} \beta$

Alpha decay:  ${}^A_Z X \rightarrow {}^A_{Z-2} Y + {}^4_2 \alpha$

**PHYSICAL PROPERTIES OF THE RADIONUCLIDE**

**TARGETED ALPHA THERAPY (TAT)**

- Shorter range in tissue
- Higher linear energy transfer (LET) x 100
- DNA damage incidence is proportional to the absorbed dose
  - 40 DSB /cell/Gy
  - 1000 DNA base lesions /cell/Gy

Parent → Daughter + Beta Particle

Parent → Daughter + Alpha Particle

**BEYOND VISION – AT211-PSMA ?**

Half Life 7.2 h

$\alpha$  5.9 MeV,  $\gamma$  decay, 42% Electron capture, 58%  $\beta^+$  1.02 MeV, 100%  $\beta^+$  0.5 MeV, 100%  $\beta^+$  0.5 MeV,  $\alpha$  7.4 MeV

Anil P Bidkar et al. *Theranostics* 2024

Watabe T, et al. *Eur J Nucl Med Mol Imaging.* 2023

Manual on the proper use of the <sup>211</sup>At-labeled PSMA ligand (<sup>211</sup>At] PSMA-5) for clinical trials of targeted alpha therapy (1st edition)

Watabe T, et al. *Ann Nucl Med.* 2024

19.30 **Cocktail reception**

**Wednesday October 2<sup>nd</sup>, 2024 / Nantes**

08.00 Welcome : Opening address  
**Dr. Emma Aneheim & Dr. Jean-François Gestin**

08.15 **Dr. Jean-François Gestin - COST NOAR Project**

**Objective:** Introduction of COST Action

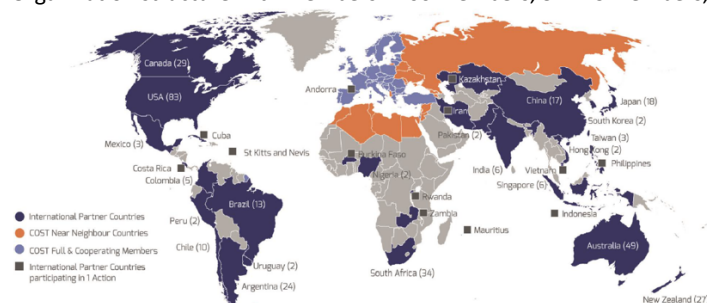
Official start : March 2020

Kick off meeting (virtual), October 22, 2020

The Action will end on Monday, October 21, 2024

- Inter-governmental program dedicated to the financing of European and international research networks
- EU funding in addition to member countries
- Management by the COST association based in Brussels

Organization structure with members - 160 members, 37 MC members, 21 EU Countries



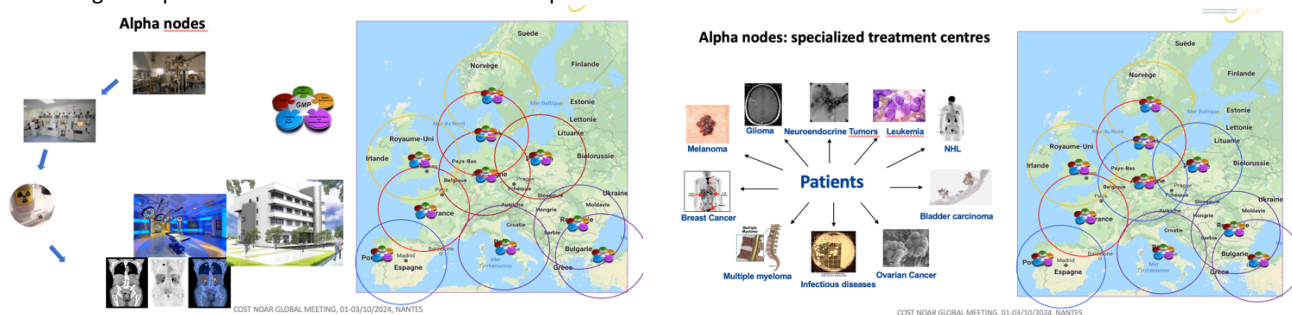
The Acting chair was presented for what is COST made

**To finance:** All disciplines, all types of partners (academic, private, associations, institutional ...), and Network activities only (**no funding for equipment or research staff**):

- Meetings, workshops, conferences,
- Short stay missions,
- Training schools,
- Dissemination actions including publication (open access).

Provided budget quite low - Approximately 100.000€/year for a duration of the project of 4 years, according to the number of countries participating in the action.

The Acting chair presented the ambition to built an European Network:



08.25 Progress and prospects

**WG 1: Production: what has been achieved -- Astatine-211 targetry, production, extraction, back-up, logistics**

WG Leader: **Dr. Sture Lindegren**

**Objective:** To ensure reliable and sustainable astatine-211 production and development of a standardized purification method. This WG will focus on astatine-211 production in order to ensure reliable access to inject patients with therapeutic doses of qualified astatine-211 within the ATNodes in Europe.

**Tasks:**

- T.1.1. Establishing producer catalogue and astatine-211 production procedure
- T.1.2. Automating processes
- T.1.3. Proposing alternative production solutions
- T.1.4. Researching the relevant intermediate (radiochemical) form(s) and final; (radiopharmaceutical) form for astatine-211 delivery
- T.1.5. Controlling stability, measuring radiolysis, defining present species
- T.1.6. Organising intra and extra cluster logistics / EU territorial grid / back-up

### Deliverables, milestones and estimated delivery month

D.1.1. Final forms for astatine-211 delivery (radiochemical or radiopharmaceutical) (m12)

D.1.2. Reference documents (including catalogue of producers) for the production of astatine-211 freely available, open source (m27)

D.1.3. Proposing alternative production solutions National and European Logistics guidelines on the production of astatine-211 and related radiopharmaceuticals (m48)

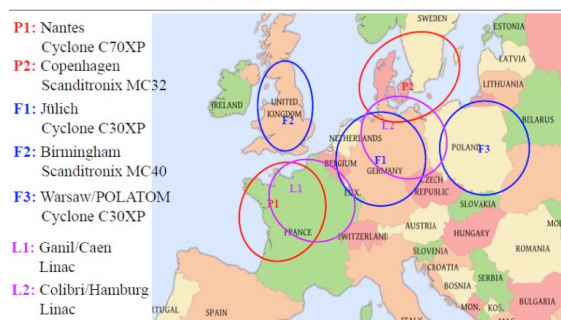
### WG1 achievements

- Final forms of Astatine-211 Delivery
- Reference documents (including catalogue of producers) for the production of astatine-211 freely available, open source
- Proposing alternative production solutions National and European Logistics guidelines on the production of astatine-211 and related radiopharmaceuticals

### Transport Challenges for <sup>211</sup>At

- $\alpha$ -emitter (stigma)
- Early state
- Half-life 7.2 h
- Require on demand production
- Regulation/cross-border transport
- Long distant transport / air cargo

### <sup>211</sup>At Production capacity overview Europe



### Dr. Holger Jan Jensen - Copenhagen cyclotron

Chief Cyclotron Physicist,  
Department of Clinical Physiology, Nuclear Medicine & PET,  
Cyclotron and Radiochemistry unit, 3982  
Copenhagen, Denmark.

### Objective: <sup>211</sup>At production status, Copenhagen, Denmark including:

- Status of the Cyclotrons in Copenhagen
- Production details , yields,
- Upgrades: Ion Source, High power int. Target,
- Re-inventing the wheel for <sup>211</sup>At Production in Copenhagen

Scanditronix MC32

**Transport range:**  
by flight or by car?

WG1:  
Flight "impossible"/  
VERY difficult due to  
long check-in and  
check-out times.

WG1:  
Car is the best option.

HJ: Rule-of-thump  
distance  $\leq T_{1/2}$ .



### Dr. Bernd Neumaier - Jülich cyclotron

Objective: Progress and prospects: INM-5 Forschungszentrum Jülich

- Presentation dedicated to the way and stage of construction of the new cyclotron facility for Radionuclide production at the cyclotron, Radionuclide production and Cleanroom with Radiopharmaceutical production.
- The presentation included detailed  $^{211}\text{At}$  Production/Separation/Chemistry, Production yield with Comparison of different target-types
- Obtained results:
  - Molten Target
  - Irradiation: 50-55  $\mu\text{A}$ , appr. 1 h, 50  $\mu\text{Ah}$
  - Yield: 1250 -1780 MBq EOB ( $\gamma$ -line, integration and efficiency)
  - Mean value: 1575 MBq (31.5 MBq/ $\mu\text{Ah}$ )
  - 0.012 % At-210
  - $\alpha$ -Beam energy: 28.7 MeV (isotope ratio  $^{211}\text{At}/^{210}\text{At}$ )
  - $\rightarrow$  Extrapolation: 35 MBq/ $\mu\text{Ah}$  x 50  $\mu\text{A}$  x 4 h = 7 GBq
- Synthesis of **4- $^{211}\text{At}$ At-I-phenylalanine**

#### $^{211}\text{At}$ -production and chemistry



$^{211}\text{At}$ -European Landscape

#### Pr. Carl Wheldon - Birmingham cyclotron

School of Physics and Astronomy, University of Birmingham

#### Objective: Astatine-211 production at the Birmingham Cyclotron Facility

The presentation contained:

- Overview of the Birmingham Cyclotron Facility - Twelve beam lines — two exit the vault and Hot filament ion source / Also 46 MeV  $^{14}\text{N}^{4+}$  and 70 MeV  $^{14}\text{N}^{5+}$  for nuclear physics.
- Current radioisotope production - Rb-81, F-18, Cu-64, Zn-62, Mn-52
- At-211 production development - Birmingham is part of a project funded by the UK Government with the Medical Radionuclide Innovation Programme (MRIP). The project is led by **Queen Mary's University London** (PI: Jane Sosabowski) involving King's College London. This project aims to establish the first UK production of Astatine-211. **Production will take place at Birmingham.**
- At-211 production: **Atley Solutions Ltd** is supporting in design of target station and the Bi-209 target and are supplying the targets for irradiation
- At-211 purification and synthesis: Atley will provide a C100 module for purification of astatine and synthesis of at-211-labelled compounds in Lon
- Targets and irradiations - Target-holder for external beam is a modified design based on the one used by Copenhagen Hospital (Holger Jensen) with the first irradiations planned for mid-October 2024 with  $\sim 5 \mu\text{A}$ .
- Advert of the new High Flux Accelerator-Drive Neutron Facility (HF-ADNeF)

#### Dr. Renata Mikolajczak - Polatom cyclotron

#### Objective: CERAD – a 30 MeV cyclotron in Poland (POLATOM cyclotron)

The presentation started by introducing CERAD - Center of Design and Synthesis of Radiopharmaceuticals for Molecular Targeting,

#### Action 4.2: Development of modern research infrastructure of the science sector with Coordinator: National Centre for Nuclear Research

- Cyclone<sup>®</sup> 30 XP ; proton- deuteron- alpha,
  - Proton (H- accelerated) 15 - 30 MeV 350 $\mu\text{A}$  and 2 exits
  - Deuteron (D- accelerated) 9 - 15 MeV 50  $\mu\text{A}$  with 2 exits
  - Alpha (He<sup>2+</sup> accelerated) (29) - 30 MeV 50  $\mu\text{Ae}$  with 1 common exit with H<sup>+</sup>

The presentation included detailed CERAD – layout of the ground floor and stages of Installation and commissioning planned, technical specifications (Proton and deuteron acceleration system, Alpha particle acceleration system).

The conclusion of this presentation was presenting the question and suggestion how to choose the right cyclotron for Therapy stressing the point what is the best for Alpha radio immuno therapy, is  $^{211}\text{At}$  is one of the best using IBA Cyclone 30 XP (proton- alpha)

#### Dr. Gilles de France- Ganil LINAC

#### Objective: Activities on the production of $^{211}\text{At}$ at GANIL



The presentation provided :

- GANIL overview
- Opportunities at GANIL using the LINAC
- Current limitations for <sup>211</sup>At
- The REPARE Project - Research and dEvelopements for the Production of innovAtive RadioElements, including their own objectives
- To study ways to increase <sup>211</sup>At production through the <sup>209</sup>Bi(α,2n) reaction and to take advantage of the characteristics of SPIRAL 2 beam (up to 80MeV and mAe of α)

The speaker presented the main results:

- WP1: - measurements of production cross section using an alpha beam and evaluation of calculation codes (inventory calculations)
- WP2: - design and manufacturing of a high power solid Bi target and test production run
- WP3: - design study of high power liquid Bi target and No to go
- WP4: - Test bench and measurements of physico-chemical properties of Rn for a possible Rn/At generator

As a next steps are predicted following:

- Installation of the irradiation station in a dedicated area
- Plan more production runs (1-2/months of LINAC time)
- Shipments to ARRONAX, CYCERON
- Structure the activity at various levels (ongoing actions):
  - Local: radiolabelling of VLA4 antibody with At as a POC
  - Regional: reinforce the link with the Nantes area
  - National: create a network of labs/hospitals/industrial partners interested in alphatherapy

International: PRISMAP+, ITN MC network, COST

## 09.25 **WG2A: Chemistry & Radiochemistry: what has been achieved**

**WG2A Leader: Dr. François Guérard**

**Objectives:** Development of radiolabelling strategies adapted to different vectors.

This WG was focused on building different astatine-211 radiolabelled vectors in order to establish the preclinical proof of concept for some of them that will be pushed forward through the clinical development.

### Tasks:

T.2.1. Setting up couples: vector / astatine-211:

- Innovating the design of more stable ligands.
- Developing modelling techniques confronted with physico-chemical measurements in order to optimize the astatine-211 ligand binding.

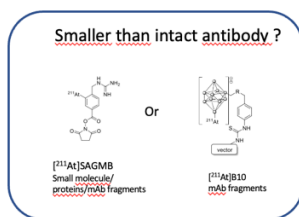
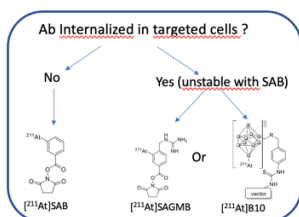
T.2.2. Setting up theranostic aspects: vector / imaging agents.

T.2.3. Sharing aspects of toxicology studies to prepare drug files.

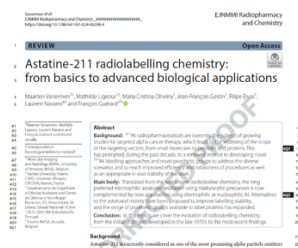
T.2.4. Automating, optimizing, and standardizing of radiolabelling protocols for clinical trials.

### What has been achieved:

- Identification of the most advanced prosthetic groups for the Proof of concept



This work has been synthesized in a review article (in press)



**Dr. Matthias Herth** - University of Copenhagen

**Objective:** ASTATINATIONS and their in vivo applications

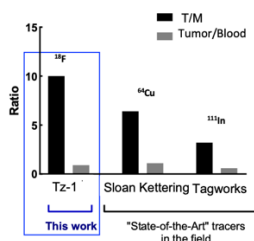
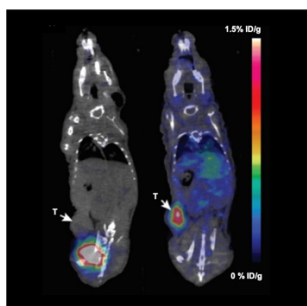
- Development of Labeling Methods
- Development of Small Molecule and Peptide <sup>211</sup>At-based Radiopharmaceuticals
- Minimize De-Astatination
- Increase Cell Internalization - as therapeutic efficacy is positively correlated
- Internalized alpha-emitters increase therapeutic efficacy due to recoil energy of the daughter (ca. 5% of the total release energy)
- DE ASTATINATION – rational drug design
- Hypothesis - De-Astatination is reduced when the <sup>211</sup>At is attached to an area that lies deep down in the pocket of the receptor and <sup>211</sup>At can be substituted for a phenyl ring of the naphthyl moiety of PSMA-617
- Receptor-Ligand-Binding

### DRUG DEVELOPMENT

- Cmpd Library and In Vitro Characterisation, In vivo Selection - Selected to be translate as a compromise between affinity and internalization, in vivo tumo uptake and retention and excretion profile

HOW TO SYNTHESIZE THE PSMA REFERENCE CMPDS AND PRECURSORS - Solid Phase Peptide Synthesis and Precursor Synthesis

CHALLENGES AND SOLUTION TO ASTATINATE PSMA DERIVATIVES and NEW CHEMISTRY - Precursor Synthesis and Labeling  
 DRUG DEVELOPMENT - Precursor Synthesis and <sup>211</sup>At-Labeling, In vivo Evaluation and Correlation between lipophilicity, diffusion & non-specific binding  
 IN VIVO SELECTION, CELL INTERNALIZATION AND TUMOR BINDING and TREATMENT STUDIES IN TUMOR-BEARING MICE – PILOT DATA  
 PRETARGETING STRATEGIES - Proof-of-Concept



**Dr. Yawen Li** - University of Washington  
 Department of Radiation Oncology  
 University of Washington, Seattle, WA, United States

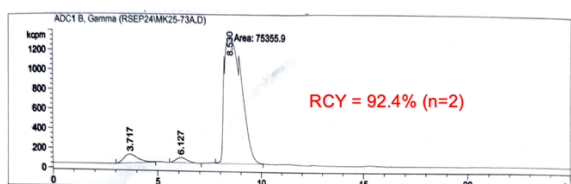
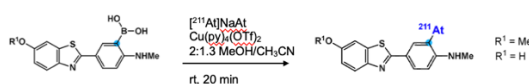
**Objective:** Validation of the Semi-Automated At-211 Isolation Process Using Te-packed Columns for Routine Production

- At-211 Isolation Using Tellurium-Packed Columns
- Previous Semi-Automated At-211 Isolation System
- Current Semi-Automated At-211 Isolation System
- Semi-Automated At-211 Isolation Process
- At-211 Production Runs
- Radiochemical Purity - Radio-iTLC
- Radiochemical Purity - Radio-HPLC
- ICP-MS analysis
- Secondary Te Column
- *Closo*-Decaborate(2-) Astatination
- Cu-Catalyzed Astatination

The semi-automated Te-column consistently achieved high isolation yield, along with superior radiochemical and chemical purity, demonstrating its potential for use in routine production

Modifications such as chemical-resistant equipment and the addition of a 0.2-micron filter to reduce tellurium impurities have ensured process robustness and consistent product quality

The isolated <sup>211</sup>At demonstrated high RCYs for astatination reactions using *closo*-decaborate(2-) and boronic acid labeling methods



Sean W. Reilly et al., *Org. Lett.* 2018, 20, 7, 1752–1755  
 Emily K. Kirkeby, et al., *Appl. Radiat. Isot.*, 2023, Vol 191, 110555

## 10.00 Industrial Presentations

- IBA - Leading particle accelerator technologies  
 Bruno Scutnaire RadioPharma Solutions

**Objective :** IBA – Global leader in particle beam technology







IBA Radiopharma Solutions – Installed Base Europe

IBA as a key partner – one stop shop for equipment, and more

- IBA Radiopharma Solution offers the widest range of cyclotron, from 9 MeV up to 70MeV, extensive targetry, chemistry modules and associated services
- IBA solutions will allow you to reach **highest production capacity** as demonstrated in more than 300 radiopharmacies around the world.

