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A digital real-time high-resolution imaging system to quantify and identify all emitted charged particles



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Currently, the **characterization of the nature and spatial distribution of radionuclides** in a sample is **time consuming and fastidious**. Indeed, it necessarily requires the use of two distinct analytical techniques and detectors of different nature.

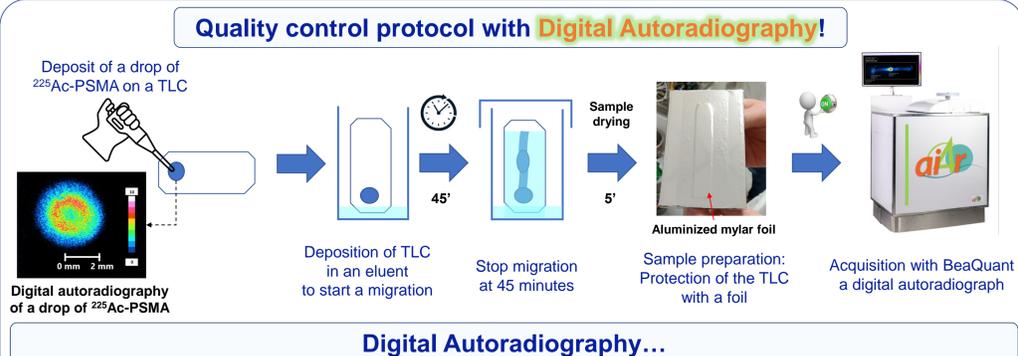
Moreover, the spatial resolutions of the two methods are often detector dependent, which makes it difficult to integrate and interpret these two measurements together.

Can we perform a fast and accurate quality control of radiopharmaceuticals with a single system?

Quality control ²²⁵Ac

| RCY [1] | RCP [1] |
|------------------|--|
| X? | Y? |
| Yield = (100-x)y | Purity = $\frac{\sum^{225Ac}}{\sum^{Tot}}$ |
| >95% | >90% |

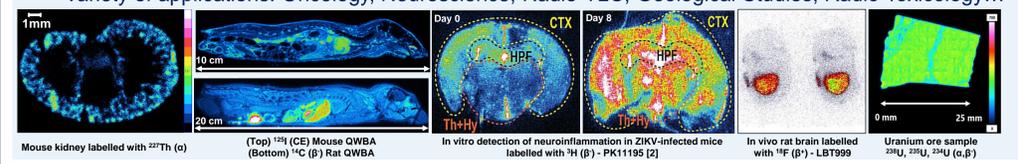




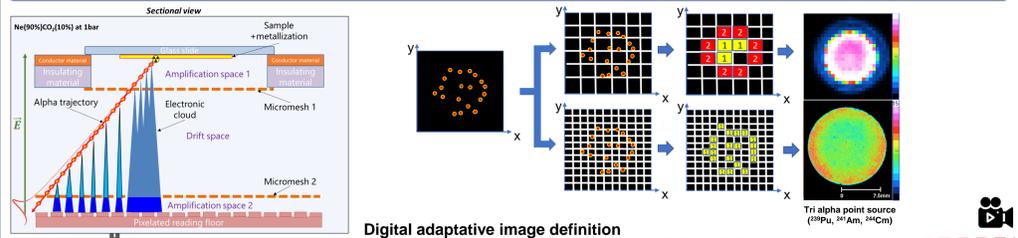
Digital Autoradiography...

→ an accurate up-to-date emission imaging technique !

- Allows to study and locate in 2 dimensions the radioactivity emanating from a surface sample at scales until **10 micrometer**.
- Well suited for pre-clinical TAT: allows **understanding and quantifying biodistributions** in tissues at **high spatial resolution and low activity**.
- Digital autoradiography** → Ability to analyze and reanalyze endlessly the digital data acquired!
- Variety of applications: Oncology, Neuroscience, Radio-TLC, Geological Studies, Radio Toxicology...



BeaQuant: a particle by particle digital autoradiography system



Digital adaptive image definition

Data analysis

Image processing:

- Localization (ROI)
- Quantification

Additional data available of each detected particle:

- Time
- Kinetic energy (α) [3]

The Spatio Temporal Spectroscopic Autoradiography Analysis (STSA)

