

10

Pediatric

# Standard Pediatric Imaging Methods

## Overview

### 1. Introduction

Thoughtless imaging examinations should not be made in the evaluation of children, who have long lives ahead and represent the future. Thoughtless and inappropriate examinations occur as a result of improper justification and optimization. The basic approaches and procedures for the diagnostic imaging of children are discussed in the overview at the beginning of these guidelines (p. 32 to 35), and the reader is encouraged to refer to them. Although they are essentially the same as for adults, justification and optimization must be implemented with particular rigor for children.

Because pediatric diagnostic imaging covers all of the organs, further detailed discussion of each examination modality by patient age and disease type would far exceed the scope of the preface to the pediatrics section. Consequently, this section discusses basic approaches in general terms.

### 2. Justification of imaging examinations: best examination first!

Justification starts with an examination of whether an examination is truly necessary. A requirement is that the risk associated with factors such as the invasiveness of an examination be less than the benefit it contributes to diagnosis and treatment. Even if an examination is found to meet this requirement, it is essential that the examination most suitable for the purpose of examination be performed first. Another important consideration in justification is examining whether a procedure that does not involve radiation exposure, such as ultrasonography or MRI, can provide diagnostic performance comparable to that of one that does involve radiation exposure, such as CT, and be used instead of the latter. This is the process involved in the justification of pediatric diagnostic imaging. It is synonymous with performing the best examination first.

## Detailed discussion

### 1. Optimization of pediatric CT: not more nor less

The optimization of pediatric radiography is based on the as-low-as-reasonably-achievable (ALARA)<sup>1</sup> principle. The most important type of optimization in pediatric diagnostic imaging is the optimization of CT, which can be performed often and in a short time, but is associated with radiation exposure. The point that should be emphasized most is that pediatric CT is fundamentally single-phase imaging. One should not be bound to the bygone rule that non-contrast CT combined with contrast-enhanced CT is the standard. Modern CT systems, which represent marked advances in technology, enable lung fields, bone, and calcification all to be evaluated by contrast-enhanced CT alone. Non-contrast CT is of course sufficient for evaluating the lung fields, airways, and bony structures, including the middle and inner ear. If a truncal

tumor or inflammatory disease is suspected, the use of single-phase contrast-enhanced CT is the overriding rule. Non-contrast CT alone is the rule for emergency cranial CT for conditions such as status epilepticus and consciousness disturbance. MRI is indicated if there are no findings on CT and neurological symptoms persist. However, if MRI cannot be performed, non-contrast CT is repeated. Only in special cases (e.g., there is reason to suspect a condition such as vascular malformation) is contrast-enhanced CT performed without non-contrast CT. The indications for multiphase contrast-enhanced imaging are very limited to cases where information on the arteries is needed, such as before surgery and with severe trauma.

With regard to CT imaging conditions, the lowest dose that can provide the necessary information is generally used. Moreover, multiple protocols specific to children, separate from the protocols used for adults, must be prepared depending on the performance of the system used, the body size of the patient, and the purpose of the examination. Of course, losing diagnostic information by using a radiation dose so low that the required information cannot be obtained would defeat the purpose of the examination. Consequently, a dose that is not too high or too low should be selected by applying specialized knowledge and collaborating with radiological technologists.

Preparing pediatric CT protocols that are varied and appropriate for the body sizes and circumstances of the patients and generally involve single-phase imaging is the essence of pediatric CT optimization, and the principle of "not more nor less" should be applied. Diagnostic reference levels, which serve as standards for reviewing doses used at your facility, are provided in the Overview section at the beginning of these guidelines (p. 33).

## **2. Optimization of Pediatric MRI**

MRI involves no radiation exposure, provides excellent density resolution, and involves little need for contrast medium administration. It should therefore be the procedure that is most used for children. Because the examination time is long, however, it requires appropriate restraint or sedation for children who cannot remain motionless. With regard to sedation measures, a system that can respond to emergencies is essential. Such a system should be established based on the MRI sedation recommendations issued by the relevant academic societies (first edition published in May 2013, revised editions published in February and April 2020).<sup>2)</sup>

Many children are physically small, and their respiratory and heart rates are higher than those of adults. Moreover, many very difficult situations are often encountered in MRI that cannot be addressed with an adult protocol, such as the usually difficult breath-hold examination. To overcome these difficulties, k-space sampling techniques, such as radial sampling, which suppresses artifacts caused by movements of the rib cage, diaphragm, and heartbeat, respiratory gating using techniques such as navigator echo, and body motion correction methods using techniques such as PROPELLER/BLADE need to be tailored to the various sequences and imaging angles and optimized for the system used. In addition, diffusion-weighted imaging and the ADC values it yields often provide useful information on body and pathological tissues,

and pathophysiology, whether in the central nervous system, trunk, or bone and soft tissue. Its routine use is therefore recommended.

Physiological signal changes in the brain (myelination) and bone marrow (change from red to yellow marrow) occur from the neonatal period through childhood, necessitating measures to tailor sequences to those changes. Because the volume of fluid in the brain is large in premature infants and neonates, it is difficult to establish contrast with the cerebrospinal fluid. It is therefore necessary to specify a longer effective TE ( $\geq 120$  at a minimum) than for adults and older children when performing FSE T2-weighted imaging, particularly with 1.5T systems. When evaluating the brains of premature infants, diagnosis should be undertaken based on the corrected age in weeks or months (the chronological age added to the gestational age at birth).<sup>3)</sup>

A gadolinium contrast medium should be used after thoroughly examining whether its use will provide additional information. With MRI of the central nervous system (CNS), sites of failure of the blood-brain barrier undergo contrast enhancement just as with iodinated contrast agent-enhanced CT. However, for non-CNS examinations, MRI, which fundamentally provides excellent tissue contrast, lacks the significant anatomical contrast seen with CT contrast agents. Consequently, the additional information obtained with contrast medium administration is limited. Therefore, examinations for tumors or inflammation in the CNS, trunk, bone, or soft tissue for a purpose such as evaluating posttreatment efficacy should not be automatically performed using a contrast medium without proper justification. Rather, its indication should be rigorously determined by considering the effects of tissue accumulation of free gadolinium, particularly in children. It has been reported that, when the findings of a plain examination were normal, the use of a gadolinium contrast medium in the brain detected imaging abnormalities in just 0.3% of cases, indicating that it did not provide additional clinical information.<sup>4)</sup>

### **3. Optimization of pediatric ultrasonography**

Ultrasonography is even more useful for diagnosis in children, who are physically small and have very little subcutaneous and visceral fat, than it is in adults. The small size of children enables deep areas to be observed even with the use of a high-frequency probe. The resulting spatial resolution provides images overwhelmingly superior to those obtained by modalities such as CT. Special measures or training are needed to perform ultrasonography in children who are uncooperative. However, because ultrasonography does not involve radiation exposure and is not invasive, there is no reason not to try it.

Moreover, sites where ultrasonography is used in children but cannot be considered in adults include the mediastinal organs such as the thymus (probe placed in the intercostal area near the sternum or over the sternum) and, from the neonatal period to infancy, the intracranial region and spine using the fontanel and cranial sutures as acoustic windows (observed from between vertebrae in the case of direct scanning from the dorsum or if ossification has advanced). These are useful for screening for changes such as dimples.

#### **4. Optimization for pediatric nuclear medicine**

Nuclear medicine is a useful modality for obtaining information that cannot be obtained with other imaging procedures. Because it involves radiation exposure, however, the question of whether it is indicated needs to be carefully examined. For example, it is not an exaggeration to say that an examination such as gallium-67 ( $^{67}\text{Ga}$ ) scintigraphy is a thing of the past and far from the first choice of examination methods for a fever of unknown origin. Optimization is performed according to the ALARA principle.<sup>1)</sup> It is recommended that pediatric nuclear medicine examinations be performed, and dose and indication determined based on the consensus guidelines for the proper implementation of pediatric nuclear medicine examinations and by referring to the nuclear medicine section of these guidelines.<sup>5)</sup>

#### **Summary: The role of the diagnostic radiologist**

In addition to the high carcinogenic risk of radiation exposure in children, the effects of agents such as contrast media (e.g., adverse reactions to cumulative effects and their consequences) need to be considered in the context of the long remaining life expectancy of children, which can be 60 to 80 years or longer. Pediatric imaging procedures therefore should be carefully selected based on the judgement of specialists and performed using the most appropriate method in a way that is minimally invasive and avoids the loss of important diagnostic information. This is where diagnostic radiologists can best show their capabilities as a specialist, and also an area where their active involvement that uses their specialized knowledge makes a direct contribution to children, with whom the future rests.

#### **Secondary source materials used as references**

- 1) Multidisciplinary conference organized by the Society of Pediatric Radiology: The ALARA (as low as reasonably achievable) concept in pediatric CT intelligent dose reduction. *Pediatr Radiol* 32: 217-313, 2001
- 2) Japan Pediatric Society, Japanese Society of Pediatric Anesthesiology, Japanese Society of Pediatric Radiology: Joint Recommendations on Sedation During MRI. *Journal of the Japan Pediatric Society* 124(4): 771-805, 2020
- 3) Aida N: A Key to Brain MRI Interpretation (3rd Edition): Important Points and Normal Images. Gakken Medical Shujunsha. pp.316-323, 2012
- 4) Dunger D et al: Do we need gadolinium-based contrast medium for brain magnetic resonance imaging in children? *Pediatr Radiol* 48: 858-846, 2018
- 5) Study Panel on the Proper Implementation of Pediatric Nuclear Medicine Tests, Japanese Society of Nuclear Medicine: Consensus Guidelines for the Proper Implementation of Pediatric Nuclear Medicine Tests. Japanese Society of Nuclear Medicine, 2013

## **BQ 84 In which cases is CT recommended for minor head trauma in children?**

### **Statement**

With minor head trauma in children, the risk of intracranial injury is evaluated using criteria such as the PECARN criteria for cranial CT indications, the CHALICE rule, and the CATCH rule. If the risk is low, CT should not be performed.