IBA's joint venture PanTera  
secures EUR 93 million in  
oversubscribed Series A round  
to accelerate global actinium-  
225 production

Corporate / 11.09.2024

| Cyclone @ Key   | Cyclone @ Kiube   | Cyclone @ Ikon  | Cyclone @ 30XP   | Cyclone @ 70  | Rhodotron TT-300HE  |
|---|---|---|--|---|---|
| 3Ci of F18 in 2h  | Up to 300 FDG dose in 2h  | Up to 1500µA on target  | Proton, Deuteron and Alpha acceleration  | (5) Only running 70MeV on the field   | <b>PANTERA</b><br>A BETTER FIRST STEP   |
| 9 MeV<br>Optimized robustness   | 18 MeV<br>8 exit port   | 13 to 30 MeV  | 15 to 30 MeV<br>IBA only   | 30 to 70 MeV<br>IBA only  | IBA only  |
|  |  |  |  |  |  |

**- IONETIX - Astatine-211 Commercial Supply**  
**David M. Eve, Vice President, Ionetix Alpha**

**Objective:** Ionetix Astatine-211 Commercial Supply Chain with Ionetix Commercial At-211 Cyclotron Platform, Ionetix Commercial At-211 Manufacturing Platform including Ionetix Commercial At-211 Program Status

U.S. Based Astatine-211 Services:

- At-211 supply
- CDMO/CMO services
- FDA Regulatory support
- Logistics

**- NUSANO - supplying the fight against cancer**  
**Greg Moffitt, Director of Target Development**

**Objective:** Commercial operations begin 2025

Production Capabilities

<sup>211</sup>At: Worldwide Production

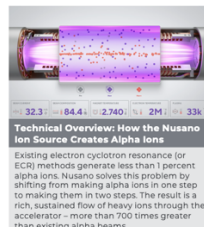
Capability of production – 25+ different isotopes, up to 12 simultaneously

<sup>211</sup>At Production - <sup>211</sup>At yields: 0.44-1.1 mCi/µAhr<sup>1</sup>

<sup>211</sup>At Production - <sup>211</sup>Rn generator for <sup>211</sup>At - expand our service region

**Technology Overview Videos**

Watch at <https://nusano.link/tech-overview>



**10.15 Dr. Ferid Haddad - Arronax cyclotron for Lu-177 and Ac-225 on behalf of the GIP Arronax Team and Prisma@subatech, Nantes Université**

**Objective:** Radionuclides and radiopharmaceuticals development at ARRONAX

ARRONAX - Accelerator for Research in Radiochemistry and Oncology at Nantes AtlantiX

- Creation date 2008
- End of commissioning (dec 2010)
- 70 workers (including Phd students)
- Soon 2 cyclotrons (C70XP and Kiube 180)
- ISO 9001 certify since 2014

ARRONAX is at the heart of a pluridiciplinary cluster

Beam characteristics:

- Multi-particles: proton, deuteron and alpha particles
- High energy: up to 70 MeV (protons, alpha particles)
- High intensity: up to 750 µA in dual proton beam mode

A versatile facility:

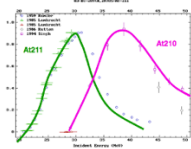
- 2000 m<sup>2</sup> of restricted area / 6 vaults / 3 lines of hot cells for radionuclides production / 3 lines of hot cells for sterile radiopharmaceuticals production

Aronax radiopharmacy (Nantes university hospital/ Arronax)

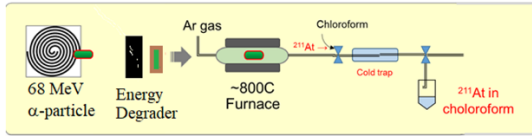
Arronax PIPELINE

Astatine – 211 - Astatine-211 production route used @Arronax:

$^{209}\text{Bi} + \alpha \rightarrow ^{211}\text{At} + 2n$   
coproduction of  $^{210}\text{At}$



**Production scheme:**



The beam energy degrader made of graphite  
→ changing its thickness allows to change the At210/At211 ratio

Target preparation using evaporation under vacuum  
Dry extraction of  $^{211}\text{At}$   
Improving our  $^{211}\text{At}$  production process

10.30 Break - Industrial exhibition

**11.00 WG2B: Biology: what has been achieved**  
WG2B Leader: **Dr. Joelle Gaschet/ presented by Dr. François Guérard**

**Objectives:** Inventory of vectors properties proposed and selected for astatine labelling in order to establish the preclinical proof of concept for some of them that will be pushed forward through the clinical development

**Deliverables & Milestones:**

Catalogue of validated radiolabelling techniques dependent on vectors including advantages and disadvantages, and multi-centre diffusion  
Preclinical proof of concept

- Overview of the in vivo preclinical studies using  $^{211}\text{At}$ ,  $^{213}\text{Bi}$ ,  $^{149}\text{Tb}$ ,  $^{225}\text{Ac}$  and  $^{227}\text{Th}$
- Only studies presenting 3 sets of data: Efficacy, Toxicity, Biodistribution

What has been achieved:

**$^{211}\text{At}$  Preclinical studies : Joëlle Gaschet & Mathilde Allard**

| Vector  | Name | Local | Inj      | Type | Tumor    | Spec.   | Graft | Model | Biod  | Effic | Tox | Ref |
|---------|------|-------|----------|------|----------|---------|-------|-------|-------|-------|-----|-----|
| peptide | PSMA | A11   | ext      | IV   | Prostate | PC3     | human | SC    | 211At | Nude  |     | 16  |
| peptide | PSMA | 3Lc   | internal | IV   | Prostate | PC3-PIP | human | SC    | SCID  |       |     | 2   |
| peptide | PSMA | L1    | internal | IV   | Prostate | PC3-PIP | human | SC    | NSG   |       |     | 9   |

**$^{225}\text{Ac}$  Preclinical studies : Joëlle Gaschet & Mathilde Allard**

| Type    | Target | Name | Local    | Inj | Type     | Tumor   | Spec. | Graft | Model | Biod | Effic | Tox | Ref |
|---------|--------|------|----------|-----|----------|---------|-------|-------|-------|------|-------|-----|-----|
| peptide | PSMA   | A11  | ext      | IV  | Prostate | PC3     | human | SC    | 225Ac | Nude |       |     | 16  |
| peptide | PSMA   | 3Lc  | internal | IV  | Prostate | PC3-PIP | human | SC    | SCID  |      |       |     | 2   |

**$^{213}\text{Bi}$  Preclinical studies : Sanja Vranjes-Djuric & Drina Jankovic**

| Type    | Target | Name | Local    | Inj | Type     | Tumor   | Spec. | Graft | Model | Biod | Effic | Tox | Ref |
|---------|--------|------|----------|-----|----------|---------|-------|-------|-------|------|-------|-----|-----|
| peptide | PSMA   | A11  | ext      | IV  | Prostate | PC3     | human | SC    | 213Bi | Nude |       |     | 16  |
| peptide | PSMA   | 3Lc  | internal | IV  | Prostate | PC3-PIP | human | SC    | SCID  |      |       |     | 2   |

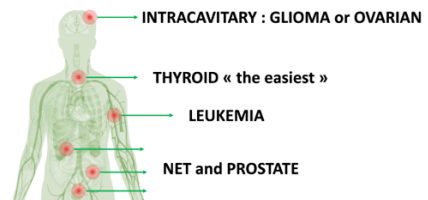
**What has been achieved**

➤ Fruitful inter-WG discussion about the « best » clinical indications in Coimbra, May 2023 (to be continued by WG4...)

**What has been achieved**

**$^{149}\text{Tb}$  Preclinical studies : Sanjav Vranjes-Djuric & Zorana Milanovic**

| Vector  | Name | Local    | Inj | Type | Tumor    | Spec.    | Graft | Model | Biod | Effic | Tox | Ref |
|---------|------|----------|-----|------|----------|----------|-------|-------|------|-------|-----|-----|
| peptide | PSMA | PSMA-617 | int | IV   | prostate | PC-3 PIP | human | IV    | SCID |       |     | 6   |



**Dr. Emma Aneheim** - University of Gothenburg  
**Tom Bäck, PhD, Researcher**  
Targeted Alpha Therapy group, University of Gothenburg, SWEDEN

**Objective:**

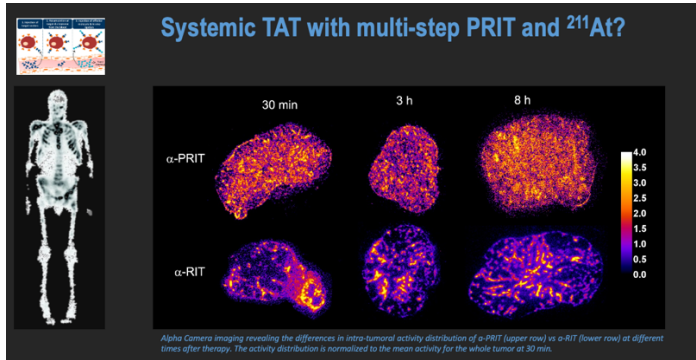
- Develop and evaluate TAT
- Derive parameters for dosimetry
- Verify and validate dosimetry

Intra-peritoneal  $\alpha$ -TAT with  $^{211}\text{At}$  for Ovarian Cancer

- Clinical Trial Phase I a/b,  $^{211}\text{At}$ -MX35-F(ab')<sub>2</sub>
- Preparing a Phase I c,  $^{211}\text{At}$ -trastuzumab (IgG)
- Planning for a Phase II/III
- Effects on normal organs
- Derive parameters for dosimetry

**A Novel Method for Real-Time Quantification of Radioligand - Binding to Living Tumor Cells In Vitro**

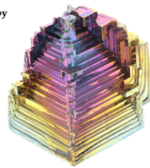
- Evaluation using micro tumours and spheroids
- Systemic TAT with multi-step PRIT and  $^{211}\text{At}$ ?



**Dr. Michel Chérel** - University of Nantes  
CRC<sup>2</sup>NA Nuclear Oncology

**Objective : Alpha particles in Nantes - A little journey with our colleagues from IETU Karlsruhe**

**Anti-Tumor Efficacy of PD-L1 Targeted Alpha-Particle Therapy in a Human Melanoma Xenograft Model**



Use PD-L1 for TAT to target the tumor, and its stroma using anti-PDL1.

- alpha RIT in solid tumors - NET
- $^{211}\text{At}$  in Multiple Myeloma
- Alpha-RIT :  $^{211}\text{At}$ -anti-mCD138 - Fractionated doses protocol, survival curves, Repeated doses protocol, Repeated doses - survival curves
- Preclinical study of Targeted Alpha Therapy using  $^{211}\text{At}$ -labeled phenylalanine derivative in a syngeneic Multiple Myeloma model
- Alpha-RIT :  $^{211}\text{At}$ -Phenylalanine - Amino acid transporter LAT-1 and Dose escalation and efficacy study of  $^{211}\text{At}$ -APA

eBioMedicine  
Part of THE LANCET Discovery Science



**eBioMedicine**  
Part of THE LANCET Discovery Science

**Brain intratumoural astatine-211 radiotherapy targeting syndecan-1 leads to durable glioblastoma remission and immune memory in female mice**

Loris Roncati<sup>1,4</sup>, Séverine Maréchal-Lambot<sup>1,4</sup>, Charlotte Roy<sup>1,4</sup>, Romain Eychemé<sup>1,5</sup>, Sébastien Guard<sup>1,4</sup>, Sylvie Avril<sup>1</sup>, Nicolas Chouin<sup>1,6</sup>, Jérémie Riou<sup>1</sup>, Mathilde Allard<sup>1</sup>, Audrey Rousseau<sup>1,4</sup>, François Guérard<sup>1</sup>, François Hindric<sup>1,4</sup>, Michel Chérel<sup>1,4,11,12</sup> and Emmanuel Garçon<sup>1,4,13,14</sup>

**Glioblastoma : an unmet clinical need**

**Locoregional targeted radiotherapy in GBM - Single injection of [ $^{211}\text{At}$ ]-9E7.4**

- [ $^{211}\text{At}$ ]-9E7.4 radiotherapy reveals a major survival benefit and generates long-term survivors
- Long-term memory response - Survivors rechallenge with a new contralateral graft in the striatum
- Radiobiology - Alpha particles can destroy cells in G0 phase
- Radiobiology of astatine-211
- $^{211}\text{At}$ -anti-CD138 induces DNA double-strand breaks
- $^{211}\text{At}$ -anti-CD138 increases cytoplasmic dsDNA levels

- $^{211}\text{At}$ -anti-CD138 can induce IFN- $\beta$  secretion
- Intravesical [ $^{211}\text{At}$ ]At-anti-CAIX mAb

### 11.30 **WG3: Improving dosimetry: what has been achieved**

WG Leader: **Dr. Stig Palm**

**Objective:** Construct and validate computer models for estimating absorbed dose to tumours and healthy tissues. This WG will focus on dosimetry to predict efficacy and risks associated to the use of the different astatine derivatives. Absorbed (radiation) dose must be estimated to both tumours and healthy tissues. This is necessary to fulfil radiation safety regulations, but also to predict efficacy and risks within the context of personalized medicine. Dosimetry is thus a crucial component for selecting and optimizing the best vectors for astatine-211 delivery. However, consensus on best dosimetry techniques for alpha-emitters such as astatine-211 are lacking and need to be developed.

#### Tasks:

- T.3.1. Collecting data on stability and biokinetics from all consortium members.
- T.3.2. Constructing biokinetic models that provide the best fit to the collected data.
- T.3.3. Proposing new experiments that will test/validate the new models.
- T.3.4. Simulating decay of astatine-211 to the predicted distribution sites.
- T.3.5. Generating (predicted) maps of absorbed dose to tumours and healthy tissues for a range of vector/astatine-211 combinations.

#### AlphaMet: Consortium

Get in touch for more information or to join as a collaborator:

- Coordinator: Jan Rusnak [jrusnak@cml.cz](mailto:jrusnak@cml.cz)
- Creating Impact WP Leader: Ana Denis-Bacelar (NPL) [ana.denisbacelar@npl.co.uk](mailto:ana.denisbacelar@npl.co.uk)
- General enquiries: [alphametproject@gmail.com](mailto:alphametproject@gmail.com)

**Consortium**

Eight metrology institutes (NMI/DI)

Eight clinical and research partners, and one affiliated entity

2.6 M€ (1.9 M€ EU)  
Sep 2023 – Aug 2026

Partners include: CCM, ENEA, sck cen, KU LEUVEN, etc.

