1
Neuroradiology

Standard Imaging Methods for the Brain and Nervous System

Introduction

MRI provides better contrast resolution than CT, and because there are no artifacts from bone, it is an excellent modality for visualizing central nervous system lesions. It is therefore the first-line choice of diagnostic imaging methods for many diseases of the head. CT is given priority if there are concerns about MRI use, such as when the patient has a device incompatible with MRI or is in poor general condition, or when evaluating a bone lesion or calcification, as well as in the case of acute brain hemorrhage or head trauma. Compared with CT, MRI is highly useful in diseases such as the following: inflammatory diseases, including demyelinating diseases such as multiple sclerosis; degenerative and metabolic diseases; congenital malformations; brainstem and spinal cord lesions; meningeal dissemination; axonal injury resulting from head trauma; and sellar lesions. MRI is in general highly useful for brain tumors, subacute and chronic cerebrovascular disorders, and bone marrow changes. In addition to morphological information, MRI can provide functional information on aspects such as water molecule diffusion, blood flow, and metabolism. SPECT and PET, which use radioactive tracers, are useful for the functional evaluation of aspects such as blood flow and metabolism.

Basic methods of head MRI

Routine MRI of the head is generally performed with a slice thickness of approximately 5 mm and involves T1-weighted and T2-weighted imaging and fluid-attenuation inversion recovery (FLAIR) imaging (or proton density-weighted imaging). In addition, because diffusion-weighted imaging can be performed in a short time and provides a large amount of information, it can also be included in routine imaging. The reference plane for transverse imaging is generally the AC-PC line (line joining the anterior and posterior commissures). Depending on the location to be imaged and the purpose of the examination, images such as coronal and sagittal images, thin-slice images, and 3D images are selected in addition. For example, coronal and sagittal images provide useful information for the cranial base, sellar, and high convexity regions.

Evaluation of contrast enhancement by contrast medium administration is necessary to determine whether the blood-brain barrier (BBB) has failed due to a lesion and whether the lesion has a solid component. If a tumor or inflammation is suspected, use of a contrast medium is considered to determine whether a tumor or inflammation is present and perform differential diagnosis. MRI is superior to CT for evaluating contrast enhancement in such a condition.

1. T1-weighted imaging

Spin echo (SE) sequences are commonly used for T1-weighted imaging, but images can also be acquired with gradient echo (GRE) sequences. Items that show hyperintensity in T1-weighted images include hemorrhagic components, fluids with high protein concentration, fat components, and melanin. The presence of a fat component can be confirmed if it is suppressed by fat suppression when hyperintense in T1-weighted images. Calcification shows hyperintensity in T1-weighted images as the result of surface effects occurring with supplementation of water molecules by sponge-like calcification foci. However, whether they show hyperintensity depends on the status of the calcification foci.

Contrast enhancement resulting from contrast medium administration is generally evaluated using pre-contrast and post-contrast T1-weighted images. When a lesion shows hyperintensity in pre-contrast T1-weighted images, contrast enhancement can be readily evaluated by pre-contrast and post-contrast image subtraction. In the orbit and cranial base, the fat signal interferes with assessment of contrast enhancement resulting from the contrast medium, and fat suppression is therefore used concurrently. To detect pituitary microadenomas and diagnose other pituitary lesions, dynamic imaging using thin slices (approximately 3-mm-thick) and rapid contrast medium injection is useful.

2. T2-weighted imaging

T2-weighted imaging is typically performed using a fast spin echo (FSE) sequence. T2-weighted imaging is essential for detecting brain parenchymal lesions and evaluating lesion characteristics, such as cysts, necrosis, and hemorrhage, and the extent of lesion progression. The characteristics represented by marked hyperintensity are mainly those of components such as fluid (cysts, mucous components, blood components) and cartilaginous components. Because many 180° pulses are used with FSE, the susceptibility effect decreases, reducing the ability to detect hemorrhage. $T2^*$-weighted imaging and susceptibility-weighted imaging (SWI) are useful for detecting small hemorrhages.

3. FLAIR imaging

With FLAIR imaging, lesions generally show hyperintensity, and cerebrospinal fluid is suppressed. It is therefore useful for detecting brain lesions that are in contact with cerebrospinal fluid. It is also useful for detecting lesions in cerebrospinal fluid, such as subarachnoid hemorrhage. However, a shortcoming of FLAIR imaging is that cerebrospinal fluid artifacts are readily apparent with 2D imaging. It should also be noted that its ability to visualize lesions in deep gray matter and the brain stem/cerebellum is inferior to that of T2-weighted imaging. Evaluation in combination with T1-weighted and T2-weighted imaging is often useful for diagnosis. For example, evaluations that combine these 3 types of imaging are useful for differentiating among old lacunar infarcts, white matter lesions, and perivascular spaces.

Basic methods of head CT

Multidetector CT enables an extensive area to be imaged at high spatial resolution. It also allows rapid imaging and improves temporal resolution, enabling CT angiography (CTA) to be performed and cerebral perfusion images to be acquired. It generally enables 0.5 to 0.6-mm isotropic volume data to be obtained over an extensive range. Image reconstruction methods such as multiplanar reformation (MPR), maximum intensity projection (MIP), and volume rendering (VR) techniques are also useful for diagnosis.

● Imaging methods used when stroke is suspected

① CT

CT can be performed easily and in a short time and is generally performed first to exclude intracranial hemorrhage. Hemorrhage and signs of early ischemia are evaluated with non-contrast CT (NCCT). Adding CTA is useful for identifying cerebrovascular lesions.

② MRI

In addition to routine imaging of the head, diffusion-weighted imaging, T2*-weighted imaging, and MRA are generally performed. Depending on the patient's condition, the MRI examination may be discontinued before its completion. Consequently, examinations are performed in sequential order, beginning with the most important imaging methods. In acute brain infarction, diffusion-weighted imaging and MRA are particularly important and should be performed early. If acute brain infarction is suspected, the following types of imaging should commonly be performed.

(1) Diffusion-weighted imaging
(2) MRA
(3) FLAIR imaging
(4) T2*-weighted imaging (SWI)
(5) T2-weighted imaging
(6) T1-weighted imaging

Intravascular hyperintensity is often seen in occluded blood vessels with FLAIR imaging, making it useful for diagnosing such occlusion (Fig. 1). In addition, because FLAIR imaging suppresses the cerebrospinal fluid signal, it is often helpful for diagnosing subarachnoid hemorrhage. T2*-weighted imaging is an effective means of detecting brain hemorrhage. An example of an MRI protocol is shown in Table 1.

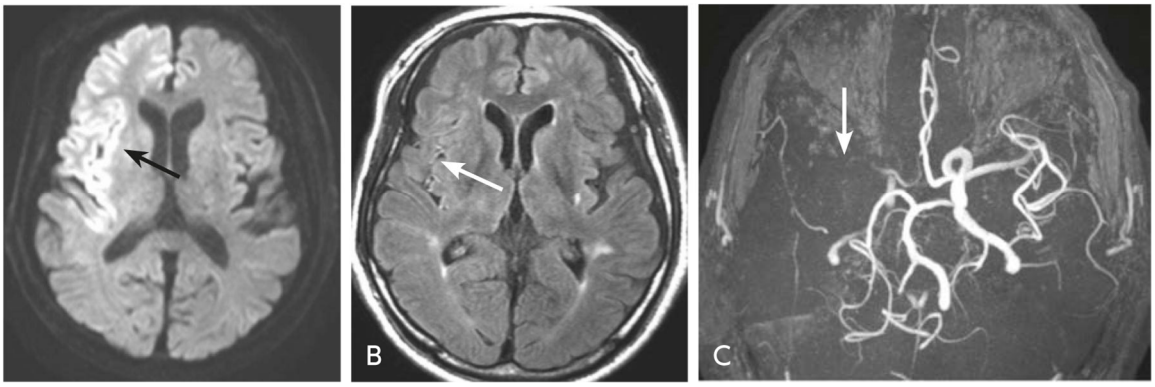


Figure 1. Acute cerebral infarction (MRI)

A: Diffusion-weighted image shows an area of hyperintensity in the right frontal lobe and insula (→).
B: FLAIR image demonstrates a hyperintense blood vessel in the right Sylvian fissure (→).
C: MRA shows decreased visualization of the right middle cerebral artery, indicating occlusive changes (→).

Table 1. An example of a MRI protocol for brain ischemia (3T system, 8-channel head coil)

Imaging Method	Sequence	TR/TE	Slice thickness	Other
Diffusion-weighted imaging	SE-EPI	3,200/60 ms	5 mm	
MRA	GRE	20/3.5 ms	0.5 mm	Time-of-flight method
FLAIR imaging	IR	10,000/120 ms	5 mm	
T2*-weighted imaging	GRE	570/40 ms	5 mm	
T2-weighted imaging	FSE	3,500/80 ms	5 mm	
T1-weighted imaging	FSE	450/10 ms	5 mm	

Note: Diffusion-weighted imaging and MRA are particularly important in evaluating acute cerebral infarction and are therefore performed early.

● Imaging methods in head trauma

① CT

CT is useful in acute head trauma. Specifically, it is useful for evaluating intracranial hemorrhage, cerebral contusion, and skull fracture. Helical imaging allows observation in multiple planes and is useful for determining the relationships among bone, brain, and hemorrhage.

② MRI

The types of MRI sequences indicated below are commonly performed when the main target condition is head trauma.

(1) T1-weighted imaging
(2) T2-weighted imaging
(3) FLAIR imaging
(4) T2*-weighted imaging (SWI)
(5) Diffusion-weighted imaging

These imaging methods are considered useful for diagnosing acute epidural/subdural hematoma, traumatic subarachnoid hemorrhage, cerebral contusion, and diffuse axonal injury (DAI) (Fig. 2). An example of a typical MRI protocol is shown in Table 2.

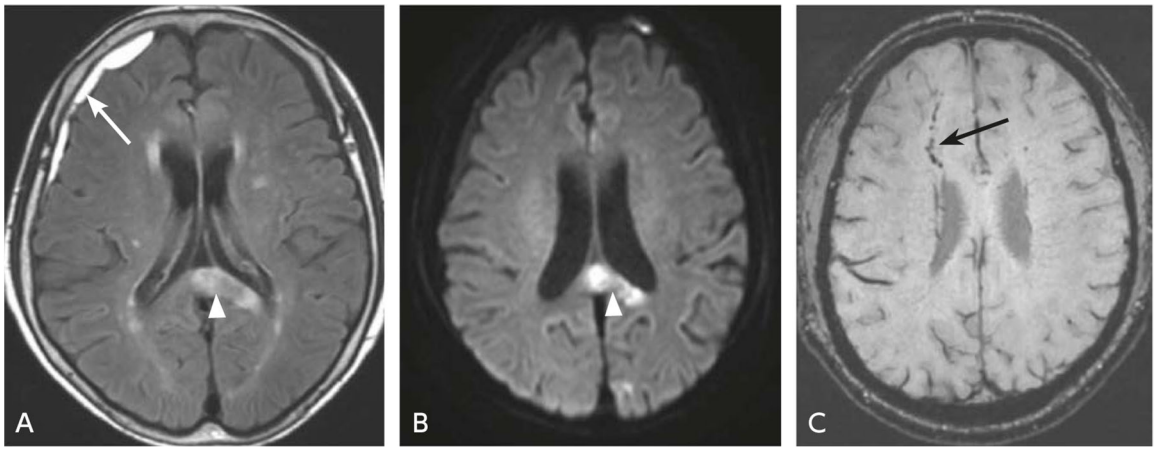


Figure 2. Subdural hematoma and axonal injury (MRI)

A: FLAIR image shows a subdural hematoma on the cortical surface of the right frontal lobe (→), and a lesion in the splenium of the corpus callosum that appears to be an axonal injury (▷).
B: Diffusion-weighted image depicts a hyperintense lesion in the splenium of the corpus callosum, likely axonal injury (▷).
C: SWI shows small hypointense areas in the right frontal lobe white matter, suggestive of an axonal injury (→).

Table 2. An example of a MRI protocol for head trauma (3T system, 8-channel head coil)

Imaging Method	Sequence	TR/TE	Slice Thickness	Other
T1-weighted imaging	SE	450/10 ms	5 mm	
T2-weighted imaging	FSE	3,800/80 ms	5 mm	Sagittal and coronal planes both useful
FLAIR imaging	IR	10,000/120 ms	5 mm	Sagittal and coronal planes both useful
$T2^*$-weighted imaging	GRE	570/40 ms	5 mm	
(SWI)	(GRE)	(27/20 ms)	(2 mm)	
Diffusion-weighted imaging	SE-EPI	3,200/60 ms	5 mm	

Note: SWI can be substituted for $T2^*$-weighted imaging.

Cerebral blood flow scintigraphy

The following are used as radiopharmaceuticals for cerebral blood flow scintigraphy: ^{99m}Tc-ethyl cysteinate dimer (^{99m}Tc-ECD), ^{99m}Tc-hexamethyl propylene amine oxime (^{99m}Tc-HMPAO), and N-isopropyl-p-I-123-iodoamphetamine (^{123}I-IMP). The radiopharmaceutical is administered by intravenous injection with the patient at rest in bed with eyes closed. The patient remains at rest until imaging is performed. Imaging begins 5 to 10 minutes after administration of ^{99m}Tc-ECD or ^{99m}Tc-HMPAO and 30 to 40 minutes after ^{123}I-IMP administration. If the objective is dynamic analysis or cerebral blood flow quantitation, dynamic acquisition is performed in addition to normal imaging. The use of a gamma camera

equipped with a high-resolution collimator for low-energy imaging is recommended. The 2008 nuclear medicine diagnostic guidelines should be referred to regarding stress testing, cerebral blood flow measurement, and statistical image analysis.

