Tele-ICU and Beyond: Developing the Intensive Care Unit of the Future

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• None

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• Ohio Board of Regents
Objectives

1. Describe the ICU of the present.

2. Review available data addressing the value of telemedicine initiatives in the ICU.

3. Outline the development of novel biomarkers of biological pattern variability in preclinical models of human disease.

4. Translation to the bedside in the ICU of the future.
ICU of the Present

Family Circus Cartoon, Bill Keane.
### ICU of the Present

Any Resident or Nurse, MICU, 2011.
ICU of the Present

- “Modern-day ICUs (...) contain easily 50 to more than 100 different pieces of electronic equipment.”

- “This equipment and these technologies do not communicate or work efficiently in an integrated fashion, posing a safety risk.”

Mathews and Provonost, JAMA 2011.
ICU of the Present

- Too much data, not enough information
- Working memory:
  - Miller’s Law: $7 \pm 2$
  - Three, sometimes four

Cognitive overload:
- Inhibits problem solving
- Worsened by stress

Clark RE, 2010; Cowan N, 1998; Luck & Vogel, 1998
ICU of the Present

ICU of the Present

- EMR is a big step forward
- But it is essentially replaces paper with a computer screen
- Current HIT initiatives do not focus on the integration and processing of information in the data-heavy ICU
ICU of the Present

Bedside Monitors
- Heart Rate
- Blood Pressure
- O$_2$ Saturation
- Temperature

Pulmonary Arterial Pressure

Central Venous Pressure

EEG

Laboratory Data

Medical Record

Intravenous (IV) Infusion Bag

Infusion Pump

Mechanical Ventilator

Electrodes

IV Catheter
ICU of the Present

- Clinicians presented with every-increasing amounts of raw data
- Often in a chaotic environment
- Expectation of filtering this data
- Need to prioritize tasks
- Hope to make informed treatment decisions

- Workarounds are commonplace

Mathews and Provonost, JAMA 2011.
ICU of the Present

- Lack of an integrated system:
  - Diagnostic errors
  - Inefficient work
  - Alarm fatigue
  - Worker stress and burnout

- “Clinicians often feel burdened rather than supported by technology.”

Mathews and Provonost, JAMA 2011.
Help is on the way?

- Interoperability and standardization of equipment
  - Health Level 7 (HL7)
  - Medical Device Plug & Play (MDPnP)
- Commercial Solutions
- Complete redesign to allow integration of disparate data streams and clinical workflows

Mathews and Provonost, JAMA 2011.
ICU Telemedicine

- 1977: Technological strategy to improve critical care outcomes by expanding the reach and availability of intensivist clinicians.
- 2011: Multiple commercial applications, Intensivist workforce shortage
- Rapid expansion covering >10% of total ICU beds

Philips VISICU eICU online content.
ICU Telemedicine

- Relay patient data to the tele-ICU center
  - Real-time physiologic data
  - Laboratory and radiographic data
  - Electronic patient and medication records
- User interface to organize patient data
  - Commercial “smart alerts” are untested
- Communication network
  - Videoconferencing technology

ICU Telemedicine

- Common Interventions:
  - Best practice adherence
  - Response to physiological instability
  - Intervention to prevent instability
  - Alterations to mechanical ventilation
  - Admission reviews
  - Adjustments to diagnosis or care plan
  - Antibiotic sensitivity targeting
  - Education/Communication

ICU Telemedicine: JAMA 2009

- Federally-funded (R01), multicenter, before-and-after observational study
- 6 ICUs, varying case mix
- Preintervention: 2034 pts
- Postintervention: 2108 pts
- Adjusted outcomes (SAPS II)
- Full delegation of intervention authority in only 31% pts

No overall benefit of tele-ICU on mortality or length of stay.

