Impact of Prolonged Sitting on Central Hemodynamics: Role of Intermittent Pneumatic Compression Therapy

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University of Southern Mississippi

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ABSTRACT

Prolonged sitting (3-6 hours) negatively impacts peripheral vascular health. Whether sitting similarly impacts central cardiovascular hemodynamics and vascular stiffness is unknown. **Purpose:** Determine if prolonged sitting increases central blood pressure, aortic pulse wave reflection and vascular stiffness. **Methods:** In 10 subjects (Age=22±2 yrs, BMI=28±4kg/m², 3 females), brachial artery pulse wave analysis was performed before (baseline-BL), during, and after 3 hours of sitting. Aortic pulse wave velocity (PWV) was examined before and after sitting using carotid applanation tonometry coupled with oscillometry performed on left upper-thigh. For mechanistic insight, intermittent pneumatic compression (IPC) was applied during sitting (i.e., 3, 120 mmHg compression cycles per minute, 30 mins on/off) in a sub-set (N=9). **Results:** During sitting, there was no change in heart rate (P>0.05); however, it tended (p=0.079) to be lower with IPC. No changes were noted for central blood pressure during sitting, with or without IPC (p>0.05). Augmentation pressure and index (AIX), wave reflection height and magnitude all exhibited significant decreases over course of sitting, most notable at 180 mins (e.g., AIX at BL=7±5, vs. 180 mins sitting=-3±3%, p=0.03). IPC appeared to mitigate these changes (sitting with vs. without IPC; AIX, 120 mins diff in mean=9.7%, p=0.018). No change was observed for aortic PWV in response to sitting, with or without IPC (p>0.05). **Conclusion:** Prolonged sitting decreases aortic pulse wave reflection but does not impact vascular stiffness. IPC tends to reduce heart rate and restrain central hemodynamic changes which may be the result of a reduction in venous pooling in the legs.
ACKNOWLEDGMENTS

I would like to thank Dr. Daniel Credeur, without whom this research would not have been completed or even devised to attain this valuable information. I would like to extend an appreciation to Dr. Scott Piland, Dr. Bill Holcomb, Dr. Trenton Gould, and the University of Southern Mississippi.
DEDICATION

I want to dedicate this thesis to my family and friends who have supported, encouraged, and helped me accomplish my dreams and hasn’t stopped believing in me.
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<th>Description</th>
</tr>
</thead>
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<tr>
<td>CD</td>
<td>Cardiovascular Disease</td>
</tr>
<tr>
<td>AUC</td>
<td>Area Under the Curve</td>
</tr>
<tr>
<td>RM (%)</td>
<td>Wave Reflection Magnitude</td>
</tr>
<tr>
<td>BP</td>
<td>Blood Pressure</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiography</td>
</tr>
<tr>
<td>HR</td>
<td>Heart Rate</td>
</tr>
<tr>
<td>PWA</td>
<td>Pulse Wave Analysis</td>
</tr>
<tr>
<td>PP</td>
<td>Pulse Pressure</td>
</tr>
<tr>
<td>MAP</td>
<td>Mean Arterial Pressure</td>
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<tr>
<td>AP</td>
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<td>Pb</td>
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<td>aPWV</td>
<td>Aortic Pulse Wave Velocity</td>
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<td>BL</td>
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CHAPTER I– INTRODUCTION

More than half (60%) of U.S. adults do not meet the recommended amount of physical activity, leading to a life of inactivity. (Facts about Physical Activity, 2017) Accumulating evidence supports that a sedentary lifestyle can increase one’s risk of developing a chronic diseases, such as metabolic disease or cardiovascular disease (CD) (Booth, Roberts, Laye, 2012). Evidence regarding the deleterious effects of being physically inactive can be dated back to 450 B.C with a quote from Hippocrates stating, “If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health.” (Booth, Roberts, Laye, 2012).