### **Background**

Pediatric trauma, typified by head contusion, is a condition often seen in emergency outpatient care. In nearly all cases, it is mild and can be addressed by watchful waiting alone. Abnormal CT findings are rare, and cases that result in surgery are even rarer. Decisions must be made regarding whether CT is needed for a mild head injury and whether it is indicated in view of the risk associated with radiation exposure.

### **Explanation**

An increasing number of studies have examined how to predict the risk of intracranial injury in minor head trauma in children and narrow the indications for CT. However, the findings have varied, and there is no standard view on the types of cases in which CT should be performed.<sup>1-8)</sup> The following 3 sets of criteria are supported by high-level evidence.<sup>9, 10)</sup>

The cranial CT indication criteria of the Pediatric Emergency Care Applied Research Network (PECARN) (Table 1) are used to assess whether CT is recommended based on considerations such as the Glasgow Coma Scale (GCS) score and consciousness status, with patients stratified as aged < 2 years or 2 to 18 years.<sup>11, 12)</sup> Severely impaired patients with a GCS score  $\leq 13$  are not considered suitable for CT.

The children's head injury algorithm for the prediction of important clinical events (CHALICE rule) (Table 2) is used for patients with head trauma who are aged 2 to 16 years. Based on the diagnostic imaging guidelines of the United States and the clinical guidelines of the United Kingdom, the rule is widely used clinically.

The Canadian assessment of tomography for childhood head injury (CATCH rule) is used for children aged 0 to 16 years with a GCS score of 13 to 15 within 24 hours after injury and abnormal clinical symptoms (the CATCH2 rule, which has additional items, was released in 2018).<sup>13)</sup> It was found to be highly sensitive in a large, multicenter cohort study (Table 3).

In the clinical setting, whether CT is indicated should be assessed by selecting from among those rules based on the circumstances. However, the judgement of the patient's primary care physician, wishes of the patient's family, and circumstances at the relevant facility also need to be given adequate consideration.

In 2019, the Recommendations and Guidelines for CT Imaging Criteria in Pediatric Head Injury were released by the Japanese Society of Child Neurology, Japanese Society for Pediatric Neurosurgery,

Japanese Society of Emergency Pediatrics, and Japanese Society of Pediatric Radiology. They cover topics such as the previously mentioned rules, figures, and tables, and the points to keep in mind when using them, along with measures to reduce radiation exposure during CT imaging. In addition, it provides examples of written explanations for families who are sent home after it is determined that CT is unnecessary based on the criteria. It is therefore a document that should be used for reference.

**Table 1. PECARN cranial CT indication criteria**

(Indications for CT tests in GCS 14 - 15 head injury)

<p>&lt; 2 years old</p> <ul style="list-style-type: none"> <li>▪ GCS = 14, altered consciousness, or palpable skull fracture</li> <li>▪ Subcutaneous hematoma other than of the forehead, loss of consciousness for <math>\geq 5</math> seconds, dangerous mechanism of injury, or parents consider appearance to be different from usual</li> </ul> <p><math>\geq 2</math> years old</p> <ul style="list-style-type: none"> <li>▪ GCS = 14, altered consciousness, or basal skull fracture finding</li> <li>▪ Loss of consciousness, vomiting, dangerous mechanism of injury, or intense headache</li> </ul>
---

CT not recommended if above are not applicable

**Table 2. CHALICE rule**

<ul style="list-style-type: none"> <li>▪ Loss of consciousness for <math>\geq 5</math> minutes</li> <li>▪ Amnesia for <math>\geq 5</math> minutes</li> <li>▪ Somnolence</li> <li>▪ Vomiting <math>\geq 3</math> times</li> <li>▪ Abuse suspected</li> <li>▪ Convulsion in a patient with no past history of epilepsy</li> <li>▪ GCS &lt; 14. GCS &lt; 15 if &lt; 1 year old</li> <li>▪ Compound fracture, suspected depressed fracture, or bulging anterior fontanel</li> <li>▪ Basal skull fracture finding (otorrhagia, raccoon eyes, cerebrospinal fluid leak, Battle sign)</li> <li>▪ Neurological abnormality</li> <li>▪ Subcutaneous hematoma or bruise <math>\geq 5</math> cm in child &lt; 1 year old</li> <li>▪ Dangerous mechanism of injury, e.g., high-speed trauma [traffic accident occurring at or greater than a certain speed (64 km/hour), fall from a height of <math>\geq 3</math> m, collision with an object moving at high speed]</li> </ul>
---

Detailed examination by CT required if any of the above are applicable

**Table 3. CATCH and CATCH2 rules (CT test indications for mild head injury and consciousness level GCS 13 - 15 on examination)**

<ol style="list-style-type: none"> <li>(1) GCS score &lt; 15 points at 2 hours post-trauma</li> <li>(2) Compound or depressed fracture suspected</li> <li>(3) Worsening headache</li> <li>(4) Agitated state on examination</li> <li>(5) Basal skull fracture suspected</li> <li>(6) Large hematoma in scalp</li> <li>(7) High-energy trauma</li> <li>[(8) Vomiting <math>\geq 4</math> times]</li> </ol>
---

Cranial CT recommended if any of the 7 items is present [8 items, including (8), for CATCH2 rule]

## Search keywords and secondary sources used as references

PubMed was searched using the following keywords: children, minor head injury, trauma, and CT.

In addition, the following were referenced as secondary sources.

- 1) Medina L et al (eds.): Evidence-based imaging in pediatrics. Springer, 2010
- 2) Kuppermann N et al: Identification of children at very low risk of clinically-important brain injuries after head trauma: a prospective cohort study. *Lancet* 374: 1160-1170, 2009
- 3) Dunning J et al: Derivation of the children's head injury algorithm for the prediction of important clinical events decision rule for head injury in children. *Arch Dis Child* 91: 885-891, 2006
- 4) Osmond MH et al: CATCH: a clinical decision rule for the use of computed tomography in children with minor head injury. *CMAJ* 182: 341-348, 2010
- 5) Japanese Society of Child Neurology, et. al, Ed.: Recommendations and Guidelines for CT Imaging Criteria in Pediatric Head Injury. Japanese Society of Child Neurology, 2019

## References

- 1) Greenes DS, Schutzman SA: Clinical indicators of intracranial injury in head-injured infants. *Pediatrics* 104: 861-867, 1999
- 2) Palchak MJ et al: A decision rule for identifying children at low risk for brain injuries after blunt head trauma. *Ann Emerg Med* 42: 492-506, 2003
- 3) Haydel MJ, Shembekar AD: Prediction of intracranial injury in children aged five years and older with loss of consciousness after minor head injury due to nontrivial mechanisms. *Ann Emerg Med* 42: 507-514, 2003
- 4) Oman JA et al: Performance of a decision rule to predict need for computed tomography among children with blunt head trauma. *Pediatrics* 117: e238-246, 2006
- 5) Boran BO et al: Evaluation of mild head injury in a pediatric population. *Pediatr Neurosurg* 42: 203-207, 2006
- 6) Atabaki SM et al: A clinical decision rule for cranial computed tomography in minor pediatric head trauma. *Arch Pediatr Adolesc Med* 162: 439-445, 2008
- 7) Dunning J et al: A meta-analysis of variables that predict significant intracranial injury in minor head trauma. *Arch Dis Child* 89: 653-659, 2004
- 8) Maguire JL et al: Should a head-injured child receive a head CT scan?: a systematic review of clinical prediction rules. *Pediatrics* 124: e145-154, 2009
- 9) Babl FE et al: Accuracy of PECARN, CATCH, and CHALICE head injury decision rules in children: a prospective cohort study. *Lancet* 389: 2393-2402, 2017
- 10) Mastrangelo M, Midulla F: Minor head trauma in the pediatric emergency department: decision making nodes. *Curr Pediatr Rev* 13: 92-99, 2017
- 11) Pickering A et al: Clinical decision rules for children with minor head injury: a systematic review. *Arch Dis Child* 96: 414-421, 011
- 12) Mihindu E et al: Computed tomography of the head in children with mild traumatic brain injury. *Am Surg* 80: 841-843, 2014
- 13) Osmond MH et al: Validation and refinement of a clinical decision rule for the use of computed tomography in children with minor head injury in the emergency department. *CMAJ* 190: 816-822, 2018



## **BQ 85 Is neuroimaging recommended for a suspected febrile seizure?**

### **Statement**

Because it does not involve radiation exposure and provides even higher detection performance than CT, MRI is recommended as an imaging examination in complex febrile seizures, frequent seizures, and seizures associated with neurological deficits. However, in patients who require sedation, the risk associated with sedation is taken into account in deciding whether to perform MRI.

