CIMIT MEETING SUMMARY 7/26/2005

In the final session of the CIMIT educational lectures on Molecular Imaging, Mary Dickinson, PhD, Baylor College of Medicine described “Dynamic Imaging of Fluid Forces and Heart Motions in Developing Embryos”. The pathogenesis of many congenital cardiovascular diseases involves abnormal flow within the embryonic vasculature, resulting either from heart malformations or from defects in the vasculature itself. Extensive genetic and genomic analysis in the mouse and in zebrafish has led to the identification of an array of mutations that result in cardiovascular defects during embryogenesis. Rapid confocal microscopy has been combined with the development of quantitative tools to analyze fluid and structural motions in order to better understand how circulation is initiated during embryogenesis and how endothelial cells respond to varying flows. The blood flow is too rapid to be resolved by video rate (20 fps) microscopy and a dedicated line-scanning confocal microscope operating at up to 120 fps is being used to image the flow. These tools have been used to study events during vascular remodeling in order to determine how fluid forces influence vasculogenesis and vessel maturation. Shear stress levels in the developing yolk sac are found to be within levels known to induce the expression of developmentally relevant genes. The group is currently studying how individual endothelial cells respond to shear stress in vivo using fluorescent protein markers and multispectral imaging. In a related series of experiments, Dr. Dickinson's lab has been characterizing the contractions of the embryonic heart to determine how the cardiac cycle influences flow. Together these experiments are providing vital information about the initiation of embryonic circulation and offer sensitive methods for understanding mutant phenotypes. The zebrafish embryo is being studied using GFP to image heart valve function and wall deformities; 3-D movies of these fish studies were shown.

Lee Josephson, PhD, MGH, described “Magneto/fluorescent Nanoparticles For Tumor Margin Delineation**”.** Imaging of cancer has multiple uses, including determination of margins, staging, detection of metastases and monitoring response to treatment. The use of imaging techniques may improve Breast Conserving Treatment (BCT), a technique of margin-guided sequential resections used as an alternative to mastectomy. Currently 25% of BCT procedures initially show some margin involvement and require a second resection. Imaging may allow more accurate margin determination, making only a single resection necessary. However, even good marking techniques may still be inadequate for tumors that lack definability and tumor motion after MRI may make the intraoperative location of a margin difficult. The ability to determine tumor margins is crucial for tumor resection in the brain, performed with the twin goals of complete tumor removal and maximal preservation of normal tissue. The use of nanoparticles having both a metal iron oxide component and a fluorescent moiety, such a Cy5.5, can allow tumor location preoperatively by MRI, followed by intraoperative fluorescence imaging. Experiments comparing the accuracy of brain margin delineation in rodents by postoperative histology, as well by fluorescence, were described. A computer algorithm was used to determine the margins objectively, allowing comparison of the techniques for various tumors. The issue of potential approval of marker systems as drugs was discussed; five “drugable” polymer-coated iron oxide systems are currently available, with four already in clinical trials. Currently, quantum dot markers, which can contain cadmium, a carcinogen, in a compound semiconductor are considered by some as not ”drugable”.