NIH Public Access
Author Manuscript
NMR Biomed. Author manuscript; available in PMC 2010 July 29.

Published in final edited form as:
NMR Biomed. 2008 November ; 21(9): 997–1002. doi:10.1002/nbm.1247.

Clinical application of MRI in ophthalmology

Kelly A. Townsend, **Gadi Wollstein**, and **Joel S. Schuman***
UPMC Eye Center, Eye and Ear Institute, Ophthalmology and Visual Science Research Center, Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Abstract

MRI has long been applied to clinical medical and neurological cases for the structural assessment of tissues as well as their physiological and functional needs and processes. These uses are at a variety of developmental stages in ophthalmology, from common use of clinical structural assessment for neuro-ophthalmology and evaluation of space-occupying lesions to the beginning stages of experimentally measuring functional activation of specific layers within the retina and measurement of physiological oxygen responses. New MRI methodologies, such as the use of orbital coils and Gd-DTPA image enhancement, have been researched, developed, and validated in the eye, opening new possibilities for this technology to enter the clinic. This review aims to summarize the clinical ophthalmological uses of MRI, focusing on the current use of the technology and future applications.

Keywords

MRI; ophthalmology; clinical use; eye; retina; optic nerve

INTRODUCTION

In recent years, ophthalmology has provided an opportunity for many varied approaches to imaging of the eye in a clinical setting. Developments in optical imaging techniques designed for the eye, such as scanning laser polarimetry, confocal scanning laser ophthalmoscopy, and optical coherence tomography, have taken advantage of the naturally clear optical pathway that provides access to the internal features of the eye. However, although these devices provide high-resolution information, these technologies can acquire only limited information beyond the level of the retinal pigment epithelium. Other techniques that have been developed for imaging elsewhere throughout the body, such as ultrasonography and MRI, also have the potential to provide clinically relevant information, particularly in cases where it is not possible to optically obtain the information needed. Using appropriate scanning probes, one can obtain high-resolution ultrasonograms, but with limited tissue penetration, or low resolution with higher penetration. Many new MRI techniques have been applied to ophthalmology, providing both structural and physiological/functional information that may be relevant for clinical diagnosis and treatment.

In this paper, ophthalmological applications of MRI relevant to clinical care are reviewed, examining the transition and application of research methods to the clinic. Research methods that have been presented which are relevant to clinical use are discussed, including structural assessment of disease, functional MRI of the retina, physiological measurements such as oxygenation, and assessment of drug-delivery methods. In addition, future MRI

*Correspondence to: J. S. Schuman, UPMC Eye Center, Department of Ophthalmology, University of Pittsburgh School of Medicine, 203 Lothrop Street, Eye and Ear Institute, Suite 816, Pittsburgh, PA 15213, USA. schumanjs@upmc.edu.

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

developments that might be translated to improve clinical relevance in ophthalmology will be presented.

MRI IN OPHTHALMOLOGY TO THE PRESENT

A wide imaging view with enhanced neural tissue visualization is a substantial advantage of MRI over any other ocular imaging technique, which can be valuable in certain clinical situations. The most notable clinical use of MRI is for neuro-ophthalmic evaluation, because it allows visualization of the cranial and intraorbital nerves and detection of space-occupying lesions in the orbit, intracranial or hypophyseal region (1–4). MRI can provide better information about the eye in the context of the orbit than any other ocular imaging device. This allows detection of the etiology of ocular abnormalities related to primary orbital pathologies (2,4–7). Another indication for MRI of the eye is where gross ocular abnormality limits the ability for clinical examination.

Techniques

An assortment of strategies for ocular MRI have been attempted in the last few years. Scans focused on the orbits can be acquired from a cranial scan, using the whole-body receiver coil in the MRI (8–10). Head coils for MRI are readily available in clinical setups, and therefore these coils have been widely tested for various ophthalmological indications (5,9–11). These coils are mainly beneficial for imaging the eye in the context of the head, as it provides signal penetration beyond the orbital apex (8). A head coil can be used to acquire images of cranial nerves, which may be most relevant in cases where it is believed that the optic nerve and beyond have been affected by disease such as optic neuropathy or tumors (3,4).

