

Award
Number: W81XWH-10-1-0981

TITLE: "A Comparison of Robotic, Body Weight-Supported Locomotor Training and Aquatic Therapy in Chronic Motor Incomplete Spinal Cord Injury Subjects."

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REPORT DATE: June 2015

TYPE OF REPORT: Final

PREPARED
FOR:
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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REPORT DOCUMENTATION PAGE			Form Approved OMB No. 0704-0188		
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1. REPORT DATE (DD-MM-YYYY) June 2015		2. REPORT TYPE Final		3. DATES COVERED (From - To) 30 Sep 2010 - 29Mar2015	
4. TITLE AND SUBTITLE "A Comparison of Robotic, Body Weight-Supported Locomotor Training and Aquatic Therapy in Chronic Motor Incomplete Spinal Cord Injury Subjects."			5a. CONTRACT NUMBER W81XWH-10-1-0981		
			5b. GRANT NUMBER		
			5c. PROGRAM ELEMENT NUMBER		
6. AUTHOR(S) Peter Gorman MD; Paula Geigle PT PhD; Keith Tansey MD PhD; Leslie VanHiel PT, DScPT email: pgorman@umm.edu			5d. PROJECT NUMBER		
			5e. TASK NUMBER		
			5f. WORK UNIT NUMBER		
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University Maryland, Baltimore 2200 Kernan Drive Baltimore, MD 21207			8. PERFORMING ORGANIZATION REPORT NUMBER		
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, MD 212702-5012			10. SPONSOR/MONITOR'S ACRONYM(S)		
			11. SPONSOR/MONITOR'S REPORT NUMBER(S)		
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release, distribution unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT At the end of study year 4 we completed all expected enrollment, intervention, and data collection as per our protocol. All necessary IRB approvals were obtained, and all regulatory documents submitted including the annual IRB continuing review, attached to this report (Shepherd IRB and University Maryland). All study personnel hold current certifications in order to participate in research. Multiple meetings occurred, both in person (at ASIA conference in San Antonio, May 2014) and via monthly teleconferencing in order to coordinate activities between the Baltimore and the Atlanta sites. Thirty seven research participants initiated the study (with 6 drop outs) by the September 30, 2014 end of enrollment date. Screening data entry and analysis is initiated and we eagerly examining our outcome data. Two manuscripts are published and 11 presentations (platform and poster) occurred from our study proposal and screening data analysis to date.					
15. SUBJECT TERMS Motor Incomplete Spinal Cord Injury, Lokomat, Aquatic Therapy, Functional and Physiological Outcomes					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 24	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			19b. TELEPHONE NUMBER (include area code)

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INTRODUCTION

The goal of this research was to compare the effects of three months, three times a week aquatic therapy with similar intensity robotically assisted, body weight supported locomotor training (RABWSLT) upon functional ambulatory ability, cardiovascular fitness, and metabolic changes in 37 individuals with chronic (> 12 months, post injury) motor incomplete spinal cord injury (CMISCI). We hypothesized aquatic therapy would be more effective than robotically assisted aerobic locomotor training in improving functional ability as measured by timed walks, a gait mat device and community step activity monitors. Furthermore, we also hypothesized aquatic therapy would be more effective than robotic locomotor therapy in improving cardiovascular fitness as measured by open circuit spirometry during arm ergometry for these same participants. This work provided preliminary evidence-based information regarding the efficacy of aquatic therapy and robotically assisted, body weight supported locomotor training in chronic spinal cord injury rehabilitation. We noticed this need for empirical data, as little objective data examining either of these two interventions after spinal cord injury existed.

BODY

Our aims and hypotheses, based on the distinct characteristics of the two therapeutic techniques, were as follows:

Aim 1. Assess the impact of prescribed, customized aquatic therapy and Lokomat training upon cardiovascular fitness of individuals after with chronic motor incomplete spinal cord injury.

Hypothesis 1: Aquatic therapy will increase cardiovascular fitness as measured by VO_2 max during exercise 20%, or 10% more than Lokomat training which will increase VO_2 max 10% as measured during both treadmill exercise and upper extremity arm ergometry.

Aim 2. Assess the impact of prescribed, customized aquatic therapy and Lokomat training upon walking capability and participation (as measured by timed walks and step activity monitoring in the community respectively) of individuals with chronic motor incomplete spinal cord injury.

Hypothesis 2: Aquatic therapy will be increase functional ambulatory distance 20% more than Lokomat training as measured by the 6-minute walk test and increase gait speed as measured by the 10 meter walk test. Community based step activity will also increase more after aquatic therapy than it will after Lokomat training.

