Three-dimensional High-Resolution Magnetic Resonance Imaging of Ocular and Orbital Malignancies

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Background: Ultrathin-section 3-dimensional fast spin-echo (3-D FSE) T2-weighted imaging is a new magnetic resonance imaging (MRI) technique that we used in the evaluation of ocular and orbital malignancies. We evaluated the usefulness of this new technique compared with conventional MRI.

Methods: Imaging data from 26 consecutive patients seen in the Ocular Oncology Unit at the University of California–San Francisco were retrospectively reviewed by physicians from the ocular oncology and neuroradiology units. For all patients, 3-D FSE T2-weighted images (27 scans) were compared with results of conventional MRI and correlated with results of computed tomography (CT), A- and B-scan ultrasonography, ultrasound biomicroscopy, clinical examinations, and histopathology, when available.

Results: The 3-D FSE T2-weighted imaging sequence resulted in an overall improvement in accuracy of imaging findings in 17 (63%) of our 27 cases compared with the standard MRI protocol. The increased resolution led to the radiographic detection of additional lesions in 11 (41%) of 27 cases and to an increase in confidence in radiographic diagnosis in 6 (22%) of the remaining cases. The improved resolution of the 3-D FSE T2-weighted sequence resulted in a change of disease management in 3 (60%) of the 5 patients with nonretinoblastoma lesions. One hundred percent of active retinoblastoma lesions could be detected by means of 3-D FSE and conventional imaging; however, inactive lesions were not always detected using conventional imaging.

Conclusions: The 3-D FSE T2-weighted sequence offers superior resolution of intraocular and orbital structures compared with conventional MRI. It is particularly useful in the evaluation of intraocular tumors and the nerve-sheath complex. This new technique contributes significantly to improved diagnosis and management in patients with ocular and orbital malignancies.

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NEUROIMAGING in ocular oncology plays an essential role in the accurate diagnosis of intraocular and orbital tumors. Increased use of globe-conserving therapies such as external beam radiation, brachytherapy, and chemoreduction with laser hyperthermia has led to an increased reliance on neuroimaging for diagnosis and monitoring of disease activity. Patients with intraocular tumors who have received radiation frequently develop cataracts that preclude visualization of the retina by indirect ophthalmoscopy. In these patients, we have traditionally relied on A- and B-scan ultrasonography to follow intraocular tumors. More recently, high-quality x-ray computed tomography (CT) and magnetic resonance imaging (MRI) have provided additional, complementary information.

In the management of retinoblastoma (Rb), MRI and CT are superior to ultrasonography in detecting orbital and optic nerve disease. Magnetic resonance or CT imaging is also required for the detection of trilateral Rb (primitive neuroectodermal tumors, or PNETs) and to define the extent of secondary orbital, head and neck, and central nervous system (CNS) malignancies. We routinely obtain thin-section (1 mm) axial unenhanced and enhanced CT scans for the initial evaluation of suspected Rb. This study provides excellent detection of intraocular calcification, narrows the differential diagnosis, and allows us to exclude a synchronous intracranial mass. We also routinely perform ophthalmic A- and B-scan ultrasonographic studies to document tumor heights and to further substantiate the presence of intraocular calcification. In straightforward cases, the initial CT scan is adequate to assess optic nerve involvement and to exclude CNS disease, although this study is less sensitive than MRI for these purposes.

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MATERIALS AND METHODS

The managing ocular oncologist (J.M.O.), in collaboration with the neuroradiology team, retrospectively reviewed 27 thin-section 3-D FSE MRI scans performed in conjunction with conventional MRI scans from 26 consecutive patients with known or suspected ophthalmic tumors (Rb, meningioma, choroidal metastasis, ciliary body melanoma, lymphoma, and lymphangioma). Two neuroradiologists (E.M.S. and N.J.F.), masked to diagnosis and clinical history, independently compared the findings on 3-D FSE T2-weighted images with those on conventional images gathered during the same imaging session.