A variety of orbit coils have been used to image the eye selectively, providing greater signal-to-noise ratio, at the cost of decreased signal penetration (4,8). One commonly used clinically available coil setup is the 3-inch diameter surface receive-only radiofrequency coil (2.5–3.15-inch inner diameter, depending on manufacturer) which provides a detailed view of the anterior orbit (6,9,12). Microscopy surface coils with smaller diameters of ~1.9 inches can be used to provide even better resolution of the structures within the eye (13). The surface coil techniques, however, can be much more sensitive to movement artifact and therefore require much greater skill by the technician.

Bert *et al*. (12) tested a variety of preparatory strategies for MRI of human eyes using commercially available systems. The 1.5 T systems of three manufacturers (Philips, GE, and Siemens) were tested using the manufacturers' 3-inch receiver coils with each, with the subject fixated on a target with the non-imaged eye and the imaged eye open, held closed, taped closed, or taped closed with water-soaked gauze over it, and the results were compared for each protocol. The water-soaked pads were added to reduce T_2 dephasing of the MRI signal due to magnetic field susceptibility differences, caused by the air interface with the cornea. The three devices were found to be comparable, and both neuroradiologists and eye pathologists subjectively graded the 'taped with water-soaked pad' procedure as the most artifact-free, and images obtained from an eye held closed by the subject were the poorest quality.

Several processing techniques may also aid the acquisition of enhanced ocular scans. Fat suppression techniques, such as short tau inversion recovery, are often needed because of the short T_1 constant of fat, which can cause registration artifacts or mask tissues near the high-signal-intensity retrobulbar fat (4,13). As in other fields, different weighting techniques, such as T_1, T_2, and diffusion weighting, can reveal details of different structures. For example, T_1-weighted images can provide better anatomical detail because of the high signal-to-noise ratio, but the strong orbital fat signal can over-saturate smaller adjacent

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

structures (4). T_2 weighting can improve visualization of the inner surface of the globe, because of the bright vitreous signal, but is more subject to motion artifact and has lower signal-to-noise ratio (4). Diffusion weighting can improve the ability to visualize stroke or other neural trauma sooner after the incident than either T_1 or T_2 weighting (14). In addition, contrast agents such as gadolinium diethylenetriaminepenta-acetic acid (Gd-DTPA) can be introduced to provide greater detail in the vascularized portions of the eye (8,15).

Structural assessment: from the optic chiasm to the retina

A variety of studies conducted in the last 10 years have examined the anterior portions of the visual system (optic nerve to the optic chiasm) using MRI (16). Several of these studies examined how glaucomatous damage relates to the structure of the optic nerve and anterior visual pathway (17,18). Glaucoma is characterized by typical changes to the retina and optic nerve head, with gradual loss of visual field. One focus of investigation is normal-pressure glaucoma, which is a sub-group where the patient presents glaucomatous features in the presence of normal intraocular pressure. In this situation, it is particularly difficult to distinguish the visual field and optic nerve head abnormalities associated with normal-tension glaucoma from compressive optic neuropathy caused by intracranial masses. Greenfield *et al*. (17) examined brain MRI or CT images of patients diagnosed with normal-tension glaucoma for the presence of anterior visual pathway compressions. It was concluded that neuroimaging has too low a sensitivity to provide cost-effective diagnosis information. In contrast, Ahmed *et al*. (18) compared the prevalence of intracranial lesions in people diagnosed with normal-tension glaucoma and subjects with primary open-angle glaucoma. A significantly higher number of subjects were found to have intracranial lesions in normal-tension glaucoma than in primary open-angle glaucoma (6.5% vs 0%), thus the authors concluded that intracranial lesions are an important differential diagnosis to be considered when assessing for normal-tension glaucoma, and that MRI is an important tool for assessment of this.

Kashiwagi *et al*. (19) used MRI to detect the presence and extent of glaucomatous damage to the optic nerve and optic chiasm. They found significantly smaller optic nerve diameter and significantly lower optic chiasm in patients with glaucoma than in healthy controls. These two parameters both correlated significantly with other structural and functional indicators of the extent of glaucomatous damage.

