Human Immunodeficiency Virus (HIV)

Magnetic resonance imaging (MRI) for the evaluation of patients infected with human immunodeficiency virus (HIV), as with most other forms of intracranial inflammatory or infectious diseases, is a powerful though largely nonspecific diagnostic tool. For imaging of these complex patients with the varied and numerous pathologies they may harbor, the Basic Protocol presented in *UNIT A4.1* is utilized to include gadolinium-enhanced sequences. Several optional imaging sequences, to include magnetic resonance diffusion (dMRI), magnetic resonance perfusion (pMRI), and magnetic resonance spectroscopy (MRS) are outlined, which can be employed should patient tolerance allow and if specific clinical situations exist to be further clarified. The parameters given here are derived from experience at 1.5 T and may need to be altered slightly depending on the field strength available and the specific equipment manufacturer.

IMAGING OF HIV

BASIC PROTOCOL

This protocol presents the authors routine MR head examination for patients with intracranial inflammatory disease, with gadolinium contrast agent sequences. The total number of sequences presented is seven (scout, T_1-weighted sagittal and transverse, fluid-attenuated inversion recover (FLAIR) and fast spin-echo (FSE) T_2-weighted transverse, and post-contrast T_1-weighted transverse and coronal). This examination may be shortened considerably by limiting the use of two planes for post-contrast imaging to a single transverse plane for exams with a lower clinical suspicion for disease, or if review of the images obtained through the transverse gadolinium-enhanced images proves unremarkable. The sequences described herein are based on the authors' experience with a Marconi Medical Systems 1.5-T scanner, but are expected to be equally applicable to machines from other manufacturers. The authors utilize the same basic scanning protocol to image HIV patients as that for other cerebral inflammatory conditions (*UNIT A4.1*), which follows below.

Table A4.3.1 lists the hardware necessary to perform the examination, along with appropriate parameters.

NOTE: Be sure that technologists and nurses have immediate access to any emergency equipment that may be relevant to a given study, or that may be needed for a particular patient, such as a crash cart or oxygen. Also ensure only magnetic field compatible oxygen tanks are utilized if wall-source oxygen is unavailable.

Materials

Extravascular contrast agent (e.g., 0.1 mmol/kg patient body weight of gadolinium chelate from Mangevist, Omniscan, or Prohance)
Normal saline (0.9% NaCl) sterile

Table A4.3.1 Equipment Parameters for Contrast-Enhanced Head Imaging Sequences

Coil type	Head
Gradient coil strength	25 mT/m (or whatever the system permits)
Gating (cardiac, respiratory, peripheral)	No
Respirator or oxygen	If required by patient
Motion cushions	Recommended
Contrast agents	Yes

Contributed by Andrew E. Auber and Clifford Belden
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Set up patient and equipment

1. Interview (screen) the patient to ensure that he/she has no contraindication for MR scanning such as cardiac pacemaker or other implants containing ferromagnetic materials. Also be sure to find out if the patient has any health conditions that may require the presence of special emergency equipment during the scanning procedure, or that necessitate other special precautions.

   Generally standard screening forms are used for all patients scanned in a magnetic resonance system.

   The presence of any ferromagnetic metals may be a health hazard to the patient when he or she is inside the magnet, and will also affect the imaging. If in doubt as to the exact composition of the items, it is best to exclude patients with any metal implants; see Shellock (1996) for discussion of what implants may be safely scanned using magnetic resonance.

   Patients may be accompanied into the magnet room by a friend or family member, who can sit in the room during the scan and comfort the patient as needed. This companion must be screened as well to ensure the absence of loose metal objects on the body or clothing.

2. If the procedure is a research protocol, have the patient sign any necessary consent form.

3. Have the patient remove all jewelry and change into a gown to eliminate any metal that might be found in clothing.

4. Have the patient remove any mascara or other metal-containing makeup to avoid local tissue heating and image artifacts.

5. Inform the patient about what will occur during the procedure, what he/she will experience while in the magnet, and how to behave, to include the following:

   a. If earphones/headphones are used to protect the ears from loud sounds produced by the scanner, the patient will be asked to wear these, but will be able to communicate with the technologist at any/all times during the procedure.

   b. The patient will be given a safety squeeze-bulb or similar equipment to request assistance at any time (demonstrate how this equipment works).

   c. For optimum results the patient should not talk, and should avoid/minimize swallowing or other movement during each scan, i.e., as long as the banging sounds continue. Between scans, talking and swallowing are allowed in most cases, but should be avoided when comparative positional studies are being performed. The patient will be informed in these instances.

   d. Nevertheless, the patient may call out at any time if he/she feels it necessary.

6. Have the patient lay supine on the scanner table. Either before or directly after the patient is positioned on the table, set up any triggering devices or other monitoring equipment necessary.

7. Establish an intravenous (i.v.) line through which the contrast agent can be injected, and attach this line securely to the patient so that movement into or out of the magnet will not pull at the patient's arm. It is preferable to insert the line prior to imaging. This allows no intervening motion between those scans performed before and those run after the contrast agent injection.

8. Center the patient in the head coil. Make sure that the head and neck are constrained to prevent unnecessary motion, especially if high-resolution scans are to be run.

9. If needed, place a pillow or other support under the knees to make the patient more comfortable.

10. Use the centering light to center on the nasion of the patient and place them into the center of the magnet.

    Once this step has been performed, so long as the patient does not move on the table, the table itself can be moved and then replaced in the same position as before without jeopardizing the positioning of one scan relative to another.

11. If the patient is unable to hold still, either provide an appropriate sedative, or arrange with anesthesiology for conscious or general anesthesia.

    Alternatively, a low-field open magnet may be sought for scanning the claustrophobic patient. There are also fast scanning techniques that may be employed for imaging of these patients (see Chapter A5).

