Contents

Members of the working group

Chair: Dr Topun Austin (Consultant Neonatologist, Cambridge, appointed by BAPM’s Executive Committee)

Members: (self-nominated from BAPM membership and approved by Executive Committee, or approached by the Executive Committee)

Dr James Boardman (Reader and Honorary Consultant, Edinburgh), Dr. Sundeep Harigopal (Consultant Neonatologist, Newcastle), Dr Axel Heep (Consultant in Neonatal Medicine, Bristol), Dr Harriet Joy (Consultant Neuroradiologist, Southampton), Dr Karen Luyt (Senior Lecturer in Neonatal Neuroscience, Bristol), Dr Christina Malamateniou (Lecturer in Perinatal Imaging, London), Dr Brigitte Vollmer (Associate Professor in Neonatal and Paediatric Neurology, Southampton), Dr Elspeth Whitby (Senior Lecturer and Honorary Consultant, Sheffield representing BMFMS), Ms Lisa Nandi (Executive Manager, BAPM)

Organisations involved in the consultation process

Members of the British Association of Perinatal Medicine, the BMFMS, the Royal College of Radiologists and the Neonatal Transport Interest Group

Executive Summary of Recommendations

1. Reporting of fetal and neonatal MRI brain scans
   - Fetal and Neonatal MRI brain scans should be reported by appropriately experienced personnel.
   - Dependent on caseload, review of scans by more than one reporter is advocated, either through double reading/reporting of the scan or within the setting of MDT/clinico-radiological meetings.
   - Where possible, the development of regional networks is recommended to share experience.
   - The pregnant woman or parent should be counselled regarding the potential limitations of the fetal or neonatal MRI scan.

2. Term infants with acquired brain injury, encephalopathy or seizures
   - Newborns with clinical signs of acquired brain injury or neonatal encephalopathy (NE) should undergo neuroimaging.
   - MRI is the imaging modality of choice for diagnostic imaging in NE.
   - Newborns with clinical and/or electrographic signs of seizures should undergo neuroimaging for diagnostic and prognostic purposes, and MRI is the imaging modality of choice.
   - MRI is useful in aiding prediction of neurological and neurodevelopmental outcome in newborns with hypoxic-ischaemic encephalopathy (HIE).
• For aiding prediction of neurological outcome in HIE, MR imaging between five to fourteen days after delivery is recommended. Injury patterns evolve over the first couple of weeks and thus it is essential to be familiar with the temporal evolution of injury patterns and to consider this in the interpretation of the findings on MRI.

3. Term infants with congenital heart disease & term infants undergoing extracorporeal membrane oxygenation
• There is currently insufficient evidence to support routine MRI in either term infants with congenital heart disease or term infants undergoing extracorporeal membrane oxygenation.
• Cerebral MRI should be performed where,
  o there are seizures or abnormal neurological signs.
  o there are significant parenchymal or midline abnormalities on the cerebral ultrasound scan.

4. Preterm infants
• MRI of the preterm infant at term equivalent age should be considered for:
  o Infants with evidence of overt parenchymal injury on cranial ultrasound including cystic periventricular leukomalacia, haemorrhagic parenchymal infarction, moderate to severe post-haemorrhagic ventricular dilatation and echodensity persisting for more than 3-4 weeks.
  o Infants with unexplained abnormal neurological signs.
• MRI of the preterm infant at term equivalent age, with a normal cranial ultrasound scan should not be performed routinely outside the context of research.
• In exceptional circumstances MRI may be performed before term equivalent age if the responsible neonatologist considers it necessary to make an early diagnosis of neurological disease and appropriate facilities for imaging the preterm infant are available.

5. Fetal imaging
Fetal MRI should be undertaken as part of a specialist fetal medicine referral.
The indications for fetal MRI are:
• To aid diagnosis.
• To aid management of a fetus with a known diagnosis.
• To provide additional information in cases where termination is considered and there is any uncertainty over the diagnosis.

Gadolinium contrast agents should not be used.
1. Background
Magnetic resonance imaging (MRI) has become increasingly available to clinicians for the evaluation of the fetus and neonate. However, with the exception of MR imaging in infants with hypoxic-ischaemic encephalopathy (HIE), there are no formal guidelines that address clinical indications and the practical aspects of MRI in these patient groups within the NHS.

1.1 Terms of reference
The purpose of this document is to:

- Provide recommendations on clinical indications for neonatal and fetal brain MRI.
- To promote best practice for acquiring and reporting of neonatal and fetal brain images.