MRI might also be useful in assessing intraocular findings that may be related to intraorbital features. Tarver-Carr and Miller (20) presented a case report of MRI identification of congenital tilted disc syndrome where the optic nerve penetrated the globe at a sharp angle and caused an atypical appearance of the intra-ocular optic nerve head. In this case, it was possible to visualize the oblique entry of the optic nerve into the globe with MRI, confirming this etiology from other differential diagnoses.

One of the predominant uses of MRI is for identification of ocular and orbital tumors, as they are often visible at the resolution it can provide, and because tumor tissue often has unique features that are identifiable on MRI. Types of tumor that have been identified on MRI scans include uveal melanocytic tumors, uveal metastasis, uveal vascular tumors, other miscellaneous uveal tumors, vascular and glial tumors of the retina, medulloepithelioma, adenoma of the non-pigmented ciliary epithelium (3,4), melanoma, hemangioma (6), and retinoblastoma (4,5,7). In addition to the ability to identify many of the tumors, MRI is of utmost value in determining the extent of tissue involvement and spread into the orbit, which is crucial for clinical decisions for treatment approaches.

In situations where the view into the eye is blocked by media opacities or large tissue abnormalities, MRI might provide valuable information on the intraocular findings. A

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

variety of retinal detachments have been documented with MRI, such as rhegmatogenous, exudative non-rhegmatogenous, and hemorrhagic retinal detachment (4) and detachment due to tumor (6). A study was conducted by Pop-Fanea *et al*. (21) to evaluate the ability of MRI to monitor retinal detachment due to experimental ocular inflammation induced in rats. MRI measurements corresponded well to histological findings, and detachments as small as 0.1 mm^2 were observed with MRI, indicating that MRI has potential for *in vivo* visualization and monitoring of retinal detachment. MRI has also been used to visualize cat scratch neuroretinitis effects and distinguish them from other optic neuropathies, even possibly before the macular star findings on the retina that typically identify the disease. MRI is often performed in these cases to rule out other causes of optic neuritis, such as multiple sclerosis (11,22,23).

Using newer methods and technology, it has become possible to visualize retinal layer details. Shen *et al*. (15) were able to visualize three layers within the cat retina using T_2- and diffusion-weighted MRI at 4.7 T, and T_1-weighted MRI before and after administration of Gd-DTPA contrast agent. The inner layer exhibited large T_2 and spin density with Gd-DTPA enhancement, and was established to include the retinal ganglion cell layer, bipolar cell layer, and their embedded vasculature. The middle layer of the retina had small T_2, and spin density enhancement without Gd-DTPA, and included a photo-receptor cell layer and the inner and outer segments. The outer layer included the tapetum, a layer that does not exist in humans, and a choroidal vascular layer, which had large T_2 and spin density with Gd-DTPA enhancement. The blood/retina barrier prevented Gd-DTPA from entering the avascular photoreceptor zone, allowing this three-layer differentiation. Georgouli *et al*. (13) used a 47 mm microscopy coil to acquire T_1- and T_2- weighted images of the whole globe, noting visualization of the retinal layers, Tenon's capsule, and tarsal plates, with higher resolution than had ever been obtained with head or eye coils.

Functional MRI: retinal function and ocular physiology

One of the prime advantages of MRI for ocular imaging is its ability to combine structural and functional imaging, to provide physiological information beyond the anatomy. Functional MRI (fMRI) techniques have been applied experimentally to map activity-evoked signal changes in the retina (24,25). The first fMRI study of the retina was performed by Duong *et al*. (25) in anesthetized cats. They mapped the activity-evoked changes using the blood-oxygenation-level-dependent (BOLD) technique in the overall retina–choroid complex to drifting and stationary gratings in both the full visual field and upper and lower visual fields separately. They found robust significantly increased activity after stimulation in the retinal areas expected on the basis of the location of the stimuli, and found no statistically significant signal change in the location of the optic nerve. Since their study, research has been carried out to isolate the functional signal in specific layers of the retina. BOLD fMRI allowed segmentation of the retina into three distinctive segments and revealed differential responses in the two vascularized retinal regions in response to hyperoxia and hypercapnia (24). MRI was also able to demonstrate changes in photoreceptor degeneration rat models, observing both structural degeneration in the outermost layer, believed to represent photoreceptors, and attenuated BOLD fMRI responses in the vascularized layers (24).

