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Neuromonitoring in the neonatal ECMO patient

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Abstract

Utilization of extraocorporeal membrane oxygenation (ECMO) has become increasingly widespread as a bridging therapy for neonates with severe, reversible respiratory or cardiac diseases. While significant risks remain, due to advances in medical and surgical management, overall mortality has decreased. However, short and long-term neurological morbidity has remained high. Therefore, increasing attention has been focused on multimodal neuromonitoring to track and optimally, minimize or prevent intracranial injury. This review will explore the the indications, advantages, disadvantages, timing, frequency, duration, and any known correlation with neurodevelopmental outcomes of common types of neuromonitoring in the neonatal ECMO population. Investigational monitoring techniques such as NIRS will be briefly reviewed.

Introduction

Extracorporeal membrane oxygenation (ECMO) is a life-saving intervention for neonates with profound, reversible respiratory or circulatory collapse that is refractory to conventional medical management. As ECMO therapy involves cannulation and ligation of large vessels (most commonly the carotid artery and jugular vein) and contact of blood with synthetic surfaces and anticoagulation (see Figure 1), the risk of neurologic consequences due to altered cerebral hemodynamics, bleeding, and/or embolic phenomena is not trivial. Treatment with anticoagulants mitigates some of this risk, but introduces the potential risk of hemorrhagic complications. While immediate mortality on ECMO related to neurologic

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complications has decreased, neurological morbidity continues to be significant.[1] Multiple single-center studies report varying rates of neonatal ECMO central nervous system (CNS) complications ranging between 0 to 52% using head ultrasound (HUS) and head computed tomography (HCT) data.[2–8] More recent studies based on magnetic resonance image (MRI) have shown higher rates of MRI abnormalities, between 52% to 62%.[9, 10]

ECMO survivors have increased rates of neurological co-morbidities including periventricular leukomalacia (PVL), cerebral palsy (CP), sensorineural hearing loss, and intellectual disability.[11–17] As the survivors age, additional long term deficits have been reported in memory, executive function, and visuospatial functioning.[18] However, distinguishing to what extent these findings are a consequence of the underlying disease that required ECMO management as opposed to ECMO itself is a challenge. Furthermore, finding a consistent association of neuroimaging outcomes with neurodevelopmental outcomes has been difficult.

Despite the potential risks of neurologic sequelae, the field of neuromonitoring during ECMO care is in its early stage. Standard evaluation for neurologic status at this time is relatively rudimentary using physical examination (which is often clouded by sedative needs), vital sign changes (which may be non-specific), and head ultrasound (which may be of limited utility in detecting subtle changes). However, as technology for enhanced neurologic monitoring evolves and becomes easier to apply at the bedside, investigators strive to gain a better understanding of the factors that lead to neurodevelopmental impairments in these patients, with the goal of preventing them altogether or diminishing their impact.

In either case, more specific monitoring for evolving neural injury may allow for earlier application of ECMO as a therapy or may lead to modifications of management during ECMO to improve future outcomes. The ideal neuromonitoring approach would be initiated around the time ECMO is being considered. It would be non-invasive, portable, provide actionable, reliable and reproducible information, and present minimal risk. Additionally, measures that reflect ongoing degree of neural integrity could be used to inform treatment decisions and weigh the many risks inherent to this therapy.

In the following sections, we will review the benefits and risks of currently available neuromonitoring techniques and how they are used to inform application of ECMO as a therapy. They are summarized below. [TABLE 1] We will review known neurodevelopmental outcomes associated with injury seen on neuromonitoring. Finally, we will evaluate new and upcoming techniques that may potentially be used as non-invasive, bedside measures of cerebral oxygenation and perfusion.

Head Ultrasound (HUS)

Head ultrasound is an essential neuroimaging technique for the care of an ECMO patient. Ultrasound technology is based on sending high-frequency sound waves that are transduced via a probe placed over the neonate’s fontanelle; these waves are differentially reflected back depending on tissue composition and distance. Injury to brain parenchyma such as ischemia,

hemorrhage, or white matter injury induces a change in tissue density that can reflect as hyperechogenic; however, at times, etiology of these lesions can be difficult to differentiate by HUS alone. HUS can also detect acute changes in ventricular size if there are concerns for communicating or non-communicating hydrocephalus. Advantages of HUS include its ease of use, bedside portability, low cost, efficiency, and lack of exposure to radiation. Finally, HUS results are readily interpretable and quickly available for medical decision-making.

