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Allogeneic and autogolous stem cell therapy combined with physical rehabilitation: A case report on a chronically injured man with quadriplegia

Abstract:

Background and Purpose: Stem cell therapy for SCI is a potentially promising treatment with increasing interest. This case report describes the use of a particular stem cell therapy protocol for a patient with chronic spinal cord injury, and describes his subsequent therapy and outcomes.

Case Description: The patient is a 29-year-old male who is chronically injured from a cervical spinal injury, resulting in quadriplegia. The patient was treated with a combined protocol of intrathecal (IT) and intravaneous (IV) allogeneic MSC and CD34+ cells and IT autologous BMMC at 6 ½ years post-injury. The results track the patient's physical therapy progress until 6 months following stem cell treatment.

Outcomes: Recovery of strength in upper extremity and lower extremity muscle groups was noted, along with a functional increase in grip strength, ability to ambulate with assistance, and a significant decrease in daily medications.

Discussion: This case supports further investigation into treatment of chronically injured SCI patients with stem cell therapy followed by physical therapy.

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Backround:

Spinal cord injury occurs worldwide in 15-40 cases per million people. In the United States alone, there are approximately 1.275 million people living with a spinal cord injury. There are around 12,000 new injuries each year.[1,2] The cost of SCI to our health system is estimated to be $40.5 billion annually,[1] with an estimated cost per individual to be up to $25 million over their lifetime[2]. The main causes of traumatic SCI are road traffic accidents, falls, and occupational and sports-related injuries.[2] Approximately 55% of these SCI occur at the cervical level.[2]

There is a wide range in severity and location of spinal cord injuries and the resulting complications and functional impairments, but some of these are: sensory, motor, and autonomic dysfunction; an increased risk of cardiovascular complications, deep vein thrombosis, osteoporosis, pressure ulcers, autonomic dysreflexia, and neuropathic pain; and emotional, social, and financial burdens.[1,2]

The physical manifestations that arise following SCI are results both of damage to a specific area of the spinal cord, and the disruption of messages from the ascending and descending fiber tracts.[1] SCI involves both a primary and a secondary injury. The primary injury is the physical injury itself, in which contusion of the spinal cord causes direct damage from membrane disruption, vascular damage, and hemorrhage.[1,3] The end result of the SCI, however, becomes much worse, as secondary injury processes

are activated. In the early stages of SCI, there is vascular destruction, a loss of neurons within the gray matter of the spinal cord, and a loss of myelinating oligodentrocytes in the white matter. There is axonopathy that leads to denervation and retraction of proximal axons. Cell death occurs, leading to further cell death as the result of excitotoxicity. Excitotoxicity occurs as there becomes an excess of excitatory molecules, such as glutamate, in the extracellular fluid, which leads to overactivation of the neurotransmitter receptors.[3] Spinal neurons typically die as a result of necrosis or excitotoxic damage within 24 hours of SCI.[1] Some of them, as well as oligodendrocytes, die as a result of apoptosis, which can last from 24 hours to several weeks after the injury.[3]

Inflammation also occurs in response to the initial injury. Macrophages, neutrophils, and T cells migrate into the area from the peripheral circulation and become activated. Microglia also become activated, and along with the macrophages, remove dead cells and debris through phagocytosis.[3] These cells produce cytokines and chemokines that propogate this inflammatory process.[3] The spinal cord is especially vulnerable to inflammation, because swelling of the cord within the confines of the spinal canals creates higher pressure than that of venous blood pressure. Therefore, blood flow to the injured area ceases, and the venous infarct deprives the interior of the cord of oxygen and nutrients. This causes cell death in the gray matter, which is where the bodies of the nerve cells reside.[4]

Analysis of spinal cords after chronic SCI shows that there is typically a white matter rim that is spared, although there is degeneration of ascending and descending axons, and demyelination due to the apoptosis of oligodendrocytes.[3] Ultimately, a scar forms at the site of the injury. This is known as a glial scar and is many times larger than the initial injury itself.[3] This glial scar impedes axonal regeneration and remyelination by acting as a physical barrier and also by providing an inhibitory environment towards axon outgrowth.[1,3]