Berkowitz *et al*. (26) used another fMRI approach to examine the retinal layers, using manganese-enhanced fMRI to look at the cellular demand for ions in different retinal layers as they are activated, rather than looking at hemodynamic responses as BOLD does. Inner and outer retinal responses were observed with and without systemic injection of $MnCl_2$ during light and dark adaptation, and signal intensity differences were com-pared. With the $MnCl_2$, the change in outer retinal signal between light and dark was significantly greater than the change observed in the inner retina. As these technologies develop beyond the

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

experimental realm and normal patterns of BOLD response or manganese ion consumption are understood, fMRI could develop into an important clinical tool for assessing the level of functional ability in a diseased eye, and the physiology of its dysfunction could be better understood.

MRI assessment of blood oxygenation in the retina can be used not just to look at functional activation in healthy eyes, but also to examine the retinal oxygenation response, particularly how it changes as a result of retinopathy. Monitoring of ocular oxygenation using MRI can help physicians understand the regulation of retinal oxygen concentrations *in vivo*, which is important for the treatment and control of a variety of retinal pathologies (27,28). Diabetic retinopathy and other similar diseases are believed to be related to retinal hypoxia, which leads to neovascularization. However, the current method for examining retinal oxygen concentrations uses oxygen electrode technology, which allows measurement only at a single point on the retina and cannot be used in either rodent models (eyes are too small) or human cases, as it is too invasive, unless the eye is already opened, as in vitreoretinal surgery, and clear media is present for placement, both of which limit their relevance for clinical use (27). Non-invasive MRI-based methods, however, can address many of these concerns. MRI allows a physician to make non-invasive measurements of oxygen concentration across the entire retina, which are unaffected by media opacity. Ito and Berkowitz (27) summarized two novel methods of measuring oxygenation in the retina. The first ^{19}F-NMR method uses a small perfluorocarbon droplet placed on the retina. This liquid is able to absorb an order of magnitude more oxygen than water, making its $(T_1)^{-1}$ more sensitive to inner retinal oxygen tension, allowing a more accurate and precise calculation. In addition to this invasive measurement technique, which is most feasible in experimental models but not for routine clinical measurement, proton MRI can be used non-invasively to generate a T_1-weighted image of the eye in both room air and a hyperoxic inhalation challenge, and the change between them gives an accurate measure of inner retinal oxygen response. This response is likely to be abnormal if the retina is poorly perfused because of retinal pathology. Retinal oxygenation response has continued to be further investigated, as described by Trick and Berkowitz (28), where they suggested that the retinopathic damage such as neovascularization is mainly due to an inability to actively regulate oxygen rather than constant hypoxic conditions. The method for acquiring this data also had to be developed and validated to minimize the blinking artifacts that confound detection of the subtle signal changes, by having patients refrain from blinking for 12 seconds, then allowing a 3 second blinking rest period (29). So far, these methods have been shown to display evidence for both subnormal oxygenation levels and responses before pathological evidence of disease in experimental models. Therefore, there may be the potential to use these techniques to identify disease before visible damage can be detected.

In addition to clinical use of the MRI, ocular MRI technology has been used recently to better understand diffusion pathways in the eye and their effects on the localization of drug doses. Bert *et al*. (30) found an anterior diffusional pathway for solutes from the ciliary body stroma to the anterior chamber, similar to that in rabbits and monkeys, by observing subjects after an intravenous injection of Gd-DTPA contrast agent. Signal intensity was observed first rising in the ciliary body, followed by a latent signal enhancement in the anterior chamber that appeared strongest in the angle near the trabecular meshwork, indicating that solutes are able to cross the blood/ocular barrier, which may also explain the presence of plasma-derived proteins in the aqueous humor. MRI was also used to directly monitor the subconjunctival and intrascleral infusion methods of drug delivery. Kim *et al*. (31) also used Gd-DTPA contrast agent to look at distribution and clearance from infusions in the subconjunctival or intrascleral space by dynamic contrast-enhanced MRI. Subconjunctival injections failed to produce detectable concentrations of Gd-DTPA in the posterior segment, where drugs are targeted. However, intrascleral injection expanded the suprachoroidal layer,

