EDITORIAL

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Recent progress and future development of MRI in ophthalmology

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Within a short span of 20 years, magnetic resonance imaging (MRI) has become a major radiological routine for soft-tissue disease diagnosis. In fact, MRI is often one of the most heavily utilised services. Its clinical potential, however, is still yet to be fully realised. This has been due to a gap between the fast pace in MRI research and the slower upgrading in clinical application. MR scans are now ordered principally for the brain, the spine, and the extremities. Interests in the imaging of other organs including the eye, the heart, and the abdominal organ systems have been strong although there is still room for improvement in image quality. MRI of the eye/orbit is no exception. The progress in MRI in clinical ophthalmology has been gradual; the potential and even the availability of ocular MRI are still not fully appreciated by most ophthalmologists. It is already known that the advantages of MRI include the lack of non-ionising radiation, multiplanar capability, the excellent anatomical details of the eye/orbit and the visual pathway, and its especial sensitivity in detecting demyelinating diseases. This editorial examines some of the more recent advances and discusses the possibilities of MRI in ophthalmology.

High-resolution MRI of the eye

The MR modality that closely resembles conventional optical imaging of the eye is perhaps high-resolution MRI of the eye. The latter is defined as MRI using the smallest available field-of-view (FOV) and the maximal matrix (for both frequency and phase). For ocular imaging, it also requires a small surface coil to collect signals from the region-of-interest (i.e., the eye/orbit), and a reasonably strong magnetic field to generate adequate NMR signals. At present, ocular MRI can be done with a 6-8 cm FOV with a 256x256 matrix, a small receive-only surface coil (1.25-3 inch in diameter), and at least a 1.5 Tesla magnet. And depending on the pulse sequence, both 2D (spin-echo) and 3D (gradient-echo) acquisitions can be done. The results are striking anatomy with readily detectable pathologies such as tumors (Figure 1), retinal and choroidal detachments (Figure 2),[2] and congenital malformations.[1]

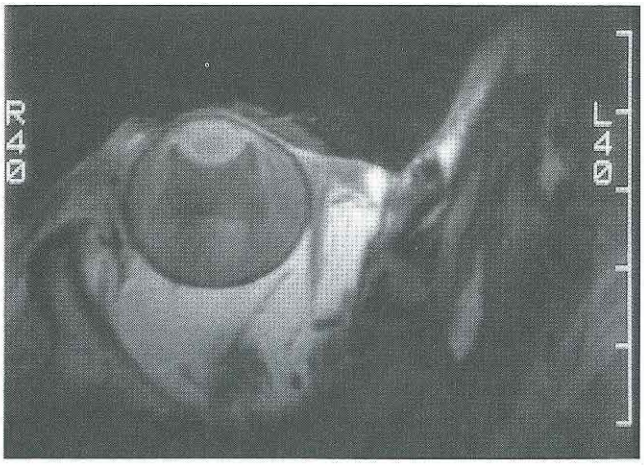

Figure 1. High resolution MRI of the eye showing a choroidal melanoma near the optic nerve head. The FOV was 8cm with a 256x256 matrix (i.e. an in-plane resolution of 0.3x0.3mm) and the slice thickness was 3mm. The rest of the eye appears normal.

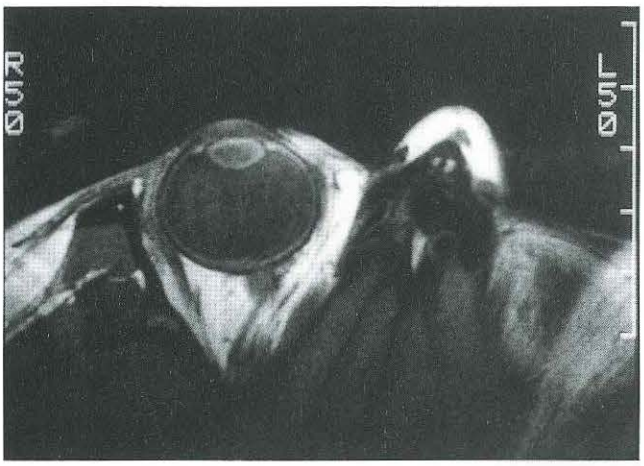

Figure 2. MR image of choroidal detachment. The MRI parameters are the same as that in figure 1.

