Potential of Neuromuscular Electrical Stimulation as a Bone Loss Countermeasure in Microgravity

Thomas J. Abitante; Mary L. Bouxsein; Kevin R. Duda; Dava J. Newman

INTRODUCTION: For future long-duration spaceflight missions, additional methods of loading the skeleton may be required to supplement exercise to minimize bone loss. Neuromuscular electrical stimulation (NMES) can elicit muscular contractions that create strain on bone. However, the potential effectiveness of NMES on the proximal femur during disuse is not known.

METHODS: We measured the maximum isometric force of NMES-induced contractions of the rectus femoris and the hamstrings of 10 subjects (5 male, 5 female), sitting with the hips and knees at 90 degrees of flexion. We employed 2-D biomechanical models of the knee and hip to estimate the hip joint reaction forces, applied these forces to a generic femur finite element analysis model, and qualitatively compared the peak principal strains of the proximal femoral neck to the peak strains modeled in previous studies for other forms of exercise.

RESULTS: The average peak tensile/compressive strains were 1380 ± 719 με/-2179 ± 1130 με and 573 ± 345 με/-900 ± 543 με for the male and female subjects, respectively. While results varied between studies, the strains achieved during NMES generally were comparable to those achieved during walking or stairs, with some individuals matching higher intensity activities.

DISCUSSION: This study demonstrated that isometric NMES contractions of the thigh muscles can create strain in the proximal femoral neck similar to that achieved during low impact activities. While NMES alone will unlikely create a sufficient daily strain stimulus to prevent bone loss, it will likely improve the current spaceflight countermeasures by adding more frequent loading throughout the day.

KEYWORDS: strain model, exercise countermeasures, long duration spaceflight.

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Astronauts aboard long duration spaceflight missions are at risk of detrimental effects associated with micro-gravity, including a substantial loss of bone mineral density (BMD), as high as 1–2% per month, in the lower body.[21] Currently, exercise is prescribed as the primary countermeasure to reduce the rate of bone loss,[22] with heavy resistance training and proper nutrition increasing the efficacy.[37,39] Nevertheless, the rate of bone loss varies greatly among astronauts, with many at an increased risk of fracture[41] on a future mission beyond Low Earth Orbit (LEO) to the Moon or Mars.[31] The difficulty in maintaining BMD can be attributed to the fact that astronauts experience negligible skeletal loading outside of the exercise block, whereas the mechanisms that trigger bone maintenance are more responsive to more frequent skeletal loading spread throughout a given day.[35] Unfortunately, the solution cannot be simply adding more exercise. The current exercise regimen (2 h per day) results in an increased need for water, food, and carbon dioxide removal, which may not be as logistically feasible beyond LEO.[36] Furthermore, an additional increased energy expenditure may be difficult to compensate for, creating a negative caloric balance which can hinder the benefits of the exercise.[19] Additionally, future long duration

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spacecraft will be significantly smaller and will not be able to accommodate the mass and power of the three exercise machines currently in use, potentially reducing the variability and intensity of exercises one can perform. While pharmacological countermeasures have been recently explored[20,37] and smaller integrated exercise devices[44] and new exercise regimens are in development,[13] investigations into nonexercise based methods to maximize the daily loads on the skeletal system are warranted.

Neuromuscular Electrical Stimulation (NMES) is a technique that uses electrical pulses to cause involuntary muscular contractions.[6] Repetitive daily muscular contractions with NMES can attenuate the bone loss in the tibia and the femur associated with disuse from spinal cord injury,[11] as well as increase bone parameters in rodent hind limbs.[16] NMES can also potentially address some of the shortcomings of the current spaceflight exercise countermeasure regimen. The energy expenditure during isometric NMES contractions of the lower limbs is less than that seen with the ISS cycle ergometer,[15,42] and it can be used in microgravity with minimal discomfort and equipment such that other work can be performed simultaneously, allowing NMES to be administered throughout the day outside of the exercise block. Additionally, simultaneous co-contractions of agonist-antagonist muscles such as the quadriceps and hamstrings muscles can reduce the net joint movement, which would be crucial for safe application in microgravity.[26]

The potential effectiveness of NMES as a bone loss countermeasure in healthy individuals is unknown. The currently accepted theory concerning bone health is that mechanosensors at the cellular level detect mechanical loading in the form of strain.[14] The total amount of loading that is required to maintain bone mass and structure is often referred to as the daily strain stimulus, which is determined by the magnitude of the strain, and the number of loading cycles or repetitions.[33] To better understand how to reduce BMD loss in the proximal femur in postmenopausal women, the bone strain associated with low impact activities like walking[4,12,17] and high intensity resistance training have been modeled using finite element analysis.[24,32] Presently, no finite element analysis model has been created to estimate the strain on the proximal femur from the internal forces produced by isometric NMES contractions in humans. Like the models used for exercise in postmenopausal women, the peak strains from the NMES contractions could indicate NMESs potential to reduce bone loss on long duration spaceflight.