HUS is performed prior to cannulation for ECMO to detect pre-existing intracranial hemorrhage (ICH). The presence of ICH at this time dramatically changes the risk-benefit considerations of ECMO therapy, and may result in a contraindication to proceeding with ECMO cannulation. Furthermore, ongoing surveillance for ICH during the course of the ECMO run is critical, as the evolution of this finding may influence decisions about continuing ECMO and may alter anticoagulation goals. Although this varies by institution, a common imaging protocol includes obtaining a baseline pre-ECMO ultrasound followed by daily monitoring HUS for the first 5–7 days after cannulation, the period during which the incidence of ICH is highest.[8, 19] Subsequent HUS monitoring is typically performed every other day for the duration of the ECMO run. Additional ultrasounds are obtained based upon clinical indications, such as new onset seizures, sudden drop in hemoglobin, or other clinical concerns.

There are some limitations of HUS, one of which is the requirement of an open fontanelle for optimal visualization of intracranial structures. In addition, the structure of the ultrasound beam affords a limited field of view; lesions in periphery and posterior fossa are thus poorly visualized and can be missed. Historically, variability and accuracy of HUS findings have depended on individual technician's skill level. There is also inter-observer variability in diagnosing ultrasound findings with lower concordance for presence of germinal matrix hemorrhage and higher for parenchymal hemorrhage.[20] Ultrasound is not a sensitive tool for reliably detecting small hemorrhages and ischemic lesions,[21] but if seen, the injury causing the lesion can be assumed to have occurred in the interval since the last HUS.

More crucially, in the ECMO population, there is growing concern for discrepancy between detection of abnormalities on HUS as compared to HCT or MRI.[3, 4, 9,22] For example, Lazar et al showed that in a series of 74 neonatal ECMO patients, only 53% of patients with confirmed structural injury by HCT or MRI brain had signs of injury on serial HUS examinations. In a case series of 70 neonates requiring ECMO with available MRI data between 2011–2015 at the Children's Hospital of Philadelelphia, CNS complications, including 1 case of ICH and 5 cases of IVH, were missed by HUS.[22] Two examples are shown in figure 2 [FIGURE 2]. In addition, of the 11 total cases of IVH, only 2 were later seen on MRI brain, raising concern not only for the sensitivity, but also the positive predictive value of HUS.

Despite the limitations of HUS, one potential utility of HUS could be as a tool to screen for early complications by using resistive indices (RI) to assess for changes in cerebral regulation and blood flow. RI is calculated by the difference in peak systolic velocity and

end diastolic velocity divided by peak systolic velocity. Variability in RI with pressure challenge has been previously shown to be associated with increased intracranial pressure.[23, 24] More recently, Zamora et al evaluated anterior cerebral resistive indices and showed that a resistive index variability of equal or greater than 10% over 24 hours predicted a greater risk of cerebrovascular complication in neonates undergoing ECMO.[25]

Finally, somewhat counter-intuitively, regardless of findings, HUS has not been shown to consistently predict long-term neurodevelopmental outcomes in the ECMO population, particularly in the absence of a catastrophic bleed. In the study by Glass et al, in 43% of children with severe brain injury and 67% of children with moderate brain injury on neuroimaging by HUS were later noted to have no disability at 5-year follow-up.[11] Conversely, a normal HUS does not rule out future developmental impairment; Lazar et al found that 13.5% of neonates treated with ECMO had delayed neurological development even without evidence of anatomic injury on serial HUS or follow-up imaging.[3] Therefore, HUS should not be used in isolation to predict neurodevelopmental outcomes.

Head Computed Tomography (HCT)

Computed tomography uses computer software to integrate multiple cross-sectional images of x-rays (tomographic images). These images are composed of units called voxel, the number of which reflects tissue density. HCT is excellent for detection of significant structural or acute vascular changes. Since the introduction of a portable HCT scanner in the early 2000s with subsequent integration into intensive care units, portable HCT has been increasingly utilized in large academic centers. In the neonatal ECMO population, portable HCT has been used for emergent evaluations after an abnormal HUS with any findings that may impact immediate survival or continued ECMO candidacy. There have been no studies to evaluate the diagnostic quality of portable HCT in the pediatric population, but review of the limited adult ICU literature indicates that portable HCT provides sufficient diagnostic yield.[26] Disadvantages of HCT include radiation exposure, artefactual distortion, and the need to move the patient with associated risk of ECMO cannulae displacement. Two small retrospective studies of ECMO patients (including neonates, children and adults) have shown intra-hospital transfer, including to CT machines, to be relatively safe if appropriate measures and guidelines are followed.[27–29]

Despite these disadvantages, multiple small studies have shown that HCT has improved sensitivity to detect intracranial pathology that was overlooked by HUS including findings of significant intracranial hemorrhages.[2, 4, 5] In a study by Bulas et al, of the 286 neonates placed on ECMO who underwent both HUS and HCT imaging, HCT provided additional information in 106 of the neonates as compared to HUS alone.[2] Of the 82 total findings that were considered “major”, 17 had significant findings on HCT that were not detected by HUS, including 3 cases of large ICH and 6 cases of ischemia. As a result, these authors recommended HCT for follow up of abnormal HUS findings.

