SOP: diagnosis and classification of brain injury

Version	Author(s)	Date	Changes	Approved by
1.0	Mathias Lühr Hansen	26.03.19	Initial version	Gorm Greisen
1.1	Mathias Lühr Hansen	30.10.10	• "These images" is changed to "the classification", section 3 line 2	Gorm Greisen

Content

1.0 Brain injury in SafeBoosC III

In SafeBoosC III, 'severe brain injury' is part of the composite primary outcome 'severe brain injury or death', evaluated at 36 weeks postmenstrual age or discharge home.

Severe brain injury is defined as having one or more of the following brain injuries:

- Intraventricular haemorrhage grade 3 or 4
- Cystic periventricular leukomalacia
- Post-haemorrhagic ventricular dilatation
- Cerebellar haemorrhage
- Cerebral atrophy

Other brain injuries are not relevant in the context of SafeBoosC III but may still be relevant for the baby's clinical care.

Only brain injuries diagnosed by routine cerebral cranial ultrasound scans may be used for SafeBoosC III. The classification must be done by someone blind to the group allocation in the trial (see '**SOP: blinding of cranial ultrasound and data entry'**) and the methods and criteria listed in this SOP must be used. A training module on cranial ultrasound scanning and classification of severe brain injury for SafeBoosC III, is available in the web-based training and certification program.

2.0 Diagnostic classification of brain injury in SafeBoosC III

Intraventricular haemorrhage

Intraventricular haemorrhage (IVH) is the typical cerebral haemorrhage in preterm infants and it develops within the first few days after birth. Low-grade IVHs (grade 1 and 2) are located in the germinal matrix (grade 1) or presents minimal intraventricular bleeding (grade 2). In its severe forms, high-grade IVH, a large intraventricular clot fills the ventricle and causes acute dilatation of the involved lateral ventricle (IVH grade 3) or a parenchymal haemorrhagic infarction is visible in the periventricular white matter (grade 4). These brain lesions can be unilateral or bilateral, and periventricular haemorrhagic infarction can co-exist with all grades IVH.

Only IVH grade 3 and 4 are classified as severe brain injury for the purpose of SafeBoosC III.

Cystic periventricular leukomalacia

Normal peritrigonal blush is symmetric, soft, radial and homogeneous with vague margins. In contrast, abnormal periventricular echodensities (PVE) are usually asymmetric, hard, sharply delineated and often inhomogeneous with nodular accents - but the distinction is difficult and somewhat subjective. So, while PVL grade 1, may be difficult to define well, cysts are easy to identify due to their rounded shape, central echolucency, and often a hyper-echoic rim.

Classification of periventricular leukomalacia according to (from Pierrat et at. Arch Dis Child Fetal Neonatal Ed. 2001)	
Grade 1	Transient periventricular echodensities (PVE) persisting for >14 days
Grade 2	PVE evolving into small localised fronto-parietal cystic lesions
Grade 3	PVE evolving into extensive periventricular cystic lesions
Grade 4	Cystic lesions extending into deep white matter, evolving to extensive subcortical cysts

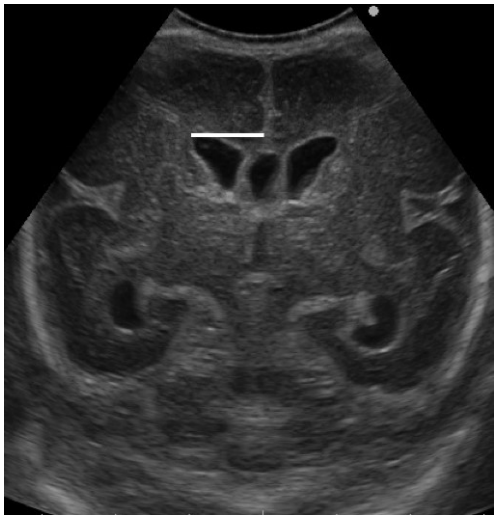
It is only PVL grade 2-4 that are classified as severe brain injury for the purpose of the SafeBoosC III trial.