In addition to anatomy, it is also possible to conduct dynamic imaging using contrast agents such as gadolinium(Gd)-DTPA and oxygen-17 water ($H_2{}^{17}O$) as the tracers for ocular fluid flow[3,4] and the non-contrast detection of blood oxygen levels in the optic nerve.[5] These techniques allow quantitation of ocular circulation which potentially can be used in the examination of the pathophysiology of primary open angle glaucoma and related diseases.

High-resolution MRI in its extreme form is MR microscopy (MRM).[6] This imaging mode was initially developed for the examination of pathological specimens. It uses a special imaging probe with radiofrequency coils fitted into a conventional high-field NMR spectrometer (e.g. 9.4 Tesla). These resonators come in several diameters ranging from 5 to 25 mm so the sample size can vary from small biopsied tissue to the whole enucleated eye. The spatial resolution can be in the micron range (Figure 3). This method requires no tissue fixation so the specimens can be processed immediately after surgical removal. Chemically-fixed specimens also can be examined for anatomy if NMR parameters, such as T1, T2, and proton density, are not crucial. An extension of MRM is chemical-shift microscopy which has been used to examine 13C-glucose metabolism in the diabetic lens.[7] There appears no clinical application of this technique at present time.

Ultra-high-resolution MRI or *in vivo* MRM can be the ultimate non-surgical biopsy. Its potential is yet to be explored. With the increasing availability of high-field magnets, this imaging mode will soon become a reality.

In vivo NMR spectroscopy (MRS)

MRS is a well-established analytical chemistry technique. It has been in use in chemical structure studies in the past several decades. However, the realisation that it can be used to examine the metabolism of tissues *in situ* is quite new. Most ophthalmic MRS studies are on normal lens metabolism and diabetic cataractogenesis.[8-10] This technique is very versatile and which can be used to examine metabolites that contain NMR nuclei such as proton, deuterium, 31P, 13C, etc. Figure 4 shows an example of the scleral response to topical 5-fluorouracil. Clinical application of MRS, however, is still experimental. Proton NMR, for example, can be used to examine the viability of human donor corneas (based on the rates of glucose consumption and lactate production) as well as the metabolic change in endophthalmitis.[11] A new application using an old solid-state NMR technique, i.e., magic-angle-spinning (MAS) spectroscopy, also has found its way into the examination of surgical specimens such as pterygium.[12] MAS spectroscopy is based on the fact that dipole couplings and chemical-shift anisotropy have an angular dependence described by (3cos2q - 1), where q = the angle between the static magnetic field and the inter-nuclear vector. At a spinning angle of 54 ° 44', (3cos2q - 1) = 0 (hence the term, " agic angle"). The effect of these interactions on spectral broadening thus can be much reduced to allow higher resolution. MAS spectroscopy, together with MRM, may prove useful tools in ocular pathology and diagnosis.

