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Magnetic Resonance Imaging in Neuro-ophthalmology

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Magnetic Resonance Imaging (MRI) of the visual system is an important new diagnostic technique used in neuro-ophthalmology. MRI has been used to detect intraocular and orbital pathology complementary to computerized tomographic (CT) scanning and ultrasound in the resolution of small anatomic structures. MRI has been able to demonstrate with exquisite detail the complete visual and oculomotor pathways, from the eye to the occipital lobe and brainstem. Laboratory studies involving MRI in both *in vitro* and *in vivo* designs have attempted to elucidate the underlying biochemical mechanism involved with specific disease processes. This may lead to earlier detection of disease, with the potential for differentiation between specific histopathologic tumor types through noninvasive means. Other studies are involved with high energy phosphate metabolism, sodium imaging, and hydration. MRI holds great potential for the future as technology continues to advance with increasing magnetic field strength and better techniques of resolution.

Magnetic Resonance Imaging (MRI) of the visual system is undergoing exciting and rapid evolution in diagnostic imaging. *In vitro* application of nuclear magnetic resonance has provided clear images with definition at the molecular level. In clinical medicine, we are witnessing this wonderful tool grow and develop in its application to *in vivo* subjects. MRI in ophthalmology has special clinical applications due to the innate and demanding quantification of clinical data in ophthalmology. Electrophysiologic testing, computerized perimetry, electro-oculography, and other specialized procedures give clinical insight to the imaging scientist.

Currently the radiologist uses only a fraction of the power of MRI. Present instrumentation looks primarily at hydration and more specifically at the activity of hydrogen atoms. Unlike CT scanning, MRI provides metabolic parameters, and in some instances finer anatomic detail. Future applications of

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MRI will include work on other targets such as sodium, phosphorus, and monoclonal antibodies. The future also holds the potential for differentiation between specific histopathological tumor types through noninvasive means. This paper will describe current clinical applications of MRI to some diagnostic problems of the visual system.

IntraOcular Pathology

Early reports suggested that prolonged T1 relaxation times were observed in tumors. Damadian, Zaner, Hor, and Dimaio (1973) found that in their study of five melanomas, two had short T1's, quite different from the other three tumors in their report. Using 2.35 Tesla (2.35T) they believed that this disparity was due to paramagnetic proton relaxation enhancement (PRE) by stable radicals known to occur in melanin. Sobel, Kelly, Kjos, Char, Brant-Zawadzki, and Norman (1984) observed a decrease in relative intensity on T2-weighted images and shortened calculated T1's and T2's in a choroidal melanoma. A total of six choroidal melanomas were studied using both nuclear magnetic resonance spectroscopy as well as magnetic resonance imaging.

Gomori, Grossman, Shields, Augsburger, Joseph, and DeSimeone (1986a) studied six freshly enucleated human eyes with a clinical diagnosis of choroidal melanoma. Initially, the *in vitro* specimens were imaged on a 1.4T super conducting magnetic resonance imaging system. For laboratory correlation, the eyes were immediately sectioned and tumor samples were analyzed on a variable field (0.19-1.4T) nuclear magnetic resonance spectroscopy unit. In tumors with a greater concentration of melanin, shorter T1 and T2 relaxation times were observed. It was thought that these observations were due to the paramagnetic effect of radicals present in melanin. It was concluded that the use of high magnetic field MRI can help to distinguish between proteinaceous effusions, pigmented melanomas, hematomas, and non-melanotic tumors. The authors were unable, however, to differentiate between fat and melanotic melanomas, or between amelanotic melanomas and non-pigmented tumors within the eye.

Eleven patients with intraocular tumors were studied by de Keizer, Vielvoye, and de Wolff-Rovendaal (1986) who used a spin-echo post-sequence 0.5T field and a multiple-slice technique with a thickness of 5 mm. The results were compared with ophthalmic ultrasound, general inspection, and histopathologic correlations. Of the eleven patients studied, seven had choroidal melanomas, six of which were detected by MRI. It was thought that demarcation was excellent when looking at the junction between the tumor and the sclera. Hemorrhage in and about the choroidal melanoma could be seen separately. MRI appeared to differentiate the choroidal tumor from surrounding intraocular and extraocular tissues better than CT scanning. The other patients in this study had lymphoma, metastatic carcinoma, hemangioma, and hemorrhage as causes for the intraocular masses.

