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Numerical assessment of CaOx renal calculi development in space using PBE coupled to urinary flow and species transport

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ABSTRACT

Recently collected astronaut data indicate that space travel has a profound impact on the nephron biochemistry with increasing risk of renal stone development during long duration missions. In this paper, a Population Balance Equation (PBE) model is developed to compute the size distribution of nucleating, growing and agglomerating calcium oxalate (CaOx) renal calculi as they are transported through the different nephron sections. The PBE model is coupled to a Computational Fluid Dynamics (CFD) model that solves for the steady state flow of urine, the concentrations of ionic species, calcium and oxalate, and the transport of the crystals along the nephron using a two-phase interpenetrating Eulerian framework. Simulation are performed based on measured averaged post-flight astronaut 24 h. urine biochemistry to assess the size distribution of the CaOx crystals developed under microgravity conditions. The important effects of agglomeration on the aggregate size distributions and the impact of wall friction on the CaOx volume fraction distributions are carefully examined. Simulations are also presented to indicate the important mixing effect that the cascading nephron configuration may induce during the passage of the particles through the various nephron subsections. Parametric numerical predictions for the microgravity astronaut biochemistry are compared to those for normal and stone-former subjects on Earth. It is concluded that under nominal conditions the largest calcium oxalate aggregate sizes developed in space will be still below the critical range for problematic stone development. However, computations also indicate that in microgravity the highest CaOx volume fractions occur next to the tubule and duct walls. This suggests that there may be an increased potential for wall adhesion and possibility of evolution towards critical stone sizes.

1. Introduction

Microgravity data collected in the past two decades has shown that space travel has a profound impact on astronauts' nephron biochemistry. Under weightlessness conditions, due to bone atrophy [1–3] and lower urine volumes caused by dehydration [4–5], both calcium (Ca) and oxalate (Ox) in the urine can become considerably more concentrated hence elevating the urinary CaOx supersaturation levels that is one of the main promoters of renal stone formation. There are other contributing factors such as the astronauts' high protein and sodium level intake that induce higher calcium and pH levels and provide nidi that serve as nucleation sites for CaOx precipitation [5–6]. The astronauts' higher pH levels will also lower the concentration of citrate, one of the primary inhibitors of CaOx growth and agglomeration [6–7]. All these changes in the astronauts' renal biochemistry tend to provide favorable conditions for increased nucleation, growth, and agglomeration of CaOx stones in the renal system.

In this light, risk of astronauts developing kidney stones has become a serious concern for NASA, especially, since the duration of future space expeditions will be increasing substantially. The concern seems to be justified since a recent survey of renal stone development in US astronauts has revealed 14 recorded episodes [1]. Several incidents occurred in the preflight period (n = 5) while other episodes (n = 9) were in the post-flight phase. The time period for the onset of symptomatic stone formation following return to earth ranged from 9 to 120 months after landing. Six out of the nine post-flight episodes occurred after 1994, which corresponded with the extension of the shuttle missions to 12 days. Four out of

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Nomenclature

B^o	nucleation rate
D	particle diameter
$D_{j,m}$	mass diffusion coefficient of species j in urine
G_D	linear growth rate
G_v	volumetric growth rate
K_b	nucleation rate constant
K_g	growth rate constant
$\dot{m}_{p,q}$	mass transfer rate from pth phase to qth phase
n_v	volume based particle population density
N	particle number density
p	pressure
R	particle radius
R_{pq}	momentum interaction force between p^{th} and q^{th} phases
RS	relative supersaturation of calcium oxalate in urine
S	supersaturation of calcium oxalate in urine
t	time
$\vec{u}$	velocity vector
h	height
Y_j	mass fraction of species j
t	time

Greek

α	volume fraction
β	particle agglomeration kernel
ρ	density
$\bar{\bar{\tau}}$	stress-strain tensor

Subscripts

Ca	calcium
Ox	oxalate
p	pth phase that transfers mass
q	qth phase that receives mass
j	species index
1	pertaining to urine
2	pertaining to calcium oxalate

the six kidney stones of known composition developed by the astronauts have also been calcium oxalate [2].

