Leg intramuscular pressures and in vivo knee forces during lower body positive and negative pressure treadmill exercise

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PREVIOUS STUDIES HAVE DOCUMENTED peak tibial forces during various daily activities of 2.2 body weight (BW) (11) to 2.5 BW (12). Determining the force magnitude over a broad range of loads on the tibia may improve prosthetic durability. Lower body positive pressure (LBPP) treadmill exercise is a relatively new rehabilitation treatment that provides significant reductions of weight bearing, improves cardiovascular safety during exercise, and minimizes alterations of gait kinematics in orthopedic patients (8, 13).

Quantifying ground reaction forces (GRF) during walking and running at various body weights will help develop exercise hardware and exercise prescriptions to prevent muscle and bone loss during long-duration spaceflight. Reduced mechanical loading to bone and muscle during microgravity exposure results in profound reductions in muscle (28) and bone mass (31). GRFs during treadmill walking and running on the International Space Station (ISS) were reduced by 25% and 46%, respectively, compared with similar activities on earth (6). Bone mineral density measured during the first six ISS expeditions was lost at a monthly rate of 1.4–1.5% at the hip and 0.9% at the spine (19). Furthermore, recent studies performed aboard the ISS demonstrate the need for development of improved exercise countermeasures that involve higher loading profiles to weight bearing muscles (14, 28). During spaceflight, exercise within lower body negative pressure (LBNPex) may enable astronauts to exercise comfortably at loads equal to, or greater than, one BW and serve as an exercise countermeasure to help mitigate muscle, bone, and cardiovascular deconditioning as well as the headward fluid shift (16–17, 22, 29).

GRF during supine LBNP treadmill exercise at 100% BW reproduces those GRFs measured during upright treadmill exercise (4). Collectively, leg intramuscular pressure, GRF, and the instrumented tibial tray force measurements provide a comprehensive assessment of leg muscle and joint biomechanical effects of gravity during exercise. The objective of this study was to determine the intramuscular pressures of the leg, axial compressive force on the tibia in vivo, vertical ground reaction force, and knee range of motion during altered body weight levels using upright LBPP and LBNP treadmill exercise. We hypothesize that peak ground reaction force (pGRF), peak tibial forces, and peak intramuscular pressures of the leg correlate linearly with percent BW, as generated across a broad range of upright LBPP and supine LBNP exercise. These data will aid the development of rehabilitation exercise hardware and prescriptions for patients and astronauts.

METHODS

This study was approved by the University of California, San Diego, Human Research Protection Program, and all subjects gave informed written consent prior to testing.

Intramuscular pressure measurements during upright LBPP and LBNP. Eight healthy subjects (age 18–30, weight 68–100 kg, 5 men, 3 women) volunteered for IMP measurements during LBPP/LBNP exercise. Four 3-Fr solid-state transducer-tipped catheters (Millar Instruments, Houston, TX) were used to measure IMP in the anterior, lateral, superficial posterior, and deep posterior muscle compartments. The insertion site was shaved and prepped in a sterile fashion. The skin and fascia around the insertion site were anesthetized with 1% lidocaine hydrochloride using a 27-gauge needle. A 16-gauge intra-

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Venous placement unit (Jelco, Critikon, Tampa, FL) was inserted at a 30° angle to the skin and advanced to shallowly penetrate the muscle fascia. The needle was retracted, leaving the outer plastic sheath in the muscle and the transducer was inserted 4–5 cm into the muscle compartment, parallel to the muscle fibers to reduce muscle trauma and bleeding. The pressure sensor’s transducing surface was directed toward the skin. The pressure transducer was connected to the personal computer-operated LabView data acquisition system, and the skin was palpated to confirm adequate response from the pressure transducer. The cannula was withdrawn, and the catheter was secured in place with a sterile transparent Tegaderm dressing (3M, St. Paul, MN). Proper placement and catheter function were confirmed by again palpating over the catheter tip and asking the subject to plantarflex and dorsiflex the ankle. Thus IMP response to these manipulations help confirm that the pressure transducers were in the posterior and anterior/lateral muscle compartments. The same trained orthopedic surgeon ensured that each catheter was placed at the same angle with the same length of penetration for all subjects. Moreover, resting pressures in the supine position ranged from 6.8 to 20.4 cmH2O, and IMPs were confirmed to be within normal limits before proceeding. Continuous pressure measurements were collected simultaneously from the anterior, lateral, superficial posterior, and deep posterior compartments using LabView data acquisition software. The subjects were positioned in the upright LBPP/LBNP chamber; the subject stood upright on only right leg, on only the left leg, then on both legs at 10%, 20%, 40%, 60%, 80%, 100%, 110%, 120%, 130%, and 140% BW to calibrate the GRF insoles (EQ Systems, PA) and determine the chamber pressure required to adjust the subjects’ BW by given percentage. LBPP was used to reduce weight bearing, and LBNP was used to increase weight bearing. Next, the subject walked in place as the treadmill speed was increased to 1.34 m/s. Following assurance from the subject that all instrumentation was comfortable, the treadmill speed increased to 2.24 m/s. The chamber pressure was increased to bring the subject to 10% BW and the subject exercised for 2 min. After exercise for 2 min at 10% BW, the chamber pressure was reduced to bring the subject to 20% BW, measurements were recorded for 2 min, and this process was continued until all data collection was complete at 40%, 60%, 80%, 100%, 110%, 120%, 130%, and 140% BW. To prevent confounding effects of order, the order of percent load was randomized.

