Cell Culture PET (CC-PET): an in vitro model for evaluation of ^{18}F-FDG and ^{18}F-fluoro-choline uptake in prostate cancer cells

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Background

Several PET tracers are under investigation for use in positron emission tomography (PET) for the imaging of prostate cancer[1,2]. However, it is difficult to compare PET tracers directly in clinical studies. In this study we established and evaluated an in vitro model for the study of PET tracers in tumor cells. Furthermore, we investigated the uptake of ^{18}F-FDG and ^{18}F-fluorocholine (FCH) in androgen-dependent (LNCaP) and androgen-independent (PC-3) prostate cancer cells.

Aims

- To establish and evaluate an in vitro model, *Cell-Culture PET (CC-PET)*
- To investigate the uptake of ^{18}F-FDG and ^{18}F-FCH in LNCaP and PC-3 prostate cancer cells.

Methods

Two prostate cancer cell lines, androgen-independent PC-3 and androgen-dependent LNCaP, and one breast cancer cell line MCF7 were obtained from ATTC and grown in RPMI medium with 10% FCS and penicillin/streptomycin. PC-3 and LNCaP cells were characterized by immunohistochemistry. For experiments cells were seeded in 6-wells plates or petri dishes. After 48 h the cells were incubated with ^{18}F- FDG or ^{18}F-FCH. Parallel cultures were used for cell counting. After washing 3 times with PBS the cells were placed in the gantry of a GE Discovery PET/CT scanner. Quantification of ^{18}F-FDG and ^{18}F-FCH uptake was determined using regions of interest (ROI) over each petri dish or well. The optimal protocol for acquisition and reconstruction of the data was investigated by scanning petri dishes with a known concentration of ^{18}F-FDG and reconstructing the resulting data with different combinations of scatter and attenuation corrections.

Results

- Androgen - and HER2 receptors were strongly expressed in PC-3 cells and to some extent in LNCaP cells (data not shown)
- For CC-PET experiments petri dishes were found to be superior to 6-wells plates because of overlap of radioactivity between the wells in the plates (data not shown)
- It is possible to scan up 100 petri dishes simultaneously
- A dose dependent ^{18}F-FDG and ^{18}F-choline uptake was demonstrated after 1 h in both PC-3 and LNCaP cells **(Fig 1A og 1B)**
- Both PC-3 and LNCaP cells showed a time dependent (0-200 min) ^{18}F-FDG uptake **(fig 2A)**
- MCF7 cells showed a similar time dependent (0-200 min) uptake of ^{18}F-FDG (data not shown)
- Addition of non-radiolabelled FDG resulted in significant dose-dependent inhibition of ^{18}F-FDG uptake (data not shown).
- Time dependent (0-200 min) uptake of 18F-FCH was also found in both PC-3 and LNCaP cells **(fig 2B)**
- Reconstruction with Attenuation Correction but without Scatter Correction (AC-SC) was superior to both Reconstruction with Attenution and Scatter Correction (AC+SC) and Reconstructin without Attenuation and Scatter Correction (NAC) **(fig 3)**.

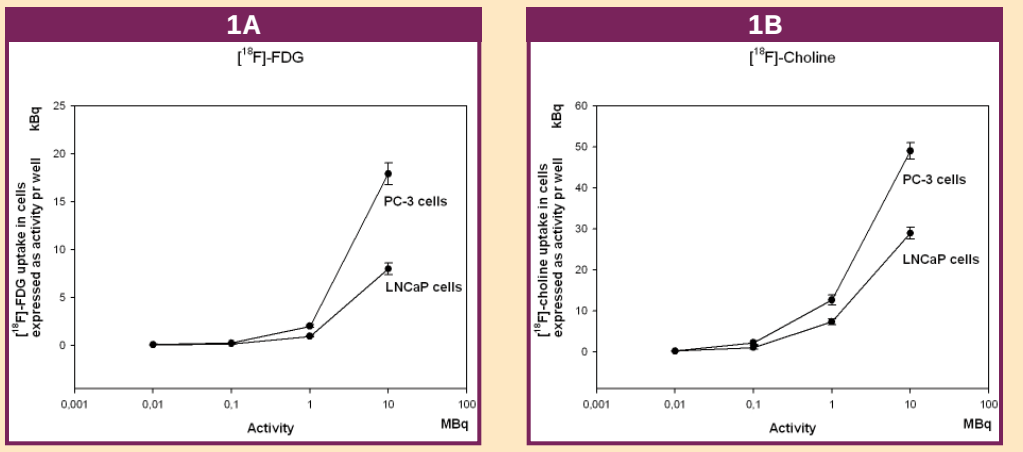

Fig 1 Uptake of ^{18}F-FDG (A) and ^{18}F-FCH (B) in LNCaP cells and PC-3 cells. The uptake was measured after 1 hour of incubation. Error bars indicate standard deviations (*n=3*).