PET in epilepsy

1. Test procedure

The patient is intravenously administered ^{18}F-FDG while at rest in the supine position with eyes closed. The dose used is adjusted as appropriate depending on the type of system used and the patient's age and weight. The patient lies at rest for 40 to 60 minutes after administration, and a PET or PET/CT system is used to perform emission and transmission scans (in the case of PET) or CT imaging (in the case of PET/CT) of the head. Data should be acquired for 10 minutes in 3D mode with administration of 185 MBq.

2. Important points for testing

① Pretreatment

The patient is fasted for at least 4 to 5 hours before the examination. Only water intake is permitted during this time (no sugar intake). Because uptake by the brain decreases if the patient's blood glucose level is high, blood glucose is checked immediately before ^{18}F-FDG administration. In addition, cerebral metabolism is altered by neuronal activity. The patient is therefore asked to try to remain at rest for 30 minutes before ^{18}F-FDG administration, and ^{18}F-FDG is administered with the patient supine with eyes closed. To the extent possible, the patient remains at rest on the bed until the examination begins.

② Points to note regarding the measurements

Because the distribution of radioactivity in the brain changes over time after ^{18}F-FDG administration, the timing of the imaging must be consistent. Up to approximately 40 minutes after ^{18}F-FDG administration, the imaging is affected by cerebral blood flow. Consequently, in the case of a single scan, imaging should be performed at approximately 60 minutes, taking into account attenuation and the examination waiting time. Steps should be taken to prevent head movement during imaging to avoid misregistration between the transmission scan and CT data using absorption correction and emission data.

Secondary source materials used as references

1) Miki Y, et al. Head MRI: Imaging protocol and latest 3T MRI findings. Japanese Journal of Magnetic Resonance in Medicine 27:156-165, 2007.
2) Sasaki M, et al. Discriminating between silent cerebral infarction and deep white matter hyperintensity using combinations of three types of magnetic resonance images: a multicenter observer performance study. Neuroradiology 50: 753-758, 2008
3) ASIST-JAPAN Committee to Formulate Clinical Practice Guidelines, Ed.: 2007 Clinical Practice Guidelines for Diagnostic Imaging of Acute cerebral infarction, Nankodo, 2007.
4) Latchaw RE, et al. Recommendations for imaging of acute ischemic stroke: a scientific statement from the American Heart Association. Stroke 40: 3646-3678, 2009
5) Essig M, et al. MR imaging of neoplastic central nervous system lesions: review and recommendations for current practice. AJNR Am J Neuro Radiol 33: 803-817, 2012

6) Hirai T, et al. Protocol for routine brain imaging with 3T MRI. Japanese Journal of Magnetic Resonance in Medicine 28: 244-254, 2008.
7) Japanese Society of Nuclear Medicine, Ed.: Nuclear Medicine Diagnostic Guidelines. Japanese Society of Nuclear Medicine, 2008.
8) Japanese Society of Nuclear Medicine, Ed.: 2020 FDG-PET and PET/CT Diagnostic Guidelines. (http://jsnm.org/archives/4372/)
9) Japanese Society of Nuclear Medicine, Ed.: Japanese Consensus Guidelines for Pediatric Nuclear Medicine. (http://jsnm.org/archives/4675/)

BQ 1 Which imaging examinations are recommended to diagnose subarachnoid hemorrhage?

Statement

The most useful imaging examination is non-contrast CT (NCCT). If diagnosis is difficult with NCCT, MRI can be considered. When subarachnoid hemorrhage is strongly suspected based on clinical findings, even if no significant findings are obtained with CT or MRI, lumbar puncture should be performed.

Background

The vast majority of headache is primary headache, such as tension headache and migraine headache. However, conditions for which an early response is extremely important, such as subarachnoid hemorrhage, are also included in this category. The main cause of non-traumatic subarachnoid hemorrhage is rupture of a cerebral aneurysm. Although CT is generally used for diagnosis in the acute phase, false-negatives are obtained with CT in some cases of subarachnoid hemorrhage (Fig. A). Lumbar puncture is therefore considered necessary. Some studies have shown that MRI, particularly FLAIR imaging, is more useful than CT for detecting subarachnoid hemorrhage (Fig. B). The advantages and shortcomings of each are outlined below.

Explanation

NCCT is the standard imaging examination for subarachnoid hemorrhage.[1)] In a study of 3,132 patients who underwent CT within 6 hours after the onset of symptoms to exclude subarachnoid hemorrhage, radiologists were able to detect it with sensitivity and specificity of 100%.[2)] However, the hemorrhage detection rate is affected by the severity of the hemorrhage and the time since it occurred. CT sensitivity has been found to decrease over time, with sensitivity of 98% to 100% within 12 hours after the onset of symptoms, 93% at 24 hours, 85% at 5 days, 57% to 85% at 6 days, and 50% at 1 week.[3-7)] Confirmation by lumbar puncture is therefore desirable 5 or more days after onset. In some cases, cerebral ventriculomegaly, particularly of the inferior horn of the lateral ventricle, may be the only finding.

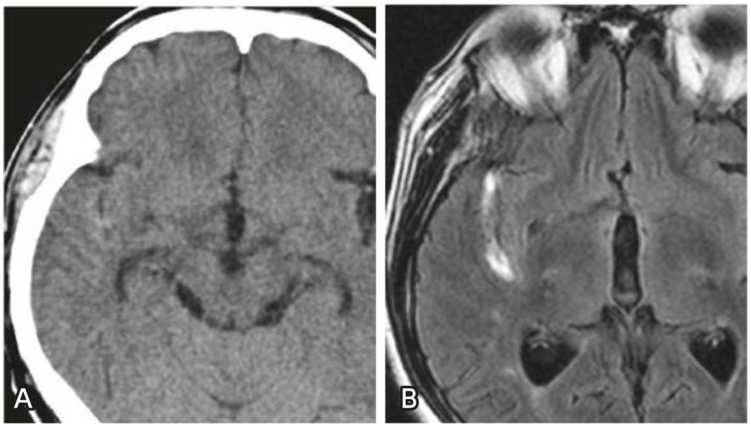


Figure. Subarachnoid hemorrhage

A: NCCT on the day of onset: The right Sylvian fissure is indistinct compared with the left and shows slightly high attenuation.

B: MR (FLAIR imaging) at 1 week after onset: Hyperintensity is seen in the right Sylvian fissure, where an abnormality was seen on CT, indicating a subarachnoid hemorrhage.

MRI (FLAIR, proton density-weighted, and T2*-weighted imaging) is also useful for diagnosing subarachnoid hemorrhage. An investigation using a 1.5T system involving 22 patients found that the sensitivity of FLAIR imaging, T2*-weighted imaging, and CT was 100%, 90.9%, and 91%, respectively, up to 5 days after onset. Subsequently, the sensitivity of FLAIR imaging and CT decreased to 33.3% and 45%, respectively, whereas that of T2*-weighted imaging increased to 100%.[8] Similarly, in an investigation using a 1.5T system involving 41 patients, the sensitivity of T2*-weighted and FLAIR imaging was 94% and 81%, respectively, up to 4 days after onset and 100% and 75% from 5 to 14 days after onset.[9] Although FLAIR imaging is useful in the acute phase, its sensitivity decreases over time, and the addition of T2*-weighted imaging to FLAIR imaging is necessary for the subacute phase. However, distinguishing between old and new subarachnoid hemorrhages may be difficult with T2*-weighted imaging.

The rate of subarachnoid hemorrhage misdiagnosis in the acute outpatient setting has been reported to range from 5% to 12%,[10, 11] and the main cause of misdiagnosis was that NCCT was not performed.[6] Moreover, one-fourth of patients with subarachnoid hemorrhage do not have headache, and approximately half have no neurological abnormalities.[1] If the patient's symptoms are mild at onset, and there is little bleeding (bleeding referred to as a sentinel bleed or warning leak), the condition cannot be diagnosed even if CT is performed.[12-14] In a prospective, cohort study of 592 neurologically normal patients with non-traumatic acute headache up to 14 days after the onset of symptoms, the sensitivity and specificity of CT in detecting subarachnoid hemorrhage were 90% and 99%, respectively. If CT was negative and lumbar puncture was added, the sensitivity and specificity (100% and 67%, respectively) were found to be sufficient to exclude subarachnoid hemorrhage.[14]

In an investigation including 12 patients with subarachnoid hemorrhage diagnosed by lumbar puncture that could not be diagnosed by CT, false negatives were obtained for 10 patients who underwent FLAIR imaging with a 1.5T system (FLAIR imaging performed within 2 days after CT for 10 patients and within 1

week for 2 patients). Thus, subarachnoid hemorrhage that could not be detected by CT was also difficult to detect with FLAIR imaging. Consequently, FLAIR imaging could not substitute for lumbar puncture.[15] Moreover, with FLAIR imaging, the cerebral sulci and cisterns may show hyperintensity due not only to subarachnoid hemorrhage, but also due to conditions such as meningitis, meningeal dissemination, acute cerebral infarction, moyamoya disease, venous thrombosis, oxygen administration, intravenous anesthesia with propofol, and artifacts.[16] The basilar cistern is particularly susceptible to ghost artifacts resulting from pulsation of the cerebrospinal fluid. Consequently, the interpretation of subarachnoid hemorrhage with FLAIR imaging requires caution.

Search keywords and secondary sources used as references

PubMed was searched using the following keywords: subarachnoid hemorrhage, subarachnoid haemorrhage, MRI, CT, fluid attenuated inversion recovery, and FLAIR. The search was limited to the article titles, and articles related to diagnosis were used in the review. The period searched was through May 2020.

References

1) Bederson JB et al: Guidelines for the management of aneurysmal subarachnoid hemorrhage: a statement for healthcare professionals from a Special Writing Group of the Stroke Council, American Heart Association. Stroke 40: 994-1025, 2009
2) Perry JJ et al: Sensitivity of computed tomography performed within six hours of onset of headache for diagnosis of subarachnoid haemorrhage: prospective cohort study. BMJ 343: 4277, 2011
3) Van der Wee N et al: Detection of subarachnoid haemorrhage on early CT: is lumbar puncture still needed after a negative scan? J Neurol Neurosurg Psychiatry 58: 357-359, 1995
4) Sames TA et al: Sensitivity of new-generation computed tomography in subarachnoid hemorrhage. Acad Emerg Med 3: 16-20, 1996
5) Sidman R et al: Subarachnoid hemorrhage diagnosis: lumbar puncture is still needed when the computed tomography scan is normal. Acad Emerg Med 3: 827-831, 1996
6) Morgenstern LB et al: Worst headache and subarachnoid hemorrhage: prospective, modern computed tomography and spinal fluid analysis. Ann Emerg Med 32: 297-304, 1998
7) Gijn J et al: The time course of aneurysmal haemorrhage on computed tomograms. Neuroradiology 23: 153-156, 1982
8) Yuan MK et al: Detection of subarachnoid hemorrhage at acute and subacute/chronic stages: comparison of four magnetic resonance imaging pulse sequences and computed tomography. J Chin Med Assoc 68: 131-137, 2005
9) Mitchell P et al: Detection of subarachnoid haemorrhage with magnetic resonance imaging. J Neurol Neurosurg Psychiatry 70: 205-211, 2001
10) Vermeulen MJ et al: Missed diagnosis of subarachnoid hemorrhage in the emergency department. Stroke 38: 1216-1221, 2007
11) van Gijn J et al: Subarachnoid haemorrhage: diagnosis, causes and management. Brain 124: 249-278, 2001
12) Kowalski RG et al: Initial misdiagnosis and outcome after subarachnoid hemorrhage. JAMA 291: 866-869, 2004
13) Tong DM et al: Predictors of the subarachnoid hemorrhage of a negative CT scan. Stroke 41: e566-567, 2010
14) Perry JJ et al: Is the combination of negative computed tomography result and negative lumbar puncture result sufficient to rule out subarachnoid hemorrhage? Ann Emerg Med 51: 707-713, 2008
15) Mohamed M et al: Fluid-attenuated inversion recovery MR imaging and subarachnoid hemorrhage: not a panacea. AJNR 25: 545-550, 2004
16) Maeda M et al: Abnormal hyperintensity within the subarachnoid space evaluated by fluid-attenuated inversion-recovery MR imaging: a spectrum of central nervous system diseases. Eur Radiol 13: L192-L201, 2003

BQ 2 Which imaging examinations are recommended to diagnose acute intracerebral hemorrhage?

Statement

Non-contrast CT (NCCT) is strongly recommended to evaluate the presence or absence of intracerebral hemorrhage.

Background

NCCT has generally been used to diagnose stroke due to its high detection performance for brain hemorrhage and its versatility. However, with the increased availability of MRI, settings in which MRI is used to diagnose stroke have increased in Japan (Fig.). However, it is unclear whether MRI can substitute for NCCT in diagnosing acute intracerebral hemorrhage. The diagnostic performance of NCCT and MRI to diagnose acute intracerebral hemorrhage was examined.

Explanation

1. CT

Intracerebral hemorrhage accounts for approximately 20% of strokes, and the presence or absence of intracranial hemorrhage is important for determining stroke treatment. Although there have been studies of the sensitivity and specificity of CT for subarachnoid hemorrhage that have used the lumbar puncture test as the reference standard, reports comparing early CT with surgery and autopsy results in intracerebral hemorrhage are limited to reports from the 1970s.[1, 2] Thus, there is insufficient evidence regarding the sensitivity and specificity of NCCT in diagnosing acute intracerebral hemorrhage. Nevertheless, NCCT has been accepted as the first choice for detecting acute cerebral hemorrhage, and it is now widely used for this purpose.[3-5] It should be noted, however, that the detection performance of CT with respect to intracerebral hemorrhage is also affected by factors such as the time from onset, the site and size of the hemorrhage, and the hematocrit concentration.