If simple febrile seizure is definitively diagnosed clinically, there is little need for diagnostic imaging (CT/MRI). However, a congenital metabolic abnormality or autoimmune disease may be involved in the background as an underlying disease. Consequently, cranial MRI can be considered for detailed examination if complex febrile seizure is still a possibility, or there are frequent seizures or seizures associated with neurologic deficit symptoms. Cranial CT is a meaningful test to perform before lumbar puncture and can be considered for this purpose.

### **Background**

According to the guidelines for the management of febrile seizures and the febrile seizure clinical practice guidelines of the Japanese Society of Child Neurology, febrile seizure is a seizure disorder (includes convulsive and nonconvulsive seizures) typically associated with fever of  $\geq 38$  °C that occurs mainly in infants at 6 to 60 months postpartum. It refers to seizures that occur in the absence of central nervous system infections such as meningitis, metabolic disease, or other obvious causes of seizures. It excludes seizures in individuals with a history of epilepsy.

More than 90% of children with a history of febrile seizure do not subsequently develop epilepsy. It is basically considered a transient, benign condition. However, it is important to differentiate it from conditions such as encephalopathy and encephalitis, which require immediate and aggressive treatment, and organic abnormalities must also be excluded if seizures occur repeatedly. Whether diagnostic imaging should be performed if febrile seizure is suspected and the important conditions from which it should be differentiated were examined.

### **Explanation**

Febrile seizure is the most frequently encountered convulsive disease of childhood. Its prevalence in Japan has been reported to be 7% to 8%, slightly higher than in Europe and the United States (2% to 5%). The convulsive seizures associated with febrile seizure are typically generalized seizures, such as generalized tonic-clonic seizures. Febrile seizures that are generalized seizures lasting less than 15 minutes that do not occur repeatedly within 24 hours are termed simple febrile seizures. Those with at least 1 of the following 3 characteristics are termed complex febrile seizures: ① has elements of focal seizures (partial

seizures); ② seizure lasts longer than 15 minutes; and ③ usually occurs multiple times within 24 hours during a single febrile episode.

The rate of recurrence of febrile seizures is approximately 30%. Risk factors are ① either parent has a past history of febrile seizure, ② onset at < 1 year of age, ③ brief intervals between febrile episodes ( $\leq$  roughly 1 hour), and ④ temperature  $\leq 39$  °C during seizures. Although the incidence of subsequent epilepsy is low, risk factors for subsequently developing epilepsy include ① the presence of a neurological abnormality before the onset of febrile seizures, ② a family history of epilepsy in a parent or sibling, ③ complex febrile seizure, and ④ brief intervals between febrile episodes ( $\leq$  roughly 1 hour). Complex febrile seizures are a risk factor for epilepsy.

No reports based on strong evidence were found that recommend diagnostic imaging (CT or MRI) for children with simple febrile seizures. The American Academy of Pediatrics recommends against CT or MRI for simple febrile seizures. However, abnormal imaging findings may be seen with complex febrile seizures.<sup>1,2)</sup>

Conditions that must be differentiated from febrile seizure include: forms of encephalitis and meningitis, such as bacterial and viral encephalitis and meningitis and tuberculous meningitis; subdural empyema, extradural empyema/subdural abscess, extradural abscess; brain abscess; and acute encephalopathy. Clinical findings are often difficult to obtain because the patients are children, and diagnostic imaging therefore plays more than a minor role. Although their frequency is lower than that of febrile seizure, early diagnosis and treatment of these conditions are important because delays in their diagnosis and treatment result in a poorer overall prognosis and functional prognosis.

Although the above-mentioned guidelines indicate that lumbar puncture is not a procedure that should be performed routinely, they indicate that it should be performed aggressively if encephalitis or meningitis is suspected. Consequently, diagnostic imaging is also meaningful to a certain extent as a means of excluding an intracranial space-occupying lesion, which is a contraindication for lumbar puncture.

MRI is recommended as an imaging examination because it involves no radiation exposure and detects lesions more sensitively than even CT. However, the risk associated with sedation should be considered in patients that require it, and a system adequate to support MRI sedation should be implemented based on the joint recommendations. Acute-phase CT is useful as a convenient method of ruling out an intracranial space-occupying lesion and increased intracranial pressure.

Acute encephalopathy is a disease in which a convulsion or a sudden consciousness disturbance is seen in the acute phase of a viral infection associated with high fever.<sup>3)</sup> The pathogenic virus and clinicopathological classification do not correspond in a 1-to-1 fashion. That is, a specific viral infection can produce a variety of clinicopathological features and, conversely, a variety of viruses can present with the same clinicopathological features. Moreover, acute encephalopathy may occur in disorders other than infection, such as: congenital metabolic abnormalities; nonviral infections such as bacterial infections, cat-scratch disease, and Q fever; and autoimmune disorders.<sup>3-7)</sup> In incipient disease without consciousness disturbance, differentiating between acute encephalopathy with biphasic seizures and late reduced diffusion

(AESD) and febrile seizures is difficult. Identifying subcortical hyperintensity (bright tree appearance) in diffusion-weighted images on day 4 to 5 after onset facilitates diagnosis.<sup>3)</sup> What are termed reversible lesions of the corpus callosum splenium appear in a variety of pathophysiologies, including after drug administration. Lesions in acute encephalopathy are known to be reversible if the lesion distribution is limited to white matter that extends to the corpus callosal splenium and Rolando's area.<sup>8,9)</sup>

In the chronic phase, hippocampal atrophy was found on MRI in 6 of 15 patients with complex febrile seizures, although the evidence level for this finding is not high.<sup>10)</sup> The risk of developing epilepsy has been reported to be high in patients with complex febrile seizures. Diagnostic imaging is also therefore regarded as having a specific role in detailed examination in the chronic phase, such as when seizures occur repeatedly.<sup>11)</sup>

## Search keywords and secondary sources used as references

PubMed was searched using the following keywords: febrile seizure, CT, and MRI.

In addition, the following were referenced as secondary sources.

- 1) Fukuyama Y, et al.: Guidelines for the management of febrile seizures. *Japanese Journal of Pediatrics* 49:207-215, 1996
- 2) Seki T: Febrile seizures—Recent findings and new management guidelines. *New Developments in Child Neurology* 26:139-152, 1997
- 3) Japanese Society of Child Neurology, Ed.: 2015 Clinical Practice Guidelines for Febrile Seizures. SHINDAN TO CHIRYO SHA, 2015
- 4) Subcommittee on Febrile Seizures, American Academy of Pediatrics: Neurodiagnostic evaluation of the child with a simple febrile seizure. *Pediatrics* 127: 389-394, 2011
- 5) Japan Pediatric Society, et al.: Joint Recommendations on Sedation During MRI. *Journal of the Japan Pediatric Society* 124(4):771-805, 2020

## References

- 1) Takanashi J et al: Diffusion MRI abnormalities after prolonged febrile seizures with encephalopathy. *Neurology* 66: 1304- 1309, 2006
- 2) Rasool A et al: Role of electroencephalogram and neuroimaging in first onset afebrile and complex febrile seizures in children from Kashmir. *J Pediatr Neurosci* 7: 9-15, 2012
- 3) Takanashi J et al: Excitotoxicity in acute encephalopathy with biphasic seizures and late reduced diffusion. *AJNR Am J Neuro Radiol* 30: 132- 135, 2009
- 4) Kubota H et al: Q fever encephalitis with cytokine profiles in serum and cerebrospinal fluid. *Pediatr Infect Dis J* 20: 318-319, 2001
- 5) Ogura K et al: MR signal changes in a child with cat scratch disease encephalopathy and status epilepticus. *Eur Neurol* 51: 109-110, 2004
- 6) Mizuguchi M: Acute necrotizing encephalopathy of childhood: a novel form of acute encephalopathy prevalent in Japan and Taiwan. *Brain Dev* 19: 81-92, 1997
- 7) Tada H et al: Clinically mild encephalitis/encephalopathy with a reversible splenial lesion. *Neurology* 63: 1854-1858, 2004
- 8) Maeda M et al: Reversible splenial lesion with restricted diffusion in a wide spectrum of diseases and conditions. *J Neuroradiol* 33: 229-236, 2006
- 9) Takanashi J et al: Differences in the time course of splenial and white matter lesions in clinically mild encephalitis /encephalopathy with a reversible splenial lesion (MERS). *J Neurol Sci* 292: 24-27, 2010
- 10) VanLandingham KE et al: Magnetic resonance imaging evidence of hippocampal injury after prolonged focal febrile convulsions. *Ann Neurol* 43: 413-426, 1998
- 11) Neligan A et al: Long-term risk of developing epilepsy after febrile seizures: a prospective cohort study. *Neurology* 78: 1166-1170, 2012

**BQ 86 Is skeletal survey by plain radiography recommended to identify child abuse?**

**Statement**

Skeletal survey of the bones is an established means of identifying bone injury in children under 2 years of age who have experienced physical abuse.

**FQ 23 Is chest CT recommended for diagnosing rib fracture for child abuse?**

**Statement**

Although rib fracture in an infant is a finding strongly suggestive of abuse, diagnosing bone fractures in the acute phase is difficult with plain radiography. By comparison, CT provides high sensitivity in the acute and subacute phases and for bone fractures in the process of healing. In circumstances where abuse is suspected, chest CT using an appropriate radiation dose is weakly recommended if rib fracture is not clearly seen on initial skeletal survey.

