Research Article

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Ultrasound assessments of lower extremity joint structures from astronauts after 18 days on board the International Space Station

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Abstract

The purpose of this observational pilot study was to determine how various lower extremity joint structures are affected by space flight and microgravity conditions on board the International Space Station (ISS) where the normal terrestrial cyclic compressive loading is absent.

Methods: This study compared pre- and post-flight mean results obtained from three Axiom-4 Astronauts in 2025 after spending 18 days onboard the International Space Station (ISS). Quantitative musculoskeletal ultrasound measurements were performed using GE LOGIQ™ e system with a 12-LRS probe to assess 12 anatomic regions including bilateral hips, knees, and ankles. More specifically, we assessed the amount of synovial fluid in the knees (with and without external pneumatic compression), cartilage depths of hips, femoral condyle and talus cartilage. Infrapatellar ligaments and achilles tendon thicknesses were measured in longitudinal and transverse views. The Radiant DICOM Viewer program linear measurement tool, was used to quantitate measured distances of the identical structures post-flight compared to pre-flight values. Power Doppler Imaging signal (PDI) was used to detect any evidence of joint capsule inflammation suggested by increased blood flow in the hips, knees, and ankles as well as the distal insertion sites of the infrapatellar ligaments and achilles tendons.

Results: No statistically significant differences were observed between pre- and post-flight measurements after this short duration low Earth orbital mission. However, each crew member performed between 3 and 4.5 total hours of cycling exercise while on board the ISS. We did not detect any abnormal increases in blood flow signals using PDI and therefore we detected no evidence of active inflammation in the synovium of the hips, knees or ankles or the distal insertion sites of the infrapatellar ligaments or achilles tendons either pre-flight or post-flight.

Conclusions: Statistical differences in ultrasound measured lower extremity joint structures were not observed which may be explained by the short duration of the space mission and/or the effects of ingested NSAIDS and/or the compressive loading exercises all crew members performed while on board the ISS. We believe however, that non-invasive quantitative real-time ultrasound assessments hold promise as a precision medicine instrument to assess cartilage and joint structure health on longer duration missions. This information could hopefully optimize the exercise protocols of compressive loading needed to preserve healthy joints and therefore reduce injury upon returning to Earth or while performing activities on the Lunar or Martian surfaces.

Background

To maintain astronaut health on long duration orbital flights and on missions to the Moon or Mars, it is important to identify and mitigate the negative effects of microgravity on joint cartilage and the supporting structures including muscles, tendons, ligaments, and subchondral bone [1-4]. A significant rate of knee injuries was reported among Space Shuttle crew with 19 of 94 Astronauts requiring surgical knee interventions and 6 United States Astronauts following long duration ISS missions were referred for total hip or knee arthroplasty consideration (Drs. Rick Scheuring and Pat McCullough-personal communication) [5, 6]. Also, a retrospective study of 242 astronauts revealed 9% sustained shoulder injuries which were positively associated with ISS mission duration greater than 6 months [7].

While exercise protocols on board the ISS have shown benefit in reducing some of the deleterious effects of microgravity such as bone loss and reduced muscle mass, it is unknown if this approach is adequate to maintain healthy joints in all crewmembers. Chronic injury to the cartilage from microgravity exposure could potentially lead to degenerative joint disease which can be career ending for Astronauts. In addition, damage to supporting joint structures including ligaments and tendons could lead to joint instability and to additional injuries due to abnormal shear stress after resuming joint loading during terrestrial activities [3]. Roberts et al have summarized results from numerous studies on unloading related tendinopathies and MRI image analysis after 21 days of bedrest revealed changes in the shape but not the volume of the Achilles tendon [8,9].

There is also research evidence documenting the deleterious effects of reduced loading on cartilage health. MRI imaging has detected cartilage loss within weeks of immobility in humans and during a -6^{O} head-down tilt bed rest study which is a common spaceflight analog model [10,11]. Elevated serum collagen breakdown biomarkers were also reported during ISS missions and during immobilization from Liphardt and colleagues [11-14]. Chondrocyte damage and cartilage thinning have also been observed in rodents exposed to specific environmental conditions such as reduced weight-bearing (hind limb suspension), microgravity during orbital flight, after being on board the ISS [15-18]. Kwok et al have found similar adverse effects during hind limb unloading and while on board the ISS with reduced cartilage glycosaminoglycan content and elevated matrix metalloproteinases [18]. The effects of simulated galactic radiation which would occur beyond Earth's protective magnetosphere has also been shown to have an additive deleterious effect of cartilage in rodents during unloading and low Earth orbital flight [19,20].