Previous studies have utilized models of bed rest and limb casting to examine the physiological impact of physical inactivity (Saltin et al, 1968). In terms of central cardiovascular parameters, these studies have demonstrated a decrease in VO$_2$ max, maximal cardiac output, maximal stroke volume, and an increased heart rate following 20 days of bed rest (Saltin et al, 1968, Owen et al, 2010, Williams et al, 2009). Furthermore, limb casting studies have shown vascular remodeling occurs very quickly, resulting in a decrease in artery size, increase in vascular resistance, and subsequent reduction in limb blood flow, most notable within the first week (Green et al, 1997, Thijssen et al, 2011, Thijssen et al, 2010, de Groot PC et al, 2006). Collectively, these results show that completely removing activity can result in detrimental physiological changes that may never fully recover with a return to physical activity (Saltin, Blomqvist, Mitchell, Johnson, Wildenthal, Chapman, 1968). However, it is highly unlikely, unless under extreme circumstances, individuals are placed on bed rest or extreme inactivity.
Previous studies have also examined short-term reductions in physical activity, such as reducing one’s step count, or prolonged single bouts of sedentary behavior like sitting. One study demonstrated that reducing daily steps (10,000 steps to <5,000 steps per day) can increase insulin resistance and decrease endothelial function in the legs, both markers of cardio-metabolic disease risk (Boyle et al, 2013, Reynolds et al, 2015). Another study examining a reduction of steps per day (~6,000 steps to 1,400 steps for three weeks) found the area under the curve (AUC) for plasma insulin progressively increased, VO\textsubscript{2} decreased, and body composition changed—increased fat mass and decrease in lean mass (Olsen, Krogh-Madsen, Thomsen, Booth, Pederson, 2008). The overall temporality for these cardio-metabolic changes in response to short-term changes in daily physical activity appear rapid, and it may be that cardio-metabolic dysfunction is initiated with single bouts of sedentary behavior such as prolonged, uninterrupted sitting.

Recently, research has shown that following a prolonged bout of sitting (6 hours), leg endothelial function was reduced with no changes occurring in the arms (Restaino, Holwerda, Credeur, Fadel, Padilla, 2015). These results suggest that rapid, localized vascular deconditioning can occur in a single day. Simple activities such as walking, prior exercise, fidgeting of a limb, or even localized heating seems to revert these negative vascular effects associated with sitting (Morishima et al, 2017, Morishima et al, 2016, Restaino et al, 2016, Restaino et al, 2015). The underlying mechanisms is still unclear, but may be related to increases in blood flow-induced shear stress on the vascular endothelium (Restaino, Walsh, Morishima, Vranish, Martinez-Lemus, Fadel, Padilla, 2016). Importantly, little is known about the plausible negative effects one bout
of prolonged sitting could have on central cardiovascular hemodynamics and aortic
vascular stiffness.

*Purpose and Hypothesis.* Given this background, the purpose of this study was to
determine whether prolonged, uninterrupted sitting could negatively impact central
cardiovascular hemodynamics and vascular stiffness. We hypothesized that prolonged
sitting would increase central blood pressure (BP), aortic pulse wave reflection (RM) and
vascular stiffness in healthy college-aged individuals. As an exploratory aim, and to
provide mechanistic insight, we applied intermittent pneumatic cuff compressions to the
lower limbs during sitting in a subset (N=9) to determine whether this simple non-
exercise therapy could prevent changes in central cardiovascular hemodynamics during
prolonged sitting.
CHAPTER II– METHODS

Experimental Design

This study was a randomized cross-over design.

Subjects

Ten young men and women (18-30 years of age) were recruited from the University of Southern Mississippi campus and surrounding Hattiesburg (MS, USA) area and participated in this study. All experimental procedures were approved by the University of Southern Mississippi Health Sciences Institutional Review Board (Approval Letter, Appendix A). Prior to participation, each participant provided a written detailed informed consent. Female subjects were studied during the early follicular phase of their menstrual cycle to account for potential influences of hormonal status on study results. All participants were considered recreationally active, non-smokers, not using vasoactive medications, and free of any diagnosed cardiovascular, pulmonary, or metabolic disease, as determined by a detailed medical health history questionnaire.

Experimental Measurements and Procedures

*Anthropometric Measures.* Height and weight were determined with a standard stadiometer and sliding scale.

*Cardiovascular Measures.* Participants were instrumented with lead II surface electrocardiography (ECG) (Powerlab, AD-Instruments, Colorado Springs, CO) to continuously monitor heart rate (HR) throughout the study. Peripheral and central cardiovascular hemodynamics were measured via automated cuff oscillometry (SphygmoCor XCEL; AtCor Medical). To do this, a blood pressure cuff was placed on the subject’s upper right arm and was inflated/deflated performed at different intervals.
(rest, 10 min, 60 min, 120 min, 180 min, post) during the study visit. Pulse wave analysis (PWA) was performed using a validated transfer function (AtCor Medical) to examine central, aortic hemodynamics, such as blood pressure (BP), mean arterial pressure (MAP), pulse pressure (PP), augmentation pressure (AP), augmentation index (Alx), wave reflection (Pb), and wave magnitude (RM%). Rate pressure product (RPP), an index of myocardial oxygen demand, was measured by using the following equation:

\[
\text{Heart rate (bpm)}/\text{systolic blood pressure (mmHg)}
\]

