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## EFFECT OF LOWER BODY POSITIVE PRESSURE ON CARDIOVASCULAR RESPONSE AT VARIOUS DEGREES OF HEAD UP TILT

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EFFECT OF LOWER BODY POSITIVE PRESSURE  
ON CARDIOVASCULAR RESPONSE AT VARIOUS DEGREES OF HEAD UP TILT

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THESIS

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A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in Exercise Physiology in the College of Education at the University of Kentucky

By

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2012

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## ABSTRACT OF THESIS

### EFFECT OF LOWER BODY POSITIVE PRESSURE ON CARDIOVASCULAR RESPONSE AT VARIOUS DEGREES OF HEAD-UP TILT

Various models of simulated weightlessness and resulting cardiovascular effects have been researched in the last 50 years of space exploration. Examples of such models are the Alter-G (Alt-G) treadmill used for body unweighting and head-up-tilt (HUT) model each providing similar cardiovascular effects, but differing in their stimulation of vestibular centers. Advantages of using the Alt-G include: use of lower body positive pressure (LBPP) to simulate hypogravity, it acts as a countermeasure to alleviate negative cardiovascular effects of standing and provides a constant vestibular stimulus. In addition, the Alt-G shorts themselves may be providing a certain degree of LBPP, acting as a compression garment. Therefore the purpose of this study was to determine the cardiovascular effects of Alt-G shorts and how effective they are as countermeasure to deconditioning effects of space flight.

This study tested cardiovascular changes in 12 men and women at 0 and 80 degrees head-up-tilt (HUT0 / HUT80) with and without Alt-G shorts using 5-lead ECG, 10-lead impedance, heart rate, systolic and diastolic blood pressure measurements at finger and arm. The tilt-induced increase in mean heart rate (HR) was significantly smaller when subjects wore the Alt-G shorts. Shorts ended up reducing HR by 2.3 bpm in supine control and by 6.7 bpm at HUT80 ( $p < 0.05$ ). The tilt effect was also significant (HUT/control, vs. HUT80), 66.4 vs. 91.5 bpm with no shorts and 64.1 vs. 84.8 bpm with shorts ( $p < 0.0005$ ). In addition, the tilt-induced decrease in systolic blood pressure (SBP) was significantly smaller when subjects wore the Alt-G shorts. Shorts helped maintain SBP when moving from 0 to 80 degree tilt, avg. 6.6 vs. 10.8 mmHg ( $p < 0.05$ ) decrease in SBP for shorts vs. no shorts. The tilt effect (HUT0, vs. HUT80) was not significantly different ( $p > 0.05$ ). Other cardiovascular variables did not show any significant effect from shorts.

In conclusion, this study was in line with results from other studies that used compression garments to determine cardiovascular effects of LBPP.

**KEYWORDS:** Lower body positive pressure, cardiovascular effects, compression garments, head-up-tilt, orthostatic intolerance

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Date \_\_\_\_\_ 3/28/12 \_\_\_\_\_

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allowed me to learn about their cardiovascular system and who made this project a complete success.

## TABLE OF CONTENTS

|  |      |
|--|------|
| Acknowledgments.....   | iii  |
| List of Tables.....  | vii  |
| List of Formulas.....  | viii |
| List of Figures.....   | ix   |
| Chapter One. Introduction.....                                     | 1    |
| Chapter Two. Review of literature.....                             | 4    |
| Chapter Three. Methodology.....                                    | 11   |
| Protocol.....  | 11   |
| Qualification Phase.....   | 11   |
| Orientation Phase.....   | 12   |
| Preparation/Instrumentation Phase.....                             | 13   |
| Measurements/Data Acquisition Phase.....                           | 18   |
| Statistical Analysis.....  | 22   |
| Chapter Four. Results.....   | 23   |
| Effect of Shorts and HUT on HR.....                                | 25   |
| Effect of Shorts and HUT on SBP .....                              | 26   |
| Effect of Shorts and HUT on DBP.....                               | 28   |
| Effect of Shorts and HUT on Mean Arterial Pressure (MAP).....      | 29   |
| Effect of Shorts and HUT on Segmental Impedance Change.....        | 30   |
| Effect of Shorts and HUT on stroke volume (SV).....                | 33   |
| Effect of Shorts and HUT on Cardiac Output (Q).....                | 34   |
| Effect of Shorts and HUT on total peripheral resistance (TPR)..... | 36   |



|   |    |
|---|----|
| Chapter Five. Discussion.....                                       | 37 |
| Chapter Six. Summary and conclusions.....                           | 43 |
| APPENDIX A. Recruitment script.....                                 | 45 |
| APPENDIX B. Research procedures.....                                | 46 |
| APPENDIX C. Informed consent.....                                   | 48 |
| APPENDIX D. Medical history form.....                               | 54 |
| APPENDIX E. Par-Q form.....   | 55 |
| APPENDIX F. Raw data.....   | 56 |
| APPENDIX G. Subject and impedance data.....                         | 58 |
| APPENDIX H. Resulting Cardiovascular Values and T-test Results..... | 59 |
| References.....   | 60 |
| Vita.....   | 62 |

## LIST OF TABLES

|  |    |
|--|----|
| Table 3.1. Order of HUT activities matrix for male and female subjects ..... | 14 |
| Table 4.1. Age, sex, height and body mass of the 12 subjects. ....           | 23 |
| Table 4.2. Resulting cardiovascular mean values $\pm$ S.E.M.....             | 24 |
| Table F.1. Raw cardiovascular data.....                                      | 56 |
| Table G.1. Subject demographic and impedance data.....                       | 58 |
| Table H.1. Resulting cardiovascular values and t-test results.....           | 59 |

## LIST OF FORMULAS

|  |    |
|--|----|
| F. 4.1. Fluid volume and impedance/resistance formula.....               | 31 |
| F. 4.2. Sramek-Bernstein formula for calculating stroke volume (SV)..... | 31 |
| F. 4.3. Formula for calculating cardiac output.....                      | 34 |
| F. 4.4. Formula for calculating total peripheral resistance.....         | 36 |

## LIST OF FIGURES

|  |    |
|--|----|
| Fig. 3.1. Subject fitted with Alt-G shorts.....                              | 13 |
| Fig. 3.2. Subject supine (HUT0 degrees) during tilt test.....                | 15 |
| Fig. 3.3. Electrode placement on subjects for determining impedance.....     | 16 |
| Fig. 3.4. Data acquisition while subject is tilted to HUT80. ....            | 19 |
| Fig. 3.5. "Windaq" file with signals from 9 channels for one subject.....    | 21 |
| Fig 4.1. Mean heart rate with and without Alter-G shorts at HUT0, HUT80..... | 26 |
| Fig. 4.2. Mean systolic blood pressure with and without shorts.....          | 28 |
| Fig. 4.3. Mean diastolic blood pressure with and without shorts.....         | 29 |
| Fig. 4.4. Mean arterial blood pressure with and without shorts.....          | 30 |
| Fig. 4.5. Mean segmental impedance response.....                             | 32 |
| Fig. 4.6. Mean stroke volume with and without shorts.....                    | 34 |
| Fig. 4.7. Mean cardiac output with and without shorts.....                   | 35 |
| Fig. 4.8. Mean total peripheral resistance with and without shorts.....      | 36 |

## Chapter One

### Introduction

Orthostatic hypotension (OH) and orthostatic intolerance (OI) are less serious, but more pervasive, manifestations of adrenergic failure, in the progression of autonomic disorders such as autonomic neuropathies, autonomic failure and multiple system atrophy (Denq et al., 1997). OI is a common problem in aging populations and it affects approximately 30% of short duration and 80% of long-duration astronauts post-flight (Stenger et al., 2011) due to cardiovascular de-conditioning (i.e., heart shrinkage, body dehydration and plasma volume reduction) occurring with microgravity. Therapeutic approaches to OI primarily consist of vasoconstrictor drugs, increasing blood volume and the use of compression garments due to the lower body positive pressure (LBPP) they create. The latter is the main topic of this study.

Crile introduced LBPP with the antigravity suit (G suit) or medical anti-shock trousers in 1903. The principle of the G suit has been applied to the treatment of OI. The development of new materials allowed the fabrication of elastic suits that are able to apply even or gradient pressure. However, there is little systematic information about the effects of compression of various venous capacitance beds and their use as a significant counter-measure for returning astronauts.

The efficacy of compression of specific body compartments (calves, thighs, low abdomen, calves and thighs together, and all compartments combined) has been looked at by Denq (1997). The main finding was that compression garments significantly reduced the deficit in standing blood pressure (BP) if both legs and the abdomen are compressed or if the abdomen alone is compressed due to substantial amount of fluid in the human gut area.

Compression in the region of calves, thighs or combined calves and thighs did not show results as impressive as the abdomen data, nevertheless, in a study by Stenger et al.(2010), thigh-high, graded compression garments were found to be an effective counter-measure to mitigating the symptoms of OI. However, full-body compression suits, showed the most significant effect, as in a study by Platts et al.(2009), who compared NASA's inflatable antigravity suit (AGS) and the Russian Federal Space Agency's non-inflatable compression garment "Kentavr" (a.k.a. "Centaurus"). In all the studies above, compression garments prevented the symptoms of OI by decreasing venous pooling of the calves and thighs, thereby improving venous return and stroke volume (SV). Systolic blood pressures (SBP) and total peripheral resistances (TPR) were higher with garments, while heart rates (HR) were lower.

The present study focuses on a garment that compresses the abdominal and upper legs with the use of Alt-G shorts. The Alt-G shorts are an integral part of the Alt-G treadmill, which uses LBPP to reduce body weight and therefore simulate reduced gravity. In the Alt-G, the subject, wearing special Alt-G shorts is sealed at the waist inside the LBPP enclosure and positive air pressure is applied to the subject's lower body while they stand, walk or run on an enclosed treadmill.

The selection of Alt-G shorts as a compression garment in this study was based on several studies (Evans JM et al., 2010; Kostas V. et al. 2011 – in progress), which compared the cardiovascular effects between Alt-G and head up tilt (HUT) models of reduced gravity. Specifically, data obtained at four body weights (BW) produced by the Alt-G were compared to data acquired from four degrees of HUT (Moon stand=20% BW [AG] vs 10° HUT), (Mars stand=40% BW [AG] vs. 20° HUT), (Earth stand =100% BW [AG] vs. 80° HUT), (Earth supine = 0% BW [AG] vs. 0° HUT).

Preliminary results from this study showed that cardiovascular effects from the two models were similar at the corresponding Alt-G body weights and HUT angles as shown above, especially as related to HR and cardiac output (CO) responses. However, comparison between Alt-G and HUT data were difficult because it was not clear how much of the cardiovascular effect was from the air pressure inside the Alt-G chamber and how much was from the Alt-G shorts themselves.

The hypothesis of the present study is that, by their nature (the shorts are tight), Alt-G shorts result in fluid shifts towards the abdomen and thorax and significantly contribute to the increases in stroke volume, systolic and diastolic BP seen when lower body positive pressure is applied. At the same time heart rate should go down and total peripheral resistance should go up.

Therefore the purpose of this study is to determine the effects of shorts on heart rate, systolic and diastolic blood pressure, mean arterial pressure, stroke volume, cardiac output, total peripheral resistance and volume shifts (as determined by thoracic, abdominal, upper and lower leg impedance) at 0 and 80 degrees head-up tilt.

## Chapter Two

### Review of Literature

The purpose of this literature review is to investigate past and current literature involving compression garments, the lower body positive pressure (LBPP) they create and their effect on the cardiovascular system (heart rate, blood pressure, stroke volume, cardiac output, total peripheral resistance, fluid shifts, etc) in normal and reduced gravity conditions, as experienced by astronauts. With respect to blood pressure, compression garments are used to treat orthostatic intolerance. Orthostatic intolerance (OI) and orthostatic hypotension (OH) are serious manifestations of adrenergic failure, occurring in the progressive autonomic disorders such as autonomic neuropathies, autonomic failure and multiple system atrophy (Denq et al., 1997). OI is a common problem in the aging population and affects ~30% of short duration and 80% of long-duration crewmembers post-flight (Stenger et al., 2010).

Therapeutic approaches to OI and OH primarily consist of the use of vasoconstrictor drugs, increasing blood volume and the use of compression garments. The latter method is the topic of our discussion.

Crile introduced LBPP with the antigravity suit (G suit) or medical anti-shock trousers in 1903. The development of new materials since, allowed the fabrication of elastic suits that are able to apply evenly distributed or gradient pressures. However, there is little systematic information about the effects of compression of various venous capacitance beds. Testing of compression garments for their ability to provide a significant counter-measure to lower body



blood pooling in returning astronauts is in its infancy (Gaffney F. et al., 1981; Williamson, J. et al., 1994; Nishiyasu T. et al., 1998; Fu Q. et al., 2000)

The efficacy of compression of specific compartments (calves, thighs, low abdomen, calves and thighs together, and all compartments combined) has been investigated by Deng J. et al., 1997. His study was carried out on 14 patients who were confirmed to have neurogenic OH. Each patient donned a modified (Crile) G suit which had five separate compartments: one lower abdominal, two thigh and two calf bladders. The suit was filled with air and a regulator connected to the bladders made it possible to control pressure continuously. In randomized order, the different bladders were inflated with a pressure of 40 mmHg. Five minutes of data were recorded with each subject supine, as well as five minutes tilted at 80 degrees with or without the selected compartments inflated.

One of the findings in the above study was that head-up tilt (HUT) resulted in a significant reduction in blood pressure (BP), cardiac output (CO) and total peripheral resistance (TPR). However, the main finding was that compression of capacitance beds reduced significantly ( $p < 0.01$ ) the deficit in standing BP if both the legs and the abdomen (13/14 subjects) were compressed or if the abdomen alone was compressed (9/14), due to substantial amount of fluid in the human gut area. The improvement was due primarily to an increase in TPR. The improvement in BP was accompanied by improvement in orthostatic symptoms. Compression in the region of calves, thighs or combined calves and thighs was not as impressive as compression of the abdomen. The degree of improvement correlated relatively well with the amount of blood in the regional vascular beds involved. On standing up there was an orthostatic shift of approximately 500ml of blood to the limbs. The splanchnic mesenteric bed is two- to three-fold larger, comprising 20-30% of total blood volume. In the postprandial state, there is a further increase of two- to three-fold. Presumably, improvement in TPR or BP did not occur with compression of the calves, thighs

or both, since the capacity of those regions was relatively small. Compression of the limbs is nevertheless important, since the combination of limb, with abdomen, compression increased the proportion of subjects with moderate to large improvement in orthostatic tolerance from 5/14 to 13/14. Moreover, due to relatively low cost, comfort and ease of donning, lower limb compression garments continued to be investigated.

In a study by Stenger M. et al., 2010, thigh-high, custom-fit, graded compression garments by “BSN-JOBST, Inc.” were used on five male astronauts following a 13-day mission to International Space Station (ISS). Graded compression consisted of 55 mmHg pressure at the ankle, degrading to ~18 mmHg at the knee and 6 mmHg at the thigh. These compression garments were worn beneath their flight suits during the Space Shuttle “walk around” and media events. Two hours after landing, the crewmembers participated in NASA’s operational test of orthostatic tolerance, which consisted of 6 min of supine rest followed by 80-degree HUT for 10 min or until the onset of presyncope. Hemodynamic responses to tilt in these crewmembers were compared to nine male astronauts (control group) who underwent an identical tilt test protocol in a different lab but without any compression garments. As a result, following spaceflight, all astronauts wearing thigh-high compression garments completed the full 10 min HUT test. In contrast, only six out of nine subjects in the non-countermeasure group completed the tilt test without developing presyncopal symptoms. However, there was no statistically significant difference between the survival rates of the countermeasure and non-countermeasure groups ( $P=0.171$ ). Systolic BP was not affected by position, but was elevated in the counter-measure group ( $P=0.006$ ). Diastolic BP was not affected by position or group. HR was elevated by tilt ( $P<0.001$ ), but was not different between groups. SV and CO were decreased by tilt ( $P<0.001$ ), but were both significantly higher in the countermeasure group (SV,  $P=0.028$ ; CO,  $P=0.017$ ).

Therefore in that study, thigh-high, graded compression garments were an effective countermeasure in mitigating the symptoms of orthostatic intolerance by decreasing venous pooling of the calves and thighs, thereby improving venous return and stroke volume. That study had several limitations, first, only a small number of subjects (five astronauts) and no females were tested. In addition, although the compression garments were custom fit to each astronaut, the measurements were made pre-flight. Crewmembers often lose leg volume, through a combination of dehydration and muscle atrophy so the magnitude of the compression was probably less than originally intended. The level of protection from the compression garments used may be improved by the addition of abdominal or full body compression.