Leukocoria is the appearance of a white reflex through the pupil, and it is an important clinical sign. According to Haik et al. (1985), leukocaria is the most common presenting finding in the pediatric ocular malignancy of retinoblastoma. Haik and colleagues used four MRI parameters (proton density, T1, T2, and flow) in their series of fourteen patients presenting with leukocoria. Using a Technicare 0.5T MRI unit with a slice thickness of 7.5 mm, they compared the results of MRI with extensive clinical ultrasound, and radiographic evaluation. They were able to demonstrate a spectrum of primary retinal and vitreal abnormalities with morphologic specificity. In children, MRI was felt to be much more advantageous than exposing the pediatric age group to the ionizing radiation of CT scanning.

Orbital Pathology

One of the early pioneers in MRI is Worthington. His team in Nottingham (Worthington, Wright, Curati, Steiner, and Rizk, 1986) studied various orbital and ocular pathology to determine the role of MRI in the evaluation of these disease states. The improvement in quality of MRI with surface coil data acquisition allowed the authors to achieve spatial resolution of less than 1 mm. This small resolution can allow one to distinguish between the cortex and nucleus of the lens. Pathology demonstrated by these techniques includes thyroid ophthalmopathy, with its associated thickened extraocular muscles, and tumors. The relationship between the tumor and the optic nerve can also be delineated.

This team then compared the advantages and disadvantages of these new MRI techniques to those of current CT scans. One obvious advantage to MRI of the orbit is the avoidance of ionizing radiation. The radiation dose associated with high-resolution studies of the orbit in CT scans is significant, and with repeated examinations, can approach a level known to induce a cataract. Other advantages of MRI include the direct multiplanar facility and the use of flow-dependent sequences to identify pathological vessels without the need for contrast medium. In addition, while MRI allowed only a limited discrimination between different tumor types by assessment of their MRI characteristics, this was found to be superior to that offered by CT scans. CT scans are limited in the assessment of orbital pathology because they are relatively non-specific with respect to tissue characterization. CT scans frequently fail to give an accurate indication of the degree of encapsulation, can not reliably predict tumor consistency, and are often inferior to MRI in distinguishing between intrinsic and extrinsic tumors. MRI also demonstrates cerebellopontine angle tumors of the brainstem more readily than CT scans. However, CT scans are superior in showing bone detail compared to the lack of signal from cortical bone and areas of calcification in MRI.

MRI has further disadvantages to CT scans. The potential presence of ferromagnetic material renders MRI inapplicable to the detection of foreign

bodies. Secondly, imaging times are frequently longer making it difficult to avoid artifact caused by movement of the globes. Finally, the high signal from retrobulbar fat significantly detracts from image quality.

Current work is being done to overcome these drawbacks. Daniels et al. (1986) were able to minimize the chemical shift misregistration from bulbar fat by positioning the patients so that the optic nerve was parallel to the frequency gradient. Worthington et al. (1986) found that with the appropriate choice of T1 in an inversion recovery sequence it was possible to suppress the signal from the retrobulbar fat and therefore remove the spatial blurring from this cause. Data acquisition time can also be reduced with methods which allow multiple slices to be acquired during a single exposure.

In their evaluation of lateral orbital lesions, Char, Sobel, Kelly, Kjos, and Norman (1985) studied six patients with the Diasonics 0.5T scanner operating at 0.35T. Slice thickness was 7.5 mm with 2.5 mm spacing between adjacent slices. It was felt that MRI had sensitivity equivalent to CT scanning, but it did not provide sufficient tissue specificity with the current technology to allow reliable differentiation between malignant and benign tumors of the lateral orbit.

Zimmerman et al. (1985) used a 1.5T MRI system from General Electric to study four cases of orbital pathology including an orbital hemangioma, dysthyroid ophthalmopathy, myositis, and a meningioma. Using partial saturation and spin-echo techniques, they concluded that MRI scanning showed anatomic detail superior to those of third and fourth generation conventional CT scanners.