**Vascular Stiffness.** Aortic pulse wave velocity (aPWV) was performed at pre-sitting baseline and post-sitting during each experimental visit. Aortic PWV was assessed by performing carotid applanation tonometry along with oscillometry using a thigh cuff at the femoral artery site, in accordance with published recommendations (Stoner, Credeur, Dolbow, Gater, 2015). Carotid-femoral artery pulse transit time (sec) was determined with applanation tonometry performed over the left common carotid artery pulse site, coupled with oscillometry method performed over the left upper thigh. Transit time (\(\Delta t\)) was calculated as the time interval between the diastolic foot of the pressure wave from tonometer and the thigh cuff arterial waveform. Prior to this, distance measures (m) between carotid pulse site and sternal notch (\(L1\)), and sternal notch to top edge of the thigh cuff (\(L2\)) were obtained using a standard tape-measure. Along with pulse transit time, distance was applied to the following equation to calculate aortic Pulse Wave Velocity (aPWV) which is considered the gold standard for measuring arterial stiffness (Stoner, Credeur, Dolbow, Gater, 2015):

\[
aPWV \text{ (m/s)} = \frac{\text{Length } (L2 - L1)}{\Delta t}
\]
**Intermittent Pneumatic Compression.** Intermittent pneumatic compression—IPC is an FDA approved therapy commonly used to treat lymphedema, venous insufficiency, peripheral arterial disease, and even improve vascular health in people with spinal cord injury (Tran et al, 2017, Credeur et al, 2017, Delis et al, 2005, Husmann et al, 2008). This technology works by sequentially inflating and deflating a series of air cuffs (120 mmHg) positioned around the foot, ankle and calf region. This treatment has been shown to not only increase arterial inflow, but increase venous outflow due to a mechanical pumping effect, which in theory, could prevent venous pooling during prolonged bouts of sitting. For the present study, IPC was administered on one day during sitting as a means to reduce venous pooling. During sitting, IPC was implemented during the last 30 mins of every hour during sitting.

**Experimental Protocols**

*Experimental Study Visit One.* Participants reported to the laboratory between the hours of 8:00am-12:00pm, and at least two hours fasted. The last meal consumed was logged and participants were instructed to consume the same meal for subsequent study visits. Participants were also required to abstain from intake of alcohol for 12 hours and strenuous activity 24 hours prior to each study visit. On the day of the study, individuals were presented and signed a detailed written informed consent (**Appendix B**) and completed a medical health history questionnaire (**Appendix C**). Participants were familiarized with experimental procedures before any data was collected. Following an explanation of procedures, participant rested quietly on an exam table, positioned semi-recumbent and instrumented for all study measurements: ECG, BP, PWA and PWV. Following 10 mins of rest, a 5 min resting baseline was performed (continuous ECG and
2-3 PWA), followed by a single PWV measurement. Following these initial baseline measures, the participants were repositioned upright in an adjacent chair where they remained for the next 3 hours. During sitting, the participants were allowed to perform normal desk related work such as reading a book, or working on their personal device. Importantly, participants were instructed to refrain from any leg movement or engaging in any arousing types of activities which could alter cardiovascular hemodynamics, such as listening to fast-paced music, and watching certain types of movies (e.g., comedies, action or horror). Central BP and PWA were assessed during the three hours of sitting at the time points of 10, 60, 120, 180 minutes. Following 3 hours of sitting, participants were transferred back to the exam table using a mechanical lift (Invacare Reliant 450), where post-sitting measurements of HR, BP, PWA, and PWV were performed (Figure 1).

**Experimental Study Visit Two.** For visit 2, the same experimental procedures performed in visit 1 were repeated with the addition of IPC performed on both legs using a commercially available device (Art-Assist) (Figure 2). IPC treatment was initiated during the last 30 mins of each hour during the sitting time points (IPC compression cycles: 120 mmHg compressions, 4 sec on, 16 sec off, 3 cycles per min). All data were collected immediately following completion of ICP for each study time point. Importantly, the order of experimental study visits was randomized by choice, and each study visit was separated by a minimum of 48 hours and maximum of one week. In the case for female subjects, if studied during the latter portion of the follicular phase of menstrual status, then they were asked to return to the laboratory at the same time of the month for the second visit.
Figure 1. Study Visit one Timeline.

Subject Arrival (Consent, etc.)

Rest

Start Sitting

Post-Assess.

Participant completed informed consent.

Participant rested semi-recumbent for ten mins.

Three hours of sitting began.

IPC cuffs

IPC treatment administered

Participant transferred. Post assessments (HR, BP, PWA, and PWV)