**Explanation**

**1. Plain radiography for identifying child abuse**

Bone fracture is common in cases of physical abuse ("abuse" below), following skin and soft tissue injury in frequency.<sup>1)</sup> The first choice of imaging for evaluating bone fracture is plain radiography ("XR" below). Because physically abused young children cannot describe their own symptoms, the clinical diagnosis of bone fracture is difficult, and it is not unusual to detect latent bone fractures by XR in such patients.

A background pathophysiology (conditions that predispose the patient to bone fracture, such as rickets and osteogenesis imperfecta) may also be involved in bone fractures in children. However, if the cause of bone fracture is abuse, overlooking this places the life of the child in serious danger. Skeletal survey is a test method that comprehensively images the whole body to detect latent bone fractures when abuse is suspected. Latent bone fractures have been reported to be detected by skeletal survey in 11% to 34% of children suspected of having experienced abuse.<sup>1-3)</sup> Consequently, the appropriate use of skeletal survey is important.

With the skeletal survey typically performed in the United Kingdom and United States, standard imaging consists of cranial imaging from 2 angles, imaging of the bones of the extremities from 1 to 2 angles, and imaging of the bones of the trunk from 2 angles. Reference examples of skeletal surveys based on secondary sources 1 and 2 are shown in the table. There is no categorically established method of skeletal

survey. Consequently, the method used must be determined by each facility. The details of the imaging are explained below.

① Classification according to age

Approximately 90% of abused children are < 2 years old, and more than 80% of those with bone fractures due to abuse are < 18 months old.<sup>1,4)</sup> The proportion of patients examined for bone fractures at hospitals who were found to have experienced abuse was 20% to 25% for those < 1 year old and 6 to 7% for those between 1 and 2 years old.<sup>2)</sup> Because age is inversely related to the risk of bone fracture, it is recommended that a skeletal survey be performed for all patients < 2 years old and according to the circumstances of the individual for those 2 to 5 years old.

② Both oblique views of the chest

The likelihood of abuse is high with rib fractures with no clear mechanism of injury.<sup>4)</sup> However, the ribs overlap with the cardiac and mediastinal shadows in the normal frontal view of the chest, making it difficult to diagnose bone fractures with little deviation. Sensitivity and specificity in detecting bone fractures increase with the addition of both oblique views, resulting in imaging from 4 angles, as compared with the 2 angles of the frontal and lateral chest views.<sup>5)</sup> Consequently, including both oblique views in the skeletal survey is recommended.

Even combining the above-mentioned 4 types of chest imaging, diagnosing rib fractures by XR may be difficult. Evaluation by chest CT has been suggested in such cases.

**Table. Skeletal survey**

		RCR-RCPCH (2017), <small>secondary source 1</small>	ACR-SPR (2017), <small>secondary source 2</small>	Skeletal survey reference examples
Skeletal survey	Cranium	Frontal AP Lateral	Frontal AP Lateral	Frontal AP (**1) Lateral
	Chest	Frontal AP (to the shoulders)* Both obliques (ribs)*	Frontal AP*, lateral (includes ribs, thoracic vertebrae, upper lumbar vertebrae) Both obliques (ribs)*	Frontal AP*, lateral (thoracic vertebrae) Both obliques (ribs)*
	Abdomen, pelvis	Frontal AP (abdomen to pelvis)	Frontal AP (middle lumbar vertebrae to pelvis)	Frontal AP (abdomen to pelvis)
	Spine	Lateral (cervical vertebrae to lumbosacral vertebrae) < 1 year old: imaging performed once ≥ 1 year old: imaging divided into multiple procedures	Frontal AP, lateral (cervical vertebrae) Lateral (lumbosacral vertebrae)	Lateral (cervical vertebrae) Lateral (lumbosacral vertebrae)
	Upper extremities	Young children (small children): Frontal AP (upper arm to forearm)* Lateral (elbow, wrist) Older children: Frontal AP (upper arm; shoulder to elbow, forearm; elbow to wrist)* Lateral (elbow, wrist)	Bilateral upper arm AP* Bilateral forearm AP*	Bilateral upper arm AP* (**2, 3) Bilateral forearm AP*
	Lower extremities	Young children (small children): Frontal AP (hip to ankle)* Lateral (Knee, ankle) Ankle mortise AP view Older children: Frontal AP (femur, lower leg)* Frontal AP (knee, ankle) Lateral (knee, ankle)	Bilateral femur AP* Bilateral lower leg AP*	Bilateral femur AP (hip)* (**2, 3) Bilateral lower leg AP*
	Hands and feet	Bilateral hand PA Bilateral foot PA	Bilateral hand PA* Bilateral foot PA or AP*	Bilateral hand PA* Bilateral foot PA*
Follow-up skeletal survey (FUSS)	Imaging performed 11 to 14 days later Initial imaging performed within 28 days FUSS imaging is performed for the sites indicated with *, in addition to sites where the initial skeletal survey showed or were suggestive of abnormalities.		FUSS is performed for the sites indicated with * approximately 2 weeks after the initial imaging.	FUSS is performed for the sites indicated with * approximately 2 weeks after the initial imaging.

\*\* 1: Cranial XR unnecessary when cranial CT performed.

\*\* 2: In small children, imaging can be performed at the same time from the upper arm to the forearm and from the femur to the lower leg.

\*\* 3: Lateral view added if bone fractures suspected based on frontal view of arms and legs.

### ③ Long bones lateral view

Although the addition of a lateral view of the long bones does not affect the detection of diaphyseal fractures, it has been found to improve sensitivity in detecting metaphyseal fractures.<sup>6)</sup> Because metaphyseal fractures in infants are highly specific to abuse, the addition of a lateral view is recommended if the frontal view is suggestive of a lesion.

### ④ Imaging of the spine, pelvis, hands, and feet

The view has been expressed that these sites should not be included in a skeletal survey because fracture frequency is low at these sites and in view of the radiation exposure involved.<sup>1)</sup> However, another report indicated that the frequency of bone fracture was 5.5% at these sites in children who were suspected of experiencing abuse and underwent a skeletal survey, and it also indicated there were cases in which bone fracture was seen at only these sites.<sup>7)</sup> This suggests that there is a high risk of overlooking abuse if these sites are excluded. Including them in a skeletal survey is therefore recommended.

### ⑤ Head

When a patient is examined, cranial CT may be performed before the skeletal survey to evaluate head injury. CT is highly sensitive in detecting bone fractures, and it is recommended that multiplanar imaging be performed in addition to transverse imaging. In addition, the use of 3D reconstruction imaging facilitates differentiation from normal structures such as sutures and vascular grooves.<sup>8, 9)</sup> Consequently, in patients who undergo cranial CT, generating multiplanar and 3D reconstruction images can substitute for cranial XR.

### ⑥ FUSS

The repair of bone fracture progresses in 1 to 2 weeks after injury, and union occurs in approximately 2 months. At 10 to 14 days after injury, aspects of the healing process such as the periosteal reaction and soft callus are seen on XR. This can contribute to improvement in the lesion detection rate, evaluation of suspicious lesions, and estimates of the time of injury.<sup>1, 2)</sup> Bone fractures in the healing process were seen with a FUSS in 9% to 12% of infants whose initial skeletal survey findings were negative. Consequently, if suspicion of abuse remains, a FUSS is recommended approximately 2 weeks after the initial skeletal survey.

However, methods that limit a FUSS to specific sites to avoid unnecessary radiation exposure have been proposed, and the cranium is excluded from a FUSS in the United Kingdom and the United States (because evaluating the process of cranial repair is difficult with XR). Moreover, it was found that if the initial skeletal survey findings for the spine and pelvis were negative, excluding them from the FUSS did not impede treatment.<sup>10)</sup> Consequently, exclusion from the FUSS can be considered.

## 2. Chest CT for rib fractures resulting from child abuse

Rib fractures in infants that have no clear mechanism of injury are strongly suggestive of abuse.<sup>4)</sup> An oblique view of the rib cage is therefore added in the skeletal survey to improve bone fracture detection sensitivity. However, diagnosing acute bone fractures with little deviation in infants is difficult with XR. They often cannot be diagnosed with XR due to decreased lung field permeability and overlap with the cardiac shadow and mediastinal structures.

By comparison, some reports indicated that chest CT provides higher detection sensitivity for rib fractures than XR in the acute phase and during the healing process.<sup>11-15)</sup> In investigations that compared post-mortem images with autopsy data, sensitivity for rib fractures ranged from 14% to 46% with XR and from 45% to 85% with CT.<sup>11, 12)</sup> CT was also found to provide higher detection sensitivity than XR in surviving patients.<sup>13-15)</sup>

Generating CT multiplanar and 3D reconstructed images facilitates the identification of lesion location and is useful for detecting bone fractures of the scapula and vertebrae.<sup>15)</sup>

However, although the diagnostic performance of CT is high, it poses problems such as radiation exposure and sedation. Although bone fractures may also be newly identified with a FUSS, early chest CT can be considered if abuse is suspected, in view of the dramatic effect that a definitive diagnosis of rib fracture has on a child's vital prognosis. When CT is performed, the radiation dose should be reduced to a level that still ensures diagnostic quality.

## Search keywords and secondary sources used as references

PubMed was searched using the following keywords: abuse, fracture, skeletal survey, bone survey, non-accidental injury, rib, and CT.