2. MRI

There have been few studies that have compared MRI methods for detecting intracerebral hemorrhage.[6] Consequently, there is insufficient evidence regarding which MRI method is the best. With the change from oxyhemoglobin to deoxyhemoglobin after hemorrhage, acute hemorrhage shows a signal ranging from isointense to mildly hyperintense in T1-weighted images and from hyperintense to hypointense in T2-weighted and diffusion-weighted images. In $T2^{*}$-weighted images (GRE), oxyhemoglobin shows a signal ranging from isointense to hyperintense, whereas deoxyhemoglobin, because it is a paramagnet, shows strong hypointensity due to the susceptibility effect. T2*-weighted imaging is therefore considered useful for diagnosing acute hemorrhage.[5]

In a retrospective study of 43 patients with hemorrhagic stroke and 43 patients with nonhemorrhagic stroke (41 patients with arterial cerebral infarction and 2 with transient ischemic attack), the sensitivity and specificity of T2*-weighted imaging were 100% and 95% to 97.5%, respectively. Chronic hemorrhage was concluded to be acute hemorrhage in 1 patient based on T2*-weighted imaging.[6] In a prospective investigation involving 217 patients with stroke, acute intracerebral hemorrhage was seen in 12 patients, and the sensitivity and specificity of T2*-weighted imaging [diffusion-weighted imaging (b-value = 0) performed when image quality was poor with T2*-weighted imaging] for acute intracerebral hemorrhage, with NCCT used as the reference standard, were 83% and 100%, respectively.[7]

In a study of 200 patients with suspected stroke within 6 hours of onset, acute hemorrhage was seen in 25 patients on both CT and MRI. Acute hemorrhages were seen only on MRI in 4 patients, and all were hemorrhagic changes in an ischemic area. Acute hemorrhages were identified only on CT in 3 patients. With MRI, they were diagnosed as old hematomas. Although a small subarachnoid hemorrhage was detected on CT in 1 patient, it was not identified on MRI. In 52 patients, chronic hemorrhage was seen only on MRI and was difficult to identify with CT. The inter-reader agreement rate for acute hemorrhage was higher with CT.[8]

The diagnostic performance of MRI was examined in 62 patients with acute cerebral hemorrhage within 6 hours of onset, with NCCT used as the reference standard. With diagnosis by physicians skilled in the diagnostic imaging of stroke, the sensitivity and specificity of MRI were both 100%.[5] However, the diagnostic accuracy of MRI in diagnosing hemorrhage differs depending on the experience of the diagnostician. Skill is therefore required to diagnose acute cerebral hemorrhage by MRI.[5] If the time of onset is unclear or the MRI assessment is uncertain, it is important to obtain confirmation by CT.

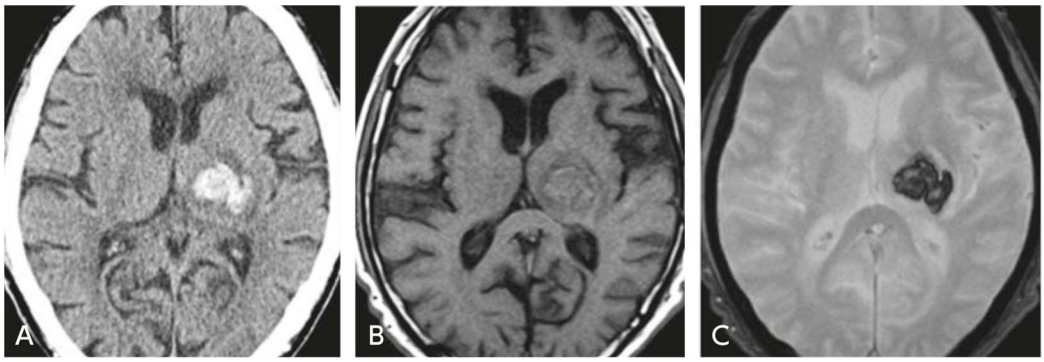


Figure. Acute thalamic hemorrhage 3 hours after onset

A: NCCT: High-attenuation hemorrhage is seen in the left thalamus.

B: MRI, T1-weighted image: The area shows non-homogeneous hyperintensity, and acute hemorrhage is suspected.

C: MRI, T2*-weighted image: The area shows strong hypointensity due to the presence of deoxyhemoglobin.

There is currently no evidence that MRI is superior to CT for evaluating acute intracerebral hemorrhage, though many reports indicate that they perform equally well in this role. Particularly in severe cases, measures such as limiting physical activity of the patient and biomonitoring during the examination should be considered.[7]

Search keywords and secondary sources used as references

PubMed was searched using the following keywords: CT, MRI, imaging, stroke, hemorrhage, guideline, and systematic review.

In addition, the following were referenced as secondary sources.

1) Salmela MB et al: ACR Appropriateness Criteria®: cerebrovascular disease. J Am Coll Radiol 5S: S34-S61, 2017
2) Brazzelli M et al: Magnetic resonance imaging versus computed tomography for detection of acute vascular lesions in patients presenting with stroke symptoms. Cochrane Database Syst Rev (4): CD007424, 2009
3) Goyal MS et al: Hyperacute ischemic stroke in adults. Kelly A et al (eds.): Evidence-based emergency imaging. Springer, pp.91-112, 2018
4) Hemphill JC 3rd et al: Guidelines for the Management of Spontaneous Intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 46: 2032-2060, 2015

References

1) Paxton R and Ambrose J: The EMI scanner: a brief review of the first 650 patients. Br J Radiol 47: 530-565, 1974
2) Jacobs L et al: Autopsy correlations of computerized tomography: experience with 6,000 CT scans. Neurology 26: 1111-1118, 1976
3) Hacke W et al: Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II): Second European-Australasian Acute Stroke Study Investigators. Lancet 352: 1245-1251, 1998
4) Berkhemer OA et al: A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med. 372: 11-20, 2015
5) Fiebach JB et al: Stroke magnetic resonance imaging is accurate in hyperacute intracerebral hemorrhage: a multicenter study on the validity of stroke imaging. Stroke 35: 502-506, 2004
6) Oppenheim C et al: Comparison of five MR sequences for the detection of acute intracranial hemorrhage. Cerebrovasc Dis 20: 388-394, 2005
7) Chalela JA et al: Magnetic resonance imaging and computed tomography in emergency assessment of patients with suspected acute stroke: a prospective comparison. Lancet 369: 293-298, 2007
8) Kidwell CS et al: Comparison of MRI and CT for detection of acute intracerebral hemorrhage. JAMA 292: 1823-1830, 2004

BQ 3 Which imaging examinations are recommended to determine whether reperfusion therapy is indicated for patients with acute cerebral infarction?

Statement

Diagnostic imaging by CT or MRI is essential for determining whether reperfusion therapy is indicated. Note, however, that they are imaging examinations whose use should be minimized and should not delay the start of treatment.

We recommended the use of noncontrast CT (NCCT) for excluding hemorrhage.

We also recommended regional evaluation of early ischemic changes (EICs) with NCCT using the Alberta Stroke Program Early CT Score (ASPECTS) for determining whether thrombolytic therapy is indicated and predicting prognosis.

MRI provides information similar to CT in evaluating hemorrhage, and diffusion-weighted imaging (DWI) is more sensitive than CT in detecting ischemic lesions. The use of MRI, with attention paid to safety, is therefore recommended.

If mechanical thrombectomy within 6 hours after onset is considered, it is recommended that the site of vascular occlusion be examined by CTA or MRA.

DWI-FLAIR mismatch is useful for estimating the time of onset in patients for whom the onset time is unknown. DWI and FLAIR imaging are therefore recommended in such cases.

Ischemic core evaluation using diffusion-weighted or CT perfusion images and ischemic penumbra (perfusion-core mismatch) evaluation using CT/MR perfusion images are considered useful for determining whether mechanical thrombectomy is indicated for patients 6-24 hours after onset. Their use is therefore recommended.

Background

In 2005, intravenous therapy with recombinant tissue plasminogen activator (rt-PA, alteplase) for acute cerebral infarction within 3 hours of onset became covered by national health insurance in Japan. The coverage was expanded to include acute cerebral infarction within 4.5 hours of onset in 2012. Subsequently, thrombus removal by catheterization was shown to be effective in cases of internal carotid artery or proximal middle cerebral artery occlusion.[1-6] In recent years, there have been reports of the indications for intravenous rt-PA therapy for acute cerebral infarction with an unknown time of onset[7] and on the expansion of the time during which thrombectomy is indicated.[8, 9] This discussion summarizes the evidence regarding the usefulness of diagnostic imaging in determining whether thrombolysis and thrombectomy are indicated, with a focus on NCCT and MRI.

Explanation

To predict the efficacy of thrombolytic therapy, it is important to evaluate the region that would be saved (ischemic penumbra) by recanalization. The revised version of the guidelines for appropriate treatment calls for the use of diagnostic imaging with NCCT or MRI to exclude intracranial hemorrhage and determine whether EICs (Fig.1) are present.

NCCT is excellent for detecting acute intracranial hemorrhage and highly useful for diagnosing intracranial hemorrhage by exclusion. EIC evaluation by CT has in the past been performed by assessing whether the extent of EICs is ≤ 1/3 of the territory of the middle cerebral artery (MCA, the 1/3 MCA rule).[10, 11] However, EICs and territory assessment have not been clearly defined, and there is variability between readers.[12] ASPECTS is therefore currently in general use. ASPECTS (Fig. 2) divides the MCA territory into 10 regions, and EICs in each region are evaluated and scored by subtracting from a perfect score of 10 points. It is a relatively easy method of assessment, and it has higher interrater agreement rate than the 1/3 MCA rule.[13] The relationships of ASPECTS with functional prognosis and the mortality rate have been examined.[14, 15] However, both methods of evaluation are limited to the MCA territory, and there has been insufficient examination of the scoring, such as the fact that the distribution of scores is the same regardless of the localization of brain function. Moreover, there have been reports indicating that these methods of evaluation are not useful for treatment selection.[15, 16] Thus, there are limitations to evaluating the ischemic penumbra by NCCT alone when assessing whether thrombolytic therapy is indicated.

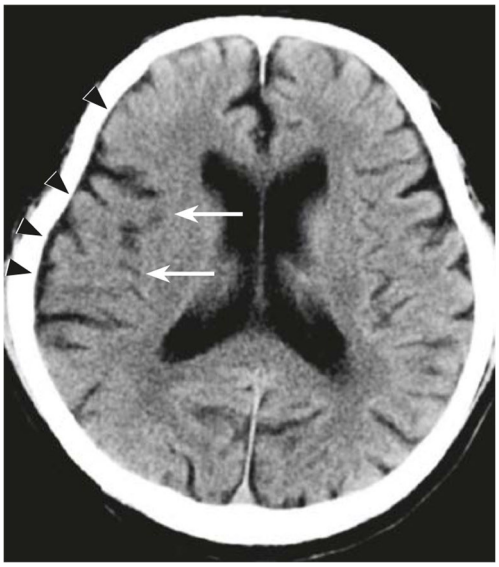


Figure 1. Early ischemic changes (EICs)

CT 2.5 hours after onset: Loss of the insular ribbon (→) and loss of gray-white differentiation (►) are seen. Obscuring of the lentiform nucleus, loss of the insular ribbon, loss of gray-white differentiation, and effacement of the cortical sulci are known EICs.

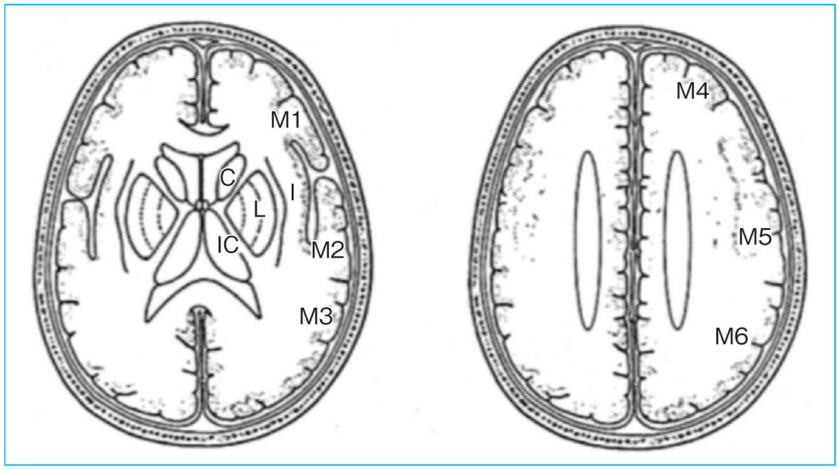


Figure 2. ASPECTS study form (taken from secondary source 4 with permission)

The unilateral middle cerebral artery territory is divided into 10 regions, and each region is evaluated for the presence or absence of EICs, which are scored by subtraction. A score of 10 points is assigned if EICs are completely absent, and the score is 0 points if EICs are seen in all MCA regions.

C: area of the head of the caudate nucleus; L: lentiform nucleus; IC: posterior limb of the internal capsule; I: insular cortex; M1 to M3: middle cerebral artery territory, basal ganglia level; M4 to M6: middle cerebral artery territory, corona radiata level.