Exercise interventions to prevent bone loss report varying results, but generally high impact activities like running or jumping and high intensity resistance training can inhibit bone loss.[5] If NMES can create sufficiently high strains comparable to that of high impact or resistive exercise, it could replace some components of the current exercise regimen or allow for a greater frequency of exercise-like forces throughout a given day. Low impact activities such as walking alone are not sufficient to inhibit bone loss unless at very high repetitions,[7] but walking in combination with other activities such as high impact or resistance training can potentially reduce bone loss.[25] If NMES can only replicate low impact activities such as walking, it could be used to supplement exercise by adding additional loading throughout the day, without compounding the negative side effects of excessive exercise. In short, is it possible to add "walking" throughout the astronauts' day?

The purpose of the current study was to model the internal forces produced by isometric NMES contractions of the rectus femoris and hamstring complex on the bone and estimate the strain induced on the proximal femur using finite element analysis to allow a qualitative comparison of the peak strains to that of other exercises modeled in previous studies in order to access the potential of NMES as a spaceflight countermeasure, and whether it could supplement, or even replace some of the current spaceflight exercise regimen.

METHODS

Subjects

There were 10 subjects who volunteered to participate in this study (5 male, 27 ± 2.7 yr old, and 5 female, 28.5 ± 4 yr old). The experimental procedures were approved by the Institutional Review Board at the Massachusetts Institute of Technology, protocol number 1810570889. All subjects were recruited from the Massachusetts Institute of Technology student population. All subjects were required to be free of any ongoing knee injury and provided written informed consent prior to participating in the study. Subjects were instructed to avoid strenuous lower body exercise for at least 24 h prior.

Upon arrival, we recorded anthropometric measurements, including weight, femur length, medial distal femoral condyle radius (measured from the center of knee rotation to the lower edge of the condyle while the knee is at 90°), and pelvic height (measured as the distance from the greater trochanter of the femur to the superior edge of the lateral iliac crest while seated with the hip at 90°).

Equipment

The NMES device we used in this study was a custom built, single channel, voltage-controlled device developed at the Massachusetts Institute of Technology (MIT) Human Systems Lab (HSL) in collaboration with MIT Portugal. The device is comprised of an Arduino microcontroller, controlled via the Arduino software,[27] and a muscle stimulation unit (MSU), which has two connections for cutaneous electrode attachment. The electrodes used were 4" x 2" rectangular electrodes (Ultrastim X, Axelgaard Manufacturing Co., Fallbrook, CA). The MSU delivers a biphasic pulse with four individually customizable parameters: pulse amplitude (V), pulse frequency (Hz), and positive and negative pulse widths (μs), which when combined are referred to jointly as the pulse width or pulse duration. Additionally, the duty cycle can be customized through the Arduino software.

We built a custom knee dynamometer rig in the MIT HSL for use in this study (**Fig. 1**). The rig was designed to prevent movement, resulting in isometric, thigh muscle contractions.

