Centrifuge-Simulated Spaceflight After Aortic Valve Replacement and Atrial Septal Defect Repair

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INTRODUCTION: Human access to space is expanding rapidly in the commercial environment, with various private companies offering commercial flights to spaceflight participants (SFPs). SFPs are more likely than career astronauts to have medical conditions novel to spaceflight and may not have undergone as rigorous a medical screening process as that used for career astronauts, representing new and unstudied risks in the spaceflight environment. We report participation of a subject with recent median sternotomy for aortic valve replacement and atrial septal defect closure in centrifuge-simulated dynamic phases of orbital and suborbital spaceflight.

CASE REPORT: A 40-yr-old man with a history of congenital bicuspid aortic valve and atrial septal defect with successful repair 8 mo prior participated in an ongoing human centrifuge research study. The subject had the opportunity to participate in up to five centrifuge runs in an 8-h period, with profiles simulating commercial spaceflight. Maximum exposures included +4.0 G_z, +4.5 G_x, 6.1 G resultant, and maximum onset rate < 0.5 $G_z \cdot s^{-1}$ and +1 $G_x \cdot s^{-1}$. Physiological data acquisition included hemodynamics, electrocardiogram, neurovestibular exams, and postrun questionnaires covering motion sickness, disorientation, and similar. The subject tolerated the physiological aspects of hypergravity well, noting progressive sternal pain with increasing $+G_x$, ultimately leading him to opt out of the final profile.

DISCUSSION: Postcardiothoracic surgery risks to SFPs are largely unknown, especially within 12 mo of a significant surgical procedure. This case provides an approach for risk stratification, preparticipation evaluation, and medical management of a postsurgical patient with significant cardiac history in spaceflight and analog environments.

KEYWORDS: commercial spaceflight, acceleration, open heart surgery, patent foramen ovale, atrial septal defect, human centrifuge.

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Structural cardiovascular abnormalities, such as valvular and septal defects, represent a particular area of concern for aerospace medical professionals with respect to medical suitability and physiological tolerance of spaceflight. Environmental stressors associated with spaceflight can result in cardiovascular sequelae, including alterations of preload, afterload, and cardiac output.[26,27] In an individual with structural or functional cardiovascular abnormalities, exposure to spaceflight and associated stressors may result in poor tolerance or even adverse clinical sequelae. Aviators with structural disease, such as valvular disease or prior replacement, are often limited in maximum allowable hypergravity exposure.[28,29] For career astronauts, cardiovascular health is a requirement; prior publications have highlighted cardiovascular disease as a common cause for disqualification of astronaut applicant candidates[18] at the National Aeronautics and Space Administration (NASA) and have detailed the extensive cardiovascular risk assessment tools used for screening, monitoring, and prevention of cardiovascular disease in the astronaut corps.[14,19] Even guidance documentation provided for medical evaluation of commercial spaceflight participants (SFPs) has highlighted cardiac structural abnormalities and valvular defects as highly concerning for intolerance of hypergravity and indicative of a need for close

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medical evaluation and extensive stratification of risk prior to considering participation.[1,27] Consequently, there are limited data regarding the effects of sustained hypergravity in individuals with significant structural cardiovascular history, particularly those with structural abnormalities or prior surgical correction.

Previous studies have shown that individuals with a variety of medical conditions, including known cardiovascular disease, can tolerate the acceleration profiles of suborbital spaceflight.[2,5,6] In one notable case report, an individual with a history of Tetralogy of Fallot, including a membranous ventricular septal defect, overriding aorta, pulmonary atresia, right ventricular hypertrophy, pulmonary artery stenosis, and remote surgical correction of his structural abnormalities, was able to successfully participate in human centrifugation simulating suborbital spaceflight.[2] Even so, this unique case report provides limited data by which to evaluate other individuals of varied cardiovascular health or structural defects. Further, suborbital spaceflight is, by nature, limited in duration, thus incurring relatively brief hypergravity exposures and a similarly limited timeframe in which an SFP would be unable to receive medical support.[5,27] In contrast, the longer-duration acceleration profiles of orbital spaceflight may pose increased risk to an abnormal cardiovascular system, with definitive medical support potentially unavailable for a prolonged period.

