NASA Laboratory Analysis for Manned Exploration Missions

06 May 2014

Michael K. Krihak\textsuperscript{a}, PhD

Tianna E. Shaw\textsuperscript{b}

\textsuperscript{a}University of California Santa Cruz, University Affiliated Research Center, Moffett Field, CA

\textsuperscript{b}National Aeronautics and Space Administration (NASA) - Ames Research Center, Moffett Field, CA

Sensing Technologies for Global Health, Military Medicine, and Environmental Monitoring IV

Paper #: 9112-67
Overview

- Background
- Mission Operations
- Requirements
- Technology Development
- Summary
• The Human Research Program is divided into 6 major elements:
  – Provide the Program’s knowledge and capabilities to conduct research, addressing the human health and performance risks
  – Advance the readiness levels of technology and countermeasures to the point of transfer to the customer programs and organizations
• The National Space Biomedical Research Institute (NSBRI) is a partner with the HRP in developing a successful research program.
Exploration Medical Capability Element

• The Exploration Medical Capability (ExMC) Element is charged with: Reducing the risk of unacceptable health and mission outcomes due to limitations of in-flight medical capabilities for exploration missions.
• To reduce this risk, ExMC
  – Defines requirements for health maintenance
  – Develops treatment protocols
  – Extrapolates from the protocols to health management modalities
  – Evaluates the feasibility of these modalities
  – Develops technology and informatics that will enable medical care and decision systems
  – Utilizes ground, analog, and flight resources

Intravenous Fluid Generation (IVGEN) Assembly that Purifies Water Coming from the Space Vehicle
## Exploration Medical Care

Objective: Ensure astronaut health and safety due to injury or illness on extended (>30 days) human exploration missions beyond LEO - Level IV & V standards of care.

<table>
<thead>
<tr>
<th>Level of Care</th>
<th>Mission</th>
<th>Capability</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>LEO &lt; 8 days</td>
<td>Space Motion Sickness, Basic Life Support, First Aid, Private Audio, Anaphylaxis Response</td>
</tr>
<tr>
<td>II</td>
<td>LEO &lt; 30 days</td>
<td>Level I + Clinical Diagnostics, Ambulatory Care, Private Video, Private Telemedicine</td>
</tr>
<tr>
<td>III</td>
<td>Beyond LEO &lt; 30 day</td>
<td>Level II + Limited Advanced Life Support, Trauma Care, Limited Dental Care</td>
</tr>
<tr>
<td>IV</td>
<td>Lunar &gt; 30 day</td>
<td>Level III + Medical Imaging, Sustainable Advanced Life Support, Limited Surgical, Dental Care</td>
</tr>
<tr>
<td>V</td>
<td>Mars Expedition</td>
<td>Level IV Autonomous Advanced Life Support and Ambulatory Care, Basic Surgical Care</td>
</tr>
</tbody>
</table>

LEO – Low-Earth Orbit
Ref: NASA CxP 70024 – Constellation Program Human-Systems Integration Requirements (Revision B), March 3, 2008.
Currently Available for Spaceflight

- International Space Station (ISS) medical diagnostics capability maintains very limited capability for in-flight analysis of bodily fluids (urine, blood, saliva).
- Upmass availability for re-supply
- Two diagnostic instruments are onboard the ISS
  - Portable Clinical Blood Analyzer (PCBA) or i-STAT (Abbott) provided by United States
  - Reflotron (Roche) provided by Russians
- Though some in-situ diagnostic capability demonstrated, several drawbacks for space exploration persist
  - Refrigerated disposables; limited shelf-life
  - Unable to provide blood cell analysis
  - Waste/consumables

ISS i-STAT PCBA
Ref: http://www.nasa.gov/mission_pages/station/research/experiments/373.html#images

M. Krihak, PhD
Exploration Laboratory Analysis
Exploration Laboratory Analysis (ELA)

ExMC Gap 4.05*

– We do not have the capability to measure laboratory analytes in a minimally invasive manner during exploration missions.