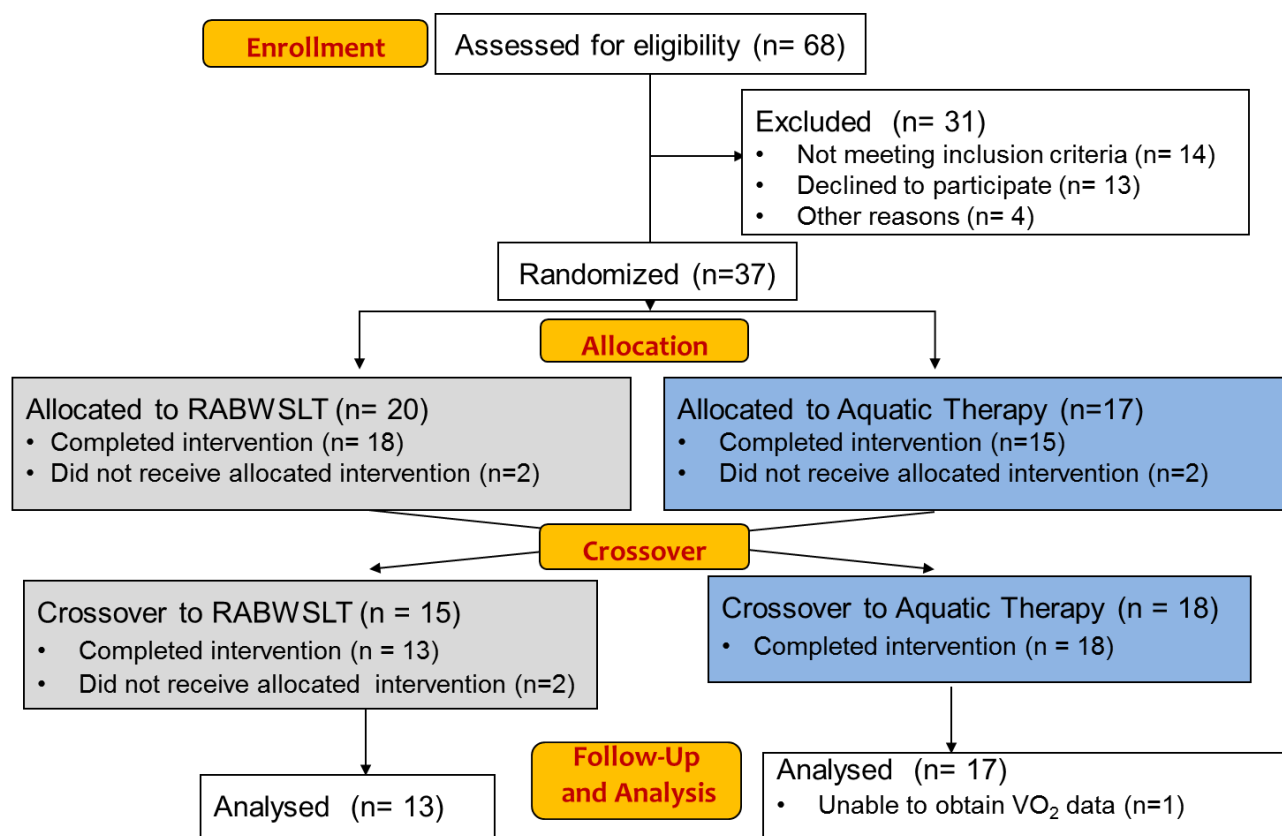
Aim 3: Assessed the impact of prescribed customized aquatic therapy and RABWSLT upon gait quality as measured by a gait mat device. Specific outcome parameters assessed included stride length, walking velocity and cadence. These assessments were secondary outcome measures, not considered as part of the experimental hypotheses. Nonetheless these evaluations helped to determine mechanism of action as well as planning future studies.

1. STUDY DESIGN

We proposed a randomized controlled crossover study of aquatic therapy versus robotically assisted body weight supported locomotor training with individuals experiencing chronic motor incomplete spinal cord injury. We recruited participants as a convenience sample from the outpatient spinal cord injury clinics at the University Maryland Healthcare Network, University Maryland Rehabilitation

and Orthopaedic Institute (UMROI), Shepherd Rehabilitation Center, and the Atlanta VA Medical Center. Block randomization by a computer program enrolled consecutive participants into either aquatic therapy or Lokomat therapy. Participants received the initial randomized therapy for three months and crossed over to the other intervention for an additional three months.

Participants: We eligibility screened a total of 68 individuals with 31 excluded secondary to inclusion criteria (n = 14), declining to commit to full participation (n = 13), or for other reasons (n=4). Therefore 37 individuals randomized to either RABWSLT first (n=20) or Aquatic Therapy first (n = 17). Figure 1 represents a modified Consolidated Standards of Reporting Trials (CONSORT) diagram. Of the 20 individuals randomized to RABWSLT first, 18 completed both that therapy and the subsequent AT therapy after crossover. In one individual, arm ergometer peakVO₂ data was not obtainable secondary to limited hand function. (demographic information included later in report as requested in final report manual)



Outcome Variables: The outcome variables measured baseline, after three months of initial therapy, and after an additional three months of subsequent crossover therapy aligned with the two major hypotheses: assessment of cardiovascular fitness (hypothesis 1) measured by peak VO₂, or peak oxygen consumption during exercise and HOMA-IR; and assessment of functional ambulatory capacity (hypothesis 2) measured by a) 10-meter walk, b) six minute walk, c) the walking index for spinal cord injury II (WISCI II), d) ambulation analysis, e) community step activity monitoring (SAM) for 5-7 days, and f) Spinal Cord Independence Measure III (SCIM-III).

Arm Cycle Ergometry Test: We accomplished the arm cycle ergometer test with an electronic-braked Monark, positioned in front of a laboratory chair or personal wheelchair with the ergometer height

adjusted to align the shoulder joint with the axis of rotation. Participants quietly sat for 5 minutes before the start of the test and then initiated a brief 3-minute warm-up phase with the ergometer work rate set at zero watts. Participants pedaled at 50 revolutions per minute during this initial phase and maintained this pace throughout the test. In subsequent phases, work rate was modified by 5 watts every minute until the session terminated at volitional fatigue or if the participant failed to maintain the pedal cadence at 50-rpm at any given work rate.

Robotic Assisted Body Weight Supported Locomotor Training Test: We used a Lokomat (Hacoma), a computer interfaced robotic device with a treadmill component, to complete both the RABWSLT and to perform RABWSLT cardiovascular testing. As during the RABWSLT we gathered participant anthropometric measurements to configure the device according to manufacturer guidelines. Participants suspended in the device above the stationary treadmill, were instructed to limit movement and communication for a 5-minute period prior to treadmill test initiation. A three-minute warm-up phase at a predetermined treadmill speed and BWS (work rate) occurred during the initial phase of the walking test. This work rate was previously determined during a 20-minute acclimation training session and reflects a speed and BWS with minimal effect on gait pattern quality (i.e., without foot drag, stumbling, or excessive spasticity). Work rate (speed, BWS, or guidance force) was adjusted every minute during the walking test until the participant reached volitional fatigue or failed to maintain a safe gait pattern (without tripping or stumbling).

A COSMED Quark Cardiopulmonary Exercise Test (CPET) unit measured aerobic capacity with unit calibrated according to manufacturer guidelines prior to each peak aerobic test. A Hans Rudolph mask with a flow meter attachment covered the participant's mouth and nose region connecting to the metabolic unit through capillary tubing, permitting collection of expired air flow and gas concentrations. A computer software program integrated this information to calculate oxygen consumption. We determined peak oxygen consumption by averaging highest observed values from 3 consecutive 10- second sampling periods.

