RISK ASSESSMENT OF BONE FRACTURE DURING SPACE EXPLORATION MISSIONS TO THE MOON AND MARS

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Abstract

The possibility of a traumatic bone fracture in space is a concern due to the observed decrease in astronaut bone mineral density (BMD) during spaceflight and because of the physical demands of the mission. The Bone Fracture Risk Module (BFxRM) was developed to quantify the probability of fracture at the femoral neck and lumbar spine during space exploration missions. The BFxRM is scenario-based, providing predictions for specific activities or events during a particular space mission. The key elements of the BFxRM are the mission parameters, the biomechanical loading models, the bone loss and fracture models and the incidence rate of the activity or event. Uncertainties in the model parameters arise due to variations within the population and unknowns associated with the effects of the space environment. Consequently, parameter distributions were used in Monte Carlo simulations to obtain an estimate of fracture probability under real mission scenarios. The model predicts an increase in the probability of fracture as the mission length increases and fracture is more likely in the higher gravitational field of Mars than on the moon. The resulting probability predictions and sensitivity analyses of the BFxRM can be used as an engineering tool for mission operation and resource planning in order to mitigate the risk of bone fracture in space.

Introduction

It is widely accepted that mechanical strain of bone is a stimulus for bone growth [1-6]. Studies have shown a correlation between engaging in physical activities that result in bone strain and an increase in bone mineral density (BMD) [7-11]. Consequently, prevailing theory holds that bone is maintained as a result of the repetitive strain experienced over the course of daily activities in Earth's gravity [12-22]. A decrease in BMD results when the mechanical stimulus is absent due to inactivity or the reduction of gravity. This phenomenon has been observed in individuals with a sedentary lifestyle, as a result of prolonged bed rest, after spinal cord injury and after spaceflight [23-34]. On Earth, reduced BMD is one factor which indicates a risk of bone fracture during the activities of everyday living. [30;35-37].

A bone fracture can be considered a structural failure of the bone, which occurs when the load placed upon the bone exceeds its structural strength [38-41]. Apparent bone strength is dependent on several factors including mineral content, prior microdamage, geometry, architecture, age and the nature of the applied load [30;35-37;42-47]. Loading that exceeds the strength of the bone can occur during an accident, such as a fall, where a high impact load is experienced. Bones can also be subject to fracture loads during normal activities, such as lifting an object, particularly for bones with compromised bone strength. Bone fracture at certain locations, such as the femoral neck and the lumbar spine, are usually highly traumatic injuries, especially in damaged or osteoporotic bone [48-53]. Treatment of these injuries requires, at best, immobilization or, at worst, surgery, and often leave the patient temporarily disabled [54-60].

During the exploration missions to the moon and Mars the astronauts will be in a reduced gravity environment for a period of months to years. Studies that have measured pre- and post-flight BMD through dual energy X-ray absorptiometry (DXA) report that astronauts lose an average of 1 – 1.6% of their bone mass per month in the spine, femoral neck, throchanter and pelvis [24] and an average of 1.7% in the cancellous tibia after one month of space flight [25]. Success of the future space exploration missions will depend on the astronauts' ability to perform physical activities, such as construction of a lunar or Martian base, with minimal threat of injury. However, there is a legitimate concern that their weakened bones will be more prone to fracture even during moderate physical activities, such as bending and lifting. There is also a risk of fracture due to the occurrence of an unexpected event, such as a fall from a ladder. Space missions are severely constrained in resources, and by their very nature, provide limited access to medical care. This can have a serious impact on the necessary time for healing, and could even lead to permanent disability and/or loss of mission or crew member [61-64]. Since the possibility of fracture exists and the impact to the mission could be substantial, it is crucial to quantify the risk of bone fracture during space exploration missions so that mitigation strategies can be engineered.