In vivo forces during upright LBPP treadmill exercise and supine LBNP treadmill exercise. An 83-yr-old male volunteer (68 kg) with a custom instrumented titanium alloy tibial prosthesis placed in the right lower extremity (11) was exercised in a LBPP chamber. The

![Diagram A](https://example.com/diagram1.png)

**A** upright lower body pressure treadmill exercise device: ground reaction force (GRF) is a function of body mass (M) multiplied by gravity (g) along with an additional force determined by the area of the waist seal ($A_{xy}$) multiplied by the difference in pressure ($\Delta P$) between the inside ($P_1$) and outside ($P_2$) of the chamber.  

$$GRF = M \cdot g + A_{xy} \cdot \Delta P$$

![Diagram B](https://example.com/diagram2.png)

**B** supine LBNP treadmill exercise device: GRF in the LBNP chamber is a product of the body cross-sectional area at the waist seal ($A_{xy}$) and the pressure differential between the external ambient and internal chamber pressures ($\Delta P$); GRF = $A_{xy} \cdot \Delta P$.  

Fig. 1. Custom force-sensing titanium alloy tibial prosthesis (eKnee) was implanted into 1 patient for in vivo measures during upright lower body positive pressure (LBPP) and supine lower body negative pressure (LBNP) exercise. A: upright lower body pressure treadmill exercise device: ground reaction force (GRF) is a function of body mass (M) multiplied by gravity (g) along with an additional force determined by the area of the waist seal ($A_{xy}$) multiplied by the difference in pressure ($\Delta P$) between the inside ($P_1$) and outside ($P_2$) of the chamber. B: supine LBNP treadmill exercise device: GRF in the LBNP chamber is a product of the body cross-sectional area at the waist seal ($A_{xy}$) and the pressure differential between the external ambient and internal chamber pressures ($\Delta P$); GRF = $A_{xy} \cdot \Delta P$.  

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The same 83-yr-old male (68 kg) with a custom instrumented titanium alloy tibial prosthesis was exercised in a supine LBNP chamber (Fig. 1B). The subject was instrumented with the same measurement hardware as described above. The subject was positioned in the supine LBNP chamber with a neoprene skirt at the superior iliac crest, sealing his lower extremity within the chamber from the waist down. Data were collected at 10%, 20%, 40%, 60%, 80%, 100% BW with supine LBNP used to simulate gravity and allow for treadmill exercise at 0.67 and 1.34 m/s. In addition, data were collected at 0% BW with the treadmill stopped while in the supine LBNP chamber.

Statistical analyses. All data are expressed as means ± SD and evaluated using the statistical package SPSS (v.17, Chicago, IL). IMPs were analyzed using a two-factor ANOVA (muscle group and %BW) to compare differences between the four muscle compartments over the LBPP loading range. GRFs were analyzed using a two-factor ANOVA (treadmill speed and %BW) to compare differences between treadmill speed over the LBPP loading range. Linear regression analysis was performed on the in vivo peak tibia force, GRF, and ROM data to determine $R^2$. For all data, statistical significance was accepted at $P < 0.05$. 

Fig. 2. A: intramuscular pressure (IMP) of the deep posterior and superficial posterior muscle compartments when standing were significantly increased in the transition from high LBPP to low LBPP and from low LBNP to high LBNP. This transition produced more weight bearing [60% body weight (BW) to 140% BW] to the lower body ($n = 8, P < 0.001$). B: IMP of the anterior and lateral muscle compartments when standing were significantly increased in the transition from high LBPP to low LBPP and from low LBNP to high LBNP. This transition produced more weight bearing (60% BW to 140% BW) to the lower body as well ($n = 8, P < 0.001$).