Conventional MRI, performed in a standard head coil, included orbital imaging with sagittal, axial, and coronal T1-weighted images; axial and coronal fat-suppressed 2-D FSE T2-weighted images; and post-gadolinium fat-suppressed axial and coronal T1-weighted images. Slice thickness was 3 to 4 mm. When indicated (in all cases with the exception of a ciliary body melanoma and an orbital lymphangioma), whole-brain sections were added, including axial dual-echo spin-echo T2-weighted and post-gadolinium axial and sagittal T1-weighted images.

The thin-section 3-D FSE T2-weighted sequence was also performed in the head coil, with a typical effective slice thickness of 0.4 mm, matrix of 256 × 256, and field of view of 18 cm. A fat-suppression pulse was added without a time penalty. The high resolution was achieved by the addition of zeros to each end of the data set before performing the Fourier transform required to produce the images. This zero filling allows for a doubling in the number of data points that pass through the reconstruction process, thereby achieving, in effect, twice as many slices from the original volume of data (Figure 1). The slices are partially overlapped, which increases the signal-to-noise ratio and provides high-quality submillimeter slices. This technique is similar to that currently used for MR angiography.10,11

The MRI findings on conventional and 3-D FSE T2-weighted studies were correlated with results of CT, A- and B-scan ultrasonography, ultrasound biomicroscopy, clinical examination, and histopathology when available. In addition, the ocular oncologist (J.M.O.) retrospectively assessed the impact of the 3-D FSE T2-weighted findings on patient management.

In patients with Rb in whom CT or ultrasonographic studies suggest optic nerve extension of disease, or when superior CNS imaging is mandated by advanced disease at presentation, we also routinely obtain an MRI scan of the brain and orbits with contrast. Orbital T2-weighted MRI of the eye with fast spin-echo (FSE) and surface coils improves image resolution compared with conventional T2-weighted imaging,3 and this represents the standard of care at many institutions. Despite this improved resolution, lesions less than 2 mm thick cannot be recognized with confidence by MRI technology, even with surface coils.6,7 In addition, the use of surface coils may impair the assessment of deep but important adjacent structures such as the orbital apex and the intracanalicular orbital nerve,8 and surface coils may exacerbate motion and chemical-shift artifacts.9 Surface coils require additional time and technologist expertise for proper positioning and setup. Their use also requires purchase of separate, dedicated coils and an interruption of the imaging session to transition from surface coil to head coil for whole-brain imaging, which is indicated in patients with Rb to exclude concomitant PNETs. Coil placement results in increased anesthesia time and additional expense for these children.

For these practical reasons, we have focused on improving the quality of ocular/orbital imaging that can be performed using a standard volumetric head coil. For T2-weighted imaging, we previously acquired 2-dimensional (2-D) FSE T2-weighted images in the coronal plane with fat saturation, as fat remains bright on FSE T2-weighted sequences. Recently, we evaluated an ultrathin-section 3-dimensional (3-D) FSE T2-weighted sequence. This technique uses a modification of current 3-D FSE imaging by adding another interpolation step during data processing, which greatly improves spatial resolution. We believe the ability to obtain submillimeter sections and to reformat this volumetrically acquired data in 3 dimensions provides superior delineation of intraocular and orbital tumors and contributes to more accurate diagnosis.

RESULTS

The 3-D FSE T2-weighted sequence resulted in an overall improvement in accuracy of findings in 17 (63%) of our 27 cases (Table). The increased resolution led to the radiographic detection of additional lesions in 11 (41%) of our 27 studies. These additional lesions usually represented previously treated sites of Rb in regression (Figure 2); however, the confirmation of a second contralateral lesion in a patient with a non-Rb lesion that was not visualized by clinical examination or conventional imaging led to a change in management (Table; bilateral metastatic adenocarcinoma).

