Effects of passive standing, dynamic standing and dynamic standing augmented by functional electrical stimulation on urinary calcium, spasticity and bowel function in a person with paraplegia: an N=1 study.

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ABSTRACT
Persons with spinal cord injury (SCI) are at elevated risk of osteoporosis and metabolic calculi due to the effects of immobility, lack of weight bearing and lack of normal neurological regulation. Static standing in a frame is a common SCI rehabilitation intervention to address reductions in bone mass density, spasticity, and bowel dysfunction. Other research findings suggest that dynamic repetitive loading activities may be more successful in promoting osteogenesis after SCI. An n=1 crossover design was executed to compare static standing, dynamic standing in the Easy Stand Evolv Glider (Glider), and Glider augmented by functional electrical stimulation (FES) in a person with T-8 complete paraplegia. All interventions resulted in urinary calcium output within normal range. Subjective report of spasticity was lowest using FES/Glider compared to Glider only, which was lower than static standing. Bowel program time was statistically equal in both Glider interventions but less compared to static standing.

KEY WORDS: stand; functional electrical stimulation; spinal cord injury; calcium; spasticity

BACKGROUND

Renal calculi occur at a rate of 1.5% in the first year and 1.9% in the first five years post spinal cord injury (SCI) (1). Statistics for the general population have not been established (2). Persons with SCI are at elevated risk of osteoporosis and metabolic calculi due to the effects of immobility, lack of weight bearing and lack of normal neurological regulation (1,3,4,5,6,7).

Research prior to bone mass density (BMD) measurement explored the effects of immobility on osteogenesis by tracking calcium output in the urine and feces under the assumption that osteoclastic activity increases when less stress is applied to bone (8,9,10,11). In a series of trials on bed-rested healthy men, recumbent cycling and supine lower extremity (LE) exercises failed to reduce hypercalciuria. Standing and resumption of normal walking in all subjects restored normal calcium excretion (11). Multiple studies since have documented improved bone density, improved bowel function and improvements in spasticity after passive standing in persons with SCI (12,13,14,15,16,17).

Repetitive loading and dynamic stress on bone has been correlated with increased osteogenesis compared to prolonged static stress in theoretical models and animal subjects (18,19,20,21). Studies on animals support a hypothesis that BMD increases more with short cycles of stress separated by recovery periods compared to the same number of cycles applied in a single episode (20,22).

Functional electrical stimulation (FES) to create bone straining muscular contraction is an ongoing area of investigation as a means to promote osteogenesis after SCI. Studies published on the combined effects of standing weight bearing and FES in persons with SCI document cardiovascular effects, metabolic costs and a decrease in upper extremity load during long leg braced standing (23,24,25). Published reports of FES alone, in cycling, in standing, and in gait training after SCI indicate that success in promoting osteogenesis depends on dosing (7,26,27,28,29). Best practice parameters for cycles of stress, magnitude, frequency and length of treatment are not

yet possible due to a lack of evidence although it does seem that higher intensity protocols are more successful (7). Other documented benefits of FES and cycling after SCI include cardiovascular benefits, muscle changes, and decreased spasticity immediately post intervention (26,30,31,32).

Devices such as the Easy Stand Evolv Glider (Glider) are another possible means of repetitive loading. The device positions the user in passive standing, then allows the user to drive the lower extremities in a hemi-elliptical motion via upper extremity levers. Depending on the height of the user, the trailing hip rises in height approximately 1", suggesting cyclic loading.

A literature review of Pubmed, Medline and Cinhal yielded no studies that specifically examined calciuria, spasticity, or bowel function dependent upon FES augmented standing or use of Glider after SCI.

Hypothesis

Dynamic standing in the Glider will successfully promote osteogenesis and decrease calciuria more than static standing. Also, greater effects will result from the same activity augmented by FES due to the muscular stress on bone. The objective was to compare the relative effectiveness of static standing, Glider and Glider augmented by FES on calciuria, bowel function and spasticity. Calciuria was used as a dependent variable instead of BMD because of its relationship to metabolic renal calculi.

