Is there a Species Specific Uptake of [^{11}C]Choline and [^{18}F]FECh in Xenograft-Models in Prostate Cancer ?

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INTRODUCTION

Prostate cancer is the second leading cause of death in men in industrial nations. The PET tracer [^{18}F]FDG is a gold-standard for cancer detection. Unfortunately it seems to be not applicable for the detection of prostate cancer. Therefore new tracers like [^{11}C]Choline and [^{18}F]F-Ethyl-Choline have been developed. However, in clinical use there is controversy about the benefit of these tracers especially in early diagnosis of prostate cancer.

To investigate the applicability of the tracers for imaging prostate cancer we use the Xenograft-models PAC120 rats and PAC120 mice to exclude species-dependent effects in tracer accumulation as well as CWR22 mice. The focus lies on the changes in tumor entity before and after castration. Thus, it is possible to mimic an androgen ablation therapy.

In previous studies investigating BALB/c-nude male mice with the hormone-independent tumors PC-3 and DU145 we found only very faint uptake of [^{18}F]FECh and [^{11}C]Choline in the tumors yielding a low tumor to muscle ratio (T/M), summarized in table 1.

	[^{11}C]Choline	[^{18}F]FECh
DU145	T/M: 1.60±0.34 n = 7	T/M: 1.42±0.04 n = 11
PC-3	T/M: 1.17±0.41 n = 7	T/M:1.24±0.25 n = 10

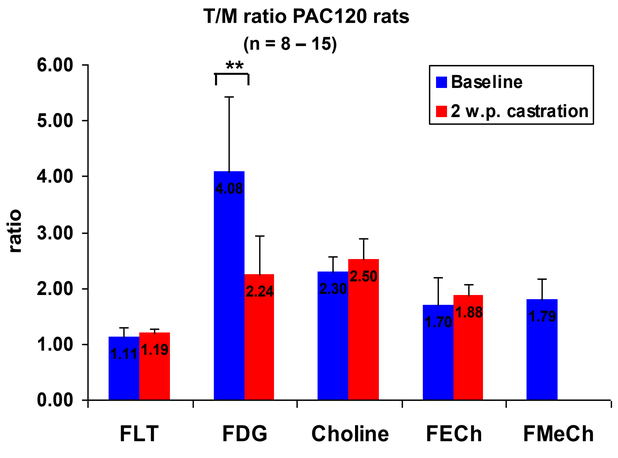
Table 1: The T/M ratio for the two hormone independent cell lines DU145 and PC-3.

MATERIAL & METHODS

For the PAC120-rat-model viable tumor tissue (30 to 40mg) is implanted into a subcutaneous bag on the right side of the animal. For PAC120 mice as well as for CWR22 mice viable tumor tissue by the size of 2x2x1mm³ is used. After a tumor size of a certain volume was reached baseline PET measurements with [^{18}F]FLT,[^{18}F]FDG, [^{11}C]Choline, [^{18}F]FECh and [^{18}F]FMeCh are performed. After surgical castration the measurements are repeated at different time points (Figure 1-3). PET and MRI scans were measured in parallel focusing on the tumor anatomy (Figure 4) and spectroscopy. A 3D Chemical-Shift-Imaging (CSI) MR sequence was obtained from the rats (3D PRESS, TR=1800 ms, TE=135 ms, voxel size: 1.3x1.3x1.3 mm³, scanned FOV: 12x12x12 voxel, which equals: 16xs16x16 mm³, interpolated FOV: 16x16x16 voxel, water saturation bandwith: 40 Hz, vector size: 1024, 2 averages). CSI-metabolic maps were calculated (Figure 4).