There is no cure at this time for SCI, and though there have been some SCI clinical trials over the past two decades, the only therapeutic intervention shown to have statistically significant efficacy is Methylprednisolone, which is given within 8 hours of the injury.[5]

Stem cells

Since the identification and characterization of stem cells, there has been increased interest and research determining their potential for use in SCI and other disorders.[6] Researchers in this field appear to have two main goals, which are to prevent the secondary tissue loss that occurs at the spinal cord, and to achieve partial regeneration of the damaged axons and neuronal circuits.[4]

A stem cell is defined by its ability of self-renewal and its totipotency.[6] Self-renewal is characterized by the ability to undergo asymmetric cell division, where there is production of one daughter cell that is identical to the mother cell and another daughter cell that becomes restricted to one of the germ layers (ectoderm, mesoderm, or endoderm).[1,6] Totipotency means that the cell can become any cell type that is present in an organism. Some consider the zygote to be the only totipotent (stem) cell because it has the ability to differentiate into either a placenta cell or an embryonic cell.[6] Embryonic cells (ESCs) are defined as pluripotent, because they cannot become a placenta cell, but they can give rise to lineages

derived from any of the three primary germ layers.[1,6] Besides ESCs, there are also adult stem cells (or "somatic stem cells") that have been found to differentiate into the any of the three germ layers.[6]

Stem cells can be divided into these two main categories – embryonic stem (ES) cells and somatic stem cells.[3] Somatic stem cells are otherwise known as adult stem cells. This cell category also includes endogenous progenitor cells that repair and replace tissue in our bodies, and cells derived from fetal tissues, neonatal tissues, and adult tissues.[3]

In most cases, ES cells are obtained from an embryo that was derived through in vitro fertilization.[4] ES cells have several features that set them apart from somatic stem cells – 1) they can replicate indefinitely without aging, 2) they are pluripotent, meaning they can give rise to all the different types of cells in the body, 3) they are more likely than other types of dividing cells to give rise to genetically normal cells, and 4) they can be easily manipulated genetically.[4] Although ES cells show the greatest potential for the widest range of cell replacement therapies,[3] there are also some risks involved with using these cells. Transplanting ES cells can cause problems, because pluripotent cells can deposit normal tissue in the wrong places.[4] They can also generate teratomas, which are tumors made up of more than one tissue,[4,6] and they are prone to being rejected after injection into adult tissue, for which long-term treatment of immunosuppressive drugs could be required.[6] For these reasons, as well as ethical dilemmas, ES cells are not currently being used as widely as somatic stem cells.

There are many categories and types of somatic stem cells that have been used in experimental treatments for SCI.[1,3,7,8,9,10,11] This paper will focus on the characteristics and research relating to cord blood derived cells, mesenchymal stem cells, cells that have CD34+ expression, and bone marrow mononuclear cells, as those as these are the stem cells that were used with the patient in this case report.

Human stem cells derived from the umbilical cord are a promising candidate for use in stem cell therapy for SCI because of their great availability, weak immunogenicity, and low risk of mediating viral transmission.[12] Umbilical cord and Wharton's jelly derived mesenchymal stem cells also seem to offer greater therapeutic characteristics when compared to bone marrow derived MSCs. The characteristics are specifically: longer telomeres, increased passage ability without loss of differentiation potential, and more potent cytokine release activity.[7] Cells derived from cord blood have been described by investigators to stimulate post-infarct neurogenisis through stimulation of angiogenesis.[13] In addition, it appears that cord blood CD34+ cells mediate effects partially through the secretion of glial line derived neurotrophic factor (GDNF) and vascular endothelial growth factor (VEGF).[8] GDNF has been shown to promote axonal growth and cellular protection in injured adult motor neurons, and VEFG has been shown to accelerate endogenous neurogenesis.[8]

