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MAGNETIC RESONANCE IMAGING IN MEDICINE

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Magnetic resonance imaging has evolved as an important imaging modality to the last two decades. In this review, we describe the application of MRI in the field of medicine.

Key Words : MRI; Medicine; Brain; Diffusion Imaging; MR Spectroscopy; MR Angiography; Functional Imaging

1 Introduction

In the seventeenth century people dreamt about a machine to get rid of evil spirits and obsessions that were thought to be the main source of misfortune and diseases. They dreamt of a machine that could display images from the inner world of men that could be easily identified and named. Somehow these are the roots of Magnetic Resonance Imaging. Of course, we now view diseases from a different point of view but our objectives remain the same, namely to make diseases visible and to try to characterize them in order to cure them.

About 300 years later the clinical introduction of MRI has great potential for making this dream comes true. The name NMR is succinctly descriptive - ***N***uclear because the fundamental phenomenon arises from the spin of those atomic nuclei that have it (all those containing uneven numbers of protons &/or neutrons); ***M***agnetic because the spin and positive charge make the nucleus behave like a tiny magnet which will interact with externally applied magnetic fields and ***R***esonance because the use of the technique depends on first exciting and then detecting resonant frequencies.

The very word "nuclear" sends shudders down the spines of many patients even though the energy per quantum of the radiofrequency employed is some 10^{10} less than that of ionizing radiations. Nevertheless for clinical purposes the "N" has been dropped from the name and "MR" is used instead.

Damadian's article in 1971 about differences in T1 relaxation times between healthy and pathological tissues was a milestone in tissue characterization. His results initiated intensive research into MR imaging and tissue parameters. Since the initial clinical introduction in early 80's, the indications and applications of MRI in the field of medicine have shown exponential growth and refinement.

In the first decade of its existence, MR imaging rapidly became the predominant technique for imaging the nervous system, supplanting to a large extent other methods such as computed tomography, myelography, and diagnostic angiography. The extraordinary technical progress that has been made over the past decade has significantly broadened the scope of clinical applications in MR imaging to include the musculoskeletal system, abdomen and pelvis, breast, and cardiovascular system, to name just a few. Presently MRI is used for imaging from head to foot; and from bone marrow imaging to bone and soft tissue.

Conventional imaging sequences (e.g., spin echo) and traditional image contrasts (e.g., T1 and T2-weighting) have been complemented by an astounding variety of newer and faster acquisitions techniques, providing an unprecedented wealth of new information.

With the development of advanced systems hardware, work stations, phased array coils and advanced software program including fast imaging techniques and high resolution options (1024 acquisition matrices, volume acquisition and reformation) MR has been established as the leading cross-sectional imaging modality. The range of contrast agents has increased tremendously as well, ranging from organ-specific agents to contrast-enhanced three-dimensional angiograms.

"In order to understand the principles of MRI, one must successfully navigate through an elaborate structure whose essence is very much like a mathematical subject." - Alfred L. Horowitz (1995)

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MRI has found major applications in medicine and vibes for supremacy with its main competitor Computed Tomography (CT). The main advantages of MRI are its noninvasive nature and the flexibility with which it can be applied to obtain different sorts of information from various tissues and pathologies. The static magnetic fields and RF strengths currently in clinical use cause no known harmful effects, and studies can be repeated safely even on newborn.

Other diagnostic modalities such as ultrasound and CT give mainly structural information and except for ultrasound, involve the use of ionizing radiation. MR can give information on nuclear density, nuclear relaxation properties, metabolite and metallic ion concentrations, metabolite exchange rates, intercellular pH and 3D macroscopic tissue structure. Magnetic Resonance Spectroscopy strives to resolve the frequencies of signals from the vast multitude of metabolites, many found only in minute concentrations, in the living system.

Frequently MRI is the definitive examination, providing invaluable information to help the surgeon not only to understand the underlying pathology but also to make the critical decision regarding surgical intervention. Unprecedented developments have taken place that has catapulted this imaging modality to the forefront of modern medical imaging. During this development, complex novel techniques have been introduced, including magnetic resonance angiography, diffusion imaging, perfusion images and functional MR imaging.