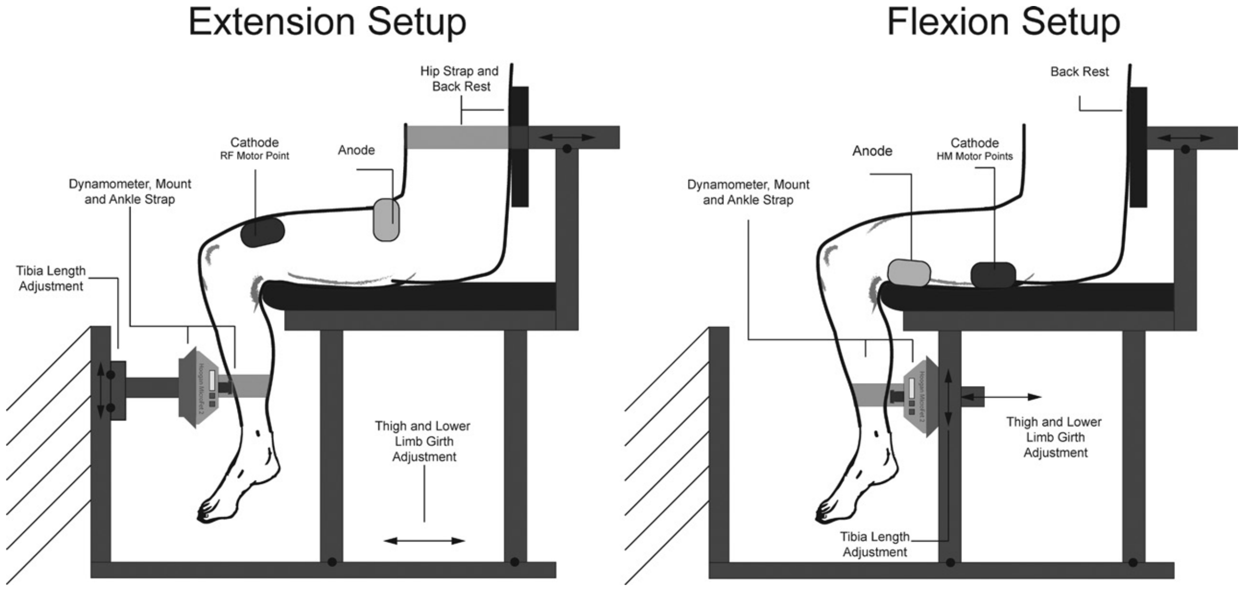

Fig. 1. NMES dynamometer rig built in the Massachusetts Institute of Technology Human Systems Lab for this study. The Hoggan MF2 dynamometer could be adjusted vertically to account for different lower limb lengths, the seat could be adjusted horizontally to account for different lower limb girths, and the backrest could be adjusted horizontally to account for different thigh lengths.

Therefore, the NMES administered in this fashion can be considered NMES against a fixed resistance (NMES-FR). The rig utilizes a Hoggan MicroFET 2 (MF2) handheld dynamometer for force measurement, which was secured with a 3D printed mount. The rig could be set up in either knee extension, or knee flexion configuration. The seat of the rig could be slid forward or backward to ensure that firm, constant contact between the lower leg and MF2 was achieved. A backrest was utilized to prevent hip extension during hamstring contractions, and a seatbelt was utilized to prevent hip flexion during rectus femoris contractions.

Procedures

We recorded the isometric muscle contraction force of two different muscles: the rectus femoris (RF), and the hamstring complex (HM). We placed the distal RF electrode longitudinally on the muscle belly, as identified with the leg at full extension, and the proximal electrode transversely across the proximal thigh, below the hip crease and in line with the distal electrode. We placed the distal HM electrode laterally above the knee crease, just medial to the bicep femoris tendon, and the proximal electrode over the muscle bellies of the HM muscles, as found when the subject was flexing the HM while standing. Both electrodes were placed longitudinally. The HM muscles were treated as a singular unit based on the inability to place the electrode in a way that would reliability delineate between the bicep femoris long head, semitendinosus, and the semimembranosus. Each muscle was activated individually with the rig either in the extension or flexion configuration for the RF or HM respectively. We followed an identical calibration and testing protocol for the RF and the HM.

First, with the subject not sitting within the knee dynamometer rig, three NMES-FR contractions were delivered at a cadence of 1 s on, 3 s off at a low power. The power level of the pulse was determined by changing the pulse width of the electrical signal with the amplitude held constant. The pulse width was then slightly increased, and the three NMES-FR contractions were delivered again. We repeated this process until the subject stated that the intensity of the three contractions was at a maximum tolerable level. The maximum tolerable level was a subjective metric, defined as the point at which the subject felt they would be able to talk or read without distraction from the contractions. This metric was used as the goal would be that astronauts could perform other tasks during the administration of a NMES treatment. During this process, we instructed the subjects to either read or talk during the contractions to aid in this determination.

Following the determination of the peak power for a particular muscle, we slightly reduced the intensity of the NMES-FR, and the subject was positioned within the dynamometer rig. The intensity was reduced to ensure that any discomfort from the contractions was at a tolerable level. For both muscles, we measured the knee angle and the distance from the knee center of rotation to the MF2. Additionally, when in the extension configuration, we measured the vertical distance from the hip joint (measured as the greater trochanter of the femur) to the center of the seatbelt, and when in the flexion configuration, we measured the vertical distance from the hip join to the top of the posterior edge of the iliac crest (assumed to be the center of pressure on the back rest). The subject then received two bouts of four contractions at a cadence of 1 s on, 3 s off, with the isometric force being recorded by the MF2.

To estimate the internal forces from the measured external muscle forces, we constructed simple biomechanical models of the knee and hip. The knee model was used to take the external measured force and determine the internal muscle forces for the RF and the HM. The hip model was used to take the internal muscle forces as determined by the knee model and estimate the hip joint reaction forces (HRF) from the RF and HM. Additionally, we used these models to estimate the net joint torques at the knee and hip, which could result in unwanted movement while in microgravity.

