

SUMMARY OF CLINICAL RESEARCH INVOLVING THE ALTERG ANTI-GRAVITY TREADMILL®

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At AlterG, we are committed to proper scientific investigation of the potential clinical and athletic performance benefits of using our device. We are pleased to have multiple studies in clinically relevant areas currently underway by independent researchers, at highly reputable institutions in the U.S. and Internationally. Out of respect for the integrity of the scientific process, we will not cite specific authors or institutions until the studies have been published in peer-reviewed journals, presented at professional meetings, or until the author gives us permission. In the following sections, I will outline for you our published or presented research, present in aggregate format findings from studies already completed but not yet published, and a brief overview of planned studies and questions to be answered for 2010.

PREMARKETING STUDIES AND TECHNOLOGY VALIDATION

The concept of using advanced differential air pressure technology for weight support was originally conceived by Dr. Robert Whalen and Dr. Alan Hargens while they were studying the biomechanics of exercise in space as part of an effort to design effective exercise regimens for NASA's astronauts. AlterG has developed this concept into a technology for use in training and rehabilitation and developed a user friendly platform with ergonomics and adjustability that suit an extraordinarily wide range of users.

The earliest published technology validation research was performed at the Palo Alto VA Medical Center:

Charles G Burgar, MD; Douglas Schwandt, MS; James Anderson, JEM; Robert Whalen, PhD; Gregory Breit, PhD; NASA-ARC: Differential Walking Assist: an inflatable walking support *Rehabilitation R&D Center Progress Report, 1994.*

This study demonstrated the effectiveness of lower body positive pressure and a flexible enclosure for reducing ground reaction force. The technology was effectively that of the AlterG without an enclosed treadmill. It also demonstrated nominal cardiovascular changes due to the positive pressure. In this early prototype, study participants were able to reduce body weight up to 74% with an average pressure of 45mm Hg.

Additional studies were performed for premarketing validation:

Ellie L. Buckley, MS PT; Charles G. Burgar, MD; Yang Cao, MB; and Douglas F. Schwandt, MS: Partial Body Weight Support Using Air Pressure: Safety and Unloading.

Second National Department of Veterans Affairs Rehabilitation Research and Development Conference Proceedings, 2000.

For this second investigation, a new fabric chamber was constructed and a treadmill was placed inside the chamber to provide exercise. The goal was to determine if subjects suffering from stable cardiovascular disease would demonstrate any ill effects or aberrant physiological response to exercise with body weight support. Walking with air pressure support proved to be subjectively comfortable and safe for subjects tested with medically stable cardiac, vascular and respiratory disorders. Intra-chamber pressures of less than 1.1 psi provided up to 75% body weight support with concomitant reduction in ground reaction force.

Eastlack, Robert K MD; Hargens, Alan R PHD; Groppo, Eli R BS; Steinbach, Gregory C PHD; White, Klane K MD; Pedowitz, Robert A MD, PHD: Lower Body Positive-Pressure Exercise after Knee Surgery. *Clinical Orthopaedics & Related Research. 431:213-219, February 2005.*

This study assessed the preliminary feasibility of lower body positive pressure exercise as a rehabilitation technique by examining its effects on gait mechanics and pain, postoperatively. Ground reaction forces for surgically treated and contralateral extremities were reduced 42% and 79% from normal body weight conditions when ambulating at 60% and 20% body weight, respectively. After meniscectomy, ambulatory knee range of motion decreased only at 20% body weight (37°), compared with normal body weight conditions (49°). Peak electromyographic activity of the biceps was maintained at all body weight conditions, whereas that of the vastus medialis was reduced at 20% body weight. Pain relief was significant with lower body positive pressure ambulation after ante-

rior cruciate ligament reconstruction. This study showed that lower body positive pressure exercise is effective at reducing ground reaction forces, while safely facilitating gait postoperatively.

Cutuk, A.A., Groppo, E.R., Quigley, E.J., White, K.W., Pedowitz, R.A., Hargens, A.R.: Ambulation in Simulated Fractional Gravity Using Lower Body Positive Pressure: Cardiovascular Safety and Gait Analyses. *J Appl Physiol* 101: 771-777, 2006.