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

allowing delivery of Gd-DTPA to the posterior portion of the eye. This expansion normalized after intrascleral infusion was stopped, and no permanent change to the suprachoroidal layer was observed. The knowledge gained from their study was useful for designing clinical drug treatment for macular disease. Metrikin *et al*. (32) used contrast-enhanced MRI in rabbits receiving endotoxin-induced endophthalmitis to determine the amount of blood-retinal barrier breakdown. This disease results in profound visual consequences, due to severe inflammation, and blood-retina barrier breakdown is believed to have an important relationship with the amount of inflammation. MRI was able to provide images despite ocular media clarity loss, which hinders fluorescein angiography, a common technique used to assess the blood-retina barrier. They found inner barrier breakdown with all levels of endotoxin administered, with leakage increasing with increasing amounts of endotoxin. The blood-retinal barrier regained structural and functional integrity by day 28 post-endotoxin dosage. This knowledge of the breakdown could help in future assessment of therapies.

Ocular MRI limitations

When considering the use of MRI for ocular evaluation, several limitations of the technology should be taken into account, especially when compared with optical techniques. MRI is an expensive procedure, and the machine is bulky and can be uncomfortable for many patients. It has a relatively slow acquisition rate which makes the images prone to motion artifacts and has limited resolution in comparison with optical techniques. Although the resolution of MRI is in the range 200–250 μm for in-plane resolution on 1.5 T commercial systems (12), some of the optical imaging devices have an axial resolution at the level of 3 μm (33).

FUTURE DIRECTIONS FOR MRI

Improvements in structural MRI methodology leading to improved resolution and image quality will help visualization of the retina and optic nerve. Resolution is a vital consideration for ocular imaging. As the retina is ~400 μm thick at the optic nerve head margin and further thins as it moves toward the periphery (34), MRI currently does not have the resolution to compete with optical imaging devices for structural imaging within the eye (12,33). However, as progress is made towards improved image quality and resolution, structural MRI may still be relevant in ocular cases where the use of optical imaging devices is not possible because of optical pathway opacities. Improved resolution could be of benefit in monitoring clinical situations, such as ocular nevi that may be malignant choroidal melanoma, allowing physicians to track changes in size or shape. Optic disc drusen, or deposition of calcified material within the nerve head, would be more identifiable using MRI with better resolution. This improvement is expected as clinical MRI system standards move from the 1.5 T devices to 3 or even 7 T devices, providing better resolution at higher speeds, resulting in less motion artifact. In addition, the development of more stable surface coil systems for localized imaging would provide better resolution. Currently, nearly all clinical MRI scans are acquired using whole-body or head coils, because the mechanical stability of surface coils is highly affected by any patient motion. If a more solid system for coil placement were developed to prevent motion artifacts, scans of the eye with much greater resolution could be obtained faster.

The physiological monitoring abilities of MRI are a unique feature of this technology that shows promise for future use. fMRI provides an objective assessment of the ocular tissue function and, when combined with the structural features, can lead to a better understanding of the pathophysiology of numerous ocular pathologies. Further improvement in MRI oxygenation-assessment techniques should provide additional information for understanding and monitoring of ocular pathologies (27,28).

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

In conclusion, many new research methods for ocular MRI have been proposed recently. In addition to clinical uses that currently exist, particularly in neuro-ophthalmology, many of these new methods that have only been used in research so far could be of future use for improving the understanding of pathological ophthalmic processes.

Acknowledgments

Financial Support: Supported in part by NIH grants R01-EY013178-08 and P30-EY08098-21 (Bethesda, MD, USA), The Eye and Ear Foundation (Pittsburgh, PA, USA) and an unrestricted grant from Research to Prevent Blindness, Inc (New York, NY, USA).

Contract/grant sponsor: NIH; *contract/grant number:* R01-EY013178-08 and P30-EY08098-21.

Contract/grant sponsor: The Eye and Ear Foundation.

Contract/grant sponsor: Research to Prevent Blindness, Inc.

