The effectiveness of a home-based, patient-specific, functional exercise program on patients with inclusion body myositis (IBM)

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The Effectiveness of a Home-Based, Patient-Specific, Functional Exercise Program on Patients with Inclusion Body Myositis (IBM)

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Supervisor: Dr Dylan Edwards

Date of Submission: 07 - 11 - 2006
ABSTRACT

Previous research has shown exercise to be beneficial in the treatment of myositis-affected patients. However, the potential of functional exercises to improve muscle strength and function in the absence of disease progression markers in patient’s with Inclusion Body Myositis (IBM) is not well understood. It is believed that the initial exercise dose and patient specificity is of paramount importance in the successful use of this modality in the routine management and long term treatment of such patients. The objective of this study was to investigate the effects of a home-based, patient-specific functional exercise programme, including aerobic exercise and resistance training, on muscle strength, endurance and function, and the aerobic capacity of the patient.

Pre muscle strength and functional assessments, and a maximal aerobic exercise test were conducted on seven IBM patients’ prior to a 12-week training period. As part of the patient’s routine management, the patients maintained their scheduled visits to the neuromuscular clinic whereby their serum creatine kinase (CK) levels were assessed pre- and post-training intervention. The patients’ were gently and selectively overloaded in the early stages of their 12-week exercise program to encourage compliance and gradual adaptation, and to prevent ‘overtraining’ early in the program. The exercise program combined upper and lower body resistance training exercises with an aerobic component.

It was anticipated that the patients would exercise frequently at low intensities and at volumes that would optimally induce muscular strength and endurance improvements. Integral to the prescription of exercise for this patient group was the patient-specificity of the exercise dose being prescribed and the method of exercise overload. The patient’s progress was monitored by fortnightly phone calls; maintenance of the patients scheduled visits to their specialist at the neuromuscular clinic, and a ‘training diary’ was given to the patient to fill out daily. At the conclusion of the training intervention period, all parameters of muscle strength and function were reassessed, and the patients undertook follow-up testing of their maximal aerobic capacity.
The results show that, a diseased muscle, having undergone exercise training, maintained its strength (knee extension [100.9±10%]) (mean±standard error [SE]), whilst significant improvements (p < 0.05) were observed in otherwise healthy, trained muscles, with hip abduction strength improving by 59.1±31%, shoulder abduction strength increasing by 66.1±12% and hip flexion strength increasing by 83.7±35%. Functional assessments showed that there was not a statistically significant improvement in the time taken to perform a stair climb and walk 30 metres, and also the amount of paces used during the walk. However, the patient group improved in all functional tasks.

Research suggests that muscle strength and function can be improved by resistance training and an aerobic exercise program. However, further research is required to evaluate the effects of a mild, daily, exercise program performed in the patient’s home. Exercise guidelines for this clinical population are substantially lacking. However, this study has added to the current depth of knowledge regarding exercise and Inclusion Body Myositis patients’. Program adherence, exercise prescription and progression and program monitoring are areas which require further examination in long-term, multi-centre exercise intervention trials. It would appear that an exercise program tailored to the individual is important for the clinical management of the disease.
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Signed...... ...........................................................

Dated...... ........................................................... 2008
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1. Introduction

Inclusion Body Myositis (IBM) is an idiopathic inflammatory myopathy (IIM) that is characterized by progressive muscle weakness and reduced muscle strength, endurance and function (Alexanderson & Lundberg, 2005; Mastaglia, Garlepp & Phillips, 2003). It is the most common inflammatory myopathy amongst adults over 50 years of age and is more common in men than women (Felice, Relva & Conway, 1998; Ranque-Francois, Maisonobe, Dion, Piette, Chauveheid, Amoura & Papo, 2005; Sivakumar & Dalakas, 1997; Vogel, 1998). Prominent clinical findings include asymmetric weakness in both distal and proximal muscle groups, in particular the quadriceps femoris muscles and wrist and finger flexors (Amato, Gronseth, Jackson, Wolfe, Katz, Bryan & Barohn, 1996; Arnardottir, Alexanderson, Lundberg & Borg, 2002; Felice, Relva & Conway, 1998; Lotz, Engel, Nishino, Stevens & Litchy, 1989).

In patients with IBM, serum creatine kinase is often elevated, whilst histological findings include rimmed vacuoles, endomysial inflammation, beta-amyloid accumulation and atrophic fibres (Arnardottir, et al., 2002; Spector, Lemmer, Koffman, Fleisher, Feuerstein, Hurley & Dalakas, 1997). The rate of progression of IBM is relatively slow compared to other forms of IIM, with muscle weakness developing insidiously (Felice, Relva & Conway, 1998; Lotz, Engel, Nishino, Stevens & Litchy, 1989; Mastaglia, Garlepp, Phillips & Zilko, 2003). This can result in a diagnosis not being made for several years after the patient initially complains of symptoms (Phillips, Zilko & Mastaglia, 2000).

The pattern of muscle weakness in IBM patients is primarily the early atrophy of the quadriceps femoris muscle, which often leads to the patient falling due to their 'knees buckling' or the patient tripping over an obstacle due to their inability to raise their foot to the height they perceive they are raising it to safely clear the obstacle. The initial presentation is often due to the patient having experienced a fall or near-fall which the patient has difficulty explaining or justifying why it occurred (Mastaglia, et al., 2003). The selective pattern of muscle involvement in IBM patients can result in the clinical diagnosis of the disease (Mastaglia, et al., 2003). However, a muscle biopsy is commonly used and is thought to be the definitive diagnostic process, enabling not only a diagnosis to be made, but it can also indicate the severity
of the disease in its current state and confirm the actual form of myositis that is affecting the patient (Mastaglia, et al., 2003). The use of magnetic resonance imaging (MRI) can assist in the confirmation of a diagnosis, in particular if a muscle biopsy is inconclusive or when atypical muscle involvement is prevalent (Mastaglia, et al., 2003).

Corticosteroids and immunosuppressive agents are generally accepted as the medical treatment for patients with IBM, but even short-term benefits from using these are rare (Isenberg, Allen, Farewell, Ehrenstein, Hanna, Lundberg, Oddis, Pilkington, Plotz, Scott, Vencovský, Cooper, Rider & Miller, 2004; Mastaglia, 2000). Immunoglobulin therapy has been shown to elicit a mild improvement and possibly slow the disease progression (Amato, Barohn, Jackson, Pappert, Schenk & Kissel, 1994; Dalakas, Sonies, Dambrosia, Sekul, Cupler & Sivakumar, 1997; Soueidan & Dalakas, 1993). A typical characteristic of IBM is its resistance to the commonly accepted forms of immunotherapy (Amato et al., 1996; Oldfors & Lindberg, 1999).

It was previously thought that physical exercise should be avoided due to the concern that it would enhance the inflammatory process (Alexanderson & Lundberg, 2005; Dalakas, 1989; Jones, Newham, Round & Tolfree, 1986). However, studies have shown physical training of patients with polymyositis (PM) and dermatomyositis (DM) resulted in muscle strength improvements in the absence of an inflammatory reaction (Alexanderson, Stenstrom & Lundberg, 1999; Wiesinger, Quittan, Aringer, Seeber, Vole-Platzer, Smolen & Graninger, 1998A; Wiesinger, Quittan, Graninger, Seeber, Ebenbichler, Sturm, Kerschan, Smolen & Graninger, 1998B). Exercise training programs targeting improvements in muscular strength should include isotonic, isometric and isokinetic exercises (Aitkens, McCory, Kilmer & Bernauer, 1993; Mastaglia, et al., 2003).

Falling due to lower body weakness and the increased risk of cardiovascular disease due to reduced mobility are significant health issues that often lead to disability and a decreased quality of life in IBM patients. Exercise programs can result in strength gains, prevent strength loss and can be performed without muscular fatigue or inflammation in IBM patients (Arnardottir, et al., 2002; Spector, et al., 1997). Physical activity has been shown to be a safe and appropriate enablement
strategy in other inflammatory myopathies. Exercise has been shown to improve a patient's muscular strength and endurance, and importantly, can improve the patient's well being (Wiesinger, et al., 1998A). There is evidence to suggest exercise could potentially play an important role in the delaying of the disease progression, with an investigation into the pattern of muscle weakness in IBM patients presenting relatively novel findings (Felice, Relva & Conway, 1998). It was found that weakness and muscle atrophy in the forearms was particularly more profound on the non-dominant side of the body. The investigators in this study suggested that daily, functional activities such as washing, buttoning and writing delay the atrophy and progressive weakness associated with this muscle disease, and therefore concluded that performing exercise may result in a delaying of the disease progression (Felice, Relva & Conway, 1998).

The purpose of this study is to investigate the effectiveness of a functional, home-based, patient-specific exercise program on muscle strength, endurance and function in an IBM patient group. The potential of functional exercises to improve muscle strength and function in the absence of disease progression markers is not well understood. It is believed that an exercise program tailored to the individual is important for the routine management and long-term treatment of the disease.

Integral to this study is the correct prescription of both resistive and aerobic exercise, in particular the type and amount of the chosen exercises, and the individuality of the exercise programs to be given to these patients. In undertaking this study, it was believed that an aggressive exercise program will result in either non-compliance in the program or excessive muscle fatigue/soreness leading to withdrawal from the study. Consequently, the patient specific exercise programs that were prescribed to the IBM patients were initially very conservative to account for these important issues and to ensure the technical aspects of the exercises are learnt so that the patient employed the correct technique and applied the adequate loading onto their muscles.
2. Literature Review

2.1 Idiopathic Inflammatory Myopathies

Idiopathic Inflammatory Myopathies (IIM) is a diverse group of disorders with various clinical and pathological presentations that are typically characterised by muscle weakness and chronic muscle inflammation (Oddis, Rider, Reed, Ruperto, Brunner, Koneru, Feldman, Giannini & Miller, 2005; Phillips & Mastaglia, 2000). Mastaglia, Phillips and Zilko (1997) report the cause of some IIM's to be "identifiable viral, bacterial, fungal, or parasitic micro-organisms". They can be localised and restricted to a single muscle, or extensive and involve a range of skeletal muscles (Mastaglia, et al., 2003). Three common forms of IIM's are polymyositis (PM), dermatomyositis (DM) and inclusion body myositis (IBM), and each has distinctive clinical, histological and pathological manifestations (Bohan & Peter, 1975; cited in Isenberg, et al., 2004; Mastaglia, et al., 2003). Idiopathic inflammatory myopathies are immune-mediated myopathies which can occur in isolation, in conjunction with other autoimmune disorders or with connective tissue disorders (Mastaglia, et al., 2003).

2.2 Inclusion Body Myositis

Originally developed in 1971 (Yunis & Samaha, 1971; cited in Tawil & Griggs, 2002), the term 'inclusion body myositis' was applied to an idiopathic inflammatory myopathy variant clinically and pathologically different to other known myopathies. Yunis and Samaha (1971; cited in Derk, Vivino, Kenyon & Mandel, 2003) used it to describe a patient with abnormal tubular filaments found within muscle fibres on electron microscopy. It was further elaborated on in 1978 by Carpenter, Karpati, Heller and Eisen (1978; cited in Derk, et al., 2003) who found distinguishing features to dissociate it from polymyositis and dermatomyositis. 'Inclusion' refers to the inclusion bodies found in the prominently affected muscle cells, whilst 'myositis' is an acknowledgement of the inflammation that is found in the involved muscles.

IBM is the most common inflammatory myopathy in individuals over the age
of 50, and is believed to be more common in males (Felice, Relva & Conway, 1998; Lotz, Engel, Nishino, Stevens & Litchy, 1989; Oldfors & Lindberg, 1999; Phillips, Zilko & Mastaglia, 2000). In a 10-year retrospective study on the prevalence of IBM in Western Australia, Phillips, Zilko and Mastaglia (2000) reported the prevalence of IBM to be 9.3 per million population in Western Australia (using population figures adjusted for sex, the gender differentiated figures were 10.9 and 7.7 for males and females respectively per million). Due to the diagnostic process, the time differential between the onset of symptoms and diagnosis, and the chronicity of the disorder, the authors acknowledge their figures to most likely be an underestimation and conclude that further population studies are required.

Ninety five IBM patients were identified in a study in The Netherlands, with 43 males and 21 females comprising the subject population (31 were unable to complete the study for various reasons) (Badrising, Maat-Schieman, van Houwelingen, van Doorn, van Engelen, Faber, Hoogendijk, de Jager, Koehler, de Visser, Verschuuren & Wintzen, 2005). Badrising, Maat-Schieman and van Duinen (2000) estimated the prevalence of IBM in The Netherlands to be 4.9 per million population (the investigators thought this to be an underestimation though). However, in respect to the two described studies, different criterion was used to diagnose the IBM, which may affect the resultant prevalence figures. Worldwide figures of the prevalence of IBM are unknown, and certainly more research is required to systematically determine how common IBM is, and to account for other epidemiological aspects of the disease.

2.3 Clinical Presentation

A slowly progressive muscle disease of insidious onset, muscle weakness in IBM patients is typically selective, with initial atrophy and weakness found in the quadriceps femoris muscles in the lower limbs (Mastaglia, et al., 2003; Oldfors & Lindberg, 1999; Tawil & Griggs, 2002). The weakened knee extensors, and the falls they predispose the patient to, are often the initial presenting symptom of IBM (Mastaglia, et al., 2003). The forearm flexors are also selectively involved in the earliest stages of the disease progression, in particular the flexor digitorum profundus muscles, resulting in an increasing difficulty in maintaining flexion of the distal
Phalanges when the patient is performing a task requiring grip strength (Mastaglia, et al., 2003).

Phillips, Cala, Thickbroom, Melsom, Zilko and Mastaglia (2001) suggest the involvement of the medial gastrocnemius is also typical of IBM. Finger extensors, thumb hyperextension and flexor digitorum sublimis gradually become involved, along with the more proximal muscles in the upper limbs (Mastaglia, et al., 2003). Difficulty swallowing has also been recorded by IBM patients due to the involvement of pharyngeal and oesophageal muscles (Badrising, et al., 2005; Mastaglia, et al., 2003; Ranque-Francois, et al., 2005; Tawil & Griggs, 2002).