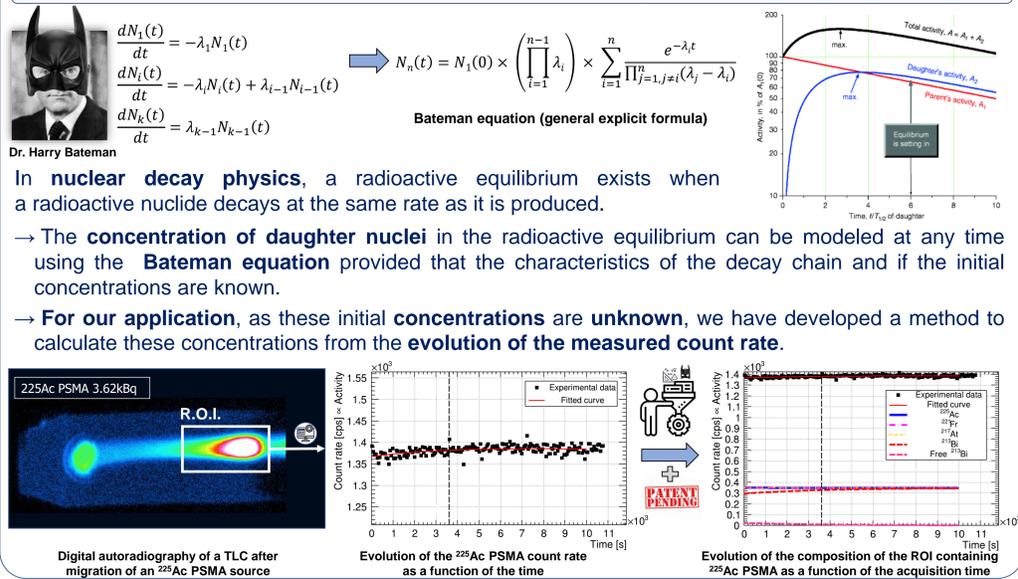
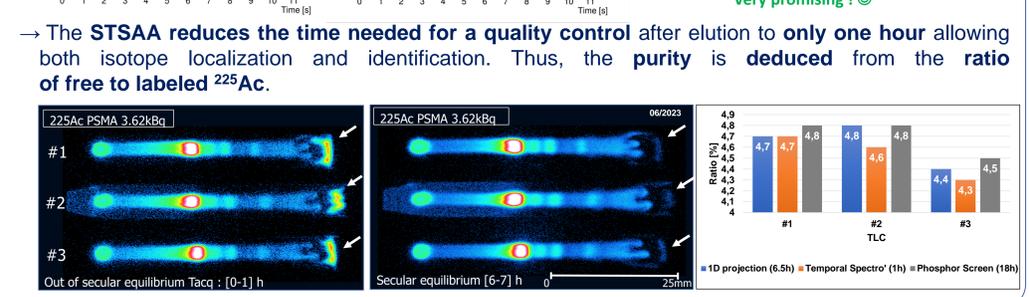
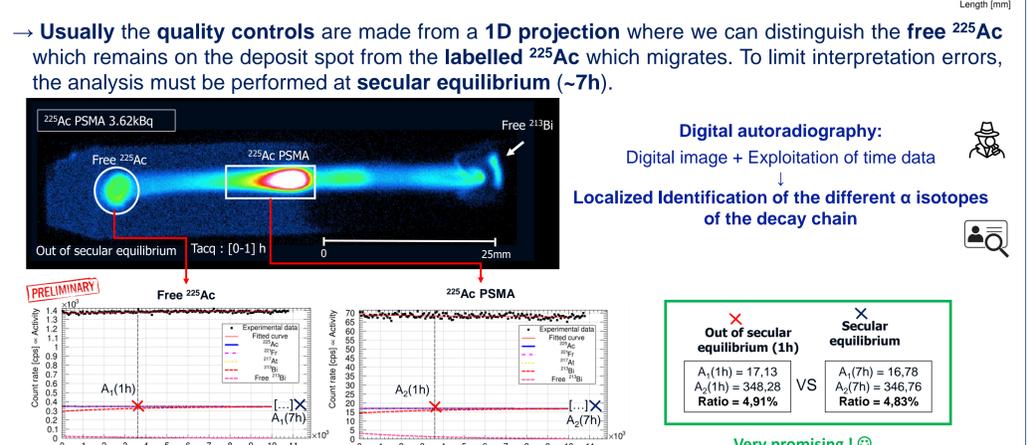
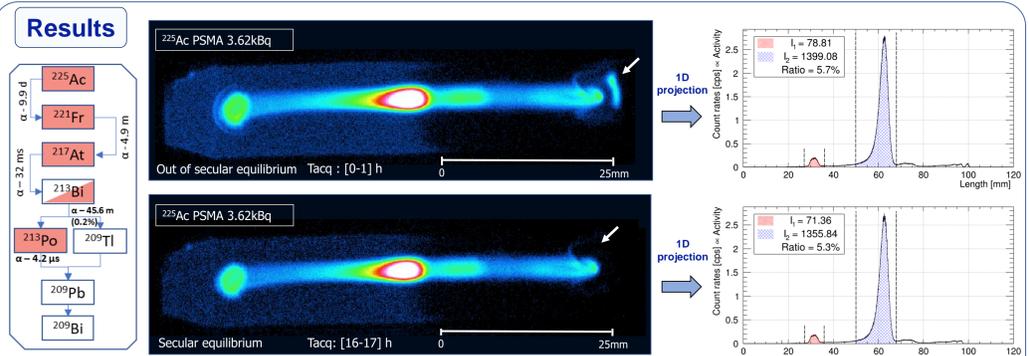
Dr. Harry Bateman