This paper provides an introduction to the Bone Fracture Risk Module (BFxRM), a mathematical model that has been constructed to calculate the probability of bone fracture during specific astronaut activities during space exploration missions. An overview is given of the key elements of model, including the mission parameters, the biomechanical loading models, the bone loss and fracture models, and the incidence rates of mission-related activities or events. Insight is given into the underlying uncertainties and assumptions of the model and the interaction of the key elements which ultimately produce predictions of fracture probability. The probability of bone fracture is presented for several mission scenarios and an analysis of the most sensitive parameters is given, exemplifying the value of the BFxRM for mission operation and resource planning.

Methods

The BFxRM is a scenario-based model. It estimates the probability of fracture at a particular skeletal site during a mission by considering the key activities or events of a mission, the resultant skeletal loading, and the dynamically evolving bone strength. See Figure 1 for a block diagram of the model. Inputs to the model include gender, gravitational environment, mission duration (see Table 1 for mission duration definition), whether the activities are internal (IVA) or external (EVA) to the vehicle, astronaut body mass, EVA suit mass and the pre-flight BMD level. At the core of the BFxRM is the calculation of a fracture risk index (FRI), which is the ratio of the actual skeletal load to the maximal load (Ultimate Load) that the bone can sustain. FRI is also commonly referred to as factor of risk. An FRI substantially below one indicates that the bone is likely to be strong enough to support the load. Conversely, an FRI above one indicates that there is a significant risk of bone fracture [39;65;66]. The load transmitted to the bone in question was estimated using biomechanical models, and a relationship between BMD and Ultimate Load (UL) was established to determine the maximal load. The probability of fracture for the mission is the combined probability of a fracture occurring during an event, which is calculated from the FRI, and the probability of the event occurring during the mission, which is based on the incidence rate of the event (See Figure 1). Fracture probabilities were calculated with Crystal Ball software (Oracle, Denver, CO), using Monte Carlo and Latin Hypercube simulations. For each activity or event, the fracture probability was calculated during 100,000 trials. An estimate of the fracture probability was defined by the mean, standard deviation and 5% and 95% percentiles of the 100,000 fracture probability calculation trials. Multiple trials were performed in order to account for uncertainty in the model parameters, which were defined as a distribution of values. In addition, the multiple trials were used in order to calculate the probability for the entire mission by using a different mission day (from a uniform distribution) during each trial.