About 2% of the human umbilical cord blood cells are positive selection of CD34+ expressing cells.[8] Cells observed as CD34+ are of an undifferentiated, primitive form; they are pluripotential hemopoietic stem cells. It has been shown by researchers that CD34+ cells can improve functional recovery and reduce infarction and apoptosis in the injured spinal cord.[8] This is believed to be through production of GDNF and stimulated production of VEGF in the injured spinal cord area. These findings support the

researchers' hypothesis that transplanting CD34+ cells promotes an environment conducive to neovascularization of ischemic spinal cord so that neural regeneration can occur.[8]

Bone marrow mononuclear cells have typically been used as a hemopoietic stem cell source for bone marrow transplants, however their use has been shown to benefit various disorders, including SCI.[8] It has been demonstrated that BMMC administered via lumbar puncture, poses no serious adverse risk to the patient.[11] In addition, these cells have an advantage of being autologous, thereby avoiding possible graft rejection.[1] Small studies have been conducted with the use of autologous BMMC, and the authors have observed improvement in bladder function, ASIA scores, and quality of life.[9] These improvements, however, do appear greater in acute rather than chronic patients.[10]

It has been demonstrated in animal models that mesenchymal cells, CD34 hemapoietic stem cells, and BMMC all possess some capacity for SCI regenerative activity.[8] It has also been stated by previous researchers that a combined approach is appealing as MCS are known anti-inflammatory and growth factor producers, and CD34 cells have been found to produce angiogenic factors and in some cases have even demonstrated to differentiate into neurons directly.[7] This case report is necessary because the research and results regarding chronically injured spinal cord patients are lacking, and the potential for stem cell therapies with these patients has not been fully explored. The purpose of this case report is to describe the treatment and outcomes associated with a specific combined stem cell therapy protocol and subsequent physical therapy in a patient with chronic spinal cord injury.

Case description

The patient is a 29-year-old male, who was 22 at the time of his injury. He sustained a spinal cord injury in August 2005 of unknown cause. The patient was found lying approximately 20 feet from his bed, with no recollection of a fall or assault. At the time of the injury, he was taken to the hospital and found to have a C5 lamina fracture with cord compression. An MRI was taken of his cervical spine, and revealed cord edema at C4 – C6 and cord edema with bleed C4-C5. The patient subsequently underwent C3, C4, C5 laminectomies with spinal cord decompression. Physical therapy and occupational therapy evaluations in the next 24 hours revealed the patient to be "dependent" with bed mobility and activities of daily living. Neurological testing of the patient within 24 hours revealed the information found in Table 1.

The patient was also found to have bilateral LE strength at 0/5 and absent sacral sensation. The diagnosis at this time was C4 complete quadriplegia.

After 12 days of being hospitalized, the patient was transferred to an inpatient rehabilitation center. He showed some neurological improvement since the initial injury and upon evaluation at the rehabilitation center, was said to be "roughly C5 incomplete." MMT revealed shoulder abduction 5/5, elbow flexion 5/5, elbow extension 1/5, and wrist extension 2/5. The patient was found to have no finger movement and the only LE movement he had was some flexion of his left 5th toe. The patient was found to have some sacral sensation to light touch at this time, but absent for pin prick.

The patient spent 2 months in the inpatient rehabilitation center. The patient's inpatient rehabilitation focused on maximizing function to live as independently as possible, including strengthening and functional mobility exercises. The patient and his family were taught range of motion and stretching exercises to be performed on a daily basis, and also how to transfer the patient to his wheelchair. The patient was fitted with a powerchair and taught how to use it. At discharge, the patient left with a diagnosis of incomplete C4 spinal cord injury. His ASIA score was AIS C, meaning that the SCI was incomplete and that motor function below the neurological level was preserved, with key muscles above the neurological level having a strength grade <3/5.[14]

Within 2 months of discharge from inpatient rehabilitation, the patient began outpatient physical and occupational therapy for further rehabilitation. At just over 4 months past his injury, his outpatient evaluation revealed the MMT scores located in Appendix 1. His ASIA motor score was 39/100. His ASIA sensory score was 66/112 for pin prick and 67/112 for light touch.