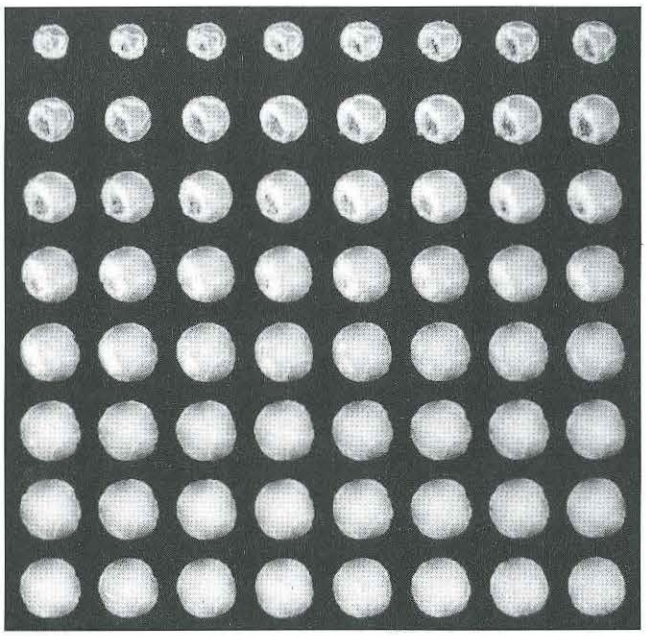

Figure 3A

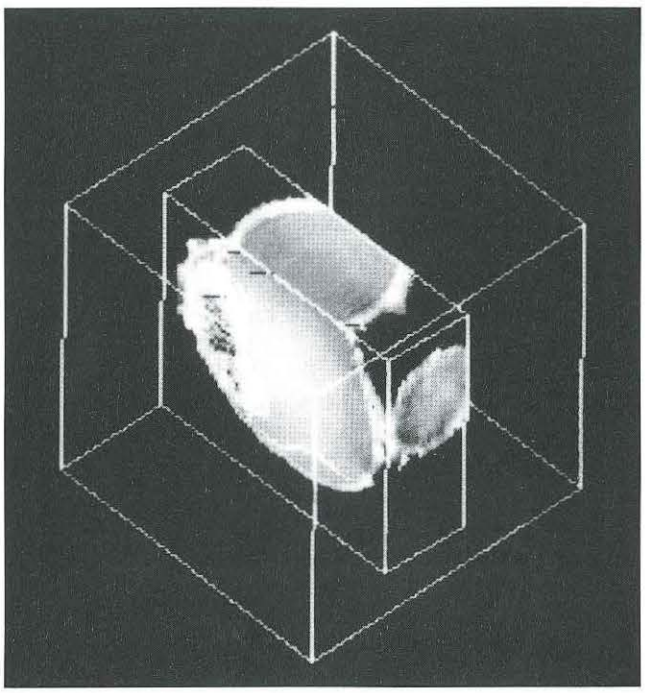

Figure 3B. MR microscopy of an enucleated eye with retinoblastoma. The FOV was 20mm and the images were obtained in the volume acquisition mode (A) which allows recognition and display in 3D (B). Calcification can be seen as black, signal-void lesions within the tumor.

Also in the offing are Naturally Abundant Chemical-Shift Imaging and Image-Guided NMR Spectroscopy. Both of which allow localisation of metabolites in large organs such as the brain. The eye, because of the small component tissues hence limited number of NMR nuclei, will require long acquisition times at relatively high fields (e.g., 3-4 Tesla). It is uncertain at present if MRS will prove practical in clinical ophthalmology despite its demonstrated efficacy in metabolic studies of ocular tissues. Indeed it will be quite advantageous if it is possible to detect sorbitol in the diabetic lens *in vivo* and normalisation when treated with aldose reductase inhibitors.[7] This is a true molecular diagnosis of the disease process.

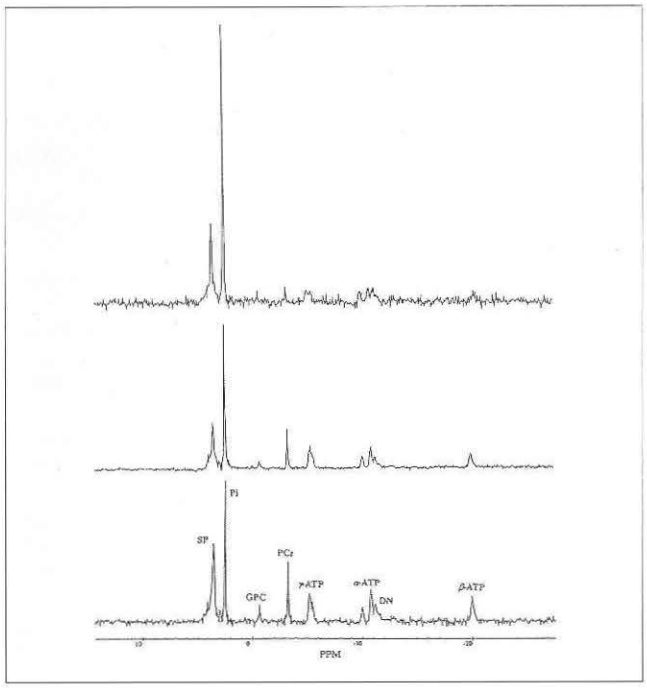

Figure 4. 31P NMR spectra of the scleral response to topical 5-fluorouracil (bottom): control (middle): 5mg/ml and (top): 50mg/ml 5FU. 5FU appears toxic to the sclera as indicated by loss of ATP and increase in Pi.