Extent of injury seen on HCT may provide some insight into neurodevelopmental outcomes, although this has not been consistently replicated in all studies.[9, 30] Small retrospective studies have demonstrated an association between abnormal head CT findings with adverse

neurodevelopmental outcomes.[5, 11, 31, 32] In the study of 5-year outcomes in 152 neonatal ECMO survivors by Glass et al, severity of neuroimaging findings was associated with worsened neurocognitive outcomes.[11,33] However, in the same group, a small subset (10%) had no signs of injury on neuroimaging findings and were also later classified as disabled, a result which has been found by other groups as well.[30] Therefore, acquired intracranial injury (or the lack thereof) by HCT may need to be more clearly delineated by additional imaging for prognostication purposes.

Magnetic Resonance Imaging (MRI)

MRI is the gold standard for detection of intracranial injury and pathology. MR technology relies on measuring magnetic field perturbations as a result of introduction of energy pulsation to hydrogen atoms at the cellular level. Modifying factors such as the pulsation energy or hydrogen atom relaxation time produce different MRI sequences that are best at evaluating certain tissue contrasts or specific physiologies. ECMO equipment is incompatible with MRI and as a result, MRI of the brain is contraindicated during ECMO therapy and can only be performed after decannulation.

Clear advantages of obtaining MRI imaging are its lack of radiation exposure as well as the high sensitivity and specificity for intracranial pathology. In neonatal ECMO survivors, MR imaging detects a high prevalence of stroke and white matter injuries,[9, 10] for which HUS and HCT are typically less sensitive. [FIGURE 4] Disadvantages are that post-ECMO, patients often remain critically ill and may not tolerate the transport, the duration of the examination, or the sedation required for an optimal study. Moreover, unlike HUS, dating the timing of an injury seen on MRI can be difficult with a few key exceptions. Diffusion restriction visualized on MRI is well known to have occurred within a window of a few minutes to 10 days post an acute ischemic injury [FIGURE 3]. The hemoglobin in blood degrades in stages and therefore timing of acute, subacute versus chronic hemorrhage can be roughly estimated by using MR brain T1 and T2-weighted images. The gradient recalled echo (GRE) sequence also contributes additional information; hemosiderin staining can be still seen in areas of prior hemorrhage that may have long-resolved.

Despite the sensitivity of MR for detection of intracranial pathology, the role of MR findings and their association with neurodevelopmental outcomes remain unclear. In the study by Rollins et al, of the 26 neonates followed up post ECMO, there was no association between HUS or MRI findings and neurodevelopmental outcomes.[9] This conclusion is complicated by variability in timing of image acquisition, sensitivity of MRI for minor abnormalities that have unclear significance, and lack of correlation with long-term outcomes in modern cohorts of ECMO patients. These issues, combined with a lack of specific interventions for documented injuries and increased attention to value and healthcare spending, have led some to question whether routine post-ECMO brain MRI studies are necessary.[9] Interestingly, in an older study by Lagos et al, presence of increased size of cerebrospinal fluid spaces found on MRI after ECMO correlated with worse outcomes at 6 and 12 months of age.[30] This is corroborated by studies in the congenital diaphragmatic hernia population where a large proportion of children have required ECMO. The presence of increased extra-axial cerebrospinal fluid spaces and intracranial hemorrhage predicts worse neurodevelopmental

outcomes at one year of age.[34] As a result, the optimal timing of MRI still remains unclear and indications and timing for MR imaging for screening purposes in individual institutions vary widely. Larger longitudinal studies will be needed to investigate neurodevelopmental outcomes of ECMO patients and MRI findings, especially considering the association between white matter injury, increased extra-axial cerebrospinal fluid spaces and global atrophy. Most studies have not evaluated the emerging burden of white matter injury and its association with neurodevelopmental outcomes in the ECMO population. [FIGURE 5] Interestingly, in the congenital cardiac population population, there is a high incidence of white matter injury of up to 48–54% post corrective cardiac surgery.[35–37] In a long-term follow up of patients with d-transposition of great arteries (d-TGA), diffusion tensor imaging (DTI) was used to measure fractional anisotrophy (FA) with a correlation found between FA and cognitive measures, specifically visual-spatial reasoning.[38] The authors hypothesized that these areas of white matter injury occur in critical locations interrupting crucial networks between visual cortices, spatial reasoning, and integration of these information including memory tracts which lead to these higher cognitive deficits later in development.