The roles of MRI in post-mortem examination and perinatal research are beyond the scope of this document, as are detailed technical recommendations for image acquisition.

1.2 Recommendations for best practice
MRI acquisition of the fetus and neonate should be undertaken in a facility with experience of examining these patient groups. Specialists with specific expertise in interpreting fetal and neonatal MRI should report these images; a network or regional approach can facilitate this.

1.3 Audit standards
1. Infants born at term (>37 weeks postmenstrual age, PMA) with acquired brain injury, neonatal encephalopathy (NE) or seizures should undergo MRI.
2. MRI is the modality of choice for diagnostic and prognostic imaging in NE and in neonatal seizures. For prognostic purposes, the optimal timing for image acquisition in cases of HIE is between 5 and 14 days after birth.
3. In infants with congenital heart disease and those who have undergone extracorporeal membrane oxygenation (ECMO), MRI should be considered if there are abnormal neurological signs or evidence of parenchymal brain injury or intracranial haemorrhage on cranial ultrasound examination.
4. MRI of the preterm infant at term equivalent age (38-42 weeks postmenstrual age, PMA) should be performed if there is evidence of parenchymal injury on cranial ultrasound (intraparenchymal haemorrhage, haemorrhagic parenchymal infarction, cystic periventricular leucomalacia or post haemorrhagic ventricular dilatation) or if there are unexplained abnormal neurological signs.
5. Fetal MRI should be undertaken as part of a specialist fetal medicine referral to aid diagnosis, to aid management of a pregnancy or fetus, or to provide additional information in cases where there is diagnostic uncertainty.
2. Reporting of fetal and neonatal MRI brain scans

2.1 Background
The acquisition and interpretation of fetal and neonatal brain MRI is challenging compared with older patient groups because during the perinatal period:

- Anatomic variability is wide.
- Resolution is limited.
- Movement artifact is common.
- Tissue contrast changes rapidly due to myelination, decreases in brain water content and increases in tissue density.
- Contrast to noise ratio between grey and white matter is lower.
- Abnormalities may be subtle.

Although subspecialty trainees will encounter neonatal MRI scans (and possibly fetal MRI scans) during training, there is no specific accreditation for reporting fetal and neonatal MRI scans, nor any mechanism for determining that those who undertake this role after completion of training maintain their competence (1). Therefore, consideration needs to be given to who should report these scans and what other processes might be put in place to ensure an accurate and valid report.

2.2 What the reporter wants to know
In order to provide a knowledgeable and reasoned assessment of an MRI scan it is important to correlate the image with the clinical history of the patient (2). Essential requirements include: the gestational age (for fetal MRI), gestational age at birth and scan (neonatal MRI), and the differential diagnosis of the referring clinical team. It is important that request forms facilitate sufficient clinical detail to be entered.

2.3 What the referrer wants to know
The referrer requires a detailed review of the images, with particular detail of features that may be of diagnostic and prognostic value (e.g. the location of acquired parenchymal lesions, features consistent with a specific CNS malformation, congenital infection or neuro-metabolic disorder, or patterns of injury that are associated with adverse outcome). Consideration may be given to the use of a structured or graded reporting system to ensure that all areas are reviewed. Use of a proforma style of reporting may assist in auditing results.
2.4 Reporting

The reporter needs to be knowledgeable about the normal appearances of the fetal and neonatal brain and the range of expected findings for this population group. Images should be viewed on high quality imaging monitors because abnormalities may be subtle. The reporter should provide a permanent written record of the scan report (3).

It may be possible for an MRI scan to be performed in a local centre but there may not be a person with appropriate expertise available to report the images. Arrangements may be made for tertiary reporting of scans; in this situation, it is appropriate for the tertiary/reporting centre to advise on technical aspects of image acquisition, in particular detailing the sequences to be obtained.

In those centres where reporting of fetal and/or neonatal MRI scans is undertaken but the number of cases is not large, review of these scans by more than one reporter with provision of a consensus report is recommended. A number of studies reported in the literature have shown improved reporting rates for various imaging investigations with the introduction of a second reader and double reporting also serves to increase the experience of those involved (4).

2.5 Multidisciplinary teams and networks

Secondary review of both fetal and neonatal MRI scans is advocated within the setting of a multidisciplinary team (MDT) which may be convened at local, network or regional level depending on available expertise. An MDT review is advocated because coordinated expert review has potential:

- To improve communication between the professionals involved and consequently result in more appropriate and consistent information being offered to the pregnant woman or parents.
- To share knowledge, expertise and experience among a range of professionals and therefore serve as a platform for training; and to reduce variation in the service provided nationally.

