SMRI '93 Eleventh Annual Meeting

Plenary Symposia

Sunday Morning • Imperial Ballroom
Plenary Symposia 001–004

BASICS OF CONTRAST

MODERATOR: GK Sze, MD
8:00 AM–10:00 AM

PS 001 • 8:00 AM

Tissue Contrast in MR Imaging: Basic Principles and Abdominal Applications

DG Mitchell, MD
Department of Radiology, Thomas Jefferson University Hospital, Philadelphia, PA

The greatest strength of MR imaging lies in its versatile depiction of tissue contrast. The variety of abdominal tissues and pathologic processes provide an especially challenging model for development of a comprehensive examination to potentially replace a battery of other tests. T1, T2, chemical shift, and flow contrast can be achieved with spin-echo, inversion-recovery, gradient-echo, RARE, and echo-planar techniques. The liver and pancreas have shorter T1 than most other nonfatty tissues, possibly due to high intracellular surface area. Damaged parenchyma and most tumors have longer T1, rendering them conspicuous on T1-weighted MR images, while well-differentiated hepatocellular tumors may have similar or even shorter T1. T2-weighted images depict most inflammatory or neoplastic abnormalities as hyperintense. Iron overload in the liver, pancreas, and spleen can be identified, excluded, and/or quantified on T2- and T2*-weighted images, allowing diagnosis and grading of and distinction between iron-overload states, potentially obviating biopsy. The chemical shift between triglyceride and water allows the accurate identification or exclusion of lipid by fat/water opposed-phase or signal suppression techniques. Suppression of lipid signal also reduces lipid-induced image degradation and increases the conspicuity of tissues enhanced by paramagnetic contrast agents. Flow can be detected and measured by physical displacement of protons or by phase changes relative to static tissue. MR angiographic techniques can help assess suspected vascular pathology, including aortic disease or stenosis/occlusion of many abdominal arteries and veins. Comprehensive MR imaging can help diagnose or exclude a greater range of diseases than any other modality.

PS 002 • 8:30 AM

Basics of MR Contrast Agents

RC Brasch, MD
Department of Radiology, University of California, San Francisco, CA

The purpose of this presentation is to familiarize and update the practicing diagnostician on MR contrast media, including modes of action, current indications, safety, dose considerations, and new applications. Similarities and potential differences in available or "soon-to-be-released" gadolinium chelate formulations will be discussed. Current indications for using intravenously infused paramagnetic contrast media for central nervous system (CNS) diagnosis include leptomeningeal disease, metastases, distinction of residual tumor from postoperative changes, pituitary microadenomas, acoustic neuromas, and epidural fibrosis versus herniated disk. Relatively newer applications of small-molecular gadolinium complexes, outside the CNS, include characterization of breast masses, evaluation of the female pelvis, and musculoskeletal enhancement. Differences between the modes of action of paramagnetic and magnetic susceptibility agents will be detailed. The strategies for the design of newer agents that have unique distribution and enhancement patterns will be explained. These include oral agents for the gastrointestinal tract, macromolecular agents for perfusion and capillary integrity imaging, and particulates for imaging the reticuloendothelial system (liver, spleen, and lymph nodes). The potential utility for liver imaging with small-molecule chelates with specific uptake by the hepatocyte can be shown from preclinical studies. The potential of a new generation of smaller superparamagnetic nanoparticles (MIONs) that can be linked to a variety of bioactive carriers will also be demonstrated.

PS 003 • 9:00 AM

Central Nervous System Applications of Contrast Agents

MN Brant-Zawadzki, MD
Department of Radiology, Hoag Memorial Hospital, Newport Beach, CA