METHODOLOGY

One subject was recruited from a sample of convenience. Subject: a 23-year-old community dwelling female with a 16 month history of T-8 ASIA A paraplegia due to trauma. Past medical history: T6 - T11 instrumented fixation and inferior vena cava filter placement. She was negative for urinary tract infections, calculi and other kidney, bladder or bowel dysfunction prior to injury. Bladder management: clean intermittent catheterization. Bowel care: seated digital stimulation and suppositories as needed every morning. Post injury the subject had reoccurring urinary tract infections and two episodes of renal calculi requiring lithotripsy. Laboratory analysis of calculi composition indicated a metabolic nature. Previous urine collections indicated hypercalciuria. Past urinary analyses were positive for pseudomonas aeruginosa, enterococcus, or were normal. Medications: gabapentin, baclofen, and ditropan. Passive LE range of motion was within functional limits for planned interventions. Subject reported flexor spasticity in the morning resulting in difficulty performing transfers requiring passive extension of lower extremities: wheelchair to car, and achieving the long sitting position. She also complained of difficulty maintaining a regular bowel pattern, bowel accidents and protracted amounts of time required for evacuation. Prior to the study, the subject performed passive standing without regularity, with no occurrence within 3 months of the beginning of the trial. Prior to and during the trial, she exercised regularly through resistance training, upper extremity ergometry and hand cycling. She was instructed to maintain her normal routine. Dietary intake was not controlled. She was considered a good candidate for therapeutic standing and selected because of her problems with metabolic hypercalciuria, calculi, spasticity and bowel maintenance.

The institutions ethical review board approved the study and informed consent was obtained. Intervention took place in the physical therapy gym of a rehab center. Personnel were available for assistance if needed. Five consecutive phases each 6 weeks in length were executed in an A-B-C-B-A design. Phases are hereafter noted in order of occurrence A/1, B/1, C, B/2, A/2. During each phase intervention took place three times per week and never on consecutive days.

Phases A1 and A2 involved passive standing only, 45 minutes per trial, using the Easy Stand Evolv stander. Phases B/1 and B/2 involved dynamic standing using the Glider. Set up of the handles accommodated patient comfort. The resistance pistons on the device were removed since upper extremity resistance training was not a goal. Using a digital clock, the subject performed a one minute dynamic standing, then one minute resting protocol. The subject performed one full cycle every two seconds to create consistency with phase C, where the Functional Electrical Stimulation (FES) unit utilizes one second increments. Phase C used the Hasomed RehaStim eight channel programmable FES system along with the Glider from phase B. The FES protocol consisted of two phases lasting one second each, resulting in one full cycle of the Glider every two seconds. FES time interval 0.0-1.0 second muscles and intensity were right quadriceps(90 mA), right gastrocnemius/soleus(40 mA), left gluteals(90 mA), left hamstrings(90 mA). FES time interval 1.0-2.0 seconds muscles and intensity were left quadriceps(90 mA), left gastrocnemius/soleus(40 mA), right gluteals(90 mA), right hamstrings(90 mA). Other FES parameters were 0 ramp, 50 Hz frequency and 150 microseconds phase width. During initial setup, these parameters produced a 2+/5 or greater muscle grade contraction, and were used throughout phase C.