Full-body compression suits showed the most significant effects, as in the study by Platts et al.. 2009, who compared NASA's inflatable antigravity suit (AGS) and the Russian Federal Space Agency's non-inflatable compression garment "Kentavr" (a.k.a. "Centaurus"). That study involved 35 male and female subjects, randomly assigned to one of the three groups, AGS, Kentavr or control (no counter-measure) groups. Thirty-six hours before the tilt test (0 degrees HUT to 80 degrees HUT), used to assess orthostatic tolerance, the subjects were dehydrated using a dose of furosemide (diuretic, 0.5 mg/kg) infused into an antecubital vein followed by a low salt diet (10 mEq Na<sup>+</sup> per day). As a result, all subjects wearing either AGS or Kentavr full body garments during the tilt test completed the test without symptoms of orthostatic hypotension. In contrast, only 56% of control subjects were able to complete the test.

The tilt-induced decrease in systolic BP of control subjects ( $-16 \pm 5$  mmHg) was significantly greater than in AGS subjects ( $8 \pm 4$  mmHg) and Kentavr ( $2 \pm 3$  mmHg). There was no difference between countermeasure groups. The increase in HR was greater in

control subjects ( $38 \pm 4$  bpm) than in the AGS subjects ( $15 \pm 3$  bpm) and in the Kentavr ( $16 \pm 2$  bpm). The drop in SV at the end of tilt was significantly less in the AGS ( $21 \pm 3$  ml) compared to control subjects ( $36 \pm 3$  ml). Standing SV for the AGS and Kentavr subjects were significantly higher than for controls at the end of tilt. Therefore, both the NASA AGS and the Russian Kentavr full body compression suits proved to be effective countermeasures against OH throughout passive tilt during pharmacologically induced hypovolemia. Wearing a compression garment reversed the effect of hypovolemia (as experienced after a space flight) on the response to tilt.

Although both garments provided effective countermeasures, both have negative features. The AGS requires a compressed gas source to inflate the bladders and maintain compression. Once AGS is disconnected, the bladders slowly leak, especially during movement. In contrast, Kentavr is a non-inflatable garment that consists of elastic, laced bicycle type shorts and gaiters (which cover the calves), thus the area around the knees and groin are not compressed, which may lead to edema formation during chronic use (after landing and egress). In addition, the utility of full-body suits could be decreased in some scenarios. For example, inflation of an AGS during emergency egress from the Space Shuttle may limit crewmember's capacity to move to a safe distance from the vehicle by restricting movement in the lower body. Use of the AGS and Kentavr are complicated because both require aid from others crew members to don. Both also interfere with the adult diaper worn by all astronauts under the advanced crew escape suit (ACES). Therefore additional research is needed in development of compression garments that can be optimized for crewmember protection without interfering with critical mission tasks. These garments are also quite expensive and would be quite impracticable for the general population with OI condition.

In addition to thigh-high and full-body garments, several studies focused on abdomen compression. While Denq et al.. 1997, used air-pressurized garments to improve blood pressure, comparison studies between the efficacy of air-pressurized garments versus elastic counterpressure with respect to orthostatic hypotension were not published until A. Smit et al.. 2004. In the Smit study, 23 patients with neurogenic orthostatic hypotension underwent three protocols. Protocol 1 evaluated a 40-60degree HUT position and the effect of abdominal compression using an anti-gravity suit on caval vein and femoral diameter, arterial BP and hemodynamics. Protocol 2 documented the relationship between the level of compression and the arterial pressure response. Protocol 3 investigated the ability to maintain standing BP by an abdominal elastic binder. During HUT, compression (40 mmHg) resulted in a reduction in diameter of the caval vein without a change in femoral vein diameter while SV increased by 14%, CO by 13%, HR decreased by 4% and BP (systolic/diastolic) by 30%/14%, both  $p < 0.05$ , with no change in TPR. Forty mmHg compression was associated with a higher blood pressure than 20 mmHg compression. Elastic abdominal binding increased standing BP with 15/6 mmHg (systolic/diastolic range - 3/3 to 36/14). Elastic binding and air-pressurized binding increased standing BP to a similar extent. However, in some patients in above study, low level abdominal compression did not increase standing BP. Hypothetically, the distribution of disturbed autonomic innervation and thereby capacity for venous pooling in the abdomen, differs among patients.. Further studies are needed to assess whether, and how, the efficacy of abdominal compression can be optimized.

As in the study above, the present study focuses on a garment that compresses the abdominal area with the use of Alt-G shorts. The Alt-G shorts are an integral part of the Alt-G treadmill, which uses LBPP to reduce body weight and therefore simulate reduced gravity. In the Alt-G, the subject, wearing special Alt-G shorts is sealed at the waist inside the LBPP

enclosure and positive air pressure is applied to the subject's lower body while they stand, walk or run on an enclosed treadmill. The selection of Alt-G shorts as a compression garment in this study was based on several other studies (Evans JM et al., 2010, Kostas V. et al., 2011 – in progress to be published), which compared cardiovascular effects between Alt-G and HUT models of reduced gravity. Specifically, data obtained at four body weights (BW) produced by the Alt-G were compared to data acquired from four degrees of HUT (Moon stand=20% Gz BW [AG] vs 10° HUT, Mars stand=40% Gz BW [AG] vs. 20° HUT, Earth stand =100% Gz BW [AG] vs. 80° HUT, Earth supine = 0% Gz BW [AG] vs. 0° HUT). Results from this study showed that cardiovascular effects from the two models were similar, especially as related to HR responses and CO. However, comparison between Alt-G and HUT data were difficult because it was not clear what percentage of the cardiovascular effect was from the air pressure inside the Alter-G chamber and how much was from the Alt-G shorts themselves.

The hypothesis of the present study is that, by their nature (the shorts are tight), Alt-G shorts result in fluid shifts towards the abdomen, and significantly contribute to increases in stroke volume and systolic BP and reduction of heart rate when lower body positive pressure is applied. A secondary purpose of this study is to provide insight into effects of the compression shorts on results from the simulated Moon and Mars gravity environments study (Kostas V. et al., 2011). In that study subjects inside the Alt-G treadmill were affected by LBPP but how much of that effect was contributed by the shorts themselves was unknown. Finally, another purpose was to determine how effective the Alter-G shorts were in preventing symptoms of orthostatic intolerance in comparison to compression garments used in other studies.

## Chapter Three

### Methodology

The subjects in this study were 12 healthy, non-smoking, properly-hydrated adults, 6 male and 6 female (height= $176.9 \pm 3.5$  cm, weight= $77.4 \pm 6$  kg, mean  $\pm$  S.E.M.). They were recruited by word of mouth. While subjects of any ethnic background were recruited, all 12 subjects were Caucasian, between 18 and 45 years of age (age= $27.2 \pm 2.5$ , mean  $\pm$  S.E.M.). Subjects were excluded if they failed any of the criteria in the qualification phase provided below.

The study was approved by University of Kentucky Institutional Review Board. All subjects gave written informed consent prior to participation. The study took place at the University of Kentucky Aeronautical Research Laboratory, “Wenner-Gren” Center for Biomedical Engineering.

#### Protocol:

Subjects were asked to complete several phases in one session (one day) lasting no longer than 1.5 hrs total.

#### Qualification Phase:

There was an initial screening/qualification phase lasting 20 minutes. The screening/qualification included signing of the Informed Consent Form, Physical Activity Readiness Questionnaire (Par-Q) and BP measurement. If the subject answered “Yes” to any of the Par-Q questions or had prior history of fainting, they were excused from participation. If

resting BP was greater than 140/90 mmHg, they were excused with a recommendation to see a physician.

This phase also identified caffeine users and their approximate daily intake, as well as smokers. Participants were asked about the amount of exercise they performed before the study, their sweat rate, as well as fluid intake. This information was used during the data interpretation phase to determine if any of these activities/conditions had a significant influence on results.

#### Orientation Phase:

Subjects who passed the initial screening were allowed to participate in the study following a verbal orientation. In this phase, the subject's height ("American Std., Union, WA") and weight ("Taylor Professional Scale", Crestwood, VA) were recorded. Body cross sectional area at hip, waist and thigh were measured using a measuring tape. Then subjects were fitted with "Alter-G" ("Woodway, Alter-G-SML") LBPP garments of various sizes (S, M, L, XL, XXL). The Alter-G (Alt-G) shorts had to fit tightly and comfortably on the subject's body (Fig. 3.1). If a subject's physique did not allow them to fit in any of the garments available onsite, they would have been excused. Criteria for elimination were unusually large or small waist or thigh circumference which would have made the garments uncomfortably tight or too loose. None of the recruited subjects were excused.





**Fig. 3.1. Subject fitted with Alt-G shorts.**

Subjects were also familiarized with the HUT table operation and impedance/ECG electrode placement. The orientation phase lasted about 20 minutes.

#### Preparation / Instrumentation Phase:

The order of stages/conditions (stage 1/with shorts or stage 2/without shorts) as well as order of HUT angle/activity (0 degrees/supine or 80 degrees/standing) was randomized and entered into a matrix in such a manner that an equal number of subjects, both male and female, participated in each activity and each condition. This was accomplished by dividing the total number of subjects in half, as well as dividing male and female in half, and

randomly assigning subjects from each half to each condition. The matrix for 12 subjects is shown in Table 3.1.

| Subj. | Female subjects     |                  |                  |                  |
|-------|---------------------|------------------|------------------|------------------|
| #     | Order of activities |                  |                  |                  |
| 1     | HUT0, No Shorts     | HUT80, No Shorts | HUT0, Shorts     | HUT80, Shorts    |
| 2     | HUT80, No Shorts    | HUT0, No Shorts  | HUT80, Shorts    | HUT0, Shorts     |
| 3     | HUT0, Shorts        | HUT80, Shorts    | HUT0, No Shorts  | HUT80, No Shorts |
| 4     | HUT80, Shorts       | HUT0, Shorts     | HUT80, No Shorts | HUT0, No Shorts  |
| 5     | HUT0, No Shorts     | HUT80, No Shorts | HUT0, Shorts     | HUT80, Shorts    |
| 6     | HUT80, No Shorts    | HUT0, No Shorts  | HUT80, Shorts    | HUT0, Shorts     |
| Subj. | Male subjects       |                  |                  |                  |
| #     | Order of activities |                  |                  |                  |
| 1     | HUT0, No Shorts     | HUT80, No Shorts | HUT0, Shorts     | HUT80, Shorts    |
| 2     | HUT80, No Shorts    | HUT0, No Shorts  | HUT80, Shorts    | HUT0, Shorts     |
| 3     | HUT0, Shorts        | HUT80, Shorts    | HUT0, No Shorts  | HUT80, No Shorts |
| 4     | HUT80, Shorts       | HUT0, Shorts     | HUT80, No Shorts | HUT0, No Shorts  |
| 5     | HUT0, No Shorts     | HUT80, No Shorts | HUT0, Shorts     | HUT80, Shorts    |
| 6     | HUT80, No Shorts    | HUT0, No Shorts  | HUT80, Shorts    | HUT0, Shorts     |

**Table 3.1. Order of HUT activities matrix for male and female subjects.**

Subjects were asked to either wear or not wear the Alt-G shorts, according to the matrix above. Then he/she was asked to lay or stand still on the HUT table (“Bailey Mfg. 9505”, Louisville, KY) according to the matrix, while all devices were calibrated, Fig. 3.2.



**Fig. 3.2. Subject supine (HUT0) during tilt test.**

The subject's left arm was placed on a platform at heart level for accurate BP measurements and strapped to the platform with "Velcro" to prevent movement. The subject's legs and abdomen were strapped to the HUT table to prevent shifting or falling during tilting.

For placing the ten impedance leads, appropriate skin areas were treated with alcohol and shaved (with subject's permission). Monitoring electrodes ("3M, Red Dot -2560") were placed as follows: lead 1 on back of the neck, lead 2 on top of left foot, lead 3 on right shoulder, leads 4 and 5 under left rib, leads 6 and 7 on left upper thigh, lead 8 above left knee, lead 9 below left knee, lead 10 on lower leg, above the foot. The segment between leads 3 and 4 determined the fluid in the thorax, between leads 4 and 7 – in the abdomen,

between 7 and 8 – in the upper leg, between 9 and 10 – in the lower leg as shown in Fig.

3.3.

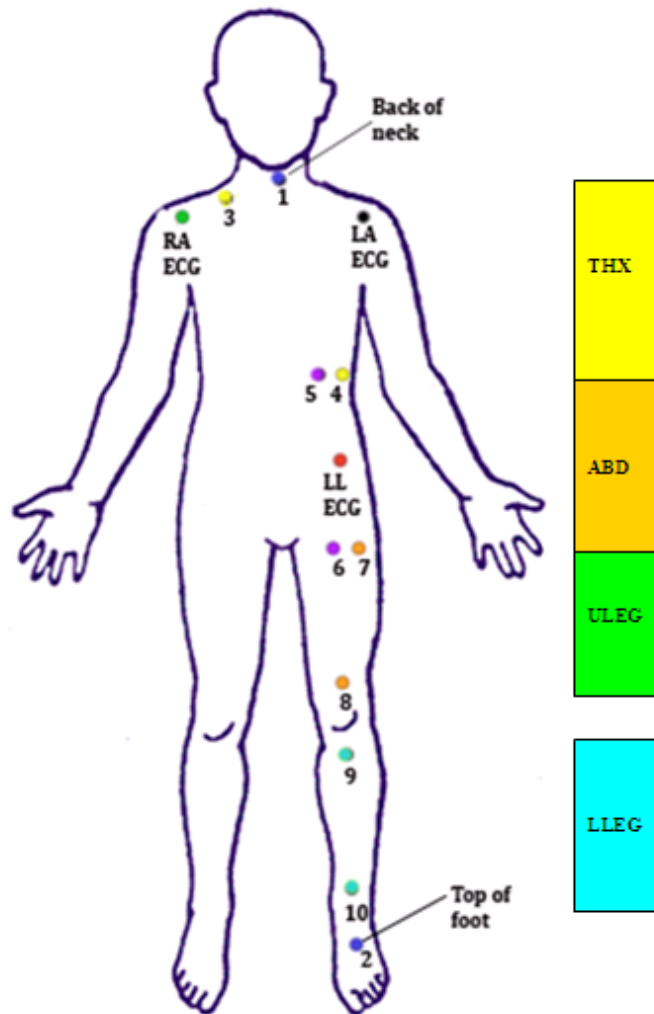


Fig. 3.3. Electrode placement on subjects for determining impedance.

Impedance leads detected segmental tetrapolar body impedance (“Thrim Tetrapolar Impedance Meter – 2994”, San Francisco, CA) which was transmitted to a “Dell” laptop

("Dell Latitude D-600"). Lengths of each of the four body segments were measured with a tape and data were recorded for later use in impedance formulas for each subject (thorax= $39.6 \pm 1.0$  cm, abdomen= $45.3 \pm 1.8$  cm, upper leg= $23.9 \pm 1.1$  cm, lower leg= $24.5 \pm 1.4$  cm, mean  $\pm$  S.E.M.)

The five ECG leads were placed as follows: one on right shoulder, one on left shoulder, one above left hip, one above right hip and one on chest. The ECG leads were connected to the ECG unit ("Spacelab") which in turn transmitted data to the laptop.

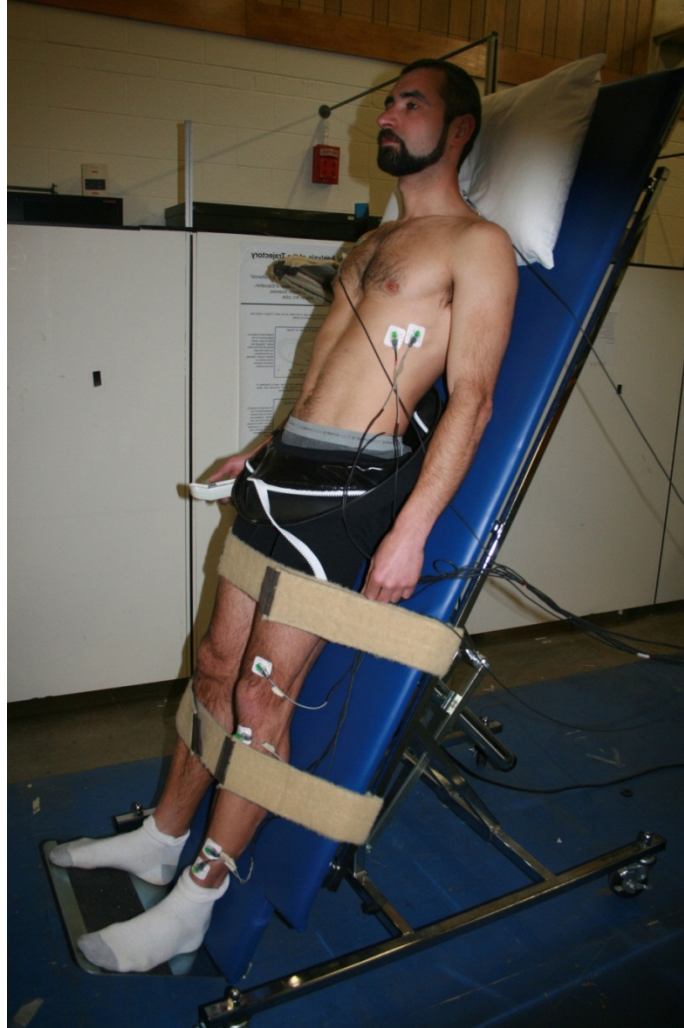
The continuous BP device consisted of a small cuff with a "Portapres" sensor, fitted on the subject's middle finger according to size (S, M, L, XL) and connected to the "FMS Portapres" front end unit ("Finapres Medical Systems") which was secured to the subject's wrist with Velcro to prevent sliding. In turn, this unit transmitted data to the computer. The technology used by the Finapres Medical Systems finger BP device is based on the volume-clamp method, first introduced by Czech physiologist J. Penaz in 1967. With this method, finger arterial pressure is measured using a finger cuff and an inflatable bladder in combination with an infrared plethysmograph, which consists of an infrared light source and detector. The infrared light is absorbed by the blood and the pulsation of arterial diameter during a heart beat causes a pulsation in the light detector signal. A special algorithm then is able to determine the blood pressure wave form.

