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# Technology – Considerations for the NICU of the Future☆

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ABSTRACT

Modern neonatal intensive care arose from, and will forever depend upon, technology. There are increasing pressures to leverage new technologies to make care safer, more efficient and cost-effective. Changes in the delivery room will bring better monitoring and data display for the resuscitation team. Sensing and monitoring advances will be used in the NICU, measuring a wider range of physiologic parameters. Better integration of technologies with the EMR will be the basis for decision support and predictive analytics. Communication will be improved between the EMR, NICU staff and parents of newborns. Advances in conventional, CT, MRI and ultrasound imaging of neonates will aid in our diagnostic efforts. Ventilators are getting smarter, with wider ranges of support options and monitoring, in parallel with improvements in non-invasive respiratory support. New technologies can be used to evaluate and support neurodevelopment and to optimize nutrition. Laboratory testing can be done more rapidly, with smaller sample size and reduced costs, bringing more testing to the bedside. All these new technologies should optimize the NICU physical environment, improving the experience for patients, their families and hospital staff.

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Technology has long been the backbone of modern neonatal intensive care. Starting with the basic needs to provide warmth and protection from the elements, technological advances now give us the opportunity for continuous monitoring of multiple physiological processes and supporting complex communication between patients, medical staff and families.

The need to reduce costs is a major driver for technological change in health care. In the U.S., the economic impact of preterm births is well over $25 billion per year.[1] As more care is being provided to patients on capitated, or based on diagnosis-based, rates, there is increasing pressure to be more deliberate about utilization of resources. Thus, technologies that reduce the length of stay for neonatal patients will have an immediate appeal. There is also a need to have technologies that reduce expensive laboratory testing and radiologic imaging. The charge from a

*Abbreviations:* CLABSI, central line-associated blood stream infection; CPAP, continuous positive airway pressure; EMR, electronic medical record; ETCO2, end-tidal transcutaneous carbon dioxide; FDA, Food and Drug Administration; HIE, hypoxic-ischemic encephalopathy; NEC, necrotizing enterocolitis; NICU, neonatal intensive care unit; NNS, non-nutritive sucking.

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costly MRI usually comes off the bottom line and does not add to it. Thus, there is a drive to seek and develop new technologies that replace older, more expensive ones. New technologies may be applied to reduce medication use, which accounts for approximately 5% of NICU costs. Greater cost savings can be derived from technology that reduces labor costs, as NICU RN and respiratory therapy labor expenses account for over 60% of total neonatal care.

In the midst of being cost-conscious, there is an increasing awareness and accountability for the safety and quality outcomes of our NICUs. Most NICUs choose, or are required, to track, benchmark and often publicly report certain complications of care such as central line-associated blood stream infection (CLABSI). Some of these more avoidable complications may be used for negative financial incentives; for California state health reimbursement, NICUs currently are subjected to a withholding of $6K from a neonatal patient's bill for each CLABSI. Pressure ulcers and unplanned extubations are among many other hospital-acquired conditions attracting the attention of payors enough to incentivize development and implementation of new technologies.

Not surprisingly, there are also resistors to change beyond the current reimbursement models that reward longer stays and greater charges. The relatively small market size of neonatal intensive care is less likely to attract commercial health care interests. There is limited awareness of how to partner with others having design and engineering expertise. There are significant startup costs for the designing and clinical testing of new technologies; these may be prohibitive for traditional investors seeking a quicker return on investment than device development normally affords. Established medical device companies with traditional medical equipment in the NICU are not likely to support the development of new, disruptive technologies. Often the long lead-in for technology and device development depends on a combination of self-funding, angel investing, government monies (e.g. SBIR grants), and sometimes institutional support by hospitals or medical centers. Nonprofit consortia supporting the development of such devices include the Institute for Pediatric Innovation and the FDA's Pediatric Device Consortia. Conducting clinical trials that lead to FDA device approval is often challenging financially and complicated by the potential need for multi-center recruitment and collaboration.