Twenty-four hour urine collections were obtained initially, then every two weeks, and analyzed for calcium content. Before every session the subject recorded bowel information (time required, method used), as well as spasticity information (on a scale ranging from one through ten based on the following question: "Please rate the amount that your spasticity negatively affected your ability to perform daily activities such as dressing, bathing and transfers in the past 24 hours?"). General comments were also recorded, and the researcher periodically interviewed the subject. Heart rate and blood pressure were monitored periodically, especially at the beginning of a new phase. Researchers were blinded to results of urinary calcium, but not to self-report data.
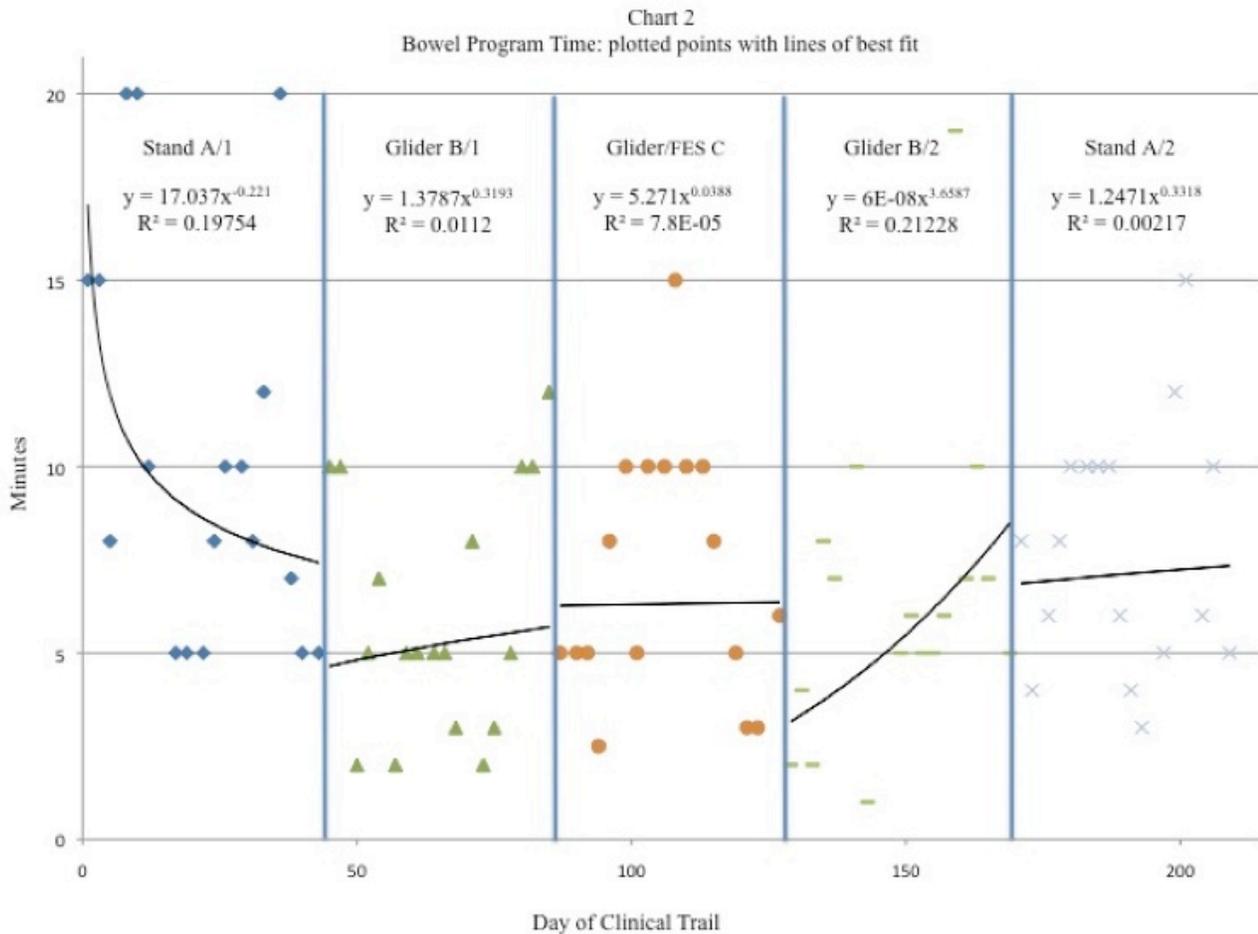
RESULTS

Approximately 10 minutes post intervention on day four of 18 of phase B/1 while sitting, the subject reported bilateral upper extremity and facial numbness and tingling lasting approximately seven minutes. Systolic blood pressure was normal, diastolic blood pressure and heart rate were both elevated. The study's physician examined the subject. Physical exam was negative but a urinalysis was positive requiring ampicillin 1500 mg TID for 10 days. The protocol was changed from 1 minute active, 1 minute rest for 45 minutes to 35 minutes then 10 minutes of passive standing to allow for a "cool down" effect. There was no recurrence of symptoms. She had difficulty with recurrent urinary tract infections and used macrobid, cipro and trimethoprim at different times during the trial. Since neither medications nor bacteria present in urinary analysis were considered to affect urinary calcium, the trial was allowed to continue.