Functional ambulation measurement: Functional testing at baseline visits included the Walking Index for Spinal Cord Injury (WISCI II) assessment and for participants who were able, a timed 10-meter walk and an assessment of total distance walked in 6 minutes in one attempt. We repeated the 10-meter walk 2 times each for normal walking speed and for fast as safely possible speed to obtain average values and minimize the training effect. The Spinal Cord Independence Measure (SCIM) mobility section was completed by research participant report and therapist observation. An ankle based step activity monitor (SAM) worn for 5 to 7 days at each time point (baseline, three months and six months) assessed daily activity. Additionally, ambulation analysis with or without an assistive device occurred for all ambulatory participants. GAITRite software extracted the timing of each step and stride event to summarize the stance and swing phase patterns for each limb. The step and stride lengths are also recorded, along with toe-in /-out angles for foot orientation.

Metabolic: Blood draws for HOMA-IR, glucose, and insulin occurred at initial screening, cross over and completion of this study. HOMA-IR is a surrogate marker for glucose tolerance. Risk factors specific to SCI for heart disease include prevalence of a pattern of arterogenic metabolic alterations, including low high density lipoproteins (HDLs), glucose intolerance, insulin resistance, and reduction in metabolic rate. These changes in glucose uptake and use are often identified as a part of the "metabolic syndrome".

Interventions: Participants randomized into either the aquatic or robotic exercise intervention for 3 months followed by 3 months of the exercise intervention not performed during their initial randomization. Participants exercised 3 days a week in both interventions at 65-75% heart rate

reserve. We individualized training sessions to focus on strength, flexibility, gait, and cardiovascular needs. These categories were met in the robotic intervention by manipulating treadmill speed, bodyweight support, and guidance force. Water depth, position in water, speed of movement, and equipment used addressed individual needs in aquatic exercise arm.

Aquatic Exercise Protocol: Aquatic intervention parameters included:

- Water depth: work at the level providing highest functional level while challenging core stability and balance
- Position in water: upright, horizontal, semi reclined based on individual needs & abilities
- Activities: Gait training, cardiovascular conditioning and strengthening activities
- 40-45 minutes of continuous exercise is goal with 1 minute rest/change of activity
- Effort level goal: aquatic adjusted heart rate for strengthening and cardiovascular component at 65 to 75% heart rate reserve (RPE=16-17)
- water temperature 90 degrees Fahrenheit

Include water safety assessment, typically completed on second in pool training session.

Consisting of:

- Breath control—demonstrates blowing bubbles with face in water
 - Float prone or supine
 - Change from prone to supine position
 - Change from prone or supine to standing position
 - Swimming w/wo floatation devices
- Rate of Perceived Exertion: Borg scale 6-20. Participant recommendation to ask cardiovascular difficulty level AS WELL AS task difficulty level.
 - We actually added what task participants reported most difficult to complete, not solely CV challenge?
 - Added this question as participants wanted to tell us what task was most difficult for them as well as what level of overall CV difficulty. These two tasks did not always align.

Blood pressure: wrist BP and HR monitor—makes vital sign easier especially midpoint and deep water work, also in RABWSLT

Activity	Frequency/Reps/Sets	Duration (mins)	Potential equipment	Comments
Warm Up: Water walking	1 set @: forward, backward, sideward	5 mins	No ↑ surface area to start, slowly ↑ to include paddles for UEs and wrap cuffs for Les	Core stability focus, open chest expansion in all planes
LE muscle group	8 reps, 1-3 sets both legs for each of the following muscle groups: hip flex, ext, ABD, ADD; knee flex, ext	9 mins	Use small to increasing in surface area cuffs	Start facing wall 2 hand support; turn parallel one hand support; move away from wall no UE support
Cardio Function	Lunge walking/semi reclined paddling/kickboard	7 mins	As needed to support participant in functional cardio positions	
Cardio Function	Step ups, push off wall tethered, cycling UE and LE seated/semi reclined, adapted swim strokes	7 mins	As needed to support participant in functional cardio positions	
Cool Down	Water walking/Ai Chi	5 mins		Address any tight muscle groups as needed

Robotic Training Program Included the following parameters. Each included category parallels the aquatic intervention categories and occurred in each robotic intervention within the study confines. However the categories required customization both in aquatic and robotic arms for each participant to achieve optimal outcomes and tolerate the exercise condition. For example, one participant's increased tone permitted him from walking faster than 1.6 miles per hour. So guidance force and body weight support were customized to provide the highest level of both cardiovascular conditioning and strengthening possible.

- Cardiovascular: 65-75% heart rate reserve
- Functional Gait Training: specific gait components requiring attention identified for each participant
- Cardiovascular Component as well:
- Three Factors to Adjust:
 - 1) Body Weight Support
 - 2) Speed
 - 3) Guidance Force

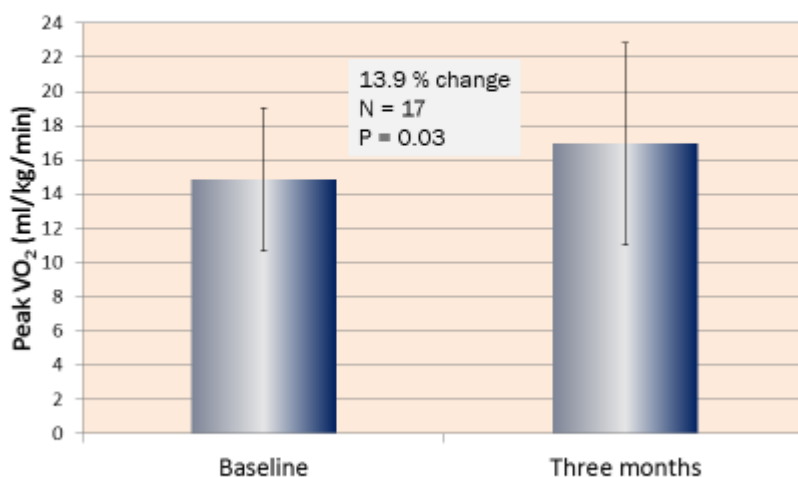
Results

All data were assessed and examined for viability. Using a general linear model we examined relationships both linked and independent based upon interventions. We found covariances and wide data dispersion made significance determination difficult. With such wide variance in data (even with rigid inclusion criteria) we moved toward chi-square goodness of fit based on equality of proportions to further assess the data.