Fortunately, concerned and creative caregivers, as well as recipients of health care, are often motivated enough to overcome these barriers to new technology and device development. The creation of new NICU technology may arise from a perceived or demonstrated need – to change a process to become more efficient, less expensive or safer. Alternatively, there may be well-established technologies being applied in medicine outside of the NICU, and possibly not even from within the health care sector, that can be imported and applied to babies and their care. These technologies might include new hardware, such as miniaturization, and software to automate a process, using new communication tools (smart phones, wireless connectivity) and interfacing with information technology.

## Delivery Room

Many practices and technologies supporting delivery and resuscitation have changed little in the last few decades. However, one of the most significant recent changes in NRP guidelines is the application of sensor leads to measure saturation and heart rate during resuscitation.[2] A recent study has shown the relative inaccuracy of auscultatory assessment of newborn heart rate compared to these other technologies.[3] Several other technologies are being developed to assess neonatal heart rate during resuscitation, including sensors within an umbilical cord clamp,[5] and optical reflectance (photoplethysmography).[4,5] The available physiological information can be displayed in a more integrated fashion, along with more interactive, decision-support feedback reminding the resuscitation team what needs to be done next. New devices such as specialized resuscitation tables and sensor displays are being designed to provide physical platform and to monitor support for resuscitations that start with delayed cord clamping. Laryngoscope blades incorporating small LED screens may prove helpful to those intubating during neonatal resuscitation.[6]

The visual information presented to the resuscitation team could be further refined and designed to provide more timely feedback to the care providers. Gaze-tracking technology can be used to see from where an individual is seeking visual information, as well as provide insight into that person's autonomic status based on pupillary constriction. The next generation of training mannequins for neonatal resuscitation will be much more realistic – with internal speakers generating heart beat and breath sounds, pulsatile umbilical stumps, and visible cyanosis that can be adjusted remotely.[7]

The birth process can greatly benefit from emerging technologies that better support communication and feedback to and from the mother and her partner. This can start with apps or websites for submitting a birth plan that is better integrated with the hospital electronic medical record (EMR) system. Mothers frequently report extreme anxiety and worry during separation after delivery of a baby who is then transported and admitted to a distant NICU. Smart phones, tablets, Google Glasses and other audiovisual devices have recently been used to keep mothers in Skype® or FaceTime® contact with fathers or others accompanying the newborn to these remote locations.

## Sensing and Monitoring

Many of the new technologies being applied within the resuscitation suite are also being used within the NICU setting. Using non-invasive methods such as optical sensing of heart rate can obviate the need for EKG leads. Alternatively, EKG leads and other sensors such as saturation monitor leads can be connected to a wireless transmitter that communicates the information confidentially to the local display monitor and the patient's EMR. Eliminating these monitoring cables should greatly facilitate transferring the baby to be held for skin-to-skin kangaroo care by parents. Blood pressure measurement should soon be available with placement of small patch-like pressure transducers over extremity arteries.

Other forms of physiologic monitoring are being facilitated by new and improved technologies. Transcutaneous monitoring of oxygen and carbon dioxide, while available for decades, is now more reliable with less chance of local thermal injury by the associated skin probes.[8] Tissue saturation of target organs including the brain and abdominal organs has been more widely adopted with new technologies.[9,10] Having too high or too low cerebral saturations in babies less than 32 weeks gestational age was associated with adverse neurodevelopmental outcomes.[11] Another recent multi-centered study showed no change in EEG and other biomarkers when care was adjusted to target optimal cerebral saturation in infants less than 28 weeks gestational age.[12] Further studies should help us better understand how to better incorporate tissue saturation into our care practices and predictive analytics.

