Metastatic Intra-Axial Neoplasia

Magnetic resonance imaging (MRI) is a sensitive noninvasive means by which to evaluate intracranial pathology. The role of imaging in the metastatic work-up is to detect the spread of tumor to the brain parenchyma, and define the location. Intravenous contrast (gadolinium-DTPA) provides the greatest sensitivity for detecting brain lesions (Healy et al., 1987) and is almost always indicated except when there is no intravenous access. This unit presents the set of MR sequences used for imaging intra-axial brain metastases (see Basic Protocol) and specific modifications will be discussed where necessary (see Alternate Protocol). The sequences described in this unit are based on the authors' experience with a 1.5 T scanner (Echospeed GE Medical Systems, Milwaukee, Wisconsin), but can be expected to be equally applicable to other field strengths and scanners from other manufacturers.

RULE OUT (R/O) NON-HEMORRHAGIC METASTATIC DISEASE

BASIC PROTOCOL

The vast majority of metastases are located in the intra-axial supra-tentorial compartment, are typically multiple and subcortical, and have a considerable amount of surrounding vasogenic edema (Atlas and Lavi, 1996). In general, T_1-weighted and T_2-weighted images provide tissue-specific information by elucidating the water content, hemorrhagic components, and cellularity of lesions. Contrast enhancement of intra-axial brain lesions indicates breakdown of the blood-brain barrier. Imaging following triple-dose MRI contrast agent administration detects a greater number of small (<10 mm) metastatic lesions than the standard dose (0.10 mmol/kg) (Yuh et al., 1995). Delayed imaging (10 to 30 min) after the administration of either the standard dose or high dose contrast improves the detection of small metastatic lesions. In most institutions, patients receive the standard dose and are scanned without any significant delay in the transverse and coronal planes. Beyond generating a second plane of imaging, the coronal plane acquisition following the transverse sequence allows for a small delay (several minutes) following intravenous contrast administration. In pediatric patients and other subjects requiring sedation, the authors feel that a third post-contrast acquisition, in the sagittal plane, is worthwhile in evaluating brain tumor patients. Sequences 1 to 5 comprise the preferred protocol.

Table A3.1.1 lists the hardware necessary to perform the procedure, along with appropriate parameters.

NOTE: Be sure that technologists and nurses have immediate access to any equipment such as crash carts or oxygen that may be necessary in the event of an emergency. Reactions to contrast agents are rare, but the resources are necessary.

Table A3.1.1 Equipment Parameters for Imaging Brain Tumors

Coil type	Quadrature head coil
Gradient coil strength	25 mT/m (or whatever the system permits)
Cardiac gating	No
Peripheral gating	For safety only
Respiratory gating	No
Respirator	If required by patient
Oxygen	If required by patient
Motion cushions	No

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Materials

Normal saline (0.9% NaCl), sterile
Intravenous contrast agent (e.g., Magnevist, Omniscan, or Prohance)

Set up patient and equipment

1. Interview (screen) the patient to ensure that he or she has no contraindications such as cardiac pacemakers 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 necessitate any other 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 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 wash off any mascara and other makeup to avoid local tissue heating and image artifacts.

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

   a. If earphones or headphones are used to protect the ears from the loud sounds produced by the gradients, the patient will be asked to wear these, but will be able to communicate with you at any time during the imaging.
   b. The patient will be given a safety squeeze-bulb or similar equipment to request assistance at any time (demonstrate how this works).
   c. For good results the patient should not talk, and should avoid or 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 when this is the case.
   d. Nevertheless, the patient may call out at any time if he or she feels it necessary.

6. Have the patient mount onto the table in the supine position. Either before or right after the patient lies down, set up any triggering devices or other monitoring equipment that is to be used.

7. Center the patient in the head coil at the region where the key information is desired. Make sure the head and neck are constrained to prevent motion.

   Generally the patient's head is fixed so that the head is horizontal (not tilted) and the neck and head lie along the axis of the patient table.

8. If needed, place a pillow or other support under the knees to make the patient more comfortable.
9. Use the centering light to position the patient (centered on the nasion) and put him or her 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.

