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.
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
## 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
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 Chloride</td>
<td>pH</td>
<td>Neutrophils</td>
<td></td>
<td>ALT</td>
<td>Proteins</td>
</tr>
<tr>
<td>BUN</td>
<td></td>
<td>Abs. Neutrophils Count</td>
<td></td>
<td></td>
<td>Glucose</td>
</tr>
<tr>
<td>Creatinine</td>
<td></td>
<td>Lymphocytes</td>
<td></td>
<td></td>
<td>Ketones</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monocytes</td>
<td></td>
<td></td>
<td>Urobilirubin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Eosinophils</td>
<td></td>
<td></td>
<td>Bilirubin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PLT</td>
<td></td>
<td></td>
<td>Blood</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Urate</td>
</tr>
</tbody>
</table>

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 Technology

Spiral Vortexer
Capillary Collector, Saline/Waste
Nanostrips
Optical Block

M. Krihak, PhD
Exploration Laboratory Analysis

Courtesy of The DNA Medicine Institute
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)

rHEALTH (counts/run)

r² = 0.9978

Mean RU

Log[TNF-alpha] pg/ml

rHEALTH (counts/run)

ABX Micros 60 (counts/μL)

r² = 0.9978

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)

FLOW THROUGH CELL
- Sensor film (O₂)
- Optical window
- Sensor film (CO₂)
- Substrate
- Optical cable
- Water equilibrated with O₂/CO₂

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-TEMPORAT MAPPING OF DISEASES AND CONDITIONS

M. Krihak, PhD

Exploration Laboratory Analysis

Courtesy of Holomic, LLC
Holomic Mobile Phone Labs

Courtesy of Holomic, LLC

M. Krihak, PhD

Exploration Laboratory Analysis
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