In addition, the following were referenced as secondary sources.

- 1) The Royal College of Radiologists and The Society and College of Radiographers: The radiological investigations of suspected physical abuse in children, 2017
- 2) Wootton-Gorges SL et al: ACR Appropriateness Criteria®: suspected physical abuse-child. J Am Coll Radiol 14: S338-S349, 2017

## References

- 1) Karmazyn B et al: The prevalence of uncommon fractures on skeletal surveys performed to evaluate for suspected abuse in 930 children: should practice guidelines change? AJR Am J Roentgenol 197: W159-W163, 2011
- 2) Wood JN et al: Development of guidelines for skeletal survey in young children with fractures. Pediatrics 134: 45-53, 2014
- 3) Duffy SO et al: Use of skeletal surveys to evaluate for physical abuse: analysis of 703 consecutive skeletal surveys. Pediatrics 127: e47-e52, 2011
- 4) Kemp AM et al: Patterns of skeletal fractures in child abuse: systematic review. BMJ 337: a1518, 2008
- 5) Marine MB et al: Is the new ACR-SPR practice guideline for addition of oblique views of the ribs to the skeletal surveys for child abuse justified? AJR Am J Roentgenol 202: 868-871, 2014
- 6) Karmazyn B et al: Long bone fracture detection in suspected child abuse: contribution of lateral views. Pediatr Radiol 42: 463-469, 2012
- 7) Kleinman PK et al: Yield of radiographic skeletal surveys for detection of hand, foot, and spine fractures in suspected child abuse. AJR Am J Roentgenol 200: 641-644, 2013
- 8) Prabhu SP et al: Three-dimensional skull models as a problem-solving tool in suspected child abuse. Pediatr Radiol 43: 575-581, 2013



- 9) Culotta PA et al: Performance of computed tomography of the head to evaluate for skull fractures in infants with suspected non-accidental trauma. *Pediatr Radiol* 47: 74-81, 2017
- 10) Harper NS et al: The utility of follow-up skeletal surveys in child abuse. *Pediatrics* 131: e672-e678, 2013
- 11) Shelmerdine SC et al: Chest radiographs versus CT for the detection of rib fractures in children (DRIFT): a diagnostic accuracy observational study. *Lancet Child Adolesc Health* 2: 802-811, 2018
- 12) Hong TS et al: Value of postmortem thoracic CT over radiography in imaging of pediatric rib fractures. *Pediatr Radiol* 41: 736-748, 2011
- 13) Sanchez TR et al: Characteristics of rib fractures in child abuse: the role of low-dose chest computed tomography. *Pediatr Emerg Care* 34: 81-83, 2018
- 14) Sanchez TR et al: CT of the chest in suspected child abuse using submillisievert radiation dose. *Pediatr Radiol* 45: 1072- 1076, 2015
- 15) Wootton-Gorges SL et al: Comparison of computed tomography and chest radiography in the detection of rib fractures in abused infants. *Child Abuse Negl* 32: 659-663, 2008

## **BQ 87 In which cases is fetal MRI recommended?**

### **Statement**

Fetal MRI is recommended when a lesion of the head, head and neck, or trunk (excluding the heart) is suspected. However, the imaging and interpretation should be performed by a radiology technologist and diagnostic radiologist with as much experience as possible.

### **Background**

Fetal MRI is useful for diagnosing fetal diseases and provides information beneficial for perinatal management and counseling parents. However, ultrasound is the standard test for fetal screening. MRI is performed when ultrasound shows an abnormality of the fetus and further information is needed, when evaluation by ultrasound is insufficient for reasons such as maternal obesity or oligohydramnios, and when no abnormalities are seen by ultrasound but a fetal abnormality is considered likely. To determine whether it is indicated, information is needed regarding how useful MRI is and the conditions and disorders that are good indications for fetal MRI. Consequently, these were the topics examined.

### **Explanation**

Detailed examination of fetal malformations and masses accounts for many of the indications for fetal MRI. Moreover, as fetal therapy develops and its indications expand, evaluation by fetal MRI is becoming important. The gestational week at which diagnosis is possible depends on the disorder. However, it has been shown that no adverse events are seen in the fetus even when typical 1.5T non-contrast MRI is performed from the 1st trimester.<sup>1)</sup>

There have been several reports comparing the diagnostic performance of ultrasound and MRI. Ultrasound was found to be superior in 4%, MRI in 39% (of which, MRI contributed to a change of diagnosis in 56%, to new findings in 31%, and to confirmation of the diagnosis in 13%), and the 2 modalities were found to be comparable in 57%.<sup>2)</sup> A review by Bekker et al. found that MRI provided additional information useful for diagnosis in 23% to 100% of patients and changed fetal care in 13% to 39%.<sup>3)</sup> Examination by anatomical region showed that the addition of MRI to ultrasound contributed significantly to diagnosis in the central nervous system, urogenital tract, gastrointestinal tract, and chest.<sup>2)</sup> Abnormalities in these regions are therefore good indications for MRI. However, MRI was not shown to be useful for the skeletal system (limbs), face, and heart.<sup>2)</sup>

Typical indications for fetal MRI are shown in the table below. In addition, indications for each anatomical region are described in the following.

## **1. Head (central nervous system), spine, and spinal cord**

Cerebral ventriculomegaly, brain parenchymal malformation (e.g., callosal dysgenesis, cortical dysplasia, and posterior fossa malformation), and destructive changes of the brain parenchyma (e.g., hemorrhage, infarction, and inflammation) are good indications. In addition, twin-to-twin transfusion syndrome is associated with a high risk of intracranial complications and therefore necessitates an intracranial evaluation.

In a prospective study by Goncalves et al., MRI was found to be superior to ultrasound for diagnosing central nervous system conditions, and MRI added information related to prognosis and counseling to that obtained by ultrasound in 22.2% of patients. Therefore, central nervous system evaluation is the best indication for fetal MRI.<sup>4)</sup>

A review by Jarvis et al. regarding cases in which brain malformation was suspected found that the MRI diagnostic accuracy rate was 91%, which was 16% higher than that evaluated with ultrasound alone.<sup>5)</sup> In 55% of the patients, the MRI and ultrasound findings were concordant for the correct diagnosis. In 15%, the information obtained with MRI added to that obtained with ultrasound. In 19%, an erroneous ultrasound diagnosis was corrected based on MRI.<sup>5)</sup> In addition, MRI resulted in a change in the counseling provided to the parents or in perinatal management in 41.9%.<sup>5)</sup> In addition, it has been reported that additional findings were obtained by MRI in 55% of patients.<sup>2)</sup> Another report showed that, among patients with an abnormality on ultrasound, the counseling the parents received changed based on MRI in 49.6%, the diagnosis changed in 31.7%, and perinatal management changed in 18.6%.<sup>6)</sup>

**Table Typical indications for fetal MRI**

Indication: Major Category		Indication: Minor Category
Head	Malformation	e.g., cerebral ventriculomegaly, callosal dysgenesis, holoprosencephaly, posterior fossa malformation, cortical dysplasia, and cephalocele (encephalocele, meningocele)
	Vascular disorder	vascular malformation, hydranencephaly, cerebral infarction, cerebral hemorrhage, complication of monochorionic twin pregnancy
Spine and spinal cord	Tumor (mass)	sacroccygeal teratoma
	Malformation	neural tube defect (e.g., myelomeningocele), vertebral body malformation
Head and neck	Tumor (mass)	vascular malformation (venous malformation, lymphatic malformation (LM)), teratoma, goiter
	Malformation	facial cleft, gnathoschisis
Chest	Tumor (mass), malformation	congenital lung anomalies (congenital pulmonary airway malformation (CPAM), pulmonary sequestration, bronchial atresia, congenital lobar emphysema), congenital diaphragmatic hernia, mediastinal mass (teratoma, vascular malformation, thymic mass), esophageal atresia
	Other	pulmonary hypoplasia (evaluation of lung volume and signal intensity resulting from congenital diaphragmatic hernia, oligohydramnios, tumor, skeletal dysplasia, etc.), pleural effusion, pericardial effusion
Abdomen, pelvis, and retroperitoneum	Tumor (mass)	Abdominopelvic tumor, cyst (e.g., hemangioma, neuroblastoma, sacroccygeal teratoma, suprarenal mass, renal mass, ovarian cyst)
	Malformation	e.g., urinary tract malformation (e.g., renal malformation, lower urinary tract obstruction, cloacal malformation, bladder exstrophy), intestinal tract malformation (anorectal malformation, intestinal atresia), abdominal wall abnormality (gastroschisis, omphalocele)
	Other	meconium peritonitis; fetal ascites, such as chylous ascites
Monochorionic twin complications		1 fetal death, conjoined twins

Not all disorders could be covered, and the usefulness of MRI varies between individual patients. The indications for MRI are therefore not limited to these.