Atypical patterns of muscle involvement are not rare, with a more proximal or asymmetric pattern of muscle involvement having been reported (Lindberg, Persson, Bjorkander & Oldfors, 1994). This is supported by a study by Phillips et al (2001) which concluded that the common pattern of muscle involvement is not always the case in IBM patients. Whilst it has been widely acknowledged as being the most common myopathy in individuals over the age of 50 (Ranque-Francois, et al., 2005; Sivakumar & Dalakas, 1997; Vogel, 1998), a study by Badrising et al (2005) reported the onset of symptoms to be generally after the age of 40 as a common characteristic. There is often a substantial time differential between the onset of symptoms and actual diagnosis, with Phillips, Zilko and Mastaglia (2000) reporting an average delay of 4.4 years.

2.4 Etiology

The etiology of IBM is largely unknown (Tawil & Griggs, 2002). Clinically, IBM has been linked to mild increases in other systemic autoimmune disorders and there is strong evidence to suggest it is an immune-related disease (Tawil & Griggs, 2002). Mastaglia, Phillips and Zilko (1997) support this by claiming in IBM “cellular immune mechanisms have been directly implicated in causing the muscle fibre injury”: Cytotoxic CD8+ T-cells are prominent within endomysial infiltrations, major histocompatibility complex (MHC) class 1 expression by muscle fibres, and the infiltration of non-necrotic fibres by CD8+ lymphocytes and macrophages are typically found at the cellular level (Mastaglia, Phillips & Zilko, 1997; Mastaglia, et
The muscle tissue of an IBM patient exhibits pro-inflammatory cytokines interleukin-1 (IL-1\textalpha{}), interleukin H1 (IL-1\beta{}), interferon-\gamma{}, lymphotoxin and tumour necrosis factor (TNF-\alpha{}) predominantly produced by macrophages and monocytes (Lundberg, 2000; Lundberg & Nyberg, 1998; Mastaglia, et al., 2003). These play important roles as up-regulating and down-regulating factors of molecules integral to the homing process of inflammatory cells to the tissue (Lundberg & Nyberg, 1998). Cytokines can perform functions such as T-cell activation, lymphocyte and mononuclear phagocyte recruitment, stimulation of expression of major histocompatibility complex molecules and potentially can directly damage target cells (Mastaglia, et al., 2003). These functions can then aid in the generation or further enhancement of autoimmune responses and assist in the local inflammatory response (Mastaglia, et al., 2003).

Inflammatory inhibiting cytokines, such as transforming growth factor-\beta{} and interleukin 4 (IL-4), have been found in idiopathic inflammatory myopathies (Lundberg, 2000). Chemotactic and inflammatory chemokines have also been observed in IIM’s, including monocyte chemoattractant protein-1 (MCP-1), macrophage inflammatory protein-1\alpha{} (MIP-1\alpha{}) and regulated-upon-activation normal T-cell expressed and secreted (RANTES) (Confalonieri, Bernasconi, Megna, Galbiati, Cornelio & Mantegazza, 2000; Lundberg, 2000; Mastaglia, et al., 2003).

The presence of T-cell receptors in the incursive lymphocytes indicates a possible case of restrictive gene rearrangements, raising the prospect that the T-cell activation is due to a potential superantigen (Lindberg, Oldfors & Tarwoski, 1994; Tawil & Griggs, 2002). The persistence of this pattern throughout the disease progression implies that the primary antigenic stimulus continues to cause the immune-mediated muscle disease post-presentation of the initial symptoms (Tawil & Griggs, 2002). However, the absence of long term and complete responses to immunosuppressive agents indicates that there maybe more to the cause of IBM than the immune-mediated etiological belief (Tawil & Griggs, 2002).

Abnormal accumulation of proteins, including beta-amyloid, within the
vacuolated muscle fibres is commonly reported in IBM patients, however, it is unclear as to what initiates their deposition and whether or not they result from or cause the inflammatory process (Askanas & Engel, 2003; Derk, et al., 2003; Tawil & Griggs, 2002). The relationship between these accumulated proteins and immune mechanisms prevalent in IBM patients is unknown (Mastaglia, Phillips & Zilko, 1997). Evidence of nitric oxide induced oxidative stress, the contributions of genetics and the possibility of the overexpression of αB-crystallin in IBM patients further confounds the process of establishing a definitive etiology for this inflammatory myopathy (Alexanderson & Lundberg, 2005; Mastaglia, et al., 2003; Ranque-Francois, et al., 2005; Tawil & Griggs, 2002).

2.5 Diagnosis

Early and accurate diagnosis is important to guide the treatment process and enable a definitive prognosis to be made as early as possible. This is particularly important when distinguishing the various forms of idiopathic inflammatory myopathies, as PM/DM often respond favourably to treatment, whilst IBM has been shown to be quite resistant to various therapeutic interventions (Mastaglia, et al., 2003; Mastaglia, Phillips & Zilko, 1997; Ranque-Francois, et al., 2005).

IBM patients have a selective pattern of muscle involvement of the quadriceps femoris muscles and the forearm flexors of the upper limbs (Phillips, et al., 2001). The greater susceptibility of some muscles to the muscle disease IBM is currently an unresolved issue. Phillips et al (2001) lists possible reasons for this selectivity, including muscle size differences, fibre-type proportions, physiological roles and functional reserve of different muscles, and the possibility of an accumulation of mutant DNA deletions that occur with ageing. This characteristic muscular selectivity can be more difficult to identify in the latter stages of the disease, and atypical patterns of muscle involvement and asymmetric weakness have been found (Mastaglia, Phillips & Zilko, 1997). The insidious onset of proximal and distal weakness in an individual over the age of 50 should raise initial suspicions of IBM (Ranque-Francois, et al., 2005)

As a prominent marker of muscle damage, elevated serum creatine kinase
(CK) has been used to support the diagnosis of IBM, however normal or slightly elevated levels of CK are typically found in IBM patients (Badrising, et al., 2005; Derk, et al., 2003; Mastaglia, Phillips & Zilko, 1997; Ranque-Francois, et al., 2005; Tawil & Griggs, 2002). The extent and severity of the myositis can be indicated by electromyography, but ultimately, a muscle biopsy is the most definitive standard in providing a conclusive confirmation of IBM (Derk, et al., 2003; Mastaglia, et al., 2003; Mastaglia, Phillips & Zilko, 1997; Tawil & Griggs, 2002). A muscle biopsy should ideally be performed prior to the commencement of treatment and will not only allow confirmation of the diagnosis but will also provide an insight into the severity and extent of the muscle inflammation and exclude any other forms of myopathies (Mastaglia, Phillips & Zilko, 1997; Mastaglia, et al., 2003).

An open biopsy is preferable, and using magnetic resonance imaging (MRI) to assist in selecting a biopsy site may prevent a potential sampling error that could possibly interfere with the identification of characteristic clinical features or if the clinical picture is not obvious (Mastaglia, et al., 2003; Oldfors & Lindberg, 1999). The muscle biopsy should identify a number of features, including endomysial inflammation and invasion of non-necrotic fibres, rimmed vacuoles and intracellular amyloid deposits (Tawil & Griggs, 2002). The presence of these features provides a definite diagnosis of IBM, and other clinical and pathological criteria are not required. Griggs, Askanas, DiMauro, Engel, Karpati, Mendell & Rowland (1995) developed a distinct criteria to enable diagnosis that took into consideration typical biopsy findings to allow rapid diagnosis, and also other clinical and laboratory features (refer to Appendix B) that enable diagnosis despite possible atypical muscle involvement or the absence of the primary clinical diagnostic features (Refer to Appendix B for the diagnostic criteria of IBM)

2.6 Treatment

The treatment of Inclusion Body Myositis can be considered to currently be a work in progress (Arnardottir, et al., 2002; Ranque-Francois, et al., 2005). The unknown etiology of the disease presents clinicians with a challenging task in developing strategies or therapeutic measures to treat IBM. The current options available to patients are all non-selective in relation to their impact on the immune
system (Mastaglia, et al., 2003; Mastaglia, 2000). It has been shown that the conventional method of pharmacological treatment prescribed to IBM patients often has little, if any effect, on the progression of the disease (Alexanderson & Lundberg, 2005; Griggs & Rose, 1998). However, most IBM patients are initially placed on a course of medication, such as a corticosteroid (most commonly prednisone) and an immunosuppressive agent, such as methotrexate, to combat the disease to some degree, with the patient’s responses to these drugs varying greatly (Mastaglia, 2000).

Immunoglobulin therapy has been trialled previously, with findings to suggest it could play a role in the treatment of the muscle disease (Mastaglia, Phillips and Zilko, 1998; Soueidan & Dalakas, 1993). A slowing of the disease and possible moderate improvement has been reported in a number of short-term studies (Amato, Barohn, Jackson, Pappert, Sahenk & Kissel, 1994; Dalakas, et al., 1997; Soueidan & Dalakas, 1993; Walter, Lochemler, Toepfer, Schlotter, Reilich, Schroder, Muller-Felber & Pongratz, 2000). In a study by Mastaglia, Phillips and Zilko (1998), muscle myometry scores improved following intravenous immunoglobulin (IVIg) in some cases, however, only slight functional improvements were observed, and on the basis of this, it can be difficult to justify considering the expensive nature of the treatment (Mastaglia, Phillips & Zilko, 1998).

Other forms of therapy have been proposed, including, L-carnitine, coenzyme Q, antioxidants and testosterone, but are yet to be clinically assessed (Engel & Askanas, 1998). Despite the uncertainty regarding various drug therapies and their ultimate effect on IBM patients, these treatment modalities deserve further research in the form of multi-centre, long-term, randomized, placebo-controlled therapeutic trials (Mastaglia, 2000; Walter, et al., 2000). Exercise therapy has been trialled with some positive results for IBM patients in the absence of disease progression markers (Arnardottir, et al., 2002; Spector, et al., 1997).

2.7 Exercise and IBM

2.7.1 Strength Training

Strength training in otherwise healthy individuals is well established as a means of increasing muscle strength, endurance and size (Feigenbaum & Pollock,
1999), but it can also play an important role in the rehabilitation of patients with neuromuscular disorders (McCartney, Moroz, Garner, McHomas, 1988; Milner-Brown & Miller, 1988; Spector, Gordon, Feuerstein, Sivakumar, Hurley & Dalakas, 1996). Phillips and Mastaglia (2000) have demonstrated its benefits in the management of various myopathies; however, its presence in the long-term treatment and clinical management of inflammatory myopathy patients is not well understood. Further research is required in regards to the establishment of training protocols that will optimally induce muscle strength, endurance and functional changes, and the development of outcome measures that are suitably sensitive, and provide reliable and valid results in assessing the impact of exercise as a therapeutic means in neuromuscular disordered patient groups (Mastaglia, et al., 2003). The repetitive nature of resistance training should not prevent the patient’s muscles from responding positively to the strength tasks (Taivassalo, De Stefano, Chen, Karpatic, Arnold & Argov, 1999).

Two key studies provide the current basis of knowledge in regards to the effect of an exercise training program on IBM patients. These investigations were warranted on the basis of positive findings from physical training in PM/DM patients and other myopathic patients. Wiesinger et al (1998A) found significant improvements in muscle strength, oxygen uptake and overall wellbeing. The six week training intervention also saw improvements in ‘activities of daily living’ (ADL) scores, whilst there was no significant increase in disease activity compared to the control sample.

Wiesinger et al (1998B) reported a clinically significant increase in the aerobic capacity of the sample population. Peak oxygen uptake, peak isometric torque in the lower extremities and ADL scores all rose to significant levels in the absence of a rise in serum creatine phosphokinase (CPK). The six-month study included a combination of stationary cycling and step aerobics, as did the earlier study by Wiesinger et al (1998A). However, the duration of the 1998A study (6 weeks) and the sample size of the later study (1998B) (n=8) must be considered when analysing their results.

Alexanderson, Stenstrom and Lundberg (1999) performed a study investigating the effects of a home exercise program on PM/DM patients, with
positive results reported. In accordance with the Functional Index (FI) scale, six of ten cases were found to have significantly improved muscle function in the absence of a rise in CPK. The remaining four patients all reported functional improvements. Muscle biopsies and MRI's were also used to confirm the safety of the exercise program in terms of monitoring potential muscle inflammation as a result of the exercises performed.

The Short Form-36 (SF-36), which is a widely used assessment tool in inflammatory myopathy studies (Isenberg, et al., 2004), was used to assess changes in health and wellbeing, and significant improvements in health status were found as a result of the exercise program. Various other investigations have been performed to assess the impact of exercise, in particular strength-training programs, on patients with myopathies (Phillips & Mastaglia, 2000). Despite the small sample sizes that are prevalent in the majority of these studies, muscle strength improvements are typically seen as a result of various exercise protocols and training periods.

An investigation into the asymmetrical patterns of muscle weakness and atrophy observed in IBM patients suggests that exercise may potentially delay the progression of the muscle disease (Felice, Relva & Conway, 1998). The study found the non-dominant forearm flexor was significantly more atrophied and weaker than the dominant forearm flexor. From this, the investigators concluded that dominant side, daily activities, such as writing, washing and buttoning, delay the progression of the disease, and evidence of less pronounced atrophy in other groups that rarely perform unilateral exercises support this conclusion (Felice, Relva & Conway, 1998). The investigators recommend the prescription of moderate resistant exercise, in particular targeting the weakened forearm flexors and quadriceps muscles, and acknowledge the need for further studies in this area (Felice, Relva & Conway, 1998).

Spector et al (1997), conducted a 12-week progressive resistance strength-training program, primarily designed to target the predominantly weakened muscles in 5 IBM patients. The exercise program was prescribed with upper and lower extremity exercises alternated between exercise sessions to minimize fatigue, and suitable recovery periods, and volumes and intensities of workload were chosen. These ‘training’ variables were prescribed on the basis of previous resistance training
studies in a Post-Polio Muscular Atrophy patient group, in which dynamic muscle strength increased following a 10-week progressive resistance strength training program (Spector, Gordon, Feuerstein, Sivakumar, Hurley & Dalakas, 1996).

