

## Hepatobiliary Cancer

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### **Contrast-Enhanced Magnetic Resonance Imaging: A Reliable Method to Evaluate Tumor Progression/Regression in a Murine Model of Hepatocellular Cancer**

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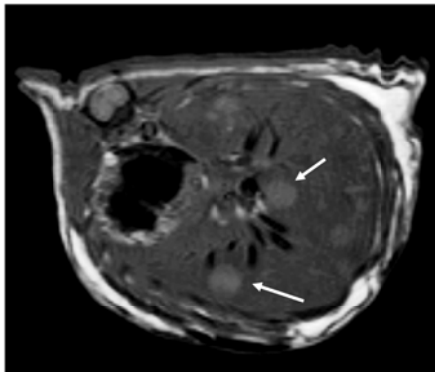
**Introduction:** Hepatocellular cancer (HCC) is a leading cause of cancer mortality worldwide. Its incidence is increasing in the United States as a result of hepatitis C. This tumor is refractory to chemotherapy, and radiation is not possible due to liver toxicity. Surgery is the only effective form of therapy; unfortunately, due to associated liver disease, most patients are not candidates for surgical resection. While liver transplantation is an effective therapy in some cases, donor organs are scarce. For these reasons, the overwhelming majority of patients with HCC succumb to their disease. Recent work has demonstrated that active specific immunotherapy is a promising approach to the treatment of HCC. Our lab has recently developed a spontaneous model of HCC, created by injecting tumorigenic hepatocytes (HCCT) into the spleens of normal, immunocompetent mice. These animals provide a realistic model of HCC, allowing the study of specific immunotherapies. We propose the use of contrast-enhanced magnetic resonance imaging (MRI) to study the progression/regression of HCC in a model of spontaneous HCC.

**Methods:** C57BL/6 mice underwent intrasplenic injection of  $0.5 \times 10^6$  HCCT. Gadolinium-enhanced MRI was performed using a 7 Tesla MRI on a cohort of normal C57BL/6 mice (control group) and a cohort of animals injected intrasplenically with

HCCT (experimental group). Eight weeks (5 mice), 12 weeks (1 mouse), and 16 weeks (2 mice) after injection, animals from the experimental group were imaged and compared with negative controls (3 mice). MRIs were acquired using a spin echo sequence with a TR/TE of 700 ms/10.5 ms, 1.0 mm section thickness and in-plane resolution of  $168 \mu\text{m} \times 168 \mu\text{m}$ . Prior to imaging, animals were anesthetized with isoflurane and a tail vein intravenous line was placed for contrast administration. Axial pre- and post-contrast images were obtained in 1 millimeter sections.

**Results:** One millimeter axial sections produced high quality images demonstrating normal liver anatomy in the control cohort. MRIs of the control animals demonstrated normal perfusion with no focal abnormalities. In the experimental group, pre-contrast images obtained at 8 weeks demonstrated focal hepatic nodules, which were easily distinguished from normal liver parenchyma (Figure 1). Post-contrast images demonstrated further enhancement of the tumor foci. At 12 and 16 weeks after injection, images demonstrated progressive enlargement of tumors that coalesced and replaced hepatic parenchyma.

**Conclusions:** MRI provides a powerful tool for the evaluation of hepatic tumor presence in our model of spontaneous HCC. Subsequently, MRI is a reliable method to follow the progression and/or regression of HCC in conjunction with the study of specific immunotherapy.



**Figure 1.** MRI liver image 8 weeks following splenic injection of cells, demonstrating multifocal lesions (arrows).