ICU Telemedicine: Mixed Results

- Meta-analysis of 13 studies involving 35 ICUs
- 9 MICU, 8 SICU, 8 mixed, 7 other, 3 not specified

<table>
<thead>
<tr>
<th>Source</th>
<th>No. of ICUs</th>
<th>Data Presented at ICU Level</th>
<th>Baseline Period, mo</th>
<th>No. of Baseline ICU Patients</th>
<th>Intervention Period, mo</th>
<th>No. of Tele-ICU Patients</th>
<th>Authors Affiliated With Tele-ICU Vendor</th>
<th>Newcastle-Ottawa Scale Score</th>
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</thead>
<tbody>
<tr>
<td>Breslow et al, 2004</td>
<td>2</td>
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<td>1396</td>
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<td>744</td>
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<td>Kohl et al, 2007</td>
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<td>Marcin et al, 2004</td>
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<td>47</td>
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<td>McCambridge et al, 2010</td>
<td>3</td>
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<td>16</td>
<td>954</td>
<td>10</td>
<td>959</td>
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<td>Morrison et al, 2010</td>
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<td>4</td>
<td>1371</td>
<td>4</td>
<td>1430</td>
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<td>Norman et al, 2009</td>
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<td>2</td>
<td>356</td>
<td>5</td>
<td>477</td>
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<td>Rosenfeld et al, 2000</td>
<td>1</td>
<td>Yes</td>
<td>8</td>
<td>427</td>
<td>4</td>
<td>201</td>
<td>Yes</td>
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<td>Shaffer et al, 2005</td>
<td>6</td>
<td>No</td>
<td>19</td>
<td>6205</td>
<td>14</td>
<td>3954</td>
<td>Yes</td>
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<tr>
<td>Siek et al, 2008</td>
<td>2</td>
<td>No</td>
<td>3</td>
<td>148</td>
<td>3</td>
<td>128</td>
<td>...</td>
<td>3</td>
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<tr>
<td>Thomas et al, 2009</td>
<td>6</td>
<td>Yes</td>
<td>32</td>
<td>2035</td>
<td>25</td>
<td>2107</td>
<td>No</td>
<td>9</td>
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<tr>
<td>Van der Kloot et al, 2009</td>
<td>1</td>
<td>Yes</td>
<td>24</td>
<td>1277</td>
<td>21</td>
<td>2012</td>
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<td>Zawada et al, 2009</td>
<td>4</td>
<td>No</td>
<td>12</td>
<td>696</td>
<td>30</td>
<td>6379</td>
<td>No</td>
<td>6</td>
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</table>

Total 35 15870 25707

Figure 2. Effect of telemedicine intensive care unit (ICU) coverage on ICU mortality. Weights are calculated from random-effects analysis. CI indicates confidence interval; OR, odds ratio.

Figure 3. Effect of telemedicine intensive care unit coverage on in-hospital mortality. Weights are calculated from random-effects analysis. CI indicates confidence interval; OR, odds ratio.
**Figure 5.** Effect of telemedicine intensive care unit (ICU) coverage on **ICU length of stay (LOS)**. Weights are calculated from random-effects analysis. CI indicates confidence interval; SMD, standardized mean difference.

**Figure 6.** Effect of telemedicine intensive care unit coverage on **hospital length of stay (LOS)**. Weights are calculated from random-effects analysis. CI indicates confidence interval; SMD, standardized mean difference.
ICU Telemedicine: Mixed Results

- Why a reduction ICU but not in-hospital mortality?
  - Tele-ICU is a multi-factorial intervention
  - Upgraded EMR
  - Enhanced quality improvement programs
  - Changes in patient acuity due to improved admission triage decisions (palliative care?)

- Why a reduction ICU but not in-hospital LOS?
  - More aggressive ventilator weaning
  - Greater willingness to transfer on off-shifts

Limitations/Editorial Comments:
- Study designs don’t allow for causal inference
- Are nighttime complications the problem?
- Or systematically implementing evidenced-based practices

