

1st Bergen meeting on PET chemistry and applications Auditorium 2, Science building at University of Bergen, May 19, 2011

Organized by Department of Chemistry at University of Bergen





1st Bergen meeting on PET chemistry and applications

Program

09:30 Registration & coffee

10:00 Welcome

Professor Hans-René Bjørsvik Department of Chemistry University of Bergen

Introduction / Opening

Dean Dag Rune Olsen Faculty of Mathematics and Natural Sciences, University of Bergen

10:15 Centre for Nuclear Medicine and PET: Possibilities and

expectations

Chief Radiochemist / Assoc. prof II Tom Christian Holm Adamsen Centre for Nuclear Medicine and PET Haukeland University Hospital. Department of Chemistry

University of Bergen.

11:00 Clinical PET-CT: What more?

Assoc. prof. Martin Biermann University of Bergen and Acting medical chief, PET-centre Haukeland University Hospital

11:45 Coffee break

12:00 Imaging of renal function using a novel PET-probe Professor Olav Tenstad Institute of Biomedicine University of Bergen

12:45 Break / Lunch

13:30 Optimization and simplification of a fully automated synthesis process for manufacture of the PET tracer

¹⁸F-Fluciclatide using FASTlab[®] Research scientist Torgrim Engell GE Healthcare, Oslo

14:15 Positron Emission Tomography (PET) Radiochemistry and Imaging in Aberdeen: Tradition and Innovation

Professor Matteo Zanda Institute of Medical Sciences, College of Life Sciences and Medicine, University of Aberdeen, Aberdeen, Scotland (UK)

15:00 End of meeting

Abstracts

10:15 • • • • • • • • • • • • • • • • • •

Centre for Nuclear Medicine and PET: Possibilities and Expectations

<u>Tom Christian Holm Adamsen</u>^{1,2} ¹Centre for Nuclear Medicine and PET, Dept. of Radiology, Haukeland University Hospital, ²Department of Chemistry, University of Bergen

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The Centre for Nuclear Medicine and PET was established in 2005 because of a grand philanthropic donation from Trond Mohn. With the donation to both Haukeland University Hospital and the University of Bergen, research is to play a big role in the utilisation of this technology.

The past, present and future of nuclear medicine, and PET in particular, relies on solid and broad range of knowledge. The research and design pipeline for new tracers needs cooperation from medicine, biology, physics and mathematics to mention a few. However, the search for the optimal imaging probe is futile without broad knowledge in chemistry and involvment from chemists. Chemistry is in such way both the driving force, and perhaps the bottleneck, for new tracer development.

The PET-center at Haukeland University Hospital has a dedicated area for both GMP-production, as well as for research. Our own cyclotron can produce all relevant PET-isotopes, and can be expanded for solid target irradiation. We also hope to install a small animal imaging PET/CT before the end of 2012.

In March 2011 we were granted a licence to produce [¹⁸F]FDG for clinical use from the Norwegian Medicinal Agency. The time is now ripe to expand our tracer portfolio and to develop new molecular probes for PET-imaging.

Due to the expected increase in demand for knowledge in PET, we will offer a course in radiochemistry and radioactivity, as well as a more pharmaceutical/medicinal chemistry focused course in medical imaging. The latter drawing on expertise from various related fields, in addition to chemistry.

11:00 • • • • • • • • • • • • • • • • • •

Clinical PET-CT: What more?

Martin Biermann^{1,2}

¹Centre for Nuclear Medicine and PET, Haukeland University Hospital and ²Section for Radiology, Institute for Surgical Sciences, University of Bergen

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The approval of our own F-18-FDG-production facilities by the Norwegian Drug Agency in March 2011 marked a big milestone in the development of our centre – but is FDG-PET-CT enough to meet the challenges posed by modern medicine? In the first half of my talk, I am going to present our latest results in multimodal imaging of thyroid cancer. By integrating multiple modalities in patients with differentiated thyroid cancer - ultrasound (US) including US-elastography, US-guided fine and core-needle biopsies, I-131-SPECT-CT, F-18-FDG-PET and contrast-enhanced CT – we have been able to find recurrent disease in 63 % of the 35 patients studied so far, changing therapy in half the patients with diagnosed recurrence. I will also present preliminary data on the use of PET for radiation therapy planning at Haukeland University Hospital (HUH). F-18-FDG-PET has become routine since April 2010 for dose planning in patients to receive external beam radiotherapy for cancer in the epipharynx.

In the second half of my talk I will outline what clinical benefit we can expect of new tracers in Bergen. I will present sample cases studied with O-15-water for coronary heart disease, C-11-choline for prostate cancer and Ga-68-DOTATOC for neuroendocrine tumours.

Positron emission tomography and nuclear medicine is more than just F-18-FDG-PET.

Imaging of single kidney function using a novel PET-probe.

<u>Olav Tenstad</u>¹, Tom C.H. Adamsen,^{2,3} Aurora Brønstad,⁴ Bodil Næss,² Geir Espen Abell² and Torfinn Taxt².

¹Deparment of Biomedicine, University of Bergen, ²Department of Radiology, Haukeland University Hospital, Bergen. ³Department of Chemistry, University of Bergen. ⁴Laboratory Animal Facility, University of Bergen.

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We have developed a new probe for molecular imaging of renal function that is highly specific for filtering nephrons. The two normal human kidneys filter plasma at a rate of 180 liter pr day, remove waste from the blood, regulate the amount of salt and water in the body and control long term blood pressure. The technology can visualize as well as quantify glomerular filtration rate (GFR) in each of the approximately 1 million filtering units per kidney as illustrated in Fig.1.