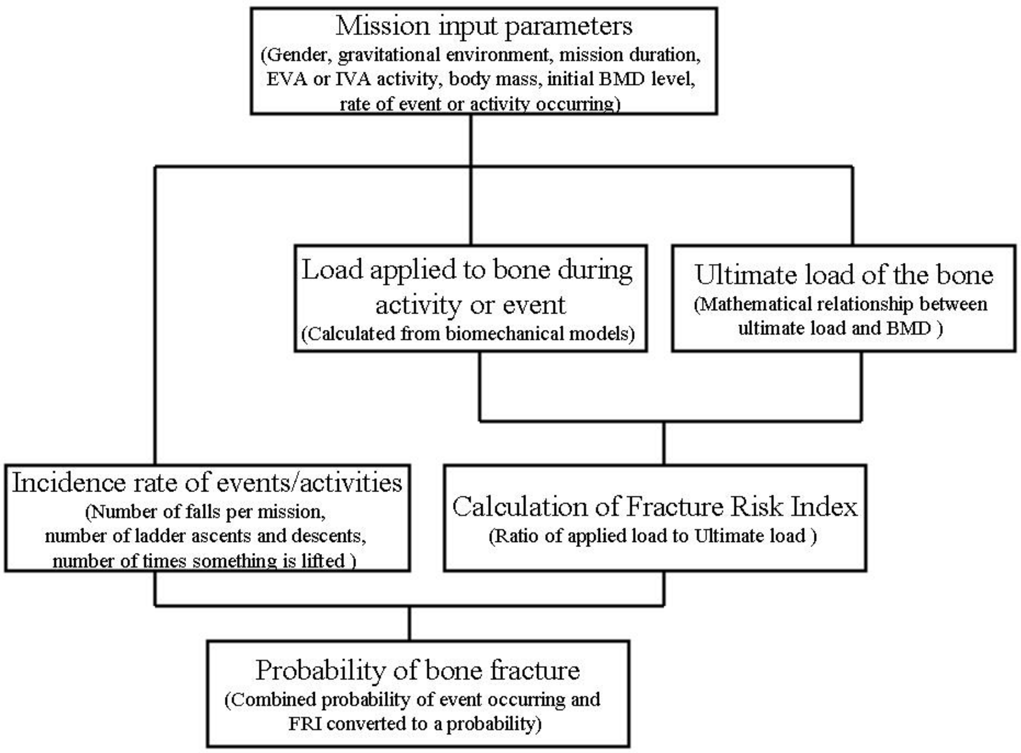


Figure 1. *Block diagram of the Bone Fracture Risk Module.*

Table 1. *Definition of mission durations.*

Duration length	Mission location	Transit time to location (days)	Length of stay (days)	Transit time back to Earth (days)
Short	Moon	3	8	3
Long	Moon	5	170	5
Short	Mars	162	40	162
Long	Mars	189	540	189

A library of biomechanical loading models was developed to estimate the loading experienced at different skeletal sites for a variety of loading conditions. The loading models that will be discussed in this paper include 1) the load on the femoral neck during a fall to the side (FN-side fall); 2) the load on the lumbar spine while holding a load with the trunk flexed (LS-flexed trunk); 3) the load on the lumbar spine at impact after a fall from a height but landing on two feet (LS-feet first fall). The FN-side fall loading model was based on models developed by Robinovitch et al for side falls [67]. These models were augmented with data regarding the direction of fall [68-71], the active response to the fall [72;73] and estimates regarding the contribution of the EVA suit to fall impact dynamics [74]. The integration of these contributors was used to estimate the skeletal forces imparted to the proximal femur during standing falls in the reduced gravity environments of the moon and Mars.

The LS-flexed trunk model used a linked-segment model of the body in a flexed trunk body posture. The forces and moments at the lumbar spine level due to the weight of the upper body and the load held were assumed to be balanced by the erector spinae muscle force and were computed assuming static equilibrium. The sum of the forces and moments were used to compute the vertebral compressive force [65;75-77]. The LS-feet first fall model was based on a mass-spring-damper model, similar to those developed by others [78-81]. As shown in Figure 2, the LS-feet first model incorporated three masses (head, arms and trunk (HAT), pelvis and legs (PL), and feet (F)), a spring and damper between the HAT mass and the PL mass to represent the stiffness and damping characteristics of the lumbar spine [82-85], a spring between the PL mass and the F mass to represent the stiffness characteristics of the legs [78;86-95] and a spring and damper between the F mass and ground to represent the stiffness and damping characteristics of the ground [78;87;89;91;96;97]. The load on the lumbar spine was calculated using a system of linear first order differential equations, with impact velocity as the initial condition.

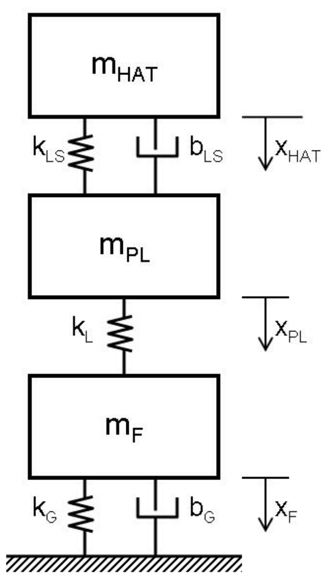


Figure 2. *Mass-spring-damper model of the LS-feet first model. The mass of the head arms and trunk (m_{HAT}), pelvis and legs (m_{PL}), and feet (m_F); the stiffness of lumbar spine (k_{LS}), legs (k_L), and ground (k_G); the damping characteristics of lumbar spine (b_{LS}), and ground (b_G); and the displacement of m_{HAT} (x_{HAT}), m_{PL} (x_{PL}), and m_F (x_F) are shown.*

Bone-loss data resulting from space travel is sparse and does not clearly establish the time course that should be expected in long-duration spaceflight. In an attempt to bound the problem, the available data on astronaut BMD [27] were fitted to define bone loss as a function of time using both linear and exponential approximations. These relationships were used to calculate the decrease in bone density as a function of mission elapsed time. The predicted BMD at the time of fracture was then used to determine the maximal loading above which fracture occurs.

