Evaluation of PET Tracer Uptake in Mouse Xenograft Models of Hormone-Dependent Prostate Cancer

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INTRODUCTION

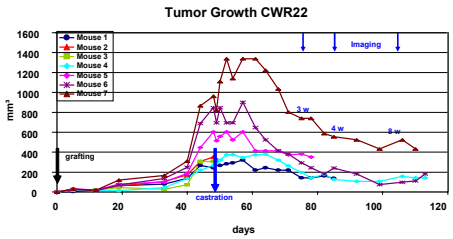
Prostate cancer is the most common oncologic disease in men and the one with the highest accession rate. The evaluation of new PET biomarkers is therefore important. Aim of this study was to investigate PET biomarkers for in vivo delineation of human prostate tumours in xenograft mouse models. We studied the different tracer pharmacodynamics and uptake characteristics of [18F]FLT, [18F]FDG, [11C]Choline and [18F]FECh in the two hormone-dependent tumour models CWR22 and PAC120 using small animal PET imaging.

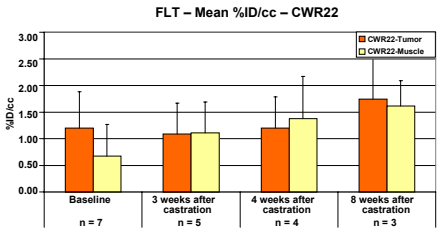
MATERIAL & METHODS

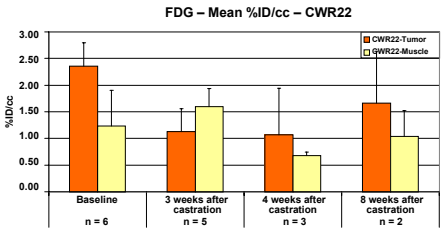
BALB/c-nude male mice at an age of 6 to 8 weeks old were subcutaneously grafted with a 2x2x1mm³ viable tumour zone. After tumour formation followed baseline PET scans on four consecutive days with all four tracers. After this baseline scan the animals were surgically castrated to mimic an androgen ablation therapy. On three different time points after castration mice were imaged again with the four different tracers on four consecutive days.

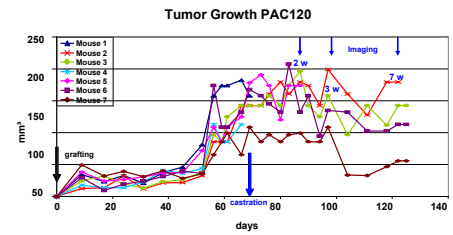
Tracers were administered by intra venous injection of an activity of 10 - 12MBq (F-18) or 14 – 18MBq (C-11) into the tail vein. After the last scan with [18F]FECh, tumours were harvested for further evaluation by immunohistochemistry and histology. Tracer uptake was analyzed by retrieving time activity curves (TACs), percent injected dose per cc (%ID/cc), standard uptake value (SUV) and tumour-to-muscle-ratios (T/M). The optimal uptake time for the static scans were determined from the first dynamic data set (data not shown). PET image reconstruction was performed with an OSEM 2D algorithm.

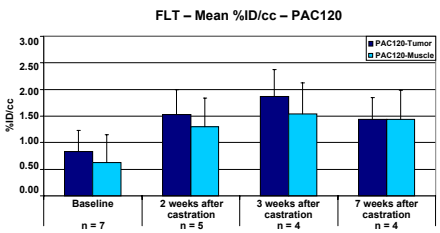
RESULTS

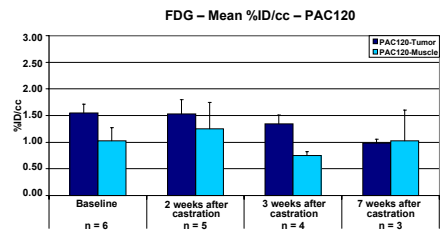




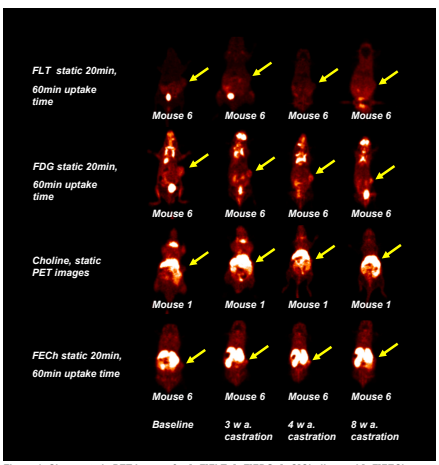


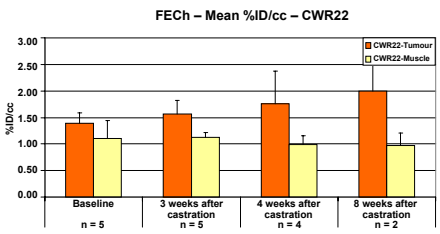






CWR22





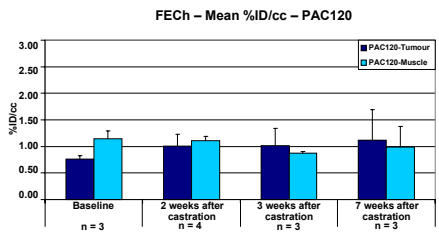


Figure 1: Shows static PET Images for [18F]FLT, [18F]FDG, [11C]Choline and [18F]FECh for the CWR22 tumour model.

PAC120

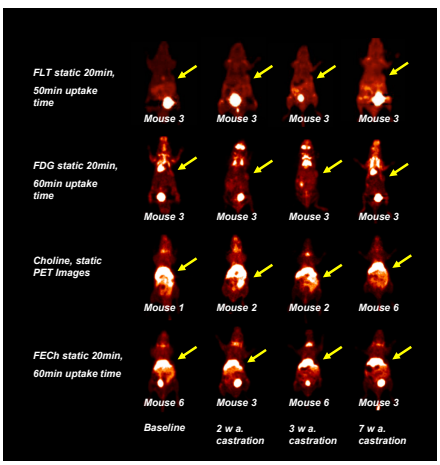


Figure 2: Shows static PET Images for [18F]FLT, [18F]FDG, [11C]Choline and [18F]FECh for the PAC120 tumour model.

SUMMARY

We observed only a moderate uptake with [18F]FLT and [18F]FDG (Figure 1 and 2) in the hormone-dependent tumour models. For imaging the tumours with [18F]FECh we found faint uptake and no tracer uptake with [11C]Choline. Castration induced a decrease of [18F]FLT and [18F]FDG tumour-to muscle ratio in the CWR22 model. Over time we found a constant increase of FLT uptake in the CWR22 tumour and muscle. Four weeks after castration the uptake starts to increase. That could mean there is a transformation from a hormone-dependent to a hormone-independent tumour. But with [18F]FDG there is a decrease of 1.5 fold into the tumour three weeks after castration. The data eight weeks post castration show an increase of [18F]FDG uptake. Thus, we have a notedly change of the tumour environment three and eight weeks after castration. The PAC120 tumour model demonstrates an increase of [18F]FLT into the tumour and the muscle. Seven weeks after surgically castration we found a decrease of the [18F]FLT and [18F]FDG uptake characteristic.

For both tracer we found seven weeks after castration the same uptake level into tumour and muscle in the PAC120 model. With [18F]FDG we observed a continuently decrease of tracer uptake into the tumour over time for that tumour model. Very interesting is the different growing of the two hormone-dependent tumour models. The PAC120 model grows significantly slower than the CWR22 model. That tumour model shows a clear reduction of the tumour volume after castration.

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