While ambulating in LBPP at 3 mph (1.34 m/s), HR decreased significantly from 9934 bpm in ambient pressure to 8432 bpm at 50 mmHg LBPP ($p < 0.009$). Blood pressure, brain oxygenation, blood flow velocity through the middle cerebral artery and head skin microvascular blood flow did not change significantly with LBPP. As allowed by LBPP, ambulating at 60% and 20% body weight (BW) decreased ground reaction force (GRF) ($p < 0.05$), while knee and ankle sagittal ranges of motion remained unaffected. The study concludes that ambulating in LBPP has no adverse impact on the systemic and head cardiovascular parameters while producing significant unweighting and minimal alterations in gait kinematics. Many individuals exercising on the AlterG may have concurrent cardiovascular disease, and this study demonstrates safety in the cardiovascular profile.

PUBLISHED STUDIES CONDUCTED ON THE ALTERG ANTI-GRAVITY TREADMILL®

These studies were performed at the lab of internationally renowned researcher Dr. Rodger Kram. They used the commercially available AlterG P200 model, and provide the foundation for the biomechanics of running and walking on the AlterG. They also show that for each individual a “metabolic prescription” can be achieved, thus maintaining metabolic load while reducing the ground reaction forces. The principles shown here can be applied to a wide variety of medical and athletic rehabilitation settings.

Grabowski, Alena and Kram, Rodger: Effects of Velocity and Weight Support on Ground Reaction Forces and Metabolic Power During Running. *J Appl Biomech* 24:288-297, 2008

This study was performed at the University of Colorado, and validated several core biomechanical principles associated with usage of the AlterG:

- For any given running speed, weight support reduced metabolic demand by the runner
- For any given amount of weight support, metabolic demand can be increased by increasing running speed
- Ground reaction forces are reduced at all levels of weight support

- Surface EMG electrode activity shows that muscle firing patterns and gait mechanics are maintained for all levels of weight support and running speeds.
- The interaction of speed and weight on gross metabolic power is summarized as:
 - $MP = 6.11BW + 2.29v - 2.65$ ($R^2 = 0.49$)

Grabowski, Alena: Metabolic and Biomechanical Effects of Velocity and Weight Support Using a Lower Body Positive Pressure Device During Walking. *Archives of Physical Medicine and Rehabilitation, In Press, 2010.*

This study uses similar methods to the running study by Dr. Grabowski referenced above but now focusing on individuals during walking. Proof of basic principles during walking is very important for the post-injury, post-operative, and other groups who would not be expected to run on the AlterG.

- At faster velocities, peak GRFs and metabolic demands were greater. In contrast, walking at lower BW attenuated peak GRFs, and reduced metabolic demand compared to normal weight walking.
- Many combinations of velocity and BW resulted in similar aerobic demands, yet walking faster with weight support lowered peak GRFs compared to normal weight walking.
- Manipulating velocity and weight support during walking with the AlterG may be a highly effective strategy for rehabilitation, recovery following surgery, and gait re-training.

THE FOLLOWING STUDIES HAVE BEEN PRESENTED AT NATIONAL MEETINGS, BUT NOT YET PUBLISHED

Several studies were completed during 2009, many of which have been presented at scientific meetings. These studies are either in the review process for journal publication, or have manuscripts that are being prepared for submission.

Basic Science: Biomechanics

Jensen, Bente R., Hovgaard-Hansen, Line, Cappelen, Katrine L: Effects of Lower Body Positive Pressure on Muscle Activity and Joint Loads. (University of Copenhagen, Denmark). *Presented at The International Society of Biomechanics meeting, South Africa, July 2009*

Eight experienced male runners were studied for vertical and horizontal ground reaction forces, surface EMG muscle activity, heart rate and perceived exertion. This study showed that maintained horizontal ground reaction forces are most likely responsible for the normal gait patterns seen with all levels of weight support.