Figure 2. Study Visit Two Timeline.
Data Analysis

For brachial artery pulse wave analysis, oscillometric BP waveforms were recorded and analyzed through the SphygmoCor XCEL device [32]. Each assessment cycle (baseline and post sitting, and during sitting time points) lasted approximately one minute, consisting of a brachial BP recording and then a 10-sec sub-systolic recording. An aortic BP waveform was generated by the device using a validated transfer function (Butlin, Qasem, Avolio, 2012), from which the central hemodynamic indices were derived: systolic BP, diastolic BP, pulse pressure, augmentation pressure, augmentation index, backward pressure components (Pb) and reflection magnitude (RM%). The AIx is defined as augmentation pressure (AP) expressed as a percentage of pulse pressure, where AP is defined as maximum systolic pressure, minus pressure at the inflection point. The generalized aortic pressure waveform is decomposed into its forward—Pf and backward—Pb components by assuming a triangular flow wave (Westerof et al, 2006, Qasem et al, 2008). This methodology generates a triangular-shaped wave by matching start, peak, and flow-wave end to timing of the foot, inflection point, and incisura of aortic pressure wave. The Pb and Pf are constructed with the following equations: Pf = [P + Zc × Q]/2 and Pb = [P – Zc × Q]/2, respectively, where P is the aortic pressure wave, Q is the approximated pseudo-flow wave, Zc is the characteristic impedance. The RM% was calculated as Pb/Pf*100.

Statistical Analysis

To examine the difference in cardiovascular hemodynamics between the various sitting time points (BL, 10, 60, 120, 180, post sitting), two-way repeated measures
ANOVA’s were performed on dependent variables (HR, SPB, DPB, PP, MAP, RPP, AP, AIX, Pb, RM).

To examine the difference in vascular stiffness from pre-sitting to post-sitting a univariate ANOVA was performed on aortic PWV. Cohen’s $d$ effect sizes were calculated to examine meaningfulness of changes in primary dependent variables over the course of sitting. All statistical analyses were performed using Sigma Plot Analysis software and SPSS (IBM, Watson Analytics). Statistical significance was set $a$ priori at $p<0.05$, and moderate to large effect sizes were considered clinically meaningful.
CHAPTER III - RESULTS

Subjects

Ten subjects were recruited and studied. Participants consisted of three females and seven males. The average age, height, weight, and BMI were 22±2 yrs, 168 ± 10 cm, 80 ± 17 kg, and 28±4 kg/m², respectively. All participants were free of any chronic disease and/or prescribed vasoactive medications that could alter study results.

Central hemodynamic responses to sitting, with and without IPC

All central hemodynamic data from baseline (pre) to post-sitting time points are presented in Table 1. From pre-post sitting there was a significant decrease in heart rate (e.g., baseline=66±10 vs. post sit=62±9 bpm, p=0.038). During sitting, there was no change in heart rate (P>0.05); however, heart rate tended (p=0.079) to be lower with the application of IPC (Figure 3). No changes were noted for central blood pressure measures during sitting, with or without IPC (p>0.05) (Figure 4). Augmentation pressure and index (AIx), exhibited significant decreases over the course of sitting, most notable at 180 mins (Figure 5). Interestingly, IPC appeared to mitigate these changes (sitting with vs. without IPC; AIx, 120 mins diff in mean=9.7%, p=0.018). Figure 5 illustrates the impact of sitting on central pulse pressure (cPP) and rate pressure product (RPP).

Following sitting, there was a significant decrease in cPP and RPP (p<0.05), both with and without IPC application. The changes in backward wave height (Pb) and wave reflection (RM) are illustrated in Figure 6. Both Pb and RM were significantly lower from pre- to post-sitting time points both with (p=0.040) and without IPC (p=0.037). No
change was observed for aortic PWV in response to sitting, with or without IPC (p>0.05).

**Table 1. Central Cardiovascular Hemodynamics from Pre- to Post-Sitting**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre IPC No</th>
<th>Post IPC No</th>
<th>Pre IPC</th>
<th>Post IPC</th>
<th>Time</th>
<th>Visit</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (bpm)</td>
<td>66±10</td>
<td>62±9</td>
<td>63±9</td>
<td>60±10</td>
<td>0.03</td>
<td>0.34</td>
<td>0.89</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>105±11</td>
<td>107±10</td>
<td>108±12</td>
<td>106±8</td>
<td>0.85</td>
<td>0.66</td>
<td>0.12</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>74±8</td>
<td>76±7</td>
<td>73±9</td>
<td>76±6</td>
<td>0.08</td>
<td>0.69</td>
<td>0.59</td>
</tr>
<tr>
<td>PP (mmHg)</td>
<td>31±7</td>
<td>30±5</td>
<td>35±7</td>
<td>30±5</td>
<td>0.02</td>
<td>0.36</td>
<td>0.09</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>86±10</td>
<td>88±9</td>
<td>87±10</td>
<td>87±7</td>
<td>0.58</td>
<td>0.85</td>
<td>0.64</td>
</tr>
<tr>
<td>RPP (bpm*mmHg)</td>
<td>6910±1713</td>
<td>6574±1570</td>
<td>6881±1567</td>
<td>6353±2353</td>
<td>0.02</td>
<td>0.58</td>
<td>0.25</td>
</tr>
<tr>
<td>AP (mmHg)</td>
<td>3±5</td>
<td>-2±2</td>
<td>4±5</td>
<td>-2±2</td>
<td>0.001</td>
<td>0.27</td>
<td>0.28</td>
</tr>
<tr>
<td>AIx (%)</td>
<td>7±14</td>
<td>-8±7</td>
<td>11±14</td>
<td>-8±8</td>
<td>&lt;0.001</td>
<td>0.33</td>
<td>0.33</td>
</tr>
<tr>
<td>Pb (mmHg)</td>
<td>12±3</td>
<td>12±2</td>
<td>16±5</td>
<td>12±2</td>
<td>0.020</td>
<td>0.22</td>
<td>0.04</td>
</tr>
<tr>
<td>RM (%)</td>
<td>46±7</td>
<td>44±2</td>
<td>51±8</td>
<td>43±3</td>
<td>0.07</td>
<td>0.01</td>
<td>0.04</td>
</tr>
</tbody>
</table>