$$\frac{dN_1(t)}{dt} = -\lambda_1 N_1(t)$$

$$\frac{dN_2(t)}{dt} = -\lambda_2 N_2(t) + \lambda_1 N_1(t)$$

$$\frac{dN_k(t)}{dt} = \lambda_{k-1} N_{k-1}(t) - \lambda_k N_k(t)$$

Bateman equation (general explicit formula)

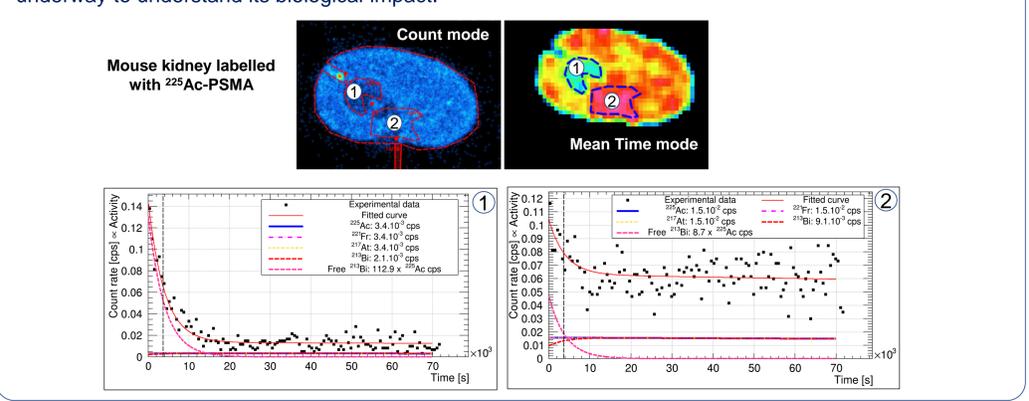
$$N_n(t) = N_1(0) \times \left(\prod_{i=1}^{n-1} \lambda_i \right) \times \sum_{j=1}^n \frac{e^{-\lambda_j t}}{\prod_{i=1, i \neq j}^n (\lambda_j - \lambda_i)}$$



Discussion

Digital autoradiography combined with a temporal spectroscopy method allows the quick and accurate identification of different radioisotopes and to observe their localization.

The increased robustness of this method comes from its low dependence on the operator's choices compared to 1D method.

From the results, we can observe the **contribution** of a radioisotope called "**free ²¹³Bi**". Clearly visible on the migration front, free ²¹³Bi corresponds to ²¹³Bi which is not radiolabeled and whose parent, ²¹⁷At, has **not decayed locally**. The most probable hypothesis is that the **free ²¹³Bi** comes from the **mother solution**. This free ²¹³Bi has also been observed in biological samples. Studies are underway to understand its biological impact.



Conclusions

Digital Autoradiography with spectroscopic method:

- Promising** in the acquisition of nuclear data for the production of radionuclides for nuclear medicine applications like **quality control of radiopharmaceuticals** !
- A **precise tool** to understand the temporal behavior of a chain of labeled isotopes.
- Precise image & quantification from mBq to kBq.

Perspectives

More experiments !

- Develop standard methods for **quality control**.
- New field** of application, source control, contamination, environmental studies.
- Set up of **AIDA Lab**, a common laboratory with **Inserm U982**.

References

- Gillings et al., EANM guideline on the validation of analytical methods for radiopharmaceuticals, EJNMMI Radiopharmacy and Chemistry, 2020.
- C.B.L. Victorio et al., TSPO expression in a Zika virus murine infection model as an imaging target for acute infection-induced neuroinflammation, Eur J Nucl Med Mol Imaging, p. 742-755, 2023.
- H. Lefeuve et al., « Spectroscopic autoradiography of alpha particles using a parallel ionization multiplier gaseous detector », Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment, vol. 1035, p. 166807, 2022.

Acknowledgments

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