The knee was treated as a 2-D joint, with no forces acting in the transverse plane. The hip model was also treated as 2-D, with only the sagittal moments arms of the muscle being included, as the muscles overwhelmingly acted in the direction of the femur. This allowed the seatbelt and back rest reaction forces to be calculated. However, the joint reaction forces in the hip model were treated as 3-D, with the transverse joint reaction forces being equal to the transverse components of each of the HM and RF muscle forces. Additionally, in both the knee and hip, we assumed the joint reactions were placed at the center of the joint to greatly simplify the calculations. This was deemed acceptable as the differences in the estimated muscle forces were minute. OpenSim static optimization was also used to determine the muscle activation of the individual muscles in the HM contractions.[8]

Due to the nature and capabilities of this study, we were unable to obtain accurate anthropometric data of the internal structures of the knee and hip for each subject. Therefore, we used literature derived moment arms of the muscles and joints in question: male knee extension,[38] female knee extension,[30] knee flexion,[38] hip rectus femoris,[10] male and female hip hamstrings.[10,29] When female data were not available, we extrapolated it based on the numerical differences between male and female moment arms found in other muscles.

To account for the different anthropometric characteristics across individuals, we then scaled the literature-derived moment arms based upon the anthropometric measurements taken: knee moment arms based upon the medial distal femoral condyle radius and hip moment arms based on pelvic height. The moment arm was scaled an equal number of standard deviations of the literature derived moment arm to the number of standard deviations of the individual's anthropometric measurement from the average of the group.[28]

With the Abaqus CAE software (Dassault Systems), we created a finite element model of the femur to model the effects of the muscle contractions. A 4th generation standard model femur geometry was obtained with literature derived and validated material properties applied.[23] The hip reaction force from the RF and HM were applied to 20 nodes on the superior surface of the femoral head in the direction of the knee. We applied physiologically realistic boundary conditions in accordance with Speirs et al.[40] to minimize femoral head deflection. The model was then meshed with tetrahedral elements, sized in accordance with a performed convergence test (1.2 mm for the femoral head, neck and trochanter, and 3 mm elsewhere).

The FE model was solved for each subject. The model assumed the knee and hip extensors and flexors would be contracted simultaneously in an agonist-antagonist co-contraction, and that the forces produced during the co-contraction would equal the forces produced when contracted individually. For each subject, we extracted the peak maximum (tensile) and peak minimum (compressive) principal strains on the cortical femoral neck. As each subject model utilized the same femur geometry as well as the same HRF input vector, differences in strain will be attributed solely due to differences in muscle force production during the NMES-FR.

Table I lists the six studies that measured or modeled the strain in the proximal femur during various exercises that we used as comparison to the results of the NMES-FR. Low Impact includes walking and stair climbing and descending. Resistance Exercise includes exercises such as squats with or without added weight. Where possible, resistance exercises that exceed 70–80% of maximum effort were used, due to the increased likelihood of positive results for bone maintenance.[5]

Due to the variability in study methods and materials, as well as the unavailability of individual data points from the associated studies, we could only perform a qualitative comparison. Additionally, the qualitative comparison was performed due to an inability to concretely compare the osteogenic potential of any individual activity modeled in one study to another, as there remains many unknowns concerning the interactions of peak strain, loading cycle count, and loading cycle distribution on a total daily strain stimulus and the subsequent osteogenic effect, especially when one activity is used in combination with another.

Table I. List of the Six Studies Obtained for the Qualitative Comparison.

STUDY	MUSCLE DATA SOURCE	FEMUR MODEL SOURCE	SUBJECT POPULATION	LOW IMPACT	VERTICAL JUMP	RESISTANCE EXERCISE
Aamodt 1997[1]	In-Vivo	N/A	Women (*N* = 2)	X		
Martelli 2014[24]	Obtained Model Simulation*	Obtained Model†	N/A	X	X	X
Edwards 2016[12]	Obtained Model Simulation	Obtained Model	N/A	X		
Kersh 2018[17]	Subject Inverse Kinematics/ Dynamics	Individual Subject CT	Post-Menopausal Women (*N* = 20)	X	X	
Pellikaan 2018[32]	Subject Inverse Kinematics/ Dynamics	Obtained Model	Post-Menopausal Women (*N* = 14)	X	X	X
Altai 2021[4]	Subject Inverse Kinematics/ Dynamics	Individual Subject CT	Post-Menopausal Women (*N* = 5)	X		

*Obtained Model Simulation states that muscle forces were obtained computationally using subject kinematics or dynamics inputs from a previous study.
†Obtained Model states that a previously constructed femur geometry was obtained.