In their evaluation of orbital tumors, Hawkes, Holland, Moore, Rizk, Worthington, and Kean (1983) reported on their study of twenty-eight patients with orbital space-occupying lesions. In this early study, a comparison was made with other conventional neuroradiologic procedures, including CT scanning. It was thought that the multiplanar facility of nuclear magnetic resonance was of special value. It could provide accurate volumetric information and could establish precise topographical relationships of the normal structures to the tumor. Li et al. (1984) compared MRI imaging with ultrasound and CT scanning of orbital tumors. Fourteen patients with space-occupying lesions in the orbit were studied with a 0.15T imager using spin-echo and inversion-recovery full sequences. Tissue characterization was best performed by MRI scanning. Using their early results, the authors concluded that this preliminary experience showed no distinct advantage of MRI over CT scanning or ultrasound in the diagnosis of orbital tumors. Sobel et al. (1984) used a 0.5T magnet operating at 0.35T with a 7 mm slice thickness and a 2.6 mm interslice gap. On their twenty-seven patients with ocular and orbital pathology, Sobel et al. (1984) concluded that MRI was very sensitive in detecting ocular, extraconal, and intraconal lesions larger than 5 mm, but was insensitive in imaging smaller lesions and in detecting pathology at the optic

nerve. It should be emphasized that this work was done three years ago, and that the authors predicted that further development should improve diagnostic accuracy. Figure 1 demonstrates an optic nerve glioma in a fourteen year-old with neurofibromastosis.

Bilaniuk et al. (1985) studied nine patients, five of whom had orbital masses. Using a surface coil at 1.5T they were able to detect 3.9 to 4.5 mm of elevation of ocular tumors. Using two different pole sequences, they saw separation of melanoma from adjacent retinal detachment. The authors concluded that the contrast obtained between orbital lesions and the adjacent normal structures was better than that demonstrated with high resolution CT scanning.

Trauma to the eye can cause orbital blow-out fractures which may present with double vision. McArdle, Amparo, and Mirfakhraee (1986) described one case of a blow-out fracture involving the medial and inferior walls of the orbit. When compared to CT scanning, they found that the masking of intraorbital contents by isodense hemorrhage on CT scanning was not a problem with MRI

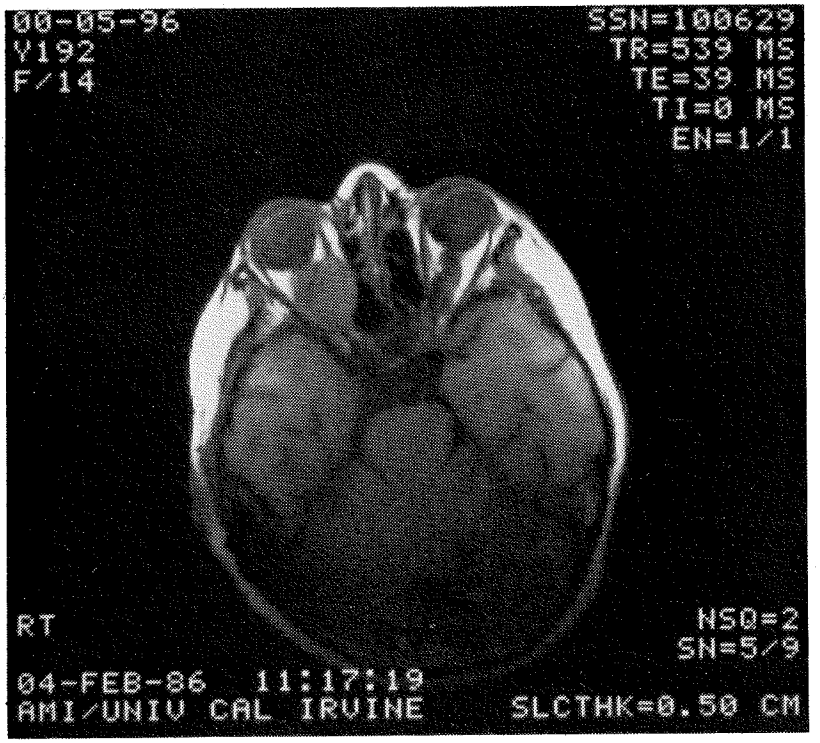

Figure 1: T1 weighted image of a right optic nerve glioma in a 14 year-old female with neurofibromatosis. A left optic nerve glioma was previously resected. The image was taken with a saddle coil placed anteriorly over the orbits using a 2.0 Tesla Superconductive Technicare Teslacon System operating at 0.6 Tesla.

imaging if the hemorrhage was small or non-acute. Figures 2 and 3 illustrate an orbital floor blow-out fracture in both saggital and frontal views respectively.