This case report details the experience and physiological response to centrifuge-simulated dynamic phases of suborbital and orbital spaceflight in a subject with cardiac structural abnormalities, including a history of atrial septal defect and congenital bicuspid aortic valve following recent median sternotomy and surgical repair. This subject's participation was a part of a larger study which has already been published.[4]

CASE REPORT

A 40-yr-old Caucasian man with a history of congenital bicuspid aortic valve and atrial septal defect in the form of a patent foramen ovale volunteered to participate in a centrifuge study performed at the National AeroSpace Training and Research (NASTAR) Center centrifuge and approved by the University of Texas Medical Branch Institutional Review Board. The subject's congenital cardiac abnormalities had become progressively more symptomatic after age 30. These symptoms included intermittent and worsening lightheadedness, presyncopal events, and two episodes of visual field deficits initially concerning for transient ischemic attacks, but ultimately attributed by his cardiologists to cardiogenic presyncopal peripheral vision loss. In the 4-yr period leading up to his surgical intervention, his serial echocardiograms and medical evaluations documented reduction in his ejection fraction from >65–55% to 42%, development of mild left ventricular enlargement, progression of aortic regurgitation from moderate to severe with the development of leaflet prolapse, and enlargement of his aortic root from 3.8 cm to 4.4 cm. Additional medical history included hyperlipidemia, mild but frequent headaches, gastroesophageal reflux, and anxiety. His family history was significant for first-degree relatives with hypertension, diabetes, and hyperlipidemia; two second-degree relatives with congenital bicuspid aortic valves; and multiple other second-degree maternal relatives with history of coronary artery disease, myocardial infarction, and cardiac surgical interventions, including percutaneous stenting procedures and bypass grafting.

The subject underwent median sternotomy for complete replacement of his native aortic valve with a bioprosthetic porcine tissue valve 8 mo prior to study participation; his atrial septal defect was also oversewn during this surgery. He followed a nominal postoperative recovery timeline with regular cardiothoracic follow-up and imaging and progressive return to activities. In the postoperative period, the subject reported complete resolution of lightheadedness and no further episodes of syncope or presyncope. Echocardiogram performed at 3 mo postprocedure showed significant improvement with resolution of left ventricular size to normal and return of left ventricular systolic function with an ejection fraction of 60%, a well-positioned bioprosthetic aortic valve without intra- or paravalvular regurgitation, and peak and mean aortic gradients of 30 and 18 mmHg, respectively. Mild diastolic dysfunction was present (grade 1), with associated mild dilated right ventricular size but normal right ventricular systolic function and no evidence of pulmonary hypertension. The calculated aortic valve area was 1.9 cm^2, and the aortic root/ascending thoracic aorta were normal in size. Repeat echocardiogram at 7 mo postprocedure demonstrated no interval change and stability of operative interventions. The subject additionally performed serial Valsalva maneuvers during echocardiogram with no evidence of valve dysfunction or leak. The subject was fully cleared by both the surgical team and his cardiologist at 7 mo postprocedure to return to all normal activity without restriction.

The participant volunteered for the centrifuge study approximately 5 mo after his surgery and participated in centrifuge profiles 8 mo postsurgery. Prior to being medically approved for participation, he was required to complete all initial screening documentation, including a comprehensive medical history questionnaire, as described in prior publications.[4,5,24] He was subsequently required to submit additional documentation, including a complete operative report and all follow-up visit documentation, clearance to return to unrestricted physical activity from his cardiothoracic surgeon and cardiologist, recent laboratory results (including blood chemistries, blood counts, coagulation studies, and lipid panels), postoperative imaging reports including radiography and echocardiogram results, and pre- and postprocedure electrocardiogram (ECG). These documents and results were initially reviewed by an Aerospace Medicine-certified study investigator. Following initial review, this investigator interfaced directly with the subject to review and confirm submitted information and to obtain additional information regarding his current state of health. The subject obtained a physical exam from his personal physicians (including his primary care physician, his cardiologist,

and his cardiothoracic surgeon) under guidance by the study physicians (as previously described[24]). He was able to demonstrate tolerance of moderate exercise for up to an hour, 4–5 times weekly, and the ability to rapidly climb 3–5 flights of stairs without dyspnea. Physical exam documentation indicated a well-developed, moderately obese man with body mass index of 32. Baseline vitals included heart rate (HR) of 66 bpm and resting blood pressure of 132/92. His ECG at time of exam demonstrated sinus rhythm of 67 bpm, left axis deviation, a right bundle branch block and left anterior fascicular block, no ectopy, and no evidence of strain or ischemia; this was unchanged from his immediate postoperative ECG. Physical exam was notable for a well-healed midline sternal incision scar, otherwise unremarkable. The subject's medication regimen included carvedilol 12.5 mg twice daily, atorvastatin 20 mg daily, and aspirin 81 mg daily; he had been stable on these medications since the time of his surgery.