#### AlphaMet: Technical Work Packages

AlphaMet aims to address the unique and unmet metrological challenges of alpha emitters to support its clinical implementation before wide routine adoption

| WP1: Standards   | WP2: Activity (QI)  | WP3: Absorbed dose   | WP4: Bone marrow  |
|--|---|--|---|
| Standards: $^{225}\text{Ac}$ , $^{212}\text{Pb}$ , $^{211}\text{At}$<br>$^{225}\text{Ac}$ activity intercomparison | Improve QI methods<br>Accuracy, reproducibility, uncertainties: SPECT Intercomparison | Uncertainty analysis in biokinetic modelling<br>Impact of macro/ micro-dosimetry assumptions | Bespoke bone phantom<br>Quantitative Bone marrow morphological imaging (DECT & MRI) |

End-to-end metrology

#### AlphaMet: Survey on the Use of Alpha Emitters

**Dr. Tom Bäck** - University of Gothenburg  
Researcher

Targeted Alpha Therapy group, University of Gothenburg, SWEDEN

**Objective:** Summary from Gothenburg – Dosimetry/ Dosimetryology

#### Can dosimetry predict biological outcome of TAT?

- TAT with  $^{211}\text{At}$  → Same mean absorbed dose to whole kidney
- Different kidney toxicity due to different sub-organ dose distribution?

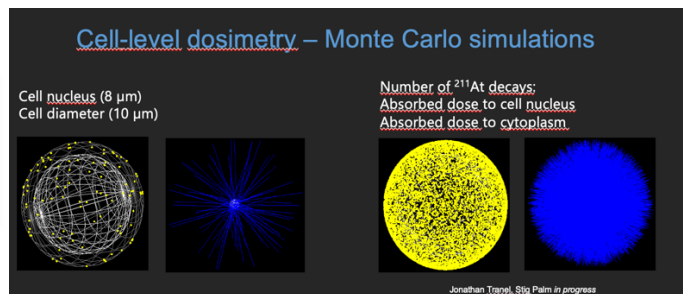
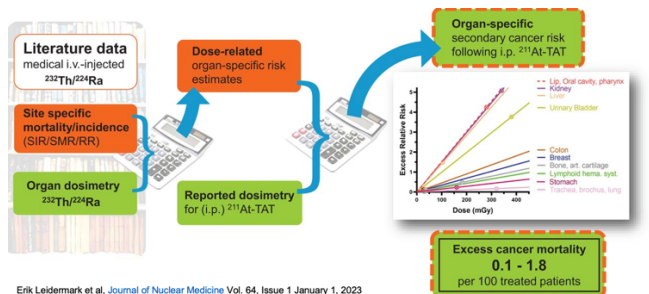
Non-uniform dose distribution in tumours - Both in macro tumours and micro tumours

Dynamic simulation and dosimetry model - Intra-peritoneal  $^{211}\text{At}$ -RIT for ovarian cancer

Estimating the risk for secondary cancer following TAT with  $^{211}\text{At}$  intraperitoneal radioimmunotherapy

Dynamic simulation and dosimetry model - Intra-theical TAT with  $^{211}\text{At}$ -RIT for children with neuroblastoma

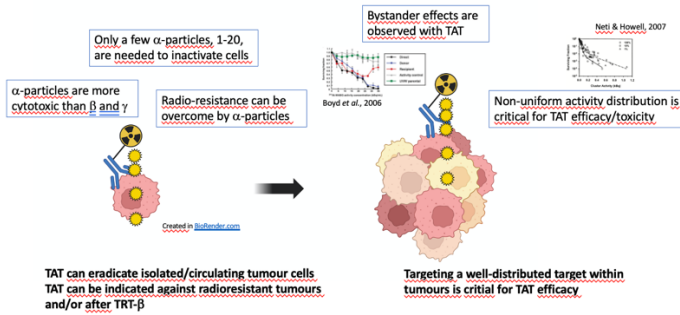
Dynamic simulation and dosimetry model - Intra-theical TAT with  $^{211}\text{At}$ -RIT for children with neuroblastoma



**Dr. Nicolas Chouin** - University of Nantes  
CRCI<sup>2</sup>NA Inserm U1307, Nuclear Oncology research team

**Objective :** TAT a translational journey - What we learn as a group and as a community... with dosimetry

Summary from the history:



Comparison of alpha-emitters – At-211 and Bi-213 in Multiple myeloma Breast cancer metastases model (Song *et al.*, Cancer Res, 2009)

2010: (non-uniform) activity distribution at micrometric scale... revealed

The <sup>211</sup>At-9E7.4 radiotherapy is efficient against glioblastoma

Mean asorbed dose delivered to GB tumours - Estimated mean absorbed dose to GB tumour > 300 Gy (for 100 kBq of <sup>211</sup>At-9E7.4)

**On-going work :**

- Comparison of alpha-emitters <sup>225</sup>Ac vs <sup>211</sup>At - Impact on haematological toxicity
- Spectroscopic autoradiography (<sup>225</sup>Ac)
- Standardization of practice in autoradiograph

**12.00 WG4: Clinical applications: what has been achieved**

WG Leader: **Dr. Alexandre Lugat/ presented by Mickaël Bourgeois**

**CRCI2NA, team 2 : nuclear oncology**

**Nuclear Medicine Department,**

**GIP ARRONAX**

**CHU Nantes**

**Objective:** Feedback and standardization of clinical practices.

This WG will focus on establishing which pathologies are best adapted to benefit from treatment with astatine-211 targeted therapy and prove the clinical potential. It will also focus on the organizational, regulation and economic aspects in order to evaluate the European practices and to propose a standardization of practices.

**Tasks:**

- T.4.1. Identifying relevant pathologies for the use of astatine-211.
- T.4.2. Analysing the practices of each member country and regulatory aspects.
- T.4.3. Evaluating the cost of therapy in each member country.
- T.4.4. Logistics and patient networking.
- T.4.5. Assessing the issue of radioactive waste.

| MALADIE | TRAITEMENT       | VECTEUR             | RADIOISOTOPE      | OPTIMISATION | PRECLINIQUE | IMAGERIE | PHASE 1 | PHASE 2 | PHASE 3 |
|---------|------------------|---------------------|-------------------|--------------|-------------|----------|---------|---------|---------|
| CNMIV*  | Imagerie TEP     | Anticorps (TLX-250) | <sup>89</sup> Zr  | PERTINENCE   |             |          |         |         |         |
| CNMIV*  | α IMMUNOTHERAPIE | Anticorps (TLX-250) | <sup>211</sup> At |              |             |          |         |         |         |

**Dr. Scott Wilbur** - University of Washington

<sup>1</sup>Translation Science and Therapeutics Division and Clinical Research Division  
Fred Hutch and Fred Hutch Cancer Center

<sup>2</sup>Department of Radiation Oncology and <sup>3</sup>Division Of Hematology and Oncology  
School of Medicine, University of Washington  
Seattle, WA USA

**Objective:** Update Of Fred Hutch/UW Clinical Trials Using <sup>211</sup>At-labeled mAb-B10 Conjugates

**Status of Fred Hutch/UW <sup>211</sup>At Clinical Trials**

- Introduction to Allogeneic Hematopoietic Cell Transplantation
- Reduced-intensity HCT For AML
- Treatment Plan of FH 9595
- Peripheral Blast Clearance After <sup>211</sup>At-BC8-B10
- Treatment plan and Results

**Clinical Hold of <sup>211</sup>At-BC8-B10 Protocols**

- FDA requiring dosimetry based on imaging
- While not part of the Clinical Hold - FDA requiring size-exclusion HPLC (UV & radio) in validation runs

**Dr. Tadashi Watabe** - University of Osaka  
Department of Radiology, Graduate School of Medicine,  
Osaka University

**Objective:** Clinical Application of Targeted Alpha Therapy using Astatine (<sup>211</sup>At)

**ASTATINE-211: JAPAN'S STRATEGIC WEAPON AGAINST CANCER**

Japan is working to develop a new and interesting ACCELERATOR-BASED RADIONUCLIDE THERAPY.

Researchers in Japan are developing and testing the alpha particle emitter, astatine-211 (<sup>211</sup>At), which has potential for use as a direct radionuclide therapy for treating cancer. Although clinical trials in humans are just beginning, collaborative initiatives are currently looking at astatine-211 in Japan, some European countries, and the United States.

In Japan, Osaka University and Kansai Medical University (KMC) are among five centers using cyclotron accelerators to make the radionuclide. Says Tadashi Watabe, a nuclear medicine physician at Osaka University,

Researchers at these centers hope that the radionuclide will be useful in radiotherapy treatments – one of the three key weapons in our anti-cancer arsenal. Radiotherapy harnesses radiation to kill cancer cells, and it's used in the treatment of many types of cancer. However, it's not always effective at eradicating DNA and killing cancer cells, with a potential of about five times that of conventional therapy.

But alpha particles are also a relatively new option for radiotherapy compared to gamma rays or beta-particles, which have already been used for a long time against cancer. One challenge, explains Watabe, is that alpha particles, unlike some other radiation therapies, cannot be applied externally as they have a very short penetration beyond the skin.

Alpha particles are therefore being developed for intravenous administration, or direct injection into the tumor. Recently, improved targeting of tumors has been reported for radionuclides from other parts of the world, explains Kazuya Kuboyama, a radiologist at Osaka University.

Alpha particles are therefore being developed for intravenous administration, or direct injection into the tumor. Recently, improved targeting of tumors has been reported for radionuclides from other parts of the world, explains Kazuya Kuboyama, a radiologist at Osaka University.



- Five cyclotron facilities for <sup>211</sup>At supply.
- Three clinical trials are currently underway in Japan.

Naka et al. EJNMMI Radiopharmacy and Chemistry (2024) 9:29  
https://doi.org/10.1007/s11368-024-00271-4

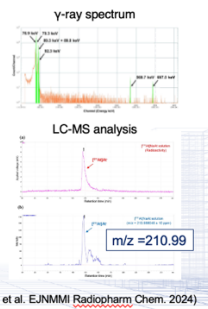
**RESEARCH ARTICLE** Open Access

**Production of [<sup>211</sup>At]NaAt solution under GMP compliance for investigator-initiated clinical trial**

Sadahiro Naka<sup>1,2</sup>, Kazuhiro Ooe<sup>3</sup>, Yoshifumi Shinakami<sup>3</sup>, Kenta Kurimoto<sup>1,2</sup>, Toshihiro Sakai<sup>4</sup>, Kazuhiro Takahashi<sup>5</sup>, Atsushi Toyoshima<sup>1</sup>, Yang Wang<sup>6</sup>, Hiromitsu Nishida<sup>1</sup>, Hiroki Kato<sup>1,2</sup>, Nanyuki Tomiyama<sup>1</sup> and Tadashi Watabe<sup>1,2\*</sup>

\*Correspondence: watabe@med.osaka-u.ac.jp  
Department of Radiology, Graduate School of Medicine, Osaka University, Suita, Osaka 565-0871, Japan  
Department of Hematology, Osaka University Hospital, 2-15 Yamadaoka, Suita, Osaka 565-0871, Japan

**Abstract** Background The alpha emitter astatine-211 (<sup>211</sup>At) is garnering attention as a novel targeted alpha therapy for patients with refractory thyroid cancer resistant to conventional therapy using beta-emitter radioiodine (<sup>131</sup>I). Herein, we aimed to establish a robust method for the manufacturing and quality control of [<sup>211</sup>At]NaAt solution for intravenous administration under the good manufacturing practice guidelines for investigational products to conduct an investigator-initiated clinical trial. **Results** [<sup>211</sup>At]NaAt was separated and purified via dry distillation using irradiated Bi-platelets complexing [<sup>211</sup>At] obtained by the nuclear reaction of <sup>209</sup>Bi with <sup>207</sup>Pu. After purification, the <sup>211</sup>At trapped in the cold trap was collected in a reaction vessel using



(Naka S, et al. EJNMMI Radiopharm Chem. 2024)

**From basic research to clinical trials – preclinical to clinical Research collaboration in Osaka University**

- Biodistribution in rats (3hrs) : <sup>211</sup>At vs <sup>123</sup>I
- [<sup>211</sup>At]NaAt: cellular uptake (K1-NIS)
- DNA double strand break : <sup>211</sup>At vs <sup>131</sup>I
- [<sup>211</sup>At]NaAt: treatment effect (K1-NIS)
- Extended single intravenous toxicity study
- In the blood test, males (50 MBq/kg) and females (50 MBq/kg) showed a decrease in white blood cell and platelet counts on day 5, and recovery on day 14.
- Toxicity tests of [<sup>211</sup>At]NaAt (50MBq/kg) in mice
- Clinical trial drug manufacturing for [<sup>211</sup>At] drugs - under GMP standard in Osaka University Hospital. from Bi-target irradiated alpha-beam containing At-211 is brought in from an external accelerator facility.
- Alpha-T1 study: [<sup>211</sup>At]NaAt for thyroid cancer
- PSMA Theranostics using <sup>211</sup>At
- [<sup>211</sup>At]PSMA-5 : new alpha therapy for prostate cancer
- Histology of normal mice ([<sup>211</sup>At]PSMA-5): Day1
- Alpha-PS1 clinical trial (Phase-1: First in human)
- Manufacturing of clinical trial drug: [<sup>211</sup>At]PSMA-5

**12.45 Industrial Presentations**

- **GLOBAL FIA**  
**Graham Marshall, Global FIA, Fox Island WA, USA**

**Objective:** Modular Isotope Purification – the Production of <sup>211</sup>At

Presentation related to the flow-based fluid handling modules developed and demonstrated to automate the processing of an <sup>211</sup>At-bearing cyclotron target into A<sub>0</sub>-labelled <sup>211</sup>At in <2 hours with minimal product handling from one processing module to the next.



What was included:

- three fluid handling modules to achieve the desired automated isotope-handling procedures
- flow-based sensors for measuring temperature, pressure, pH, conductivity, and radiation were incorporated into the flow manifold for closed-loop control of time-sensitive process steps as well as real-time feedback of critical process steps and monitoring of system performance
- A simplified dose measuring device based on a Geiger–Müller tube was built and tested

<sup>211</sup>At Process Unit Operations - Product Processing Modules:

- Target dissolution and matrix exchange
- Solid phase extraction (SPE) and pH adjustment
- Radio-labeling and de-salting (SEC)
- (Optional) Product de-watering for transportation of solid

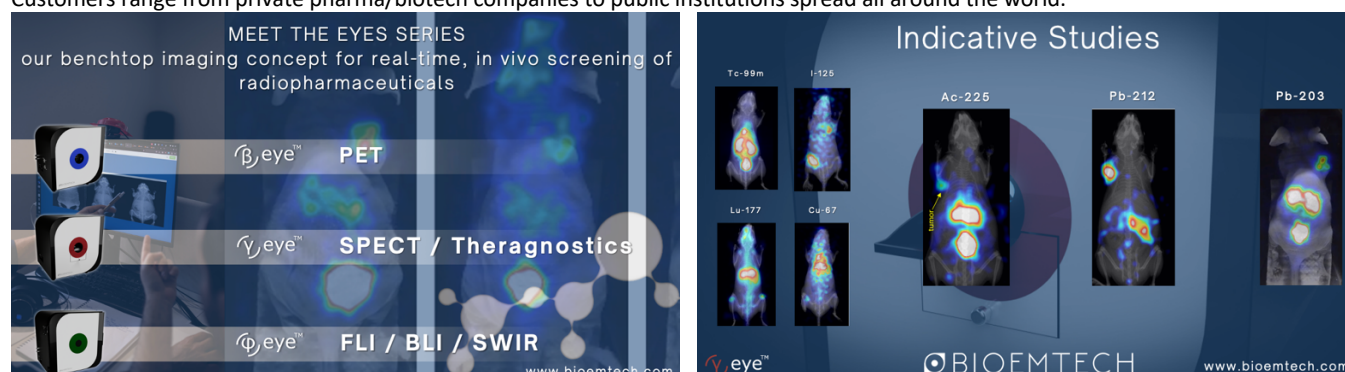
#### - BIOEMTECH

**Objective:** Embracing scientists translate ideas into results

BIOEMTECH's mission is to accelerate preclinical research of promising drugs, towards clinical translation, through high quality services and products.

Infrastructure: Headquarters and Preclinical Platform inside NCSR Demokritos (Athens, Greece).

Customers range from private pharma/biotech companies to public institutions spread all around the world.



Features

Field-Of-View of 50 mm x 100 mm, suitable for whole body mouse imaging

AI generated x-ray for anatomical mapping purposes

Small footprint of 44 cm (L) x 46 cm (W) x 40 cm (H) – Truly desktop

#### - INVISCAN

**Objective:** Applications on small Animals - Internal Vectorised Radiotherapy Lu-177 At-211 Ac-225

Imaging of [<sup>68</sup>Ga/<sup>177</sup>Lu]-AZ-93 for diagnosis and radiotherapy

- Mice bearing PSMA-positive tumours
- Tracer: [<sup>68</sup>Ga]Ga-AZ-093 5.5 to 7.4 MBq (PET/CT imaging)
- [<sup>177</sup>Lu]Lu-AZ-093 41 MBq (SPECT/CT imaging)
- PET : 8 min acquisition time at 10, 30, 60, 90, 120 min post injection
- SPECT : 20 min acquisition time at 1, 3, 24, 48 h post injection (SPECT/CT)

Imaging of [<sup>68</sup>Ga/<sup>89</sup>Zr/<sup>177</sup>Lu] based teranostic pairs in tumors

- Balb/c nude mice, injected with tumor cells at right posterior flanks
- Tracer: [<sup>68</sup>Ga]Ga-NOTA-ABDC2 4.3 MBq PET : 10 min at 1h, 4h, 8h post injection
- [<sup>89</sup>Zr]Zr-DFO-ABDC2 4.1 MBq PET : 10 min at 6h, 72h, 144h post injection
- [<sup>177</sup>Lu]Lu-DOTA-ABDC2 13.5 MBq SPECT imaging 1 week after treatment (SPECT/CT)

Comparison of the energy spectra : Alpha-SPECT-mini system

Siemens Symbia Clinical SPECT System (Johns Hopkins University School of Medicine)

13.00 Lunch Break - Industrial exhibition

14.30 **WG5:**

WG Leader: **Dr. Dana Niculae** - Dissemination: what has been achieved

**Objective:** Made the technology visible and accessible to researchers, patients, EU practitioners, and industries. This working group focused on creating conditions to overcome barriers to the development of astatine therapy by identifying therapeutic candidates and facilitating their transfer and development.