An advantage of MRI is that diffusion-weighted images can be obtained (Fig. 3). In some cases, faint hyperintensity on diffusion-weighted images is reversible. Although the significance of this has not been established, it enables infarcts to be distinctly visualized from an early stage, with little inter-reader variability. It is also excellent for detecting small lesions of the brain stem, cerebellum, cortex, and subcortex. Consequently, the diagnostic performance of (DWI) with respect to acute cerebral infarction is considered high. A method of evaluation that matches areas of hyperintensity in DWI with ASPECTS (DWI-ASPECTS) is used to evaluate EICs. The scores obtained with DWI-ASPECTS are approximately 1 point lower than those obtained by CT. Although the scores obtained with both methods are good predictors of posttreatment symptomatic cerebral hemorrhage and functional prognosis after 3 months, DWI-ASPECTS has been found to be superior.[17)]

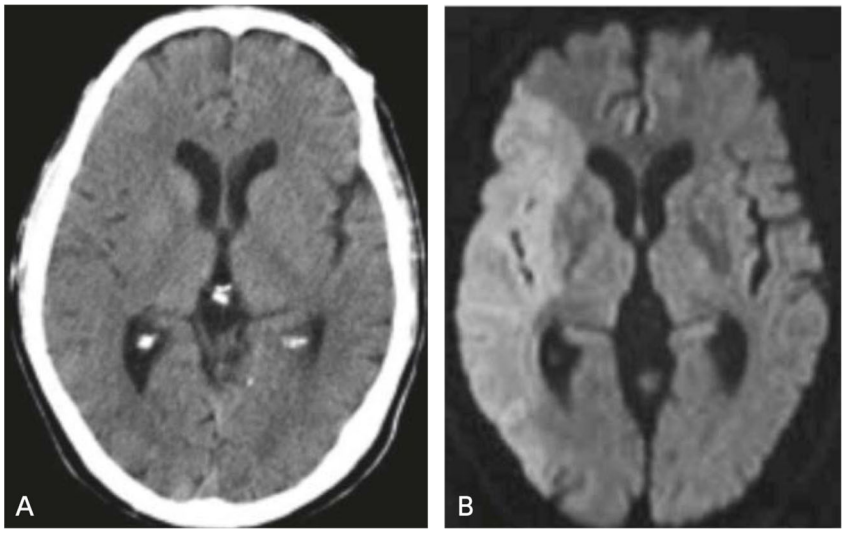


Figure 3. Patient with acute cerebral infarction

A: CT 50 minutes after onset, B: MRI 1 hour and 10 minutes after onset (diffusion-weighted image)
During hospitalization for heart failure, acute cerebral infarction occurred with consciousness disturbance and left hemiplegia. National Institutes of Health Stroke Scale (NIHSS) score of 29 points at onset.
EICs seen extensively in the right hemisphere on both CT and MRI (diffusion-weighted imaging). However, the extent of ischemia is more clearly identifiable with MRI. ASPECTS score of 3 points on both CT and MRI. Watchful waiting was adopted because rt-PA was not indicated. CT the next day showed clear hypodensity in the same region.

The detection performance of MRI is also high in acute intracranial hemorrhage (see the section on brain hemorrhage for details). In particular, susceptibility-weighted imaging such as T2*-weighted imaging is excellent for detecting microbleeds (MBs). However, the basis for using the presence of MBs as the criterion for careful administration of thrombolytic therapy is weak.

Moreover, it has been reported that, if the ischemic lesion is hyperintense on diffusion-weighted images, but does not show hyperintensity on FLAIR images (DWI-FLAIR mismatch), it can be estimated that the patient is within 4.5 hours after stroke onset.[18] An RCT called WAKE-UP, published in 2018, showed that intravenous rt-PA therapy was useful in patients with DWI-FLAIR mismatch for whom the time of onset was unknown.[7]

Endovascular thrombectomy is strongly recommended for patients within 6 hours of onset and with acute occlusion of the internal carotid artery (ICA) or proximal MCA (M1) for whom intravenous rt-PA therapy is indicated by an ASPECTS score ≥ 6 points and NIHSS score ≥ 6 points on head CT or diffusion-weighted images. In 2018, 2 RCTs, the DAWN and DEFUSE 3 trials, reported that thrombectomy was useful for acute occlusion of the ICA or M1 area occurring more than 6 hours from the time last known well.[8, 9] In Japan, it is recommended that thrombectomy begin within 16 hours for patients with a modified Rankin Scale (mRS) score of 0 or 1 before onset, an NIHSS score ≥ 10 points, and a DWI-ASPECTS score ≥ 7 points, and within 24 hours for patients judged to have a mismatch between the ischemic core volume on CT perfusion images or diffusion-weighted images and neurological symptoms or the delayed perfusion area in perfusion images.

Although identification of a vascular lesion is not essential for intravenous rt-PA therapy, evaluation of intracranial vessels by CTA or MRA is necessary if endovascular therapy is considered. However, intravenous therapy should be given priority in patients for whom intravenous rt-PA therapy is indicated, and the start of therapy should not be delayed by additional examinations. In other countries, CTA is often the first choice for diagnosing occluded vessels.[6] CTA can be used to evaluate thrombus size as the area of contrast deficit, as well as the site of an occlusion. CTA imaging in multiple time phases has been reported to enable collateral blood flow to be evaluated and to provide an estimate of the extent of the ischemic core.[3] MRA is also useful for evaluating occluded blood vessels. Compared with other countries, its use in acute cerebral infarction is particularly common in Japan, where MRI is frequently performed. An advantage of MRA is its low invasiveness, due to the fact that a contrast agent is not used, and no radiation exposure is involved. Another advantage is that it enables the extent of the ischemic core to be evaluated by DWI almost simultaneously during a sequence of MRI examinations. Because slow blood flow results in poor visualization, careful interpretation of the images is needed.

Perfusion imaging with CT involves rapidly injecting an iodinated contrast medium intravenously and performing continuous scanning to acquire images of cerebral perfusion. MRI methods of perfusion imaging are dynamic susceptibility contrast, which involves rapid intravenous injection of a gadolinium contrast agent, and arterial spin labeling (ASL), which does not use a contrast agent. However, only a limited number of facilities can use ASL, and its adoption has been slow. Recent RCTs in acute cerebral infarction have included trials that have measured pretreatment ischemic core volume using cerebral blood flow (CBF) on CT perfusion images.[2, 4, 8, 9] In an RCT that examined the period beginning from 6 hours after onset, not only the ischemic core volume, but also the extent of the delayed perfusion area based on Tmax was measured on CT/MR perfusion images. Whether endovascular thrombectomy was indicated was determined with the mismatch region considered the salvageable region.[9] Thus, the number of studies that used perfusion images to determine whether reperfusion therapy is indicated has been increasing, and most of the published RCTs from other countries have used automated analysis software called RAPID™ (Rapid AI). Software that can rapidly measure ischemic core volumes, delayed perfusion areas, and mismatch regions, such as RAPID™, has not yet been widely adopted in Japan. Care must therefore be exercised in determining whether reperfusion therapy is indicated for individual patients.

Search keywords and secondary sources used as references

PubMed was searched using the following keywords: acute ischemia, thrombolysis, thrombectomy, brain, CT, and MRI.

In addition, the following were referenced as secondary sources.

1) Working Group on Revised Guidelines for Intravenous Thrombolysis, Committee for Medical Improvement and Social Insurance in Stroke, Japan Stroke Society, Ed.: Guidelines for Appropriate Intravenous Thrombolytic Therapy (rt-PA), 3rd Edition. Japanese Journal of Stroke 41:205-245, 2019.
2) Japan Stroke Society, et al., Ed.: Guidelines for the Appropriate Use of Percutaneous Transluminal Thrombectomy Devices, 4th Edition. Japan Stroke Society, Japan Neurosurgical Society, Japanese Society for Neuroendovascular Therapy, 2020.
3) Powers WJ et al: Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association / American Stroke Association. Stroke 50: e344-e418, 2019
4) Barber PA et al: Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study Group. Alberta Stroke Programme Early CT Score. Lancet 355: 1670-1674, 2000

References

1) Berkhemer OA et al: MR CLEAN investigators: a randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 372: 11-20, 2015
2) Campbell BC et al: EXTEND-IA investigators: endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med 372: 1009-1018, 2015
3) Goyal M et al: ESCAPE trial investigators: randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med 372: 1019-1030, 2015
4) Saver JL et al: SWIFT PRIME investigators: Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med 372: 2285-2295, 2015
5) Jovin TG et al: REVASCAT trial investigators: thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med 372: 2296-2306, 2015
6) Goyal M et al: HERMES collaborators: endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet 387: 1723-1731, 2016
7) Thomalla G et al: WAKE-UP investigators: MRI-guided thrombolysis for stroke with unknown time of onset. N Engl J Med 379: 611-622, 2018
8) Nogueira RG et al: DAWN trial investigators: thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. N Engl J Med 378: 11-21, 2018
9) Albers GW et al: DEFUSE 3 investigators: thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. N Engl J Med 378: 708-718, 2018
10) von Kummer R et al: Acute stroke: usefulness of early CT findings before thrombolytic therapy. Radiology 205: 327-333, 1997
11) Hacke W et al: Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II): Second European-Australasian Acute Stroke Study Investigators. Lancet 352: 1245-1251, 1998
12) Grotta JC et al: Agreement and variability in the interpretation of early CT changes in stroke patients qualifying for intravenous rtPA therapy. Stroke 30: 1528-1533, 1999
13) Pexman JH et al: Use of the Alberta Stroke Program Early CT Score (ASPECTS) for assessing CT scans in patients with acute stroke. AJNR Am J Neuroradiol 22: 1534-1542, 2001
14) Hill MD et al: Selection of acute ischemic stroke patients for intra-arterial thrombolysis with pro-urokinase by using ASPECTS. Stroke 34: 1925-1931, 2003
15) Demchuk AM et al: Importance of early ischemic computed tomography changes using ASPECTS in NINDS rtPA Stroke Study. Stroke 36: 2110-2115, 2005
16) Patel SC et al: Lack of clinical significance of early ischemic changes on computed tomography in acute stroke. JAMA 286: 2830-2838, 2001
17) Nezu T et al: Early ischemic change on CT versus diffusion-weighted imaging for patients with stroke receiving intravenous recombinant tissue-type plasminogen activator therapy: stroke acute management with urgent risk-factor assessment and improvement (SAMURAI) rt-PA registry. Stroke 42: 2196-2200, 2011
18) Thomalla G et al: DWI-FLAIR mismatch for the identification of patients with acute ischaemic stroke within 4.5 h of symptom onset (PRE-FLAIR): a multicentre observational study. Lancet Neurol 10: 978-986, 2011

BQ 4 Is MRI recommended for diagnosing diffuse axonal injury (DAI)?

Statement

Detailed examination by MRI is recommended when DAI is suspected.

Background

With prolonged consciousness disturbance following head trauma, CT findings may be weak. DAI is suspected when there is a discrepancy like this between the neurological symptoms and CT findings or when traumatic subarachnoid hemorrhage or intraventricular hemorrhage is seen on CT.[1] In such cases, detailed examination by MRI is often performed. Various imaging methods have been reported to be useful for evaluating such cases by MRI. The lesion detection performance of MRI in head trauma and its usefulness for evaluating neurological prognosis are summarized below.

Explanation

1. CT and MRI

For the diagnosis of brain hemorrhage, cerebral contusion, and DAI occurring with head trauma, MRI provides higher contrast resolution and superior diagnostic performance than CT.[2-6] DAI in particular is often not detected by CT and normal MRI imaging such as T1- and T2-weighted imaging, and caution is therefore required in its diagnosis.[4-6] Dionei et al. compared CT and MRI in 55 patients with head trauma and found that T2- and T2*-weighted and FLAIR MRI were significantly superior to CT for lesion detection in acute subdural hematoma, traumatic subarachnoid hemorrhage, cerebral contusion, and DAI.[2]

2. FLAIR and diffusion-weighted imaging

Of the general imaging methods, FLAIR and diffusion-weighted imaging are excellent for lesion detection in conditions such as non-hemorrhagic DAI. In a retrospective examination of 56 patients by Ashikaga et al. that compared evaluation with FLAIR and T2-weighted images, FLAIR imaging was significantly superior for detecting DAI, cerebral contusion, and subdural hematoma, its detection performance being equal to or better than that of T2-weighted imaging in all patients.[7] In a retrospective examination of 36 patients by Kinoshita et al. that compared the detection performance of FLAIR and diffusion-weighted imaging with respect to DAI, the evaluations were comparable, suggesting that FLAIR and diffusion-weighted imaging are useful in this role.[8]

3. T2*- and susceptibility-weighted imaging

DAI is often associated with microscopic hemorrhagic lesions, and T2*- and susceptibility-weighted imaging, which strongly reflect differences in susceptibility, are useful for its diagnosis. Compared with other imaging methods, T2*-weighted imaging provides higher detection performance for DAI and is

superior for detecting microscopic lesions.[9, 10] In an investigation of 66 patients with head trauma, Scheid et al. reported that normal T2-weighted imaging detected DAI at a total of 233 locations, whereas T2*-weighted imaging detected it at 608 locations. Thus, the detection performance of T2*-weighted imaging was significantly better than that of normal T2-weighted imaging.[10] In a comparison of T2*-weighted imaging and SWI with respect to the number of DAIs detected in 7 patients with severe head trauma, Tong et al. reported that T2*-weighted imaging detected DAI at a mean of 28.8 ± 8 locations per patient, whereas SWI detected DAI at a mean of 134 ± 27 locations. Thus, the detection performance of SWI was significantly better than that of T2*-weighted imaging (Fig.).[11] In addition, SWI has detected microscopic petechiae in the brain parenchyma of individuals who regularly sustain mild head trauma, such as boxers, suggesting that it can also detect microscopic DAI in diagnosing head trauma.[12]

4. Neurological prognosis evaluation

With regard to neurological prognosis based on DAI and the Glasgow Coma Scale, the number of lesions detected with T2*-weighted imaging has been found not to be correlated with the prognosis.[10] However, an increase in the number of lesions detected with SWI has been found to be correlated with prognosis in terms of indices such as prolongation of consciousness disturbance.[13, 14] SWI is recommended if feasible.

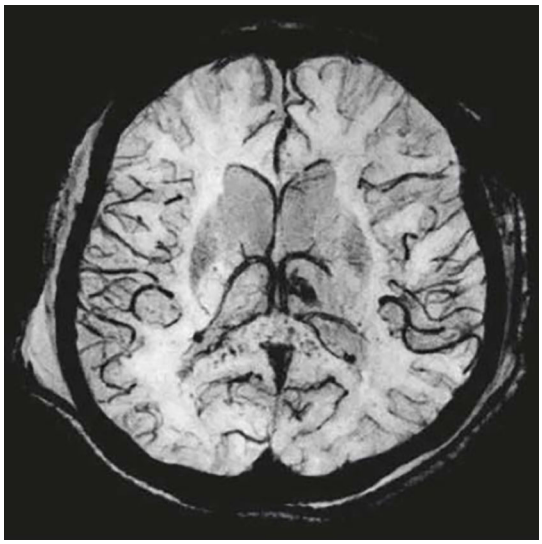


Figure. Patient with prolonged consciousness disturbance following a traffic accident (MRI)

SWI: Multiple punctiform hypointensities are seen in the splenium of the corpus callosum, and DAI was diagnosed.