Given the novelty of the subject's medical history in an aerospace environment associated with hypergravity exposure as well as the recent surgical history, subject medical documentation was additionally reviewed by a panel of Aerospace Medicine-certified physicians, including those with additional certification in Internal Medicine, Emergency Medicine, and Critical Care Medicine, for risk profiling. With his reassuring postoperative course, contemporaneous cardiac evaluation, and evidence of cardiovascular fitness, he was approved to participate in the study. The subject was extensively counseled on the centrifuge profiles and associated hypergravity. He was further educated regarding risks associated with hypergravity, including the potential risks for significant chest discomfort (particularly with $+G_x$ exposures), risk of hypergravity-induced dysrhythmias, and risk of G-induced alterations of cardiac output and associated clinical sequelae (including near or complete loss of consciousness, lightheadedness, or similar). The participant's cardiologist was informed of his intent to participate; the cardiologist further recommended a third echocardiogram 7.5 mo after surgery and 2 wk prior to study participation, which was obtained and showed stability over time as well as reaffirming both successful repair of the atrial septal defect and normal velocity gradient across the aortic valve without additional abnormalities. His cardiologist additionally expressed comfort with prolonged Valsalva during anti-G straining maneuvers (AGSM) as needed. The subject provided written informed consent prior to participation and was able to independently verbalize understanding of risk as well as expected and potential adverse symptoms or experiences related to hypergravity exposure in each vector.

On arrival at the centrifuge facility, the subject reviewed his submitted medical history and exam paperwork with study medical personnel to verify the validity and currency of all submitted information; a brief physical exam was completed including resting vital signs and a repeat ECG. No interval change in health of functional status from submitted documentation was identified and ECG remained unchanged from prior postoperative ECGs. Prior to participation, he was taught basic AGSM and the "hook" (L-1 closed-glottis variant) maneuver. Given his medical history and risk factors, his initial centrifuge profile was performed at half (50%) intensity compared to the intended study profile to provide familiarization and ensure tolerance prior to progressing to subsequent profiles; he was advised not to use the AGSM during this low-intensity profile but to report any feelings of lightheadedness or other discomfort. He was additionally educated on how to prevent Coriolis symptoms by reducing provocative head movements during the runs. He was given a detailed overview of the centrifuge gondola, including familiarization with restraint systems and floor foot panels, prior to each run.

The subject had the opportunity to participate in up to five centrifuge profiles in a single day as a part of the larger study (detailed profile information is provided below). Study profiles included two profiles approximating suborbital spaceflight hypergravity exposures in winged vehicles and three profiles approximating capsule launch, reentry, and launch abort profiles; the centrifuge gondola multimedia system provided audiovisual stimulation during profiles to increase the fidelity of the experience. In all profiles, maximum G-onset rates remained $\leq 0.5\ G \cdot s^{-1}$ along the $+G_z$ axis and $\leq 1.5\ G \cdot s^{-1}$ along the $+G_x$ axis. The subject received a break of ≥45 min between profiles. Results as discussed below include comparison of this subject's hemodynamic parameters, physiological tolerance, and subjective symptoms to those of participants in the larger study as previously published.[4]

As above, the subject participated in Run 1 at 50% intensity, with maximum exposure +1.8 G_z and +3.0 G_x. The subject experienced no adverse events during the profile, reporting general enjoyment and noting a very brief period of transient nausea; he otherwise denied symptoms, including dizziness, chest pain, dyspnea, palpitations, headache, and greyout or tunnel vision. He did not use AGSM during the profile given the limited intensity. Vital signs remained within expected boundaries when compared to other study participants and prior investigations of this type[3–5] (see **Fig. 1**). He then proceeded to full intensity profiles as described in a prior publication,[4] including Run 2 consisting of a capsular launch profile ($+G_x$ exposure only, maximum +3.2 G_x), Run 3 representing a capsular reentry profile ($+G_x$ exposure only, maximum +4.2 G_x), and Run 4 simulating a suborbital winged vehicle profile with sequential $+G_z$ and $+G_x$ exposures during launch phases and simultaneous $+G_x$ and $+G_z$ exposures during descent (maximum exposure +4.0 G_z, +4.5 G_x, 6.1 G resultant). After participation in Run 4, the subject opted out of further centrifugation. Data collected during profiles included HR at predetermined profile intervals as well as continuous, telemetered 3-lead ECG. Throughout all profiles, the participant was actively monitored by multiple NASTAR operational staff and two board-certified Aerospace Medicine and Emergency Medicine physicians via multiple video angles and two-way voice communication, and real-time medical telemetry including 3-lead ECG, HR, and respiratory rate (RR). The subject was additionally evaluated with pre- and postrun vital signs, postrun neurovestibular examination, and postrun questionnaires regarding motion sickness and other symptoms.