The ECG, impedance and BP device signals transmitted to the computer were monitored on the screen using "Windaq" software ("Windaq Pro Data Acquisition Sftw. V. 2.59" and "Windaq Playback", "DATAQ Instruments", DI-7x0 USB0). In addition, subjects were fitted with a cuff around the left bicep connected to a manual BP/HR device ("AND UA – 767") for validation of "Portapres" BP and "Spacelab" ECG data.

The temperature in the room was monitored using a “LaCrosse Technologies” thermometer. The preparation/instrumentation phase duration was 20 minutes.

Measurement/Data Acquisition Phase:

This phase included confirmation of working condition of all devices. Subjects were asked to lay still and not talk for five minutes at a time while data acquisition (length=three minutes) took place in each of the four conditions from matrix above. The tilting of the table took less than one minute between all conditions (Fig. 3.4). Time allotted for equilibration of fluids and cardiovascular variables between activities took one minute, while changing into/out of shorts took about five minutes, with a total of about 20 minutes for the data acquisition phase.



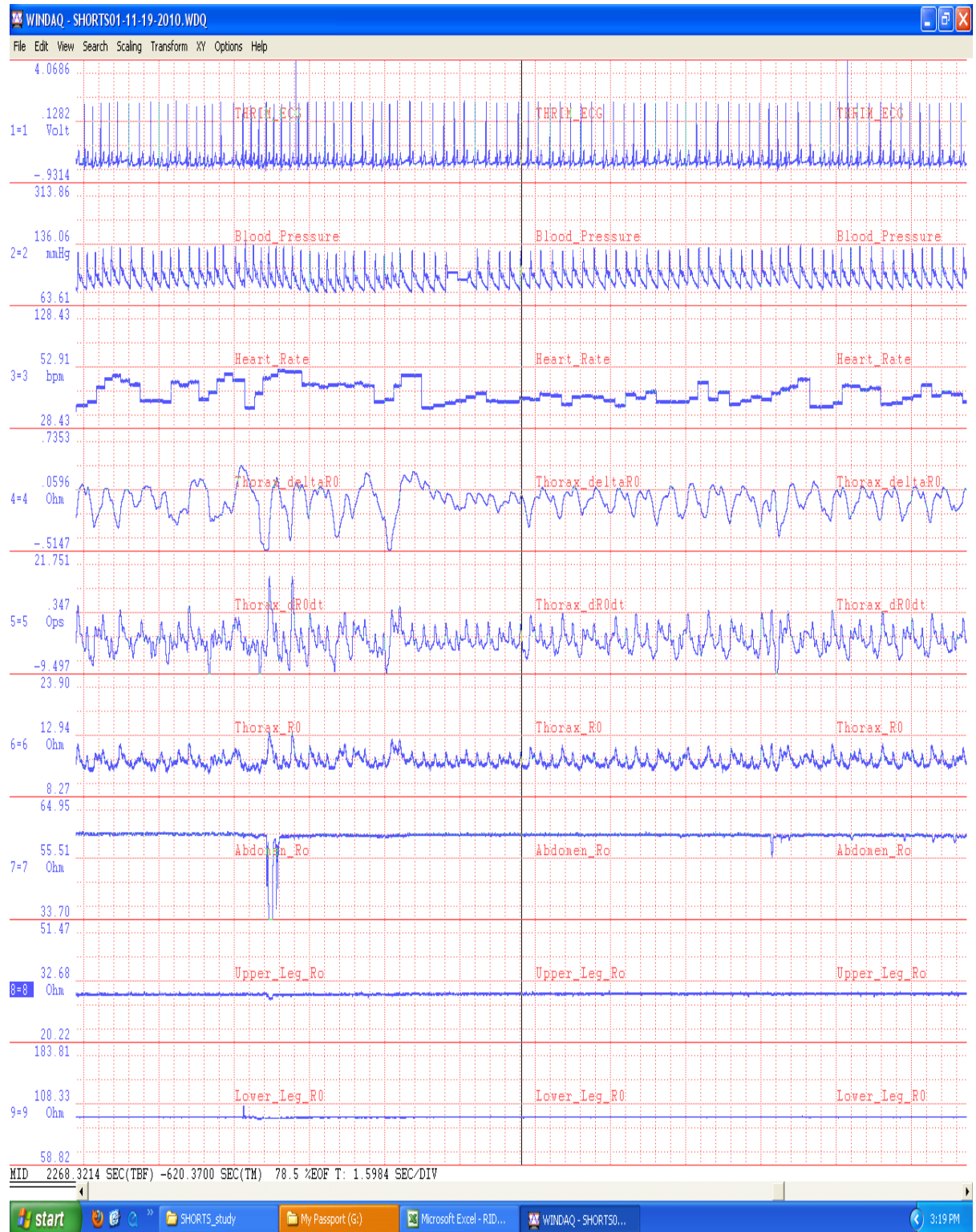
**Fig. 3.4. Data acquisition while subject is tilted to HUT80.**

Measurements of subjects' HR (both ECG and manual BP device), BP (SBP, DBP and MAP, both continuous and manual), TPR, fluid shifting measurement/ segmental body impedance (thoracic, abdominal, upper leg and lower leg segments) took place at this time. All manual data were hand-written into each subject's data sheet.

Automated signals were collected and monitored using pre-set channels in Windaq Software on the computer, as shown in Fig. 3.5, where channel 1=ECG data, channel 2 =

BP data, channel 3 = HR, channel 4 = thorax Delta RO (changes in impedance of the thorax filtered to give respiratory impedance), channel 5 =  $d RO / dt$  (derivative of impedance filtered to give heart synchronous impedance), channel 6 = thorax RO (raw impedance of the thorax), channel 7 = abdomen RO (impedance of the abdomen), channel 8 = upper leg RO (impedance of the upper leg), channel 9 = lower leg RO (impedance of the lower leg).





**Fig. 3.5. “Windaq” file with signals from 9 channels for one subject.**

Each signal from subjects' "Windaq" file was analyzed with "Physiowave" Software ("Physiowave 6.21, Visual Numerics Corp."). Each signal was filtered and transformed through derivation formulas with sample frequency of 1000Hz, with low bandpass filter = 0.5Hz and high bandpass filter=20Hz. "Physiowave" software was also used to perform signal peak detection and to insert new markers into the Windaq file to indicate R-R interval, minimum and maximum values, etc. Beat-to-beat and breath-to-breath tables were generated. Spectral analyses of R-R intervals and BP were performed.

Even though each activity contained approximately 180-200 sec worth of data, cleanup reduced it to about 130 sec of good data. The cleanup consisted of removal of bad data (from calibration, from artifact, from weak signal and/or from loose electrodes). The remaining data were averaged through Physiowave for each activity/condition and imported into Excel (Microsoft Office Excel 2003).

### Statistical Analysis

Data were analyzed in Excel and also imported into SAS (SAS Enterprise Guide v. 4.2, SAS Institute Inc.) for statistical analysis. To evaluate the effect of shorts, a paired two-sample t-test of the change in the mean for each change in condition (for example the change from HUT0 to HUT80 was compared for shorts vs. no shorts condition). This test was chosen over any other test, like an ANOVA, due to limited amount of subjects and large variability between subjects. Data were expressed as means  $\pm$  S.E.M. The hypothesis that the shorts condition would be different from the no shorts condition was tested for each activity. Significance was rejected when  $p > 0.05$ .

## Chapter Four

### Results

Six male and six female subjects, all Caucasians, passed all qualification criteria and successfully completed the study over an 8-week period. Subject demographic data are shown in Table 4.1.

| Basic demographic data |            |           |                        |                           |
|------------------------|------------|-----------|------------------------|---------------------------|
| Subj. ID               | Sex (M, F) | Age (yrs) | Height (cm) (in *2.54) | Weight (kg) (lbs/ 2.2046) |
| shorts1                | F          | 26        | 168.9                  | 63.8                      |
| shorts2                | M          | 30        | 190.5                  | 93.0                      |
| shorts3                | M          | 23        | 193.0                  | 88.5                      |
| shorts4                | F          | 20        | 177.8                  | 120.7                     |
| shorts5                | F          | 45        | 167.9                  | 84.4                      |
| shorts6                | M          | 18        | 188.0                  | 65.8                      |
| shorts7                | F          | 19        | 162.6                  | 52.2                      |
| shorts8                | F          | 36        | 162.6                  | 62.1                      |
| shorts9                | M          | 21        | 175.3                  | 73.9                      |
| shorts10               | M          | 22        | 180.8                  | 96.2                      |
| shorts11               | M          | 38        | 193.0                  | 81.2                      |
| shorts12               | F          | 28        | 162.6                  | 47.6                      |
| TOTAL                  | 12         | 326       | 2122.9                 | 929.3                     |
| MEAN                   |            | 27.166667 | 176.9                  | 77.4                      |
| S.E.M.                 |            | 2.5       | 3.5                    | 6.0                       |

Table 4.1. Age, sex, height and body mass of the 12 subjects.

Inter-subject variability was high for all measurements. Age varied from 18 to 45 with an average of 27.2 years. Height ranged from 162.6 to 193.0 cm with an average of 176.9 cm. Weight range was 47.6 kg to 120.7 kg with an average of 77.4 kg. Temperatures in the room varied between 77.5 and 79.2 F during testing.

Effects of the tilt tests on HR, BP and impedance measures with and without the compression shorts are shown in Table 4.2. The values have been averaged for twelve subjects with standard error of the mean shown.

| RESULTING CARDIOVASCULAR MEAN VALUES +/- S.E.M. |                   |                    |                        |                 |                                      |                       |                   |
|---|-------------------|--------------------|------------------------|-----------------|--------------------------------------|-----------------------|-------------------|
| Activity \ Variable                             | Systolic BP, mmHg | Diastolic BP, mmHg | Mean Arterial BP, mmHg | Heart Rate, bpm | Total Periph. Resistance, mmHg/L/min | Cardiac Output, L/min | Stroke Volume, ml |
| TILT 0 deg NO SHORTS                            | 117.3 ± 4.5       | 71.2 ± 2.4         | 86.5 ± 3.1             | 66.4 ± 4.8      | 18.8 ± 1.9                           | 4.6 ± 0.2             | 69.3 ± 4.2        |
| TILT 80 deg NO SHORTS                           | 106.4 ± 5.1       | 67.0 ± 3.2         | 80.1 ± 3.8             | 91.5 ± 7.7      | 26.4 ± 1.9                           | 3.0 ± 0.2             | 33.2 ± 1.9        |
| TILT 0 deg WITH SHORTS                          | 115.9 ± 3.8       | 70.1 ± 2.5         | 85.4 ± 2.9             | 64.0 ± 4.1      | 18.4 ± 2.4                           | 4.6 ± 0.2             | 72.3 ± 4.1        |
| TILT 80 deg WITH SHORTS                         | 109.3 ± 4.4       | 65.9 ± 3.5         | 80.4 ± 3.8             | 84.8 ± 6.7      | 26.2 ± 2.6                           | 3.1 ± 0.2             | 36.2 ± 1.9        |

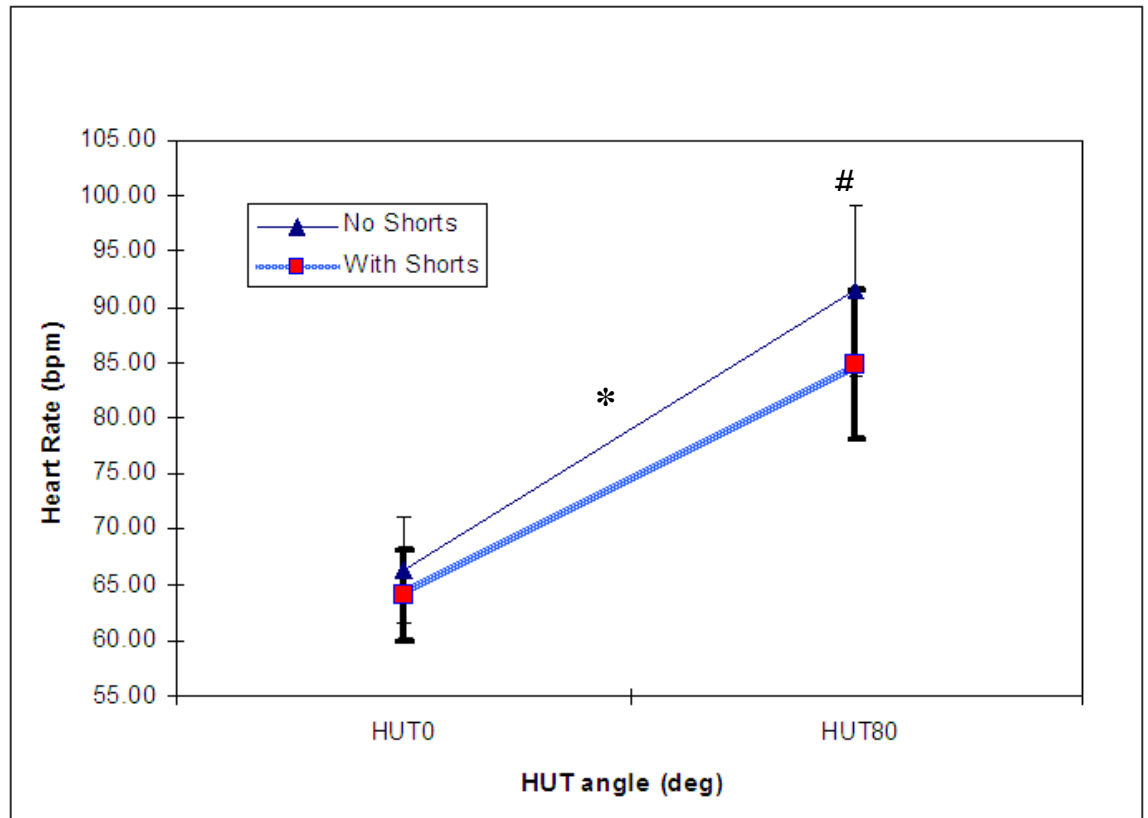
**Table 4.2. Resulting cardiovascular mean values ± S.E.M.**

The effect of shorts on each cardiovascular variable is shown in each of the corresponding sections below.

### Effect of Shorts and HUT on HR

Effects of shorts and HUT on HR are shown in Fig. 4.1. Without shorts, the average HR was  $66.4 \pm 4.8$  bpm supine (HUT0), which is the control condition. Tilting to 80 degrees (HUT80) caused HR to increase to  $91.5 \pm 7.7$  bpm. A similar effect was seen when the subjects wore shorts, where the average HR increased from  $64.0 \pm 4.1$  bpm at HUT0 to  $84.8 \pm 6.7$  bpm at HUT80. The tilt effect was significant, both with and without shorts ( $p < 0.05$ ). The tilt effect on HR was in line with that seen in other studies (Denq et al., 1997; Platts et al., 2009; Stenger et al., 2010).

When examining the effect of shorts, notice that the tilt-induced increase in mean HR was smaller when subjects wore the Alter-G shorts. The shorts reduced HR by 2.3 bpm in the supine and by 6.7 bpm in the HUT80 position. The paired t-test was used to test the change in HR with shorts and no shorts. This method was selected because it provided the most sensitive indicator considering the following factors: 1) small effect of stimulus (shorts), 2) small number of subjects, 3) large inter-subject variability (see Table 4.1). In the case of HR, the change in means between  $\Delta_{\text{shorts}} = 25.1$  bpm vs.  $\Delta_{\text{no shorts}} = 20.7$  showed that the effect of shorts was statistically significant ( $p < 0.05$ ).