12. This Basic Protocol can be performed in <30 min.

Sequence 1: Rapid three-plane pilot

13. Run the three-plane pilot (Table A4.3.2) sequence to evaluate the patient positioning in the magnet.

14. This sequence runs in <10 sec and is used to position the remainder of the sequences. It is particularly useful to correct off-axis positioning in the coronal plane.

Sequence 2: T_1-sagittal head

15. This sequence serves as a true T_1-weighted sagittal study of the head. Bring the sequence for a sagittal T_1-weighted scan up onto the console and utilize the parameters in Table A4.3.3.

16. Use the pilot sequence to set up the scan levels.

17. Let the patient know you are ready, and begin the scan.

Table A4.3.2 Primary Clinical Imaging Parameters for Sequence 1: Rapid Three-Plane Pilot

Patient position	Supine
Scan type	Gradient echo
Imaging plane (orientation)	Sagittal, transverse, and coronal
Central slice or volume center	Midline head
Echo time (T_E)	3.7 msec
Repeat time (T_R)	16 msec
Flip angle (FA)	20°
Fields of view (FOV_x, FOV_y)	300 mm, 300 mm
Resolution (Δx, Δy)	2.34 mm, 2.34 mm
Number of data points collected (N_x, N_y)	128, 128
Display matrix (D_x, D_y)	256, 256
Slice thickness (Δz)	10 mm
Number of slices	3
Slice gap	NA
Number of acquisitions (N_{acq})	1
Read direction	Left–right
Slice locations	At isocenter, 3 orthogonal planes
Saturation pulses	None
RAM[a]	2X
Scan time	6 sec

[a]Zero padded from 128 by 128 points to 256 by 256 points.

Sequence 3: T_1-transverse head

18. Bring the sequence for a transverse T_1-weighted scan up onto the console. Set the imaging parameters as shown in Table A4.3.4.
19. Use the pilot sequence to set up the scan levels.
20. Let the patient know you are ready, and begin the scan.

Table A4.3.3 Primary Clinical Imaging Parameters for Sequence 2: T_1-Sagittal Head

Patient position	Supine
Scan type	Spin echo
Imaging plane (orientation)	Sagittal
Central slice or volume center	Midline head
Echo time (T_E)	12 msec
Repeat time (T_R)	300 msec
Flip angle (FA)	90°
Fields of view (FOV_x, FOV_y)	240 mm, 240 mm
Resolution (Δx, Δy)	1.25 mm, 0.94 mm
Number of data points collected (N_x, N_y)	192, 256
Display matrix (D_x, D_y)	256, 256
Slice thickness (Δz)	4 mm
Number of slices	15
Slice gap	1 mm
Number of acquisitions (N_{acq})	1
Read direction	Superior–inferior
Slice locations	Cover brain parenchyma
Saturation pulses	None
Scan time	1 min, 55 sec

Table A4.3.4 Primary Clinical Imaging Parameters for Sequence 3: T_1-Transverse Head

Patient position	Supine
Scan type	Spin echo
Imaging plane (orientation)	Transverse (planum sphenoidale line)
Central slice or volume center	Mid-cranium
Echo time (T_E)	12.1 msec
Repeat time (T_R)	500 msec
Flip angle (FA)	90°
Fields of view (FOV_x, FOV_y)	240 mm, 180 mm
Resolution (Δx, Δy)	0.94 mm, 0.94 mm
Number of data points collected (N_x, N_y)	256, 192
Display matrix (D_x, D_y)	256, 256
Slice thickness (Δz)	5 mm
Number of slices	24
Slice gap	1 mm
Number of acquisitions (N_{acq})	2
Read direction	Anterior–posterior
Slice locations	Foramen magnum to vertex
Saturation pulses	None
Scan time	2 min, 36 sec

Sequence 4: FLAIR transverse head

21. Bring the sequence for a transverse FLAIR scan up onto the console. Set the imaging parameters as shown in Table A4.3.5.
22. Use the pilot sequence to set up the scan levels and a caudal saturation pulse.
23. Let the patient know you are ready, and begin the scan.

Sequence 5: FSE transverse head

24. Bring the sequence for a transverse FSE scan up onto the console. Set the imaging parameters as shown in Table A4.3.6.
25. Use the pilot sequence to set up the scan levels.
26. Let the patient know you are ready, and begin the scan.

Sequence 6: T_1-transverse post-gadolinium head

27. Bring the sequence for a transverse T_1-weighted scan up onto the console. Set the imaging parameters as shown in Table A4.3.7.
28. Use the pilot sequence to set up the scan levels.
29. Leaving the patient in the magnet, inject the contrast agent. This may be by either hand or by a mechanical injector. Observe the injection to insure there is no extravasation of the contrast agent. Flush the line with 10 ml of sterile normal saline. The scan may begin as soon as the injection is completed.

    Alternatively, the scanning table may be advanced out of the magnet for the injection, but the patient must remain in place.

    A dose of 0.1 mmol/kg of contrast agent is usually given.

    This is essentially the same sequence as the pre-gadolinium scan, but can be performed with the addition of a flow compensation (FC) pulse to better delineate the cerebral vessels, and a magnetization transfer (MT) pulse to optimize enhancing lesion detection.