The above results are not surprising since cartilage has mechanoreceptors which stimulate anabolic pathways in response to normal compressive loading and chondrocyte apoptosis occurs during lack of load bearing, aging, as well as chronic inflammation [21]. Unlike bone or muscle, cartilage has no afferent sensory receptors therefore symptoms develop only after substantial loss and tissue damage have already occurred. The knee femoral cartilage is only 3-5 mm thick and has minimal capacity to regenerate once damaged. Since cartilage is avascular, it receives nutritional support from the surrounding synovial fluid which is facilitated during compressive loading [22]. Synovial fluid is an ultrafiltrate of plasma and synoviocytes produce Hyaluronan and other proteins, which reduce cartilage damage during loading [23].

In flight immunology studies by Crucian et al have reported elevated circulating pro-inflammatory cytokines from crew during ISS missions [24,25]. These circulating cytokines and other proteins may be deleterious to cartilage and could also reduce synoviocyte production of hyaluronan or alter normal synovial capillary permeability. Circulating or synovial tissue produced vasoactive and pro-inflammatory proteins may also reduce synovial fluid viscosity and increase volumes. It is also becoming clear that osteoarthritis is not simply a mechanical wear and tear degenerative process but is also caused by ongoing chronic inflammation [26,27]. We have also identified that synovial fluid cytokines analyzed from many osteoarthritis patients have a pro-inflammatory profile like some patients with Rheumatoid arthritis [28]. An observed increase in knee synovial fluid volumes and a concomitant decrease in viscosity is also a useful clinical biomarker of joint disease progression.

Ultrasound (US) is a non-invasive painless imaging modality, demonstrated to have multiple medical uses including biomedical research on board the ISS [29]. The amount of knee synovial fluid can be more precisely quantitated using ultrasound and in conjunction with a proprietary gravity-independent external pneumatic compression device (KneeTap™). This device facilitates more accurate synovial fluid measurement and simplifies joint fluid aspiration (arthrocentesis) by redistributing the synovial fluid from various communicating compartments of the knee to one specific target area under positive pressure [30,31]. Ultrasound imaging can also identify cartilage depths as well as thickness and integrity of larger tendons and ligaments [32].

This proof-of- concept technical feasibility study also addresses several knowledge gaps including developing a non-invasive real time tool needed to assess the efficacy of personalized countermeasures such as exercise, to reduce the adverse effects of microgravity on cartilage and tendons. No prior studies have determined if inflammation occurs within synovial tissue or the enthesis or if volumes of joint fluid are altered after spaceflight. To our knowledge, this is also the first study to perform quantitative ultrasound measurements of various lower extremity joint structures in humans immediately following spaceflight [Figure 1].

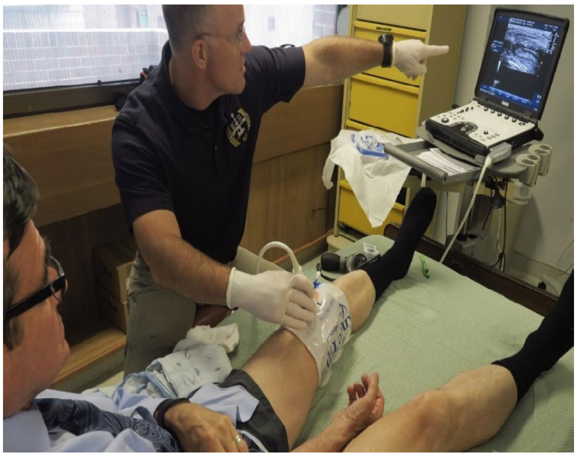


Figure 1. Image below, NASA/ JSC Flight Surgeon Dr Rick Scheuring performing knee ultrasound examination with KneeTap™ external pneumatic compressive device on RM at National Jewish Health Denver CO.

Methods

Astronaut Subject Demographics

This was an observational, within-subject, pre-and post-flight pilot study. Three Crewmembers of the Axiom Space AX-4 mission signed consent forms and agreed to participate in this IRB approved study (HS 4090). US images were obtained pre-flight at Axiom Space Headquarters (Houston, Texas, USA) on April 7 and 8, 2025. The mission launched on June 25, 2025, at 2:31 AM and returned to Earth on July 15, 2025, at 5:31 AM. All 3 crew were examined within 4 hours after splashdown in the Axiom Space post-flight testing facility in Long Beach, California USA.