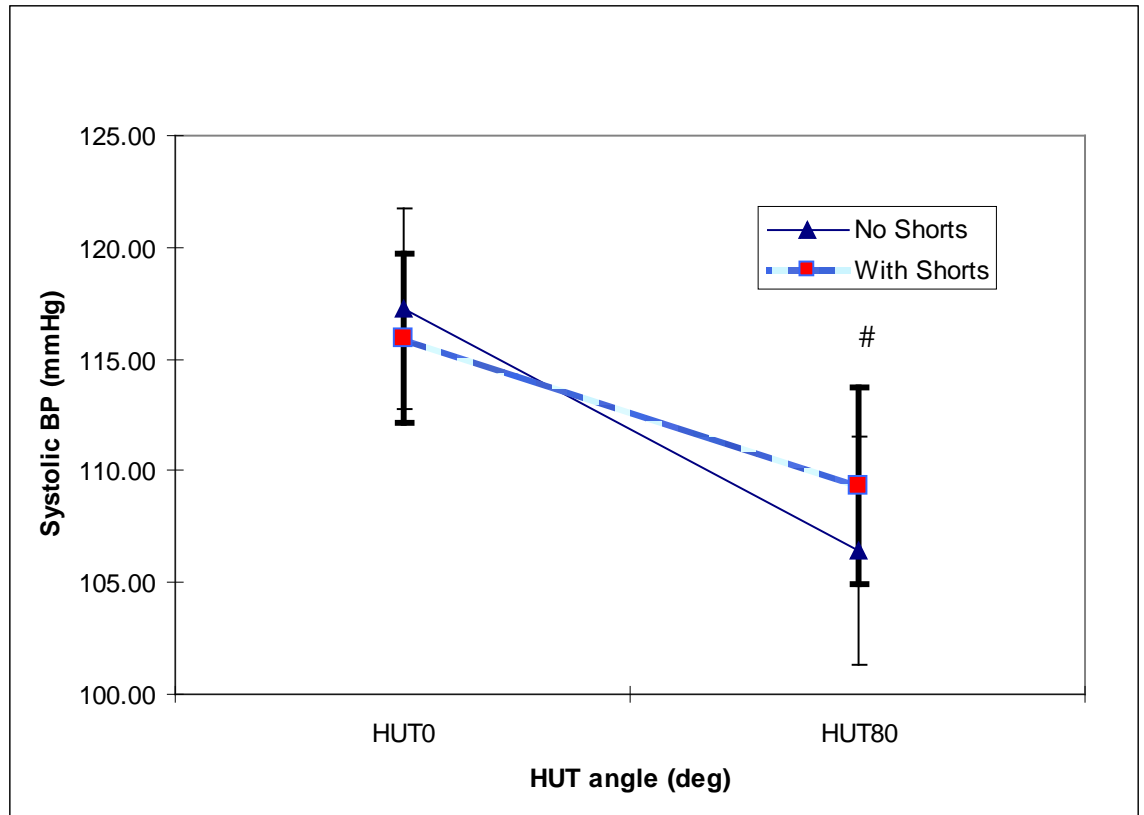
**Figure 4.1. Mean heart rate of twelve subjects with and without Alter-G shorts at HUT0, HUT80. \* Effect of tilt significant. # Change in HR significantly less with shorts than without shorts.**

#### Effect of Shorts and HUT on SBP

Effects of shorts and HUT on SBP are shown in Fig. 4.2. Without shorts, the average SBP decreased from  $117.3 \pm 4.5$  mmHg supine at HUT0 to  $106.4 \pm 5.1$  mmHg at HUT80. A similar effect was seen when subjects wore shorts. The average SBP decreased from  $115.9 \pm 3.8$  mmHg at HUT0 to  $109.3 \pm 4.4$  mmHg at HUT80. While the changes in

blood pressure could be of physiological significance, they were not statistically significant due to large standard deviations ( $p > 0.05$ ). However, the effect of tilting on SBP was in line with that seen in other studies (Denq et al.; 1997, Platts et al.; 2009, Stenger et al., 2010).

When examining the effect of shorts, notice that the tilt-induced decrease in mean SBP was smaller when subjects wore the Alter-G shorts, basically the shorts had the effect of maintaining control SBP during tilt. The shorts reduced SBP by 1.3 mmHg in the supine and increased it by 2.9 mmHg in the HUT=80 position (a net effect of 4.2 mmHg). The paired two sample t-test for change in means between  $\Delta\text{shorts} = 6.6$  mmHg vs.  $\Delta\text{no shorts} = 10.8$  mmHg showed that the effect of shorts on SBP was statistically significant ( $p < 0.05$ ).

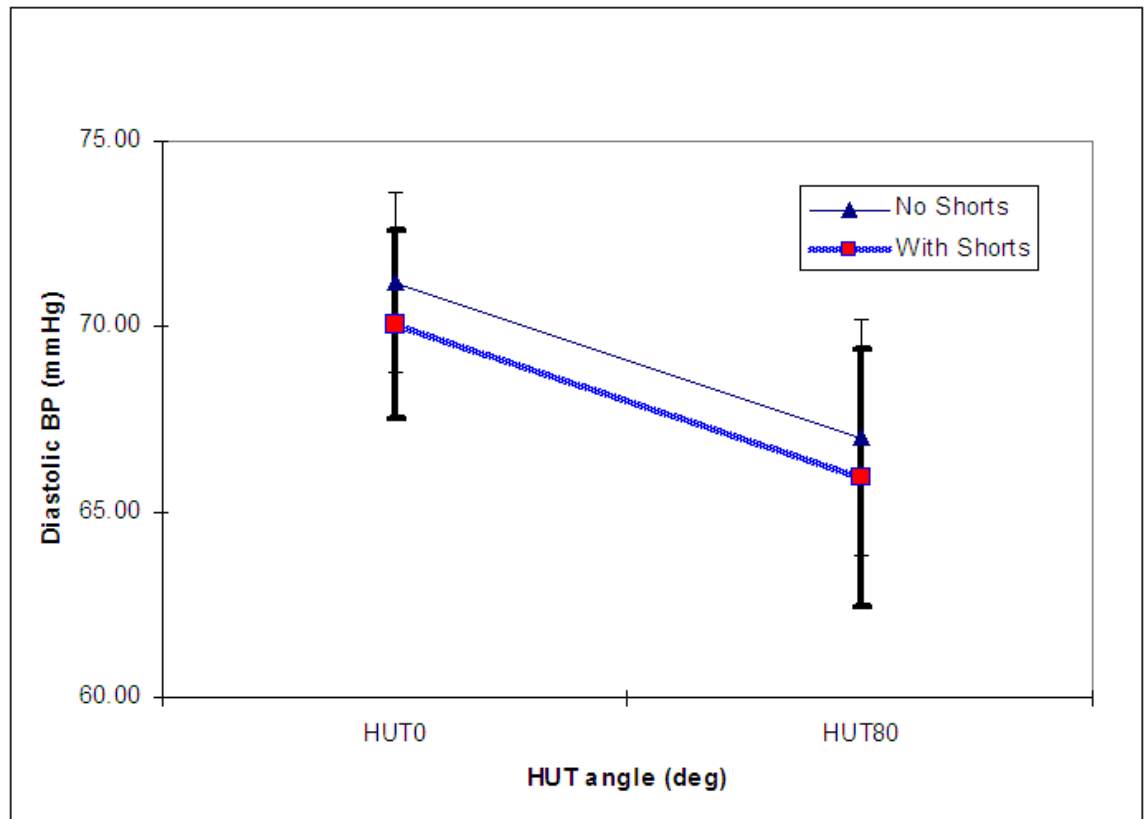


**Fig. 4.2. Mean systolic blood pressure with and without shorts. # Change in SBP significantly less with shorts than without shorts.**

#### Effect of Shorts and HUT on DBP

Effects of shorts and HUT on DBP are shown in Fig. 4.3. In the supine position without shorts, the average DBP was  $71.2 \pm 2.4$  mmHg. Tilting to 80 degrees decreased the average DBP to  $67.0 \pm 3.2$  mmHg. A similar effect was seen when the subjects wore shorts. The average DBP decreased from  $70.1 \pm 2.5$  mmHg at HUT0 to  $65.9 \pm 3.5$  mmHg at HUT80. Neither tilt nor shorts effects were significant on DBP.

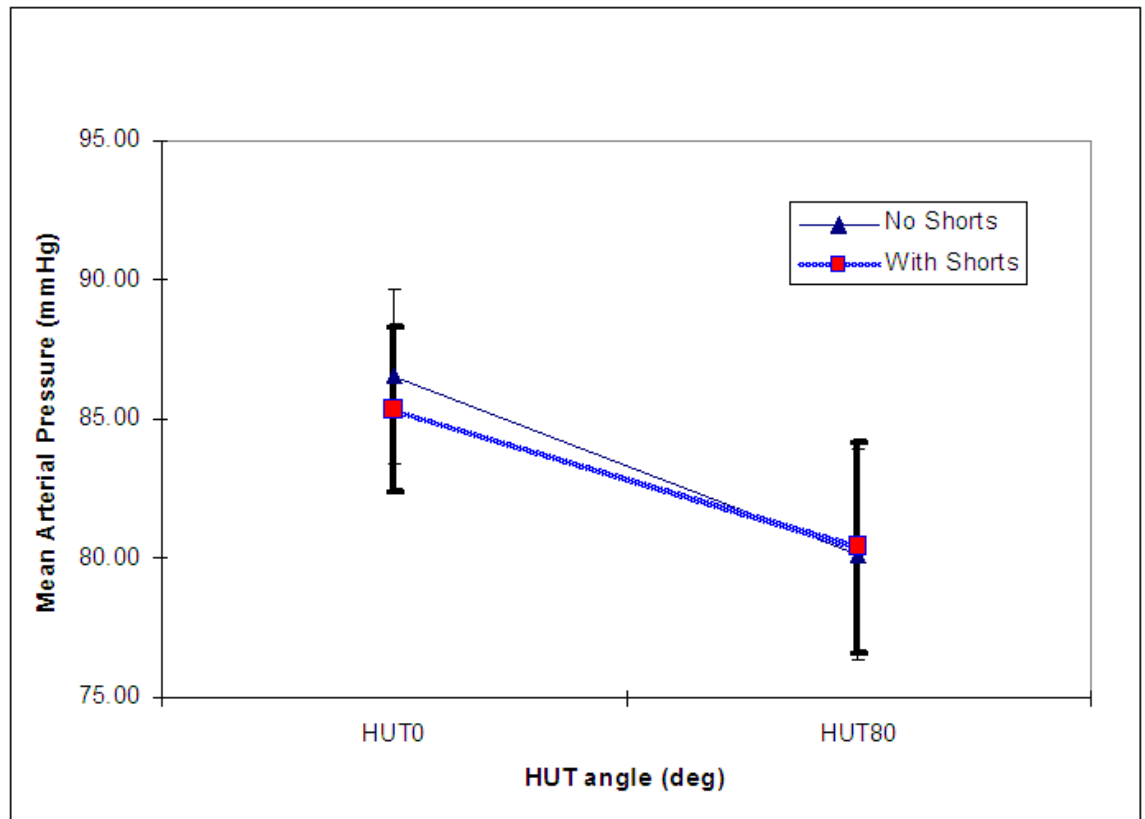




**Fig. 4.3. Mean diastolic blood pressure with and without shorts. No significant shorts effect.**

#### Effect of Shorts and HUT on Mean Arterial Pressure (MAP)

Effects of shorts and HUT on MAP are shown in Fig. 4.4. In the supine position without shorts, the average MAP was  $86.5 \pm 3.1$  mmHg . Tilting to HUT80 decreased average MAP to  $80.1 \pm 3.8$  mmHg. A similar effect was seen when the subjects wore shorts. The average MAP decreased from  $85.3 \pm 3.0$  mmHg at HUT0 to  $80.3 \pm 3.8$  mmHg at HUT80 degrees. The tilt effect was not significant, neither with nor without shorts ( $p > 0.05$ ).



**Fig. 4.4. Mean arterial blood pressure with and without shorts. No significant tilt nor shorts effect.**

#### Effect of Shorts and HUT on Segmental Impedance Change

Measurements of Impedance were performed for several reasons. Due to the inverse relationship between impedance and fluid volume (Formula 4.1), the higher the impedance value, the less fluid that is in the measured area/segment and vice versa:

$$\text{Vol} = L^2 * \delta / R,$$

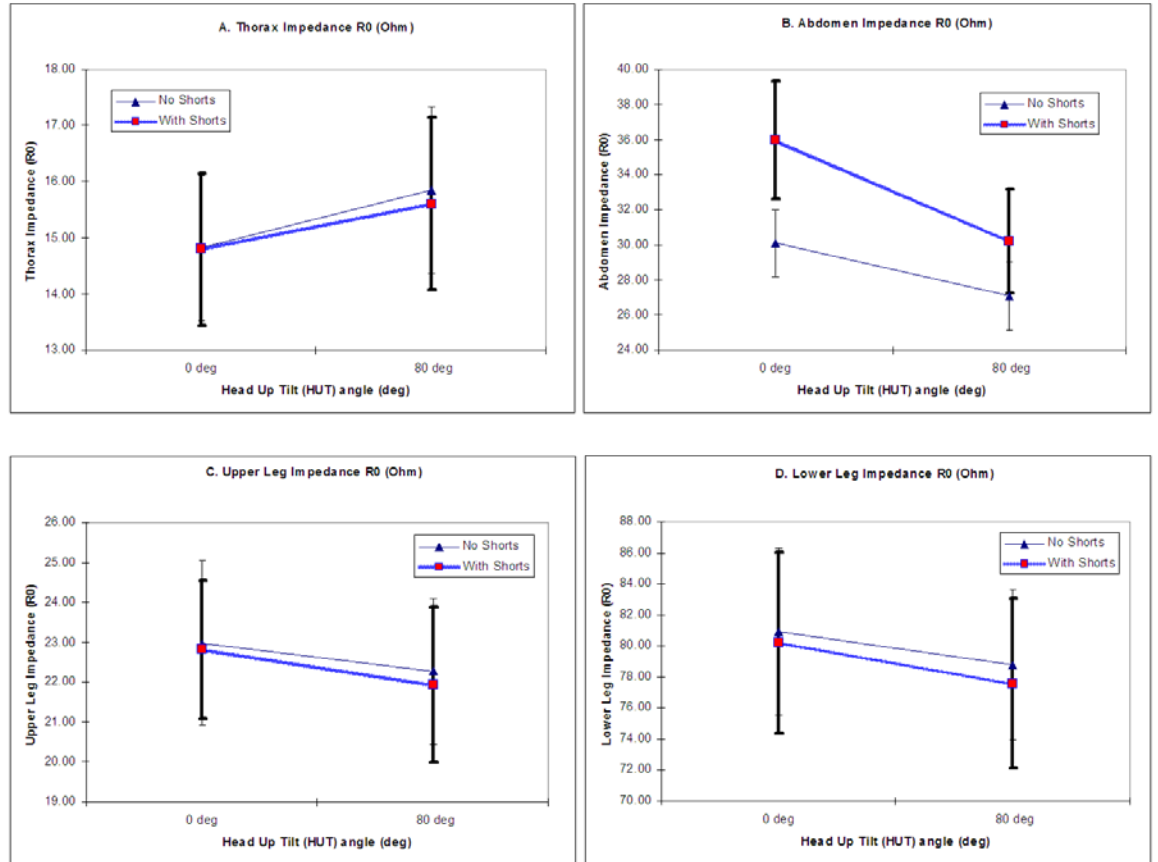
**Formula 4.1. Fluid volume and Impedance/resistance formula (where  $L$  = segment length,  $\delta$  = effective resistance for plasma (0.8 – 1.0 Ohm),  $R$  = segment Impedance (device measured)).**

Tracking the changes in fluid volume (of blood, interstitial fluid, etc) allows us to explain why the human cardiovascular system responds the way it does to the tilt and to compression by shorts. In addition, impedance is used to calculate heart stroke volume and cardiac output, using the Sramek-Bernstein formula 4.2.

$$\text{SV} = \delta * ((0.17 * H)^3 / 4.25) * (dZ/dt_{\text{max}} / Z_0) * \text{LVET}$$

**Formula 4.2. Sramek-Bernstein formula for calculating stroke volume (SV), where  $\delta$  is a weight correction factor,  $H$ - person's height,  $dZ/dt_{\text{max}}$  – maximal impedance change,  $Z_0$  – basic thoracic impedance, LVET – left ventricular ejection time.**

Effects of shorts and HUT on segmental impedance in thorax (THX), abdomen (ABD), upper leg (UL) and lower leg (LL) are shown in Fig. 4.5. In the case of THX, looking at the tilt alone, notice that without shorts, THX impedance,  $R_0$  (Fig. 4.5.A) averaged  $14.8 \pm 1.3$  Ohm at HUT0, which is the control condition. Tilting to HUT80 did not increase the average THX  $R_0$  significantly. A similar trend was seen when subjects wore shorts.



