SPECT and PET imaging in porcine inflammation and infection models

UCPH pig model network seminar

Friday November 21. 2014, 8.30 - 12.00, auditorium A2-70.02, Thorvaldsensvej 40, 1871 Frederiksberg C.

See **abstracts** and **campus-map** below

Programme

8.30-9.00: Coffee

9.00-9.05: Welcome

9.05-9.30: Pia Afzelius, MD, PhD, Department of Diagnostic Imaging, North Zealand Hospital, Hillerød, Denmark
Imaging of Osteomyelitis in Humans; State of the Art

9.30-9.55: Ole Lerberg Nielsen, DVM, PhD, Department of Veterinary Disease Biology, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark
Comparison of autologous ^{111}In-leukocytes, ^{18}F-FDG, ^{11}C-methionine, ^{11}C-PK11195 and ^{68}Ga-citrate for diagnostic nuclear imaging in a juvenile porcine haematogenous *Staphylococcus aureus* osteomyelitis model

9.55-10.30: Aage Kristian Olsen Alstrup, DVM, Ph.D., Department of Nuclear Medicine and PET Centre, Aarhus University Hospital, DK-Aarhus, Denmark
An overview of the use of pigs in PET research

10.30-10.45: Break

10.45-11.30: Erik H.J.G. Aarntzen, MD, PhD, Department of Radiology and Nuclear Medicine, Radboudumc, Nijmegen, The Netherlands
Imaging immune cells at work; the dendritic cell vaccination model in melanoma patients

11.30-12.00: Thomas L. Andresen, Cand Polyt, PhD, Technical University of Denmark, Department of Micro- and Nanotechnology, Center for Nanomedicine and Theranostics, Denmark
Nanoparticle imaging probes for studying inflammatory disease

Registration to Benedicte Kragh, mbhk@sund.ku.dk, no later than November 19th 2014

Organizeres: Professor Lisbeth Høier Olsen, associate professor Ole Lerberg Nielsen, University of Copenhagen

IN VIVO PHARMACOLOGY
GRADUATE PROGRAMME FOR IN VIVO PHARMACOLOGY & EXPERIMENTAL ANIMALS

Abstracts

Imaging of Osteomyelitis in Humans; State of the Art

Pia Afzelius (pia.afzelius@dadlnet.dk)

Plain radiography, technetium-99 bone scintigraphy, and magnetic resonance imaging (MRI) are the most used modalities for diagnosing osteomyelitis in humans. Plain radiography usually does not show abnormalities caused by osteomyelitis until about two weeks after the initial infection. Although computed tomography is superior to MRI in detecting necrotic fragments of bone, its overall value is generally less than that of other imaging modalities. MRI can detect osteomyelitis within three to five days of disease onset. The sensitivity and specificity of MRI may be as high as 90 percent, and MRI is even superior to bone scintigraphy in diagnosing and characterizing osteomyelitis. However, three-phase technetium-99 bone scintigraphy and leukocyte scintigraphy are usually positive within a few days of the onset of symptoms. The sensitivity of bone scintigraphy is comparable to MRI, but the specificity is poor. Leukocyte scintigraphy also has poor specificity, but when combined with three-phase bone scintigraphy, sensitivity and specificity are improved. Other imaging modalities seem promising for the diagnosis of osteomyelitis, but they are not routinely used. Positron emission tomography has the highest sensitivity and specificity —more than 90 percent. The role of musculoskeletal ultrasonography in the diagnosis of osteomyelitis is evolving.

