Detection of prostate tumor metabolism using hyperpolarized [1-13C]-acetate

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Introduction

Prostate cancer is the most common cancer in the elderly men and the second leading cause of cancer death in men. It has been known for many years that the metabolic fate of acetate in tumors differs from that in normal tissue. Recently the role of acetate has been recognized as probe of tissue metabolism trough entry into catabolic or anabolic pathways as mediated by Acetyl-CoA. Prostate tumor as well as other cancers is characterized by altered energy metabolism and up-regulation of fatty acid synthesis. Here we report for the first time that hyperpolarized (HP) 13C-acetate can be used to investigate prostate tumor metabolism through measurement of the tracer uptake and the metabolic conversion to Acetyl-carnitine (ALCAR) (fig. 1). The conversion to ALCAR was considered low therefore it was necessary to develop a SNR optimal pulse sequence.

Methods

[1-13C]-acetate sodium salt was polarized in a 3.35T Hypersense DNP polarizer (Oxford Instruments, UK). Then the HP solution was injected into the rat tail vein inside the MR scanner (injected dose 5ml/kg; acetate concentration 130mM). All in vivo studies were performed on male Nude rats (n = 6) on a 3T GE HTX system equipped with a dual-tuned 1H-13C volume coil. All animals were injected subcutaneously in the neck region with PC-3 (human prostate cancer cells, 2x10⁶). All of them underwent to MRI session one for 13C spectra acquisition and the second one for 13C MRI and uptake quantification. A spectral-spatial RF-pulse (8 sublobes, duration 15.5ms, isodelay 7.0ms) was designed for exciting the whole tumor was excited. Spiral imaging (FOV 8cm; real resolution 5mm) after the described SPSP excitation was used to detect a cetate tumor uptake with FA=15°; TR=2s. For ALCAR imaging each image was acquired every 6s, with three spiral ideal encoding steps (Δ) could be detected by simple display of integrated [1-13C]-acetate images with corresponding Fast Spin Echo anatomical images (Fig. 3a). ALCAR SNR in the tumor region was too small for imaging purpose. In order to define the time evolution of acetate signal and detect the agent uptake one region of interest was drawn in the tumor and one in the blood vessel (Fig. 3b). Higher uptake in tumor region was clearly visible.

Results and discussion

The spectra time evolution of HP acetate (182.5 ppm) and its metabolic product ALCAR (174.5 ppm) recorded in the tumor slice of an exemplary dataset are shown in Fig. 2. In all animals increased [1-13C]-acetate signals in the tumor area could be detected by simple display of integrated [1-13C]-acetate images with corresponding Fast Spin Echo anatomical images (Fig. 3a). ALCAR SNR in the tumor region was too small for imaging purpose. In order to define the time evolution of acetate signal and detect the agent uptake one region of interest was drawn in the tumor and one in the blood vessel (Fig. 3b). Higher uptake in tumor region was clearly visible.

Conclusion

This study reveals that the visualization of prostate cancer with HP 13C-acetate is feasible in rats. Such baseline data could be important when following the modifications in metabolism and to monitor FAS expression in prostate cancer. Further investigations have to be done to evaluate the possibility to correlate cancer aggressiveness with quantitative analysis of prostate cancer metabolism and HP 13C-acetate tumor uptake.

References

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