*Note: HR, Heart rate; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; PP, Pulse Pressure; MAP, Mean Arterial Pressure; RPP, Rate Pressure Product; AP, Augmentation Pressure; AIx, Augmentation Index; PB, Backward Pressure Component; RM, Reflection Magnitude.*
Figure 3. Heart rate response during sitting with IPC and without IPC.

Note: There was a tendency (p=0.079) for heart rate to be lower during sitting with IPC.

A. 

B. 

Figure 4. Augmentation pressure and augmentation index alterations during sitting with IPC and without IPC.

Note: Panel (A) depicts central augmentation pressure measures with IPC and without IPC during sitting. Panel (B) depicts augmentation index measures with IPC and without IPC during sitting.

A. 
Figure 5. Central pulse pressure and rate pressure product measures during sitting with IPC and without IPC.

Note: Panel (A) depicts central pulse pressure measures with IPC and without IPC during sitting. Panel (B) depicts rate pressure product measures with IPC and without IPC during sitting.

Figure 6. Wave Reflection and Wave Reflection Magnitude measures during sitting with IPC and without IPC.

Note: Panel (A) depicts wave reflection measures with IPC and without IPC during sitting. Panel B) depicts wave reflection magnitude measures with IPC and without IPC during sitting. Error bars indicate the SD of the mean at each time point.
**Vascular Stiffness Responses to Sitting**

*Figure 7* illustrates the effects sitting on vascular stiffness via pulse wave velocity. To note, the figure depicts sitting with IPC (n=8) and without IPC (n=9). PWV data were not collected in one subject due to technical difficulties (leg size surpassed cuff length), and one subject did not return to the following-up study visit. Overall, aortic PWV was not significantly altered from pre-sit to post-sit, either with IPC or without IPC application.

![Figure 7](image)

*Figure 7.* Aortic stiffness measures pre-sit and post-sit, both with IPC and without IPC.
CHAPTER IV– DISCUSSION

This study sought to determine whether prolonged sitting could negatively impact markers of central cardiovascular health and vascular stiffness in relatively healthy individuals. Contradictory to our initial hypothesis, sitting did not increase central BP indices. Uniquely, our data also indicate that sitting causes a significant reduction in augmentation pressure, most likely the result of blood pooling in the legs. Importantly, IPC seemed to restrain some of the reduction in augmentation and tended to produce a lower heart rate response to sitting, both likely the results of less venous pooling in the legs.

Effects of Sitting on Central Cardiovascular Hemodynamics

Previous research has shown a decrease in peripheral vascular function after a single bout of prolonged, uninterrupted sitting (Restaino, Walsh, Morishima, Vranish, Martinez-Lemus, Fadel, Padilla, 2016, Thosar, Johnson, Johnston, Wallace, 2012). Given this data, we set out to determine whether or not a prolonged period of sitting would have similar effects on the central hemodynamics and vascular stiffness. Our findings demonstrate that central blood pressure indices are not significantly impacted by sitting; however, augmentation pressure appeared to be lower following sitting. This leads to question why these cardiovascular changes are occurring during sitting. One potential mechanism could be related to blood pooling in the legs, which may dampen pulse wave reflection (Stone et al, 2016, Stoner et al, 2017). Recently, a similar observation was noted for when subjects were subjected to a modified head-up tilt. The authors of this work also examined perfusion changes in the legs using near-infrared spectroscopy.

Although only correlative, these data suggests that increases in total perfusion (a marker
of blood pooling) during the postural shift are directly related to reduction in augmentation pressure. The overall clinical significance for a reduction in augmentation pressure during prolonged sitting is unclear and will require future work. Uniquely, our study shows for the first time, applying IPC during a prolonged bout of sitting may restrain reduction in augmentation pressure and lower heart rate. This has important clinical implications, especially for people who are subjected to prolonged periods of sitting due to occupational circumstances, or due to physical imitations such as people with neurological disease or injuries. Future studies will be needed to evaluate the long term impact of IPC application, particular in patient groups, as it relates to overall cardiovascular health and function.