### Table 4. Impact of Tele-ICU on LOS

<table>
<thead>
<tr>
<th>Study Subgroup</th>
<th>ICU LOS, Mean (95% CI), d</th>
<th>Sources Included</th>
<th>Hospital LOS, Mean (95% CI), d</th>
<th>Sources Included</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>-1.26 (-2.21 to -0.30)</td>
<td>27-29, 40, 51-53</td>
<td>-0.64 (-1.52 to 0.25)</td>
<td>28, 29, 40, 51-53</td>
</tr>
<tr>
<td>Higher-quality study</td>
<td>-1.11 (-2.11 to -0.11)</td>
<td>27-29, 51, 52</td>
<td>-0.67 (-1.69 to 0.36)</td>
<td>28, 29, 51-53</td>
</tr>
<tr>
<td>Lower-quality study</td>
<td>-2.10 (-2.26 to -1.95)</td>
<td>40</td>
<td>-0.47 (-0.62 to -0.33)</td>
<td>40</td>
</tr>
<tr>
<td>Studies with vendor affiliation</td>
<td>-3.54 (-4.02 to -3.07)</td>
<td>28, 51</td>
<td>-1.74 (-5.43 to 1.96)</td>
<td>28, 51</td>
</tr>
<tr>
<td>Studies without vendor affiliation</td>
<td>0.05 (-0.05 to 0.16)</td>
<td>29, 52, 53</td>
<td>0.05 (-0.01 to 0.10)</td>
<td>29, 52, 53</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; LOS, length of stay; ICU, intensive care unit; tele-ICU, telemedicine ICU.

ICU Telemedicine: JAMA 2011

- Prospective stepped-wedge clinical practice study
- Funded by the University of Massachusetts
- 6290 adults in 7 ICUs (3 MICU, 3 SICU, 1 CVICU)
- Single academic medical center (2 campuses)
- Telemedicine team had full discretion
- All tele-MDs also worked in the target ICUs

Complex intervention:
- Enforce daily goals
- Review adherence to evidence-based practices
- Respond to bedside alarms

Lilly CM et al., JAMA 305(21):2175, 2011
# ICU Telemedicine: JAMA 2011

## Table 1. Comparison of Intensive Care Unit (ICU) Processes Before and After Tele-ICU Intervention

<table>
<thead>
<tr>
<th>Preintervention</th>
<th>Tele-ICU Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bedside monitor alarms</td>
<td>Physiological trend alerts</td>
</tr>
<tr>
<td></td>
<td>Abnormal laboratory value alerts</td>
</tr>
<tr>
<td></td>
<td>Review of response to alerts</td>
</tr>
<tr>
<td></td>
<td>Off-site team rounds</td>
</tr>
<tr>
<td>Daily goal sheet</td>
<td>Electronic detection of nonadherence</td>
</tr>
<tr>
<td></td>
<td>Real-time auditing</td>
</tr>
<tr>
<td></td>
<td>Nurse manager audits</td>
</tr>
<tr>
<td></td>
<td>Team audits</td>
</tr>
<tr>
<td>Telephone case review initiated by house staff or affiliate practitioner</td>
<td>Workstation review initiated by intensivist includes electronic medical record, imaging studies, interactive audio and video of patient, interaction with nurse and respiratory therapist, and assessment of response to therapy</td>
</tr>
</tbody>
</table>
Figure. Enrollment of Study Participants

6465 Intensive care unit (ICU) admission registrations from 7 academic medical center adult ICUs (mean [SD], 899 [274] cases per ICU; range, 525-1388 cases)

1546 Validated preintervention group ICU admissions

17 Excluded
16 Registrations not admitted to an ICU
1 Pediatric patient (age, 17 y)

4901 Validated tele-ICU group ICU admissions

140 Excluded
131 Registrations not admitted to an ICU
9 Exclusions for hospital stay (admissions to both a preintervention ICU and tele-ICU during the same hospital stay)

1529 Preintervention patients included in analysis
1510 Complete APACHE III acuity data
9 Without scores for burn diagnosis
6 Without scores for short ICU stay
4 With incomplete APACHE III data

4761 Tele-ICU patients included in analysis
4751 Complete APACHE III acuity data
10 Without scores for burn diagnosis

APACHE indicates Acute Physiology and Chronic Health Evaluation.
Table 2. General Characteristics of Adult Critically Ill Patients<sup>a</sup>