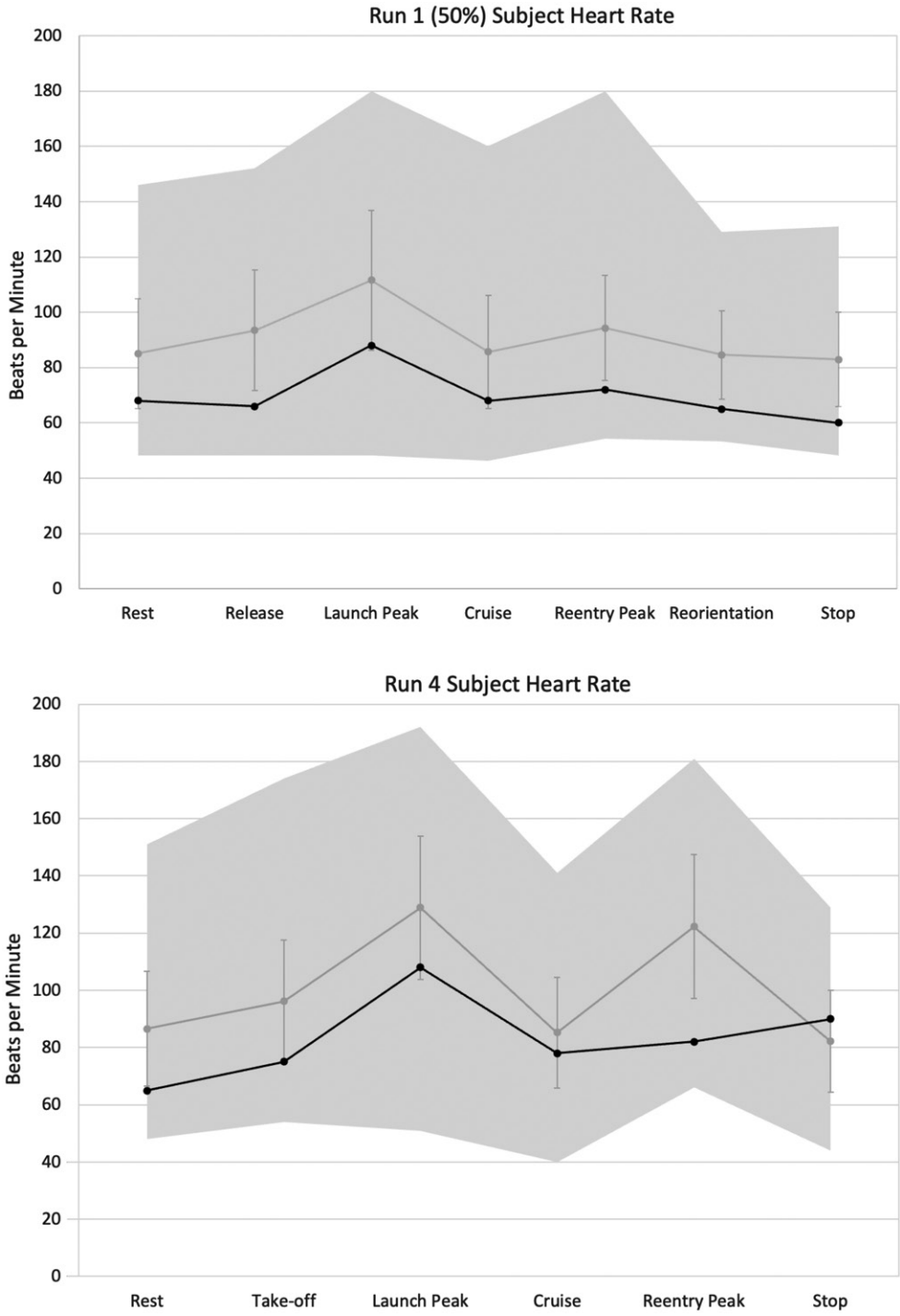

Fig. 1. Subject heart rate during winged vehicle profiles, including A) 50% Run 1 profile and B) Run 4 profile, compared to other subjects experiencing these profiles. Heart rate values are presented at rest before and after the profile as well as during dynamic profile events. Subject heart rate is indicated by the dark black line; cohort average is indicated by the light gray line, with standard deviation indicated by vertical bars. The gray shaded area represents minimum and maximum cohort heart rate ranges. Note that the subject's heart rate is persistently lower than the cohort average; while not a statistically significant difference, this may be secondary to the subject's beta-blocker usage.

During Run 2, vital signs continued to remain within expected ranges (see **Fig. 2**). Subjectively, the subject noted increased work of breathing during peak $+G_x$, which is common during $+G_x$ exposures among subjects from all study groups, regardless of cardiovascular health status and history.[4–6] However, this participant additionally noticed mild to moderate chest wall discomfort with onset at peak $+G_x$, originating midsternum and radiating outwards along the ribs, worse with inspiration and associated chest wall expansion. All symptoms resolved by the end of the profile. Notably, in the larger study