Many studies have sought to correlate bone quality with the loading conditions leading to fracture. There are varied approaches predicated on a critical skeletal loading, or, alternatively, a critical skeletal stress. Dependent variables include some measure of bone density, and, in some cases, bone geometry, load orientation, and bone structure, among others. Ebbesen et al. quantitatively compared some of these correlations by characterizing BMD, bone mineral content (BMC), ash density, and vertebral cross-sectional area in L3 vertebrae (n = 101) and then loading the specimens to failure [98]. They concluded that BMD is better correlated to the Ultimate Load (UL) than to the Ultimate Stress. Due to the availability of data on BMD, we therefore used UL as a measure of bone strength. Several *ex vivo* cadaver studies in terrestrial populations, identified in Table 2, were used as a basis for specifying the relationship between the UL and BMD in our model [52;98-100]. In all cases, vertebrae were exposed to steadily increasing uniaxial compression until fracture occurred.

Table 2. *Key parameters from studies of bone fracture where individual vertebral specimens were subjected to uniaxial compressive loading.*

Population	Age (yrs) Mean ± Std Range	Number of Specimens	Vertebral Level	Loading rate (mm/s)	BMD (g/cm^2) Mean ± Std	UL/BMD Slope ($kN/g/cm^2$)	Ref
8F, 10M	66 ±17.3 29-89	287	T1-L5	0.004	0.515± 0.178	11.6	[98]
51F, 50M	57.1 18-96	101	L3	0.083	0.617± 0.133	17.3	[100]
13F	72.5±9.7	18	T7-T11	0.423	0.294± 0.672	5.3	[52]
6F, 16M	52-75	61	L3–L5	1.500	0.809± 0.201	7.5	[99]

Little data is available in the literature to quantify the effect of loading rate on fracture, but it does suggest that the slope of the UL vs. BMD curve decreases with increasing loading rate (See Table 2; this trend continues in [101;102], albeit with relatively sparse data). The dominant failure mode under static loading is a crush fracture. More complex failure modes, such as burst fracture are possible with dynamic loading. While we are not attempting to model extremely high-energy impacts, we wanted to examine moderate energy impacts, as in a relatively low fall onto two feet. Consequently, for dynamic loading, we used a dataset at a higher loading rate [99] (yellow line in Figure 3). For static loading, as in holding a load with the trunk flexed, we pooled two of the studies with similar demographics and experimental conditions to broaden the dataset and introduce the effect of spinal location (blue line in Figure 3). Ebbesen et al. concluded that a linear fit was adequate in his BMD range, although a quadratic fit was slightly superior [98]. Certainly, the quadratic fit would be necessary at BMDs below his experimental range to avoid a negative Ultimate Load. In order to accommodate the possibility of very low BMD in our fracture model we used data from a severely osteoporitic population [52] for BMD falling below 0.4 under any loading conditions (red line in Figure 3). The fracture model in Figure 3 shows the linear fits used for BMD below 0.4 (red line), static loading with BMD above 0.4 (blue line), and dynamic loading for BMD above 0.4 (yellow line).