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Preintervention Group (n = 1529)</th>
<th>Tele-ICU Group (n = 4761)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>62 (17)</td>
<td>64 (16.8)</td>
<td>.003</td>
</tr>
<tr>
<td>Male sex</td>
<td>874 (57)</td>
<td>2701 (57)</td>
<td>.77</td>
</tr>
<tr>
<td>Body mass index, mean (SD)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>28.5 (6.3)</td>
<td>28.3 (7.7)</td>
<td>.48</td>
</tr>
<tr>
<td>APACHE III score, mean (SD)</td>
<td>45 (22)</td>
<td>58 (27)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>APS score, mean (SD)</td>
<td>33 (19)</td>
<td>46 (24)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>572 (37)</td>
<td>1492 (31)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Postoperative case</td>
<td>546 (36)</td>
<td>1221 (26)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Primary admission diagnosis classified by organ system&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>473 (31)</td>
<td>1924 (40)</td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>297 (19)</td>
<td>897 (19)</td>
<td></td>
</tr>
<tr>
<td>Neurological</td>
<td>260 (17)</td>
<td>688 (14)</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>234 (15)</td>
<td>593 (12)</td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td>125 (8)</td>
<td>260 (5)</td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td>50 (3)</td>
<td>145 (3)</td>
<td></td>
</tr>
<tr>
<td>Endocrine</td>
<td>34 (2)</td>
<td>100 (2)</td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>32 (2)</td>
<td>89 (2)</td>
<td></td>
</tr>
<tr>
<td>Hematological</td>
<td>13 (1)</td>
<td>41 (1)</td>
<td></td>
</tr>
<tr>
<td>Transplant</td>
<td>11 (1)</td>
<td>24 (0.5)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; APS, acute physiology score; ICU, intensive care unit.

<sup>a</sup>Values are expressed as number (percentage) unless otherwise indicated.

<sup>b</sup>Calculated as weight in kilograms divided by height in meters squared.

<sup>c</sup>For the difference in distribution between the 2 groups, the P value was less than .001.
**Table 3. Mortality and Length-of-Stay Outcomes**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Preintervention Group (n = 1529)</th>
<th>Tele-ICU Group (n = 4761)</th>
<th>Unadjusted P Value</th>
<th>Tele-ICU Effect Estimates&lt;sup&gt;a&lt;/sup&gt;</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality rate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital</td>
<td>208 (13.6)</td>
<td>562 (11.8)</td>
<td>.07</td>
<td>0.40 (0.31-0.52)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.005</td>
</tr>
<tr>
<td>ICU</td>
<td>164 (10.7)</td>
<td>410 (8.6)</td>
<td>.01</td>
<td>0.37 (0.28-0.49)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.003</td>
</tr>
<tr>
<td>Length of stay</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital</td>
<td>13.3 (17.1) 7.9 [0.2-15.0]</td>
<td>9.8 (10) 6.8 [0.2-12.0]</td>
<td>&lt;.001</td>
<td>1.44 (1.33-1.56)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ICU</td>
<td>6.4 (11) 2.5 [0.2-6.5]</td>
<td>4.5 (6.7) 2.4 [0.1-4.6]</td>
<td>&lt;.001</td>
<td>1.26 (1.17-1.36)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: ICU, intensive care unit; IQR, interquartile range.

<sup>a</sup> Estimate of effect size after adjustment for differences in acuity score, admission source, admission ICU, time after enrollment of first case in group, and other predictive factors including laboratory values and physiological measurements as detailed in the eSupplement at http://www.jama.com.

<sup>b</sup> Indicates odds ratio (95% confidence interval).

<sup>c</sup> Indicates hazard ratio (95% confidence interval).
Table 4. Association of Tele-ICU Intervention Group With Best Practice and Complication Measures