Table A4.3.5 Primary Clinical Imaging Parameters for Sequence 4: FLAIR Transverse Head

Patient position	Supine
Scan type	FLAIR-FSE
Imaging plane (orientation)	Transverse (parallel to AC-PC line)
Central slice or volume center	Mid-cranium
Echo time (T_E)	125 msec (effective)
Echo train length (ETL)	Fixed (generally 12)
Repeat time (T_R)	6000 msec
Inversion time (T_I)	1900 msec
Flip angle (FA)	180°
Fields of view (FOV_x, FOV_y)	240 mm, 197 mm
Resolution (Δx, Δy)	0.94 mm, 0.87 mm
Number of data points collected (N_x, N_y)	256, 204
Display matrix (D_x, D_y)	256, 256
Slice thickness (Δz)	5 mm
Number of slices	24
Slice gap	1 mm
Number of acquisitions (N_{acq})	1
Read direction	Anterior–posterior
Slice locations	Foramen magnum to vertex
Saturation pulses	Caudal to saturate arterial flow
Scan time	2 min, 48 sec

Table A4.3.6 Primary Clinical Imaging Parameters for Sequence 5: FSE Transverse Head

Patient position	Supine
Scan type	Fast spin echo (FSE)
Imaging plane (orientation)	Transverse (planum sphenoidale line)
Central slice or volume center	Mid-cranium
Echo time (T_E)	105 msec (effective)
Echo train length (ETL)	16
Repeat time (T_R)	5616 msec
Flip angle (FA)	90°
Fields of view (FOV_x, FOV_y)	240 mm, 180 mm
Resolution (Δx, Δy)	0.63 mm, 0.70 mm
Number of data points collected (N_x, N_y)	384, 256
Display matrix (D_x, D_y)	384, 384
Slice thickness (Δz)	5 mm
Number of slices	24
Slice gap	1 mm
Number of acquisitions (N_{acq})	2
Read direction	Anterior–posterior
Slice locations	Foramen magnum to vertex
Saturation pulses	Caudal to saturate arterial flow
Scan time	3 min, 22 sec

Table A4.3.7 Primary Clinical Imaging Parameters for Sequence 6: T_1-Transverse Post-Gadolinium Head

Patient position	Supine
Scan type	Spin echo
Imaging plane (orientation)	Transverse (planum sphenoidale line)
Central slice or volume center	Mid-cranium
Echo time (T_E)	12.1 msec
Repeat time (T_R)	500 msec
Flip angle (FA)	90°
Fields of view (FOV_x, FOV_y)	240 mm, 180 mm
Resolution (Δx, Δy)	0.94 mm, 0.94 mm
Number of data points collected (N_x, N_y)	256, 192
Display matrix (D_x, D_y)	256, 256
Slice thickness (Δz)	5 mm
Number of slices	24
Slice gap	1 mm
Number of acquisitions (N_{acq})	2
Read direction	Anterior–posterior
Slice locations	Foramen magnum to vertex
Saturation pulses	None
Scan time	2 min, 36 sec

Table A4.3.8 Primary Clinical Imaging Parameters for Sequence 7: T_1-Coronal Post-Gadolinium Head

Patient position	Supine
Scan type	Spin echo
Imaging plane (orientation)	Coronal (perpendicular to planum sphenoidale line)
Central slice or volume center	Mid-cranium
Echo time (T_E)	12.1 msec
Repeat time (T_R)	500 msec
Flip angle (FA)	90°
Fields of view (FOV_x, FOV_y)	220 mm, 178 mm
Resolution (Δx, Δy)	0.86 mm, 0.93 mm
Number of data points collected (N_x, N_y)	256, 192
Display matrix (D_x, D_y)	256, 256
Slice thickness (Δz)	5 mm
Number of slices	24
Slice gap	1 mm
Number of acquisitions (N_{acq})	2
Read direction	Superior–inferior
Slice locations	Frontal to occipital cerebral poles
Saturation pulses	None
Scan time	2 min, 36 sec

Sequence 7: T_1-coronal post-gadolinium head

30. Bring the sequence for a T_1-weighted scan up onto the console. Set the imaging parameters as shown in Table A4.3.8.
31. Use the pilot sequence to set up the scan levels.
32. Let the patient know you are ready, and begin the scan.

Small abscesses may be much better delineated with a smaller field of view (FOV; e.g., FOV_x = 200 mm, FOV_y = 150 mm) and higher resolution thinner slice thickness (e.g., 3 mm). Please note that this modification should be performed with one acquisition, and limited to the area of abnormality to avoid prolonged scan times.

When scanning pediatric patients (under 24 months) modify the transverse and coronal sequences by placing the FOV at 200 mm, and the slice thickness and gap at 4 mm and 1 mm, respectively. For neonates, premature infants, and other extremely small patients an extremity coil may be used.

This sequence may be performed with the addition of a flow compensation (FC) pulse to better delineate the cerebral vessels, and a magnetization transfer (MT) pulse to optimize enhancing lesion detection.

SPECIAL SITUATIONS

ALTERNATE PROTOCOL

The three sequences that follow (gradient echo; 3-dimensional gradient echo post-gadolinium; magnetic resonance angiogram or venogram) are presented here for consideration by the radiologist in those patients suspected of significant intracranial HIV-related inflammatory conditions for whom the Basic Protocol has failed to elucidate a clearly defined abnormality. These patients can suffer intracranial lesional hemorrhage, for which the gradient echo sequence is extremely useful for demonstrating microhemorrhage. This can produce not only the helpful diagnostic clue of a hemorrhagic lesion but may well bring other lesions to the attention of the radiologist. This may in turn impact upon patient

prognosis, or guide more effective follow-up imaging. The second optional sequence (3-dimensional gradient echo post-contrast) is usually reserved for higher resolution of small lesions or adjacent structures that may be affected by the pathology. It can also be an effective aid in operative planning, and may indeed serve as the base MRI sequence for several of the commercially available image-guided surgery tools presently on the market and utilized by many neurosurgeons. This sequence can be utilized in lieu of the transverse and coronal post-gadolinium sequences outlined in the Basic Protocol, if desired. It is easily manipulated in post-processing to yield a desired projection of a lesion, or simply to give a multiplanar assessment of the brain in a given patient. Magnetic resonance angiography or venography can aid in detection of an associated (inflammatory) angiitis, most often manifest in the HIV patient as venous thrombosis. Gadolinium administration may disclose such abnormalities more effectively, as it provides greater signal-to-noise within the vascular tree. This improves conspicuity of subtle findings in the larger vessels and increases visibility of the smaller vascular structures.