FES induced LE motion proved difficult to capture in the glider, and on the second day of phase C, the left knee pad on the Glider created a small blister inferior to the left patella. Two intervention days were missed for healing. ROHO cells and alternative setups were tried unsuccessfully, but a 2 inch x 2 inch Mepalex pad placed over the wound, wrapped with an Ace bandage allowed healing and provided protection.
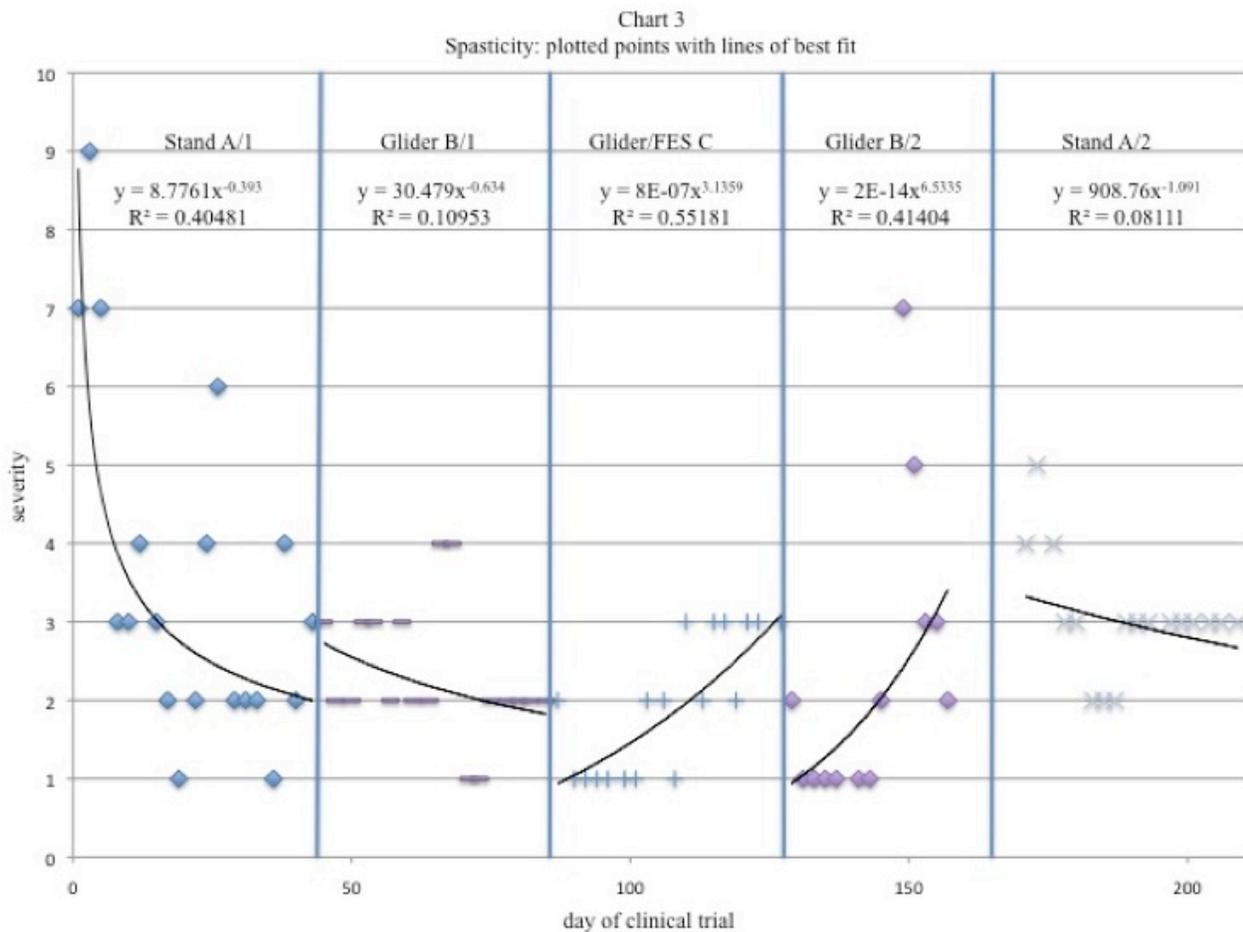
The protocol was to collect at least three data points for UC during each phase. Due to lab error and subject illness, two phases have only two values, thus not allowing trend analysis of these phases. Averages with standard deviations are displayed in Chart 1. All values are within the locally calculated norm reference range. Data distribution is unstable both within and between phases.