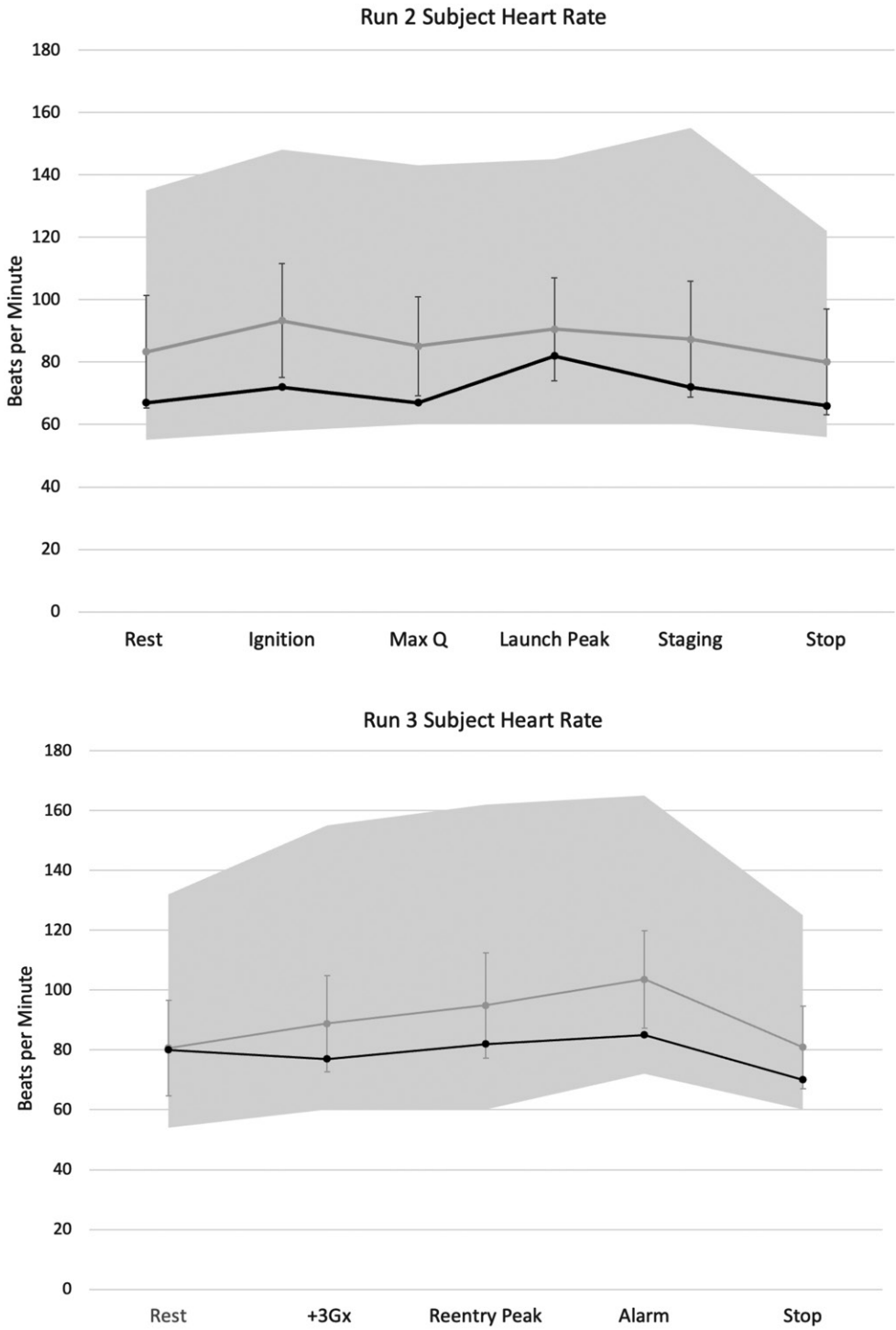

Fig. 2. Subject heart rate during capsule profiles, including A) Run 2 launch profile and B) Run 3 reentry profile, compared to other subjects experiencing these profiles. Heart rate values are presented at rest before and after the profile as well as during dynamic profile events. Subject heart rate is indicated by the dark black line; cohort average is indicated by the light gray line, with standard deviation indicated by vertical bars. The gray shaded area represents minimum and maximum cohort heart rate ranges. Note that the subject's heart rate is persistently lower than the cohort average; while not a statistically significant difference, this may be secondary to the subject's beta-blocker usage.

cohort, chest discomfort was not a symptom otherwise reported during or after this profile. Postrun neurovestibular exam was again unremarkable, and the participant elected to continue with the subsequent profile.

Run 3 was again associated with vital signs within expected ranges (see Fig. 2), though the subject again noted increased work of breathing and mild to moderate chest wall pain, particularly with sustained $+G_x$. During the highest $+G_x$ exposures,

the subject noted a transient sensation of fingertip paresthesias and commented that he felt he was hyperventilating. RR peaked at 24 breaths per minute concurrent with reported symptoms; similar RR and associated symptoms of paresthesias were seen in the larger study cohort. The subject additionally reported a brief period of a "spinning" vertigo and associated nausea concurrent with transient reentry accelerations simulating drogue and parachute deployments; vertigo and nausea were frequent complaints observed in ∼26% of the study population, associated with capsule-type profiles and likely attributable to discordant visual cues.[4] The subject reported that all symptoms resolved with hypergravity offset and he was asymptomatic at profile completion. Neurovestibular exam and postspin vitals were unremarkable, and the participant again elected to continue.