Electroencephalogram (EEG)

While the above neuromonitoring techniques provide crucial insight into acquired structural brain injury, the electroencephalogram (EEG) is a tracing that yields information about the network of cerebral electrical activity. In addition to detection of seizures, EEG gives invaluable information about the background, organization, and interictal burden (such as presence of epileptiform discharges or focal slowing) of a neonate's cerebral activity. For example, in the neonatal hypoxic ischemic encephalopathy (HIE) population, early EEG findings of abnormal low background amplitude, prolonged discontinuity of the background, or presence of electrographic seizures have independently predicted worsened neurodevelopmental outcomes at two years of age.[39] Similarly, in a follow up of 36 neonatal ECMO patients, a burst suppression background was associated with severe outcome or death.[40] EEG provides acute, actionable information; for example, development of acute focal abnormalities such as seizures would be one indication to consider urgent imaging. Other benefits of EEG are that it offers very little risk to patients and can be used in combination with other neuromonitoring techniques. There are a few disadvantages to EEG. If the EEG electrodes are placed for extended periods of time, there may be compromise to neonatal scalp integrity. The neonatal EEG suffers from difficulty of differentiating pathology versus artifact, requiring an experienced reader for appropriate interpretation. There are many sources in the ICU environment that can potentially introduce artifact including patient or medical-care induced movements, the respiratory support machines, or the ECMO pump, to name a few. Another common source is tissue edema, especially in gravity dependent locations such as the scalp, which can attenuate the cortical electrophysiological signal received by scalp EEG electrodes. Finally, benzodiazepams and other sedative medications can potentially introduce an attenuation (that is reversible) in the background EEG activity as well.

Commonly used forms of EEG in the neonatal intensive care environment are amplitude-integrated EEG (aEEG) or continuous EEG (cEEG). Amplitude-integrated EEG compresses raw EEG information from 1–2 channels with clear advantages in costs, ease of set up, and

ease of interpretation by bedside team and neonatologists. It can be used to provide information about background and detection of seizures, but sensitivity for seizures can be poor, detecting less than 34% of individual seizures in some studies.[41, 42] Use of the combined aEEG with raw EEG data improves seizure detection rates as compared to aEEG alone.[43] In clinical practice, the limitations of aEEG are well-recognized and thus, aEEG is more often used as a screening tool or in a resource-limited area. Continuous EEG, on the other hand, requires trained EEG technicians to set up the montage according to the international 10–20 system,[44] modified for neonates, and requires a trained neurologist for interpretation. Note that many of the modern-day EEG software programs that provides continuous EEG data can also analyze and provide an amplitude-integrated data (the converse, however, does not hold true). Thus, the amplitude-integrated EEG can be customized as shown in Figures 6 and 7 for improved seizure detection by adjusting the locations of seizure detection. [FIGURE 6 and 7] A routine EEG uses the same electrode set up as that of the continuous, but is typically 60 minutes or less in duration.

In 2015, the American Clinical Neurophysiology Society published guidelines recommending continuous EEG for monitoring as a standard of care in the monitoring of critically ill children and neonates for multiple reasons.[45] First, differentiating between non-epileptic and epileptic-movements in a neonate is difficult, even by experienced neonatologists and neurologists.[46] Second, in the critically ill neonatal population, there is a high burden of seizures, up to 19% in the neonatal ECMO population.[47–49] Third, seizures that were seen clinically and effectively treated with anti-epileptic medications, are subsequently then often only seen electrographically (without clinical signs), known as an “uncoupling” phenomenon[50] hence requiring EEG for identification and further treatment.

In a recent large, single-center study, Lin et al found the incidence of seizures in neonates on ECMO was 18%, with 92% of these exclusively electrographic;[48] these numbers are consistent with other prior studies with a mixed population of cardiac and non-cardiac ECMO patients.[13, 51] They also found that the presence of electrographic seizures and status epilepticus was associated with worse neurological outcomes.[48] This finding is corroborated by other small studies of EEG in the ECMO population, [40, 52] and by the pediatric critical care literature where multiple studies have demonstrated that the presence of electrical status epilepticus has an increased risk of in-hospital mortality and worsened functional status at discharge.[47, 53] Therefore, continuous EEG monitoring in the neonatal ECMO population is indicated, even when there may not be signs or symptoms concerning for ongoing seizures.

Optical Technologies

Due to the limitations of the neuromonitoring techniques as described above, there is growing interest in a bedside, portable, continuous and non-invasive technique to potentially monitor cerebral perfusion as a parameter to assess for intracranial injury and also for the adequacy of ECMO therapy. One such technique under investigation is near infrared spectroscopy (NIRS). NIRS technology uses a probe that emits a near-infrared spectrum of light through the skin to reach the red blood cells in the interrogated tissue to measure relative changes of oxy and deoxyhemoglobin, thereby reflecting changes in tissue blood volume and tissue oxygenation.[54, 55] NIRS has multiple advantages, including the fact that it

is non-invasive, does not require ionizing radiation, is easily utilized at the bedside, and can be used in conjunction with other neuromonitoring modalities such as EEG. In the future, it may be an additional tool to help titrate ECMO parameters to optimize cerebral perfusion, and perhaps, to aid decision making if conversion from VV to VA ECMO is being considered.