Some crew demographics including gender and age are not reported to prevent loss of individual subject identity. All subjects were healthy, had BMIs between 25.5 and 26.3 Kg/M2, active and fit at the time of launch and none had any knee or ankle effusions on physician examination. However, they all reported prior lower extremity joint injuries and interventions ranging from >1 year to several years before launch. These included anterior cruciate knee ligament repair, lateral ankle ligament reconstruction, knee arthroscopy, hyaluronic acid knee injections and mesenchymal stem cell injections.

Non-steroidal anti-Inflammatory drugs (NSAIDs) were reportedly used in flight by their respective flight surgeons by all 3 crewmembers. All astronauts were placed in below knee compression stockings by their flight surgeons immediately after splashdown to reduce the risk of post-flight orthostatic intolerance and these were removed while recumbent before performing US examinations.

The amount of self-reported exercise during the 18-day ISS mission was variable among each crew. One crewmember averaging 30 minutes of stationary cycling for 6 days (total 180 minutes) and one crewmember performed 6 days of cycle exercise averaging 40 minutes per session (total 240 minutes). Another crew member participated in an exercise research study and performed three 90-minute exercise sessions on a cycle (total 270 minutes).

Ultrasound Image Acquisition and Measurements

All ultrasound measurements were performed by study Rheumatologists (RM and SS) certified by the American College of Rheumatology in Musculoskeletal Ultrasound. Each physician obtained US images on the same subject post-flight as they did on their pre-flight examinations. Ultrasound images were acquired using a GE LOGIQ™ e ultrasound machine (Fairfield, CT, USA) with a 12-LRS linear array probe. Power Doppler Imaging (PDI) of blood flow signals were performed on bilateral knee, ankle, and hip synovium as well as the distal insertion sites of the infrapatellar ligaments and achilles tendons. Stored images were transferred via a portable USB drive from the US machine onto a National Jewish Health Dell desktop computer and analyzed using the linear measurement instrument on the Radiant DICOM Viewer program (Pozan, Poland).

Twelve anatomic regions were imaged on each astronaut during both thirty-minute examination sessions. The following sequence was selected to minimize time needed to re-position subjects: while prone, the left knee was first examined in 90-degree flexion for transverse views of the femoral cartilage, and the infrapatellar ligament was then imaged (longitudinal and transverse views). The knee was then flexed 20-30^{O} to image the medial and lateral infrapatellar recess compartments with longitudinal views to determine which side had the largest effusion. That specific side was then imaged using the KneeTap™ pneumatic compression device first deflated and then inflated to 100 mmHg as previously described [28,30,31]. Next the left ankle was imaged in a neutral position with the knee flexed 90^{o} to obtain longitudinal and transverse views of the talus cartilage. Subjects were then positioned prone to image the left achilles tendon (longitudinal and transverse views) with the foot in a neutral position off the table followed by longitudinal and transverse images of the right achilles tendon in the same position as the left ankle. Finally, the subjects were repositioned supine, for imaging the right anterior ankle and right knee as previously described above for the left lower extremity structures. The right hip was then imaged with the knee extended and the hip in slight external rotation. Firm pressure was applied on the probe to acquire images on the deeper hip structures with the probe in an oblique orientation followed by image acquisition of the left hip using the identical technique. Probe placements are represented by drawings in figure 2 and actual pre-and post-flight US images from one astronaut, are displayed in panels 1-3. [Figure 2, all panel fig.]

Immediately after capturing and recording gray scale ultrasound images, Power Doppler Images (PDI) were obtained of the following bilateral structures: infrapatellar ligaments and achilles tendons at the distal insertion sites, knee synovium (medial or lateral), ankle synovium and hip synovium.