2 New MRI Techniques

2.1 Magnetic Resonance Angiography (MRA)

MRA has enjoyed clinical success in the assessment of the cranial, carotid and peripheral vessels[1]. The main advantage of MRA is the visualization of blood vessels without the use of contrast (Fig. 1). The use of short echo time reduces the susceptibility artifacts. Fat saturation and magnetization transfer saturation provide background suppression. Three-dimensional time-of-flight (TOF) increase the range of cover. Contrast enhanced MRI tends to further increases the resolution, thus allowing visualization of smaller vessels with slow flow.

Improvement in gradient performance has resulted in the lowering of achievable echo time and repeat time. This has enabled an increase in the saturation of MR signal from background tissues, hence an increase in vessel conspicuity.

A technique analogous to X-ray angiography, termed MR DIGITAL SUBSTRATION ANGIOGRAPHY (MR-DSA), is being developed[2]. The multiplanar capability offered by MR-DSA is advantageous, particularly in the example of AVM where improvement in treatment accuracy of conformal radiotherapy will be added by more accurate 3-D representation of the nidus. Moving bed (patient couch) technology in combination with first-pass techniques permits the large anatomical coverage often required for effective peripheral vascular assessment.

2.2 Magnetic Resonance Pancreatocholangiography (MRCP)

MRCP is emerging as an exciting tool for the non-invasive evaluation of pancreatic and biliary ductal systems and is gradually replacing PTC and ERCP for diagnostic purposes. Duct dilatation, stricture and ductal filling defects are clearly seen and the diagnostic information obtained is equivalent to ERCP in most patients.

A variety of "bright bile" MRCP techniques with different approaches depending on scanner hardware and software are available including 2D, 3D breath-holding or respiratory triggering. Simple breath-held approach with a RARE sequence uses a thick slab with long TEs and an angulated coronal image that requires no further post- processing. The commonly used multi-section techniques use a HASTE sequence with thin sections and post-processing to generate maximum intensity projections. However, consideration of source images together with post-processed images is mandatory for clinical analysis.

Hepato-biliary contrast agents also exhibit high signal intensity within the bile and thus directly visualize the duct lumen. Gadolinium- enhanced T1-WI shows ducts with intra-luminal low signal intensity and can be

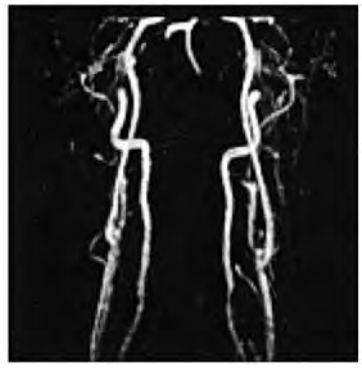

Fig. 1 MR Angiogram of the neck showing normal carotid and vertebral arteries bilaterally.

used as a "dark-fluid" technique. Gadolinium-enhanced FS T1WI, preferably with breath-held techniques, is ideal to image the ducts and adjacent soft tissues.

2.3 Magnetic Resonance Urography (MRU)

MR urography is being used in the diagnosis of obstruction. The coronal images using FISP or HASTE sequences rapidly portray a dilated collecting system and demonstrate the site of obstruction. It avoids radiation to the patient.

2.4 MR Myelography

It is a non-invasive modality that gives myelography-like pictures without the need for injection of contrast agent into the subarachnoid space. It is done by two techniques namely RARE (highly T2 WI) and FISP 3D.

2.5 MR Cisternography

This is a non-invasive way of detection of CSF leaks with no need of lumbar puncture and injection of intra-thecal contrast or use of ionizing radiation.

2.6 Diffusion MR Imaging

It is possible to non-invasively measure and depict molecular diffusion coefficients *in vivo* with MR imaging[3]. Studying molecular displacements over distances comparable to cell dimensions has provided information about the geometry and spatial organization of the tissue compartments and about water exchange between these compartments in normal and diseased states.

Diffusion-weighted images are obtained by incorporating strong magnetic field gradient pulses into an imaging pulse sequence. In a diffusion-weighted image, structures with fast diffusion are dark because they are subject to greater signal attenuation, whereas structures with slow diffusion are bright (Fig. 2). Quantitative diffusion images are generated from a series of diffusion-weighted images (Fig. 3). The term apparent diffusion coefficient (ADC) is used to quantitatively describe the results of diffusion imaging *vivo*. This can be used in the early diagnosis of stroke, assessment of white matter diseases and monitoring of tissue temperature changes during hyperthermia or laser surgery.