(Prepared based on secondary source 2)

## 2. Head and neck

Evaluation of masses such as vascular malformations (lymphatic malformation (LM), venous malformations), teratomas, and goiters is common. Differentiating goiters from other masses is facilitated by characteristic hyperintensity in T1-weighted images. In evaluating masses, not only qualitative diagnosis but also evaluating the presence or absence of airway narrowing is important for determining perinatal management that includes ex utero intrapartum treatment (EXIT; a procedure in which the fetus is treated by placing the mother under general anesthesia, laparotomy is performed, the exposed uterus is incised, and blood circulation is maintained in the umbilical cord while maintaining the airway). An investigation by Poutamo et al. found that MRI provided information useful for diagnosis or the exclusion of lesions in 6 of 8 patients with head and neck lesions.<sup>7)</sup>

As mentioned previously, there are also reports that MRI was not useful for evaluating the face. On the other hand, the diagnostic accuracy rate for orofacial cleft was found to be 59% with ultrasound and 92% with MRI.<sup>8)</sup>

### 3. Chest

Congenital diaphragmatic hernia and congenital lung anomalies are the main indications. Evaluations for complicating pulmonary hypoplasia and hydrops fetalis are also performed. Adding MRI to ultrasound was found to provide additional information for lesions of the chest in 38% to 44% of patients.<sup>2, 9)</sup> In congenital lung anomalies, MRI was found to be superior to ultrasound for visualizing abnormal blood vessels from the systemic circulation.<sup>10)</sup>

MRI was not found to be useful with respect to fetal heart malformations, with ultrasound reported to be superior for their diagnosis.<sup>2)</sup>

### 4. Abdomen, pelvis, and retroperitoneum

Abdominal masses and malformations (e.g., urinary tract malformation, gastrointestinal obstruction, gastroschisis) are the main changes evaluated. Meconium shows hyperintensity in T1-weighted images beginning from approximately 20 weeks, making it useful for evaluating the intestine. Adding MRI to ultrasound has been reported to provide additional information on abdominal gastrointestinal lesions in 38% of patients and on urogenital tract lesions in 29% of patients.<sup>2)</sup>

## Search keywords and secondary sources used as references

PubMed was searched using the following keywords: magnetic resonance imaging, and fetus.

In addition, the following were referenced as secondary sources.

- 1) American College of Radiology: ACR-SPR practice parameter for the safe and optimal performance of fetal magnetic resonance imaging (MRI), 2015
- 2) Patenatude Y et al: The use of magnetic resonance imaging in the obstetric patient (SOGC CLINICAL PRACTICE GUIDELINE). *J Obstet Gynaecol Can* 36: 349-363, 2014
- 3) Prayer D et al: ISUOG practice guidelines: performance of fetal magnetic resonance imaging. *Ultrasound Obstet Gynecol* 49: 671-680, 2017

## References

- 1) Ray JG et al: Association between MRI exposure during pregnancy and fetal and childhood outcomes. *JAMA* 316(9): 952-961, 2016
- 2) Kul S et al: Contribution of MRI to ultrasound in the diagnosis of fetal anomalies. *J Magn Reson Imaging* 35(4): 882-890, 2012
- 3) Bekker MN, van Vugt JM: The role of magnetic resonance imaging in prenatal diagnosis of fetal anomalies. *Eur J Obstet Gynecol Reprod Biol* 96(2): 173-178, 2001
- 4) Gonçalves LF et al: Diagnostic accuracy of ultrasonography and magnetic resonance imaging for the detection of fetal anomalies: a blinded case-control study. *Ultrasound Obstet Gynecol* 48(2): 185-92, 2016
- 5) Jarvis D et al: A systematic review and meta-analysis to determine the contribution of mr imaging to the diagnosis of foetal brain abnormalities In Utero. *Eur Radiol* 27(6): 2367-2380, 2017
- 6) Levine D et al: Fast MR imaging of fetal central nervous system abnormalities. *Radiology* 229(1): 51-61, 2003
- 7) Poutamo J et al: Magnetic resonance imaging supplements ultrasonographic imaging of the posterior fossa, pharynx and neck in malformed fetuses. *Ultrasound Obstet Gynecol* 13(5): 327-334, 1999
- 8) Zheng W et al: The prenatal diagnosis and classification of cleft palate: the role and value of magnetic resonance imaging. *Eur Radiol* 29(10): 5600-5606, 2019
- 9) Levine D et al: Fetal thoracic abnormalities: MR imaging. *Radiology* 228(2): 379-388, 2003
- 10) Mon RA et al: Diagnostic accuracy of imaging studies in congenital lung malformations. *Arch Dis Child Fetal Neonatal Ed* 104(4): F372-F377, 2019

## **BQ 88 Which imaging examinations are recommended when retinoblastoma is suspected?**

### **Statement**

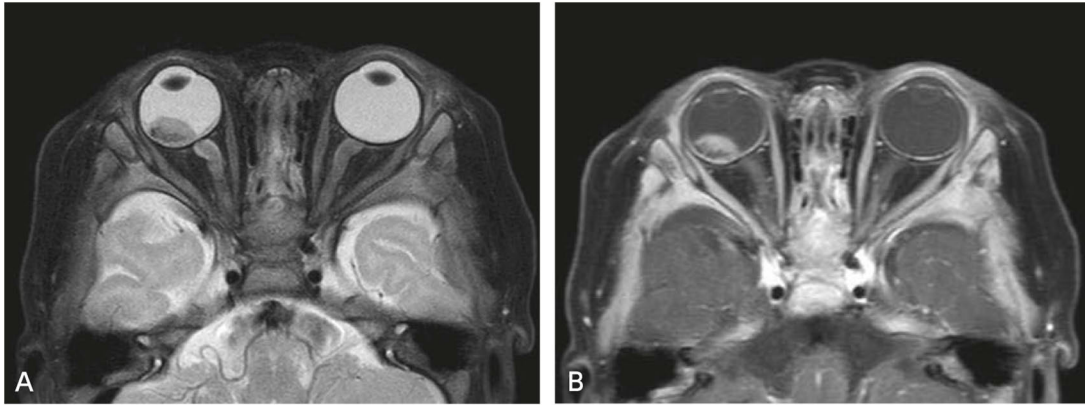
MRI, which involves no radiation exposure and provides excellent tissue resolution, is recommended. Although CT provides high detection performance with respect to calcification and is useful for diagnosis on initial examination, it is associated with radiation exposure and is therefore not always necessary. Posttreatment follow-up and periodic CT are not recommended.

### **Explanation**

Retinoblastoma is the most common childhood intraocular tumor and occurs unilaterally in 2/3 of patients and bilaterally in 1/3, according to a report published in Japan.<sup>1)</sup> Left-right and male-female differences are unclear.<sup>1)</sup> Approximately 90% of retinoblastoma cases are diagnosed by 3 years of age and approximately 40% by 1 year of age.<sup>1)</sup> The initial diagnosis is performed by funduscopy and ocular ultrasound. MRI and CT are used to more definitively determine whether there has been local progression and confirm the diagnosis.<sup>2-11)</sup>

In developed countries, nearly all intraocular lesions are detected while in a localized state. Consequently, the main objectives of treatment are to preserve the eye and visual function rather than to save the patient's life. Treatments such as laser and radiation therapy are selected for early lesions. Invasion of the optic nerve, choroid, and sclera is related to the presence or absence of distant metastasis. However, from the perspective of preserving visual function and based on the risk of metastasis associated with the manipulation, pathological findings cannot be obtained for all patients.<sup>12)</sup> For lesions that are not limited to within the eyeball and pose a high risk of metastasis, eye enucleation is considered, and multimodal treatment that includes chemotherapy is selected. Given this context, the use of MRI, which provides excellent tissue resolution, is encouraged to evaluate the risk of metastasis.

MRI can be used to evaluate metastasis-related factors such as pathological optic nerve and choroid invasion. Aspects related to these factors are evaluated. These include: the volume, long-axis diameter, morphology, and location of the tumor; enlargement and contrast enhancement of the optic nerve; and the signal intensity and degree of diffusion restriction in T2-weighted images.<sup>2-6, 8, 11)</sup> Optic nerve invasion is suspected if the tumor is large, the lesion covers the optic nerve, or the optic nerve is enlarged and shows contrast enhancement. However, none of these findings can be used to diagnose invasion with 100% certainty. Consequently, the findings are considered in combination to evaluate the risk of metastasis comprehensively (Figs. 1 and 2). In a study by de Jong et al. (370 patients), the minimum tumor volume and long-axis diameter that resulted in optic nerve invasion and apparent choroid invasion were 0.59 cm<sup>3</sup> and 13.90 mm and 0.19 cm<sup>3</sup> and 8.15 mm, respectively.<sup>2)</sup>

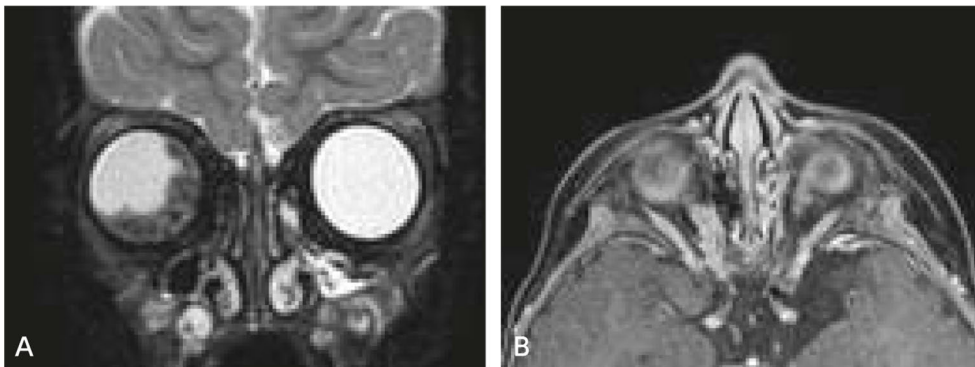


**Figure 1. Patient without optic nerve invasion**

A: MRI, fat-suppressed T2-weighted transverse image: A right intraocular tumor is seen. The long-axis diameter was measured at approximately 11 mm, but the tumor volume was 0.33 cm<sup>3</sup>.