Set up patient and equipment

1. Use the same equipment and the same patient set-up as for the previous method (see Basic Protocol, steps 1 to 11).
2. Run the pilot scan as sequence 1 in the Basic Protocol.

Sequence 8: Coronal gradient echo (head)

3. Bring the sequence for a gradient echo scan up onto the console. Set the imaging parameters as shown in Table A4.3.9.
4. Use the pilot sequence to set up the scan levels.
5. Let the patient know you are ready, and begin the scan.

Sequence 9: 3-Dimensional post-gadolinium transverse gradient echo (head)

6. Repeat step 29 in the Basic Protocol.
7. This sequence is often employed when scanning patients with HIV and may do so in lieu of the routine post-contrast 2-D transverse and coronal spin echo sequences described in the Basic Protocol, or when surgery is contemplated. It can be used to better delineate smaller lesions and can be reformatted into any desired plane as it is a volume-acquired sequence performed with high resolution parameters as described in Table A.4.3.10.
8. This scan generates 120 images as a whole brain study, but higher resolution image sets with 32 or 64 images, with a resolution as low as 1 mm can be produced, but may be restrictive in area of coverage.
9. Planar reformations of the 3-D data set can be performed on- or off-line using the reformation software. One can coordinate with the neurosurgeon to obtain the most useful projections, which can then be saved and/or filmed.
10. Note that the cerebral vasculature is quite bright on this sequence as this 3-D gradient echo sequence is the base-sequence for time-of-flight (TOF) magnetic resonance angiography (MRA).

Sequence 10: Magnetic resonance angiography (MRA) and venography (MRV)

11. These sequences may be employed when the specific history provided for a patient suggests possible arterial or venous pathology, or if review of the spin echo images indicates this possibility. MRV is routinely employed when evaluating patients with suspected meningitis, but will usually reserve the use of MRA to those patients

Table A4.3.9 Primary Clinical Imaging Parameters for Sequence 8: Coronal Gradient Echo (Head)

Patient position	Supine
Scan type	2-D gradient echo
Imaging plane (orientation)	Coronal
Central slice or volume center	Mid-cranium
Echo time (T_E)	24.6 msec
Repeat time (T_R)	719 msec
Flip angle (FA)	25°
Fields of view (FOV_x, FOV_y)	220 mm, 220 mm
Resolution (Δx, Δy)	0.86 mm, 1.15 mm
Number of data points collected (N_x, N_y)	256, 192
Display matrix (D_x, D_y)	256, 256
Slice thickness (Δz)	5 mm
Number of slices	21
Slice gap	1 mm
Number of acquisitions (N_{acq})	2
Read direction	Superior–inferior
Slice locations	Frontal to occipital cerebral poles
Saturation pulses	None
Scan time	4 min, 36 sec

Table A4.3.10 Primary Clinical Imaging Parameters for Sequence 9: 3-D Post-Gadolinium Transverse Gradient Echo (Head)

Patient position	Supine
Scan type	3-D gradient echo
Imaging plane (orientation)	Transverse (option sagittal, or coronal)
Central slice or volume center	Mid-cranium for whole brain, or area of abnormality
Echo time (T_E)	5 msec
Repeat time (T_R)	11.2 msec (or minimum)
Flip angle (FA)	35°
Fields of view (FOV_x, FOV_y)	240 mm, 187 mm
Resolution (Δx, Δy)	0.94 mm, 0.97 mm
Number of data points collected (N_x, N_y)	256, 192
Display matrix (D_x, D_y)	256, 256
Slice thickness (Δz)	1.2 mm
Number of slices	120
Slice gap	0 mm
Number of acquisitions (N_{acq})	1
Read direction	Anterior–posterior, if imaging plane is transverse
Slice locations	Whole brain
No phase wrap (NPW)[a]	Yes
Saturation pulses	NA
Scan time	4 min, 19 sec

[a]Phase oversampling or anti-alrasing.

demonstrating concerning arterial findings on spin echo images, or with suspicious hemorrhage noted. The reader is referred to the scanning parameters outlined for these sequences in Chapter A1 of this series.

COMMENTARY

Background Information

Human immunodeficiency virus (HIV) is the virus responsible for the AIDS epidemic. In the United States, an estimated 650,000 to 900,000 people are infected with HIV, and >200,000 of these individuals are unaware of their infection (Fauci, 1999; Wong and Quint, 1999). There are 40,000 new infections per year with the infection rate in heterosexuals, and especially women, accelerating greatly in the 1990s. Worldwide in 1998 there were >33 million people worldwide with HIV infection and AIDS was listed as the fourth leading cause of death, with an estimated number of 2.3 million. However, the age-adjusted death rate from AIDS in the United States declined 48% from 1996 to 1997. This improvement in the death rate is multifactorial in origin, but largely the result of new treatment advances, in particular the development of highly active antiretroviral therapy (HAART). These developments underscore the need for early and accurate diagnosis and follow-up of these challenging patients. There remain subsets of pathologies in the AIDS population that are refractory to treatment at this time. Chief among these is progressive multifocal leukoencephalopathy (PML). This fulminant opportunistic central nervous system (CNS) infection occurs in 4% of AIDS patients and is caused by the Jakob-Creutzfeldt (JC) papovavirus (JCV). It carries a mean survival of 2.5 to 4 months from the time of diagnosis. Whereas brain biopsy was previously the mainstay for the diagnosis of PML, recent advances in cerebrospinal fluid (CSF) analysis (>92% specific for JCV) when coupled with typical MR changes of the disease and a clinical presentation consistent with PML, have produced an accepted and much less invasive diagnostic regimen (Donovan-Post et al., 1999).