Chart 1
Urinary Calcium
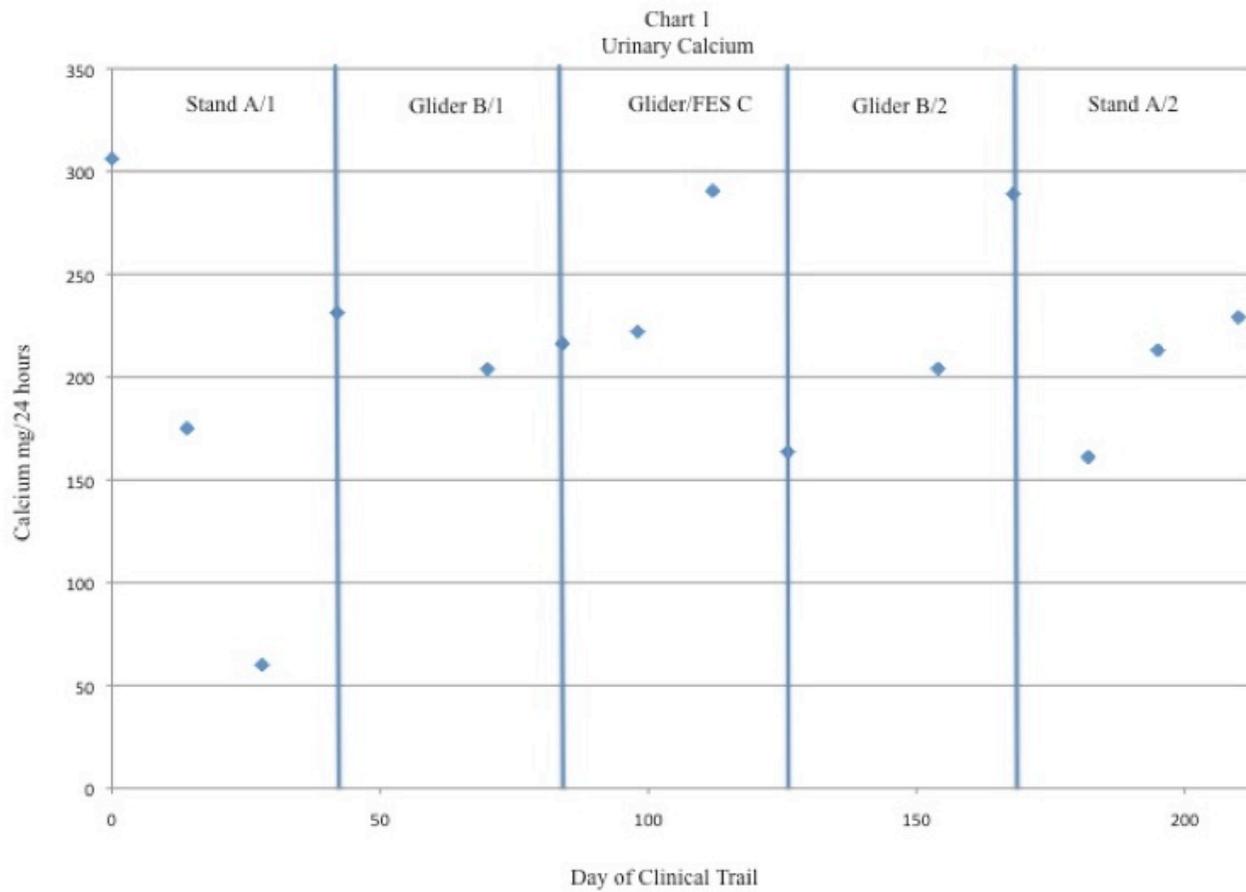
Bowel management was performed only by digital stimulation throughout the trial. The subject recorded frequent difficulty during the first three weeks, then never again. Data points, inter-phase lines of best fit, equations and r-squared values are displayed in Chart 2. All trend lines are positive except for phase A/1. Phase C is positive but near zero slope. Phase averages followed by standard deviations are A/1 10.8(5.4), B/1 5.7(2.9), C 7.4(3.6), B/2 6.5(4.1), A/2 7.6(3.2).

