

Quantitative proton MR spectroscopy as a biomarker of tumor necrosis in the rabbit VX2 liver tumor

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Purpose: The aim of our study was to compare metabolic (quantification of tumor choline concentration) MR imaging findings to percent necrosis at pathology in rabbits bearing VX2 liver tumors.

Materials and Methods: Adult New Zealand White rabbits (n = 13) underwent implantation of a VX2 tumor in the left lobe of the liver. MR imaging and spectroscopic imaging were performed 2 - 3 weeks after the implantation to reach various degrees of necrosis. All animals were sacrificed immediately after MR imaging and their livers were explanted and submitted to pathology. 1H MRS was performed using clinical 1.5T MR systems (MAGNETOM Espree, Siemens Healthcare, Erlangen, Germany) and dedicated phased-array body coils. Localized MR spectroscopy was performed with a point-resolved spectroscopy spin-echo sequence (repetition time 1500 msec; echo time 30 msec; averages 128; spectral width 1000 Hz; and vector size of 1024 data points). The field homogeneity was optimized over the selected voxel of interest using an automated 3D-shim followed by optimization with manual shimming as needed. Spectra were processed using the Spectroscopy taskcard available on a Siemens workstation. The choline concentration was calculated with the internal water reference technique using Equation 1. All animals were euthanized after the completion of MR imaging and tumors analyzed using ImageJ software (NIH, Bethesda, MD) to estimate the percentage of necrosis. The mean ratio of necrotic/total tumor size was calculated for each liver tumor. A correlation was made between the choline concentration and the percentages of necrosis on pathology.

Results: On 1H MRS the spectroscopic voxel size ranged from 1.7-6 cm³, depending on the size of the tumor. A choline resonance was detected at 3.22 ppm in 13 of the 16 (81%) spectra. The calculated choline levels ranged from 0.21-8.96 mmol/kg. Mean percentage of necrosis at pathology was 22% (Range: 4-44). Choline concentration correlated well with percentage of necrosis on pathology and showed an R value of 0.78 (Figure 1). A typical example is shown in Figure 2.

Conclusion: Choline concentration showed a relatively high correlation with the percentage of tumor necrosis on pathology. Thus proton MR spectroscopy may be useful to assess tumor necrosis.

$$[Cho] = \frac{S_{Cho}}{S_{water}} \times \frac{n_{water}}{n_{Cho} \times MW_{water}} \times \frac{fT1_{water}}{fT1_{Cho}} \times \frac{fT2_{water}}{fT2_{Cho}}$$

Equation 1: [Cho] is concentration of choline in the tumor; S_{Cho} is the integral value of choline at 3.22 ppm; S_{water} is the integral value of the unsuppressed water signal; n_{Cho} and n_{water} are the numbers of 1H nuclei contributing to the choline and water resonances respectively; MW_{water} is the molecular weight of water; $fT1$, or $(1 - \exp(-TR/T1))$, is the T1 correction factor for partial saturation; $fT2$, or $(\exp(-TE/T2))$, is the correction factor for signal loss from T2 relaxation. Relaxation times T1 and T2 of choline and water in tumor voxels of two rabbits were measured. The resulting relaxation times are $T1_{cho}$ of (1293 ± 75) ms, $T1_{water}$ of (912 ± 200) ms, $T2_{cho}$ of (276 ± 30) ms and $T2_{water}$ of (86 ± 11) ms.

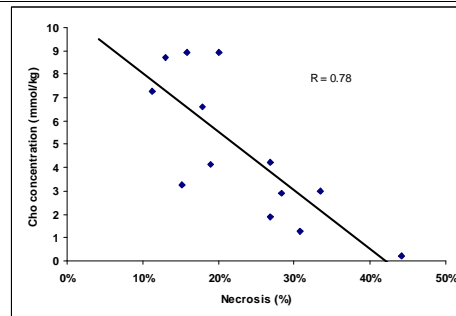


Figure 1: Correlation between choline concentration and % necrosis (n=13).

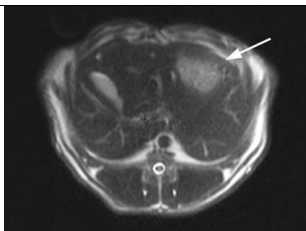


Figure 2a: A typical example of a rabbit VX2 tumor in the left lateral lobe of the liver two weeks after implantation.

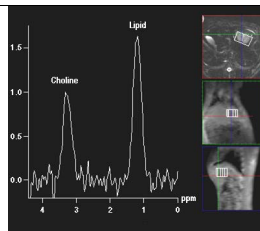


Figure 2b: Water suppressed spectrum. The Gaussian model fitting of the choline peak produces a measurement of $[Cho] = 8.71 \pm 2.18$ mmol/kg.

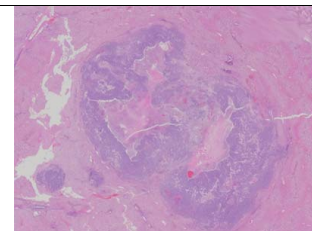


Figure 2c: The tumor after H&E staining.

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