- Vertical ground reaction forces are decreased with weight support but horizontal ground reaction forces are maintained, thus leading to normal gait patterns at all levels of support
- Joint loads are reduced at the knee and ankle, with knee reduced slightly more than the ankle (data estimated)
- Surface EMG activity reveals reduced muscle contraction amplitudes with weight support, quadriceps and gastroc/soleus are reduced more than hamstrings and tibialis anterior

Forrest, Dana M., Dufek, J.S., Masumoto, K., Mercer, J.A.: Muscle Activity During Running at Reduced Body Weight (University of Nevada, Las Vegas). Presented at American College of Sports Medicine Annual Meeting, Indianapolis, Indiana, May 2008.

Appelquist, B., Mercer, J.A.: The Effect of Simulated Anti-Gravity on Muscle Activity (University of Nevada, Las Vegas). Presented at Southwest Meeting of ACSM, San Diego, October 2009

Liebenberg, J., Scharf, J., Forrest, D., Dufek, J., Mercer, J.A.: Muscle Activity During Running at Reduced Body Weight (University of Nevada, Las Vegas). Presented at Southwest Meeting of ACSM, San Diego, October 2009

Three papers have been presented by members of Dr. John Mercer's lab, demonstrating several important fundamental principles of running on the AlterG.

- Ground reaction forces are reduced for running with weight support
- Running mechanics are maintained with weight support
- Surface EMG activity reveals normal muscle firing patterns during running
- Muscle EMG peak amplitude is decreased with reduced body weight but can be maintained with increased running speed
- Pressure inside the AlterG does not change muscle firing patterns by itself

Saxena, Amol; Granot, Allison: Use of an Anti-Gravity Treadmill in the Rehabilitation of the Operated Achilles Tendon: A Pilot Study. Presented at American College of Foot and Ankle Surgeons Annual Conference, Las Vegas, Nevada, February 2010

This observational study was performed at a busy private clinical practice from one of the world's premier foot and ankle surgeons. Two important conclusions were reached:

- Individuals are able to perform closed chain walking and jogging early on in the postoperative period after Achilles tendon repair, maintaining a training effect in spite of partial weight bearing

- Subjects training on the AlterG may be able to return to overland running sooner than those undergoing conventional postoperative rehabilitation

STUDIES CURRENTLY UNDERWAY

Several studies have ongoing data collection. General topics and hypotheses/questions are presented below for reference. We will provide updates as the studies are completed, data presented, and the paper published.

Basic Science: Biomechanics

EMG running comparison of AlterG to Harness system (UNLV)

EMG running comparison of AlterG to Hydroworx® system (Texas A+M University)

- Several studies comparing AlterG to harness suspension and pool running. What is the effect of the various systems on muscle firing patterns, gait patterns, muscle amplitude, joint reaction forces, etc.?
- Effects of weight support on stride length and stride rate during walking and running

Basic Science: Cardiovascular

Segmental Volume and Cardiovascular Responses to Changes in Body Position at Rest and During Walking Under Normal and Reduced Weight Conditions (Univ. of Kentucky)

- What is the effect of lower body positive pressure on fluid volume shifts in the lower extremity, abdomen, and thorax?
- What is the effect of lower body positive pressure on cardiac output?
- What is the correlation between applied pressure and weight reduction?
- How are the above findings influenced by volume depletion with a diuretic?

Orthopaedics: Arthritis

Arthritis Gait Pain and Exercise Study (Univ. of California, Davis)

The effect of treadmill walking exercise with a partial reduction of body weight on knee osteoarthritis disease progression (Boise State University)

Nonsurgical management of knee osteoarthritis using the AlterG (Pan Am Clinic, Manitoba, Canada)

- What is the effect of the AlterG on perceived pain levels during exercise for patients with knee osteoarthritis?
- Will patients with knee osteoarthritis choose to exercise more on the AlterG compared to other forms of exercise?
- What are the quality of life improvements for exercise on the AlterG?
- Prospective study comparing AlterG to conventional walking exercise. Does the AlterG lead to a reduced rate of osteoarthritis disease progression, reduction in biomarkers for osteoarthritis, and improved quality of life?
- Do individuals with osteoarthritis improve balance and stability compared to other forms of exercise?
- Does exercise on the AlterG lead to an increase in work productivity for young individuals with early knee osteoarthritis?