**Tasks:**

T.5.1. Identifying the exploitable results (patent potential check) and constituting patent application files.

T.5.2. Industrial transfer.

T.5.3. Dissemination of project results to relevant stakeholders.

T.5.4. Participating in existing lobbying groups.

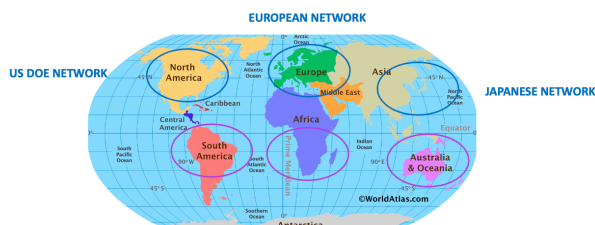
T.5.5. Communicating to patients and practitioners.

T.5.6. Creating referent contacts for research and industry.

This working group was successful in achieving all its desired outcomes. Some of these may be less visible due to the novelty of the treatment approaches for malignant diseases, highlighting the need for both clinicians and patients to be better informed and involved in the future.

What has been achieved so far:

- Meetings
- Dissemination
- Budget
- European initiatives NMEU, Japan Astatine Community



Project Communication Coordinator: **Dr. Emilija Janevik** - Communication: what has been achieved

**Implementation of the Communication Plan with Key Messages - planned and realized**

- Highlight the significance of Astatine-labeled radiopharmaceuticals in medical research.
- Showcase the goals and expected outcomes of the NOAR project.
- Emphasize the potential impact on advancements in cancer diagnosis and treatment.

The NOAR COST project effectively disseminated information, engaged stakeholders, and fostered collaboration within the radiopharmaceutical research community, ultimately contributing to the success and impact of the project.

Communication Objectives realized :

- Ensured effective communication between groups, provide timely notices for requirements and meetings, optimize results for all communications and project expectations, and measure the outcomes of the communication strategy to revise it as needed.

Engaging Partners in the Project:

- Created a bridge between the project and the networks they are involved in, provided input for the project's website, communication materials, and media channels.
- Disseminated the activities and results of the project through their social media channels.
- Shared the activities and results of the project at specific events and fairs.

Preparation of Science Communication plan

Communication Channels used for implementation of the Science Communication Plan

COST Academy / training - Education and Outreach by developing educational materials and resources for the professionals

Impact of Scientific Publications to increase the interest and investment in Astatine-211

Impact of Scientific Publications to increase the interest and investment in Astatine-211

Impact of Scientific Publications to increase the interest and investment in Astatine-211

Regular Core Group meetings of the Core Group, on Zoom every Monday at 3 p.m.

**14.50 Young researcher pathways**

**Short Term Scientific Mission: what has been achieved - Dr. Marek Pruszyński & Dr. Penelope Bouziotis**

**STSM committee:**

- Dr. Marek Pruszyński (STSM Chair)
- Dr. Petra Kolenc Peitl (STSM Co-Chair)
- Dr. Penelope Bouziotis (Committee Member)
- Dr. Andreas Tue Ingemann Jensen (Committee Member)

The STSM applicants were engaged in an official research programme as a PhD Students, postdoctoral fellow or employed by, or affiliated to, an institution, organisation or legal entity which has within its remit a clear association with performing research. STSMs were intended and realised to promote young researchers: PhD students and Early Career Investigators (ECI).  
**STSM done since 2021**

**2021**

| Applicant's name              | Dates                 | Days | Title   | Home Institution   | Host Institution   |
|-------------------------------|-----------------------|------|---|--|--|
| <b>Matthijs Bart Sevenois</b> | 2021.08.30-2021.09.12 | 14   | Investigation of production strategies to increase the At-211 yield | Research Cluster Imaging and Physical Sciences (BEFY), In vivo Cellular and Molecular Imaging Lab (ICMI), Laarbeeklaan 103 - 1090 Brussel, <b>Belgium</b><br><br>Prof. Dr. <b>Peter Covens</b> , Radiation Protection & Dosimetry Expert | Copenhagen University Hospital, PET and Cyclotron unit, KF3982, Blegdamsvej 9, DK2100 Copenhagen, <b>Denmark</b><br><br>Dr. <b>Holger Jan Jensen</b> , Chief Cyclotron Physicist |

**2022**

|                               |                       |    |   |   |   |
|-------------------------------|-----------------------|----|---|---|---|
| <b>Chiara Timperanza</b>      | 2022.02.14-2022.03.18 | 33 | Poly-L-Lysine radiolabeling with astatine-211 using arylboronic acid chemistry                                | University of Gothenburg, Department of Medical Radiation Sciences, Sahlgrenska Academy, Gula stråket, 2b, Gothenburg, <b>Sweden</b><br><br>Dr. <b>Emma Aneheim</b>                                   | Nantes Université, CRCI2 NA, INSERM U1307-CNRS U6075, 8 quai Moncousu, BP 70721, 44007 Nantes cedex 1, <b>France</b><br><br>Dr. <b>François Guérard</b> |
| <b>Matthijs Bart Sevenois</b> | 2021.08.30-2021.09.12 | 14 | Investigation of production strategies to increase the At-211 yield   | Medical Imaging Research Group, In vivo Cellular and Molecular Imaging Lab (ICMI), Vrije Universiteit Brussel, Laarbeeklaan 103, 1090 Brussels, <b>Belgium</b><br><br>Dr. <b>Matthias D'Huyvetter</b> | GIP ARRONAX, 1 rue Aronnax, CS 10112, 44817 Saint-Herblain cedex, <b>France</b><br><br>Prof. <b>Férid Haddad</b> , Directeur GIP Arronax                |
| <b>Paulina Apostolova</b>     | 2022.09.15-2022.10.16 | 32 | Antibody labeling and quality control using 211At - a new experiment and a new challenge for cancer treatment | Goce Delcev University, Faculty of Medical Sciences, Krste Misirkov 10A, 2000 Stip, <b>Republic North Macedonia</b><br><br>Prof. <b>Emilija Janevik-Ivanovska</b>                                     | Nantes Université, CRCI2 NA, INSERM U1307-CNRS U6075, 8 quai Moncousu, BP 70721, 44007 Nantes cedex 1, <b>France</b><br><br>Dr. <b>Joëlle Gaschet</b>   |

**2023**

| Applicant's name                | Dates                 | Days | Title  | Home Institution  | Host Institution  |
|---------------------------------|-----------------------|------|--|---|---|
| <b>Lucas Mues genannt Koers</b> | 2023.08.27-2023.09.01 | 6    | Target processing, separation and labelling of Astatine-211                      | Forschungszentrum Juelich, Juelich, <b>Germany</b>  | University of Gothenburg, Department of Medical Radiation Sciences, Sahlgrenska Academy, Gula stråket, 2b, Gothenburg, <b>Sweden</b><br><br>Dr. <b>Emma Aneheim</b> |
| <b>Paulina Apostolova</b>       | 2023.09.08-2023.10.06 | 29   | Preparation and characterization of bioconjugates for astatine-211 radiolabeling | Goce Delcev University, Faculty of Medical Sciences, Krste Misirkov 10A, 2000 Stip, Republic North <b>Macedonia</b><br><br>Prof. <b>Emilija Janevik-Ivanovska</b> | Nantes Université, CRCI2 NA, INSERM U1307-CNRS U6075, 8 quai Moncousu, BP 70721, 44007 Nantes cedex 1, <b>France</b><br><br>Dr. <b>Joëlle Gaschet</b>               |

**2024**

| Applicant's name           | Dates                 | Days | Title   | Home Institution  | Host Institution   |
|----------------------------|-----------------------|------|---|---|--|
| <b>Clemence Maigneueau</b> | 2024.04.01-2024.04.18 | 12   | Development of electrophilic astatine-211 labelling of antibodies modified by boronic derivatives                       | Nantes Université, CRCI2 NA, INSERM U1307-CNRS U6075, 8 quai Moncousu, BP 70721, 44007 Nantes cedex 1, <b>France</b><br><br>Prof. <b>Jean-Francois Gestin</b> | University of Gothenburg, Institute of Clinical Sciences, Department of Medical Radiation Sciences, Gothenburg, <b>Sweden</b><br><br>Dr. <b>Emma Aneheim</b> |
| <b>Tomasz Janiak</b>       | 2024.07.15-2024.07.19 | 5    | Gaining experience with the preparation of Bi targets for producing 211At in a cyclotron                                | <b>National Centre for Nuclear Research, Radioisotope Centre POLATOM, Poland</b><br><br>Prof. <b>Renata Mikołajczak</b>                                       | Forschungszentrum Jülich GmbH Institute of Neuroscience and Medicine INM-5: Nuclear Chemistry, <b>Germany</b><br><br>Prof. Dr. <b>Bernd Neumaier</b>         |
| <b>Max Palmer</b>          | 2024.09.22-2024.09.26 | 5    | Queen Mary University of London: Sharing best practice for setup and operation of an astatine-211 facility with CRCI2NA | Queen Mary University Of London, London, <b>United Kingdom</b><br><br>Prof. <b>Jane Sosabowski</b>  | Nantes Université, CRCI2 NA, INSERM U1307-CNRS U6075, 8 quai Moncousu, BP 70721, 44007 Nantes cedex 1, <b>France</b><br><br>Dr. <b>François Guérard</b>      |

15.00 **STSM Testimonies (round table):**  
Who am I? Where I have been? What was my topic? What did I learn?

**Paulina Apostolova**



Who am I?



**Paulina Apostolova**  
PhD student in Pharmacy  
  
Faculty of Medical Sciences,  
Goce Delchev University, Shtip,  
Republic of North Macedonia



COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES



What was my topic?



**1. Title: Antibody labelling and quality control using  $^{211}\text{At}$  – a new experiment and a new challenge for cancer treatment**  
15/09/2022 to 06/10/2022

- To become familiar with the methods and possibilities of working and learning some basic techniques in the laboratories of the host institution;
- Learn techniques related to cell culture/in vitro experiments;
- To see the procedures for At-211 labelling of protein molecules (antibodies) and the methods of control after labelling, which are of special interest to me.

**2. Title: Preparation and characterization of bioconjugates for astatine-211 radiolabeling**  
08/09/2023 to 06/10/2023

- Optimization of protocols for preparing bioconjugates using anti-CD138 mAb with a specific prosthetic group ready for radiolabeling with astatine-211;
- Training for characterisation of prepared bioconjugates using various analytical techniques;
- Radiochemical assessment of the practical approach for radiolabeling the prepared bioconjugates with astatine-211.

COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES

**Matthijs Seve- nois**



Who am I?

- Studies
  - Industrial engineering medical nuclear sciences
  - Biomedical engineering
  - Specialization Medical physics, nuclear medicine



Started a PhD with topic:

**“The impact of  $^{210}\text{At}$  and  $^{210}\text{Po}$  after optimised production of  $^{211}\text{At}$ ”**

- WP: Characterization of  $^{211}\text{At}$ ,  $^{210}\text{At}$  and  $^{210}\text{Po}$  on targets irradiated at different energies



COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES



Where did I go?

- STSMs
  - University hospital of Copenhagen, Rigshospitalet in Denmark
  - GIP Arronax, Nantes, France



Rigshospitalet



ARRONAX

Characterize at different incident energies the increase in yield of  $^{211}\text{At}$ ,  $^{210}\text{At}$  and  $^{210}\text{Po}$  activity



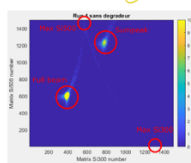
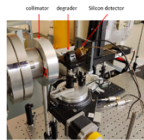
COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES



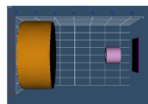
What was my topic?



- Energy determination
  - Using TOF technique with Si detectors
  - PHITS Monte Carlo technique
    - Repeated with Al degrader



- Determining yields
  - Modest  $^{211}\text{At}$  at yield improvement 1,57 to 1,56 mm degrader



- Linearity experiment
  - No evaporation observed



COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES



What did I learn?

- Being part of NOAR & STSMs
  - Gained a lot of know-how
  - Resulted in reliable and long-lasting network
  - Helped initiating my PhD research in finding way to PRISMAPP
    - Peer reviewed publications



Optimized cyclotron production of  $^{211}\text{At}$ : The challenge of  $^{210}\text{Po}$  cross-contamination  
Matthijs Seve-nois, Stine Vink, Mikkel, Holger, Jan, Heide, Mathias, D'Agostino, Peter, Clavier



Optimized alpha-particle reactions of  $^{211}\text{At}$ : Activity balance of  $^{211}\text{At}$ ,  $^{210}\text{At}$  and  $^{210}\text{Po}$  after new chemistry target dissolution  
Matthijs Seve-nois, Holger, Jan, Heide, Peter, Clavier, Yves Billaud  
Matthijs Seve-nois, Landerik, Mathias, Peter, Clavier

COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES


**Clémence Maingueneau**

**Short Term Scientific Mission**

**NOAR**

- Who am I?
- Where I have been?
- What was my topic?
- What did I learn?

Post doctoral researcher in CRCl<sup>2</sup>NA lab in Nantes



Research Center in **cancerology** and **immunology** in Nantes

COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES

**Short Term Scientific Mission**

**NOAR**

- Who am I?
- Where I have been?
- What was my topic?
- What did I learn?

**Göteborg Sweden**




1<sup>st</sup> to 18<sup>th</sup> April 2024

Department of Medical Radiation Sciences



COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES

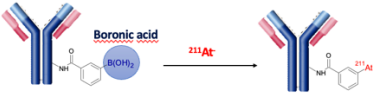
**Short Term Scientific Mission**

**NOAR**

- Who am I?
- Where I have been?
- What was my topic?
- What did I learn?

**<sup>211</sup>At labelling of modified Antibody with boronic acid functions**

Berdal, Marion, et al. 2021 [1]



- What about electrophilic way?

[1] Investigation on the Reactivity of Nucleophilic Radiohalogen with Arylboric Acids in Water: Access to an Efficient Single-Step Method for the Radioiodination and Astatination of Antibodies » *Chemical Science* 12:1458-68.

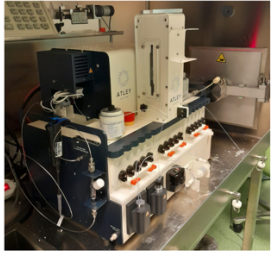
COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES

**Short Term Scientific Mission**

**NOAR**

- Who am I?
- Where I have been?
- What was my topic?
- What did I learn?

A lot !



COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES


**Lucas Koers**

**Tomasz Janiak**

**Who am I?**

**NOAR**

**POLATOM** **NCBJ**



**Tomasz Janiak**

Education: 2000-2006  
Warsaw University of Technology  
Faculty of Production Engineering - Msc. Eng  
Field of Study: Automation and Robotics  
Specialty: Flexible manufacturing systems

Research Scientist in Laboratory of Radionuclides

- Development of methods for the preparation of solid targets for irradiation in cyclotron;
- Development of methods for the manufacture of sealed sources for medical and industrial applications;
- GMP-compliant production of radiopharmaceuticals for clinical trials - somatostatin analogues with <sup>90</sup>Y and <sup>177</sup>Lu

GMP production in RC POLATOM

RESEARCH TEAM LEADER

COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES

**Short-Term Scientific Mission**

**NOAR**

**What was my topic?**

Gaining experience with the preparation of Bi targets for producing <sup>211</sup>At in a cyclotron.

**Where I have been?**

The visit of the STSM was carried out at 15-19.07.2024 in Forschungszentrum Jülich GmbH, Institute of Neuroscience and Medicine, INM-5: Nuclear Chemistry, Jülich, Germany.




Supervisor during the visit - Mr. Lukas Koers.

COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES

**Methods of preparing Bi targets:**

**NOAR**

**What did I learn?**



Electrochemical



Melting




Sedimentation




Pressing Bi Powder

COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES


**NOAR**



IBA CYCLONE 30XP in Jülich



Target station for irradiation in cyclotron



Dry distillation of At-211, produced on the IBA cyclotron, from a target prepared by the sedimentation method

COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES

**Max Palmer**



Who am I?

