

## Chapter 16

### Liver Imaging and Biotechnology

#### **A1a. Develop standardized definitions, diagnostic criteria, and methodology for liver imaging.**

A workshop entitled “Measurement of Hepatic Vein Pressure Gradient: Role in Management of Portal Hypertension” was held in June 2006. One of the recommendations from this workshop was to standardize the procedure and methods of measuring the pressure gradient. The Society of Interventional Radiology has published standards for terminology and reporting of image-guided tumor ablation (Goldberg SN. *Radiology* 2005;235:728). (2006 10%; Total 10%)

#### **A1b. Better define the role, efficacy, and safety of image-guided local therapies for HCC, such as radiofrequency and thermal ablation.**

A prospective study of percutaneous radiofrequency ablation in patients with hepatocellular carcinoma (HCC) and cirrhosis has been initiated by the American College of Radiology Imaging Network (<http://www.acrin.org/RFAprotocol.html>). (2006 0%; Total 10%)

#### **A2a. Create a liver tissue bank with correlative imaging data to facilitate clinical research.**

Serum and tissue banks of patients with early HCC and liver disease controls are being established through the NCI-supported Early Detection Research Network (EDRN), which will enroll 190 early-stage HCC and 400 cirrhosis control samples of tissue, serum, and plasma. Radiological images are also included for the HCC cases. Pathological imaging correlations of small nodules in patients with cirrhosis have demonstrated that focal nodular hyperplasia occurs not infrequently in patients with cirrhosis and can be misdiagnosed as HCC based on CT or MR imaging (Libbrecht L. *Am J Gastroenterol* 2006;101:2341). (2006 10%; Total 20%)

#### **A2b. Develop improved techniques for established imaging methods for liver disease, such as optical, MRI, or PET/CT scanning.**

PET scanning is more accurate than MR, CT, or ultrasound in detecting small and unsuspected cholangiocarcinoma in patients with sclerosing cholangitis awaiting liver transplantation (Prytz H. *Hepatology* 2006;44:1572). Fluorocholine was superior to fluorodeoxyglucose as a tracer in PET scanning for detection of HCC (Talbot J-N. *Eur J Nucl Med Mol Imaging* 2006;33:1285). Diffusion-weighted MR imaging and measurement of choline levels by MR spectroscopy have been used to detect HCC and to assess responses to therapeutic embolization of HCC in humans (Deng J. *J Vasc Interv Radiol* 2006; 17:1195; Chen CY. *Radiology* 2006;239:448; Nasu K. *Radiology* 2006;239:122). (2006 10%; Total 30%)

#### **A3. Evaluate molecular imaging techniques in animal models of liver disease.**

Use of micro-bubble contrast agents was found to be helpful in visualizing small bile ducts in a pig model (Roberts JP. *Clin Transplant* 2006;20:740). Radio-labeled antibody to vascular endothelial growth factor (VEGF) has anti-tumor effects against human HCC in immunodeficient mice (Chen J. *Cancer Lett* 2006;231:169). Finally, an animal model using implantation of rhabdo-

- myosarcoma into liver provides a means of assessing the accuracy of MR techniques in detecting morphologic and functional characteristics of tumors (Chen F. *Radiology* 2006; 239:554). (2006 0%; Total 10%)
- B1a. Validate standardized definitions, diagnostic criteria, and methodology for liver imaging in prospectively studied patients with liver disease.** This goal will follow the development of definitions and diagnostic criteria. (2006 0%; Total 0%)
- B1b. Extend studies on validation to international populations.** This goal will follow development of definitions and diagnostic criteria. (2006 0%; Total 0%)
- B2. Develop bioinformatics such that computer-aided diagnostics are useful in evaluation of liver disease.** Many bioinformatics efforts were funded by the NIH in 2006 including the Roadmap Bioinformatics and Computational Biology initiatives. Evaluation of liver disease can benefit from these non-disease specific initiatives. (2006 0%; Total 10%)
- B3. Apply promising molecular imaging techniques to human liver diseases or processes using antibody, receptor ligand, metabolically active, or substrate-defining probes.** Molecular imaging techniques developed in animal models deserve evaluation in humans with liver disease. (2006 0%; Total 0%)
- C1a. Apply definitions, criteria, and methodology for liver imaging as surrogate endpoints to therapy of liver diseases.** A conference organized by the American Association for the Study of Liver Diseases (AASLD) on “Endpoints in Clinical Trials for Hepatocellular Carcinoma” was held on December 7-8, 2006, which focused on standardization of design and endpoints, including use of imaging in trials of therapy for HCC. (2006 0%; Total 0%)
- C1b. Develop practical means of assessing liver (fat content, fibrosis, inflammation, functionality) for population-based studies.** Studies of double contrast MR imaging suggests that it is reasonably reliable in separating advanced from early or mild fibrosis (Aguirre DA. *Radiology* 2006; 239:425). More promising is ultrasound elastography as a means of assessing liver stiffness, which appears to be accurate in assessing degree of fibrosis, the presence of portal hypertension and esophageal varices (Carrion JA. *Liver Transpl* 2006;12: 1791; Kazemi F. *J Hepatol* 2006;45:230). Preliminary studies indicate that MR elastography, by reflecting whole-liver stiffness, may be more accurate than ultrasound (Rouvière O. *Radiology* 2006; 240:440). Elastography may be less accurate in assessing fibrosis in fatty liver disease. Multiple studies of MR assessment of hepatic fat are underway, and are attempting to correlate MR measurement of percent hepatic fat with clinical and histological features of nonalcoholic fatty liver disease. Doppler ultrasound evaluation of hepatic vein waveforms also shows promise as a noninvasive means of assessing degree of portal hypertension (Baik SK. *Radiology* 2006;240:574). (2006 20%; Total 20%)
- C2. Develop imaging techniques that are fully integrated into therapy of liver disease.** Real-time, three-dimensional ultrasound has been applied to robotic laparoscopic abdominal surgery in animals in preparation for studies in humans

(Pua EC. IEEE Trans Ultrason Ferroelectr Freq Control 2006;53:1999). (2006 0%; Total 10%)

**C3. Develop molecular imaging methods that provide individualized information for monitoring and therapy of liver disease, including pharmacokinetics and pharmacodynamics of targeted therapies.** Accurate molecular imaging methods are needed before they can be applied to individualized monitoring and therapy of liver disease. (2006 0%; Total 0%)

Figure 18. Estimated Progress on Liver Imaging and Biotechnology Research Goals, 2006 (Year 2) [Cross-hatching indicates recent year's progress.]