Chart 2
Bowel Program Time: plotted points with lines of best fit

Stand A/1	Glider B/1	Glider/FES C	Glider B/2	Stand A/2
$y = 17.037x^{-0.221}$ $R^2 = 0.19754$	$y = 1.3787x^{0.3193}$ $R^2 = 0.0112$	$y = 5.271x^{0.0388}$ $R^2 = 7.8E-05$	$y = 6E-08x^{3.6587}$ $R^2 = 0.21228$	$y = 1.2471x^{0.3318}$ $R^2 = 0.00217$

Day of Clinical Trail

Spasticity data points, inter-phase lines of best fit, equations and r-squared values are displayed in chart 3. During phase B/2, the subject ran out of gabapentin and waited several days before it could be refilled. This coincides with the values greater than 1 standard deviation above the mean and could artificially increase the slope angle. Phase averages followed by standard deviations are A/1 3.6(2.3), B/1 2.4(0.8), C 1.9(0.8), B/2 2.4(1.6), A/2 3.0(0.8).

Chart 3
Spasticity: plotted points with lines of best fit

Stand A/1	Glider B/1	Glider/FES C	Glider B/2	Stand A/2
$y = 8.7761x^{-0.393}$	$y = 30.479x^{-0.634}$	$y = 8E\text{-}07x^{3.1359}$	$y = 2E\text{-}14x^{6.5335}$	$y = 908.76x^{-1.091}$
$R^2 = 0.40481$	$R^2 = 0.10953$	$R^2 = 0.55181$	$R^2 = 0.41404$	$R^2 = 0.08111$

severity

day of clinical trial

DISCUSSION

All interventions correlated with UC values within normal limits and between phase analysis was not possible. If the intervention had taken place sooner after injury, when hypercalciuria was likely greater, then a between phases difference might have been apparent. Future investigation of this might also require dietary control to enhance stability. Otherwise outcomes are inconclusive.

Bowel pattern followed the hypothesis between phases A and B but not between B and C, though they were not statistically significant. More in depth analysis of phase C revealed that values peak mid phase then decreased in a symmetrical fashion suggesting that another factor influenced bowel program time in this phase.

Spasticity outcomes follow the hypothesis between all phases, though not statistically significant. This was subjective and the subject was aware of the intended benefit. The tool lacks an objective anchor and values could be subject to drift. Phase C showed a low average, but an unexplained strong positive slope, which does not continue in the next phase. Spasticity was measured subjectively and susceptible to placebo effect. Modified Ashworth Scale was considered as a dependent variable, but because the subject had specific complaints about her own transfers, the subjective method was considered to be more appropriate.

Positive slopes in both bowel and spasticity might be explained by a habituation, but a longer protocol would be needed to investigate this trend. The B and C interventions not only provided repetitive loading of the skeletal system, they also included cardiovascular exercise, passive and active LE range of motion, and increased social interaction, all in a standing position. None of these has been fully investigated for effectiveness on spasticity and bowel function post SCI.

The Glider is designed primarily for passive LE movement. RehaStim currently only allows for programming in whole second loops. This is a promising combination, but in this protocol it was suboptimal in terms of skin protection and coordination. Due to the compromise of skin integrity in phase C more development should take place before attempting to replicate that protocol.

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Chart 1 Alternative text description
This chart shows urinary calcium output in milligrams per twenty-four hours plotted on the Y-axis with day of clinical trial on the X-axis. Each phase is labeled so that phases can be visually analyzed. On visual analysis it is clear that the data is unstable and lines of best fit would be inappropriate or not possible. All values are within the locally calculated normal reference range.

Chart 2 Alternative text description
This plot chart displays time required for bowel program with day of clinical trial on the X-axis and time in minutes on the Y-axis. Lines of best fit are displayed for each phase. Equations for these lines of best fit and the corresponding R squared values are embedded in the chart. Text descriptions for these are at the end of the paper.

Chart 3 Alternative text description
This plot chart displays subjective report of spasticity with the day of clinical trial on the X-axis and severity from zero to ten on the Y-axis. Lines of best fit are displayed for each phase. Equations for these lines of best fit and the corresponding R squared values are embedded in the chart. Text descriptions for these are at the end of the paper.

Alternative text descriptions for equations displayed on charts.