Whether performed and reviewed locally or performed locally with tertiary review of the imaging, there needs to be clear process for communication between referrer and reporter so that an appropriate clinically based opinion of the imaging can be given.

2.6 Levels of certainty of a diagnosis

The level of certainty of a diagnosis made on an MRI scan will be affected by the quality of the scan obtained; movement artifact in particular can affect fetal and neonatal MRI scans. Abnormalities detected are often subtle, making it more difficult to be certain that they are
present. The level of certainty of any finding on a scan needs to be conveyed adequately by
the reporter to the referrer because it may contribute to the decision-making process regarding further management. It is important that the pregnant woman or parent is appropriately counseled regarding these limitations prior to the fetal or neonatal MRI scan.

2.7 Conclusion
Reporting of fetal and neonatal MRI brain scans should be performed by experienced personnel and reported promptly if they are to be of clinical value. Lack of local expertise may require tertiary referral for reporting, and access to multidisciplinary review by MDTs is advised.

3. Neonatal MRI
3.1 Term infants: neonatal encephalopathy

3.1.1 Background
Neonatal encephalopathy (NE) is a clinically defined syndrome of altered neurological function, characterised by difficulties establishing respiration, depression of tone and reflexes, alteration of consciousness, and often seizures.

The differential diagnosis of NE includes cerebral injury caused by a hypoxia-ischaemia, focal cerebral injury (arterial ischaemic stroke, cerebral venous sinus thrombosis, primary intracranial haemorrhage), metabolic disorders, infection, drug exposure, congenital brain malformations, neuromuscular disorders, and birth trauma. Acute bilirubin encephalopathy can result in permanent damage to the basal ganglia; although there is an imprecise relationship between total serum bilirubin levels and adverse neurological outcome, MRI can be informative if the clinical suspicion of neurological injury is high.

3.1.2 Role of neuroimaging in NE
Neuroimaging is important for determining the aetiology of NE, guiding clinical decision-making and prognosis, especially after hypoxic-ischaemic injury (5) and informing risk management and medicolegal proceedings.

3.1.3 Diagnostic imaging in NE
The Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society published practice parameters on neuroimaging of the neonate in 2002 (6). The practice parameter concludes that in the evaluation of NE, MRI is the imaging modality of choice and should include conventional
structural T1-w and T2-w images, diffusion weighted images, and, where available, single-voxel MR spectroscopy. Cranial ultrasound can be easily performed at the bedside and is helpful in the acute assessment of NE but it does not possess the wider diagnostic and prognostic utilities of MRI for evaluating children with NE.

There is growing evidence of potential long term harm of CT scanning in infancy (7); early (non-contrast) CT should be limited to emergency situations when there is evidence of birth trauma and urgent imaging is required because acute neurosurgical intervention is being considered. In all other situations MRI is the imaging modality of choice.

3.1.4 MRI as an aid for prediction of outcome in hypoxic-ischaemic encephalopathy (HIE)

A number of studies have shown that MRI is useful in aiding prediction of outcome in HIE (8-11). A recent systematic literature review on the prognostic value of clinical tests performed in the first week after birth in infants with HIE indicated considerable heterogeneity in test performance and studied outcomes (12). Nevertheless, neurophysiological studies were shown to have both the best sensitivity and specificity. Among the neuroimaging tests evaluated, diffusion weighted MRI (dMRI) had the best specificity, and conventional T1-w and T2-w MRI the best sensitivity. Neonatal MRS has fair sensitivity but poor specificity for neurodevelopmental outcome in early childhood and confidence intervals around these estimates are wide, which limits clinical utility (12). Although specific metabolites measured in specific regions of interest are reported to have higher predictive values in HIE (13), further evaluation of clinical utility is required before it is recommended in the routine clinical evaluation of children with NE.