Search keywords and secondary sources used as references

PubMed was searched using the following keywords: brain contusion, diffuse axonal injury, hemorrhage, and MRI.

References

1) Vieira GFR et al: Early computed tomography for acute post-traumatic diffuse axonal injury: a systematic review. Neuroradiology 2020 Mar 4
2) Dionei FS et al: Clinical application of magnetic resonance in acute traumatic brain injury. Arq Neuropsiquiatr 66: 53-58, 2008
3) Yokota H et al: Significance of magnetic resonance imaging in acute head injury. J Trauma 31: 351-357, 1991
4) Mittl RL et al: Prevalence of MR evidence of diffuse axonal injury in patients with mild head injury and normal head CT findings. AJNR Am J Neuroradiol 15: 1583-1589, 1994
5) Paterakis K et al: Outcome of patients with diffuse axonal injury: the significance and prognostic value of MRI in the acute phase. J Trauma 49: 1071-1075, 2000
6) Chelly H et al: Diffuse axonal injury in patients with head injuries: an epidemiologic and prognosis study of 124 cases. J Trauma 71: 838-846, 2011
7) Ashikaga R et al: MRI of head injury using FLAIR. Neuroradiology 39: 239-242, 1997
8) Kinoshita T et al: Conspicuity of diffuse axonal injury lesions on diffusion-weighted MR imaging. Eur J Radiol 56: 5-11, 2005
9) Scheid R et al: Comparative magnetic resonance imaging at 1.5 and 3 tesla for the evaluation of traumatic microbleeds. J Neurotrauma 24: 1811-1816, 2007
10) Scheid R et al: Diffuse axonal injury associated with chronic traumatic brain injury: evidence from T2*-weighted gradient-echo imaging at 3T. AJNR Am J Neuroradiol 24: 1049-1056, 2003
11) Tong KA et al: Hemorrhagic shearing lesions in children and adolecents with posttraumatic diffuse axonal injury: improved detection and initial results. Radiology 227: 332-339, 2003
12) Hasiloglu ZI et al: Cerebral microhemorrhages detected by susceptibility-weighted imaging in amateur boxers. AJNR Am J Neuroradiol 32: 99-102, 2011
13) Tong KA et al: Diffuse axonal injury in children: clinical correlation with hemorrhgic lesions. Ann Neurol 56: 36-50, 2004
14) Jing Z et al: Hemorrhagic shearing lesions associated with diffuse axonal injury: application of T2 star-angiography sequence in the detection and clinical correlation. Br J Neurosurg 25: 596-605, 2011

BQ 5 Are CT and MRI recommended for diagnosing primary headache in adults?

Statement

CT and MRI are of very little use for primary headache not associated with a neurological deficit, and their use is therefore not recommended for this purpose. However, CT and MRI may be useful for atypical headache, headache that does not fit a specific definition, thunderclap headache, and trigeminal autonomic cephalalgia, and its use can be considered for such conditions.

Background

The 3rd edition of the International Classification of Headache Disorders (ICHD-3), published by the International Headache Society (IHS), broadly categorizes headache as primary and secondary headaches and cephalalgias as central/primary facial pain and other types of headache (secondary source 1). Primary headache is classified as migraine headache, tension headache, cluster headache and other trigeminal autonomic cephalalgia, and other types of headache. Secondary headache encompasses headache associated with a variety of conditions, such as trauma, vascular disorders, non-vascular intracranial disorders, infection, and psychiatric disorders. ICHD-3 added reversible cerebral vasoconstriction syndrome (RCVS) to the secondary headache disorders. Primary headache and chronic headache are generally treated as synonymous, and their diagnosis centers on a detailed examination of medical history and neurological findings. The role of neuroimaging is considered small. In the clinical setting, however, CT or MRI is often performed before a headache is classified, and it therefore cannot be said that assessment of primary headache is common. For this discussion, the usefulness of diagnostic neuroimaging for primary headache was examined.

Explanation

The only studies that have examined the usefulness of neuroimaging for primary headache have been observational studies such as cohort and case-control studies. Its usefulness is therefore estimated based on the results of those studies. In 1985, Joseph et al. examined 48 patients who underwent CT or MRI for headache and reported that brain tumors were seen in 5 patients, and an arteriovenous malformation was seen in 1 patient.[1)] Of these patients with abnormal imaging findings, 5 showed neurological abnormalities, and 1 had an unclassifiable type of headache referred to as exertional headache. In an investigation of 100,800 patients with adult migraine headache, Weingarten et al. reported that, among patients with chronic headache with no symptoms of a neurological deficit, the detection rate of patients who required surgical treatment was approximately 0.01% with CT.[2)] In 1994, the American Academy of Neurology published diagnostic neuroimaging guidelines for patients with headache not associated with symptoms of a neurological deficit (secondary source 2). The recommendation in those guidelines was based on an

investigation by Fishberg, which was also published in 1994.[3] Fishberg reviewed 17 articles published between 1974 and 1991 and examined the findings from a total of 897 CT and MRI examinations performed in patients with migraine headache. Only 4 patients (0.4%) showed abnormalities that required treatment: 3 patients with brain tumors and 1 with an arteriovenous fistula. Based on these findings, the guidelines indicated that there was little need for neuroimaging examinations in patients with typical migraine headache. However, they also mentioned that organic disease that requires treatment may actually be present and indicated that CT or MRI may be indicated if the patient has atypical headache, a history of convulsions, or symptoms of a neurological deficit. In 2004, based on an examination of the literature, Sandrini et al. published guidelines on the usefulness of neurological and neuroimaging examinations in patients with non-acute headache (secondary source 3). The guidelines were revised and the 2nd edition published in 2010 (secondary source 4). The revised edition cited a prospective study by Sempere et al. of 1,876 patients with non-acute headache.[4] All of the patients in that study underwent CT or MRI. Significant organic disease was seen in only 1.2%, and intracranial disease was seen in only 0.9% of patients with headache not associated with symptoms of a neurological deficit. Based on this investigation, the authors concluded that the frequency of intracranial disease is low in patients with headache, and that the factors that can predict such cases are neurological findings, clinical course, and the history of the present illness. In 2005, Tsushima et al. examined MRI images of 306 patients with chronic headache not associated with symptoms of a neurological deficit.[5] They saw no abnormal findings in 169 patients and mild abnormalities in 135, and significant organic abnormalities were seen in only 2 patients (0.7%): pituitary adenoma and chronic subdural hematoma in 1 patient each. Thus, the literature consistently shows that imaging for chronic headache not associated with symptoms of a neurological deficit is of little use. However, the reports also indicate that imaging is to a certain extent necessary for atypical headache and headache that does not fit a specific definition. A recent report of a population-based study indicated that the presence of migraine headaches in women is a risk factor for deep white matter lesions. In addition, migraine headache associated with aura has been found to increase the risk of asymptomatic ischemic brain lesions.[6, 7] However, no causal relationship has been shown between detected lesions and headache, and further investigation is needed. Willbrink et al. examined 56 reports of patients with trigeminal autonomic cephalalgia, which is characterized by frequent, short-lasting headache attacks that are associated with unilateral autonomic symptoms of the face. They found that many of the patients had secondary causes associated with organic lesions such as brain tumors and vascular lesions.[8] Based on this finding, they concluded that neuroimaging is indicated when trigeminal autonomic cephalalgia is suspected based on an appropriate assessment. Besides routine cranial MRI, additional imaging should be performed as needed to evaluate the cervical blood vessels and the parasellar and paranasal sinus areas.

Search keywords and secondary sources used as references

PubMed was searched using the following keywords: chronic headache, diagnostic imaging, guideline, migraine, and cephalalgia.

In addition, the following were referenced as secondary sources.

1) Japanese Headache Classification Committee, Japanese Headache Society, Translation: International Classification of Headache Disorders, 3rd Edition. Igaku Shoin, 2018.
2) Practice parameter: the utility of neuroimaging in the evaluation of headache in patients with normal neurologic examinations (summary statement): report of the quality standards subcommittee of the American Academy of Neurology. Neurology 44: 1353-1354, 1994
3) Sandrini G et al: Neurophysiological tests and neuroimaging procedures in non-acute headache: guidelines and recommendations. Eur J Neurol 11: 217-224, 2004
4) Sandrini G et al: Neurophysiological tests and neuroimaging procedures in non-acute headache, 2nd ed. Eur J Neurol 18: 373-381, 2011

References

1) Joseph R et al: Intracranial space-occupying lesions in attending a migraine clinic. Practitioner 229: 477-481, 1985
2) Weingarten S et al: The effectiveness of cerebral imaging in the diagnosis of chronic headache. Arch Intern Med 152: 2457-2462, 1992
3) Fishberg BM: The utility of neuroimaging in the evaluation of headache in patients with normal neurologic examinations. Neurology 44: 1191-1197, 1994
4) Sempere AP et al: Neuroimaging in the evaluation of patients with non-acute headache. Cephalgia 25: 30-35, 2005
5) Tsushima Y, Endo K: MR imaging in the evaluation of chronic or recurrent headache. Radiology 235: 575-579, 2005
6) Swartz RH, Kern RZ: Migraine is associated with magnetic resonance imaging white matter abnormalities: a metaanalysis. Arch Neurol 61: 1366-1368, 2004
7) ETMinan M et al: Risk of ischemic stroke in people with migraine: systematic review and meta-analysis of observational studies. Bmj 330: 63, 2005
8) Wilbrink LA et al: Neuroimaging in trigeminal autonomic cephalgias: when, how, and of what ? Curr Opin Neurol 22: 247-253, 2009

BQ 6 Which imaging examinations are recommended to diagnose temporal lobe epilepsy?

Statement

MRI is the first-choice imaging modality for diagnosing temporal lobe epilepsy, and its use is therefore recommended for this purpose.

CT is less sensitive than MRI for detecting culprit lesions. However, it is useful for detecting calcification, and its use can be considered.

To identify epileptic foci for surgery, functional imaging is recommended, such as cerebral blood flow SPECT or glucose metabolism PET performed during a non-seizure period and cerebral blood flow SPECT performed during a seizure.

Background

Epileptogenic lesions in temporal lobe epilepsy are varied and include conditions such as hippocampal (amygdaloid) sclerosis, focal cortical dysplasia (FCD), tumors, vascular malformations, trauma, and pathological inflammatory changes such as limbic encephalitis and herpes simplex encephalitis. The importance of diagnostic imaging lies in the localization and qualitative diagnosis of these epileptogenic lesions. Moreover, for surgical treatment, the addition of functional neuroimaging using nuclear medicine examinations is recommended to identify epileptic foci. For this discussion, the usefulness of functional neuroimaging using nuclear medicine examinations was also examined.

Explanation

1. CT

Few studies have evaluated the usefulness of CT in detecting epileptogenic lesions. A retrospective study in children that included a comparison with MRI found that the sensitivity of CT for the culprit lesion was 31%, lower than that of MRI, at 64%.[1)] However, additional screening by CT may be useful when a pathological change associated with tissue calcification is suspected, as in the case of tumors and cavernous angiomas. Focal cortical dysplasia (FCD) type IIb was reported to be an area of high density on CT, which was thought to reflect a rich density of balloon cells.[2)] In addition, CT is selected when the patient's condition is poor; MRI cannot be performed due to the presence of a device such as a pacemaker; or there is a finding suggestive of increased intracranial pressure, such as intracranial hemorrhage, and surgical treatment is considered if possible.

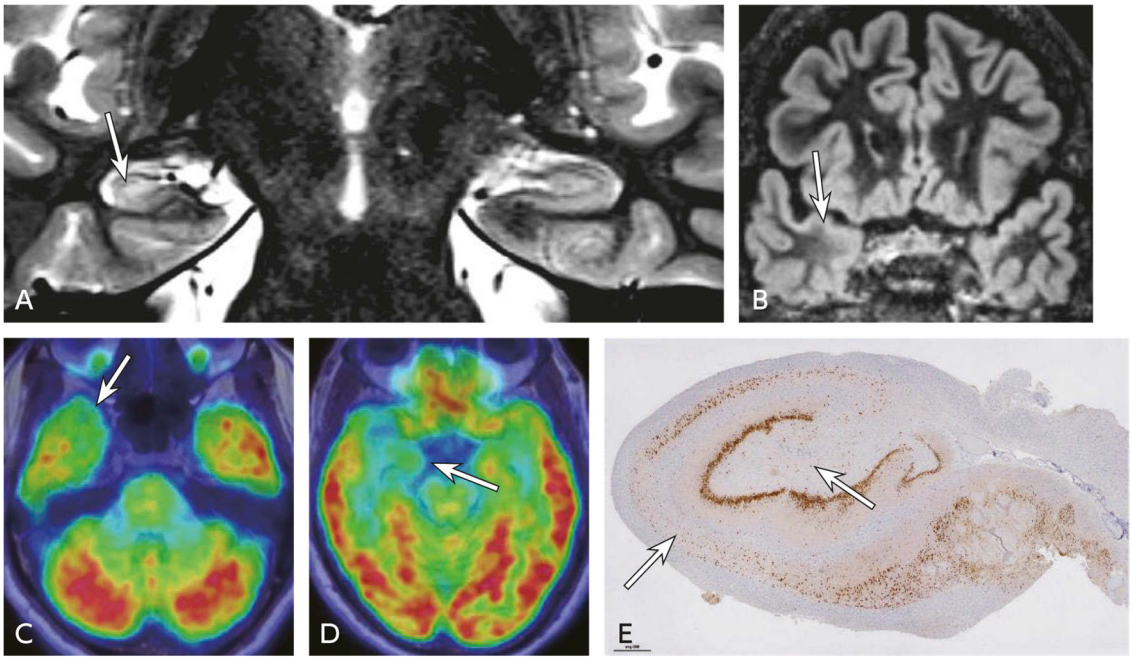
2. MRI

MRI is recommended, along with electroencephalography, as a routine examination for epilepsy. For epilepsy diagnosis, appropriate imaging with high spatial resolution and contrast is important.