<table>
<thead>
<tr>
<th>Clinical Practice Guideline Adherence</th>
<th>No./Total (%) of Patients Eligible&lt;sup&gt;a&lt;/sup&gt;</th>
<th>OR (95% CI)</th>
<th>P Value</th>
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<tbody>
<tr>
<td></td>
<td>Preintervention Group</td>
<td>Tele-ICU Group</td>
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<tr>
<td>Prophylaxis</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Stress ulcer</td>
<td>1253/1505 (83)</td>
<td>4550/4760 (96)</td>
<td>4.57 (3.91-5.77)</td>
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<tr>
<td>Deep venous thrombosis</td>
<td>1299/1527 (85)</td>
<td>4707/4733 (99.5)</td>
<td>15.4 (11.3-21.1)</td>
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<tr>
<td>Best practice</td>
<td></td>
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<td></td>
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<tr>
<td>Cardiovascular protection</td>
<td>311/391 (80)</td>
<td>2866/2894 (99)</td>
<td>30.7 (19.3-49.2)</td>
</tr>
<tr>
<td>Prevention of ventilator-associated pneumonia</td>
<td>190/582 (33)</td>
<td>770/1492 (52)</td>
<td>2.20 (1.79-2.70)</td>
</tr>
<tr>
<td>Ventilator-associated pneumonia</td>
<td>76/584 (13)</td>
<td>32/1949 (1.6)</td>
<td>0.15 (0.09-0.23)</td>
</tr>
<tr>
<td>Catheter-related bloodstream infection</td>
<td>19/1529 (1)</td>
<td>29/4761 (0.6)</td>
<td>0.50 (0.27-0.93)</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>174/1452 (12)</td>
<td>540/4565 (12)</td>
<td>1.00 (0.71-1.69)</td>
</tr>
<tr>
<td>After hours care plan review for ICU admissions, No. (%)</td>
<td>705/1529 (46)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2287/4761 (48)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.00 (0.71-1.69)</td>
</tr>
<tr>
<td>Interventions for physiological instability</td>
<td>All bedside clinician initiated</td>
<td>483&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>37,573&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; ICU, intensive care unit; OR, odds ratio.

<sup>a</sup>Unless otherwise indicated.

<sup>b</sup>Off-hours admission reviews not using a workstation.

<sup>c</sup>Off-hours admissions reviews using a workstation.

<sup>d</sup>Initiated by bedside clinician.

<sup>e</sup>Initiated prior to action by bedside clinicians.

5.05/d managed without tele-ICU
1.75/d managed with tele-ICU

Lilly CM et al., JAMA 305(21):2175, 2011
ICU Telemedicine: Mixed Results

- Limitations/Editorial Comments:
  - Unable to establish causal inference
  - Group heterogeneity, secular trends
  - Relative importance of interventions
    - Best-practice adherence
    - Regular review of daily goals
    - Electronic physiologic surveillance
  - Single center, shared physicians, full discretion
  - No comparison to in-house intensivists

Kahn JM, JAMA 305(21):2227, 2011
Lilly CM et al., JAMA 305(21):2175, 2011
ICU Telemedicine: Future Research

- Biases of available studies:
  - Unmeasured changes in case mix
  - Temporal trends
  - Coincident quality improvement projects
  - Random variation

- Implementation of ICU telemedicine associated with multiple interventions including:
  - Staffing changes
  - Decision-support tools
  - New electronic medical records

Khan JM et al. for Critical Care Societies Collaborative, CHEST 140(1):230, 2011
ICU Telemedicine: Future Research

Future studies:
- Standardized approach to assessing the preimplementation ICU environment
- Standardized lexicon for defining the telemedicine intervention

Key topic areas:
- Structure
- Process
- Outcomes

Khan JM et al. for Critical Care Societies Collaborative, CHEST 140(1):230, 2011
ICU of the Future

- Situational Awareness
  - Discrepancy between what is happening and what should be happening

- Move from a reactive model to a proactive model of clinical care
  - Anticipate patient deterioration and intervene to prevent it


ICU of the Future

- Clinical informatics tools:
  - Bedside patient management decision support
  - Reduce the number of variables that need to be interpreted
  - Complexity of the system exceeds the ability of any one individual

Biological Variability

- Biological systems are complex and measured outputs exhibit variability.
- Homeokinesis: "functioning in a variable external environment to maintain a highly organized internal environment fluctuating within acceptable limits ... in a far-from equilibrium state”.
- Variability itself is neither good nor bad, and may increase or decrease with stress or disease.
- Growing appreciation that changes in variability are clinically relevant (changes occur in disease states).