Fig. 3. A: when running, the IMP of deep posterior and superficial posterior muscle compartments significantly increased over the loading range of 60% BW to 140% BW with LBPP and LBNP ($n = 8, P < 0.001$). B: when running, the IMP of anterior and lateral muscle compartments significantly increased over the loading range of 60% BW to 140% BW with LBPP and LBNP ($n = 8, P < 0.001$). IMPs of the deep posterior compartment were significantly higher compared with the other 3 muscle compartments ($P < 0.002$). IMPs of the anterior muscle were significantly less than the other 3 muscle compartments ($P = 0.01$).
RESULTS

Intramuscular pressure measurements during upright LBPP and LBNP treadmill exercise. When standing, the IMP of all four muscle compartments (deep posterior, superficial posterior, anterior, and lateral) were significantly increased as LBPP was reduced and LBNP was increased, thus providing more weight from 60% BW to 140% BW ($P < 0.001$; Fig. 2). However, when standing, the magnitude of IMP of the four muscle compartments measured over the nine weight-bearing levels was not significantly different. When running at 2.24 m/s the IMP of all four muscle compartments significantly increased over the loading range of 60% BW to 140% BW with LBPP and LBNP ($P < 0.001$). Also, as expected, the IMP of all four muscle compartments was significantly higher when running compared with standing ($P < 0.001$; Fig. 3). Moreover, when running, IMPs of the deep posterior compartment were significantly higher compared with the other three muscle compartments ($P = 0.002$). However, the IMPs of the anterior muscle were significantly less than the other three muscle compartments ($P = 0.01$). Peak GRF during upright LBPP and LBNP exercise at 1.34 m/s significantly decreased as body weight was reduced from 140% BW to 60% BW ($P < 0.001$; Fig. 4). In addition, GRF was significantly higher when running at 2.24 m/s than walking at 1.34 m/s ($P < 0.001$). GRF data from only the right leg are presented from these eight normal healthy subjects.

In vivo knee forces during upright LBPP treadmill exercise and supine LBNP treadmill exercise. Total axial force at the knee increased linearly as a function of BW at 0 m/s in upright LBPP ($R^2 = 0.93$) and supine LBNP ($R^2 = 0.85$; Fig. 5). Knee force data transmission was not received by the data acquisition system for the standing supine LBNP 10% BW and upright LBPP 20% BW measurements. Total axial force at the knee increased linearly as a function of BW when walking in upright LBPP (Fig. 6). Similarly, total axial force at the knee increased linearly as a function of BW when walking during supine LBNP (Fig. 7). During upright LBPP exercise, GRF on the right and left side increased linearly as a function of BW at 0.67 m/s and at 1.34 m/s (Fig. 8). During supine LBNP exercise the GRF tended to be higher on the nonoperated right leg compared with the left intact leg. Conversely, during upright LBPP exercise GRF tended to be higher on the left leg. Still, during supine LBNP, GRF on the left and right side increased linearly as a function of BW at 0.67 and 1.34 m/s (Fig. 9). Right and left knee ROM increased with increasing body weight at 0.67 and 1.34 m/s (Fig. 10).

DISCUSSION

In support of our hypothesis, peak GRFs, total peak tibial forces, and peak intramuscular pressures of the leg increase linearly with percent BW as generated across a broad range of decreasing upright LBPP and increasing upright LBNP; in addition, peak GRF and peak tibial forces during supine LBNP exercise increase linearly with percent BW. Moreover, the
The present study is the first to measure IMP and peak tibial forces in vivo during upright LBPP and supine LBNP exercise.

Titration of body weight by supine LBNP can reproducibly modulate IMP within the muscle compartments of the leg (24). Several techniques reduce a patient’s effective weight (which reduces lower limb muscle and joint forces) during ambulatory rehabilitation, such as water immersion, parallel bars, walkers, crutches, and overhead suspension harnesses (3, 26). Similarly, treadmill exercise within upright LBPP may serve as a rehabilitation modality for postoperative patients undergoing rehabilitation to prevent complications of inactivity, for example, muscle atrophy, fibrous tissue contractures following knee surgery (13). Therefore, the present data extend previous work demonstrating that upright LBPP treadmill exercise and supine LBNP treadmill exercise modulate IMP, an index of muscle force, as a function of percent weight bearing. The present data are consistent with previous studies that document that the postural muscles such as soleus, produce significantly higher IMP (300 mmHg) compared with the anterior tibialis muscle (150 mmHg) during treadmill walking and running (2). Moreover, IMPs serve as a surrogate for dynamic muscle force production, with a strong linear correlation when dynamometric calibrations are performed with IMP measures of the soleus and anterior tibialis muscles (2). The present study did not include a dynamometric calibration measurement; however, prior work show that an IMP of 300 mmHg in the soleus is associated with a torque of 200 to 120 N·m (2). Therefore, the present IMP data suggest that peak muscle torque production during running would change linearly with percent weight bearing by LBPP or LBNP exercise.