Intracranial Pathology

Worthington (1984) summarized his early work on imaging of intracranial and orbital tumors. The images were produced using inversion recovery, saturation recovery, spin echo, and steady-state free precession (SSFP) sequences. By increasing both the scan cycle and the interpost interval, the separation between edema and the tumor could be improved when the tumor had a very long T1 relaxation time. This technique still does not seem to achieve the enhanced contrast which can be obtained with CT scanning. The state of the art does not allow the delineation of small areas of calcification

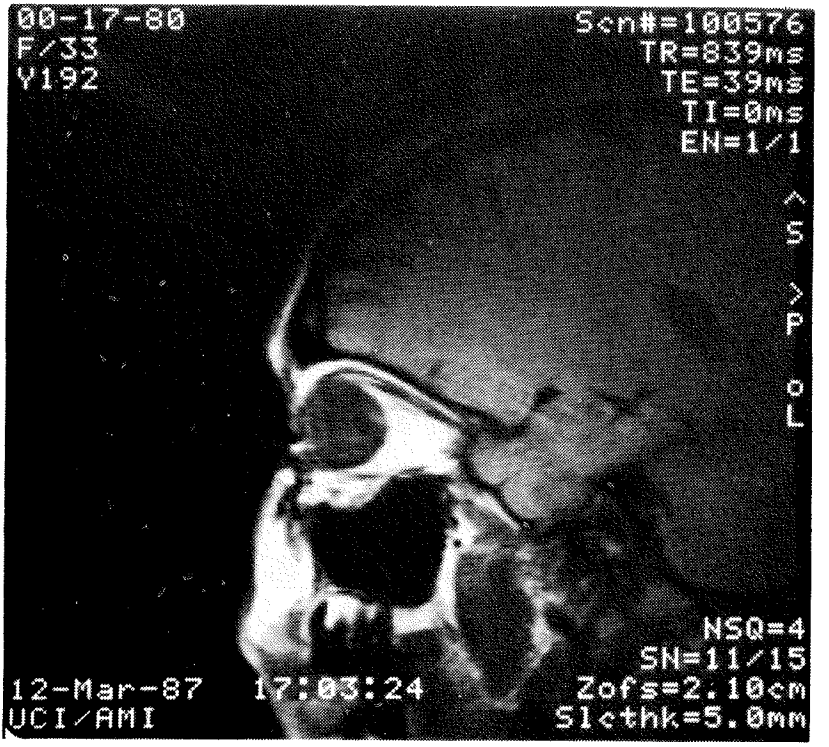

Figure 2: Saggital view of an orbital blow-out fracture with protruding fatty tissue in a 33 year-old female. This T1 weighted image was taken with a 2.0 Tesla Superconductive Technicare Teslacon System operation at 0.6 Tesla.

