PROBABILISTIC MODELING OF THE RENAL STONE FORMATION MODULE

Integrated Medical Model
Exploration Medicine Capabilities Project

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Outline

• Overview of IMM
• Renal Stone Risk Module
• Probabilistic Wrapper – Front End
• Biochemistry Model
• Probabilistic Wrapper – Back End
**Integrated Medical Model (IMM)**

- IMM is a probabilistic tool – quantifies the probability and consequences of medical risks
- Identifies medical resources necessary to optimize health and mission success

**Potential Medical Condition**

Evaluate with IMM

**Likelihood of occurrence, probable severity of occurrence, and optimization of treatment and resources**
Renal Stone Risk Module

- Astronaut urine samples have exhibited characteristics associated with renal stone formation, demonstrating an increased risk that clinically significant renal stones could form in flight
- External module to IMM
  - Adds higher fidelity to model where little data is available
- Deterministic Model (*Kassemi et. al*)
  - Integrates physics and physiology into formation of renal stone based on probabilistic input
- Probabilistic Wrapper – feeds needed information into deterministic model and transforms output into a useful distribution of risk of renal stones
Probabilistic Wrapper: Front-End

Through Monte Carlo methods, randomly samples array of probability distributions to compile a set of random inputs into biochemistry and deterministic model.
Monte Carlo Sampling

- Lognormal probability distributions formed from $\bar{x}$ and $\sigma$ and number of desired MC samples (N) in MATLAB
  - Truncated to the 95th CI
  - Example:

$$P_{Ca} = \begin{bmatrix} X_{Ca_1} \\ X_{Ca_2} \\ \vdots \\ X_{Ca_N} \end{bmatrix}$$

- Parameters randomly sampled and placed into matrix
- Parameter matrix is divided by randomly sampled volume to create total concentrations (mol/L)

$$[M] = \left[ \frac{P_{Ca} \quad P_{Ox} \quad \cdots \quad P_{Creat}}{V} \right]$$

Parameters:
- Calcium
- Oxalate
- Uric Acid
- Citrate
- Sulfate
- Phosphate
- Magnesium
- Sodium
- Potassium
- Ammonium
- Creatinine (Creatine)

Example histogram of Calcium (truncated)
Biochemistry Model

- JESS Biochemistry model – compiles 100+ applicable urine chemistry reactions and computes outputs based on system parameters and thermodynamics
- Transforms total concentration matrix, M, via system of equations into free ion concentrations \( (c_i) \) based on urine chemistry reactions
- Free ion must be converted to activity \( (a_i) \) for deterministic model:

\[
a_i = \frac{\gamma_i c_i}{c^\ominus}, \quad \gamma_i = \text{species activity coefficient}
\]

\[
c^\ominus = \text{standard concentration}
\]
Biochemistry Model

• Relative Supersaturation calcium oxalate ($RS_{CaOx}$)
  – More of the dissolved material than could be dissolved by the solvent
  – RS: Metric that represents the ability of spontaneous crystallization of the solution
    \[ RS = \left[ C_{Ca} C_{Ox} \gamma_{CaOx} \right]^{1/2} \]

• Necessary outputs to deterministic model: activity (indirect), pH, temperature, pressure, $RS_{CaOx}$
**Probabilistic Wrapper: Back-End**

- Couples deterministic model output and randomly sampled input parameters to quantify the risk of stone formation and treatment
- Utilizes two major sections: (Initially design by Mike McRae and Travis Jackson)
  1. Probability of stone formation
  2. Probability that a stone passes spontaneously (without treatment)
Back-End Continued…

• **Stone Formation:**
  – Determined by Multivariate logistic regression equation below via MATLAB statistical functions
  – Additional parameters can be added with additional $\beta$ factors
    \[
    P(SF) = \frac{1}{1 + e^{-(\alpha + \beta_1[RS] + \beta_2\left[Cit/Ca\right] + \beta_3[TV] + \beta_4[pH] + \beta_5[Mg])}}
    \]

• **Stone Passage:**
  – Determined via spontaneous passage rates related to renal stone width and ureter stone location
  – Treatment determined by the probability of stone passage:
    \[
    P(Treatment) = 1 - P(Passage)
    \]
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