**Barts  
Cancer Institute**

**Queen Mary  
University of London**



**Department for  
Energy Security  
& Net Zero**

**UNIVERSITY OF  
BIRMINGHAM**

COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES



Where have I been?

- 3-day visit to the facility at CRCINA last week.



Queen Mary University of London: Sharing best practice for setup and operation of an astatine-211 facility with CRCINA

**Max Palmer  
Queen Mary University of London**

COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES



What was the topic?

- Preparing for setup of At-211 hub in UK – but we have no experience with the radionuclide.
- Visit a working, experienced lab to see equipment and setup, as well as observing At-211 radiochemistry methods and practicalities.
- To share our proposed setup and arrangements, to receive advice, comments, questions.
- Fact-finding mission, to inform UK users of best practices in radiolabelling, most robust labelling methodologies for initial At-211 work.

COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES



What did I learn?

- Observed complete target-to-antibody radiolabelling and purification.
- How the techniques used here (manual) can be translated to the UK (automated).
- Safe handling of At-211 inside and outside contained environment.
- Multiple possibilities for extraction of At-211 from bismuth target, radiolabelling methodologies, flexibility of our automated systems.
- Comments and ideas for improving robustness of our designs and plans.
- Key materials for manipulation, storage, transfer of At-211 and labelled compounds and waste materials.

COST NOAR GLOBAL MEETING, 01-03/10/2024, NANTES

- 15.30 The «Scandinavia» Ecosystem- Moderators: **Milton Lönnroth & Dr. Andreas Ingemann Jensen**  
Sweden - **Milton Lönnroth**  
Gothenburg ecosystem and on-going projects Atley Solutions  
Denmark - **Dr. Andreas Ingemann & Dr. Francesco Sergi-Lindell** Copenhagen ecosystem and on-going efforts: Infrastructure developments around Copenhagen, start-up projects, TetraKit Technologies, Theranostic Solutions & PreTT
- 16.00 Break - Industrial exhibition
- 16.30 The «Pays de la Loire» Ecosystem - Moderators: **Dr. Joelle Gaschet & Dr. Jean-François Gestin**  
**Joelle Martin-Gauthier** - Nantes Metropole

**Dr. Ferid Haddad** - Arronax Nantes

The **ARRONAX** project is supported by:

- **Regional Council of Pays de la Loire**
- **Université de Nantes**
- **French government (CNRS, INSERM)**
- **European Union**

**Objective:** The development of a radiopharmaceuticals is a multidisciplinary adventure

- **A cluster of academic labs have been set to cover all expertise**
- **Academic cluster is part of a stronger network which includes industry**

**<sup>211</sup>At as a case study : from bench to bedside**

- Astatine-211 production scheme used @Arronax:
- Production batches are use to fuel the whole research scheme
- Chemical properties and quantum chemistry of astatine-211
- Development of innovative radiolabelling methods
- Biological studies of Astatine in different models
- Astatine-211-labeled anti-mCD138 in mouse syngeneic multiple myeloma
- Translation to clinics

**Pr. Jen-Luc Harousseau** - West Institute of Cancerology (ICO)

Johanna Rolland, Nantes Mayor, Nantes Métropole President

**Pr. Françoise Kraeber Bodéré** - University Hospital Center (CHU)

**Pluridisciplinary research since more than 15 years in a favorable ecosystem in 3 Research Axis**

- Axis 1-Radiotheranostics and radionuclide therapy (Dr C. Bailly)
- Axis 2-Innovative radiopharmaceuticals (Pr C. Bodet-Milin)
- Axis 3-Quantitative imaging, data processing and AI (Dr T. Carlier)

**Clinical Research unit - 106 clinical studies**

- Non interventional research: 4
- Diagnostic studies : 8
- Studies phase III : 6
- Studies phase I/II : 6
- In faisability studies 18
- Imaging studies (prestation) : 82

**CHU NANTES** Main results in radiotheranostics

**Phase II Trial of Anticarcinoembryonic Antigen Pretargeted Radioimmunotherapy in Progressive Metastatic Medullary Thyroid Carcinoma: Biomarker Response and Survival Improvement**  
Pierre-Yves Salaun<sup>1</sup>, Lucie Campion<sup>2</sup>, Claire Boumanou<sup>3</sup>, Alain Faivre-Chantal<sup>4</sup>, Jean-Philippe Vaillat<sup>5</sup>, David Toubi<sup>6</sup>, Catherine Amougou<sup>7</sup>, Caroline Bessonnet<sup>8</sup>, Florence Biondi-Chavan<sup>9</sup>, Stéphanie Bissot<sup>10</sup>, Jeanne Oudinet<sup>11</sup>, Bertrand Caron<sup>12</sup>, Eric Miralbes<sup>13</sup>, Chan-Hong Chang<sup>14</sup>, Robert M. Sharkey<sup>15</sup>, David M. Glicksberg<sup>16,17</sup>, Jean-François Claret<sup>18</sup>, Jacques Barbet<sup>19,20</sup>, and Françoise Kraeber-Bodéré<sup>21</sup>  
J Natl Med 2012; 53:1180-1192

**Targeting, Toxicity, and Efficacy of 2-Step, Pretargeted Radioimmunotherapy Using a Chinese Bispesic Antibody and <sup>111</sup>In Labeled Biotiners Happen in a Phase I Optimization Clinical Trial**

**Pharmacokinetics and Dosimetry Studies for Optimization of Pretargeted Radioimmunotherapy in CEA-Expressing Advanced Lung Cancer Patients**  
Carole Oudinet<sup>1</sup>, <sup>111</sup>In Labeled Anti-<sup>125</sup>I Anti-HER2/neu<sup>2</sup>, Fabrice Mouton<sup>3</sup>, Lucie Campion<sup>4</sup>, <sup>125</sup>I Capromab P2C2<sup>5</sup>, Jean-François Claret<sup>6</sup>, Jacques Barbet<sup>7</sup>, Françoise Kraeber-Bodéré<sup>8</sup>, and Jean-François Claret<sup>9</sup>  
Anticancer Res 2014; 34:2003-2014

**CHU NANTES** Main results in radiotheranostics

**Phase 3 Trial of <sup>177</sup>Lu-Dotatate for Midgut Neuroendocrine Tumors**  
J. Strobel, G. El-Haddad, E. Wirth, A. Hinderle, J. Van, B. Chavan, E. Milten, P.L. Kavan, M.H. Kuchel, H. Gerner, D. Baudinet, T.M. O'Donovan, R.P. Ryan, H.R. Kulkarni, M. Caplin, R. Lellrich, T. Probst, E. Delgado, E. Van Cutsem, A. Bressan, E. Cengiz, M. Pineda, M. J. Molina, J. Garcia, S. Gnanapavan, E. B. Sargent, K. Ching, M. Lopez-Lopez, P. Barriac, T. Theodoris, J.L. Soria, F. Ruemmele, D. Vucelja, and E. Krenning, for the NETTER-3 Trial Investigators

**Dosimetry for targeted radionuclide therapy in routine clinical practice: experts advice vs. clinical evidence**  
Arnaud Drouot<sup>1,2,3,4</sup>, Clément Bailly<sup>5</sup>, Florent Cachot<sup>6</sup>, Agathe Edet-Sanson<sup>7</sup>, Françoise Kraeber-Bodéré<sup>8</sup>, Sébastien Haplay<sup>9</sup>, Charles Meillet<sup>10</sup>, Philippe Ribot<sup>11</sup>, Pierre-Yves Salaun<sup>12</sup>, Paul Schwaert<sup>13</sup>, David Tournet<sup>14</sup>, Pierre Vera<sup>15</sup>, Frédéric Courbon<sup>16</sup>, Thomas Carlier<sup>17</sup>  
European Journal of Nuclear Medicine and Molecular Imaging (2024) 51:947-960

**First real-life data on <sup>177</sup>Lu-PSMA-617 : Descriptive analysis on the largest metastatic castration-resistant prostate cancer (mCRPC) cohort treated in early access in France**  
Arnaud Drouot<sup>1</sup>, Pierre-Philippe Vignat<sup>2</sup>, Sébastien Haplay<sup>3</sup>, Clément Bailly<sup>4</sup>, Clémentine Bessonnet<sup>5</sup>, Clémentine Bessonnet<sup>6</sup>, Clémentine Bessonnet<sup>7</sup>, Clémentine Bessonnet<sup>8</sup>, Clémentine Bessonnet<sup>9</sup>, Clémentine Bessonnet<sup>10</sup>, Clémentine Bessonnet<sup>11</sup>, Clémentine Bessonnet<sup>12</sup>, Clémentine Bessonnet<sup>13</sup>, Clémentine Bessonnet<sup>14</sup>, Clémentine Bessonnet<sup>15</sup>, Clémentine Bessonnet<sup>16</sup>, Clémentine Bessonnet<sup>17</sup>, Clémentine Bessonnet<sup>18</sup>, Clémentine Bessonnet<sup>19</sup>, Clémentine Bessonnet<sup>20</sup>, Clémentine Bessonnet<sup>21</sup>, Clémentine Bessonnet<sup>22</sup>, Clémentine Bessonnet<sup>23</sup>, Clémentine Bessonnet<sup>24</sup>, Clémentine Bessonnet<sup>25</sup>, Clémentine Bessonnet<sup>26</sup>, Clémentine Bessonnet<sup>27</sup>, Clémentine Bessonnet<sup>28</sup>, Clémentine Bessonnet<sup>29</sup>, Clémentine Bessonnet<sup>30</sup>, Clémentine Bessonnet<sup>31</sup>, Clémentine Bessonnet<sup>32</sup>, Clémentine Bessonnet<sup>33</sup>, Clémentine Bessonnet<sup>34</sup>, Clémentine Bessonnet<sup>35</sup>, Clémentine Bessonnet<sup>36</sup>, Clémentine Bessonnet<sup>37</sup>, Clémentine Bessonnet<sup>38</sup>, Clémentine Bessonnet<sup>39</sup>, Clémentine Bessonnet<sup>40</sup>, Clémentine Bessonnet<sup>41</sup>, Clémentine Bessonnet<sup>42</sup>, Clémentine Bessonnet<sup>43</sup>, Clémentine Bessonnet<sup>44</sup>, Clémentine Bessonnet<sup>45</sup>, Clémentine Bessonnet<sup>46</sup>, Clémentine Bessonnet<sup>47</sup>, Clémentine Bessonnet<sup>48</sup>, Clémentine Bessonnet<sup>49</sup>, Clémentine Bessonnet<sup>50</sup>, Clémentine Bessonnet<sup>51</sup>, Clémentine Bessonnet<sup>52</sup>, Clémentine Bessonnet<sup>53</sup>, Clémentine Bessonnet<sup>54</sup>, Clémentine Bessonnet<sup>55</sup>, Clémentine Bessonnet<sup>56</sup>, Clémentine Bessonnet<sup>57</sup>, Clémentine Bessonnet<sup>58</sup>, Clémentine Bessonnet<sup>59</sup>, Clémentine Bessonnet<sup>60</sup>, Clémentine Bessonnet<sup>61</sup>, Clémentine Bessonnet<sup>62</sup>, Clémentine Bessonnet<sup>63</sup>, Clémentine Bessonnet<sup>64</sup>, Clémentine Bessonnet<sup>65</sup>, Clémentine Bessonnet<sup>66</sup>, Clémentine Bessonnet<sup>67</sup>, Clémentine Bessonnet<sup>68</sup>, Clémentine Bessonnet<sup>69</sup>, Clémentine Bessonnet<sup>70</sup>, Clémentine Bessonnet<sup>71</sup>, Clémentine Bessonnet<sup>72</sup>, Clémentine Bessonnet<sup>73</sup>, Clémentine Bessonnet<sup>74</sup>, Clémentine Bessonnet<sup>75</sup>, Clémentine Bessonnet<sup>76</sup>, Clémentine Bessonnet<sup>77</sup>, Clémentine Bessonnet<sup>78</sup>, Clémentine Bessonnet<sup>79</sup>, Clémentine Bessonnet<sup>80</sup>, Clémentine Bessonnet<sup>81</sup>, Clémentine Bessonnet<sup>82</sup>, Clémentine Bessonnet<sup>83</sup>, Clémentine Bessonnet<sup>84</sup>, Clémentine Bessonnet<sup>85</sup>, Clémentine Bessonnet<sup>86</sup>, Clémentine Bessonnet<sup>87</sup>, Clémentine Bessonnet<sup>88</sup>, Clémentine Bessonnet<sup>89</sup>, Clémentine Bessonnet<sup>90</sup>, Clémentine Bessonnet<sup>91</sup>, Clémentine Bessonnet<sup>92</sup>, Clémentine Bessonnet<sup>93</sup>, Clémentine Bessonnet<sup>94</sup>, Clémentine Bessonnet<sup>95</sup>, Clémentine Bessonnet<sup>96</sup>, Clémentine Bessonnet<sup>97</sup>, Clémentine Bessonnet<sup>98</sup>, Clémentine Bessonnet<sup>99</sup>, Clémentine Bessonnet<sup>100</sup>

**Assessment of acquisition protocols for routine imaging of Y-90 using PET/CT**  
Thomas Carlier<sup>1</sup>, Françoise Kraeber-Bodéré<sup>2</sup>, Sébastien Haplay<sup>3</sup>, Clémentine Bessonnet<sup>4</sup>, Clémentine Bessonnet<sup>5</sup>, Clémentine Bessonnet<sup>6</sup>, Clémentine Bessonnet<sup>7</sup>, Clémentine Bessonnet<sup>8</sup>, Clémentine Bessonnet<sup>9</sup>, Clémentine Bessonnet<sup>10</sup>, Clémentine Bessonnet<sup>11</sup>, Clémentine Bessonnet<sup>12</sup>, Clémentine Bessonnet<sup>13</sup>, Clémentine Bessonnet<sup>14</sup>, Clémentine Bessonnet<sup>15</sup>, Clémentine Bessonnet<sup>16</sup>, Clémentine Bessonnet<sup>17</sup>, Clémentine Bessonnet<sup>18</sup>, Clémentine Bessonnet<sup>19</sup>, Clémentine Bessonnet<sup>20</sup>, Clémentine Bessonnet<sup>21</sup>, Clémentine Bessonnet<sup>22</sup>, Clémentine Bessonnet<sup>23</sup>, Clémentine Bessonnet<sup>24</sup>, Clémentine Bessonnet<sup>25</sup>, Clémentine Bessonnet<sup>26</sup>, Clémentine Bessonnet<sup>27</sup>, Clémentine Bessonnet<sup>28</sup>, Clémentine Bessonnet<sup>29</sup>, Clémentine Bessonnet<sup>30</sup>, Clémentine Bessonnet<sup>31</sup>, Clémentine Bessonnet<sup>32</sup>, Clémentine Bessonnet<sup>33</sup>, Clémentine Bessonnet<sup>34</sup>, Clémentine Bessonnet<sup>35</sup>, Clémentine Bessonnet<sup>36</sup>, Clémentine Bessonnet<sup>37</sup>, Clémentine Bessonnet<sup>38</sup>, Clémentine Bessonnet<sup>39</sup>, Clémentine Bessonnet<sup>40</sup>, Clémentine Bessonnet<sup>41</sup>, Clémentine Bessonnet<sup>42</sup>, Clémentine Bessonnet<sup>43</sup>, Clémentine Bessonnet<sup>44</sup>, Clémentine Bessonnet<sup>45</sup>, Clémentine Bessonnet<sup>46</sup>, Clémentine Bessonnet<sup>47</sup>, Clémentine Bessonnet<sup>48</sup>, Clémentine Bessonnet<sup>49</sup>, Clémentine Bessonnet<sup>50</sup>, Clémentine Bessonnet<sup>51</sup>, Clémentine Bessonnet<sup>52</sup>, Clémentine Bessonnet<sup>53</sup>, Clémentine Bessonnet<sup>54</sup>, Clémentine Bessonnet<sup>55</sup>, Clémentine Bessonnet<sup>56</sup>, Clémentine Bessonnet<sup>57</sup>, Clémentine Bessonnet<sup>58</sup>, Clémentine Bessonnet<sup>59</sup>, Clémentine Bessonnet<sup>60</sup>, Clémentine Bessonnet<sup>61</sup>, Clémentine Bessonnet<sup>62</sup>, Clémentine Bessonnet<sup>63</sup>, Clémentine Bessonnet<sup>64</sup>, Clémentine Bessonnet<sup>65</sup>, Clémentine Bessonnet<sup>66</sup>, Clémentine Bessonnet<sup>67</sup>, Clémentine Bessonnet<sup>68</sup>, Clémentine Bessonnet<sup>69</sup>, Clémentine Bessonnet<sup>70</sup>, Clémentine Bessonnet<sup>71</sup>, Clémentine Bessonnet<sup>72</sup>, Clémentine Bessonnet<sup>73</sup>, Clémentine Bessonnet<sup>74</sup>, Clémentine Bessonnet<sup>75</sup>, Clémentine Bessonnet<sup>76</sup>, Clémentine Bessonnet<sup>77</sup>, Clémentine Bessonnet<sup>78</sup>, Clémentine Bessonnet<sup>79</sup>, Clémentine Bessonnet<sup>80</sup>, Clémentine Bessonnet<sup>81</sup>, Clémentine Bessonnet<sup>82</sup>, Clémentine Bessonnet<sup>83</sup>, Clémentine Bessonnet<sup>84</sup>, Clémentine Bessonnet<sup>85</sup>, Clémentine Bessonnet<sup>86</sup>, Clémentine Bessonnet<sup>87</sup>, Clémentine Bessonnet<sup>88</sup>, Clémentine Bessonnet<sup>89</sup>, Clémentine Bessonnet<sup>90</sup>, Clémentine Bessonnet<sup>91</sup>, Clémentine Bessonnet<sup>92</sup>, Clémentine Bessonnet<sup>93</sup>, Clémentine Bessonnet<sup>94</sup>, Clémentine Bessonnet<sup>95</sup>, Clémentine Bessonnet<sup>96</sup>, Clémentine Bessonnet<sup>97</sup>, Clémentine Bessonnet<sup>98</sup>, Clémentine Bessonnet<sup>99</sup>, Clémentine Bessonnet<sup>100</sup>

**Dr. Franck Lethimonnier** - ITMO Santé

**Address major biomedical research challenges**

**In France**

- 300 research units
- 34 clinical investigation centers
- 50 support service units

**National Thematic Institutes**

**Health Technologies Institute**

- Exploration/diagnosis
- Intervene/treat
- Real life follow-up & prevention
- Modeling

**Targeted Alpha Therapy: Inserm initiative**

In 2021, Inserm and CNRS identified alphatherapy:

- As a strategic axis supporting innovation and reindustrialization in France, within the framework of the national Biotherapy-Bioproduction acceleration strategy
- As an opportunity to develop partnerships with key french industrials
- As a promising approach to address the challenges of the French Cancer Plan (2021-2030)

A national research program currently under development and seeking funding, including:

- Innovative radiopharmaceutical-biotherapies,
- Anti-cancer antibodies coupled with alpha-emitting radioisotopes, including Astatine-211.