Comparison of autologous ^{111}In-leukocytes, ^{18}F-FDG, ^{11}C-methionine, ^{11}C-PK11195 and ^{68}Ga-citrate for diagnostic nuclear imaging in a juvenile porcine haematogenous *Staphylococcus aureus* osteomyelitis model

Ole L. Nielsen[1] (oleni@sund.ku.dk); Pia Afzelius[2]; Dirk Bender[3]; Henrik C. Schønheyder[4,5]; Páll S. Leifsson[1]; Karin M. Nielsen[1,6]; Jytte O. Larsen[7]; Svend B. Jensen[6,8]; Aage K. O. Alstrup[3]

[1]Department of Veterinary Disease Biology, University of Copenhagen, Copenhagen; [2]Department of Diagnostic Imaging, North Zealand Hospital, Hillerød; [3]Department of Nuclear Medicine and PET Centre, Aarhus University Hospital, Aarhus; [4]Department of Clinical Microbiology, Aalborg University Hospital, Aalborg; [5]Department of Clinical Medicine, Aalborg University, Aalborg; [6]Department of Nuclear Medicine, Aalborg University Hospital, Aalborg; [7]Department of Neuroscience and Pharmacology, University of Copenhagen, Copenhagen; [8]Department of Chemistry and Biochemistry, Aalborg University, Aalborg, Denmark

The aim of this study was to compare ^{111}In-labeled leukocyte single-photon emission computed tomography (SPECT) and ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) to PET with tracers that potentially could improve detection of osteomyelitis. We chose ^{11}C-methionine, ^{11}C-PK11195 and ^{68}Ga-citrate and validated their diagnostic utility in a porcine haematogenous osteomyelitis model. Four juvenile 14-15 weeks old female pigs were scanned seven days after intra-arterial inoculation in the right femoral artery with a porcine strain of *Staphylococcus aureus* using a sequential scan protocol with ^{18}F-FDG, ^{68}Ga-citrate, ^{11}C-methionine, ^{11}C-PK11195, ^{99m}Tc-Nanocoll and ^{111}In-labelled autologous leukocytes. This was followed by necropsy of the pigs and gross pathology, histopathology and microbial examination. The pigs developed a

total of five osteomyelitis lesions, five lesions characterized as abscesses/cellulitis, arthritis in three joints and five enlarged lymph nodes. None of the tracers accumulated in joints with arthritis. By comparing the 10 infectious lesions, ^{18}F-FDG accumulated in nine, ^{111}In-leukocytes in eight, ^{11}C-methionine in six, ^{68}Ga-citrate in four and ^{11}C-PK11195 accumulated in only one lesion. Overall, ^{18}F-FDG PET was superior to ^{111}In-leukocyte SPECT in marking infectious and proliferative, i.e. hyperplastic, lesions. However, leukocyte SPECT was performed as early scans, approximately 6 h after injection of the leukocytes, to match the requirements of the 18 h long scan protocol. ^{11}C-methionine and possibly ^{68}Ga-citrate may be useful for diagnosis of soft issue lesions.

An overview of the use of pigs in PET research

Aage Kristian Olsen Alstrup (aage@pet.au.dk)

Current interest in studying molecular processes as they occur in the living organism has accelerated the use of laboratory animals for imaging of novel radiolabeled compounds. In particular, PET has contributed to the development of radiolabeled compounds for assessing molecular processes. The dynamics of PET typically require a relatively large organ size and blood supply in order to properly evaluate radioligand binding kinetics. To fulfil these requirements, pigs have often been used in such studies. At least four factors have contributed to the ever-growing interest in using pigs for PET imaging. First, a wealth of information has become available concerning similarities of physiologic and pathologic processes in pigs and humans. Second, the size of most pig organs permits studies to be carried out in PET scanners otherwise designed for human use. Third, multiple blood samples can be drawn from pigs to carry out accurate metabolite analyses in studies of new PET radioligands. Fourth, pigs can easily be maintained in anaesthesia for long-term PET studies with multiple injections of radiotracers. Clearly, pigs have much to offer PET studies. In this presentation I will also give an overview over how pig studies in practice can be performed in human PET scanners.