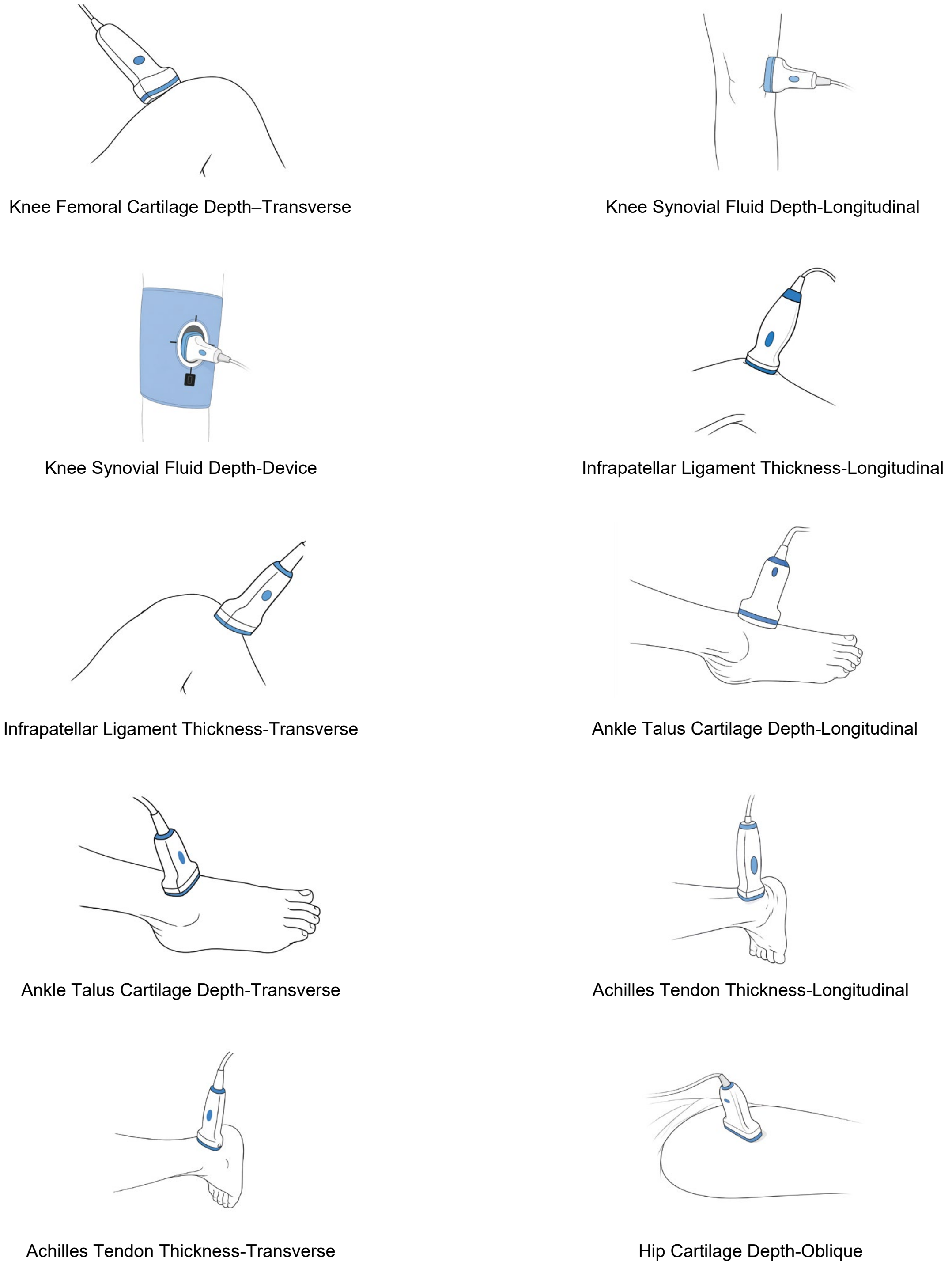
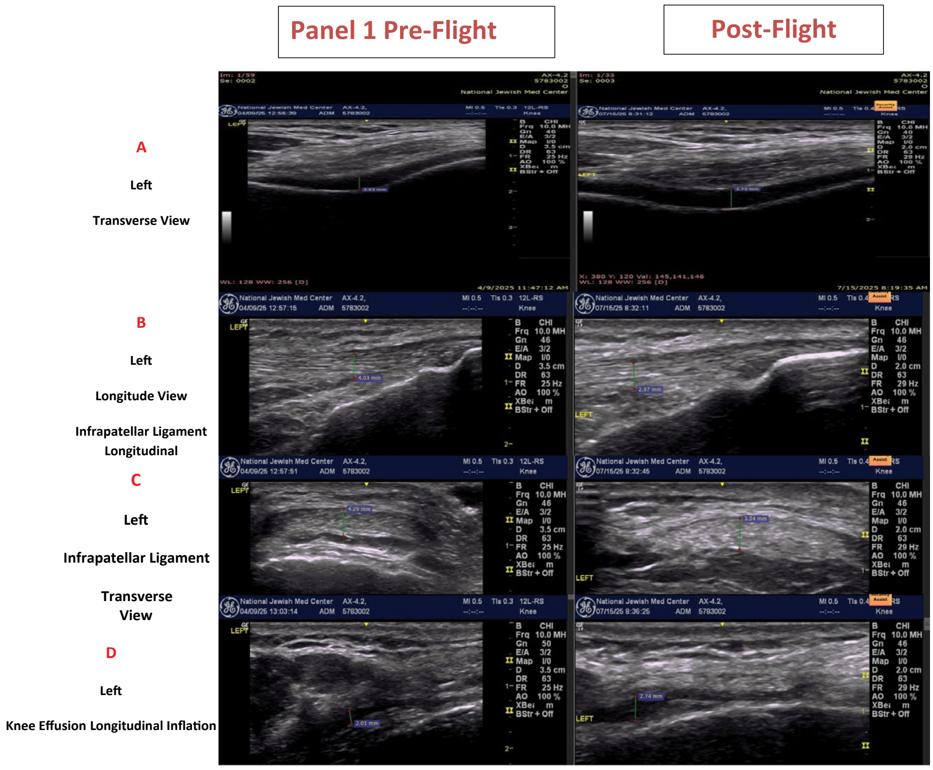
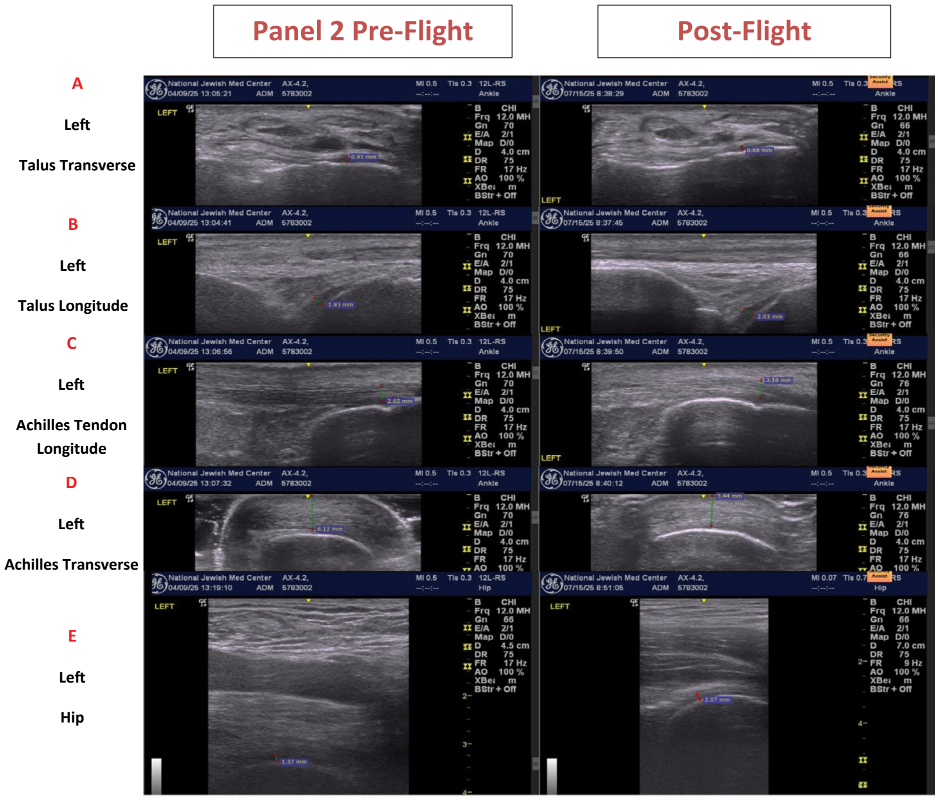