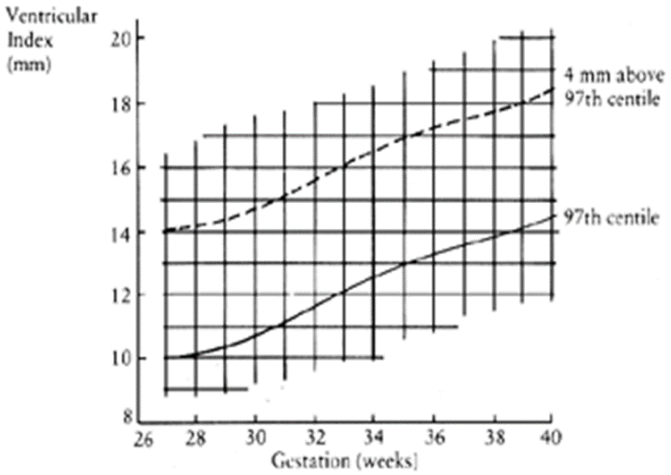
Post-haemorrhagic ventricular dilatation

Post-haemorrhagic ventricular dilatation is a common complication of IVH. Post-haemorrhagic ventricular dilatation usually begins to develop some days to a few weeks after the haemorrhage but may exceptionally occur after term corrected age. A transient dilatation with subsequent regression is also a common event. When the lateral ventricles appear dilated, standardized measurements must be made and will influence decisions regarding removal of CSF. In order to diagnose post-haemorrhagic ventricular dilatation, it is important to estimate 1) *ventricular index,* 2) *anterior horn width*, and 3) *thalamo-occipital distance.*

Ventricular index

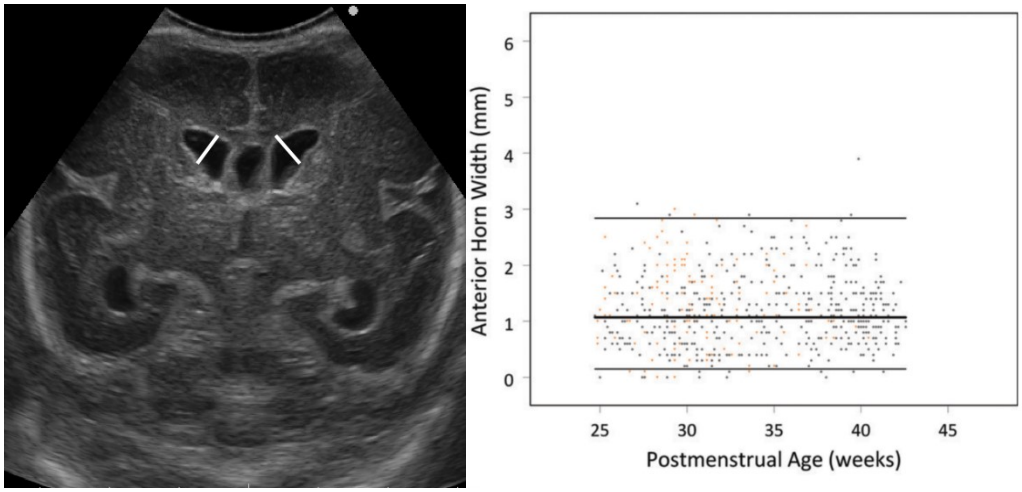
The ventricular index (sometimes called the Levene index) is the horizontal distance between the lateral corner of the ventricle and the midline. The upper limit of normal values increases from 10 mm to 14 mm with gestation because the brain grows.





Anterior horn width

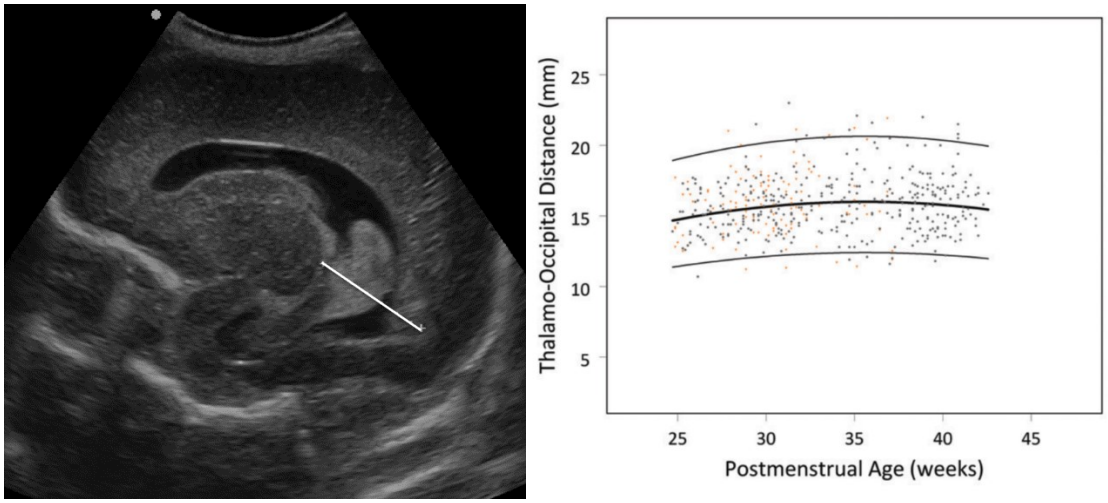
The anterior horn width is the maximal width of the lateral ventricle measured perpendicularly to its long axis. The normal value is independent on postmenstrual age or brain size and should be less than 3 mm.