Neurologic

Use of the Alter-G Trainer as a Rehabilitative Device for the Improvement of Walking in Children with Spastic Diplegic Cerebral Palsy (Munroe Meyer Clinic at the University of Nebraska)

Parkinson's Disease Randomized Clinical Trial (University of California, San Francisco)

- Does exercise on the AlterG improve functional indices, fall risk, and quality of life for patients with mild to moderate Parkinson's Disease?
- Does exercise on the AlterG improve functional indices, fall risk, and quality of life for patients with acute and chronic stroke?
- Does exercise on the AlterG improve gait mechanics and ambulatory capacity for children with spastic diplegic cerebral palsy?
- Range of motion data for healthy subjects during walking were measured in the cerebral palsy study, and are roughly as follow:
 - Hip: flexion 0-15 degrees
 - Knee: flexion 0-35 degrees
 - Ankle: 10 degrees dorsiflexion to 10 degrees plantar-flexion

Athletic Performance

Comparison of AlterG to stretching and treadmill in recovery from downhill running muscle injury (Baylor University)

Comparison of AlterG to stretching and cycling recovery from uphill cycling muscle injury

- Comparison of AlterG to stretching and running in recovery from exercise induced muscle injury during strenuous running. Will runners recover faster from muscle injury with the AlterG?
- Comparison of AlterG to stretching and cycling in recovery from exercise induced muscle injury during strenuous cycling. Will cyclists recover faster from muscle injury with the AlterG?
- Do recovery runs on the AlterG lead to reductions in delayed onset muscle soreness?

STUDIES PLANNED TO BEGIN IN 2010

Going forward, new studies will be initiated in several clinical areas. Our focus will be to emphasize applications in core areas of orthopaedics, neurology, and obesity. We will of course continue to support the foundation research in basic science and athletic performance. We are pleased to note that researchers approach us often with many ideas for innovative studies designed to answer clinically relevant questions. The studies range from case reports designed to provide practical information, to long term studies that will take several years to complete and yield very high quality results with high levels of evidence. We encourage independent thinking and conduct of the research to minimize bias. ***Please note that many of these studies are in the early planning stages. Study protocols are being developed and IRB approval may not have been granted. We provide this information as reference, but cannot guarantee that the studies will be started or completed.***

Sports Medicine: AlterG Usage in the Elite Athlete for Lower Extremity Rehabilitation

- The AlterG is used extensively for rehabilitation in all intercollegiate athletes for more than two years at a major west coast university. The authors are embarking on a retrospective review of all their clinical conditions, protocols, and outcomes in which the AlterG was used for rehabilitation. The goal of the study is to compile a comprehensive listing of indications for AlterG use in the athlete.e.

Orthopaedics: Real-Time Telemetry Data Utilizing the e-Knee

- One of the world's leading total knee arthroplasty surgeons has implanted 4 total knee replacements that include special load-bearing sensors embedded in the total knee replacements. The sensors allow these four patients to transmit real-time telemetry data on knee joint loading in a variety of activities.
- AlterG anticipates the start of a study that will pro

vide objective data on actual knee joint unloading at various levels of body weight reduction on the AlterG.

- This one-of-a-kind data will be invaluable to clinicians and researchers designing rehabilitation protocols for use with the AlterG.

Orthopaedics: Total Knee Arthroplasty

- Evaluation of functional outcomes, pain scores, range of motion, gait, and satisfaction scores after total knee arthroplasty. Randomized, prospective studies have been proposed for the AlterG vs conventional rehabilitation.
 - It is hypothesized that patients using the AlterG will have improved near term functional outcome, and decreased time off crutches/walker due to the patient's ability to achieve pain relief from unweighting during ambulation training.

Orthopaedics: Hip Arthroscopy

- Evaluation of functional outcomes, range of motion, gait, and bone density after hip arthroscopy for femoro-acetabular impingement. Randomized, prospective studies have been proposed to evaluate patients undergoing rehab with the AlterG vs conventional methods.
- Evaluation of functional outcomes, range of motion, gait, and bone density after hip arthroscopy for labrum repair. Randomized, prospective studies have been proposed to evaluate patients undergoing rehab with the AlterG vs conventional methods.

