Correlation between choline concentration (H-MRS) and choline uptake (Cho-PET) and early effect of external radiation therapy on both parameters in an experimental tumor model

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Introduction:

MRI and PET are synergistic tools in cancer imaging giving complementary anatomical and functional/molecular information of which coregistration in a composite multimodal image improves detection and localization of abnormal tissue. High-grade polymitotic processes are known to exhibit both increased choline concentration at H-MRS [1] and increased uptake at PET using labelled choline [2]. H-MRS has been advocated to monitor early treatment efficacy in human malignancies [3]. The purpose of our study was to investigate in a rodent tumor model the correlation between choline concentration at H-MRS and ^{18}F labelled choline uptake at PET and to compare the potential of each modality to monitor early treatment effect of external radiation therapy.

Materials and methods:

Micro-fragments of a human rhabdomyosarcoma were subcutaneously implanted in both thighs of male WAG/RijHsd rats. After having grown 2 to 3 weeks, the tumors reached a sufficient size for efficient MR imaging (ranging from 1 to 3 cm in diameter). All animals underwent MR examination and ^{18}F-Cho-PET under general anesthesia, being embedded within a homemade and individually-tailored alginate mold (Henry Schein Demedis dental, Vilvoorde, Belgium) equipped with an external system of flexible Teflon micro catheters (VWR International, Leuven, Belgium) for inter-modality coregistration. MR studies were performed on a clinical 3 .0 T system (Achieva , Philips medical Systems, Best, The Netherlands) using a 4 channel wrist coil (In Vivo, Gainsville, Florida). High-resolution axial T2-weighted fast spin echo thin slices were acquired for coregistration with the PET images using the Pmod ® software (PMOD Technologies Ltd., Adliswil, Switzerland) (Fig1). Single voxel spectroscopy was performed using a water suppressed PRESS-sequence with TR/TE=2000/144 ms and a spectral resolution of 2 Hz .The volume of interest (VOI) was taken as the largest rectangular volume fully included into the tumor (as done in clinical practice). The whole spectrum was fitted and the concentration of choline was calculated relative to the reference water data. The quantitative analysis of the spectra was performed using jMRUI. Immediately after the completion of the MR procedure, the anesthetized rat was transferred within alginate block to a Micro PET dedicated to small animal experimentation (Mosaic, Philips, Best, The Netherlands). The vein of the tail was then catheterized and ~ 1 mCi (37 MBq) of ^{18}F-Choline was injected intravenously to image the animal 25 min later during 30 minutes. Prior to PET imaging, the external fiduciary tubes were filled with a solution of ^{18}F-Choline to enable accurate depiction on PET images for further co-registration. PET VOIs were contoured on co-registrated MR/PET images to include all tumor voxels into the analysis. Percentage of injected doses and Standardized Uptake Values (SUV) were calculated for each tumor. 13 rats (22 tumors) which constituted the initial 'static' cohort were included into the statistical analysis (Fig. 3). In a second 'dynamic' cohort of 3 rats (5 tumors), the animals received external radiation therapy (14 Gy in one fraction) the same day of and were re-imaged by both Cho-PET and MR using the same protocol as the pre-therapeutic examination and the same mold. Recruitment of 'dynamic' cohort is ongoing.

Results and discussion:

Perfect co-registration between PET and MR images were obtained in both cohorts assessing the value of an empirical method of embedding the animals in an alginate mould equipped with external fiducials (Fig. 1). High quality H-MRS spectra were obtained with obvious choline peaks of which relative concentration was measured (Fig.2) No significant correlation was observed between quantitative values of ^{18}F-Choline uptake at PET and choline concentration at H-MRS (Fig. 3; R=-0.042), using the Pearsons' linear correlation coefficient, thereby revealing absence of matching between the two parameters of concentration and affinity as previously suggested in few human studies [4]. All five tumors showed paradoxical and strong increase in ^{18}F-choline uptake 72 hours after radiation therapy. In turn, significant decrease was observed at H-MRS peak quantification (Fig. 4). The early and major increase in Choline uptake was interpreted to be due to reactive vasodilatation and inflammatory changes.

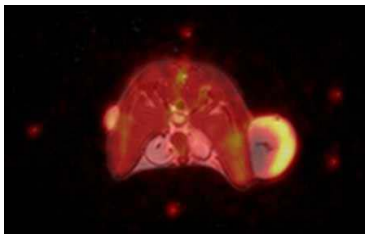

Figure 1

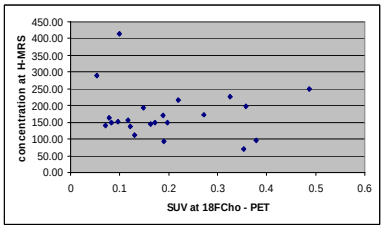

Figure 3

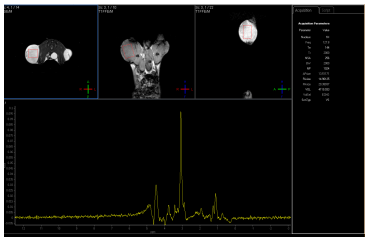

Figure 2

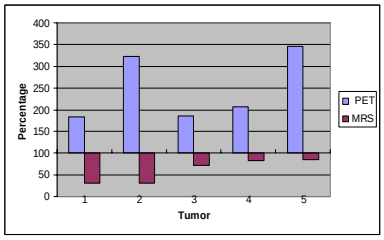

Figure 4

Figure 1: PET/MR co-registration showing perfect matching of both tumor contours and external fiducials.
Figure 2: SV-PRESS spectrum and VOI on localizer images for non irradiated tumor.
Figure 3: plotted graph with choline uptake at PET (X-axis) and choline concentration (Y-axis) at H-MRS showing absence of correlation between the two parameters.
Figure 4: Relative increase (%) in ^{18}F-Choline uptake (above baseline) and decrease (%) in MRS choline concentration (under baseline) for the five irradiated tumors of the 'dynamic' cohort.

Conclusion:

No significant correlation between choline concentration at H-MRS and choline uptake at PET was observed. Coherent early decrease of choline concentration after radiation therapy (72 hours) was observed. Paradoxical increase in choline uptake was observed at PET within the same period, precluding the use of the method to monitor early sensitivity of the tumor to radiation treatment.

References:

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