Aquatic therapy will increase cardiovascular fitness by 20% as measured by upper extremity arm ergometry VO_2 peak, or 10% more than RABWSLT, which will increase VO_2 peak 10% as measured during both treadmill and upper extremity arm ergometry.

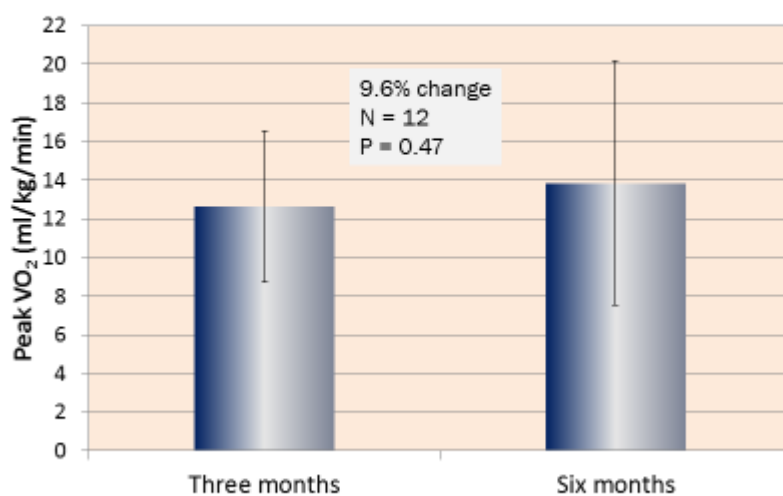
Statistically significant ($p=0.030$) increase in RABWSLT VO_2 of 13.88% in the group randomized to the RABWSLT. Group 1 (Aquatic) came close with a 9.56% clinical increase in RABWSLT VO_2 after RABWSLT, but this increase was not statistically significant. Cardiovascular fitness increased significantly (statistically) with RABWSLT and improved more than VO_2 peak with aquatic exercise. However, peak VO_2 did increase with aquatic exercise approaching statistical significance with a 9.56% improvement. Clinically this is a significant cardiovascular gain for both interventions.

*Results: Peak Lokomat VO_2 :
Initial Robotic Group before and after RABWSLT*



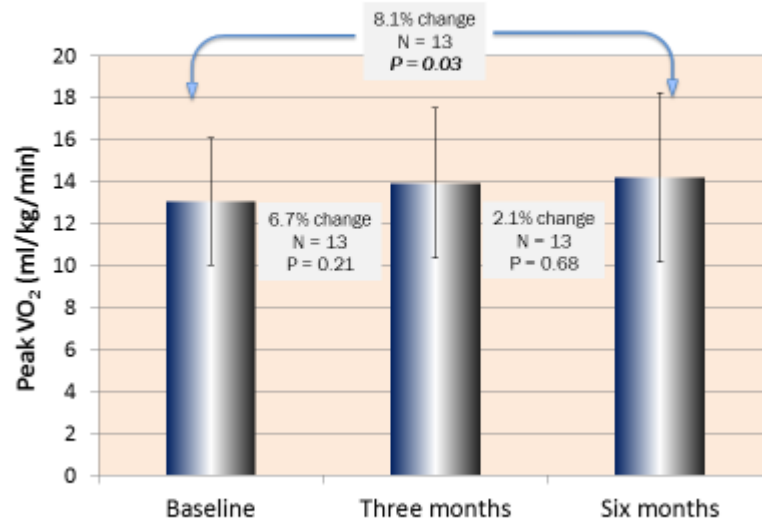
Key to column colors: Blue to grey = Aquatic First; Grey to blue = RABWSLT first

*Results: Peak Lokomat VO_2 :
Initial Aquatic Group before and after RABWSLT*

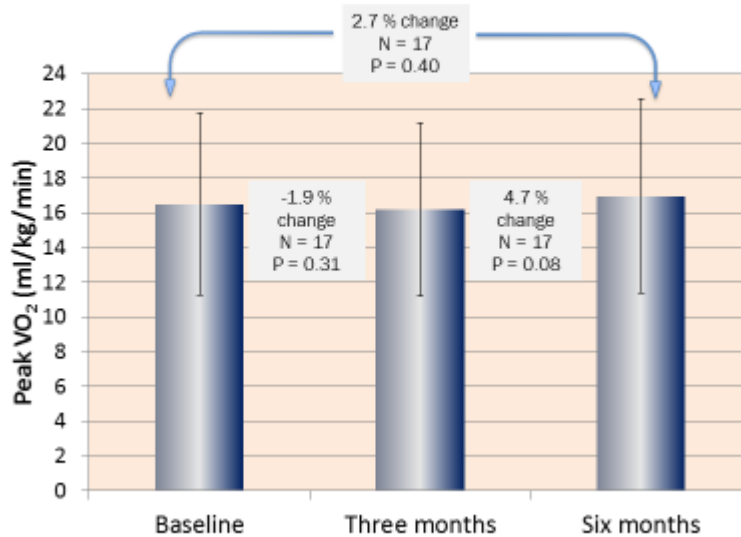


Key to column colors: Blue to grey = Aquatic First; Grey to blue = RABWSLT first

Results Peak Arm Ergometer VO_2 : Aquatics First Randomized Group



Results Peak Arm Ergometer VO_2 : RABWSLT First Randomized Group



Conclusions

- 1) Lokomat based peak VO_2 detected significant improvement in peak VO_2 with 3 months RABWSLT.
- 2) Arm ergometry peak VO_2 detected significant improvement across 6 months of exercise, aquatic first followed by RABWSLT, but not in the reverse order.
- 3) Arm ergometry peak VO_2 may not prove to be as sensitive an outcome measure of lower extremity cardiovascular training, perhaps indicating a lack of content validity.
- 4) Sub category assessment of responders may help prospective identification of subjects who would be more likely to mount a cardiovascular response to combined exercise.

