Cancer Imaging with Succinate Hyperpolarization

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Background: The Enhanced MR laboratory at HMRI is at the forefront of hyperpolarizing ^{13}C sodium succinate [1,2] and its derivatives like ethylsuccinate by PASADENA method of hyperpolarization. Succinate can be now be hyperpolarized at over 20% level of polarization routinely and reproducibly [3,4]. Succinate is biomedically interesting as it can potentially assess the *in vivo* activity of succinate dehydrogenase (SDH), the enzyme that was recently tagged as an oncogene due to its crucial role in cell energetics [5].

Purpose: The goal of research is to apply hyperpolarized succinate for imaging cancer in different tumor models in mice.

Methods: We utilized PASADENA to hyperpolarize 1-^{13}C-succinate-d2 at pH=10 in a home-built polarizer and the hyperpolarized solution is injected via the tail vein of a BALB/c mouse bearing a Colon 26 tumor (N=5). A home made ^{1}H/^{13}C dual resonance two turn loop coil and a ^{1}H/^{13}C dual resonance Litz volume coil (Doty Scientific, Inc., Columbia, SC) are utilized for ^{13}C hyperpolarized *in vivo* imaging and spectroscopy. Gradient echo and simple pulse and acquire sequences are used for hyperpolarized imaging and spectroscopy at Bruker Avance 4.7T animal scanner at HMRI.

Results: We have demonstrated that succinate is delivered to the tumor (Colon-26) of a mouse by tail vein injection (Fig. left). A ^{13}C image was acquired with a large flip angle (40°) every 3.5 seconds with polarization re-supplied by inflowing blood. The hyperpolarized succinate signal from the inflowing blood allowed for imaging up to 1 minute after injection. The 2-D ^{13}C image acquired was five 3.2 mm slices, 32 x 32 matrix, with an in-plane resolution of 1.9 mm. Proton images of the tumor verified that hyperpolarized succinate was localized primarily in the tumor space (Fig. center A). ^{13}C MR spectroscopy of the tumor localized by the coil reveal a broad peak at hyperpolarized succinate resonance and the presence of metabolites is not confirmed in this mouse model where the succinate oncogene is absent (Fig. center B). *In vivo* ^{13}C T_1 of succinate. Note that the first data point is excluded from T_1 simulation due to ongoing saturation of tumor by the succinate arriving to the tumor area. ^{13}C in vivo T_1*=43.7±0.3 s. (Fig. right)

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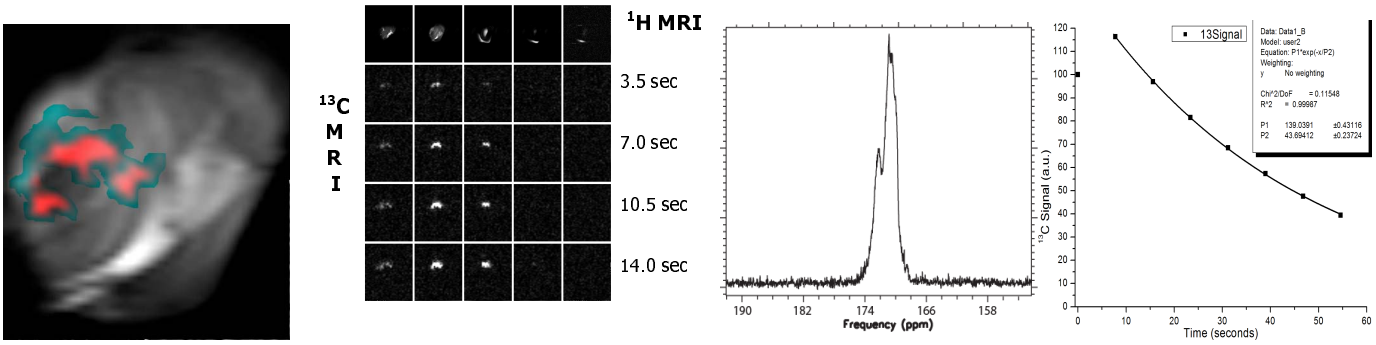

Left Center A Center B Right

Conclusions: Succinate is taken up by the Colon-26 mice model of cancer. No metabolites are detected in this model where the succinate oncogene is absent. *Ex vivo* solid state ^{13}C NMR spectra of the tumor reveal resonances from Glutamine and Citrate. Hyperpolarized succinate can be used to test permeability and uptake in a tumor as well as tissue heterogeneity. Experiments are underway with various other models of rodent cancer (e.g. 4T1 breast carcinoma). *In vivo* trials using hyperpolarized succinate derivatives like ethylsuccinate are also in progress in our laboratory.

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