The subject demonstrated vital signs within expected ranges (see Fig. 1) during Run 4, but reported significantly more symptoms than other study participants, particularly at or above +3 G_x. Symptoms reported included chest pain, back pain, increased work of breathing, transient nausea, and headache. Chest wall discomfort was particularly notable by the subject at the time of peak +G_x (+4.5 G_x), worsened with inspiration and chest wall expansion, and was associated with left-sided thoracic back pain; chest pain was not otherwise associated with this profile for other study participants. During the rise in +G_x, around +4 G_x sustained acceleration, the subject was noted to be shifting his torso in his seat. The medical monitor immediately recommended that he avoid unnecessary body movements under acceleration as muscle strain would be likely. He acknowledged this recommendation and held his position for the remainder of the profile. Around the same time, he reported shortness of breath during the acceleration profile, but attributed the sensation to difficulty in expanding his lungs under acceleration. He declined termination of the run or other limitation of acceleration during the profile and opted to continue the profile to completion.

The subject reported resolution of all symptoms by the time of profile completion except for a mild residual headache and a persistent, moderate soreness over his sternum. Neurovestibular exam was again unremarkable and postspin hemodynamic parameters were unchanged from baseline. Given his persistent symptoms, inclusive of chest wall discomfort and midback discomfort during the profile, he opted out of any further hypergravity experiences. A physical exam was performed without any concerning findings and repeat ECG demonstrated no interval change. He was monitored for an additional 2 h without adverse sequelae, and an additional repeat ECG was performed demonstrating no interval change prior to his release from the testing facility. The subject subsequently reported approximately 24 h of "soreness" in the sternal area that improved over time and was entirely resolved by the following evening. He was evaluated by his personal physician after returning home, with no reported abnormalities, longitudinal or recurrent symptoms, or side effects of participation. In subsequent follow-up with the subject in the weeks and months after participation, the subject confirmed that symptoms did not recur at any time after participation.

Following participation, the subject was asked to provide any additional insight regarding the centrifuge experience and any discomfort reported. His gondola video and subjective questionnaires were reviewed with the study medical monitor and he confirmed the discomfort he had reported as worst during Run 4, primarily recalling pain to the sternum and left-sided midthoracic back. He provided additional qualification of the discomfort, describing it as similar to postoperative pain that he had reported to his cardiothoracic surgeon in the first month after surgery; in the postoperative timeframe, his surgeon noted that this pain was consistent with commonly reported back discomfort associated with intercostal strain or dislocation during thoracotomy and rib retraction.[12] This pain had entirely resolved at >1 mo postoperative recovery, but the discomfort experienced at sustained acceleration of greater than +3.5 G_x was reminiscent of that pain. The subject also noted that the slow-deformation foam of the gondola seat and lack of ergonomic fitting of that foam to his body habitus seemed to contribute to this pain, and that his torso movements midprofile were in response to that discomfort. He did note that this torso movement while under acceleration did seem to contribute to muscle strain and stated that he thought some of his postparticipation chest discomfort was likely related to this self-induced strain rather than any discomfort associated with acceleration.

DISCUSSION

Despite the study subject's recent and extensive cardiac surgical procedures, he demonstrated physiological tolerance of the profiles. While this subject's data demonstrated a persistently lower HR than the broader cohort average of individuals participating in these centrifuge profiles, potentially secondary to beta-blocker use, his hemodynamic data revealed expected cardiovascular response during hypergravity with no statistically significant deviation from study norms. Further, this finding was not associated with any clinically significant sequelae or symptoms. All monitoring, examination, and ECG data remained reassuring throughout his participation.

Risk profiling for this subject's participation was challenging and numerous concerns were considered prior to his inclusion. While individuals with history of prior cardiac surgeries have successfully participated in human centrifuge studies, including subjects with history of coronary artery bypass grafting, repair of congenital malformations, and valve replacements (including pulmonary, aortic, and mitral), those cases included individuals with remote surgical history and longitudinal follow-up for many years prior to their participation.[2,5,6]