However, while NIRS technology has been present for the past 20 years,[56] it is still undergoing study in clinical application. Two small observational studies report use of NIRS in conjunction with ECMO in a total of 28 neonates[57, 58] and were largely meant to validate measurements of cerebral oxygenation with blood sampling[57] or evaluate for changes in oxygenation during periods of cannulation or trialing off.[58] Most recently, a case series of 34 neonates and infants less than 3 months of age was published and reported use of NIRS throughout the duration of ECMO therapy.[59] These authors reported reduction of measured brain tissue oxygenation in both non-survivors and patients who demonstrated cerebral injury on later imaging, suggesting a possible role for NIRS in prognostication.

NIRS has been used more widely in the population of critically ill infants outside of ECMO as a monitoring technique. In a large, international randomized controlled trial of application of NIRS, NIRS was shown to be able to detect cerebral oxygenation changes in extremely preterm infants; however, there were no changes in outcomes including mortality or findings of injury on HUS.[60] In the congenital cardiac population, NIRS has been used to monitor cerebral oxygen levels before, during and after cardiac surgery, and showed an association between NIRS oxygen saturation and predictors of outcome, including mortality.[61, 62] In 32 very low birth weight premature infants, 8 of 10 neonates that later developed severe germinal matrix hemorrhage had signs of impaired cerebral autoregulation as measured by NIRS.[63] Utilization of NIRS in changing clinical outcomes, however, is rare; in one small study of neonates with hypoplastic left heart syndrome, NIRS was used to minimize duration of mechanical ventilation required pre-operatively.[61]

Despite these potential insights that can be gained from NIRS, there are significant limitations to this instrument. NIRS is not quantitative and cannot measure the absolute level of cerebral blood perfusion or oxygenation. It also suffers from poor reproducibility and poor inter-subject reliability and should be only used to monitor trends. Finally, there is not yet confirmatory data that monitoring with NIRS has changed neurological outcomes in the neonatal ECMO and non-ECMO population or has been found to be useful in the selection of patients for ECMO or titration of this therapy.

Newer applications of NIRS, such as frequency- or time-domain diffuse optical tomography (DOT) and diffuse correlation spectroscopy (DCS), offer promise of improved monitoring capacity. In brief, DOT incorporates NIRs data with using expanded sensor arrays to then generate three-dimensional images reflecting hemodynamic changes in the brain.[64] Somewhat similar to NIRS in mechanism, DCS measures fluctuations of light intensity flow across tissues after which a mathematical model is applied to then correlate with blood flow or perfusion.[65, 66] These technologies are more quantitative (allowing for improved inter-subject reliability) and measure cerebral blood flow. They are starting to show early results, for example where the ECMO pump rate may be able to be adjusted to maintain sufficient

cerebral oxygenation. These technologies are, however, expensive and require significant expertise to use.

Conclusion

Evaluation of brain function and integrity is crucial for the ECMO patient. This begins prior to cannulation, to determine candidacy, and continues throughout treatment with ECMO to constantly weigh risks and benefits of ongoing therapy. Neuroimaging techniques such as HUS, HCT and MRI can demonstrate injury or concerns for injury, but are not continuous and cannot always provide an exact timing or etiology of injury. Furthermore, the correlation of neuroimaging findings with neurodevelopmental outcomes has not been consistently replicated. There is a increasing focus on continuous, non-invasive techniques such as EEG and NIRS to assess for neurological injury in real time and offer treatment with the intent of improving outcomes. A few studies have shown that multi-modality neuromonitoring may be helpful for predicting outcomes. For example, the combination of abnormal HUS and HCT with abnormal EEG predicted worse outcomes.[51] In a population of 32 patients with HIE who underwent therapeutic cooling, combining both aEEG and NIRS predicted short term outcome with increase in specificity from 52–59% to 73–91%.[67] Current studies on multimodal neuromonitoring in the neonatal ECMO population are limited.[68] Further, large-scale studies are necessary to determine the role of current and emerging technologies in the care of this growing population of patients.