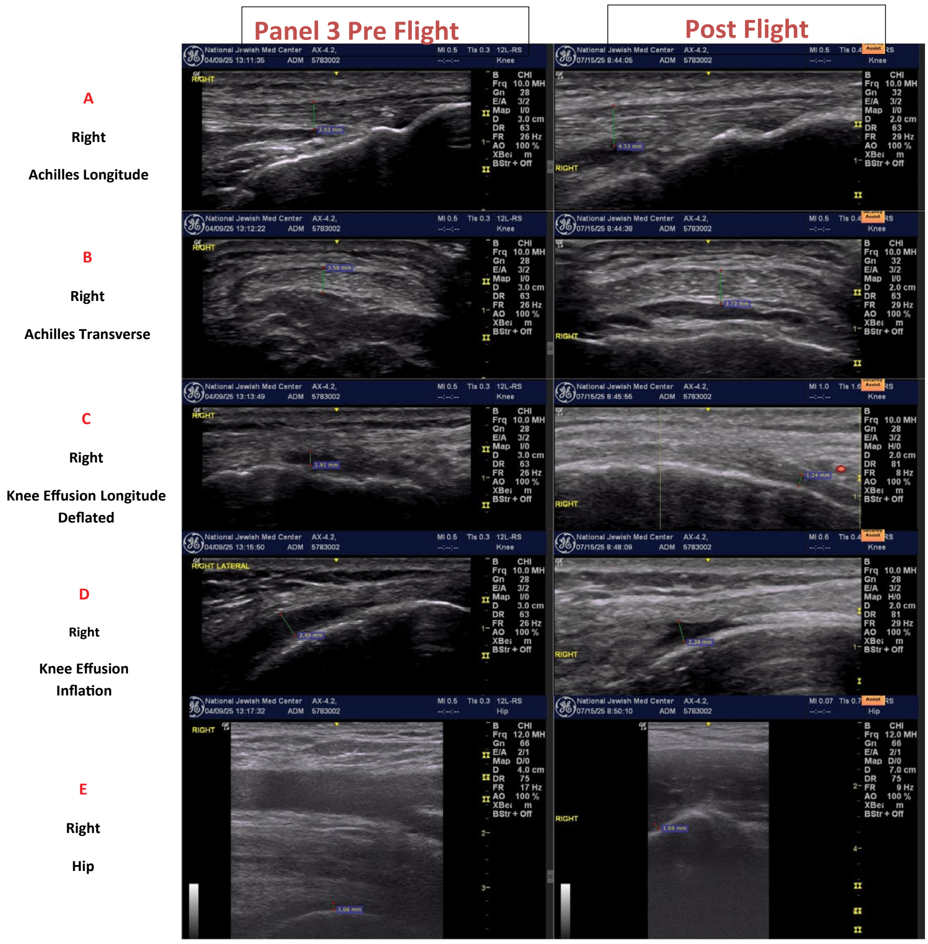
Figure 2: Probe positions for the various ultrasound images of joint structures.