Approximately 40% to 90% of patients with AIDS will develop CNS manifestations during the course of the illness (Walot et al., 1996). The most common of these opportunistic infections are caused by toxoplasma, cytomegalovirus (CMV), cryptococcus, and the JCV causing PML. Less commonly observed agents include herpes simplex virus (HSV), varicella-zoster, histoplasmosis and tuberculosis. The imaging diagnosis of these many varied pathologies found in HIV patients is most developed presently with MRI, but may require the addition of other imaging techniques such as computed tomography (CT), single-photon emission computed tomography (SPECT), and positron emission tomography (PET). A simple method to add a degree of specificity to the diagnostic workup is to search for primary infection sources in the patient, such as the lungs for many of the infectious agents. Different pathologies may occur synchronously or sequentially, confusing attempts at simplified diagnosis in these patients. The most common example of this being the problematic differentiation of the lesions of toxoplasmosis from lymphoma. Clinical presentation depends more on anatomic location within the CNS than on lesion etiology. A categorization scheme is discussed below (see Anticipated Results), consisting of four lesion classes, (1) focal lesions with mass effect; (2) focal lesions without significant mass effect; (3) diffuse global CNS abnormalities; and (4) ventriculitis, meningitis, and infarcts (Walot et al., 1996).

Critical Parameters and Troubleshooting

Please see the discussions presented in *UNITS A4.1* and *A4.2* for useful remarks in optimizing the Basic Protocol. Some additional discussion related to the imaging of HIV infected patients is warranted. Considering the utility and benefits of the contrast-enhanced 3-D gradient echo sequence if used as a whole brain sequence, it can either supplement or replace the post-contrast transverse and coronal spin echo sequences. It affords superior spatial resolution and some time savings, but at some mild loss of signal-to-noise contrast. The sequence is routinely performed as a problem-solver in that the high resolution images (especially when limited to area of interest with thinner slice thickness) can give the exact location of subtle lesions (i.e., in the subarachnoid space of a cerebral sulcus or within adjacent cerebral cortex). This determination is readily aided by the ability to reformat the sequence into any desired plane.

There is a distinct though rare association of HIV and AIDS with CNS vasculopathy, particularly in the pediatric AIDS population (Shah et al., 1996). The prudent MR imager will remain vigilant for this occurrence and employ either 3-D gradient echo or directed MRA studies to further evaluate the patient. The findings can be subtle when early in their development, but can rapidly advance to a markedly abnormal vessel contour, rupture and associated hemorrhage, or thrombosis and infarction. Alternatively, when infarction or hemorrhage are noted, clues to the presence, location, and severity of vasculopathy should be assessed. The authors have found it occasionally useful to perform MRA/MRV after the administration of gadolinium in order to obtain superior signal-to-noise from the vessels. This can be especially important when examining the small and hyperdynamic vessels found in the pediatric age group. Also, contrast administration may allow for the evaluation of more distal arterial vessels of the brain (i.e., M2 segment of the middle cerebral artery and beyond) that would not otherwise afford sufficient signal for scrutiny. Such is the case in cooperative patients, but in uncooperative patients, there is often a delay obtaining motion sensitive studies such as MRA until adequate sedation can be obtained. Though specifically in difficult patients, gadolinium enhanced MRA may give sufficient signal in the larger arterial structures of the circle-of-Willis for sufficient diagnostic confidence.

The occurrence of the AIDS dementia complex (ADC) in AIDS patients, as well as altered sensorium related to more focal pathologies in this population make fast scanning technique familiarization important. For a more detailed discussion of fast-scan techniques, please refer to Chapter A5 of this series. Additional time savings for imaging these patients can be found by limiting pre-contrast and post-contrast T_1-weighted sequences to one plane each, performing only one acquisition (N_{acq}) on each sequence, or alternatively by utilizing FSE T_1-weighted sequences rather than routine T_1-weighted sequences. These maneuvers will limit all SNR and sensitivity for detection of abnormal contrast enhancement and subtle lesions but will afford faster exam times. The marked speed of acquisition for dMRI make it a desirable sequence in these patients, as well. It can provide both T_2-weighted and diffusion data.

For the always difficult differentiation of toxoplasmosis from lymphoma, several helpful clues should be sought. The presence of microhemorrhage within lesions is a good indicator of toxoplasmosis. This determination is aided by the judicious use of the gradient echo sequence (sequence 8), which can readily display hemorrhagic blood products that might otherwise be extremely subtle, or even invisible on routine spin echo sequences (Figure A4.1.3). MRS and pMRI can also be helpful, if the reader's scanner is equipped for these studies.

Finally, the utility of MR for follow-up imaging cannot be overstressed for HIV infected patients. The pathologies found in this group demand repeat imaging, often over extended periods of months and years and after multiple associated interventions such as surgery, biopsy, and of course, anti-infectious therapies. It is important to attempt standardization of protocols from one imaging session to the next to avoid the "apples-to-oranges" effect that can handicap the radiologist's ability to assess for lesion change over time.

Imaging of HIV by magnetic resonance diffusion, perfusion, and spectroscopy

The Basic Protocol outlined above is quite sufficient in most instances and represents the standard for imaging of the patient with HIV. However, in certain clinical instances there may remain confusion as to the diagnosis, or in order to gain a higher degree of specificity in labeling a lesion, further imaging can be performed utilizing dMRI, pMRI, or MRS. Recent literature (Chang et al., 1995; Ernst et al., 1998) has indicated diagnostic benefit in some clinical and imaging differential situations with these functions, with the greatest added utility in HIV patients presently residing with MRS. Please refer to the scan parameters and set-up outlined in detail in *UNIT A4.1* of this chapter for performance of these sequences.

pMRI of the brain. This sequence is performed to assess vascular perfusion of the brain and pathologic foci. pMRI can help in differentiating abscess from necrotic neoplasm. It is a rapid acquisition with moderate spatial resolution which can yield information on the entire brain and multiple lesions, even in agitated patients.