The patient attended outpatient physical therapy for approximately 5 months, which was in the timeframe of 4-9 months after his injury. There are no MMT scores available at the patient's discharge, as he had to stop attending therapy before being formally discharged due to medical complications. The patient had progressing hyperlordosis, otherwise known as "swan neck deformity" since his injury. This complication resulted in more pressure on the patient's spinal cord and a decrease in muscle strength. At 1 ½ years post-injury, the patient underwent a spinal fusion of vertebrae C3-C5.

Over the course of the next five years post-injury, the patient also developed bowel and bladder complications, being hospitalized multiple times for bowel impaction and UTIs. The patient sustained a completely fractured and displaced left femur following a stretching session with an occupational therapist at his nursing facility. He subsequently underwent surgery for an ORIF of his left femur. The patient at this time also had a past medical history significant for a bleeding ulcer, chronic pain, pain at night, low blood pressure, and difficulty sleeping.

Clinical impression:

At 6 years past his initial injury, the patient had experienced no significant functional improvements, or improvements in strength. He was also on a significant amount of medication for pain, nerve pain, and spasms. The patient decided to seek out stem cell therapy as an intervention with a potential for functional and strength improvements. He was also interested in pain, spasm, and medication reduction. He applied for treatment at a location in Panama and was accepted as a patient. His intention was to undergo stem cell treatment and then return to the United States for physical and occupational therapy.

The plan for examination and results of this patient following treatment and therapy were MMT scores, medication reduction, and self-reported functional improvements.

The next set of MMT scores available for the patient are from 6 years and 4 months post injury, when the patient returned to outpatient physical therapy just prior to having stem cell treatment. This set of scores can be found as Table 2. The scores that worsened since his last motor testing (prior to his

decline and subsequent cervical fusion) are in red. Any scores that improved are in bold. It should be noted that the majority of his lower extremity muscles did decline in strength. It can also be noted that his pin prick score on the ASIA had increased to 106/112, and his light touch to 111/112.

Treatment and subsequent therapy:

The patient received stem cell treatment beginning at approximately 6 years, 5 months after his injury. He was treated with a combined approach of intrathecal and intravenous injections of allogeneic MSC & CD34+ cells (from umbilical cord donors) and intrathecal autologous BMMC cells (extracted from his own bone marrow). He received a total of 8 intrathecal injections of expanded/non-expanded donor mesenchymal and CD34+ cells, 2 intrathecal injections of autologous bone marrow stem stells, 4 intravenous injections of expanded donor mesenchymal and expanded CD 34+ cells, and 2 intravenous injections of autologous bone marrow stem cells. All injections were done in an outpatient setting over the course of a five week time period. A table with the cell doses can as Table 3.

The patient also attended physical therapy sessions while in Panama. He received 2 hours of physical therapy/day in an outpatient clinic. His therapy sessions focused on core exercises and upper extremity strengthening, with some inclusion of Bobath techniques to facilitate lower extremity function and reduce spasticity.

Upon returning home after his stem cell treatment, the patient resumed physical and occupational therapy with an emphasis on mobility and progression toward standing and ambulation. The patient attended approximately 6 months of physical and occupational therapy twice per week after his stem cell treatment. The sessions were each 45 minutes in length. His therapists worked with him once per week on "functional mobility," including bed mobility, transfers, and sitting balance, and once per week on standing upright with use of a tilt table. The functional mobility was progressed by decreasing the level of assistance needed for rolling in bed, supine to sit, sit to stand, transfers from one surface to another, and sitting with no support. The therapy sessions using the tilt table were focused on standing upright and maintaining blood pressure for up to 30 minutes at one time. At approximately 5 months after the stem cell treatment, when the patient was able to achieve standing for 30 minutes on the tilt table without a major decrease in blood pressure, he was progressed to ambulating with a partial weight bearing harness. The goals of the patient's therapy were to increase patient's ability to perform a therapeutic HEP, increase strength in UE and LE muscles, increase independence with mat transfers, increase independence with rolling in bed, tolerate standing for longer times at a greater angle on the tilt table, and tolerate dependent walking with partial weight bearing. The patient's results are seen below in the outcomes section.