**Fig. 4.5. Mean segmental impedance response.**

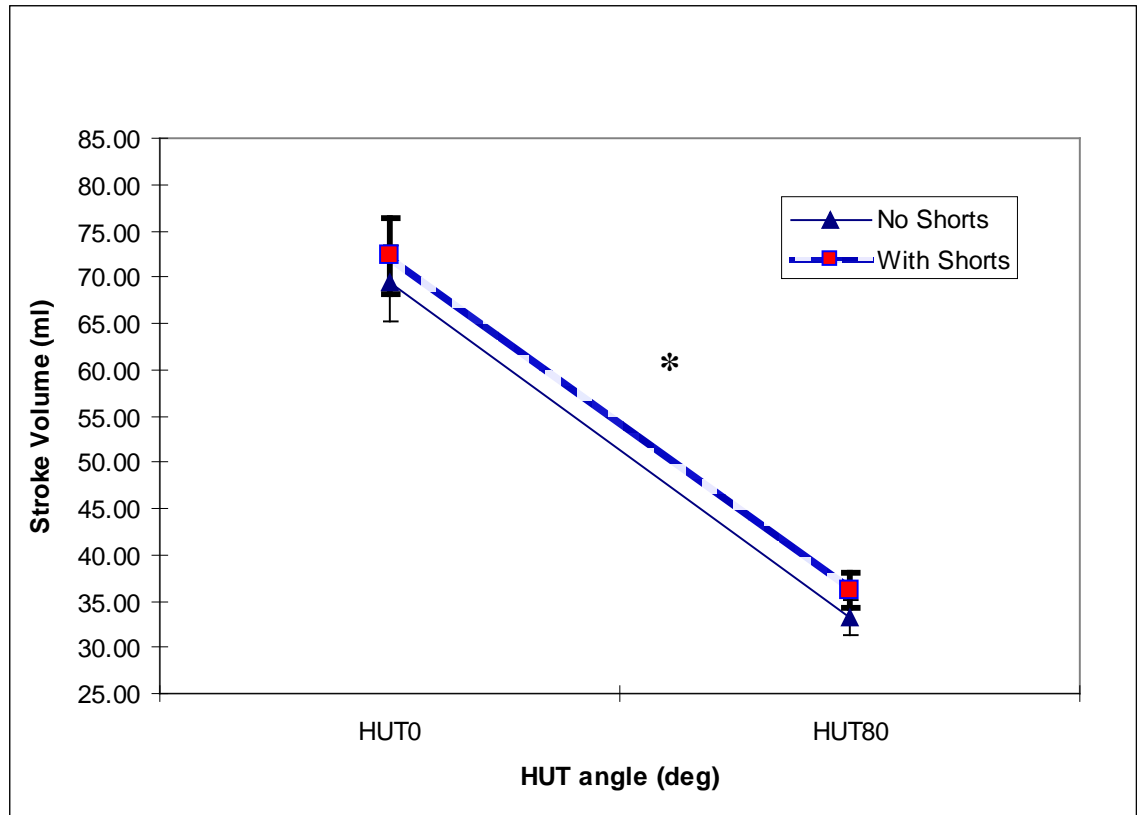
In the case of ABD, looking at the tilt alone, notice that without shorts, ABD impedance, R0 (Fig. 4.5.B) averaged  $30.1 \pm 1.9$  Ohm at HUT0. Tilting to HUT80 decreased the average ABD R0 to  $27.1 \pm 1.5$  Ohm, which means more fluid volume was available in this segment. A similar trend was seen when the subjects wore shorts. The average ABD R0 decreased from  $35.9 \pm 3.4$  Ohm at HUT0 to  $30.2 \pm 2.9$  Ohm at HUT80. Neither the tilt effect nor the shorts effect on ABD was significant ( $p > 0.05$ ).

Looking at UL R0(Fig 4.5.C) and LL R0 (Fig. 4.5.D), although both the tilt and the shorts did lower overall impedance, neither the tilt nor the presence of shorts produced any statistically significant effects ( $p > 0.05$ ).

#### Effect of Shorts and HUT on stroke volume (SV)

SV was calculated using the Sramek-Bernstein formula, 4.2. The effect of shorts and HUT on SV are shown in Fig. 4.6. Without shorts, the average SV was  $69.3 \pm 4.2$  ml at HUT0. Tilting to HUT80 decreased the average SV to  $33.2 \pm 1.9$  ml. A similar effect was seen when the subjects wore shorts. The average SV decreased from  $72.3 \pm 4.1$  ml at HUT0 to  $36.2 \pm 1.9$  ml at HUT80. The tilt effect was significant ( $p < 0.05$ ).

When examining the effect of shorts, notice that overall the shorts increased SV by 3.0 ml in the supine and increased it by the same amount (3.0 ml) in the HUT80 position. The paired two sample t-test for change in means between  $\Delta$ shorts vs.  $\Delta$ no shorts showed that the effect of shorts on SV was not statistically significant ( $p > 0.05$ ).



**Fig. 4.6. Mean stroke volume with and without shorts. \* Significant tilt effect.**

**No shorts effect.**

#### Effect of Shorts and HUT on Cardiac Output (Q)

Cardiac output was calculated using the following formula:

$$Q = HR * SV / 1000$$

**Formula 4.3. Formula for calculating cardiac output (where HR=heart rate and SV=stroke volume (see formula 4.2))**

Effect of shorts and HUT on Q is shown in Fig. 4.7. Without shorts, the average Q was  $4.6 \pm 0.2$  L/min at HUT0. Tilting to HUT80 decreased the average Q to  $3.1 \pm 0.2$  L/min. A similar effect was seen when the subjects wore shorts. The average Q decreased from  $4.6 \pm 0.2$  L/min at HUT0 to  $3.1 \pm 0.2$  L/min at HUT80. The tilt effect was significant ( $p < 0.05$ ), but the shorts themselves had no effect on Q.

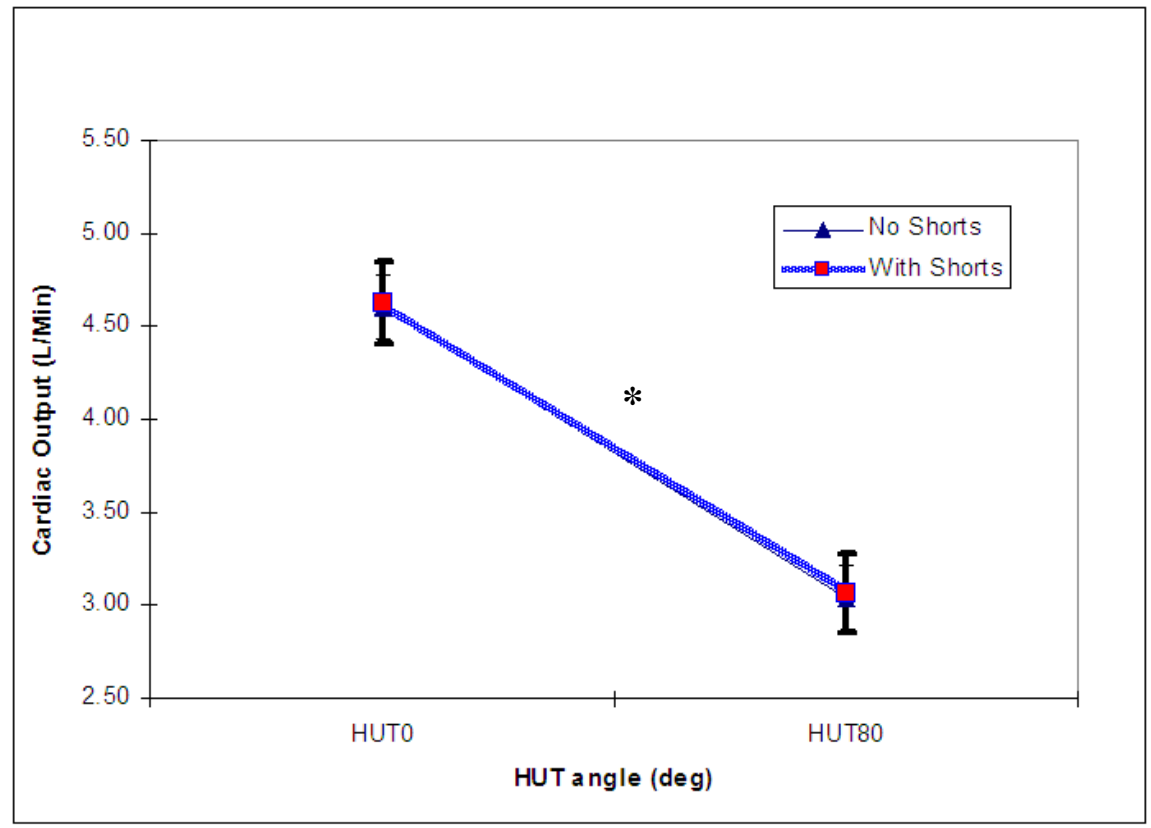


Fig. 4.7. Mean cardiac output with and without shorts. \* Significant tilt effect.

No shorts effect.

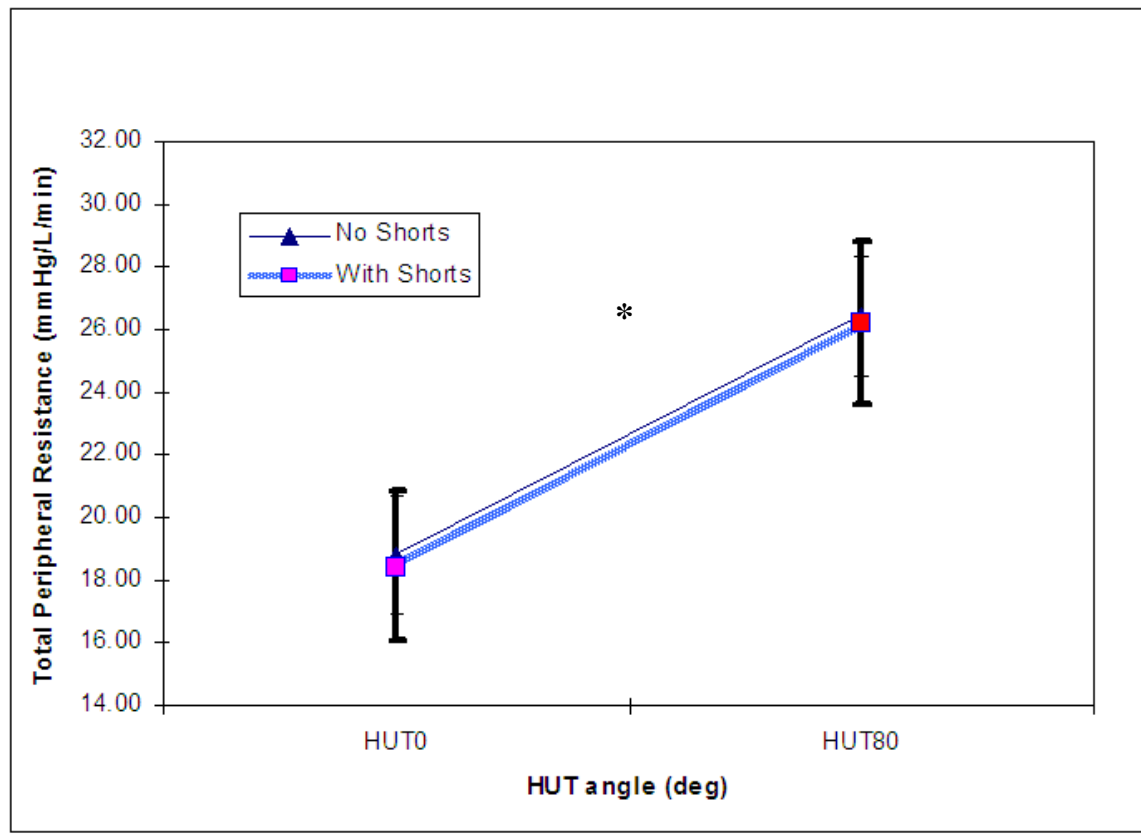
### Effect of Shorts and HUT on total peripheral resistance (TPR)

TPR was calculated using this formula:

$$\text{TPR} = \text{MAP} / \text{Q}$$

**Formula 4.4. Formula for calculating total peripheral resistance (where MAP=mean arterial pressure and Q=cardiac output)**

Effects of shorts and HUT on TPR are shown in Fig. 4.8. Tilting subjects to HUT80 caused a significant increase in TPR, but wearing shorts had no effect.



**Fig. 4.8. Mean total peripheral resistance with and without shorts.**  
**\* Significant tilt effect. No shorts effect.**



## Chapter Five

### Discussion

The present study was designed to determine the physiological effects of the Alter-G compression shorts on cardiovascular parameters during supine resting and head up tilt. The hypothesis of the present study was that, by their nature, Alter-G shorts would result in fluid shifts toward the abdomen or thorax, and significantly contribute to maintaining stroke volume and systolic BP when the body is tilted (to simulate what happens to astronauts upon return from microgravity to Earth). The main finding of this study was that, as seen in Fig. 4.2, the shorts significantly attenuated a reduction in SBP, compared to no shorts condition. However, this increase in SBP did not manifest itself with any significant change in stroke volume (SV), (see Fig. 4.6), nor with any significant changes in cardiac output (Q) (see Fig. 4.7) during the tilt test. Instead, a major change was found in heart rate (HR), (see Fig. 4.1), especially at 80 degrees tilt, where the HR was lower on average by 6.7 bpm when subjects wore shorts vs. the condition without shorts. The lower HR is possible due to higher stroke volume, even though it could not be determined exactly due to impedance formula used (see Formula 4.2).

In this small group of subjects, the Alter-G compression garments were an effective countermeasure to mitigate symptoms of orthostatic intolerance and pre-syncope throughout passive upright tilt by maintaining SBP. Compared to thigh-high or knee-high garments from other studies (Stenger et al., 2010), these symptoms were not prevented by decreasing venous pooling in the legs, which in turn improved venous return, SV and Q. Instead, the abdomen contains a large, highly compliant, venous bed which contains approximately 25% of the blood volume at rest. During orthostasis, its capacity is reduced

by baroreflex-mediated arteriolar vasoconstriction (Rowel, et al., 1972). Compression of the abdomen increases intra-abdominal pressure and thereby reduces vein diameter (Holcroft, et al., 1984) and splanchnic blood volume. Measurements in healthy subjects and autonomic dysfunction patients from other studies disclose that the subsequent abdomino-thoracic blood shift increases thoracic blood volume (see Impedance Fig. 4.6 A and B) and central venous pressure (Smit, et al., 2004). This leads to a better filling of the heart and increases SV and Q. In this study Q did not change significantly, as the increase in SV was offset by the drop in HR.

Note, that in all literature on this subject there is excellent agreement that positive pressure raises BP, and that there is a reduction in volume and flow in the compressed region (Denq et al., 1997). However, there is some disagreement in the literature on the mechanism of improvement, as to whether the effect is mediated by increasing peripheral resistance alone, i.e. afterload increase (Tenny S.M., et al. 1955) or by improving venous return, i.e. preload increase (Tanaka H., et al., 1996). The findings from our study seem to adhere to the last group, although the results are inconclusive, since as we have seen, preload has increased and stroke volume was higher, although by an insignificant amount.

As far as the effects of tilt alone are concerned, this study was in line with other studies (Denq et al., 1997, Platts et al., 2009, Stenger et al., 2010) which looked at cardiovascular responses of subjects tilted from 0 degrees to either 70 or 80 degrees. The tilt test was administered as it mimics very closely weightlessness (at 0 degrees tilt) and also Earth gravity (at 70 or 80 degrees tilt) and allows the investigator to examine fluid shifts within the subject's body while it changes angle, as well as its effect on the cardiovascular system. The tilt was performed passively, while subjects were resting on the tilt table with their feet on a sturdy platform. They were quiet without any talking, movement or muscle

contractions which could trigger venous return from lower extremities, therefore minimizing effects of external influences on Q and SV. As expected, HR increased after the tilt (significantly, in this study), as more fluid shifted toward lower extremities, the heart had to work harder to return blood to the upper body; systolic (SBP), diastolic blood pressures (DBP) and mean arterial pressure (MAP) decreased slightly, while SV and Q decreased significantly. Total peripheral resistance (TPR) increased significantly with the tilt.

Looking at segmental impedance (Fig. 4.7 A, B, C, D), thorax (THX) impedance increased slightly with the tilt. Due to an inverse relationship between impedance and fluid volume (see Formula 4.1) less fluid was present in the thorax after the tilt. Most of that fluid shifted into the abdomen, as confirmed by (not significantly) lower abdominal impedance (Fig. 4.5. B) (therefore, higher fluid volume), while some went into upper leg and lower leg segments, as shown by slightly lower impedance in those segments during tilt (Fig. 4.5. C and D). The presence of compression shorts during the tilt led to more fluid being retained in the thorax (Fig. 4.5 A) and less left in the abdomen (in addition to thorax, some of the fluid went from the abdomen into the upper and lower leg segments). A possibility for a future study would be to add compression socks which could possibly increase venous return and affect stroke volume, heart rate and other cardiovascular variables, but that could be a topic of research for another study.