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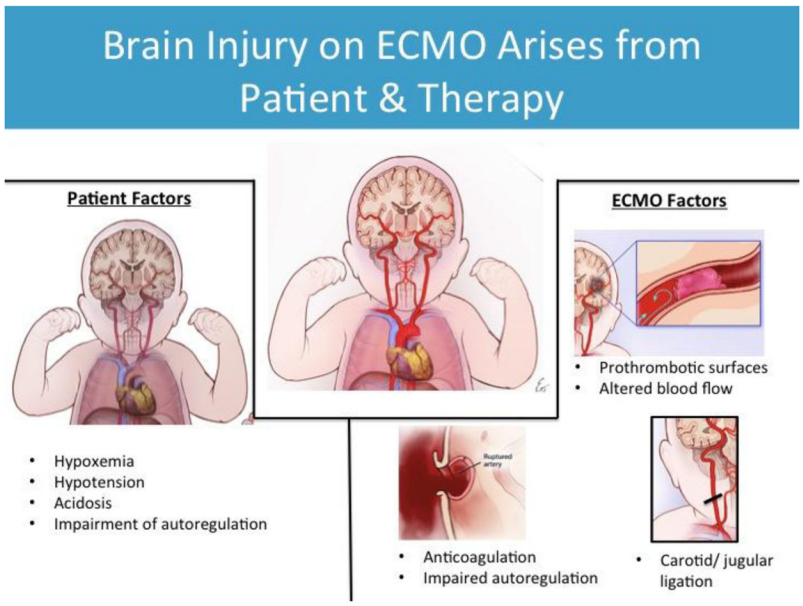

Figure 1.

Patient and ECMO factors that may contribute to brain injury. Source: John Flibotte, MD. Illustrations by Eo Trueblood, © Stream Studios at the Children's Hospital of Philadelphia.

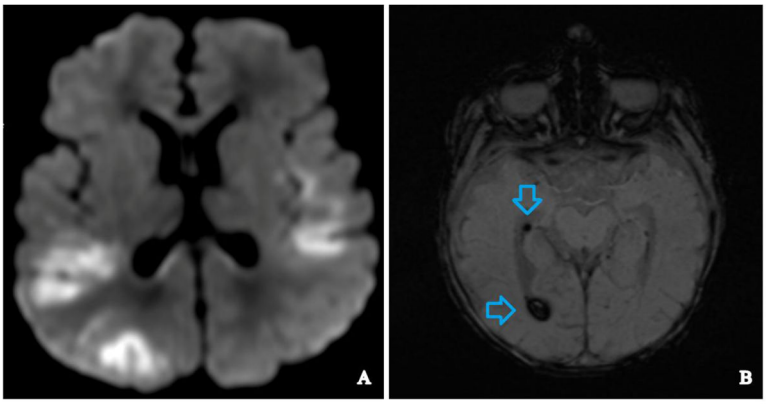

Figure 2.

Images of two different neonates demonstrating discrepancy between at the last normal HUS followed by subsequent MRI brain. A) MRI axial DWI sequence obtained 3 days post ECMO decannulation demonstrating a multifocal stroke. All HUS obtained during ECMO were normal. B) MRI GRE axial sequence, 5 days post ECMO decannulation. All HUS on ECMO were read as normal. However, MRI GRE sequence shows presence of hemosiderin staining (arrows) in the lateral horns of the ventricles suggesting prior intraventricular hemorrhage.

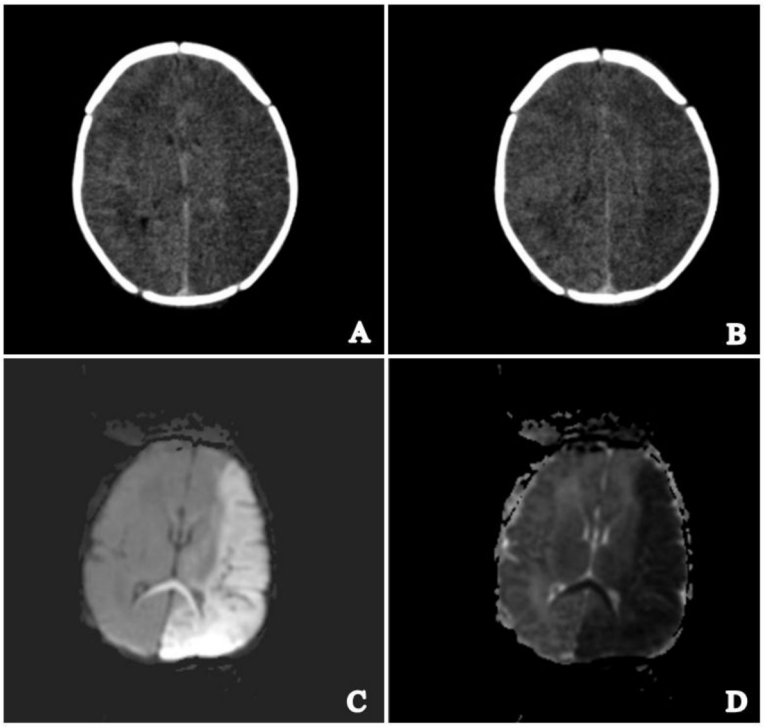

Figure 3.