The investigators also minimised the eccentric phase of the chosen activities. Resistance training exercises cause damage to the muscle, but in an otherwise healthy population, neural adaptation and muscle hypertrophy occur as a result of this, and the muscles repair and regrow to become larger and stronger (Sale, 1988). Eccentric exercises damage the muscle and can disrupt the muscle cell membrane, as evidenced by the release of serum CK from the damaged fibres (Jones, Newham, Round & Tolfree, 1986), an increase in cytokines in the muscle (Fielding, Manfredi, Wenjing, Fiatarone, Evans & Cannon, 1993) and local inflammation (Fielding, et al., 1993; Luthi, Howald, Claasen, Rosler, Vock & Hoppeler, 1986). Concentric exercises minimise this muscle damage whilst still being beneficial to the patient, such that muscle strength and size gains typically occur (Hurley, Redmond, Pratley, Trueth, Rogers & Goldberg, 1995). In this study, the concentric phase of the prescribed resistance exercises was a particular focus. Strength assessments, fatigue and activities of daily living scales, MRI’s and muscle biopsies to analyse the immunochemistry and histopathological changes, and markers of muscle damage were used as assessment tools to quantify the effect of the training program. It was concluded from this study that IBM patients are able to safely participate in regular resistance training in the absence of excessive muscle fatigue, immunological and histological abnormalities, and strength gains, in particular in the least weak muscles, can be expected.

Arnardottir et al (2002) investigated the effect of exercise on IBM patients with their study on the effects of a home-based exercise program on muscle function and it’s implications for the inflammatory response by the muscle. Seven IBM patients were subject to a 12-week, 5 days-a-week exercise program designed to be implemented in the patients home. Easy and moderate exercise programs were prescribed to the patients based upon their Functional Index (FI) score, and they included both resistive exercises, mobility exercises and a stretching routine. The study also included an aerobic component, with the patients instructed to take a 15-minute self-paced walk 5 days a week. The prescription of exercises and the
associated training variables was based upon work done on a PM/DM training study which resulted in positive muscle function effects being observed following the intervention (Alexanderson, Stenstrom & Lundberg, 1999).

In Arnardottir’s et al (2002) investigation, the exercise program was shown to be a safe treatment option with muscle inflammation and the histopathology of the disease remaining stable throughout the intervention period. Whilst there was an absence of significant strength gains across all parameters tested, the program was well tolerated by the group and there was not a reduction in muscle strength whilst the patients underwent the exercise training. The investigators acknowledged experimental deficiencies and the relatively low intensity of the prescribed exercise program may have contributed to the lack of significant data. However, this study provides further evidence of the delaying capacity exercise may have on the progression of the disease.

The small sample size’s in both studies, the duration of the training periods, and the absence of statistically significant improvements in muscle function and strength measures, reductions in fatigue and increases in ADL scores suggests further research is required before conclusive statements regarding the effect of exercise on IBM patients can be made. This is acknowledged by both Spector et al (1997) and Arnardottir et al (2002). However, from their studies it can be concluded that exercise can be safely tolerated by IBM patients and can be confidently prescribed in the knowledge it will not lead to a decrease in muscle strength as a result of the training program.

These studies highlight the need for the development of standardised training protocols that will lead to optimal gains in muscle strength, endurance and functional improvements which will, importantly, translate to a higher quality of life and provide the patients with a greater capacity to perform ADL’s. For exercise as an evidence-based, therapeutic intervention to be established and integrated into the daily lives of IBM patients, further research is required. Patient-centred, resistance training protocols, sensitive and reliable outcome measures and disease-specific health status measures for idiopathic inflammatory myopathy patient groups are areas which should be of particular interest in future studies.
2.7.2 Aerobic Exercise

The health benefits derived from aerobic exercise are numerous and far-reaching and have been well established, with 30 minutes or more per day the prescribed amount for disease prevention and the promotion of good health in healthy individuals (Pate, Pratt, Blair, Haskell, Macera, Bouchard, Buchner, Ettinger, Health & King, 1995; Pollock, Gaesser, Butcher, Despres, Dishman, Franklin & Garber, 1998). Adaptations in the heart and skeletal muscle systems, disease prevention, improved respiratory function and overall well-being highlight the importance of exercise for all individuals, including patients with inflammatory myopathies (Mastaglia, et al., 2003; Taivassalo & Haller, 2005). Taivassalo et al (1999) demonstrated aerobic exercise training can elicit benefits in nonmetabolic myopathies and mitochondrial myopathies, with significant improvements found in estimated aerobic capacity, heart rate and blood lactate at submaximal exercise intensities. A lifestyle change and appropriate physical therapy habits should be the aim in the prescription of an exercise program designed to attain maximum benefit whilst minimising the risk to the participant (Pollock, et al., 1998).

These findings are supported by Taivassalo, Shoubridge, Chen, Eng, Kennaway, Phil, DiMauro, Arnold and Haller (2001) and Taivassalo and Haller (2005). However, as Taivassalo and Haller (2005) and Taivassalo et al (1999) have stated in regards to patients with mitochondrial myopathies and other various neuromuscular disorders, exercise intolerance can be a prominent manifestation of the muscle disease and the reduced activity level of the IBM patient. Characterised by fatigue at low exertion levels, weakness of active muscles and lactic acidosis, the resultant deconditioning and increased functional limitations not only further emphasises the individual’s sedentary lifestyle, but also increases the risk of disease (Taivassalo & Haller, 2005; Trenell, Sue, Kemp, Sachinwalla & Thompson, 2006).

The muscle weakness, reduced endurance and increased fatigue which tend to dominate the lives of patients with inflammatory myopathies are impairments which negatively affect the patient’s quality of life, independence and general health and well-being (Phillips & Mastaglia, 2000). The reduction in aerobic capacity results in the patient’s mobility being severely affected and subsequently cardiac and
respiratory function is impaired, putting the patients at an increased risk of cardiovascular disease (Alexanderson & Lundberg, 2005; Hebert, Byrnes, Baethage, Wolf & Kinasewitz, 1990).

Wiesinger, Quittan, Nuhr, Volc-Platzer, Ebenbichler, Zehetgruber and Graninger (2000) reported PM/DM patients to have reduced peak oxygen uptake values compared to age and sex-matched controls. It was concluded from this study that a number of factors possibly contribute to why PM/DM patients are aerobically impaired; including the sedentary lifestyle the disease tends to impart upon the patient, cardiac involvement, pulmonary involvement or muscle atrophy or inflammation as a result of the disease. Whilst further clarification is required to determine the primary cause of their reduced aerobic capacity, it was shown that a carefully constructed, exercise testing regimen can be safely used to determine the aerobic capacity of myositis patients.

Wiesinger et al (1998B) reported an aerobic capacity increase following their physical training program in PM/DM patients. Using a patient-specific cycling protocol, the patients combined this with a step aerobics exercise session to develop their aerobic capacity. The use of the cycling protocol to aerobically train the patients was justified by the investigators on account of the concentric exercises causing less muscle damage than eccentric exercise (this is when the active muscle is lengthened). (Wiesinger, et al., 1998B). The patient’s aerobic capacity was increased by 28%, which was a significant improvement. A 9% reduction in resting heart rate was also found, whilst the ventilatory threshold of the patients was increased by 8%, which was another statistically significant result.

Hicks, Drinkard, Summers and Rider (2002) found similar findings in their study into the effects of aerobic exercise in juvenile DM patients. Taivassalo et al (1999) demonstrated an aerobic exercise program can provide physiological and functional benefits in the absence of disease progression markers in chronic myopathy patients. Taivassalo et al (1999) reported positive adaptations from a patient-specific training program that was prescribed at low intensities, but acknowledged the long-term effects of an aerobic exercise program was yet to be established. Exercise as a therapeutic intervention has been shown to improve balance in the elderly, and with
falling a major risk factor in IBM patients, improvements in balance that will reduce the risk of falling is desirable (Barnett, Smith, Lord, Williams & Baumand, 2003).

Numerous other studies have been conducted in assessing the impact of an aerobic training program on patients with various forms of myopathies, with generally positive results having been found. Aerobic capacity, maximum VO2 consumption and exercise tolerance has been demonstrated to improve to significant levels following an aerobic exercise program (Phillips & Mastaglia, 2000). Phillips and Mastaglia (2000) question the relative importance of the duration of the training period, stating that there may not be any additional benefit of implementing a longer training period (>24-weeks) in comparison to a short-term program (>6-weeks). Rather, the intensity of the exercise may have a greater influence on the resultant aerobic capacity changes. To date, there is an absence of information regarding the effect of aerobic exercise training on IBM patients.
3. Materials & Method

3.1 Study design

3.1.1 Patients

Seven Patients (2 women and 5 men, mean age 66.7±6.2 years) with IBM were recruited from the Australian Neuromuscular Research Institute at Sir Charles Gardiner Hospital, Perth, Western Australia. Diagnosis was confirmed by clinical and histological findings, and all have been in a state of progressive decline in muscle strength and function, and overall functional ability, for 5-9 years. This study had ethical approval from Sir Charles Gardiner Hospital and Edith Cowan University, and the each patient signed an informed consent prior to the beginning of this study (refer to Appendix C).

3.1.2 Experimental Design

Clinical examination, muscle strength and function assessments, and a maximal aerobic exercise test were conducted prior to a 12-week exercise training intervention. Serum CK levels were assessed pre- and post-training intervention as part of the patients’ routine management. A Penny and Giles Transducer hand-held myometer (refer to Appendix F) was used to ascertain the patients muscle strength in the following movements bilaterally: shoulder abduction/external rotation, elbow flexion/extension, wrist extension, hip abduction/flexion, and knee flexion/extension. As per Figure 1, trained/untrained movements were tested pre and post intervention in diseased and healthy muscles. Grip strength was also measured using a Spiedel and Keller, Stabil 3 grip dynamometer. Functional tasks evaluated were walking 30 meters unaided, walking up one flight of stairs (11 steps) (Refer to Appendix D for muscle assessment recording worksheet and Appendix E for strength assessment positions for hand-held myometry). Standard instructions and levels of positive reinforcement were implemented throughout the testing occasions for each patient, pre- and post-training intervention.

The patients were also required to fill out the SF-36 instrument to ascertain potential changes in the patients overall health status as a result of the intervention (refer to Appendix G for a sample SF-36). Each patient undertook a maximal aerobic
exercise test on a stationary bike, with the Metamax 3B portable VO₂ system utilised to assess their aerobic capacity. Each patient undertook a familiarisation session prior to the initial test, whereby the patient was prepared with a standard 5-lead ECG and equipped with the Metamax 3B system harness. Resting heart rate (RHR) (beats per minute [bpm]) and blood lactate levels (taken via the fingertip) was taken from the patient, whilst the Borg 0 – 10 Rating of Perceived Exertion (RPE) scale (Borg, 1982), which was to be used at one minute intervals during the test to monitor the patient’s exertion levels, was explained to the patient. The patient was advised to cease the test if they felt unwell for any reason, and this was reinforced by the supervising Doctor who attended the test to ensure a safe test was being conducted and no undue stress was being placed on the patient.

Due the variability in the aerobic capacity of each patient within the patient group, the protocol for the aerobic exercise testing was individualised based on the patients’ familiarisation tests, but only with regards to the wattage amount the patients were to increase every two minutes. Common to the entire patient group was the initial starting load of 20 Watts (W), the timing of the incremental increases in wattage (every two minutes of the test), and the maintenance of a cycling cadence between 40 and 50 revolutions per minute (RPM). The testing protocol was based on similar research previously applied in inflammatory populations (Jeppesen, Olsen & Vissing, 2003; Trenell, et al., 2006) and preliminary tests completed by a number of the IBM patient’s. VO₂ (ml/kg/min⁻¹) peak, heart rate (bpm), blood lactate (mmol⁻¹) and RPE were recorded for analysis and cardiac rhythm was monitored during the test for safety purposes by the trained Doctor in attendance. The tests were performed in the cardio-pulmonary department of Sir Charles Gardiner Hospital, administered by a trained Honours student and a laboratory technician.

3.1.3 Training Program

Each patient undertook a home-based, patient-specific 12-week exercise program integrating stretching exercises, resistance exercises and an aerobic component. The patients’ were very gently overloaded in the early stages of the program to encourage compliance and gradual adaptation, and to prevent ‘overtraining’ in the initial stages of the program. The total amount of exercise prescribed per week, which will be referred to as the training load, comprised the
number of repeated sets, duration of recovery period between exercises, and number of exercises per week. To begin with, the load prescribed was very light in order to assess the patients' tolerance to the tasks assigned, ensure the correct techniques and movements were employed and to monitor the patients' compliance to the overall program.

The patients were presented with an exercise booklet (refer to Appendix H), containing illustrations and exercise descriptions, which entailed the range of stretches and exercises the patient could potentially perform during the intervention period. Exercises were selected that emphasised patient function, and so where possible, multi-joint exercises were preferentially used as opposed to single-joint and movements were performed in functional positions involving balance and stabilizing aspects. Where functional and body weight exercises were considered too difficult, isometric, single joint muscle contractions were performed (American College of Sports Medicine, 2003, p.243).

A range of stretches was prescribed on the basis of increasing joint mobility and improving the patients' muscular flexibility, with particular attention paid to the wrist and finger flexors and extensors which are prominent areas of weakness and exhibit a reduced range of motion in this clinical population. The patients were given approximately 6-8 different stretches to perform, with 2-3 sets to be performed of each exercise and for either 10-15 breaths, or a specific number of repetitions as assigned by the investigator. Counting by number of breaths was encouraged to avoid the patients holding their breaths, which can occur during resistance training exercises, particularly when performing isometric exercises in older trainees (Fleck & Kraemer, 2004, p.21). Exercise selection was patient-specific and prescribed based upon observation of the patient's ability to perform certain movements and areas of reduced joint range of motion. The patient's were instructed to perform their selected stretches once daily.

The resistance exercises were selected on an individual basis and were also prescribed upon observation of the patients' ability to perform various functional movements. Exercises were selected or modified such that between 8-15 repetitions could be performed, then two repetitions less than the maximum number of
repetitions the patient could perform during the initial assessment was prescribed. The exercise program was separated into upper and lower extremity components, with approximately 3 exercises performed 2-3 times each (separated by 3-4 minutes rest), once daily, 3 times per week. With the aerobic component of the patients exercise program to be performed 3 times per week, the patients were encouraged to perform the resistance exercises and the aerobic training on separate days. Accordingly, the patients were to perform the upper and lower extremity exercises on the same day, but to avoid overloading the patient’s, the two components of the resistance exercises were to be performed separately, with one component to be trained in the morning, and then one later in the day. This was to prevent overtraining and enable the patient to recovery between tasks. The patients were also instructed to have one day of rest each week. A study by Kilmer, Wright and Aitkens (2005) on the impact of a home-based physical activity and dietary intervention in people with neuromuscular diseases supports this conservative approach.

