IN VIVO SODIUM MRI RELAXOMETRY OF NORMAL AND PATHOLOGICAL MOUSE LIVER AT 4.7 T

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Objective:

^{23}Na has a 3/2 nuclear spin and an electric quadrupole moment. Relaxation mechanisms are dominated by the interaction of this quadrupole moment with the electrical field gradients generated by the environment. That is why, structural changes of the external side of the cellular membrane, likely to occur in pathological tissues or the changes in tissue density or necrosis found in tumors may be evidenced by sodium concentration modification as well as by different relaxation parameters. The purpose of this study was to detect the tumor presence in a liver tumor model in mice by changes in extracellular sodium concentration and/or significant changes in the spin-spin relaxation parameters, as compared to control.

Methods Experiments were performed on XVII nc/z female mice (Institut Curie breeding facility), on a Bruker Biospec system operating at 4.7 T. The RF coil was a home-made quadrature (sodium), linear (proton) birdcage coil, operating at 53/200 MHz. Hepatocellular Carcinoma (HCC) were chemically induced by three subcutaneous injection of a specific carcinogen for mouse liver (5,9-dimethyl-7H-dibenzo-[c,g]-carbazole). Multi-slice, multi-echo ^{1}H images were recorded for localization purpose, (respiratory trigger, FOV=6.8 cm, TE=7 ms, NE=16, matrix 256x256, slice thickness 1 mm). Single slice, multi-echo (16-32 echoes) images were recorded for sodium studies, (TR=350 ms, TE=6.04 ms, FOV=6.8 cm, matrix 64x64, slice thickness 6 mm) using 160 averages. In order to get proper decay curves, the images were post-processed. Firstly, the images were phase-corrected in order to avoid the Rician noise created by modulus reconstruction. The relaxation curves, measured in regions of interest (ROI) were forward linear projected in order to reduce the noise amplitude and to reach the base line, required for a proper multiexponential fitting. This was done by singular value decomposition method that needs no initial input for fitting [1]. Error estimations were performed by Monte Carlo simulations on 100 runs.

Results and Discussion:

Normal liver results. The normal liver proved to be highly homogeneous respective to the Na relaxation parameters. The relaxation curves allowed a monoexponential fitting, with time constants in the range 17-20 ms for all ROIs. These values are similar to those already reported for the human liver [2].

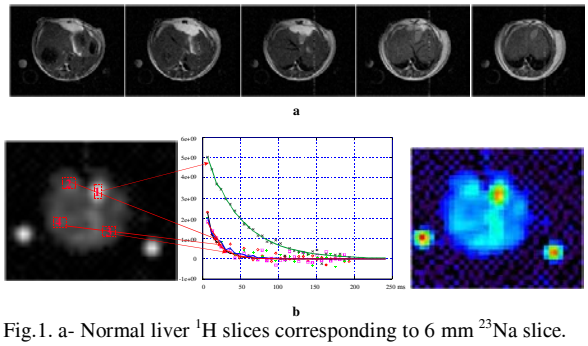

Fig.1. a- Normal liver ^{1}H slices corresponding to 6 mm ^{23}Na slice. b-sodium image and the relaxation curves of the ROIs shown on left.

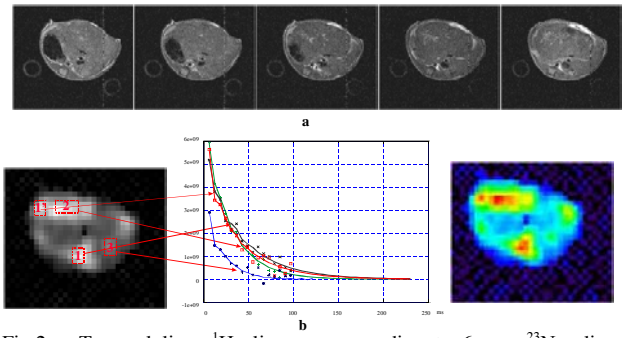

Fig.2. a-Tumoral liver ^{1}H slices corresponding to 6 mm ^{23}Na slice. b-sodium image and the relaxation curves of the ROIs shown on left.

The only distinguishable region was the gallbladder characterized by higher signal intensity as well as by a monoexponential decay with longer relaxation times (47 ms) as compared to liver (Fig.1, Table 1). Similar relaxation parameters were obtained for all investigated normal mice (n=3). *Tumoral liver results* (Fig.2., Table 2) The tumoral liver was characterized by an important heterogeneity in signal intensity, very high intensity areas appearing as compared with control. The relaxation study allowed to evidence three different regions. Region 1 was best fitted by a biexponential (with a short component T_{2fast}, in the range of 6 ms, poorly determined due to the experimental conditions (TE=6 ms, SNR=9) and a longer component T_{2slow}, in the range 37- 40 ms) characterizing the inferior vena cava, as revealed by ^{1}H images. It is interesting to notice that the inferior vena cava region was hardly noticeable on the normal liver sodium image, probably due to faster blood flow. The increase in signal intensity for inferior vena cava region was noticed for all investigated HCC livers. Similar relaxation parameters are obtained for the region labeled 1' that might represent a haemorragic area at the lobe periphery, frequently encountered in this tumor model. Region 2 corresponded to a tumoral area (hypersignal region on ^{1}H images). The apparent relaxation is monoexponential, with a corresponding relaxation time (27 ms), increased as compared to control. It may indicate a presence of necrosis with lower cellular packing, hence the increase in the T_2 value. ROI 3 was attributed to a normal tissue region, characterized by a monoexponential with a decay time constant of 18 ms, similar to the values obtained for normal mice.

Table 1. Relaxation results on normal liver

Tissue Type	T_2 (ms)
ROI 2	19 ± 3
ROI 3	17 ± 4.5
ROI 4	14 ± 4.
Gallbladder	47 ± 4

Table 2. Relaxation results on tumoral liver

Tissue Type	T_{2slow} (ms)	T_{2fast} (ms)
ROI 1 & 1'	40 ± 4	6 ± 5
ROI 2	27 ± 1.5	-
ROI 3	18 ± 3.5	-

Conclusions:

To our knowledge, this is the first ^{23}Na relaxometry study performed on mouse liver, revealing differences between normal and HCC bearing liver and moreover, possibly allowing to distinguish haemorragic areas from tumor regions. The use of a spin-echo sequence allowed to evidence the multiexponential behaviour especially for regions with higher SNR in tumoral liver. The main advantage of sodium MRI consists in its sensitivity to the environmental changes. Sodium ions spin-spin relaxation holds great potential to become an endogeneous marker for tumor diagnosis and possibly for therapy response .

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References: 1. Lupu M & Todor D, Linear Prediction and Singular Value Decomposition in NMR Signal Analysis, Elsevier, 1996, pp.164-190.
2. Steidle G, Graf H & Schick F, Sodium 3-D MRI of the human torso using a volume coil, Magn.Reson.Imag., 22, 2004, pp.171-180.