Imaging immune cells at work; the dendritic cell vaccination model in melanoma patients

Erik H.J.G. Aarntzen (Erik.Aarntzen@radboudumc.nl)

Our lab has been among the first to exploit dendritic cell (DC) based vaccinations to treat melanoma patients. These experimental clinical studies provide a unique model for multimodal imaging of immune cells and their function as 1. *ex vivo* isolation and culture allows specific labeling and QC of cell subsets, 2. loading with defined tumor-antigens and 3. delivery of antigen-presenting cells to lymph nodes, offer the possibility to study antigen-specific responses and the route of administration. Over the past years, imaging tools for *in vivo* tracking of DC based vaccines and response monitoring have been pivotal for our understanding of the processes underlying success or failure of this intensive, costly and highly personalized therapy. This presentation will give an overview of our approach to optimize DC based vaccinations using multiple imaging modalities, such as scintigraphy, MR and PET/CT, to provide complementary information. We have developed

protocols to quantify the number of ^{111}In-labeled- and USPIO-labeled DCs at the relevant site, with high resolution to allow differentiation of LNs and the possibility of longitudinal data acquisition. Furthermore, *in vivo* assessment of the ensuing immune response has been investigated using positron emission tomography (PET), exploiting [^{18}F]-labeled 3'-fluoro-3'-deoxy-thymidine ([^{18}F]FLT) and a [^{18}F]-labeled fluoro-2'-deoxy-2'-D-glucose ([^{18}F]FDG).
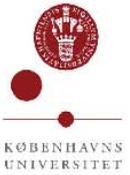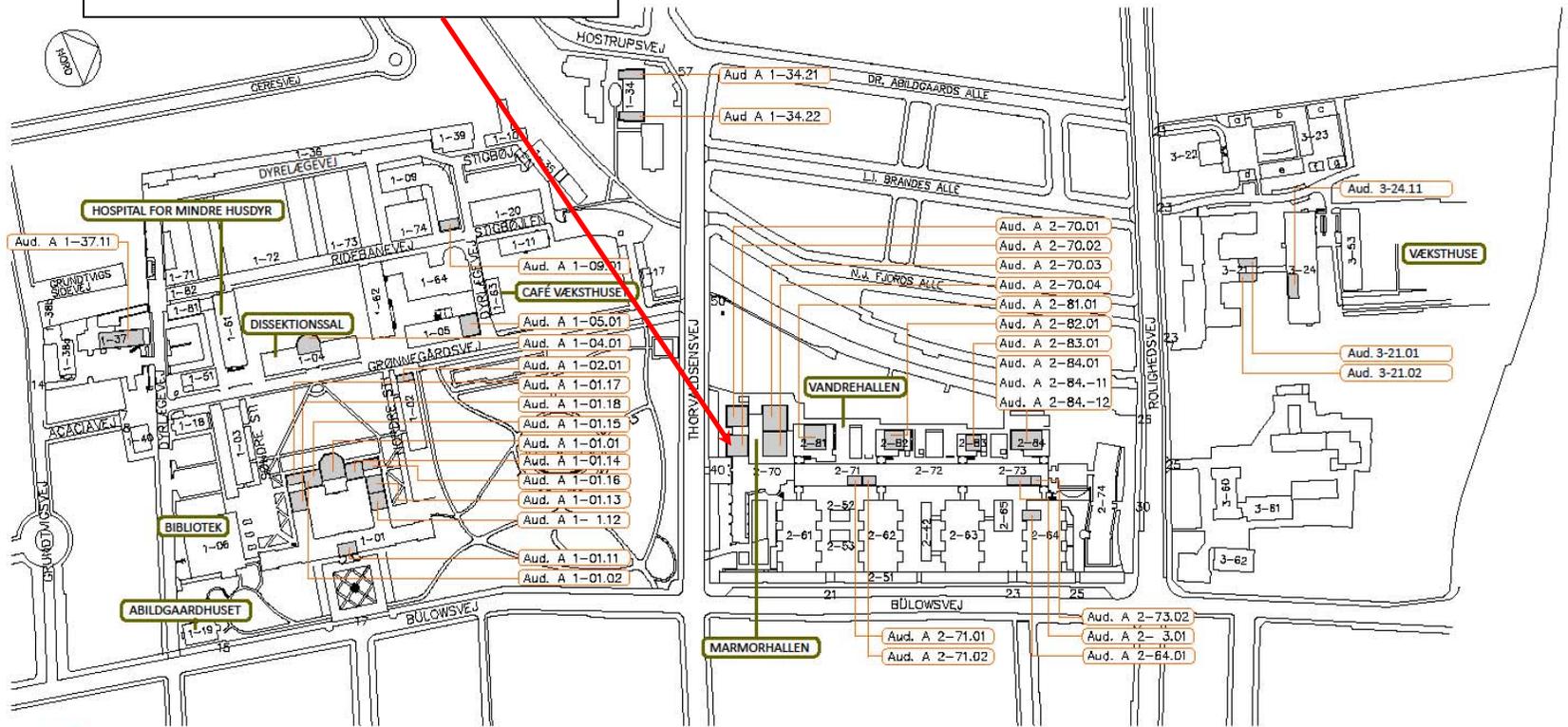
Nanoparticle imaging probes for studying inflammatory disease