<table>
<thead>
<tr>
<th>Imaging test</th>
<th>No. of studies</th>
<th>No. of patients</th>
<th>Pooled sensitivity</th>
<th>Pooled Specificity</th>
</tr>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Point estimate</td>
<td>95% CI</td>
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<td>MRI DWI first week</td>
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<td>36</td>
<td>0.58</td>
<td>0.24–0.84</td>
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<tr>
<td>ADC first week</td>
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<td>0.79</td>
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<td>T1/T2 first week</td>
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<td>T1/T2 first 6 wk</td>
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<td>0.40–0.97</td>
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<tr>
<td>MRS first week</td>
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<td>0.75</td>
<td>0.26–0.96</td>
</tr>
<tr>
<td>MRS first 2 wk</td>
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<td>0.73</td>
<td>0.24–0.96</td>
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<tr>
<td>Cranial US</td>
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<td>60</td>
<td>0.79</td>
<td>0.30–0.97</td>
</tr>
</tbody>
</table>

Table 1: Pooled sensitivities and specificities with confidence intervals for different MR imaging sequences and cranial ultrasound in the first week after birth. Adapted from van Laerhoven et al (12).
3.1.4.1 Timing of MRI for assessment of injury severity and prediction of outcome in HIE

During the first two weeks, injury patterns on conventional structural T1-w and T2-w imaging, on diffusion imaging, and also on MR spectroscopy vary (14); therefore, in order to correctly interpret imaging findings, it is important to understand the temporal evolution of lesion patterns on the different MR sequences. While dMRI will detect injury on early imaging, changes on T1-w and T2-w may not be apparent until after day 5. Although there is currently no consensus on the optimal timing for performing MRI in HIE, and practice varies depending on the local setting, it is clear that very early conventional structural MRI may underestimate the severity of injury and for accurate interpretation of conventional structural MRI, images should be obtained between 5 and 14 days of age (14). The withdrawal of life-sustaining treatment should not be delayed while MRI is sought if criteria for discontinuing intensive care, as described in RCPCH and GMC guidance, are met.

3.2 Term newborns with seizures

3.2.1 Background

Neonatal seizures occur in 1 to 5 per 1000 live births (15). Aetiologies include HIE, perinatal stroke (arterial ischaemic stroke and neonatal cerebral venous sinus thrombosis), intracranial haemorrhage (ICH), transient metabolic disturbances (hypoglycaemia, hypomagnesaemia, hyponatraemia), acute infections, inborn errors of metabolism, brain malformations, neonatal onset epilepsy syndromes, and vitamin-responsive epilepsies (15,16). Important early predictors of long-term outcome are the seizure aetiology and EEG background patterns (16); neuroimaging plays an important role in establishing the aetiology of neonatal seizures.

3.2.2 Neuroimaging in neonatal seizures

MRI is the imaging modality of choice (14,16). In addition to conventional structural MRI, additional sequences such as magnetic resonance angiography and magnetic resonance venography may be required when e.g. stroke is suspected; dMRI will be helpful in detecting early hypoxic-ischaemic injury or ischaemic stroke; MR spectroscopy can provide useful information when metabolic disorders are suspected (for example and elevated glycine peak in neonatal non-ketotic hyperglycinaemia).

Tekgul et al 2006 were able to establish the aetiology of seizures in 77% of a large cohort of newborns based on a combination of clinical history, examination, laboratory tests and CT/MRI examination (16). Weeke et al reported a diagnostic accuracy of 37.9% of cranial ultrasound (CUS) compared to 93.7% with MRI (18). Similarly, Osmond et al found that MRI
was able to identify the cause of neonatal seizures in 95% of cases, and demonstrated that MRI is valuable for both establishing the aetiology of seizures and for prediction of neurological outcome (19).

3.3 Term infants: congenital heart disease

3.3.1 Background

Congenital heart disease (CHD) is a common cause of childhood morbidity, occurring in 6 – 8/1000 live births, with up to 50% of patients requiring open-heart surgery to correct the defect. Due to advances in cardiothoracic surgical methods and intensive care medicine, it is now possible to undertake corrective surgery early in life, and survival rates have increased over the past two decades.

Survivors of CHD are at increased risk of neurodevelopmental impairment: a systematic review of infants undergoing cardiac surgery in the first 6 months of life concluded that cognitive scores are almost 1SD, and motor scores almost 2SD below the population mean in those assessed before 3 years of age (20). These neurodevelopmental deficits may contribute to increases in need for educational support (25%) and rehabilitative services (25%) seen among survivors (21).

Infants at highest risk are those with complex anomalies needing surgery in the neonatal period, such as transposition of the great arteries (TGA), univentricular anatomy, aortic arch obstruction and total anomalous pulmonary venous drainage) (22).