RESULTS

Knee and Hip Torques

For each subject, we assumed that the thigh muscles would be simultaneously contracted, resulting in both knee and hip extension and flexion. To aid in predicating the feasibility of using NMES in microgravity, we calculated the net knee torques and hip torques using the estimated internal muscle forces and moment arms. Positive torque denotes extension and negative torque denotes flexion. In 9 of 10 subjects, the rectus femoris produced a greater force than the hamstrings, resulting in net knee extension and hip flexion. **Table II** displays the net joint torques for each subject.

Table II. The Net Torques of the Knee and Hip for Each Subject, as Calculated from the Estimated Internal Rectus Femoris and Hamstring Complex Muscle Forces and Measured Anthropometric and Experimental Data.*

	NET TORQUE (N-cm)	
	KNEE	HIP
Male		
1	918.176	−1246.5
2	156.670	−132.45
3	1543.408	−1854.13
4	168.270	−79.5462
5	−486.223	2306.756
Female		
1	891.434	−936.135
2	772.864	−1155.67
3	860.066	−1049.37
4	258.150	−335.458
5	647.700	−1011.44

*Positive net torque denotes extension, and negative net torque denotes flexion.

Peak Strains

The peak maximum (tensile) strains occurred on the distal portion of the superior femoral neck, and the peak minimum (compressive) strains occurred on the proximal portion of the inferior femoral neck (**Fig. 2**). The peak strain locations were at identical nodes for all subjects as we had a single femur FEA model and used identical HRF vector across each subject.

This also resulted in a direct correlation between the sum of the modeled HRFs and the peak strains. The average peak tensile strains were 1380 ± 719 με and 573 ± 345 με for the male and female subjects, respectively. The average peak compressive strains were −2179 ± 1130 με and −900 ± 543 με for the male and female subjects, respectively. All of the peak strains by subject are listed in **Table III**.

Comparative Metrics

We obtained the peak strains on the cortical proximal femur from six prior studies. When not published, the exact quantitative data was obtained from the authors, with the exception of the Pellikaan 2018 study,[32] where we visually estimated the average peak strains from the published figures. We created four different categories for the qualitative comparison: Walking, Stairs, Vertical Jump, and Resistive Exercise. The following resistive exercises were used: Weighted Squat (Sqt), Hip Extension (HE), Hip Flexion (HF), Knee Extension (KE), and Knee Flexion (KF). The only exercises with a listed percentage of maximum effort were HE and HF in Pellikaan 2018.[32] All studies, with the exception of Martelli 2014,[24] published both superior proximal (tensile) and inferior proximal (compressive) peak strains. If a study further divided the superior and inferior peak strains of the proximal femur by sub region, those most closely matching this study's FEA results were used (superior-distal, inferior proximal). **Fig. 3** displays the peak strains of the various activities to the peak strains achieved by the male and female subject groups.