Approximately 35% of all clinical MR studies of the central nervous system (CNS) use contrast agents. The first of the paramagnetic agents approved for use was gadopentetate dimeglumine. Millions of doses of this agent have been used worldwide. Recently, 2 nonionic agents have been clinically tested and approved for human use (gadodiamide, gadoteridol). These agents have a theoretically improved safety margin, particularly with higher doses, given the lower osmolar load they present. Preliminary experience suggests that a double or triple dose (up to 0.3 mmol/kg) of these agents can improve sensitivity in the detection of metastatic disease (and potentially other lesions). The most widespread use of paramagnetic contrast agents in MR imaging of the CNS involves screening and following up patients with metastatic disease involving the brain or the spinal canal. Leptomeningeal disease can easily be missed without the use of intravenous contrast agents. Contrast agents can be used to differentiate the effects of therapy from new, recurrent, or residual disease. In the spine, the most common use for these agents is the differentiation of postsurgical epidural granulation tissue from residual or recurrent disk herniation. New uses of contrast agents exploit the magnetic susceptibility effects of these agents, particularly on their first pass through the intracranial circulation, for perfusion imaging of the brain. Also, these agents can enhance MR angiogra-

phy, particularly in the venous circulation. Finally, 3D image rendition of MR imaging studies benefits from the use of these agents, making segmentation of lesions easier. This plenary session will serve to summarize the clinical utility of paramagnetic contrast agents in the CNS and focus on the newer developments in this arena.

PS 004 • 9:30 AM

Contrast Agents in the Spine

MT Modic, MD
Cleveland Clinic Foundation, Cleveland, OH

Contrast-enhanced MR imaging has emerged as an important adjunct technique for the diagnosis of both intrinsic and extrinsic lesions of the spine. The common pathway for enhancement in both normal and abnormal structures relates to a prominent vasculature, a permeable capillary endothelium, and a capacious extravascular space. In healthy subjects, enhancement can be identified in the epidural venous plexus, basivertebral veins, and both cartilage and ossification centers in children. Enhancement within the vertebral body in an adult, however, is usually abnormal. Data to date would suggest that contrast-enhanced MR imaging is becoming routine in patients with suspected intramedullary disease, neoplasms, infection, vascular abnormalities, and in the postoperative lumbar spine. Its use in the nonoperated spine for degenerative disease, while interesting, is not yet established. This presentation will summarize the known limitations and potential benefits of the use of contrast agents in the spine.

Sunday Afternoon • Imperial Ballroom
Plenary Symposia 005–007

FUNCTIONAL AND HEPATOBILIARY IMAGING

MODERATOR: D Le Bihan, MD, PhD
1:30 PM–3:00 PM

PS 005 • 1:30 PM

Hepatobiliary Contrast Media

DD Stark, MD
University of Massachusetts Medical Center, Worcester, MA

Intensive efforts to improve the diagnostic utility of body MR imaging have resulted in a variety of specialized methods for pharmaceutical manipulation of contrast and tissue signal-to-noise ratios. Paramagnetic ions such as gadolinium (III), iron (III), and manganese (II) have unpaired outer-shell electrons that align (magnetic susceptibility) with an externally applied magnetic field (B_0). Fluctuations in the orientation of these electrons relative to adjacent water protons produce electron-proton dipole-dipole interactions that enhance (increase) the rate of longitudinal (T1) relaxation. Crystalline iron oxides are related to the particles that serve as recording materials on magnetic tapes. Ferro- or ferrimagnetic crystal structures pool the unpaired electrons of constituent atoms and therefore have a net magnetic susceptibility that is approximately a hundredfold larger than the sum of individual paramagnetic atoms. Transverse relaxation (T2) is enhanced to a greater degree than possible with paramagnetic materials. Paramagnetic complexes and composite particles have been designed to target specific cellular receptors or transport proteins located on the cell surface. Examples of such cell-specific targeting mechanisms include the hepatocyte anionic receptor targeted by Gd-BOPTA, the hepatic-binding protein targeted by galactose-linked macromolecules, and phagocytosis of opsonized particles by reticuloendothelial cells (hepatic Kupffer cells). While much of this work is in experimental stages, Mn-DPDP, targeted to hepatocytes and excreted in bile, was the first paramagnetic hepatobiliary MR agent to begin clinical trials. Superparamagnetic iron oxide is undergoing clinical trials in several countries. Both classes of contrast agents have shown enhanced detection of liver cancer in humans.