3.3.2 Neuroimaging of the infant with CHD

Two recent systematic reviews summarise the pre-operative neuroimaging findings in infants with CDH (23, 24). 29-59% of cases had significant developmental or acquired abnormalities on CUS or MRI. There is only one study reporting the relationship of cerebral MRI findings with neurodevelopmental outcome at age two years in infants with high-risk cardiac anomalies. The results suggested that the strongest MRI determinant of neurodevelopmental outcome was the degree of brain maturation, rather than structural brain lesions (25). However, much more data is required before routine brain MRI is recommended for all infants with CHD. It should however, be considered if there are abnormal unexplained neurological signs in the neonatal period or if there is evidence of parenchymal brain injury or ICH on CUS examination. The working group concurs with guidance from the American Heart Association (22) that all **high-risk infants** with CHD should undergo structured neurodevelopmental surveillance, and MRI should be undertaken if there are abnormal neurological signs or evidence of parenchymal brain injury or ICH on cranial ultrasound examination.
3.4 Term infants: extracorporeal membrane oxygenation

3.4.1 Background
Extracorporeal membrane oxygenation (ECMO) is a modified form of cardiopulmonary bypass that provides cardio-respiratory support in severe respiratory or cardio-respiratory failure. It is effective at reducing mortality and morbidity in eligible neonates (26). However, intracranial injury can occur in neonates who receive ECMO because of illness severity prior to treatment (including prolonged periods of hypoxia, hypocarbia, cardiovascular instability, acidosis, and altered cerebral autoregulation), and / or ECMO related phenomena (including complications associated with cannulation of central arterial / venous vessels, diminished pulsatility in VA ECMO, use of anticoagulants, and microthrombi from the circuit (27-34). Long-term neurodevelopmental impairment ranges from 15% to 50% in infants who have undergone ECMO; those having congenital diaphragmatic hernia having a higher incidence (42-43).

3.4.2 Patterns of brain injury and neurological complications
Neurological complications are relatively common in infants supported with ECMO (32,33,36,37). The Extracorporeal Life Support Organization registry (ELSO) report a 20% neurological complication rate, the most frequent being ICH (13%). Other lesions include infarction with cortical involvement, generalized atrophy, ventricular dilatation and periventricular leukomalacia (34,35,38,39) The high-risk group for neurological complications included preterm infants and infants less than 3kg, VA ECMO, severe acidosis and pre-ECMO cardiac arrest (40).

3.4.3 Neuroimaging of the patient treated with ECMO
The value of routine neuroimaging following ECMO and the optimal time and type of study remains unclear. The most commonly used mode of neuroimaging is CUS; this is sensitive to intracranial, which usually occurs within 72 hours of initiation of ECMO (41). However, the sensitivity of CUS may be significantly less: Rollins et al showed CUS to be abnormal in 24% during ECMO, whereas MRI detected abnormalities in 62% after decannulation (42).

3.4.4 Prediction of neurodevelopmental outcome
Although MRI is more sensitive than ultrasound for detecting intracranial lesions, there are uncertainties about its prognostic value in this group because of limited data. Glass et al reported that 43% of children with severe and 67% with moderate brain injury on neuroimaging had no disability at 5-year follow-up (43). Therefore, neuroimaging results should be interpreted with caution in regards to predicting outcome. In the absence of more
data MRI should only be undertaken if there are abnormal neurological signs or evidence of parenchymal brain injury or ICH on CUS.
3.5 Preterm infants

3.5.1 Neurodevelopmental outcome after preterm birth

Preterm birth (<37 weeks’ postmenstrual age, PMA) is a leading cause of neurodevelopmental impairment in childhood. Cerebral palsy affects 14% of surviving infants born before 27 completed weeks of gestation, and the risk remains elevated across the preterm gestational age range up to 36 weeks (44,45).

Preterm birth is an important determinant of cognitive dysfunction and educational underperformance: the effects are most severe in the extremely preterm infants, but even among relatively mature preterm infants cognitive function is impaired compared with children born at 39 to 40 weeks’ gestation (46,47). Two large population based studies in the UK have shown an increase in special educational needs that is proportional to degree of prematurity at birth for infants born at less than 39 weeks of gestation (48,49).

3.5.2 Neuroimaging of the preterm infant

Neuroimaging is used to provide information about patterns of tissue injury associated with preterm birth because diagnostic information may guide care, and some patterns of injury are closely associated with prognosis.

Sequential CUS is the standard imaging modality and will reliably detect germinal matrix-intraventricular haemorrhage, cystic periventricular leukomalacia, ventricular dilatation, and post-haemorrhagic hydrocephalus (50-52).