2.7 Perfusion Imaging

Perfusion weighted imaging provides an inexpensive, safe, reliable and accurate technique in evaluating blood flow measurements in brain compared to PET (Fig. 4). Ultra-fast imaging techniques such as

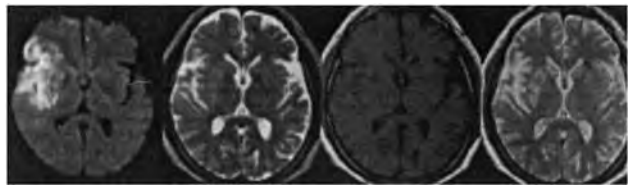

Fig. 2 Acute stroke in the middle cerebral artery territory seen as an area of hyperintensity on Diffusion weighted image.

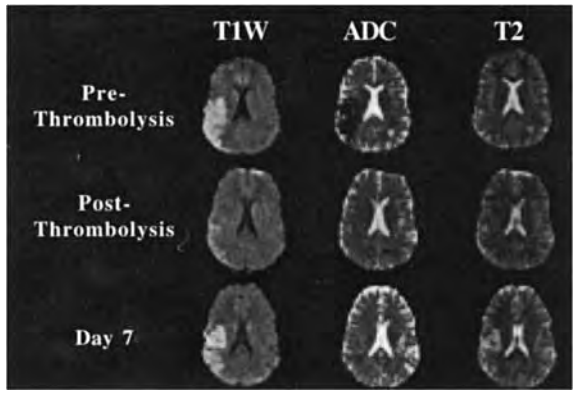

Fig. 3 Use of diffusion weighted image in stroke management by intra-arterial thrombolysis.

echo planar imaging (EPI) can monitor the first passage of contrast agents through the brain tissue within a few seconds of time. Thereafter the quantification of blood flow is performed, a procedure not so easy.

Perfusion imaging has widespread applications in hyper-acute stroke management, treatment monitoring in brain tumors and functional studies. It has been used to differentiate active recurrent brain tumors from fibrous tissue occurring secondary to operation or radiotherapy.

2.8 Functional MR Imaging (f MRI)

The first attempt to investigate brain activity was made in 1991. Studies have been performed at 1.5 Tesla MR Units using EPI and conventional fast gradient echo images. The most common approach has been the Blood Oxygen Level Development (BOLD) contrast technique[4].

Using the cooperation of the patient, who is told to perform certain tasks, different brain centres can be activated to detect activation in the primary cortices like the visual, sensory-motor and auditory cortices and association areas during higher order cognitive functions (Fig. 5).

Functional MRI has been used to study certain clinical problems like pre-surgical mapping (Fig. 6), imaging of the epileptic foci, monitoring recovery after