Of the remaining cases, the neuroradiologists noted an increased confidence in anatomic detail and lesion conspicuity in 6 scans (22%), which resulted in a change in management in 2 of these cases (Table; lymphangioma and orbital lymphoma). Overall, management was changed in 3 (60%) of 5 non-Rb cases. Of the active Rb
lesions, 100% could be detected by means of 3-D FSE T2-weighted and conventional imaging; however, inactive lesions were not always detected using conventional imaging. No change in radiographic diagnosis or confidence resulted in 10 (37%) of the 27 scans. Superior resolution compared with conventional imaging sequences was achieved in all but 2 scans, in which motion degradation occurred in 2 awake adults.

Specifically, 3-D FSE T2-weighted scanning was superior to more traditional MRI in the following respects:

1. Increased resolution of normal intraocular structures and intraocular tumors was evident, particularly for those tumors that were small, low-lying, or previously treated. This finding had particular clinical importance in this series in patients with media opacities due to cataract or vitreous hemorrhage, in which indirect ophthalmoscopy was less sensitive. These studies provided verification of findings obtained on A- and B-scan ultrasonography.

2. Increased resolution and improved delineation of the optic nerve–dural sheath complex and associated cerebrospinal fluid space, as well as of normal orbital structures, were found. For example, after enucleation, atrophic optic nerves were extremely well delineated, with 3-D FSE T2-weighted imaging demonstrating decreased nerve size, increased nerve signal, and prominence of the surrounding cerebrospinal fluid space. Although no patients with extraocular extension confirmed by histopathology were part of this study, our experience suggests that the 3-D FSE sequence with fat saturation has the potential to improve resolution of optic nerve extension in patients with Rb. This imaging approach also allowed better characterization of orbital tumors compared with conventional MRI.

3. The 3-D data set offers the opportunity to perform multiplanar reformations of data with no stair-step artifacts or penalty in terms of resolution.

4. Improved resolution of intracranial structures was achieved, compared with conventional 2-D FSE T2-weighted images.

We found a few limitations of 3-D FSE T2-weighted imaging compared with conventional imaging that should be noted. First, 3-D FSE imaging is more susceptible to motion, phase, and pulsation artifacts. Second, 3-D FSE imaging involves a longer acquisition time (9-11 minutes) compared with conventional 2-D FSE imaging (4-5 minutes). Both sequences are compatible with and should be performed with fat saturation. Third, less coverage can be achieved in a reasonable duration when 3-D FSE is used compared with 2-D FSE. Therefore, for example, the pineal region was not included on all of our 3-D FSE studies. In all patients, conventional MRI of the pineal region was completed.

**COMMENT**

The 3-D FSE T2-weighted sequence offers a new approach to ocular and orbital MRI that uses ultrathin slices to achieve superior image resolution. The potential to perform multiplanar reformations to assist in clinical interpretation is a unique feature of this technique that may contribute to the superior assessment of intraocular and orbital structures. The 3-D FSE technique provides improved resolution compared with conventional head-coil 2-D FSE T2-weighted imaging with fat saturation without a requirement for surface coils. We expect this technique could be easily implemented by other centers.

**RETINOBLASTOMA**

Because of the increasing use of eye-conserving treatments, neuroimaging has assumed greater importance in the management of Rb in children.12 In many cases, histopathologic examination is never performed.12 Neuroimaging is therefore important in the initial diagnosis and staging of the disease as well as in the continued care and follow-up of these patients, who are subject to multiple intraocular recurrences throughout the first 6 years of life.13 Second primary tumors, PNETs within the CNS, also develop at an early age in up to 10% of patients with bilateral Rb,14,15 and a recent description of successful treatment for trilateral disease suggests that screening with improved detection is of increasing importance.16 Older children are subject to additional second tumors, primarily sarcomas within the orbital radiation field.13,14 The use of free flaps after orbital exenteration for these dis-