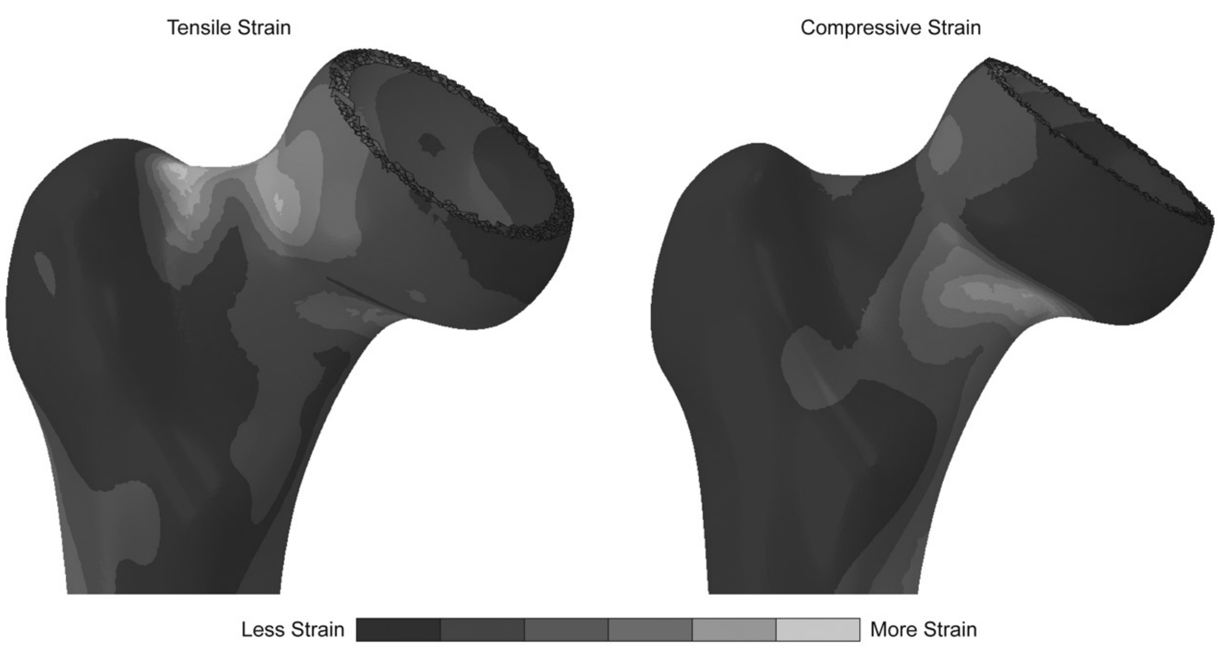

Fig. 2. Strain on the proximal cortical femoral neck as calculated by the Abaqus finite element analysis model. The strain profile was equal across all 10 subjects. A section of the femoral head was removed to eliminate nodes with erroneous peak strains resultant from the loading boundary condition.

Table III. Peak Strains for Each Individual Subject.*

	PEAK STRAINS (με)			
	MALE		FEMALE	
SUBJECT	MAXIMUM	MINIMUM	MAXIMUM	MINIMUM
1	965	−1520	1110	−1750
2	786	−1240	505	−794
3	2290	−3600	589	−925
4	844	−1330	152	−238
5	2040	−3200	508	−797
Average	1380	−2170	573	−900
SD	719	1130	345	543

*Maximum peak strains refer to the peak tensile strain on the superior cortical femoral neck, and minimum peak strains refer to the peak compressive strain on the inferior cortical femoral neck.

Of the four studies with walking (Fig. 3A), the male subject's peak maximum and minimum strains were similar to three studies[1,4,17] and less than one,[32] and the female peak strains were less than all but one.[1] Of the three studies with stairs (Fig. 3B), the men again had peak strains similar to if not greater than all three, whereas the female peak strains were less than all but one.[1] For the three studies with vertical jumping (Fig. 3C), both the male and female's peak strains were similar to one study,[17] and less than the other two.[24,32] Lastly, for resistive exercises (Fig. 3D), the male peak strains were similar to Weighted Squats and Knee extension per Martelli 2014,[24] and less than all others. The female peak strains were less than all recorded exercises.[24,32]

DISCUSSION

The aim of this study was to estimate the feasibility of using Neuromuscular Electrical Stimulation (NMES) as a bone loss countermeasure in space. This feasibility was determined by qualitatively comparing the strain induced on the femur by NMES of the rectus femoris and hamstring muscles to that of other exercises.

Our results show that NMES, or in this case NMES-FR, could produce peak strains on the femur similar to those of low impact activities, including walking and stair ascending/descending, potentially replicate the strain from higher impact activities like jumping, but could not replicate the strains from most resistive exercises. The ability of these NMES-FR contractions, or an equivalent co-contraction in microgravity without a fixed resistance, to prevent bone loss, however, is still unknown. The current theory of the bone mechanostat states that the total daily strain stimulus, which is determined by the peak strain of a loading cycle and the total number of loading cycles, drives the osteogenic response in bone tissue.[33] However, it is still not known if there is an exact threshold that must be reached, or how such a threshold can vary between individuals, as noted by the wide range of BMD changes following resistive exercise regimens targeting bone loss in older individuals.[5] Also less understood is the influence of lower strain, but higher frequency loading. For example, studies of vibration therapies, where low magnitude, high frequency loading is applied have had mixed results on preventing bone loss.[18] Therefore, while NMES can produce strains akin to walking, our data indicate that NMES alone would not reduce bone loss in microgravity, as walking alone generally does not produce sufficient daily stimulus to reduce bone loss unless at very high repetitions (10,000+).[7] Additionally, the fatigability associated with repetitive NMES contractions makes achieving a high enough number of productive repetitions difficult.[2]