Hypothesis 2. Significantly increased functional ambulation as measured by the 10 Meter Normal Pace walk test for Group 1 (Aquatic Therapy First). Gait speed increased 9.4% on this functional outcome measure after aquatic therapy, whereas it decreased 9.9% after RABWSLT, a relative difference of 19.3%. An additional t-test confirms the difference in gait speed change after the two interventions is statistically significant ($p=0.046$).

Shows the greatest differences in outcomes after the two interventions with a 33.7% relative different outcome with aquatic therapy over RABWSLT. An additional t-test determines the difference between the two interventions is also statistically significant ($p=0.024$). This result was consistent with a general linear model assessment as well.

Using a general linear model insulin levels demonstrate consistent percentage of improvement across both interventions; this variable also achieved chi-square goodness of fit based on equality of proportions.

Responders = > 10% improvement Non-responders = < 10% improvement

Aquatic Intervention First, Peak VO_2 Arm Cycle Ergometer

2

Responders ($n = 5$); Non-responders ($n = 8$)

- The responders (40.6 ± 13.6) were **11 years** younger than the non-responders (51.6 ± 5.3)
- The responders were lighter (**14.9 kg**) than the non-responders (79.7 ± 26.0 vs. 94.7 ± 18.6)
- The time since injury was **10.8 years greater** in non-responders (15.6 ± 15.1) compared to responders (4.8 ± 5.3)
- The responders displayed **higher (10.7) PASIPD scores** compared to non-responders (30.2 ± 38.5 vs. 19.5 ± 27.9)

- Lower extremity scores were **7.0 points higher** in responders (38.4 ± 7.0 ; $n = 5$ vs. 31.4 ± 10.8 ; $n=8$)

RABWSLT Intervention First, Peak VO₂ Arm Cycle Ergometer

Responders; $n = 4$ vs. Non-responders; $n = 13$

- The time since injury was **4 years greater** in the non-responders (7.5 ± 4.4 vs. 3.5 ± 3.1)
- The non-responders displayed **higher arm cycle ergometer peak VO₂** values (17.0 ± 5.4 ; $n = 13$ vs. 14.7 ± 5.7 ; $n=4$)
- **Lower extremity motor scores were 5.4 higher** in responders compared to non-responders (36.5 ± 10.4 ; $n = 4$ vs. 31.1 ± 11.3 ; $n = 13$)

Peak RABWSLT VO₂ , RABWSLT intervention first

Responders $n = 11$; non-responders $n = 6$

- **Body mass was 5.5 kg less** in responders (78.7 ± 23.0 vs. 84.3 ± 13.8)
- **Time since injury 1.8 years less** in responders (5.4 ± 2.9 vs. 7.2 ± 4.9)
- **Baseline Peak RABWSLT VO₂** values were **lower (1.1 ml/kg)** in responders (14.5 ± 5.3 vs. 15.6 ± 1.3)
- The **average speed was faster (.25 m/sec)** for the responders during the 10 meter self-paced walk test ($.53 \pm .26$; $n = 9$ vs. $.28 \pm .30$; $n = 5$)
- The **average speed was faster (.17 m/sec)** for the responders during the 10 meter fast paced walk test ($.75 \pm .40$; $n = 9$ vs. $.58 \pm .58$; $n = 3$)
- The **average distance was greater (74.11 meters)** for the responders during the six-minute walk test (196.5 ± 101.2 ; $n = 9$ vs. 122.4 ± 134.1 ; $n = 4$)

Discussion: What Understandings Do We Hold

Demonstrated selected improvement occurred in RABWSLT peak VO₂ ; AT ambulation speed; and SAM activity with response variability in all outcome categories.

Subgroup analysis suggested response predictors exist based on distinct categories for each intervention, supporting the need to individualize exercise prescription and dosage.

Examples: P8—TBI undiagnosed, P7 peak VO₂—27-28 ml/kgs; P4—central cord

Lessons Learned

- General
 - Compliance to training schedule
 - Practical issues – e.g. lightning closures, code browns
 - HR into training zone difficult for some participants for example individuals with central cord dysfunction
- RABWSLT
 - Risk of atypical autonomic dysreflexia
 - Skin abrasion issues for both pool and RABWSLT
- Pool training
 - Need for customization while maintaining standardized conditions same for RABWSLT
 - Equipment and water safety considerations

Additional Study Benefits

- Increased attendance at SCI support meetings
- Enrollment in other site studies
- Regional conference on aquatic exercise and robotics to improve quality of life for individuals with SCI (PVA educational grant 2014)
- Participants assisted in American Physical Therapy Association Aquatics for Baby Boomers video
- Articles: atypical autonomic dysreflexia occurrence with RABWSLT training in JSCM and relationship between arm and RABWSLT ergometer VO_2 values in Spinal Cord
- Research participants volunteering at facility
- Engagement in local social and recreational activities

What Will We Do Differently

- Assess VO_2 more critically
 - with portable device for aquatic exercise
 - Training sessions half function and half CV: 25 mins. each
 - Increase exercise intensity during CV training 75-85% HRR
- Assess metabolic changes more critically
 - Other factors: clamp procedure? Participant burden?
- Assess adiposity changes more critically
- Reassess appropriate use of SCIM III and WISCI II for individuals with this chronicity MISCI
 - Post intervention follow up at 4 wks? 8 wks? 12 wks?
 - Intervention carry over CV as well as PASIPD
 - PASIPD at pre/crossover/post/follow up as surrogate marker of activity –general involvement in community??
 - Shorter intervention periods
 - 7 months is a huge commitment
 - How many interventions are enough?
 - Mid-point outcome assessment next study

Future Undertakings

- Metabolic
 - Abdominal adiposity, adipoectin, resting metabolic rate
- Quality of Life
 - Focus Groups: to gather concurrent qualitative changes occurring:

I can stand longer to rake leaves, I am now using my wheelchair less at home, I am less fatigued mid afternoon

- Survey Tools
 - PASIPD pre and post study administration
- Community education regarding aquatic exercise for individuals with spinal cord injury
- Cardiovascular
 - Peak VO_2 in pool with portable metabolic cart