<table>
<thead>
<tr>
<th>Contribution of 3-D FSE T2-Weighted Imaging*</th>
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<tr>
<td><strong>Ophthalmic Diagnosis</strong></td>
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<tr>
<td>(No. of Scans)</td>
</tr>
<tr>
<td>Rb (21)</td>
</tr>
<tr>
<td>Unilateral (7)</td>
</tr>
<tr>
<td>Bilateral (14)</td>
</tr>
<tr>
<td>Mimicking lesions (1)</td>
</tr>
<tr>
<td>PHPV (1)</td>
</tr>
<tr>
<td>Other neoplasms (5)</td>
</tr>
<tr>
<td>Meningioma (1)</td>
</tr>
<tr>
<td>Retinal metastases (1)</td>
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<td>Ciliary body melanoma (1)</td>
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<tr>
<td>Orbital lymphoma (1)</td>
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<tr>
<td>Lymphangioma (1)</td>
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<tr>
<td>All (27)</td>
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*3-D FSE indicates 3-dimensional fast spin-echo; Rb, retinoblastoma; and PHPV, persistent hyperplastic primary vitreous.

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ease processes makes improved resolution imperative to diagnose subclinical disease recurrence.

Although A- and B-scan ultrasonography plays an important role in the management of intraocular Rb, the presence of massive intraocular calcification can impede visualization of the optic nerve and orbit, making evaluation of these structures more difficult. In these cases, it is essential to obtain additional information through the use of neuroimaging. To confirm the initial diagnosis, we obtain a CT scan for documentation of intraocular calcification. For subsequent evaluations, we believe that MRI is useful to exclude optic nerve disease, to evaluate for orbital and intracranial extension, and to exclude the possibility of PNETs. We follow children with low-stage Rb routinely every 6 months with MRI, including 3-D FSE T2-weighted imaging, and we believe this technique reliably surveys for the development of PNETs. Children with high-stage disease at presentation are followed more frequently with neuroimaging to evaluate the optic nerve and orbit and to assess the CNS for relapse.

Three-dimensional FSE T2-weighted technology is particularly useful in the evaluation of intraocular tumors in patients with opaque media limiting indirect ophthalmoscopy. This is especially important in children treated with external beam radiation, because cataracts almost invariably develop in these patients. In the setting of cataract, ultrasonography is required to visualize tumors, to evaluate for tumor growth, and to assess tumor activity. We find that 3-D FSE T2-weighted MRI very accurately evaluates tumor size and is useful as an adjunct to ultrasonographic measurements in patients with massive disease at presentation and extensive calcification, which is highly reflective and results in shadowing of the orbit and optic nerve.

Magnetic resonance imaging is most useful in children with advanced Rb, in which optic nerve and orbital extension significantly affect treatment planning and prognosis. We presently perform preenucleation chemoreduction in patients with orbital extension to avoid exenteration. After 2 to 3 cycles of chemoreduction, we repeat neuroimaging studies and perform orbital biopsies.
The increased resolution of intraocular structures with 3-D compared with 2-D FSE T2-weighted imaging has the potential to improve diagnosis of choroidal invasion and optic nerve extension. Optic nerve extension and massive choroidal invasion are associated with significant morbidity and mortality. This technique, then, has immediate clinical implications for those patients who are candidates for ocular conservation, as they may require adjuvant chemotherapy for increased survival. No patients with histopathologically confirmed risk factors were available to include in this series, limiting our certainty that these processes can be reliably diagnosed by any currently available imaging technique.

Despite its superior resolution compared with conventional 2-D FSE T2-weighted imaging, 3-D FSE T2-weighted imaging does not necessarily provide a clear advantage in the evaluation of intracranial structures. This is largely due to the relatively limited anatomic coverage available when using standard scan times. We generally rely most heavily on post-gadolinium T1-weighted sequences to detect intracranial extension, metastatic foci, and trilateral disease.