**17.20 Industrial Presentations**

**- AI4R – Atlantic Instrument for Reserch**

**Objective:** The BeaQuant and BeaQuant-S / New instrument based on new technologies, developed from latest technologies in particle physics.

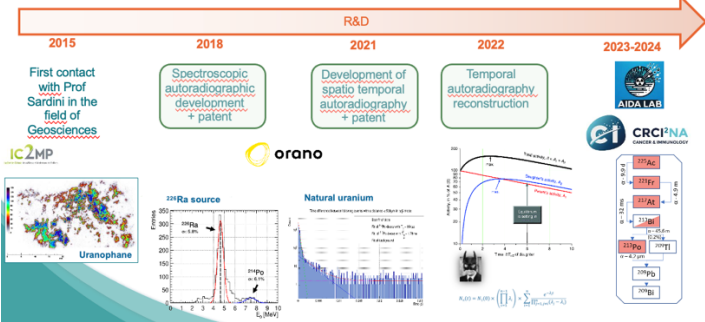
Main goal: Visualize and quantify precisely radiopharmaceuticals in biological tissue sections and in rock slices for geological studies

Sensitive to every charge particle:

- Insensitive to X and  $\gamma$  radiation
- Linearity on 5 magnitude
- Sensitivity: order of mBq



**Alpha development**



Real-time imaging  
Direct quantification in counts  
Large field of view: 20x20 cm<sup>2</sup>, 18 slides on the BeaQuant  
Image with a high spatial resolution with every emitter β<sup>-</sup>, β<sup>+</sup> and α  
A very high performance tool to analyse alpha emitters  
Sensitivity: 5.10<sup>-4</sup> cpm/mm<sup>2</sup>, order of mBq  
Linearity: 5 orders of magnitude  
Safety: No toxic gas

**The perfect complementary tool for preclinical imaging**

- CHELATEC

- ATONCO - Astatine against cancer

**What is ATO-101 and How ATO-101 could revolutionize bladder cancer treatment**

**At-211 - Next generation of Radiotherapeutics (vs emerging Ac-225)**

- Stable targets and shorter half live (7.2h)
- Easier and safer production
- Preserve the rivers and the planet
- Larger and easier patient care

Intravesical alpha-radiation therapy for non-muscular-invasive bladder cancer unresponsive to standard BCG therapy. Phase I-IIa Clinical trial project following completion of preclinical and on-going clinical proof-of-concept studies.

Sylvain Fankler, Jean-François Chatalet, Atomec, Saint Herblain, France

- Founded in 2019 in Saint Herblain, France, by Dr F Chatalet
- Clinical-stage radiopharmaceutical company
- Next-generation therapy with astatine-211, a radioactive element emitting alpha radiation that targets the last cancer cell.
- 1st drug: **ATO-101** targets bladder cancer
- Alternative to local bladder ablation. Improved patient lives, Reduced healthcare costs
- Proprietary IP (patent, license and sub-license)

**The medical need**

Patients with high-grade or intermediate-grade non-muscle-invasive bladder cancer are treated with invasive intravesical BCG instillations. However, 30% to 50% of patients are refractory or no longer respond after variable lengths of time. In these cases, the only option is a radical cystectomy, which is quite debilitating. The aim of intravesical alpha-radiation therapy with an antibody coupled to astatine-211, an alpha particle emitter, is to avoid cystectomy.

**Targeted Therapy using astatine-211**

Currently, targeted radiotherapy with Lutetium-177, an electron emitter (beta<sup>-</sup>), has shown its clinical efficacy and renewed interest in targeted therapy. Atomec is developing such a targeted radiotherapy with astatine-211 (7.2 hours half-life), an alpha particle emitter with significant advantages compared to currently used Lutetium-177 such as:

- a much higher Linear Energy Transfer of alpha particles
- a short path of less than 0.1 mm to preserve adjacent normal cells
- The antibody used is an anti-CAIX antibody (Brentuximab, TLX250) which recognizes, with excellent affinity, over 80% of tumor cells.

The scientific approach is to target tumor residues after cytoreductive resection using an intra-vesical instillation with an anti-CAIX antibody coupled with astatine-211.

**Pre Clinical Study**

**Cytotoxicity study**  
The cytotoxicity of ATO-101 (211At) as an alpha emitter, is evaluated against bladder cancer cells in vitro. The results show that ATO-101 is highly cytotoxic to bladder cancer cells, with a much higher Linear Energy Transfer of alpha particles than that of beta particles.

**Biodistribution study in healthy mice**  
As expected, the biodistribution study showed low radioactivity uptake in healthy organs and tissues. The optimal dosing of ATO-101 is being defined in the bladder which allows precise intravesical administration.

**Cytotoxicity evaluation in healthy mice**  
Histological examination of the bladder tissues showed no macroscopic abnormal observations which could be correlated to the experimental procedure. The toxicology of these data in healthy mice is being evaluated in order to optimize the ATO-101 administration protocol to be used in the Phase I-IIa clinical trial.

**Clinical feasibility study**  
ATO-101 (211At) is being produced in a GMP-compliant facility. The first patient will be treated in September 2022. The study is designed to evaluate the safety, biodistribution and dosing parameters of ATO-101 in patients with bladder cancer. The first dose received, the next step could be to combine therapeutic radionuclides with astatine-211 (211At) for targeted alpha therapy (TAT).

**Phase I-IIa clinical trial**  
Phase I-IIa clinical trial using 211At-CAIX antibody (ATO-101) in bladder cancer patients is being prepared in collaboration with University of Michigan, Ann Arbor, MI, USA. Clinical trial applications for ATO-101 for a Phase I, IIa study in Europe are still pending.

**Clinical strategy**

- Optimize agenda of time to Marketing Authorization in EU and USA
- Accomodate to Astate-211 production capacity in EU and USA and patient recruitment rates
- Comparing Single dose versus Fractional dose instillation
  - Proposed phase I/IIa study - single doses in the US >> FDA
  - Proposed phase I study - fractional instillations in Europe >>EMEA

17.45 Photos + Interviews + Press

19.30 Gala Dinner

**Thursday, October 3<sup>rd</sup>, 2024 / Nantes**

08.00 Welcome – What’s next?  
**Dr. Emma Aneheim & Dr. Jean-François Gestin**

08.15 The European Ecosystem & The European initiatives - Moderators: **Dr. Emma Aneheim & Dr. Jean-François Gestin**

**Dr. Jean Bonnet – NMEU**

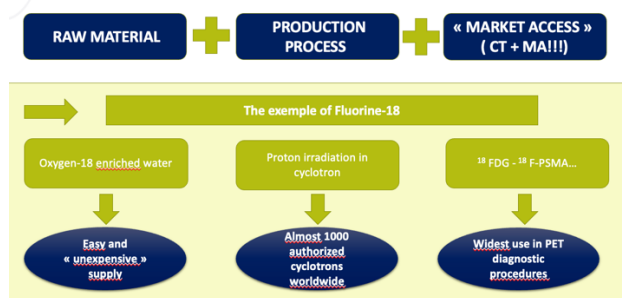
The Radioisotopes and Nuclear Medicine Industry - Facing the Challenge of Theragnostics

**The industrial challenges linked to theragnostics:**

- Never forget the basics of the Value Chain of Production of Radioisotopes
- Secure the supply of currently approved isotopes
- Be prepared for the next « champion isotope »



## Value Chain of Production of Radioisotopes



## Prerequisites to become a RLT champion

| TAILWINDS   | HEADWINDS  |
|---|--|
| Starting material <u>unexpensive</u> and in easy access | Reliable GMP supply to support clinical development      |
| Adequate physical properties in energy and T1/2         | Low availability of a network of dedicated cyclotrons    |
| Be produced in the purest form                          | Challenging QC procedures                                |
| No dependence on research reactors                      | CapEx needed to extend the 30MeV cyclotron network       |
| Good capacity to be linked to different compounds       | Obligation to set highly efficient production operations |
| Easier demand planning                                  |  |
| Fairly simple waste management process                  |  |

**Dr. Renata Mikołajczak** -PRISMAP - The European medical radionuclides programme / Isotopes for imaging and medical treatment

PRISMAP on track:

- 32 projects from 4 calls - <https://www.prismap.eu/access/user-projects/>
- >60 deliveries of 15 different radionuclides for 28 projects
- Technical manager hired
- Helpdesk in place - <https://www.prismap.eu/access/helpdesk/>
- 5 projects completed
- 2 projects published already
- One abstract highlighted as oral presentation at EANM'24 congress

PRISMAB:

1. Provide access to new radionuclides and new purity grades for medical research/ The development of the services
2. Create a common entry port and web interface for the starting research community
3. Enhance clarity and regulatory procedures to promote research with radiopharmaceuticals
4. Unlock the biomedical research through better data on radionuclides
5. Ensure the long-term sustainability of PRISMAP

**Dr. Jérôme Harray** - IHI: accelerate EU

**Dr. Alice Viana** - Oncidium foundation

**Objective:** Supporting Cancer Patients and Enhancing Access to Radiotheranostics Worldwide

Oncidium is a Belgian based, patient focused foundation. The mission is to support, promote & accelerate the development of radiotheranostics for cancer care worldwide, notably through a network of Ambassadors representing the work of the foundation on a local and global scale.

Important preliminary remarks :

- non-profit foundation
- public-interest organization
- fully independent from any other company, organization, hospitals etc.

Oncidium activities are based around 3 pillars: Access, Education and hope.

The foundation is committed to improve **ACCESS** to radiotherapeutics-based treatments for patients that could benefit from it.

The idea is to have Key Opinion Leaders, experts etc. , join this network and lead the mission of Oncidium as we are the ones that know about the challenges and opportunities in the country.

**Education** is also targeted on the website and initiatives for the healthcare community (oncologists, urologists, nuclear medicine and industry).

Each month is published "Theranostics Insights" focusing on a specific radiopharmaceutical.

Every year they share a review, called "Radiotheranostics TODAY" with exclusive content by Ambassadors and friends of the foundation about challenges and opportunities in the radiotheranostics field.

On the education page of the website, we maintain a regularly updated list of radiopharmaceuticals on the market and under development.

Oncidium collaborate with some organizations and companies to host webinars regarding radiotheranostics matters.

RLT-Connect: a collaborative platform to enable radioligand therapy for patients who could not otherwise afford it.

### 09.00 The International Ecosystem

**Dr. Koshin Washiyama** - Japan Astatine Community network - A Hub for Skills and Knowledge of <sup>211</sup>At and the Gateway to the World Astatine Community

Development of a biostable <sup>211</sup>At labeling method aimed at application to targeted alpha therapy of cancer

Prof. Hiroyuki SUZUKI (Chiba University)

To know how Japan Astatine Community have selected Astatine among many promising therapeutic radionuclides and under what strategy we've been working, please read our advertisement article on Astatine, which was published this year in Nature. You can take our reprints from the backside table with two Japanese sweets free!



Don't forget to take our reprints from the backside table with two Japanese sweets free!

**Nature Focal Point on Radiology in Japan**  
ADVERTISEMENT FEATURE  
21 March 2024

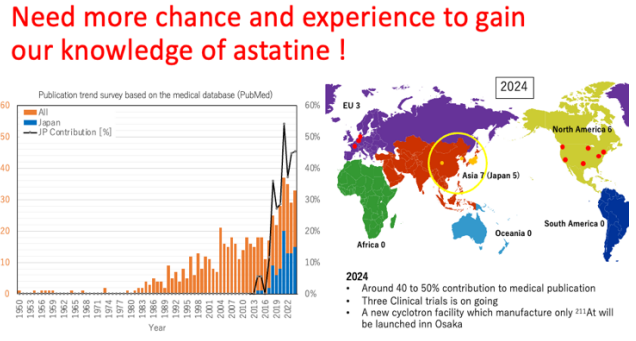
**ASTATINE-211: JAPAN'S STRATEGIC WEAPON AGAINST CANCER**  
Japan is working to develop a new and interesting ACCELERATOR-BASED RADIONUCLIDE THERAPY

**Researchers in Japan are developing world-leading expertise in making and using the alpha particle emitter, astatine-211, which is essential for use as a strong radioactive therapy for treating cancer.** Although cyclotron facilities in Japan are just beginning, collaborative initiatives are currently looking at astatine-211 in Japan, some European countries, and the United States. In Japan, Osaka University and Fukushima Medical University (FMU) are among five centers using cyclotron accelerators to make the radionuclide, says Tadaaki Vatabe, a nuclear medicine physician at Osaka University.

**Researchers at these centers hope that the radionuclide will be used in radiotherapy treatments — one of the three key regions for cancer care around the world. Radiotherapy harnesses radiation to kill cancer cells and shrink tumors, explains Vatabe, and it's used in the place of, or in combination with, surgery and chemotherapy. The advantage of alpha particles is that their relatively large mass makes them very effective at damaging DNA and killing cancer cells. Recently, improved targeting of tumors has been the focus for Osaka University and FMU researchers, with alpha-emitting particles also a relatively new option for radiotherapy compared to gamma ray or beta particles, which have already been used for a long time against cancers. One challenge, explains Vatabe, is that alpha particles, unlike some other radionuclides, cannot be applied externally as their large mass prevents penetration beyond the skin.**

**Alpha particles are therefore being developed for intravenous administration, or direct injection into affected tissue, in a manner that seeks out and targets the cancer cells. Recently, improved targeting of tumors has been the focus for Osaka University and FMU researchers, with alpha-emitting particles showing promise in treating pancreatic cancer' and malignant adrenal medullary tumours.'**

**ALPHA THERAPY** Japan has just become a leader in exploring the potential of astatine-211, which is made by bombarding bismuth with helium ion particle accelerators. This expertise has been developed out of necessity as in recent years Japanese nuclear reactors are highly regulated and are not in a position to produce many medical radionuclides. There has therefore been a need to import the alpha emitters used for radiotherapy from other parts of the world, explains Kazuo Kikunaga, a radiochemist at Osaka University.