End-tidal carbon dioxide (ETCO2) measurements can be used as a continuous, non-invasive assessment adequacy of mechanical ventilation.[13] The rapidity and small volume of breathing in neonates often limit the reliability of this measurement, especially for smaller babies, although ETCO2 measurement can be helpful for trending. Future advances in gas sampling techniques should make ETCO2 measurements more reliable and accurate. In-line blood gas measurements were previously available to be used within arterial catheters[14]; improvements in micro-analytic techniques may lead to their re-adoption in the NICU in the future. Acoustical monitoring and analysis can also be used to interpret cardiac and respiratory sounds.[15,16]

## Information Technology

U.S. hospitals are increasingly adopting information technologies and EMR, including features such as computerized physician order entry, bedside charting, progress notes, billing and integration with

clinical laboratory and radiology. For many NICUs, the EMR has been more a burden than a value added, but changes in information technology are being brought to change this. Cumbersome data entry, such as typing clinical assessments onto multiple computer screens, can be replaced by voice entry and dictation. Many new devices such as IV pumps can provide wireless communication with EMR, decreasing the need for manual data entry. Future generations of other medical equipment including ventilators and external physiology sensors should have wireless interfaces with EMR and cloud data storage systems.

Human–machine interactions within the NICU will also change with new technology. Clinical decision support will be automated to decrease medical errors, e.g. prescribing contraindicated medications or incorrect dosages, as well as to improve adherence to clinical pathways and protocols. Suggestions for limiting or substituting alternative medications based on clinical evidence can further save costs. Medical informatics systems are now commercially available to help predict sepsis risk in neonates based on heart rate variability.[17,18] Predictive analytics similar to those now used in pediatric ICUs are likely to be applied to the NICU.[19] Models using a combination of vital sign, physiologic data (arterial saturation, tissue saturation, etc.) and laboratory data should provide more accurate risk prediction of various neonatal conditions, including sepsis and necrotizing enterocolitis (NEC).

## Communication

Information helps health care providers only if it reaches them by effective communication. Parents of newborns depend upon communication with NICU staff to aid in their understanding of their babies' present condition and care options. Technological advances should be applied to support parental education and can include simulation and virtual training to better prepare them for discharge. NICUs with single patient rooms rely more highly on alert notification and communication between bedside providers and may put more pressure on family members present to be able to contact staff in a timely and effective manner. One recent study showed that a daily update report generated by the EMR was well received by NICU parents, nursing staff and physicians.[20] Systems are now available that allow for more continuous visualization of babies by their parents, with cameras that can be placed within incubators or that are built-in. Given recent information of the importance of auditory stimulation to neonatal speech development,[21,22] it will be helpful to figure out how to give beneficial auditory input, e.g. parental voices and laughter, to babies when they are in the optimal state of alertness.

Unfortunately, the auditory environment of the NICU frequently is disrupted by a variety of alarms, even though they are an integral safety element for vital sign monitoring, incubators, IV pumps and more. Technological advances can be brought to address and reduce alarm fatigue, starting with better understanding of alarm settings of defaults and delays.[23] Alarms need not only be beeps and bells of various tones and volume, but instead can be made smarter, notifying caregivers by smart phone or other communication device with a specific alert ("Baby Jones has low blood pressure.").

RFID chips and other locater technologies are being introduced into the health care setting, tracking everything from expensive equipment to individual care providers. Bar-coding technology has already been applied to reduce breast milk administration errors. It is now possible to tag individual syringes from a centralized pharmacy with specific patient identifiers that would trigger alarms when brought into the room of a different patient.

## Imaging Technology

There are several new and emerging technological improvements in neonatal imaging. Portable radiographic equipment can provide plain chest and abdominal radiographs with near-immediate display, higher resolution and reduced radiation compared to previous techniques. Ultrasound studies are being used to better assess blood flow to various organs including the brain and the gut, the latter being used in the diagnosis of NEC. CT scanning technology now allows for reduced radiation, rapid studies and higher resolution, including high resolution cardiac and other angiographic imaging studies. Portable CT scanners are now available, which may be helpful in diagnosing brain injury for babies too unstable to transport to the radiology suite. MRI technology has better resolution with stronger magnets, better sequences and neonatal coils; new MRI systems made with fixed magnets, and not needing elaborate shielding and quenching hardware, can be built closer to patient units such as the NICU. Keeping pace with this new imaging equipment, radiology interpretation will increasingly be supported by machine learning analysis.