The exercises the patients were to perform were initially demonstrated to them, and then performed by the patient themselves under supervision to ensure the correct techniques and movements were being employed. This also allowed the investigator to evaluate the patients’ current levels of muscular strength, endurance and function and to prescribe exercise volume and frequency that would slightly challenge the patient, but would also be achievable. Specifically, mild increments in training load were scheduled fortnightly, although modified according to patient tolerance and compliance. Patients were instructed that if the exercise became ‘easy’ during a given two week period, they could increase the number of repetitions by a maximum of four, for each exercise. The scheduled load increments did not increase all variables simultaneously, but one variable in a given fortnight, and in the following order: exercise number (increased to ~4-6 exercises), then number of repetitions (15 maximum), and lastly, number of sets (maximum of 3). The patients were also asked to contact the investigator to inform them of any program changes when they occurred.

The aerobic component of the training program involved the patients cycling on a Monark Ergomedic 894E stationary cycle ergometer at an intensity corresponding to 80% of their maximum heart rate achieved during their maximal
aerobic test (Taivassalo, De Stefano, Argov, Matthews, Chen, Karpati & Arnold, 1998). Polar A3 Heart rate monitors to enable the patients to exercise at the prescribed intensity were borrowed by the patients from the Edith Cowan University Sports Science Department for the duration of the training period. Volume and frequency of this component of the patients exercise programs was individually assessed and administered in consultation with Senior Physicians at the Hospital. The patients were instructed to cycle 3 times per week, and progression of the patients’ aerobic training component was achieved in much the same way as the resistance training component of their exercise program. If the patient felt the cycling became too ‘easy’, they were instructed to increase the duration for which they were cycling at, with a maximum increase of 2 minutes for any fortnightly period. This subscribes to the basic aim of this program, which was to have the patients exercising at greater frequencies and lower intensities to induce optimal strength and functional gains (American College of Sports Medicine, 2000, p.145).

3.1.4 Program Monitoring

This consisted of fortnightly phone calls; the patients’ maintaining their scheduled visits to their specialist at the clinic, and a ‘training diary’ was given to the patient to fill out daily. A diary template (refer to Appendix I) was provided for the patient to record certain training information and subjective feelings related to their training performance. This included daily recordings of exercise data, such as the specific exercises undertaken by the patient and the training load they subscribed to. The investigator also asked the patients’ to record in their diaries subjective feelings of fatigue, soreness and breathlessness immediately following the completion of the daily exercises, and also each morning of each day. These ratings were based on a 1 to 10 visual analogue scale, with ‘1’ being ‘no fatigue, soreness or breathlessness at all’ and ‘10’ representing ‘extreme fatigue, soreness or breathlessness’. The patients were also asked to provide a rating of perceived exertion (RPE) of each exercise session they completed, which was based on the Borg 0-10 scale (Borg, 1982), immediately following the conclusion of each session. Any incidence of falls or near falls, and why, was to be recorded by the patients, and they were encouraged to provide any other information they felt necessary to disclose that may have impacted on their ability to perform the exercise program. Presentation of the training program was conducted through a home-visit by the investigator. At the conclusion of the
training intervention period, all parameters of muscle strength and function were reassessed, and the patients also undertook follow-up testing of their maximal aerobic capacity.

3.2 Data Analysis

Muscle strength and function was compared pre and post a 12-week exercise training intervention and analysed in both group and individual data sets. Pre and post data was averaged and tested for normality using the Kolmogorov Smirnov test before a paired two sample t-test was applied for each subject and muscle action. For each subject, the post-intervention score was normalised to pre-intervention values, averaged across all subjects and represented by means and standard error (±SE). The exercise program included the training of both diseased and non-diseased muscles, and the investigation used both within-subject and within-study controls to evaluate the effect the exercise program had on the various muscle groups tested. The lack of compliance to the exercise program by two of the patient group resulted in an additional analysis being utilized in this study. Thus, a comparison between the compliant (n=5) and non-compliant (n=2) patient groups (compliance defined as adhering to the exercise program and performing the prescribed exercises for greater than 70% of the training period) evolved during this study.
4. Results

Mean group data normalised to pre-training levels shows that the diseased muscle in the absence of training experienced a decrease in strength levels, as shown by the 19.6±10% (mean±SE) decline in grip strength (Figure 1). Yet, the healthy, untrained muscle (shoulder external rotation) experienced maintenance, or in this case, a slight increase in strength (4.2±6%). With training however, the diseased muscle, having undergone exercise training, maintained its strength (knee extension [100.9±10%]), whilst significant improvements (p < 0.05) were observed in otherwise healthy, trained muscles, with hip abduction strength improving by 59.1±31%, shoulder abduction strength increasing by 66.1±12% and hip flexion strength increasing by 83.7±35%.

A comparison between the compliant (n=5) and non-compliant (n=2) patient groups that evolved during this study shows the substantial difference the training intervention had on the patients muscle strength (Figure 2). Normalised to pre-training levels, the compliant patient group experienced a mean increase in muscle strength across all trained muscles tested of 38.4±12%, and there was a significant difference (p < 0.05) in improvement when compared to the non-compliant subset of patients. The non-compliant group that trained infrequently showed an overall mean increase in muscle strength of 12.2±9%.

Table 1 presents a breakdown of the compliant patients mean muscle strength data pre and post training, accounting for a sample of a number of distinct subsets of muscles tested, including diseased and otherwise healthy muscles, and, trained and untrained muscles. This table shows the respective one and two-tailed p-values for the sampled muscles. The two-tailed p-values were assigned to the muscle subsets that cannot be hypothesized as increasing in strength as a result of the exercise training due to either the muscles being diseased or untrained. Whereas, the healthy/trained muscles were assessed by one-tailed p-values in support of the hypothesis that an otherwise health muscle should increase in strength following a period of exercise training. It can be observed from the table that shoulder abduction, hip flexion, hip abduction and knee flexion all resulted in significant improvements by the group.
In assessing the impact of the exercise intervention on a single, compliant patient, there was a significant difference \((p < 0.05)\) between mean pre and post scores for all trained muscles (Figure 3a). The patient improved from an average of \(5.9\pm0.6\) Kg-f pre-training to \(7.3\pm0.8\) Kg-f post-training. The mean change in muscle strength for all muscle's involved in training following the exercise intervention of a single, non-compliant patient is shown in Figure 3b, and it can be seen that the patient experienced a mild decrease in muscle strength having not completed the exercise training. The patient's muscle strength averaged \(12.7\pm1.2\) Kg-f post intervention, slightly lower than the mean muscle strength pre-intervention \((13.2\pm1.3\) Kg-f).

Group stair climb and walk time/pace number data are presented in Table 2. It can be seen from this table that whilst there was not a statistically significant improvement in any of the functional tasks, on average, the patient group improved in all tasks. It can be seen that the patients developed a larger amplitude gait as indicated by the reduction in the number of paces used to complete the 30m walk. The sample size used in this study should be considered as possibly a contributing factor that affected the power of the statistical analysis.

The functional improvements of a single compliant patient are illustrated in Figure 4, with the patient's time taken to complete both the stair climb and 30m walk reduced following the exercise training period. The patient completed the post-intervention stair climb in 39 seconds, an improvement of over 64% on their pre-training effort (64 seconds). Additionally, the patient reduced their walk time by over 95%, with a post-training walk time of 64 seconds compared to a pre-training time of 125 seconds.

The functional deficits experienced by a single, non-compliant patient, as shown in Figure 5, with time taken to walk 30m and perform a stair climb increased following the exercise program. The patient's time to climb the 11 steps of the stair climb increased from 19 seconds to 22 seconds, just over a 13% increase in time taken. There was an increase in time taken to perform the 30m walk also, with the patient completing the task in 50 seconds post-intervention compared to 31 seconds.
the patient took pre-intervention, an increase by over 61% in time taken to perform the task.
Fig. 1. Mean group data (±SE) of compliant patients (n=5) normalised to pre-training, showing that in the absence of training, a diseased muscle experiences a mild strength loss, while a healthy untrained muscle does not. Yet with training, a diseased muscle can maintain its strength and other non-diseased muscles can experience a substantial improvement in strength.

* P < 0.05
** P < 0.001
Fig. 2. Mean group data (±SE), including diseased and healthy muscles that were involved in the training, normalised to pre training. There is a significantly greater muscle strength improvement of trained muscles for the compliant patient group when compared to the non-compliant patients' (p < 0.05).
Table 1. Trained group (n=7) mean (±SE) muscle strength data pre and post exercise intervention, where $P(T\leq t)$ one-tail was used for any healthy/trained muscles, and $P(T\leq t)$ two-tail for any diseased/trained or untrained and healthy/untrained muscles.

* $P < 0.05$

** $P < 0.001$

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Mean±SE</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td><strong>Diseased/Untrained</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grip Strength</td>
<td>194.57±49.99</td>
<td>182.85±55.32</td>
</tr>
<tr>
<td><strong>Diseased/Trained</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knee Extension</td>
<td>8.60±1.46</td>
<td>8.08±1.46</td>
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<tr>
<td>Wrist Extension</td>
<td>9.96±1.49</td>
<td>9.00±1.16</td>
</tr>
<tr>
<td><strong>Healthy/Untrained</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shoulder External Rotation</td>
<td>6.77±0.57</td>
<td>6.83±0.48</td>
</tr>
<tr>
<td><strong>Healthy/Trained</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elbow Extension</td>
<td>7.34±0.96</td>
<td>6.68±0.99</td>
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<tr>
<td>Elbow Flexion</td>
<td>10.09±1.19</td>
<td>10.26±0.72</td>
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<td>Shoulder Abduction</td>
<td>10.25±1.07</td>
<td>16.79±1.68</td>
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<tr>
<td>Hip Flexion</td>
<td>9.57±0.92</td>
<td>15.09±1.41</td>
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<tr>
<td>Hip Abduction</td>
<td>7.65±1.13</td>
<td>10.17±0.88</td>
</tr>
<tr>
<td>Knee Flexion</td>
<td>9.75±1.09</td>
<td>10.56±1.08</td>
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</table>
Fig. 3a). Mean individual data (±SE) of changes in muscle strength of all trained muscles of a single, compliant patient. Fig. 3b). In the same muscle groups of a non-compliant patient over this time period, muscle strength remains unchanged.
Table 2. Group (n=7) mean (±SE) functional task data, showing the mean time taken (seconds) pre and post intervention to perform a stair climb and 30 metre walk, and also the number of paces used by the patient during the walking task.

<table>
<thead>
<tr>
<th>Functional Task</th>
<th>Mean±SE</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td>Stair Climb</td>
<td>19.4±10.7</td>
<td>15.2±6.1</td>
</tr>
<tr>
<td>30m Walk</td>
<td>43.4±20.4</td>
<td>29.8±8.8</td>
</tr>
<tr>
<td>Paces during 30m walk</td>
<td>67.0±20.0</td>
<td>52.8±7.2</td>
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Fig. 4. Mean (±SE) individual functional capacity data of a single, compliant participant.
Fig. 5. Mean (±SE) individual functional capacity data of a single, non-compliant participant following the exercise intervention.
5. Discussion

The present study has shown that a 12-week home-based, patient-specific functional exercise program performed by the IBM patient, can lead to significant strength gains in muscles not affected by the disease, the maintenance of strength in diseased muscle groups and improvements in the performance of functional tasks in the absence of muscle damage. Figure 1 illustrates the positive impact an exercise program can have on an IBM patient's muscle strength if they adhere to the training program as prescribed. Strength training can result in an increase in strength in healthy muscles, and can delay the loss of strength in diseased muscles, whilst functional improvements, despite not reaching statistical significance, could potentially be viewed as clinically significant improvements for the positive effect these improvements have on the day-to-day functioning of the patients in this study.

It has been previously thought that exercise programs should be avoided by patients with inflammatory myopathies due to the concern that the exercise may enhance the inflammatory process (Alexanderson & Lundberg, 2005; Dalakas, 1989; Jones, et al., 1986). However, studies in other forms of idiopathic inflammatory myopathies showed a positive response to physical training in the absence of an adverse inflammatory reaction (Alexanderson, Stenstrom & Lundberg, 1999; Wiesinger, et al., 1998A; Wiesinger, et al., 1998B). Furthermore, studies with IBM patients using strength training and aerobic exercise as part of the patient’s treatment concluded that exercise can be performed by the IBM patient safely and can lead to dynamic strength improvements and possibly prevent loss of muscle strength (Armadottir, et al., 2002; Spector, et al., 1997).

Optimal exercise guidelines resulting in improvements in muscle strength and function have not been established in either a home-based or laboratory setting. The emphasis this study placed on the improvement of patient function by having the patients perform exercises specifically designed to improve function, including the use of multi-joint exercises and the integration of balance and stabilizing components to the exercises, distinguishes this study from previous exercise intervention studies in this clinical population. The training program in this investigation was also quite novel in that it included the training of both diseased and non-diseased muscles, and
uses within-subjects and within-study controls to assess the impact strength training had on these various muscle groups.

From subjective interviews with the patients, it was noted that previously these patients received physical therapy that was too strenuous and resulted in exacerbated muscle pain and further muscular weakness. However, this study has shown that carefully considered exercise load prescription can result in the attainment of functional benefits and strength gains. The conservative approach this study has taken supports a study by Kilmer, Wright and Aitkens (2005). A pilot study undertaken prior to the commencement of the present study identified program adherence and excessive muscle fatigue/soreness leading to possible non-compliance and/or withdrawal from the study as potential challenges this study would encounter.

The pilot study performed on a group of IBM patients (including a number of patients in this study) provided an insight into the compliance of the patients to perform their exercise program at home when not under the direct supervision of the investigator to be a limiting factor in strength and functional improvements. In the present study, compliance was defined as adhering to the program and undertaking the exercises as prescribed for greater than 70% of the intervention period. The diaries given to the patients to record their daily activities in, and the regular patient/investigator contact via the telephone, was expected to minimise the degree of non-compliance and to provide the impetus for the patient to maintain a detailed record of what they were actually performing in their exercise sessions. Positive reinforcement from the investigator and the patients’ partners and the maintenance of the patients’ scheduled visits to the Neuromuscular clinic are other measures that were put in place to ensure program adherence. However, upon post-intervention interviews, two of the group were assessed as being non-compliant, having not completed the majority of the exercise program as instructed. For various reasons, both subjects exercised infrequently and applied a training load not specified by the investigator. As a result of this, the results of this study have at times been analysed as two separate entities; a compliant group and a non-compliant group.