PS 006 • 2:00 PM

Functional MR Imaging of the Brain

BR Rosen, MD, PhD
NMR Center, Massachusetts General Hospital, Charlestown, MA

Fundamental aspects of brain function can be investigated by using the well-established interrelationship between cerebral activity, metabolism, and regional hemodynamics. Several techniques have been proposed to measure changes in regional hemodynamics with MR imaging. Of these, magnetic susceptibility contrast is one of the most powerful means of affecting tissue signal intensity. Dynamic paramagnetic contrast techniques, based on exogenous or endogenous agents, have shown considerable promise in providing the ability to generate maps of hemodynamic parameters. Exogenously administered contrast agents, after intravenous injection, produce significant signal changes during first-pass cerebral transit. Because cerebral transit times are on the order of seconds, a rapid imaging technique is needed to resolve the passage of an intravascular agent through the capillary bed. Several groups have employed high-speed echo-planar imaging (EPI) methods to evaluate the time course and regional distribution of injected contrast agents. For endogenous (deoxyhemoglobin) contrast agents, the intrinsic hemodynamic response time to changes in brain activation state is under 2 seconds. The use of high-speed techniques is again required to provide 3D coverage of the brain with adequate temporal resolution. Noninvasive measurement of cerebral blood volume and flow and blood oxygenation has been shown to have significant impact on the diagnosis and management of patients with ischemia, neurodegenerative disorders, and cerebral neoplasms and will play a fundamental role in improving our understanding of normal brain function. With ischemic disease, functional MR imaging data offer the potential to both detect hypoperfusion well before conventional MR studies and to quantify the degree of hypoperfusion within the central lesion and the surrounding ischemic penumbra. The unique ability of MR imaging to show tissue microvasculature may allow MR imaging to directly show the phenotypic expression of tumor angiogenic growth factor genotypes. Microvascular insult may also lie at the heart of neurodegenerative disorders such as Alzheimer disease. Direct imaging of cortical activation will have a direct effect on cognitive and behavioral neuroscience and also opens new clinical possibilities for presurgical planning, improved specificity in evaluating dementias, and development of quantitative tools for studying neuropsychiatric disorders at a functional level.

PS 007 • 2:30 PM

Diffusion

ME Moseley, PhD
Department of Radiology, University of California, San Francisco, CA

Diffusion-weighted MR imaging (DWI) has had a dramatic effect in neurophysiology through the mapping of information relating to the molecular environments of cerebral water. Measurements of the apparent diffusion coefficient (ADC) of water are determined by normal as well as pathologic translations of water populations along specific anatomic planes averaged over distances smaller than or

larger than cell sizes, depending on the operator-selected observation parameters. Within the last 4 years, DWI has provided unique tissue contrast in differentiating lesions from normal tissues, in determining the spatial orientation of white matter tracts, and in the creation of "MR neurograms" for the rapid and noninvasive determination of the degree, severity, and status of stroke-induced brain damage in a variety of experimental models and clinical studies and in the observation of status epilepticus. It is becoming clear that decreases in the measured ADC observed in pathologic tissues follow similar time and severity scales with correlated histopathology, potentially linking changes in the physical environment of water to the loss of ion homeostasis. Sudden increases in ADC measured in these tissues appear to be related to a loss of cellular integrity or necrosis. It is anticipated that quantitation of the changes in the biophysical environments of water will lead to a better understanding of the mechanisms involved in pathologic brain damage. As high-speed MR methodologies mature, DWI will find further applications in noncerebral tissues such as muscle, kidney, the eye, and tumors.