CONCLUSION: At the conclusion of year 4 of the DOD study we met all planned proposal activities: regulatory compliance, recruitment, data collection, and fiscal responsibility; and are well positioned to complete data entry and analysis as well as craft publications to disseminate these findings within our no cost 6-month extension. The study offered substantial clinical cardiovascular improvement from both exercise interventions with RABWSLT improving peak VO_2 more than aquatic exercise. We will be able to report more specific outcomes as we rework the cardiovascular

data using metabolic equivalent units (METs). In a landmark systematic review of cardiorespiratory fitness (CRF) in healthy men and woman, Kodama et al reported a robust CRF association with lower overall mortality risk, coronary heart disease, and cardiovascular disease (CHD/CVD). Furthermore, people with a measured maximal aerobic capacity (MAC) of 7.9 metabolic equivalent units (METs) or greater displayed substantially lowered CHD/CVD rates compared with those with a MAC less than 7.9 METs. Based on the American College Sports Medicine, in otherwise healthy individuals, one MET (the amount of oxygen used at rest by a person) is equivalent to 3.5 ml VO_2 /kg/min. For individuals living with SCI, resting metabolic rates are different. The VO_2 equivalent to one MET for individuals with SCI is on average 2.7 ml VO_2 /kg/min, or approximately 77% of able-bodied individuals. Interpreting the Kodama paper with this information, for individuals with SCI (admittedly a heterogeneous group), the MET inflection point to predict a reduced CHD/CVD risk might be 6.1. A more achievable exercise target for individuals with partial paralysis and a reduced, recruitable muscle mass. We are currently reviewing our data and results from an adjusted METs point of view.

Both interventions increased activity measured via activity monitors with aquatic exercise facilitating greater normal daily activity. Aquatic exercise demonstrated a 33.7% relative normal daily activity difference over RABWSLT. Additionally, **normal** walking speed improved 9.4% after aquatic exercise, whereas it decreased 9.9% after RABWSLT, a relative difference of 19.3%. An additional t-test confirms the difference in gait speed change after the two interventions is statistically significant ($p=0.046$). While not in primary outcomes, gait parameters collected via an electronic gait mat, appear to show changes in gait mechanics with both interventions. We will assess this data later this year to investigate kinematic gait changes.

REFERENCES: NA

REPORTABLE OUTCOMES: One published papers related to this DOD award:

- 1) Geigle P, Frye S, Perreault J, Scott W, Gorman P. Atypical Autonomic Dysreflexia during Robotically Assisted Body Weight Supported Treadmill Training in an Individual with Motor Incomplete Spinal Cord Injury. *J Spinal Cord Medicine*. 36(2): 153-156 (2013).
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3595964/>

Presentations:

Relationships among Physical Activity Scale for Individuals with Physical Disability (PASIPD), Body Mass Index (BMI), and Peak Oxygen Consumption ($\text{V}_{\text{O}_2\text{peak}}$) in Persons with Motor Incomplete SCI. Presented at:

- 1) Both as Best Neurological Research Presentation and poster at American Academy of Physical Medicine and Rehabilitation, Washington DC, October 2013.
- 2) ASIA conference Chicago, IL, April 2013
- 3) Baltimore VA Research Day April 2013
- 4) Accepted for Combined Sections Meeting, American Physical Therapy Association, February 2014

Atypical Autonomic Dysreflexia during Robotically Assisted Body Weight Supported Treadmill Training in an Individual with Motor Incomplete Spinal Cord Injury. Presented at

- 1) ASIA conference Chicago, IL, April 2013
- 2) Baltimore VA Research Day April 2013
- 3) Accepted for Combined Sections Meeting, American Physical Therapy Association, February 2014

Motor Incomplete Spinal Cord Injury Randomized Trial Comparing Aquatic Therapy & Robotic-Assisted Body Weight Support Treadmill Training.

- 1) Platform presentation by Peter Gorman MD: American Spinal Cord Professionals Annual Conference, Las Vegas, NV, Sept 2012.
- 2) Invited Healthcare Presentation by Paula Richley Geigle PT PhD: Motor Incomplete Spinal Cord Injury Randomized Trial Comparing Aquatic Therapy & Robotic-Assisted Body Weight Support Treadmill Training. World Aquatic Health Conference: Norfolk, VA, October 2012.
- 3) Multi-Section, 2 hour Presentation by Paula Richley Geigle PT PhD and William H. Scott MA: Motor Incomplete Spinal Cord Injury Randomized Trial Comparing Aquatic Therapy & Robotic-Assisted Body Weight Support Locomotor Training. Combined Section Meeting of American Physical Therapy Association. Indianapolis, February 2015.
- 4) Invited Keynote Presentation Paula Richley Geigle PT PhD: Motor Incomplete Spinal Cord Injury Randomized Trial Comparing Aquatic Therapy & Robotic-Assisted Body Weight Support Locomotor Training. European International Aquatic Conference, Leuven, Belgium, April 2015.
- 5) Poster presentation by Peter Gorman MD: Motor Incomplete Spinal Cord Injury Randomized Trial Comparing Aquatic Therapy & Robotic-Assisted Body Weight Support Locomotor Training. Montreal, Canada, May 2015.
- 6) Invited Keynote Presentation Paula Richley Geigle PT PhD: Invited Keynote Presentation Paula Richley Geigle PT PhD: Motor Incomplete Spinal Cord Injury Randomized Trial Comparing Aquatic Therapy & Robotic-Assisted Body Weight Support Locomotor Training. Queensland, Australia, National Physiotherapist Conference, October 2015.

We are currently reworking the cardiovascular outcomes paper and anticipate a February 2016 submission date. We will forward all subsequently published articles to Patricia Henry, our science officer.