In addition to therapy, the patient also worked with a personal trainer at a local gym twice per week for 1 -1 ½ hrs per session, focusing on upper body strengthening and cardiac endurance.

Outcomes:

Muscle Strength

After the patient underwent the stem cell treatment and returned to outpatient physical therapy in his hometown clinic in the United States, his MMT scores were tested over the period of 5 months post-stem cell treatment. The scores are found as Table 4. Once again, any decline in scores is in red, any improvement since prior to the stem cell treatment is in bold.

The patient did not decrease in strength in any of the muscles tested, and experienced improvements in 6/13 upper extremity muscle groups, and 8/9 lower extremity muscle groups.

The patient did meet the treatment goals of being able to perform a HEP, increasing strength in UE and LE muscle groups, increasing standing time on the tilt table, and tolerating dependent ambulation with partial weight bearing. The patient was not able to independently perform bed mobility or transfers, but did increase in the amount of effort he was able to contribute to these activities.

The patient also had an increase in grip strength. His grip strength was measured by his occupational therapist to be 5 lbs on the right and 25 lbs on the left at one month before his stem cell treatment. Six months later, his grip strength was measured to be 22 lbs on the right and 36 lbs on the left. The patient reported that this increase in grip strength led to functional improvements, such as being able to self-catheterize, which he was completely unable to do since his injury.

Ambulation

The patient was also able to ambulate for the first time in 5 years at approximately 4 months after finishing his treatment. He was able to ambulate in partial weight bearing with the harness and max assist of two for 40 yards at .5 MPH.

Medication Use

The patient was also able to decrease some of his medications. He had been on a daily medication regimen including Baclofen (80 mg/day) for spasms, Lyrica (600 mg/day) for nerve pain, Opana (100 mg/day) for chronic pain, and Valium (20 mg/day) for spasms. After his treatment, he was able to completely stop taking the Baclofen, with the exception of 5 mg on occasion (PRN), and decrease his Opana to 90 mg/day.

Discussion:

It has been noted that caution must be used when viewing experimental stem cell transplantation, as success is not always translated from the laboratory to the clinic.[1] Additionally, the International Campaign for Cures of Spinal Cord Injury Paralysis has now set guidelines for the conduct ethics of clinical trials on stem cell therapy for SCI.[1,5] It has been pointed out in that paper[5] that almost all people that sustain a spinal cord injury will achieve some recovery of motor function below their initial level of injury. Most of this recovery occurs in the first 3 months after the injury, but the individual can continue to improve up to 18 months after the injury. The spontaneous recovery of motor function in a patient classified as motor-complete (AIS A/AIS B) is thought to be fairly limited and predictable, and usually occurs in the zone of partial preservation, but it is sometimes enough to reclassify the injury level to a

lower spinal level. Patients classified as motor-incomplete (AIS C/AIS D), however, tend to have more substantial and variable recoveries.

Because the patient in this case report received stem cell treatment, but also underwent physical and occupational therapy, and physical training sessions, it is impossible to determine the exact cause of any improvements. It should be given thought, however, that many patients with chronic SCIs do not recover strength so many years post injury with physical therapy alone. In fact, when previous studies are analyzed, it has been found that the rate of recovery is most rapid during the first three months, and that motor improvement is almost complete by 9 months, then eventually plateaus at 12-18 months after injury.[5] It is noted, though, that the rate and extent of recovery is greater in patients with incomplete lesions.[5] It is difficult to classify the patient in this report initially as having an incomplete vs. complete lesion, as his first diagnosis was "complete C4 quadriplegia," but this was in the first 24 hours of injury. For numerous reasons, such as spinal shock or medical instability, the ASIA assessment within the first 24 hours after injury has been shown to be an unreliable predictor of the patient's future functional level.[5] It has been suggested that an assessment after 72 hours would have a more accurate prognostic value.[5] This patient's next ASIA scores, however, were not taken until 12 days after hospitalization, at which time he was said to be "roughly C5 incomplete." Therefore, it is difficult to determine whether this patient was initially truly "complete" or not and to what extent this patient could have been expected to improve based on other similar patients.