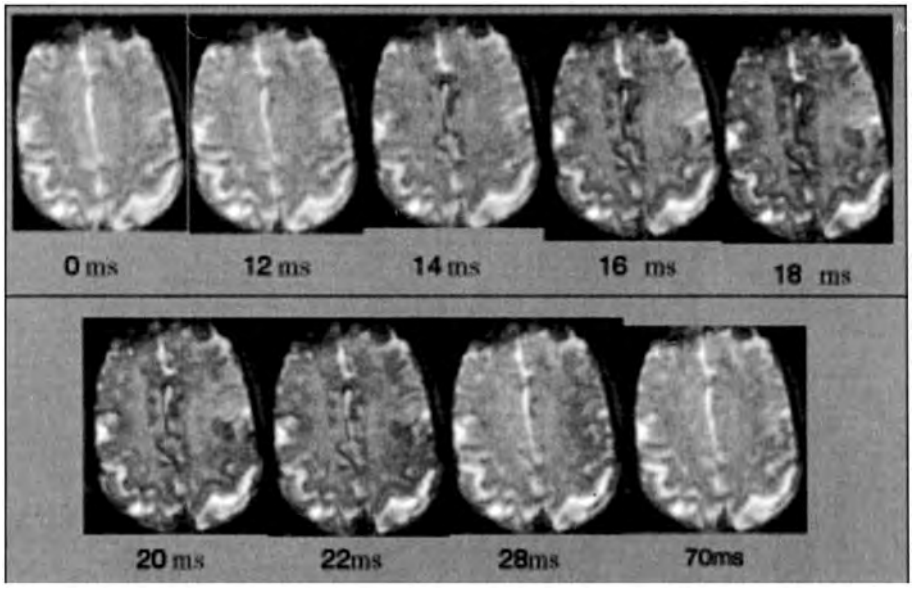

Fig. 4 Perfusion weighted contrast MR image showing an area of under perfusion in the left frontal lobe.

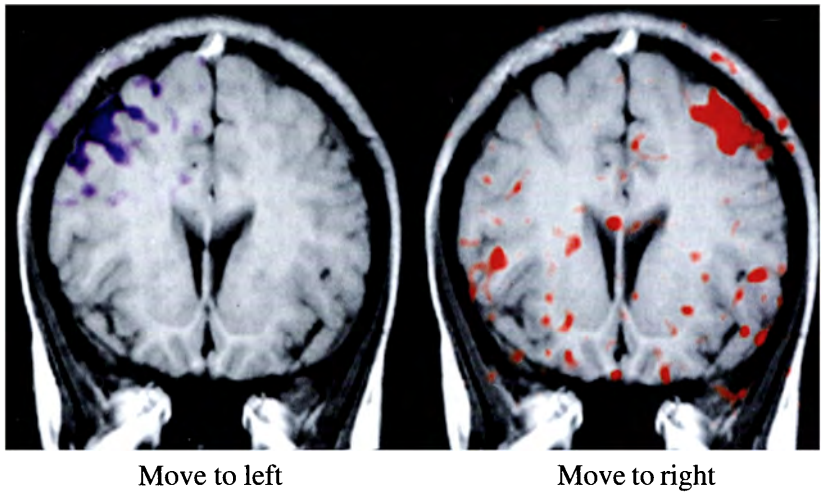

Fig. 5 Functional MRI showing activation of motor cortex on hand movement.

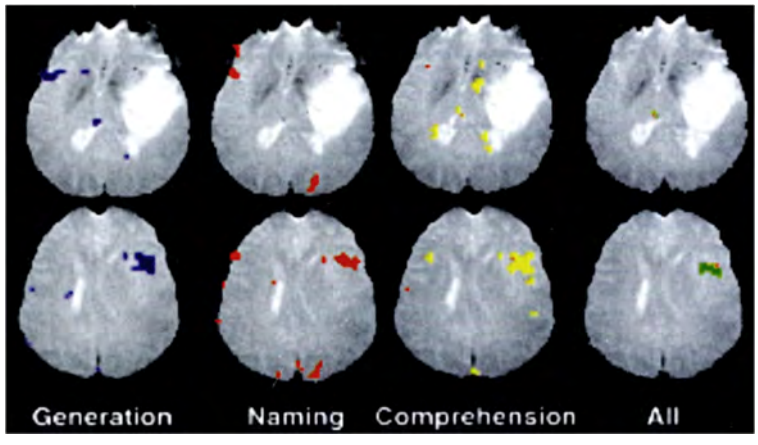

Fig. 6 Use of fMRI to outline the eloquent brain area in relation to the mass for preoperative planning.

stroke or head trauma and following treatment using neuro-pharmaceutical agents. In addition to being a tool to study anatomy of the brain, it is becoming a powerful functional tool to understand, detect and manage functional disorders of the brain.

2.9 Magnetic Resonance Spectroscopy (MRS)

MRS has become a major clinical tool for the diagnosis, prognosis and monitoring of a large variety of pathologies with metabolic as well as structural consequences[5]. Proton MR Spectroscopy is becoming a routine for several clinical assessments. Spectroscopy with other nuclei like carbon-13, nitrogen-15, fluorine-19 present major challenges associated with low natural abundance.