Magnetic resonance imaging at term equivalent age (38-42 weeks’ PMA) provides more anatomic detail than cranial ultrasound, which has led to:

- A greater appreciation of the nature and extent of white matter abnormalities including diffuse white matter injury and punctate white matter lesions (53-56);
- Detailed visualization of the posterior limb of the internal capsule and cerebellum, injury to both of which may carry prognostic significance (57, 58);
- The development of schemes for classifying brain injury (59).

In the research setting, this additional information, as well as advanced MRI processing techniques that provide quantitative measures of tissue microstructure and morphology, are useful for investigating causal pathways to injury and for biomarker development (60-63).

Neuroimaging at term equivalent age with CUS or MRI is more valuable than early CUS for predicting outcome (64). Although some centres have adopted MRI into the standard care pathway of preterm infants (65-67), there is doubt as to whether it should be adopted by the NHS at this time because accurate assessment of its added value over CUS for predicting outcome is lacking, the effect that additional information with inherent uncertainties has on
caregivers is unknown, and health economic and capacity assessments for roll-out across
the NHS have not been carried out. These matters are being investigated in a large UK
randomized controlled trial funded by the NIHR (ePrime: Evaluation of Magnetic Resonance
(MR) Imaging to Predict Neurodevelopmental Impairment in Preterm Infants,

3.5.3 Prediction of neuromotor outcome

3.5.3.1 Cranial ultrasound

CUS is highly specific for predicting outcome without cerebral palsy: a scan with no major
abnormality (defined absence of grade 3-4 IVH, cystic PVL or focal infarction) is highly
predictive of survival without cerebral palsy (specificity 95%, NPV 99%) (52). This finding is
supported by Nongena and colleagues’ analysis of relevant studies (50,52,68-70), which
estimates that a ‘normal’ scan defined as absence of haemorrhage within parenchyma or
ventricles, cysts or ventricular dilation, has a pooled probability of survival without CP of 94% (95% CI 92%-96%, heterogeneity I² 88%) (71).

Although CUS is highly specific, its sensitivity for CP is low, with estimates ranging from 18%
to 67% (59, 72-74).

3.5.3.2 Magnetic resonance imaging

The specificity of MRI at term equivalent age for predicting survival without CP is similar to
that of ultrasound, with reported values between 85% and 96% (59,72,74-76). The similarity of
these estimates is likely to be explained by the equivalence of sequential CUS and MRI for
detecting the major destructive lesions that are closely associated with CP (77).

MRI at term equivalent age appears to be more sensitive than ultrasound for predicting CP
with estimates ranging from 60% - 92% (66, 72, 74, 76); however, confidence intervals are wide
or unreported. The apparent increased sensitivity of MRI may be due to its improved
characterization of the nature and extent of white matter injury (53, 59, 78), and abnormalities of
the posterior limb of the internal capsule and cerebellum, which are associated with adverse
outcome (54,57,58,79).

3.5.4 Prediction of cognitive outcome

3.5.4.1 Cranial ultrasound

The specificity of CUS for predicting cognitive outcome is lower than it is for neuromotor
outcome: the pooled probability of a normal cognitive outcome with a normal ultrasound
scan has been estimated at 82% (95% CI 79%-85%) (71), but the extent to which the imaging
abnormalities are separable from the major destructive lesions associated with neuromotor impairment is unclear. While gross abnormalities on ultrasound including cerebral atrophy are associated with cognitive impairment, the technique is not generally considered to be a sensitive predictor of cognitive or sensorineural deficits (80).

3.5.4.2 Magnetic resonance imaging
A small number of studies show that MRI in the neonatal period is sensitive to predicting cognitive impairment but predictive values are low: Setanen et al showed that moderate to severe white matter injury on MRI has a PPV for cognitive impairment at 2 years of 34% (95% CI 20%-52%), which was similar to 5 to 9-year follow-up of the PIPARI cohort, where the PPV of major lesions on term equivalent MRI for predicting full-scale IQ < 85 was 44% (81).

3.5.5 Conclusions
Sequential CUS and MRI at term equivalent age are both highly specific for predicting outcome without cerebral palsy. If sequential CUS scans including one at term equivalent age (37-42 weeks) do not show parenchymal haemorrhage, grade 3 or 4 intraventricular haemorrhage, cystic PVL or post haemorrhagic ventricular dilatation then cerebral palsy is unlikely, it is unlikely that conventional MRI will provide any significant additional diagnostic or prognostic information.

MRI should be considered however, if there is evidence of overt parenchymal injury on cranial ultrasound because it may reveal unrecognized abnormalities in the white matter, cerebellum and posterior limb of internal capsule that may be of prognostic significance.