A left MCA stroke on the same neonate with different imaging modalities. A,B) Head CT on a term neonate. Note the decreased gray-white matter differentiation throughout the left hemisphere with increased hyperdensity in the left middle cerebral artery territory concerning for an ischemic stroke. C, D) In the same neonate, 2 days later, the MRI brain of DWI and ADC sequences, respectively, demonstrating concordance with prior HCT findings of an acute left MCA ischemic stroke.

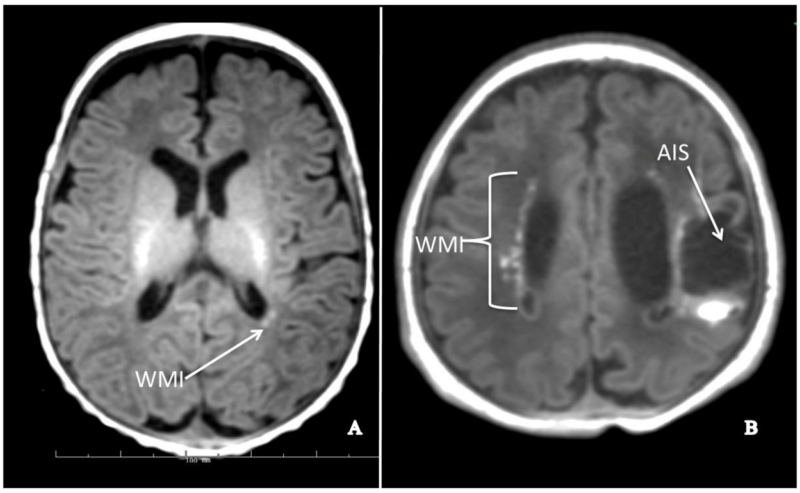

Figure 4.

Examples of white matter injury (WMI) in different neonates. A) MRI T1-weighted axial slice showing left periventricular injury as well as increased extra-axial space B) Another MRI T1-weighted axial slice demonstrating periventricular white matter injury in the right lateral ventricle, and separately, an old acute ischemic stroke (AIS) injury with associated encephalomalacia seen in the left parietal lobe.

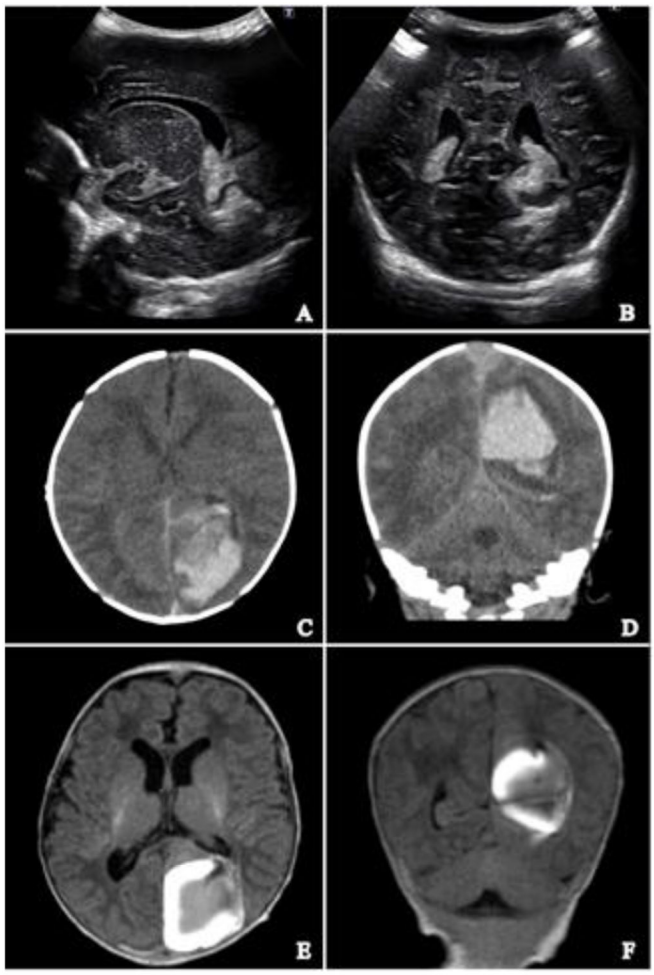

Figure 5.

Images all obtained from the same neonate demonstrating findings of intraparenchymal (IPH) and intraventricular hemorrhage (IVH) across different imaging modalities. A,B) HUS with LT sagittal and RT coronal views, respectively, demonstrating hyperechogenicity periventricularly and in parenchymal tissue. C,D) Axial HCT on same day as HUS showing hyperdensity in the same areas. E,F) MRI T1-weighted axial and coronal images, respectively, obtained 2 days later from HCT.