MRS is a non-invasive technique used to determine the molecular metabolites within the body. The metabolites are measured due to their slightly different magnetic frequencies and chemical shifts. MR spectroscopy coupled with MR imaging techniques allows for the correlation of anatomic and physiologic changes with changes in the metabolic and biochemical processes.

Since in many pathologic processes metabolic changes precede anatomic changes during disease progression and treatment, MRS offer a method for early detection of new disease and can influence the therapeutic success or failure. There is a rapid growth of clinical MRS in brain as head can be immobilized easily, brain is close to the surface and is virtually devoid of lipid signals that contaminate proton MRS spectra.

In vivo Proton MRS has also been performed in a wide variety of bone marrow lesions to quantify the cellularity of the infiltrative lesions and assess apoptosis.

Two important factors *in vivo* MRS are the volume localization technique used and how the signal measurement is affected by the type of localization procedure employed. At present there are two types of single volume localization techniques used in clinical MRS and they are the stimulated echo acquisition mode (STEAM) and point resolved spectroscopy (PRESS) techniques.

2.10 Fast Spin Echo (FSE) Imaging and Other New MR Sequences

FSE imaging is a modified rapid acquisition relaxation enhanced technique that affords rapid MR imaging while retaining true spin-echo contrast features. By manipulating the echo train length, echo spacing and order of phase encoding, images may be obtained many times faster than with conventional spin echo images. The use of FSE has reduced the imaging times considerably, an advantage to the sick patient.

Fast fluid attenuated inversion recovery (fast FLAIR) is being increasingly used in detecting subarachnoid hemorrhage in addition to detecting brain parenchyma lesions situated near the cerebrospinal fluid spaces.

Magnetization transfer (MT) images are being increasingly used to detect sub clinical lesions in the white matter that are not detected by conventional MRI. The use of this new technique is mainly focused in diseases like multiple sclerosis, AIDS, epilepsy and infections like neurocysticercosis and tuberculosis[6] (Fig. 7).

CISS is a 3D volume imaging, which gives clear images of nerve as black, while CSF appears bright. There is no need of lumbar puncture and injection of contrast as done for CT - cisternography.

2.11 Fibre Tracking and Diffusion-Tensor MRI

Fibre tracking procedures model the most probable anatomic connections between different parts of the brain. White matter visualization procedures segment white matter on the basis of its anisotropic diffusion characteristics. DTI provides formal analysis of anisotropic diffusion which is relevant to biological structures that restrict water diffusion in certain directions e.g. brain white matter and muscles.

2.12 Interventional Magnetic Resonance Imaging (i MRI)

MRI is increasingly being applied to guide various forms of intervention. Considerable progress has been in MR imaging guided interventional and intra-operative MR imaging. Several studies have shown that MR can be used to aid biopsy guidance or treatment of a lesion and to monitor laser, radio frequency and cryo-ablation therapies[7].

Several attributes of MRI make it very attractive for a potential use in interventional radiological procedures. The free choice of imaging planes,

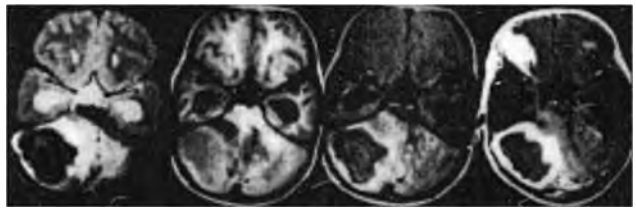

Fig. 7 Hyperintense rim seen in case of tuberculoma on pre and post-contrast Magnetic Transfer weighted image.

excellent soft-tissue contrast, plus simultaneous information on vasculature while avoiding radiation is particularly useful for many interventions. The capability of monitoring functional and physical changes of the tissue (fMRI, MR thermometry) is even more striking tool, highly attractive for minimal invasive MR-guided therapies.

Clinical experiences with iMRI are very promising, although there is still a lot of work to do in terms of hard and software development to keep up with the current standards of conventional radiology .The physical nature of MR has led to a range of compatible tools being developed, whose properties are specific to the MR environment. MRI compatible iMRI instruments usually contain nickel, chrome and titanium alloys to reduce susceptibility artifacts.

Better direct access to the patient in the imaging field (open magnet design), faster fluoroscopic imaging technique having good spatial resolution, the ability to interactively control the image scan-plane and the development of novel contrast mechanisms are all approaches that are helping to expand this exciting area.

