Clinical Guideline: IMAGING THE ENCEPHALOPATHIC INFANT, NEUROPROTECTION GUIDELINES FOR THE EAST OF ENGLAND

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Guidance specific to the care of neonatal patients.

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Audit Standards:

Audit points

1. Introduction

Neuroimaging is important in determining the aetiology of neonatal encephalopathy, guiding clinical decision making, providing prognosis after hypoxic ischaemic injury and informing risk management and medicolegal proceedings [1].

2. Cranial Ultrasound Scanning (CUS)

Standard: All infants with suspected neonatal encephalopathy should have a cranial ultrasound scan on admission and ideally before transfer to a regional cooling centre.

Standard: CUS should be performed, including assessment of the resistance index, on admission, D1, D4 (post rewarming) and later if needed (depending on the MRI).

Cranial ultrasound (CUS) remains the most utilised mode of imaging in these infants offering the advantage of bedside imaging; however, it is examiner dependent and there is poor inter-observer agreement. Cranial ultrasonography is valuable in identifying other causes of neonatal encephalopathy such as congenital abnormalities as well as identifying cerebral haemorrhages and antenatal brain injury. In HIE normal cranial ultrasound findings can be reassuring whereas abnormalities in the thalamus and basal ganglia have been shown to be associated with adverse outcome [2]. However, predictive accuracy is poor, (sensitivity 0.76 95%CI 0.3-0.97, specificity 0.55 95% CI 0.39-0.7) [3, 4]. The combination of abnormal cranial ultrasound and neurological examination may improve prediction of neurological outcomes [5]. There is no data suggesting that hypothermia alters the interpretation of cranial ultrasonography.

2.1. Doppler Studies

Pourcelot's Resistive index (RI) is calculated as peak systolic velocity minus end diastolic velocity divided by peak systolic velocity). Normal RI of >0.6 is reassuring. Low RI of $\leq$0.55 is associated with adverse neurodevelopmental outcome although specificity varies [6-8].

The positive predictive value of the resistance index was just 60% (95% CI 45-74%) in infants treated with hypothermia for HIE, considerably less than that reported in normothermic infants [9]. The

negative predictive value of the cerebral resistance index in the cooled infants was 78% (95% CI 67-86%) similar to that reported in non-cooled infants with HIE [9].

When scanning, it is important to bear in mind that high diastolic flow associated with resistive index <0.55 is rarely seen before 6 hours of age [10].

2.2 Possible CUS Findings in HIE [11]

- Early cerebral oedema – generalised increase in echogenicity, indistinct sulci and narrow ventricles.
- Intracranial bleed (eg, IVH, subdural or extradural hematoma)
- Cortical highlighting
- After 2-3 days of age, increased echogenicity of thalami and parenchymal echodensities.
- After day 7 cystic degeneration of the white matter
- Increased echogenicity in the white matter seen on day of birth does suggest antenatal onset of neonatal encephalopathy

3. Magnetic Resonance (MR) Imaging

MR imaging has been shown to have greater diagnostic and prognostic accuracy than grey scale ultrasonography and is now considered the imaging modality of choice in neonatal encephalopathy (NE) [1, 12]. CT imaging should be limited to emergency situations where there is evidence of birth trauma and urgent imaging is required because acute neurosurgical intervention is being considered. However, successfully obtaining and interpreting images requires careful preparation and planning.

Standard [1]: All neonates with clinical signs of acquired brain injury or neonatal encephalopathy should undergo neuroimaging. MRI is the imaging modality of choice for diagnostic imaging in NE.

3.1 Preparation

MR imaging of a sick neonate can be difficult and requires careful preparation in order to obtain optimal images enabling accurate interpretation. There are a number of safety issues that need to be carefully considered.

3.1.1 Timing

The very real anxiety and need for early information about long-term prognosis needs to be tempered by ensuring that as much information as possible is obtained from imaging. 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. In neonates with HIE, specific patterns of injury on conventional MR imaging have been identified as being associated with long term neurodevelopmental problems [13-16]. Ideal timing for an MR examination is between 5 and 14 days. Before this time, conventional imaging may be relatively normal [17, 18]. In addition, the infant is often more stable after the first few days from delivery and is better able to tolerate being transported to the MR scanner and the scanning procedure. If imaging during the first week diffusion weighted imaging (DWI) is essential but may underestimate the extent of the injury, particularly in the basal ganglia and thalami [16, 18-20]. Furthermore, in instances of widespread injury, and no normal appearing tissue for comparison, it is essential to measure the regional apparent diffusion coefficient (ADC) on the diffusion ADC map. DWI normalises by the end of the second week.