Effects of Sitting on Aortic Vascular Stiffness

Indeed, previous research has shown the deleterious impact of sitting on vascular health. Given this, research, one could speculate that alterations in vascular function in response to acute sedentarism, like sitting, may also alter other important cardiovascular variables such as stiffness. In light of this, we examined a gold standard measure of central vascular stiffness, aortic pulse wave velocity, before and after prolonged sitting. Interestingly, sitting did not appear to alter vascular stiffness in the present cohort. Given that intermediate measures of atherosclerotic risk, like aortic PWV, tend to be more structural in nature (i.e., dependent on arterial size and wall thickness), thus, a longer period on inactivity may be needed see noticeable changes in this measurement.
CHAPTER V– CONCLUSION

In summary, this preliminary data indicates that a single bout (3 hours) of prolonged, uninterrupted sitting results in a significant alteration in central cardiovascular hemodynamics (decreased aortic pulse wave reflection). Importantly, the application of IPC tended to reduce heart rate and restrain some of the observed central hemodynamic changes, most notably AP, which may be result of a reduction in venous pooling in the legs. Future studies are needed to fully elucidate the clinical implications for a reduction in AP in response to prolonged, uninterrupted sitting.
APPENDIX A- IRB APPROVAL

INSTITUTIONAL REVIEW BOARD
118 College Drive #5147 | Hattiesburg, MS 39406-0001
Phone: 601.266.5097 | Fax: 601.266.4377 | www.sou.edu/research/institutional-review-board

NOTICE OF COMMITTEE ACTION

The project has been reviewed by The University of Southern Mississippi Institutional Review Board in accordance with Federal Drug Administration regulations (21 CFR 26, 111), Department of Health and Human Services (45 CFR Part 46), and university guidelines to ensure adherence to the following criteria:

- The risks to subjects are minimized.
- The risks to subjects are reasonable in relation to the anticipated benefits.
- The selection of subjects is equitable.
- Informed consent is adequate and appropriately documented.
- Where appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of the subjects.
- Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of all data.
- Appropriate additional safeguards have been included to protect vulnerable subjects.
- Any unanticipated, serious, or continuing problems encountered regarding risks to subjects must be reported immediately, but not later than 10 days following the event. This should be reported to the IRB Office via the ‘Adverse Effect Report Form’.
- If approved, the maximum period of approval is limited to twelve months.
  Projects that exceed this period must submit an application for renewal or continuation.

PROTOCOL NUMBER: 16061301
PROJECT TITLE: Impact of Prolonged Sitting on Cardiovascular Health: Role of Intermittent Pneumatic Compression Therapy
PROJECT TYPE: New Project
RESEARCHER(S): Daniel P. Cradeur, Ph.D.
COLLEGE/DIVISION: College of Health
DEPARTMENT: School of Kinesiology
FUNDING AGENCY/SPONSOR: N/A
IRB COMMITTEE ACTION: Expedited Review Approval
PERIOD OF APPROVAL: 06/28/2016 to 06/27/2017
Lawrence A. Hosman, Ph.D.
Institutional Review Board
VISIT 2: During the experimental study visit, you will be asked to report to the laboratory at your scheduled time. All experimental study sessions will be scheduled to begin in the morning hours (6:00-11:00am) following an overnight fast and having been refrained from caffeine intake and alcohol for 12 hours, and any strenuous physical activity for 24 hours prior to participating.

Upon arrival to the laboratory, you will be asked to use the restroom. Next, you will be transferred to the exam table and positioned slightly upright. You will then be instrumented for baseline assessments of heart rate using electrocardiography (ECG), blood pressure, and vascular health testing (described below in detail). After baseline assessments, a blood pressure cuff positioned around your calf and/or foot will be periodically inflated and deflated (3 inflations/deflations per minute) for an hour. Ultrasound measurements on your leg will be taken twice during this time period (after 5 mins and 45 mins) to determine blood flow. Lastly, the flow-mediated dilatation tests will be repeated on both legs.

Procedures to be performed:

Height and Weight - Your height will be determined with a tape measure while you are supine on the examination table, and your weight will be determined using a specialized wheelchair scale (you will be weighed while in your wheelchair, then the wheelchair will be weighed separately after you are transferred to the exam table).

Doppler-Ultrasound - An ultrasound probe will be placed over the skin on the inside both of your ankles and also behind your knees in conjunction with a water-based gel to improve the conduction of the signal. This safe, non-invasive procedure will determine the size of your artery and also the speed of blood moving through it.

Body Composition - You will be transferred from your wheelchair onto a table to undergo Dual-Energy X-Ray Absorptiometry (DEXA) scanning. Your legs will be secured with special straps for your safety. This scanning will determine your body composition, including lean and fat mass, and bone mineral density.