RESULTS

a)



b)

PET Images – PAC120 Rats

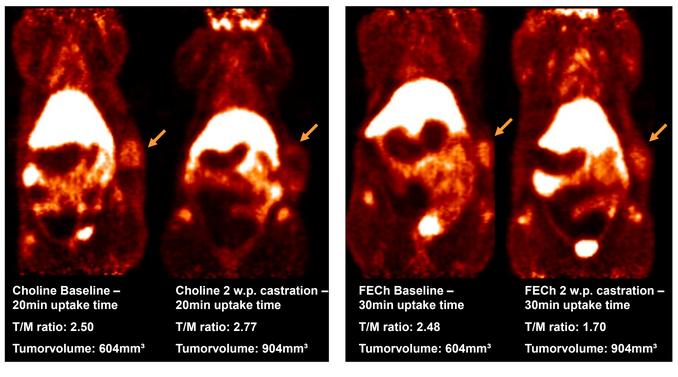
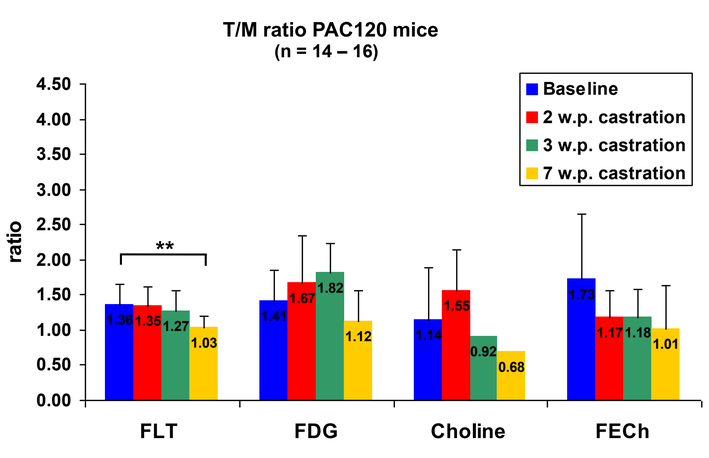


Figure 1: a) Tumor to muscle ratio for PAC120 rats, studied with different PET tracers. In our study the most effective tracer for delineation of subcutaneous prostate cancer is [^{18}F]FDG, followed by choline. b) PET images for two different PET tracers.

a)



b)

PET Images – PAC120 Mice

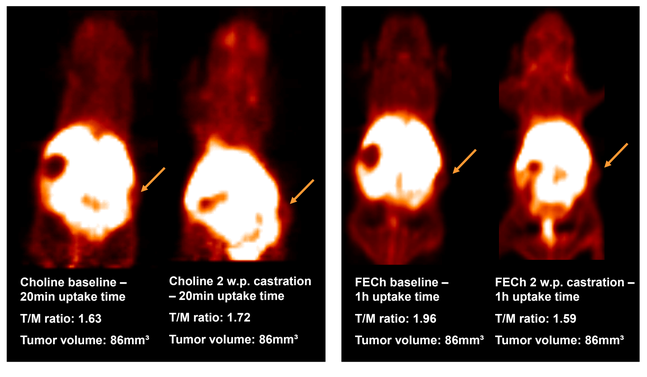
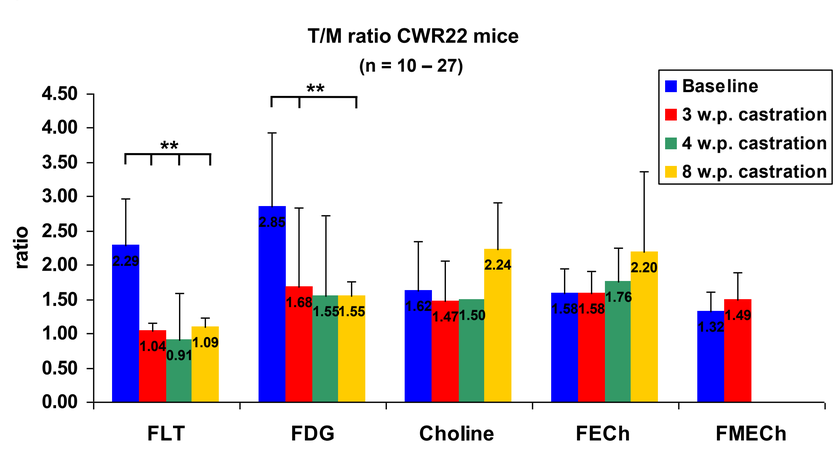


Figure 2: a) Tumor to muscle ratio for PAC120 mice, studied with different PET tracers. No tracer could be identified to be favorable. b) PET images for two different PET tracers.

a)



b)