Consequently, 3T MRI is recommended. Recommended sequences include high-resolution 3D T1-weighted imaging and 2D T2-weighted/FLAIR imaging (transverse and coronal planes). High-resolution 3D T1-weighted imaging should be performed with thin slices (≤ 1 mm) if possible and should be used to examine cerebral cortical morphology in fine detail.[3] For coronal imaging, imaging is performed in the plane orthogonal to the long axis of the hippocampus and must include the tip of the temporal lobe, which may be associated with an abnormal signal (Fig.). For 2D, a slice thickness of 3 mm is recommended (2 mm for infants). The 3D double inversion recovery (DIR) sequence, which suppresses the signal not only for cerebrospinal fluid, but also for white matter, is excellent for visualizing slight abnormal signal intensity in subcortical white matter.[4] $T2^*$-weighted or susceptibility-weighted imaging (SWI) is added if a vascular malformation, such as a cavernous angioma or arteriovenous malformation, or trauma or a tumor associated with hemorrhage is suspected. In addition, contrast-enhanced imaging is added if a nascent tumor is suspected.

3. SPECT

The tracers ^{99m}Tc-ethyl cysteinate dimer (^{99m}Tc-ECD) and ^{99m}Tc-hexamethyl-propylene amine oxime (^{99m}Tc-HMPAO) are taken up by the brain approximately 30 seconds after contrast medium administration. This is not true of ^{123}I-N-isopropyl-p-iodoamphetamine (IMP). Consequently, radiopharmaceuticals with the former 2 tracers are generally used when locating epileptic foci. Blood flow is decreased in foci on SPECT performed during a non-seizure period and increased on SPECT performed during a seizure. Sensitivity for identifying foci in temporal lobe epilepsy is ≤ 50% with SPECT performed during a non-seizure period. In contrast, it is a high 70% to 90% with SPECT performed during a seizure.[5] Moreover, subtraction of ictal SPECT-coregistered MRI (SISCOM), which involves subtracting SPECT images acquired during non-seizure periods from those acquired during seizures and superimposing them on MR images, is considered the best method for detecting foci.[6]



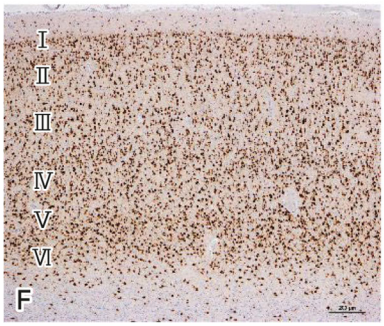


Figure. Right hippocampal sclerosis

A: MRI, T2-weighted coronal image; B: MRI, DIR coronal image
C, D: FDG-PET; E: Anti-NeuN immunostaining, right hippocampus
F: Anti-NeuN immunostaining, tip of the right temporal lobe
The patient was a woman in her 50s. Right temporal lobe epilepsy first occurred when she was 18 years old.
The right hippocampus is atrophied. On T2-weighted MRI, it shows hyperintensity, and the laminar structure is indistinct. In particular, strong hyperintensity is seen in regions C1 and C4 (A →). With the MR DIR sequence, the signal of the white matter at the tip of the right temporal lobe is higher than that of the contralateral side (B →). This may indicate changes secondary to epilepsy or a complication of FCD. In the FDG-PET images, decreased glucose metabolism is present not only in the interior of the right temporal lobe, but it also extends to the tip and lateral area (C, D →). The pathological appearance of the right hippocampus shows neuronal loss in regions C1, C3, and C4 (E →) with NeuN staining of the neurons, indicating hippocampal sclerosis type 1. This pathological finding corresponds well with the MRI findings (A). The pathology of the tip of the right temporal lobe is not associated with disturbance of the 6-layer laminar structure (F), and no complicating FCD is seen, indicating it resulted from secondary changes.

4. PET

FDG-PET assessment of glucose metabolism has long been used to identify epileptic foci in the temporal lobe.[5)] Although uptake at the site of a focus decreases during non-seizure periods, the decrease is more extensive than the focus site (Fig.). One study found no significant difference in post-temporal lobectomy prognosis between a group of patients with negative MRI and positive FDG-PET findings (decreased temporal lobe uptake) and a group with a positive MRI finding (hippocampal sclerosis),[7)] indicating that FDG-PET was useful.

Search keywords and secondary sources used as references

PubMed was searched using the following keywords: CT, MRI, SPECT, PET, temporal lobe, and epilepsy.

In addition, the following was referenced as a secondary source.

1) Japanese Society of Neurology, Ed.: Clinical Practice Guidelines for Epilepsy 2018. Igaku Shoin, 2018.

References

1) Sinclair DB: Pathology and neuroimaging in pediatric temporal lobectomy for intractable epilepsy. Pedia Neurosurg 35: 239-246, 2001
2) Kimura Y: Radiologic and pathologic features of the transmantle sign in focal cortical dysplasia: the T1 signal is useful for differentiating subtypes. AJNR Am J Neuroradiol 40: 1060-1066, 2019
3) Ahmed R: Utility of additional dedicated high-resolution 3T MRI in children with medically refractory focal epilepsy. Epilepsy Res 143: 113-119, 2018
4) Rugg-Gunn FJ: Imaging the neocortex in epilepsy with double inversion recovery imaging. Neuroimage 31 (1): 39-50, 2006
5) Kumar A, Chugani HT: The role of radionuclide imaging in epilepsy, part 1: sporadic temporal and extratemporal lobe epilepsy. J Nucl Med 54 (10): 1775-1781, 2013
6) O'Brien TJ et al: Subtraction ictal SPECT co-registered to MRI improves clinical usefulness of SPECT in localizing the surgical seizure focus. Neurology 50: 445-454, 1998
7) Carla LK: Surgical outcome in PET-positive, MRI-negative patients with temporal lobe epilepsy. Epilepsia 53 (2): 342-348, 2012

BQ 7 Are MRI and cerebral blood flow SPECT recommended to diagnose Alzheimer's disease (AD)?

Statement

MRI can detect the medial temporal lobe atrophy that is characteristic of AD, and it is also useful for diagnosing diseases that result in cognitive impairment other than AD. It is therefore recommended.

Cerebral blood flow SPECT can visualize the decreased blood flow in the bilateral temporoparietal lobes and posterior cingulate gyrus/precuneus that is characteristic of AD and is therefore recommended.

Background

The prevalence of dementia is increasing throughout the world, and the increase in mild dementia, particularly AD, is becoming a social problem in Japan, which has entered an era of extreme population aging. This BQ summarizes the evidence regarding the usefulness of MRI, cerebral blood flow SPECT, and PET in diagnosing AD.

Explanation

Advances in diagnostic imaging technology have made it possible to detect the mild cerebral atrophy and decreases in blood flow and metabolism that occur in dementia. Consequently, the role played by diagnostic imaging in AD diagnosis has changed from an adjunctive one of excluding dementing disorders other than AD to being an important method that supports early AD diagnosis. Assessment of cerebral volume and blood flow and glucose metabolism by statistical image analysis or amyloid PET provides high diagnostic accuracy in predicting conversion from mild cognitive impairment (MCI) to AD and is regarded as clinically important.

1. MRI

Beginning early in AD, a decrease in the number of neurons in the medial temporal lobe is seen, resulting in cerebral parenchymal atrophy (Fig. 1). A meta-analysis of 12 investigations that evaluated medial temporal lobe atrophy with MRI showed sensitivity and specificity of 85% and 88%, respectively, in differentiating patients with AD from healthy individuals.[1)] Based on statistical image analysis using voxel-based morphometry (VBM), atrophy was seen in areas such as the posterior cingulate gyrus/precuneus, fusiform gyrus, and medial frontal lobe in AD, in addition to the medial temporal lobe (hippocampus, entorhinal area).[2)] However, caution is required because the sites of atrophy differ depending on the patient's age at onset (with onset at a young age, medial temporal lobe atrophy is mild, and parietal lobe atrophy is pronounced).[3)] The use of special software had previously been required for VBM analysis. Since 2006, however, the voxel-based specific regional analysis system for AD (VSRAD®) has been available for use in Japan. The diagnostic accuracy rate of VBM analysis with the

hippocampus/entorhinal area as the region of interest was 87.8%.[4] In clinical use, however, VBM cannot be used alone, but rather must always be used as an adjunct to interpretation of the original image. MR examinations other than morphological diagnosis that have been shown to be useful are ^{1}H-MR spectroscopy and diffusion tensor imaging, which reflect changes in brain tissue in AD. In differentiating AD patients from healthy individuals, the sensitivity and specificity of ^{1}H-MR spectroscopy based on the myo-inositol/N-acetyl aspartate ratio (MI/NAA) have been reported to be 83% and 98%, respectively.[5] With diffusion tensor imaging, a decrease in diffusion anisotropy in the limbic system and uncinate bundle has been found to be characteristic.[6] However, these methods have not reached the stage of routine clinical use. The use of arterial spin labeling (ASL) in differential diagnosis by acquiring non-contrast cerebral blood flow images with MRI has been attempted.[7] However, this too has not reached the stage of routine clinical use. Methods of AD diagnosis by artificial intelligence using deep learning have also been developed in recent years, but they have not reached the stage of routine clinical use.

2. Blood flow SPECT

Compared with healthy individuals of similar age, individuals with AD have decreased blood flow in the temporoparietal association cortex and posterior cingulate gyrus/precuneus, and cerebral blood flow SPECT can detect it (Fig. 2). In a large, prospective study, the sensitivity and specificity of cerebral blood flow SPECT in differentiating individuals with AD from healthy individuals were 89% and 80%, respectively.[8] When cerebral blood flow SPECT was compared with standard clinical diagnosis, the sensitivity of cerebral blood flow SPECT was lower (74% vs. 81%), but its specificity was higher (91% vs. 70%). Methods of statistical image analysis that have been widely adopted in the clinical setting and are used as diagnostic aids include medi+FALCON®, which uses three-dimensional stereotactic surface projection (3D-SSP), and the easy Z-score imaging system (eZIS®), which uses statistical parametric mapping (SPM). Furthermore, the sensitivity and specificity of cerebral blood flow SPECT in differentiating AD from other dementing disorders (frontotemporal dementia, vascular dementia) range from 70% to 79%, indicating that blood flow SPECT is also useful for differentiating AD from dementing disorders other than AD.[9]

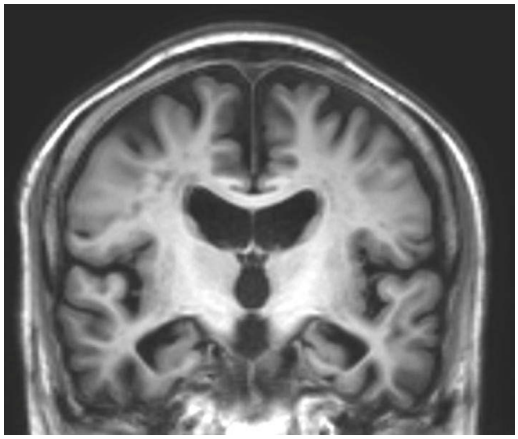


Figure 1. Alzheimer's-type dementia (1)

MRI, T1-weighted coronal image: Atrophy of the bilateral medial temporal lobes (hippocampus, parahippocampal gyri) is seen.

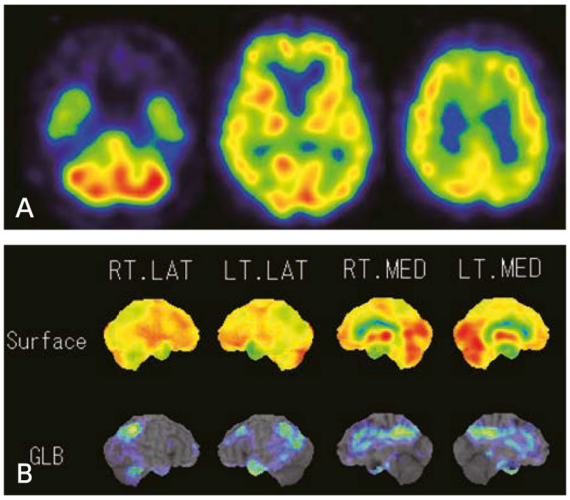


Figure 2. Alzheimer's-type dementia (2)

A: Cerebral blood flow SPECT (^{123}I-IMP, axial image)
B: Statistical image analysis (3D-SSP image)
Decreased blood flow is seen in disease-specific regions (posterior cingulate gyrus/precuneus, temporoparietal association cortex).