In aviation, pilots with bioprosthetic and mechanical cardiac valve replacement can be granted Special Issuances by the Federal Aviation Administration (FAA) to receive all classes of medical certificate; in such cases, a minimum postsurgical period of 6 mo is required to ensure stabilization.[8,9] A similar

risk analysis process is undertaken by the FAA, including review of operative records, imaging, current physical examination, and functional studies (such as echocardiography), and a report by the pilot's treating cardiologist.[9] A panel of Aerospace Medicine and Cardiology physicians review all records and reach a consensus agreement regarding the pilot's ability to safely return to flight.[9] International practices are similar, though prior literature has raised concerns about high performance flight, particularly regarding pilots with prior aortic valve replacement and performance under $+G_z$ exposure.[13,15,29] In both commercial and military aviation, pilots with aortic valve replacement are frequently required to limit $+G_z$ exposure (generally to $\leq$+3 G_z).[28,29] In commercial spaceflight activities, there may be some flexibility allowable regarding $+G_z$ limits as SFPs presumably would not be heavily tasked with critical flight operations. While G-induced loss of consciousness would be undesirable, high-performance capability may not be a strict requirement, allowing for a slightly expanded acceptable hypergravity envelope than that imposed for high-performance pilots after aortic valve replacement. Here the subject was able to demonstrate >6 mo stabilization of his replacement valve with no perivalvular leak, preserved valve function including under Valsalva, and resolution of all preexisting symptoms that had prompted surgical intervention.

Atrial septal defects, particularly when associated with clinical sequelae, can be disqualifying for aviation activities.[23] The primary aeromedical concern would be for sudden or subtle incapacitation of a pilot, which could occur from right-to-left shunting across the defect, resulting in embolic cerebrovascular accident. Prior case reports of such events have been published.[17,20] Use of AGSM, including Valsalva, for $+G_z$ protection raises the risk of shunting. However, surgical closure of such defects is generally quite successful, with very low rates of adverse sequelae.[22,30,32] In aviation, successful surgical repair of patent foramen ovale has led to reinstatement of certification for flight activities, though often with limitations in maximum allowable $+G_z$ exposure.[17,20] For the subject described here, surgical repair was successful, with postoperative evaluations demonstrating no persistent shunting even under Valsalva strain.

Given the complexity of the subject's cardiac conditions and operative interventions as well as the short time frame since surgery, consultation with the participant's cardiologists, cardiothoracic surgeons, and additional Aerospace Medical subject matter experts was essential for thorough risk analysis and discussions of informed consent. Given the participant's excellent postsurgical recovery and overall health, and after comprehensive discussions with the subject in which he was able to demonstrate exceptional understanding of all study procedures risk factors, the decision was ultimately made to include him in the study. Even so, his inclusion prompted careful monitoring beyond study baseline, including repeat examinations and imaging prior to participation, as well as extensive monitoring and reevaluation during participation. At each profile interval, his health status and desire to continue were confirmed prior to further study participation.

Despite the objective parameters indicating physiological tolerance, the patient subjectively felt enough discomfort, particularly with $+G_x$ exposure, to terminate his participation prior to study completion. With each successive acceleration profile, the maximum $+G_x$ conferred to the participant increased: during Run 1 he experienced up to +3 G_x, followed by a maximum of +3.5 G_x in Run 2, a sustained period of +4.3 G_x in Run 3, and a peak of +4.5 G_x during Run 4. The participant first noted chest discomfort negatively affecting his enjoyment of the experience during 4.5 min of sustained and steadily increasing $+G_x$ during Run 3; as discomfort resolved after profile completion, he elected to proceed with Run 4 without hesitation. However, recurrence of this discomfort during Run 4 and the persistence of discomfort after profile completion prompted his withdrawal; study monitors similarly noted his apparent discomfort and indicated their intent to terminate his participation had he not voluntarily withdrawn.

Thoracostomy is frequently associated with substantial postoperative pain, particularly in the first 12 mo after surgery. Concern for exacerbation of chest discomfort during hypergravity was a risk explicitly expressed to the subject prior to his participation. Prior literature reviews of predictive factors have highlighted a number of concerns relevant to this subject, including a history of anxiety, male sex, and young age, all of which can be positively correlated to increased sensitivity to post-thoracostomy pain.[16,21] Even so, these risk factors were likely overshadowed by simple mechanistic exacerbation of pain by compression of the thoracic cavity during $+G_x$ exposures. The subject's body habitus was considered an additional factor likely to contribute to discomfort under hypergravity.[5] Preparticipation, it was communicated to the subject that there was an expectation that the centrifuge would likely exacerbate thoracic discomfort, and that he could opt out of exposures for this or any other reason at any time of the study. It was considered that mechanical exacerbation of chest wall discomfort could mask cardiac origins of pain; this was additionally communicated to the subject and increased monitoring during the subject's participation was implemented to mitigate this risk where possible (such as repetition of ECG and examinations throughout the day).