B: Gadolinium contrast-enhanced MRI, fat-suppressed contrast-enhanced T1-weighted transverse image: No optic nerve or extraocular invasion is seen.

Based on these findings, the risk of metastasis was judged to be low. Eyeball enucleation was selected, and there was judged to be no optic nerve invasion.



**Figure 2. Patient with optic nerve invasion**

A: MRI, fat-suppressed T2-weighted coronal image: A right intraocular tumor with a long-axis diameter of 22 mm is seen.

B: Gadolinium contrast-enhanced MRI, fat-suppressed contrast-enhanced T1-weighted transverse image: Increased contrast enhancement and enlargement of the right optic nerve are seen.

Based on these findings, there was judged to be extraocular extension and a high risk of metastasis. Eyeball enucleation was performed, optic nerve invasion observed, and aftertreatment implemented.

Few cases of retinoblastoma are associated with metastasis on initial examination, and nearly all can be evaluated for the presence or absence of optic nerve invasion by fundoscopy. Consequently, whole-body screening on initial examination is not necessary in all patients.<sup>13)</sup>

Screening for calcification is important for diagnosing retinoblastoma.<sup>10)</sup> However, calcification has been reported to be visualized by MRI in  $\geq 90\%$  of cases, and CT is therefore not always necessary.<sup>4)</sup>

## Search keywords and secondary sources used as references

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

In addition, the following were referenced as secondary sources.

- 1) Japanese Society of Pediatric Hematology/Oncology, Ed.: 2016 Practical Guidelines for Pediatric Cancer, 2nd Edition. KANEHARA & Co., 2016

## References

- 1) Committee for the National Registry of Retinoblastoma: The national registry of retinoblastoma in Japan (1983-2014). *Jpn J Ophthalmol* 62: 409-423, 2018
- 2) de Jong MC et al: Diagnostic accuracy of intraocular tumor size measured with MR imaging in the prediction of postlaminar optic nerve invasion and massive choroidal invasion of retinoblastoma. *Radiology* 279: 817-826, 2016
- 3) Li Z et al: Diagnosis of postlaminar optic nerve invasion in retinoblastoma with MRI features. *J Magn Resonance Imaging* 51(4): 1045-1052, 2020
- 4) Lemke AJ et al: Retinoblastoma - MR appearance using a surface coil in comparison with histopathological results. *Eur Radiol* 17: 49-60, 2007
- 5) Kim U et al: Accuracy of preoperative imaging in predicting optic nerve invasion in retinoblastoma: a retrospective study. *Ind J Ophthalmol* 67: 2019-2022, 2019
- 6) Hiasat JG et al: The predictive value of magnetic resonance imaging of retinoblastoma for the likelihood of high-risk pathologic features. *Eur J Ophthalmol* 29: 262-268, 2019
- 7) de Jong MC et al: Diagnostic performance of magnetic resonance imaging and computed tomography for advanced retinoblastoma: a systematic review and meta-analysis. *Ophthalmology* 121: 1109-1118, 2014
- 8) Cui Y et al: Correlation between conventional MR imaging combined with diffusion-weighted imaging and histopathologic findings in eyes primarily enucleated for advanced retinoblastoma: a retrospective study. *Eur Radiol* 28: 620-629, 2018
- 9) Chawla B et al: Magnetic resonance imaging for tumor restaging after chemotherapy in retinoblastoma with optic nerve invasion. *Ophthalmic Genet* 39: 584-588, 2018
- 10) Arrigg PG et al: Computed tomography in the diagnosis of retinoblastoma. *Br J Ophthalmol* 67: 588-591, 1983
- 11) Kim JW et al: Clinical significance of optic nerve enhancement on magnetic resonance imaging in enucleated retinoblastoma patients. *Ophthalmol Retina* 1: 369-374, 2017
- 12) Shields CL et al: Vitrectomy in eyes with unsuspected retinoblastoma. *Ophthalmology* 107: 2250-2255, 2000
- 13) Chantada G et al: Results of a prospective study for the treatment of retinoblastoma. *Cancer* 100: 834-842, 2004



## **BQ 89 Which imaging examinations are recommended to diagnose and stage neuroblastomas?**

### **Statement**

CT and MRI are useful and recommended for diagnosing masses suspected of being neuroblastomas. <sup>123</sup>I-MIBG scintigraphy is useful for staging neuroblastomas, and its use with CT or MRI for a comprehensive evaluation is strongly recommended.

### **Background**

Neuroblastoma is a commonly seen pediatric cancer, following leukemia and brain tumors in frequency. According to the registry of the Research Project on Specific Pediatric Chronic Diseases, approximately 320 children are newly affected by neuroblastoma each year in Japan. Approximately half of cases occur before 1 year of age and approximately 80% by 3 years of age. It occurs in the sympathetic ganglia of the trunk and the adrenal medulla. Approximately half of neuroblastomas occur in the adrenal glands, followed by areas such as the extra-adrenal retroperitoneum (25%), chest (16%), neck (3%), and pelvis (3%). Metastasis is seen at the time of diagnosis in approximately 70% of cases, occurring preferentially in the bone marrow (70%), bone (55%), and regional lymph nodes (30%). Metastasis is also seen in areas such as the liver; distant lymph nodes, such as the supraclavicular lymph nodes; and skin. Its prognosis is strongly correlated with age at the time of diagnosis, clinical stage, and biological factors, and it is a cancer known to show diversity.

The treatment strategy is generally selected according to risk classification.<sup>1)</sup> The risk classification is assessed by evaluating a combination of clinical factors, such as age at the time of diagnosis, disease stage, and tissue classification, along with biological factors, such as MYCN gene amplification and tumor cell ploidy. The International Neuroblastoma Staging Risk Group Staging System (INRGSS), proposed in 2009, is based on diagnostic imaging performed before the start of treatment. Consequently, diagnostic imaging plays a major role in neuroblastoma staging.

### **Explanation**

#### **1. Diagnosis and staging**

Neuroblastomas are often first detected due to abdominal distension or palpation of an abdominal mass. It is also not unusual for them to be diagnosed based on metastatic lesion symptoms (e.g., bone or joint pain). Ultrasonography is selected to establish the presence of an abdominal tumor. It is easy to perform and involves no radiation exposure.

CT and MRI are excellent for evaluating the localization and extent of tumors and are also useful for staging. Their use is therefore recommended.<sup>2)</sup> They are useful for evaluating the presence or absence of invasion of major blood vessels and adjacent organs and extension into the spinal canal. In addition, they

are useful for determining a treatment strategy that includes surgical resection. CT and MRI are also useful for evaluating the presence or absence and extent of lymph node metastasis and the presence or absence of bone marrow, bone, and liver metastases and for staging. In a multicenter, prospective study by Siegel et al., the diagnostic performance of contrast-enhanced CT and MRI in neuroblastoma with distant metastasis was 81% and 83%, respectively, the difference being nonsignificant. The positive and negative predictive values with respect to detection performance in lymph node metastasis were 20% and 95%, respectively, for CT and 19% and 99%, respectively, for MRI. The positive and negative predictive values with respect to tumor extent were 73% and 83%, respectively, for CT and 81% and 79%, respectively, for MRI.<sup>2)</sup> CT and MRI are regarded as equally useful for evaluating primary lesions and local invasion.

With regard to neuroblastoma staging, the International Neuroblastoma Risk Group (INRG) proposed an international preoperative staging system based on imaging findings in 2009, and its use has grown (Table 1). Under this new classification system, surgical risk is evaluated based on imaging findings (image-defined risk factors, IDRFs). Localized tumors are classified as L1 and L2 based on the presence or absence of IDRFs and M and MS based on the type of distant metastasis. Items checked for IDRFs of the abdominopelvic region are shown in Table 2. In addition, diagnostic imaging is used to evaluate 20 checked items, such as the presence or absence and extent of extension into the trachea and spinal canal and the presence or absence of major organ invasion. The IDRF evaluation is an important index for determining a treatment strategy, and evaluation in multiple planes is useful.