10. If the patient is unable to hold still, provide an appropriate sedative.

Sequence 1: Localizer

11. Run sequence 1 according to Table A3.1.2. The sagittal scout view is used to prescribe the transverse or coronal planes.

Sequence 2: T_1-weighted scan

12. Run sequence 2 according to Table A3.1.3.

Sequence 3: T_2-weighted scan

13. Run sequence 3 according to Table A3.1.4.

Sequence 4: Fast FLAIR (fluid-attenuated inversion recovery) scan

14. Run sequence 4 according to Table A3.1.5.

Sequence 5: Post-contrast imaging

15. Remove the patient from the scanner. The patient should not move on the table. Establish an intravenous line from 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. Move the patient back into the scanner.

Table A3.1.2 Primary Clinical Imaging Parameters for Sequence 1 (T_1-Weighted)

Patient position	Supine
Scan type	Spin echo
Imaging plane (orientation)	Sagittal
Central slice or volume center	Laser light centered on nasion
Echo time (T_E)	11 msec (or select "minimum full" echo time)
Receiver bandwidth (RBW)	10 kHz
Repeat time (T_R)	500 msec
Flip angle (FA)	90°
Fields of view (FOV_x, FOV_y)	240 mm, 240 mm
Resolution (Δx, Δy)	0.94 mm, 1.25 mm
Number of data points collected (N_x, N_y)	256, 192
Slice thickness (Δz)	5 mm
Number of slices	20 or as many as needed to cover the region of interest
Slice gap	2 mm
Number of acquisitions (N_{acq})	1
Swap read and phase encoding	No
Saturation pulses	Not applicable
Scan time	1 min, 28 sec

Table A3.1.3 Primary Clinical Imaging Parameters for Sequence 2 (T_1-Weighted)

Patient position	Supine
Scan type	Spin echo
Imaging plane (orientation)	Transverse
Central slice or volume center	Laser light centered on nasion
Echo time (T_E)	11 msec (or select "minimum full" echo time)
Receiver bandwidth (RBW)	10 kHz
Repeat time (T_R)	500 msec
Flip angle (FA)	90°
Fields of view (FOV_x, FOV_y)	240 mm, 240 mm
Resolution (Δx, Δy)	0.94 mm, 1.25 mm
Number of data points collected (N_x, N_y)	256, 192
Display matrix (D_x, D_y)	256, 192
Slice thickness(Δz)	5 mm
Number of slices	20 or as many as needed to cover the region of interest
Slice gap	2.5 mm
Number of acquisitions (N_{acq})	1
Swap read and phase encoding	Yes
Saturation pulses	Not applicable
Scan time	1 min, 28 sec

Table A3.1.4 Primary Clinical Imaging Parameters for Sequence 3 (T_2-Weighted)

Patient position	Supine
Scan type	Fast spin echo
Imaging plane (orientation)	Transverse
Central slice or volume center	Laser light centered on nasion
Echo time (T_E)	102 msec (effective)
Receiver bandwidth (RBW)	16 kHz
Echo train length (ETL)	8
Repeat time (T_R)	3600 msec
Flip angle (FA)	90°
Fields of view (FOV_x, FOV_y)	240 mm, 240 mm
Resolution (Δx, Δy)	0.94 mm, 1.25 mm
Number of data points collected (N_x, N_y)	256, 192
Display matrix (D_x, D_y)	256, 192
Slice thickness (Δz)	5 mm
Number of slices	20 or as many as needed to cover the region of interest
Slice gap	2.5 mm
Number of acquisitions (N_{acq})	1
Swap read and phase encoding	Yes
Saturation pulses	Not applicable
Scan time	~2 min

Table A3.1.5 Primary Clinical Imaging Parameters for Sequence 4 (Fast FLAIR)