Sunday Afternoon • Imperial Ballroom
Plenary Symposia 008–010

ENDOGENOUS CONTRAST MECHANISMS

MODERATOR: RM Henkelman, PhD
3:30 PM–5:00 PM

PS 008 • 3:30 PM

Magnetization Transfer Contrast in MR Imaging

RS Balaban, PhD
National Institutes of Health, Bethesda, MD

Magnetization transfer contrast (MTC) is the result of selectively observing the dipolar interaction of bulk water protons (H_f) with the protons contained in macromolecules (H_r) of a tissue. The extent of the dipolar interaction of H_f and H_r has been shown to be dependent on the molecular dynamics and surface chemistry of the macromolecules contributing to the selectivity of MTC. MTC is generated by combining saturation transfer techniques with standard MR imaging procedures. Generally, MTC is produced by selectively saturating H_r with RF energy off resonance from H_f. The specific practical and theoretical aspects of saturation transfer between H_r and H_f is an area of current debate. Of major importance is the specificity and power deposition of the irradiation scheme used to saturate H_r to generate MTC. By the appropriate choice of frequency and power for H_r irradiation, the power deposition for generating MTC can be reduced by factors of 10. In addition, the specific lineshapes of H_r and H_f is important in the interpretation of the magnetization transfer results. H_r has been shown to have a complex lineshape composed of both Gaussian and Lorentzian characteristics that can change with molecular dynamics, providing unique information on tissue structure. In the last 3 years, MTC has been applied in clinical MR imaging with useful applications in the study of the knee, eye, brain, breast, and heart. The application of MTC to accentuate MR angiography and contrast agent studies has also been demonstrated. Thus, MTC is quickly becoming another tool in maximizing the quality and diagnostic potential of MR imaging.

The U. S. government holds a patent on the MTC approach discussed in this presentation.

PS 009 • 4:00 PM

Calcium Contrast Mechanisms

W Kucharczyk, MD, RM Henkelman, PhD
Department of Radiology, University of Toronto, Toronto, Ontario, Canada

Tissue calcification occurs in many diseases. The ability of an imaging modality to ascertain the presence of calcification may enable detection of lesions that are otherwise occult or indicate the type of disease process that is present. It follows therefore that the ability to detect calcification is diagnostically important. However, in contradistinction to the well-characterized effect of calcification on x-ray attenuation, the effect of calcium on MR signal intensity is not as well understood. The purpose of this presentation is to review the mechanisms through which calcium affects MR signal intensity and explain how image contrast is dependent on operator-controlled pulse sequence parameters. Finally, the detectability of calcification with CT and various MR imaging methods will be compared. This will be done through a review of the literature as well as presentation of original work. A series of 2% agarose gel phantoms were made containing different calcium salts at various concentrations. Gradient-echo (GRE) and SE MR imaging were performed while systematically altering TR, TE, and flip angle, with and without the use of spoilers. Relaxation times were determined from the appropriate MR images. The surface area of the calcium salts was determined by an analytic method known as BET analysis, wherein a layer of inert gas is adsorbed on the crystal surface and subsequently quantitated. CT attenuation was independently measured for each type of calcium sample. T1 and T2* relaxivity were found to be directly linearly related to the BET surface area. The image contrast that occurred depended on whether the pulse sequence highlighted the T1 or T2* shortening effect. T1-weighted SE sequences showed high surface area samples as hyperintense, whereas T2 SE and T2*-weighted GRE sequences demonstrated hypointensity. The hypointensity could be emphasized by using long TE and flip angles close to the Ernst angle. Visually apparent high signal intensity on T1-weighted images occurred at calcium concentrations between 5 and 30 g% by weight; this was always apparent on CT scans as hyperattenuation, as were calcium concentrations below 5 g%. T2*-weighted imaging showed visually apparent hypointensities at calcium concentrations well below 5 g% but not as sensitively as CT. T1 and T2* shortening occurs with tissue calcification. This may result in hyperintensity on T1-weighted SE images or hypointensity on T2- and T2*-weighted images. The T1 shortening is due to relaxation enhancement of bulk water at the calcium salt surface. T2* shortening can be partially explained by the same surface effect, but a more important mechanism is susceptibility-induced signal loss. The hypointensity that T2* shortening creates can be best accentuated on GRE sequences with long TE. T2*-weighted images depict calcium more sensitively than do T1-weighted images, but neither is as sensitive as CT.

PS 010 • 4:30 PM

Susceptibility Contrast and Brain Iron

EK Fram, MD
Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, Phoenix, AZ

The effects of iron and susceptibility will be discussed. Pulse sequences will be compared, including gradient-echo, SE, and fast SE sequences. Gradient-echo pulse sequences provide high sensitivity for detecting susceptibility gradients generated by iron because, unlike SE imaging techniques, they fail to correct for field inhomogeneities. The deposition of nonheme brain iron will be