The selective pattern of muscle involvement that characterises IBM patients ensured that the exercise program had varying effects on the muscle groups tested in
The significant increases in muscle strength observed in four of the trained/healthy muscles tested indicates the importance of strength training in this patient group, as whilst these muscle are not directly involved in the disease, they play important roles in the patients capacity to perform daily, functional activities. The maintenance of strength through training of an involved muscle is another important finding. When analysed in light of the mild strength loss in the untrained/diseased muscle (grip strength), this clearly suggests strength training can delay the loss of muscle strength in muscles typically involved in IBM, thus supporting findings reported by Spector et al (1997).

The progressive nature of IBM results in the gradual deterioration of strength in the muscles selectively involved in this disease. This must be taken into consideration when analysing the effect of a strength training exercise program on the diseased muscle groups. A definitive rate of decline in strength is unknown in this pathological group; however, a study by Rose, McDermott, Thornton, Palenski, Martens and Griggs (2001) found a mean decline in muscle strength of 4% from baseline in IBM patients over a six month period. Lindberg, Persson, Bjorkander and Oldfors (1994) reported a 1.4% loss of strength from baseline per month. The loss of strength in IBM patients' is likely to vary between individuals and the stage of disease progression they are at (Dawes, Korpershoek, Freebody, Elsworth, van Tintelen, Wade, Izadi & Jones, 2006). It can be seen from Figure 1 that untrained/diseased muscle groups can experience a noticeable decrement in strength over a 12-week period.

The variability in the degree of weakness and level of endurance between different IBM patients, and their general level of fitness makes it necessary to design exercise programs that are specific to each patient. The patient-specific aspect of this study allowed the investigator to overload each patient in consideration of the progression of the disease and the muscle selectivity that characterises IBM. It also enables the investigator to integrate the exercise program into the patients’ homes with greater ease by allowing for greater flexibility in the prescription of exercises in consideration of the availability of space and resources that are present in each patient’s home.
The involvement of the wrist and finger flexors in this muscle disease affects the force output of the patients hand and wrist, causing them to have reduced grip strength. At the completion of the exercise intervention, the compliant patients in this study exhibited an average decline in muscle strength of 19.6%. This is despite the fact that the wrist and finger flexors were involved in the performance of other exercises prescribed to the patients, such as bicep curls. For the entire patient group, grip strength decreased on average by almost 8% (Table 3 – refer to Appendix N). The importance of grip strength in the performance of everyday activities should not be understated, it is required in simple, menial tasks such as hanging out the washing, drying dishes and serving food, thus the implications of having a reduced grip strength, that is declining continuously, are serious and a limiting factor in the patient’s ability to independently function.

The decline in grip strength should be kept in mind when examining the effect of the exercise program on other muscles primarily involved in this disease, but which were trained in this study. Grip strength can be viewed as a within-subject control for diseased/trained or untrained muscles, thus the maintenance of strength as shown by the knee extensors of the compliant patients is particularly promising. The knee extensors have been shown to maintain their strength over the intervention period and knee extensor exercises were a major part of the exercise program. The prominent atrophy and weakness of the quadriceps muscles indicates the extent of damage this muscle group experiences as a result of the disease (Amato, Gronseth, Jackson, Wolfe, Katz, Bryan & Barohn, 1996; Arnardottir, Alexanderson, Lundberg & Borg, 2002; Felice, Relva & Conway, 1998) (refer to Appendix L for pictures of a patient in this study).

The serious consequences this has, as being a core reason as to why this patient group experiences falls frequently, validates the place of knee extension exercises in any exercise program to be prescribed in this patient group. Using sit-to-stand exercises, which have important functional applications, to improve the patients muscle strength in the knee extensors, the compliant patients averaged a 0.9% improvement in strength. Whilst only a small improvement, this supports findings by Spector et al (1997), who found muscle groups with the lowest Medical Research Council (MRC) ratings pre-training showed the least amount of improvement post-
However, Table 3 shows the average knee extensor strength pre-training to be 7.32 Kg-f, whilst post-training, the patients averaged 6.66 Kg-f of the total patient group. This is a 10% loss in strength over the 12-week intervention period. This is obviously offset by the inclusion of non-compliant patients in the data used to calculate these figures, which further emphasizes the importance of the exercise program, and the potential benefits that can be derived, by the patients by exercising the diseased muscle groups. The maintenance of strength in the knee extensors has implications in the patients capacity to perform functional tasks such as a 30m walk and a stair climb, with knee extensor strength a key factor in the ability of the patients to perform these functional tasks, and in particular the ability to climb stairs.

Shoulder external rotation, a healthy/untrained muscle group, was used as a 'control' in this study to establish strong evidence that supports the effect of the strength training on healthy/trained muscles. It forms a within-subject control variable to show that by not adhering to the exercise program, there will effectively be no net change in muscle strength of an untrained/healthy muscle at the completion of the intervention period. The collected data of the compliant patients shows they increased their strength in this muscle by 4.2%, whilst the patient group as a whole, increased in strength by just over 2% (7.45 Kg-f pre-training compared to 7.64 Kg-f post-training) (refer to Table 3). The slight increase in strength may be a secondary effect of the patients exercising the shoulder muscles involved in shoulder external rotation in the performance of other exercises directed at improving other muscle actions, such as shoulder abduction. Greater movement at the shoulder joint would also be expected to have resulted from the patient having undertaken shoulder strengthening exercises and upper limb stretching movements to enable a more flexible movement pattern, thus potentially encouraging a greater force production.

Figure 1 shows the statistically significant improvements in shoulder abduction as a result of the strength training program the IBM patients performed. As expected, the healthy/trained muscles that perform the shoulder abduction muscle action responded well to the training, with the compliant patients shoulder abduction strength improving by over 66%. The improvements seen here support previous
evidence of the benefits that can be derived by using an isometric contraction to target a particular area (Skelton & Dinan, 1999). The gain in muscle strength achieved in the shoulder abductors has important applications in the performance of activities of daily living. Daily chores such as hanging out the washing to dry and washing the dishes, require upper limb muscle strength, and the inability to perform these tasks due to a lack of strength reduces the independency of these patients, which negatively impacts on the patient’s ability to care for themselves. Thus, the importance of strengthening a non-diseased muscle cannot be understated, for its valuable contribution to undertaking the most basic, functional tasks should be recognized.

The statistically significant improvement in hip abduction strength in a healthy/trained muscle in this study has important implications for the daily functioning and general health and well-being of this patient group. A 59% increase in hip abduction strength was found in the compliant patient group, whilst statistical significance was also found when comparing pre and post muscle strength scores of the total patient group (Table 3). Hip abduction strength has practical applications as a key factor in balance and stabilizing tasks. The lower limbs abduction muscles are vital during walking to maintain the body’s weight over the limb that is in contact with the ground. Hip abduction strength is also a necessary tool for stabilizing tasks, which is particularly useful in this patient group that is prone to falls. Developing strength in this area is advantageous to the patient as a balance strategy to resist falling or correcting displacement. Postural control and improved gait are other functional benefits derived from a lower limb strength training exercise program (Campbell, Robertson, Gardner, Norton, Tilyard & Buchner, 1997; Simpson, Harrington & Marsh, 1998).

In addition to hip abduction strength, hip flexor strength is another vital component of an exercise program that aims to primarily improve the functional capacity of this patient group by improving the patients muscular strength, endurance and function. Hip flexor strengthening has been shown to play an important role in developing greater postural control and improving the gait of the elderly, and in particular those that are more susceptible to falls, which is prominent in IBM patients due to their weakened quadriceps (Campbell, et al., 1997; Simpson, Harrington & Marsh, 1998; Skelton & Dinan, 1999). IBM patients tend to develop abnormal gait
patterns due to lower limb weakness, resulting in either increased risk of falling, or reduced mobility as a consequence of a fear of falling (Lord, Lloyd & Li, 1996). By improving hip flexor strength, it is anticipated the patients will be less susceptible to falls and experience improved dynamic stability when trained in combination with other lower limbs, which will have a follow-on effect on the patients’ confidence to be more mobile, which in turn has numerous secondary health benefits for the patients (Kannus, Sievänen, Palvanen, Järvinen & Parkkari, 2005; Lord, Ward & Williams, 1996).

In the compliant subset of patients, hip flexor strength significantly improved by over 83% over the 12-week intervention period, and statistical significance was also attained when analysing the strength gains of the entire patient group, as shown in Table 3. Muscle strength improvements in healthy muscles as a result of exercise training are to be expected, and the results of the present study provide ample evidence of the benefits that can be gained from a patient-specific, functional exercise program. The highly favourable response to training is likely to be due to the low-level of pre-training fitness, as the majority of this patient group have been sedentary for a number of years, due to the reduced mobility and the fatigue they experience when they are active (Spector, et al., 1997).

Figure 2 presents the overall mean change in muscle strength of both the compliant and non-compliant patient groups at the completion of the exercise program. The compliant patients experienced over a 38% increase in muscle strength for all muscles trained, which was significantly different to the average change in muscle strength experienced by the non-compliant patients. This figure emphasizes the importance of undertaking the exercises as prescribed and instructed, and supports the hypothesis that an exercise training program can result in muscle strength improvements in this patient group. The findings in this study support work by Spector et al. (1997) who found significant strength changes following a short-term exercise program in IBM patients.

Almost all healthy muscles (trained or untrained) showed an increase in strength post-training (Table 1). One exception to this is elbow extension, which on average experienced a loss of strength over the study. The elbow extensors were
‘trained’ in as much as they were involved in the sit-to-stands all patients were
required to undertake. Each patient was asked to use their upper limbs to lower
themselves back into a seated position after each repetition for each sit-to-stand set
performed by the patient. The limitation of this is that the effort and concentration
required by the patients to perform the sit-to-stands may have potentially resulted in
the patients not following the instructions of using their arms to lower themselves
back into a sitting position.

However, this study was initially designed to exercise the patients using,
where possible, functional and multi-joint exercises to make the program time and
energy efficient but also with transfer into activities of daily living. The muscular
fatigue experienced by this patient group, limits the amount of time and the intensity
of effort the patients can apply to their program, so an exercise plan that has the
patient training numerous muscles through a small number of exercises will not only
be well tolerated by the patients, but encourage compliance as opposed to longer
exercise sessions.

In analysing the results, and using information provided by the patients in both
subjective interviews and diary recordings, it is possible to present some interesting
figures through a case study. Figures 3a and 3b are a comparison between two
patients, with Figure 3a a pre-post comparison of the mean muscle strength data for a
single, compliant patient, whilst 3b presents the same values, but for a single, non­
compliant patient. The compliant patient recorded a statistically significant difference
between pre mean muscle strength score for all trained muscles. This patient was
highly compliant, undertaking the exercise program as instructed, and was assisted
through positive reinforcement and constant and strict supervision by their partner.
The patient’s diaries were very detailed and both the patient and their partner strongly
expressed the view that very few, if any, exercise sessions were not completed. The
patient’s mean strength improved from 5.9±0.6 Kg-f pre-training, to 7.3±0.8 Kg-f
post-training.

This is in contrast to the non-compliant patient, who not only missed exercise
sessions, but also failed to perform the exercises in each session as instructed. This
patient failed to record any exercise information, which makes it difficult to quantify
how much exercise the patient performed, despite the encouragement and close monitoring provided by the investigator. However, in interviews with the patient, it was clear that they had performed very little of the exercise programme, and thus were assessed as being non-compliant in this study. The patient averaged 13.2±1.3 Kg-f in muscle strength pre-training, but experienced a non-significant loss in strength over the 12-week intervention period and recorded a mean value of 12.7±1.2 Kg-f post-training.

In comparing the muscle strength results of these two patients, they provide further evidence of not only the capacity of the exercise program to enable the patients to attain muscle strength improvements due to a patient-specific, functional exercise plan, but also the importance of adhering to the exercise program. Figure 3b shows non-compliance can potentially result in a loss of muscle strength which this individual patient experienced, which supports the findings presented earlier in Figure 1 detailing the loss of muscle strength in grip strength in the absence of training.

The change in functional capacities of the compliant patients in this study, whilst not statistically significant, should not be understated. As can be observed from Table 2, in all three functional tests, the compliant patients improved following the training intervention. The time taken to climb one flight of stairs was reduced from an average of 19.4±10.7 seconds pre-training to 15.2±6.1 seconds post-training. The 30 metre walk time also decreased following the training intervention, from 43.4±20.4 seconds to 29.8±8.8 seconds. The reduced walk time was accompanied by a reduction in the number of paces used by the patient to perform the walk, with the compliant patients averaging 67.0±20.0 steps pre-training and 52.8±7.2 steps post-training. This reduction in number of paces used to perform the walk is indicative of the patients developing a larger amplitude gait.

In the absence of statistical significance, a clinical perspective can be applied to the functional improvements seen in this study, whereby for various reasons, such as small subject numbers and the insensitivity of the tests in detecting change (Rider, 1996), the patients did not achieve statistical significance, the improvements seen may be viewed as an example of clinically significant results. Additionally, the progressive nature of the disease, which has been shown to cause the patients to lose muscle
strength, may have had a limiting effect on the improvements in functional capacity over the 12-week intervention period. However, mild improvements, as seen in this study group, have important functional implications in the patients’ activities of daily living. The ability to walk faster over a set distance means less energy is expended and the patient can therefore walk further in the absence of fatigue. This enables the patient to be more independent, such that they can go to the shops with their partner; they can spend an afternoon in a park without becoming over-fatigued from any walking they may have to undertake.

The ability to walk further and faster may also result in the patient delaying the need to use a wheel chair or motorised buggy to locomotor. The immobility that accompanies these movement aids has serious implications for future health issues, in particular cardiovascular disease and other secondary co-morbidities, as a consequence of the sedentary lifestyle the patient is forced to live (American College of Sports Medicine, 2000, p.5). Being able to walk more and climb stairs with greater ease can simply mean the patient is able to move around their house without the assistance of their partner or carer, and activities of daily living can be performed with greater ease and confidence by the patient. This would potentially have positive psychological benefits for the patients, who are able to feel more independent and confident in their ability to perform tasks on their own and contribute to the community, and less dependent on their partner, carer or others to assist them.