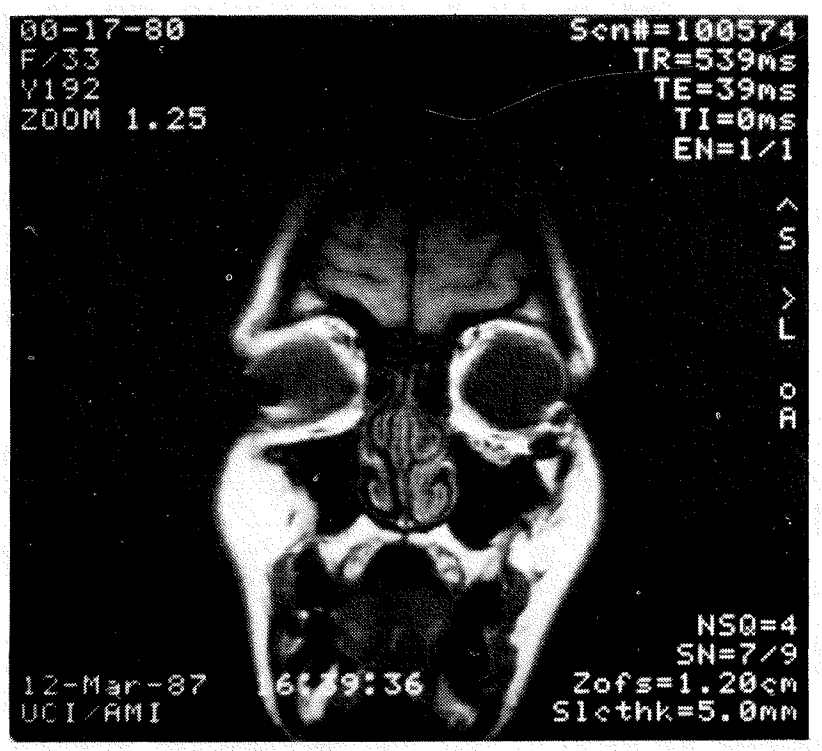

Figure 3: Frontal view of the same patient described in Figure 2. This T1 weighted image was taken with a 2.0 Tesla Superconductive Technicare Teslacon System operating at 0.6 Tesla.

within tumors, while CT scanning may do this, allowing a useful diagnostic sign to be obtained. MRI may be helpful in monitoring the response to radio-therapy, because initial changes in tissue following radio-therapy may result in edema with consequent increase in relaxation time. As the edema subsides there will be reduction of the relaxation time to more normal values. Perhaps this will allow radiologists to measure the efficacy of treatment as well as the diagnosis of recurrence by observing an increase in relaxation times.

In the region of the optic chiasm, SSFP sequences demonstrate that pituitary adenomas appear denser than brain tissue. Flow-dependent sequences can diagnose juxtaceller aneurysms, and the empty sella turcica syndrome is easily confirmed on a midline sagittal section when the suprasellar cisterns can be seen extending into the upper part of the fossa. Using a T1 weighted image, we were able to obtain good delineation of a pituitary adenoma (see Figure 4). An empty sella turcica is clearly demonstrated with the infundibulum dropping into the sella turcica in Figure 5.

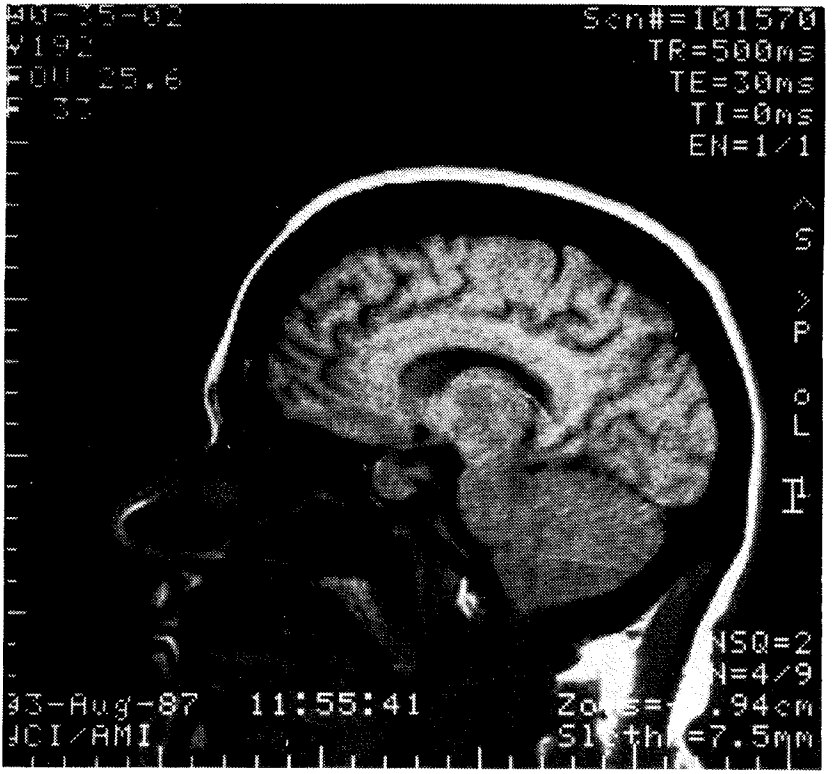

Figure 4: Pituitary adenoma in a 33 year-old female. T1 weighted image taken with a 2.0 Tesla Superconductive Technicare Teslacon System operating at 0.6 Tesla.