In a minority of infants early MR imaging (i.e. within the first week) may be clinically indicated, either to clarify the diagnosis and exclude other pathologies (e.g. intracranial haemorrhage, perinatal stroke, metabolic conditions) or in infants where withdrawal of intensive care is being considered. 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.

Sensitivities and specificities for different MR imaging sequences in the first week after birth is shown in Table 1.

Imaging Test	No of studies	No of patients	Pooled sensitivity		Pooled specificity	
			Point estimate	95% CI	Point estimate	95% CI
MRI DWI first week	2	36	0.58	0.24-0.84	0.89	0.62-0.82
ADC first week	3	113	0.79	0.5-0.93	0.85	0.75-0.91
T1/T2 first week	3	60	0.84	0.27-0.99	0.9	0.31-0.99
T1/T2 first 2 weeks	3	75	0.98	0.8-1.0	0.76	0.36-0.94
MRS first week	3	66	0.75	0.24-0.96	0.58	0.23-0.87
MRS first 2 weeks	3	56	0.73	0.3-0.97	0.84	0.27-0.99

Table 1: Pooled sensitivities and specificities with confidence intervals for different MR imaging sequences in the first week after birth for neurodevelopmental outcome in early childhood [1, 3].

Standard [1]:
For aiding prediction of neurological outcome in HIE, MR imaging between 5-14 days after delivery is recommended

3.1.2 Requesting an MR Image

It is important to provide clear and concise clinical details to the radiology team not only to facilitate interpretation of the scans in the light of the clinical history but also to ensure that the department are aware of the current clinical status of the infant and can prepare for the scan appropriately (See Appendix A- MR request form).

3.1.3 Sedation

Imaging the neonatal brain relies on the infant being still. Neonates may be imaged during natural sleep following a feed. Swaddling can aid this ('feed and wrap' method). However, the quality of MR images is often compromised by movement artefact, thus diminishing the reporting accuracy and the ability to predict neurodevelopmental outcome. In non-ventilated infants, light sedation can be achieved with chloral hydrate enabling better quality images. With strict protocols and adequate monitoring, chloral hydrate sedation for MR scanning can be safely performed for both preterm and term infants [21, 22]. Chloral hydrate 30-50 mg/kg should be administered via oral or nasogastric route on an empty stomach (1 hr fast) about 15 minutes before the anticipated start of the scan. The rectal route may be used if oral/nasogastric administration is not possible. The chosen dose should be judged via careful clinical assessment and adjusted accordingly depending on concomitant administration of sedatives and anticonvulsants. Sedation may result in hypoventilation and the need for supplemental oxygen although the incidence of significant complications was 1% [21]. Therefore, oxygen saturation is monitored continuously from time of sedation to time of full waking and neonatal-trained staff must be present throughout. Infants who are already properly sedated for ventilation do not routinely need any additional sedation.

3.1.4 Monitoring

All infants, sedated or not, should be monitored during transportation to and from the scanner as well during the procedure itself. MR compatible pulse oximeters are available in all MR departments for this purpose. Electrocardiogram monitoring should also be undertaken during transportation and during the scan where appropriate MR compatible equipment is available. Two neonatal-qualified staff should be in attendance throughout the scan for all ventilated infants. The assistance of a paediatric anaesthetist can also be helpful. At least one neonatal/paediatric nurse should be in attendance for all patients requiring sedation. Observations should be documented regularly during both transport and scanning.

Standard: All infants undergoing MR imaging should have continuous monitoring (oxygen saturations and heart rate as a minimum).

3.1.5 Equipment

Transferring sick neonates to the MR department is challenging. It requires careful planning and an understanding of the potential risks involved. It is therefore vital that staff accompanying the infant should be familiar with all the equipment (e.g. transport incubator, infusion pumps, MR compatible equipment) and be competent in the stabilisation of a sick neonate. In addition to MR compatible monitoring equipment, ventilated infants will require a MR compatible ventilator. Such infants often have multiple infusions. Prior to leaving the neonatal unit, check stability and that baby is metal free with all appropriate lines secure- See checklist (Appendix C)

A metal check of the baby (e.g. for arterial lines with terminal electrode, poppers on clothes, electronic name tags etc.) and of all staff needs to undertaken before entering the MRI scanner room. Careful consideration also needs to be given to the procedure to be followed in the event of clinical deterioration of the infant during the scan. Only MR compatible resuscitation equipment can be taken into the scanner room. If this is not available, the infant needs to be brought out of the scanner room before resuscitation and stabilisation. It is important that all members of staff are aware of the resuscitation procedure during transportation and scanning.

4. MR Details

Neonates present specific challenges to the practicalities of acquiring a scan because of their size and the increased water content of their developing brain.