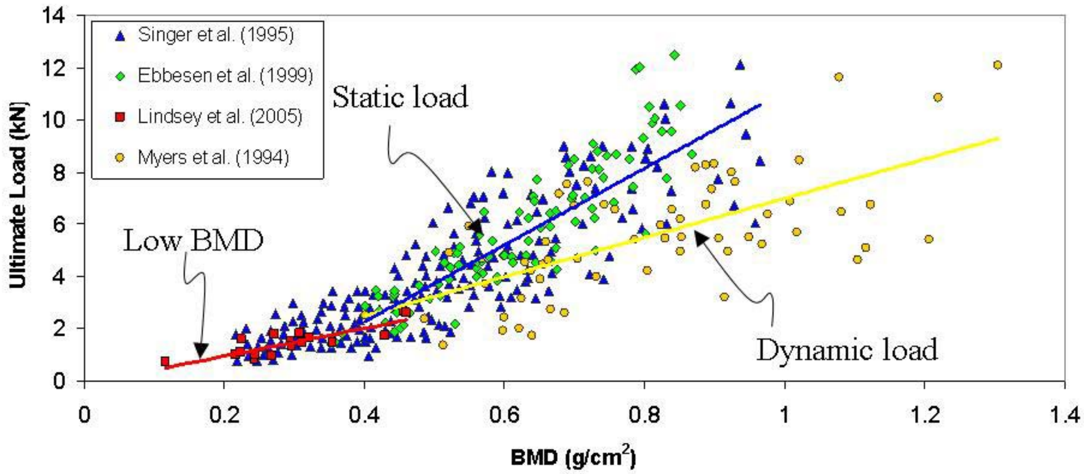


Figure 3. *Fracture load model with underlying datasets. For BMD<0.4, the fracture model follows the red line. For higher BMD, static loads follow the blue trendline, and dynamic loads follow the yellow line.*

In our model, the FRI was calculated as the ratio of the applied load, calculated from the biomechanical loading models, to the Ultimate Load, determined from Figure 3 using the predicted BMD at the time of the event. The FRI was converted to a probability based on the work of others [80], where a logistic regression was used to identify a mathematical relationship between FRI and fracture probability by comparing post incidence fractures to controls. For our model, the parameters of the equation used by Davidson et al. were modified to incorporate the findings of Kannus et al. The references therein utilize the relation that a fracture is most likely when the load applied to the bone is within one standard deviation of the Ultimate Load [74].

The rates of occurrence from past missions were used to calculate the probability that particular events would happen in the modeled mission scenarios. Using Apollo EVA films and astronaut reports, the rate of occurrence of a fall to the side was qualitatively estimated to be once per EVA. The rate of occurrence of a fall onto two feet was estimated from the number of ascents and descents of the Lunar Lander ladder. The frequency at which astronauts engage in activities that require holding a weight with a flexed trunk was estimated from a list of the tasks performed during the deployment of an Apollo lunar surface experiments package (ALSEP) during an Apollo 15 EVA [103]. The rate of occurrence of these events and activities was converted to a probability assuming a Poison distribution.

The model parameters contain aleatory uncertainty and epistemic uncertainty. Aleatory uncertainty is the uncertainty associated with the natural variation in population. This type of uncertainty is present in the parameters of the model, such as body mass, body segment mass and lengths, preflight BMD levels, etc., due to the anatomical variation present among the astronaut corps. Assuming the use of accurate data for defining these parameters, the ability to reduce this uncertainty is minimal. To account for the variations, distributions of values were created for the model parameters. Epistemic uncertainty results from incomplete information about the parameters or the interaction of the parameters within the model, either because measurements haven't been made, because the measurements are difficult to make, or because equally valid, competing assumptions must be considered within the model. Examples of epistemic uncertainty in our model include location of the center of mass of the upper body, the linear or exponential rate of bone loss in space, the mass of an object the astronauts might lift, etc. To bound the epistemic uncertainty in the model, a range of possible values, based on the best available data, for the uncertain parameters were incorporated into a distribution of values. During each simulation trial, a different value from each parameter distribution was used in the calculation of fracture probability.

Results

Example output

Figure 4 provides an example of the output of the BFxRM. Shown in the figure is a distribution of the calculated probability of lumbar spine fracture in a male astronaut landing on two feet after a 1 m drop during an EVA of a long duration mission to Mars. The mean probability, standard deviation, 5th and 95th percentile probability for this scenario and several other mission and event scenarios are tabulated in Table 3. The probability of fracture is less during short-duration missions to the moon due to decreased time in space and therefore, less severe bone loss, as well as lower gravitational level (roughly one-sixth of Earth gravity) The probability increases as the missions become longer and in the higher gravity environment of Mars (roughly two-thirds of Earth gravity). These results can be seen in Figure 5, a graphical illustration of the probability of bone fracture for different activities during missions to the moon and Mars.