Echo-planar imaging (EPI) dMRI of the brain. This sequence is performed to assess water motion (proton diffusion) within the brain parenchyma. Diffusion imaging may help in the differential diagnosis of cerebral abscess vs. necrotic neoplasm. It is a rapid acquisition (scan time 28 sec) with moderate spatial resolution that can yield information on the entire

brain and multiple lesions, even in agitated patients.

MRS of the brain. This sequence will provide information as to the specific molecular substrate(s) within an area of interest, which may indicate the presence of abnormal tissue or metabolic processes. MRS can be used in the diagnosis and follow-up of cerebral abscess, encephalitis, regions of demyelination, or tumors. The sequence acquisition time is ~10 min per T_E performed, making useful results difficult to obtain in agitated patients. A tracing of the magnetic spectra of the molecular contents of the voxel is produced for analysis.

Anticipated Results

Focal brain lesions with mass effect are found in 15% to 20% of AIDS patients and, as a class, represent the most important pathologies for accurate identification as generally effective therapies are available (Walot et al., 1996). As AIDS is fundamentally an immune system compromising illness, there can be distinct and confusing differences in the appearance of pathologic entities in the AIDS patient when compared to similar pathologies in the normal population. Specifically, the inflammatory response can be weak in the immunocompromised patient, which may lead to a decrease in reactive edema found around inflammatory or neoplastic lesions, and poor contrast enhancement. However, tumors that would normally enhance will usually continue to do so, as neoplasia involves the formation of abnormal tumor vessels that leak contrast agent and are not subject to an inflammatory factor. *Toxoplasma gondii* is the protozoan responsible for the most common opportunistic CNS infection in AIDS patients (13% to 33% of AIDS patients with CNS disease). Encephalitis and abscess can result from reactivation of the organism in the immunocompromised host. The primary means of differentiating toxoplasmosis from lymphoma in the CNS remains a satisfactory response to antitoxoplasma therapies, with noticeable lesion regression seen on imaging studies by 2 weeks. Toxoplasmosis tends to present with multiple lesions and the presence of small lesional hemorrhages is supportive of the diagnosis (Taveras and Pile-Spellman, 1996). However, a solitary lesion at presentation is not uncommon (~30%). Primary lymphoma is the most common neoplasm in AIDS patients, and is almost always of the high-grade B-cell type. It is also most often multifocal at presentation (80% to 100%) and hemorrhage in these lesions is distinctly unusual. Though typically solid tumors, lymphoma may display necrosis (an unusual finding in non-AIDS patients) and ring enhancement, especially when larger. The ring enhancement is often less distinct and thicker (>3 mm) than that seen with toxoplasmosis. Lymphoma is isointense to brain on both T_1-weighted and T_2-weighted MR images, with occasional hypointensity seen on T_2-weighted images due to the high cellularity of the process and the high nuclear/cytoplasmic ratio. It occurs centrally in the basal ganglia, corpus callosum, and periventricular white matter. Subependymal spread and ventricular encasement are also common.

Despite these appearances and their seeming differences, the imaging characteristics of toxoplasmosis and lymphoma overlap to a significant degree, and in fact have been reported to occur together in the same patient (Walot et al., 1996; Wong and Quint, 1999). With therapy all lesions must thus be closely monitored. pMRI and MRS have been used to further differentiate these pathologies (see discussion in *UNIT A4.1*; Chang et al., 1995; Ernst et al., 1998). Toxoplasmosis tends to demonstrate marked elevation of the lactate and lipid peaks on MRS and normal metabolite depletion, while lymphoma produces an elevated choline peak with moderate elevation of the lactate and lipid peaks. These spectra are thought secondary to the more infiltrating and solid nature of the neoplasm compared to the more typically necrotic and abscessed infectious lesion.

Cryptococcosis, an infection from the yeast *Cryptococcus neoformans*, occurs in 5% of AIDS patients and can be varied in presentation and structural involvement of the CNS (Harris and Enterline, 1997). However, meningitis is certainly most common at presentation. Inflammatory response by the CNS to invasion by cryptococcus is muted as the organism elaborates a mucinous capsule. Thus, meningeal enhancement is rarely noted. However, the organism proliferates in the subarachnoid space and characteristically settles in the perivascular spaces of Virchow-Robin, where it fills these spaces with organisms and mucoid exudate leading to lesions termed "gelatinous pseudocysts" (Figure A4.3.1). These pseudocysts have signal characteristics similar to CSF, but may be detected on FLAIR or proton-density images with abnormal high T_2 signal in dilated and unusually numerous Virchow-Robin spaces, which are seen mostly at the base of the brain and in the brainstem (predominantly the midbrain).

AIDS patients do not have a particular susceptibility to pyogenic abscess formation or tuberculosis, but these infections can still be seen in the i.v. drug abusing subset of the AIDS population (Walot et al., 1996). Neurotuberculosis presentations are varied with cerebritis, or focal parenchymal or meningeal lesions seen typically with prominent and diffuse enhancement, though true abscess formation may occur. The simultaneous occurrence of basilar meningitis and associated hydrocephalus is a strong indicator of tuberculous infection, or another granulomatous process such as fungal infection by coccidioidomycosis.

The second broad category of CNS abnormalities in AIDS patients is focal lesions without significant mass effect. These processes generally involve only white matter without producing significant edema, and usually without associated enhancement after administration of gadolinium chelates. The lesions are of low signal on T_1-weighted MR images, and demonstrate high T_2 signal intensity. This appearance is nonspecific, being produced by lesions of multiple sclerosis, post-infectious demyelinating conditions such as acute disseminated encephalomyelitis (ADEM) and ischemic processes in the elderly population. Of paramount concern among these is PML that represents a reactivation of the dormant JCV found in 80% of the normal adult population. The virus infects and destroys oligodendrocytes causing the demyelination. The lesions are usually multiple, confluent and bilateral (though asymmetric) at presentation, and found in the white matter, primarily in subcortical, periventricular, and centrum semiovale locations. The process rarely enhances (2%) and may have mild associated cortical atrophy (Donovan-Post et al., 1999). The main differential consideration with PML is that of primary HIV or CMV cerebritis. These conditions characteristically have advanced associated atrophy of the cerebral structures on presentation. Additionally PML, as the name implies, can progress. This progression may be startlingly rapid with serial MR studies depicting marked progression in many patients within 9 weeks.