![Fig. 6. During upright LBPP, total axial force at the knee increased linearly as a function of BW at *0.67 m/s ($R^2 = 0.90$) and #1.34 m/s ($R^2 = 0.98$).](image1)

![Fig. 7. During supine LBNP, total axial force at the knee increased linearly as a function of BW at *0.67 m/s ($R^2 = 0.98$) and #1.34 m/s ($R^2 = 0.91$).](image2)
Peak GRFs during exercise correlate linearly with added or reduced weight bearing. For example, Chang et al. (7) reports that running on the externally applied horizontal force treadmill harness system at 100% BW give GRF of 983 and 724 N at 50% BW (7). In waist-deep water, weight-bearing loads are reduced by ~40% and in chest-deep water by nearly 60% (18). Peak GRF during zero-gravity locomotion simulator (ZLS) exercise at a slow walk (0.5 m/s), fast walk (1.0 m/s), slow run (3 m/s), and fast run (4 m/s) were 445, 709, 857, and 953 N, respectively (9). The present data show similar effects of increased gait speed and magnitude of weight bearing on peak GRF during LBPP and LBNP exercise.

We sought to measure in vivo peak axial loads at the tibia during two walking conditions at various body weight loads to determine how upright LBPP and supine LBNP exercise affect maximal knee loads. These in vivo knee force data were from one subject instrumented with an in vivo force-measuring total knee implant. The tibial forces and GRF show a significant linear relationship as a function of BW by LBPP and LBNP. Thus tibial forces at the knee can be accurately adjusted to a given BW to increase loading of the knee gradually to theoretically improve healing and return to full weight bearing sooner. Therefore, these peak axial forces on the knee may help improve rehabilitation of total knee-replacement patients. Tibial forces during level walking (0.67 m/s) 3-days postoperative are ~45% of those (1.25 times BW) at 1 yr postoperative (2.8 times BW) (10). There are few data that measure invasive human tibial strains. During walking (1.39 m/s) invasive strain gauge measures show mean compressive and tensile strains are ~544 μE and 437 μE, respectively (5). When this subject
donned a 17-kg backpack, the principal strains only changed a few percent when walking on a level surface; however, when walking downhill with the added weight, compressive strain increased by 45% and tensile strain by 12%. Thus in vivo strain measures alone may not enable detection of graded reduction of BW during ambulation at the tibia. The peak tibial forces during supine LBNP exercise were markedly similar to those during LBPP exercise. A 40% BW reduction with supine LBNP exercise provided a reduction in peak tibial loading on the range of 13–17%; this difference may be explained by a 90° shift in the gravity vector or perhaps by some interaction with thigh, ankle, or waist seal supports. Nonetheless, both upright LBPP treadmill exercise and supine LBNP treadmill exercise at walking speeds effectively reduced in vivo peak tibia loads. Current exercise hardware and exercise prescriptions performed during ISS missions (~6 mo) do not completely prevent musculoskeletal deconditioning (14, 19, 28). For example, Trappe et al. (28) report that leg muscle mass loss of 10 ISS crew members (~6 mo mission) was 13%. This leg muscle loss on ISS is slightly less than the 17% loss observed on Russian Space Station Mir missions (20). Moreover, these muscle mass decrements on ISS and Mir are ~50% of the calf muscle volume loss (~29%) after long-duration (60–120 day) bed rest studies, the ground-based human model for simulated spaceflight (1, 21, 27, 30). These data suggest that mechanical loading to skeletal muscle with previous resistance exercise and endurance exercise prescriptions on ISS partially mitigate muscle mass loss.

The inability to reproduce the GRF profile on ISS compared with those obtainable on earth when exercising on a treadmill may explain the inability to completely mitigate muscle and bone loss during spaceflight. The highest active peak in-shoe force was 1.77 BW with the subject load device (at 210-lb setting) on the ISS treadmill, referred to as vibration isolation and stabilization (TVIS) (15). Moreover, Cavanagh et al. (6) reports that the GRFs during walk and running on TVIS onboard ISS were 25% less and 46% less than when walking and running on earth. It has yet to be shown if the newly deployed advanced resistive exercise device (aRED) will better protect against muscle and bone loss. The present data show that ground-based tests of the exercise LBNP exercise device can provide sufficient load to the musculoskeletal system at less than, equal to, or greater than one BW. In addition, the present data show that supine LBNP was able to attain similar in vivo tibial loads compared with walking upright on a treadmill. Unfortunately, assessments at high treadmill speeds of in vivo tibial loads were not performed and future work over a broad range of speeds are required.

In conclusion, upright LBPP and supine LBNP exercise modalities produce peak GRF, peak tibial forces, and peak intramuscular pressures of the leg in a linear relationship across a broad range of simulated reductions in gravity or added gravity ranges. The development and utilization of exercise modalities that enable rehabilitation of patients to comfortably load muscle and bone may help facilitate more rapid recovery from injury; similarly, exercise hardware and prescriptions for astronauts that load the body at earthlike gravitational levels may help better prevent muscle and bone loss during space-flight.

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DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS
REFERENCES