Blood Pressure - A blood pressure cuff will be wrapped around your upper-arm to periodically measure blood pressure.

Heart Rate - After cleaning your skin with an alcohol swab, electrodes (patches) will be placed on the surface of your chest just below your shoulders and also on the side of your abdomen for heart rate measurements per the ECG.

Vascular Health Testing - A blood pressure cuff will be placed around your calves. This cuff will be inflated, as is done when your blood pressure is being measured, but instead of deflating the cuff immediately it will remain inflated for 5 minutes. We will measure the blood flow to your foot by placing a probe over the artery of your ankle or behind your knee, during and after inflating the cuff. The probe will provide a measure of the speed at which your blood is traveling through your artery as well as the size of your blood vessel.

Intermittent Pneumatic Compression (IPC) - IPC is a non-invasive FDA-approved therapy which includes the administration of brief 120 mmHg cuff compressions (4 sec each) around your calf and foot region performed sequentially over the course of an hour (~3 compressions/min). Blood flow in your ankle and behind your knee will be measured using the ultrasound machine periodically during the IPC session. The FMD procedure will be performed on both ankles and/or behind the knees before and after 60 minutes of IPC.

3. Benefits:

If you agree to take part in this study, there may or may not be a direct medical benefit to you. You may expect to benefit from taking part in this research to the extent that you are contributing to medical knowledge. Our hope is that the information gained from this study will develop future recommendations for the prevention and/or treatment of vascular diseases among individuals with spinal cord injury.

4. Risks:

While in the study, you are at risk for the side effects described below. You should discuss these with the investigator and/or your doctor. There may also be other side effects that we cannot predict:
ECG: Some people may experience skin irritation from the patches that connect the wires on the chest to the computer. Skin and hair are pulled slightly when the patches are removed after the test. Research personnel will attach and remove the patches as carefully as possible.

Blood pressure cuff inflation: The blood pressure cuff will squeeze the arm tightly; however, any discomfort will be alleviated as soon as the pressure in the cuff is released.

DEXA Scanning: The DEXA scan measurements emit small amounts of radiation, however, they have been found to have no biological effects and are equivalent in radiation exposure to that of natural background radiation.

Participant Transfers: The risks of transferring you to and from your wheelchair includes bumping of your limbs and falling. However, trained personnel will be there to assist with transfers using a specialized heavy-duty lift equipped with a harness system and straps to transfer you from your wheelchair to various testing apparatuses.

Intermittent Pneumatic Compression: There are no known risks associated with the use of low frequency IPC. In fact, this therapy is routinely used in patients subjected to bedrest to improve circulation through peripheral arteries and veins, thus, reducing occurrence of blood clots.

For the reasons stated above the investigators will observe you closely while giving the treatment described herein. If you have any worrisome symptoms or symptoms that has described to you, notify the investigators immediately.

5. Confidentiality:

Information produced by this study will be stored in the investigator's file and identified by a code number only. The code key connecting your name to specific information about you will be kept in a separate, secure location. Information contained in your records may not be given to anyone unaffiliated with the study in a form that could identify you without your written consent, except as required by law. It is possible that your medical and/or research record, including sensitive information and/or identifying information, may be inspected and/or copied by the study sponsor and/or federal or state government agencies in the course of carrying out their duties. If your record is inspected or copied by the study sponsor (and/or its agents), or by any of these agencies, the University of Southern Mississippi will use reasonable efforts to protect your privacy and the confidentiality of your medical information. The results of this study may be published in a medical book or journal or used for teaching purposes. However, your name or other identifying information will not be used in any publication or teaching materials without your specific permission.

6. Alternative Procedures:

An alternative is to not participate in this research study.

7. Participant's Assurance:

This project has been reviewed by the Institutional Review Board, which ensures that research projects involving human subjects follow federal regulations.

Any questions or concerns about rights as a research participant should be directed to the Chair of the IRB at 601-266-5997. Participation in this project is completely voluntary, and participants may withdraw from this study at any time without penalty, prejudice, or loss of benefits.

Any questions about the research should be directed to the Principal Investigator using the contact information provided in Project Information Section above.

CONSENT TO PARTICIPATE IN RESEARCH
# APPENDIX C – MEDICAL HISTORY QUESTIONNAIRE

<table>
<thead>
<tr>
<th>University of Southern Mississippi, School of Kinesiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Health History Form</td>
</tr>
<tr>
<td>All of the information provided in this form is voluntary.</td>
</tr>
</tbody>
</table>

**Date:**

**Biographical information:**

**Last Name:**

**First:**

**Mi:**

**Occupation:**

**Email:**

**Home Phone:** ( )

**Work:** ( )

**Cell:** ( )

**Address:**

**DOB:** / /  

**Age:**

**Gender M / F**

**Height:**

**Weight:**

**Highest Education Achieved:**

**Race:**

- **Hispanic or Latino** - A person of Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race. The term "Spanish origin," can be used in addition to "Hispanic or Latino."