Chart 2 within phase equations for lines of best fit and R squared values.
Phase A one:
$y = 17.037x^{-0.221}$: Y equals seventeen point zero three seven X to the negative zero point two two one power
$R^2 = 0.19754$: R squared equals zero point one nine seven five four
Phase B one:
$y = 1.3787x^{0.3193}$: Y equals one point three seven eight seven X to the zero point three one nine three power
$R^2 = 0.0112$: R squared equals zero point zero one one two
Phase C
$y = 5.271x^{0.0388}$: Y equals five point two seven one X to the zero point zero three eight eight power
$R^2 = 7.8E\text{-}05$: R squared equals seven point eight E negative zero five
Phase B two
$y = 6E\text{-}08x^{3.6587}$: Y equals six E negative zero eight X to the three point six five eight seven power
$R^2 = 0.21228$: R squared equals zero point two one two two eight
Phase A two
$y = 1.2471x^{0.3318}$: Y equals one point two four seven one X to the zero point three three one eight power
$R^2 = 0.00217$: R squared equals zero point zero zero two one seven

Chart 3 within phase equations for lines of best fit and R squared values.
Phase A one:
$y = 8.7761x^{-0.393}$: Y equals eight point seven seven six one X to the negative zero point three nine three power
$R^2 = 0.40481$: R squared equals zero point four zero four eight one
Phase B one:
$y = 30.479x^{-0.634}$: Y equals thirty point four seven nine X to the negative zero point six three four power
$R^2 = 0.10953$: R squared equals zero point one zero nine five three

Phase C :

$y = 8E\text{-}07x^{3.1359}$: Y equals eight E negative zero seven X to the three point one three five nine power