(from Bouwer MJ et al Radiology 2012)

Thalamo-occipital distance

The posterior horn of the lateral ventricle is particularly prone to dilate. The most robust measure is the maximal distance from the posterior margin of the thalamus to the tip of the posterior horn. This measure is surprisingly independent of postmenstrual age. A typical value is 15 mm, the upper limit of the normal range is 20 mm.



(from Bouwer MJ et al Radiology 2012)

For the diagnosis of post-haemorrhagic ventricular dilatation, which can be made at any time in the course

after an IVH, the lateral ventricles must be enlarged. All three measures should be above the cut-off. If the dilation is asymmetric, the measures for the most dilated ventricle is used.

At corrected age of 36 weeks of gestation	Cut-off
Ventricular Index	97% centile
Anterior horn width	3mm
Thalamo-occipital distance	20mm

The diagnosis can also be made, if repeated removal of cerebrospinal fluid is done to reduce the ventricular dilation.

Cerebellar haemorrhage

Cerebellar haemorrhage (CBH) represents the most commonly acquired posterior fossa brain lesion in preterm infants, with an impact on motor, cognitive and behavioural long-term outcomes.

Different CBH patterns were described in preterm infants:

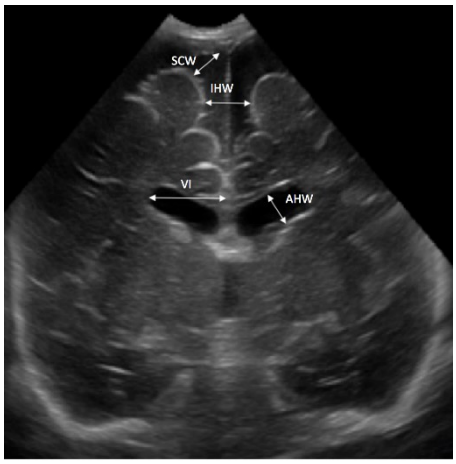
- Microhaemorrhages within the hemispheric parenchyma
- Large focal CBH in the parenchyma of the cerebellar hemispheres or the vermis

On cUS scans, large focal CBHs appear as globular areas of increased echogenicity within the cerebellar parenchyma. Minor CBHs can only be seen in mastoid views – if available - and are also classified as severe brain injury for the purpose of SafeBoosC-III. In the chronic phase, focal atrophy of the cerebellum is seen.

Cerebral atrophy

Brain atrophy is defined as the combination of an enlarged subarachnoid spaces and a widened interhemispheric fissure with a large, rather than compressed, ventricular system. All measurements for diagnosing cerebral atrophy are performed on the standard coronal image (at the level of the foramen Monroi). The extracerebral space is measured from the lateral edge of the triangular sagittal sinus to the surface of the cortex perpendicular to the latter (SinoCortical Width – SCW) and the interhemispheric fissure

width (IHW) is calculated as the maximum horizontal distance between the hemispheres, measured between the top gyri. For the definition of cerebral atrophy at 36 weeks corrected age, the subarachnoid space (measured by the sinocortical width), the interhemispheric fissure as well as the lateral ventricles (measured by the ventricular index) must be enlarged.



At corrected age of 36 weeks of gestation	Cut-off
Sinocortical width (SCW)	3mm
Interhemispheric width (IHW)	6mm
Ventricular index (VI)	13mm