Acknowledgements

- Funding from the Department of Defense Congressionally Directed Medical Research Program Spinal Cord Injury Research Program Clinical Trial Award - FY2009
- Research participants
- Research staff
 - Sarah Frye
 - Naomi Price-Miller
 - Jean McQuaid
 - Gertrude Morrison
 - Leigh Casey
 - Kevin Chen
 - Angela Pihera
 - Brian Smith
 - Neshella Braga
 - Michelle Daniels
 - Rosalyn Lobo
 - Marnie Kallins
 - John Perreault
 - R. Sandy Alexander
 - Lauren McCollough
 - Michelle Deyton



Statement of Work (SOW) Tasks are listed below, and are followed (in blue and bold font) with description of the actual accomplishments during this annual study period.

Task 1: Implement plans, obtain IRB study approval and start up. Completed the formal study protocol, case report forms, data collection sheets, and informed consent documents.

1a. Ensure consistency in these documents across the two sites.

1b. Annually submit the protocol and regulatory documents to the University of Maryland at Baltimore and the Shepherd Center IRBs.

1c. Maintain research certification for all study personnel, renewing as required.

1d. Continue regular meetings phone and face to face allowing for coordination of the research study and efficient dissemination of study results.

All these tasks successfully. We did request and receive approval for a no cost extension to insure thorough data analysis. This is the final study report (April 30, 2015).

Task 2: Implement Randomized Clinical Trail (Months 7-42)

2a. Initiate screening of potential individuals for the research study (General medical and ASIA examination, blood tests, EKG, Standing frame challenge) (Months 7-9)

2b. Obtain baseline measurements (VO₂max, Timed walked tests, GAITRite, Step activity monitor studies) on individual study participants as they pass screening.

- 2c. Initiate the stratified randomization of subjects into the Lokomat versus aquatic therapy protocols with exercise occurring 3 times per week for 3 months. (Months 7 -9)
- 2d. Recruit twelve individuals across both sites during year one (approximately six per site approximately equally divided between tetraplegic and paraplegic individuals (Months 7-19).
- 2e. Obtain 3 month outcome measurements after participants complete their first exercise intervention (Months 10-39).
- 2f. Cross over participants to the other exercise intervention after outcome measurements have been performed (Months 10-42).
- 2g. Obtain 6 month outcome measurements after participants complete their second exercise interventions (Months 12-42).

31 individuals were screened in Baltimore with 27 progressing to study participation and five individuals dropping out of the study. Three potential participants failed to meet screening criteria and one potential participant deferred secondary to an orthopedic issue which required attention. Fifteen individuals were screened and enrolled in Atlanta at Shepherd Center with fourteen progressing to study completion. At the end of this final reporting year, 31 participants completed the final data collection.

Task 3. Implement Analysis of Data, Presentation and Publication (Months12-45).

- 3a. Provide annual reports to the Data Safety Monitoring Board at the Baltimore site (Months 12-36).
- 3b. Complete proposed statistical analysis of the study data and submit the results for scholarly presentation and publication. In addition provide outcome information in the form of a report to the granting agency. (Months 36-45).

3a. The eighth DSMB report was submitted November 2014. The preceding seven DSMB reviews were positive and we anticipate no issues with the eighth DSMB report as all participant involvement ended before this review period initiated. University of Maryland Baltimore and the Shepherd Center IRB annual reviews are attached to this document with no issues reported. 3b. Data analysis is now completed except the Gaitrite data and two publications and 11 study related presentations completed to date.

Prose Summary Description of Recruitment Accomplishments:

The first Baltimore recruitment actually started in April 2011. Since then 31 individuals were screened with 27 progressing to study participation. Atlanta study recruitment began in July 2011 with 15 individuals screened and engaged in study participation. Recruitment at both sites began as soon as the Department of Defense (DOD) IRB review was complete. In Baltimore 17 participants and at Shepherd 14 participants completed the entire study. Demographic breakdown for all screened individuals includes the following:

Status key: I=first exercise arm, II=second exercise arm

Site key: 1=Baltimore, 2=Atlanta

gender	Race/ethni	veteran	Age	Level	status	site
M	AA	no	41	C7	withdrawn-II	1
M	Asian	no	20	C5	withdrawn--I	1
F	Caucasian	no	48	T9	completed	1
M	Caucasian	no	36	T6	Screen failure: Open skin lesions	1
F	AA	no	28	T12	Screen failure: ASIA B	1
M	Caucasian	no	60	C5-6	completed	1
M	Caucasian	no	61	C5-6	completed	1
M	AA	yes	61	C4	completed	1
M	Caucasian	no	41	T1	withdrawn--I	1
M	Caucasian	yes	35	C4	completed	1
M	AA	no	51	T1	deferred start	1

M	AA	yes	65	L2	screen failure	1
M	Caucasian	no	51	C4	completed	1
F	Caucasian	no	44	T10	Withdrew -II	1
M	AA	no	27	T1	withdrawn-I	1

M	Am Indian	yes	49	C8	completed	1
M	Caucasian	no	46	C4	completed	1
M	Caucasian	no	55	T1	completed	1
F	Caucasian	no	30	C7	completed	1
F	AA	no	53	C3	completed	1
M	AA	yes	48	C8	completed	1
F	Islander	no	65	T1	completed	1
M	Hispanic	no	46	C4	completed	1
F	Caucasian	no	58	T1	completed	1
M	AA	no	57	T7	screen failure	1
M	AA	no	27	C6	completed	1
M	Caucasian	no	32	C8	completed	1
F	Caucasian	no	54	T3	completed	2
M	Caucasian	no	39	C5	completed	2
M	Caucasian	no	60	C4	completed	2
M	Caucasian	no	37	T8	completed	2
F	Caucasian	no	27	T1	completed	2
M	Caucasian	yes	65	C2	completed	2
M	AA	no	41	T6	completed	2
M	AA	no	50	C2	completed	2
F	Caucasian	no	25	C4	completed	2
M	Caucasian	no	31	C4	completed	2

M	Caucasian	no	40	T4	completed	2
M	AA	no	50	C2	enrolled-II	2
M	AA	no	39	C2	enrolled-II	2
M	Caucasian	no	51	C1	enrolled-I	2
F	AA	no	47	C4	withdrawn bowel program, HTN	2

Participants who were withdrawn:

Five individuals at the Baltimore site were withdrawn from study participation. One enrolled participant (at the Baltimore site) was withdrawn at his fourth training Lokomat exercise session secondary to his inability to tolerate Lokomat setup. Specifically, the fourth and final session was terminated during the warm-up period after the participant reported experiencing a “burning” sensation in the left foot. This participant reported similar symptoms during the two prior Lokomat training sessions but he did not report this symptom to the research team during the set-up and acclimation sessions. The reported paresthesia was not in a classical neuroanatomic distribution. For two of the last four attempted training sessions the participant actually reported paresthesia before leaving the exercise mat and being suspended in the Lokomat harness. To diminish or prevent this problem, the research team attempted to reposition the Lokomat straps, but was unsuccessful in ameliorating the condition during Lokomat suspension. The PI ultimately terminated the subject’s participation for safety reasons.