Clear communication of risk and expected sequelae is a vital component of informed consent and management of expectations in spaceflight and analogs (and indeed one of the few requirements imposed by FAA regulatory oversight[7,10,11]). In this case, the subject did express after his termination that the study medical team prepared him to expect such discomfort and that he was able to recognize the correlation between his pain and the hypergravity exposures, providing him some reassurance that the pain was likely mechanical in nature and related to the sternotomy rather than cardiac etiologies. Further, he was able to qualify the pain as feeling musculoskeletal in origin in both the chest and the back, similar to musculoskeletal discomfort he had experienced during recovery. Repeat examinations, vital signs, and ECGs that demonstrated no interval change despite the pain experienced were further reassuring for the patient and study monitors. It is possible that a longer

postoperative recovery period would have mitigated the subject's discomfort and allowed for better enjoyment of the experience. This case highlights an important distinction between physiological tolerance and individual enjoyment; overall enjoyment is certainly a driver in commercial operations, and a longer delay between surgical intervention and participation may increase the likelihood that postoperative SFPs enjoy their commercial spaceflight experience. Further, while in this case the subject's pain was most likely musculoskeletal and relatively benign in origin, it is worth noting that even benign pain can be operationally distracting and negatively affect performance. In the case of an actual spaceflight, an SFP experiencing similar pain could potentially be unable to perform critical actions such as contingency tasks or self-egress, which could increase risk to themselves or others.

While this individual's experience should not be considered representative of all persons with similar history, we have presented a means by which such medical history can be evaluated and risk assessed for participation in spaceflight or analog activities through careful review by subject matter experts (particularly those with Aerospace Medicine training and prior hypergravity experience) and extensive education and discussion with the participant prior to informed consent. This patient's physiological tolerance should not be considered universally representative of all individuals with valve replacement, atrial septal defect repair, or other cardiac abnormalities. Further, this subject was particularly knowledgeable about the aerospace environment and his own medical conditions; as a result, he was able to readily grasp his own relative risk in the hypergravity environment, greatly facilitating informed risk discussions. The subject was exceptionally proficient at describing symptoms as they occurred and noting suspected etiologies (for example, his description of sternal pain as a muscular chest wall soreness rather than a deeper pain), while simultaneously demonstrating a willingness to be forthcoming with symptoms rather than masking them to pursue further experiences.

It is worth noting that participant enthusiasm for spaceflight or analog experience could obscure symptoms or reduce the likelihood of a participant sharing even critical symptoms with medical personnel due to a fear of being removed from a highly desired opportunity. Fortunately, this did not seem to be a concern in the case of this subject but could mask or delay symptom reporting in a different circumstance. A participant with less comprehension of aerospace stressors and physiological sequelae or his own medical history may not have been as capable of engaging in an in-depth discussion of informed consent or in providing the same level of insight into symptoms as they occurred. Similarly, physicians lacking in aerospace medical training or experience, in particular hypergravity experience, may misinterpret or even fail to recognize symptoms, etiologies, and associated risks in such a complex patient. Ensuring adequate understanding of the aerospace stressors to be experienced and likely symptom sequelae is critical for subject informed consent. In parallel, ensuring adequately experienced Aerospace Medicine practitioners are performing the screening, monitoring, and risk stratification of such a subject in this unique environment is equally critical for the safety of the subject and those around them.

This study was not designed to extensively evaluate cardiovascular response or compensation, particularly in a subject with severe disease or a decompensated state. There was no invasive monitoring, measurement of cardiac output, or measurement of chamber or valve pressures during participation. Similarly, there was no ability to perform cardiac imaging (for example, echocardiogram) immediately before, during, or after centrifuge profiles. Further, a hypergravity study of this nature is unable to evaluate the effects of microgravity exposure or associated risks. Potential microgravity risks include fluid shifts and alterations of cardiac output,[25,26,31] which could result in adverse sequelae in an individual with this subject's medical history and recent procedural interventions. Further, long-term stays in the microgravity environment could alter hypergravity tolerance or response during reentry acceleration phases or compound any of the reported symptoms noted here.

Despite this single subject physiologically doing well through multiple centrifuge runs, the need for extensive medical review, screening, and real-time monitoring during future hypergravity exposures for all participants with cardiac history is not diminished in any way. The purpose of this study was not to produce a generalization regarding the tolerance of similar individuals to centrifuge profiles simulating suborbital and orbital spaceflight, but to identify an effective means of screening individuals with complicated medical histories, the importance of including the appropriate specialists, including Aerospace Medicine specialists with hypergravity experience, and to determine the subjective level of tolerance for the aforementioned profiles in a comprehensive and collaborative manner. The subject in this study was young and relatively healthy with an uncomplicated postoperative course, exceptional insight into both the aerospace stressors and his own medical risk factors, and an abundant enthusiasm for the centrifuge experience. He physiologically tolerated the profiles and subjectively enjoyed the experience despite his transient chest wall pain, though discomfort ultimately led him to terminate his experience. As the field of commercial spaceflight broadens, similar individuals with complex medical histories may present themselves to commercial companies as candidates for spaceflight. Adequate screening and evaluation of these individuals may further contribute to the growing catalog of medical conditions able to withstand hypergravity exposure and lead to novel opportunities for these medically complex individuals. This study lays the groundwork for additional evaluation of individuals with complex but well-controlled medical conditions in an aerospace environment.

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