Using the same two patients that were identified in Figure’s 3a and b, Figures 4 and 5 provide a contrasting observation of the difference in functional capacity changes over the 12-week intervention period by a compliant and non-compliant patient. Figure 4 further highlights the importance of adhering to the exercise program and the benefits of the patient-specific program itself, as this figure shows the functional improvements that can be made by an individual, compliant patient over a 12-week period. The patient reduced their stair climb time by 25 seconds, a 64% improvement in time taken to perform the task, whilst their 30 metre walk time was reduced from 125 seconds pre-training to 64 seconds post-training, an improvement by over 95%. This descriptive data clearly shows the influence the exercise program had on this patient and their capacity to perform simple functional task such as a stair climb and 30 metre walk.
Figure 5 presents data from the same functional tests, but shows the reduction in functional capacity resulting from non-compliance to the exercise program. In the patient’s post-training functional assessment, their time taken to walk 30 meters and perform the stair climb increased from their pre-training levels. In the case of the stair climb, the patient’s time increased by 13%, from 19 seconds pre-intervention to 22 seconds post-intervention. Their 30 metre walk time went from 31 seconds pre-training to 50 seconds at the completion of the exercise intervention, an increase in time by over 61%. This data adds further weight to the evidence this study provides in support of the importance of an exercise program for this patient group in the prevention or delaying of a loss of muscle strength and functional capacities.

The careful and selective prescription of exercise load was primarily based upon exercise rehabilitation guidelines for other pathological groups. According to the American College of Sports Medicine (2000, p.145) guidelines, for optimal strength and functional gains to be attained, the patient should adhere to an exercise program that emphasises higher frequencies and longer duration exercise sessions at lower intensities. This was adhered to by the investigator when prescribing each patient’s exercise program. In establishing the patients’ exercise programs, the investigator deliberately avoided emphasising eccentric muscle contractions for the damaging effect on muscles they have been shown to cause (Jones, Newham, Round & Tolfree, 1986). Rather, multi-joint exercises, isometric and concentric muscular contractions were preferentially prescribed along with movements and functional positions that emphasised balance and stability within the training program.

Class-based versus home-based exercise rehabilitation therapy has been investigated in a variety of pathological groups (Ashworth, Chad, Harrison, Reeder & Marshal, 2005), and the cost-effectiveness, compliance rates, and overall results from both strategies have merit (Carmelli, Sheklow, & Coleman, 2006). Home-based programs are easy to implement (Ashworth, et al., 2005), accessible to the patient (Lim, Moon & Lee, 2005), and encourage compliance (McCarthy, Mills, Pullen, Richardson, Hawkins, Roberts, Silman & Oldham, 2004). The impaired mobility that typifies an IBM patient gives a home-based exercise program advantages over a class-based program. Such advantages include the safety and familiarlarity of exercising in
the familiar surroundings of their own home, the assistance and encouragement of partners, the flexibility to perform the exercises according to their own schedule, and the avoidance of having to arrange suitable transport.

Despite being an integral component of this study, the home-based setting with which the exercise program was designed for and performed in presented the investigator with a number of challenges. Program monitoring is comprehensively more challenging in this home-based study compared to a laboratory or clinic setting whereby constant observation and supervision can be applied. Ensuring the patients perform the exercises, use the correct techniques and apply the appropriate training load are just a number of the issues that confront the investigator when establishing a home-based therapeutic intervention. Controlling external factors, such as other activities and chores the patient undertakes which may impact on the patients fatigue and muscle weakness levels whilst partaking in the exercise program, is also an issue that requires further examination. Verbal instructions with regards to the importance of recovering between exercise sessions and limiting the amount of strenuous activities performed during the study period was impressed upon the patients.

However, it is both unethical and unfeasible to ask the patient to abstain from any activities that may make them tired or weak on the premise that this will negatively impact on their capacity to consistently perform their exercise program. Future studies need to consider this point, and it is recommended that a specific rating system of energy exertion during the undertaking of regular, daily activities could be useful in attempting to quantify the fatigue levels being experienced by the patients when performing these activities of daily living. This would enable the investigator to closely monitor the patients’ energy and fatigue levels, and then prescribe exercise accordingly. In order to establish if exercise should be prescribed as part of the routine clinical management of IBM patients’, it was felt that it should be determined if exercise training in the patients’ home is practically achievable and therefore we considered that the nature of home-based exercise was integral to this study.

In evaluating the completed diaries of the patients, there was much variability in the amount of the exercise program performed by each patient. Two of the patient group did not attempt to fill out a diary, so it is difficult to make a formal conclusion
on the adherence to the program by the patient’s, other than what was verbally communicated to the investigator by each patient in subjective interviews at the completion of the exercise program. For reasons such as an illness, having friends staying with them, or having to go away from home, five of the patient’s felt that they missed a small percentage of days within the intervention period, but never for more than 5-6 days at a time, and this is supported by diary entries by this subset of patients. The non-compliance of two of the patient’s in the study group was the reason why the investigator took the approach of analysing the results in two separate data sets.

Despite rigorous efforts to encourage and monitor patient compliance, ensuring the patients adhered to the exercise program and performed the training as prescribed was challenging. Physicians should therefore consider this when prescribing exercise to this clinical population. The program was developed to ideally exist in the absence of daily interactions with the investigator and the associated constant supervision, as it was the intention of the investigator to develop the program in such a way so as to make the exercise program a behavioural change and an addition to the patients’ everyday lifestyle, not something the patients were forced to do and travel to and from a gym or clinic to undertake.

Despite encouraging self assessments from each patient with regards to their adherence to the exercise program throughout the intervention period, it is difficult to make any formal conclusion of overall compliance to the program with the variability that existed between each patient in their diary entries and without the factual information of how often the patient actually performed the exercises that the diary was intended to provide. In consideration of the non-compliance by two patients in this study, some viable recommendations could go some way to ensuring future similar studies are not hindered by the issue of non-compliance, or at least the lack of indisputable facts needed to make sufficiently justified statements of the training load each patient performed. A more interactive method of program monitoring could provide the necessary stimulus required to ensure the patients are not only undertaking their exercises, but also to further encourage them to maintain their exercise diaries, regardless of what they did or did not do. More regular contact via phone calls and possibly more home-visits by the investigator are two realistic means
of increasing the investigator/patient contact.

A more direct involvement by each patient's personal support network could also lead to improvements in patient self-assessment and exercise recording. This could involve simply having the patients' wife/husband/child listening in on all meetings between the investigator and patient and being involved in the implementation of the exercise program into the patients' home. Obviously, the patient is given the opportunity to involve who they wish and invite them along to any and all meetings between themselves and the investigator, but additional encouragement to do this by the investigator could ensure every patient has the necessary support to undertake the exercise program. Taking this a step further, it would be quite possible to involve the patient's partner in the actual exercise program and make the exercise therapy a joint interest the patient and their partner could share with potential positive benefits for both. Having someone in the patients' home to act as 'interactive supervisors' in the absence of the investigator to ensure the exercises are correctly undertaken and recorded, provide encouragement and positive reinforcement and to ensure the safety of the patient is an important facet of home-based exercise programs if they are to be successful.

Another option that may potentially have a positive effect on the compliance of the patients to the program and also stimulate them more to record their progress is the establishment of a once-weekly group exercise session delivered in a gym-type setting. Balance and physical performance has been shown to be improved as a result of class-based, supervised exercise programs in older adults (Carmelli, Sheklow & Coleman, 2006; Judge, 2003). This would provide the patients with motivation to do their exercises in the knowledge that their progress will be more closely followed by the investigator when they attend these sessions each week. It would also provide the investigator with the opportunity to deliver more specialised exercise programming and work more hands on with the patients in a rehabilitative setting. The social aspect of having a group of patients with the same disease interacting and supporting each other would likely have a positive influence on the patients and provide further motivation to attend each week knowing a friend will be there and is facing the same problems and daily issues as them. This is particularly prevalent in this pathological group exhibiting a muscle disease that is seemingly quite uncommon. Whilst
conflicting evidence surrounds the impact of home-based and class-based exercise programmes, further research is required to assess why patients are/are not adhering to exercise programs and diligently recording their performance, regardless of the setting. This would then provide investigators with the fundamentals necessary to establish research projects designed to enable investigators to make conclusive statements on the type of exercise setting that will best induce optimal training effects.

The role CK plays during exercise has been comprehensively examined, resulting in CK levels being the primary biochemical marker of muscle damage following a bout of exercise (Clarkson & Tremblay, 1988; Houmard, Costill, Mitchell, Park, Fink & Burns, 1990; Shahbazpour, Carroll, Riek & Carson, 2004; Totsuka, Nakaji, Suzuki, Sugawara & Sato, 2002). It is felt that CK is a reliable measure of muscle damage following exercise in myopathic patients (Phillips & Mastaglia, 2000). However, studies on inflammatory myopathy patients have shown that despite an immediate rise in CK levels following strength training, the rise does not seem to be sustained for any more than a few hours, and certainly with no long-lasting changes in the patients CK levels following exercise have been observed (Arnadottir et al., 2002; Escalante, Miller & Beardmore, 1993; Hicks, Miller, Plotz, Chen & Gerber, 1993; Spector, et al., 1997). This study did not result in significant serum CK changes, thus supporting previous findings that exercise can be safely tolerated by this patient group.

The small number of subjects in this study has implications for the statistical power of the results and the subsequent conclusions drawn from the data. However, with the muscle disease being quite rare, the actual numbers which make up this study are comparative to other exercise therapy studies involving neuromuscular disorders. The progressive disabling nature of the disease and the symptomatic muscle weakness and fatigue caused a number of patients to withdraw from the study either prior to it beginning or during the intervention period. The decision to withdraw was often made apologetically and whilst most wanted to continue or start the exercise program, they simply felt that the exercises were not going to help them and it would therefore be a waste of their time and effort.

The assessment of muscle strength by a hand-held myometer, which is
employed regularly in clinical settings, provided accurate, valid and reliable results (Agre, Magness, Hull, Wright, Baxter, Patterson & Stradel, 1987; McMahon, Burdett & Whitney, 1992), as did the testing of the patient’s functional ability. The functional tests performed by the patients are commonly clinically applied in the testing of a variety of muscle disorders. The aerobic testing of the patients was quite a novel procedure for this pathological group, but it was carefully planned and designed to account for individual differences between the patients and any co-morbidities that were present. The testing procedure was thoroughly researched and critically assessed prior to being used, and was based on a number of similar protocols established in the testing of other symptom-limited pathologic groups.

The testing procedures used in this study were reliable and valid measures of both muscle strength and functional capacity and inter-rater reliability was confirmed for all measures tested. However, the importance of assessing the impact of any exercise intervention on a clinical population’s quality of life (QOL) should be prioritised and should be a key outcome measure in studies such as this one. Improvements in muscle strength and endurance are vital, but it is how these changes advantage the everyday lives of the patients and improve their functionality that is the key issue. Currently, further research is required to develop valid, reliable and sensitive QOL scales for this particular patient group.

The use of the SF-36 as the quality of life instrument to assess general health and functional changes as a result of the training intervention is based on it’s prevalence in the literature pertaining to similar studies of neuromuscular patient groups. Despite it not being a muscle disease specific measure, it has been shown to be a valid and reliable measure of a patient’s overall health status (Alexanderson, Stenstrom & Lundberg, 1999). The SF-36 was trialled in this study, but in reviewing the patients’ pre- and post-intervention questionnaires, the investigator found the questionnaire lacked specificity when applied to this particular clinical population. Despite its application in a number of IIM studies (Isenberg, et al., 2003; Sultan, Ioannou, Moss & Isenberg, 2002), the validity of the SF-36 as a QOL measure for IBM patients needs further clarification.
6. Conclusion

In IBM patient’s, significant strength gains can be attained in non-diseased muscles, strength can be maintained in the diseased muscles, and functional improvements can be made in the absence of muscle damage as a result of a home-based, patient-specific, functional exercise program. In normal populations, a muscle that has experienced atrophy can regain size and strength through resistance training, however, studies have shown that strength training does not seem to cause muscle hypertrophy in IBM patient’s, or at least it does not do so to a sufficient number of muscle fibres required to make a significant contribution to result in a change in muscle size (Phillips & Mastaglia, 2000; Spector, et al., 1997). Other possibilities which may explain the increase in muscle strength observed in this patient group following the exercise intervention include a change in fibre type (Alexanderson & Lundberg, 2005; Arnadottir, et al., 2002) and recruitment patterns. An increase in muscle fibre cross sectional area has been seen in muscle biopsies following an exercise intervention in IBM patients; however, a significant result was not established and questions remain as to whether or not muscle undergoes hypertrophy in response to a strength training program (Arnardottir, et al., 2002).

Motor learning and an improvement in the co-ordination of muscles activated during the performance of a task may also contribute to strength gains and functional improvements. We propose that the present approach has been beneficial to the patient’s by slowing muscle atrophy and improving co-ordination and activation of muscle groups to perform a given task. Although improvement in the functional tasks did not reach significance, the use of functional weight-bearing activities in the exercise program may assist the patient in average daily living activities (Littbrand, Rosendahl, Lindelöf, Lundin-Olsson, Gustafson & Nyberg, 2006; Wilson, Murphy & Walshe, 1996). It should be considered that the sample size used in this study is likely to have affected the statistical power of the data analysed. The results are particularly promising when taking into consideration that the training did not include an aerobic component that could potentially specifically enhance the patient’s ability to move with greater control, therefore, a reduction in energy expenditure resulting from excessively co-contracting muscles.
Exercise guidelines are substantially lacking for this patient group; however, exercise has been shown to have a positive effect on an IBM patient's muscle strength in previous studies (Arnardottir, Alexanderson, Lundberg & Borg, 2002; Spector, et al., 1997). This study provides evidence to support the prescription of a carefully controlled, patient-specific exercise program. In the absence of disease progression markers, this study shows that muscle strength and function can be improved by mild daily exercises performed in the patient's home. Key factors such as adherence, exercise prescription, the initial training load and the subsequent progression of the training program must be considered and thoughtfully planned in any future investigations. Exact training protocols and the relevance such strength and functional improvements have on the patients quality of life, requires further investigation with large sample sizes in controlled, long-term training interventions using validated, disease-specific quality of life scales. This would perhaps require a coordinated multi-centre, randomized controlled, clinical trial. However, this study has shown that exercise, in particular, strength training, may be an important component of the routine management and long-term treatment of patients with Inclusion Body Myositis.
7. References


Wiesinger, G.F., Quittan, M., Nuhr, M., Volc-Platzer, B., Ebenbichler, G.,
dermatomyositis/polymyositis patients and healthy controls. *Archives of
Physical Medicine and Rehabilitation, 81*(1), pp.1-5.