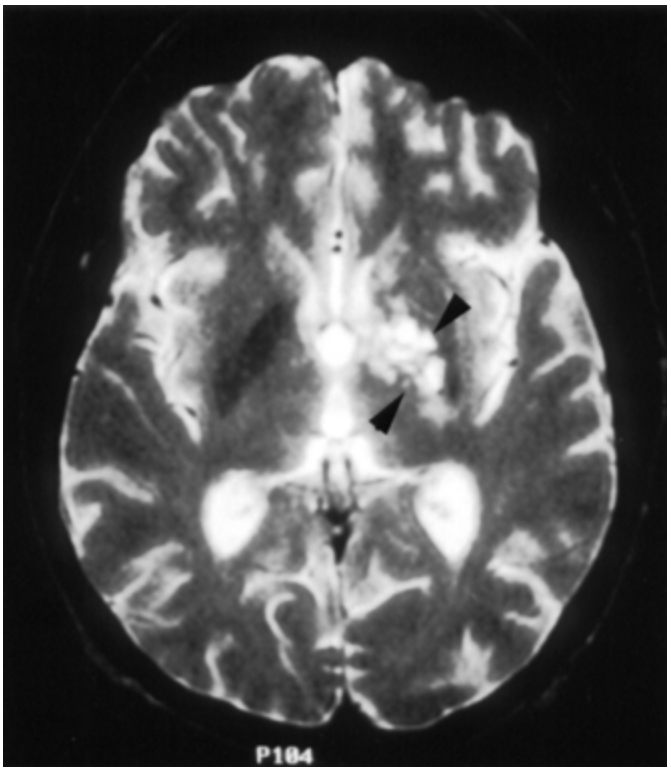

Figure A4.3.1 This T_2-weighted (T_R = 2500 msec, T_E = 80 msec, N_{acq} = 0.75) transverse image at the basal ganglia level demonstrates a cluster of rounded lesions (arrowheads) in the left globus pallidus and posterior limb of the internal capsule with mild increased T_2 signal in adjacent brain. Minimal mass effect is present. The CSF disclosed cryptococcal infection, and "gelatinous pseudocysts" within the perivascular spaces of Virchow-Robin were diagnosed.

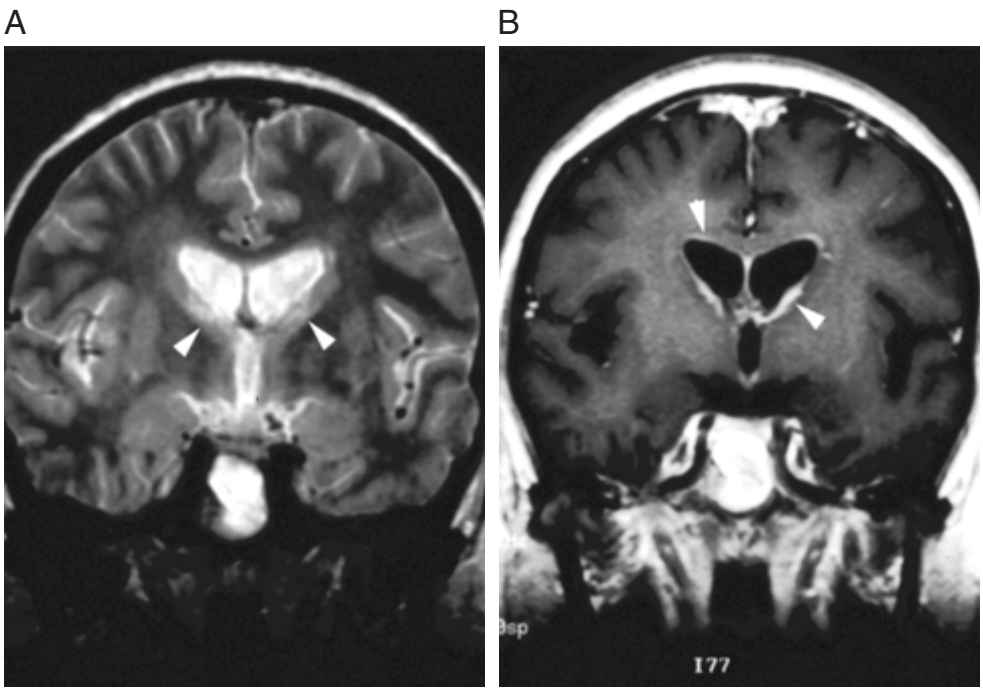

Figure A4.3.2 A coronal (**A**) FSE T_2 image through the third ventricle (T_R = 5600 msec, T_E = 105 msec, N_{acq} = 2; echo train length = 8) discloses abnormal increased T_2 signal in the subependymal and immediate periventricular white matter (arrowheads). The corresponding post-contrast T_1-weighted (**B**) coronal image (T_R = 500 msec, T_E = 12 msec, N_{acq} = 1) shows linear ependymal enhancement (arrowheads) compatible with presumed CMV ventriculitis and ependymitis. This diagnosis was supported in this 33-year-old female with AIDS by a concurrent CMV retinitis. The authors utilized the additional coronal FSE sequence (A) in this patient primarily as a means of evaluating the optic pathways in this patient with CMV retinitis.

MRS has been described for AIDS patients and PML (Chang et al., 1995) and suggests a significant contribution to specificity in distinguishing amongst the many differential diagnostic possibilities when coupled with the results of spin-echo examination.