Daniels et al. (1984) used the GE scanner weighted at 0.5 to 1.4 T. A normal group was compared with four patients with tumors involving the visual axis. Two patients had anterior clinoid meningiomas, one had an optic nerve glioma, and one had an optic nerve sheath meningioma. It was reported that MRI demonstrated the optic nerve, the associated structures, and particularly the intra-canalicular portion of the nerve which was found to be difficult to image with CT scanning. Inversion recovery and spin echo techniques were less successful than partial saturation recovery imaging. Since axial views could not always distinguish ethmoid sinus tissue from the optic nerve it was recommended that both axial and coronal images be utilized. A recurrent meningioma in the region of the optic chiasm is demonstrated in Figure 6.

Albert, Lee, Saint-Louis, and Deck (1986) compared MRI with both CT scanning and metrizamide CT scanning in the evaluation of lesions in the optic tract, chiasm, and optic radiations. The MR images were performed using a 0.5 T

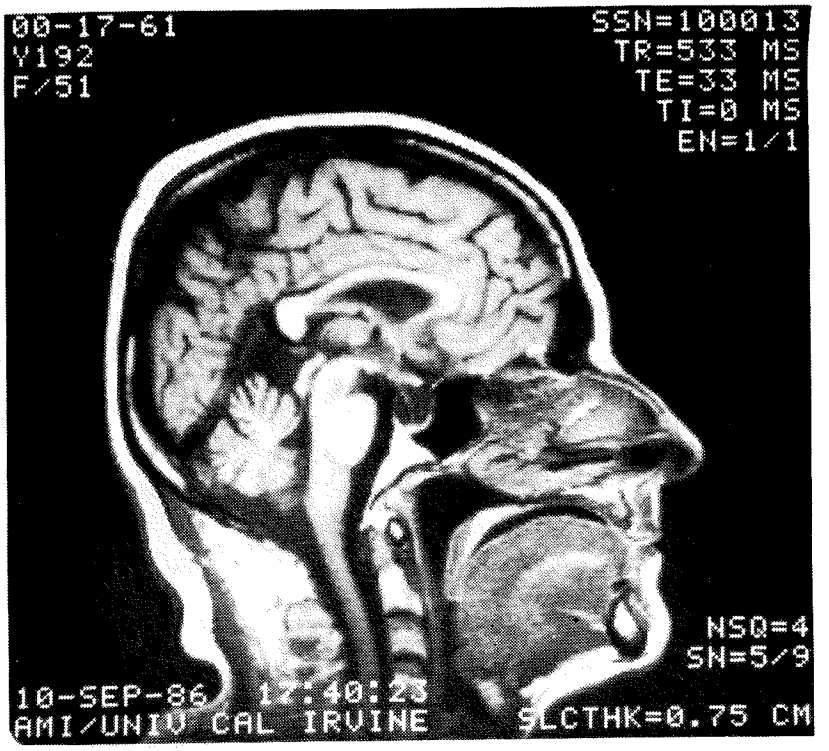

Figure 5: 51 year-old female with the pituitary stalk protruding into the empty sella turcica. T1 weighted image taken with a 2.0 Tesla Superconductive Technicare Teslacon System operating at 0.6 Tesla.

magnet while the CT scans were taken by a General Electric 8800 or 9800 model. The authors reported that abnormalities of the optic chiasm were difficult to detect on CT scans because of the poor contrast difference between the chiasm and the subarachnoid space, as well as the frequent occurrence of streak artifacts in the region. Primary lesions were also seldom distinguished from secondary involvement by adjacent pathology. Metrizamide CT is usually performed for detailed delineation of lesions in this location. Lesions of the optic tract were poorly seen on CT scans without contrast enhancement or pronounced compression of the brain stem. The extent of such involvement was shown well on axial MRI.

In studying patients with optic neuritis for the possibility of having disseminated sclerosis elsewhere in the central nervous system, Ormerod et al. (1986) studied thirty-five adults and two children with isolated optic neuritis, making sure to eliminate patients with medical conditions known to be

