Intelligent Data Analysis in the Neonatal Intensive Care Unit

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The Artemis Project...
The Artemis collaboration . . .

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An important caveat . . . exciting innovative project, preliminary results very encouraging, requires robust evaluation . . .

A warning . . . some slides contain dense, technological information . . . viewer discretion is advised.
Roadmap for the presentation . . .

An overview of neonatal intensive care
The information environment
The Artemis Project
Clinical informatics research
Future directions . . . and opportunities
Neonatal Intensive Care
Neonatal intensive care . . .

The neonatal intensive care population includes, but is not limited to, newborn infants with . . .

Birth asphyxia

Congenital malformations

Infection

Jaundice

Low birth weight

Respiratory disorders
Newborn infants require surgery . . .
Neonatal intensive care . . .

The intensive care of critically ill newborn infants includes:

Respiratory support, surfactant replacement therapy
Antimicrobial chemotherapy
Fluid, electrolyte and nutritional management
Phototherapy, exchange transfusion
Anticonvulsant therapy, therapeutic hypothermia
Surgery
Care of the parents . . .
The challenges of prematurity . . .

5-12% babies worldwide are born prematurely
Rate increasing in developing countries
Extremely immature babies born 12-16 weeks early
They may reside in the NICU for 3-4 months . . .
Some graduates have neurodevelopmental sequelae . . .
Others have chronic medical problems . . .
Cost of intensive care is significant . . . $$$
Life time costs impressive for some NICU graduates
Complications of intensive care . . .

Brain injury
Cerebral palsy
Cognitive impairment
Visual impairment
Hearing impairment

Chronic lung disease
Gastrointestinal failure
Psychosocial problems
Intelligent data analysis in the NICU

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Paper notes . . . detail enormous data collection
Hand-annotated records of nursing staff, usually at 60 minute intervals . . orders of magnitude of data loss

As many as 16 different streams of physiological data being displayed . . . rates ranging from one to 512 readings/sec, observed for 1-2 months in some cases

Very common for critically ill babies to have significantly abnormal variation in the measured parameters minute by minute that are not recorded in the medical record
Three persistent problems . . .

The data problem . . .
Data, data everywhere . . . . but not the data I need

The information paradox . . .
The information I have is not the information I want
The information I want is not the information I need
The information I need is not available

The knowledge gap . . .
The knowledge I need has not been discovered . . .

Adapted from Sir Muir Gray, Chief Knowledge Officer, NHS, UK (2007, 2008)
The data challenge . . .
Data loss . . .

<table>
<thead>
<tr>
<th></th>
<th>Heart rate</th>
<th>Respiratory rate</th>
<th>Blood oxygen saturation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actual frequency</td>
<td>140/min</td>
<td>40/min</td>
<td>60/min</td>
</tr>
<tr>
<td>Record rate</td>
<td>Hourly</td>
<td>Hourly</td>
<td>Hourly</td>
</tr>
<tr>
<td>Hourly data loss</td>
<td>8399</td>
<td>2399</td>
<td>3599</td>
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<tr>
<td>Daily data loss</td>
<td>201576</td>
<td>57576</td>
<td>86376</td>
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<tr>
<td>Weekly data loss</td>
<td>1411032</td>
<td>403032</td>
<td>604632</td>
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</table>

There is no value in collecting data unless the use of that data adds value to the care of the critically ill newborn infant.
Retinopathy of Prematurity Classification

Data visualisation . . .

O₂ saturation percent frequency using top of the hour spot readings, day 28

- 8.33% at 7am - 7pm Day Shift
- 25.00% at 7pm - 7am Evening Shift
- 66.67% at 7am - 7pm Day Shift
- 25.00% at 7pm - 7am Evening Shift
- 41.67% at 7am - 7pm Day Shift
- 33.33% at 7pm - 7am Evening Shift

Legend:
- <85% Below
- 85% - 92% Target
- 93% - 100% Above
Retinopathy of Prematurity Classification

Distortion of reality . . .
Intelligent data analysis in the NICU

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Early detection of subtle changes in physiological data that represent condition onset predictors for selected conditions that . . . make a major contribution to neonatal morbidity and mortality, and have an impact on long term outcomes.

Recognition of condition onset markers . . . would enable the earlier use of currently available, or newly discovered biophysical, interventions . . . that have the potential to minimize the severity of the condition, or even prevent its occurrence . . .
From the beginning . . .

- Implementation at SickKids: August 2009
- Implementation in Rhode Is: March 2010
- Implementation in Shanghai: April 2013

Prospective data collection > 750 babies
Physiological data streams (HR, RR, BP, SpO$_2$)
90 million data points per day
Represents approximately 15 patient years
Data storage requirements 5 TB per year
Stream computing . . .
High throughput real-time analytics with ultra low latency

Continuous ingestion  Continuous queries/analytics on data in motion

Marion Blount, 2010
New computational paradigm . . .

Traditional analytics and stream analytics open up new opportunities and provide greater value . . .

Marion Blount, 2010
Artemis functionality . . .
Algorithmic data processing . . .
Artemis architecture . . .
Data management processes . . .

Dynamic physiological data from NICU bedside monitoring devices captured in real-time

Robust, real-time temporal data analysis to identify features that are temporally associated with conditions of interest

Clinical data extracted from Clinical Information Management System . . . integrates context

Data storage for reuse

Reporting

Clinical research
Capturing relevant data . . .

Physiological data streams . . . synchronous data
Respiratory rate
Heart rate
Blood oxygen saturation
Blood pressure
Other data streams . . .