**<sup>211</sup>At production site (5+1) in Japan**

| Manufacturing sites   | Production route and Separation method  | History                 | Location  |
|---|---|-------------------------|-----------|
| Research Center for Nuclear Physics (RCNP), Osaka University  | <sup>211</sup> Bi (α, <sup>209</sup> Bi) At Dry distillation                        | 1980. Medical use 2015- | Osaka     |
| Takasaki Ion Accelerators for Advanced Radiation Application (TIARA), Takasaki Advanced Radiation Research Institute, National Institutes for Quantum and Radiological Science and Technology (QST) or QST (Takasaki) | <sup>211</sup> Bi (α, <sup>209</sup> Bi) At Dry & Wet chemistry                     | Since 2012              | Takasaki  |
| Quantum Medical Science Directorate, National Institute of Radiological Sciences (NIRS), National Institutes for Quantum and Radiological Science and Technology (QST) or QST (Chiba)                                 | <sup>211</sup> Bi (α, <sup>209</sup> Bi) At Dry distillation                        | Since 2013              | Chiba     |
| Nishina Center for Accelerator-Based Science, Institute of Physical and Chemical Research (RIKEN)   | <sup>211</sup> Bi (α, <sup>209</sup> Bi) At Dry distillation                        | Since 2015              | Wakusa    |
| Advanced Clinical Research Center (ACRC), Fukushima Medical University (FMU)  | <sup>211</sup> Bi (α, <sup>209</sup> Bi) At Dry distillation                        | Since 2016              | Fukushima |
| The tandem accelerator facility, Nuclear Science Research Institute, Japan Atomic Energy Agency (AEA)   | <sup>211</sup> Bi (LLS) → <sup>211</sup> Rn → <sup>211</sup> At Dry & Wet chemistry | Since 2011              | Osaka     |

**What have we learned over the past decade?**

**Dispersal rates of astatine-211 from aqueous solutions and chelation**  
Authors: TOYOSHIMA<sup>1</sup>, Kojima NAGATA<sup>2</sup>, Kurokawa OOE<sup>1,3</sup>, ZHANG<sup>1,4</sup>, HIRATAKE<sup>1,5,6</sup>, Saitoh RIBBERG<sup>1,6</sup>, Shimada OKUDA<sup>1</sup>, Takahashi YOSHIMIZU<sup>1,6</sup>, and Anahita SHINOHARA<sup>1,7</sup>

**Low radioactivity levels → High stability against in vivo dechelation**

**Radiotherapeutic system with radiolodine and <sup>211</sup>At**

**Neopentyl Glycol as a Scaffold to Provide Radiohalogenated Therapeutic Pairs of High in Vivo Stability**

**Dr. Sunao Fujioka - Alpha Fusion Inc., <sup>211</sup>At based drug development biotech**

What Alpha Fusion is doing

- <sup>211</sup>At pipeline R&D - Focus on <sup>211</sup>At clinical development to achieve earliest commercialization
- <sup>211</sup>At supply chain - Work closely with supply key stakeholders across Japan and WAC given the short half-life

JAC – industry perspective - Efficient transportation to cover 125M population across Japan – approx. 2000Bn JPY (12Bn Euros) oncology drug market overall

Summary:

- Astatine is a promising alpha-emitting radionuclide for TAT
- Astatine is provided to many users through the short-lived RI supply platform and Fukushima Medical University's own network in Japan
- Astatine-related medical articles with Japanese involvement accounted for 40-50% of the world's astatine publications in the last five years.
- These continuous effort since 2011 resulted in the first milestone (Phase-1 studies).
- We are still running towards next milestone with the bottom-up activities of the Japan Astatine Community collaborating with the World Astatine Community.

**Dr. Ethan Balkin - American network**  
Federal Program Manager for Radioisotope Production R&D  
Office of Isotope R&D and Production  
Office of Science  
U.S. Department of Energy

**Objective:** DOE Isotope Program Update on the University Isotope Network vis-à-vis At-211 - Production of <sup>211</sup>At to develop a new market and meet US domestic demand

- Produce and/or distribute radioactive and stable isotopes that are in short supply; includes by-products, surplus materials and related isotope services
- Maintain the infrastructure required to produce and supply priority isotope products and related service
- Conduct R&D on new and improved isotope production and processing techniques which can make available priority isotopes for research and application. Develop workforce.
- Ensure robust domestic supply chains. Reduce U.S. dependency on foreign supply to ensure National Preparedness.

The DOE Isotope Program University Isotope Network (UIN):

- Invest in R&D and develop production capabilities
- Unique infrastructure capabilities & expertise
- Workforce Development

<sup>211</sup>At Production Capabilities in the U.S.

- University of Washington
- University of California – Davis
- Texas A&M University
- Duke University
- University of Pennsylvania

DOE Isotope Program UIN Evolving Strategy:

- DOE IP recognizes that the production and isolation of <sup>211</sup>At can be challenging. However, we believe that success dramatically increases with cooperation.
- Generation of a notable new literature and general knowledge of the stability and robustness of the product supply chain to encourage clinical evaluation and eventual adoption.
- Maximize the UIN's capability to support U.S. domestic <sup>211</sup>At researchers.
  - Continue to develop production capability at the university sites via grant funding.
  - Gas trapping and generator development can extend shipping range, two approaches are being explored.
  - Explore opportunities for commercialization of <sup>211</sup>At with U.S. private industry.
  - Explore opportunities for development of bench-top accelerators optimized for <sup>211</sup>At production.

**Promote international cooperation and technology exchange.**

09.45 Industrial Presentations

- **ACS - TR-ALPHA Cyclotron**

**Objective: TR-ALPHA Cyclotron**

- purchased by Alpha Nuclide (Ningbo) Medical Tech. Ltd: Jan 2023
- Design & Manufacturing Completion: Apr 2024
- Factory Testing: Oct 2024
- Installation/Commissioning: Jan 2025
- Isochronous cyclotron accelerating He<sup>2+</sup> to a max. energy of 30 MeV.
- External ECR ion source providing stable, low emittance He<sup>2+</sup> beam up to 1.1 e-mA at 30 kV.
- Designed for production of large quantities of At-211.
- No beam extraction.
- Configured for irradiation of internal targets.

Highlights:

- Dedicated to alpha production.
- Easy to operate.
- fully automated.
- Vertical acceleration plane; allowing easy maintenance.
- Smaller Vault/Facility required.

- **ALPHA NUCLIDE**

- **TELIX, Burnaby, BC, Canada**

**Telix company provide turnkey solutions for commercial radioisotope production:**

- ISO 9001:2015 Registered
- registered Engineering Firm in BC, Canada
- have a Service License with Canadian Nuclear Safety Commission
- have a traceable supply chain and inventory of enriched stable isotopes
- operate R&D and manufacturing activities within our Quality and Safety programs

Intentionally Focused on Cu-64, Ga-68, Zr-89, Tc-99m and:

- Technology transfer with SOPs, draft MBRs and checklists
- Applications training hands-on training for on-site staff
- We spend a lot of effort on regulatory alignment, US being our first focus – it is very important to us that our products can be used commercially (goes back to our intentionally focused product line)
- Responsive and highly trained technical support

10.00 Coffee Break - Industrial exhibition

10.30 New Actors - Moderators: **Dr. Antero Abrunhosa**

**Dr. Kazunobu Ohnuki** - National Cancer Institute of Japan. New perspective on handling the Astatinated compounds (virtual)

**Dr. Choong Mo Kang** - Korea Institute of Radiological and Medical: At-211 production and R&D at KIRAMS Science, Seoul

- Introduction of KIRAMS and Division of Applied RI
- Medical Cyclotrons in KIRAMS
- MC-50 Cyclotron Beam Lines
- Bi-209 target preparation
- Production of Astatine-211 in KIRAMS – production record (2023-2024)
- Radiolabeling test – labeling of small molecules and antibody conjugates
- Targeted alpha therapy – treatment of HER2 expressing gastric cancer, pheochromocytoma, neuroendocrine tumors
- Theranostic research using 211At/123I pair
- HPLC control of labeled antibodies with Astatine-211 – trastuzumab
- In vitro therapeutic efficacy

**Dr. Yutian Feng** - Chinese Network

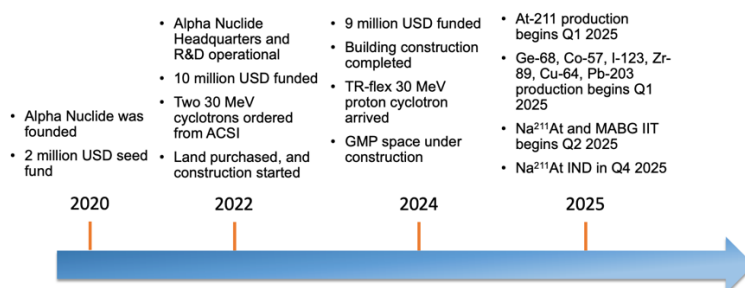
**CEO, Alpha Nuclide Inc.**

**Assistant Professor, Duke University Medical Center**

**Objective:** Innovation Driven Solutions to the <sup>211</sup>At Supply Chain in China: The Alpha Nuclide Model

- Radiopharmaceuticals in China: Challenges and Opportunities - Radionuclide Production, Radiopharmacy/CDMO, Nuclear Medicine/Hospital
- Radiopharmaceuticals in China: Challenges and Opportunities -
- Alpha Nuclide: First and Only TRT focused - Radionuclide Supplier + CRO + CDMO in China
- Alpha Nuclide Radiochemistry R&D
  - Level B RAM licensed radiopharmaceutical lab was completed in 2022 – 16 radionuclides including <sup>211</sup>At, <sup>225</sup>Ac, <sup>212</sup>Pb and <sup>68</sup>Ge are licensed
  - 2 cGMP processing labs, fully equipped radiochemistry R&D lab
  - In-house cell culture lab and animal facility
  - Suitable for preclinical and R&D studies
- Alpha Nuclide Cyclotron facility
  - Innovation 1 – the TR-Alpha cyclotron
    - Co-developed with ACSI, first in the world
    - First cyclotron that is designed specifically to produce At-211
    - Small footprint – cost effective and more regulation-oriented
  - Innovation 2 – compact facility for At-211 production and radiopharmaceutical formulation
    - Maximize efficiency
    - Cost effective
    - Quick turn around – 24 h lead time for patient dose
- Alpha Nuclide Model: Localized Production and Supply

### Alpha Nuclide Model: Timeline



**Dr. Feize Li** - Sichuan University (virtual)

**Dr. Fei Yu**, Institute of Nuclear Medicine at Tongji University, China

**Objective:** Chinese researchers working on At-211 radiopharmaceuticals

- Unique advantage – higher energy, shorter range, better hypoxia tolerance and easier shielding

China started in 1990 while international research on astatine -211 and gradually progressing

Stable production of astatine-211 using the CS-30 cyclotron in 2003 with outstanding contribution to the synthesis, separation and application

First research using astatine-211 octreotide targeting somatostatin receptor2 (SSTR2) and continue with various small peptides, monoclonal antibodies, single domain antibodies and biomimetic nanomaterials as carriers.

Efforts in preclinical studies and less in clinical investigations

Book published in 2022 by Prof. Yutian Feng and co-invited “strategies and Application of Targeted Alpha-Particle Therapy”

**Dr. Gabriel Tabacaru** - Texas A&M University

**Objective:** Fundamental research (Astrophysics and Fundamental nuclear physics and nuclear chemistry), Aerospace industry chip testing (NASA, JPL, Boeing, Lockheed Martin, Amazon, SpaceX, Intel, Texas Instruments,...) and Radioactive Isotopes production for medical research Production

- K150 Cyclotron (88")
- Use of newly acquired ion source (D-Pace Inc., versatile, produces negative ions and positive ions) or ECR Ion Source (home made)
- Energy 28.8 MeV, external irradiation

Target system

- Bismuth deposit on aluminum
  - Melted, pressed and machined
  - Fused using ultrasonic soldering device
- Slanted rectangular (10 deg) – obsolete
- Disk – current setup

Target extraction

- Manual extraction
- Air in the target chamber checked for airborne astatine

Target processing

- Target dissolved in HNO<sub>3</sub>
- Automated system reduces hands-on time

Target processing<sup>211</sup>At separation

Shipments - Texas A&M is the newest member of the DOE Isotope Program's UIN! We joined in 2023.

Q&A

11.50 Future of the Network

**Dr. Jean-François Gestin** - NOAR Europe

**Objective:** NOAR EUROPE - Network for Optimized Astatine labelled Radiopharmaceuticals <sup>211</sup>At users community in EU

- Capitalize on COST NOAR activities
- Consolidate the network of academic and industrial users
- Provide access to a dedicated community with up-dated knowledge
- Facilitate the development of <sup>211</sup>At in EU
- Favor transfer to industry for patient benefits
- Communicate and disseminate
- Make it happen!

**Several topics to address –**

Securing EU supply

- Establish a network (Back-up) of producers & close delivery
- Favor repurposing of existing 30 MeV cyclotrons for astatine-211 production
- Favor Increasing astatine-211 output per irradiation time
- Giving supports to acquire new dedicated cyclotrons in European countries
- Contribute to the development of new technologies (LINAC, Generators, ...)
- Contribute to the delivery to EU laboratories

Radiochemistry

- Improvement of extraction, radiolabeling yield and stability
- Establishment of best practices for labeling targeting vectors
- Establishment and up-scaling of drug manufacture under GMP
- Automatization of the full process
- Transfer of knowledge to EU academic labs

Preclinical

- Provide more evidence of efficacy and comparative studies with other radionuclides, in different pathologies
- Development of innovative vectors (scaffolds, targets, delivery strategies, ...)
- Stay tuned to new approaches in biology

Regulatory & Clinical

- Regulatory and stability concerns during transportation by road or air
- Regulatory landscape and available clinics for astatine-211 drug trials
- Radiation safety / Handling of astatine-211 and decay products at laboratories and clinics

Meetings & Dissemination

- Organization of virtual WG meetings (4/Year)
- Organization of Scientific meetings only for members (1/Y)
- Co-organization within the WAC of International meetings (1/2Y)
- Organization of Pre-symposium bringing together academic and industrials
- Lectures: Scientific presentations or presentation to a panel of non-experts
- Common communication, paper review, .....

Improve communication to practitioners & patients.

## Europe

Identification and common answer to EU calls to finance:

- Improvement in production yield & sites
- Preclinical research
- Clinical POC
- Network consolidation

Participation to NMEU (therapy group & lobbying)

Participation to PRISMAP+ (thematic node)

European Network - European Network & Research platform

### Dr. Koshin Washiyama

**Objective:** The Past and Current of the World Astatine Community

Roots of the World Astatine Community:

- Formation of the WAC was catalyzed by the 66th International Atomic Energy Agency General Conference At-211 Side Event hosted by the Atomic Energy Commission of the Cabinet Office of Japan on September 27, 2022.
- During the side event Dr. Jean-François Gestin of the University of Nantes, France, Dr. Mitsuru Uesaka, Chairperson of the Japan Atomic Energy Commission and Dr. Ethan Balkin of the United States Department of Energy Isotope Program (DOE IP) shared the views and status of At-211 production capabilities of their respective countries/unions, and agreed to continue an open exchange of information, technology transfer as permitted, and collaborative research among regional production networks established by individual countries and organizations.

Cape Town, the birthplace of WAC

- Subsequently, at the 12th International Symposium on Targeted Alpha Therapy (TAT'12) held in Cape Town, South Africa, astatine-related stakeholders from the European Union (EU), Japan and the United States of America (U.S.), along with an IAEA observer, gathered to formally announce the formation of the WAC and begin to codify a frame work for its form and function.



### Dr. Ethan Balkin - WAC

**Objective:** Changes and New Additions

For the European community, while the COST action is ending, NOAR Europe is an exciting opportunity! And pleased to welcome China to the WAC

- Outreach to New & Potential Producers - South Africa and Latin America\
- Upcoming Events

Prof. Jean-François Gestin will be jointly organizing a session on Alpha-emitters at the upcoming iSRS Conference in Australia (May 11-15, 2025).

WAC will begin rotating workshops to provide a forum to discuss At-211 scientific and clinical developments and to encourage collaborations.

