

Six questions to ...



Anna Pacelli, PhD

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Eckert & Ziegler

Summary

Anna Pacelli is one of the co-authors of

Manual and automated Cu-mediated radiosynthesis of the PARP inhibitor [¹⁸F]olaparib

recently published in the peer reviewed journal **Nature Protocols**. A major goal of their study was the automation of the synthesis process for the promising tracer, in which Eckert & Ziegler's **Modular-Lab Standard** played a central role.

We have been in touch with Anna to find out more about the group's research and what opportunities arise from their work.



About Anna

Anna Pacelli has a PhD in Medicinal Chemistry and Radiochemistry. At the moment she is working as a postdoctoral researcher and research translational radiochemist at the University of Oxford, one of the most recognised research institutes in the UK and worldwide.

A major task in the PET radiochemistry department is the development of novel PET tracers and automation of radiosynthesis processes.

In February 2020 Anna was co-author of *Manual and automated Cu-mediated radiosynthesis of the PARP inhibitor [¹⁸F]olaparib*, published in the peer reviewed journal **Nature Protocols**.

This publication is a great representation of the department's work and shows why they are at the forefront of nuclear medicine research.

About the publication in *nature protocols*

ABSTRACT - Positron emission tomography (PET) is a diagnostic nuclear imaging modality that relies on automated protocols to prepare agents labeled with a positron-emitting radionuclide (e.g., ^{18}F). In recent years, new reactions have appeared for the ^{18}F -labeling of agents that are difficult to access by applying traditional radiochemistry, for example those requiring ^{18}F incorporation into unactivated (hetero)arenes. However, automation of these new methods for translation to the clinic has progressed slowly because extensive modification of manual protocols is typically required when implementing novel ^{18}F -labeling methodologies within automated modules. Here, we describe the workflow that led to the automated radiosynthesis of the poly(ADP-ribose) polymerase (PARP) inhibitor [^{18}F]olaparib. First, we established a robust manual protocol to prepare [^{18}F]olaparib from the protected N-[2-(trimethylsilyl)ethoxy]methyl (SEM) arylboronate ester precursor in a $17\% \pm 5\%$ ($n = 15$; synthesis time, 135 min) non-decay-corrected (NDC) activity yield, with molar activity (A_m) up to $34.6 \text{ GBq}/\mu\text{mol}$. Automation of the process, consisting of copper-mediated ^{18}F -fluorodeboronation followed by deprotection, was achieved on an **Eckert & Ziegler Modular-Lab** radiosynthesis platform, affording [^{18}F]olaparib in a $6\% \pm 5\%$ ($n = 3$; synthesis time, 120 min) NDC activity yield with A_m up to $319 \text{ GBq}/\mu\text{mol}$.

Guibbal, F., Isenegger, P.G., Wilson, T.C. et al. Manual and automated Cu-mediated radiosynthesis of the PARP inhibitor [^{18}F]olaparib. *Nat Protoc* 15, 1525–1541 (2020). <https://doi.org/10.1038/s41596-020-0295-7>

About Modular-Lab

Modular-Lab Standard was already introduced in 2006 to fully automate radiosynthesis processes using a modular approach. By combining different modules, connecting these with tubings and further accessories, and using an open programmable software, users are able to establish their own syntheses on the system.

Since its introduction, ML Standard has been used by more than 100 research groups worldwide and therefore become a Gold Standard for research and development of novel radiotracers with almost any isotope including ^{18}F , ^{11}C , ^{68}Ga and many more.

Nowadays, it is used by several well-known university hospitals, institutes and pre-clinical research companies. In UK alone more than 20 ML Standard Systems have been installed and put into operation in the past years.



1 What potential does [¹⁸F]olaparib have? Which patients may benefit?

Olaparib is a PARP inhibitor that could be used in chemotherapy, in combination with radiotherapy or with other chemotherapeutic agents, to increase their efficacy. However, some patients are resistant to PARP inhibitors. [¹⁸F]olaparib could be a good tool to screen patients who can actually benefit from this treatment regimen.

2 What drove your desire to automate the process?

Automation ensures reproducibility and is safer for the operator (less exposure to radioactivity). If the process is used to make a tracer for clinical studies, it is also safer for the patients because it reduces contact with the operators, who are the main source of contamination in a GMP laboratory.

3 What is special about the process described in the publication?

Copper-mediated radiofluorination is a great tool to make fluorine-18 labelled molecules that couldn't be synthesised with other procedures. The main criticism of this method was its applicability. In this publication, which was the result of a collaboration between Véronique Gouverneur's and Bart Cornelissen's groups, we show that this process can be used in good yields and can be automated, which are two key factors for application to routine production of PET tracers.

The experiences we got during the development can now be used for other applications in this class and we are confident that now further interesting tracers will become approachable.

4 Why did you choose the Modular Lab system to develop your chemistry?

It is a very flexible system with a large variety of available modules, perfect for Research and Development. Also, the software is very user-friendly which allowed us to design the process specifically to our needs

5 **Are there any plans to transfer the process to the clinic and routine?**

There are plans to move to validation of this tracer for clinical studies. It is very much a group effort, with R&D, QC, Production and QA members working together to make this tracer safe for humans.

6 What further exciting projects are you currently working on?

I am working on the development of another novel PET tracer; it is still early days, so I cannot say much. However, I can definitely say that I will use Modular Lab for the radiosynthesis.



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Thank you!

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