Figure 1. Conceptual properties describing biological variability and selected tools to quantify sources of variability.
Preclinical Models of Diseases Common in the ICU

- Respiratory Insufficiency/Failure
- Cardiac Arrest
- Stroke
- Heart Failure
- Sepsis
- Ventilator-Associated Lung Injury
- Drug Overdose
Preclinical Models of Diseases Common in the ICU

- Understanding the neurophysiological mechanisms responsible for the genesis of biological variability
- Develop markers of disease severity
- Identify prognosis and reversible pathophysiology leading to recovery
- Novel therapeutics targeted at modulating pattern variability
- Feasibility for translational studies
Respiratory Failure

Hypotheses:
- Acute lung injury will alter breathing pattern variability
- Changes in breathing pattern variability will reflect the severity of lung injury, and will be predictive of progression or resolution of lung injury

A

![Graph showing the relationship between BALF protein (µg/µL) and respiration rate (bpm).](image)

- Equation: \( y = 0.0016x - 0.1133 \)
- \( r^2 = 0.8279 \)

B

![Graph showing the probability of lung injury versus NLCI.](image)

- OR: 1.13
- \( p = 0.04 \)

C

![ROC curves comparing different metrics.](image)

- **NLCI**
  - AUC = 0.933
- **Mutual Information**
  - AUC = 0.935
- **Coefficient of Variation of \( T_{\text{Tot}} \)**
  - AUC = 0.779

Medullary Coronal Sections Stained for IL-1β

**Area Postrema**

- PBS
- Bleomycin

**Nucleus Tractus Solitarii**

- PBS
- Bleomycin

---

Fig. 9. IL-1β was co-localized with neurons in the nTS, as identified by fluorescent staining.
Cardiac Arrest & Resuscitation

- Transient global brain ischemia (12 min) was achieved using a rat model of cardiac arrest and resuscitation.
- Intra-atrial injection of d-tubocurare (0.3 mg) and ice-cold KCl solution (0.5 M; 0.12 ml/100 g body weight).
- Resuscitation: Intubation, ventilation, chest compressions, infusion of normal saline until ROSC.
- Epinephrine (4–10 μg) infused to establish MAP greater than 80% of the pre-arrest value.

Xu, K et al. Brain Research 2009.
## Table 1 – Physiological variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Survivor (n=10)</th>
<th>Non-survivor (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (g)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-arrest</td>
<td>357 ± 28</td>
<td>364 ± 33</td>
</tr>
<tr>
<td>1 d post</td>
<td>340 ± 27</td>
<td>339 ± 32</td>
</tr>
<tr>
<td>2 d post</td>
<td>328 ± 26*</td>
<td>325 ± 33</td>
</tr>
<tr>
<td>3 d post</td>
<td>325 ± 25*</td>
<td>330 ± 30</td>
</tr>
<tr>
<td>4 d post</td>
<td>334 ± 24</td>
<td>NA</td>
</tr>
<tr>
<td>HVR pre-arrest</td>
<td>2.9 ± 0.3</td>
<td>2.9 ± 0.3</td>
</tr>
<tr>
<td>MABP (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-arrest</td>
<td>113 ± 6</td>
<td>113 ± 7</td>
</tr>
<tr>
<td>1 h post</td>
<td>97 ± 8*</td>
<td>98 ± 10*</td>
</tr>
<tr>
<td>Arterial pH (unit)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-arrest</td>
<td>7.43 ± 0.03</td>
<td>7.41 ± 0.04</td>
</tr>
<tr>
<td>1 h post</td>
<td>7.38 ± 0.08</td>
<td>7.35 ± 0.08</td>
</tr>
<tr>
<td>PaO₂ (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-arrest</td>
<td>96 ± 17</td>
<td>92 ± 7</td>
</tr>
<tr>
<td>1 h post</td>
<td>99 ± 14</td>
<td>95 ± 8</td>
</tr>
<tr>
<td>PaCO₂ (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-arrest</td>
<td>38 ± 3</td>
<td>40 ± 2</td>
</tr>
<tr>
<td>1 h</td>
<td>36 ± 4</td>
<td>38 ± 3</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-arrest</td>
<td>48 ± 2</td>
<td>48 ± 2</td>
</tr>
<tr>
<td>1 h post</td>
<td>48 ± 2</td>
<td>48 ± 2</td>
</tr>
<tr>
<td>Glucose_plasma (mM)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-arrest</td>
<td>7.9 ± 1.1</td>
<td>8.2 ± 0.3</td>
</tr>
<tr>
<td>1 h post</td>
<td>9.6 ± 1.2</td>
<td>9.3 ± 0.8</td>
</tr>
<tr>
<td>Lactate_plasma (mM)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-arrest</td>
<td>1.5 ± 0.3</td>
<td>1.7 ± 0.4</td>
</tr>
<tr>
<td>1 h post</td>
<td>2.9 ± 0.8*</td>
<td>3.3 ± 0.6*</td>
</tr>
</tbody>
</table>
Xu, K et al. Brain Research 2009.
Cardiac Arrest & Resuscitation