A secondary purpose of this study was to separate effects of the compression shorts from effects of Alter-G lower body positive pressure created by air pressure and in turn provide answers to questions from the comparative study of simulated Moon and Mars gravity environments between Alter-G and head-up tilt (Kostas V., et al., 2011). While no data from the Alter-G were collected during the present study, we can speculate on the effects, based on comparing the findings of a previous study, to data collected here. For

example, in the previous study (Kostas., et al., 2011), the average difference between systolic blood pressure at 100% body weight (up-right subject in Earth gravity) in the Alter-G (117.3 mmHg) versus 80 degree head-up tilt (104.1 mmHg) was 13.12 mmHg. From the results of the present study we can estimate that approximately 4.0 mmHg of the pressure changes were due to the shorts and approximately 9.0 mmHg was due to air pressure inside the Alter-G chamber.

There are several limitations to this study. First, the study was conducted using a small number of subjects and inter-subject variability was high. For example, subject 4 was a 20 y.o. female 177.8 cm high and weighing 120.7 kg, while subject 12 was a 28 y.o. female 162.6 cm high and weighing 47.6 kg. Secondly, the compression garments were not custom fit to each subject, as is the case in other studies. Instead, the garments in this study came in only 5 sizes (S, M, L, XL, XXL) and some subjects possibly had garments that were not an exact fit, which could have distorted the results. The tightness of shorts was determined by using the index finger and pulling slightly on the shorts, both around legs and waist. This was a very subjective measurement and did not take into consideration other factors, like the circumference of the thighs or the waist and other factors. To better control for this variable, an improvement could have been to design a bladder device that would have been inserted between the subject's skin and the Alter-G shorts and could be used to determine the direct pressure exerted by each pair of shorts on the subject's skin. This might have allowed a determination of a relationship between the pressure exerted by the shorts and changes in physiological parameters. Finally, the values for stroke volume, and subsequently for cardiac output ( $Q = HR \cdot SV / 1000$ ) and TPR ( $TPR = MAP / Q$ ) were obtained from the Sramek-Bernstein electrical impedance formula (see Formula 4.2). This method for determining SV was used due to its non-invasiveness and low cost. Note that this formula assumes that the volume of the electrically participating tissue in the thorax is a truncated

cone, while other similar equations, (like Kubicek's,  $SV = \delta * (L^2 / Z0^2) * (dZ/dtmax / Z0) * LVET$ , where **L- distance between electrodes**) assume it is a cylinder. The validity of these SV equations has been investigated by many researchers (Woltjer, H. et al., 1997; Donovan K.D., et al., 1986). In general, most investigators have found a significant correlation (assuming normal hydration levels of subjects) between SV measured with impedance cardiography and SV measured with other methods, such as MRI or echo-cardiography (ultra-sound), which were not available for this study due to their high cost. However, various investigators also reported a wide dispersion of the impedance SV data (Goldstein et al., 1986). It also appears from these studies that the impedance method is not equally valid under all physiological conditions. Thus, no consensus can be reached on the accuracy of impedance cardiography in measuring of SV. In some studies, the method is evaluated as highly accurate (Koon-Kang, et al., 1985); in others more dispersion between the two methods is found (Donovan, et al., 1986). In most studies, however, the mean difference between the two methods and its standard deviation are not shown, which makes it difficult to draw conclusions about precision. In order to establish the validity of impedance cardiography, more research is needed and more studies need to be performed comparing both impedance methods with each other and with other methods (MRI, echo-cardiography, etc).

One such attempt was made in the comparative study of simulated moon and Mars gravity environments between Alter-G and head-up tilt (Kostas, et al., 2011). The average values for SV in that study were obtained using two methods, through ultra-sound and also using the impedance formula. Even though in absolute terms, the average SV values were different (92 vs. 190.5 ml for HUT0 degrees, as well as 63.8 vs. 140.6 ml for HUT80 degrees, ultra-sound vs. impedance respectively), the relative change from HUT0 degrees to HUT80 degrees was in the same vicinity, 30.6% vs. 26.2%, ultra-sound vs. impedance

respectively. Therefore the absolute values for average SV obtained in current study (72.3 vs. 36.2 ml, HUT0 to HUT80 degrees, respectively), could be ignored, since they are on the low side, and instead, the relative change of 50% of going from HUT0 degrees to HUT80 should be taken into account.

Based upon results obtained from this study, the level of protection from Alter-G compression shorts may be improved in future studies by the addition of thigh-high compression, as demonstrated by Denq et al., 1997, or breast-high compression. However, re-designing the Alter-G shorts to become Alter-G socks or pants or a full-body Alter-G suit, may also change lower body positive pressure exerted on the subject by the Alter-G air enclosure. During unweighting in the Alter-G device, with the shorts on, most of the pressure is concentrated in the perineum region of each subject, which also makes it quite uncomfortable over time, especially for males, as it may lead to edema. Switching to Alter-G pants with feet would most likely redistribute the pressure from the perineum to the soles of the feet and other body parts to make it more comfortable for subjects to withstand the unweighting process. More research is needed in the area of compression garments as it relates to simulating spaceflight and re-entry into Earth gravity using the Alter-G device, as well as well as for the purpose of other Earth related activities, such as athlete rehabilitation and injury prevention.

## Chapter Six

### Summary and Conclusions

The present study was designed to determine physiological effects of the Alter-G compression shorts while resting in the supine position and during a head-up tilt position. The main finding of this study was that the shorts significantly increased SBP by approximately 4 mmHg when compared to the no shorts condition during tilt. However, this increase in SBP did not manifest itself with any significant change in stroke volume (SV), nor with any significant changes in cardiac output (Q). Instead, a major change was found in heart rate (HR), especially at 80 degrees tilt, where the HR increased 6.7 bpm less in subjects wearing the shorts. The smaller increase in HR could be due to higher stroke volume, even though this could not be established from the data we obtained.

In this small group of subjects, the Alter-G compression garments were an effective countermeasure to mitigate the severity of the symptoms of orthostatic intolerance and pre-syncope throughout passive upright tilt by maintaining SBP. As far as the effects of the tilt alone are concerned, this study was in line with other studies performed on this topic.

A secondary purpose of this study was to separate effects of the compression shorts from effects of Alter-G lower body positive pressure created by air pressure and in turn provide answers to questions from the comparative study of simulated Moon and Mars gravity environments between Alter-G and head-up tilt. From the results of this study we were able to estimate that approximately 4.0 mmHg of the pressure changes were due to the shorts and approximately 9.0 mmHg was due to air pressure inside the Alter-G chamber.

Based upon results obtained from this study, the level of protection from Alter-G compression shorts may be improved in future studies by the addition of thigh-high compression, or breast-high compression. More research is needed in the area of compression garments as it relates to simulating spaceflight and re-entry into Earth gravity using the Alter-G device, as well as well as for the purpose of other Earth related activities, such as athlete rehabilitation and injury prevention.



## Appendix A

### Recruitment Script

My name is Vladimir Kostas and I am Master's Degree student in Exercise Physiology at the University of Kentucky. I am studying how the human body responds to microgravity, in particular what astronauts' heart and blood go through in long duration space flights, as well as upon re-entry into Earth atmosphere and how various garments could decrease the negative effects of space-flight and allow humans to reach such far-away worlds as Planet Mars and beyond.

I am trying to find healthy subjects between the ages of 18 – 45 to participate in my study. To participate in this study, you must be overall healthy, without prior history of fainting. If you are pregnant, had major surgery within the past year, your doctor has restricted you from activity, you know your resting blood pressure is above 140/90, or if you have an HIV/AIDS diagnosis, you should not participate.

The study will take place at the Biodynamics Laboratory in the center for Biomedical Engineering on the University of Kentucky campus. You will need to come to the Biodynamics Laboratory one time during the study. The visit will take about 1.5 hrs. You will be asked to try on lower body compression garments of various sizes, lay or stand still while your Heart Rate, Blood Pressure and other measurements are taken on a tilt table.

You will be compensated for your time in the amount of \$25.

If you are interested in participating, feel free to contact me for more information (859)227-2074 or through email [vlad.kostas@uky.edu](mailto:vlad.kostas@uky.edu) (preferred method)

Thank you !

## Appendix B

### Research procedures

#### Qualification Phase:

- signing of the informed consent \_\_\_\_\_
- Par-Q questionnaire \_\_\_\_\_
- Medical history/history of fainting \_\_\_\_\_
- Exercise the day of testing /sweat rate \_\_\_\_\_
- Fluid intake the day of testing \_\_\_\_\_
- BP measurement \_\_\_\_\_

#### Orientation Phase:

- verbal orientation / questions/ answers \_\_\_\_\_
- fitting with Alter-G shorts \_\_\_\_\_

#### Preparation / Instrumentation Phase:

- record height \_\_\_\_\_ cm
- record weight \_\_\_\_\_ kg
- determine order of activities according to table/matrix \_\_\_\_\_
- Place subject on HUT table (HUT = 0 deg) \_\_\_\_\_
- Place ECG and IMPDN electrodes / connect leads \_\_\_\_\_
- Strap subject / place hand on platform / connect BP, etc \_\_\_\_\_
- Record distance between THRIM leads
- Chest (LThorax) \_\_\_\_\_ cm
- Abdomen \_\_\_\_\_ cm
- UL \_\_\_\_\_ cm
- LL \_\_\_\_\_ cm

#### Measurement/Data Acquisition Phase:

- confirm working condition of all devices (PC, BP, WindaQ signals, ECG signals) \_\_\_\_\_
  - place subject according to matrix (HUT=0 or HUT=80 with or without SHORTS) \_\_\_\_\_
  - ask subject to sit still / no talk for 1 min \_\_\_\_\_
  - take manual BP / HR and record on data sheet. \_\_\_\_\_
  - Take 3 min of continuous BP + Impedance measurements \_\_\_\_\_
  - Tilt table (up / down),
  - ask subject to sit still / no talk for 1 min \_\_\_\_\_
  - take manual BP / HR and record on data sheet. \_\_\_\_\_
  - Take 3 min of continuous BP + Impedance measurements \_\_\_\_\_
  - Allow subject to get off HUT table and remove/put on SHORTS \_\_\_\_\_
  - Re-connect Impedance/ ECG Leads \_\_\_\_\_
  - Repeat above CV data Acquisition (1+3 +1+3 min)
- for another NO SHORTS/ SHORTS condition \_\_\_\_\_

#### De-instrumentation Phase

- Remove Straps \_\_\_\_\_
- Remove BP cuff / finger/ hand \_\_\_\_\_
- Remove Leads / Electrodes \_\_\_\_\_
- Allow subject to stand up / remove shorts \_\_\_\_\_
- Check subject feeling good / Release subject \_\_\_\_\_
- Disinfect shorts \_\_\_\_\_

## Appendix C

### Informed Consent (IRB form C)

#### Consent to Participate in a Research Study

#### **EFFECT OF LOWER BODY POSITIVE PRESSURE ON CARDIOVASCULAR RESPONSE AT VARIOUS DEGREES OF HEAD UP TILT**

##### **WHY ARE YOU BEING INVITED TO TAKE PART IN THIS RESEARCH?**

You are being invited to take part in a research study about the effects of lower body positive pressure on cardiovascular response at rest and at various degrees of head up tilt. You are being invited to take part in this research study because you are a healthy person between the ages of 18 and 45. If you volunteer to take part in this study, you will be one of about 40 people to do so.

##### **WHO IS DOING THE STUDY?**

The person in charge of this study is Vladimir Kostas, a graduate student at the University of Kentucky Department of Kinesiology and Health Promotion. He is being guided in this research by J. W. Yates, PhD. There may be other people on the research team assisting at different times during the study.

##### **WHAT IS THE PURPOSE OF THIS STUDY?**

By doing this study, we hope to learn how the body responds to fluid shifts from lower extremities towards the chest area, a condition which might be experienced by an astronaut while in zero-gravity in space or while in an anti-gravity suit upon return to Earth, as well as fluid shift towards the lower extremities when no compression garment is present.

##### **ARE THERE REASONS WHY YOU SHOULD NOT TAKE PART IN THIS STUDY?**

If you are under 18 or over 45 years of age, are prone to fainting, are pregnant, had major surgery in the past year, your doctor has restricted you from activity, your blood pressure is greater than 140/90 or you have a diagnosis of HIV/AIDS, you should not participate in this study.

##### **WHERE IS THE STUDY GOING TO TAKE PLACE AND HOW LONG WILL IT LAST?**

The research procedures will be conducted at the Biodynamics Laboratory in the Center for Biomedical Engineering on the University of Kentucky campus. You will need to come to the Biodynamics Laboratory one time during the study. The visit will take about 1.5 hrs.

##### **WHAT WILL YOU BE ASKED TO DO?**

You will be asked to review this document and provide informed consent to continue as a subject in the study. If you agree to participate, you will be asked to fill out a short questionnaire to

help the investigators determine if you can participate. If you are prone to fainting, have experienced dizziness or lightheadedness getting out of bed or standing up from a chair in the past, you will be excused.

Next, one of the investigators will take your resting blood pressure. If your pressure is less than 140/90 mmHg, you can continue. At this point your weight, height and waist circumference will be measured. Then you will be asked to try on several pairs of shorts to determine the ones that fit best. You will also get familiarized with the tilt table operation.

In addition to wearing shorts, you will also wear a blood pressure cuff on one of the arms and also on one finger and 12 electrodes placed on various body parts (chest, leg, arm, neck).

During the whole study you will be asked to stay quiet and still four times for 3 minutes at a time at various phases of the study with or without the shorts on while your body is tilted on the table to various positions. Your body will be strapped to the table while you are tilted to prevent you from shifting forward or sideways too much.

Several measurements will be taken while you are lying down on the table or tilted into standing position. You will not feel anything during these measurements, except the blood pressure cuff on your arm and finger inflating. If you feel lightheaded or dizzy anytime during the study or experience any other sign of discomfort, you should tell the attending personnel immediately.

After data collection is complete, you will be helped in removing the electrodes from your skin. Then you will be allowed to leave the tilt table and remove the shorts in the dressing room, after which you will be excused.

### **WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?**

This is a minimal level of activity and represents a minimal risk to healthy subjects. Potential Risks could occur from the Tilt Test, Electrode Placement, Alter-G shorts and Electrical Instrumentation.

#### **Tilt Test**

A. Potential Hazard Cause: There is some risk of feeling lightheaded or fainting with upright tilt.

B. Effects of the Hazard: Patient could become presyncopal or syncopal.

C. Assessment-Severity & Probability: Reasonable/Medium

D. Protection to Minimize Risks: If the subject feels lightheaded, blood pressure or heart rate begins to fall (see below) or faints while standing, the tilt table will be returned to a supine or head-down position and the test will be terminated. Subject restraints will be used during the tilt test to keep the subject from falling. The tilt test will be terminated if any of the following instances occur while the subject is tilted upright:

1. A sudden drop in heart rate greater than 15 beats per minute
2. A sudden drop in blood pressure (systolic fall > 25 mmHg or diastolic fall > 15 mmHg in one minute)
3. Significant cardiac arrhythmias
4. Heart rate < 40 beats per minute for people whose resting heart rate is > 50 beats per minute

5. Tachyarrhythmias (three or more beats in a row of supraventricular or ventricular tachycardia)
6. Evidence of heart block other than first degree
7. Premature ventricular contractions (PVC) which meet the following criteria:
  - 6 or more PVC's/minute
  - PVC's that are closely coupled
  - PVC's that fall on the T wave of the preceding beat
  - PVC's which are multiformed
  - PVC's in couplets or runs (ventricular tachycardia)
8. An absolute systolic blood pressure of 70 mmHg or less
9. Severe nausea
10. Clammy skin
11. Profuse sweating
12. Pallor
13. Light-headedness
14. Dizziness or tingling
15. Sudden chest tightness or difficulty breathing
16. Subject request at any time
17. Prolonged loss of ECG signal

#### Electrodes

- A. Potential Hazard Cause: Allergic reaction or skin irritation due to electrode application process
- B. Effects of the Hazard: Subject discomfort due to skin irritation
- C. Assessment-Severity & Probability: Marginal/Low
- D. Protection to minimize risks: Only standard, medically approved, electrodes are used. Electrodes will not be worn more than 1hr at a time.

#### Alter-G Shorts

There is small risk of infection when the "Alter-G" garment is worn. As this study will enroll only healthy subjects, the risk is considered extremely small. To reduce the risk further, each subject will be provided with a clean pair of "Alter-G" garments, after they have been washed in an anti-microbial and bleach solution.

#### Electrical Instrumentation

- A. Potential Hazard Cause: Improperly grounded instrumentation, or failure of electrical protection circuitry
- B. Effects of the Hazard: Subject injury due to electrical shock
- C. Assessment-Severity & Probability: Critical/Extremely low
- D. Protection to Minimize Risks:
  1. Grounding will be confirmed through scheduled preventative maintenance.
  2. All cables will be insulated and properly strain-relieved to avoid breakage during voluntary movements.
  3. Physiological amplifiers for monitoring will limit electrode current, even under fault conditions, to less than 50  $\mu$ amps for all electrode leads combined, which is within the guidelines established by Human Research Policy and Procedures.