However, it can be posited that adding a daily NMES regimen to the current or future exercise regimen could potentially improve the effects and further reduce bone loss in long duration spaceflight missions. The bone's mechanotranducers have a sensitivity that declines with repetitive loading cycles, and requires time to recovery this lost sensitivity.[34] Loading that is more distributed throughout a given day, therefore, has a significantly greater osteogenic response than the same volume of loading applied at a single time point.[35] While NMES alone may not generate strains that would fully replicate the loading one experiences on Earth, astronauts currently experience negligible forces on the lower body throughout the day outside of the prescribed exercise period.[21] A countermeasure that induced strains akin to walking periodically throughout the day could theoretically have significant benefits. It is recommended that a long term, head down bed rest study comparing the bone loss with an exercise block vs. an exercise block with distributed NMES be performed to investigate these possibilities. Additional metabolic analysis studies of multiple muscle repetitive NMES contractions should also be completed to further conclude that NMES will not exacerbate the negative energy balance seen with ISS astronauts.[19]

These potential benefits will vary significantly individual to individual, as observed by the variation in peak strains between subjects. The source of the individual variation can be attributed to an individual's potential force production, which is affected by the neuromuscular composition, muscle fiber type distribution and the muscle's maximum voluntary contractile force. Neuromuscular composition refers to the distribution of the motor endplates, where a particular motor neuron branches out to innervate its respective muscle fibers. Those who have more clustered motor endplates can have more under a given electrode size and therefore have more muscle fiber innervated by a given strength NMES electric field.[3,6] The muscle fiber type distribution refers to the spatial distribution of the high twitch, high force producing muscle fibers. As all muscle fiber within reach of the NMES electric field will contract, individuals with more of the high force producing fast twitch muscle, normally recruited during strenuous activity, near the electrodes could generate higher forces.[6] Last, the inherent strength of a muscle will determine the potential strength of a NMES contraction. A greater percentage of muscle fibers innervated, with a greater percentage of those fibers being fast twitch, will generate a greater percentage of the total maximum force capability. The individual variation in results can also be attributed to an individual's tolerance to NMES. The pain of NMES can be attributed to purely subjective measures as well as physical characteristics, such as body fat and hair. Thicker subcutaneous fat requires a