Abbreviations used

BOLD	blood-oxygenation level-dependent
fMRI	functional MRI
Gd-DTPA	gadolinium diethylenetriaminepenta-acetic acid

References

1. Atlas, S.; Galetta, S. The orbit and visual system. In: Atlas, S., editor. Magnetic Resonance Imaging of the Brain and Spine. Raven Press; New York: 1991.
2. Harms, S. The orbit. In: Edelman, R.; Hesselink, J., editors. Clinical Magnetic Resonance Imaging. WB Saunders; Philadelphia: 1990.
3. Sobel D, Mills C, Char D, Norman D, Brant-Zawadski M, Kaufman L, Crooks L. NMR of the normal and pathologic eye and orbit. American Journal of Neuroradiology 1984;5:345–350. [PubMed: 6431768]
4. De Potter, P.; Shields, JA.; Shields, CA., editors. MRI of the Eye and Orbit. J.B. Lippincott Company; Philadelphia, PA: 1995. p. 304
5. de Graaf P, Knol DL, Moll AC, Imhof SM, Schouten-van Meeteren AY, Castelijns JA. Eye size in retinoblastoma: MR imaging measurements in normal and affected eyes. Radiology 2007;244(1): 273–280. [PubMed: 17581906]
6. Bilaniuk LT, Schenck JF, Zimmerman RA, Hart HR Jr, Foster TH, Edelstein WA, Goldberg HI, Grossman RI. Ocular and orbital lesions: surface coil MR imaging. Radiology 1985;156(3):669–674. [PubMed: 4023227]
7. O'Brien JM. Retinoblastoma: clinical presentation and the role of neuroimaging. AJNR Am J Neuroradiol 2001;22(3):426–428. [PubMed: 11237961]
8. Wirtschafter, J.; Berman, E.; McDonald, C. Magnetic Resonance Imaging and Computed Tomography. Vol. 6. American Academy of Ophthalmology; San Francisco: 1992.
9. Schenck, JF.; Leue, W. Instrumentation: Magnets, coils, and hardware. In: Atlas, S., editor. Magnetic Imaging of the Brain and Spine. Raven Press; New York: 1991.
10. De Marco, J.; Bilaniuk, LT. Magnetic resonance imaging: Technical aspects. In: Newton, T.; Bilaniuk, LT., editors. Radiology of the Eye and Orbit. Vol. 4. Clavadel Press; San Anselmo, CA: 1990.
11. Schmalfuss IM, Dean CW, Sistrom C, Bhatti MT. Optic neuropathy secondary to cat scratch disease: distinguishing MR imaging features from other types of optic neuropathies. AJNR Am J Neuroradiol 2005;26(6):1310–1316. [PubMed: 15956488]
12. Bert RJ, Patz S, Ossiani M, Caruthers SD, Jara H, Krejza J, Freddo T. High-resolution MR imaging of the human eye 2005. Acad Radiol 2006;13(3):368–378. [PubMed: 16488850]