- **American Indian or Alaska Native** - A person having origins in any of the original peoples of North, South, of Central America, and who maintain a tribal affiliation or community attachment.

- **Asian** - A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent, including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam. (Note: Individuals from the Philippine Islands have been recorded as Pacific Islanders in the previous data collection strategies.)

- **Black or African American** - A person having either origins in any of the black racial groups of Africa. "Haitian" can be used in addition to "Black" or "African American."

- **Native Hawaiian or Pacific Islander** - A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

- **White** - A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

**Primary Care Physician:**

**Name:**

**Office Phone:**

**Address:**

**Emergency Contact:**

**Name:**

**Relationship:**

**Phone #**

**Medications:** Include over the counter drugs/ oral contraceptive/ dietary supplements

**Name/ Dosage/ How often taken:**

**Allergies:**

**Smoking History:**

**Do you smoke** Cigarettes? Pipe/ Cigar? Other? If you quit, what year did you quit?

**# of packs smoked per day** For how many years
### Medical Health History Form  Page 2

**Alcohol Consumption History:**

Do you currently drink alcohol? \[\text{YES} / \text{NO}\]

If you drank alcohol previously, when did you stop?

If you ever did drink alcohol, what is (was) the volume consumed?

\[\text{# ounces / day for } \text{# of years} \]

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**Medical History:**

<table>
<thead>
<tr>
<th>NO</th>
<th>YES</th>
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<tbody>
<tr>
<td></td>
<td><strong>Please explain any &quot;YES&quot; answers</strong></td>
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<tr>
<td></td>
<td>high blood pressure</td>
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<tr>
<td></td>
<td>chest pain/ history of heart attack</td>
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<td></td>
<td>extra heart beats or racing</td>
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<td>abnormal electrocardiogram (ECG)</td>
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<td>other heart trouble (e.g. murmur, valve problems)</td>
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<td></td>
<td>high cholesterol</td>
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<td>diabetes</td>
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<td>seizures</td>
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<td></td>
<td>stroke</td>
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<td></td>
<td>fainting spells</td>
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<td></td>
<td>anxiety (diagnosed)</td>
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<td>depression (diagnosed)</td>
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<td>recurrent fatigue</td>
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<td></td>
<td>insomnia</td>
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<td>thyroid problems</td>
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<td>difficulty breathing</td>
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<td>emphysema/ asthma/ chronic bronchitis</td>
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<td></td>
<td>tuberculosis</td>
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<td></td>
<td>chronic infection</td>
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<td>stomach/ GI problems</td>
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<td>hepatitis</td>
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<td></td>
<td>bleeding disorder</td>
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<td>kidney/ urinary problems</td>
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<td>joint injuries/ joint pain</td>
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<td></td>
<td>arthritis (rheumatoid or osteoarthritis)</td>
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<td></td>
<td>migraine headaches</td>
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<td></td>
<td>vision problems (exclude corrected near/ far sightedness)</td>
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<tr>
<td></td>
<td>surgical procedures</td>
</tr>
</tbody>
</table>
### Medical Health History Form

**Inclusion Criteria for SCI Participants:**
1. Adults with chronic T3 – L5, (AISA- A, B, or C) SCI (2 years post injury)
2. Wheelchair reliant (unable to walk with or without support)
3. Between 18 and 75 years of age

**Exclusion Criteria:**
1. No evidence of pressure wounds on buttocks or feet
2. Unhealed bone fracture or history of low trauma (fragility) fracture
3. Severe Osteoporosis (T score of -4 or less or a history of fragility fractures)
4. Uncontrolled autonomic dysreflexia
5. Less than 2 years post injury

**Where is the location of your injury?**

**How long have you had the diagnosis of SCI?**

### Injury Questions:

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>Please explain any “YES” answers</th>
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</thead>
<tbody>
<tr>
<td>NO</td>
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<tr>
<td></td>
<td></td>
<td>Do you have a history of uncontrolled autonomic dysreflexia?</td>
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<td>Have you suffered a bone fracture recently?</td>
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<td></td>
<td>Have you been diagnosed with orthostatic hypotension?</td>
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<tr>
<td></td>
<td></td>
<td>Have you been diagnosed with Osteoporosis?</td>
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<tr>
<td></td>
<td></td>
<td>Do you have a history of bone fragility fractures?</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Do you have any decubitus ulcers or ulcers on the feet?</td>
</tr>
</tbody>
</table>

**Please sign and date:**

Signature: ___________________________ Date: ___________
BIBLIOGRAPHY


Corretti, M., Anderson TJ, Benjamin , E., Celermajer , D., Charbonneau, F., Creager, M., . . . International Brachial Artery Reac