4.1 MR Coil

A standard adult head coil should produce a sufficiently high signal to noise ratio. In a large coil care must be taken to place the neonatal head in the centre of the coil (padding underneath the head), to avoid uneven signal intensity in the acquired images. High signal to noise and even signal intensity may be acquired using a smaller coil such as an adult knee coil or a dedicated neonatal head coil. Poor coil choice or head position can result in poor quality images.

4.2 MR Sequences

Essential MR Sequence		Recommended MR sequence	
Axial T1	To visualise basal ganglia & thalami & for assessing myelination in the posterior limb of internal capsule.	**Fluid attenuated inversion recovery**	Useful for detecting late gliotic changes in older infant.
Sagittal T1	Ideal for visualising midline structures (eg pituitary, corpus callosum, cerebellar vermis).	**Venogram**	Exclude sinus thrombosis & differentiate from subdural haemorrhage.
Axial & coronal T2	Ideal for identifying early ischaemic changes. and for assessing grey-white matter differentiation. Detection of haemorrhage.	**Angiogram to include proximal cerebral arteries and neck vessels**	Visualise cerebral vessels in focal stroke and exclude carotid dissection.
Gradient Echo Axial	Greatest sensitivity for detecting intracranial haemorrhages.	**MR spectroscopy**	Deep grey matter Lac/ Naa ratios have demonstrated greatest prognostic sensitivity (18) detection of elevated lactate or glycine in certain metabolic disorders.
Diffusion Weighted image	Detects ischaemic changes earlier than conventional MRI. Particularly useful if	**Motion resistant Sequences**	Propeller/ BLADE or T2 single shot FSE.

	focal stroke suspected		

5. Reporting

In order to provide an informed and accurate assessment of an MRI scan it is important to correlate the image with the clinical history and current findings of the patient. MRI scans should be reported by appropriately experienced personnel and reviewed within the setting of MDT/clinicoradiological meetings. It may be possible for an MRI scan to be performed in a local centre but there may not be appropriate expertise to report the images. Arrangements may be made for tertiary reporting in these cases. Images should be transferred to tertiary radiologists using appropriate NHS routes (e.g. PACS).

A standardised reporting scheme ensures all areas are reviewed, promotes accessibility of results, facilitates interpretation of subsequent imaging and helps in auditing the results. (Appendix B).

Clear process for communication between the referrer and reporter should be available so that an appropriate clinically based opinion of imaging can be given and communicated to family.

6. Serial Imaging

The accuracy of early, appropriately timed MR imaging in predicting neurodevelopmental outcome is well documented and negates the need for routine serial scans in the majority of infants [3]. However, it may be appropriate to repeat MR scans where the initial scan has been undertaken within the first week of life when MR changes are still evolving or when indicated by the clinical course of the infant, or in the case of significant movement artefact on previous scan precluding satisfactory interpretation. Subsequent imaging should be undertaken at the discretion of the clinician responsible for the infant in discussion with consultant radiologists.

7. Features of HIE on MR imaging

Following moderate or severe HIE, particularly following a documented sentinel event, abnormal signal intensity is most commonly detected in the basal ganglia and thalami, corticospinal tracts, the subcortical white matter, and regional cortex [15] and images have high predictive values for detecting adverse outcomes (See Table 1). Extensive and dominant white matter and cortical injury is suggestive of additional chronic hypoxic ischaemic compromise as may be indicated by fetal growth restriction (FGR) and/or poor fetal movements. It may also complicate symptomatic hypoglycaemia and /or bacterial or viral infection e.g. Parecho virus.

On MR spectroscopy high lactate (suggestive of tissue hypoxia and ischaemia) and low N-acetyl aspartate (reflects neuronal injury) within the basal ganglia and thalami is often seen.

The predictive accuracy of MRI is unchanged following therapeutic hypothermia [23, 24].

7. Communication with Parents

This is a very stressful time for parents and the uncertainty about long term prognosis adds to this. Timely and repeated communication with parents and family should be a key aspect of caring for these sick infants. With regard to imaging, it is important to discuss beforehand what information may be obtained by imaging the infant at that particular time and the limitations of the imaging modality. Whilst MR imaging can provide reliable prognostic indicators, it is important to also consider all neurological assessment tools and information when discussing long term prognosis (including clinical examination and course, resistive index on CUS and aEEG/ conventional EEG findings). It is also important to stress the need for long term developmental follow up and support for these infants. It is vital that results of imaging are communicated to parents at the earliest opportunity by the most senior clinician available, ideally the consultant responsible for the infant. This should ideally be undertaken face to face.

Neuroimaging is an important aspect of neuro-intensive care of infants with HIE. It can provide vital information to guide management and prognosis of these babies.