MRI may also excellently visualize tissue ablation based on cooling, as opposed to heating, since the T2 of frozen tissue is so short that there is effectively no RF signal from the frozen region. Ice formation within the tissues can thus be seen as a signal-free area in T1W SE, GRE and rapid-acquisition relation-enhancement imaging (RARE) sequence. Clinical experiences are derived from treatment of superficial organs, ophthalmology, dermatology), endoscopically treatable organs (pulmonology, gastroenterology) as well as intraoperative applications.

2.13 Intraoperative Use of MRI

MRI in combination with active visualization methods and fast imaging techniques will significantly increase the positional accuracy of the lesion and thus decrease the time of surgery. MRI images may, for this purpose be linked to functional MR images, MR angiographies and other 3D data sets, such as positron emission tomography (PET) and CT, offering a new dimension of anatomical and functional neuro-navigation for the surgeon.

2.14 Cardiac MRI and Cine MRI

In addition to the anatomical depiction of CHD, MRI is capable of functional imaging, including measurement of intra-cardiac shunts, differential pulmonary blood flow, and pressure gradients across valvular and vascular stenoses and valvular regurgitant fraction.

Trans-thoracic echocardiography in adults suffers from poor acoustic penetration through the thoracic cage and mediastinal scar tissue. The advantage of MRI over echocardiography is that it can demonstrate cardiovascular anatomy without the limitation of acoustic windows. Supra-cardiac region and posterior aspect of the heart can be clearly seen. Because ventricular anatomy may be distorted in CHD, MRI may have an advantage over both echocardiography and angio-cardiography, since the latter two rely on geometrical assumptions.

Cine MRI attains a temporal resolution almost equal to cine angiography, which is sufficient to calculate stroke volume, ejection fraction, regional ventricular wall motion and wall-thickening dynamics.

MRI flow techniques (velocity-encoded cine MRI) can produce images depicting a map of blood velocity within the multiple cine MR images acquired throughout a cardiac cycle. Cine MRI and velocity-encoded cine MRI can be used to assess cardiac chamber dimensions and functional as well as blood flow in the central circulation.

Much progress has been made recently in MRA of acquired coronary artery disease, although these techniques have yet to see widespread clinical applications.

MR velocity mapping, or velocity-encoded cine technique, is a more recently developed and powerful technique for the functional assessment of CHD. Quantitative phase images provided by this technique contain two-dimensional velocity maps similar to duplex Doppler colour flow mapping. Flow velocity in cardiac chambers along a desired direction can be displayed as gray-scale differences on MRI.

2.15 Myocardial Tagging

MRI with myocardial tagging is the only non-invasive method for quantitatively assessing myocardial mechanics in three-dimensional manner. Myocardial tagging involves labelling a region or strip of voxels via magnetic saturation. This labeled zone can be followed anatomically throughout the cardiac cycle.

Measurement of local myocardial wall motion using myocardial tagging has become a simple and reproducible examination using single breath-hold cine methods. Direct visualization of the myocardium provides important insights into regional

myocardial mechanics. In contrast to global measures of systolic function, such as ejection fraction, MRI myocardial tagging makes it possible to quantify the severity and extent of subtle regional heart wall motion abnormalities both at rest and during stress.

Contrast enhanced MRI has a significant role in the evaluation of MI, as well as in assessing micro-vascular perfusion. First-pass myocardial perfusion methods may be applied to assess coronary flow reserve[8].

2.16 High Field MR Imaging

Higher field whole body research systems operating at 3T and above (images have been acquired using a 8T head only system) have been installed. The initial experiences of imaging at 3T or higher are very encouraging. The main advantage is the high resolution obtained due to higher signal to noise ratio allowing thinner slices.

2.17 Lung Imaging with Hyperpolarised Noble Gases

Hyperpolarized 3-helium and 129-xenon have recently shown great promise for use in imaging of ventilation and perfusion[9]. When these atoms are brought into a MR system, a low flip angle FLASH sequence can be used to make an image of the hyperpolarized nuclei.