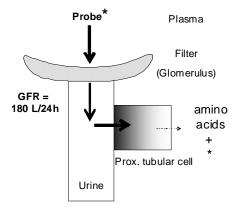


Fig. 1 Probe* is freely filtered and quantitatively taken up into proximal tubular cells, close to its parent glomerulus by adsorptive endocytosis. Probe* is then digested in the lysosomes and its constituent amino acids can be detected together with free label in plasma 20-30 min after i.v.

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injection. By recording the uptake in different layers of the renal cortex by PET, detailed and accurate information of single kidney function can be visualized and quantified without urine sampling.

Since the probe is rapidly and exclusively up-concentrated in functional nephrons, the dose can be reduced by two orders of magnitudes as compared to conventional contrast agents. Furthermore, potential side effects are minimized by utilizing endogenous polypeptides already present in human body fluids. Two patent applications are filed and initial results are ready for publication.

As an illustrative example, the blood supply to the lower part of the left kidney in an anaesthetized pig was ligated prior to PET (Fig 2). The regional loss of glomerular filtration is, as expected, easily detected. The 124I-uptake is strictly confined to renal cortex containing filtering nephrons and the marker intensity is directly related to function, i.e glomerular filtration rate. The function in the healthy part of the left kidney is well preserved at this stage and the total loss of renal function of about 20% is less than detectable by conventional methods.

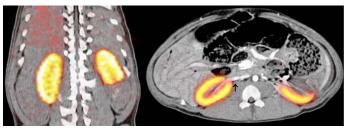


Fig. 2 Left kidney infarction. Coronal and transverse fused *PET-CT-slice at the level of the ligated artery. Color (PET)* represent function (*GFR*). Arrow: *CT-contrast filling of a large artery supplying kidney cortex where the glomerular filtration takes place.*

13:30 • • • • • • • • • • • • • • • • • •

Optimization and simplification of a fully automated synthesis process for manufacture of the PET tracer ¹⁸F-Fluciclatide using FASTlab[®]

<u>Torgrim Engell</u>¹, Julian Grigg², Roger Pettitt², Dimitrios Mantzilas¹, Knut Dyrstad¹, Nigel Osborn², Carina Wickmann¹, Erlend Hvattum¹

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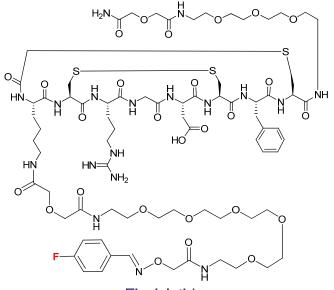
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¹⁸F-Fluciclatide is currently in development as a PET tracer for oncology diagnosis. The compound is produced using a fully automated synthesis platform; FASTlab[®] (GE Healthcare) within a disposable cassette which contains all the required reagents. The process involves two synthetic steps and two purification steps in addition to trapping and pre-treatment of ¹⁸F-fluoride.

Outline of the process

Radioactive fluoride, ¹⁸F-fluoride, from a cyclotron is transferred in to the FASTlab[®] cassette and trapped on a SPE anion exchange cartridge (Waters QMA). The trapped

 18 F-fluoride is released from the cartridge by a solution of water and acetonitrile containing Kryptofix 222 (K222) and K₂CO₃ and transferred to the FASTlab[®] reaction chamber where the fluoride is pre-treated.



Fluciclatide

During the pre-treatment, the water level is reduced (drying) to a low and controlled level and the reactivity of ¹⁸F-fluoride is enhanced by establishing a non-hydrate salt between a K222/K⁺complex and ¹⁸F-fluoride (conditioning). ¹⁸F-fluoride then reacts with the synthon precursor 4- (trimethylammonium)-benzaldehyde (AH111360) to form the synthon 4-fluorobenzaldehyde (FBA). FBA is purified over a mixed bed cation/C-18 cartridge (Waters MCX) before reaction with a bio-active peptide (AH111695) to form ¹⁸F-Fluciclatide. Fluciclatide is finally purified over two C2 SPE cartridges in series (Waters tC2). The yield as recovered ¹⁸F in ¹⁸F-Fluciclatide is 40 % not decay corrected, which equals a chemical yield of above 50 % depending on the reaction time.

This presentation will include: A general introduction to PET-tracer production, the automated platform FASTlab[®], the¹⁸F-fluciclatide process, optimization performed on each synthetic step, and analytical data.

14:15•••••••••

Positron Emission Tomography (PET) Radiochemistry and Imaging in Aberdeen: Tradition and Innovation

Professor Matteo Zanda Chair in Medical Technologies (NRP) Institute of Medical Sciences, Foresterhill, Aberdeen, AB25 2ZD, College of Life Sciences and Medicine University of Aberdeen, Scotland (UK)

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The University of Aberdeen has a strong tradition in molecular imaging, as witnessed by the fact that the first British radioisotope tomographic scanner was installed in Aberdeen in the 70s. Currently, the development of novel experimental tracers for PET Imaging represents a research priority at the University of Aberdeen, with an emphasis on three main topics: oncology, cardiovascular and CNS. The first part of this talk will describe the research facilities at the John Mallard Scottish PET Centre and the activity of the Centre in the area of radiochemistry, pre-clinical and clinical PET imaging. The second part will give an overview of the research projects currently developed at the Centre, which can be listed as follows: (1) 18F-labelled tumour-homing peptides and their trifluoroethylamine mimics; (2) radiotracers for the Alzheimer's Disease; (3) novel analogues of 18F-FAZA for the imaging of hypoxia; (4) brain mapping with radiolabelled cannabinoid CB1 receptor ligands.

PÅMELDING

Deltagelse på seminaret er *gratis,* men det kreves påmelding. Send påmelding i form av en e-mail til Nina.Berg-Johannesen@kj.uib.no Skriv i emne felt: "PET meeting"

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