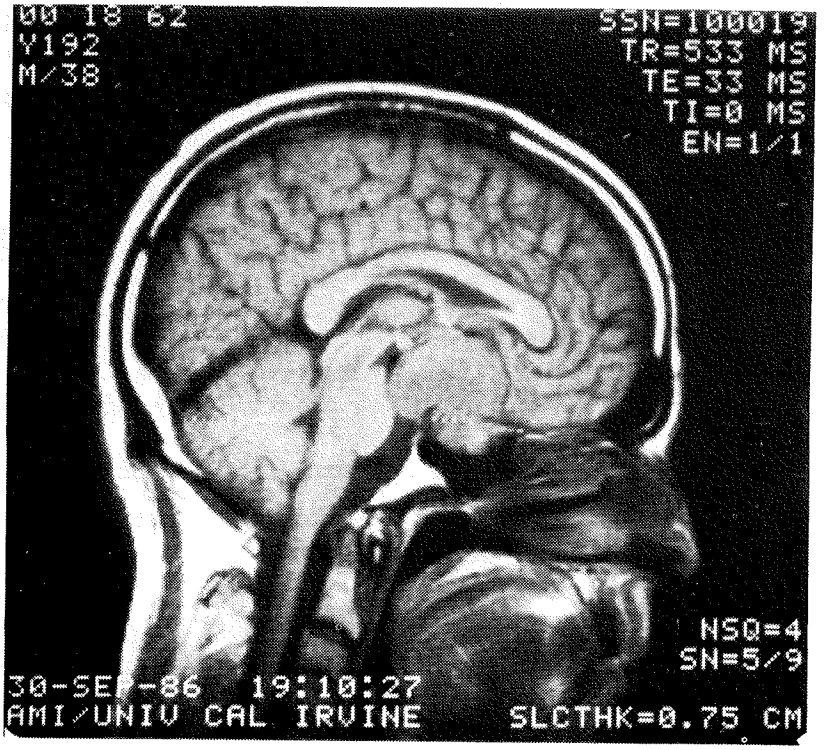

Figure 6: Post-resection recurrent meningioma in a 38 year-old male with bilateral blindness. T1 weighted image taken with a 2.0 Tesla Superconductive Technicare Teslacon System operating at 0.6 Tesla.

associated with optic neuropathy. He used the Picker proton MRI at 0.25 T, and later at 0.5 T, to study at least two sequences per patient, namely spin echo and inversion recovery. Comparisons were made between the sensitive measurement of evoked potentials and MR imaging. Of the thirty-five adult patients, evoked potentials suggested the presence of lesions outside the visual system in 30% while MRI demonstrated disseminated lesions in 61% of these patients. It was concluded that in patients with uncomplicated optic neuritis, MRI may be a sensitive method for detecting clinically unsuspected disseminated lesions, confirming the diagnosis of multiple sclerosis. While the above study was able to isolate disseminated lesions in the central nervous system, Seiler, Wollensak, and Miszalok (1986), in their study of optic nerve disease, attempted unsuccessfully to diagnose optic neuritis via MRI.

Rudick, Jacobs, Kinkel, and Kinkel (1986) analyzed free kappa-light chains in cerebrospinal fluid with the hope of finding some correlation with MRI in

patients suspected of having disseminated disease of multiple sclerosis. It was discovered that in eight patients with isolated optic neuritis, elevated kappa-light chains were found in 63% (five out of eight patients diagnosed). Of the five patients with optic neuritis and elevated kappa-light chains, four demonstrated disseminated lesions in the brain with MRI. Rudick et al. (1986) concluded that the presence of free kappa-light chains in cerebrospinal fluid appeared to correlate with disseminated disease in patients with isolated optic neuritis. Currently these authors are using MRI as the reference point for laboratory evaluations to predict the development of multiple sclerosis using kappa-light chains of cerebrospinal fluid.

Metabolic Studies via MRI

Glonek and Kopp (1985) described their work as an attempt to elucidate the underlying biochemical mechanisms which help distinguish between the different pathological processes, with the hope that *in vivo* diagnosis of the affected tissue can be made with direct noninvasive techniques of nuclear magnetic resonance. Using *ex vivo* studies of Phorphorus-31 chemical shifts of biomolecules, they studied tissue of the lens, cornea, brain, and heart. Preliminary studies suggest that tissue energy status can be determined by comparing the relative tissue content of high-energy phosphate signals (ATP, ADP, NAD, and the uridine diphosphohexoses) to that of the low-energy phosphate signals (inorganic phosphate and the sugar phosphates) to provide an indication of the metabolic state of the tissue.

An *ex vivo* study performed by Gomori, Grossman, Shields, Augsburger, Joseph, and DeSimeone (1986b) studied ocular MRI and spectroscopy of freshly enucleated eyes with choroidal melanomas. In their study of six eyes, which were imaged within 2 to 5 hours of enucleation, they described detailed ocular anatomy with a variable field (0.19–1.4T) resistive unit. The nuclear magnetic resonance spin relaxation times correlated with the MRI intensive patterns. The authors believed that the sensitivity of MRI to states of hydration could provide excellent demonstrations of ocular anatomy. It should be noted that these were not *in vivo* studies and were with eyes that could be scanned for an extended length of time without movement.