Thomas L. Andresen (tlan@nanotech.dtu.dk)

Nanoparticles have been investigated as imaging probes in a range of disease areas in recent years, and have been developed as contrast agents for multiple imaging modalities including PET, MR and CT imaging. Our own research has been focused on developing companion diagnostics for nanoparticle based chemotherapeutics, particularly within cancer. We have developed a number of nanoparticle imaging agents for PET/CT imaging that have been investigated in cancer disease models. These systems have interesting properties for investigating inflammatory disease, which we aim to utilize in forthcoming studies. The nanoparticles can be used to visualize inflammatory tissue due to the leaky vasculature that occurs during inflammation and also be targeted to over-expressed receptors in the tissues. We are particularly interested in targeting over-expressed receptors on endothelial cells and immune cells in relation to inflammation.

AUDITORIEOVERSIGT, FREDERIKSBERG CAMPUS

Thorvaldsensvej 40, auditorium A 2-70.02

HOSTRUPSVEJ

CERESVEJ

DYRLÆGEVEJ

Aud A 1-34.21
Aud A 1-34.22

DR. ABILDGAARDS ALLE

L.J. BRANDES ALLE

3-22   3-23

Aud. 3-24.11

HOSPITAL FOR MINDRE HUSDYR

Aud. A 1-37.11

GRUNDTVIGS SIDEVEJ

RIDEBANEVEJ

STIGBØJLEN

Aud. A 1-09.01

CAFÉ VÆKSTHUSE

DISSEKTIONSSAL

Aud A 1-05.01
Aud. A 1-04.01
Aud. A 1-02.01
Aud. A 1-01.17
Aud. A 1-01.18
Aud. A 1-01.15
Aud. A 1-01.01
Aud. A 1-01.14
Aud. A 1-01.16
Aud. A 1-01.13
Aud. A 1- 1.12

Aud. A 1-01.11
Aud. A 1-01.02

ACACIAVEJ

GRØNNEGÅRDSVEJ

BIBLIOTEK

ABILDGAARDHUSET

BÜLOWSVEJ

GRUNDTVIGSVEJ

THORVALDSENSVEJ

N.J. FJORDS ALLE

Aud. A 2-70.01
Aud. A 2-70.02
Aud. A 2-70.03
Aud. A 2-70.04
Aud. A 2-81.01
Aud. A 2-82.01
Aud. A 2-83.01
Aud. A 2-84.01
Aud. A 2-84.-11
Aud. A 2-84.-12

VANDREHALLEN

2-81   2-82   2-83   2-84

2-70   2-71   2-72   2-73   2-74

2-61   2-52   2-62   2-63   2-65   2-64

2-53   2-51

BÜLOWSVEJ

MARMORHALLEN

Aud. A 2-71.01
Aud. A 2-71.02

Aud. A 2-73.02
Aud. A 2- 3.01
Aud. A 2-64.01

ROLIGHEDSVEJ

VÆKSTHUSE

3-53

3-21

3-24

Aud. 3-21.01
Aud. 3-21.02

3-60   3-81
3-62

KØBENHAVNS UNIVERSITET

AUDITORIUM BYGNINGSNUMMER ETAGE AUDITORIENUMMER

A 1-01.12

SIGNATURFORKLARING:

KÆLDER	-1
STUE	0
1.SAL	1
2.SAL	2