There is not a lot of evidence for chronically injured individuals recovering motor and sensory function over 2 years post-injury with any type of treatment. There is one study of a severely injured man (ASIA grade A) that was able to improve to ASIA grade C between 5 and 8 years after his injury, which is almost unheard of.[14] This man underwent a program known as "activity-based recovery" that was being instituted based on the hypothesis that patterned neural activity might stimulate the CNS to become more functional, as it does during development. This type of therapy is very different from that of the patient in this case report, as the "activity-based recovery" consisted primarily of training on an FES bicycle. This "activity-based recovery" therapy could be a beneficial component to add to the post-treatment phase of patients receiving stem cell therapy, since it has shown such positive results on its own.

The main form of outcome measures used in this case study was MMT scores, which is the clinical measure most often used to examine strength in patients with SCI.[15] The face and content validity of MMT are high,[16] and inter-tester reliability in patients with SCI is excellent (r = .94).[17] However, it has been suggested that the MMT is not sensitive enough to distinguish between increments at higher levels of strength or to detect small or moderate increases seen in patients with SCI.[18] Therefore, a patient may have had a real increase in strength, but not have it reflected as a change in the MMT. Researchers have explored the relationship between muscle performance and functional abilities in patients with SCI, and it has been determined that critical levels of strength in key muscle groups do relate to independence in function.[18,19] One finding in particular has been that individuals with 3+/5 MMT scores in triceps were more independent than those with less than a 3+/5 score.[18] In particular, it has been found that elbow extension strength is strongly correlated to transfers in different settings (bed to wheelchair, wheelchair to toilet, wheelchair to tub).[19] The patient in this case study had 2/5 triceps

strength bilaterally both before and after the stem cell treatment and physical therapy. This could likely be the reason that independent mobility goals, for transfers specifically, were not fully met.

The reduction of medication following stem cell treatment in this case report is something the patient was pleased with, as the combination of medications with serious side effects can affect cognition and quality of life. The patient stated that he could think more clearly and was no longer in a "brain fog" after reducing two of his medications. Medication reduction as a treatment result is not reported on as frequently as motor and sensation increases, but can have a serious impact on daily functioning. Reduction of medication for nerve pain in another patient has been demonstrated in a similar case report.[7]

Further research into stem cell therapy followed by physical therapy with chronically injured patients is warranted, as this case report shows that even at 7 years post-injury, functional and strength gains are possible with the right combination of stem cell treatment and physical therapy. Different approaches of stem cell treatment and physical therapy should be explored, as some combinations may be more beneficial than others. It must be remembered, however, as noted by previous writers, that no SCI therapy will be considered to be effective for treatment of patients unless it improves the ability of the patients to function in their daily routines and activities.[5]

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Table 1. Neurological testing within 24 hours of injury.

Muscle	**Left**	**Right**
Deltoids	2/5	2/5
Biceps	4-/5	4-/5
Wrist extensors	4-/5	3/5

Triceps	1/5	0/5
Flexor digitorum profundus	0/5	0/5

Table 2. MMT scores at 6 years, 4 months post-injury.