MRI should also be considered for preterm infants at term equivalent age with unexplained abnormal neurological signs because of its increased sensitivity for detecting acquired lesions and CNS malformations.

The optimal timing for MR imaging of the preterm infant is 38-42 weeks because this allows for assessment of brain maturation and myelination in the posterior limb of the internal capsule. In exceptional circumstances an earlier MRI may be beneficial if neurometabolic disease, congenital infection, or CNS malformation is suspected.
4. Fetal MRI

4.1 Background
Fetal imaging with ultrasound is the main imaging modality for antenatal anomaly screening, however interest in fetal MRI of the brain has grown steadily over the past two decades, given both the relatively high frequency of developmental abnormalities and the number of clinically significant pathologies which can give rise to quite subtle imaging changes. As a result fetal MRI has become part of clinical practice in centres where the expertise is available. The NIHR are currently funding a large study to assess the value of fetal MRI for CNS abnormalities (MERIDIAN: Magnetic resonance imaging to enhance the diagnosis of fetal developmental brain abnormalities in utero, http://www.shef.ac.uk/meridian/studysummary).

4.2 Indications for fetal MRI
Fetal MRI is indicated for reasons that fall into 3 main categories:

1. To aid diagnosis
2. To aid management of a fetus with a known diagnosis
3. To provide additional information in cases where termination is considered and there is any uncertainty over the diagnosis.

4.2.1 Fetal MRI to aid diagnosis
In a number of cases ultrasound can detect an abnormality but the extent of the abnormality is difficult to determine with accuracy. This may be due to maternal factors including raised BMI, and oligohydramnios (109); late gestation also reduces the ultrasound quality due to the ossification of the fetal skull (101). In other cases, the associated abnormalities are often subtle, for example, agenesis of the corpus callosum, the associated sulcal and gyral malformations cannot easily be identified with ultrasound. A recent systematic review (including 710 fetuses) indicates that for fetal CNS anomalies, the diagnosis was confirmed by MRI in 65.6% of cases and in 22.1% there were additional anomalies (82).

4.2.2 Fetal MRI to aid management decisions
The Meridian trial is a prospective cohort study investigating whether diagnosis is improved by performing in utero MRI where the fetus is known or suspected of having some form of developmental brain abnormality based on antenatal ultrasound examination. The results of this study, when published, are likely to influence clinical practice in the UK; however, there is a growing literature demonstrating the value of fetal MRI in a range of conditions affecting the brain:
1. **Difficult deliveries**: e.g. face and neck tumours requiring EXIT procedures (83,84), spina bifida (85,86), macrocephaly, sacrococcygeal teratomas.

2. **Mild-moderate ventriculomegaly (10-15mm)**: 5-10% of cases have associated abnormalities which may affect the diagnosis and prognosis (87,88). Although cases of severe ventriculomegaly (>15mm) have a higher incidence of associated abnormalities, the additional information provided by fetal MRI may not alter the counselling and management plans. Cases of ventriculomegaly do not require a routine follow up fetal MRI but should be followed up with serial ultrasound examinations (89-91).

3. **Posterior fossa abnormalities**: these are difficult to assess with ultrasound and fetal MRI may add valuable information. These include Dandy Walker malformations, isolated cerebellar vermis hypoplasia, Blake’s Pouch Cysts, and mega cisterna magna (92,93).

4. **Agenesis of the corpus callosum**: fetal MRI enables an assessment of whether the corpus callosum is intact along its entire length and to look for associated abnormalities that affect the prognosis (94-98). It can also aid in the differentiation of the 4 types of holoprosencephaly, severe ventriculomegaly, hydranencephaly and septo-optic dysplasia (99).

5. **Non-visualisation of the Cavum Septum Pellucidum** on ultrasound: this may be an indication of other underlying abnormalities, such as septo-optic dysplasia (100).

6. **Encephaloceles**: fetal MRI can be helpful, especially the encephalocele is small, as neural tissue involvement is difficult to see on ultrasound and again there may be additional abnormalities (98).

7. **Abnormal shaped head**: distortion makes interpretation of any underlying brain pathologies with ultrasound difficult. Spinal dysraphism is clearly demonstrated by ultrasound (102,103), however, fetal MRI may provide additional information on any involvement of the neural tissue (104,105). Fetal MRI may help in the prognosis by accurate identification of the level of the defect and also the degree of severity of any associated Chiari ii malformation that is difficult to assess using ultrasound.