Wiesinger, G.F., Quittan, M., Aringer, M., Seeber, A., Volc-Platzer, B., Smolen, J., &
polymyositis/dermatomyositis patients by a training programme. *British

Wiesinger, G.F., Quittan, M., Graninger, M., Seeber, A., Ebenbichler, G., Sturm, B.,
8. Appendices
Appendix A

Published abstract in the Scholarly Journal ‘Neuromuscular Disorders’. This abstract was presented as a poster presentation at the XI. International Congress on Neuromuscular Diseases, 02-07 July, Istanbul – Turkey. This abstract was pilot study work the investigator undertook prior to the commencement of their Honours investigation.
This mechanism might be the cause of increased myostatin precursor demonstrated in s-IBM muscle fibers. Increased myostatin precursor/myostatin might contribute to muscle-fiber atrophy and other changes in s-IBM.

Support: grants (to VA) from the NIH, TMA, MDA and the Helen Lewis Research Fund.

M-P.6.04
Granulysin expression in polymyositis and inclusion body myositis
Koji Ikezoe*, Sachiko Oshima, Manabu Osoegawa, Masato Tanaka, Kazuyuki Ogawa, Kinya Nagata, Jun-ichi Kira
Japan

Background: Granulysin, a recently defined cytolytic molecule, is expressed in cytokitic T and natural killer cells; similar to perforin, which is reported to play a major role in the pathogenesis of polymyositis (PM) and inclusion body myositis (IBM). Objective: To clarify the role of granulysin in PM and IBM. Methods: We examined the expression of granulysin and perforin by double-staining with CD8, CD4, and CD56 in endomysial infiltrating cells and autoinvasive cells in 17 muscle biopsies of PM (6 steroid resistant, and 11 steroid responsive), and 7 IBM. Results: Similar to perforin, granulysin was expressed in CD8+, CD4+, or CD56+ cells in PM and IBM. However, only the ratio of cells double positive for granulysin and CD8 to all CD8+ cells at endomysial sites was significantly higher in steroid resistant PM than in steroid responsive PM and IBM. Conclusion: Granulysin expression in CD8+ cells appears correlated with steroid resistance in PM.

M-P.6.05
A pilot study on the effects of a patient-specific, home based, functional exercise program on patients with Inclusion Body Myositis (IBM)
Liam Johnson*, Dylan Edwards, Gary Thickbroom*, Frank Mastaglia*
Centre for Neuromuscular Disorders, The University of Western Australia; School of Exercise, Biomedical and Health Sciences, Edith Cowan University; *Centre for Neuromuscular Disorders, The University of Western Australia

Previous research has shown exercise to be beneficial in the treatment of myositis-affected patients. The potential of functional exercises to improve muscle strength and function in the absence of disease progression markers is not well understood. We believe that an exercise program tailored to the patient is important for routine management and long-term treatment. The present study investigated the effects of a home-based, patient-centered functional exercise program, on muscle strength and patient mobility. Patients were tested pre and post, a 16 week, patient-specific, home exercise program involving mild, daily functional exercise. Outcome measures included a hand-held dynamometer for muscle strength, whilst a 30 m walk and stair climb was performed to ascertain changes in overall functional ability. Inter-tester reliability was confirmed for the measures used. Creatine Kinase (CK) was monitored over the intervention period. Strength improved for all muscles tested, with results as follows; shoulder abduction 39.4±10SEM%, shoulder external rotation 7±18, elbow extension 39.2±8, elbow flexion 57.7±14, wrist extension 57.7±21, wrist flexion 169.5±56, hip abduction 56.1±20, knee extension 36.1±10 and knee flexion 62.0±24. There was a post-intervention improvement in average time taken to climb one flight of stairs (13.8±3 s reduced to 11.5±3 s) and walking unaided for 30 meters (41±5 s reduced to 34±6 s). The number of paces to perform the 30m walk was also reduced (58.8±3 to 54.8±4). Serum creatine kinase levels remained constant throughout the intervention period. Results from this preliminary study show that muscle strength and function can be improved by mild daily exercises performed in the patient’s home. In the absence of disease progression markers, our individually prescribed home exercise program over 16 weeks has shown that simple functional exercise activities can be beneficial in the clinical management of myositis patients.

CONGENITAL MYOPATHIES; POSTER PRESENTATIONS
M-P.15.01
A comparative morphological study of heart and skeletal muscle in mutation-proven desminopathy
Hans H. Goebel*, Rolf Schroeder*, Walter Schulz-Schaefferb, Lev Goldfarb*
Department of Neuropathology, Johannes Gutenberg University Medical Center, Mainz, Germany; *Center for Biochemistry, University of Cologne, Germany; †Department of Neurology, Georg-August University, Goettingen, Germany; ‡National Institute of Neuromuscular Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, USA

Background: Desminopathies are molecularly marked by mutations in the desmin gene, clinically by muscle weakness, often of late onset and more distal than proximal, and frequently cardiac disease, morphologically of degeneration of sarcomeres and aggregation of desmin and many other proteins appearing as inclusions or wide spread granulofilamentous material within muscle fibers. Purpose: To assess the morphology of cardiac pathology and compare it with myopathy in skeletal muscle fibers in mutational desminopathy. Material: Cardiac tissue obtained by biopsy or explantation for heart transplantation of three genetically affected patients. Methods: Histology, immunohistochemistry, electronmicroscopy. Results: Myocytes in both skeletal muscle and heart gave identical disruption of sarcomeres and accumulation of granulofilamentous material often amased at the intercalated discs of cardiomyocytes and beneath the sarcolemma in skeletal muscle fibers. Conclusion: As desmin is the intermediate filament of both skeletal muscle fibers and cardiomyocytes encoded by the same gene with, hence, mutations in the DES gene affecting both organs the similar pathomorphology underscores such genotype-morphotype correlation and forms the basis for clinical involvement of skeletal muscle and heart.

M-P.15.02
Severe nemaline myopathy caused by mutations of the stop codon of the skeletal muscle alpha actin gene (ACTA1)
William Wallefeld*, Sabine Krause*, Kristen Nowak; Rina Horvath*, Zoltan Molnar*, Miklos Szabo*, Ichiro Nishino*, Hans Lochmüller*, Nigel Laing Molecular Neurogenetics Laboratory, Centre for Medical Research, University of Western Australia, Western Australian Institute for Medical Research, B Block, Queen Elizabeth II Medical Centre, Nedlands, Western Australia; *Molecular Myology Lab, Friedrich-Baur-Institute, Department of Neurology, Ludwig-Maximilians-University of Munich, Marchioninistr. 17, 81377 München, Germany; †First Department of Pediatrics, Semmelweis University, Bókay u. 53, 1085 Budapest, Hungary; ‡Department of Neuromuscular Research, National Institute of Neuroscience, National Center of Neurology and Psychiatry (NCNP), 4-1-1 Ogawahigashi, Kodaira, Tokyo 187-8502, Japan

Purpose: Most nemaline myopathy patients have mutations in the nebulin (NEB), or alpha-skeletal actin (ACTA1) genes. We have performed screening of the ACTA1 gene in multiple patients with congenital myopathies from Europe and Japan. Here we report for the first time mutations of the ACTA1 stop codon in two patients, one from Hungary and one from Japan, with severe nemaline myopathy with dystrophic changes on muscle biopsy. Methods: All six coding exons of the alpha-skeletal actin gene were sequenced from genomic DNA using our previously published methods. Western blotting performed using an antibody to sarcomeric actins. The stop codon mutations were cloned into pEGFP-N1 (Clontech) and expressed in C2C12 cells according to our previously published protocols. Results: A heterozygous TAG>CAG (glutamine) mutation of the ACTA1 stop codon was identified in the patient from Hungary and a heterozygous TAG>TAT (tyrosine) mutation in the Japanese patient. Both mutations will cause inclusion of an additional 47 amino acids, translated from the 3'UTR of the gene, into the mature actin protein. Western blotting performed on
Appendix B

Diagnostic criteria for the diagnosis of sporadic-IBM
Table 3.2. Diagnostic criteria for s-IBM

I. Characteristic features
   A. Clinical
      1. Duration of illness: more than 6 months
      2. Age of onset: more than 30 years old
      3. Muscle weakness must affect the proximal and distal muscles of
         arms and legs, and
         the patient must exhibit at least one of the following features:
         (a) Finger-flexor weakness
         (b) Wrist-flexor weakness greater than wrist-extensor weakness
         (c) Quadriceps-muscle weakness (grade 4 MRC)
   B. Laboratory
      1. Serum creatine kinase less than 12 times normal
      2. Muscle biopsy
         (a) Inflammatory myopathy characterized by mononuclear-cell inva-
             sion of non-necrotic muscle fibers
         (b) Vacuolated muscle fibers
         (c) Either
             (i) Intracellular amyloid deposits (must use fluorescence
                 method of identification before excluding the presence of
                 amyloid) or
             (ii) 15–18-nm tubulofilaments shown by electron microscopy
      3. Electromyography findings must be consistent with the features of
         an inflammatory myopathy (i.e., irritable myopathy); long-duration
         potentials are commonly observed and do not
         exclude a diagnosis of s-IBM
   C. Family history
      Rarely, s-IBM can be observed in families. This condition is
different from h-IBM without inflammation. Familial cases of s-IBM
require documentation of the inflammatory component by
muscle biopsy, in addition to vacuolated muscle fibers, intracellular
(within muscle fibers) amyloid, and 15–18-nm tubulofilaments.
D. Associated disorders
   IBM can occur with a variety of other disorders, especially immune-
mediated conditions. The presence of an associated condition does not
preclude a diagnosis of s-IBM if the following diagnostic criteria are
met.

II. Diagnostic criteria for s-IBM
   A. Definite s-IBM
      Patients must exhibit all muscle biopsy features, including invasion of
      non-necrotic fibers by
      mononuclear cells, vacuolated muscle fibers, and intracellular (within
      muscle fibers) amyloid deposits or 15–18-nm tubulofilaments. None of
      the other clinical or laboratory features are mandatory if the muscle
      biopsy features are diagnostic.
   B. Possible s-IBM
      If the muscle shows only inflammation (invasion of non-necrotic muscle
      fibers by mononuclear cells) without other muscle biopsy features of
      IBM, then a diagnosis of “possible s-IBM” can be made if the patient
      exhibits the characteristic clinical (I.A.1,2,3) and laboratory (I.B.1,3)
      features. Neither I.C nor I.D should exclude a diagnosis of s-IBM.

Griggs, R.C., Askanas, V., DiMauro, S., Engel, A., Karpati, G., Mendell, J.R., &
Neurology, 38(5), pp.705-713.
Appendix C

Patient consent form signed by each patient that took part in the study
CONSENT FORM

The Effectiveness of a Home-Based, Patient-Specific, Functional Exercise Program on Patients with Inclusion Body Myositis (IBM)

Investigators: Professor Frank Mastaglia, Dr G Thickbroom, Dr Merrilee Needham, Dr Dylan Edwards and Liam Johnson

Subject Name: ____________________________

Date of Birth: __________

1. I have been given clear information (verbal and written) about this study and have been given time to consider whether I want to take part.

2. I have been told about the possible advantages and risks of taking part in the study and I understand what I am being asked to do.

3. I have been able to have a member of my family or a friend with me while I was told about the study. I have been able to ask questions and all questions have been answered satisfactorily.

4. I know that I do not have to take part in the study and that I can withdraw at any time during the study without affecting my future medical care. My participation in the study does not affect any right to compensation, which I may have under statute or common law.

5. I agree to take part in this research study and for the data obtained to be published provided my name or other identifying information is not used.

If you are unclear about anything you have read in the Patient Information Sheet or this Consent Form, please speak to your doctor before signing this Consent Form.

Name of Patient ____________________________ Signature of Patient ____________________________

Date ____________________________

Name of Investigator ____________________________ Signature of Investigator ____________________________

Date ____________________________

The Sir Charles Gairdner Hospital Human Research Ethics Committee has given ethics approval for the conduct of this project. If you have any ethical concerns regarding the study you can contact the secretary of the Sir Charles Gairdner Hospital Human Research Ethics Committee on telephone No. (08) 9346.3528.
Appendix D

Muscle Assessment form used by investigator to record the patients muscle strength results
MUSCLE ASSESSMENT

NAME: ___________________________ CLINIC NO: ______ DATE: ______

ISOMETRIC TESTING

<table>
<thead>
<tr>
<th>Muscle Group</th>
<th>MRC</th>
<th>Right</th>
<th>Left</th>
<th>MRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoulder abductors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shoulder ext. rotators</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elbow extensors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elbow flexors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist extensors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip flexors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip abductors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neck flexors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grip strength</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knee extensors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knee flexors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ankle dorsiflexors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TIMED TESTS

1 Stairs
2 Walking 30m/10m _______ No. Paces _______
3 Timed Stands _______

FUNCTIONAL TESTS

1 Sit up from lying Yes/No
2 Rise from squat Yes/No

Weight
Medications
Appendix E

Muscle strength assessment positions for hand-held myometry
<table>
<thead>
<tr>
<th>MUSCLE GROUP</th>
<th>POSITION OF LIMB SEGMENT</th>
<th>MYOMETER POSITION</th>
<th>STABILISATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoulder abductors</td>
<td>Shoulder abducted 20 deg, elbow flexed 90 deg</td>
<td>Immediately proximal to lateral epicondyle</td>
<td>Nil</td>
</tr>
<tr>
<td>Shoulder external rotators</td>
<td>Arm at side, elbow flexed 90 deg, forearm mid-prone</td>
<td>Immediately proximal to ulnar styloid process</td>
<td>Nil</td>
</tr>
<tr>
<td>Elbow extensors</td>
<td>Shoulder abducted 10 deg, elbow flexed 90 deg, upper arm in contact with plinth during test, forearm supinated</td>
<td>Immediately proximal to ulnar styloid process</td>
<td>Nil</td>
</tr>
<tr>
<td>Elbow flexors</td>
<td>Shoulder abducted 10 deg, elbow flexed 90 deg, forearm supinated</td>
<td>Immediately proximal to proximal wrist crease</td>
<td>Nil</td>
</tr>
<tr>
<td>Wrist extensors</td>
<td>Shoulder abducted 10 deg, elbow extended, forearm pronated and in contact with plinth, wrist extended 20 deg, fingers flexed</td>
<td>Centre of dorsum of hand</td>
<td>Forearm stabilised on plinth by examiner</td>
</tr>
<tr>
<td>Hip flexors</td>
<td>Hip and knee flexed 90 deg, lower leg supported by examiner</td>
<td>Immediately proximal to upper border of patella</td>
<td>Nil</td>
</tr>
<tr>
<td>Hip abductors</td>
<td>Hip abducted 20 deg, knee extended</td>
<td>Immediately proximal to lateral femoral condyle</td>
<td>Subject holding side of plinth, other leg stabilised by examiner</td>
</tr>
<tr>
<td>Ankle dorsiflexors</td>
<td>Hip abducted 10 deg, knee extended, foot plantigrade</td>
<td>Centre of dorsum of foot</td>
<td>Nil</td>
</tr>
<tr>
<td>Neck flexors</td>
<td>Head raised to 30 deg with chin tucked in</td>
<td>Centre of forehead</td>
<td>Nil</td>
</tr>
</tbody>
</table>
Appendix F

Penny and Giles Transducer Muscle Myometer used to assess the patients muscle strength in selective muscles bilaterally
Penny and Giles Transducer hand-held myometer – used to measure the patients muscle strength in selected muscle bilaterally.
Appendix G

Short Form-36 Health Survey used to assess the patients change in general health and well-being as a result of the exercise intervention
### SF36 Health Survey

**INSTRUCTIONS:** This set of questions asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Answer every question by marking the answer as indicated. If you are unsure about how to answer a question please give the best answer you can.