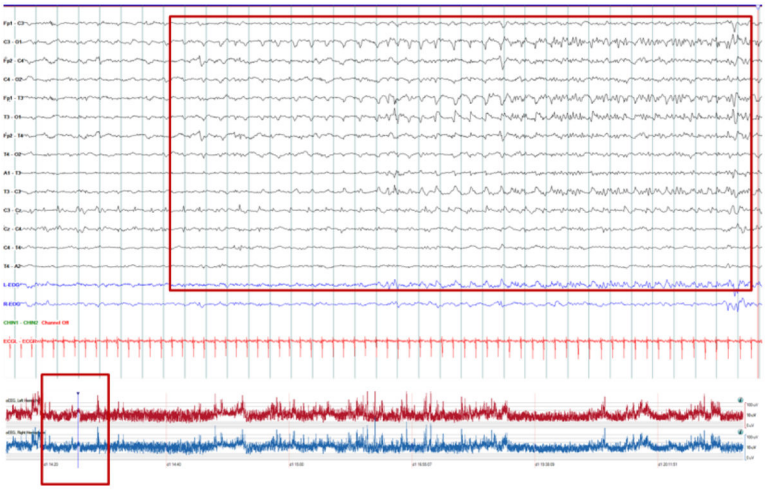

Figure 6.

Top panel - continuous EEG neonatal montage showing evolution of an electrographic seizure (box) in a term neonate. Bottom panel – multiple seizures are captured in the 24 hour amplitude EEG as shown by the presence of the epochs (smaller box) This has been set up with the default mode of left (red) and right (blue) hemispheric detection. (Figure courtesy of Katherine Holland-Bouley, MD, PhD, with permission)

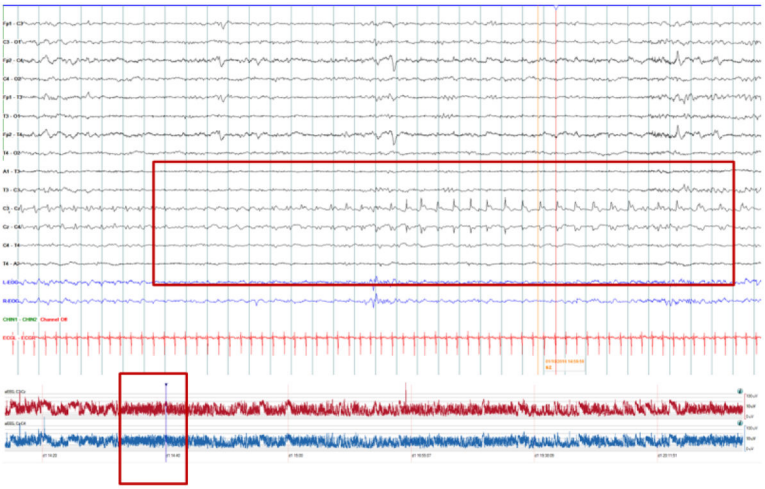

Figure 7.

Top panel - In the same neonate as above, another seizure (box) arising from a different location that is missed by the default parameter of aEEG detection. Bottom panel – one can tailor the aEEG by adjusting the setting from left hemisphere to left mid-central (C3Cz, red) and right hemisphere to right mid-central (C4Cz, blue) seizures. Note the increase in the number of epochs (small box) detected by aEEG that were previously not seen in the same 24 hour aEEG montage. aEEG can miss a significant number of neonatal seizures if they are focal and outside of the conventional 1–2 channel set up. (Figure courtesy of Katherine Holland-Bouley, MD, PhD, with permission)

Table 1

Neuromonitoring	Indications	Advantages	Limitations
Head ultrasound	Surveillance pre-ECMO and during ECMO for detection of hemorrhage	Ease of use	May miss significant ICH
		Portability	
		Low cost	Does not predict neurodevelopmental outcomes
		Highly efficient	
		No risk of radiation	
		Provides fast, actionable data	
Head CT	Follow up of abnormal HUS that would change ECMO management	Sensitive and specific for ICH	Radiation
		May help predict neurodevelopmental outcomes	Artifact distortion
	As clinically indicated		Transfer risk
MRI brain	Follow up of prior abnormal imaging	Most sensitive and specific for pathology	Cannot be done during ECMO
	As clinically indicated	No radiation risk	Optimal timing of MRI unclear
		May help predict neurodevelopmental outcomes	
EEG	Detection of electrographic and clinical seizures	Provides fast, actionable data	May require significant resources for set up and interpretation
		May help predict neurodevelopmental outcomes	
NIRS	Measure trends in cerebral oxygenation	Non-invasive	Not widely-available
		Portable	