Hepatocellular carcinoma: assessment of tumor oxygenation with BOLD MRI.

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Introduction

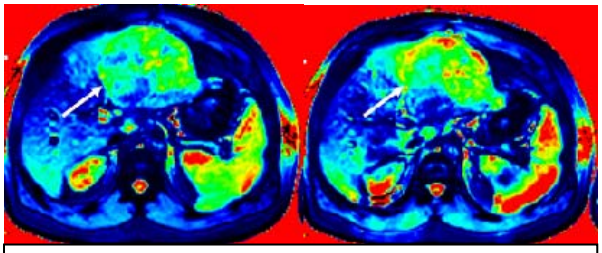
Tumor hypoxia is an important marker of angiogenesis and has been shown to correlate with tumor invasiveness, response to treatment and survival in several types of cancers (1). BOLD MRI is a noninvasive diagnostic method for assessing tumor hypoxia, by detecting signal changes secondary to changes in blood flow and oxygenation. Various animal studies have demonstrated significant increases in tumor T2* (decrease in R2*) when modifying O_2 concentration in animal models of hepatocellular carcinoma (HCC) (2-5). To date, there is no published data validating the ability of BOLD MRI to assess tumor hypoxia in human HCC. We are reporting our early experience using BOLD with oxygen challenge to quantify tumor hypoxia in human HCC.

Methods

After IRB approval, we prospectively performed BOLD MRI on 13 patients (9 males, 4 females, mean age 57 y) on a 1.5 T multichannel clinical system (Avanto, Siemens Medical Solutions) using axial and coronal T2* GRE sequence (TR 80, TE 1-40, slice thickness 1 cm, FOV 300-366*400-450, matrix 126-208*256, number of slices 4-6 in mid liver) before and after inhalation of 10 L/min. of pure oxygen via nasal cannula. 8 patients had cirrhosis and HCC, while 5 subjects (3 with cirrhosis, 2 volunteers) did not have evidence of HCC. Three of the patients with HCC were imaged prior to any treatment, 3 were imaged following transarterial chemoembolization (TACE), and 2 were imaged both prior to and following TACE. T2* maps were created using commercial software and ROIs were placed over HCCs, surrounding liver parenchyma and lumbar muscles to determine T2* (in msec.) and R2* (=1/T2*, in sec^{-1}) values before and after O2 administration. ΔR2* [=(R2* before O2– R2* after O2)/ R2* before O2 x 100%] was determined for untreated HCC (n=5) and compared to HCC post TACE (n=5), liver parenchyma (n=13) and muscle (used as reference, n=13).

Results (Table)

10 HCCs (mean size 4.9 cm, range 1.8-12.0 cm) were evaluated in 8 patients. There was a significant increase in T2* values in untreated HCCs (Fig.) with decreased R2*, with higher ΔR2* compared to HCC post TACE (p=0.01, see Table), liver parenchyma (p=0.002) and muscle (p=0.0012). There was no change in T2* values in treated HCC and muscle. We observed differences in ΔR2* values in 2 patients with HCC who were scanned before and after TACE (average ΔR2* before TACE 21.19, after TACE 2.06).



T2* maps before (left) and after (right) O2 administration demonstrate increased T2* values in a left lobe HCC (arrow, ΔR2* tumor 20%, ΔR2* liver 3.8%).

	Untreated HCC (n=5)	Treated HCC (n=5)	Liver (n=13)	Muscle (n=13)
R2* before O2	31.72±10.78	37.77±11.32	43.54±10.18	45.19±8.45
R2* after O2	25.63±8.46	38.07±11.78	42.11±10.25	45.45±7.83
ΔR2* (%)	19.15±6.71	-0.66±3.29	3.36±4.96	-0.94±4.96

Discussion

Tumor R2* has been shown to be a sensitive indicator of tissue oxygenation, correlating directly with deoxyhemoglobin concentration. Administration of oxygen increased T2* (decreased R2*), enhancing differences between treated and untreated HCCs. The decrease in R2* in tumors likely reflects a reduction in deoxyhemoglobin due either to increased blood perfusion and/or to increased oxygen consumption, this could be used as a biomarker of HCC hypoxia. In addition, BOLD could be used to predict and follow HCC post TACE as shown in our data on pre- post-TACE BOLD (n=2).

Conclusion

Untreated HCC demonstrates significantly higher oxygen uptake compared to HCC post TACE and liver parenchyma. These preliminary results demonstrate the potential utility of BOLD in quantifying tumor hypoxia in HCC.

References
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