At this stage, the main clinical use is focused on imaging of the lung and major airways with 3-helium. 129-Xenon can be used both as a ventilation agent and as a diffusible tracer for organ perfusion studies[10]. More recently, additional functional data on lung physiology parameters have been obtained; resulting in the development of regional oxygen tension measurement for gas exchange.3-Helium MRI may also be used for the measurement of apparent diffusion coefficient as a measure for alveolar size and perfusion / ventilation correlation using a combination of perfusion imaging and 3-helium imaging. Nevertheless, the technique is still in its infancy and its further development will probably take several years.

2.18 Exogenous Contrast Agent Development

Gadolinium chelates -the standard exogenous contrast agents in clinical MR imaging are neither organ nor pathology specific[11]. Some agents are under development that will remain within the blood circulation, while others are aimed at target organs.

Blood Pool Agents

Agents have been developed to remain within the circulation, resulting in an increased plasma half-life. This creates a great advantage for imaging: it allows more prolonged investigation time by enabling the acquisition of greater numbers of repeated data sets. This is beneficial if one wants to image small vessels (e.g. accessory renal arteries or coronary arteries), vessels with slow flow (e.g. pulmonary embolism and deep vein thrombosis, and vessels with complex flow patterns (e.g. AVM). Furthermore, perfusion studies can be repeatedly performed, rather than being solely dependent on the first-pass changes of a single infusion of the traditional gadolinium- based contrast agents. This has considerable potential if one wishes to image moving targets, such as the heart, where ECG-gating and respiratory gating were previously limiting factors.

Liver Contrast Agents

Gadobenate dimeglumine is actively taken up by hepatocytes and excreted into the bile. This results in long-lasting enhancement of liver parenchyma. Also the excretory function of liver can be assessed.

Small iron particles are actively taken up by the Kuffer cells of the reticuloendothelial system in the liver and spleen (comparable to the technetium sulphur colloid scan in nuclear medicine). They are metabolized into the iron pools of the body and excreted over a period of weeks. The particles are ferromagnetic, which leads to a local loss of coherence in the MR signal (spin dephasing) with a shortening of T2.It has been demonstrated that the uptake of these iron particles is diminished in patients with liver cirrhosis, resulting in a brighter liver signal on T2 weighted images[12].

Coated, ultra small, iron oxide particles directed specifically at the asialoglycoprotein (AG) receptors of hepatocytes promise even better distinction between normal and pathological liver tissue.

Manganese containing contrast agents are absorbed in the liver, pancreas and cortex of kidneys. The result is a decrease in the T1 relaxation time and thus an increased signal on T1 weighted image. This facilitates the detection of hypointense focal lesions within these organs. Mn DPDP, a paramagnetic agent, is excreted into the bile by the hepatocytes and is comparable to HIDA scanning in nuclear medicine.

"There is nothing that nuclear spins will not do for you, as long as you treat them as human beings." - Erwin Louis Halin (1949)

Endoluminal Contrast Agents

Various compounds have been used for the evaluation of endoluminal diseases of the small bowel, colon and rectum. These include a negative contrast agent based on iron particles for use in MR Enteroclysis and MR imaging of rectal cancers[13].

Gadolinium-based oral positive contrast has been applied with some success. Most recently, good results have been obtained in patients with suspected inflammatory bowel disease of small bowel obstruction, using a combination of methylcellulose solution for bowel distension and intravenous gadopentate diglumine for bowel wall enhancement. Using fast imaging techniques, it was feasible to assess both static and dynamic (MR fluoroscopic) bowel images in these patients.

Finally, natural compounds, such as blueberry juice, may act as negative contrast agent in upper abdominal MR investigations, such as MRCP[14].

Targeted Contrast Agents

The latest development is the use of targeted agents. Examples are necrosis-specific agents[15], lymphographic contrast agents[16] and agents targeted at inflammation detection[17]. The exact role of these agents is currently unclear, but they could considerably alter the practice of radiology.

Conclusion

We conclude that MR imaging is the modality of the future with a possibility of developing in to the walk through imaging technique with advancement in computer technology and hard ware. Passage of the human body through the scanner gantry would be a non-invasive, efficient and elaborate means of providing information about the anatomical, physiological and metabolite and functional aspects of the whole body.

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