**PERSISTENT HYPERPLASTIC PRIMARY VITREOUS**

In patients referred with leukocoria, the possibility that the child has a lesion that can mimic Rb, such as persistent hyperplastic primary vitreous (PHPV) or Coats’ disease, should receive serious consideration in the initial diagnosis and management. Intraocular biopsy is contraindicated in children with a potential diagnosis of Rb because of the possibility that the tumor can spread along the needle track, and because increased mortality is associated with extraocular disease. These children must, therefore, undergo evaluation using indirect diagnostic approaches. In this series, a patient with bilateral PHPV and dystrophic calcification was followed using A- and B-scan ultrasonography and 3-D FSE MRI. A subretinal hemorrhage that evolved over time was documented. The 3-D FSE data increased our confidence in the diagnosis of PHPV, as the persistent tunica vasculosa lentis was well defined, the globes were confirmed to be small, and no mass developed over serial observation (Figure 4).

**OTHER NEOPLASMS**

Any ocular oncology service will evaluate many patients with other neoplasms, including choroidal melanoma, choroidal metastases, meningiomas of the optic nerve, and a variety of orbital masses. In this series, we obtained useful information in patients with non-Rb intraocular and orbital malignancies. Superior resolution of these lesions enhanced our ability to make accurate diagnoses and to provide immediate treatment planning.

For example, in an elderly man, the MRI appearance of a right lateral orbital mass, associated with proptosis and medial displacement of the right lateral rectus and superior rectus, was most compatible with lympho-
phoma (Figure 5). The increased confidence in anatomic detail provided by 3-D FSE T2-weighted imaging favored this diagnosis and demonstrated that CT-guided needle biopsy could be safely performed. The patient, who was in poor health, was spared an open surgical orbital biopsy, and treatment was expedited.

In addition, 3-D FSE T2-weighted data changed the management of a right orbital mass in a child. Improved visualization of a cystic mass with internal septations and fluid-fluid levels only apparent on 3-D FSE T2-weighted findings favored a diagnosis of a venolymphatic malformation and obviated the need for open biopsy (Figure 6).

Finally, 3-D FSE T2-weighted imaging confirmed an additional lesion in the contralateral eye of a patient who was thought to have metastatic disease rather than a primary process, e.g., a hemorrhagic retinal detachment or melanoma. Indirect ophthalmoscopy was limited in the second eye by a dense cataract, an inability to dilate, and patient disability. The detection of bilateral disease favored a metastatic process and led to a search for a primary lesion. A CT-guided biopsy of an abdominal mass on the day of presentation subsequently led to the diagnosis of metastatic adenocarcinoma of an unknown primary lesion and expedited ocular radiation therapy.

The 3-D FSE T2-weighted technique was comparable to conventional imaging in the evaluation of a ciliary body melanoma. The pigmented mass was not well resolved by 3-D FSE T2-weighted imaging, conventional MRI, or A- and B-scan ultrasonography. However, ultrasound biomicroscopy accurately demonstrated the melanoma in the ciliary body (Figure 7). The efficacy of ultrasound biomicroscopy...
for the resolution of tumor margins in ciliary body and anterior uveal melanoma is supported by a recent study at our institution and is an additional tool for the evaluation of potentially subtle anterior intraocular masses.

**CONCLUSIONS**

This initial retrospective review of 3-D FSE T2-weighted technology suggests that this MRI sequence provides significant additional information to the treating ophthalmologist in patients with intraocular and orbital malignancies. This technology provides information that is not currently available by means of ultrasonography or CT scanning, as well as providing improved information compared with conventional MRI sequences. We believe that 3-D FSE T2-weighted technology represents a significant step forward in the diagnosis and management of such tumors, particularly with the increasing use of eye-conserving measures.

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**REFERENCES**

10. Du YP, Parker DL, Davis WL, Cao G. Reduction of partial-volume artifacts with...
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