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

13. Georgouli T, James T, Tanner S, Shelley D, Nelson M, Chang B, Backhouse O, McGonagle D. High-Resolution Microscopy Coil MR-Eye. Eye. 2007
14. Albers GW, Lansberg MG, Norbash AM, Tong DC, O'Brien MW, Woolfenden AR, Marks MP, Moseley ME. Yield of diffusion-weighted MRI for detection of potentially relevant findings in stroke patients. Neurology 2000;54(8):1562–1567. [PubMed: 10762494]
15. Shen Q, Cheng H, Pardue MT, Chang TF, Nair G, Vo VT, Shonat RD, Duong TQ. Magnetic resonance imaging of tissue and vascular layers in the cat retina. J Magn Reson Imaging 2006;23(4):465–472. [PubMed: 16523482]
16. Villablanca P, Curran J, Arnold A, Lufkin R. Orbit and optic nerve. Top Magn Reson Imaging 1996;8(2):87–110. [PubMed: 8784966]
17. Greenfield DS, Siatkowski RM, Glaser JS, Schatz NJ, Parrish RK 2nd. The cupped disc. Who needs neuroimaging? Ophthalmology 1998;105(10):1866–1874. [PubMed: 9787356]
18. Ahmed II, Feldman F, Kucharczyk W, Trope GE. Neuroradiologic screening in normal-pressure glaucoma: study results and literature review. J Glaucoma 2002;11(4):279–286. [PubMed: 12169963]
19. Kashiwagi K, Okubo T, Tsukahara S. Association of magnetic resonance imaging of anterior optic pathway with glaucomatous visual field damage and optic disc cupping. J Glaucoma 2004;13 (3): 189–195. [PubMed: 15118461]
20. Tarver-Carr ME, Miller NR. Tilted optic discs visualized by magnetic resonance imaging. J Neuroophthalmol 2006;26(4):282–283. [PubMed: 17204924]
21. Pop-Fanea L, Vallespin SN, Hutchison JM, Forrester JV, Seton HC, Foster MA, Liversidge J. Evaluation of MRI for in vivo monitoring of retinal damage and detachment in experimental ocular inflammation. Magn Reson Med 2005;53(1):61–68. [PubMed: 15690503]
22. Mafee MF. Ocular manifestations of cat-scratch disease: role of MR imaging. AJNR Am J Neuroradiol 2005;26(6):1303–1304. [PubMed: 15956483]
23. Reddy AK, Morriss MC, Ostrow GI, Stass-Isern M, Olitsky SE, Lowe LH. Utility of MR imaging in cat-scratch neuroretinitis. Pediatr Radio 2007;37(8):840–843.
24. Cheng H, Nair G, Walker TA, Kim MK, Pardue MT, Thule PM, Olson DE, Duong TQ. Structural and functional MRI reveals multiple retinal layers. Proc Natl Acad Sci USA 2006;103(46):17525–17530. [PubMed: 17088544]
25. Duong TQ, Ngan SC, Ugurbil K, Kim SG. Functional magnetic resonance imaging of the retina. Invest Ophthalmol Vis Sci 2002;43 (4):1176–1181. [PubMed: 11923263]
26. Berkowitz BA, Roberts R, Goebel DJ, Luan H. Noninvasive and simultaneous imaging of layer-specific retinal functional adaptation by manganese-enhanced MRI. Invest Ophthalmol Vis Sci 2006;47(6):2668–2674. [PubMed: 16723485]
27. Ito Y, Berkowitz BA. MR studies of retinal oxygenation. Vision Res 2001;41(10–11):1307–1311. [PubMed: 11322975]
28. Trick GL, Berkowitz BA. Retinal oxygenation response and retinopathy. Prog Retin Eye Res 2005;24(2):259–274. [PubMed: 15610976]
29. Berkowitz BA, McDonald C, Ito Y, Tofts PS, Latif Z, Gross J. Measuring the human retinal oxygenation response to a hyperoxic challenge using MRI: eliminating blinking artifacts and demonstrating proof of concept. Magn Reson Med 2001;46(2):412–416. [PubMed: 11477648]
30. Bert RJ, Caruthers SD, Jara H, Krejza J, Melhem ER, Kolodny NH, Patz S, Freddo TF. Demonstration of an anterior diffusional pathway for solutes in the normal human eye with high spatial resolution contrast-enhanced dynamic MR imaging. Invest Ophthalmol Vis Sci 2006;47(12):5153–5162. [PubMed: 17122097]
31. Kim SH, Galban CJ, Lutz RJ, Dedrick RL, Csaky KG, Lizak MJ, Wang NS, Tansey G, Robinson MR. Assessment of subconjunctival and intrascleral drug delivery to the posterior segment using dynamic contrast-enhanced magnetic resonance imaging. Invest Ophthalmol Vis Sci 2007;48(2): 808–814. [PubMed: 17251481]
32. Metrikin DC, Wilson CA, Berkowitz BA, Lam MK, Wood GK, Peshock RM. Measurement of blood-retinal barrier breakdown in endotoxin-induced endophthalmitis. Invest Ophthalmol Vis Sci 1995;36(7):1361–1370. [PubMed: 7775114]

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

33. Wollstein G, Paunescu LA, Ko TH, Fujimoto JG, Kowalevicz A, Hartl I, Beaton S, Ishikawa H, Mattox C, Singh O, Duker J, Drexler W, Schuman JS. Ultrahigh-resolution optical coherence tomography in glaucoma. Ophthalmology 2005;112(2):229–237. [PubMed: 15691556]

34. Scheie, H.; Albert, DM., editors. Textbook of Ophthalmology. 9. W.B. Saunders Company; Philadelphia: 1977. p. 616