Panel 1: Ultrasound images from one Crew member. Row A images are of the left femoral cartilage transverse view. Row B images are the left Infrapatellar ligament (longitudinal view). Row C is the transverse view of the left infrapatellar ligament. Row D are longitundinal views of the left infrapatellar recess demonstrating a small knee effusion during inlation of the external pneumatic compression device.



Panel 2: Ultrasound images from one Crew member. Row A are transverse views of the left ankle demonstrating the talus cartilage. Row B are the longitudinal views of the left talus cartilage. Row C are the longitudinal views of the left achilles tendon. Row D are the transverse views of the left achilles tendon. Row E are oblique images of the left hip.



Panel 3: Ultrasound images from the identical astronaut as in panels 1 and 2. Row A are longitudinal views of the right Achilles tendon. Row B are transverse views of the right Achilles tendon. Row C are longitudinal views of the right infrapatellar recess demonstrating a small knee effusion with the external pneumatic compression device deflated. Row D displays the same region as in Row C but with the device inflated which demonstrates a larger knee effusion. Row E displays oblique views of the right hip.

Ultrasound measurements were performed on side by side displayed US images using the DICOM viewer and the linear measurement instrument with a consensus of 3 investigators (RM, SS and EH). This approach ensured that the measurement cursor was placed as accurately as possible on the post-flight target image structures as the site selected for measurement on the pre-flight recorded images. The following structures were measured in millimeters (mms): cartilage depths (femoral transverse, talus cartilage transverse and longitudinal, hip oblique images) and knee synovial fluid depth (inflation and deflation of the external pneumatic compressive device) and infra-patellar tendon thicknesses in transverse and longitudinal views as well as the achilles tendon thicknesses in the transverse and longitudinal views.

Data Processing and Analysis

All measured results were entered into the REDCap data storage program at National Jewish Health and statistical analysis was performed for all linear measurements using paired t tests comparing pre-flight values to post-flight measurements in each structure or compartment imaged. A p-value of 0.05 was considered to indicate statistically significant differences. All analyses were performed in the R language version 4.4.2 [33]. Using the pwr package, a post hoc power calculation was performed to estimate the minimum % change that would be required to yield a detectable association given 80% power and the observed standard deviations in each compartments' measurements [34].

Results

Cartilage Measurements

The mean pre- and post-flight values (in mms) of the various joint structures from the 3 Astronauts and p values are reported in Table 1. There were no statistical differences between the pre-flight and post-flight

Table 1: US measurements of mean values from 3 crewmembers in mms and p values of various joint structure pre-flight compared to post-flight values.