The second participant was withdrawn on his 11th Lokomat session (after he completed the entire Aquatic therapy arm of the study with no problems) when asymptomatic autonomic dysreflexia (AD) occurred. This was detected after the participant described a ‘feeling of warmth’ while exercising on the Lokomat. The blood pressure taken at the time was 210/100 mmHg. The subject was otherwise asymptomatic, i.e. there was no headache or diaphoresis. The blood pressure returned to normal after the subject was taken out of the Lokomat straps. Several attempts were made to modify the straps to see if this elevation in BP could be avoided. Unfortunately it could not.

Autonomic dysreflexia is a known complication of persons with spinal cord injury at or above the T6 level, usually caused by some sensory irritation below the level of injury. We discussed this incident with the IRB at the time it occurred. Since AD is a known complication, no reportable new information (RNI) report was required. Because of the persistent elevation in BP during the Lokomat component of the protocol (i.e. silent AD), this individual was withdrawn from the study.

An unfortunate non-study activity related, lower leg fracture necessitated withdrawal of the third participant. He was casted for 6 weeks sp fracture.

An unreported skin irritation on the plantar surface of his foot facilitated the removal of the fourth research participant. This individual does not routinely examine his skin integrity, or follow up with recommended and scheduled clinical care. Once the irritation was researcher identified, the area was examined and treated until the participant no longer returned to our facility. Attempts were made to contact him via phone and mail with no success.

The fifth participant successfully completed the aquatic intervention and 30 sessions of Lokomat and was hospitalized for a non-study condition. One participant was withdrawn in Atlanta after 1 week of study involvement for medical conditions prohibiting ongoing study participation. She was referred to services to address these medical conditions.

All of these withdrawn individuals but the fifth who was directly admitted to the hospital from home, were medically evaluated by the PI (PHG) who determined that no further intervention was necessary other than withdrawal from participation. Two withdrawn individuals are currently engaged in our wellness aquatic programs as a secondary outcome of study participation. We diligently monitored all study participants to insure safe participation in this DOD protocol. Additionally, study withdraws were reported through our established DSMB.

KEY RESEARCH ACCOMPLISHMENTS

No study papers published yet. Cardiovascular outcome paper will be submitted by February 2016. Two related but not directly linked to DOD study include:

Gorman PH, Geigle PT, York H, Scott W. Reliability and Relatedness of Peak VO₂ Assessments during Body Weight Supported Treadmill Training and Arm Cycle Ergometry in Individuals with Chronic Motor Incomplete Spinal Cord Injury. *Spinal Cord*. 2014 Apr;52(4):287-91. <http://www.ncbi.nlm.nih.gov/pubmed/24534779>

Improvement in Weight Loss and Ambulation Outcomes after Gastric Sleeve Surgery for a Person with Chronic Motor Incomplete Tetraplegia: Clinical Case Report. *Spinal Cord*. 2016.

<http://www.nature.com/sc/journal/vaop/ncurrent/full/sc201622a.html>

- At the 2014 ASIA Meeting, members of the University of Maryland Department of Neurology and UM Rehabilitation Research Center presented the following:

Paula Richley Geigle PT PhD, and **Sara Kate Frye OTR/L, MS**, presented a two-part course: Aquatic Exercise for Individuals with Spinal Cord Dysfunction: Clinical Guidelines, didactic and in-pool experiences.

John Perreault CRNP, William H. Scott MA, Peter Gorman MD, and Paula Richley Geigle PT, PhD Adjunct Assistant Professor presented: Gastric Sleeve Surgery in a Person with Chronic Motor Incomplete Tetraplegia: A Clinical Case Report. (poster presentation)

William H. Scott MA, Peter Gorman MD, John Perreault CRNP, Peter Kuchonov PhD, Paula Richley Geigle PT PhD, presented: Abdominal Adiposity, Insulin Resistance, and Prescribed Exercise for a Woman with Chronic Motor Incomplete Spinal Cord Injury: A Clinical Case Report. (platform presentation)

- Study protocol, case report forms, data collection sheets, and informed consent documents were maintained in a consistent manner across both study sites
- Filed all required regulatory documents for 4 years of study enrollment and intervention
- Obtained/maintained research certification for all study personnel
- Orchestrated organizational face to face meetings in Baltimore, Atlanta, and at national professional meetings to allow for efficient coordination of the research study
- Held weekly DOD research study meetings (in Baltimore) including all local team members
- Planned and executed monthly phone conferencing between both study sites
- Submitted local IRB modification to clarify exclusion criteria so that they better align with the current clinical definition of diabetes; and to offer optional participation in MRI screening at pre, mid, and post data assessment for abdominal adiposity.
- Two manuscripts from screening data and study execution only
- Nine presentations from proposal, screening data, and study execution only.
- The majority of our team members from both University Maryland Rehabilitation and Shepherd Center were present and met together at the American Spinal Injury Association (ASIA) annual meeting, San Antonio, TX, May 2014. We discussed

specific details of the data analysis plan. Also at this meeting we were fortunate to meet Dr. Patricia Henry our Science Officer for this award.

Our plan for the 6 month no cost extension:

- Submitted our eighth DSMB report in November 2014 which did not include any new participant information as all intervention and outcome collection was completed
- Analyze both screening and outcome data
- Draft publication(s) discussing: clinical concepts; cardiovascular; functional; and metabolic information acquired from this DOD funded study
- Draft manuscript(s) for publication submission and study closure reports for both UM and Shepherd