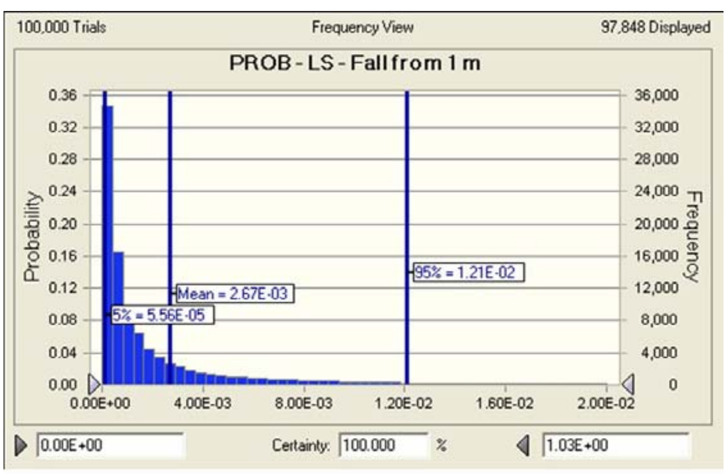
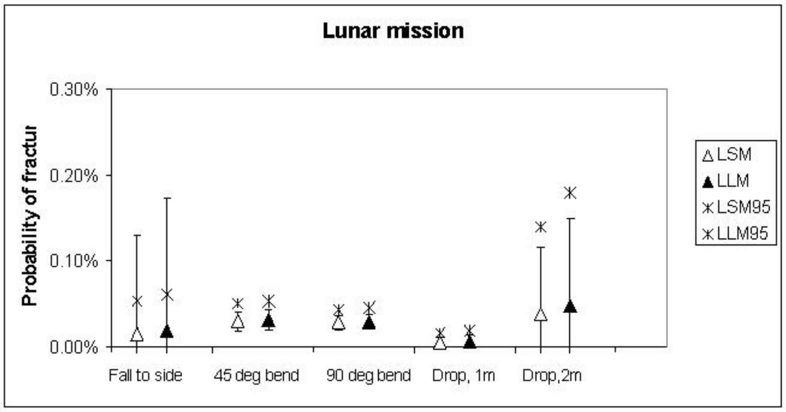


Figure 4. *Example output of the BFxRM showing the probability distribution for fracture of the lumbar spine by a male astronaut due to a 1m fall during an EVA during a long duration, Martian mission. Shown here is a screen shot from Crystal Ball software (Oracle, Denver, CO).*

Table 3. *Probability of fracture for several different mission scenarios for male astronauts.*