## Cardiorespiratory Care

Providing respiratory support has been the lynchpin of the care of premature and other critically ill newborns. While synchronized ventilation has been used for decades, newer methods for triggering breaths are more recent, including Neurally Adjusted Ventilator Assist.[24] Hybrid ventilators providing high-frequency and conventional modes of ventilation are being used in Europe and are likely to be brought to the U.S. for FDA approval. Several investigators are developing servo-controlled oxygen administration, which leads to greater compliance with targeted oxygen saturation ranges.[25,26] New technologies now can provide continuous, non-invasive monitoring of endotracheal tube position and obstruction.[27]

A growing percentage of premature neonates are avoiding mechanical ventilation by increasing their use of CPAP. Different CPAP drivers[28] and masks[29] are being developed to support non-invasive ventilation and to reduce the incidence of complications such as nasal septum erosion. The use of 3D printing could lead to customized prong manufacturing for each individual newborn needing CPAP. New technologies are also being developed to provide less invasive transient intubation for the administration of surfactant.[30,31] The introduction of aerosolized surfactants will obviate the need for intubation solely being done for drug administration, but this may depend on new aerosolizing technology.[32] There is increasing evidence of the benefit of providing nasal intermittent positive pressure ventilation (NIPPV) especially post-extubation.[33] While there is increasing experience with heated, humidified high-flow nasal cannula systems,[34] their use remains challenging due to the wide variability of effective CPAP pressure being applied for any given flow rate.[35] It should be possible to incorporate intrathoracic pressure monitoring, e.g. with a transducer in a gavage tube, that would allow for better titration of high-flow nasal cannula flow to achieve targeted CPAP pressures.

Babies have been supported with ECMO bypass for 40 years. Ventricular assist devices, now only available for larger infants, may get small enough to be used in neonates. Liquid ventilation using perfluorocarbons has been used on a limited basis in neonates.[36] Artificial placenta/womb systems have recently been able to support premature lambs *ex utero* for several weeks[37]; NICUs of the future may be called upon to extend the gestation age of extremely preterm fetuses using similar technology.

## Neurologic Care

Optimizing neurodevelopment potential remains the principal focus of NICU care. New tools for monitoring neurophysiology include amplitude-integrated EEG (EEG)[38] and near-infrared monitoring of brain tissue saturation (NIRS).[39] Many larger NICUs are incorporating the use of such monitoring into the development of neuro-NICUs,[40] where neonatology care teams collaborate with pediatric neurologists and developmental specialists. We have learned from recent sophisticated MRI imaging and EEG studies the importance and beneficial impact of skin-to-skin kangaroo care.[41] Hypothermia has become the

standard of care for the treatment of hypoxic-ischemic encephalopathy (HIE) in term and near-term infants[42]; its use in premature infants is currently being more thoroughly studied by the NICHD Neonatal Network. Xenon gas is also being studied as an adjunctive therapy for HIE, but its use requires the development and application of a scavenger system within the ventilator circuit to prevent excessive loss of this expensive gas.[43] Neonatal critical care would benefit from more reliable, objective measurement of pain in order to optimize comfort and limit the use of pain medications, including opiates and benzodiazepines, that are associated with withdrawal and that may adversely affect brain development. Such pain assessment could come from rapid point-of-care measurement of cortisol or possibly from facial recognition software.

## Nutrition and Feeding Technology

Neonatal care depends on the provision of optimal nutrition, both parenteral and enteral, in the most appropriate environment. The use of banked breast milk for targeted populations in the NICU, particularly very low birth weight infants, has been increasing in recent years.[44] The use of human milk-derived human milk fortifier has been associated with reduction in NEC and sepsis in such infants.[45] The clinical benefits of other specialized human milk products such as cream and oligosaccharides are now being studied. With the advent of improved milk analysis, it is increasingly possible to "lacto-engineer" milk from an individual mother to optimize caloric, protein and fat content.[46] Such optimization will depend on the development of better biomarkers to define what is the ideal nutrition and growth for an individual neonate. The neonatal microbiome, being affected by nutrition choices, genetics and antibiotic use, may also be significantly influenced by NICU environmental factors.[47]