In considering the third broad category of CNS lesions found in AIDS patients, diffuse global CNS abnormalities, the most common presentation is that of iso-intense to hypo-intense T_1 signal relative to brain, with subtle and diffuse abnormal increased T_2 signal located predominantly in the cerebral white matter in a symmetric manner. This is seen with associated diffuse and often marked cerebral atrophy (which in itself may be the only finding). The most common cause of this constellation of findings is direct CNS infection by HIV, a neurotropic virus. No enhancement is present in the regions of abnormal signal and MRS shows neuronal loss with a decrease of the *N*-acetylaspartate (NAA) peak (a neuronal marker). Clinically, an associated encephalopathy may be noted (ADC). Autopsy studies have shown a high prevalence of a concurrent CMV infection, though this pathogen is believed to invade the brain later in the course of the illness.

Finally, ventriculitis, meningitis, and infarcts comprise the fourth category of CNS abnormality. CMV may cause an aggressive ventriculoencephalitis, the diagnostic clue to which can often be found with CMV infection elsewhere in the body (most notably CMV retinitis). The ventricles are enlarged, generally from associated atrophy, with increased T_2 signal seen in subependymal location along with poorly defined periventricular enhancement (Figure A4.3.2). This viral agent also has a tendency to spread to the meninges and adjacent cranial nerves. CNS vasculopathy, which can lead to ischemic or hemorrhagic infarction, will rarely affect the larger arterial structures (circle-of-Willis) at the base of the brain and can lead to fusiform aneurysm formation, as well as sclerosis and thrombosis (Figure

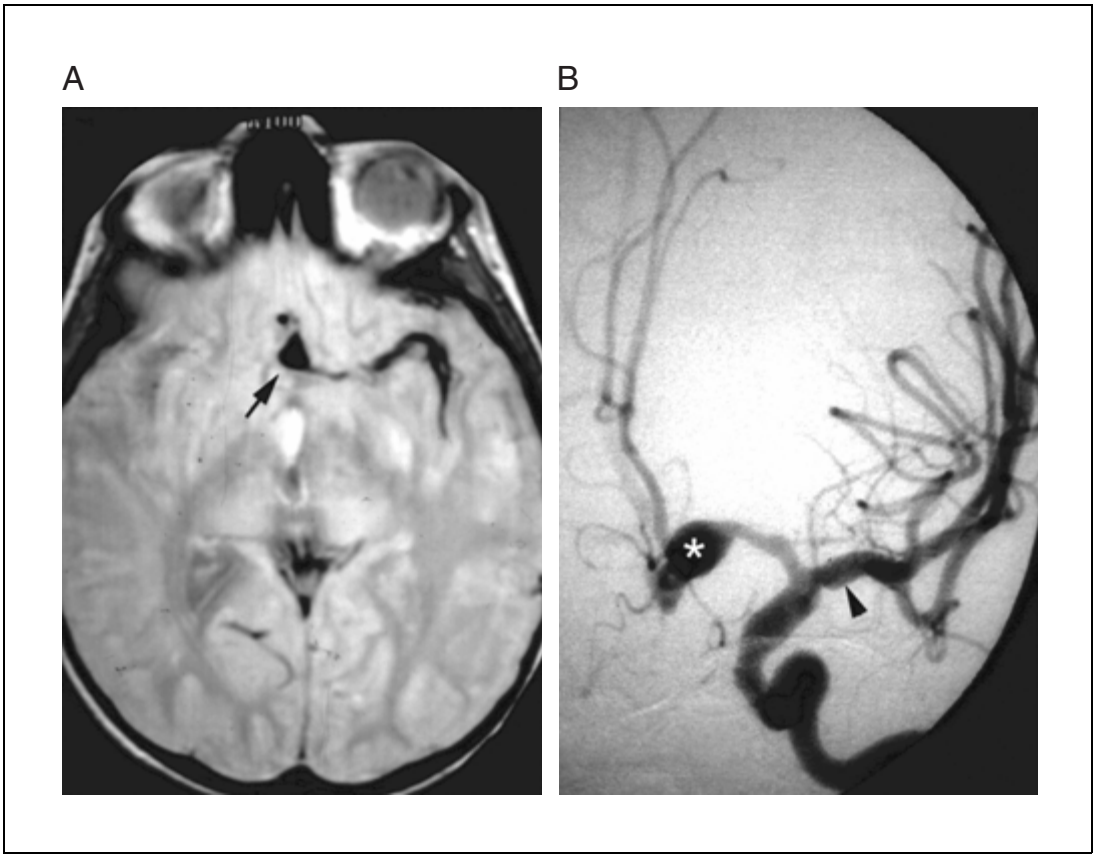

Figure A4.3.3 This 9-year-old boy with congenitally acquired HIV infection began complaining of headaches. The proton-density T_2-weighted (**A**) transverse image (T_R = 2500 msec, T_E = 30 msec, N_{acq} = 0.75) shows prominent fusiform aneurysmal dilatation of the anterior cerebral artery (arrow). A subsequent cerebral angiogram (**B**) reveals diffuse aneurysmal involvement of the supraclinoid internal carotid artery (ICA), as well as the A1 (asterisk) and M1 (arrowhead) portions of the ICA branch vessels. The child was treated conservatively, but several months later experienced severe subarachnoid hemorrhage and died.

A4.3.3). This may be the result of spread to the vessel wall (presumably the adventitia primarily) via meningeal infection and inflammation, or possibly a direct vascular infection via the hematogenous route. This vasculopathy has a particular incidence in the pediatric AIDS population and is a late manifestation of the disease (Shah et al., 1996). It is rare to see vasculopathy without associated abnormalities present on spin echo images of the brain (Pomper et al., 1999).

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Key Reference

Walot et al., 1996. See above.

Presents a directed and concise summary of the myriad imaging appearances encountered in this complex patient population.

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