Validation and diagnostic accuracy of quantitative measurement of tumor characteristics by MRI, PET and histology of mice tumor

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Abstract: Increased PET and MRI image intensities of mouse prostate tumors were correlated with immunostaining apoptosis indices. Hypothesis was: Increased signal intensities of intracellular sodium (μMRI) and flouro-2-deoxy-glucose utilization (μPET) in apoptosis rich regions in tumors were positively correlated.

Introduction: The apoptosis rich prostate tumors are sodium MRI visible and show high FDG glucose uptake due to high glycolysis (1). By MRI/PET tumor physiology and metabolism may be assayed.

Methods: Sequential scanned MRI (1 mm slice) and PET images over PC-3 tumor area were acquired. Biotransformation data was acquired at different 4 time points of 10, 20, 50, 80 minutes after injection of FDG. Further, image data were corrected for uniformity, sensitivity, and attenuation and images were reconstructed using Hanning filtered convolution back-projection with cut off value of 1.0. PET images were fused with transaxial MR images using MEDEX software. MRI and PET images and histology slices were digitally captured and correlated with immunostaing apoptosis indices in tumors. For validation of PET image intensities, biotransformation was optimized and correlated with malignancy by histology. Comparison was done using MRI/PET image intensity, histology and ss-DNA antibody immunostaining data from PC3 tumor imaging.

Results: SQ images of a large tumor are shown (see Figure 1). The effects of varying inversion time (TI) and echo time (TE) were indicative of the intracellular sodium signal dependence on these parameter values. The tumors were comparable on sodium images with phantom images(Figure 1). In tumors increase in IC-Na signal 30 % ($p<0.001$) increase and FDG uptake increased 15 %($p<0.001$) at optimal biotransformation rate of 70 % using 150 μCi FDG. Malignancy stages were identified (see Figures1,2). Histological features were analyzed for high tumor risk (high mitotic index and apoptotic index). These features in co-registered IC-Na, μPET hypermetabolic and monoclonal antibody (ss-DNA) sensitive regions were identified that showed (% difference <6%). Distinct Na peak was seen on NMR spectroscopy from the apoptosis rich tumor regions (see Figure 2).

Discussion: FDG-PET is tumor sensitive and tumor specific imaging method. Integrated sodium MRI and PET imaging approach may offer *in vivo* tumor physiological, functional and morphological tumor insights for rapid drug monitoring time-dependent method. These tumor imaging techniques were based on sodium(for MRI) and FDG uptake(for PET) images. The ss-DNA staining was suggestive of apoptosis.

Conclusion: Increased intracellular sodium and flouro-2-deoxy-glucose utilization in tumors may be associated with apoptosis and malignancy.

References:

1. Sharma,R., Esser, P.D., Van Heertum, R.L. (2002) Abstract #10-5039 at 93rd Annual Meet of AACR at San Francisco, CA on June, 2002.

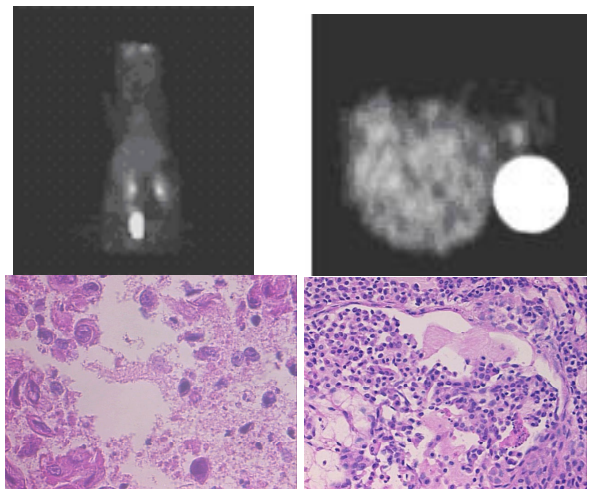

Figure1: Top: Mouse FDG-PET image(left); Na-MRI image(right). Bottom: Malignant stages (carcinoma on left and sarcoma on right) are shown on tumor H&E slice high power field from the center of tumor.

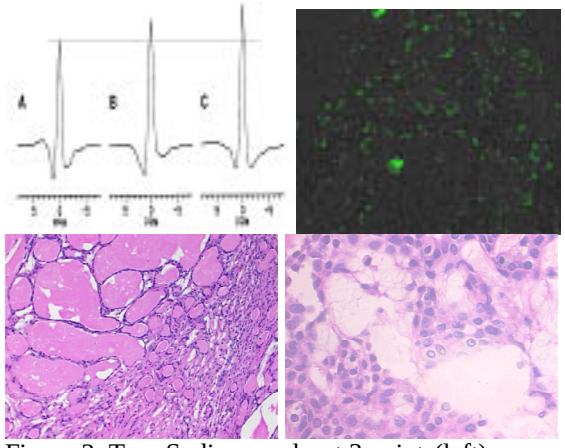

Figure 2: Top: Sodium peaks at 3 points(left); apoptosis staining(right). Bottom: Ductal carcinoma(left); Apoptosis rich cyst(right) on high power fields on H&E slices.