In addition to the risks and discomforts listed above, you may experience a previously unknown risk or side effect.

#### **WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?**

You will receive information regarding your heart rate, blood pressure, stroke volume and cardiac output response measured during rest. In addition, your willingness to take part may help better understand this research topic.

#### **DO YOU HAVE TO TAKE PART IN THE STUDY?**

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any benefits or rights you would normally have if you choose not to volunteer. You can stop at any time during the study and still keep the benefits and rights you had before volunteering.

#### **IF YOU DON'T WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?**

If you do not want to be in the study, there are no other choices except not to take part in the study.

#### **WHAT WILL IT COST YOU TO PARTICIPATE?**

You may have to pay for the cost of getting to the study site and a parking fee.

#### **WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THIS STUDY?**

You will receive monetary compensation for taking part in the study . When you arrive for the study, you will receive \$10. Then, if you are admitted to participate in the study (i.e. if you meet the qualification criteria for the study ) you will receive an additional \$15 at the end of the study for a total of \$25.

#### **WHO WILL SEE THE INFORMATION THAT YOU GIVE?**

We will make every effort to keep private all research records that identify you to the extent allowed by law.

Your information will be combined with information from other people taking part in the study. When we write about the study to share it with other researchers, we will write about the combined information we have gathered. You will not be personally identified in these written materials. We may publish the results of this study; however, we will keep your name and other identifying information private.

This study is confidential. That means that only study personnel will know who participates. We may be required to show information, which identifies you to people who need to be sure we have done the research correctly; these would be people from such organizations as the University of Kentucky.

### **CAN YOUR TAKING PART IN THE STUDY END EARLY?**

If you decide to take part in the study you still have the right to decide at any time that you no longer want to continue. You will not be treated differently if you decide to stop taking part in the study.

The individuals conducting the study may need to withdraw you from the study. This may occur if you are not able to follow the directions they give you, if they find that your being in the study is more risk than benefit to you, or if the agency funding the study decides to stop the study early for a variety of scientific reasons.

If you only partially complete the study, you will be monetarily compensated in the amount of \$25.

### **WHAT HAPPENS IF YOU GET HURT OR SICK DURING THE STUDY?**

If you believe you are hurt or if you get sick because of something that is due to the study, you should call Vladimir Kostas at (502) 407-7916 or Dr. J.W. Yates at 859-257-5879 immediately. They will determine what type of treatment, if any, that is best for you at that time.

It is important for you to understand that the University of Kentucky does not have funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. Also, the University of Kentucky will not pay for any wages you may lose if you are harmed by this study.

Medical costs that result from research related harm can not be included as regular medical costs. Therefore, the medical costs related to your care and treatment because of research related harm will be your responsibility.

You do not give up your legal rights by signing this form.

### **WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS, CONCERNS, OR COMPLAINTS?**

Before you decide whether to accept this invitation to take part in the study, please ask any questions that might come to mind now. Later, if you have questions, suggestions, concerns, or complaints about the study, you can contact the investigator, Vladimir Kostas at (859) 227-2074 / [vlad.kostas@uky.edu](mailto:vlad.kostas@uky.edu) or his advisor, Dr. J.W. Yates at 859-257-5879. If you have any questions about your rights as a volunteer in this research, contact the staff in the Office of Research Integrity at the University of Kentucky at 859-257-9428 or toll free at 1-866-400-9428. We will give you a signed copy of this consent form to take with you.

### **WHAT ELSE DO YOU NEED TO KNOW?**



At this time, there is no additional info that you, as a subject, need to know, while participating in this study.

\_\_\_\_\_  
Signature of person agreeing to take part in the study

\_\_\_\_\_  
Date

\_\_\_\_\_  
Printed name of person agreeing to take part in the study

\_\_\_\_\_  
Name of [authorized] person obtaining informed consent

\_\_\_\_\_  
Date

## Appendix D

### Medical History Form

#### **Medical History**

Name (First, Last) \_\_\_\_\_

Birth Date \_\_\_\_\_

#### Personal:

- | Y   | N   |   |
|-----|-----|---|
| ___ | ___ | Have you ever been diagnosed as having heart disease?               |
|     |     | Yes, _____  |
| ___ | ___ | Have you ever had any other significant medical conditions?         |
|     |     | Yes, _____  |
| ___ | ___ | Have you had a major surgery in the past year?                      |
|     |     | Yes, _____  |
| ___ | ___ | Do you smoke?   |
|     |     | Yes, _____  |
| ___ | ___ | Are you currently using any prescription medication                 |
|     |     | Yes, _____  |
| ___ | ___ | Are you prone to fainting/dizziness / have you fainted in the past? |
|     |     | Yes, _____  |
| ___ | ___ | Are you pregnant? (F)   |
|     |     | Yes, _____  |
| ___ | ___ | Have you been diagnosed with HIV/AIDS ?                             |
|     |     | Yes, _____  |

#### Family:

- | Y   | N   |   |
|-----|-----|---|
| ___ | ___ | Has a member of your family ever been diagnosed with heart disease?     |
|     |     | Yes, _____  |
| ___ | ___ | Has anyone in your family ever died from heart attack or cardiac event? |
|     |     | Yes, _____  |
| ___ | ___ | Has anyone in your family died suddenly before 50 years of age?         |
|     |     | Yes, _____  |

## Appendix E

### Par-Q form

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day.

Being more active is very safe for most people. However, some people should check with their physician before they

start becoming more physically active. **Please complete this form as accurately and completely as possible.**

#### **PAR-Q FORM** Please mark YES or No to the following: YES NO

Has your doctor ever said that you have a heart condition and recommended only medically supervised physical activity? \_\_\_\_ \_\_\_\_

Do you frequently have pains in your chest when you perform physical activity? \_\_\_\_ \_\_\_\_

Have you had chest pain when you were not doing physical activity? \_\_\_\_ \_\_\_\_

Have you had a stroke? \_\_\_\_ \_\_\_\_

Do you lose your balance due to dizziness or do you ever lose consciousness? \_\_\_\_ \_\_\_\_

Do you have a bone, joint or any other health problem that causes you pain or limitations that must be addressed when developing an exercise program (i.e. diabetes, osteoporosis, high blood pressure, high cholesterol, arthritis, anorexia, bulimia, anemia, epilepsy, respiratory ailments, back problems, etc.)? \_\_\_\_ \_\_\_\_

Are you pregnant now or have given birth within the last 6 months? \_\_\_\_ \_\_\_\_

Do you have asthma or exercise induced asthma? \_\_\_\_ \_\_\_\_

Do you have low blood sugar levels (hypoglycemia)? \_\_\_\_ \_\_\_\_

Do you have diabetes? \_\_\_\_ \_\_\_\_

Have you had a recent surgery? \_\_\_\_ \_\_\_\_

If you have marked YES to any of the above, please elaborate below:

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Do you take any medications, either prescription or non-prescription, on a regular basis?

Yes/No

What is the medication for?

How does this medication affect your ability to exercise or achieve your fitness goals?

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**Please note: If your health changes such that you could then answer YES to any of the above questions, tell your trainer/coach. Ask whether you should change your physical activity plan.**

**I have read, understood, and completed the questionnaire. Any questions I had were answered to my full satisfaction.**

Print Name: \_\_\_\_\_ Signature: \_\_\_\_\_

Date: \_\_\_\_\_

# Appendix F

## Raw Data (subject data acquisition phase)

|             |             |           |                                      |             |        |         |         |         |         |         |         |         |            |             |         |
|-------------|-------------|-----------|--------------------------------------|-------------|--------|---------|---------|---------|---------|---------|---------|---------|------------|-------------|---------|
|             |             |           | # File : SHORTS01-11-19-2010_ICG.b2b |             |        |         |         | s1      |         |         |         |         |            |             |         |
| Activity    | tbegin(sec) | tend(sec) | man_SYS_BP                           | man_DIAS_BP | man_HR | SV_b2b  | CO_b2b  | TPR_b2b | Thx_b2b | Abd_b2b | UL_b2b  | LL_b2b  | SYS_BP_b2b | DIAS_BP_b2b | man_MAP |
| HUT_0_NOSH  | 870.09304   | 1004.0789 | 110                                  | 67          | 55     | 76.2262 | 4.19244 | 19.4    | 13.2    | 25.2    | 30.8209 | 106.682 | 178.2      | 122         | 81.33   |
| HUT_80_NOSH | 1274.0327   | 1409.0256 | 99                                   | 43          | 78     | 30.6433 | 2.39018 | 25.8    | 14.7    | 22.8    | 31.9985 | 101.847 | 142.3      | 100.1       | 61.67   |
| HUT_0_WISH  | 2099.0908   | 2230.0557 | 115                                  | 68          | 54     | 82.414  | 4.45035 | 18.8    | 12.9    | 55.6    | 32.5625 | 108.175 | 173        | 99          | 83.67   |
| HUT_80_WISH | 2409.0485   | 2539.0624 | 100                                  | 43          | 80     | 30.2734 | 2.42188 | 25.6    | 14.4    | 31      | 30.5811 | 102.507 | 137.6      | 78.8        | 62.00   |
|             |             |           |                                      |             |        |         |         |         |         |         |         |         |            |             |         |
|             |             |           | # File : SHORTS02-12-14-2010_ICG.b2b |             |        |         |         | s2      |         |         |         |         |            |             |         |
| Activity    | tbegin(sec) | tend(sec) | man_SYS_BP                           | man_DIAS_BP | man_HR | SV_b2b  | CO_b2b  | TPR_b2b | Thx_b2b | Abd_b2b | UL_b2b  | LL_b2b  | SYS_BP_b2b | DIAS_BP_b2b | man_MAP |
| HUT_0_NOSH  | 2596.0374   | 2771.0622 | 129                                  | 65          | 60     | 78.6278 | 4.71767 | 18.3    | 11.2788 | 25.4755 | 14.4618 | 97.3079 | 136.6      | 66.6        | 86.33   |
| HUT_80_NOSH | 3061.0079   | 3197.0717 | 128                                  | 73          | 75     | 45.9539 | 3.44654 | 26.5    | 12.3354 | 23.4055 | 18.7986 | 93.1758 | 140.9      | 85.5        | 91.33   |
| HUT_0_WISH  | 1092.0429   | 1282.0527 | 133                                  | 67          | 62     | 79.7491 | 4.94444 | 18      | 11.0932 | 26.5204 | 19.2124 | 90.0029 | 145.5      | 67.1        | 89.00   |
| HUT_80_WISH | 1730.0402   | 1866.0041 | 131                                  | 70          | 69     | 50.1601 | 3.46105 | 26.1    | 11.603  | 23.5947 | 18.9058 | 88.1248 | 133.4      | 66.6        | 90.33   |
|             |             |           |                                      |             |        |         |         |         |         |         |         |         |            |             |         |
|             |             |           | # File : SHORTS03-12-21-2010_ICG.b2b |             |        |         |         | s3      |         |         |         |         |            |             |         |
| Activity    | tbegin(sec) | tend(sec) | man_SYS_BP                           | man_DIAS_BP | man_HR | SV_b2b  | CO_b2b  | TPR_b2b | Thx_b2b | Abd_b2b | UL_b2b  | LL_b2b  | SYS_BP_b2b | DIAS_BP_b2b | man_MAP |
| HUT_0_NOSH  | 2993.0799   | 3127.0458 | 117                                  | 61          | 45     | 96.2158 | 4.32971 | 18.4    | 10.9    | 30.2    | 18.5771 | 101.327 | 139        | 67.6        | 79.67   |
| HUT_80_NOSH | 3370.0626   | 3503.0295 | 98                                   | 58          | 64     | 43.0341 | 2.75418 | 25.9    | 11.8    | 27.4    | 17.9575 | 98.5343 | 125.2      | 65.2        | 71.33   |
| HUT_0_WISH  | 1381.0096   | 1540.0504 | 119                                  | 60          | 44     | 100.033 | 4.40147 | 18.1    | 10.8    | 29.9    | 18.8136 | 102.911 | 139.4      | 57.4        | 79.67   |
| HUT_80_WISH | 1898.06     | 2040.0179 | 113                                  | 59          | 63     | 47.7431 | 3.00781 | 25.6    | 12.3    | 27.7    | 18.2423 | 98.3883 | 124.7      | 60.9        | 77.00   |
|             |             |           |                                      |             |        |         |         |         |         |         |         |         |            |             |         |
|             |             |           | # File : SHORTS04-12-27-2010_ICG.b2b |             |        |         |         | s4      |         |         |         |         |            |             |         |
| Activity    | tbegin(sec) | tend(sec) | man_SYS_BP                           | man_DIAS_BP | man_HR | SV_b2b  | CO_b2b  | TPR_b2b | Thx_b2b | Abd_b2b | UL_b2b  | LL_b2b  | SYS_BP_b2b | DIAS_BP_b2b | man_MAP |
| HUT_0_NOSH  | 3382.0685   | 3513.0474 | 90                                   | 68          | 64     | 63.9719 | 4.0942  | 18.4    | 15.8769 | 22.9677 | 17.895  | 75.3066 | 139.5      | 82.3        | 75.33   |
| HUT_80_NOSH | 3055.0639   | 3186.0428 | 87                                   | 66          | 102    | 26.5069 | 2.7037  | 27      | 16.0738 | 17.0581 | 14.8412 | 72.1058 | 139.2      | 96.2        | 73.00   |
| HUT_0_WISH  | 2752.0432   | 2882.0431 | 97                                   | 70          | 78     | 56.8018 | 4.31694 | 18.3    | 15.3995 | 22.4413 | 16.812  | 75.9927 | 120.2      | 69.9        | 79.00   |
| HUT_80_WISH | 2240.0117   | 2370.0116 | 98                                   | 78          | 100    | 31.7104 | 3.17104 | 26.7    | 16.2192 | 24.1578 | 11.2233 | 76.9415 | 122.7      | 85.7        | 84.67   |
|             |             |           |                                      |             |        |         |         |         |         |         |         |         |            |             |         |
|             |             |           | # File : SHORTS05-1-2-2011_ICG.b2b   |             |        |         |         | s5      |         |         |         |         |            |             |         |
| Activity    | tbegin(sec) | tend(sec) | man_SYS_BP                           | man_DIAS_BP | man_HR | SV_b2b  | CO_b2b  | TPR_b2b | Thx_b2b | Abd_b2b | UL_b2b  | LL_b2b  | SYS_BP_b2b | DIAS_BP_b2b | man_MAP |
| HUT_0_NOSH  | 2300.0477   | 2431.0166 | 134                                  | 93          | 84     | 64.7878 | 5.44218 | 19.6    | 12.8061 | 33.108  | 13.1322 | 82.4094 | 193.1      | 108.5       | 106.67  |
| HUT_80_NOSH | 2633.6038   | 2790.0472 | 132                                  | 83          | 105    | 35.4319 | 3.72035 | 26.7    | 12.4653 | 29.8871 | 15.8758 | 81.9261 | 191.4      | 105.1       | 99.33   |
| HUT_0_WISH  | 209.02277   | 354.02762 | 139                                  | 90          | 83     | 67.7844 | 5.6261  | 18.9    | 11.6136 | 34.9026 | 24.4379 | 80.9971 | 229.2      | 130.8       | 106.33  |
| HUT_80_WISH | 987.014     | 1131.0198 | 134                                  | 83          | 100    | 38.0228 | 3.80228 | 26.3    | 11.8758 | 31.1376 | 26.8718 | 79.9433 | 199.7      | 107.9       | 100.00  |
|             |             |           |                                      |             |        |         |         |         |         |         |         |         |            |             |         |
|             |             |           | # File : SHORTS06-1-8-2011_ICG.b2b   |             |        |         |         | s6      |         |         |         |         |            |             |         |
| Activity    | tbegin(sec) | tend(sec) | man_SYS_BP                           | man_DIAS_BP | man_HR | SV_b2b  | CO_b2b  | TPR_b2b | Thx_b2b | Abd_b2b | UL_b2b  | LL_b2b  | SYS_BP_b2b | DIAS_BP_b2b | man_MAP |
| HUT_0_NOSH  | 2373.0486   | 2509.0624 | 116                                  | 74          | 68     | 72.2971 | 4.9162  | 17.9    | 11.8715 | 23.9821 | 32.9764 | 90.936  | 125.3      | 73.5        | 88.00   |
| HUT_80_NOSH | 2832.0032   | 2974.049  | 88                                   | 57          | 120    | 20.7052 | 2.48462 | 27.1    | 12.4211 | 18.6269 | 26.6359 | 80.5337 | 100.1      | 67.9        | 67.33   |
| HUT_0_WISH  | 653.09026   | 797.09611 | 112                                  | 66          | 69     | 66.5957 | 4.5951  | 17.7    | 11.8442 | 41.1731 | 22.4462 | 91.4551 | 111.3      | 64.6        | 81.33   |
| HUT_80_WISH | 1371.0156   | 1507.0295 | 86                                   | 52          | 112    | 20.9436 | 2.34568 | 27      | 10.9322 | 20.078  | 13.5863 | 77.6302 | 98.8       | 64.4        | 63.33   |