**Table 1. International Neuroblastoma Risk Group Staging System**

Stage	Description
L1	A localized tumor confined to one body compartment without IDRF (image-defined risk factor)
L2	A localized tumor with at least one IDRF
M	Distant metastasis (excluding MS)
MS	< 18 months of age with metastasis confined to skin, liver, and/or bone marrow bone marrow metastasis: tumor cells in bone marrow < 10% of nucleated cells and MIBG scintigraphy negative

IDRF = image-defined risk factor, prepared from secondary source 1

**Table 2. IDRFs for the abdominopelvic region**

Anatomic Region	Description
Multiple body compartments	Ipsilateral tumor extension within $\geq 2$ compartments (e.g., chest and abdomen, abdomen and pelvis)
Abdomen and pelvis	Tumor infiltrating porta hepatis or hepatoduodenal ligament Tumor encasing branches of superior mesenteric artery at mesenteric root Tumor encasing celiac artery and/or superior mesenteric artery root Tumor invading one or both renal pedicles Tumor encasing aorta and/or inferior vena cava Tumor encasing iliac vessels Pelvic tumor crossing sciatic notch
Intraspinal tumor extension	Intraspinal tumor extension (any level) provided that $\geq 1/3$ of spinal canal in the axial plane is invaded, the perimedullary leptomeningeal spaces are not visible, or spinal cord intensity is abnormal
Infiltration of adjacent organs and structures	Infiltration of the pericardium, diaphragm, kidney, liver, duodenum, pancreas, and mesentery

Prepared from secondary source 1

As a method of tumor scintigraphy with neuroblastoma-specific uptake,  $^{123}\text{I}$ -MIBG scintigraphy ("MIBG scintigraphy" below) is useful for evaluating primary and metastatic lesions.<sup>3, 4)</sup> In an examination of the diagnostic performance of MIBG scintigraphy by Vik et al., sensitivity and specificity of 88% and 83%, respectively, were reported. The causes of false positives were found to be the effects of physiological uptake by organs and structures such as the heart, salivary gland, brown fat, lacrimal gland, liver, and urinary bladder. The causes of false negatives were found to include tumor cell maturity and intratumoral necrosis and cystic changes.<sup>5)</sup> MIBG scintigraphy requires that imaging be performed 24 hours after radionuclide administration. Its diagnostic performance is improved by including SPECT in addition to planar imaging.<sup>5)</sup> SPECT/CT further improves resolution and is therefore useful not only at the time of diagnosis, but also when evaluating treatment efficacy.<sup>6, 7)</sup>

The sensitivity and specificity of bone scintigraphy in evaluating bone metastasis were found to be 70% to 78% and 51%, respectively. Thus, the diagnostic performance of bone scintigraphy was lower than that of MIBG scintigraphy and MRI. However, bone scintigraphy is recommended to evaluate skeletal system metastasis in patients negative on MIBG scintigraphy.<sup>7)</sup> Because the liver shows strong physiological uptake with MIBG scintigraphy, ultrasonography, CT, or MRI is needed to evaluate liver metastasis.<sup>1, 8)</sup> Moreover, when it is difficult to interpret abnormal uptake with MIBG scintigraphy at a site where metastasis may have occurred, another modality must be added to assess whether there is metastasis.

The number of reports comparing  $^{18}\text{F}$ -FDG PET ("PET" below) and MIBG scintigraphy has increased in recent years.<sup>7-9)</sup> Although PET provides excellent visualization of small lesions, it has been found to be inferior to MIBG scintigraphy in overall diagnostic performance, including the diagnosis of metastatic lesions.<sup>8, 9)</sup> PET involves higher levels of radiation exposure than MIBG scintigraphy, which is highly tumor-specific, and it produces many false positives and false negatives. Its use is therefore limited to special cases, such as patients negative on MIBG scintigraphy.

Based on the above considerations, contrast-enhanced CT or MRI is recommended for the local evaluation of neuroblastomas, and MIBG scintigraphy, in addition to CT and MRI, is strongly recommended to evaluate distant metastasis.

## 2. Selection of CT and MRI

A disadvantage of CT is that it generally requires the use of a contrast agent and is associated with radiation exposure. However, its advantages are that it enables the entire trunk to be evaluated in a short time and can be performed relatively easily at any facility. MRI, because of its high tissue resolution, does not require the use of a contrast agent. However, its shortcomings are that it is noisy, its tests take a long time, its imaging range is limited, and it often requires sedation for even longer than CT. Moreover, contrast-enhanced CT is superior for preoperatively evaluating blood vessels, whereas MRI is superior for evaluating tumors that extend to the central nervous system or spinal canal. Performing both CT and MRI is more useful for diagnosis. However, the modality should be selected according to the condition of the affected child and the circumstances of the facility.

## Search keywords and secondary sources used as references

PubMed was searched using the following keywords: neuroblastoma and diagnostic imaging.

In addition, the following were referenced as secondary sources.

- 1) Brisse HJ et al: Guidelines for imaging and staging of neuroblastic tumors: consensus report from The International Neuroblastoma Risk Group project. *Radiology* 261: 243-257, 2011
- 2) Bar-Sever Z et al: Guideline on nuclear medicine imaging in neuroblastoma. *Eur J Nucl Med Mol Imaging* 45: 2009-2024, 2018
- 3) Monclair T et al: The International Neuroblastoma Risk Group (INRG) Staging System: an INRG task force report. *J Clin Oncol* 27: 298-303, 2009

## References

- 1) Brodeur GM: Neuroblastoma: biological insights into a clinical enigma. *Nat Rev Cancer* 3: 203-216, 2003
- 2) Siegel MJ et al: Staging of neuroblastoma at Imaging: report of the Radiology Diagnostic Oncology Group. *Radiology* 223: 168-175, 2002
- 3) Matthay KK et al: Criteria for evaluation of disease extent by 123I-metaiodobenzylguanidine scans in neuroblastoma: a report for the International Neuroblastoma Risk Group (ONRG) Task Force. *British Journal of Cancer* 102: 1319-1326, 2010
- 4) Fendler WP et al: High 123I-MIBG uptake in neuroblastic tumours indicates unfavorable histopathology. *Eur J Nucl Med Mol Imaging* 40: 1701-1710, 2013
- 5) Vik TA et al: 123I-mIBG scintigraphy in patients with known or suspected neuroblastoma: results from a prospective multicenter trial. *Pediatr Blood Cancer* 52: 784-790, 2009
- 6) Rozovsky K et al: Added Value of SPECT/CT for correlation for MIBG scintigraphy and diagnostic CT in neuroblastoma and pheochromocytoma. *AJR Am J Roentgenol* 190: 1085-1090, 2008
- 7) Mueller WP et al: Nuclear medicine and multimodality imaging of pediatric neuroblastoma. *Pediatr Radiol* 43: 418-427, 2013
- 8) Sharp SE et al: 123I-MIBG scintigraphy and 18F-FDG PET in neuroblastoma. *J Nucl Med* 50: 1237-1243, 2009
- 9) Papathanasiou ND et al: 18F-FDG PET/CT and 123I-metaiodo- benzylguanidine imaging in high-risk neuroblastoma: diagnostic comparison and survival analysis. *J Nucl Med* 52: 519-525, 2011

## **BQ 90 Is MIBG scintigraphy recommended for the posttreatment follow-up of neuroblastomas?**

### **Statement**

MIBG scintigraphy is useful and recommended for the follow-up of neuroblastomas.

### **Background**

Neuroblastomas are fetal tumors that arise from the sympathetic nervous system. They can occur anywhere from the base of the skull to the pelvis. Neuroblastomas are the most common extracranial tumors that occur between the ages of 1 and 4 years. Neuroblastomas are the cause of approximately 15% of cancer deaths in young children. They account for 7% to 10% of pediatric cancers, peak in their occurrence at < 2 years of age, and 90% are diagnosed by 5 years of age. Metastasis is seen at the time of diagnosis in approximately 70% of patients with neuroblastomas. However, the prognosis is strongly correlated with age at diagnosis, disease stage, and biological factors.<sup>1-3)</sup> The evaluation of distant metastasis by MIBG scintigraphy has been reported to be correlated with prognosis in neuroblastoma.<sup>4)</sup> Although MIBG scintigraphy is already being widely used in Japan for patients with neuroblastomas, its usefulness in posttreatment follow-up was examined.

### **Explanation**

Using <sup>123</sup>I-MIBG planar imaging and SPECT for the posttreatment follow-up of 40 patients, Okuyama et al. visualized 10 of 11 recurrent tumors in 8 patients (91%) Of these 10, no elevation of tumor markers was seen in 3 patients.<sup>5)</sup> In an investigation of 11 patients with neuroblastoma, Rozovsky et al. reported that recurrence was detected in 5 patients with whole-body imaging and SPECT, but in only 2 patients with diagnostic CT. They suggested that contrast-enhanced CT can be omitted in the absence of MIBG SPECT/CT findings.<sup>6)</sup>

### **Search keywords and secondary sources used as references**

PubMed was searched using the following keywords: neuroblastoma, MIBG, scintigraphy, and follow. Four articles were selected from the results.

### **References**

- 1) Brodeur GM et al: Revisions of the international criteria for neuroblastoma diagnosis, staging, and response to treatment. *J Clin Oncol* 11(8): 1466-1477, 1993
- 2) Shimada H et al: International neuroblastoma pathology classification for prognostic evaluation of patients with peripheral neuroblastic tumors: a report from the Children's Cancer Group. *Cancer* 92(9): 2451-2461, 2001
- 3) Bown N et al: Gain of chromosome arm 17q and adverse outcome in patients with neuroblastoma. *N Engl J Med* 340(25): 1954-1961, 1999

- 4) Schmidt M et al: The prognostic impact of functional imaging with (123) I-MIBG in patients with stage 4 neuroblastoma >1 year of age on a high-risk treatment protocol: results of the German Neuroblastoma Trial NB97. *Eur J Cancer* 44(11): 1552-1558, 2008
- 5) Okuyama C et al: Utility of follow-up studies using meta-[123 I] iodobenzylguanidine scintigraphy for detecting recurrent neuroblastoma. *Nucl Med Commun* 23(7): 663-672, 2002
- 6) Rozovsky K et al: Added value of SPECT/CT for correlation of MIBG scintigraphy and diagnostic CT in neuroblastoma and pheochromocytoma. *AJR Am J Roentgenol* 190(4): 1085-1090, 2008