Learning to nipple feed is often the rate-limiting factor determining when a premature infant can be discharged home. New technologies have been developed to better assess feeding metrics. Placing a sensor within a nipple during feeds allows the display and documentation of objective feeding metrics in real time, enabling clinicians to see impact of feeding interventions and to track a baby's progress over time.[48] Pacifier-based technology can also be used to assess non-nutritive sucking (NNS) skills and to promote the development of NNS by providing rhythmic oral stimulation.[49]

## Laboratory Testing

The advent of microfluidics and improved microanalytics should lead to more rapid, less costly laboratory testing that can be done on smaller and smaller blood samples. More studies will be done as point-of-care testing, allowing for nearly immediate result availability. Transcutaneous measurement of bilirubin has proven to be helpful in the assessment of jaundice.[50] Related technologies can be used to measure glucose transcutaneously,[51] and possibly serum electrolytes and hematocrit. Breath analysis is now being used to measure hemolysis based on exhaled carbon monoxide[52] and may be extended to include other gases including nitric oxide, methane and ammonia.

Genomic testing is increasingly being incorporated into neonatal intensive care. An increasing number of diseases have been linked to genetic defects that can be identified by fluorescent in situ hybridization, comparative gene hybridization or single gene sequencing. Rare single nucleotide variations are very common in an individual human's genome[53]; such variations have recently been associated with risk and severity of BPD in neonates.[54] The day may come when large populations of babies will have genetic sequencing done at birth, and their health status will be followed thereafter, leading to a much better understanding of the effects of many different genetic variations, and possibly their interactions with the environment. Meanwhile, there are a number of commercial genetic labs focusing on testing for mutations associated with specific symptoms and clinical findings, such as respiratory failure or immunodeficiency. Such testing may be helpful in more rapidly diagnosing a fatal condition, e.g. surfactant protein deficiency, and thereby allowing us to limit futile intensive care. Genetic testing may help us better understand an individual baby's metabolism, e.g. being a slow or rapid metabolizer of phenobarbital, thereby helping us guide pharmacologic therapies. There are significant confidentiality and ethical issues raised by detailed genetic analyses being available from birth, especially when there remains much uncertainty about the clinical implications of most mutations.[55] Newborn screening will eventually be expanded to include a wider range of genetic and metabolome measurements to provide risk assessment for a number of diseases seen in the NICU.

## NICU Environment and Family Integrated Care

Technological advances can help us to achieve the environment that is optimal for a baby's neonatal development as well as the staff's workflow and well-being.

Most neonates in the NICU spend the vast majority of their stay inside an incubator or an open warmer or crib. The newest generation of incubators will provide better thermal support as well as help monitor and track auditory and visual stimuli, while trying to be more ergonomic for staff and parents interacting with the baby. One of the biggest needs of incubators and NICU furniture is to facilitate safe transfer of babies between incubator and chair and back, thereby encouraging kangaroo care. Sound monitoring should be done throughout the NICU or at each bedside and can be used to give feedback to NICU personnel to help limit their noise production. Lighting technology can be adapted for the NICU to better stimulate circadian rhythm.

Efforts to declutter the NICU setting will include eliminating cables from EKG leads and saturation monitors connecting to monitors and bedside computers. More equipment may be driven by batteries that are recharged by local magnetic fields, which would thereby obviate the need for power cords. However, there is a growing concern about the effects of electromotor radiation on neonates and their developing brains. One recent study showed that turning on the power to incubators affected heart rate variability of newborns within them.[56]

## Summary

Recent and upcoming technologies will change how we deliver neonatal intensive care and how we support babies and their parents through their NICU journey, from delivery to discharge. Introducing new technologies should be done with the same combination of enthusiasm and skepticism used to evaluate new drugs. Careful consideration should be applied as to how these technologies will change the communication, workflow and environment of the NICU. Caregivers and families should be encouraged to provide input on the development and design of new NICU technologies, collaborating as needed with design and engineering partners from academic institutions and industry.

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