3. PET (^{18}F-FDG PET, amyloid PET, tau PET)

The use of PET for AD is not covered by national health insurance in Japan (FDG-PET is being performed under Advanced Medical Care Category B, pharmaceutical approval has been received for 3 devices to synthesize ^{18}F-labeled amyloid PET agents and 2 delivery agents, and the results will be reported with the aim of insurance coverage). However, it has been reported to be useful in diagnosing AD and differentiating it from other types of degenerative dementia.[10, 11] FDG-PET can detect decreases in glucose metabolism in the temporoparietal association cortex and posterior cingulate gyrus/precuneus in AD more sensitively than cerebral blood flow SPECT. The sensitivity and specificity of FDG-PET in differentiating individuals with AD from healthy individuals range from 86% to 96% and from 80% to 90%, respectively, its diagnostic performance in this role being superior to that of blood flow SPECT.[12-14] The use of statistical image analysis methods such as 3D stereotactic surface projection (3D-SSP) further improves diagnostic accuracy (sensitivity, 95% to 97%; specificity, 100%).[15] Amyloid PET shows amyloid beta-protein accumulation in the brain in AD (senile plaque formation). Reports on ^{18}F-labeled amyloid PET have increased in recent years, particularly reports on the use of ^{11}C-Pittsburgh compound-B (PiB). Although its diagnostic sensitivity is high,[16] amyloid beta-protein accumulation is also seen in some healthy elderly individuals (10% to 30%), in non-AD types of degenerative dementia, such as Lewy body dementia, and in cerebral amyloid angiopathy. Consequently, the presence of amyloid deposits does not necessarily indicate AD.[11, 17] Because the half-life of ^{11}C is a very short 20 minutes, efforts are currently underway to have diagnostic agents labeled with ^{18}F, which has a long half-life, covered by national health insurance so that they can be used in routine clinical practice.[15] For tau PET, which shows tau protein

deposition, next-generation tau PET agents are currently being developed, and their clinical application is expected.[18)]

Search keywords and secondary sources used as references

PubMed was searched using the following keywords: Alzheimer's disease, diagnosis, MRI, SPECT, and PET. The search was limited to investigations described by the following terms: meta-analysis, practice guideline, randomized controlled trial, and review.

In addition, the following were referenced as secondary sources.

1) Japanese Society of Neurology, Ed.: Clinical Practice Guidelines for Dementing disorders 2017. Igaku Shoin, 2017.

References

1) Scheitens P et al: Structural magnetic resonance imaging in the practical assessment of dementia: beyond exclusion. Lancet Neurol 1: 13-21, 2002
2) Karas GB et al: A comprehensive study of gray matter loss in patients with Alzheimer's disease using optimized voxel-based morphometry. Neuroimage 18: 895-907, 2003
3) Ishii K et al. Voxel-based morphometric comparison between early- and late-onset mild Alzheimer's disease and assessment of diagnostic performance of z score images. AJNR Am J Neuroradiol. 26: 333-340, 2005
4) Hirata Y et al: Voxel-based morphometry to discriminate early Alzheimer's disease from controls. Neurosci Lett 15: 269-274, 2005
5) Shonk TK et al: Probable Alzheimer disease: diagnosis with proton MR spectroscopy. Radiology 195: 65-72, 1995
6) Nakata Y et al: Tract-specific analysis for investigation of Alzheimer disease: a brief review. Jpn J Radiol 28: 494-501, 2010
7) Wolk DA et al: Arterial spin labeling MRI: an emerging biomarker for Alzheimer's disease and other neurodegenerative conditions. Curr Opin Neurol 25: 421-428, 2012
8) Jobst KA et al: Accurate prediction of histologically confirmed Alzheimer's disease and the differential diagnosis of dementia: the use of NINCDS-ADRDA and DSM-III-R criteria, SPECT, X-ray CT, and Apo E4 in medial temporal lobe dementias: Oxford Project to Investigate Memory and Aging. Int Psychogeriatr 10: 271-302, 1998
9) Dougall NJ et al: Systematic review of the diagnostic accuracy of ^{99m}Tc-HMPAO-SPECT in dementia. Am J Geriatr Psychiatry 12: 554-570, 2004
10) Nasrallah IM et al: Multimodality imaging of Alzheimer disease and other neurodegenerative dementias. J Nucl Med 55: 2003-2011, 2014
11) Ishii K: PET Approaches for diagnosis of dementia. AJNR Am J Neuroradiol 35: 2030-2038, 2014
12) Zakzanis KK et al: A meta-analysis of structural and functional brain imaging in dementia of the Alzheimer's type: a neuroimaging profile. Neuropsychol Rev 13: 1-18, 2003
13) Patwardhan MB et al: Alzheimer disease: operating characteristics of PET-a meta-analysis. Radiology 231: 73-80, 2004
14) Bohnen NI et al: Effectiveness and safety of ^{18}F-FDG PET in the evaluation of dementia: a review of the recent literature. J Nucl Med 53: 59-71, 2012
15) Minoshima S et al: A diagnostic approach in Alzheimer's disease using three dimensional-stereotactic surface projections of fluorine-18-FDG PET. J Nucl Med 36: 1238-1248, 1995
16) Edison P et al: Amyloid, hypometabolism, and cognition in Alzheimer disease: an [11C] PIB and [18F] FDG PET study. Neurology 13: 501-508, 2007
17) Jack CR Jr et al: Serial PIB and MRI in normal, mild cognitive impairment and Alzheimer's disease: implications for sequence of pathological events in Alzheimer's disease. Brain 132 (Pt 5): 1355-1365, 2009
18) Matsuda H et al: Neuroimaging of Alzheimer's disease: focus on amyloid and tau PET. Jpn J Radiol 37: 735-749, 2019

BQ 8 Which imaging examinations are recommended when an intracranial space-occupying lesion is suspected based on the patient's subacute and chronic clinical course?

Statement

MRI is recommended.

CT is recommended if an urgent response is required in circumstances where MRI cannot be promptly performed.

Background

CT and MRI are widely used to diagnose intracranial space-occupying lesions. However, there is no clear indicator of which examination should be given priority. Following is a summary of the evidence regarding the usefulness of CT and MRI for intracranial space-occupying lesions with a subacute or chronic course other than stroke and traumatic lesions.

Explanation

For nearly all abnormal intracranial findings, the sensitivity of MRI is comparable to or greater than that of CT.[1-6)]

MRI provides even better contrast resolution and visualization of details than CT, and it allows imaging to be performed in any arbitrary plane. It is also excellent for detecting lesions associated with no clinical symptoms.[1, 2, 5-8)] Furthermore, MRI is excellent for visualizing areas surrounded by bone, enabling more accurate evaluation of lesions in the posterior cranial fossa, brain stem, and middle cranial fossa than can be performed with CT (Fig.).[2, 9-11)] In particular, MRI is superior to CT for evaluating the status of structures near lesions of the sellar and suprasellar areas, such as the optic nerve, optic chiasm, and internal carotid artery.[7, 8)] On the other hand, CT is better for detecting calcification in lesions and evaluating associated bone changes.[1, 10, 12)]

A review that compared MRI with other modalities, including CT, found that, although MRI affected the treatment strategy, it did not have a major effect on quality of life (QOL).[2)] Although dramatic advances in CT and MRI hardware have been made in the past 30 years, CT still allows imaging to be performed in a shorter time than MRI in nearly all cases. Moreover, MRI is more expensive than CT and, depending on the circumstances of the individual facilities, MRI examinations often cannot be performed expeditiously. CT is adequate for detecting large intracranial masses and hemorrhage of the type that requires immediate intervention.[1-3)] In addition, MRI requires caution regarding the fact that some internal metal products are contraindications for MRI, as typified by the pacemaker. On the other hand, since CT involves radiation exposure, unnecessary examinations should not be performed.

The use of an iodinated contrast agent in CT and of a gadolinium contrast agent in MRI is useful for improving the ability to detect intracranial neoplasms and to determine the overall appearance of lesions.[1, 13-16] In general, contrast-enhanced MRI is superior to contrast-enhanced CT with respect to the ability to detect and visualize lesions. Many intracranial neoplasms are observed more distinctly with contrast-enhanced MRI than with contrast-enhanced CT, such as primary intraaxial brain tumor and metastatic neoplasms, typified by gliomas, as well as meningiomas and schwannomas. This makes contrast-enhanced MRI useful for evaluating the extent of lesion progression (Fig.).[1, 2, 16-20] Particularly for brain metastasis and meningeal dissemination, the detection rate of contrast-enhanced MRI is higher than that of contrast-enhanced CT according to many reports.[3, 16-18, 20] Contrast-enhanced MRI is therefore recommended for detailed examination of intracranial masses using a contrast agent.

However, large meningiomas and schwannomas often can also be evaluated with non-contrast MRI.[13] Moreover, it should be noted that not all intracranial neoplasms exhibit contrast enhancement.

Search keywords and secondary sources used as references

PubMed was searched using keywords such as the following: brain, intracranial, central nervous system, tumor or neoplasm or mass or occupying, CT, MR, and sensitivity or specificity. In selecting articles to use, preference was given to articles with large sample sizes and strong evidence.

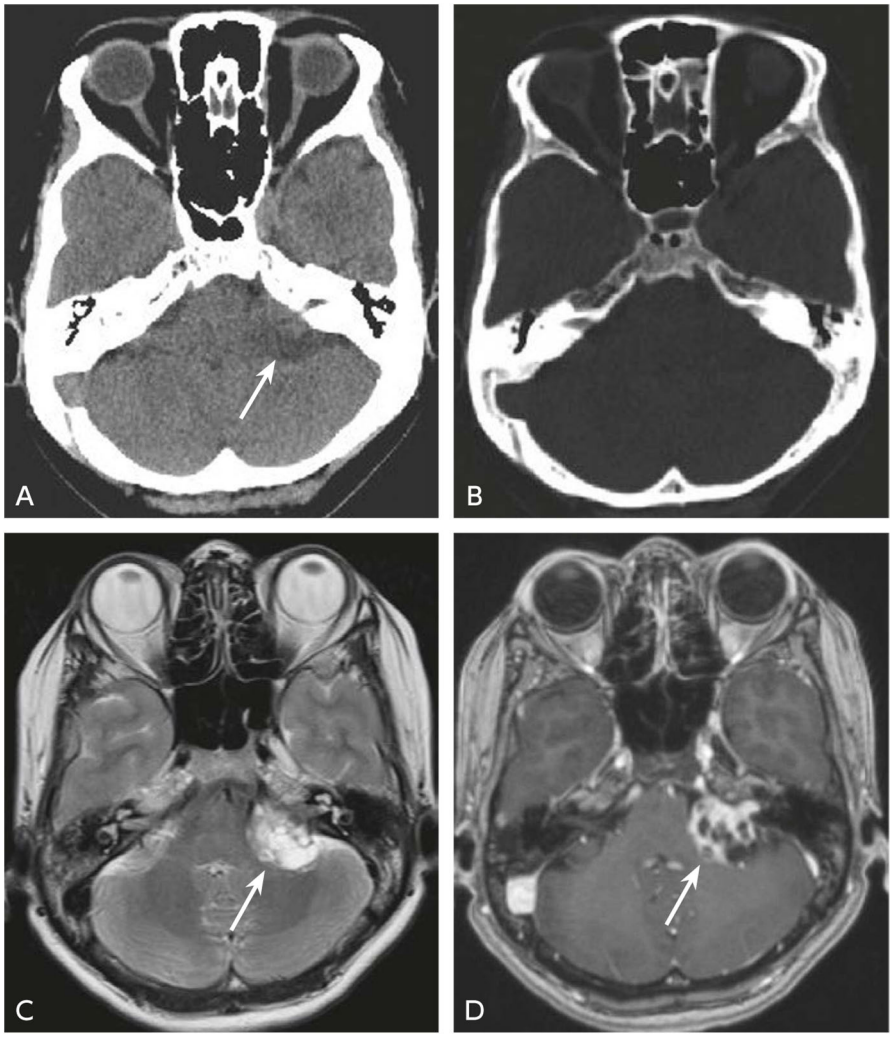


Figure. Left acoustic schwannoma

A: NCCT; B: NCCT, bone imaging conditions; C: MRI, T2-weighted image; D: MRI, contrast-enhanced T1-weighted image. Both CT and MRI enable the presence of the mass to be established (→). However, the overall appearance of the lesion is clearest with contrast-enhanced MRI. The enlargement of the left internal auditory canal is indistinct even on CT under bone imaging conditions.

In addition, the following was referenced as a secondary source.

1) Medina LS, Blackmore C (eds.): Evidence-based imaging: optimizing imaging in patient care. Springer, 2011

References

1) Hutter A et al: Brain neoplasms: epidemiology, diagnosis, and prospects for cost-effective imaging. Neuroimaging Clin N Am 13: 237-250, 2003
2) Kent DL et al: The clinical efficacy of magnetic resonance imaging in neuroimaging. Ann Intern Med 120: 856-871, 1994
3) Medina LS et al: Adults and children with headache: evidence-based diagnostic evaluation. Neuroimaging Clin N Am 13: 225-235, 2003
4) Kucharczyk W et al: Central nervous system tumors in children: detection by magnetic resonance imaging. Radiology 155: 131-136, 1985
5) Price AC et al: Primary glioma: diagnosis with magnetic resonance imaging. J Comput Tomogr 10: 325-334, 1986
6) Orrison WW et al: Comparison of CT, low-field-strength MR imaging, and high-field-strength MR imaging: work in progress. Radiology 181: 121-127, 1991

7) Lee BC et al: Sellar and juxtasellar lesion detection with MR. Radiology 157: 143-147, 1985
8) Karnaze MG et al: Suprasellar lesions: evaluation with MR imaging. Radiology 161: 77-82, 1986
9) Lee BC et al: MR imaging of brainstem tumors. AJNR Am J Neuroradiol 6: 159-163, 1985
10) Barloon TJ et al: Lesions involving the fourth ventricle evaluated by CT and MR: a comparative study. Magn Reson Imaging 7: 635-642, 1989
11) Loneragan R et al: Magnetic resonance imaging evaluation of cerebellopontine angle tumours. Australas Radiol 33: 47-55, 1989
12) Schubeus P et al: Intracranial meningiomas: how frequent are indicative findings in CT and MRI ? Neuroradiology 32: 467-473, 1990
13) Felix R et al: Brain tumors: MR imaging with gadolinium-DTPA. Radiology 156: 681-688, 1985
14) Haughton VM et al: Sensitivity of Gd-DTPA-enhanced MR imaging of benign extraaxial tumors. Radiology 166: 829-833, 1988
15) Elster AD et al: Is Gd-DTPA required for routine cranial MR imaging ? Radiology 173: 231-238, 1989
16) Sze G et al: Detection of brain metastases: comparison of contrast-enhanced MR with unenhanced MR and enhanced CT. AJNR Am J Nueroradiol 11: 785-791, 1990
17) Sze G et al: MR imaging of the cranial meninges with emphasis on contrast enhancement and meningeal carcinomatosis. AJR Am J Roentogenol 153: 1039-1049, 1989
18) Chamberlain MC et al: Leptomeningeal metastasis: a comparison of gadolinium-enhanced MR and contrast-enhanced CT of the brain. Neurology 40: 435-438, 1990
19) Schörner W et al: Intracranial meningiomas: comparison of plain and contrast-enhanced examinations in CT and MRI. Neuroradiology 32: 12-18, 1990
20) Davis P et al: Diagnosis of cerebral metastases: double-dose delayed CT vs contrast-enhanced MR imaging. AJNR Am J Neuroradiol 12: 293-300, 1991

BQ 9 Which imaging examinations are recommended to detect metastatic brain tumors?