Functional MRI (fMRI)

fMRI is the newest entrant in the field of MRI. It is useful not only for neuroscience research but also the examination of brain lesions.[13, 14] It became possible largely because of advances in both hardware-ultrafast echo-planar imaging, and software -image analysis, and it is truly a product of joint efforts by physicists, engineers, scientists, and clinicians.[15] fMRI is based on measurements of circulation parameters such as blood volume (the first-pass effect using a contrast agent[16]), blood flow (changes in T1), and blood oxygenation (changes in T2*).Clinically, fMRI can provide anatomica l and functional correlation in lesions of, for example, the visual pathway. This information can aid the diagnosis and the planning of surgery now available only from PET. The T2*-weighted method also known as BOLD (blood oxygen level dependent) MRI is now the most popular fMRI technique. It was introduced by Kwong *et al*[17] demonstrated activation of the visual cortex by visual stimuli. This technique requires no contrast agents, so repeated scans can be done on the same patient. An example is shown in Figure 5, in which activation of the visual cortex by a simple eye convergence exercise is seen.

The literature on fMRI of vision has now become too vast to allow appropriate citation. Readers are encouraged to consult recent radiological and neuroscience journals. It should be noted that fMRI is still evolving and expanding.

So far, it has already elevated psychophysical research onto a higher level.[18] And indeed, this is one of the rare cases when an entire scientific discipline gained a renewed momentum using just one simple technique. fMRI studies on normal and diseased visual pathway will no doubt benefit neuro-ophthalmological patients as well.

Conclusion

In the US, the indiscriminate use of MR scans has long been considered a contributing factor in the escalating cost of healthcare. Part of it can be attributed to the so-called "defensive medicine". To avoid this pitfall, MR scans must be based on absolute necessity and should be ordered judiciously. Indeed the socioeconomic-legal factor is not necessarily an impediment to a wider application of MRI in general and imaging of the eye/orbit in particular. In fact, the obstacle may be simply a lack of communication between general ophthalmologists and MRI subspecialists (neuroradiologists).

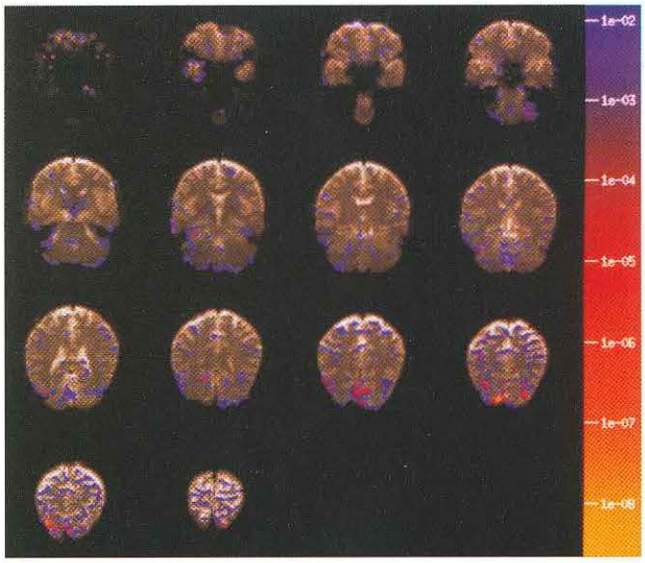

Figure 5. An fMRI study of eye convergence. This is a multi-slice T2* series of the t-maps superimposed onto the corresponding anatomy. Color areas show activation of the visual cortex by repeated eye convergence.

Since the eye and orbit contain soft tissues ideally represented by MR imaging, the ophthalmologists are strongly urged to include MRI in their diagnostic arsenal. In the examination of non-trauma cases, and certainly in cases where ocular media are too opaque to allow optical observation,[19-23] MRI should be regarded as the first alternative to ultrasonography X-ray and CT. (CT of course remains the first choice for acute orbital trauma - to allow examination of bony structures and to rule out ferromagnetic foreign bodies.) Increasing utilisation of high-resolution ocular and orbital MRI and fMRI of the brain, and perhaps in the future *in situ* NMR spectroscopy and chemical-shift imaging, will prove indispensable for the management of ocular diseases in the advanced mode.

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