ESTIMATING THE RATE OF OCCURRENCE OF RENAL STONES IN ASTRONAUTS

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Renal Stone Likelihood during Space flight

- Evidence of altered urine volume and chemistry
  - Lower output
  - Elevated Calcium (diet and bone demineralization)
  - Alterations in oxalate uptake
  - Countermeasures
    - Citrate treatments
    - Bisphosphonates
    - Individualized diet and intense exercise (ARED)
One way to estimate incidence

• Based on Bayesian analysis including
  – Summary of Urological Diseases in America 2004
  – JSC Control Population Data
  – Inflight/Post Flight Data (up to ~2012)

Astronaut - inflight 3.65 (+/- 0.46) events per 1000 person years
  – Purely related to incidence/diagnosis of a stone
  – Does not account for changes in urine chemistry or counter measures

Gilkey et al 2012 – NASA/TP -2012-217120
Can we do better?

• **Consider**
  – Kassemi et al* population balance equation (PBE) model has been shown to differentiate stone forming potential based on urine chemistry and crystallization kinetics in idealized representations of space flight and ground urine chemistry

• **Surmise**
  – The ability to quantitatively differentiate stone forming potential from a given set of urine chemistries can be used to better estimate the likelihood of stone formation in astronauts

• **Approach**
  – Develop a probabilistic simulation model utilizing the PBE model to distinguish the stone forming potential across the expected range of urine chemistry combinations for astronauts.

*Kassemi et al.  HRP-IWS 2016*
Renal Stone occurrence model
- Complex Simulation model of renal stone growth
- Couples deterministic model output and randomly sampled input parameters to quantify the risk of stone formation and treatment using MATLAB

Probabilistic model for Renal Stone Incidence Likelihood

Urinalysis Data → JESS → Stone Growth Model → Data Fit Model → Risk of Renal Stone
Key Components

Urinalysis Data
• Taken from astronaut pre-flight data, and Cleveland Clinic stone former data

JESS
• A commercial code that calculates the chemical speciation
• Outputs the RSS (SI) which is a measure of supersaturation

Stone Growth Model-Kassemi et al population balance model
• Takes in speciated urine chemistry
• Produces a population density of steady state crystal growth sizes distributed from 20 nm to 2 mm

Data Fit Model
• Takes in the crystal sizes for various data types and correlates to known incidence rates for those data types such as stone formers and non-stone formers

Risk Model Output
• Outputs the risk of renal stones
Data Fit Model Input: Kidney Stone Size

- Max Stone Size is defined as 1 stone/mL of urine

Datasets taken from
- Piertzky et al Renal Stone Formation Among Astronauts, Aviation, Space, and Environmental Medicine • Vol. 78, No. 4, Section II • April 2007, Pre and Post-flight
- Cleveland Clinic Stone former dataset
## Simulation Analysis – Incidence data

<table>
<thead>
<tr>
<th>Distributions</th>
<th>Minimum per 100,000 person years</th>
<th>Maximum per 100,000 person years</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postflight</td>
<td>396</td>
<td>1676</td>
<td>Maximum-Gilkey et al. “Bayesian Analysis for Risk Assessment of Selected Medical Events in Support of the Integrated Medical Model Effort”, NASA/TP - 2012-217120 Maximum- Derived from 2015 LSAH data request ID#: 10669; 6 CaOx events in 358 person years, interval 1 year post-flight</td>
</tr>
</tbody>
</table>

- All Distributions except the Post Flight max are multiplied by the a uniform distribution to remove the kidney stones of other varieties. 70.7 to 78.1% of kidney stones are calcium oxalate stones per Lieske et al 2006.
- **Only Non-Stone former, Stone former, and Post Flight values are currently used by the model**
Simulation analysis – Data Fit Model Flow Chart

1. **Takes in Data** - Max Stone size and Incidence rates
2. **Samples the number of incidences over 100,000 years for each data point of max stone size with the corresponding incidence distribution**
3. **Matches each set of incidences to a Poisson distribution with the form**
   
   \[ e^{b_1 + b_2 \times \text{maxStoneSize}} \]

4. **Repeats 10,000 times**
5. **Averages the total distributions and calculates the standard deviation**
Datasets Used for Mean Curve
• 8 Preflight Non-Stone formers
• 9 Post Flight Stone formers
• 9 Cleveland Clinic Stone formers
Conclusions and future work

Conclusion

• Prototype Completed
  – Designed to expand prior Bayesian estimates
  – Includes multiple factors related to renal chemistry and crystal formation
  – Relies on population and astronaut data to make rate estimates
  – Further data is needed before the model validation

Future Work

• Expand the training dataset to incorporate the entire application range
  – LSAH/LSDA correlated data request
  – Length of time from astronaut urinalysis measurement to stone formation
  – More astronauts pre, post flight, and post stone formation
  – More terrestrial stone former and non-stone former sample sets

• Address remaining programming and CM requirements
  – Final review and documentation to NASA standards

• Validation
  – Select data removed prior to model training
  – Used as referent data for performance assessment and validation