Activity or event	Mission location	Mission duration	EVA or IVA	Mean	Std	5th	95th
Femoral Neck Fracture							
Fall to side	Moon	Short	EVA	1.50E-04	1.15E-03	3.30E-07	5.36E-04
Fall to side	Moon	Long	EVA	1.94E-04	1.54E-03	3.47E-07	6.15E-04
Fall to side	Mars	Short	EVA	1.44E-03	7.66E-03	1.15E-06	4.85E-03
Fall to side	Mars	Long	EVA	2.47E-03	9.95E-03	1.68E-06	1.15E-02
Lumbar Spine Fracture							
45º trunk flexion, holding a load	Moon	Short	EVA	3.03E-04	1.06E-04	1.80E-04	5.03E-04
90º trunk flexion, holding a load	Moon	Short	IVA	2.87E-04	7.83E-05	1.92E-04	4.35E-04
Fall from 1m, landing on two feet	Moon	Short	EVA	5.42E-05	6.18E-05	4.80E-06	1.64E-04
Fall from 2m, landing on two feet	Moon	Short	EVA	3.86E-04	7.67E-04	1.77E-05	1.40E-03
45º trunk flexion, holding a load	Moon	Long	EVA	3.18E-04	1.17E-04	1.84E-04	5.39E-04
90º trunk flexion, holding a load	Moon	Long	IVA	2.97E-04	8.58E-05	1.95E-04	4.59E-04
Fall from 1m, landing on two feet	Moon	Long	EVA	6.21E-05	7.64E-05	5.26E-05	1.91E-04
Fall from 2m, landing on two feet	Moon	Long	EVA	4.81E-04	1.02E-03	2.00E-05	1.79E-03
45º trunk flexion, holding a load	Mars	Short	EVA	2.32E-03	2.71E-03	5.09E-04	6.59E-03
90º trunk flexion, holding a load	Mars	Short	IVA	1.13E-03	9.57E-04	3.71E-04	2.79E-03
Fall from 1m, landing on two feet	Mars	Short	EVA	1.11E-03	2.32E-03	3.85E-05	4.38E-03
Fall from 2m, landing on two feet	Mars	Short	EVA	5.30E-03	5.60E-05	1.78E-04	2.01E-02
45º trunk flexion, holding a load	Mars	Long	EVA	6.21E-03	1.94E-02	6.11E-04	2.01E-02
90º trunk flexion, holding a load	Mars	Long	IVA	2.13E-03	5.53E-03	4.20E-04	6.05E-03
Fall from 1m, landing on two feet	Mars	Long	EVA	2.67E-03	5.45E-03	5.71E-05	1.21E-02
Fall from 2m, landing on two feet	Mars	Long	EVA	8.30E-03	1.03E-02	2.90E-04	2.94E-02



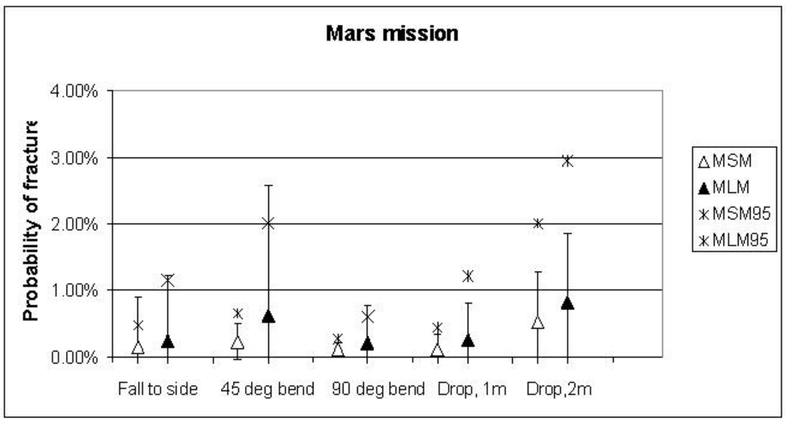


Figure 5. *A graphical illustration of the probability of bone fracture for male astronauts during various activities or events during a lunar or Martian mission. LSM = Lunar short mission, LLM = Lunar long mission, LSM95 = LSM 95th percentile, LLM95 = LLM 95th percentile, MSM = Martian short mission, MLM = Lunar long mission, MSM95 = MSM 95th percentile, MLM95 = MLM 95th percentile.*

Sensitivity analysis

An analysis was performed in order to determine the most sensitive model parameters, where small changes to these parameters cause a large variance in the probability calculations. The four most sensitive parameters in the FN-side fall models are associated with the loading calculation. The fifth most sensitive parameter in the FN-side fall model is the starting BMD value. For the LS-flexed trunk model, the most sensitive parameters are the anthropometric values used in the loading model, the mass of the lifted object, the starting BMD value and the astronaut mass. For the LS-feet first fall model, the most sensitive parameter is the incidence rate of a fall from a ladder, followed by loading model parameters, the relationship between BMD and UL and then astronaut mass.

Discussion

A model that quantifies the risk of a bone fracture during a long duration space mission has been developed. The uncertainties associated with the conditions that are necessary for a fracture to occur have been bounded in the model. The model predicts an increase in the probability of fracture as the mission length increases and fracture is more likely in the higher gravitational field of Mars than on the moon. The resulting probability predictions and sensitivity analyses of the BFxRM can be used as an engineering tool for mission operation and resource planning in order to mitigate the risk of bone fracture in space.