	Pre-flight mms	Post-flight mms	P values
Left Knee Femoral Cartilage Depth-Transverse	3.5	3.7	0.52
Right Knee Femoral Cartilage Depth-Transverse	3.9	3.9	0.57
Left Infrapatellar Ligament Thickness-Longitudinal	3.4	3.1	0.08
Right Infrapatellar Ligament Thickness-Longitudinal	3.7	3.7	0.65
Left Infrapatellar Ligament Thickness-Transverse	4.3	4.4	0.70
Right Infrapatellar Ligament Thickness-Transverse	3.6	3.5	0.31
Left Knee Synovial Fluid Depth-Deflated Device	2.4	2.9	0.70
Right Knee Synovial Fluid Depth-Deflated Device	3.3	3.2	0.47
Left Knee Synovial Fluid Depth-Inflated Device	4.7	4.3	0.35
Right Knee Synovial Fluid Depth-Inflated Device	4.7	4.8	0.94
Left Ankle Talus Cartilage Depth-Longitudinal	1.5	1.7	0.06
Right Ankle Talus Cartilage Depth -Longitudinal	1.3	1.3	0.62
left Ankle Talus Cartilage Depth- Transverse	1.5	1.3	0.29
Right Ankle Talus Cartilage Depth-Transverse	1.1	1	0.47
Left Achilles Tendon Thickness-Longitudinal	4.2	4.4	0.34
Right Achilles Tendon Thickness-Longitudinal	4.4	4.6	0.62
Left Achilles Tendon Thickness-Transverse	4.8	4.4	0.24
Right Achilles Tendon Thickness-Transverse	5.8	5	0.12
Right Hip Cartilage Depth-Oblique	1.9	2.1	0.57
Left Hip Cartilage Depth-Oblique	2	1.9	0.77

measurements of cartilage depths of the femoral, talus or hip [Table 1].

Knee Synovial Fluid Depth

We identified slightly more synovial fluid in the initial pre-flight medial compartments than the lateral compartments in 3 of the 6 knees so the site which had the largest anechoic region was selected for synovial fluid measurement for each knee. We chose to measure synovial fluid depths from that compartment (medial or lateral) during inflation of the external pneumatic compressive device because it was determined to be the most sensitive to accurately quantify synovial fluid depths on small effusions. Therefore, we decided to apply this procedure for each individual crew member and compare pre-vs post-spaceflight measurements. Out of 6 knees, only two knees demonstrated an increase in the amounts of measured synovial fluid post-flight 4.4% and 21%. In contrast, the remaining 4 knees had decreases in synovial fluid ranging from 5% to 25% compared to pre-flight values.

Post-Hoc Power

We calculated that the change in the measured synovial fluid depths knee compartments during inflation of the KneeTap™ external pneumatic compressive device would need to increase by 75% in the right knees of subjects and by 190% in the left knee to reach statistical significance given the sample size of only 3 subjects and 80% power.

Tendon and Ligament Thickness

There were no differences in the infrapatellar ligament or achilles tendon thicknesses post-flight compared to pre-flight measurements in either the transverse of longitudinal views.

Power Doppler Imaging

No synovial tissue sites in the knees, ankles, hips, or infrapatellar ligament or achilles tendon insertion sites displayed a positive PDI signal that would be associated with active inflammation in either pre-flight or post-flight examinations.

Discussion

We hypothesized in this observational pilot study that brief microgravity exposure in low Earth orbit and while onboard the ISS may result in an increase in knee synovial fluid volumes compared to pre-flight values, possibly because of a decrease in synovial fluid viscosity caused by elevated circulating pro-inflammatory cytokines which has been observed by other investigators. Ultrasound is uniquely suited for spaceflight and post-flight monitoring because it is portable, non-ionizing, repeatable in real time, and capable of assessing dynamic soft-tissue and synovial changes without the logistical constraints, radiation exposure, or cost associated with MRI or CT.

That fact that we did not observe differences in the depth of the anechoic regions in the medial or lateral infrapatellar knee compartments after space flight might have been related to several factors. It is possible that this 20 day microgravity exposure with 18 days on board the ISS was an inadequate duration to cause any alterations in synovial fluid volumes. The concomitant use of NSAIDs (Ibuprofen or meloxicam)at some time by all 3 crew while onboard the ISS and the amount of cycling exercise (180-270 total minutes of cycling) may have been a sufficiently effective countermeasure to prevent any statistical changes in the measured synovial fluid and other structural changes such as tendinopathies from being observed. Another explanation could be that the known cephalad fluid shifts which occur in microgravity might have resulted in a reduced hydrostatic pressure gradient on the knee synovial capillary membrane relative to what normally occurs on Earth and therefore could have prevented changes in synovial fluid volumes. Finally, the very tight compressive leggings worn for 3 hours before post flight examinations could have also affected knee synovial fluid volumes.