Statement

Contrast-enhanced MRI is strongly recommended to detect metastatic brain tumors.

Background

In cancer-bearing patients, whether brain metastasis has occurred is important for determining a treatment strategy. In addition to detecting brain metastatic foci, it is important to accurately determine their number, size, and location to select a treatment. CT and MRI have often been used for this evaluation. With the increase in concern over healthcare resources, an emphasis on avoiding unnecessary examinations has recently emerged. In addition, FDG-PET is becoming ever more widely adopted. For this BQ, the question of which imaging examination should be the first choice for detecting metastatic brain tumors was examined, including an assessment of whether to screen for metastatic brain tumors in cancer-bearing patients.

Explanation

Reports investigating the usefulness of imaging studies for metastatic brain tumors are limited to observational studies, such as cohort studies and case-control studies. Their usefulness is therefore evaluated based on the results of those studies.

Many comparative studies of CT and MRI for the detection of metastatic brain tumors have been conducted since the late 1980s.[1-4] With a normal contrast medium dose, contrast-enhanced MRI detected more metastatic foci than contrast-enhanced CT.[2] Even when compared with contrast-enhanced CT using a double dose of contrast medium, normal contrast-enhanced MRI provided higher detection performance.[3] A comparison of the detection performance of contrast-enhanced CT, T1-weighted and T2-weighted imaging, and contrast-enhanced MRI using the normal contrast dose and triple dose found that the number of metastatic foci detected was highest with MRI using the triple contrast dose, followed in descending order by MRI using the normal contrast dose, contrast-enhanced CT, and T2-weighted and pre-contrast T1-weighted imaging. MRI using the triple contrast dose was significantly better than the other methods, the differences being particularly striking in the detection of metastatic foci ≤ 5 mm in size.[4] These reports consistently showed the superiority of contrast-enhanced MRI. Consequently, contrast-enhanced MRI, rather than contrast-enhanced CT, is the imaging examination recommended for detecting metastatic brain tumors.

The contrast medium dose, timing of the imaging, magnetic field strength, and the imaging method used have been examined as factors affecting the performance of contrast-enhanced MRI in detecting lesions.

With regard to the contrast medium dose, several reports indicate that sensitivity for detecting metastatic foci is improved with a triple dose of gadolinium contrast medium.[4-6] Using a 1.5T system, an investigation examined the effects of contrast medium dose and the time from contrast medium administration to imaging on visualization performance with respect to metastatic foci ≤ 10 mm in size. The results showed that contrast dose had the strongest effect on the detection of small lesions. A comparison of immediate-post-administration images showed that, compared with the normal contrast dose, approximately 3 times as many metastatic foci were detected with a triple dose. Moreover, with images acquired immediately after administration of contrast at a triple dose, more metastatic foci were detected than with images acquired 20 minutes after administration of the normal contrast dose.[5] An examination of metastatic foci < 5 mm in size showed that, with administration of a triple dose, detection performance was significantly better than with administration of the normal dose. This was true for both 1.5T and 3T systems.[6] On the other hand, a prospective investigation using a 1.5T system in patients suspected of having metastatic brain tumors found that administration of a triple dose of contrast medium was associated with an increase in false positives and was not useful for any of the patients. It was concluded that the use of a triple dose should be limited to patients with ambiguous findings with the normal dose or when a single metastasis is seen with the normal dose.[7] In Japan, additional administration of up to a double dose of gadoteridol is approved for patients suspected of having metastatic brain tumors for whom visualization with a single administration is judged to be inadequate. Although a single administration of a double dose of gadoteridol has been found to improve visualization compared with additional divided administration of a double dose of gadoteridol,[8] the latter has been approved in Japan. Thus, although administration of double and triple doses of contrast has been considered useful, important issues have been raised. Nephrogenic systemic fibrosis (NSF) is a well-known serious adverse reaction to gadolinium contrast media.[9] In addition, intracerebral deposition of gadolinium contrast media has been identified, although no clinical symptoms have been observed as a result.[10] Based on these considerations, even with a single administration, renal function should be evaluated when contrast media are used, and they should be administered carefully. In Japan, contrast-enhanced MRI is normally performed to detect metastatic brain tumors using a single dose of gadolinium contrast medium. The above findings indicate that additional administration of up to a double dose of gadoteridol is desirable in patients whose findings with a single dose are ambiguous, or if a single metastasis is seen with a single dose.

With regard to timing of the imaging, in the above-mentioned study of metastatic foci ≤ 10 mm in size that used a 1.5T system, although contrast medium dose had the strongest effect on the detection of small lesions, detection performance of small lesions was higher approximately 20 minutes after contrast medium administration than immediately after.[5] Improved detection performance at 7 to 10 minutes after administration compared with immediately after was also noted in the investigation of a single double-dose described above.[8] The above findings indicate that, even with administration of a single dose of contrast medium, improved detection of metastatic brain tumors is likely if the time after administration until imaging is appropriately selected.

With regard to magnetic field strength, an investigation comparing metastatic foci detection performance with a triple dose and normal dose using 3T and 1.5T systems found that performance was highest with the 3-fold dose using the 3T system. Moreover, with either dose, detection of metastatic foci < 5 mm in size was the best with the 3T system.[6] In addition, an increase in the contrast-noise ratio of metastatic brain tumors was reported with a 3T system compared with a 1.5T system.[11] These findings indicate that the use of a 3T system results in improved detection performance with respect to metastatic brain tumors.

With regard to imaging methods, 3D imaging has been found to be useful.[8, 12-14] Differentiation from blood vessel signals is often problematic, particularly for detecting small metastatic foci. However, with 3D high-speed SE using a variable flip angle (VISTA, CUBE, SPACE), blood vessels signals often decrease, facilitating detection and diagnosis of metastatic foci.[15] With contrast-enhanced FLAIR imaging, although metastasis detection sensitivity is low with this method alone, blood vessel signals are low. Consequently, the addition of another imaging method to contrast-enhanced MRI facilitates the differentiation of small metastatic foci and blood vessels.[16] In addition, excellent visualization of metastasis to the pia mater has been reported with contrast-enhanced FLAIR imaging.[17] The presence or absence of pia mater lesions is important information for determining a strategy for treatments such as stereotactic radiation therapy.

FDG-PET/CT is used for whole-body metastasis screening. Although there have been few systematic investigations regarding brain metastasis, in a prospective study of 104 patients with lung cancer, 100 metastatic brain tumor lesions were detected by contrast-enhanced MRI, whereas just 17 lesions were detected with FDG-PET/CT. Moreover, the patient-based sensitivity, specificity, true positive rate, and true negative rate with FDG-PET/CT were 27.3%, 97.6%, 75.0%, and 83.3%, respectively.[18] On the other hand, by expanding the imaging range of FDG-PET/CT whole-body screening to include the brain, brain metastasis may be detected by chance. In a retrospective investigation of 227 patients with lung cancer, brain metastasis was detected by chance in 5 patients.[19] In a study in 1,000 cancer-bearing patients, expanding the imaging range to include the head resulted in detection of brain metastasis by chance in 13 patients.[20] These findings indicate that, though the sensitivity of FDG-PET/CT alone is low for detecting metastatic brain tumors, expanding the imaging range to include the brain during whole-body screening may enable such tumors to be detected by chance.

With the increasing concern about healthcare costs, the need for imaging examinations to screen for metastatic brain tumors in cancer-bearing patients has also been evaluated. Although lung cancer is the primary tumor most commonly responsible for metastatic brain tumors, the guidelines for non-small cell lung cancer developed by the National Comprehensive Cancer Network (NCCN) of the United States recommend brain MRI screening for metastasis in stages II to IV, but they indicate that it is optional in stage Ib, whereas screening by routine brain MRI is not recommended in stage Ia. Supporting this approach, an investigation in 1,751 patients with non-small cell lung cancer found that the incidence of metastatic brain tumors was 0.5% in stage T1 and 0.7% in stage N0.[21] Moreover, in an examination of pretreatment MRI in 109 patients with lung cancer with pure ground-glass nodules, no metastatic brain tumors were detected.[22] These findings indicate that imaging examinations to screen for metastatic brain tumors are unnecessary in stage Ia lung cancer.

Search keywords and secondary sources used as references

PubMed was searched using the following keywords: brain metastasis, CT, and MRI.

In addition, the following was referenced as a secondary source.

1) David S et al: NCCN Guidelines®: non-small cell lung cancer Ver 2. 2021. National Comprehensive Cancer Network, 2021

References

1) Russell EJ et al: Multiple cerebral metastases: detectability with Gd-DTPA-enhanced MR imaging. Radiology 165 (3): 609-617, 1987
2) Sze G et al: Detection of brain metastases: comparison of contrast-enhanced MR with unenhanced MR and enhanced CT. AJNR Am J Neuroradiol 11 (4): 785-791, 1990
3) Davis PC et al: Diagnosis of cerebral metastases: double-dose delayed CT vs contrast-enhanced MR imaging. AJNR Am J Neuroradiol 12 (2): 293-300, 1991
4) Akeson et al: Brain metastases: comparison of gadodiamide injection-enhanced MR imaging at standard and high dose, contrast-enhanced CT and non-contrast-enhanced MR imaging. Acta Radiologica 36 (3): 300-306, 1995
5) Yuh WT et al: The effect of contrast dose, imaging time, and lesion size in the MR detection of intracerebral metastasis. AJNR Am J Neuroradiol 16 (2): 373-380, 1995
6) Ba-Ssalamah A et al: Effect of contrast dose and field strength in the magnetic resonance detection of brain metastases. Invest Radiol 38 (7): 415-422, 2003
7) Sze G et al: Comparison of single- and triple-dose contrast material in the MR screening of brain metastases. AJNR Am J Neuroradiol 19 (5): 821-828, 1998
8) Ochi T et al: Comparison between two separate injections and a single injection of double-dose contrast medium for contrast-enhanced MR imaging of metastatic brain tumors. Magn Reson Med Sc 3 (4): 221-229, 2014
9) Wang Y et al: Incidence of nephrogenic systemic fibrosis after adoption of restrictive gadolinium-based contrast agent guidelines. Radiology 260 (1): 105-111, 2011
10) Kanda T et al: High signal intensity in the dentate nucleus and globus pallidus on unenhanced T1-weighted MR images: relationship with increasing cumulative dose of a gadolinium-based contrast material. Radiology 270 (3): 834-841, 2014
11) Krautmacher C et al: Brain tumors: full- and half-dose contrast-enhanced MR imaging at 3.0 T compared with 1.5 T: initial experience. Radiology 237 (3): 1014-1019, 2005
12) Kakeda S et al: Detection of brain metastasis at 3T: comparison among SE, IR-FSE and 3D-GRE sequences. Eur Radiol 17 (9): 2345-2351, 2007
13) Kato Y et al: Usefulness of contrast-enhanced T1-weighted sampling perfection with application-optimized contrasts by using different flip angle evolutions in detection of small brain metastasis at 3T MR imaging: comparison with magnetization-prepared rapid acquisition of gradient echo imaging. AJNR Am J Neuroradiol 30 (5): 923-929, 2009
14) Nagao E et al: 3D turbo spin-echo sequence with motion-sensitized driven-equilibrium preparation for detection of brain metastases on 3T MR imaging. AJNR Am J Neuroradiol 32 (4): 664-670, 2011
15) Komada T et al: Contrast-enhanced MR imaging of metastatic brain tumor at 3 tesla: utility of T1-weighted SPACE compared with 2D spin echo and 3D gradient echo sequence. Magn Reson Med Sci 7 (1): 13-21, 2008
16) Terae S et al: Contrast-enhanced FLAIR imaging in combination with pre- and postcontrast magnetization transfer T1-weighted imaging: usefulness in the evaluation of brain metastases. J Magn Reson Imaging 25 (3): 479-487, 2007
17) Fukuoka H et al: Comparison of the added value of contrast-enhanced 3D fluid-attenuated inversion recovery and magnetization-prepared rapid acquisition of gradient echo sequences in relation to conventional postcontrast T1-weighted images for the evaluation of leptomeningeal diseases at 3T. AJNR Am J Neuroradiol 31 (5): 868-873, 2010
18) Krüger S et al: Brain metastasis in lung cancer. Comparison of cerebral MRI and ^{18}F-FDG-PET/CT for diagnosis in the initial staging. Nucl Med 50 (3): 101-106, 2011
19) Nia ES et al: Incidence of brain metastases on follow-up (18) F-FDG PET/CT scans of non-small cell lung cancer patients: should we include the brain? J Nucl Med Technol 45 (3): 193-197, 2017
20) Abdelmalik AG et al: The incremental added value of including the head in (18) F-FDG PET/CT imaging for cancer patients. Front ncol 3: 71, 2013
21) Diaz ME et al: Non-small cell lung cancer brain metastasis screening in the era of positron emission tomography-CT staging: current practice and outcomes. J Med imaging Rad Oncol 62 (3): 383-388, 2018
22) Cho H et al: Pure ground glass nodular adenocarcinomas: are preoperative positron emission tomography/computed tomography and brain magnetic resonance imaging useful or necessary ? J Thorac Cardiovasc Surg 150 (3): 514-520, 2015