The large uncertainty bands illustrate the need for additional information. As new data becomes available it can be easily incorporated into the model to increase fidelity and to reduce epistemic uncertainty surrounding the risk of bone fracture during space exploration missions. The sensitivity analysis provides guidance on the key factors controlling fracture risk. This insight can be used to most efficiently mitigate risk through, e.g., potential modifications to the astronaut's habitat, equipment, training, and operations plan.

Simplifications were made during model development, particularly in the biomechanical loading models. Quantification of loading forces is not easily achieved. In vivo measurements require invasive implantation of strain gauges or pressure sensors. Therefore, instead of direct measurements, the loads on the bone were found indirectly, through mathematical estimation with biomechanical models. Skeletal loading results from a complex interaction between external objects, skeletal muscles, tendons, ligaments, other tissues and bones. Simplifications of these interactions were essential to produce a practical, useful biomechanical model. Examples of the simplifications used in our biomechanical models include the assumption that the erectae spinal muscle is the only muscle that counteracts the weight of the torso and the assumption that the stiffness and damping characteristics of the spine, legs and ground are linear.

Data available in the literature that most closely matched our demographics and loading situations were used to develop our relationship between UL and BMD. However, due to the lack of available information, we were not able to distinguish differences in UL based on gender, nor did we include effects of off-axis or torsional loading. It is also important to note that experimental studies of bone strength tend to have a preponderance of elderly subjects, as opposed to athletic, middle-aged astronauts, which may lead to conservative model predictions early in the mission. Finally, aging imposes a loss in the mineral content of bone as well as a modification of the bone microarchitecture, both of which contribute to fracture susceptibility. From the standpoint of the microarchitecture, it is unclear whether "space aging" of bone is comparable to aging bone on earth.

Since the aim of this work is prediction of a medical event, validation methods that compare our results to clinical observation are needed. Validation of our model against data in the literature will be reported in detail elsewhere [104], but summarized here. For the FN-side fall model, the FRI calculated with our model for a fall to the side on Earth from a 1m fall height was in good comparison to that calculated in a study by Lang et al [105]. For the LS-flexed trunk model, the loads on the lumbar spine calculated with our model were compared to those reported by Duan et al. and Bouxsein et al [65;76]. For the LS-feet first fall, the peak ground reaction force calculated with our model was compared to the peak ground reaction force measured with force plates in the studies of others [87-89;106;107]. All of the literature data fit within the uncertainty bands of our calculations. For the LS-feet first fall model, 100,000 FRI calculations were made with a distribution of fall heights which corresponded to the fall height distribution reported in Goonetillike et al [108]. This study reported the percentage of patients who fractured their lumbar spine after experiencing a fall from a height within the distribution. The percentage of our FRI calculations above 1, matched well with the percentage of fractures from the patient population Goonetillike et al. studied. Additional clinical validation efforts are also underway to further validate the model.

This model has applications as an engineering tool. For example, it could be used to determine the height for ladders above which guards should be added to prevent falling. It could be used to determine the limits on the size of a load that can be safely lifted by an astronaut after so many days in space. It can be used to determine the optimal type and amount of medical resources that should be taken on the mission and it can be used to determine the most beneficial medical training for the crew.

Conclusion

A model has been developed that bounds the uncertainty associated with the risk of bone fracture in space. It is focused on fractures of the femoral neck and the lumbar spine, since these regions are particularly sensitive to bone loss and their fracture could lead to catastrophic consequences for the crew and/or mission. Biomechanical models of the most likely activities that would lead to fracture were developed to determine the applied loads at specific skeletal sites. Models of bone loss as a function of mission duration were built on the best available astronaut data. Bone fracture models were created for both the femoral neck and the lumbar spine, based on data from terrestrial populations subjected to comparable loading conditions. Several mission scenarios were examined, resulting in fracture probabilities, as well as sensitivity analyses. This model shows great promise as an engineering and planning tool to reduce the risk of bone fracture during space missions.

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