1. In general, would you say your health is: (Please tick one box.)
   - Excellent
   - Very Good
   - Good
   - Fair
   - Poor

2. Compared to one year ago, how would you rate your health in general now? (Please tick one box.)
   - Much better than one year ago
   - Somewhat better now than one year ago
   - About the same as one year ago
   - Somewhat worse now than one year ago
   - Much worse now than one year ago

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? (Please circle one number on each line.)

<table>
<thead>
<tr>
<th>Activities</th>
<th>Yes, Limited A Lot</th>
<th>Yes, Limited A Little</th>
<th>Not Limited At All</th>
</tr>
</thead>
<tbody>
<tr>
<td>3(a) Vigorous activities, such as running, lifting heavy objects,</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>participating in strenuous sports</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3(b) Moderate activities, such as moving a table, pushing a vacuum</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>cleaner, bowling, or playing golf</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3(c) Lifting or carrying groceries</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3(d) Climbing several flights of stairs</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3(e) Climbing one flight of stairs</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3(f) Bending, kneeling, or stooping</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3(g) Walking more than a mile</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3(h) Walking several blocks</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3(i) Walking one block</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3(j) Bathing or dressing yourself</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health? (Please circle one number on each line.)

<table>
<thead>
<tr>
<th>Problem</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>4(a) Cut down on the amount of time you spent on work or other activities</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>4(b) Accomplished less than you would like</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>4(c) Were limited in the kind of work or other activities</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>4(d) Had difficulty performing the work or other activities (for example, it took extra effort)</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (e.g. feeling depressed or anxious)? (Please circle one number on each line.)

<table>
<thead>
<tr>
<th>Problem</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>5(a) Cut down on the amount of time you spent on work or other activities</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>5(b) Accomplished less than you would like</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>5(c) Didn’t do work or other activities as carefully as usual</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
6. **During the past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups? (Please tick one box.)

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>Slightly</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
</table>

7. **How much physical pain** have you had during the **past 4 weeks**? (Please tick one box.)

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Very mild</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Very Severe</th>
</tr>
</thead>
</table>

8. **During the past 4 weeks**, how much did pain interfere with your normal work (including both work outside the home and housework)? (Please tick one box.)

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>A little bit</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
</table>

9. These questions are about how you feel and how things have been with you during the past 4 weeks. Please give the one answer that is closest to the way you have been feeling for each item.

<table>
<thead>
<tr>
<th>(Please circle one number on each line.)</th>
<th>All of the Time</th>
<th>Most of the Time</th>
<th>A Good Bit of the Time</th>
<th>Some of the Time</th>
<th>A Little of the Time</th>
<th>None of the Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>9(a) Did you feel full of life?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>9(b) Have you been a very nervous person?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>9(c) Have you felt so down in the dumps that nothing could cheer you up?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>9(d) Have you felt calm and peaceful?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>9(e) Did you have a lot of energy?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>9(f) Have you felt downhearted and blue?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>9(g) Did you feel worn out?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>9(h) Have you been a happy person?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>9(i) Did you feel tired?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

10. **During the past 4 weeks**, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives etc.)? (Please tick one box.)

<table>
<thead>
<tr>
<th></th>
<th>All of the time</th>
<th>Most of the time</th>
<th>A Good Bit of the Time</th>
<th>Some of the time</th>
<th>A Little of the Time</th>
<th>None of the time</th>
</tr>
</thead>
</table>

11. How **TRUE or FALSE** is each of the following statements for you?

<table>
<thead>
<tr>
<th>(Please circle one number on each line.)</th>
<th>Definitely True</th>
<th>Mostly True</th>
<th>Don't Know</th>
<th>Mostly False</th>
<th>Definitely False</th>
</tr>
</thead>
<tbody>
<tr>
<td>11(a) I seem to get sick a little easier than other people</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>11(b) I am as healthy as anybody I know</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>11(c) I expect my health to get worse</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>11(d) My health is excellent</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

Thank You!
Appendix H

Exercise Training booklet each patient was given, illustrating and describing sample exercises
Personal Exercise Program

Chest and Anterior Shoulder (Right arm)

Hold on to a high object with the right hand, keeping the right arm straight. Turn the feet to the left and rotate the body to the left feeling the stretch across the front of the shoulder.

Hold for ____ secs.
Repeat ____ times.

Stand or sit.

Stretch one arm over to the opposite shoulder by pushing it at the elbow with your other arm. Hold the stretching approx. 20 secs. - relax.

Repeat ____ times.

Calf Stretch (Soleus) (Right leg)

Begin in a half-lunge position with your front leg bent, hands supported on the wall. Lower your body towards the wall, pressing your leading foot into dorsiflexion.

Hold for ____ secs.
Repeat ____ times.

Half Lunge (Right leg)

Begin half kneeling, and tighten your abdominal muscles to stabilise your trunk. Press your trailing leg forwards, forcing your right hip into extension.

Hold for ____ secs.
Repeat ____ times.
Gluteal Stretch (Right leg)

Lie on the floor with left leg straight. Flex the right knee and pull it upwards and across towards the opposite shoulder.

Hold for ____ secs.
Repeat ____ times.

Hamstring Stretch (Active knee extension) (Right leg)

Lie on the floor, flex your hip to 90°. Grip your hands behind the knee and actively straighten the knee using your quadriceps muscles.

Hold for ____ secs.
Repeat ____ times.

Lying on your back or sitting.

Bend and straighten your ankles briskly. If you keep your knees straight during the exercise you will stretch your calf muscles.

Repeat ____ times.

Sitting with your foot on the floor.

Alternately raise the inner border of your foot (big toe) and then the outer border (little toe).

Repeat ____ times.

Support your elbow on a table with your wrist straight and your fingers pointing towards the ceiling.

Make a fist (thumb over fingers). Straighten your fingers and bring them apart.

Repeat ____ times.
Support below the finger joint to be exercised.

Bend the middle joint of the finger. Assist the movement with your other hand. Hold ___ secs.

Repeat ___ times.

Support the wrist of the hand to be exercised.

Bend your wrist and assist the movement with your other hand. Hold ___ secs.
Then straighten your wrist and assist the movement with your other hand. Hold ___ secs.

Repeat ___ times.

With your thumb touch each finger-tip.

Repeat ___ times.
Personal Exercise Program

Provided for: Liam Johnson  

3 Months

Shoulder Flexion

Stand facing a wall with your arms straight and hands on the wall.

Do push-ups against the wall keeping your body in a straight line.

Repeat ___ times.

Shoulder Extension

Stand with your back against the wall. Keep your upper arm close to the side and elbow at a right angle.

Push the elbow back against the wall.

Repeat ___ times.

Elbow Flexion

Stand or sit with arms hanging down. Hold ___ kg handweights and turn your palms forward.

Bend alternate elbows briskly.

Repeat ___ times.

Elbow Extension

Sit or stand holding a ___ kg handweight.

Bring the arm to be exercised up with the elbow pointing to the ceiling. Support the elbow with the other hand. Straighten the arm holding the weight.

Repeat ___ times.
Upper Trunk Flexion

Stand or sit.

Push shoulders forward, stretch the arms diagonally forwards and down keeping your chin in. Hold stretching 20 secs.

Repeat ___ times.

Upper Trunk Extension

Sit with your back straight and feet firmly on the floor.

Pull your shoulder blades together while turning your thumbs and hands outwards.

Repeat ___ times.

Horizontal Shoulder Abduction

Stand sideways next to a wall. Lift your arm so that your shoulder and elbow are at right angles.

Push your forearm against the wall. Hold approx. ___ secs.

Repeat ___ times.
Personal Exercise Program

**Hip Flexion**

Sit on the floor with one leg straight and the other bent with your arms around it.

Try to straighten your bent leg while resisting any movement with your arms for 5 secs. - relax. Then pull the leg closer to your body. Hold approx. 20 secs.

Repeat ___ times.

**Hip Extension**

Stand straight holding on to a chair.

Bring your leg backwards keeping your knee straight. Do not lean forwards.

Repeat ___ times.

**Hip Abduction**

Stand straight holding on to a support.

Lift your leg sideways and bring it back keeping your trunk straight throughout the exercise.

Repeat ___ times.

**Knee Extension**

Sitting with your arms crossed or using your arms to raise yourself up.

Stand up and then sit down slowly on a chair, using your arms to decelerate your movement. (This can be made easier and more difficult by changing the height of the chair). Maintain straight back throughout

Repeat ___ times.
Knee Flexion

Stand. Hold onto a support and bring one leg slightly backwards.

Bend your knee and lift your foot off the floor. Hold ___ secs.

Repeat ___ times.

Calf Raises (Using block or step)

Place the ball of the foot on a small (5 cm) block or step. Press the heel to the floor, keeping your legs straight. Pull your hip forwards over the toes to feel the stretch in the calf, then slowly raise up, then back down again.

Hold for ___ secs.
Repeat ___ times.
Appendix I

Diary template given to each patient with a workbook to record training information and subjective feelings experienced by the patients' as requested by the investigator
- Date
- Time of day
- Duration of exercise session (minutes)
- Exercises Performed and Quantity
- VAS Rating upon waking
  - Fatigue (F)
  - Muscle soreness (MS)
  - Breathlessness (B)
- VAS Rating immediately post-exercise session
  - Fatigue (F)
  - Muscle soreness (MS)
  - Breathlessness (B)
- Visual Analogue Scale (1-10 rating system)

1 = Not at all 10 = Very much so

- Rating of Perceived Exertion (RPE) for the exercise session (Borg 0-10 scale to be completed 30 minutes post-exercise session)
  - 0 = Rest
  - 1 = Very, very easy
  - 2 = Easy
  - 3 = Moderate
  - 4 = Somewhat hard
  - 5 = Hard
  - 6 =
  - 7 = Very hard
  - 8 =
  - 9 =
  - 10 = Maximal

- Falls
  - When?
  - Why?
  - Injuries sustained as a result of the fall?

- Any other comments (for example, other strenuous activity undertaken, other health issues, general feeling of wellbeing)
Appendix J

Photos of IBM study participant consented by patient to be shown in investigators Thesis
An IBM patient from the Australian Neuromuscular Research Institute. The photo on the right clearly shows the muscular atrophy that is prominent in IBM patients' knee extensors. Upon closer inspection of this photo, scars on the knee can also be seen, which is also a common feature of IBM patients as a result of falls they are pre-disposed to with the quadriceps weakness they are afflicted by. The two photo’s on the right show the decreased joint range of motion these patients have in their finger and wrist flexors and extensors. Particularly reduced finger flexion, and particularly the two fingers shown and their distal joints more so than the proximal joints.
Appendix K

Honours Study Budget and Timeline
Project Budget

1. Edith Cowan University vehicle hire to transport exercise bikes to patients homes ~ $300
2. Transport fare for patients to attend the Centre for Neuromuscular and Neurological Disorders for patient assessment ~ $300

Project Timeline

<table>
<thead>
<tr>
<th>Pre-testing</th>
<th>16-week training intervention</th>
<th>Post-testing</th>
<th>Data analysis</th>
<th>Complete Thesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>March</td>
<td>April</td>
<td>August</td>
<td>September</td>
<td>November</td>
</tr>
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</table>
Appendix L

Table 3. Mean changes in muscle strength of total patient group
Table 3. Total group (n=7) mean (±SE) muscle strength data pre and post exercise intervention, where $P(T<=t)$ one-tail was used for any healthy/trained muscles, and $P(T<=t)$ two-tail for any diseased/trained or untrained and healthy/untrained muscles.

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Mean</th>
<th>P-value</th>
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<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td><strong>Diseased/Untrained</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grip Strength</td>
<td>150.18</td>
<td>138.27</td>
</tr>
<tr>
<td><strong>Diseased/Trained</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knee Extension</td>
<td>7.32</td>
<td>6.66</td>
</tr>
<tr>
<td>Wrist Extension</td>
<td>9.87</td>
<td>9.08</td>
</tr>
<tr>
<td><strong>Healthy/Untrained</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shoulder External Rotation</td>
<td>7.45</td>
<td>7.64</td>
</tr>
<tr>
<td><strong>Healthy/Trained</strong></td>
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<td></td>
</tr>
<tr>
<td>Elbow Extension</td>
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<td>6.83</td>
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<td>Elbow Flexion</td>
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<td>11.05</td>
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<td>Shoulder Abduction</td>
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<td>Hip Flexion</td>
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<tr>
<td>Hip Abduction</td>
<td>9.02</td>
<td>10.57</td>
</tr>
<tr>
<td>Knee Flexion</td>
<td>10.46</td>
<td>11.53</td>
</tr>
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</table>