To address this gap, an exploration lab analysis platform technology for long-duration, exploration missions should:

– Be minimally invasive
– Be easy to use
– Promote crew autonomy
– Exhibit expanded assay capability
– Have extended shelf-life of consumables (e.g. reagents, cartridges)
– Minimize mass, volume, power, and consumables

*https://humanresearchwiki.jsc.nasa.gov

M. Krihak, PhD
ELA Operational Concept

User
- Crewmember
  - Sample acquisition
  - Sample preparation

Hardware
- Sample Analysis
  - Analyzer 1
  - Analyzer 2

Data Management
- Integral to hardware
- Data processing, storage, transmission
- Wired/wireless communication to PC

EMS
- Wired/wireless integration hardware
- Medical diagnosis, evaluation
- Ground support

EMS – Exploration Medical System

M. Krihak, PhD
Exploration Laboratory Analysis
## ELA Performance Considerations

<table>
<thead>
<tr>
<th>Performance Consideration</th>
<th>Value</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shelf life, durables and consumables</td>
<td>36 months</td>
<td>Storage under the exploration vehicle’s ambient environment conditions; no refrigeration</td>
</tr>
<tr>
<td>Operational life in space</td>
<td>36 months</td>
<td>Survive possible high-energy and background radiation exposure</td>
</tr>
<tr>
<td>Reliable usage time</td>
<td>144 hours</td>
<td>Battery power operability</td>
</tr>
<tr>
<td>Gravitational/residual acceleration</td>
<td>1, 0.38, 0.17, $10^{-5}$ g</td>
<td>Must operate on Earth, moon, near-Earth asteroid, Mars, and in low-Earth orbit</td>
</tr>
<tr>
<td>Consumables volume (includes reagents and disposables)</td>
<td>TBD (cm³)</td>
<td>Depends on medical kit dimensions</td>
</tr>
<tr>
<td>Mass</td>
<td>TBD (kg)</td>
<td>Depends on medical kit dimensions</td>
</tr>
<tr>
<td>Power consumption</td>
<td>TBD (W)</td>
<td>Battery operation; vehicle back-up</td>
</tr>
<tr>
<td>Volume</td>
<td>TBD (cm³)</td>
<td>Depends on medical kit dimensions</td>
</tr>
</tbody>
</table>
## ELA Functional Requirements

### MEASUREMENT PANELS

<table>
<thead>
<tr>
<th>Basic Metabolic</th>
<th>Blood Gases</th>
<th>Hematology</th>
<th>Cardiac</th>
<th>Liver</th>
<th>Urinalysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>PaO₂</td>
<td>WBC Count</td>
<td>Troponin I CK-MB</td>
<td>Total Bilirubin</td>
<td>Specific Gravity</td>
</tr>
<tr>
<td>Calcium</td>
<td>PaCO₂</td>
<td>RBC Count</td>
<td></td>
<td>Direct Bilirubin</td>
<td>pH</td>
</tr>
<tr>
<td>Sodium</td>
<td>SaO₂</td>
<td>HCT</td>
<td></td>
<td>ALP</td>
<td>Leukocytes</td>
</tr>
<tr>
<td>Potassium</td>
<td>HCO₃</td>
<td>Hgb</td>
<td></td>
<td>AST</td>
<td>Nitrites</td>
</tr>
<tr>
<td>CO₂, Total</td>
<td>pH</td>
<td>Neutrophils</td>
<td></td>
<td>ALT</td>
<td>Proteins</td>
</tr>
<tr>
<td>Chloride</td>
<td></td>
<td>Abs. Neutrophils</td>
<td></td>
<td></td>
<td>Glucose</td>
</tr>
<tr>
<td>BUN</td>
<td></td>
<td>Count</td>
<td></td>
<td></td>
<td>Ketones</td>
</tr>
<tr>
<td>Creatinine</td>
<td></td>
<td>Lymphocytes</td>
<td></td>
<td></td>
<td>Urobilirubin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monocytes</td>
<td></td>
<td></td>
<td>Bilirubin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Eosinophils</td>
<td></td>
<td></td>
<td>Blood</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PLT</td>
<td></td>
<td></td>
<td>Urate</td>
</tr>
</tbody>
</table>


M. Krihak, PhD

Exploration Laboratory Analysis
NASA SBIR Technologies

Solicitation/Subtopic/Title:

- NASA SBIR 2007 solicitation, Exploration Medical Capability
  - Reusable Handheld Electrolytes and Lab Technology for Humans (rHEALTH Sensor), DNA Medical Institute
- NASA SBIR 2008 solicitation, In Flight Diagnosis and Treatment
  - Nanoscale Test Strips for Multiplexed Blood Analysis, DNA Medicine Institute
- NASA SBIR 2011 solicitation, Smart Phone Driven Blood-Based Diagnostics
  - Cell Phone-based Lateral Flow Assay for Blood Biomarker Detection, Intelligent Optical Systems, Inc./Holomic
rHEALTH Capabilities