PET Images – CWR22 Mice

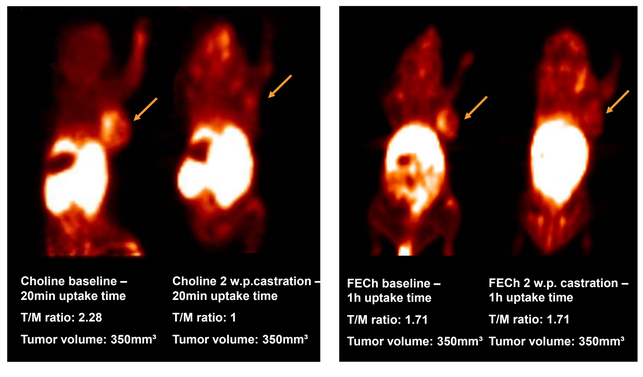


Figure 3: a) Tumor to muscle ratio for CWR22 mice, studied with different PET tracers. [^{18}F]FLT and [^{18}F]FDG are the tracers best suited for these studies. b) PET images for two different PET tracers.

DISCUSSION

PAC120 rats: The tracers that showed the highest T/M ratio are [^{18}F]FDG and [^{11}C]Choline (Figure 1). Before castration, the [^{18}F]FDG T/M ratio is nearly doubled in contrast to the [^{18}F]FDG T/M ratio 2 weeks post castration (*p.c.*). This change is not observed with the other tracers studied. Also the CSI-MR data (Figure 4) shows no difference in choline metabolite concentration before and *p.c.*. Tumor glucose metabolism seems to be strongly impacted by changes in androgen production. In contrast to this, membrane activity, as tracked with [^{11}C]Choline, is not observed to be hormone depended.

PAC120 mice: All tracers show approximately the same T/M ratios (Figure 2). Interestingly, in contrast to the PAC120 rats, there is no significant change in [^{18}F]FDG uptake before and 2 weeks *p.c.*. Therefore changes in androgen production seem not to influence [^{18}F]FDG T/M ratios in the PAC120 mice.

CWR22 mice: [^{18}F]FLT and [^{18}F]FDG tracers are the most suitable tracers for this tumor model. A strong change in [^{18}F]FLT uptake, that represents cell proliferation, as well as [^{18}F]FDG uptake is observed before and 3 weeks *p.c.*. In this tumor model, androgen production seems to influence cell proliferation as well as glucose metabolism.

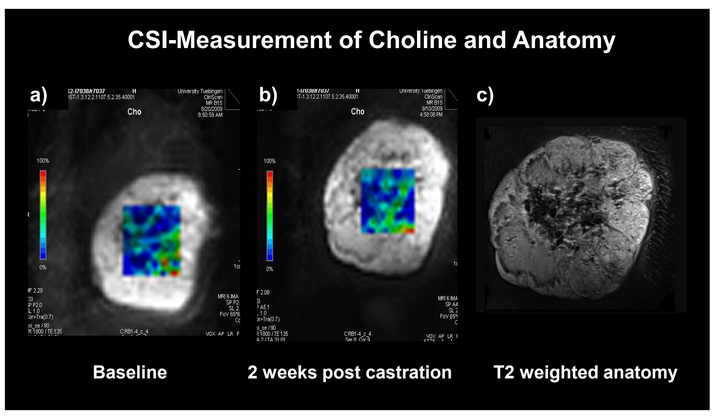


Figure 4: CSI images of a rat before a) and after b) castration. A change in the CSI-choline metabolite concentration is not observed between baseline and two weeks post castration. c) The tumor anatomy shown in the T2-weighted MR image. The heterogeneity of the tumor tissue is clearly depicted in these high resolution images.

CONCLUSIONS

Our studies on different tracer uptake in PAC120 rats and mice as well as CWR22 mice revealed the following:

- There is no species specific difference in PET tracer uptake of [^{11}C]Choline and [^{18}F]FECh observed in the studied animal models
- A species specific difference in [^{18}F]FDG tracer uptake was observed for PAC120 rats and mice. Glucose utilization was only suppressed in rats by androgen ablation through surgical castration.
- A tumor model specific difference in [^{18}F]FDG and [^{18}F]FLT tracer uptake was observed for PAC120 mice and CWR22 mice, despite the fact that both mice were from the same strain.

➔ Therefore a careful selection of tracers is needed, depending on the tumor model as well as the species. This should be considered in the interpretation and use of small animal oncological study data.

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