Since all the subjects had experienced at least one orthopedic lower extremity intervention, we also anticipated that the previously injured joint might have been more susceptible to identifying any deleterious effects of spaceflight compared to the contralateral uninjured joint. However, those previously injured individual joints did not appear to respond with greater changes in knee synovial fluid volumes or evidence of tendinopathy compared to their non-operated joints.

Study Limitations and Strengths

A major limitation in this study, and for most human spaceflight research, is the small number of available study subjects. Our group was also heterogenous regarding prior lower extremity joint injuries and the amount of exercise performed onboard the ISS. Another potentially confounding variable which could have prevented measured changes in joint structures due to microgravity per se, is that all study subjects ingested anti-inflammatory medications while onboard the ISS.

The strengths of this study include that US images were acquired by experienced musculoskeletal ultrasound sonographers with more than 15 combined years of performing similar US examinations on hundreds of patients with several types of inflammatory arthritis as well as osteoarthritis. We were also extremely fortunate and grateful to Axiom Space to allow us crew access within 4 hours of splashdown for repeat US examinations since some changes might have been transient including knee synovial fluid volumes upon resumption of ambulation activities on Earth.

We suggest the following changes in future study designs to improve the sensitivity of US in detecting changes in joint structures caused by microgravity exposure. Crew ideally should be studied from longer duration missions (3-6 months), and ideally with in-flight examinations which could be obtained by a physician or crew member trained in US assessments. Also, US results could be correlated with any changes in circulating pro-inflammatory or vasoactive cytokines. We also think the precision of US measurements could be improved by AI directed placement of the US probe in the identical position and angle when obtaining sequential images to ensure identical anatomical images are acquired on the same subject during repeated examinations [35]. Improvement in imaging technologies will also continue to evolve such as point of care handheld ultrasound devices such as the Butterfly iQ3™ and or the GE Vscan Air™ handheld units, which currently provide excellent musculoskeletal image quality. Alternately a 3-dimensional US technique might become available in handheld devices to improve the sensitivity of detecting small, measured changes.

Summary

The results from this 18-day ISS low Earth orbital mission did not result in any statistically meaningful differences in the mean values of lower extremity cartilage thicknesses, knee synovial fluid depths measured with and without pneumatic compression or the thickness of infrapatellar ligaments or Achilles tendons among these three Astronauts. We also did not observe any increase in blood flow signals on power doppler imaging (PDI) in the knee, ankle, or hip synovium or from infrapatellar ligament or Achilles tendon distal insertion sites to suggest any active inflammation was present post-flight. Additional studies on crew from longer mission durations and including more study subjects might validate the value of non-invasive US examinations of joint structures to serve as a useful biomarker of the amount of compressive loading exercise needed for an individual astronaut to prevent cartilage damage or tendinopathy injuries. This information might also prove useful in guiding rehabilitation protocols post-flight to prevent joint injuries as crew resume exercise upon returning to Earth. A similar approach might also help aging patients or those recovering from prolonged bedrest or immobility to safely resuming weight bearing exercises without sustaining any joint injury.

Conflicts of interest and acknowledgements

The authors declare that they have no conflict of interest. This study was approved by Axiom Space (Houston, Texas, USA), the European Space Agency (ESA), and by BRANY (Biomedical Research Alliance of New York) which is an Independent Review Board contracted by National Jewish Health for all biomedical research experiments involving humans. The KneeTap™ is a device invented by RM and it is protected by a 2008 issued US patent #7,468,040 owned by National Jewish Health. Since the device is not commercially available nor licensed to any commercial entity, there is no potential monetary interest to any of the authors. We wish to acknowledge the dedicated AX-4 crew who took time from their rigorous training schedules to participate in this study and the outstanding pre- and post- flight support from Lucie Low, PhD, Michelle Griffin MPH, and Rahul Goel, PhD at Axiom Space. We also acknowledge the contribution of Allen Stevens and Dr. John Hill for their assistance with validating our US methodology in the NJH Clinical Research Unit. We also thank Ms Ruthie Knowles MSW, CCRP for constructing the unique REDCAP system used for data acquisition and analysis of this study and Ms Chavi Miles for manuscript technical and editing support. This research study was conducted as part of a Space Research Initiative led by Dr. Emmanuel Hilaire at National Jewish Health. We gratefully acknowledge Dr. Hilaire for his valuable advice and the National Jewish Health Technology Transfer Office, under his direction, for providing financial support to accomplish this project. We are also grateful to the vital support of the Diane K Shah Foundation for their commitment to advancing rheumatology research.

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