Patient position	Supine
Scan type	Inversion recovery fast spin echo
Imaging plane (orientation)	Transverse
Central slice or volume center	Laser light centered on nasion
Echo time (T_E)	120 msec (effective)
Receiver bandwidth (RBW)	16 kHz
Echo train length (ETL)	8
Repeat time (T_R)	10000 msec
Inversion time (T_I)	2200 msec
Flip angle (FA)	180°
Fields of view (FOV_x, FOV_y)	240 mm, 240 mm
Resolution (Δx, Δy)	0.94 mm, 1.25 mm
Number of data points collected (N_x, N_y)	256, 192
Display matrix (D_x, D_y)	256, 192
Slice thickness (Δz)	5 mm
Number of slices	20 or as many as needed to cover the region of interest
Slice gap	2.5 mm
Number of acquisitions (N_{acq})	1
Swap read and phase encoding	Yes
Saturation pulses	Not applicable
Scan time	~5 min

It is preferable to insert the line prior to imaging and to leave the patient in the magnet, with no intervening motion, between the scans run before and after contrast agent injection and those run after injection.

16. Leaving the patient in the magnet, inject the contrast agent, flush the line with 10 ml saline.

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

    A delay in scanning may actually be beneficial when evaluating for metastases, which is one of the reasons we scan in multiple planes after intravenous contrast administration.

17. Acquire the post-contrast images using the same parameters as sequence 2 (T_1-weighted).

    In addition to the transverse plane, the coronal plane is routinely obtained, with the following changes to the parameters in sequence 2: (a) flow compensation is on; (b) T_E is 20 msec (prolonged due to flow compensation gradients); and (c) it is not necessary to swap read and phase encoding directions. We also routinely obtain a third post-contrast plane of imaging (sagittal) in patients requiring sedation and in all pediatric patients.

R/O HEMORRHAGIC METASTATIC DISEASE/METASTATIC MELANOMA

ALTERNATE PROTOCOL

A small percentage of metastatic brain tumors will demonstrate evidence of hemorrhage. These most commonly include melanoma, choriocarcinoma, renal cell, bronchogenic, and thyroid carcinomas. The appearance will vary according to the stage of the hemorrhage (acute-chronic) on the T_1-weighted and T_2-weighted images (Thulborn et al., 1990; Thulborn and Atlas, 1996; Atlas and Thulborn, 1998) and gradient-echo imaging demonstrates evidence of hemorrhage that may not be seen with conventional spin-echo imaging (Atlas et al., 1988). Intracranial metastatic melanoma (if melanotic) exhibits the typical

Table A3.1.6 Primary Clinical Imaging Parameters for Sequence 6 (Gradient Echo)

Patient position	Supine
Scan type	2-D gradient recalled echo
Imaging plane (orientation)	Transverse
Central slice or volume center	Laser light centered on nasion
Echo time (T_E)	30 msec
Receiver bandwidth (RBW)	4 kHz
Repeat time (T_R)	500 msec
Flip angle (FA)	15°
Fields of view (FOV_x, FOV_y)	240 mm, 240 mm
Resolution (Δx, Δy)	0.94 mm, 1.25 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	20 or as many as needed to cover the region of interest
Slice gap	2.5 mm
Number of acquisitions (N_{acq})	1
Swap read and phase encoding	Yes
Saturation pulses	Not applicable
Scan time	~2 min

imaging appearance of any paramagnetic lesion (Atlas et al., 1987), causing shortening of T_1 and T_2 on MR images. However, the imaging appearance may be quite variable depending on melanin content and hemorrhage.

Setup equipment and patient

1. Use the same equipment and perform patient setup as for the previous method (see Basic Protocol).

Pre-contrast T_1-weighted scan should be acquired in the same plane as the post-contrast T_1-weighted scan to look for intra-lesional enhancement.

Sequence 6: Gradient echo sequence

2. In addition to sequences 1 to 5, obtain gradient echo images (sequence 6, Table A3.1.6).

COMMENTARY

Background Information

Brain metastases are common intracranial tumors (Johnson and Young, 1996) affecting between 80,000 and 170,000 individuals in the United States per year (Davey, 1999). While computed tomography (CT) may often be more readily available and therefore the first examination performed for suspected intracranial pathology, magnetic resonance imaging (MRI) has proven to be invaluable in refining the diagnosis. MRI with intravenous contrast provides the greatest sensitivity and exquisite anatomical information for the detection of brain metastases. The neuroanatomic location of metastases and the associated edema and mass effect determine the clinical presentation of the patient. The most common primary sites of brain metastases in adults include lung, breast, skin (melanoma), and the gastrointestinal tract. In younger patients, brain metastases often arise from sarcomas and germ cell tumors.