Because of unavailability of adequate and statistically significant microgravity and space data and the considerable danger that a clinically significant renal stone incident can pose to the astronauts' health and to the success of future missions, NASA has focused on using both probabilistic [8] and deterministic [9] computational models to assess the risks of renal colic for various mission scenarios. To address this need, in the present work, we present a comprehensive deterministic model for renal stone formation and transport through the nephron. This is accomplished by coupling the Population Balance Equation (PBE) for nucleation, growth and agglomeration of renal calculi to a Computational Fluid Dynamics (CFD) model that solves for flow of urine, the concentrations of the ionic species, calcium and oxalate, and transport of renal calculi along the nephron using a two-phase interpenetrating Eulerian approach.

CaOx stone development has been subject to various theoretical considerations; both in isolation [10,11] and in the context of its passage through the renal system [12–16]. The physical mechanisms that govern nucleation and crystal growth are relatively well known and have been subject to a comprehensive monograph by Nielsen and Christoffersen [11]. A coupled kinetics-transport treatment of CaOx crystal precipitation has been presented by Kassemi et al. [10] where special attention was devoted to urinary stone formation.

Finlayson [12] was the first to consider the ducts of Bellini and the pelvis as a system of continuous crystallizers in series and applied a Mixed Suspension Mixed Product Removal (MSMPR) analysis similar to the ones employed extensively in chemical reactor engineering to predict the size distributions for a population of nucleating and growing crystals. Subsequently, Finlayson and Reid [13] and later Kavanagh [14] concluded that in order for the calculi to become large enough to cause blockage, some kind of particle fixation or retention such as wall adhesion must take place. This became known as the *fixed particle* concept [13]. Finlayson's analysis, however, considered only nucleation and growth and neglected the important effects of agglomeration.

Roughly two decades after Finlayson's *fixed-particle* concept, Kok and Khan [15] used more appropriate data for the tubular dimensions and accounted for particle agglomeration, albeit, in a quite simplified manner, to show that tubular blockage may be possible even without particle fixation when agglomeration is taken into account. This has come to be known the *free-particle* concept. Robertson [16] complemented the previous theoretical treatments of the problem by considering the effects of tube wall, fluid drag and gravity and concluded that there is still a possibility that wall drag and gravity may delay the passage of stones travelling close to the tube walls to an extent that they would grow large enough to create an obstruction.

Although the precise mechanisms for kidney stone formation and growth are still not well-understood, recent studies by Kim et al. [17] and Evan et al. [18] using advanced endoscopic imaging and comprehensive physiological biopsies suggest three possible free/fixed pathways to stone formation: (a) nucleation and growth on the Randall plaque deposits in the papillae; (b) growth after adherence to a possibly injured section of collecting or Bellini ducts; (c) homogeneous nucleation and growth in the urine during passage through the nephron. The Randall plaque overgrowth mechanism seems to be the most common pathway for CaOx stone development in idiopathic stone formers.

In a previous work [9] that adopted the MSMPR treatment of the kidney as put forth by Finlayson, we developed an analytical PBE model for renal calculi formation and showed that alterations in astronauts' renal biochemistries due to exposure to microgravity and space environment can increase the propensity for development of larger CaOx crystalline sizes in the kidney during long duration missions. Subsequently, we also demonstrated through numerical simulations that the risk of renal stone development in Space can be mitigated, to a large extent, through dietary countermeasures such as citrate administration and enhanced hydration [19]. Unfortunately, due to the system level "lumped analysis" approach taken in these two studies [9,19], the crystallization process could not be coupled in a meaningful manner to the transport of the renal calculi through the nephron which is crucial for proper risk assessment.

In the present work, we assume that regardless of where the stone formation originates in the kidney, it is accomplished through the three coupled mechanisms of nucleation, growth, and agglomeration as described by the Population Balance Equation [20,21],. Using a coupled PBE-CFD model, we study both the formation and the transport of the CaOx crystalline through the