 Survivors vs. Non-Survivors:

C. Sample Entropy

- **Original Data**
- **±Uncertainty**
- **Surrogate Data**
- **±SD**

No-arrest control
1 day recovery

Neu-N, Caspase-3, Merge

Rostral Ventrolateral Medulla (RVLM)
Kui Xu in Prabha Kc's laboratory

Xu, K et al. Experimental Biology 2012 International Conference (Submitted).
The ICU is a bit more complicated...
Liberation from Mechanical Ventilation

• Multi-step Process

• Readiness Testing
  – Weaning Predictors: RSBI, $V_T$, $V_E$, NIF, etc.

• Weaning
  – Spontaneous Breathing Trial (SBT)
    – Gradual reduction in ventilator support

• Decision to Extubate
Liberation from Mechanical Ventilation

• Timing of extubation is a daily dilemma

• Risks of prolonged mechanical ventilation
  – VAP, VALI, VTE, GI bleeding, prolonged sedation, mortality

• Incidence of failed extubation: average 15% (5-20%)

• Failed extubation associated with increased mortality, ICU & hospital LOS, tracheostomy, cost, long term & rehab care

• Need for improved prediction of extubation failure
**Weaning and Variability Evaluation**

**Multicenter Trial**

**Principal Aim:** Evaluate the thresholds of altered HRV & RRV occurring during an SBT that optimally predict extubation failure
6-min Epoch of Data for Analysis Pre-Weaning Trial

End-tidal PCO₂

ECG

R-Wave Detection from Phillips

Actual Time (h. ½/10 h)
Detection & Confirmation of Waveforms Pre-Weaning Trial

End-tidal $\text{PCO}_2$

- Onset of Inspiration
- Onset of Expiration

ECG

R-Wave Detection from Phillips

Actual Time (h. $\frac{1}{1000}$ h)
Poincaré Plots

Before

During Weaning Trial

After

Instantaneous HR (bpm, n)

Instantaneous RR (Brhspm, n)

6-min Epochs
The Future of Critical Care?

Transforming multi-modal patient data to actionable information to improve patient outcomes and reduce healthcare costs.

Critical Care Medicine

What do we need?

• Reliable predictions of outcomes of multiple, simultaneous events and actions in individual patients

• Aggregate predictions of sequential outcomes from the interaction of these events and actions (physiological signatures)

• Precise forecasting of individual patient trajectories in the intensive care unit

• Refinement of predictive modeling based on better understanding of complex physiology and modified by comparison with actual outcomes

Our approach:

1. Develop an open source information architecture that supports the acquisition, time-synchronization and archiving of multi-modal physiological waveform data at the device level in the ICU.

2. Develop computational models and algorithms using preclinical models to investigate which measures have the greatest promise for improving real-time clinical decision-making in the ICU.

3. Design and implement human research and clinical studies that can provide the necessary data to reliably address utility (cost verses benefits).

The Future of Critical Care?

- Device communication with the EMR
- Real-time signal analysis
- Smart Alarms
  - Multimodal to reduce false positives
  - Early detection to promote proactive care
- Support workflow to bring providers back to the bedside
- Decision support to improve diagnosis
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  - Mary Andrews, RRT, Barry Bertagnolli, CBET, Geoff Green, Dave Haney, RRT, Steve Slaughter, RRT

- Lab
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