Critical Parameters and Troubleshooting

Intravenous contrast (gadolinium-DTPA) is essential when evaluating the brain for the full

extent of metastatic disease. A delay in scanning is actually beneficial and at least two planes of imaging should be obtained following the administration of intravenous contrast. Three planes of imaging (transverse, coronal, and sagittal) should be acquired post-contrast in patients requiring sedation and in all pediatric patients. Not uncommonly, metastatic lesions (particularly to the cortex) are detected solely on the post-contrast images, which is due to similar signal characteristics with the adjacent brain tissue and the lack of surrounding edema. Where small lesions (1 mm) can be mistaken for vessels, the use of a first and second dose of contrast can be used to distinguish lesions (more conspicuous after the second dose) from vessels (no change in appearance between doses).

Anticipated Results

The goal in evaluating the brain for metastases is to demonstrate the total number of lesions, and to depict the full extent of disease burden in terms of edema, brain herniation and hemorrhage. Magnetic resonance imaging offers superb anatomical detail and tissue characterization of brain metastases and provides the greatest sensitivity for detecting lesions.

Time Considerations

The protocols detailed in this unit should take ~30 min to complete.

Literature Cited

Atlas, S.W. and Lavi, E. 1996. Intra-axial brain tumors. *In* Magnetic Resonance Imaging of the Brain and Spine, 2nd ed. (S.W. Atlas, ed.) pp. 315-422. Lippincott-Raven, Philadelphia.

Atlas, S.W. and Thulborn, K.R. 1998. MR detection of hyperacute parenchymal hemorrhage of the brain. *Am. J. Neuroradiol.* 19:1471-1477.

Atlas, S.W., Grossman, R.I., Gomori, J.M., Guerry, D., Hackney, D.B., Goldberg, H.I., Zimmerman, R.A., and Bilaniuk, L.T. 1987. MR imaging of intracranial metastatic melanoma. *J. Comput. Assist. Tomogr.* 11:577-582.

Atlas, S.W., Mark, A.S., Grossman, R.I., and Gomori, J.M. 1988. Intracranial hemorrhage: Gradient-echo MR imaging at 1.5 T. *Radiology* 168:803-807.

Davey, P. 1999. Brain metastases. *Curr. Probl. Cancer* 23:59-98.

Healy, M.E., Hesselink, J.R., Press, G.A., and Middleton, M.S. 1987. Increased detection of intracranial metastases with intravenous Gd-DTPA. *Radiology* 165:619-624.

Johnson, J.D. and Young, B. 1996. Demographics of brain metastasis. *Neurosurg. Clin. N. Am.* 7:337-344.

Shellock, F.G. 1996. Pocket Guide to MR Procedures and Metallic Objects. Lippincott-Raven, Philadelphia.

Thulborn, K.R. and Atlas, S.W. 1996. Intracranial hemorrhage. *In* Magnetic Resonance Imaging of the Brain and Spine, 2nd ed. (S.W. Atlas, ed.) pp. 265-314. Lippincott-Raven, Philadelphia.

Thulborn, K.R., Sorensen, A.G., Kowall, N.W., McKee, A., Lai, A., McKinstry, R.C., Moore, J., Rosen, B.R., and Brady, T.J. 1990. The role of ferritin and hemosiderin in the MR appearance of cerebral hemorrhage: A histopathologic biochemical study in rats. *Am. J. Neuroradiol.* 2:291-297.

Yuh, W.T., Tali, E.T., Nguyen, H.D., Simonson, T.M., Mayr, N.A., and Fisher, D.J. 1995. The effect of contrast dose, imaging time, and lesion size in the detection of intracerebral metastasis. *Am. J. Neuroradiol.* 16:373-380.

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