Audit Standards

1. Infants with neonatal encephalopathy should undergo MRI Ideally sedation should be used.
2. Optimal timing for MR imaging in cases of HIE is between 5-14 days after birth.
3. Standardised reporting by a radiologist with appropriate experience.
4. Documentation of monitoring during MR imaging.
5. Adverse events related to sedation and MR imaging.

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Appendix A: MRI Expert Reporting – Referral Proforma (Adapted from Prof. Rutherford London Perinatal Imaging Proforma)

Consultant		**Hospital**	
Baby details			
Name		**GA at birth**	
dob		**CGA @ MRI**	
NHS no		**Birth weight**	
Address		**Current weight**	
		Birth OFC	
		Current OFC	
Antenatal			
Gravida		**Para**	**TOP/Misc**
Serology			
Scans			
Any other concerns			
Labour			
Onset			
Sepsis risk factors			
Antenatal steroids			
Delivery		**Resuscitation**	
Mode		**Apgars**	
Indication		**Cord pH**	
Ventilation			
Day on ventilator			
CPAP			
High FLow			
Current status			
CVS			
Inotropes			
GI/Fluids			
Full feeds by			
NEC			
Hypoglycaemia			
Neurology			
Encephalopathy			

Seizures	
Cranial US	
Neurological exam	
Summary	

Appendix B: MRI Expert Reporting – Reporting Proforma (Adapted from Prof. Rutherford London Perinatal Imaging Proforma)

PERINATAL IMAGING REPORTING SERVICE

Radiologist Details

Date of report:

NAME	

D.O.B.		Date of scan		NHS No.	

Hospital		Consultant	

Clinical Details:
GA: **Birth weight (g):** **OFC (cm):**
Apgars **Arterial pH** **Venous pH**
Antenatal:
Labour and Delivery:
Condition at Birth:.
Presenting Issues:
CFM/EEG:
Metabolic:
Sepsis.
Cranial US:
Current neurology:
Feeding:
Discharged:
Age at scan

MR Summary

MRI DETAILS: Images were obtained with T_1 and T_2 weighted sequences in the axial and sagittal planes and diffusion weighted sequences

MRI REPORT:

Bi Parietal Diameter:
Cortex:
White Matter:

NAME:

MRI REPORT CONTINUED:

Basal Ganglia and Thalami:
Internal Capsule:
Corpus Callosum:
Cerebellum:

Brainstem:

Extracerebral Space:
Ventricles:
Lateral:
3rd:
4th:
Germinal matrix:
Cavum Septum Pellucidum:

Myelination:
Pituitary:

Orbits:
Globe diameter:
Lenses:
Optic nerves:

Other Comments:
ADC Map:
FLAIR:
Gradient echo:
SWAN:

MRV:
MRA:

Appendix C

Checklist for MR imaging

		Yes/No/N.A.	Comment
1	Confirm date and time of scan		
2	Confirm with neonatal registrar/consultant baby is stable for scan		
3	Confirm verbal consent from parents		
4.	Confirm if baby requires sedation If sedation required check baby is nil by mouth for atleast one hour prior to administration		
5.	Prescribe choral hydrate		
6.	Baby's clothing metal free i.e. no poppers, hat on		
7.	Remove EEG leads, ECG leads, rectal probes electronic name tags before transfer		
8.	If long line in situ- check compatibility with radiographer		
9.	Remove bionectar (needle free connectors) and all lines are metal free		

10.	All lines with infusions have 4 extra extensions or MR compatible infusion pumps are used		
11	TPN is changed to clear fluids		
12	Portable pulse oximeter monitor is attached to the baby		
13	Check with radiographer ok to proceed with giving choral sedation or feed to be given e.g. scanner and staff ready		
14.	Check chloral hydrate administered and well tolerated (if no e.g. large vomit or have concerns please inform neonatal team)		
15	Check 2 neonatal/paediatric staff for ventilated babies and 1 neonatal/paediatric staff for sedated babies present during scan		
13	Put ear muffs/plugs		
14	Post scan continue monitoring till baby awake		

reproduction. The document only applies to the East of England region with due process followed in agreeing the content.

Exceptional Circumstances Form

Form to be completed in the **exceptional** circumstances that the Trust is not able to follow ODN approved guidelines.

Details of person completing the form:	
Title:	Organisation:
First name:	Email contact address:
Surname:	Telephone contact number:
Title of document to be excepted from:	
Rationale why Trust is unable to adhere to the document:	
Signature of speciality Clinical Lead: Date:	Signature of Trust Nursing / Medical Director: Date:
Hard Copy Received by ODN (date and sign):	Date acknowledgement receipt sent out:

Please email form to: mandybaker6@nhs.net requesting receipt.

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