1. First workshop will be held either just prior to or just after the 2025 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging in New Orleans, Louisiana USA (June 21-24)
2. Second workshop will be held just prior to the 2026 Workshop on Targetry and Target Chemistry in Nara, Japan
3. Additional Workshops will be announced annually

### Dr. Jean-François Gestin - Survey presentation

Q&A

## 12.10 Industrial Presentations

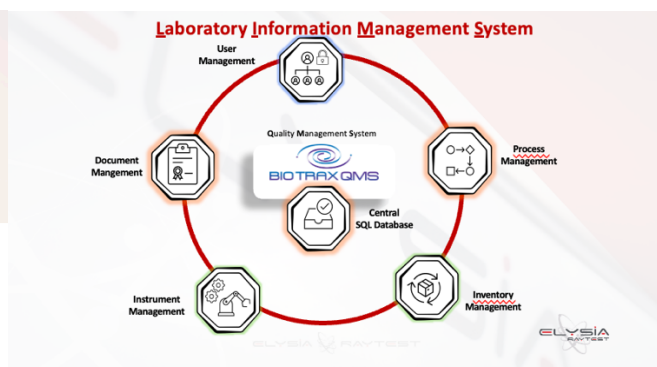
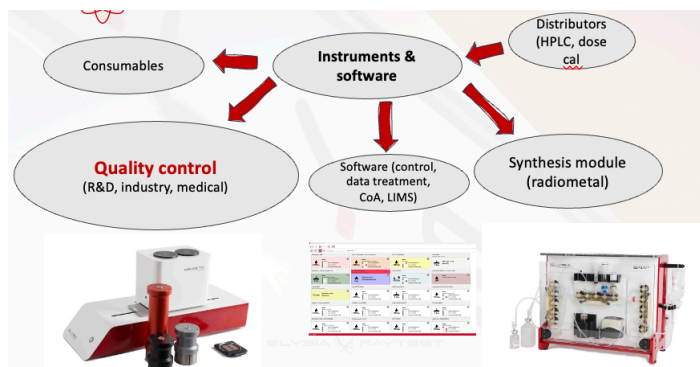
- ELYSIA

**Elysia Spin-off Uliège (2014) and Raytest (radiodetection, 90's)**

**Elysia QC solutions**

- Complete Radio-HPLC
- Radio Detector (GABI)
- TLC scanners (miniGita)
- Multi Channel Analyzer (Mucha NOVA)
- Filter Integrity Test > Safira
- Preparative HPLC detectors

- Ionization Chambers
- Automated Radio Active Sample Preparation Module
- QC Tests covered
- Alpha- Beta-LC-flow Monitors : radio-HPLC
- Flow cells
- At-211 measurements : RAMONA
- Alpha, beta, Gamma and MCA probes for MINIGITA



#### - TRISKEM

- Based in Rennes (France)
- Main product line: extraction chromatographic resins
- Staff : 20
- R&D and TechSupport group: 4 RadChem PhD, 2 Technicians + 1 PhD student
- R&D: Development of new resins, techniques and applications
- Products used in several domains

#### Working in the field of Extraction chromatography and interests in Radiopharmacy:

- Radionuclide production/purification
  - o Resin and method development 'cold'
    - Cooperation with cyclotrons & reactors (NL, RN producers,...)
    - Equipment provider (targetry, synthesizer,...)
  - o Separation of radionuclides (mainly radiometals) from irr. targets
    - Diagnostics: Zr-89, Cu-64, Ga-68, Ge-68, Ti-44/5, Tc-99m, Sc-43/4...
    - Therapy: alpha emitters (Ac-225, Pb-212,...), Lu-177, Tb-161, Cu-67, Sc-47...
  - o Requirements for resins:
    - No selectivity for target material, high selectivity for product
    - Elution under 'soft' conditions in small volume => labelling/injection
    - Fast kinetics
    - Combining several resins can facilitate the separation
      - Conversion (high acid to dilute acid, e.g. Ga-68)
      - Removal of impurities upfront (e.g. Cu-64)

#### Quality control

- Cartridge based methods (e.g. Sr-90 in Y-90,...)
  - Use of "TK-SrScint cartridges"?
- "Sheets"
  - p.ex. DGA sheets (functionalized TLC for Ra-223, Ga-68, Pb-212,... => CVUT Prague),

#### CU Sheets (QC of Cu labelled compounds),...

- Decontamination of effluents/waste (Ge-68, lanthanides, radioiodine,...)
- 'Recycling'/valorization of long-lived RNs (Ge-68,...) and target materials
- Radiolysis stability (polymer, radical scavengers,...)
- Determination of radionuclides (mainly used in therapy, generally Lu-177 and Ac-225) in environmental and bioassay samples

#### Interest on Astatine-211

- Looking for collaboration
- At separation on a cartridge after target dissolution
  - o Option: TK400 Resin (long-chained alcohol based), elution typically in NaOH
  - o Interested to test other resins (TK401/2, TK200,...)
- Rn-211/At-211 generator
  - Inert support impregnated e.g. with with long-chained alkenes, alcohols,...
  - Mixture of several extractants on a resin bead
  - Possibility to retain Rn and Po, elution of At?

**12.30 Dr. Richard Zimmermann - Will <sup>211</sup>At really happen?**

**Objective:** Switching from betas to alphas

- <sup>177</sup>Lu exclusively based on nca <sup>177</sup>Lu
- <sup>161</sup>Tb: same profile, same production tools, ... same issues
- <sup>67</sup>Cu: still one isolated company developing drugs labeled with <sup>67</sup>Cu
- <sup>131</sup>I non metallic atom of interest for BBB crossing - main use: thyroid
- <sup>90</sup>Y high energy, no gamma - main market in local therapy (liver - brachytherapy)
- Alphas in general are considered for relapsing patients
- <sup>225</sup>Ac tested as substitute for all <sup>177</sup>Lu drugs developed so far
- <sup>225</sup>Ac mainly used in patients non-responsive to <sup>177</sup>Lu
- ... but, if <sup>177</sup>Lu is inefficient, <sup>225</sup>Ac-analogues will do the job, is not true

RVT further evolution

*Thinking out of the box: beyond today's standard use of Radiotheranostics*

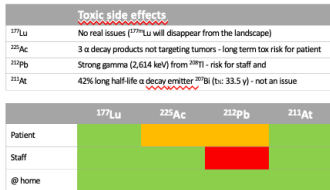
- From third to second to first line treatments
- Combined or cocktail therapies
  - Evolution of RVT will follow evolution of chemotherapy
  - Need of approved drugs (alpha and betas) and 15-20 years
  - <sup>225</sup>Ac + <sup>177</sup>Lu already tested: better efficacy proven
  - Future: combined betas+ alphas, introducing AEs/CEs, mix with chemo, ...
  - Important role to play for <sup>161</sup>Tb (beta+AE) or <sup>212</sup>Pb (beta+alpha)
  - <sup>211</sup>At: Probably major role for combined <sup>131</sup>I/<sup>211</sup>At (beta/alpha) or <sup>123</sup>I/<sup>211</sup>At (AE/alpha)
  - Other advantage: same production tool for <sup>123</sup>I and <sup>211</sup>At
- Evolution of NM in pediatry
- Evolution of veterinary nuclear medicine

**Safety**

2034: From 30,000 to 1,000,000 patients treated a year

Safety issues to take in account

| Issue       | Consequences   |
|-------------|--|
| Production  | Everything under control<br>But waste storage issues                             |
| Hospital    | Ambulatory vs Hospitalization<br>Human waste storage<br>Staff radiation exposure |
| Patient     | Contact with healthy relatives<br>Long term irradiation<br>(Side effects)        |
| Environment | Waste issues   |



Ecological issues that led to class action lawsuits  
Risks for human health in drinking water

| Pollutant                 | Issue                       |
|---------------------------|-----------------------------|
| Methylmercury             | Minnesota, 1990-01s         |
| Diverse chemicals         | Nagasaki Falls, 1970s       |
| Lead                      | Flint water crisis, 2014    |
| Arsenic                   | Bangladesh, USA, ...        |
| Nitrate                   | Blue baby syndrome          |
| Fluorides                 | Bone, thyroid, neurological |
| Chlorine (trihalides THM) | Cancer, liver, CNS          |
| Pesticides - herbicides   | Cancer                      |
| Organophosphates          | Acute life alteration       |
| Pharmaceuticals           | under evaluation            |
| Nanoparticles             | under evaluation            |
| PFAS                      | under evaluation            |

Influence from environmentalists:  
mainly a political issue to anticipate

| Radionuclide   | Type  |
|----------------|---|
| Natural        | <sup>238</sup> U, <sup>235</sup> U, <sup>232</sup> Th, <sup>210</sup> Pb, <sup>210</sup> Bi |
| Artificial     | <sup>137</sup> Cs, <sup>90</sup> Sr, <sup>137</sup> La, <sup>137</sup> Ba                   |
| Medical origin | <sup>131</sup> I  |

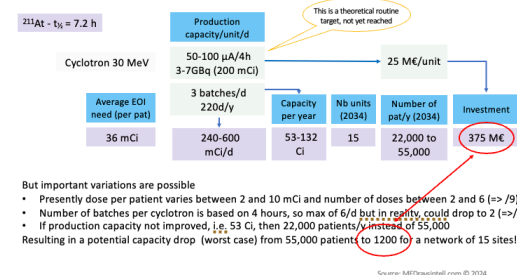
| Radionuclide              | 177Lu | 225Ac | 212Pb | 211At |
|---------------------------|-------|-------|-------|-------|
| Industrial waste handling | Low   | High  | High  | High  |
| Hospital waste handling   | Low   | High  | High  | High  |
| Water pollution           | Low   | High  | High  | High  |
| Ecological issues         | Low   | High  | High  | High  |

Worldwide incidence:  
20 Mt (Stibian 2022)  
Worldwide prevalence:  
43.8 Mt (Ward, 2018)

**2034: Long term needs' assumptions**

|   | Average dose per patient | Average dose (pre-labeling) | EOI dose per patient | Nb doses Per patient | Average amount per patient (EOI) |
|---|--------------------------|-----------------------------|----------------------|----------------------|----------------------------------|
| <sup>177</sup> Lu - t <sub>1/2</sub> = 6.7 d  | 75 mCi                   | 200 mCi                     | 400 mCi              | 2 to 6 – average 3   | 1.2 Ci                           |
| <sup>225</sup> Ac - t <sub>1/2</sub> = 10.0 d | 200 μCi                  | 300 μCi                     | 330 μCi              | 2 to 6 – average 3   | 1.0 mCi                          |
| <sup>212</sup> Pb - t <sub>1/2</sub> = 10.6 h | 3 mCi                    | 6 mCi                       | 20 mCi               | 2 to 6 – average 3   | 60 mCi                           |
| <sup>211</sup> At - t <sub>1/2</sub> = 7.2 h  | 3 mCi                    | 6 mCi                       | 12 mCi               | 2 to 6 – average 3   | 36 mCi                           |

**2034: <sup>211</sup>At production capacity**



<sup>177</sup>Lu-Pluvicto is approved on the basis of 6 times 200mCi injected. On this basis, the average amount EOI per patient would be 6 Ci, not 1.2. Real life average reported number of doses per full cycle is 3.5 (due to drop out, no-show, death, ...)

**2034: Future <sup>211</sup>At-labelled drug world manufacturing capacity**

- If we trust these figures, a full network of 15 dedicated production centers will cover the main US+EU markets and will be sufficient to treat a maximum of 55,000 patients a year
- Each additional target of 55,000 patients/year will need an investment of €375M
- <sup>211</sup>At is adapted for orphan drug indications, not blockbuster indications (prostate, breast, lung ...)
- Each drug/company will want to control its own network, so there will be as many networks of 15 cyclotrons as marketed drugs
- ... as € 375M is a small amount compared to a potential yearly revenue of 55K pat x 100K€ = €5.5B
- ... and a small investment compared to an additional reactor (> 1B€), sources for <sup>225</sup>Ac (presently 3x200M€), and even to the investment realized so far for giving access on this same territory to <sup>18</sup>F (800+ cyclotrons - €4B)

Producing <sup>211</sup>At will NOT lead to exceptional CoGs - there is no reason not to invest in <sup>211</sup>At

Why should I invest in Astatine-211 rather than in ... ?

Two types of investors

- A: Companies investing in the manufacturing tools: €20 to 400M
- B: Companies investing in the drug development : €200M to €10B

If development of drug is successful, B will acquire A

The existing <sup>211</sup>At-producing network is mainly based on academic centers

Of the utmost importance for developing new technologies and new drugs in the field

... providing that the research activities are covered by IP

Also of high importance for industry as part of their learning curve



That can be used during the ramping up phase but not further than Clinical Phase II (GMP)  
 ... but, as they cannot be acquired at a later stage for commercial production (except lonetix, Nusano, ...), of no interest for investors  
 The cost of development of a drug targeting 27,000 patients is almost the same as for a drug targeting 5M patients  
 Development of a 'me-too' drug can become really expensive

Summary and conclusions

- <sup>211</sup>At production yields need to be improved
- <sup>211</sup>At is best appropriate in development of drugs for orphan diseases (<50K patients)
- Each player will want to control its own production network (15 cyclotrons)
- To keep the control and to reach market target, he will have to invest about € 375M /drug/indication
- On the long term, <sup>211</sup>At may have a role to play in brain disease (together with <sup>123</sup>I/<sup>131</sup>I)
- <sup>212</sup>Pb will put pressure on <sup>225</sup>Ac, but <sup>211</sup>At will not jeopardize <sup>225</sup>Ac or <sup>212</sup>Pb
- We are missing molecules with IP in original indications

**Q&A**

13.10 Lunch Break - Industrial exhibition

14.40 **Dr. Antero Abrunhosa** - Survey analysis

14.55 **Dr. Emma Aneheim & Dr. Jean-François Gestin**  
 Closing remarks & Farewell

15.10 **All MC representatives - MC meeting**

- 1) End of Action NOAR
- 2) Creation of NOAR EUROPE/WAC
- 3) Discussion on the survey result
- 4) Discussion on future NOAR EUROPE membership and budget

**Presentation of the budget during the 4 years:**

All Grant Periods have been approved by MC and Scientific Officer of the COST Action :

From 01/11/2020- 31/10/2021 = 73.841,50€

From 01/11/2021- 31/10/2022 = 95.699,55€

From 01/11/2022- 31/10/2023 = 132.653,08€

From 01/11/2023- 21/10/2024 = 152.490,00€

Total amount = 454.687€/4years

**Presentation of the 01/11/2023- 21/10/2024 period**

[Actions / CA19114 / Periods / Period 4 / Grant](#)

Financial period: **AGA-CA19114-4**  
 From **01/11/2023** to **21/10/2024**

[? Contact Us](#)

| Total   | Grant budget<br>(a) | Expenditure      |                 |                  |                   | Total<br>(f=d+e)  | Delta<br>(g=f-a) |
|---|---------------------|------------------|-----------------|------------------|-------------------|-------------------|------------------|
|   |                     | Actuals<br>(b)   | Accruals<br>(c) | Total<br>(d=b+c) | Forecast<br>(e)   |                   |                  |
| Meeting   | 74 235.00           | 11 006.75        | 1 632.43        | 12 639.18        | 54 640.00         | 67 279.18         | -6 955.82        |
| Training School   | 1 585.00            | 1 212.64         | 0.00            | 1 212.64         | 0.00              | 1 212.64          | -372.36          |
| Short-Term Scientific Mission Grant                     | 40 780.00           | 5 100.00         | 0.00            | 5 100.00         | 35 680.00         | 40 780.00         | 0.00             |
| Virtual Mobility Grant                                  | 0.00                | 0.00             | 0.00            | 0.00             | 0.00              | 0.00              | 0.00             |
| Inclusiveness Target Countries Conference Grant         | 4 000.00            | 0.00             | 0.00            | 0.00             | 4 000.00          | 4 000.00          | 0.00             |
| Dissemination Conference Grant                          | 6 500.00            | 4 000.00         | 0.00            | 4 000.00         | 2 500.00          | 6 500.00          | 0.00             |
| Dissemination and Communication Products                | 4 500.00            | 0.00             | 0.00            | 0.00             | 4 500.00          | 4 500.00          | 0.00             |
| Other Expenses Related to Scientific Activities (OERSA) | 1 000.00            | 0.00             | 0.00            | 0.00             | 1 000.00          | 1 000.00          | 0.00             |
| Virtual Networking Support Grant                        | 0.00                | 0.00             | 0.00            | 0.00             | 0.00              | 0.00              | 0.00             |
| Networking expenditure                                  | <b>132 600.00</b>   | <b>21 319.39</b> | <b>1 632.43</b> | <b>22 951.82</b> | <b>102 320.00</b> | <b>125 271.82</b> | <b>-7 328.18</b> |
| Eligible Networking expenditure                         | 132 600.00          | 21 319.39        | 1 632.43        | 22 951.82        | 102 320.00        | 125 271.82        | -7 328.18        |
| FSAC 15% of Eligible Networking expenditure             | 19 890.00           | 3 197.91         | 244.86          | 3 442.77         | 15 348.00         | 18 790.77         | -1 099.23        |
| Eligible Costs  | <b>152 490.00</b>   | <b>24 517.30</b> | <b>1 877.29</b> | <b>26 394.59</b> | <b>117 668.00</b> | <b>144 062.59</b> | <b>-8 427.41</b> |

**Grant budget** - Budget as per Contractual Grant Agreement  
**Actuals** - expenditure recorded for payment and sent to bank  
**Accruals** - expenditure to be/ or claimed pending to be reimbursed  
**Forecast** - value/amount of future activities planned or committed

16.30 Coffee Break & End of meeting

**Friday, October 4<sup>th</sup> , 2024 / Nantes**

**08.00 Core Group meeting**

**Revision of the final work and budget**

The final work was presented to the Core Group members by the Action Chair. The discussion focused on how to continue in the coming months and create a platform for future work and collaboration. NOAR-EU was promoted, highlighting its goals, development path, and as a starting point for new projects and industrial collaboration.

A draft version of the budget was presented and discussed. The budget aligned with the planned and realized activities.

**Discussion and preparation of the content for the Final Achievement Report, as well as the progress of the Final Action Dissemination, including deliverables**

The Action Chair opened the discussion about the submission of the Final Achievement Report, which needs to be submitted after the end date of the COST Action.

The main objective of the Final Assessment of the COST Action was to identify how well the Action has:

- Implemented networking activities
- Developed S&T activities toward the Action's MoU objectives
- Achieved its MoU deliverables
- Achieved additional outputs and achievements, including projects resulting from Action activities and co-authored Action
- Engaged the TAT and WAC communities
- Promoted NOAR-EU
- Produced publications and achieved communication, dissemination, and exploitation of Action results

In addition, the Final Assessment of the Action will include:

- Information on potential success stories, emerging topics, and potentially important future developments
- Identification of impacts (the short- to long-term scientific, technological, and/or socioeconomic changes produced by the Action, whether directly or indirectly, intended or unintended)
- Collection of data necessary to demonstrate COST performance and impact

**Preparation on the Newsletter No4**

The final newsletter for the COST NOAR project will address topics from the 3rd Global Meeting, as well as the mission, responsibilities, and duties carried out during the project. T

his newsletter will provide important information about the project's outputs and key insights as we conclude the story.

16.30 – 18:00 **Conclusion – Minutes writing**