Race against the clock

Interview with Dr. Anna Pees, Amsterdam UMC

Dr. Anna Pees (Mainz, Germany) obtained her BSc and MSc degree in Biomedical Chemistry at the Johannes Gutenberg University (Mainz, Germany). From 2016-2021 she pursued her PhD at AmsterdamUMC (Amsterdam, The Netherlands) under supervision of Prof. Dr. D. J. Vugts and Prof. Dr. A. D. Windhorst on the topic of ^{18}F-labelled trifluoromethyl groups. After having briefly worked as a product specialist at BV Cyclotron VU (Amsterdam, The Netherlands) in 2021, she started a postdoctoral fellowship under Prof. Dr. N. Vasdev at the Centre for Addiction and Mental Health (CAMH) (Toronto, Canada) where she worked on the development of PET tracers for imaging the endocannabinoid system and other CNS targets. She has recently been awarded a Veni grant to return to AmsterdamUMC for a postdoctoral fellowship on the development of radiolabelling strategies for the short-lived radionuclide oxygen-15.

Race against the clock! That sounds like a challenging project. Could you briefly explain the goal of your Veni research?

My Veni project aims to develop new radiolabelling strategies with the underexplored radionuclide oxygen-15 to synthesise radiotracers for positron emission tomography. The title of my project refers to the ultrashort half-life of oxygen-15, which is just about two minutes. This means it will be literally a race against the clock to have a ^{15}O-labelled PET tracer synthesised and imaged before the activity has decayed. Commonly used PET nuclides have much longer half-lives, e.g. fluorine-18 has a half-life of two hours, which leaves more time for synthesis and imaging. But the short half-life has also its advantages and I like the added challenge.

Oxygen-15 is a relatively unknown radioisotope. Can you tell us more about it? How did you come up with the idea to use this for your research?

As I already mentioned, oxygen-15 is a PET nuclide with an ultrashort half-life. This makes working with it very challenging and therefore the radionuclide has not been used much so far, except as flow tracer in form of ^{15}O-labelled water. With all the recent innovations in the field, such as the new total body PET scanners that are much more sensitive and can image at low tracer doses, and all the automated synthesis equipment as well as dedicated cyclotrons for oxygen-15 production, imaging with oxygen-15 has become much more feasible. The only missing part is the radiochemistry, the synthesis strategies for ^{15}O-labelled PET tracers. And this is exactly what I would like to develop in my Veni project. What fascinates me most about this project is on the one hand the challenge of the time pressure, which necessitates an extremely efficient and easily applicable process. On the other hand, I love the novelty of the project. So little is known on oxygen-15 chemistry and there is a lot to discover. I think the radionuclide has a huge potential.

What is your biggest challenge in this project?

I think the biggest challenge – but also a huge opportunity – is that this project will require to 'think outside the box'. The way we typically approach PET tracer synthesis and imaging will not work for oxygen-15 because of the ultrashort half-life. The project will need creative new approaches for radiosynthesis, quality control and imaging protocols. This is challenging but also offers the chance to explore exciting new techniques and bring them into the PET field.

Even though this is very fundamental research, you probably have a vision of how this could eventually impact patients. Can you elaborate on that?

Eventually, the goal of the project is to have a positive impact in healthcare. For the patient, the ultrashort half-life of oxygen-15 is actually an advantage: it will enable scanning with multiple target-specific tracers in the same patient on the same day which

will increase accuracy of diagnosis and optimise selection of the right treatment for the right patient at the right time. The patients will also profit from safer PET scans with oxygen-15 since the radiation burden will be strongly reduced. As an example, an [^{18}F]FDG PET scan results in a radiation exposure of around 5-7 mSv while a [^{15}O]H_2O PET scan results in around 0.5 mSv. Also, I will be expanding the radiochemistry toolbox, which will allow us to synthesise new tracers and hopefully image diseases that are currently still challenging to diagnose, such as Parkinson's disease (PD).

You recently completed a post-doc at the Centre for Addiction and Mental Health (CAMH) in Canada, where you conducted research on the endocannabinoid system and other CNS targets. What is the most important thing you learned there, and can you apply it in your research in the Netherlands?

My postdoc in Canada was a great learning experience. After having worked on a fundamental radiochemistry project for my PhD, my postdoc project was much more applied. Most of my work focused on tracer development and preclinical studies, and two of the tracers I was working with are currently being validated for human use at CAMH. My new postdoc project is now again in the space of fundamental radiochemistry. With the insights I gained during my postdoc at CAMH I understand much better what is needed to make this fundamental research accessible and valuable for the application in the clinic. My aim is to not only expand our scientific knowledge but also to eventually develop something useful for the patient.

A Veni grant is an important milestone in the career of a young scientist. What does it mean to you?

I am extremely honoured and of course very happy to have been awarded a Veni grant. After my postdoc in Canada, this is a great stepping stone to come back to the Netherlands and continue my academic career. I am very passionate about the field of radiochemistry and PET imaging and hope to contribute to the field with this Veni grant but also in the future in the next steps of my academic career. The Veni grant offers me a unique opportunity to establish myself as an independent researcher with my own research interests.

If we look five years into the future, what do you hope to have achieved with this Veni? What would you be most proud of?

Of course, I hope to have achieved the goal of my proposed research project by having developed synthesis strategies for ^{15}O-labelled PET tracers. But what I really wish and what would make me proud would be if my research on this topic had impact: either in a scientific way, e.g. other researchers joining me to work on oxygen-15 radiochemistry or using my developed ^{15}O-tracers to study diseases, or in the clinic, e.g. in form of more oxygen-15 scans for patients. Nothing is more validating and satisfying for me as a researcher than seeing my work being interesting and useful to others.♦