One drop = 100s of tests

5 – 10 μL sample volume

Multiplexed Immunodx

Cell subtypes

Cell counting

M. Krihak, PhD

ABX Micros 60 (counts/μL)

r^2 = 0.9978

rHEALTH (counts/run)

TNF-alpha Standards

Mean RFU

0 1000 2000 3000

0 1 2 3 4

Log[TNF-alpha]pg/ml

r2 = 0.9978

0 2000 4000 6000

ABX Micros 60 (counts/μL)

rHEALTH (counts/run)

Courtesy of The DNA Medicine Institute
Smartphone Diagnostics – IOS Lateral Flow Assays (LFA)

Concept – develop a simple and compact point-of-care platform
- Integrate lateral flow test strip with cell phone
- Demonstrate blood biomarker detection
- Perform diagnostics in absence of medically trained personnel

Cell phone with LFTS cassette holder attachment, modified for fluorescence imaging

Courtesy of Intelligent Optical Systems (IOS)
Advantages of Smartphone Diagnostics

• Over 5 billion cellphone subscribers worldwide
  – Commodity; less expensive than fabricating a reader(s) for multiple assay configurations (i.e. immunoassays, electrochemical assays, hematology)

• Telemedicine - remote, biomedical diagnostic applications
  – Leverage development of apps and assays
  – Standardized reconfigurable user interface, communication, data processing and data storage platform.

• Highly compact analyzer, including attachments

• Cellphones in-use on ISS and Small Satellites – space ready

• Potential basis for future personalized medicine and decentralized healthcare; need for lower healthcare costs
### Smartphone Diagnostics Development

<table>
<thead>
<tr>
<th>Institution</th>
<th>Laboratory</th>
<th>Cellphone Application</th>
<th>Citation</th>
</tr>
</thead>
</table>
LFA Construction for Cardiac Panel

Assay Calibration

<table>
<thead>
<tr>
<th>Troponin I [ng/mL]</th>
<th>Peak Height (Avg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1.0</td>
<td>0</td>
</tr>
<tr>
<td>2.5</td>
<td>42.1</td>
</tr>
<tr>
<td>5</td>
<td>68.1</td>
</tr>
<tr>
<td>10</td>
<td>185.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CK-MB [ng/mL]</th>
<th>Peak Height (Avg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2.5</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>43.8</td>
</tr>
<tr>
<td>10</td>
<td>65.4</td>
</tr>
<tr>
<td>40</td>
<td>215.1</td>
</tr>
<tr>
<td>100</td>
<td>493.2</td>
</tr>
</tbody>
</table>
LFA Construction – Dissolved Blood Gas Panel

Design of test strips for blood gas panel analysis

Multi-well flow-through cell for rapidly testing sensitive materials

Response Profile of Sensor Materials

Response to dissolved ppO₂ in water (0, 75, 115, 150 mmHg).

Response to dissolved ppCO₂ in water (0, 7.5, 23, 45 mmHg)

M. Krihak, PhD

Exploration Laboratory Analysis
Smartphone Diagnostics – Lateral Flow Assay Test Strip Reader

RAPID DIAGNOSTIC TEST (RDT) READER

✓ MULTIPLEXED DIGITAL EVALUATION OF LATERAL FLOW TESTS
✓ UNIVERSAL AND QUANTITATIVE
✓ COST-EFFECTIVE
✓ ACCURATE (CV < 2%)
✓ SENSITIVE (LIMIT OF DETECTION < 0.5% OD)
✓ INTEGRATED INTO THE CLOUD
✓ ENABLES SPATIO-TEMPORAL MAPPING OF DISEASES AND CONDITIONS

Courtesy of Holomic, LLC

M. Krihak, PhD

Exploration Laboratory Analysis
Holomic Mobile Phone Labs

Courtesy of Holomic, LLC
ELA Timeline

- Select for ground demonstration – 2015
- Select for flight demonstration – 2017
- Ground demonstration – 2018
- Flight demonstration - 2020
Summary

• Space environment and missions present unique challenges for ELA
  – Microgravity (control of bubbles in microfluidics)
  – Minimizing consumables/waste
  – Accommodation by the exploration medical kit (mass, volume)
  – Extended instrument performance throughout lengthy deployments
  – Extended shelf-life

• Possible technological solutions are under investigation
• Path for closing ExMC Gap 4.05 for ELA has been identified