Table F.1. Raw cardiovascular data

# Raw Data (subject data acquisition phase), continued

|             |             |           |            |                               |        |         |           |         |                            |         |         |         |            |             |         |
|-------------|-------------|-----------|------------|-------------------------------|--------|---------|-----------|---------|----------------------------|---------|---------|---------|------------|-------------|---------|
|             |             |           | # File     | SHORTS07-08-04-2010_ICG.b2b   |        | s7      | former--> | # File  | : RID13-08-04-2010_ICG.b2b |         |         |         |            |             |         |
| Activity    | tbegin(sec) | tend(sec) | man_SYS_BP | man_DIAS_BP                   | man_HR | SV_b2b  | CO_b2b    | TPR_b2b | Thx_b2b                    | Abd_b2b | UL_b2b  | LL_b2b  | SYS_BP_b2b | DIAS_BP_b2b | man_MAP |
| HUT_0_NOSH  | 1420.0825   | 1560.1023 | 102        | 69                            | 109    | 39.0396 | 4.25532   | 18.8    | 21                         | 40.9017 | 32.2535 | 84.4728 | 116.5      | 62.2        | 80.00   |
| HUT_80_NOSH | 2080.0059   | 2194.0118 | 88         | 73                            | 119    | 24.8281 | 2.95455   | 26.4    | 23.7                       | 37.3383 | 31.3403 | 81.9294 | 89.1       | 65.2        | 78.00   |
| HUT_0_WISH  | 4499.0705   | 4597.1023 | 100        | 64                            | 99     | 41.496  | 4.10811   | 18.5    | 21.6                       | 42.6208 | 32.2592 | 82.6996 | 109.9      | 68.1        | 76.00   |
| HUT_80_WISH | 2961.004    | 3091.0738 | 97         | 67                            | 115    | 25.3623 | 2.91667   | 26.4    | 23.5                       | 38.5644 | 30.8672 | 81.2918 | 108.3      | 77          | 77.00   |
|             |             |           |            |                               |        |         |           |         |                            |         |         |         |            |             |         |
|             |             |           | # File     | : SHORTS08-08-05-2010_ICG.b2b |        | s8      | former--> | # File  | : RID15-08-05-2010_ICG.b2b |         |         |         |            |             |         |
| Activity    | tbegin(sec) | tend(sec) | man_SYS_BP | man_DIAS_BP                   | man_HR | SV_b2b  | CO_b2b    | TPR_b2b | Thx_b2b                    | Abd_b2b | UL_b2b  | LL_b2b  | SYS_BP_b2b | DIAS_BP_b2b | man_MAP |
| HUT_0_NOSH  | 785         | 927       | 117        | 73                            | 53     | 87.5179 | 4.63845   | 18.9    | 16.7                       | 28.9    | 21      | 69.4    | 134.9      | 60.7        | 87.67   |
| HUT_80_NOSH | 1292        | 1428      | 120        | 71                            | 69     | 48.8687 | 3.37194   | 25.9    | 18.7                       | 25.7    | 20      | 69.5    | 119.1      | 63.7        | 87.33   |
| HUT_0_WISH  | 3392.0885   | 3521.0314 | 122        | 82                            | 48     | 107.941 | 5.18116   | 18.4    | 18                         | 29.6    | 21.3    | 66.2    | 167.4      | 93.6        | 95.33   |
| HUT_80_WISH | 5002.039    | 5132.0968 | 119        | 80                            | 66     | 54.4051 | 3.59073   | 25.9    | 19                         | 26.5    | 20.7    | 65.8    | 174.3      | 113.8       | 93.00   |
|             |             |           |            |                               |        |         |           |         |                            |         |         |         |            |             |         |
|             |             |           | # File     | : SHORTS09-08-05-2010_ICG.b2b |        | s9      | former--> | # File  | : RID16-08-05-2010_ICG.b2b |         |         |         |            |             |         |
| Activity    | tbegin(sec) | tend(sec) | man_SYS_BP | man_DIAS_BP                   | man_HR | SV_b2b  | CO_b2b    | TPR_b2b | Thx_b2b                    | Abd_b2b | UL_b2b  | LL_b2b  | SYS_BP_b2b | DIAS_BP_b2b | man_MAP |
| HUT_0_NOSH  | 1593.1113   | 1722.1321 | 123        | 69                            | 76     | 60.8903 | 4.62766   | 18.8    | 14.1687                    | 27.3009 | 20.3263 | 78.0131 | 115.9      | 54.1        | 87.00   |
| HUT_80_NOSH | 2175.1746   | 2308.0916 | 104        | 67                            | 79     | 37.3316 | 2.94919   | 26.9    | 14.6116                    | 25.4311 | 19.2065 | 76.8143 | 106.6      | 63.1        | 79.33   |
| HUT_0_WISH  | 4593.0104   | 4717.0862 | 121        | 63                            | 64     | 69.1644 | 4.42652   | 18.6    | 14.5104                    | 28.0708 | 20.3409 | 89.9243 | 134.6      | 79.2        | 82.33   |
| HUT_80_WISH | 3443.0635   | 3600.1063 | 108        | 61                            | 78     | 36.9514 | 2.88221   | 26.6    | 14.8276                    | 25.616  | 19.3044 | 91.7336 | 126.9      | 77.4        | 76.67   |
|             |             |           |            |                               |        |         |           |         |                            |         |         |         |            |             |         |
|             |             |           | # File     | : SHORTS10-08-06-2010_ICG.b2b |        | s10     | former--> | # File  | : RID18-08-06-2010_ICG.b2b |         |         |         |            |             |         |
| Activity    | tbegin(sec) | tend(sec) | man_SYS_BP | man_DIAS_BP                   | man_HR | SV_b2b  | CO_b2b    | TPR_b2b | Thx_b2b                    | Abd_b2b | UL_b2b  | LL_b2b  | SYS_BP_b2b | DIAS_BP_b2b | man_MAP |
| HUT_0_NOSH  | 1322.1006   | 1475.0974 | 137.00     | 76.00                         | 55.00  | 90.2843 | 4.96564   | 19.4    | 11.95                      | 26.9797 | 19.1799 | 68.3958 | 142        | 84.5        | 96.33   |
| HUT_80_NOSH | 1810.148    | 1945.013  | 117.00     | 74.00                         | 60.00  | 55.978  | 3.35868   | 26.3    | 12.26                      | 27.1176 | 17.181  | 74.308  | 126.6      | 95.9        | 88.33   |
| HUT_0_WISH  | 4795.0422   | 4929.1579 | 123.00     | 76.00                         | 48.00  | 100.512 | 4.82456   | 19      | 11.73                      | 27.4928 | 18.5596 | 59.7916 | 117        | 72          | 91.67   |
| HUT_80_WISH | 5889.2748   | 6026.0539 | 117.00     | 76.00                         | 54.00  | 64.1117 | 3.46203   | 25.9    | 12.19                      | 24.1878 | 18.3682 | 58.7569 | 115.6      | 87          | 89.67   |
|             |             |           |            |                               |        |         |           |         |                            |         |         |         |            |             |         |
|             |             |           | # File     | : SHORTS11-08-04-2010_ICG.b2b |        | s11     | former--> | # File  | : RID20-08-04-2010_ICG.b2b |         |         |         |            |             |         |
| Activity    | tbegin(sec) | tend(sec) | man_SYS_BP | man_DIAS_BP                   | man_HR | SV_b2b  | CO_b2b    | TPR_b2b | Thx_b2b                    | Abd_b2b | UL_b2b  | LL_b2b  | SYS_BP_b2b | DIAS_BP_b2b | man_MAP |
| HUT_0_NOSH  | 1024.5744   | 1098.1008 | 136.00     | 76.00                         | 64.00  | 80.2139 | 5.13369   | 18.7    | 12.2                       | 32.4223 | 23.8189 | 35.7951 | 123.5      | 76.2        | 96.00   |
| HUT_80_NOSH | 1098.1008   | 1363.4352 | 128.00     | 79.00                         | 80.00  | 45.4835 | 3.63868   | 26.2    | 13.1                       | 29.9476 | 22.3238 | 36.2705 | 115.9      | 80.8        | 95.33   |
| HUT_0_WISH  | 4034.2557   | 4170.1197 | 111.00     | 72.00                         | 59.00  | 79.1581 | 4.67033   | 18.2    | 12.3                       | 33.8753 | 15.9814 | 33.3757 | 153.1      | 80          | 85.00   |
| HUT_80_WISH | 5521.5669   | 5660.0283 | 117.00     | 61.00                         | 76.00  | 40.3171 | 3.0641    | 26      | 12.6                       | 31.045  | 22.7839 | 31.9583 | 117.5      | 69          | 79.67   |
|             |             |           |            |                               |        |         |           |         |                            |         |         |         |            |             |         |
|             |             |           | # File     | : SHORTS12-08-06-2010_ICG.b2b |        | s12     | former--> | # File  | : RID22-08-06-2010_ICG.b2b |         |         |         |            |             |         |
| Activity    | tbegin(sec) | tend(sec) | man_SYS_BP | man_DIAS_BP                   | man_HR | SV_b2b  | CO_b2b    | TPR_b2b | Thx_b2b                    | Abd_b2b | UL_b2b  | LL_b2b  | SYS_BP_b2b | DIAS_BP_b2b | man_MAP |
| HUT_0_NOSH  | 636.20316   | 756.08316 | 96.00      | 63.00                         | 62.00  | 62.4894 | 3.87435   | 19.1    | 25.72                      | 43.7918 | 31.2747 | 80.431  | 143.9      | 93.9        | 74.00   |
| HUT_80_NOSH | 1161.1277   | 1301.2375 | 88.00      | 60.00                         | 72.00  | 36.3382 | 2.61635   | 26.5    | 27.92                      | 40.0741 | 31.19   | 78.1723 | 139.1      | 90.8        | 69.33   |
| HUT_0_WISH  | 1675.1132   | 1816.1221 | 99.00      | 63.00                         | 60.00  | 66.4894 | 3.98936   | 18.8    | 25.65                      | 59.2691 | 31.0843 | 80.9652 | 152.2      | 84.4        | 75.00   |
| HUT_80_WISH | 2658.1292   | 2781.1561 | 92.00      | 61.00                         | 68.00  | 39.7356 | 2.70202   | 26.4    | 27.94                      | 59.0427 | 31.7619 | 77.5903 | 120.7      | 77.6        | 71.33   |

# Appendix G

## Subject and Impedance Data

| Basic demographic data |            |           |                        |                           | Distance between impedance leads (cm) |         |           |           |
|------------------------|------------|-----------|------------------------|---------------------------|---------------------------------------|---------|-----------|-----------|
| Subj. ID               | Sex (M, F) | Age (yrs) | Height (cm) (in *2.54) | Weight (kg) (lbs/ 2.2046) | Thorax                                | Abdomen | Upper Leg | Lower Leg |
| shorts1                | F          | 26        | 168.9                  | 63.8                      | 37.0                                  | 34.5    | 30.5      | 27.0      |
| shorts2                | M          | 30        | 190.5                  | 93.0                      | 42.0                                  | 47.0    | 25.0      | 30.5      |
| shorts3                | M          | 23        | 193.0                  | 88.5                      | 42.0                                  | 54.0    | 21.0      | 32.0      |
| shorts4                | F          | 20        | 177.8                  | 120.7                     | 47.0                                  | 51.0    | 23.0      | 27.0      |
| shorts5                | F          | 45        | 167.9                  | 84.4                      | 40.0                                  | 49.5    | 22.0      | 26.0      |
| shorts6                | M          | 18        | 188.0                  | 65.8                      | 40.0                                  | 47.5    | 29.0      | 25.0      |
| shorts7                | F          | 19        | 162.6                  | 52.2                      | 34.5                                  | 41.8    | 18.5      | 21.3      |
| shorts8                | F          | 36        | 162.6                  | 62.1                      | 38.7                                  | 35.3    | 22.0      | 16.7      |
| shorts9                | M          | 21        | 175.3                  | 73.9                      | 37.0                                  | 46.0    | 22.5      | 26.0      |
| shorts10               | M          | 22        | 180.8                  | 96.2                      | 36.0                                  | 44.5    | 28.0      | 27.0      |
| shorts11               | M          | 38        | 193.0                  | 81.2                      | 43.5                                  | 51.0    | 24.5      | 17.0      |
| shorts12               | F          | 28        | 162.6                  | 47.6                      | 37.3                                  | 41.0    | 20.2      | 18.7      |
| TOTAL                  | 12         | 326       | 2122.9                 | 929.3                     | 475.0                                 | 543.1   | 286.2     | 294.2     |
| MEAN                   |            | 27.2      | 176.9                  | 77.4                      | 39.6                                  | 45.3    | 23.9      | 24.5      |
| S.E.M.                 |            | 2.5       | 3.5                    | 6.0                       | 1.0                                   | 1.8     | 1.1       | 1.4       |

Table G.1. Subject demographic and impedance data

## Appendix H

### Resulting Cardiovascular Values and T-test Results

| RESULTING CARDIOVASCULAR MEAN VALUES +/- S.E.M                                  |                   |                    |                        |                 |                                      |                           |                            |                              |                              |                       |                   |
|---|-------------------|--------------------|------------------------|-----------------|--------------------------------------|---------------------------|----------------------------|------------------------------|------------------------------|-----------------------|-------------------|
| Activity \ Variable   | Systolic BP, mmHg | Diastolic BP, mmHg | Mean Arterial BP, mmHg | Heart Rate, bpm | Total Periph. Resistance, mmHg/L/min | Thorax RO, Impedance, Ohm | Abdomen RO, impedance, Ohm | Upper Leg RO, impedance, Ohm | Lower Leg RO, Impedance, Ohm | Cardiac Output, L/min | Stroke Volume, ml |
| TILT 0 deg NO SHORTS  | 117.3             | 71.2               | 86.5                   | 66.4            | 18.8                                 | 14.8                      | 30.1                       | 23.0                         | 80.9                         | 4.6                   | 69.3              |
| TILT 80 deg NO SHORTS   | 106.4             | 67.0               | 80.1                   | 91.5            | 26.4                                 | 15.8                      | 27.1                       | 22.3                         | 78.8                         | 3.0                   | 33.2              |
| TILT 0 deg WITH SHORTS  | 115.9             | 70.1               | 85.4                   | 64.0            | 18.4                                 | 14.8                      | 36.0                       | 22.8                         | 80.2                         | 4.6                   | 72.3              |
| TILT 80 deg WITH SHORTS   | 109.3             | 65.9               | 80.4                   | 84.8            | 26.2                                 | 15.6                      | 30.2                       | 21.9                         | 77.6                         | 3.1                   | 36.2              |
| S.E.M.  |                   |                    |                        |                 |                                      |                           |                            |                              |                              |                       |                   |
| TILT 0 deg NO SHORTS  | 4.50              | 2.43               | 3.12                   | 4.81            | 1.89                                 | 1.29                      | 1.89                       | 2.05                         | 5.39                         | 0.17                  | 4.20              |
| TILT 80 deg NO SHORTS   | 5.08              | 3.19               | 3.82                   | 7.74            | 1.92                                 | 1.48                      | 1.94                       | 1.83                         | 4.86                         | 0.18                  | 1.90              |
| TILT 0 deg WITH SHORTS  | 3.78              | 2.53               | 2.95                   | 4.09            | 2.36                                 | 1.36                      | 3.36                       | 1.73                         | 5.80                         | 0.22                  | 4.11              |
| TILT 80 deg WITH SHORTS   | 4.37              | 3.48               | 3.77                   | 6.72            | 2.57                                 | 1.54                      | 2.97                       | 1.96                         | 5.48                         | 0.21                  | 1.93              |
| Paired Two Sample t-Test for change in Means (Delta Shorts vs. Delta No Shorts) |                   |                    |                        |                 |                                      |                           |                            |                              |                              |                       |                   |
| P(T<=t) one-tail  | 0.034201          | 0.500000           | 0.121070               | 0.040984        | 0.495553                             | 0.147801                  | 0.136619                   | 0.425704                     | 0.274214                     | 0.499122              | 0.499842          |
| * Signif. Different (p<0.05)  | *                 |                    |                        | *               |                                      |                           |                            |                              |                              |                       |                   |
| 2-factor ANOVA for Tilt Effect (HUT=0 deg vs. HUT=80 deg)                       |                   |                    |                        |                 |                                      |                           |                            |                              |                              |                       |                   |
| P(T<=t) one-tail  | 0.057049          | 0.163533           | 0.091172               | 0.000434        | 0.009455                             | 0.518014                  | 0.100121                   | 0.67984836                   | 0.66103634                   | 0.009288              | 0.007923          |
| * Signif. Different (p<0.05)  |                   |                    |                        | *               | *                                    |                           |                            |                              |                              | *                     | *                 |

**Table H.1. Resulting cardiovascular values and t-test results.**

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## ABSTRACT PUBLICATIONS / CONFERENCES

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