8. **In utero surgery for neural tube defects**: although predominantly carried out in the USA, accurate delineation of the spinal pathology is essential prior to such a procedure (106,107).

9. **For suspected ischaemic / haemorrhagic lesions** (108)

10. **Twin to twin transfusion syndrome**: the highest risk for neurological sequelae follows laser therapy or death of a co twin (109,110). Approximately 8% of pregnancies in women who have undergone laser ablation for twin-to-twin transfusion syndrome have fetuses with neurological sequelae (111). Single fetal death in monochorionic twins is also associated with increased neurological morbidity and diagnosis may be aided by MRI (112).
4.2.3 Fetal MRI to provide additional information in cases prior to termination of pregnancy

While definitive cases do not require fetal MRI (e.g. anencephaly), in cases of diagnostic uncertainty fetal MRI may provide additional information to inform families and clinicians (e.g. ventriculomegaly with an abnormal echogenicity of the parenchyma seen on ultrasound).

4.3 How and when to perform a fetal MRI

4.3.1 Timing of fetal MRI

The majority of fetal MRI scans are performed after the 20-week anomaly ultrasound scan as this is usually the first time a concern about the fetus has been raised (114). Earlier fetal MRI scans are performed when clinically indicated but are technically more challenging as the fetus is smaller and more mobile and there is little experience and knowledge of the imaging appearances early in gestation (115). Earlier scans should only be performed if the results are likely to change the management at that point in time. Examples include brain malformations where termination is considered. MRI scans in the first trimester for maternal reasons have been shown to be safe (e.g. maternal appendicitis) (113). Later scans, beyond 30 weeks, may provide more information than earlier scans but in general scans should be done as early as possible, as long as it does not compromise diagnostic accuracy, in order to manage the pregnancy and counsel the patient (116).

4.3.2 Repeat scans

Repeat fetal MRI scans are not routinely used in clinical practice, as ultrasound remains the modality of choice to follow up known abnormalities. Cases where a repeat MR scan may be useful include:

- Those where the diagnosis remains uncertain. For examples in disorders of neuronal migration a later scan, when the sulcal and gyral development is more advanced, may be more informative.
- Cases of Spina Bifida may also benefit from a repeat fetal MRI at 32-34 weeks. This provides information to plan the postnatal surgery, gives clearer details of any neural tissue involvement than the earlier scan and may remove the need for a postnatal scan prior to surgery.
4.3.3 Sequences chosen for fetal MRI (121,117,118)

**T2 single shot fast spin echo (SSFSE):** This sequence provides structural detail of the brain and excellent contrast between different brain anatomical structures and is obtained within 20 seconds removing the need for sedation of the mother and fetus or paralysis of the fetus as has been used in the past in Europe and the USA. It is the most important of the sequences and should be performed in three orthogonal planes. The images will provide not only the structural detail but also detail on the neuronal migration pattern and the sulcal and gyral pattern.

**T1-w:** This is important for areas of haemorrhage or dense neuronal tissue, which will show as bright areas.

**DWI:** Provides detail on structural damage not visualised on the T2 images.

**Gadolinium based contrast:** This is not indicated routinely in fetal MRI (119). It is not known if it is safe to use as it recirculates in the amniotic fluid and is at risk of dechelating to a toxic form (120). Current policy is to avoid its use as there is limited experience and knowledge on its safety (121).

4.3.4 Magnetic field

Currently clinical fetal MRI scans are routinely done at 1.5T. Given that doubling field strength increases the specific absorption rate (SAR) by a factor of 4, scanning at 3.0T is currently not performed outside a research setting. The upper limit regarding field strength safety is currently 4T (122).

4.3.5 Patient Position

The patient should ideally lie in the left lateral decubitus position to prevent compression of the inferior vena cava (123, 124). Some patients may prefer the supine position. In all cases the patient should enter the magnet feet first and be reassured that their head will never be in the middle of the ‘tunnel’.

4.4 Conclusions

Fetal MRI has moved from a pure research tool to being used increasingly in clinical practice to aid diagnosis and prognosis of a wide range of neurological pathology. Given the technical challenges of performing high quality fetal MRI scans, the rapidly changing structure of the developing brain in the second and third trimester and the frequency of often subtle lesions with uncertain prognostic significance, it is important that that fetal MRI scans are undertaken and reported in centres with expertise in this area. The evidence to date would suggest that fetal MRI can provide important additional diagnostic and prognostic information.
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