Orthopaedics: Total Hip Arthroplasty

- Evaluation of functional outcomes, pain scores, range of motion, gait, and satisfaction scores after total hip arthroplasty. Randomized, prospective study has been proposed to evaluate patients undergoing rehab with the AlterG vs conventional methods.
 - The AlterG could be used almost immediately after surgery, even when dislocation precautions for posterior approach is used due to the limited range of hip flexion required to walk on the AlterG.

Orthopaedics: Knee Arthroscopic Microfracture

- The ability for a microfracture patient to begin closed chain partial weight bearing ambulation training significantly earlier than currently done with other rehab methods could represent an entirely new paradigm in rehab methods for this commonly performed procedure.

A randomized, prospective study has been proposed by the world's leading expert in the procedure.

- Principles learned from this study can be extended to other arthroscopic/open knee procedures utilizing a period of protected weight bearing, such as meniscus repair, osteochondral autograft, or autologous chondrocyte implantation..

Orthopaedics: ACL Reconstruction

- A procedure in which the patient can be "weight bearing as tolerated" immediately after surgery, but typically chooses to use crutches for several weeks due to pain, stiffness, disuse atrophy, and muscle weakness is an opportunity in which the AlterG can be used very early. It is hypothesized that very early postoperative use will lead to improved near term functional outcomes, the ability for the patient to gain an early cardiovascular training effect, and faster return of running activity in a manner that is safe for the ACL graft. Randomized, prospective studies have been proposed to evaluate this concept.

Obesity

- The overweight individual must deal with a number of issues that make exercise very difficult, such as poor cardiovascular conditioning at baseline, and presence of painful lower extremity joints due to osteoarthritis. Modalities such as aquatic therapy, bicycle, and full body weight walking are commonly recommended, in addition to nutritional modification and lifestyle changes. It is believed that the AlterG enables overweight individuals to exercise in ways they could not otherwise.
 - The ability to "feel what their body is like at a lower weight" is highly motivational
 - Unweighting allows them to exercise in a pain free range
 - Metabolic demand can be maintained even with unweighting by increasing walking speed
 - Randomized prospective studies are set to begin in 2010

Athletic Performance: Can Strength Gains Occur from Training on the AlterG?

- It is common to see strength gains in the atrophied lower extremity that is undergoing rehabilitation after injury or surgery, but is it possible for an individual to actually increase strength above baseline through training on the AlterG? Are the conditions different for the injured vs. uninjured limb? This is a complex issue that will undergo investigation.

Athletic Performance: Can Training on the AlterG Lead to Improvements in Running Speed for the Uninjured Athlete?

- “Overspeed training” is commonly performed by high level runners on the AlterG, and anecdotal evidence suggests that competitive times are improved when traditional training is supplemented with the AlterG.
- The mechanisms behind overspeed training will be investigated.

Sports Medicine: AlterG Usage in Rehabilitation During Healing for Lower Extremity Stress Fractures

- The AlterG allows the athlete with a lower extremity stress fracture to continue running with normal mechanics, unweight the injured extremity to avoid harmful stresses during healing, and to maintain cardiovascular fitness. The authors are beginning a prospective study to evaluate functional and cardiovascular outcomes in an elite athlete population..

Case Studies and Case Reports

- Multiple clinical areas will be authored by recognized experts, and provide practical guidance to physical therapists, athletic trainers, and physicians. Planned target indications include:
 - o Lumbar disc injury
 - o Hip: nonsurgical osteoarthritis; primary total hip; revision total hip; arthroscopy for femoro-acetabular impingement; arthroscopy for labrum repair; femoral neck stress fracture
 - o Femur: stress fracture; traumatic fracture
 - o Knee: nonsurgical osteoarthritis; primary total knee replacement; revision total knee replacement; chondromalacia patella; other patellofemoral disorders; ACL reconstruction; articular cartilage procedures such as microfracture; meniscus repair; tibial plateau fracture
 - o Leg: shin splint syndrome; stress fracture; traumatic fracture
 - o Ankle and Foot: Achilles tendonitis; Achilles tendon repair; other tendonopathies; ankle ORIF for fracture; ankle sprain; plantar fasciitis; metatarsal stress fracture; diabetic foot