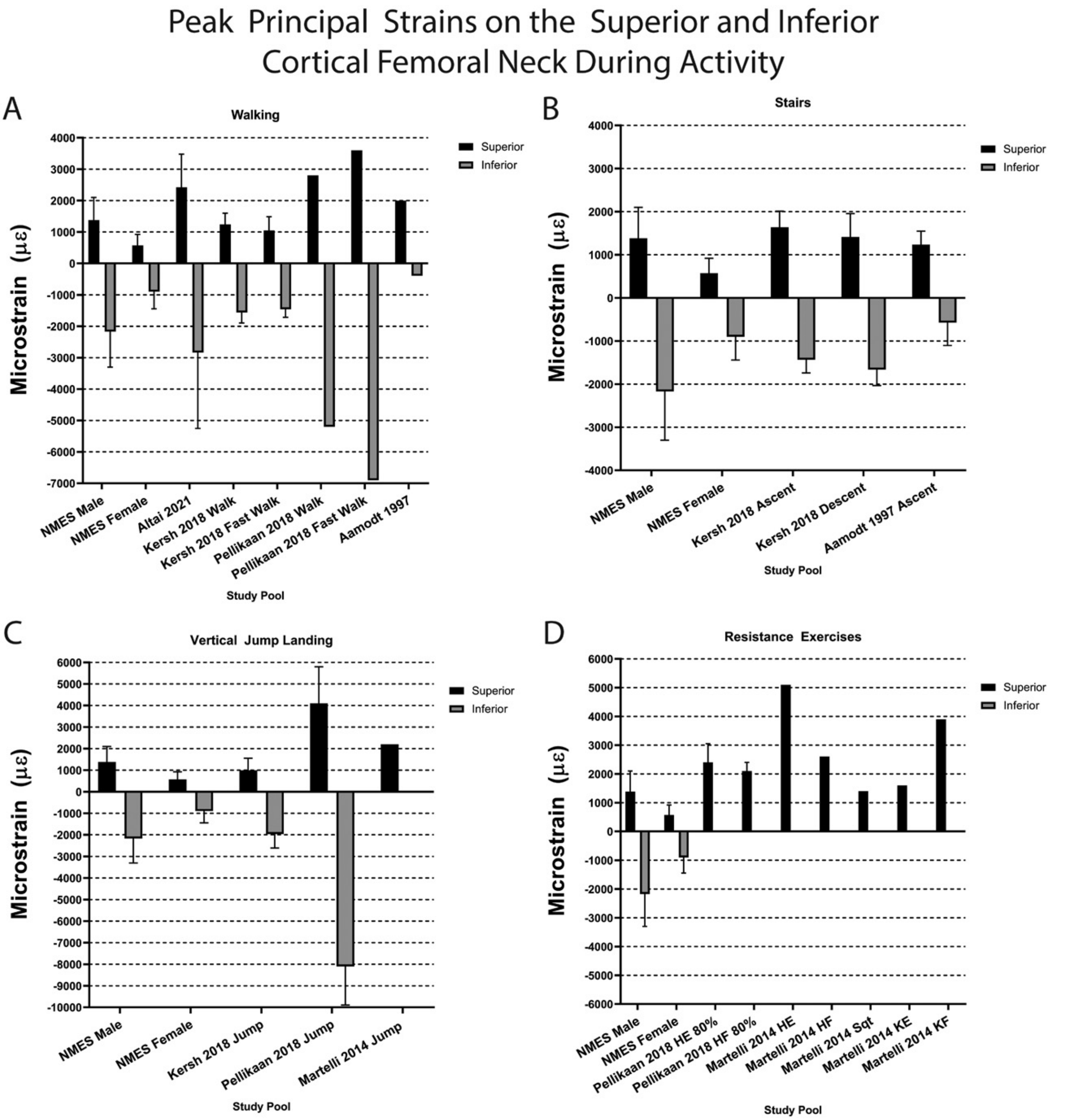

Fig. 3. Peak strains on the superior and inferior cortical femoral neck from NMES compared to A) walking, B) stairs, C) vertical jump landing, and D) various resistive exercises. Height of each bar represents the mean and the whisker represents 1 SD. If no whiskers are present, the data were not available or the study utilized a model rather than subjects. Data for the Pellikaan 2018[32] exercises were obtained visually from figures.

stronger electric field to innervate the motor endplates and results in more residual current entering tissue, resulting in pain.[9]

There were no strength, athletic, or body composition requirements for the subjects of this study, nor was any information recorded. Therefore, it is difficult to ascertain why certain subjects were more responsive and subsequently produced higher forces. However, factors like maximum voluntary contractile strength and body fat thickness likely played a role in the trend of the female peak strains being less those that of the men. Additionally, the limitations with using a single FEA model for all subjects regardless of anthropometric measures was a likely contributor to the overall differences in modeled strain between the two groups.

This study also calculated the net knee and hip torques produced from the proposed co-contraction of the rectus femoris and hamstring muscles. In microgravity, these net joint torques could result in unwanted movement that could be hazardous to the spacecraft or self. Co-contractions of the quadriceps and hamstrings have previously been performed in microgravity aboard Mir and found that at lower NMES intensity levels the resultant movement was negligible.[26] However, this may not be the case when targeting bone loss, as the higher intensity contractions would be desirable. In order to better predict the resultant movement and subsequent hazard from this study's resultant torques, a follow-on study involving a microgravity analog, such as lateral position or a 0-g flight, should be performed.

Our study utilized methods that measured external force and torque production, converted these external forces to internal muscle forces using biomechanical models, and then applied those forces to an FEA model to estimate the strain on the femur. The calculations and assumptions included in these methods have inherent limitations. First, we used an external dynamometer, which could allow for slight movements and subsequent inconsistences in force measurement between individuals. Additionally, an external measurement was required from the dynamometer to an estimated knee rotation center, which could result in slight errors in the estimated joint torque. We calculated the in-vivo muscle forces with simple biomechanical models that utilized estimated and scaled moment arms and assumed external reaction forces, which may not reflect the true internal biomechanical force transfer.[28,43] We used a single femur FEA model across all 10 subjects, whereas individuals will have varying femur geometry, lengths, and material properties. Last, due to the limitations of the biomechanical model, accurately producing an HRF vector was not possible, and instead we used an identical vector field in the direction of the knee across all subjects. These factors would all contribute to increased variation in peak strains, as well as the locations of peak strains, across each subject.

This study involved comparing the results to those of other strain models from other studies. The studies used here were all comprised of different biomechanical models and finite element models, as well as subject populations. Additionally, the activities modeled had variations between the different studies. For example, walking speeds varied and therefore exact comparisons could not be performed. These limitations necessitated that the current study be limited to a qualitative comparison.

In this study we estimated femoral strains induced by the isometric force from Neuromuscular Electrical Stimulation of the rectus femoris and hamstring complex. By comparing these strain estimates to those previously reported for other activities, we were able to determine the feasibility of using NMES as a countermeasure for bone loss in microgravity. Our results indicated that some, but not all, individuals have sufficiently high muscle forces during NMES to create strains on the femur similar to activities such as walking or stair climbing/descending, with NMES inducing strains comparable to those reported for jumping or resistance exercises in a few individuals. These results suggest that NMES is a promising approach to reduce bone loss in space and provide strong rationale for further investigations, specifically testing whether the use of NMES can prevent bone loss in a bedrest study.

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