$R^2 = 0.55181$: R squared equals zero point five five one eight one

Phase B two

$y = 2E\text{-}14x^{6.5335}$: Y equals two E negative fourteen X to the six point five three three five power
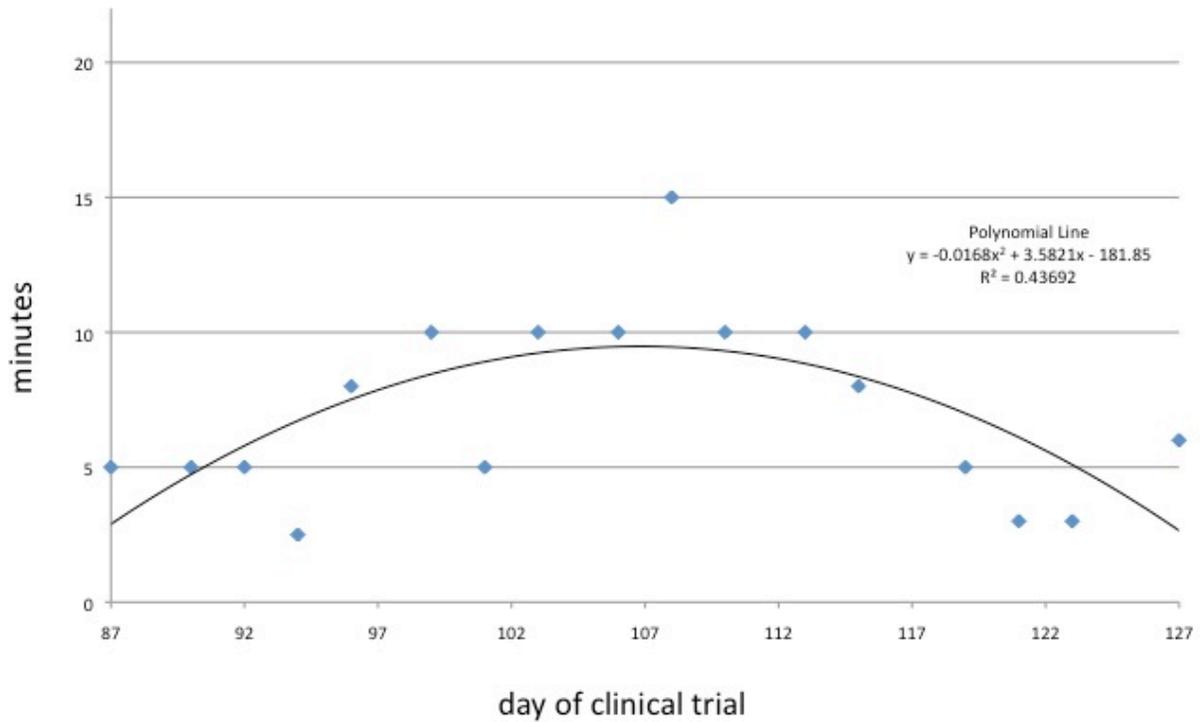
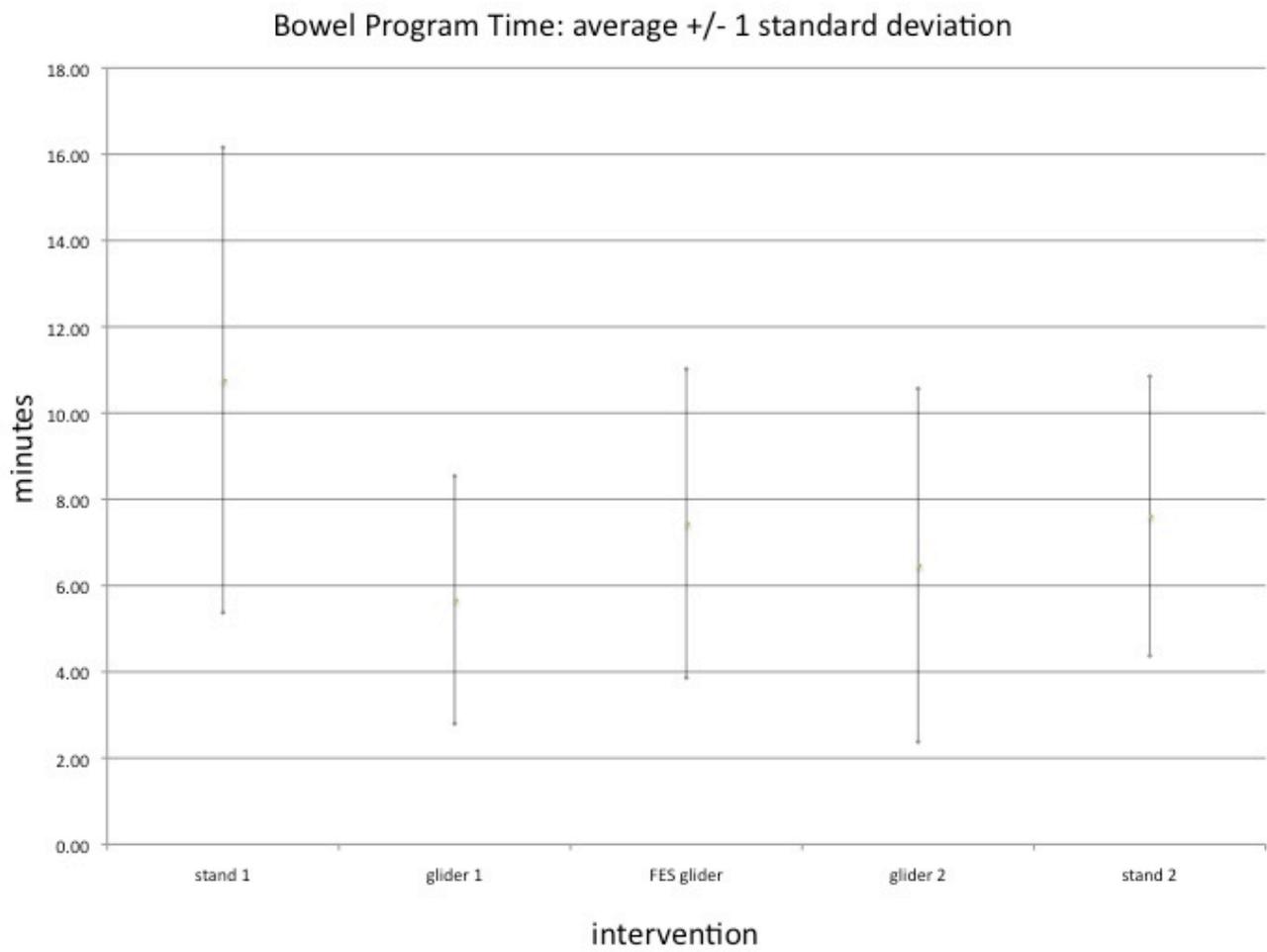$R^2 = 0.41404$: R squared equals zero point four one four zero four

Phase A two

$y = 908.76x^{-1.091}$: Y equals nine hundred eight point seven six X to the negative one point zero nine one power

$R^2 = 0.08111$: R squared equals zero point zero eight one one one

Bowel Program Time: During FES/Glider Phase

Polynomial Line
$y = -0.0168x^2 + 3.5821x - 181.85$
$R^2 = 0.43692$

Bowel Program Time: average +/- 1 standard deviation

Spasticity: average +/- 1 standard deviation