Other data . . . asynchronous data
Clinical observations; laboratory data
Interventions and responses; events
Images
Artemis platform . . .

Multidimensional approach
  multiple conditions
    with multiple streams of data
      for which multiple behaviours can exist

Data integration
  synchronous medical device data [continuous]
  asynchronous electronic clinical data [intermittent]

Data processing and aggregation
  multidimensional algorithms for one or more conditions
Intelligent data analysis in the NICU

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Development of algorithms for condition onset prediction for late onset neonatal sepsis

Development of algorithms for the detection and classification of neonatal spells

Recognition of pain

Recognition of sleep/wake cycling

Quantitation of retinal oxygen exposure in immature infants at risk for retinopathy of prematurity

Perioperative heart rate variability
Late onset neonatal sepsis . . .

Very common cause of morbidity for the newborn infant

Early diagnosis difficult . . . clinical signs are usually subtle, vague and non-specific until the infection is well established

Biological markers available to assist clinicians make an early diagnosis of LONS . . . there has not been widespread adoption of this biotechnology

Changes in heart rate variability may occur up to 24 hours prior to the clinical presentation of LONS (Griffin and Moorman, 2001)
Heart rate variability . . .
Cardiorespiratory variability . . .

Temporal abstractions to create hourly summaries for HRV and RRV

Variability — absolute value of the difference between consecutive time points

Hourly abstractions based on number of minutes where variability is below threshold
Some representative data . . .
Clinical presentation . . .

Absolute times

<table>
<thead>
<tr>
<th>Baby 1</th>
<th>15/11/06</th>
<th>16/11/06</th>
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</thead>
<tbody>
<tr>
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<td>Diagnosis</td>
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<table>
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<th>15/11/06</th>
<th>16/11/06</th>
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<tr>
<td></td>
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<table>
<thead>
<tr>
<th>Baby 3</th>
<th>15/11/06</th>
<th>16/11/06</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Diagnosis</td>
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</tbody>
</table>

Carolyn McGregor, 2013
Feature identification . . .

Absolute times

Baby 1

Baby 2

Baby 3

Carolyn McGregor, 2013
Temporal alignment . . .

**Absolute times**

- Baby 1: Diagnosis on 15/11/06 and 16/11/06
- Baby 2: Diagnosis on 15/11/06
- Baby 3: Diagnosis on 16/11/06

**Relative times**

- Baby 1: Diagnosis on 15/11/06 and 16/11/06
- Baby 2: Diagnosis on 15/11/06
- Baby 3: Diagnosis on 16/11/06

Carolyn McGregor, 2013
Abnormal HRV . . . LONS
Late onset neonatal sepsis . . .

Changes in HRV may occur up to 24h before clinical presentation of LONS (Griffin and Moorman, 2001)

Additional papers over the past decade

HeRO trial (Moorman, Carlo, Kattwinkel et al, 2011)

RCT of HRC monitoring

Mortality rate reduced in infants whose HRC monitoring was displayed from 10.2% to 8.1%

Trend toward increased days alive and ventilator-free

The mortality benefit was greater in infants <1000 g
Late onset neonatal sepsis . . .

Development of algorithms for condition onset prediction for late onset neonatal sepsis

• Prospective dataset: high fidelity physiological data streams [August 2009 – ]
• Retrospective dataset: low fidelity [2007-08]
• Prospective dataset: low fidelity [April 2010 – ]
• Prospective dataset: low fidelity [December 2012 – ]
Progress . . .

Prospec[178]ve dataset [SickKids]
More than 600 patients, representing approximately 15 patient years of data
Currently supporting 16 concurrent patients
Collecting approximately 1256 readings a second
Definitive analysis in progress . . .

Retrospective dataset [SickKids]
Nearly two years of 30 second spot reading data obtained from 1151 patients
Detailed analysis in progress . . .
WIHRI study . . .

Prospective data collection for 128 babies admitted to the WIHRI NICU for more than 4 days [March 2010 - Sep 2011]
60 second spot readings; temporal abstractions to create hourly summaries for HRV and RRV

variability — absolute value of the difference between consecutive time points

hourly abstractions based on number of minutes where variability < threshold

low HRV — 37 min/hr low RRV — 20 min/hr

t-tests and logistic regression to assess relationship between HRV, RRV and LONS status
Results . . .

LONS occurred in 13 patients (10.2%)
GA 29.2 weeks vs. 32.9 for non LONS patients (p < 0.0001)
Average LOS before LONS 18.5 days
Mean data collection 77.1 days vs. 40.7 days for non-LONS patients (p < 0.0001).

Relative alignment to point of diagnosis
Mean % low HRV for LONS patients 50.0% vs. 9.8% for non-LONS patients (p < 0.001).
Each unit increase in % low HRV — 10.3% increase in odds of LONS (c=0.944)
Some unexpected observations . . .
Some unexpected observations . . .
Perioperative HRV . . .

GA 34, BW 2504 g, Pyloric atresia Repair
Perioperative HRV . . .
Perioperative HRV . . .

GA 30, BW 1510 g, Sacrococcygeal teratoma

Resection teratoma
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Future directions . . .
Future directions . . .

Monitor every neonate in the NICU
Study additional conditions
• Early onset neonatal sepsis
• Necrotising enterocolitis
• Intraventricular haemorrhage
• Neonatal drug withdrawal

Implement the Artemis platform across the Canadian Neonatal Network . . . and beyond
Next generation informatics . . .

Real-time intelligent data analysis . . . integration with existing knowledge . . . platform for real-time clinical decision support, clinical research and knowledge discovery . . .
Integrated personalised care . . .
References . . .


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