Muscle	**Left**	**Right**
Upper Extremity: Upper Trapezius	**5/5**	**5/5**
Middle Deltoid	3/5	3/5
Anterior Deltoid	**3/5**	**2/5**
Pectoralis Major (sternal)	**4/5**	**4/5**
Biceps/Brachialis	**5/5**	**5/5**
Triceps	2/5	2/5
Pronators	**4/5**	3/5
Supinators	**5/5**	**5/5**
Wrist extension	**5/5**	**4+/5**
Abductor digiti minimi	1/5	1/5
Flexor Digitorum Profundus	2/5	**2/5**
Lumbricals	3+/5	3/5
Trunk: Abdominals	1+/5	1+/5
Lower Extremity: Iliopsoas	1+/5	1+/5
Gluteus Maximus	1+/5	1/5
Gluteus Medius	1/5	1/5
Hip Adductors	1+/5	1+/5

Quadriceps	1+/5	1/5
Hamstrings	1+/5	1/5
Gastrocnemius	2/5	1+/5
Tibialis Anterior	1+/5	0/5
Peroneals	1+/5	1/5
Extensor Hallucis	1+/5	0/5
Flexor Digitorum	2/5	**2/5**

Table 3. Cell types and doses given over the five week time period.

Cell Type	**Cell Viability**	**Cell Doses**
CD34+ (non-expanded)	>75%	500,000
CD34+	>80%	36,000,000
MSC's	>80%	72,000,000
BMMC's	>75%	294,000,000

Table 4. MMT scores over 5 month period post-stem cell treatment.

Muscle	**Left**	**Right**
Upper Extremity: Upper trapezius	5/5	5/5
Middle Deltoid	**5/5**	**5/5**
Anterior Deltoid	**5/5**	**5/5**
Pectoralis Major	**4/5**	**4/5**
Rhomboids	**4/5**	**4/5**
Biceps	5/5	5/5
Triceps	2/5	2/5

Brachioradialis	5/5	5/5
Serratus Anterior	5/5	5/5
Wrist extension	5/5	**5/5**
Abductor digiti minimi	1/5	**1+/5**
Flexor Digitorum Superficialis	3+/5	3+/5
Flexor Digitorum Profundus	2/5	2/5
Trunk: Abdominals	1+/5	1+/5
Lower Extremity: Iliopsoas	**2-/5**	1+/5
Gluteus Maximus	1+/5	**2-/5**
Gluteus Medius	**1+/5**	**1+/5**
Hip Adductors	**2+/5**	**2+/5**
Quadriceps	**2-/5**	1/5
Hamstrings	1+/5	1/5
Gastrocnemius	**2+/5**	1+/5
Tibialis Anterior	1+/5	**1/5**
Extensor Hallucis	**2/5**	0/5

Appendix 1. MMT scores at four months post-injury.

Muscle	**Left**	**Right**
Upper Extremity: Upper Trapezius	4/5	4/5
Middle Deltoid	4+/5	2+/5
Anterior Deltoid	3-/5	2+/5

Posterior Deltoid	3-/5	3+/5
Pectoralis Major – clavicle	3-/5	3-/5
Pectoralis Major – sternum	3+/5	3+/5
Pectoralis Minor	4/5	4/5
Rhomboids	3+/5	3+/5
Biceps/Brachialis	4+/5	4/5
Triceps	3+/5	3-/5
Pronators	3/5	3+/5
Supinators	4+/5	4+/5
Wrist extension	4/5	3+/5
Finger Abduction	2-/5	0/5
Flexor Digitorum Superficialis	3-/5	3-/5
Flexor Digitorum Profundus	3+/5	1/5
Lumbricals	3+/5	3/5
Trunk: Erector Spinae	 1+/5	 1+/5
Abdominals	2/5	2/5
Lower Extremity: Iliopsoas	 2-/5	 1+/5
Gluteus Maximus	2+/5	1+/5
Gluteus Medius	1+/5	1/5
Hip Adductors	2+/5	2+/5
Quadriceps	4/5	3-/5
Hamstrings	3-/5	1+/5

Gastrocnemius	2+/5	2-/5
Tibialis Anterior	3-/5	0/5
Peroneals	2+/5	0/5
Extensor Digitorum Longus	2-/5	1/5
Extensor Hallucis	4/5	0/5
Flexor Digitorum	2+/5	1+/5