Garner, Hilal, Lee and Spector (1986) reported on laboratory work on the bovine eye and lens while studying Sodium-23 MRI. Operating at 29.8 CHz (2.7T), they demonstrated a spatially localized transference relaxation time T2-weighted spin density map of the Sodium-23 within the lens, resulting in resolution better than 250 μm. Through the use of a planar-integral projection reconstruction (PPR) imaging scheme the authors were able to allow sufficient short echo-times (1 msec.) for the detection of Sodium-23. They were able to demonstrate extracellular versus intracellular sodium and found good correlation with observations based on invasive techniques that demonstrated

a sodium gradient within the lens and the existence of a pump-leak system. It was felt that surface detection coils and strong magnetic fields would eventually allow noninvasive observation of changes in the distribution and local environment of sodium prior to the formation of cataracts.

Other laboratory studies have been conducted to determine whether there were any deleterious effects of nuclear magnetic resonance upon the eye. Sacks, Worgul, Merriam, and Hilal (1986) studied the effect of a constant magnetic field of 2.7 T and radio frequency pulses of 29 MHz at 800-ms intervals for 6 hours at field strengths representing the maximum used in clinical settings. This 6 hour exposure was more than the 4 to 6 minutes currently employed in most diagnostic protocols, and the study was carried out on young maturing mammalian eyes. Radiograms of the lenses from the developing animals were studied for any disturbances in cell-cycle kinetics. A 2-year follow-up has indicated that both slit lamp biomicroscopy and light microscopy studies showed no discernable effects on the developing rat eye. Sacks et al. (1986) thus concluded that radio frequencies and tesla levels currently employed by MRI today are essentially non-hazardous to the eye.

Kolodny, Albert, Epstein, Ruzzo, and Sprengnether (1985) studied Phosphorus-31 nuclear magnetic resonance spectroscopy as a possible means of characterizing human uveal melanoma cells. They studied 3 cell lines: uveal melanoma, Greene hamster melanoma, and normal human diploid fibroblasts. Phosphorus-31 nuclear magnetic resonance spectroscopy was found helpful in the measurement of intracellular pH. The pH of the uveal melanoma cells was much higher than that of the other 2 cell lines. Uridine diphosphate-glucose appeared in the Greene hamster melanoma and human diploid fibroblast cell spectra but was not detected in the melanoma cells from the uvea. Once further laboratory studies can confirm distinctive features of Phosphorus-31 nuclear magnetic resonance spectra in human ocular melanoma, it is hoped that an *in vivo* study of human eyes will show differences separating melanoma from other tissues.

Future Technology

The new technology to enhance MRI must include the use of surface coils which have improved the high resolution of magnetic resonance images of the eye and orbit. Schenck et al. (1985) described a method using modified surface receiver coil placed adjacent to the anatomy to be studied with magnetic resonance signals. The advantage of surface coils is that they limit the patient-generated noise while increasing the sensitivity for imaging voxels close to the surface of the body. This results in improvement of signal to noise ratio, thereby reducing the size of the imaging voxel. Using the 1.5T MRI system, Schenck et al. (1985) utilized the surface coils to obtain imaging pixel sizes of approximately 1 X 1 mm and slice thicknesses of 4 mm. These authors found it

advantageous to use separate coils for transmitting and for receiving elements, although other researchers have been able to use a single surface coil for both of these functions. Wong et al. (1987) studied *in vivo* cataractous changes in rabbits using a single surface coil for both transmitting and receiving functions. The images appeared to be as clear as images obtained from *ex vivo* lenses. These images will improve as the pixel decreases in size, which depends on new surface coils currently being developed.

Current research is studying the feasibility of developing holographic images to visualize multiple CT scans and MRI scans. In this way, there will be an integrated picture with a three dimensional image. In addition, holographic techniques can be used to archive the voluminous numbers of films which are currently stored in bulk. With the advent of new superconductors which are able to function at temperatures closer to the liquid nitrogen range, the future should hold development of more efficient and more powerful MRI systems for a fraction of the current costs.

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