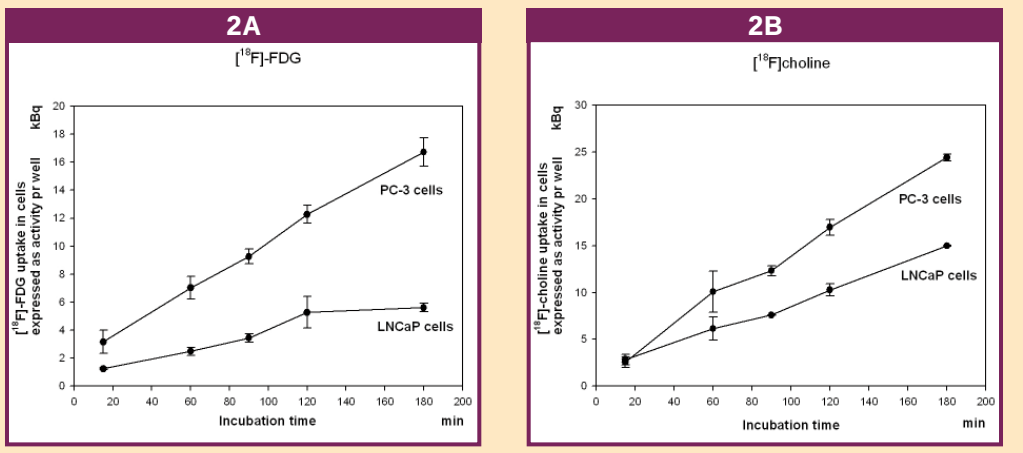

Fig 2 Uptake of (A) ^{18}F-FDG and (B) ^{18}F-FCH in LNCaP cells and PC-3 cells. The uptake was measured at different incubation time (10-200 min). Error bars indicate standard deviations *(n=3).*

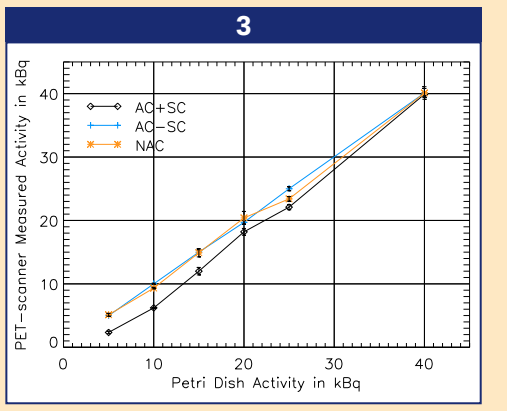

Fig. 3 Quantitation of petri dish radioactivity on the GE Discovery STE PET-scanner. Reconstruction with Attenution and Scatter Correction (AC+SC). Reconstruction with Attenuation Correction but without Scatter Correction (AC-SC). Reconstruction without Attenuation and Scatter Correction (NAC).

Conclusion

- In this study we established and optimized CC-PET as an in vitro model for evaluation of PET tracers in tumor cells.
- Time dependent ^{18}F-FDG and ^{18}F-FCH uptake was found in both androgen dependent (LNCaP) and androgen independent (PC-3) prostate cancer cells. The results indicate that *delayed PET/CT imaging* (>1 hour) is superior to early (10-15 min) imaging in prostate cancer patients.
- ^{18}F-FCH is superior to ^{18}F-FDG for PET imaging of both androgen-dependent and androgen-independent prostate cancer cells.
- Dose dependent ^{18}F-FDG and ^{18}F-choline uptake was found in both androgen-dependent and androgen independent prostate cancer cells.
- CC-PET is a very promising in vitro model for studying PET tracers in cancer cells.
- Several pitfalls may influence the results when using CC-PET as an in-vitro model.

- PC-3 cells demonstrated a significant higher uptake of both ^{18}F-FDG and ^{18}F-FCH as compared to LNCap cells **(fig 1 & 2)**
- Uptake of ^{18}F-FCH was significant higher in both PC-3 cells and LNCaP cells as compared to uptake of ^{18}F-FDG **(fig 1 & 2)**

References

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2. Bouchelouche K, Oehr P. Recent developments in urologic oncology: Positron emission Tomography molecular imaging. *Curr Opin Oncol* 2008 May;20(3):321-6.

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